Determinants of Adherence and Recurrence of Malaria Among Women of Reproductive Age in a Mixed Effects Model Analysis

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Abstract

Background: The recommended treatment for uncomplicated malaria globally since 2001 has been artemisinin-based combination treatments, or ACTs. Patient adherence to ACT is critical for curing malaria and preventing drug resistance. However, evidence on adherence levels and its impact on recurrence particularly among women of reproductive age remains limited especially in high transmission settings.

Methods: A retrospective cohort study analysed data from 1801 women of reproductive age in Homa Bay county, Kenya (2021-2025). This study quantified adherence levels and employed a mixed effects logistic regression model to identify predictors of adherence. A mixed effects Cox proportional hazards model was used to assess the effect of adherence and other factors on the time to malaria recurrence, adjusting for clustering and confounding.

Results: Overall adherence was high (86.2%). Pregnant women had significantly lower odds of adherence than non-pregnant women (aOR=0.69, 95% CI:0.53-0.92). Significant geographic variation existed with women from Mfangano and Rusinga islands showing higher adherence than those in urban Homa Bay. Contrary to expectations, treatment adherence did not significantly reduce the hazard to malaria recurrence in either the univariate (HR=1.01, p=0.94) or multivariate analysis (aHR=1.04, p=0.82) after adjusting for gravidity, marital status, income and age. The primary protective factor against recurrence was gravidity. Multigravida women under 35 years had a 26% reduced hazard of recurrence (HR=0.74, 95% CI:0.57-0.96). Model diagnostics confirmed good fit for both analysis.

Conclusion: While adherence was generally high, it was not the primary driver of malaria recurrence in this high transmission area where re-infection risk is likely a dominant factor. Pregnancy was a key risk factor for non-adherence. We recommend targeted support for pregnant women and vector control to complement treatment.

Introduction

Malaria poses a severe threat to public health worldwide, particularly in regions where it is endemic. The mainstay of malaria prevention and treatment approaches is the use of vector control methods and antimalarial drugs. However, patient compliance with recommended treatment plans is a major factor in these drugs efficacy. Designing efficient interventions to enhance treatment results and lessen the recurrence and burden of malaria requires an understanding of the rates of antimalarial medication adherence and the variables affecting adherence behaviour. In 2021, Kenya accounted for 1.3% of the total malaria cases globally(World Health Organization, 2022). Insufficient medical management of malaria during pregnancy is correlated with low birth weight , premature delivery, intrauterine development limitation, and an elevated risk of foetal, neonatal, and childhood mortality(World Health Organization, 2022). Three strategies recommended by the World Health Organisation (WHO) for preventing pregnancy related malaria include chemoprevention in trimesters two and three using intermittent preventive treatment (IPTp) with monthly sulphadoxine-pyrimethamine (IPTp-SP) in women without HIV and the implementation of durable nets treated with insecticides(World Health Organization, 2022). Nevertheless, the extent to which women of reproductive age comply with recommended antimalarial medication remains uncertain(World Health Organization, 2022). The WHO prevalence rates make it certain that malaria continues to pose a serious threat to international health, especially to vulnerable groups like pregnant women. Socioeconomic, cultural, behavioural, and healthcare-related factors are among the many that impact adherence to antimalarial treatment regimens(Steketee et al., 2001). Because of the possible hazards malaria infection poses to the health of both mother and foetus, women who are of reproductive age are especially vulnerable to its aftereffects(Desai et al., 2007). For this group to avoid negative outcomes such congenital malaria, low birth weight, maternal mortality, and severe malaria, adherence to antimalarial medications at high levels is essential(World Health Organization, 2020, 2022). Various research studies define full adherence

differently(Morrison et al., 2015). Some define a patient as fully adherent based on arbitrary thresholds like 80% prescription consumption while other studies would conduct pharmacokinetic modelling of serum drug levels resulting from a patient's dosing pattern(Morrison et al., 2015). Several variables influence and impact adherence, including patient age, education level, perceptions of the disease, costs associated with treatment(Gore-Langton et al., 2015). Adherence is a crucial factor when determining how effective a treatment is (Gore-Langton et al., 2015; Lawford et al., 2011). Poor adherence to ACT treatment can have serious repercussions because patients who don't finish their recommended treatment appropriately are more likely to experience a poor recovery, be at risk for developing drug resistance early on(Fuangchan et al., 2014; Keoluangkhot et al., 2008; White & Pongtavornpinyo, 2003), and have treatment failure(Rasmussen et al., 2022; World Health Organization, 2020). There have been numerous studies (Gore-Langton et al., 2015; Haftu et al., 2018; Lawford et al., 2011; Morrison et al., 2015) on patients compliance with ACT and factors that contribute to poor adherence. However, a significant knowledge gap exists regarding the role that factors pertaining to the patient play in enhancing adherence to ACT treatment in Women within the reproductive age group in the majority of Kenya's low-income and rural setting such as in Homa Bay county. Researching the variables driving antimalarial drug adherence in women who are fertile needs to be done, considering a range of social, environmental, and individual factors. The intricate interactions between these variables and their relationships to medication adherence can be examined. By using a multivariate analysis technique, this study seeks to close the information gap about the factors that influence women of reproductive age's adherence to antimalarial medications. To improve treatment compliance and malaria control efforts, interventions and strategies can be devised by identifying and understanding the correlates of adherence and malaria recurrence. This will ultimately improve maternal and child health outcomes in malaria-endemic countries.

Methods

Study Design

This is a retrospective cohort study analysing prospectively collected secondary data. This data was collected by a team of researchers from KEMRI MiMBa study between February 2021 and March 2025. Women of childbearing age were consented, and a unique identifier assigned. Every hospital or community health services visit attended by a woman had her record identified using the unique identifier number. Data from all visits were merged using the unique identifier. The analysis dataset was then restricted to episodes where a woman received an antimalarial prescription and had follow-up dose completion assessment within 3 days.

Study Setting and Population

Data used in this analysis was collected from women of childbearing age in Homabay county residing in community units around selected health facilities providing antenatal care and delivery services. Malaria is endemic in this area with transmission occurring throughout the year with peak during rainy seasons (typically March-May and October-December). Indoor residual spraying (IRS) has been implemented in Homa Bay County in recent years, reducing but not eliminating transmission; the area remains endemic with ongoing malaria transmission.

Outcome variables

Adherence is a binary variable. We classified a patient as adherent if she completed her ACT based antimalarials in 3 days.

Malaria recurrence was defined as a subsequent episode of confirmed malaria by microscopy or RDT occurring after completion of the index antimalarial treatment. Time to recurrence was measured in days from the date of treatment completion (day 3) to the date of the subsequent malaria diagnosis. Women were censored at the end of the study period, loss to follow-up, or death, whichever occurred first.

Independent variables

A list of demographics, pregnancy history, and socioeconomic characteristics were considered.

Statistical Analysis

We conducted descriptive analysis to characterize the overall study population and across the 4 sites. We generated frequency tables and corresponding percentages for categorical variables. For continuous variables, we generated the median and interquartile range (IQR) for each site and combined pool of women. We calculated adherence levels by dividing number of antimalarial treatment episodes where women were adherent by total number of antimalarial episodes. To identify risk factors of adherence, we fit a mixed effects logistic regression after checking that the assumptions are satisfied. Bivariate models were fitted to assess unadjusted association between each predictor and adherence. Variables which gave a p-value less than or equal to 0.2 were included in the multivariable model. We evaluated the performance of our model by estimating intraclass correlation and area under curve. Cox proportional hazards regression model was used to investigate association between time to malaria recurrence and predictor variables including adherence, patient age, pregnancy status, education level, marital status, income, gravidity, history of miscarriage, HIV status, and location of residence. Univariate Cox regression models were fitted for each covariate to assess their individual associations with the outcome. A multivariate Cox regression model was then constructed including all covariates that showed a significant association in the univariate analysis ($p<0.20$). The 0.20 cut-off is a common threshold to avoid excluding potentially important confounding variables. All statistical analysis were carried out using STATA 17.

Ethical considerations

The protocol for the parent study was reviewed and approved by the Scientific and Ethical Review Unit (SERU) of the Kenya Medical Research Institute (KEMRI) with the approvals granted under KEMRI SSC Protocol KEMRI/SERU/CGHR/346/4093. Permission to use the data for analysis has been granted by the Principal Investigator. Data for this project is anonymised to ensure data protection of the participants and compliance with Data protection Act. All the women gave informed consent to participate in the primary study. No contact was made with any of the women during this study.

Results

Baseline characteristics

A total of 1801 women of childbearing age were followed up after administration of antimalarial treatment. The overall baseline characteristics and stratified by site are shown in Table 1. These women were drawn from Homabay town (21.7%, n=390), Marindi (22.0%, n=396), Mfangano island (28.04%, n=505) and Rusinga (28.26%, n=509). The median maternal age was 25 years (IQR: 22–30), consistent across sites. Median maternal weight ranged from 62–63.5 kg, suggesting comparable nutritional status. Gravidity distribution indicated a balanced spread, with approximately 23% of participants reporting five or more pregnancies. Majority of the women were married (81%), rural residents (94%), and had at least primary education (90%). More than 50% did not have a source of income with only 5% salaried. HIV prevalence was 16.4%, and about 20% had received a COVID-19 vaccine. Previous miscarriage was reported in 9.6% of participants.

Adherence

Table 2 presents adherence to antimalarial medication across various demographic and health related characteristics. Overall adherence was high at 86.16%. Adherence differed significantly by pregnancy status ($p < 0.001$), with non-pregnant women (88.86%) showing higher adherence compared to pregnant women (82.47%). This suggests that pregnancy may be associated with lower adherence to antimalarials, possibly due to safety concerns or changes in perception and prioritization of medication during pregnancy. Residence also showed a statistically significant difference in adherence rates ($p = 0.042$), with rural residents (86.52%) more likely to adhere than their urban counterparts (80.00%). This may reflect better engagement with community health interventions or differing healthcare access between rural and urban areas. HIV-negative individuals had a slightly higher adherence (86.45%) compared to HIV-positive individuals (82.85%) ($p = 0.084$), this difference not being of statistical significance. Other factors, including marital status, income generation, and COVID-19 vaccination status, did not show significant associations with adherence levels.

Logistic regression model assumptions

The dependent variable, adherence, is binary with two distinct categories “yes” and “no” as displayed in supplement 1. This satisfies the fundamental assumption of logistic regression which requires the outcome variable to be dichotomous. To assess whether the continuous predictors age and weight have a linear relationship with the log odds of adherence, we used the Box-Tidwell test which fits adherence against the log of age and weight. From results in supplement 2, the p-values are greater than 0.05, we fail to reject the null hypothesis, suggesting that the assumption of linearity between age, weight and the log odds of adherence is satisfied. Multicollinearity was assessed using Variance Inflation Factors (VIF) for continuous variables and Generalized VIF (GVIF) for categorical variables. All VIFs in supplement 3 are below the commonly used threshold of 5, suggesting no significant collinearity in our dataset. We assessed normality of random effects using the normal Q-Q (Quantile-Quantile) plots in supplement Figure 1, the random effect by patient id was close to normal distribution. To protect our inference from the minor deviations, we used robust standard errors in our model. We predicted random effects and examined correlation between random effects and fixed effects to confirm that the random effects are independent of fixed predictors. We defined the Best Linear Unbiased Predictors (BLUPs) for random effects to estimate how much each woman deviates from the population-level (fixed-effect) prediction. The best estimator minimizes prediction error(variance), predictor predicts the unobserved random effect for each group. The BLUPs for patient id has low correlation values as displayed in supplement 4, suggesting near zero correlation between the random effect and fixed effects. We used pearson residuals to approximate residual errors and examine for patterns in residuals vs random effects. No clear pattern in the plots on supplement figure 2 suggested independence.

Model selection

Adherence was subjected to bivariate logistic regression analysis to discover potential risk factors of adherence. Risk factors with p values up to 0.20 identified in the unadjusted analyses were included in the adjusted logistic mixed effects model to assess their specific impact on adherence, while accounting for other risk factors. The 0.20 cut-off is a common threshold to avoid excluding potentially important confounding variables.

Adherence risk factors

Factors associated with adherence were evaluated using mixed effects logistic regression model. Women of unknown HIV status were two times more likely to adhere to antimalarial treatment compared to women with known HIV status (aOR = 2.19, 95% CI: 1.14–4.22, $p = 0.02$) (Table 3). Pregnant women were thirty percent less likely to adhere to treatment than nonpregnant women (aOR = 0.69, 95% CI [0.53–0.92], $p = 0.01$) (Table 3). Compared to participants from Homa Bay, those from Mfangano and Rusinga were at least twice more likely to adhere: (Mfangano: aOR = 4.01, 95% CI[2.58–6.24], $p < 0.01$), (Rusinga: aOR = 2.61, 95%

CI[1.75–3.89], p < 0.01) (Table 3). Gravidity, classification of location (rural/urban), age, experience with previous miscarriage did not have a significant effect on antimalarial adherence. These findings imply geographic disparities in health behaviour, possibly influenced by differences in health education outreach, community engagement, or accessibility of health services. Other demographic factors such as education level, marital status, income, age, and location were not significantly associated with adherence in the adjusted models.

Evaluating the mixed effects logistic model

We conducted a post estimation AUC (Area Under Curve) plot in Figure 1 and found that predictive accuracy of the logistic model was 0.86, 95% CI[0.85-0.88], standard error=0.0098. This means there is a 86.47% chance our model will give a higher score to a mother who is adherent compared to a non adherent one. We measured the proportion of total variance attributable to differences between groups (the random effects by patient) by computing the intraclass correlation coefficient. About 17% of the total variance in adherence was attributable to differences between patient. This shows moderate variation within women clustering. The remaining 83% was explained by fixed effects variation.

Survival data descriptives

Among 1801 women included in the recurrence analysis, 395 experienced at least one recurrence during 2458.5 person years of follow-up. The incidence of recurrence was 0.16 and median survival time was 2.64 years. 1406 women observations were censored due to end of follow-up.

Time to Malaria Recurrence and Associated Factors

The proportional hazards assumption was tested and the results indicated that all covariates met the assumption except pregnancy status and site. The final Cox model was stratified by pregnancy status and site. The analysis in Table 4 determines the effect of adherence and other factors on malaria recurrence. Multigravida women had a significantly lower hazard of malaria recurrence compared to paucigravida in the univariate model, with (HR = 0.73, p = 0.002). Married women had a reduced hazard of malaria recurrence (HR = 0.74, p = 0.015). Women having an income source also had reduced hazards of recurrence (HR = 0.77, p = 0.011). A unit increase in patients age reduced the hazard of infection by 2% (HR = 0.98, p = 0.004). Patient adherence, education, knowledge of HIV status, COVID vaccine and history of miscarriage did not significantly impact recurrence to malaria in the unadjusted model.

Confounding effect

Gravidity, marital status, income and age qualified to be included in the adjusted model due to having a p value less than 0.20. Running the adjusted model with the four variables did not yield significant results. The marginal benefit of age in the unadjusted model prompted checking for confounding effect on the other variables to determine how to account for it in the adjusted model. From percentage changes in hazard rates displayed in Table 10, we noted more than 10% change in hazards signifying that age distorts the observed association between malaria recurrence, gravidity, and marital status. We accounted for the confounding effect by stratifying our model into under 35 years and 35 years and above as displayed in table 5. In the under 35 years group, multigravid women had 26% reduction in hazard of malaria recurrence compared with paucigravid women (aHR=0.74, p = 0.02). Marital status and having income source did not have significant effect on hazard of malaria recurrence. Patient adherence did not significantly reduce hazards of malaria recurrence (aHR=1.21, p= 0.32).

Evaluating the Cox model

The plot on Figure 2 is a graph of the Nelson-Aalen cumulative hazard function and the Cox-Snell residual. The hazard function follows the 45-degree line very closely except for very large values of time. This is common for models with censored data. Our final model fits the data well.

Discussion

This study examined factors associated with antimalarial treatment adherence among women of childbearing age in Homa Bay County, Kenya, using a mixed effects logistic regression model. Our findings indicate that HIV status awareness, pregnancy status, and geographic location were significant predictors of adherence, whereas other socio-demographic variables such as education, marital status, income, and age did not show independent associations after adjustment.

Women of unknown HIV status were twice as likely to adhere to treatment compared to those who knew their HIV status. This may be due to confounding factors. Maybe women who do not know their status may be systematically different in their health seeking behaviour, or they may have been misclassified in the data. This finding highlights the importance of strengthening routine HIV testing during malaria treatment visits to enable better characterization of this population.

Pregnant women were approximately 30% less likely to adhere to treatment compared to their non-pregnant counterparts. This aligns with previous research indicating that pregnancy can be a period of reduced adherence to non-routine medications, particularly when women experience nausea, vomiting, or concerns about potential teratogenic effects of drugs(Lupattelli et al., 2014). Although Kenya's national malaria policy promotes intermittent preventive treatment in pregnancy (IPTp) and prompt treatment of malaria

in pregnant women(World Health Organization, 2022), our results suggest that additional counselling and reassurance may be needed to address fears and misconceptions about antimalarial safety during pregnancy.

Geographic disparities in adherence were evident. Women from Mfangano and Rusinga Islands were at least twice as likely to adhere compared to those from the Homa Bay mainland. This finding may reflect differences in health education outreach, community-based treatment programs, or perceptions of malaria severity. Island communities, often served by targeted NGO and community health initiatives, may have stronger health worker–patient relationships, which have been linked to improved adherence in other rural African settings. In contrast, urban or peri-urban settings like Homa Bay town may experience greater patient mobility and less personalized follow-up, reducing adherence rates. Interestingly, education, marital status, income, age, and other demographic variables were not significantly associated with adherence in our adjusted models.

A key and unexpected finding was that treatment adherence did not significantly reduce hazards of malaria recurrence. This null association persisted across all model specifications and age strata. This suggests that in high transmission areas like Homa Bay, reinfection from a new mosquito bite can happen very quickly, diminishing any protective benefit gained from successful clearance of the initial infection with drugs. Although indoor residual spraying has reduced transmission intensity in Homa Bay County, the area remains endemic with ongoing transmission. We could not distinguish recrudescence from reinfection since molecular genotyping was not conducted in this study. If most recurrences represent reinfection rather than recrudescence, high adherence will successfully clear the original infection but not prevent subsequent exposure. Further analysis in multivariable models is needed to explore the potential role of antimalarial adherence to malaria recurrence.

Reduced hazard of malaria recurrence in multigravida women under 35 years suggest that women with more births may have more exposure to malaria prevention strategies. This highlights the need for interventions targeting younger women of lower gravida who may be more vulnerable to malaria recurrence due to less experience with health services.

Our findings have important implications for malaria control strategies in Homa Bay County. Efforts to improve adherence should consider integrating malaria treatment counselling into HIV care programs to address potential drug fatigue and misconceptions. Tailored interventions for pregnant women are also needed, emphasizing the safety and importance of completing antimalarial regimens. Moreover, the higher adherence rates in island communities suggest that elements of their community engagement and follow-up models could be adapted for the mainland.

This study's strengths include the use of a mixed-effects logistic regression model to adjust for clustering by study site, increasing the robustness of our estimates. However, limitations include reliance on self-reported adherence, which may be subject to recall and social desirability bias, and the cross-sectional nature of the data, which precludes causal inference.

Conclusion

This study demonstrates that adherence to antimalarial treatment among women of childbearing age in Homa Bay County is influenced by HIV status awareness, pregnancy status, and geographic location, highlighting important behavioral and structural disparities. Women of unknown HIV status and those residing in Mfangano and Rusinga were more likely to adhere compared to their counterparts, while pregnant women were less adherent. A key and surprising finding was that treatment adherence did not significantly reduce the hazard of malaria recurrence. While high overall adherence may contribute to this null finding, a more plausible explanation is the high transmission intensity in Homa Bay which results to rapid reinfection.

These findings suggest that targeted interventions addressing maternal health challenges and site-specific barriers are critical to improving adherence.

Recommendations

Policy and Practice

Provide more support to pregnant women by giving them clear information on the safety of malaria drugs during pregnancy.

Strengthen malaria adherence programs in urban areas where rates are lower, possibly by learning from strategies used in rural settings.

Strengthen routine HIV testing during malaria treatment visits to enable better identification of women at higher risk of nonadherence.

Research

Longitudinal studies with varying transmission intensities could demistify the effect of adherence on malaria recurrence.

Qualitative studies to explore the specific barriers to adherence among pregnant women and urban residents.

Data and Methodology

This study demonstrates the value of using longitudinal data with repeated measures.

Future research should continue this approach to better capture the dynamics of adherence and recurrence over time.

Consider applying models that adjust for prior treatment and malaria vaccination that could provide more insights into the relationship between adherence and malaria recurrence.

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Author Contribution

Conceptualization was carried out by EO

Methodology was designed by EO and JO

Formal analysis was conducted by EO

The original draft was written by EO, with review and editing provided by JO.

Data availability

The Worldwide Antimalarial Resistance Network (WWARN) are in the process of developing a data sharing platform for antimalarial pregnancy exposure registry.

Competing interests

The authors declare no competing interests.

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	Participant Demographics				
	Overall	**Site**			
		Homabay	Marindi	Mfangano	Rusinga
Maternal age (years), N, median (IQR; range)	N=1801, 25 (22-30; 15-48)	N=390, 25 (21-30; 15-45)	N=396, 25 (21-30; 15-47)	N=505, 26 (22-30; 15-48)	N=509, 26 (23-31; 15-45)
Maternal weight (kg), N, median (IQR; range)	N=1757, 63 (57-70; 34.2-166.5)	N=389, 63 (57-71; 34.2-104)	N=395, 62 (56-69; 43-111)	N=469, 63.5 (58-70.4; 40-166.5)	N=503, 63 (56-71; 43-160)
Gravidity					
0, n/N (%)	1/1800 (0.1%)	1/390 (0.3%)	0/396 (0.0%)	0/505 (0.0%)	0/508 (0.0%)
1, n/N (%)	411/1800 (22.8%)	98/390 (25.1%)	104/396 (26.3%)	108/505 (21.4%)	100/508 (19.7%)

		Participant Demographics				
		Overall	Site			
			Homabay	Marindi	Mfangano	Rusinga
	2, n/N (%)	373/1800 (20.7%)	89/390 (22.8%)	75/396 (18.9%)	110/505 (21.8%)	99/508 (19.5%)
	3, n/N (%)	333/1800 (18.5%)	67/390 (17.2%)	70/396 (17.7%)	91/505 (18.0%)	105/508 (20.7%)
	4, n/N (%)	281/1800 (15.6%)	55/390 (14.1%)	63/396 (15.9%)	75/505 (14.9%)	88/508 (17.3%)
		401/1800 (22.3%)	80/390 (20.5%)	84/396 (21.2%)	121/505 (24.0%)	116/508 (22.8%)
Smoking, n/N (%)		1/1795 (0.1%)	1/387 (0.3%)	0/396 (0.0%)	0/503 (0.0%)	0/508 (0.0%)
Drink alcohol, n/N (%)		21/1799 (1.2%)	8/390 (2.1%)	3/396 (0.8%)	4/504 (0.8%)	6/508 (1.2%)
Marital status						
	Single, n/N (%)	306/1729 (17.7%)	73/369 (19.8%)	75/366 (20.5%)	84/484 (17.4%)	74/509 (14.5%)
	Married, n/N (%)	1399/1729 (80.9%)	293/369 (79.4%)	286/366 (78.1%)	390/484 (80.6%)	429/509 (84.3%)
	Divorced, n/N (%)	2/1729 (0.1%)	0/369 (0.0%)	1/366 (0.3%)	0/484 (0.0%)	1/509 (0.2%)
		22/1729 (1.3%)	3/369 (0.8%)	4/366 (1.1%)	10/484 (2.1%)	5/509 (1.0%)
Residence						
	Rural, n/N (%)	1685/1800 (93.6%)	311/390 (79.7%)	390/396 (98.5%)	492/505 (97.4%)	492/509 (96.7%)
		115/1800 (6.4%)	79/390 (20.3%)	6/396 (1.5%)	13/505 (2.6%)	17/509 (3.3%)
Highest level of schooling completed						
	None, n/N (%)	174/1796 (9.7%)	32/389 (8.2%)	30/393 (7.6%)	44/504 (8.7%)	68/509 (13.4%)
	Primary, n/N (%)	903/1796 (50.3%)	185/389 (47.6%)	234/393 (59.5%)	231/504 (45.8%)	253/509 (49.7%)
	Secondary, n/N (%)	538/1796 (30.0%)	132/389 (33.9%)	97/393 (24.7%)	156/504 (31.0%)	152/509 (29.9%)
		181/1796 (10.1%)	40/389 (10.3%)	32/393 (8.1%)	73/504 (14.5%)	36/509 (7.1%)
Source of income						
	Salaried worker, n/N (%)	93/1801 (5.2%)	26/390 (6.7%)	16/396 (4.0%)	27/505 (5.3%)	24/509 (4.7%)
	Business Owner, n/N (%)	370/1801 (20.5%)	92/390 (23.6%)	68/396 (17.2%)	58/505 (11.5%)	151/509 (29.7%)
	Subsistance fish farming, n/N (%)	190/1801 (10.5%)	23/390 (5.9%)	77/396 (19.4%)	68/505 (13.5%)	22/509 (4.3%)
	Commercial fish farming, n/N (%)	53/1801 (2.9%)	2/390 (0.5%)	18/396 (4.5%)	12/505 (2.4%)	21/509 (4.1%)
	None, n/N (%)	843/1801 (46.8%)	180/390 (46.2%)	157/396 (39.6%)	292/505 (57.8%)	214/509 (42.0%)
	Other, n/N (%)	11/1801 (0.6%)	1/390 (0.3%)	3/396 (0.8%)	4/505 (0.8%)	3/509 (0.6%)
	Daily wage, n/N (%)	66/1801 (3.7%)	18/390 (4.6%)	6/396 (1.5%)	3/505 (0.6%)	39/509 (7.7%)
		175/1801 (9.7%)	48/390 (12.3%)	51/396 (12.9%)	41/505 (8.1%)	35/509 (6.9%)
HIV status						
	Positive, n/N (%)	295/1797 (16.4%)	68/390 (17.4%)	58/396 (14.6%)	90/503 (17.9%)	79/507 (15.6%)
	Negative, n/N (%)	1397/1797 (77.7%)	301/390 (77.2%)	290/396 (73.2%)	398/503 (79.1%)	407/507 (80.3%)
		105/1797 (5.8%)	21/390 (5.4%)	48/396 (12.1%)	15/503 (3.0%)	21/507 (4.1%)
Covid 19 vaccine, n/N (%)		355/1788 (19.9%)	77/385 (20.0%)	39/390 (10.0%)	105/503 (20.9%)	134/509 (26.3%)
Consanguity, n/N (%)		6/1799 (0.3%)	0/390 (0.0%)	1/396 (0.3%)	4/505 (0.8%)	1/507 (0.2%)
Previous miscarriage, n/N (%)		173/1799 (9.6%)	38/390 (9.7%)	19/395 (4.8%)	56/505 (11.1%)	60/508 (11.8%)
Congenital anomaly, n/N (%)		22/1397 (1.6%)	3/291 (1.0%)	5/302 (1.7%)	3/398 (0.8%)	11/406 (2.7%)

Table 2

		adherence	p values
overall	overall	86.16%	
Marital status	married	86.60%	0.6121
	not married	85.62	
Pregnancy status	pregnant	82.47%	<0.001
	not pregnant	88.86%	
Area	rural	86.52%	0.0418
	urban	80.00%	
Income source	income genarating	85.79%	0.669
	no income	86.44%	
HIV status	HIV positive	82.85%	0.084
	HIV negarive	86.45%	

COVID-19	covid 19 positive	86.41%	0.8365
	covid 19 negative	86.02%	

Table 3: unadjusted and adjusted Odds ratios

variable description	unadjusted OR (95% CI)	p-value	adjusted OR	p-value
Gravidity				
paucigravida	ref			
multigravida	1.23(0.94-1.63)	0.12	1.05(0.74-1.49)	0.79
Married				
no	ref			
yes	1.11(0.79-1.56)	0.55		
Location				
rural	ref			
urban	0.58(0.35-0.98)	0.04	0.96(0.56-1.64)	0.87
Education				

secondary sch not completed	ref			
sec school completed	1.08(0.82-1.42)	0.60		
Income				
no	ref			
yes	0.94(0.71-1.23)	0.63		
HIV				
known status	ref			
unknown status	1.69(0.89-3.22)	0.11	2.19(1.14-4.22)	0.02
Age	1.02(1.00-1.04)	0.06	1.00(0.98-1.03)	0.76
Weight	1.01(0.99-1.02)	0.38		
Covid vaccine				
no	ref			
yes	1.01(0.73-1.42)	0.92		
Previous miscarriage				
no	ref			
yes	1.58(0.96-2.62)	0.07	1.42(0.85-2.39)	0.18
Pregnant				
no	ref			
yes	0.56(0.42-0.73)	<0.01	0.69(0.53-0.92)	0.01
Site				
homabay	ref			
marindi	1.40(0.97-2.00)	0.06	1.31(0.90-1.91)	0.154
mfangano	4.33(2.81-6.66)	<0.01	4.01(2.58-6.24)	<0.01
rusinga	2.92(1.98-4.30)	<0.01	2.61(1.75-3.89)	<0.01

Table 4: unadjusted and adjusted Hazard ratios

variable description	unadjusted HR (95% CI)	p-value	adjusted HR	p-value
Adherence				
no	ref			
yes	1.01(0.73-1.41)	0.94	1.04(0.74-1.46)	0.82
Gravidity				
paucigravida	ref			
multigravida	0.73(0.59-0.89)	<0.01	0.79(0.60-1.05)	0.10
Married				

no	ref			
yes	0.74(0.58-0.94)	0.02	0.91(0.69-1.20)	0.50
Location				
rural	ref			
urban	0.72(0.43-1.23)	0.23		
Education				
secondary sch not completed	ref			
secondary school completed	0.96(0.78-1.19)	0.71		
Income				
no	ref			
yes	0.77(0.63-0.94)	0.01	0.86(0.69-1.08)	0.20
HIV				
known status	ref			
unknown status	1.07(0.70-1.65)	0.76		
Age	0.98(0.96-0.99)	<0.01	0.99(0.97-1.02)	0.58
Weight	1.00(0.99-1.01)	0.53		
Covid vaccine				
no	ref			
yes	0.87(0.67-1.13)	0.30		
previous miscarriage				
no	ref			
yes	1.19(0.88-1.62)	0.26		

Table 5: adjusted analysis stratified by age

	stratified adjusted analysis-< 35yrs		stratified adjusted analysis->= 35yrs	
variable	adjusted HR	p-value	adjusted HR	p-value
adherence				
No	ref			
yes	1.21(0.83-1.78)	0.32	0.48(0.22-1.05)	0.07
gravidity				
paucigravida	ref		ref	
multigravida	0.74(0.57-0.96)	0.02	0.46(0.06-3.38)	0.45
married				
no	ref		ref	
yes	0.85(0.62-1.14)	0.27	1.26(0.59-2.71)	0.55
income				
no	ref		ref	
yes	0.86(0.67-1.11)	0.24	0.64(0.36-1.14)	0.13

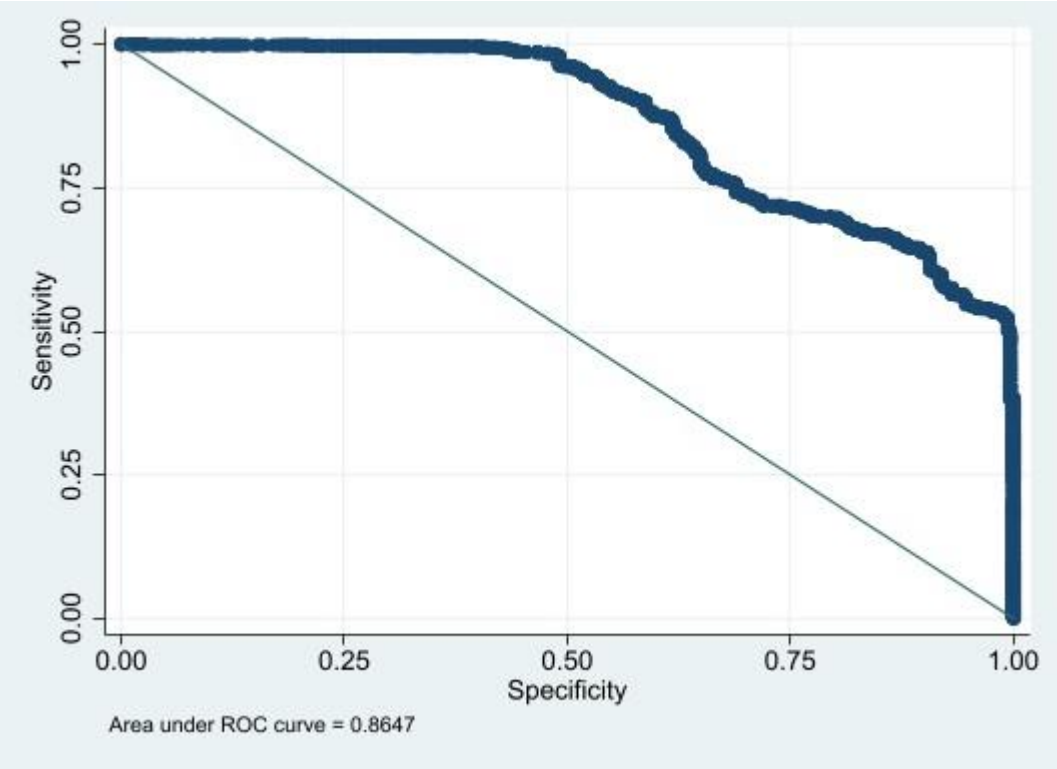


Figure 1: Area Under Curve plot evaluating the mixed effects logistic model

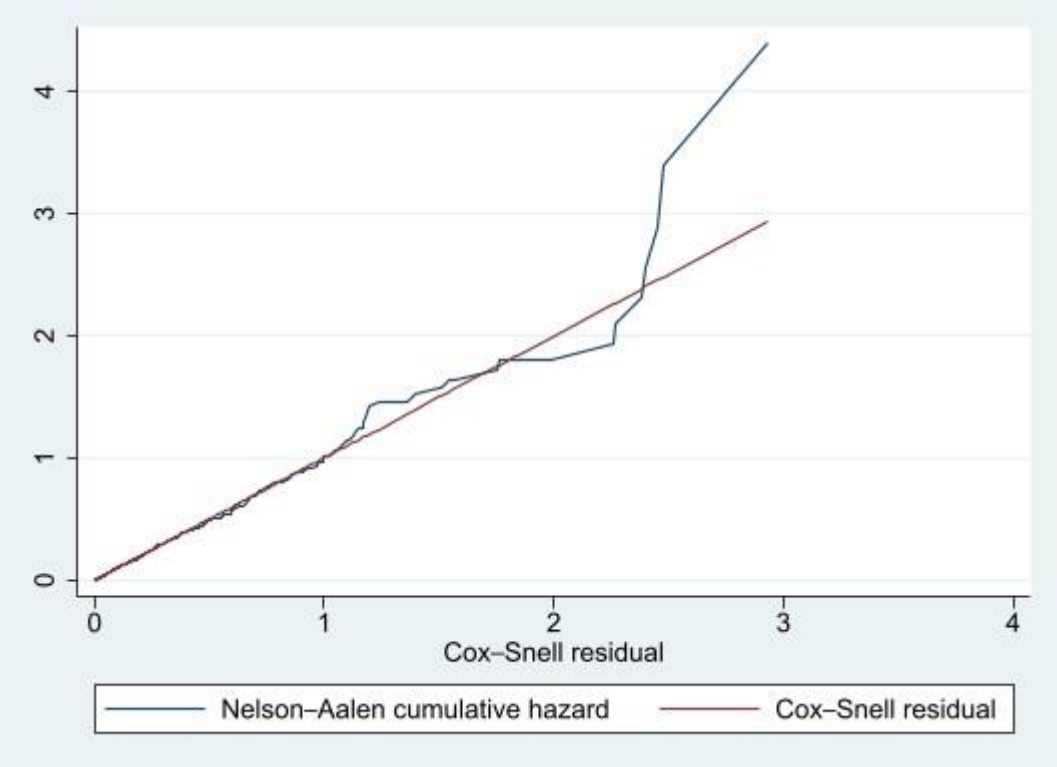


Figure 2: Graph of the Nelson-Aalen cumulative hazard function and the Cox-Snell residual.

Supplement 1: adherence distribution

adherence	frequency	percent

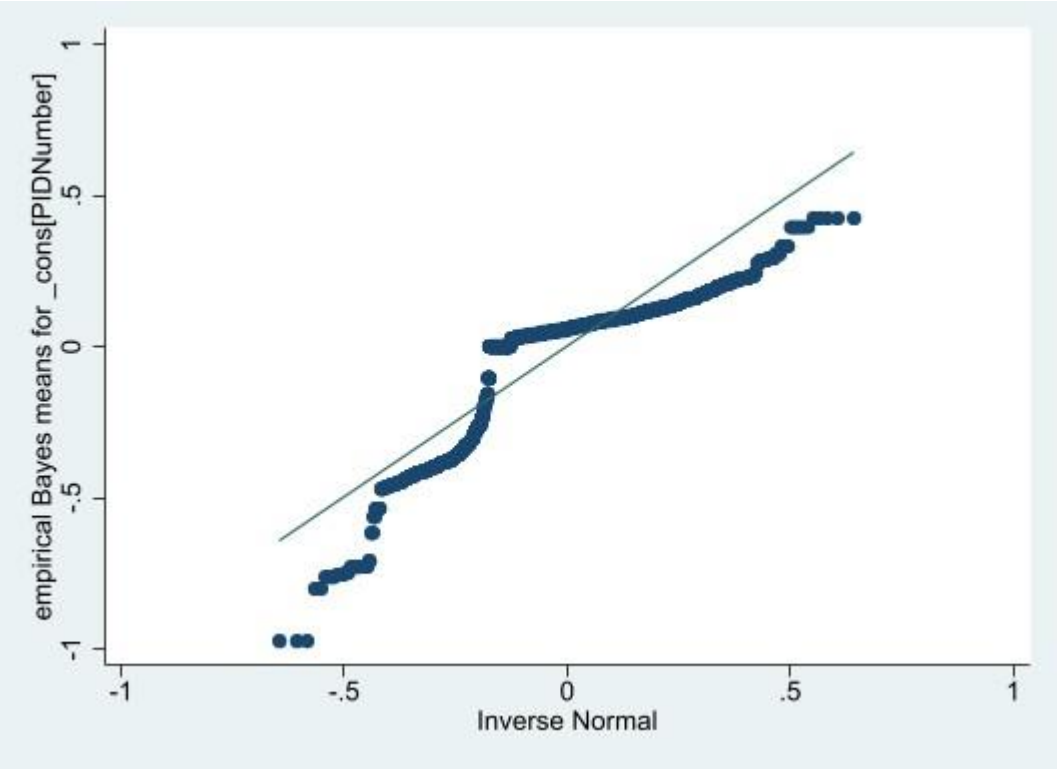
yes	2005	86.16
no	322	13.84

Supplement 2: Box-Tidwell test of linearity

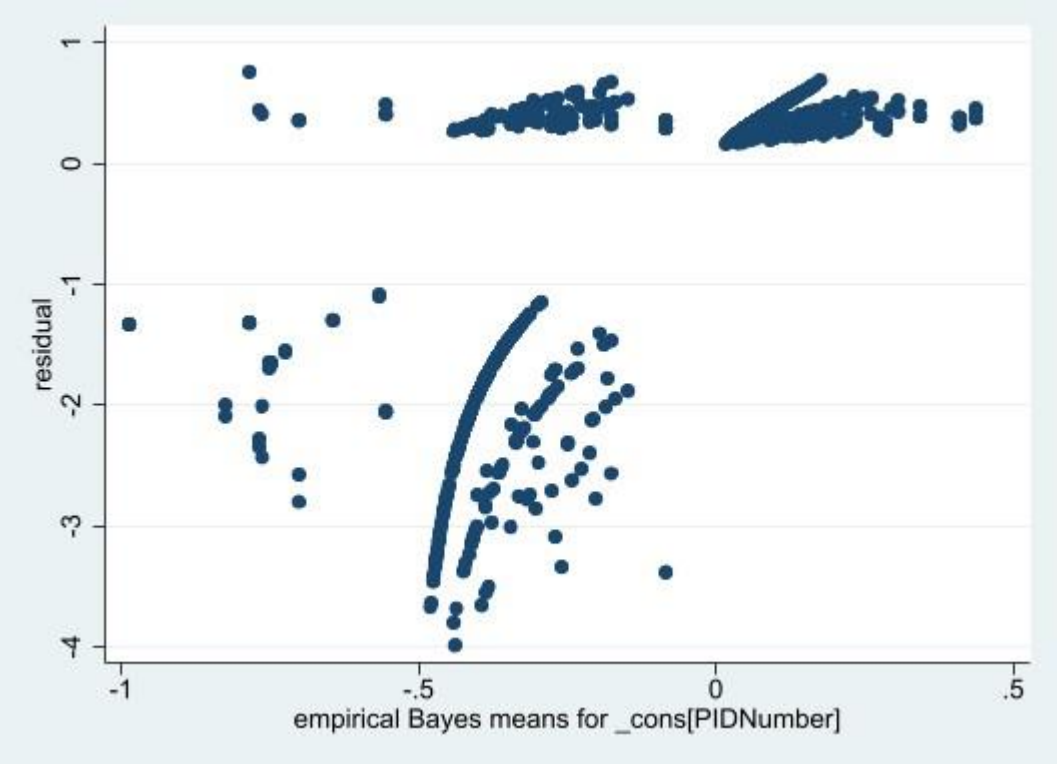
variable	p
age	0.553
weight	0.394

Supplement 3: VIF's

Variable	VIF	√VIF	Tolerance	R^2
Gravidity	2.04	1.43	0.4914	0.5086
Marital status	1.39	1.18	0.7202	0.2798
Location	1.07	1.04	0.9334	0.0666
Education	1.1	1.05	0.911	0.089
Income	1.21	1.1	0.8252	0.1748
HIV	1.02	1.01	0.981	0.019
Age	1.94	1.39	0.5156	0.4844
Weight	1.07	1.04	0.9313	0.0687
COVID Vaccine	1.03	1.02	0.9646	0.0354
Previous miscarriage	1.06	1.03	0.946	0.054
Pregnant	1.08	1.04	0.9227	0.0773
Site	1.13	1.06	0.8863	0.1137
Mean VIF	1.26			



Supplement Figure 1: Q-Q plots for random effect village



Supplement Figure 2: random effect PID and residual error

Supplement 4: BLUP for random effect village

	uhat
uhat	1
Location	0.0069
Education	-0.0291
Income	0.0012
HIV	0.005
Age	-0.0212
Weight	-0.0083
Gravidity	-0.0274
Site	-0.019
Married	-0.018
Covid vaccine	0.0144
Previous miscarriage	0.022
Pregnant	0.0184

Table 10: confounding effect of age

Covariates Included	**HR (Exposure)**	**% Change**
gravidity	0.726	—
gravidity+age	0.821	-13.09%
marital status	0.736	
marital status + age	0.823	-12%
income source	0.767	
income source + age	0.837	-9%