Examining Trends in Sepsis and Sepsis Management by Non-Physician Clinicians in a Rural Ugandan Emergency Department Over a Decade.

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Abstract

Background: There is a paucity of data from Sub-Saharan Africa regarding sepsis outcomes and the impact of sepsis care on those outcomes, including the impact of care provided by non-physician clinicians (NPCs).

Methods: Data were retrospectively analyzed from a rural Ugandan emergency department staffed by NPCs using a quality assurance database of adult and pediatric patient visits with and without sepsis from 2010 through 2018. Sepsis was defined as suspected infection with a qSOFA score ≥ 2. Mortality, disposition, and NPC adherence to intravenous fluid and anti-infective therapy were analyzed using chi-squared and multivariable linear regression.

Results: Sepsis criteria were met in 4,847 (11.0%) cases. Sepsis cases compared to non-sepsis cases were significantly older, and had higher rates of comorbid malaria, HIV, tuberculosis, and pneumonia. They had higher admission rates (86.8% versus 66.3%), were more likely to still be admitted at three days (40.2% versus 26.2%), and had higher mortality at three days (7.8% versus 2.5%). The incidence of sepsis significantly declined over time from 16.3% in 2010 to 3.1% in 2018 while the proportion of sepsis cases with qSOFA score of ≥ 3 increased significantly over time. The decrease in incidence was largely due to a precipitous drop in malaria smear-positive sepsis. Utilizing a multivariable linear regression model, annual three-day sepsis mortality did not significantly change over time, though adherence to administration of both fluids and anti-infectives increased significantly from 12.3% in 2010 to 35.0% in 2018.

Conclusions: Sepsis incidence, especially malaria smear-positive sepsis, decreased over time, while annual mortality did not change despite increased adherence to administration of anti-infectives and intravenous fluids in an NPC-staffed emergency department. Further studies are needed to investigate the contextualized use of anti-infectives and fluid resuscitation.

Background

Sepsis is one of the most significant worldwide causes of morbidity and mortality, totaling 48.9 million annual cases and accounting for 11 million annual deaths, 19.7% of all global deaths, in the most recent analysis of the Global Burden of Disease Study from 2017 data.[1] Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection, while septic shock is a subset of sepsis in which there are underlying circulatory, cellular, and metabolic abnormalities that are associated with an even greater risk of mortality.[2] These conditions disproportionately impact persons in low-and-middle income countries (LMICs).[1,3] While in-hospital mortality rates can be greater than 25–30% across resource settings, mortality rates of up to 38% are reported in LMICs, particularly in patients who have confirmed bacteremia.[2–4] In Uganda, a low-income country in sub-Saharan Africa, the primary causes of death are all infectious in nature—namely malaria, HIV/AIDs, pneumonia, tuberculosis and diarrheal-associated diseases, all of which can lead to sepsis.[5,6] Studies in Uganda have shown sepsis mortality

rates between 34–43% and 59% in those characterized as having septic shock.[7,8] The World Health Organization (WHO) has identified sepsis as an international priority, adopting a resolution in 2017 to improve the prevention, diagnosis and clinical management of sepsis.[9]

Identifying patients with sepsis and septic shock presents a significant challenge. Clinical criteria to identify patients with these syndromes have evolved over time. The most recent Sepsis-3 consensus recommendations suggest using bedside clinical criteria, termed the quick Sequential Organ Failure Assessment (qSOFA) score, which utilizes respiratory rate ≥ 22/min, altered mentation, and systolic blood pressure ≤ 100 mm Hg.[2] Adult patients with suspected infection and two or more of these findings are determined to meet sepsis criteria. Using the qSOFA score in a low-resource setting is of particular value because it does not rely on advanced diagnostic testing or resources and provides opportunity for a rapid objective clinical evaluation of the patient by a variety of providers including nurses, mid-level providers, and physicians. One study in Uganda found that stratifying patients with sepsis based on vital signs can assist in prioritizing patients who are more acutely ill.[10]

Management of sepsis globally has changed significantly over the past two decades. In the US and other high-resource settings, a single-center randomized trial published in 2001 that reported improvement in sepsis outcomes with “early goal-directed therapy” sparked widespread interest and change in practice patterns for sepsis management, yet subsequent trials published in the current era of sepsis management have failed to find similar benefits.[11–15] As such, specific interventions that may improve outcomes continue to be debated,[16] and many agree that sepsis management may need to be tailored based on patient population, disease patterns, practice environment, and resource availability.[5]

The current standard of care for managing sepsis in high-resource settings follow guidelines established by the Surviving Sepsis Campaign.[17] However, these guidelines have been deemed not only impractical in sub-Saharan Africa (SSA) due to limited resources, but also potentially detrimental as “early goal-directed therapy” interventions that increased fluid resuscitation were found to increase mortality in SSA.[18,19] This difference in impact of fluid resuscitation on septic patients across settings may be related to a difference in patient populations that carry a high burden of malaria and other co-morbidities as well as a lack of intensive care facilities to provide supportive treatment in cases where fluids may exacerbate respiratory failure, heart failure, or renal failure.[7,8,19–22] In LMICs overall, recommendations for sepsis management have included early administration of antibiotics, fluid resuscitation, using epinephrine and dopamine administration to optimize tissue perfusion in those refractory to fluid resuscitation, frequent vital sign monitoring, corticosteroid administration when necessary, supplemental oxygenation, and identification of infectious sources.[23] However, these interventions can be challenging to implement with limited staff, training, and supplies.[24] Therefore, it remains unclear if any specific sepsis-care bundle can be applied across settings due to variations in patient populations, pathogens, and clinical environments.[5]

Despite these challenges, limited studies have shown some reduction in sepsis mortality in Uganda with increased adherence to sepsis protocols including fluid resuscitation, early antimicrobial treatment, and close monitoring of patients.[21] For septic patients with Human Immunodeficiency Virus (HIV) infection, early antiretroviral therapy is recommended, in order to reduce mortality.[25,26] In patients with HIV and severe sepsis, early anti-tuberculosis therapy and intravenous fluids have demonstrated a reduction in mortality.[8,27] Although these studies suggest some approaches to sepsis management, there is still overall limited research into effective sepsis-related interventions and their outcomes in SSA and in Uganda in particular.[19] In this study, we describe patients with sepsis and their management and outcomes in a rural Ugandan Emergency Department staffed by non-physician clinicians over a nine-year period.

Methods

Description of Study Site

The study site is Karoli Lwanga Hospital, a rural district hospital located in the town of Nyakibale in the Rukungiri District of southwest Uganda. The hospital has a six-bed Emergency Department (ED) that opened in 2008 and treats 300 to 700 patients per month. Since 2010, the ED has been staffed independently by non-physician clinicians (NPCs) called Emergency Care Practitioners (ECPs). The ECPs are nurses who have completed a two-year advanced training course in emergency care described elsewhere.[28] They practice independent care unsupervised by physicians and continue to train new cadres via a train-the-trainer model. Hospital-based Ugandan physicians were on call for consultations, if required, particularly for complicated medical and surgical emergencies.

During the study period, the hospital lacked critical care units, ventilators, capabilities for invasive monitoring, and vasopressor medications. Diagnostic testing was limited to hemoglobin, blood grouping, urinalysis, blood smear for malaria, glucose, cerebrospinal fluid analysis, HIV rapid testing, brucellosis antibody, and Widal test for typhoid along with radiography (X-ray) services of variable availability and ultrasound capability.

The Karoli Lwanga Hospital ED maintains a prospectively collected quality assurance database of all ED patient visits, including three-day follow-up data on clinical status, described previously.[28] When the database was developed, three-day follow-up was chosen to minimize loss to follow-up for admitted and discharged patients in a setting where most patients do not have consistent ability to receive phone calls. Additionally, follow-up after three days was thought to be less reflective of outcomes related to acute care provided in the ED, and the database was designed specifically for quality assurance of ED care.

Data Analysis

Data were retrospectively abstracted from the Karoli Lwanga Hospital ED quality assurance database, including all consecutive patient visits for patients of all ages presenting to the ED between 2010 and

2018. Sepsis was defined as a suspected infection (a complaint or diagnosis consistent with infection [e.g. “sepsis”, “cholecystitis”, “fever”]) with a qSOFA score of two points or greater with one point each for age-adjusted tachypnea (respiratory rate (RR) ≥ 22 if age ≥ 12 years, RR ≥ 30 if age < 12 and ≥ 6 years, RR ≥ 40 if age < 6 and ≥ 1 year, RR ≥ 50 if age < 1 year and ≥ 2 months, RR ≥ 60 if age < 2 months), altered mentation (included if Glasgow Coma Scale (GCS)) < 15, or hypotension (systolic blood pressure (SBP) ≤ 100). Demographics, anti-infectives (including all classes of anti-infectives such as antifungals, antibiotics, etc.), intravenous fluid, outcomes of testing (including malaria smear status when available), presence of a high-risk comorbidity listed as a top infectious cause of death on the GBD 2017 survey (HIV, pneumonia, tuberculosis, diarrhea), and three-day mortality outcomes were analyzed for all patients. Proportions were compared using χ 2 tests and linear regression was performed to test the significance of care trends, incidence and mortality over time. The quality assurance database was approved by the Institutional Review Board at Mbarara University of Science and Technology.

Results

There were 43,910 patient visits over the nine-year period for which registry data were obtained. Of those, 27,449 (62.5%) visits were cases with suspected infection. Of these, 4,831 (17.7%) satisfied two or more qSOFA criteria and were included in the analysis (Fig. 1). Therefore, 11.0% (4831 of 43,910) of all cases were retrospectively determined to have sepsis.

The mean age for sepsis cases and non-sepsis cases was 37.1 and 29.0 years, respectively (Table 1). Pediatric cases (< 18 years) made up 18.9% of all sepsis cases, with 3.6% of sepsis cases overall accounted for by the under-five group. This is significantly lower than in the non-sepsis group where 40.9% of cases were pediatric with the under-five group representing 26.8% of all non-sepsis cases. Females accounted for 49.8% of sepsis cases and 48.1% of non-sepsis cases. Sepsis cases had significantly higher rates of malaria, HIV, tuberculosis, and pneumonia, but not diarrhea. Of those, the greatest differences were found in patients with HIV (16.4% vs 5.8%) and tuberculosis (9.5% vs 2.1%).

Table 1

Characteristics of ED patient visits with suspected infection, n = 27,449.

	qSOFA < 2	qSOFA ≥ 2	
	n = 22,618	n = 4831	P value
Age, Mean (SD)	29.0 (28.3)	37.1 (22.8)	< 0.001
Age Groups			
Under 5, n (%)	6069 (26.9)	174 (3.6)	< 0.001
5–11, n (%)	1700 (7.5)	217 (4.5)	< 0.001
12–17, n (%)	1475 (6.5)	521 (10.8)	< 0.001
18–64, n (%)	10021 (44.3)	3186 (66.3)	< 0.001
≥ 65, n (%)	3273 (14.5)	705 (14.7)	< 0.001
Unavailable (%)	80 (0.4)	28 (0.6)	< 0.001
Female, n (%)	10873 (48.1)	2404 (49.8)	0.030
Unavailable	17 (0.1)	6 (0.1)	
Malaria Smear Positive, n (%)	4563 (20.2)	1112 (22.9)	< 0.001
High-Risk Comorbidity, n (%)‡	7209 (31.9)	2016 (41.7)	< 0.001
HIV	1304 (5.8)	793 (16.4)	< 0.001
Diarrhea	2570 (11.4)	506 (10.5)	0.07
Tuberculosis	485 (2.1)	457 (9.5)	< 0.001
Pneumonia	4021 (17.8)	981 (20.3)	< 0.001

Visits lost to follow up include patient encounters with dispositions of discharged, admitted, transferred, direct to theater, died in ED.

Continuous variables are presented as M ± SD.

Categorical variables are presented as n (%) and P values were calculated using the Chi-squared test.

Percentages may not equal 100% due to rounding.

‡ Includes patients with one or more high-risk comorbidities

Patient disposition and outcomes are included as Table 2. Sepsis cases had a higher admission rate than non-sepsis cases (86.9% versus 66.3%). When follow-up was performed at three days sepsis cases were significantly more likely than non-sepsis cases to be dead (7.8% vs. 2.5%, $p < 0.001$) or still admitted to the hospital (40.2% vs. 26.2%, $p < 0.001$). Loss to follow-up for admitted cases was similar for both septic

(6.56%) and non-septic (6.63%) patients (p = 0.87). Mortality in discharged patients was extremely rare for both septic (n = 1) and non-septic patients (n = 3), and no significant difference was seen in mortality between groups (p = 0.13). Loss to follow up was much higher in discharged patients overall - because of either no phone number being provided or no answer at that number - and occurred at a higher rate amongst non-septic (45.4%) versus septic (38.8%) patients (p = 0.005). The mortality rate for sepsis cases with high-risk comorbidities was significantly greater than non-sepsis cases (10.7% versus 3.8%), with the highest mortality rates in cases with pneumonia (12.6% versus 3.8%), tuberculosis (12.0% versus 3.9%), and HIV (10.7% versus 5.9%).(Table 3)

Table 2

Comparative Outcomes for Patient Visits with Suspected Infection According to qSOFA score and disposition.

qSOFA Score	0	1	2	3	P value
Three Day Mortality Rate	1.4	3.8	7.0	16.2	< 0.001
[95% CI]	[1.2–1.6]	[3.4–4.1]	[6.2–7.7]	[12.7–19.7]	
(Deceased/Total Cases)	(173/12284)	(388/10334)	(308/4404)	(69/447)	
		qSOFA < 2	qSOFA ≥ 2		
		n = 22602	n = 4847		
Disposition, n (%)					
Discharged		7238 (32.0)	493 (10.2)		< 0.001
Admitted		15005 (66.3)	4199 (86.9)		< 0.001
Died in ED/DOA		81 (0.4)	50 (1.0)		< 0.001
Other*		240 (1.1)	70 (1.5)		0.02
Unavailable		54 (0.2)	19 (0.4)		0.03
3-Day Follow-up Status					
Deceased, n (%)		561 (2.5)	377 (7.8)		< 0.001
Still in Hospital, n (%)		5729 (26.2)	1897 (40.2)		< 0.001

Visits lost to follow up include patient encounters with dispositions of discharged, admitted, transferred, direct to theater, died in ED.

Categorical variables are presented as n (%) and P values were calculated using the Chi-squared test.

Percentages may not equal 100% due to rounding.

* Includes dispositions of left against medical advice, transferred out of hospital, direct to theatre.

‡ Includes admitted, died in ED, and other (as above)

Table 3

Mortality Outcomes for Subgroups with a High-Risk Comorbidity.

Mortality	qSOFA < 2	qSOFA ≥ 2	P value
All High Risk	272/7209	216/2016	
Deceased/Total cases, %	3.8	10.7	< 0.001
HIV*	77/1304	85/793	
	5.9	10.7	< 0.001
Diarrhea	97/2570	47/506	
	3.8	9.3	< 0.001
Pneumonia	154/4021	124/981	
	3.8	12.6	< 0.001
Tuberculosis	19/485	55/457	
	3.9	12.0	< 0.001

High-risk comorbidities were defined as a clinical diagnosis documented in the patient chart for the visit.

* Defined as a positive HIV test or a past medical history of HIV positivity

In regard to trends noted in sepsis patients over the nine-year study period, incidence of sepsis declined from a peak of 16.3% of all patients in 2010 to 3.1% of all visits in 2018, an approximate reduction of 1.1% per year (95% CI 1.3–1.0, $p < 0.001$). Over the same time period the proportion of sepsis cases with a qSOFA score of ≥ 3 (indicating greater sepsis severity and poorer prognosis) significantly increased at a rate of 0.8% per year (95% CI 0.2–0.9%, $p = 0.001$). Displayed visually in Fig. 2, with regard to malaria smear status, the incidence of sepsis without a smear and smear-negative sepsis declined over time, but the decline in smear-positive sepsis (from 207 cases in 2010 to 4 in 2018) was by far the most precipitous.

Management of sepsis cases by NPCs showed that annual adherence to treatment guidelines for both fluids and anti-infective intervention increased over time at a rate of 2.9% per year (95% CI 2.4–3.4, $p < 0.001$) from 12.3% in 2010 to 35.0% in 2018 (Fig. 3). Similarly, sepsis cases where neither fluids nor anti-infectives were given decreased at a rate of 3.6% per year (95% CI 3.0–4.1, $p < 0.001$) from 53.0% in 2010 to 22.8% in 2018. Fluids alone and anti-infectives alone did not trend significantly across years ($p = 0.20$ and $p = 0.12$, respectively).

The three-day mortality for sepsis averaged over the entire period was 7.6% [95% CI 6.9–8.4] with a low of 5.4% in 2012 and a high of 10.9% in 2016. A multiple linear regression model including year, qSOFA score,

malaria smear results and quality of sepsis care showed mortality did not vary significantly by year (p = 0.52).

Discussion

The above study describes sepsis cases in a rural Ugandan ED, reports on the outcomes of sepsis cases, and analyzes trends in sepsis cases and sepsis management by NPCs over nine years. Debate is ongoing to the applicability of qSOFA and other clinical scoring tools to pediatric populations.[29–31] The decision was made to include pediatric cases as it more accurately described the clinical environment where patients < 18 years old represented 19% of total sepsis cases and 11% of total sepsis deaths. Sepsis cases were older and more likely to carry a comorbidity known to be a common cause of death in Uganda such as diarrhea, HIV, tuberculosis, or pneumonia, and they were also more likely to have a positive malaria smear.

While it is generally accepted that early antimicrobials are a cornerstone of sepsis management,[17] context-specific agents are likely an important consideration for the diagnosis and management of sepsis in rural Uganda. Standard broad-spectrum antibiotics may not address a different host of underlying pathogens leading to a sepsis syndrome in certain patients. Therefore, sepsis care recommendations in areas with high prevalence of these conditions may need to be tailored to include antimalarial, antiretroviral, antifungal, antiparasitic, and anti-tuberculous agents. Additionally, facilities must have the diagnostic testing capabilities to identify these underlying etiologies and the aforementioned treatment options. Although clinical criteria may suffice to diagnosis the syndrome of sepsis, clinical observations alone cannot usually identify many of these high-risk co-morbidities, and availability of trained staff can be lacking.

In our analysis of sepsis outcomes, we found that NPCs admitted a greater percentage of sepsis cases than non-sepsis cases though NPCs do not routinely calculate qSOFA scores nor use it to make admission decisions. The increased mortality associated with higher qSOFA scores is in line with other research suggesting the value of qSOFA to discriminate between patients at higher risk for mortality in sepsis, particularly in SSA.[32] Trends of sepsis over time in our study demonstrate an overall decrease in sepsis case incidence, and notably, a profound decrease in annual cases of sepsis associated with a positive malaria blood smear. These findings are in accord with the observed decrease in malaria as a cause of death and disability in Uganda over the period of 2007–2017 in the Global Burden of Disease Survey.[6] The National Malaria Control Program in Uganda employed a combination of control measures including long-lasting insecticidal nets, indoor residual spraying, and intermittent preventative treatment for malaria during pregnancy during the study period. The reduction of malarial sepsis over time in our study may be related to the success of these multi-pronged approaches to malaria prevention at a community level.[33]

Another significant trend noted was in the change of management of sepsis over time with an increase in adherence to the recommended sepsis management guidelines during that time, including administration

of intravenous fluids and intravenous antimicrobials. The increase in adherence to sepsis treatment protocols over time suggests that the train-the-trainers for NPCs employed in this setting was successful in promoting ongoing practice improvement. The rates of fluid and antibiotic administration provided by NPCs compares favorably to the standard of care provided by admitting medical officers in other Ugandan hospitals during the same time period.[21] In the study cited above, the study intervention clearly improved medical officer adherence to sepsis care guidelines and reduced mortality. Some have suggested that improved training of nurses, paramedical assistants, and other NPCs could significantly improve sepsis identification and management and can be done at low cost.[5,34] Additional studies are needed to confirm whether targeted training interventions with NPCs in emergency units would improve their adherence to sepsis care bundle and whether that change would impact mortality outcomes.

Despite the increased adherence to sepsis management guidelines, no change in sepsis mortality was seen over the study period. This lack of mortality benefit seen may be due to shifting trends in the septic population presenting to the hospital where significantly fewer malaria smear-positive patients and significantly more patients with qSOFA scores of 3 or greater presented to the ED over the course of the study. Additionally, it is difficult to identify the impact of distinct interventions via retrospective study as sicker patients almost always receive more aggressive care and more interventions. Controlled clinical trial environments are likely needed to isolate the mortality impact of individual sepsis treatments or bundles for ED patients in Uganda.

Alternatively, the lack of mortality benefit associated with “improved” treatment may be related to the emerging evidence that suggests standard fluid resuscitation may increase instead of decrease mortality in SSA.[20,22] To date, no high-quality ED-based studies exist to validate these findings in an ED setting and direct ED-based sepsis care in SSA. Without additional trials to inform the standard of care, current guidelines published in 2019 continue to recommend judicious use of intravenous fluids as part of standard sepsis management for emergency providers in SSA.[35] It is hoped that future studies will be able to the generate high-quality, region-specific, ED-based data required to create context-specific sepsis guidelines and policy for EDs throughout Uganda and SSA.

Limitations

There are several limitations of the registry database. First, the registry data are limited to a single center. As sepsis patterns and care may be different in high and low-resource settings and in certain geographic areas, there may be limited generalizability of the findings above given potential region-specific practice patterns and disease prevalence. However, it seems that sepsis care does not seem to have a “one size fits all” approach, and thus more data on these understudied populations may be of benefit, particularly for similar settings in rural SSA that might share similar disease burdens and resources. As emergency care and critical care systems continue to develop, these data may inform resource allocation.

The registry data does not allow for determining the number of unique patients who presented to the ED; therefore, some patient visits reported may have been repeat visits by the same patients. Comorbid

infections were reported in the registry by clinicians based on clinical evaluation and may or may not have included supporting lab or imaging data in the low-resource context. Additionally, some vital sign information may have been incomplete, including patient temperatures and blood pressures, particularly for pediatric patients, given a lack of supplies, which may underestimate sepsis cases. Finally, specific anti-infectives utilized (antibacterial, antifungal, antiparasitic, antiviral) as well as total intravenous fluid volume administered were not included at the time of analysis of the registry data. Future studies may benefit from looking specifically at sepsis outcomes related to types of anti-infectives and volume of fluids administered.

Mortality reported in this study was lower than in similar settings. This is likely related to a limitation of the ED registry which only records three-day mortality and therefore may underestimate longer-term measures such as in-hospital mortality. Nevertheless, the findings of high-risk co-morbidities related to three-day sepsis mortality and incident ED sepsis mortality trends over time are notable, even if overall mortality is underestimated.

Conclusions

In a retrospective analysis of a rural Ugandan ED staffed by NPCs, sepsis accounted for 11.0% of patient visits. Sepsis mortality was higher in patients with high-risk comorbidities, and the mortality rate increased with increasing qSOFA score. Over the nine years of the study, the incidence of blood-smear positive malaria decreased in sepsis cases. During that same time, in the years following implementation of an NPC training program, there was increased adherence to a sepsis management protocol. Despite improved adherence to sepsis treatment protocols, sepsis mortality did not change over time. It is unclear if existing treatment protocols can improve sepsis mortality in this context, and further studies are needed to investigate the use of specific anti-infectives and the role of fluid resuscitation in particular patients and resource environments.

Abbreviations

ECP, Emergency Care Practitioner

ED, Emergency department

GCS, Glasgow Coma Scale

HIV, Human Immunodeficiency Virus

LMICs, low- and middle-income countries

NPC, Non-physician clinician

qSOFA, quick Sequential Organ Failure Assessment

RR, respiratory rate

SBP, systolic blood pressure

WHO, World Health Organization

Declarations

Ethics approval and consent to participate

Ethics approval and waiver of consent for the quality assurance database was obtained through the Institutional Review Board at Mbarara University of Science and Technology.

Consent for publication (individual)

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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Author's contributions

S. Calo, S. Chamberlain, and BR contributed to study concept and design. BR and NK conducted data acquisition. BR planned and performed statistical analysis. S. Calo, S. Chamberlain, and BR contributed to data interpretation. S. Calo primarily wrote the manuscript with revisions and contributions from S. Chamberlain, BR, JBK, and NK. All authors provided edits and final approval of the manuscript.

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Figures

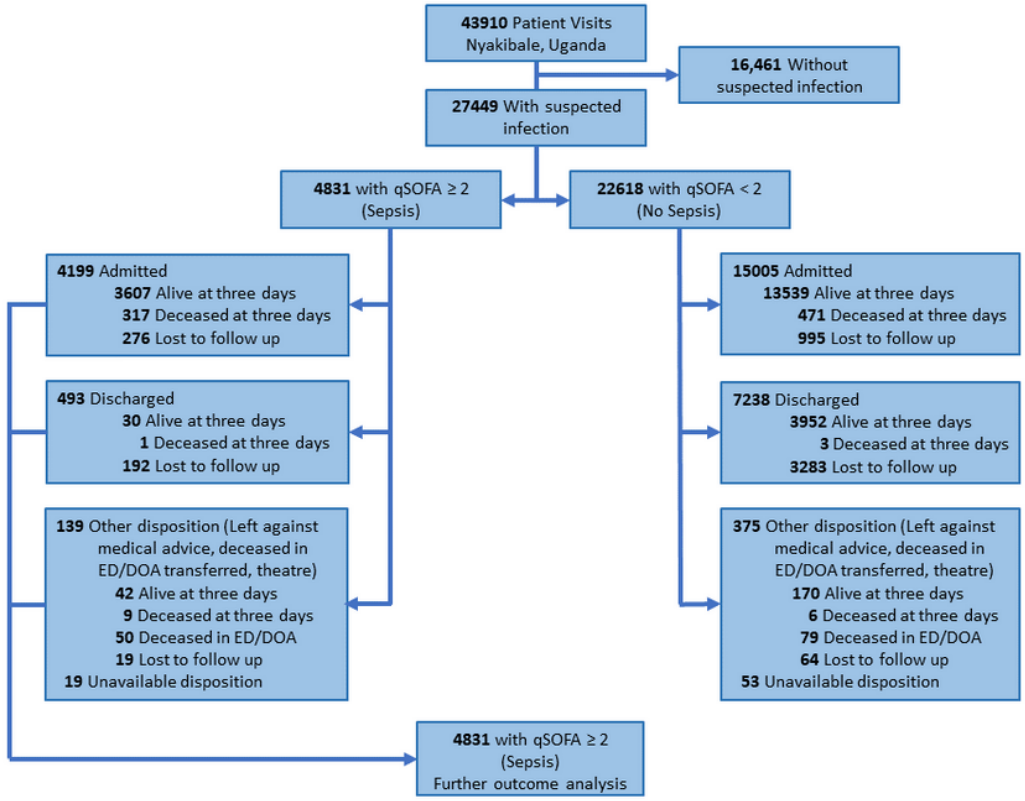

Figure 1

Flowchart demonstrating stratification of patient visits (cases) included in the analysis.

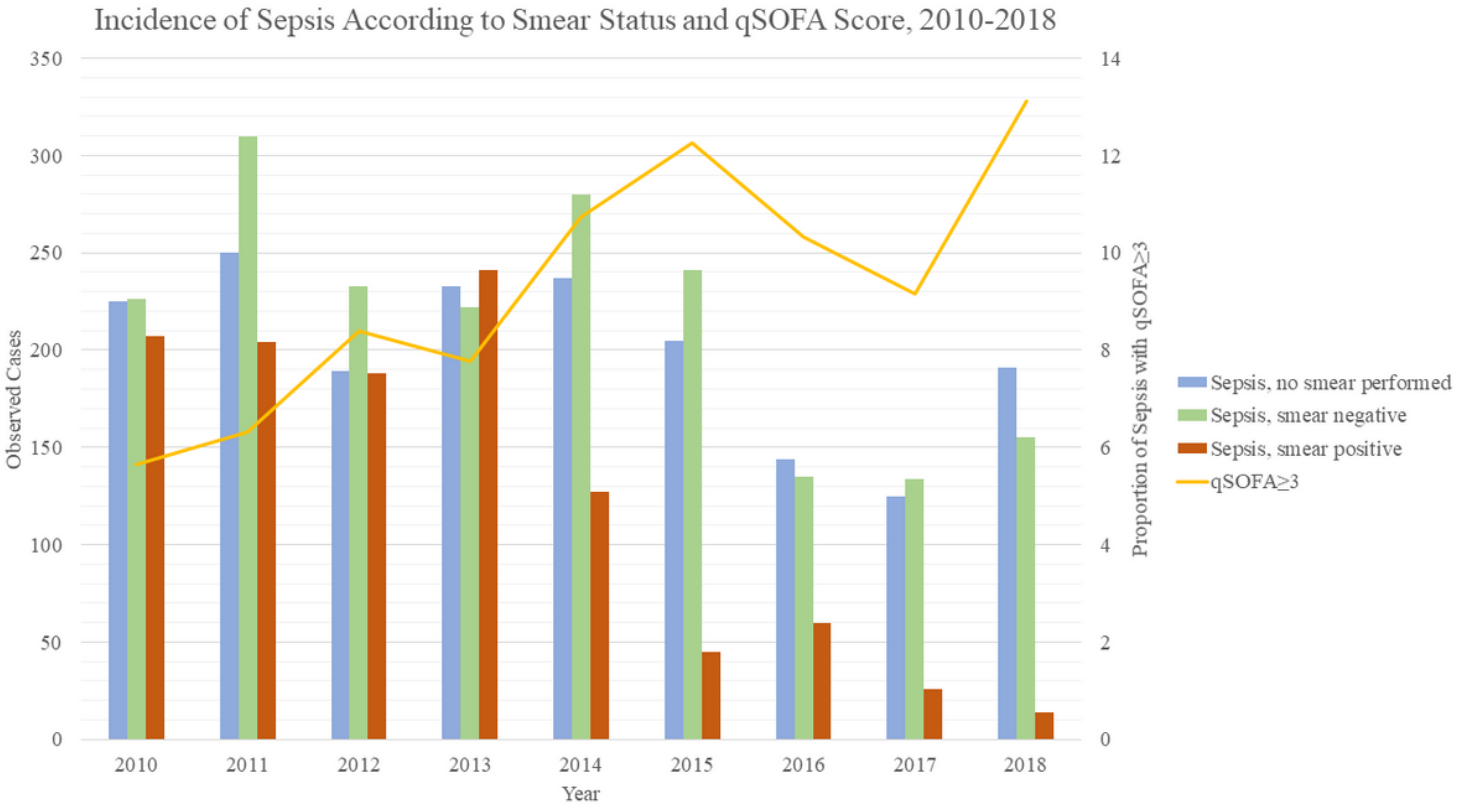

Figure 2

Incidence of Sepsis According to Smear Status and qSOFA Score, 2010-2018. For each year, the number of observed cases of sepsis are shown according to malaria smear status. The secondary ordinate axis corresponds to the trend line for mortality within the subgroup of sepsis cases with qSOFA ≥3.

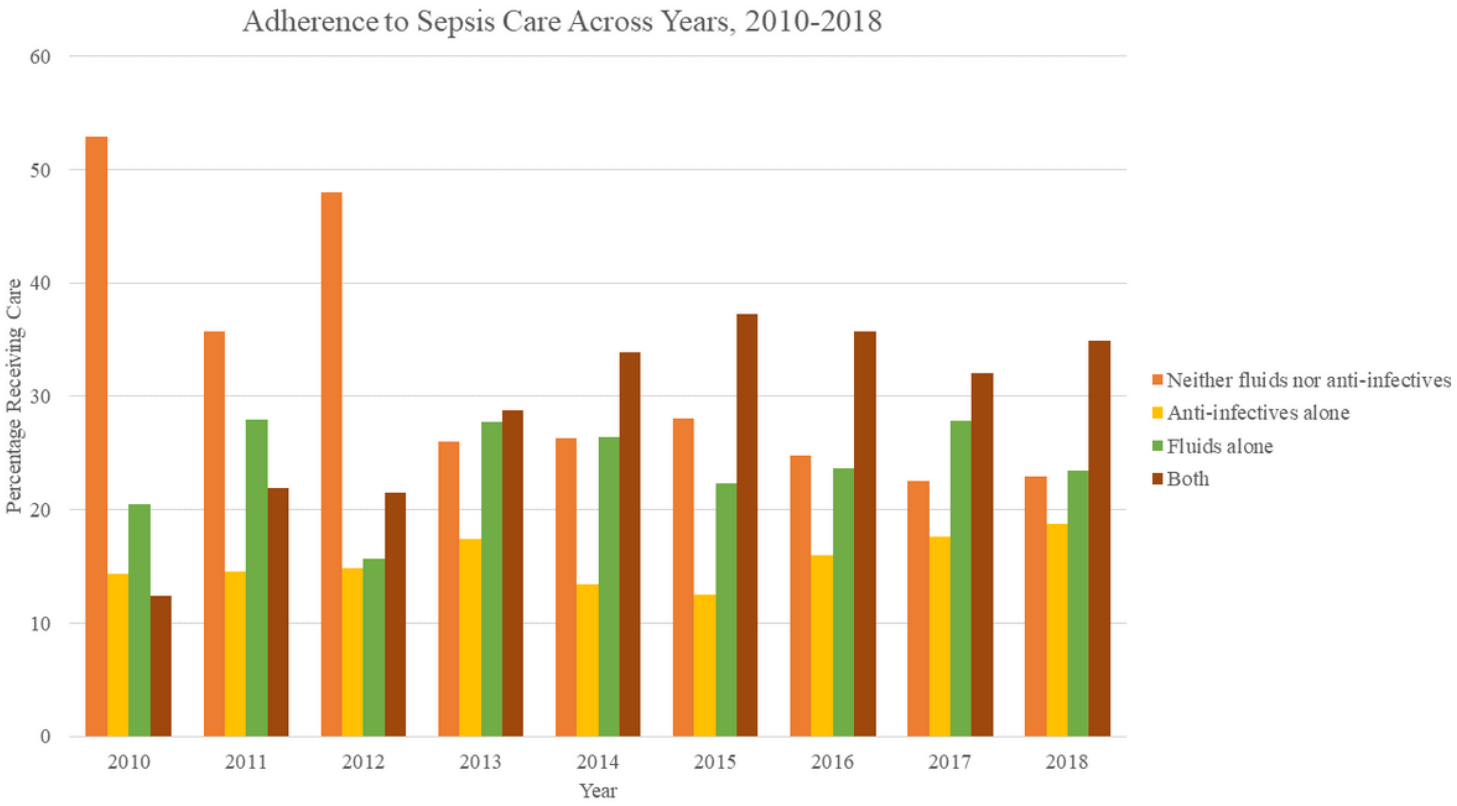

Figure 3

Adherence to Sepsis Care Across Years, 2010-2018. The magnitude of each bar is shown as a percentage. Sepsis cases were qSOFA≥2. Anti-infective administration includes antibiotic, antiviral, antifungal, and antiparasitic agents. Fluids denotes intravenous crystalloid administration.