

In-hospital malaria mortality and time to death in Mozambique: a national clinical audit and survival analysis

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Abstract

Background:

Malaria remains a leading cause of morbidity and mortality in Mozambique, yet detailed evidence on in-hospital deaths and their determinants is limited. We conducted a national clinical audit to quantify malaria mortality, describe characteristics of deaths, and identify factors associated with time to death.

Methods:

We performed a retrospective clinical audit across 80 health facilities in all 11 provinces of Mozambique, reviewing routine data from January 2020 to December 2022. Malaria cases and deaths were identified from inpatient and emergency registers, and detailed clinical information was extracted from patient records. Survival analysis was conducted using Kaplan-Meier methods and multivariable accelerated failure time (AFT) models with shared frailty at the facility level. Cox proportional hazards and piecewise exponential models were fitted for comparison.

Results:

Among 735,580 malaria cases, 1,926 in-hospital deaths were identified (case fatality rate 2.61 per 1,000 cases). Of these, 1,591 had available clinical records, and 1,391 were included in survival analyses. More than half of deaths (55.3%) occurred in children, with a median age of 4 years. A total of 57.4% of deaths occurred within 48 hours of admission. Severe clinical features, including anemia (52.6%) and prostration (54.0%), were common. Comparison with routine surveillance data indicated approximately 28% underreporting of malaria deaths. In multivariable analysis, Human Immunodeficiency Virus (HIV) infection (time ratio 0.35, 95% CI 0.33–0.37), anemia (0.79, 0.75–0.83), severe condition at admission (0.78, 0.71–0.86), and traditional treatment use (0.67, 0.58–0.77) were associated with shorter time to death, while prior malaria treatment was associated with longer survival (1.44, 1.37–1.52). Regional and facility-level differences were observed.

Conclusions:

Malaria remains a major cause of in-hospital mortality in Mozambique, particularly among children, with most deaths occurring shortly after admission. Gaps in early care-seeking, clinical management, and surveillance systems contribute to preventable mortality. Strengthening early diagnosis, improving quality of care, and enhancing routine data systems are critical to reduce malaria deaths.

Background

Malaria remains a leading cause of morbidity and mortality globally, with the greatest burden concentrated in sub-Saharan Africa. According to the World Health Organization (WHO), an estimated 282 million malaria cases and 610,000 deaths occurred worldwide in 2024, approximately 94% of cases and 95% of deaths occurred in Africa (1). Children under five years of age account for nearly 80% of malaria-related deaths, highlighting their disproportionate vulnerability (1, 2).

Mozambique is among the countries most affected by malaria and is consistently ranked among the highest burden countries globally (1, 3). Malaria accounts for a substantial proportion of outpatient visits, hospital admissions, and in-hospital deaths in the country (4, 5). Nationally it is estimated that malaria contributes to over 40% of outpatient consultations and approximately 30% of hospital admissions, with particularly higher malaria burden in northern and central regions (4, 6). Despite ongoing control efforts, malaria remains a major public health challenge, with persistent transmission and recurrent seasonal peaks associated with rainfall patterns (7, 8).

In response, the Mozambican Ministry of Health (MOH) has implemented a range of interventions aimed to reduce malaria-related morbidity and mortality, including universal testing of suspected cases, prompt treatment with artemisinin-based combination therapies, and the use of injectable artesunate for severe malaria (9, 10). National strategic plans have set ambitious targets, including a 50% reduction in in-hospital malaria mortality, from 1.4 per 100,000 population in 2021 to 0.77 per 100,000 by 2026 (9, 11). While these interventions have contributed to reductions in mortality over time, the overall number of malaria cases has remained high, and important gaps persist in the quality of care and health system performance (4, 5, 9, 12).

Clinical audits have been increasingly recognized as a critical tool to measure the quality of health care and provide evidence to improve quality of care, particularly in high-burden settings. By systematically reviewing cases and deaths, audits can identify gaps in diagnosis, treatment, and health system processes, and provide actionable evidence to inform programmatic improvements (13, 14). Evidence from other high-burden settings, including studies conducted in countries such as Uganda, has shown that mortality audits can reveal underreporting of deaths, inadequate diagnostic practices, and delays in treatment, all of which contribute to preventable mortality (14, 15).

In Mozambique, there has been limited nationally representative evidence examining the characteristics and determinants of malaria-related deaths in health facilities. Routine surveillance systems may underestimate mortality, and detailed clinical data are often incomplete or not systematically analyzed. Furthermore, few studies have applied survival analysis approaches to better understand the timing of death and factors associated with rapid progression following hospital admission (5, 16).

To address these gaps, we conducted a national clinical audit of malaria cases and in-hospital deaths across 80 health facilities in all 11 provinces in Mozambique. The objectives of this study were to quantify the burden of malaria-related mortality, describe the socio-demographic and clinical characteristics of deaths, assess survival patterns following admission, and identify factors associated with time to death. By providing a comprehensive analysis of malaria mortality in routine care settings,

this study generated evidence to inform improvements in case management and strengthen health system responses to reduce preventable deaths.

Methods

Study design and setting

We conducted a national retrospective cross-sectional clinical audit of malaria cases and in-hospital deaths in Mozambique. The study was implemented between the second half of 2023 and the first quarter of 2024 and reviewed health facility routine data collected from January 1, 2020 to December 31, 2022. The audit covered all 11 provinces of Mozambique and included a stratified sample of 80 health facilities, comprising central, provincial, general, district, and rural hospitals, as well as selected health centers with inpatient services.

Sampling and data sources

Health facilities were selected using a stratified cluster sampling design, with stratification by province and health facility type. All hospitals (central, provincial, general, district, and rural) were included, and health centers with inpatient services were randomly selected within each province. Within selected health facilities, data were collected from inpatient wards (pediatrics, medicine, obstetrics/gynecology) and emergency departments.

Data were extracted from multiple sources, including:

- Inpatient admission registers
- Emergency department registers
- Clinical records (patient files)
- Laboratory registers

Malaria cases and deaths were identified from health facility registrations and compiled into a dedicated database ("*CoMalária: contagem de casos*"). For all identified deaths, detailed clinical information was collected from patient records using a standardized data abstraction tool ("*CoMalária: Questionário de Óbitos de Malária*").

Study population

The study population consisted of all patients admitted to the selected health facilities with a diagnosis of malaria during the study period. For the detailed analysis of mortality, we included all in-hospital deaths attributed to malaria for which clinical records could be retrieved. After removal of duplicate records, 1,591 malaria-related deaths with available clinical data were included in the statistical analysis.

Variable descriptions

Outcome

the primary outcome was time to death, defined as the number of days from hospital admission to death. For patients who died on the day of admission, the time to death was set to 0.5 days to allow inclusion in survival models. This correction of 0.5 to event times of zero is a common technique used in survival data analysis to avoid computational issues, particularly in modelling or when applying logarithmic transformations.

Explanatory variables were selected based on clinical relevance and data availability and included:

- *Demographic variables*: age, sex
- *Clinical characteristics*: anemia, HIV infection, tuberculosis, severity of malaria at admission, presence of complications
- *Treatment variables*: correct malaria treatment according to national guidelines, prior malaria treatment before admission, use of traditional treatment
- *Health system factors*: ward of admission, type of health facility, region, and inter-facility transfer

Statistical analysis

Descriptive statistics were used to summarize health facility characteristics, malaria cases, and deaths. Categorical variables were presented as frequencies and percentages, and continuous variables as means with standard deviations or medians with interquartile ranges, as appropriate. Time-to-event analysis was conducted to assess factors associated with time to death. Kaplan-Meier methods were used to estimate survival probabilities overall and stratified by key variables, including sex, region, ward type, and selected clinical characteristics.

To account for the hierarchical structure of the data (patients nested within health facilities and provinces) and potential selection bias due to missing clinical records, we fitted AFT models with shared frailty at the facility level. Several parametric distributions (exponential, Weibull, log-normal, and log-logistic) were evaluated, and the final model was selected based on Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC). For comparison purposes, Cox proportional hazards (Cox PH) and piecewise exponential (PWE) models with shared frailty were also fitted. Interaction terms were included to assess whether the effect of selected variables (e.g. traditional treatment and correct treatment) varied by region. Results from AFT models are presented as time ratios ($\exp(\beta)$), and results from Cox and PWE models as hazard ratios (HRs), each with 95% confidence intervals (CIs). All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant.

Approximately 13% of cases had missing information on key variables. Given that this proportion was below 20%, complete-case analysis was performed without imputation.

All analyses were conducted using R version 4.3.3 (R Development Core Team, 2024) and Stata version 17.0 (StataCorp, 2021).

Ethical considerations

The study was approved by the Institutional Bioethics Committee of the Faculty of Medicine, Eduardo Mondlane University and Maputo Central Hospital (reference number CIBS FM&HCM/055/2022). Administrative authorization was obtained from the Ministry of Health. As this study used retrospective routinely collected data, informed consent was waived. All data were anonymized prior to analysis.

Results

Study population and health facility characteristics

A total of 80 health facilities across all 11 provinces of Mozambique were included, comprising central (5.0%), provincial (8.8%), general (7.5%), district (22.5%), rural hospitals (21.2%), and health centers with inpatient services (35.0%). Data were extracted from pediatric, medical, obstetric/gynecological wards and emergency departments. Across all health facilities, 2,282,525 admissions were reviewed, including 735,580 malaria cases between January 2020 and December 2022. A total of 1,926 malaria-related in-hospital deaths were identified.

Burden and trends of malaria mortality

The overall in-hospital malaria case fatality rate was 2.61 per 1,000 cases, with variation over time (Table 1). Mortality declined between 2020 and 2021, followed by an increase in 2022, coinciding with rising malaria case numbers in Mozambique.

Table 1
Malaria cases and in-hospital mortality, Mozambique (2020–2022)

Year	Malaria cases (n)	Deaths (n)	Case fatality rate (per 1,000)
2020	188,088	569	3.02
2021	237,408	535	2.25
2022	310,084	822	2.65
Total	735,580	1,926	2.61

Distribution of cases and deaths by clinical department

Malaria cases were predominantly managed in emergency/triage services (85.5%), while mortality was concentrated in inpatient wards, particularly pediatrics (55.3%) (Table 2).

Table 2
Distribution of malaria cases and deaths by ward

Ward	Cases (n)	% of cases	Deaths (n)	% of deaths
Paediatrics	74,143	10.1	1,101	57.2
Medicine	21,611	2.9	532	27.6
Obstetrics/Gynaecology	11,281	1.5	28	1.5
Emergency/Triage	628,545	85.5	265	13.8
Total	735,580	100	1,926	100

Seasonal patterns and underreported malaria mortality

Malaria admissions demonstrated a clear seasonal pattern, peaking in March (11.9%) and reaching a nadir in September (4.9%), consistent with known transmission dynamics in Mozambique. Despite this predictable temporal distribution, comparison with routine surveillance data (SIS-MA) revealed that the audit identified approximately 28% more malaria-related deaths than officially reported, indicating substantial underreporting within the national health information system.

Characteristics of malaria deaths

Of the 1,926 malaria-related deaths identified, 1,591 (82.6%) had complete clinical records available for analysis, and 1,391 cases were included in survival analyses. The majority of deaths occurred among males (58.3%), and the overall median age was 4 years (mean 15.4 years), with more than half of deaths (55.3%) occurring among pediatric patients.

A substantial proportion of deaths occurred shortly after admission, with 57.4% of patients dying within 48 hours and a median length of hospital stay of one day, indicating rapid clinical deterioration or late presentation to care. Clinical features consistent with severe malaria were highly prevalent. The most frequently reported signs and symptoms were mucosal pallor (54.6%), prostration (54.0%), anemia (52.6%), vomiting (44.3%), respiratory distress (40.9%), and convulsions (31.3%), while coma (13.4%) and shock (3.7%) were less documented.

Diagnostic practices at admission showed that malaria testing was performed in 86.4% of cases and hemoglobin or hematocrit testing in 73.0%, whereas glucose testing was conducted in only 20.1% of patients, indicating limited assessment of key complications despite high testing coverage for malaria itself. The most common comorbid conditions among patients who died were anemia (43.9%), HIV infection (13.3%), and pneumonia (10.3%), with HIV prevalence showing regional variation and higher proportions observed in southern Mozambique (23.1%).

In terms of treatment, most patients received injectable artesunate (93.8%); however, only 46.7% received treatment consistent with national guidelines, reflecting gaps in quality of care. Additionally,

19.7% of patients had received prior malaria treatment before admission, and 8.2% had used traditional treatments, which may have contributed to delays in accessing health facility care.

Marked geographic variation was observed across regions as shown in Table 3.

Table 3 Selected indicators by region			
Indicator	South	Centre	North
Death within 48h (%)	76.4	49.3	61.1
Correct treatment (%)	59.0	50.5	38.5
Glucose testing (%)	28.4	32.6	3.0
HIV prevalence (%)	23.1	15.1	8.1
Traditional treatment (%)	19.0	6.0	7.4

Survival data analysis and factors associated with time to death

As shown in Fig. 1, the distribution of time to death was highly skewed, with a marked decline in survival probability occurring within the first days following admission. The Kaplan-Meier survival curve for the overall sample demonstrated a steep early drop, indicating that a large proportion of deaths occurred shortly after hospital admission.

Stratified Kaplan-Meier curves in Fig. 1 showed differences in survival probability by sex, region, and type of health facility. Survival curves for male patients were consistently lower than those for female patients over time. When stratified by region, survival probability was highest in the central region, followed by the northern region, with the lowest survival observed in the southern region. Differences in survival were also observed by type of health facility, with provincial hospitals showing higher survival probabilities over time compared to other facility types.

As shown in Fig. 2, Kaplan-Meier survival curves stratified by clinical and patient-related characteristics demonstrated variation in survival probability across subgroups. Patients without HIV infection had higher survival probabilities compared to those with HIV. Similarly, patients without tuberculosis had higher survival probabilities than those with tuberculosis. Patients who did not report prior use of traditional treatment had higher survival probabilities compared to those who had used traditional treatment. Differences were also observed by ward type, with higher survival probabilities in medical and obstetric/gynecological wards compared to pediatric and emergency wards.

Survival data analysis was conducted using AFT, Cox PH, and PWE models. The AFT model with log-logistic baseline hazard and shared gamma frailty was selected based on model fit criteria (Table 4). No significant associations were observed for sex, age, transfer status, ward type, or correct malaria

treatment. Significant associations were identified for anemia, HIV infection, prior malaria treatment, severity at admission, traditional treatment use, region, and rural hospital setting. Results from Cox PH and PWE models were consistent with those of the AFT model (Supplementary Table S1).

Table 4
Multivariable survival analysis of factors associated with time to death (AFT model)

Variable	β (SE)	$\exp(\beta)$ (Time Ratio)	95% CI for $\exp(\beta)$	p-value
Sex (male)	0.007 (0.021)	1.01	0.97–1.05	0.74
Age	−0.00008 (0.001)	1.00	0.998–1.002	0.92
Transfer	−0.028 (0.025)	0.97	0.92–1.02	0.26
Anaemia	−0.236 (0.025)	0.79	0.75–0.83	< 0.001
HIV infection	−1.041 (0.025)	0.35	0.33–0.37	< 0.001
Prior malaria treatment	0.362 (0.027)	1.44	1.37–1.52	< 0.001
Correct treatment	0.051 (0.035)	1.05	0.98–1.12	0.15
Severe condition at admission	−0.251 (0.053)	0.78	0.71–0.86	< 0.001
Traditional treatment	−0.400 (0.074)	0.67	0.58–0.77	< 0.001
Region (North vs Centre)	0.137 (0.053)	1.15	1.04–1.28	0.01
Region (South vs Centre)	−0.277 (0.097)	0.76	0.63–0.92	0.004
Hospital rural (vs CS inpatient)	−0.122 (0.053)	0.89	0.80–0.99	0.02

Estimates are from the accelerated failure time (AFT) model with log-logistic baseline and shared gamma frailty; $\exp(\beta)$ represents the time ratio. Values < 1 indicate shorter time to death, and values > 1 indicate longer time to death. Reference categories are sex (female), region (center), and facility (health center with inpatient services)

Discussion

In this national clinical audit of malaria cases and in-hospital deaths across 80 health facilities in Mozambique, we identified a substantial burden of malaria mortality, with nearly 2,000 deaths recorded over a three-year period. Our findings highlight three critical patterns: a high concentration of deaths among children, a large proportion of deaths occurring shortly after admission, and significant gaps in both surveillance systems and quality of care.

First, the disproportionate burden of mortality among pediatric patients is consistent with the broader epidemiology of malaria in high-transmission settings (17, 18). More than half of all deaths occurred in children, and the median age was 4 years, underscoring the continued vulnerability of young children to severe malaria. This pattern reflects both biological susceptibility and potential delays in recognition and treatment at the community and primary care levels (17, 19, 20). The high prevalence of severe clinical features at admission including anemia, prostration, and respiratory distress, further suggests that many patients present to health facilities at an advanced stage of disease (18, 20, 21).

Second, the timing of death provides important insights into health system performance. Over half of all deaths occurred within 48 hours of admission, and the median length of hospital stay was only one day (22–24). These findings indicate that a large proportion of patients either arrive at facilities too late to benefit from treatment or experience rapid clinical deterioration shortly after admission. The steep early decline in Kaplan-Meier survival curves reinforce this pattern and highlights the critical importance of early diagnosis, timely referral, and rapid initiation of appropriate treatment (23–25). While most patients received injectable artesunate, adherence to national treatment guidelines was suboptimal (24, 26), and key diagnostic tests for complications such as glucose, were infrequently performed (22, 24). Together, these findings point to gaps not only in access to care but also in the quality and completeness of clinical management (25, 27).

Third, our results reveal important weaknesses in routine surveillance systems. The audit identified approximately 28% more malaria-related deaths than reported in the national health information system, suggesting substantial underreporting (24, 28). This discrepancy is consistent with findings from other settings, where mortality audits have demonstrated gaps in data completeness and reporting accuracy (29–31). Underestimation of malaria mortality has important implications for program planning, resource allocation, and evaluation of national targets (27, 28), and underscores the need to strengthen health information systems and reporting mechanisms (28, 29).

The survival analysis provides additional insights into factors associated with mortality. HIV infection and anemia were strongly associated with shorter time to death, reflecting the role of comorbidities in worsening clinical outcomes (32–34). The association between traditional treatment use and reduced survival time suggests that delays in seeking formal care may contribute to advanced disease at admission (35, 36). Conversely, prior malaria treatment before admission was associated with longer survival time, which may reflect earlier engagement with the health system (36, 37). Geographic differences in survival, with poorer outcomes observed in the northern and southern regions compared to the center, as well as higher mortality in rural hospitals, point to persistent inequities in access to timely and quality care across the country (38, 39).

This body of evidence highlights the multifactorial nature of malaria mortality in Mozambique, encompassing patient-level factors, health-seeking behaviors, and systemic health system challenges. Addressing these gaps will require a combination of interventions, including strengthening early case detection and referral pathways, improving adherence to clinical guidelines, expanding access to

essential diagnostics for severe malaria complications, and optimizing the completeness and accuracy of routine surveillance data.

This study has several strengths. It represents one of the first nationally representative clinical audits of malaria mortality in Mozambique, covering all provinces and multiple levels of the health system. The use of detailed clinical data from patient records allowed a comprehensive characterization of deaths, and the application of survival analysis provided insights into the timing and determinants of mortality that are not captured by routine surveillance data.

This study has several limitations. First, the analysis was restricted to cases for which clinical records could be located, which may introduce selection bias if these cases differ systematically from those without available records. Second, data were retrospectively collected from routine clinical records, which may be subject to incomplete documentation and variable data quality across facilities. Missing data for some variables further limited the inclusion of all cases in the survival analysis, although the proportion of missing data was relatively low.

Third, misclassification of cause of death is possible, as diagnoses were based on routine clinical records and may not have been systematically confirmed, particularly in the presence of co-morbid conditions. Fourth, the analysis was limited to in-hospital deaths and does not capture malaria mortality occurring in the community, potentially underestimating the overall burden of mortality.

Fifth, survival analysis was restricted to patients who died, without inclusion of censored observations, limiting interpretation to differences in time to death rather than overall mortality risk. Finally, as an observational audit based on routinely collected data, causal relationships between identified factors and mortality cannot be established, and residual confounding from unmeasured factors such as delays in care-seeking, socioeconomic status, and access to healthcare may have influenced the observed associations.

Conclusion

Malaria remains a major cause of in-hospital mortality in Mozambique, particularly among children, with a substantial proportion of deaths occurring within the first 48 hours of admission. The high frequency of early mortality, combined with evidence of underreporting in routine surveillance systems, underscores important gaps in timely access to care, quality of clinical management, and health information systems. Addressing these challenges will require strengthening early diagnosis and referral pathways, improving adherence to clinical guidelines for severe malaria, and improving the completeness and accuracy of routine data. Targeted efforts in these areas are critical to reducing preventable deaths and accelerating progress towards national and global malaria control targets.

Abbreviations

WHO

World Health Organization
MOH
Ministry of Health
SIS-MA
Health Information System for Monitoring and Evaluation
HIV
Human Immunodeficiency Virus
AFT
multivariable accelerated failure time
AIC
Akaike Information Criterion
BIC
Bayesian Information Criterion
Cox PH
Cox proportional hazards
PWE
piecewise exponential models

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Bioethics Committee of the Faculty of Medicine, Eduardo Mondlane University and Maputo Central Hospital (reference number CIBS FM&HCM/055/2022). Administrative authorization was obtained from the Ministry of Health. As this study used retrospective routinely collected data, informed consent was waived. All data were anonymized prior to analysis.

Consent for publication : Not Applicable

Availability of data and materials: Data are available from the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests

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Authors' contributions

JS, CG and BC designed the study, wrote the protocol, prepared data collection tools

JS, CG, BC, AP, AC, AS, MB and MD participated in the development of the study protocol, the supervision of the field phase, the analysis and interpretation of the data, and critically reviewed the manuscript.

ZS: performed data cleaning and data management

AM: performed statistical analyses.

JS and CG: Coordinated the implementation and validation of the results of the study.

BC and QF: participated in interpretation of the data, and critically reviewed the manuscript

All authors: reviewed and approved the manuscript.

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Figures

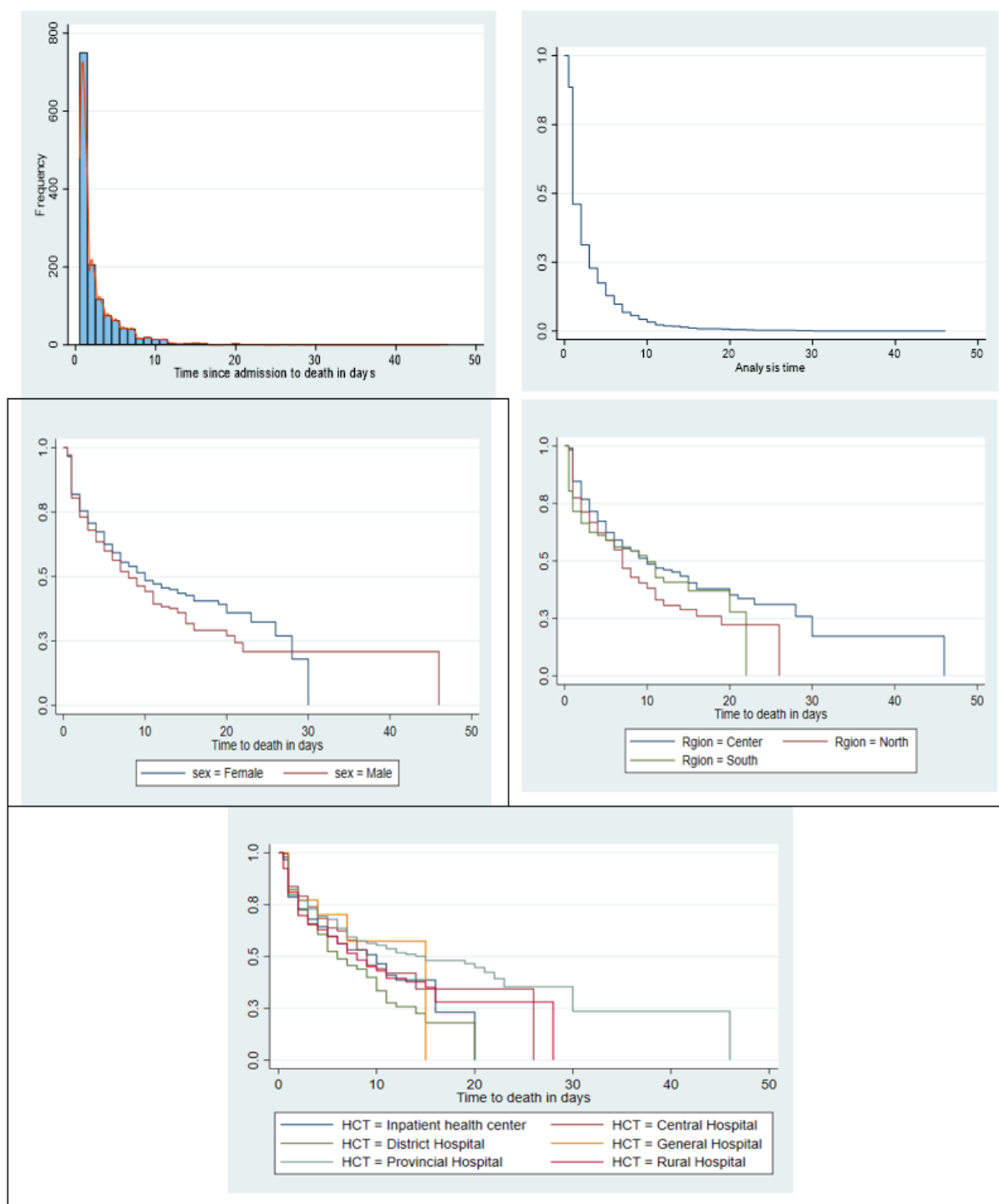


Figure 1

Distribution of time to death (upper left). Kaplan–Meier survival function: overall (top right), by sex (center left panel), by region (center right panel), and by type of health facility (bottom).

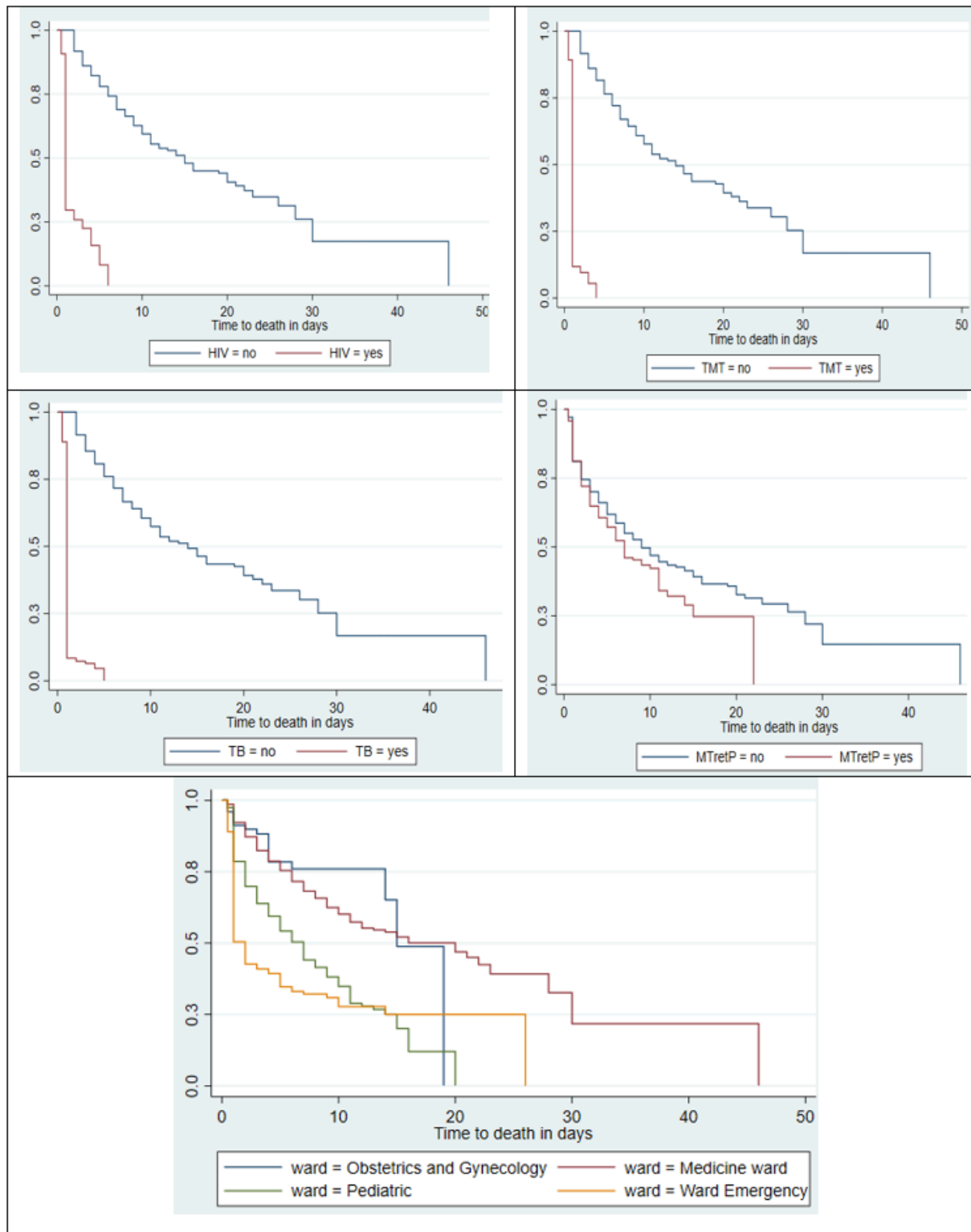


Figure 2

Kaplan-Meier estimates of survival probabilities by HIV status, traditional treatment, tuberculosis, prior antimalarial treatment, and ward type.

Supplementary Files

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- [SupplementaryTableS1JS220426.docx](#)