



# Validation of the APACHE-II scoring system in critically ill patients diagnosed with COVID-19 and admitted at a regional-level hospital intensive care unit: A retrospective study

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**Background.** The use of the Acute Physiology and Chronic Health Evaluation II (APACHE-II) scoring system to predict mortality in the intensive care unit (ICU) has not been validated for use in the coronavirus-19 (COVID-19) pandemic in the South African context.

**Objectives.** To provide data on the outcomes and clinical characteristics of ICU patients in a regional hospital diagnosed with COVID-19. The primary objective was to measure the validity of the APACHE-II scoring system in predicting mortality in these patients. Secondary objectives included the description of clinical characteristics, potential risk factors for mortality and length of ICU stay.

**Methods.** This study was a single-centre, retrospective, observational cohort study conducted from 2020 to 2022. Data were obtained from electronic databases and patient records to determine diagnosis of COVID-19, demographics, comorbidities, history, clinical parameters and patient outcome. A receiver operating characteristic (ROC) analysis was performed to assess the discriminative power of the APACHE-II score in predicting mortality.

**Results.** A total of 96 patients with confirmed COVID-19 diagnoses had sufficient data to calculate the APACHE-II score. The observed in-hospital mortality was 57.3%, while the APACHE-II score predicted a mortality of 25%. An ROC analysis showed poor discrimination (area under the ROC curve 0.58). Patients who had increased odds of death were those with increased age: odds ratio (OR) 1.01 (confidence interval (CI) 1.00 - 1.02), and those who were peripartum: OR 4.35 (CI 1.06 - 29.30). Other factors were not significantly associated with mortality. The median (interquartile range) length of hospital stay was 5.00 (4.00 - 9.25) days.

**Conclusion.** The APACHE-II scoring system is a poor discriminator between death and survival in this cohort of COVID-19 ICU patients. ICU patients who were diagnosed with COVID-19 were more likely to die despite a relatively low APACHE-II score. Information regarding clinical characteristics of these ICU patients and their outcomes provides some insight into the nature of the COVID-19 pandemic.

**Keywords.** Critical care; mortality; COVID-19; APACHE; APACHE-II; South Africa.

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## Contribution of the study

While mortality prediction models such as the APACHE-II score are valuable in general ICU populations, their applicability to novel diseases may be limited, as evidenced during the COVID-19 pandemic. Our findings highlight the limitations of these generalized prognostic tools when applied to future emerging diseases.

Towards the end of 2019, a novel respiratory virus was identified that led to the emergence of a disease later named coronavirus-19 (COVID-19).<sup>[1]</sup> On 5 March 2020, the Minister of Health of South Africa (SA) confirmed the first case of COVID-19 in the country, and on 11 March 2020, the World Health Organization declared COVID-19 a global pandemic.<sup>[2]</sup>

COVID-19 placed a massive burden on SA's healthcare system and large numbers of patients suffered significant morbidity and mortality. As of January 2023, the National Policy Data Observatory had reported 4 055 732 confirmed cases, over 500 000 hospital admissions and 102 595 deaths owing to COVID-19 in SA.<sup>[3]</sup> A retrospective cohort study performed in two public hospitals in Pietermaritzburg, KwaZulu-

Natal (KZN), reported 375 patients admitted to the intensive care unit (ICU) with COVID-19 from 5 March 2020 to 30 June 2022.<sup>[14]</sup>

The ability to accurately predict the outcomes of patients assists clinicians in optimising bed utilisation and making clinical decisions which is particularly vital in the context of scarce and expensive critical care resources.<sup>[5]</sup> One way to predict the probable outcomes of patients is to employ scoring systems. The most frequently used and cited scoring system in critical care literature to date is the Acute Physiology and Chronic Health Evaluation II (APACHE-II) scoring system.<sup>[6,7]</sup> Its popularity can be attributed primarily to its capacity to discriminate and risk-stratify critically ill patients.<sup>[8]</sup> This helps to assess the severity of disease, and therefore the extent of diagnostic and therapeutic interventions required, such as the need for intensive care.<sup>[8]</sup> It is an efficient tool that predicts expected mortality.<sup>[6]</sup>

Despite the popularity of the APACHE-II scoring system, it has many pitfalls. One such pitfall is the formulation of the APACHE-II scoring system based on population groups from North America, as well as the age of the scoring system.<sup>[8]</sup> This means it may not be well calibrated to other regions of the world due to the differences in available technology, characteristics of the patient populations, and advancement of critical care practices over the years.<sup>[8]</sup> Subsequently, a number of SA studies were undertaken in attempts to validate the APACHE-II scoring system in the critically ill SA population prior to the COVID-19 pandemic. Arregui *et al.*<sup>[9]</sup> compared disease severity scoring systems of patients in septic shock in three ICUs and found that the APACHE-II scoring system was a useful prognostic tool. Van Der Merwe *et al.*<sup>[10]</sup> found the APACHE-II score to be a good predictor of mortality at a single-centre, tertiary level, predominantly medical ICU in SA. Despite the age of the APACHE-II score, these recent studies have validated the score as a reliable tool in present-day critical care practice.<sup>[9]</sup>

Regarding the use of the APACHE-II score in patients diagnosed with COVID-19, a number of studies demonstrate mixed results. Zou *et al.*<sup>[11]</sup> and Wilfong *et al.*<sup>[12]</sup> compared multiple scoring systems and found the APACHE-II score showed excellent discrimination in this group of patients. In contrast, Stephens *et al.*<sup>[13]</sup> performed a study in the UK which found a higher than predicted mortality for relatively low APACHE-II scores, suggesting poor calibration of the score for COVID-19 patients. This finding was consistent with the results from the UK's Intensive Care National Audit and Research Centre database.<sup>[14]</sup>

Although the COVID-19 pandemic has passed, the risk of future pandemics and novel respiratory viral illnesses still exists. Given the criticisms of the APACHE-II scoring system and the mixed results regarding its utility, further research in this area may prove useful in assessing the reliability and applicability of the APACHE-II score in local clinical practice. The primary aim of this study was to determine the validity of the APACHE-II score as a discriminator between mortality and survival in critically ill COVID-19 patients in a resource-limited SA context. Secondary outcomes included the description of clinical characteristics, documenting length of ICU stay and identification of potential risk factors for mortality this group of patients.

## Ethics

The study was approved by the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal (UKZN) (ref. no. BREC/00004903/2022). The Ethics Committee waived the requirement of individual study participant consent.

## Methods

### Study design and setting

This study was a single-centre, retrospective, observational cohort study performed at Harry Gwala Regional Hospital (HGRH) ICU in Pietermaritzburg, KZN. HGRH, formerly known as Edendale Hospital, is a teaching hospital in the uMngungundlovu District and serves a population of 1.4 million people.<sup>[15]</sup> It has a total bed capacity of 897, which is the 4th largest in SA.<sup>[15]</sup>

Prior to COVID-19, HGRH ICU was a closed unit comprising 6 ICU beds and 3 high-care beds, and was managed by a multi-disciplinary clinical team.<sup>[16]</sup> HGRH ICU provided non-COVID-19 critical care services during the pandemic, and repurposed a general ward into a COVID-19 critical care unit in order to increase bed capacity for management of COVID-19-positive patients. This required the mobilisation and training of additional staff to manage these patients.<sup>[16]</sup> The nurse-to-patient ratio allocated in the COVID-19 and non-COVID-19 ICU was 1:1, while the nurse-to-patient ratio in the respective high-care units was 1:2.<sup>[17]</sup>

All patients who required ICU management regardless of COVID-19 diagnosis were referred to the ICU by means of a written request on a proforma.<sup>[17]</sup> Thereafter, a member of the ICU team reviewed the patient in person and the patient was triaged according to the Society of Critical Care Medicine (SCCM) prioritisation model.<sup>[17]</sup> Patients who were perceived as likely to benefit from admission to the ICU were accepted for admission. However, shortages in ICU resources may have resulted in delays in admission.<sup>[17]</sup> While a bed was unavailable, recommendations and reviews were offered by the critical care team until the patient was admitted to the ICU.<sup>[17]</sup> This was standard of care for triaging of all ICU candidates including those diagnosed with COVID-19.

Inclusion criteria for the study included laboratory-confirmed COVID-19 diagnosis, recorded clinical data within the first 24 hours of ICU admission needed to calculate the APACHE-II score, a known outcome of either in-hospital death or survival to discharge and age of 18 years or older.

This study was conducted over a 2-year time period from 1 July 2020 to 30 June 2022. A 2-year period was chosen to achieve a population sample large enough to achieve adequate statistical power for the study. During this time period, COVID-19 laboratory tests were still mandatory for referral to ICU.

Patients excluded from the study were those who were not admitted to the ICU, did not have a confirmed positive diagnosis of COVID-19, did not have a recorded outcome of in-hospital death or survival to discharge, did not have sufficient clinical information recorded from the first 24 hours of admission to ICU to calculate the APACHE-II score, or were below 18 years of age.

## Data collection and management

The research instrument used was the Integrated Critical Care Electronic System (iCES) database, an existing database used by ICUs in the Pietermaritzburg Metropolitan Hospital Complex. The iCES database (BREC ref. no. BCA 211/14) is an electronic database system that is updated by doctors in the ICU. It contains information regarding referral, admission and discharge information as well as the variables required to calculate the APACHE-II scores.

The admission information of all patients in the HGRH ICU was entered into the iCES database. This information included patient name, date of birth, history of presenting problem, background medical

comorbidities, previous surgical history, patient vital signs, clinical examination, blood test results, and patient discharge summaries.

The data from the iCES database was extracted and exported into a Microsoft Excel Spreadsheet. The data were analysed and the APACHE-II score of each patient was manually calculated using the APACHE-II scoring tool as reproduced in Appendix A as per Knaus *et al.*<sup>[6]</sup> The predicted mortality was derived according to the APACHE-II scores as shown in Appendix B (INSERT URL).<sup>[6]</sup>

All data were password-protected with twofold authentication and accessible to the primary investigator only. The data were anonymised to prevent identification of patients and their personal data.

## Sample size

A significance level or alpha of 0.05 was used with a statistical power of 80%. Previous studies demonstrated an estimated mean APACHE-II score of 14.5, with a predicted mortality of 25%.<sup>[11,12]</sup> Stephens *et al.*<sup>[13]</sup> and Yang *et al.*<sup>[21]</sup> observed a higher actual mortality of 37.6% and 61.5%, respectively, which is a mean excess of 27.55% mortality. Assuming an observed increase in mortality of 25% or more than predicted mortality, then a population sample of greater than 90 was required in order to demonstrate statistical significance.

## Statistical analysis

Statistical analysis was performed using R (R project, Austria; version 4.4.1). Descriptive statistics were used to present the data. Categorical data were described using frequencies and percentages and analysed by Fisher's exact or chi-square test. Numeric data were evaluated for normality, and normally distributed data were described using means with standard deviations and analysed using Student's t-test. Non-normally distributed data were described using medians with interquartile ranges (IQRs) and analysed using the Mann-Whitney *U*-test.

A receiver operating characteristic (ROC) curve of the APACHE-II score was examined and Youden's index was used to determine the best cut-off for determining mortality.

Means, as well as medians, for both predicted and observed mortality were calculated in order to draw comparisons with previous studies. The Mann-Whitney *U*-test was used to determine association between predicted and observed mortality. In addition, unadjusted and multivariable logistic regressions were performed, and odds ratios (OR), 95% confidence intervals (95% CI) and *p*-values were calculated for both the univariable and multivariable analyses.

A *p*-value of 0.05 was considered the cut-off for statistical significance.

## Results

During the study period, 1 163 patients were admitted to HGRH ICU. A total of 167 of the patients admitted to HGRH ICU had a laboratory-confirmed diagnosis of SARS CoV-2 infection; however, 71 of those patients did not have adequate clinical information or records and a total of 96 patients fulfilled the inclusion criteria for the study. A larger population sample would have been preferable; however, this was difficult to achieve in practice owing to the single-centred and exploratory nature of this study.

The demographic and clinical characteristics of the patients included are summarised in Table 1. Unadjusted logistic regression was also performed, and results are summarised in Table 2.

The mean APACHE-II score for the survivors' group was 15.8, while the mean for the non-survivors' group was 18.5. The mean (SD) APACHE-II score for the whole cohort was 17.3 (7.3). This translated to

a predicted mortality of ~29%. The observed mortality was 57.3%, more than double the predicted mortality. The Youden's Index did not produce a useful cut-off for sensitivity or specificity of the score.

There was a slightly greater overall predominance of female patients, *n*=55; 57.3%) compared with male patients (*n*=41; 42.7%) admitted to the ICU with COVID-19. Female gender was not a statistically significant risk factor for mortality (OR 1.03; CI 0.53 - 1.80).

Increased age increased the odds of death and the association was statistically significant (mean 50.6 years for non-survivors v. 44.4 years for survivors (*p*=0.04)) in our cohort (OR 1.01; CI 1.00 - 1.02). In addition, the peripartum period (OR 4.35; CI 1.06 - 29.30) significantly increased the odds of death. There were no statistically significant associations between hypertension (OR 1.61; CI 0.69 - 3.90), obesity (OR 1.06; CI 0.42 - 2.76), diabetes (OR 0.91; CI 0.68 - 1.22) or HIV (OR 3.17; CI 0.91 - 14.80) and mortality. The *p*-values for chronic respiratory disease, thyroid disease, neuropsychiatric disorders and connective tissue disorders were not calculable owing to the low prevalence within the sample population. The need for emergency surgery also did not have a statistically significant association with mortality (OR 0.84; CI 0.62 - 1.15).

The median (IQR) length of ICU stay was 5.00 (4.00 - 9.25) days. Patients with an in-hospital stay of <5 days had a mortality of 45.9%, while those who stayed ≥10 days had a mortality of over 62%; however, these were not statistically significant associations (OR 1.00; CI 0.98 - 1.01).

During the first, second and third waves of COVID-19, there were 16 (mortality of 64.0%), 17 (85.0%) and 16 (55.2%) in-hospital deaths, respectively, while there were only 6 (27.3%) in total during the fourth and fifth waves. Although, the mortality was highest in the second wave of COVID-19 (85.0%), these associations were not of statistical significance, after adjusting for other covariables.

## Discussion

The APACHE-II scores in our study were similar to the results of a multicentre study in KZN conducted a few years prior to the COVID-19 pandemic by Wise *et al.*<sup>[18]</sup> in which they calculated a median APACHE-II score of 17.0. HGRH was a significant contributor to that study and therefore the APACHE-II scores from that research serve as a good comparator. Furthermore, the similarities in population characteristics suggest some generalisability of our findings to the rest of the KZN region.

The observed in-hospital mortality of COVID-19 patients admitted to HGRH ICU was 57.3% despite a predicted mortality of 23.49% based on the median APACHE-II score of 16. This was significantly higher than the observed mortality in previous studies conducted across SA which found mortality to range between 17.5% to 33.9%.<sup>[18-20]</sup> The discrepancy between the observed mortality and the predicted mortality category suggests poor discrimination of the APACHE-II scoring system for predicting mortality in this cohort. This may be related to the pitfalls of the APACHE-II scoring system related to novel diseases, regional differences and resource availability.<sup>[8]</sup>

ROC analysis demonstrated poor discrimination by the APACHE-II scoring system as illustrated by the area under the curve (AUC) of 0.59. The greatest discrepancy between the observed mortality and the predicted mortality was found in patients with a low APACHE-II score. These findings were consistent with those of Stephens *et al.*<sup>[13]</sup> and Yang *et al.*,<sup>[21]</sup> which demonstrated a mean APACHE-II score of 16.0 and median APACHE-II score of 17.0, respectively. Stephens *et al.*<sup>[13]</sup> and Yang *et al.*<sup>[21]</sup> observed a higher actual mortality of 37.6% and 61.5%, respectively, despite a predicted mortality of 25%. ROC analysis was not performed in either

## RESEARCH

**Table 1. Baseline characteristics of COVID-19 patients admitted to HGRH ICU**

Variable	Total patients (N=96), n (%)	Non-survivors (n=55), n (%)	Survivors (n=41), n (%)	p-value
<b>Demographics</b>				
Age (years), median (IQR)	49.5 (35 - 60)	54 (38.5 - 63)	43 (34 - 55)	0.039*†
<b>Gender</b>				
Male	41 (42.7)	22 (53.7)	19 (46.3)	0.677
Female	55 (57.3)	33 (60.0)	22 (40.0)	
<b>Comorbidities</b>				
Nil comorbidities	24 (25.0)	11 (45.8)	13 (54.2)	0.236
Hypertension	34 (35.4)	22 (64.7)	12 (35.3)	0.292
Diabetes mellitus	18 (18.8)	8 (44.4)	10 (55.6)	0.292
Obesity (BMI (kg/m <sup>2</sup> ) >35)	24 (25)	14 (58.3)	10 (41.7)	1.00
HIV	14 (14.6)	11 (78.6)	3 (21.4)	0.142
Peripartum	12 (12.5)	10 (83.3)	2 (16.7)	0.065
Chronic respiratory disease	3 (3.1)	3 (100)	0	NC
Hypo-/ hyperthyroid	1 (1.0)	0	1 (100)	NC
Neuropsychiatric disorders	3 (3.1)	0 (0.0)	3 (100)	NC
Connective tissue disorders	4 (4.2)	1 (25.0)	3 (75.0)	NC
<b>Operative status</b>				
Non-operative	77 (80.2)	45 (58.4)	32 (41.6)	0.796
Emergency surgery	19 (19.8)	10 (52.6)	9 (47.4)	
<b>Length of ICU stay</b>				
Days (median, IQR)	5 (4 - 9.25)	6 (4 - 10)	5 (3 - 9)	0.199‡
< 5 days	37 (38.5)	17 (45.9)	20 (54.1)	
5-9 days	35 (36.5)	23 (65.7)	12 (34.3)	
≥ 10 days (10 - 42 days)	24 (25)	15 (62.5)	9 (37.5)	
<b>APACHE-II Score</b>				
APACHE-II Score (mean, SD)	17.3 (7.30)	18.5 (7.77)	15.8 (6.37)	0.132*
Predicted mortality (m, SD)	30.0 (19.95)	29.4 (20.18)	30.9 (19.87)	
APACHE-II Score, median (IQR)	16 (13 - 21.25)	16 (14 - 23.5)	15 (12 - 19)	
Predicted mortality (%), median (IQR)	23.49 (5.05 - 94.05)	23.49 (16.53 - 37.13)	20.97 (18.65 - 42.43)	
<b>Approximated in-hospital mortality rates (%)</b>				
0 - 10	15 (15.6)	10 (67)	5 (33)	0.805‡
10 - 20	25 (26)	13 (52)	12 (48)	
20 - 30	19 (19.8)	12 (63)	7 (37)	
30 - 40	13 (13.5)	7 (54)	6 (46)	
40 - 50	7 (7.3)	4 (57)	3 (43)	
50 - 60	9 (9.4)	6 (67)	3 (33)	
60 - 70	2 (2.1)	0	2 (100)	
70 - 80	4 (4.2)	1 (25)	3 (75)	
80 - 90	0	0	0	
>90	2 (2.1)	2 (100)	0	
<b>Mortality during each wave</b>				
Wave 1 (Mar 2020 - Nov 2020)	25 (26)	16 (64.0)	9 (36.0)	0.002†‡
Wave 2 (Dec 2020 - Apr 2021)	20 (20.8)	17 (85.0)	3 (15.0)	
Wave 3 (May 2021 - Oct 2021)	29 (30.2)	16 (55.2)	13 (44.8)	
Wave 4 - 5 (Dec 2021 - June 2022)	22 (22.9)	6 (27.3)	16 (72.7)	

HGRH = Harry Gwala Regional Hospital; ICU = intensive care unit; IQR = interquartile range; BMI = body mass index; APACHE-II score = Acute Physiology and Chronic Health Evaluation II; SD = standard deviation; NC = not calculable; chronic respiratory disease = chronic obstructive airways disease/asthma, TB and *Pneumocystis pneumonia*; neuropsychiatric disorders = bipolar, schizophrenia, epilepsy.

\*Mann-Whitney test.

†Statistically significant.

‡Chi-square.

of these studies. In contrast, the studies by Zou *et al.*<sup>[11]</sup> found a mean APACHE-II score of 23.2 which predicted a mortality of 40% and a ROC AUC of 0.966 (95% CI 0.94 - 0.99). However, only 50% of the patients included in that study were described as being critically unwell, which may raise some concerns regarding the application of the APACHE-II score.<sup>[13]</sup> Wilfong *et al.* also found the APACHE-II score to be a good discriminator

between mortality and survival in which patients with a score of less than 10 survived to hospital discharge and demonstrated a ROC AUC of 0.851 (95% CI 0.786 - 0.917).<sup>[12]</sup> However, the primary outcome was the need for ICU admission rather than for predicting mortality.<sup>[12]</sup>

Our study identified increased age as a significant risk factor which is consistent with the systematic review by Parohan *et al.*<sup>[22]</sup>

**Table 2. Unadjusted and multivariable logistic regression for predictors of mortality of patients with COVID-19**

Predictors	Unadjusted		Multivariable	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.03 (1.00 - 1.06)	0.046	1.01 (1.00 - 1.02)*	0.017*
<b>Gender</b>				
Female	1.00	1.00	1.00	1.00
Male	1.30 (0.57 - 2.95)	0.535	1.03 (0.53 - 1.80)	0.770
<b>Comorbidities</b>				
Nil	0.54 (0.21 - 1.37)	0.193	1.30 (0.93 - 1.84)	0.119
Hypertension	1.61 (0.69 - 3.90)	0.278	1.05 (0.80 - 1.38)	0.704
Diabetes mellitus	0.53 (0.18 - 1.48)	0.226	0.91 (0.68 - 1.22)	0.505
Obesity (BMI >35)	1.06 (0.42 - 2.76)	0.905	0.94 (0.73 - 1.22)	0.645
HIV	3.17 (0.91 - 14.80)	0.094	1.40 (1.02 - 1.93)	0.039*
Peripartum	4.35 (1.06 - 29.30)	0.069	1.82 (1.18 - 2.79)	0.007*
<b>Operative status</b>				
Non-operative	1.00	1.00	1.00	1.00
Emergency surgery	0.79 (0.29 - 2.20)	0.647	0.84 (0.62 - 1.15)	0.271
<b>Length of ICU stay</b>				
Days	1.01 (0.95 - 1.08)	0.755	1.00 (0.98 - 1.01)	0.552
<b>Mortality during each wave</b>				
Wave 1 (Mar 2020 - Nov 2020)	1.00	1.00	1.00	1.00
Wave 2 (Dec 2020 - Apr 2021)	3.19 (0.79 - 16.40)	0.123	1.16 (0.87 - 1.55)	0.319
Wave 3 (May 2021 - Oct 2021)	0.69 (0.23 - 2.06)	0.511	0.92 (0.70 - 1.20)	0.532
Wave 4 - 5 (Dec 2021 - June 2022)	0.21 (0.06 - 0.70)*	0.014*	0.75 (-0.55 - 1.03)	0.073

OR = odds ratio; CI = confidence interval; ICU = intensive care unit.  
\*Statistically significant.

Pregnancy was also a statistically significant risk factor for mortality; these findings are in keeping with the study by Barbera *et al.*<sup>[23]</sup> and Wang *et al.*<sup>[24]</sup> which demonstrated increased odds of severe disease and mortality.

The associations with a point estimate above 1 included the risk factors of female gender, hypertension, obesity and HIV. However, these were not statistically significant. This was evident in the wide confidence intervals and *p*-values that were greater than 0.05.

The median (IQR) length of ICU stay was 5.00 (4.00 - 9.25) days. In contrast, the median length of ICU stay found by Stephens *et al.*<sup>[13]</sup> was 14 days, which was significantly longer;<sup>[13]</sup> 17 of the 37 patients who had an ICU stay of less than 5 days died (45.9% mortality) compared with the 38 out of the 59 patients who had an ICU stay of 5 days or longer (greater than 64.4% mortality). This suggested that patients who had longer ICU stays were less likely to survive.

The mortality rates during the first, second and third waves of COVID-19 were ~64%, 85% and 55%, respectively. These were much higher compared with data from the ICUs in KZN prior to COVID-19.<sup>[18]</sup> The mortality then dropped down to 27.3% in the fourth and fifth wave. Jassat *et al.*<sup>[25]</sup> also noted similar changes in incidence and disease severity of COVID-19 during each of the pandemic waves.

Trends in mortality are notoriously difficult to interpret. Possible reasons for the observed trends may include the varied implementation of isolation and personal protection procedures, the use of non-invasive ventilation, high flow nasal oxygen, prone positioning, as well as the use of glucocorticoids.<sup>[26]</sup> Improved survival rates of critical care patients were reported over the course of the pandemic adjusting for age, sex and comorbidity which suggested a change in the COVID-19 disease or improved effectiveness of medical management.<sup>[26]</sup>

Over the course of 2021, multiple vaccines were developed and became widely available for the management of COVID-19; additionally, the SARS-CoV-2 virus continued to mutate.<sup>[27,28]</sup> These two factors may have contributed to the reduction in the severity of the disease, the number of ICU admissions and in-hospital mortality.<sup>[27,28]</sup> This should be considered when applying the findings of our study to future critically ill COVID-19 patients as the SARS-CoV-2 virus continues to mutate, and the management of COVID-19 is updated.

### Study strengths and limitations

The present study was able to achieve the required population sample of greater than 90 to achieve statistical power for a mortality difference of more than 25% between predicted mortality and observed mortality. However, a larger sample size would provide greater insight, especially in terms of identifying significant risk factors. Furthermore, the single-centred nature of the study means that the results of the study may not be representative or broadly generalisable to other populations. The study relied on historical mortality rates as a control group for the COVID-19 group. Further validity may have been improved with a concurrent non-COVID-19 control group instead.

The results of the present study should be considered in light of the novel nature of COVID-19 illness. As the pandemic unfolded, guidelines were continuously developed, updated and implemented. There were many resource limitations such as the availability of high-flow nasal oxygen, non-invasive ventilation, mechanical ventilators, ICU beds and appropriate ICU staffing.

There were periods in which hospital resources were overwhelmed and patients were triaged in terms of those who were most likely to have a good outcome as well as the need for ventilatory support. Patients who were severely ill but were eligible for ICU admission were sometimes not admitted to the ICU due to a lack of ICU beds.

ICU bed capacity was increased but this also resulted in increased patient-to-nurse and patient-to-doctor ratios. Resource constraints meant that not all patients may have received the best medical therapy. Furthermore, the high infection risk and limited availability of personal protective equipment meant that COVID-19 patients were not seen as frequently as patients who did not have COVID-19 and admission times were often delayed compared with patients without COVID-19. Waiting times in the general wards and emergency departments were sometimes prolonged owing to a lack of ICU beds, which may have resulted in suboptimal care.

Selection bias may have been present, as the database and clinical records may not have contained all the data required to calculate the APACHE-II score, resulting in exclusion of these patients from the study. Further selection bias may have been present in the exclusion of patients who were not known to have survived or died. Survival bias may exist in that some eligible patients were not admitted to ICU due to a lack of ICU bed availability.

Lead-time bias may have been present, as patients who were transferred to HGRH from other ICUs or hospitals may have had a higher mortality rate than predicted by the APACHE-II scoring system. Accurate data collection was dependent on the clinicians working in ICU which was subject to human error.

## Conclusion

In the present study's setting, the APACHE-II scoring system was a poor discriminator between mortality and survival at hospital discharge among COVID-19 ICU patients. Patients who were diagnosed with COVID-19 were much more likely to die, despite a relatively low APACHE-II score. Information regarding clinical characteristics and ICU outcomes of these patients provides some insight into the nature of the COVID-19 pandemic.

**Declaration.** This research study was conducted in partial fulfilment of YC's MMed degree at UKZN.

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**Author contributions.** YC wrote the protocol, interpreted the data and wrote the first draft, supervised by JI. CC performed statistical analysis. YC wrote the final draft and all authors assisted with and approved the final manuscript.

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