The World Federation of Societies of Intensive and Critical Care Medicine define an intensive care unit (ICU) as an organised system for the provision of care to critically ill patients. These patients have greater physiological demands, requiring specialised medical and nursing care, enhanced monitoring and greater organ support measures to manage life-threatening illnesses. The timely administration of appropriate therapy is required to reverse pathological processes, preserve organ function, and improve outcomes and survival. Delayed admission to the ICU may result from errors in triage, delays in identification of critically ill patients, lengthy waiting periods for inter-hospital ICU transfer, prolonged pre-ICU hospital length of stay (LOS) (for a variety of reasons), and ICU bed unavailability.

Prior research has cited prolonged pre-ICU hospital LOS as an independent marker of hospital mortality. Patients admitted to ICU from hospital wards have significantly higher severity of illness scores compared with those admitted directly from the emergency department (ED). Furthermore, patients admitted to ICU from another hospital have similarly displayed a higher mortality.

Several reasons have been suggested for worse outcomes in patients admitted to ICU following in-hospital ward stays, compared with direct...
ICU admissions from the ED. These include: (i) critically ill patients receiving limited/suboptimal care in hospital wards by non-specialised staff; (ii) missed warning signs of deterioration or missed opportunities for early interventions; (iii) slow deterioration of physiological function in hospital, leading to critical care admission hours to days later;[1,2] and (iv) ICU admission following events of cardiac arrest in hospital wards, which often resulted in an elevated mortality rate.[3,4] Although no international consensus exists for defining the timeframe for ICU admissions, the Society of Critical Care Medicine (SCCM) recommends that patients be admitted to the ICU within 6 hours of the decision to admit from the ED.[5] Multiple emergency medicine studies have concluded that prolonged ED LOS for patients requiring ICU admission is independently associated with higher risks of hospital mortality.[6-8] A study from Brazil showed that each hour delay in hospital wards awaiting ICU transfer was associated with a 1.5% increased risk of ICU mortality and a 1% increased risk of hospital mortality.[9] Similar results from a 2004 UK study demonstrated increased mortality in relation to increased time in hospital wards before ICU admission.[10] Furthermore, a USA study found that critically ill patients who experienced delays of more than 6 hours in ED prior to ICU transfer had a longer hospital LOS with higher ICU and hospital mortality.[11,12,13] Therefore, previous studies collectively showed a higher mortality for patients with a longer pre-ICU hospital LOS, primarily in well-resourced settings.[13] One of the key contributors to prolonged pre-ICU LOS is limited ICU capacity, which has been demonstrated in American and European studies, but chronic shortages are far more prominent in low- and middle-income countries, with larger population-to-ICU-bed ratios and greater resource limitations.[14] A South African (SA) study published in 2015 reported a 1:32 000 ICU-beds-to-population ratio in the SA public sector, in contrast to the 1:5 000 ratio noted in well-resourced settings such as Germany and the USA.[15] Moreover, longer pre-ICU hospital LOS has been associated with more costly ICU stays, with relevance to resource-limited environments.[16] This study aimed to determine the association between pre-ICU hospital LOS and ICU outcomes in a resource-limited setting. We hypothesised that longer pre-ICU hospital LOS, adjusted for other patient-level factors, would be associated with higher in-ICU mortality.

**Methods**

**Study design and data source**

We performed a retrospective cohort study to measure the association between pre-ICU hospital LOS and ICU outcomes, using data extracted from a regional hospital ICU in KwaZulu-Natal, SA. Data were analysed from the ICU’s electronic patient database, which collects detailed patient data at the time of ICU admission and discharge.[17] This database has been used in prior observational studies involving measures of patient triage and acuity.[18]

Approval for the research was obtained from the Biomedical Research and Ethics Committee (ref. no. BREC/00000962/2020) and by the Institutional Review Board of the University of Pennsylvania (Philadelphia, USA). Additional permission was obtained from the study hospital and the Provincial Department of Health prior to commencement.

**Study site**

The study hospital is a 900-bed, regional-level metropolitan hospital in KwaZulu-Natal, SA, and serves a population of ~1.4 million people. The hospital has 6 adult mixed medical-surgical ICU beds and 3 high-care beds. The ICU is run as a closed unit, led by a team of intensivists and anaesthesiologists. In light of the limited bed capacity, patient selection for ICU admission is stringent and guided by SCCM classification,[19] based on the physiological and organ support required, weighed against the reversibility of the pathology and the final prognosis.

**Study population**

The study included consecutive admissions of all patients older than 18 years of age, admitted to ICU for both medical and surgical indications. All patients admitted to the ICU and captured on the electronic patient database during the study period (September 2014 to August 2018) were reviewed. A sample of 2 119 was identified, of which 79 patients were excluded owing to missing data, making the corrected sample size 2 040 patients (Fig. 1). For pre-specified stratified secondary analyses, ICU admissions were categorised based on the source of referral, being the ED, operating theatre (OT), or hospital wards.

Patients were excluded from the study if younger than 18 years old and if the referral was an inter-hospital transfer. Inter-hospital transfers were excluded based on confounders arising from logistical and transportation delays within the provincial healthcare system. Therefore, patients included in this study were restricted to...
those admitted to ICU from within the study hospital’s ED, OT or hospital wards.

Exposures, outcomes, and adjustment variables
The primary exposure was pre-ICU hospital LOS, which was treated as a continuous variable in calendar days for the primary analysis and for the OT and ward subgroup analyses. Among the ED subgroup, pre-ICU hospital LOS was dichotomised to <1 day versus ≥1 day. The primary outcome was ICU mortality, defined as death in the ICU or a palliative discharge from the ICU. The secondary outcome was ICU LOS, which was measured from the time of ICU admission to the time of ICU discharge. Adjustment variables included age, gender, race, year, HIV status, chronic comorbidities, and Mortality Probability Admission Model-III (MPM$_{-III}$).\cite{28} A composite model based on clinical and historical data obtained at the time of ICU admission. Comorbidities included binary present or absent indicators of: cardiovascular disease, respiratory disease, diabetes, haematological malignancy, neurological disease, HIV and highly active antiretroviral therapy (HAART) status, and non-HIV-related immunosuppression. MPM$_{-III}$ includes: acute physiology indicators (heart rate ≥150 bpm, systolic blood pressure ≤90 mmHg, and Glasgow Coma Score <5); chronic diagnoses (chronic kidney disease, cirrhosis, metastatic cancer); acute diagnoses (acute kidney injury, cardiac arrhythmia, cerebrovascular accident, gastrointestinal bleeding, and intracranial mass effect); age; cardiopulmonary resuscitation attempt before ICU admission; mechanical ventilation status at ICU admission; medical or non-elective surgical admission; and resuscitation status.\cite{29}

Data analysis
Multivariable logistic regression was used to assess the primary outcome of ICU mortality, and multivariable Cox proportional hazard regression was used for the secondary outcome of ICU LOS, with death as a censoring event. Our primary analysis included all eligible patients. We performed additional pre-specified stratified secondary analyses separately among patients admitted from the ED, OT, and ward. All analyses were conducted using STATA version 14.1 (StataCorp., USA). A p-value <0.05 was considered statistically significant.

Results
Patient demographics
A total of 2 119 patients were admitted and entered onto the ICU database from September 2014 to August 2018. Seventy-nine patients were excluded owing to missing exposure or primary outcome variables, leaving a total sample size of 2 040 patients.

The mean age of the population was 39.3 years (range 18 - 95 years), and 55.6% were male (Table 1). ICU admissions were categorised as medical or surgical, based on the referring discipline and indication for admission, of which the vast majority (73.4%) were surgical admissions. The surgical category included admissions from general surgery, trauma surgery, obstetrics and gynaecology, orthopaedics, otorhinolaryngology, maxillofacial surgery, urology, burns and anaesthesia. Of the surgical admissions, n=653/1 498 (43.6%) had trauma as the primary reason for ICU admission. These findings are in keeping with a previous study conducted in 2015, which assessed referral patterns to this ICU\cite{30}

Comorbidity status/illness profile
Pre-existing comorbidities were considered, based on the primary organ system affected as depicted in Table 1. Cardiovascular comorbidities included conditions such as hypertension and ischaemic heart disease, and were present in 14.0% (n=285/2 040) of admissions. Respiratory illnesses included asthma, chronic obstructive pulmonary disease and pulmonary tuberculosis, while pre-existing neurological disease encompassed conditions such as epilepsy and cerebrovascular events. Of note, diabetes mellitus was a common comorbidity reflected in 12.0% (n=244/2 040) of all admissions. HIV was noted as the most prominent comorbidity in the study population. Patients who at presentation were known to be HIV-positive accounted for 23.4% (n=477/2 040) of all ICU admissions, of whom 77.8% (n=371/477) were on HAART. This represents a marginally higher prevalence rate than the estimated 19% reported for HIV in the general adult population of SA according to Statistics South Africa 2018.\cite{31} However, the figure quoted in our study may underestimate the burden of HIV in this critically ill population, as it recognises only patients with a known HIV status from medical history. HIV testing on admission is not routine practice in the ICU and is only performed if relevant to diagnostic testing and treatment.

ICU acuity
By MPM$_{-III}$, study patients had a mean predicted mortality of 18.3%, which compares closely with international data on ICU mortality.

Table 1. Patient characteristics (N=2 040)

| Gender          | n (%)*  |
|-----------------|---------|
| Male            | 1 135 (53.6) |
| Female          | 904 (44.3)  |

| Admission type     | n (%)   |
|--------------------|---------|
| Not specified       | 51 (2.5) |
| Medical            | 491 (24.1) |
| Surgical           | 1 498 (73.4) |
| Trauma             | 653 (43.6) |
| Non-trauma         | 845 (56.4) |

| Comorbidities       | n (%)   |
|--------------------|---------|
| HIV                |         |
| Negative or status unknown | 1 563 (76.6) |
| Positive           | 477 (23.4) |
| Positive, on HAART | 371 (18.2) |
| Positive, not on HAART | 106 (5.2) |
| Cardiac            | 285 (14.0) |
| Diabetes mellitus  | 244 (12.0) |
| Respiratory        | 75 (3.7)  |
| Neurological       | 45 (2.2)  |
| Immunosuppressed   | 5 (0.3)   |
| Haematological     | 1 (0.05)  |

ICU severity scoring

| qSOFA score | n (%)   |
|-------------|---------|
| 0 - 1       | 783 (38.4) |
| 2           | 869 (42.6) |
| 3           | 367 (18.0) |
| Missing     | 21 (1.0)  |

| MPM$_{-III}$, % | n (%)   |
|-----------------|---------|
| 25th percentile | 3.2     |
| 50th percentile | 13.4    |
| 75th percentile | 26.6    |
| 95th percentile | 57.3    |
| Mean (SD), %   | 18.3 (18.2) |
| Pre-ICU LOS (days), mean (IQR) | 1 (0 - 2) |

HAART = highly active antiretroviral therapy; qSOFA = Quick Sequential Organ Failure Assessment; MPM$_{-III}$ = Mortality Probability Assessment Model-III; SD = standard deviation; IQR = interquartile range.
*Unless otherwise specified.
Outcomes

The majority of patients, 43.8% \((n=893/2,040)\), were admitted to ICU from the ED. The pre-ICU LOS for patients admitted from ED corresponded with ED LOS, which reflected that 93.5% \((n=835/893)\) of patients were admitted to ICU within 24 hours. Further admissions from OT and the hospital wards accounted for 35.6% \((n=727/2,040)\) and 20.2% \((n=411/2,040)\), respectively (Table 2).

The median pre-ICU hospital LOS was 1 day (interquartile range (IQR) 0 - 2 days). The median length of ICU stay was 2.4 days (IQR 1.1 - 4.8 days) and the observed ICU mortality was 16.0% \((n=327/2,040)\) (Table 3).

Pre-ICU hospital LOS was not associated with ICU mortality in the unadjusted (odds ratio (OR) 1.00, 95% confidence interval (CI) 0.98 - 1.02; \(p=0.68\); \(n=2,040\)) and fully adjusted logistic regression models (OR 1.00; 95% CI 0.98 - 1.03; \(p=0.90\); \(n=1,981\) using a complete case analysis for missing patient-level covariates). In analyses stratified by admission source, pre-ICU hospital LOS was likewise not associated with ICU mortality for patients admitted from the OT (OR 1.00, 95% CI 0.97 - 1.04; \(p=0.79\); \(n=702\)), ED (OR 0.90; 95% CI 0.60 - 1.35; \(p=0.61\); \(n=871\)), or ward (OR 1.02; 95% CI 0.97 - 1.07; \(p=0.48\); \(n=394\)) (Table 3).

Discussion

In contrast to previous studies from middle- and high-income countries, pre-ICU hospital LOS was not associated with ICU LOS or ICU mortality based in a resource-limited setting. This may be attributed to a number of patient and institutional factors associated with the study population, hospital, and this particular resource-constrained environment.

International data were analysed in the ICON (Intensive Care Over Nations) audit published in 2014, which assessed the worldwide burden of critical illness across 84 countries.\(^{[21]}\) The worldwide statistics for ICU mortality were noted to be 16.2%, with a median ICU LOS of 3 days. The audit included region-specific statistics with African figures for ICU mortality of 16.9% and median ICU LOS of 2 days. The audit was skewed in its representation, with Europe comprising >50% of the study population and Africa representing 1.4%. These results may better reflect European data and should be interpreted with caution when considering Africa. Although there is a paucity of data from African countries regarding in-ICU mortality, our study reported an ICU mortality of 16% and a median ICU LOS of 2.4 days, which parallel international statistics.

Our study population was younger (median age of 35 years) compared with previous studies (median age 50 - 60 years).\(^{[22]}\) Moreover, the study population had less chronic burden of disease (37%), which is likely to influence mortality. In addition, more than 70% of the study population was admitted for surgical rather than medical indications, and of these patients >40% were admitted on the basis of severe acute traumatic injuries. This differs from studies in high-income countries in which chronic disease rates are greater and more patients are admitted with primary medical illnesses and possibly worse baseline physiology. These differences may have a marked impact on patient survival.

Although the study population was noted to have a high burden of HIV, more than 70% of these patients were on HAART. The South African

Table 2. Pre-ICU source of admission \((N=2,040)\)

| Source of ICU referral | n (%) |
|------------------------|-------|
| ED                     | 893 (43.8) |
| ≤1 day                 | 835 (93.5) |
| >1 day                 | 58 (6.5) |
| OT                     | 727 (35.6) |
| Wards                  | 411 (20.2) |
| Missing data           | 9 (0.4) |

ICU = intensive care unit, ED = emergency department, OT = operating theatre.

Table 3. Association of pre-ICU hospital LOS and ICU outcomes

| ICU LOS (days), mean (IQR) | 2.4 (1.1 - 4.8) |
|----------------------------|-----------------|

| Observed outcomes | Alive | Dead |
|-------------------|-------|------|
| ICU mortality, n (%) | 1,713 (84.0) | 327 (16.0) |

| ICU LOS | OR | 95% CI | p-value |
|---------|----|--------|---------|
| Unadjusted mortality model | 1.00 | 0.98 - 1.02 | 0.70 |
| Fully adjusted mortality model | 1.00 | 0.98 - 1.03 | 0.90 |
| Stratified mortality analysis | | | |
| Patients admitted from OT | 1.00 | 0.97 - 1.04 | 0.79 |
| Patients admitted from ED | 0.90 | 0.60 - 1.35 | 0.61 |
| Patients admitted from wards | 1.02 | 0.97 - 1.07 | 0.48 |
| ICU LOS | HR | 95% CI | p-value |
| Unadjusted univariate LOS analysis | 1.00 | 0.98 - 1.02 | 0.70 |
| Fully adjusted LOS model | 1.00 | 0.98 - 1.03 | 0.72 |
| Stratified LOS analysis | | | |
| Patients admitted from OT | 1.01 | 0.98 - 1.04 | 0.50 |
| Patients admitted from ED | 0.80 | 0.57 - 1.13 | 0.21 |
| Patients admitted from wards | 1.02 | 0.97 - 1.06 | 0.46 |

ICU = intensive care unit, IQR = interquartile range; LOS = length of stay; SD = standard deviation; OR = odds ratio; CI = confidence interval; HR = hazard ratio; ED = emergency department; OT = operating theatre.
Surgical Outcomes Study (SASOS) conducted in 2011 noted that despite the high prevalence of HIV in the SA population, HIV infection was not associated with increased in-hospital mortality, and this population may not have a significantly increased risk of mortality based on this comorbidity alone.[23,24]

Previous studies in developed, well-resourced countries varied with regard to pre-ICU placement of patients. This may impact on these study outcomes, as patients in the ED have access to constant surveillance and doctors present in attendance when compared with wards, which may be ill-equipped, with non-specialised staff inexperienced in managing critically ill patients. In turn, benefit may be attributed to the similarity between OT and ICU environments, with care by specialised staff, advanced monitoring and necessary skills available.

However, it is interesting to note that comparable studies conducted in the UK, Portugal, and Australia also demonstrated no significant adverse outcomes on ICU LOS or mortality in association with delayed ICU admissions from ED.[25-27] These studies classified timely admissions as being between 4 and 8 hours, and looked at patients admitted exclusively from the ED. These studies further depict the vast contrast in definitions used by resource-rich and resource-poor environments when classifying pre-ICU LOS and delays in ICU admission.

Moreover, a study conducted at the Royal London Hospital concluded that pre-ICU length of hospital stay is a predictor of hospital but not ICU mortality.[28] This highlights the impact that delays may have on long-term outcome, which our study was not able to evaluate.

In a 2019 publication by Santos et al.,[29] it was noted that critically ill patients with prolonged hospital stays prior to ICU may have worse outcomes as a consequence of delayed monitoring and treatment administration. The outreach system of the ICU team in our study may account for improved outcomes, as patients deemed candidates for critical care admission are followed up and reviewed by the ICU team in ED and other high-fidelity areas of the hospital. The impact of such interventions may play a key role in explaining the better-than-expected outcomes demonstrated in our results. This practice may not be possible in every institution and may impact on patient triage. ICU admissions and outcomes. Furthermore, it is not uncommon for these outlying high-fidelity patients to progress from ICU candidates to no longer requiring ICU, either by improvement or deterioration in clinical condition. Thus, it may be possible that a healthier, more resilient subgroup of patients ultimately fulfill the criteria for ICU admission and are therefore less likely to deteriorate rapidly.

International studies have described comparable practices of informal ICU care being implemented in temporary areas across hospitals, when faced with ICU bed shortages. In the USA, this often involves critical care delivered temporarily outside ICUs or within novel ‘ED long-term acute-care facilities’ which house patients that await hospital beds for longer than 6 hours.[25,28] Similarly, a UK study described the concept of ‘critical care without walls’ as one that is becoming increasingly accepted, and cites the hospital’s theatre suite being used to board patients pending ‘critical care without walls’ as one that is becoming increasingly accepted, and therefore less likely to deteriorate rapidly.

Conclusions

In contrast to previous studies, pre-ICU hospital LOS was not associated with either ICU mortality or ICU LOS in a resource-limited setting. Future studies should aim to include multicentre data and evaluate long-term outcomes.

Declaration. None.

Acknowledgements. The authors acknowledge Dr Nikki Allorto for her work in design and maintenance of the intensive care electronic database (ICED) used in this study, and Dr Carel Cairns for his prior work on data captured on the ICED system.

Author contributions. SK and RW contributed to study design, acquisition of data, interpretation of data, writing and revision of the manuscript. SMS and GLA contributed to the study design, data analysis, interpretation of data and revision of the manuscript.

Funding. This project was supported by grant number K12HS026372 (GLA) from the US Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality.

Conflicts of interest. None.

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Accepted 10 September 2021.