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ORIGINAL RESEARCH

# Incidence of Acute Myocardial Infarction in Northern Tanzania: A Modeling Approach Within a Prospective Observational Study

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**BACKGROUND:** Rigorous incidence data for acute myocardial infarction (AMI) in sub-Saharan Africa are lacking. Consequently, modeling studies based on limited data have suggested that the burden of AMI and AMI-associated mortality in sub-Saharan Africa is lower than in other world regions.

**METHODS AND RESULTS:** We estimated the incidence of AMI in northern Tanzania in 2019 by integrating data from a prospective surveillance study (681 participants) and a community survey of healthcare-seeking behavior (718 participants). In the surveillance study, adults presenting to an emergency department with chest pain or shortness of breath were screened for AMI with ECG and troponin testing. AMI was defined by the Fourth Universal Definition of AMI criteria. Mortality was assessed 30 days following enrollment via in-person or telephone interviews. In the cluster-based community survey, adults in northern Tanzania were asked where they would present for chest pain or shortness of breath. Multipliers were applied to account for AMI cases that would have been missed by our surveillance methods. The estimated annual incidence of AMI was 172 (207 among men and 139 among women) cases per 100 000 people. The age-standardized annual incidence was 211 (263 among men and 170 among women) per 100 000 people. The estimated annual incidence of AMI-associated mortality was 87 deaths per 100 000 people, and the age-standardized annual incidence was 102 deaths per 100 000 people.

**CONCLUSIONS:** The incidence of AMI and AMI-associated mortality in northern Tanzania is much higher than previously estimated and similar to that observed in high-income countries.

**Key Words:** incidence ■ mortality ■ myocardial infarction ■ sub-Saharan Africa ■ Tanzania

Although acute myocardial infarction (AMI) is a leading cause of death globally,[1] the burden of AMI in sub-Saharan Africa (SSA) remains poorly understood.[2] In particular, there are no population-based data derived from objective testing describing the incidence of AMI in any country in SSA.[1,3,4] Thus, epidemiologists rely on a small number of hospital-based studies to make inferences about disease burden. The GBD (Global Burden of Disease) study, for example, currently estimates the rate of AMI-associated mortality in SSA to be among the lowest in the world, but these estimates are based on modeling extrapolations of existing data on covariates for AMI and on very little empiric evidence directly studying AMI rates in SSA.[1,3,4] Rigorous population-based AMI incidence and mortality data would provide a more accurate description of the burden of disease in SSA and inform crucial policy decisions in resource-limited health systems.

Obtaining accurate AMI incidence data is challenging, even in high-income countries.[5] In SSA, identification of AMI cases is particularly challenging. Recent qualitative studies in Tanzania and Kenya found that

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## CLINICAL PERSPECTIVE

### What Is New?

- Based on prospective surveillance data, the incidence of acute myocardial infarction in Tanzania is much higher than previously estimated and similar to the incidence in high-income countries.

### What Are the Clinical Implications?

- Interventions are needed to improve myocardial infarction prevention, screening, and care in sub-Saharan Africa.

### Nonstandard Abbreviations and Acronyms

| | |
|---|---|
| **KCMC** | Kilimanjaro Christian Medical Centre |
| **SSA** | sub-Saharan Africa |

lack of diagnostic equipment, low levels of provider awareness, and delayed patient care-seeking all contributed to underrecognition of AMI in hospitals.[6,7] Furthermore, community-based studies from SSA have shown multiple barriers to accurate denominator determination. For example, adults with AMI symptoms often do not seek care in hospitals or they must travel long distances to reach hospitals equipped to diagnose AMI.[8,9]

The purpose of our study was to estimate the incidence of AMI and AMI-associated mortality in northern Tanzania. We conducted a hybrid prospective observational study that coupled hospital-based AMI surveillance with a community-based study of healthcare seeking. This method has been used successfully in many settings to determine the incidence of a wide variety of diseases.[10,11]

## METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

### Study Setting

Our study area consisted of 3 districts in the Kilimanjaro Region of northern Tanzania: Moshi Urban District (population 184 289[12]), Hai District (population 210 531[12]), and Moshi Rural District (population 466 740[12]). Kilimanjaro Region is fairly representative of Tanzania as a whole in terms of urbanization, population density, and unemployment.[12] For study definition purposes, Moshi Urban District (population density 2883 people/km$^2$) was considered urban and Moshi Rural District (population density 356 people/km$^2$) and Hai District (population density 231 people/km$^2$) were considered rural. Hospital-based AMI surveillance was conducted at Kilimanjaro Christian Medical Centre (KCMC), a tertiary referral center in Moshi Urban.

### Case Identification

Cases were identified through a surveillance study in the KCMC emergency department (ED), with detailed methods published elsewhere.[13] Briefly, all adults aged ≥18 years presenting to the ED with chest pain or shortness of breath were enrolled and underwent AMI testing with an ECG and point-of-care troponin-I testing (Abbott iSTAT cardiac troponin I assay, Abbott Point of Care, Princeton, NJ). AMI cases were defined as those meeting criteria for ST-segment–elevation myocardial infarction (STEMI) or non–ST-segment–elevation myocardial infarction (NSTEMI) in accordance with the Fourth Universal Definition of Myocardial Infarction criteria.[14] Specifically, STEMI was defined as pathologic elevation of the ST segment in ≥2 contiguous leads and NSTEMI was defined as a troponin value above the 99th percentile of the manufacturer-defined normal range in the absence of a STEMI. ECGs underwent review retrospectively by 3 independent, blinded physician adjudicators to determine presence of STEMI for study purposes. Enrollment was conducted from 8 AM to 11 PM, 5 days per week, from January 9 through October 12, 2019. For incidence calculations, only patients with AMI residing within the study area were included in the analysis. Thirty days after enrollment, participants with AMI were contacted via telephone to assess vital status. If a patient was unreachable by telephone, a member of the study team visited the patient's home to assess mortality.

### Community Survey

A 2-stage randomized population-based cluster survey was conducted in the study area in 2018, following World Health Organization recommendations for community cluster surveys.[15] The methods of this community survey have been described in detail elsewhere.[8,16] Briefly, 60 subdistricts within the study area were selected randomly in a population-weighted fashion. Within each selected subdistrict, 12 point locations were generated randomly using Quantum Geographic Information System (v2.18.7) and the closest household to the selected point was included in the survey. Adult residents who self-identified as household healthcare decision-makers were asked to report where they would go if they or another adult in their household were to experience

chest pain or shortness of breath. Participants were asked to choose from a picklist of healthcare facilities in the study area as well as self-treatment at home and traditional healer.

## The Multiplier Method

As the AMI cases identified in the surveillance study represented only a fraction of those occurring in the community, a widely used multiplier method was used to estimate the total number of incident cases in the study area.[17–19] We applied multipliers to the number of cases detected to account for the time surveillance was not being done, the number of cases presenting to other sites, and the number of cases not surviving to hospital presentation. Figure 1 summarizes the various multipliers used in this study, as described next.

## Prehospital Mortality Multiplier

The prehospital mortality multiplier accounts for cases who would have presented to hospital but died before hospital arrival. To our knowledge, there are no available data regarding the proportion of AMI cases in SSA who die before hospital presentation. Given this lack of data and our desire to provide a conservative estimate, we used a multiplier derived from US data. In the United States, it estimated that there are ≈72.0 sudden prehospital deaths per 100 000 people annually, of which ≈57.6 are attributable to acute coronary syndromes.[20] In contrast, the annual incidence of hospitalized cases of AMI in the United States was estimated to be 272.6 per 100 000 people in 2014.[21] Thus, the approximate proportion of AMI cases that survived to hospital presentation in the United States in 2014 was 82.6% (272.6/[272.6+57.6]). The inverse of this proportion (1.211) was used as a multiplier to account for prehospital mortality in our incidence estimation. Because patients with AMI in Tanzania typically present to hospitals much later after symptom onset than patients in the United States,[13,22] this multiplier likely underestimates prehospital mortality in Tanzania.

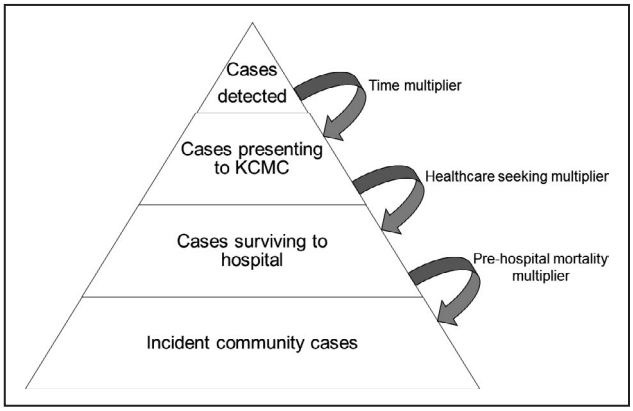


**Figure 1. AMI surveillance pyramid demonstrating multipliers used to account for cases not detected in a hospital-based surveillance study, northern Tanzania.**
AMI indicates acute myocardial infarction; and KCMC, Kilimanjaro Christian Medical Centre.

## Healthcare-Seeking Multiplier

Because there are many other hospitals within the study area and some patients with AMI may choose not to present to any healthcare facility, a multiplier was developed to account for incident community cases that would not present to KCMC. This multiplier was derived from the community survey data, consistent with the methods used in prior incidence estimation studies.[17–19] To develop this multiplier, the proportion of respondents who selected KCMC as their preferred facility for chest pain or shortness of breath was calculated, and the inverse of this proportion was used as a multiplier to account for AMI cases that would not have presented to KCMC.

## Time Multiplier

A time multiplier was developed to account for the fact that AMI surveillance was not performed 24 hours per day or 365 days of the year. Data from a 2018 study in the KCMC ED demonstrated that 82.7% of adults presenting with chest pain or shortness of breath presented between 8 AM and 11 PM.[22] Thus, ≈17.3% of AMI cases were presumably missed during the overnight period on each day of enrollment. Furthermore, enrollment during this study was conducted on a total of 176 days, representing 48.2% of the calendar year 2019. Thus, to account for all AMI cases that would have presented during the entire calendar year, a total time multiplier of 2.509 was used. As there are no available data regarding variation in MI frequency across seasons or across days of the week in Tanzania, the time multiplier was calculated based on the assumption that the frequency of AMI hospital presentation was constant across seasons and days of the week.

## Statistical Analysis

Separate sample size calculations were performed for the community survey and the surveillance study. For the community survey, the sampling frame and sample size were determined according to World Health Organization guidelines for cluster surveys,[15] assuming the proportion of the population who sought health care at KCMC was 10%, with inflation factor of 1.2, design effect of 1.5, and precision of 10%. These parameters generated a sampling frame of 60 clusters and 11 households per cluster, thus necessitating 660 household participants. The sample size calculations for the surveillance study have been previously published.[13] A previous study at KCMC found that 1.8%

of adults presenting with chest pain or shortness of breath to the ED were diagnosed with AMI by the ED physician—although diagnostic testing for AMI was rare.[22] Assuming a prevalence of AMI among adults presenting with chest pain or shortness of breath of 1.8%, then 675 participants would be required to report this proportion with 95% confidence and a 1% margin of error.

All statistical analyses were performed in the R suite (version 3.6.1). The estimated incident number of AMI cases was calculated using the number of AMI cases identified in the surveillance study who resided in the study area, adjusted by the multipliers detailed previously. The estimated non-age-standardized or crude incidence of AMI was calculated by dividing the estimated incident number of cases by the population of the study area according to the most recent Tanzanian national census.[12] So that our incidence estimates could be compared with populations with different age distributions, age-standardized incidence was calculated via direct standardization according to World Health Organization guidelines.[23] CIs were constructed around point estimates based on the Poisson distribution. The formulae used to derive estimated crude incidence, age-standardized incidence, and mortality incidence are summarized in Figure 2.

To assess the robustness of our estimates, we performed sensitivity analyses by varying 2 key parameters in our incidence calculations: the prehospital mortality multiplier and the healthcare-seeking multiplier. To determine the effect of different estimates of prehospital AMI mortality, we calculated the estimated incidence of AMI in Tanzania assuming a prehospital mortality rate twice that of the United States (34.9%) and half that of the United States (8.7%). To determine the effect of different estimates of the healthcare-seeking multiplier, 95% CIs were constructed around the proportion of community survey participants who reported they would present to KCMC for chest pain or shortness of breath, using the binomial distribution. The upper and lower bounds of this CI were used to generate alternate healthcare-seeking multipliers for incidence calculations.

## Mortality Incidence Estimation

The incidence of annual AMI-associated mortality was derived by adding estimated incident deaths among patients with AMI who survived to hospital presentation to incident deaths among patients with AMI who did not survive to hospital presentation (Figure 2). Incident deaths among patients with AMI surviving to hospital were derived from the number of enrolled patients with AMI who died within 30 days, adjusted by the time and healthcare-seeking multipliers described previously. Incident deaths among patients with AMI not surviving to hospital were derived by multiplying the total number of estimated incident AMI cases by 17.4%—the estimated proportion of AMI cases that did not survive to hospital in the United States in 2014, as detailed previously. Age-standardization of mortality rates was performed using World Health Organization guidelines.[23] Although 30-day mortality data certainly underestimate annual AMI-associated mortality, we chose to use 30-day mortality data to provide a more conservative estimate. In a further effort to provide a conservative estimate, patients who were lost to follow-up were presumed to have survived.

**Estimated incident cases:**

$$(observed\ AMI\ cases) \times (time\ multiplier) \times (seeking\ multiplier) \times (prehospital\ mortality\ multiplier)$$

**Crude incidence:**

$$\frac{(estimated\ incident\ cases)}{(study\ region\ population)}$$

**Age-standardized incidence:**

$$\sum_{Age\ 0-5}^{Age>80} \frac{(estimated\ incident\ cases\ for\ age\ group) \times (WHO\ standard\ population\ for\ age\ group)}{(study\ region\ population\ for\ age\ group)}$$

**AMI-associated mortality incidence:**

$$\frac{[(observed\ deaths) \times (time\ multiplier) \times (seeking\ multiplier)] + [(estimated\ incident\ cases) \times 0.174]}{(study\ region\ population)}$$

**Figure 2. Formulae used to calculate estimated crude incidence, age-standardized incidence, and AMI-associated mortality incidence, northern Tanzania, 2019.**
AMI indicates acute myocardial infarction; and WHO, World Health Organization.

## Ethics

This study received ethics approval from institutional review boards at Duke Health, KCMC, and the Tanzania National Institute for Medical Research. All participants provided written informed consent before enrollment.

## RESULTS

During the surveillance study period, 681 adults presented to KCMC with chest pain or shortness of breath. Of these, 152 patients had AMI, including 89 (58.6%) residing within the study area. Of patients with AMI residing within the study area, 52 (58.4%) were male and the median (interquartile range) age was 64 (55–78) years (Table 1). The median (interquartile range) duration of symptoms before hospital presentation among incident AMI cases was 3 (1–7) days. Thirty-day follow-up was achieved for all incident cases; 36 (40.4%) patients with AMI died within 30 days of presentation.

Of 718 community survey participants, 131 (18.2%) identified KCMC as their preferred facility for chest pain or shortness of breath. This resulted in a healthcare-seeking multiplier of 5.481. The estimated crude annual incidence of AMI in northern Tanzania in 2019 was 172 cases per 100 000 people (95% CI, 147–200 cases per 100 000 people), including 207 cases per 100 000 men (95% CI, 180–237 cases per 100 000 men) and 139 cases per 100 000 women (95% CI, 117–164 cases per 100 000 women). The age-standardized annual incidence of AMI was 211 cases per 100 000 people (263 per 100 000 men and 170 per 100 000 women). Table 2 summarizes the estimated crude and age-standardized annual incidence of AMI in the study area and selected subpopulations. The age-standardized incidence of AMI was highest among men, those living in Moshi Urban District, and those of age 80 years or higher. Sensitivity analyses generated estimated crude annual incidences ranging between 147 and 218 cases per 100 000 people (Table 3).

The estimated crude annual incidence of AMI-associated mortality was 87 deaths per 100 000 people, and the age-standardized incidence was 102 deaths per 100 000 people (Table 4). The crude and age-standardized incidence of AMI-associated mortality was higher among men than women.

## DISCUSSION

To our knowledge, our study presents one of the first estimates of AMI incidence in SSA using empiric observational case detection. We found that the incidence of AMI and AMI-associated mortality in northern Tanzania in 2019 was high, highlighting the urgent need both for additional AMI incidence data across SSA and for increased resources to combat cardiovascular disease in Tanzania.

Our estimates of AMI incidence in northern Tanzania are similar to what has been reported in the United States and Europe, where recent studies have projected annual incidence ranging between 167 and 209 per 100 000 people.[5,24–26] This suggests that the epidemic of ischemic heart disease in Tanzania may be more severe than previously appreciated and that interventions to improve detection and prevention of AMI across SSA are needed. Although our incidence calculations relied on multipliers to account for cases not detected at the surveillance hospital, our sensitivity analyses demonstrated similarly high estimates using a wide range of plausible multipliers. Given the well-described ongoing increase in the prevalence of cardiovascular risk factors such as hypertension and obesity across SSA,[27–29] the burden of AMI in SSA will likely continue to rise without aggressive public health interventions.

The incidence of AMI was noted to be higher among men and elderly people. This is consistent with what has been reported in high-income settings

**Table 1. Characteristics of Patients From Moshi Urban, Moshi Rural, and Hai Districts Presenting to KCMC With Acute Myocardial Infarction, 2019 (N=89)**

| Patient characteristics | Median | Interquartile range |
|---|---|---|
| Age, y | 64 | (55–78) |
| Body mass index, kg/m$^2$ | 23.2 | (20.6–27.0) |
| Duration of symptoms before presentation, d | 3 | (1–7) |
| | N | % |
| Male sex | 52 | 58.4 |
| History of hypertension | 62 | 69.7 |
| History of diabetes mellitus | 22 | 24.7 |
| History of hyperlipidemia | 4 | 4.5 |
| History of tobacco use | 36 | 40.4 |
| HIV infected | 3 | 3.4 |
| District of residence | | |
| Moshi urban | 17 | 19.1 |
| Moshi rural | 55 | 61.8 |
| Hai | 17 | 19.1 |
| Myocardial infarction type | | |
| ST-segment–elevation myocardial infarction | 39 | 43.8 |
| Non–ST-segment–elevation myocardial infarction | 50 | 56.2 |
| Vital status at 30 days | | |
| Alive | 53 | 59.6 |
| Dead | 36 | 40.4 |

KCMC indicates Kilimanjaro Christian Medical Centre.

**Table 2. Estimated Annual Incidence of Acute Myocardial Infarction per 100 000 People, Northern Tanzania, 2019**

| | Crude incidence | 95% CI | Age-standardized incidence | 95% CI |
|---|---|---|---|---|
| All people | 172 | (147–200) | 211 | (183–241) |
| Men | 207 | (180–237) | 263 | (232–297) |
| Women | 139 | (117–164) | 170 | (145–198) |
| Moshi urban district | 154 | (131–180) | 341 | (306–379) |
| Moshi rural district | 196 | (170–225) | 207 | (180–237) |
| Hai district | 134 | (112–159) | 155 | (132–181) |
| Age 20–39 y | 35 | (24–49) | … | … |
| Age 40–59 y | 334 | (299–372) | … | … |
| Age 60–79 y | 827 | (772–885) | … | … |
| Age ≥80 y | 2099 | (2010–2191) | … | … |

such as the United States[30] and also consistent with GBD estimates for SSA.[3] We also noted a higher age-standardized incidence of AMI among those living in urban settings than those living in rural settings. This may be because of the greater prevalence of cardiovascular risk factors in urban settings in SSA, as has been previously described.[29] To our knowledge, there has been no prior study comparing the incidence of AMI between urban and rural settings in SSA, and additional research is needed to determine if similar patterns in AMI epidemiology exist elsewhere in SSA.

The estimated AMI-associated mortality in our study was also high. The estimated age-standardized annual incidence of AMI-associated mortality in our study is more than double the reported rate in the United States in 2016.[30] This suggests that although the burden of incident disease in Tanzania and the United States may be similar, the burden of AMI-associated mortality in Tanzania is much higher. The reasons for disproportionately higher case fatality rate in Tanzania are likely myriad, including delayed presentation and diagnosis, weaker health systems, and low uptake of evidence-based AMI care.[6] Recent studies in Tanzania, for example, found that only few AMI cases were treated with aspirin in the ED and few patients with AMI reported taking an antiplatelet agent following hospital discharge.[13] Further epidemiologic investigation is needed to illuminate factors contributing to high AMI-associated mortality in Tanzania and to better quantify prehospital AMI mortality. Nonetheless, efforts to improve prevention and care of AMI in Tanzania would likely reduce excess AMI mortality.

Importantly, our estimates of AMI incidence and AMI-associated mortality stand in contrast to prior modeling studies that estimated that the burden of AMI in SSA was much lower than in other world regions.[1,4] For example, our estimate of annual AMI-associated mortality is more than twice that of the 2017 GBD Study, which reported an annual mortality rate of 38 deaths due to ischemic heart disease per 100 000 people in Tanzania.[1] Estimates for AMI incidence and mortality from the GBD study were largely derived from hospital-based data; however, such estimates fail to account for missed cases at the study hospital, care-seeking behavior, and out of hospital deaths from AMI. A recent observational study in Tanzania found that ≈90% of AMI cases were missed by hospital physicians,[13] and this finding may explain why reliance on retrospective hospital-based data likely underestimates disease burden. Our study benefitted from prospective AMI surveillance using standardized objective testing with ECGs and cardiac biomarkers, allowing us to detect cases that would otherwise have been missed.

Our study had several limitations. First, our surveillance methods may have missed AMI cases with atypical or delayed presentations, potentially resulting in an underestimation of AMI incidence. Second, a community survey was used to calculate a healthcare-seeking multiplier, but respondents' reported hypothetical hospital preferences may not reflect actual care-seeking behavior for actual AMI events. Because

**Table 3. Sensitivity Analyses of Estimated Annual Incidence of Acute Myocardial Infarction Per 100 000 People, Northern Tanzania, 2019**

| Assumption | Crude incidence | 95% CI |
|---|---|---|
| Prehospital mortality rate twice that of the United States | 218 | (190–249) |
| Prehospital mortality rate half that of the United States | 156 | (132–182) |
| Upper bound of 95% CI for healthcare-seeking multiplier | 202 | (175–232) |
| Lower bound of 95% CI for healthcare-seeking multiplier | 147 | (124–173) |

**Table 4. Estimated Annual Incidence of Acute Myocardial Infarction Mortality Per 100 000 People, Northern Tanzania, 2010**

| | Crude mortality incidence | 95% CI | Age-standardized mortality incidence | 95% CI |
|---|---|---|---|---|
| All people | 87 | (70–107) | 102 | (83–124) |
| Men | 105 | (86–127) | 128 | (107–152) |
| Women | 71 | (55–90) | 81 | (64–101) |

the community survey was performed by a KCMC-based team, social desirability bias may have influenced respondents to report that KCMC was their preferred facility. This would have resulted in an under-estimation of the healthcare-seeking multiplier and therefore an underestimation of the AMI incidence and mortality. Third, as described, the prehospital mortality multiplier was derived from US data, but prehospital mortality in Tanzania is likely higher for many reasons. In Tanzania, patients with AMI typically present to hospitals much later after symptom onset than patients in the United States,[13,22] and emergency medical transport services and emergency systems of care are more limited. Thus, our approach likely resulted in underestimation of prehospital mortality in Tanzania, which would have led to an underestimation of both AMI incidence and AMI-associated mortality. Furthermore, all-cause 30-day mortality following AMI diagnosis was used to estimate the annual incidence of AMI-associated mortality. Thus, AMI-associated mortality occurring beyond 30 days was not detected by our study methods, therefore resulting in an underestimation of annual AMI-associated mortality. Finally, the use of the multiplier method to generate disease burden estimates is likely to produce less precise results than a comprehensive community-based study with universal AMI screening with standardized diagnostic testing and imaging. However, in northern Tanzania, where most healthcare facilities do not have access to ECG or cardiac biomarker assays and where many residents with AMI symptoms would not present to a hospital,[6,8] such a comprehensive epidemiologic study is not currently possible. As diagnostic capacity and healthcare-seeking behavior in Tanzania continue to improve, additional study may be needed to confirm our findings. Having acknowledged these limitations, we nevertheless emphasize a principal strength of this study: the incidence estimates presented here are based on prospective surveillance data with empiric case detection that relied on rigorous screening and case definition criteria in a real-world setting.

## CONCLUSIONS

In conclusion, generating estimates based off prospective surveillance, we found that the incidence of AMI in northern Tanzania in 2019 was high, and similar to that reported in high-income countries. The incidence of AMI-associated mortality in northern Tanzania was also high and substantially higher than what has been previously reported. Additional empiric data from prospective surveillance studies are needed to more accurately describe the burden of AMI across SSA. Notably, our study did not assess disability following AMI events; thus, additional research is needed to describe the burden of disability-adjusted life years lost due to AMI in Tanzania and across SSA. Given the large burden of AMI-associated deaths observed in our study, public health interventions are needed to reduce ischemic heart disease mortality in northern Tanzania.

## ARTICLE INFORMATION

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