Modelling In-hospital Survival and Associated Factors Among Hospitalized Patients with COVID-19, Zambia, March 2020 to December 2022: A Retrospective Cohort Study

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COVID-19 mortality hazard rate varied over the hospitalization duration and was associated being male, older age, comorbidities, severe disease and vaccination

BACKGROUND

- Zambia has recorded ~349,000 COVID-19 cases and ~4,000 COVID-19 deaths.
- Likely underestimated counts due to limited testing capacity, asymptomatic infections and undetected cases [1, 2].
- Estimated that as much as 30% of COVID-19 cases get hospitalized for their acute SARS-CoV-2 infection [3].
- Among hospitalized COVID-19 patients, 11.5% are estimated to experience unfavorable outcomes such as death [4].
- In-hospital survival time of COVID-19 patients is reported to be commonly associated with older age, male gender, comorbidities and compromised immune function.
- Some studies assume proportional hazard rate of mortality throughout hospitalization while others have determined that mortality risk varies over the duration of hospitalization [5].
- We estimated the median survival time for hospitalized COVID-19 patients, identified factors associated with in-hospital mortality, and assessed whether mortality risk changed over hospitalization time.
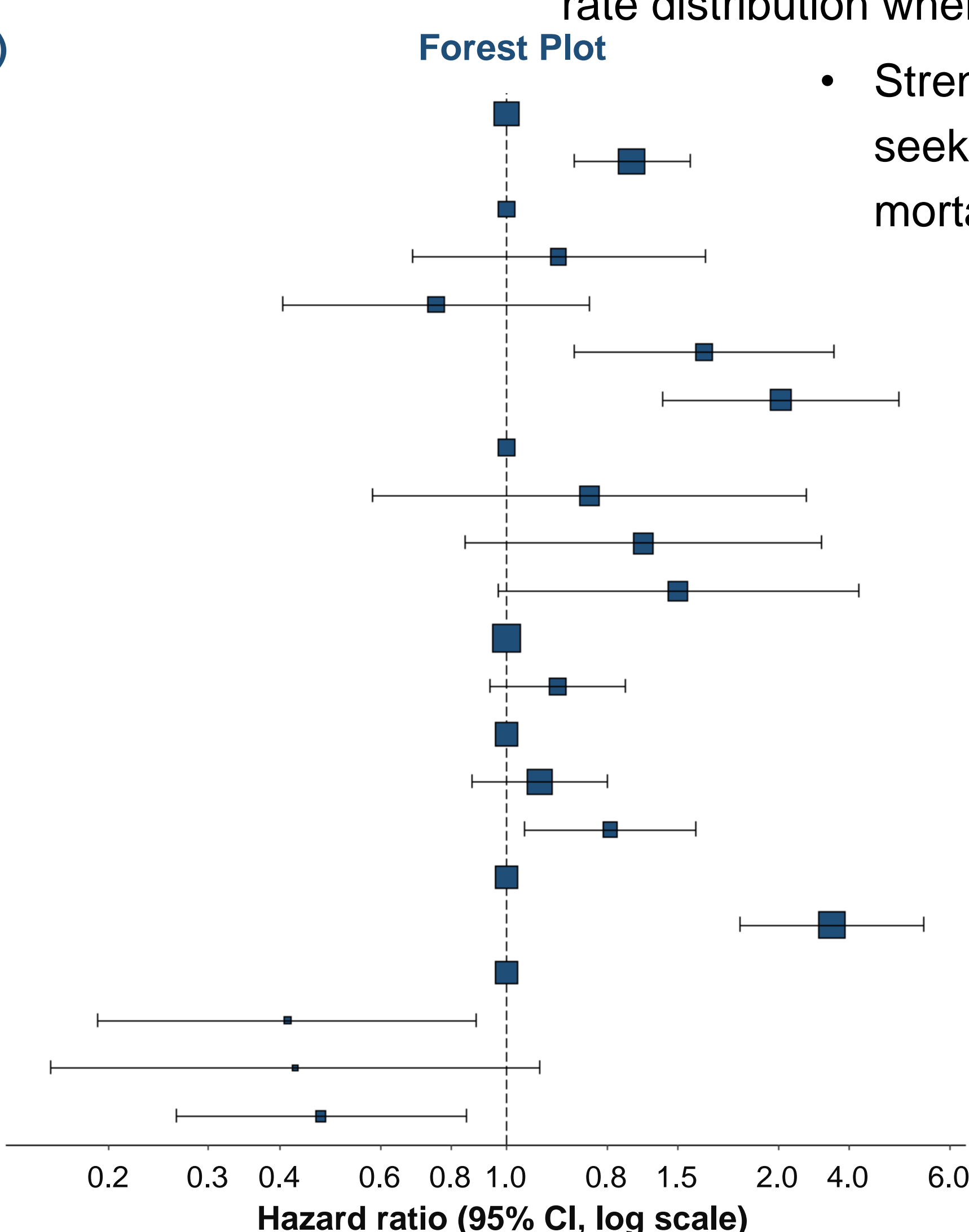
METHODS

- Analyzed routinely collected clinical information of patients admitted to COVID-19 treatment centers in five Zambian cities (Lusaka, Ndola, Living stone, Kabwe, and Kitwe) between Mar-2020 and Dec-2022.
- Data included demographic information (sex and age), medical history (comorbidity), acute COVID-19 course during hospitalization and vaccination status.
- Severe COVID-19 was defined as having oxygen saturation <90%, respiratory rate >30 breaths/minute, or oxygen therapy requirement.
- Survival time was time in days from date of admission to death or censor (discharged patients).
- Conducted descriptive and survival analysis using Kaplan-Meier estimator, Cox proportional hazard and parametric survival models in R.
- Statistical significance was considered at p<0.05.

RESULTS

- In total, 3,921 patients were followed up during their hospitalization. A majority (n = 2,140; 54.7%) were male, and the median age was 50 (interquartile range [IQR]: 35-65) years.
- Patients with comorbidities were 2,366 (60.3%). Commonly reported health conditions included hypertension 1501 (63.4%), diabetes 648 (27.4%), HIV 623 (26.3%), and tuberculosis 200 (8.5%).
- Vaccinated patients with at least ≥1 dose were 243 (13.4%). These were 57 (3.1%), 40 (2.2%) and 146 (8.0%) with full, partial and unknown dates for vaccination series, respectively (Figure 1).
- Severe COVID-19 diseases was present in 2,364 (60.6%) patients and nearly a quarter (n = 869, 22.6%) died. A majority being male (65.2%).

RESULTS

- Overall, the median survival time was 25 (IQR: 21-30) days (Figure 2). Patients with severe COVID-19 had a median survival time was 17 (IQR: 16-19) days
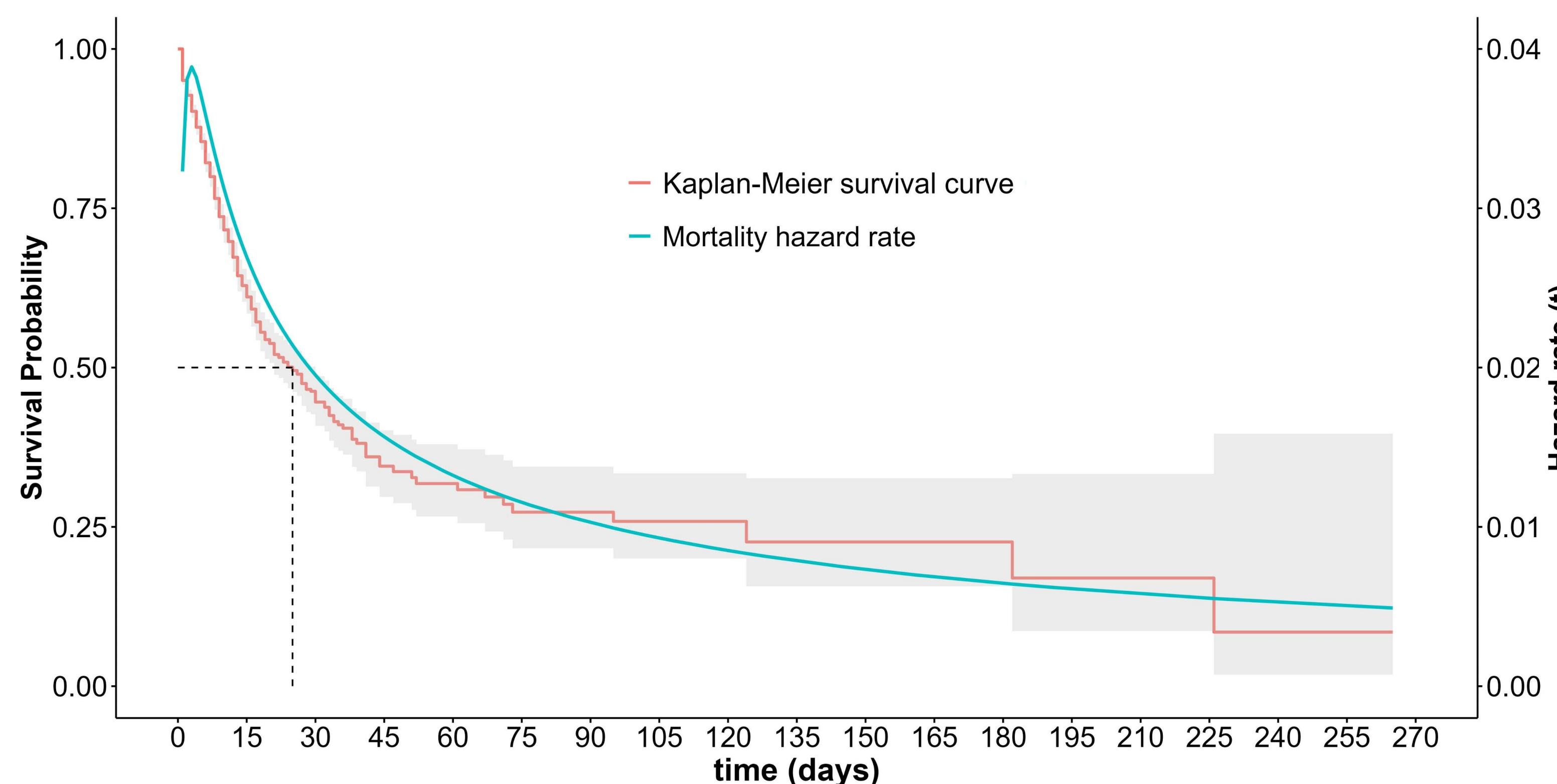
Figure 2: Kaplan-Meier curve and variable hazard for in-hospital mortality in Zambia, Mar-20 to Dec-22

- The total person time at risk was 28,797 days and the incidence rate of mortality was 3 per 100 person-days. The rate was significantly higher (p<0.001) among severe COVID-19 patients (4 per 100 person-days) than among mild cases (1 per 100 person-days).
- In-hospital mortality was significantly associated with being male (adjusted hazard ratio [aHR]: 1.66), aged 50-59 years (aHR: 2.22) and 60+ years (aHR: 3.02), having ≥3 comorbidities (aHR 1.53) and severe COVID-19 (aHR: 3.73) – Figure 1.
- Patients with full vaccination series had reduced mortality risk (aHR: 0.41).
- In-hospital mortality distribution was characterized by an increasing (up to 5 days) and then decreasing hazard rate (right-skewed tapering) over the remainder of hospitalization duration (Figure 2).

DICUSSION

- The factors associated with in-hospital mortality risk in Zambia aligns with existing literature, these being older age, being male, comorbidities and COVID-19 severity [5,6].
- Vaccination was associated with a reduced risk of in-hospital mortality as is reported by other studies.
- The increasing and then decreasing mortality hazard rate would suggest that patients may have presented late to hospital (relatively high proportion of severe COVID-19 patients).
- The initial hospitalization days with increasing mortality hazard rate may correspond to the time when complications such as respiratory distress, cytokine storms, or organ failure are more likely to occur, leading to higher mortality rates.
- The study underscore the critical nature of severe COVID-19 cases and the timing of care for effective management strategies (right-skewed mortality hazard rate distribution where the initial days are critical).
- Strengthening health systems and educating the public about seeking care for COVID-19 early may likely reduce in-hospital mortality in Zambia.

ADDITIONAL INFORMATION

References:
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Variables	Levels	n (%)	aHR* (95% CI, p-value)
Sex	Female	1,773 (45.3)	-
	Male	2,140 (54.7)	1.66 (1.31-2.10, p<**0.001**)
Age group (years)	≤29	651 (16.7)	-
	30-39	585 (15.0)	1.23 (0.68-2.23, p=0.487)
	40-49	661 (17.0)	0.75 (0.401.40, p=0.369)
	50-59	650 (16.7)	2.22 (1.31-3.76, p=**0.003**)
	60+	1,345 (34.5)	3.03 (1.88-4.90, p<**0.001**)
SARS-CoV-2 Variant	Alpha	736 (18.8)	-
	Beta	1,025 (26.2)	1.40 (0.58-3.35, p=0.454)
	Delta	1,196 (30.5)	1.74 (0.85-3.35, p=0.132)
	Omicron	961 (24.5)	2.00 (0.97-4.14, p=0.062)
HIV Infection	Negative	2,659 (81.0)	-
	Positive	623 (19.0)	1.23 (0.93-1.62, p=0.141)
No. of self-reported comorbidities	0	1,555 (39.7)	-
	1-2	1,951 (49.8)	1.14 (0.87-1.50, p=0.337)
	≥3	415 (10.6)	1.52 (1.08-2.15, p=**0.017**)
COVID-19 disease status	Mild	1,535 (39.4)	-
	Severe	2,364 (60.6)	3.37 (2.58-5.39, p<**0.001**)
Vaccination status	Unvaccinated	1,576 (86.6)	-
	Full series	57 (3.1)	0.41 (0.19-0.89, p=**0.023**)
	Partial series	40 (2.2)	0.43 (0.16-1.14, p=0.090)
	Unknown vaccination dates	146 (8.0)	0.47 (0.26-0.85, p=**0.012**)

Forest Plot

Hazard ratio (95% CI, log scale)

Figure 1: Adjusted hazard ratio (aHR*) and forest plot for factors associated with in-hospital mortality in Zambia, Mar-20 to Dec-22