BMJ Open Uptake of four or more doses of sulfadoxine pyrimethamine for intermittent preventive treatment of malaria during pregnancy in Zambia: findings from the 2018 malaria in pregnancy survey

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Dr Cephas Sialubanje; csialubanje@yahoo.com ABSTRACT

Objective To determine the prevalence and predictors of the uptake of four or more doses of sulfadoxine pyrimethamine (IPTp-SP 4+) in Zambia.

Design A cross-sectional study using secondary data from the malaria in pregnancy survey (Malaria Indicator Survey) data set conducted from April to May 2018. **Setting** The primary survey was conducted at community level and covered all the 10 provinces of Zambia.

Participants A total of 3686 women of reproductive age (15–45 years) who gave birth within the 5 years before the survey.

Primary outcome Proportion of participants with four or more doses of IPTp-SP.

Statistical analysis All analyses were conducted using RStudio statistical software V.4.2.1. Descriptive statistics were computed to summarise participant characteristics and IPTp-SP uptake. Univariate logistic regression was carried out to determine association between the explanatory and outcome variables. Explanatory variables with a p value less than 0.20 on univariate analysis were included in the multivariable logistic regression model and crude and adjusted ORs (aORs) along with their 95% Cls were computed (p<0.05).

Results Of the total sample of 1163, only 7.5% of participants received IPTp-SP 4+. Province of residence and wealth tertile were associated with uptake of IPTp-SP doses; participants from Luapula (a0R=8.72, 95% Cl (1.72 to 44.26, p=0.009)) and Muchinga (a0R=6.67, 95% Cl (1.19 to 37.47, p=0.031)) provinces were more likely to receive IPTp-SP 4+ compared with to those from Copperbelt province. Conversely, women in the highest wealth tertile were less likely to receive IPTp-SP 4+ doses compared with those in the lowest quintile (a0R=0.32; 95% Cl (0.13 to 0.79, p=0.014)).

Conclusion These findings confirm a low uptake of four or more doses of IPTp-SP in the country. Strategies should focus on increased coverage of IPTp-SP in provinces with much higher malaria burden where the risk is greatest and the ability to afford healthcare lowest.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Use of a large data set from the 2018 malaria in pregnancy survey with a nationally representative sample reduced selection bias and increased external validity and generalisability of the findings.
- \Rightarrow Use of multistage random sampling technique reduced selection bias and increased validity of the findings.
- ⇒ Inclusion into analysis only women of reproductive age who gave birth after the new IPTp-SP policy was introduced reduced information bias and increased internal validity of the study.
- \Rightarrow Use of secondary data limited the choice of variables to be included in the analysis.
- ⇒ Exclusion of participants with incomplete data could have reduced the power of the study.

INTRODUCTION

Globally, there are an estimated 247 million cases of malaria reported from 84 malariaendemic countries, with the majority (95%)being reported from the WHO African Region. Sub-Saharan Africa is disproportionately affected, accounting for an estimated 350-500 million cases, 1-3 million deaths, 10000 maternal and 200000 neonatal deaths per year.^{1 2} With an estimated 125 million pregnant women being at risk of contracting malaria globally, malaria in pregnancy (MIP) remains an important preventable cause of adverse maternal, neonatal health outcomes worldwide.¹³⁴ Out of an estimated 50 million annual pregnancies in malaria-endemic countries around the world each year, more than 50% of these live in the tropical areas of Africa where there is a high transmission of Plasmodium falciparum.⁵⁶

Malaria is a parasitic disease caused by a protozoon of the genus Plasmodium. Although there are species of malaria that infect humans-P. falciparum, P. malariae, P. ovale, P. vivax and P. knowlesi-two main species, P. falciparum and P. vivax, pose the greatest risk and contribute to adverse outcomes. P. falciparum is the deadliest malaria parasite and the most prevalent on the African continent.⁶⁷ Malaria parasites contribute to adverse pregnancy and birth outcomes due to their preferential accumulation in placental intervillous spaces, putting pregnant women and their babies at an increased risk. MIP is associated with anaemia, miscarriage, premature birth, stillbirth, congenital infection, low birth weight (lbw), maternal, foetal and perinatal death; one in four women have evidence of placental infection at the time of delivery.⁶⁻⁸ Moreover, evidence from previous studies shows that lbw is associated with a marked increase in infant mortality, high rates of cognitive impairment, learning disability and behavioural problems.^{8–11}

Zambia is a sub-Saharan African country with a high malaria burden with an approximate 5.2 million annual malaria cases and an estimated 200000 pregnancies being at risk of malaria.¹² The Zambia National Malaria Elimination Centre (NMEC) in line with WHO strategic framework of malaria prevention and control during pregnancy has developed and is implementing an MIP policy which includes the provision of four or more doses of intermittent preventive treatment of malaria during pregnancy with sulfadoxine pyrimethamine (IPTp-SP).¹³ Other interventions are insecticide treated nets (ITNs), in-door residual spraying and case management.

IPTp-SP and ITN interventions are being implemented as part of antenatal care (ANC) services¹⁴ and involve administration of sulfadoxine pyrimethamine (SP) (comprising three tablets containing 500 mg/25 mg SP, giving the total required dosage of 1500 mg/75 mg SP) as direct observed therapy to pregnant women. The first IPTp-SP dose is administered during the second trimester, 13-16 gestation weeks, followed by monthly doses until delivery for at least four doses. ANC has been identified to provide a good platform for regular and close contact between pregnant women and skilled health personnel for improved service delivery and monitoring. Zambia follows the 2016 WHO ANC model which recommends a minimum of eight ANC contacts with the first contact scheduled to take place in the first trimester, two contacts in the second trimester and five contacts scheduled in the third trimester.¹⁴¹⁵

Administration of IPTp-SP is based on the assumption that every pregnant woman living in a high malaria transmission area has malaria parasites. The parasites live in blood or placenta, whether or not she has symptoms and signs of malaria.^{16 17} Previous studies in Zambia and elsewhere have provided evidence on the effectiveness of IPTp-SP on improved maternal and newborn health outcomes. In Zambia, administration of two or more doses of IPTp-SP showed a decrease in low birth weight among paucigravid and multigravid women compared

with one dose.¹¹ A study conducted in Mali¹⁸ showed that addition of a third dose of IPTp-SP led to a reduced risk of placental malaria, lbw and preterm births in all gravidae, compared with the standard two dose regimen. A systematic review and meta-analysis on intermittent preventive therapy for malaria during pregnancy using two versus three or more doses of SP and risk of lbw in Africa by Kayentao and colleagues¹⁹ showed that three or more doses were associated with a 3.3% reduction in lbw, 3.1% reduction in placental malaria and 1.4% reduction in moderate-to-severe maternal anaemia.

However, the 2018 Malaria Indicator Survey (MIS) report²⁰ shows that the proportion of pregnant women receiving four or more doses of IPTp-SP is low at 5%. The reasons for the low coverage of IPTp-SP are not clear. Limited studies have been conducted on the predictors of the uptake of four or more doses of SP in Zambia. The reasons for the low coverage of IPTp-SP are not clear. Limited studies have been conducted on the predictors of the uptake of four or more doses of SP in Zambia.

OBJECTIVES

The aim of this study was to determine the prevalence and predictors of the uptake of four or more doses of IPTp-SP in Zambia. Information is required to inform policy and programming to improve uptake of SP in the country.

METHODS

Study design

The present study is a secondary analysis of the 2018 MIS done in Zambia. It was a cross-sectional survey conducted from April to May, 2018. The survey is periodically done to assess the malaria burden and coverages of key malaria interventions such as vector control, parasite clearance, health promotion, enhanced surveillance, monitoring, evaluation and research, health system capacity, financing and case management in the general population including MIP. The MIS 2018 was the latest comprehensive data set that was representative of the whole country and readily accessible at the time of writing the manuscript.

Study site

The study used the 2018 MIS survey data which covered all the 10 provinces of Zambia, making it nationally representative. The country is divided into 10 provinces that are further divided into districts. For statistical purposes, each district is subdivided into census supervisory areas which are in turn subdivided into enumeration areas (EAs). The listing of EAs has information on the number of households and the populations. Zambia is a sub-Saharan African country located in south-central Africa with a surface area of 752614 square kilometres. Lusaka, the capital city, is located in the south-central part of the country.²¹ The topography is characterised by a high plateau, river valleys and water bodies. The country derives its name from the Zambezi River, which drains all but a small northern part of the country. It has a tropical climate with the rainy season occurring during October to April. The climate is suitable for mosquito breeding and malaria transmission takes place throughout the year but peaks during the rainy season.^{22 23} Zambia's population as of 8 September 2022 was 19610 769. The male population was 9603 056 and the female population was 10 007 713.²⁴

Study participants and procedures

Study participants were women of reproductive age who participated in the 2018 MIS. The country conducts MIS surveys every 2–3 years to provide updates on malaria interventions and disease burden in the country. A total of 3686 women of reproductive age who gave birth in the past 5 years participated in the 2018 MIS. From this sample, a total of 1381 were included in our analysis.

Inclusion criteria

To be included in the study, participants needed to be:

- ► Pregnant women who were pregnant in the past 2 years and 5 months after the new 2016 policy on the fourth dose IPTp-SP was implemented.
- All women aged between 15 and 49 years from all the 10 provinces.

Women who did not give consent and those who did not complete the individual questionnaires were not included in the analysis.

Sample size estimation

The study participants in the main survey were selected using a two-stage cluster sampling technique which is based on a nationally representative sample of 4177 households from 179 standard EAs randomly selected from all 10 provinces. Based on these criteria, at least 2176 households were required in the rural domain. For further details on the 2018 MIS sampling technique and sample size determination see the 2018 MIS published report by the Zambian Ministry of Health.

Assumptions for the sample size determination were:

- ▶ 95% CI.
- ▶ 80% power.
- ▶ Design effect of 2.50.
- ► Z-score of 1.96.
- ▶ 10% relative SE.
- ▶ Margin of error of 2%.
- ▶ 20% adjustment for non-response.

The estimated minimum sample size in this study was determined by the formula below:

 $n = \frac{z^2 x p (1-p) (DEFF)}{d^2} = 1141 \ (25)$

where n is the calculated sample size, z=1.96 is the statistic that defines the level of confidence required, p=0.05 is a prevalence of uptake of IPTp-SP among pregnant women in Zambia, expressed as a proportion of that population, D=0.02 is the desired level of precision, DEFF=2.5 is the design effect.²⁵

Variables

The variables for the study were as follows:

- Outcome variable: uptake of four or more doses of IPTp-SP.
- Predictor variables: sociodemographic variables (age, parity, place and province of residence, religion, educational level, wealth index).
- Basic knowledge about malaria.
- ► Knowledge about malaria treatment.

The predictor variables were selected based on thorough literature review. In this study uptake means receiving any dosage of SP during pregnancy, with each dose being given at least 1 month apart starting from the second trimester of gestation, until the time of delivery as directly observed therapy.

Data sources and processing

The merged 2018 MIS data set comprising women of reproductive age (15–49 years) was extracted into the Microsoft Office Excel sheet 2013 using the data extraction tool. We subset women 15–49 years of age who were eligible to complete the questionnaire. From the eligible women, we subsetted women who consented. Further, a subset of women who completed the questionnaire and delivered in 2016 or later (after the new IPTp policy) was done using the lubridate library in RStudio. This was determined by using the age of the youngest child (ie, if a child was less than 881 days).

Statistical analysis

RStudio statistical software V.4.2.1. was used for all the analyses. Descriptive statistical analysis was carried out first on socio-demographics to obtain frequencies and proportions. The proportion of missing values on the outcome was calculated. The correlation among the predictor variables was explored. Thereafter, univariate logistic regression was carried out and explanatory variables whose p values were less than 0.2 were presented in table 1. The estimators with a p value level of 0.20 chose the adjusted estimate more frequently when confounding is present and so produced less bias than the estimators with a p value level of 0.05.²⁶ Then, a backward selection approach using stepwise method with a p value of 0.2 threshold was used to select explanatory variables to be included in the multivariable logistic regression for further analysis of the association to obtain adjusted ORs. We also compared Akaike's Information Criteria (AIC), Bayesian Information Criteria (BIC) and pseudo-R² between the multivariable model which included all variables (full model) and the model after backward selection approach (reduced model) for model fit. To account for the differences in sampling probabilities across the clusters and strata, sample weighting was used to adjust for the cluster sampling design using 'svy' function in RStudio and 'svyset' command to match the multistage cluster sampling design method. Results from univariable and multivariable analysis were presented as crude and adjusted ORs along with their 95% CIs, respectively (p value<0.05).

Table 1 Predictors for the adequate uptake of IPTp-SP (≥4 doses) during pregnancy in Zambia									
Variable	n (weighted)	n (%)	cOR	95% CI	P value	aOR	95% CI	P value	
Overall	1163	87 (7.5)							
Age group (years)									
15–24	542	46 (8.5)	1.00			1.00			
25–34	441	31 (7.0)	0.67	0.37 to 1.21	0.181	0.54	0.26 to 1.08	0.083	
35+	180	10 (5.5)	0.58	0.24 to 1.35	0.202	0.58	0.23 to 1.51	0.266	
Education level†									
Primary	542	50 (9.2)	1.00			1.00			
Secondary+	396	18 (4.6)	0.30	0.15 to 0.61	0.001*	0.55	0.27 to 1.11	0.093	
Residence									
Rural	927	70 (7.6)	1.00						
Urban	219	17 (7.2)	0.22	0.11 to 0.44	<0.001*				
Province									
Copperbelt	44	2 (4.6)	1.00			1.00			
Central	89	3 (3.4)	2.15	0.28 to 16.78	0.463	2.03	0.27 to 15.48	0.493	
Eastern	210	11 (5.2)	1.72	0.32 to 9.35	0.528	1.15	0.19 to 7.00	0.878	
Luapula	196	36 (18.4)	13.57	2.98 to 61.77	0.001*	8.72	1.72 to 44.26	0.009*	
Lusaka	70	0 (0.0)	-	-	-	-	-	-	
Muchinga	83	13 (15.7)	11.50	2.32 to 56.95	0.003*	6.67	1.19 to 37.47	0.031*	
North-Western	84	4 (4.8)	2.32	0.38 to 14.08	0.359	2.08	0.32 to 13.34	0.441	
Northern	111	16 (14.4)	8.94	1.86 to 42.87	0.006	4.13	0.73 to 23.42	0.109	
Southern	80	1 (1.3)	0.82	0.07 to 9.59	0.873	1.40	0.11 to 17.90	0.794	
Western	196	1 (0.5)	0.53	0.05 to 6.13	0.608	-	-	-	
Wealth tertile									
Low	438	50 (11.4)	1.00			1.00			
Middle	259	16 (6.2)	0.35	0.17 to 0.72	0.005*	0.52	0.19 to 1.45	0.212	
High	466	21 (4.5)	0.10	0.10 to 0.20	<0.001*	0.32	0.13 to 0.79	0.014*	
Exposure to media messages									
No	607	54 (8.9)	1.00						
Yes	556	33 (5.9)	0.49	0.28 to 0.85	0.011*				
Knowledge about malaria prevention†									
Not knowledgeable	180	22 (12.2)	1.00						
Knowledgeable	920	60 (6.5)	0.44	0.23 to 0.86	0.016*				

Note: AIC, BIC and pseudo-R² are 417.7, 490.2 and 0.09 for the reduced model, and 436.7, 496.3 and 0.08 for the model which included all the variables (full model) in the table, respectively.

*Significant at 5% level.

†The observations do not add up to the overall sample because the variables have missing values.

AIC, Akaike's Information Criteria; aOR, adjusted OR; BIC, Bayesian Information Criteria; cOR, crude OR.

The missing values were imputed using the multiple imputation by chain equation methods. The study explored the proportions of missing values and compared the estimates from the full data models and the imputed models to see whether there was an observed difference. The multiple imputation was carried on multivariable analysis only.²⁶

Patient and public involvement

The study design was determined by the research team. Participants and the public were not directly involved in the conceptualisation and design of the study. Selection of study participants for the 2018 MIS was done in collaboration with the provincial and district health managers. The public were involved in the participant recruitment for the primary survey. However, since the study used secondary data from the 2018 MIS, patients and the public were not directly involved in the selection of the variables to be included in the analysis. Rather, the team from Levy Mwanawasa Medical University and NMEC decided and agreed on the variables to be included in the analysis. Consequently, permission for access to the data set used for the analysis was granted by the NMEC in consultation with the Ministry of Health. After analysis and report writing, the research team held a dissemination meeting and study findings were shared with key stakeholders, including the Levy Mwanawasa Medical University School of Public Health, Ministry of Health and Zambia National Public Health Institute. A final report was also written and shared with the funding organisation.

RESULTS

Participants

A summary of the recruitment algorithm of study participants is shown below. A total of 4044 women of reproductive age were eligible to complete the questionnaire. Out of these, 3686 (91%) completed the questionnaire; 358 (9%) did not provide consent and were excluded from the study. A total of 1381 (34%) participants comprising women who delivered after the new IPTp-SP policy was introduced were included into the final sample for analysis (online supplemental figure 1).

Demographic characteristics of respondents

Majority (68.9%) of study participants were in the age group 15-29 years; almost one-third (30.8%) were in the age group 30-44 years and 0.3% were aged above 45 years. Close to half (48.9%) had completed primary education, 28.2% had secondary school education and 2.8% had gone up to higher education. Most respondents (81.3%) lived in rural areas. With regard to province of residence, 19.1% were from Luapula, 18.0% from Eastern, 17.2% from Western and 4.1% from Copperbelt provinces. One-fifth (21.9%) of the study participants were in lowest wealth tertile; 15.6% were in the middle tertile. Concerning religion, more than half (56.8%) of study participants were protestants followed by Catholics (22.2%); Muslims constituted 0.1% of the respondents. Majority (97.3%) attended ANC and most (92.5%) took less than four doses of IPTp-SP. Majority (71.3%) took three doses of IPTp-SP, 14.5% took two doses, 7.5% took IPTp-SP 4+ doses, 6.9% took only one dose. The proportions of IPTp-SP uptake increased from IPTp-SP 1 to IPTp-SP 3 and drastically dropped at IPTp-SP 4+. More than half (52.5%) of the study participants had three or more children and 22.2% had two children. Concerning knowledge on malaria prevention measures, most (76.4%) were knowledgeable and only 45.0% were exposed to media messages (table 2).

Predictors for the uptake of adequate doses of IPTp-SP (4+ doses)

The overall uptake of adequate (4+) doses of IPTp-SP was 7.5%. The uptake of 4+ doses of IPTp-SP decreased by level of education ranging from 9.2% for women with primary education to 4.6% for women with higher education. The same trend was observed across age groups, that is, decrease from 8.5% in the 15–24 years age group to 5.5% in the age group of 35 and above years. The women from rural areas had higher (7.6%) uptake of adequate doses compared with women from urban areas (7.2%).

Table 2Socio-demographic and clinical characteristics ofthe study participants (N=1381)

Variable	N (%)
Age (years)	
15–24	678 (49.1)
25–34	497 (36.0)
35+	205 (14.8)
Missing	1 (0.1)
Residence	
Rural	1123 (81.3)
Urban	258 (18.7)
Province	
Central	93 (6.7)
Copperbelt	56 (4.1)
Eastern	249 (18.0)
Luapula	264 (19.1)
Lusaka	87 (6.3)
Muchinga	95 (6.9)
North-Western	90 (6.5)
Northern	120 (8.7)
Southern	90 (6.5)
Western	237 (17.2)
Wealth tertile	
Low	578 (41.8)
Middle	302 (21.9)
High	501 (36.3)
Education level	
Primary	675 (48.9)
Secondary+	428 (31.0)
Missing	278 (20.1)
Religion	
Christian	1092 (79.1)
Non-Christian	289 (20.9)
Parity	
1	348 (25.2)
2	307 (22.2)
3+	725 (52.5)
Missing	1 (0.1)
Got antenatal care	
Yes	1344 (97.3)
No	35 (2.5)
Missing	2 (0.2)
IPTp-SP uptake*	
1	80 (6.9)
2	167 (14.3)
3	829 (71.3)
4+	87 (7.5)
	Continued

Table 2 Continued					
Variable	N (%)				
Exposure to media message					
No	759 (55.0)				
Yes	622 (45.0)				
Missing					
Knowledge about malaria prevention					
Not knowledgeable	241 (17.5)				
Knowledgeable	1055 (78.4)				
Missing	85 (6.1)				
Basic malaria knowledge					
Incorrect	351 (25.4)				
Correct	945 (68.4)				
Missing	85 (6.2)				
*The proportions excludes the missing values.					

The uptake of adequate doses of SP was highest for women in the low wealth tertile (11.4 %). Also, women who were not exposed to media messages had higher uptake of SP (8.9%) compared with those who were exposed to media messages (5.9%) (table 1).

The results of univariate logistic regression analysis (crude ORs) show that a woman's education level, place of residence, province, wealth tertile, exposure to media messages and knowledge about malaria prevention were significantly associated with the adequate uptake of IPTp-SP. While age group showed no evidence of association with adequate uptake of IPTp-SP. The results in table 1 show significant lower odds of taking an adequate IPTp-SP among women with at least secondary level of education (0.30, 95% CI 0.15 to 0.61, p value=0.001) compared with those with primary level of education. Luapula and Muchinga provinces show significant higher odds of taking an adequate IPTp-SP (13.57, 95% CI 2.98 to 61.77, p value=0.001 and 11.50, 95% CI 2.32 to 56.95, p value=0.003, respectively) compared with those from Copperbelt. However, this may be due to chance given the low sample size in Copperbelt province which is a reference. This is evidenced by the wide 95% CI, which increases uncertainty.

Women in the middle and high wealth tertile show significant lower odds of taking adequate IPTp-SP (0.35, 95% CI 0.17 to 0.72, p value=0.005 and 0.10, 95% CI 0.10 to 0.20, p value<0.001, respectively) compared with those in low wealth tertile. Women who were exposed to media messages had significant lower odds of taking an adequate IPTp-SP (0.49, 95% CI 0.28 to 0.85, p value=0.011) compared with those who were not exposed. Women who had knowledge about malaria prevention had significant lower odds of taking an adequate IPTp-SP (0.44, 95% CI 0.23 to 0.86, p value=0.016) compared with those who had none.

Using a backward selection method with p value threshold of 0.2, the reduced (final) model retained age group, education level, province and wealth quintile. Therefore, after adjusting for age group, education level and wealth quintile, Luapula and Muchinga provinces still showed significant higher (though reduced) odds of taking an adequate IPTp-SP (8.72, 95% CI 1.72 to 44.26, p value=0.009 and 6.67, 95% CI 1.19 to 37.47, p value=0.031, respectively) compared with those from Copperbelt. And after adjusting for age group, education level and province, only women in the higher wealth tertile had significant lower odds of taking an adequate IPTp-SP (0.32, 95% CI 0.13 to 0.79, p value=0.014) compared with those in low wealth tertile.

Comparing AIC, BIC and pseudo- \mathbb{R}^2 we have 417.7, 490.2 and 0.09 for the reduced model, and 436.7, 496.3 and 0.08 for the full model, respectively. This suggests that the reduced model is better fitted compared with the full model. This is because the AIC and BIC are lower, and pseudo- R^2 is higher for the reduced model compared with the full model. The proportion of missing values was highest under the education level variable which accounted for 20.1%. Comparing estimates of the full data model from multivariable analysis and the imputed multivariable analysis, there is not much difference in the estimates apart from the fact that the 95% CI are narrower in some instances in the imputed model compared with the full data model. However, estimates from multiple imputation are only valid when data is at least missing at random (table 1).

DISCUSSION

The study aimed to determine the predictors of IPTp-SP uptake for four or more doses in Zambia. Our findings show that uptake of four or more doses of IPTp-SP was low at 7.5%. The place and province of residence were significantly associated with adequate uptake of IPTp-SP doses. Women who were residents of Luapula and Muchinga provinces had higher odds of taking adequate doses with reference to those in the Copperbelt province. Conversely, women in the highest wealth tertile were significantly less likely to receive IPTp-SP 4+ doses compared with those in the lowest tertile.

Our findings show an association between IPTp-SP uptake and place of residence. Women from rural provinces such as Muchinga and Luapula showed higher odds of IPTp-SP uptake than those from urban provinces of Copperbelt and Lusaka. The observed variation in the odds of IPTp-SP uptake between the urban and rural provinces could be due to differences in the malaria prevalence among these provinces. For example, Luapula province has a high malaria prevalence of 63% compared with 3% in Lusaka and Southern provinces. The province is rural with many water bodies, enhancing malaria transmission. These factors also make malaria transmission likely to be longer and more intense compared with other provinces. Thus, the province continues to report

the largest malaria burden in the country. Women in provinces with low prevalence of malaria may not take adequate IPTp-SP due to low perceived risk.^{27 28} On the contrary, women from regions of high level of malaria transmission, may take adequate doses of IPTp-SP due to higher risk perception. In these regions, emphasis on SP uptake during awareness messages could be higher due to the higher risk of contracting malaria. This finding suggests that women in rural areas may consider themselves at higher risk of contracting malaria compared with those in urban areas. Exploratory studies are required to investigate the reasons for variations in uptake of IPTp-SP among different provinces. These findings corroborate those from studies conducted in Uganda²⁸ and Tanzania^{29 30} which showed that variations in IPTp-SP uptake were related to differences in malaria transmission in the regions. The study in Tanzania showed that residents of the Central, Eastern, Southern, Lake regions, Southern highlands and Southwest highlands were significantly associated with the optimal uptake of SP doses compared with the residents of Zanzibar and Northern zones where malaria transmission was low. Similarly, the Uganda study showed that pregnant women residing in Eastern and Coastal regions had higher odds of optimal uptake of SP.

Our findings show that participants who had knowledge about malaria prevention and exposure to media messages had less odds of receiving adequate IPTp-SP doses. These findings contradict the study conducted by Mutanyi *et al*^{β 1} which showed that maternal knowledge on IPTp-SP positively influenced the uptake of the intervention in Tanzania, Cameroon, Zambia and Ghana. The difference between these findings and the current study could be that our study did not assess specifically the knowledge about IPTp-SP and its benefits. Rather, the study focused on knowledge about malaria prevention in general. This calls for more awareness on malaria interventions in general and about the recommended doses of IPTp-SP during pregnancy.

Moreover, our findings showed no significant association between education level and uptake of IPTp-SP. However, unadjusted analysis showed that women who had secondary level education and above had less odds of taking four or more doses of IPTp-SP compared with those who attained primary education. Our findings contrast previous studies and surveys. Literally, one would expect that having a secondary educational level or higher may be of influence on the uptake of the recommended doses of IPTp-SP compared with women with a lower education level. A study which compared MIS results of 12 countries in sub-Saharan Africa³² found that women with higher education had higher odds of reporting receiving three or more doses of IPTp-SP. The differences in the findings could be as a result of using different methods. It could also be due to selection bias; a large proportion of our study participants were those with primary level education who mainly resided in rural areas.

This study found that women in the highest and middle wealth tertile had less odds of taking four or more doses of IPTp-SP compared with those in the lowest wealth tertile. This finding contradicts previous studies^{33 34} which revealed that wealth index has a significant effect on uptake of IPTp-SP. These studies showed that the chances of completing the recommended dose of IPTp-SP increased with increase in wealth index.³⁴ For example, a study conducted in Senegal found that women in richer or middle wealth tertile were more likely to use the recommended doses of IPTp-SP.³⁴ The reason for the difference between our findings and these studies could be due to confounding by place of residence. Our findings show that most study participants who took four or more doses of IPTp-SP were from the rural areas who are mostly in the low wealth tertile. The other reason could be the fact that IPTp-SP is provided for free in Zambia.

There was no significant association noted between age and taking four or more doses of IPTp-SP. However, the adjusted analysis showed that, compared with the youthful mothers (15–24 years), those aged between 25 and 34 years were less likely to take four or more doses of IPTp-SP. This finding contradicts previous studies^{34,35} which revealed that younger women are less likely to use health services due to inadequate access to information and communication channels used for IPTp-SP promotion which are necessary for the uptake of IPTp-SP. For example, a study conducted in Ghana³⁵ reported low uptake of the recommended dose of IPTp-SP among the youth. Many youth often hide their pregnancies and start their ANC late, when they cannot take the recommended doses before delivery.

This study further reports that the uptake of four or more doses of IPTp-SP during pregnancy is still low at 7.5%. Most women (71.3%) took up to the third dose of IPTp-SP during pregnancy. This finding could be due to lack of awareness about the new guidelines on the fourth dose. More emphasis is needed on the new guidelines and taking at least three or more doses of IPTp-SP. Health messages should focus on and emphasise the new policy on four or more doses in the country. This finding is similar to other studies in sub-Saharan Africa which reported low uptake of the recommended doses of IPTp-SP³⁶ and suggests an urgent need for strategies to increase IPTp-SP coverage for improved maternal and newborn health outcomes in the region. This may contribute to the achievement of the ambitious Sustainable Development Goals and the target of reducing maternal mortality rate from 319 to 70 per 100000 live births.^{36–42}

Study limitations

This study has potential limitations. First, we did not collect the data, but used secondary data from the 2018 MIS. This prevented the team from having control over the measurement and selection of the variables. Some important variables that would have been of interest such as distance from the health facility to the communities where people live, stocks of SP, timing of ANC and number

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of times the woman attended ANC were not contained in the data set and thus could not be analysed. Further, the MIS data were cross-sectional, the associations in this study cannot guarantee causation or directionality.

Despite these limitations, we believe our findings have provided important information on the low coverage of four or more doses of IPTp-SP and the associated factors. In addition, use of nationally representative data from the 2018 MIS that covered all the provinces increases the generalisability of our findings.

CONCLUSION

These findings confirm low uptake of four or more doses of IPTp-SP in Zambia at 7.5% and that province and place of residence and wealth tertile affect IPTp-SP uptake. Strategies and interventions should focus on increased coverage of IPTp-SP from the current very low levels, with emphasis on provinces with much higher malaria burden where the risk is greatest and the ability to afford healthcare lowest. Interventions should include dissemination messages on the new policy of four or more doses of IPTp-SP and the benefits of strengthening the linkage between IPTp-SP programme with ANC services.

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Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval Ethical approval and waiver of consent was given by ERES converge IRB (Ref No. 2021-Nov-004). Permission to conduct the study and access to the 2018 MIS data set was granted by the National Health Research Authority (NRFA) Ref No. NHRA000023/04/03/2022) and the Ministry of Health, respectively. The data set was then secured as soft copy in the computer. No information regarding names of study participants was obtained and used; the data set was only used for the purpose of this study and it was not given to any other person or organisation. No harm was inflicted to the participants, the study used secondary data and there was no direct contact with study participants.

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REFERENCES

- 1 WHO. Malaria; 2023. Available: Malaria (who.int) [Accessed 10 Apr 2023].
- 2 WHO. World malaria report 2020: 20 years of global progress and challenges; 2021. Available: World malaria report 2020: 20 years of global progress and challenges (who.int) [Accessed 10 Apr 2023].
- 3 WHO. World malaria report 2020: tracking progress and gaps in the global response to malaria; 2023. Available: World malaria report 2022 (who.int) [Accessed 10 Apr 2023].
- 4 Bauserman M, Conroy AL, North K, et al. An overview of malaria in pregnancy. Semin Perinatol 2019;43:282–90.
- 5 Dellicour S, Tatem AJ, Guerra CA, et al. Quantifying the number of pregnancies at risk of malaria in 2007: a demographic study. PLoS Med 2010;7:e1000221. 10.1371/journal.pmed.1000221 Available: https://doi.org/10.1371/journal.pmed.1000221
- 6 Gnémé A, Guelbéogo WM, Riehle MM, et al. Plasmodium species occurrence, temporal distribution and interaction in a child-aged population in rural Burkina Faso. *Malar J* 2013;12:67.
- 7 Desai M, ter Kuile FO, Nosten F, et al. Epidemiology and burden of malaria in pregnancy. *Lancet Infect Dis* 2007;7:93–104.
- 8 Greenwood AM, Armstrong JR, Byass P, et al. Malaria chemoprophylaxis, birth weight and child survival. *Trans R Soc Trop Med Hyg* 1992;86:483–5.
- 9 Steketee RW, Nahlen BL, Parise ME, et al. The burden of malaria in pregnancy in malaria-endemic areas. Am J Trop Med Hyg 2001;64:28–35.
- 10 Corbett SS, Drewett RF. To what extent is failure to thrive in infancy associated with poorer cognitive development? A review and metaanalysis. J Child Psychol Psychiatry 2004;45:641–54.
- 11 Mace KE, Chalwe V, Katalenich BL, et al. Evaluation of sulphadoxinepyrimethamine for intermittent preventive treatment of malaria in pregnancy: a retrospective birth outcomes study in Mansa, Zambia. Malar J 2015;14:69.
- 12 Chaponda EB, Chandramohan D, Michelo C, et al. High burden of malaria infection in pregnant women in a rural district of Zambia: a cross-sectional study. Malar J 2015;14:380.
- 13 Zambia National Malaria Elimination. National malaria elimination strategic plan 2017-2021. 2017. Available: Malaria Elimination Strategy – Zambia National Malaria Elimination Centre (nmec.org. zm) [Accessed 12 Apr 2023].
- 14 Ministry of Health. ANC guidelines for a positive pregnancy experience. 2018. Available: ANC guidelines for a positive pregnancy experience | WHO | Regional Office for Africa [Accessed 13 Apr 2023].
- 15 Sialubanje C, Kaiser JL, Ngoma T, et al. Postnatal care services in rural Zambia: a qualitative exploration of user, provider, and community perspectives on quality of care. BMC Pregnancy Childbirth 2023;23:39. 10.1186/s12884-023-05350-w Available: https://doi.org/10.1186/s12884-023-05350-w
- 16 Sikambale C, Halwindi H, Baboo KS. Factors influencing utilization of intermittent presumptive treatment of malaria (IpTp) services by pregnant women in Sesheke District of Western province Zambia. *Med J Zambia* 2013;40:24–32.
- 17 Zakama AK, Ozarslan N, Gaw SL. Placental malaria. Curr Trop Med Rep 2020;7:162–71.
- 18 Diakite OSM, Kayentao K, Traoré BT, et al. Superiority of 3 over 2 doses of intermittent preventive treatment with sulfadoxine-

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9

pyrimethamine for the prevention of malaria during pregnancy in Mali: a randomized controlled trial. *Clin Infect Dis* 2011;53:215–23.

- 19 Kayentao K, Garner P, van Eijk AM, *et al.* Intermittent preventive therapy for malaria during pregnancy using 2 vs 3 or more doses of sulfadoxine-pyrimethamine and risk of low birth weight in Africa: systematic review and meta-analysis. *JAMA* 2013;309:594–604.
- 20 Ministry of Health, Central Statistics Office, PATH, PMI USAID, CDC, UNICEF, and WHO. MIS 2018: Zambia malaria indicator survey 2018; 2018. Available: https://www.malariasurveys.org/documents/ Zambia_MIS2018_FINAL-withSigs_20190415.pdf [Accessed 10 Apr 2023].
- 21 Central Statistical Office (Zambia), ICF International, Ministry of Health (Zambia), University Teaching Hospital (Zambia), University of Zambia. Zambia demographic and health survey 2018-2019. Fairfax, United States of America: ICF International; 2020. Available: Zambia Demographic and Health Survey 2018-2019 | GHDx (healthdata.org)
- 22 US President's Malaria Initiative (PMI). Zambia. 2022. Available: Zambia - PMI [Accessed 14 Apr 2023].
 23 Biddel N Voustavu D Miller, IM et al. Caparaphical patterns.
- 23 Riedel N, Vounatsou P, Miller JM, et al. Geographical patterns and predictors of malaria risk in Zambia: Bayesian geostatistical modelling of the 2006 Zambia national malaria indicator survey (ZMIS). Malar J 2010;9:37.
- 24 Zambia Statistics Agency. 2022 census; 2022. Available: https:// www.zamstats.gov.zm/2022-census [Accessed 14 Apr 2023].
- 25 Pourhoseingholi MA, Vahedi M, Rahimzadeh M. Sample size calculation in medical studies. *Gastroenterol Hepatol Bed Bench* 2013;6:14–7.
- 26 Rubin DB. Inference and missing data. *Biometrika* 1976;63:581–92. 10.1093/biomet/63.3.581 Available: https://doi.org/10.1093/biomet/ 63.3.581
- 27 Okoli CI, Hajizadeh M, Rahman MM, et al. Decomposition of socioeconomic inequalities in the uptake of intermittent preventive treatment of malaria in pregnancy in Nigeria: evidence from demographic health survey. *Malar J* 2021;20:300.
- 28 Okethwangu D, Opigo J, Átugonza S, et al. Factors associated with uptake of optimal doses of intermittent preventive treatment for malaria among pregnant women in Uganda: analysis of data from the Uganda demographic and health survey, 2016. Malar J 2019;18:250.
- 29 Mchwampaka WM, Tarimo D, Chacky F, et al. Factors affecting uptake of ≥3 doses of sulfadoxine-pyrimethamine for malaria prevention in pregnancy in selected health facilities, Arusha region, Tanzania. BMC Pregnancy Childbirth 2019;19:440:440:..
- 30 Gross K, Alba S, Glass TR, et al. Timing of antenatal care for adolescent and adult pregnant women in South-Eastern Tanzania. BMC Pregnancy Childbirth 2012;12:16.

- 31 Mutanyi JA, Onguru DO, Ogolla SO, *et al.* Determinants of the uptake of intermittent preventive treatment of malaria in pregnancy with Sulphadoxine Pyrimethamine in Sabatia sub County, Western Kenya. *Infect Dis Poverty* 2021;10:106:106.:.
- 32 Darteh EKM, Dickson KS, Ahinkorah BO, *et al.* Factors influencing the uptake of intermittent preventive treatment among pregnant women in sub-Saharan Africa: a Multilevel analysis. *Arch Public Health* 2021;79:182.
- 33 Burger R. School effectiveness in Zambia: the origins of differences between rural and urban outcomes. *Development Southern Africa* 2011;28:157–76.
- 34 Mbengue MAS, Bei AK, Mboup A, et al. Factors influencing the use of malaria prevention strategies by women in Senegal: a crosssectional study. *Malar J* 2017;16:470.
- 35 Atenkperiga Ayiisi E. Knowledge and utilization of intermittent preventive treatment (IPT) for malaria control among pregnant women attending Antenatal clinics in the Sunyani West District of Ghana. *SJPH* 2017;5:254.
- 36 Odjidja EN, Kwanin C, Saha M. Low uptake of intermittent preventive treatment in Ghana; an examination of health system bottlenecks. *Health Syst Policy Res* 2017;4.
- 37 Dun-Dery F, Meissner P, Beiersmann C, et al. Uptake challenges of intermittent preventive malaria therapy among pregnant women and their health care providers in the upper West region of Ghana: a mixed-methods study. *Parasite Epidemiol Control* 2021;15:e00222.
- 38 Blystad A, Moland KM, Munsaka E, et al. Vanilla bisquits and lobola bridewealth: parallel discourses on early pregnancy and schooling in rural Zambia. BMC Public Health 2020;20:1485.
- 39 Massar K, Sialubanje C, Maltagliati I, et al. Exploring the perceived effectiveness of applied theater as a maternal health promotion tool in rural Zambia. Qual Health Res 2018;28:1933–43.
- 40 Sialubanje C, Sitali DC, Mukumbuta N, *et al.* Perspectives on factors influencing transmission of COVID-19 in Zambia: a qualitative study of health workers and community members. *BMJ Open* 2022;12:e057589.
- 41 Sialubanje C, Mukumbuta N, Ng'andu M, et al. Perspectives on the COVID-19 vaccine uptake: a qualitative study of community members and health workers in Zambia. BMJ Open 2022;12:e058028.
- 42 Sialubanje C, Kaiser JL, Ngoma T, *et al.* Postnatal care services in rural Zambia: a qualitative exploration of user, provider, and community perspectives on quality of care. *BMC Pregnancy Childbirth* 2023;23:39.