Retrospective evaluation of the APACHE II critical care scoring system in a multidisciplinary intensive care unit

Kenalemodisa Lindiwe Mogotsi

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Anaesthesiology.

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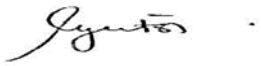
Declaration

I, Kenalemodisa Lindiwe Mogotsi, declare that this research report is my own unaided work. It is being submitted for the Degree of Master of Medicine in the branch of Anaesthesiology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



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Abstract

Background

APACHE II is one of the oldest scoring systems and it is still used globally due to its availability and ease of use. A performance evaluation is necessary when using a critical care scoring system in any particular ICU and patient population.

Objective

The aim of this study was to evaluate the performance of the APACHE II scoring systems in a multidisciplinary ICU at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

Methods

A retrospective evaluation of ICU patients' records between February and May 2018 was conducted. Follow-up was until death or hospital discharge.

Results

Of the 256 records included, 44.1% were medical and 55.9% were surgical admissions. The mean (SD) age of the patients was 43.7 (18.3) years and for the APACHE II score was 20.3 (8.4). The mean (SD) predicted mortality rate was 39.2% (23.9%) and the actual mortality rate was 33.0%. The standardised mortality ratio was 0.84 and the correct classification rate was 71%. Discrimination was good (AUROC = 0.8087), as was calibration at 10.55 (p=0.2284) for ICU mortality and 9.95 (p=0.2684) for mortality at ward discharge. The median (IQR) APACHE II score for the HIV negative and positive groups was 19.0 (13.0 – 25.0) and 23.5 (17.5 – 30.0), respectively. The predicted mortality rate was 36.3% and 49.4% and the actual mortality rate was 32.3% and 40.0% in the HIV negative and positive groups, respectively.

Conclusion

This study found a good discrimination and calibration of the APACHE II score in the multidisciplinary ICU at CMJAH.

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Abbreviations

APACHE	Acute Physiology and Chronic Health Evaluation
ART	Anti-retroviral treatment
AUROC	Area under the receiver operating characteristic
CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
MODS	Multiple Organ Dysfunction Score
MPM	Mortality Probability Model
ROC	Receiver operating statistic
SA	South Africa
SAPS	Simplified Acute Physiology Score
SMR	Standardised Mortality Ratio
SOFA	Sequential Organ Function Assessment

Statement

The Research Report consists of a literature review, draft article, study proposal and appendices. The study proposal is included for background reference and is not for examination.

The formatting of this Research Report complies with the University of the Witwatersrand's Style Guide for Theses, Dissertations and Research Reports. The formatting of the draft article may differ from the author guidelines of the South African Journal of Critical Care, the journal to which it is intended to be submitted, in order to comply with the university's style guide.

Section 1: Review of the literature

1.1 Introduction

Critical care is a fast-growing specialty, and it has become an essential part of global health care systems (1). Due to the increase in the demand for critical care services and the associated resource burden, the need for efficacious allocation of this scarce resource has become of paramount importance (2).

Systematic decision-making processes need to take place in order to decide about bed allocation to some patients over others. A variety of factors are taken into consideration when allocating intensive care unit (ICU) resources (3), and critical care scoring systems are one of the tools used to facilitate this process (4, 5).

These critical care scoring systems are primarily used to predict mortality of patients admitted to ICU, based on severity of disease and other variables (4). There are many critical care scoring systems in use, the Acute Physiology and Chronic Health Evaluation (APACHE) II, APACHE IV, Simplified Acute Physiology Score (SAPS) III and Sequential Organ Function Assessment (SOFA) score, being the most commonly used critical care scoring systems worldwide. These critical care scoring systems have been widely validated for different intensive care populations (6). The APACHE II score, which will be the focus of this research, assesses the severity of disease and provides an estimate of in-hospital mortality (7).

To reliably use the correct scoring system in any particular ICU and patient population, a performance evaluation is necessary (8). As the case-mix may be different from the one used during the development and validation of the scoring system, this may affect the accuracy of the scoring system in different populations (9). APACHE II is one of the oldest scoring systems and it is still used globally due to its availability and ease of use and has been validated in many single centre ICUs (10-13).

In the next section critical care will be discussed with regards to its history, costs, bed distribution, and patient selection. Then critical care scoring systems will be discussed, the different types (with a focus on APACHE II), how they are

classified, their uses, and their validation internationally and in South Africa (SA). Lastly there will be a focus on the burden of HIV in SA and its effect on critical care.

1.2 Critical care

1.2.1 The role and need for critical care historically and in the modern hospital

Critically ill patients require intense specialised treatment from a coordinated team of highly specialised individuals with close observation and monitoring. This is usually performed in specialised hospital wards called ICUs (14). Patients admitted to ICUs usually have acute life-threatening medical and surgical conditions, compromising one or more organ systems and require artificial organ support. The main aim of ICU care is to provide organ support while diagnosing and treating the underlying disease process (1,14). The need for a separate ICU in hospitals evolved due to the realisation that critically ill patients had better outcomes with closer monitoring and treatment by dedicated staff (14).

The idea of creating a separate area near the nurses' station to take care of severely wounded soldiers after battle and surgery was credited to Florence Nightingale, during the Crimean War in the 1850s. It is believed that this is where intensive care first started (15). This concept was also applied in World War I in the 1910s for severely injured soldiers. This was followed by Dr Walter Dandy at Johns Hopkins Hospital in 1923, who separated his critically ill postoperative neurosurgical patients in order to improve postoperative care (15). Severely ill medical patients during the poliomyelitis epidemic requiring ventilation, which was initially done manually until mechanical ventilators were developed, was done in the 1950s in specialised units called intensive therapeutic units (15).

Critical care has evolved exponentially, with many advancements in diagnostic, monitoring and therapeutic approaches being made. It is one of the fastest-growing fields of medicine, and the ICU has an important role to play in the structure and operation of every hospital globally (1, 14).

1.2.2 The cost of ICU

ICUs are one of the key cost drivers of healthcare spending and have thus come under the spotlight in debates on healthcare economics (16). This has led to rationing of healthcare resources to meet the demands on the healthcare system (16). Due to population growth, increased life expectancy, and improved access to healthcare resources, healthcare expenditure is growing in both developed (16) and developing countries (17). This has increased the demand for measures to reduce escalating healthcare costs (16).

1.2.3 ICU bed availability in South Africa

ICU beds in SA are a limited resource; this is mainly due to the steadily increasing burden on the health care system. The number of people depending on this system has increased drastically, secondary to a larger proportion of the population being able to access the system after the end of apartheid, as well as the influx of immigrants seeking better social circumstances in SA (17).

A national audit of critical care resources undertaken by the Critical Care Society of Southern Africa done by Bhagwanjee and Scribante in 2005 (18), showed that 23% and 84% of public and private hospitals, respectively had ICU and High care units, resulting in 4168 beds. Fifty seven percent of ICU beds in SA are in the private sector (18). Majority of ICU beds (86%) were located in three of the nine provinces in SA, namely Gauteng, KwaZulu Natal and Western Cape, this uneven distribution of ICU beds compounds the problem of limited ICU beds in SA.

A desktop audit done by Naidoo et al in 2013 (19), identified 4719 ICU beds in SA during the period 2008 – 2009, 75% of beds were located in the private sector. And the distribution of beds across the country remained the same, mostly in the same three provinces mentioned above (19).

1.2.4 Selecting patients for admission to the ICU

With demand for ICU beds often exceeding supply, bed allocation in times of limited bed availability is a crucial and sensitive issue (2). According to the Values, Ethics, and Rationing in Critical Care Task Force, “healthcare rationing is the allocation of potentially beneficial healthcare services to some individuals in the

face of limited availability that involves the withholding of those services from other individuals" (20).

Intensivists assess a variety of factors before granting or refusing a patient admission to an ICU (2). The Society of Critical Care Medicine (21) recommends guiding ICU admission based on specific patient needs that can only be addressed in an ICU environment such as life support therapy and available clinical expertise. An assessment of how the patient would potentially benefit from ICU admission as well as an overall prediction of their outcome based on the severity of the disease, is useful in making triage decisions (22). Predictions of outcome are often made using various critical care scoring systems (22).

1.3 Scoring systems

Critical care scoring systems reflect measures of disease severity and are typically used to predict mortality of patients admitted to the ICU (8). The characteristics of an ideal scoring system, according to Bouch and Thompson (8) are:

- "easily/routinely recordable variables;
- well calibrated;
- have a high level of discrimination;
- applicable to all patient populations,
- can be used in different countries;
- have the ability to predict functional status or quality of life after ICU discharge."

Although an ideal critical care scoring system has yet to be developed (8), there are many validated scoring systems in current use.

1.3.1 Classification of critical care scoring systems

The classification of scoring systems can be done in a variety of ways. Firstly, they can be classified according to when the variables required for the calculation of the score were collected, either on admission (first day) or repetitive scores (23). Secondly, they can be classified according to whether the score was developed subjectively, using variable weighting decided upon by experts; or objectively,

using variable weighted determined by regression analysis from a large patient database (23). Thirdly, scoring systems can be designed for use in single organ failure or multiple organ failure syndromes (5). These different types of scoring systems are complementary rather than competitive or mutually exclusive, therefore, may be used together at the same time (22). A few of the commonly used general scoring systems will be briefly discussed, followed by an in-depth discussion of APACHE II in section 1.3.4.

The SOFA score was previously known as the Sepsis-Related Organ Failure Assessment, which was developed in 1994. It was later renamed because the score has relevance for non-septic patients as well. It aimed to objectively and quantitatively describe the degree of organ dysfunction in a group of patients or in an individual patient over time (24). Six organ systems were selected to make up the SOFA score. A score of 0 (normal function) to 4 (most abnormal) was used for each organ. The worst value for each day was used (24).

Developed in 1984, as a derivation of the APACHE score, the SAPS is a physiologically based first-day scoring system that assesses 14 variables, including age but with no input for pre-existing disease. As with the APACHE score, the worst values on admission are used to calculate the probability of death (25). SAPS II includes a pre-admission status and 17 other variables, which include age (26). The latest revision is SAPS III, which is still used widely and offers much easier integration with electronic health records than the APACHE score (27).

The Mortality Probability Model (MPM) is an alternative to APACHE and SAPS, with scores being able to be calculated on admission, at 24 hours and at 72 hours. The first version of MPM was published in 1985 and was based on two models; an admission model and a 24-hour model including chronic health status and acute diagnosis (28). The MPM II was developed in 1993 also containing admission, 24-hour and 72-hour scores and includes therapeutic variables (29). It is much easier to collect information and calculate than other scoring systems, as it does not use any laboratory data, only clinical and physiological variables. The MPM may be used to calculate mortality risk throughout ICU stay (29).

Lastly, the Multiple Organ Dysfunction Score (MODS) is a repetitive score similar to the SOFA score. It also uses six organ systems, namely the respiratory, cardiovascular, renal, neurological, hepatic and hematological systems to calculate a daily score (30). It can, therefore, be used chart the patient's progress in the ICU. A final MODS score can be calculated by adding the sum of all the worst scores during the ICU stay (5). This score is still used in some units, particularly trauma units, however, it has largely been superseded by the SOFA score (30).

1.3.2 Uses of scoring systems

As mentioned in Section 1.1 critical care scoring systems are used to predict mortality in ICU patients, as audit tools to assess the performance of an individual ICU over time, for comparison of one ICU with other ICUs (4), they can also be used as tools for research purposes (6). Additionally, although not designed for this purpose, they have been used to assist in triage decisions (4, 23).

Large numbers of patients from several ICUs are generally used to develop a scoring system, using prospectively collected data. This data commonly includes chronic and current health, vital signs, and laboratory data. These are used to calculate a numeric score and a mortality prediction signifying the patients' severity of illness. (6).

When using scoring systems as an audit tool, an individual ICU's performance can be compared to a "standard" ICU. The standard ICU is defined as the theoretical ICU used to formulate the scoring system. Many ICUs are used to create a scoring system. For example, the authors of the APACHE II score used the ICUs of 13 hospitals in its formulation (7).

Performance is assessed using indicators such as the standardised mortality ratio (SMR), which is a ratio of the actual mortality per scoring category versus the expected "standard" ICU mortality for that category (5). For example, if the SMR is one for patients with an APACHE score of 20, the number of actual deaths is equal to the expected number of deaths for patients with an APACHE score of 20 in the ideal "standard" ICU. This would mean that the ICU in question has an

adequate performance. If, however, the SMR is greater than one, the death rate is higher than expected and the ICU is performing poorly (31).

When comparing one ICU to another, looking only at the mortality rate of one ICU in comparison to another ICU is not appropriate because ICU case mix, access to therapy, ICU staff, administration differences and discharge policies of the unit can affect the mortality rate in ICU. Using the SMR allows for these variations to be accounted for and a better assessment and meaningful comparison can be made (32).

SMR is also a crude measurement of calibration; calibration is one of the two methods used to validate a scoring system (5) and will be discussed in Section 1.4. Although it is generally a good instrument, the SMR has limitations including poor calibration, questionable accuracy in certain case-mixes, and inability to generalise this ratio to other countries (32).

Researchers can use critical care scoring systems to evaluate different interventions applied in ICU between patients with similar risks as quantified by critical care scoring systems (6). They can be used to compare patient populations in clinical trials and identify patients eligible for inclusion (22).

Critical care scoring systems can assist in selecting patients for admission by estimating in-hospital mortality; this is done by using routinely collected clinical and biochemical variables in the ICU. This data is then used to calculate a score, usually given as a number, and an associated probability of in-hospital mortality (8). Patients with higher scores have a higher mortality risk and, therefore, may be too severely ill to be considered for ICU admission. A patient with a lower score and higher survival probability can then preferentially receive the ICU bed in this situation (2).

The Critical Care Society of Southern Africa commented in their 2019 guidelines (33) that although critical care scoring systems are desirable to assist in triage decisions, they are inadequate if used alone. In summary, critical care scoring systems assist in allocating the highly sought-after ICU beds in critically ill patients thereby ensuring efficacious use of this resource. They do however, come with limitations (6, 22).

1.3.3 Factors influencing the accuracy of scoring systems

When using a scoring system and when interpreting the score there are important factors concerning the input variables to be considered. Factors such as inter and intra-observer reliability (34), data collection, and entry errors need to be taken into account (4). These factors affect the quality of the input variables and, therefore, the reliability and accuracy of the score generated by the scoring system (22).

Scores such as the APACHE II score are admission scores, and the timing of the recording as well as the severity of the relevant physiological variables is critical in the accuracy of the score. For example, pre-ICU admission resuscitative efforts, whether in the ambulance, the emergency department, or the medical and/or surgical wards, affect the admission variables when patients are eventually admitted into the ICU and, therefore ultimately the calculated APACHE or SOFA score. This is known as lead-time bias which affects variables, such as blood pressure, heart rate, respiratory rate, pH, blood glucose, and oxygenation most rapidly (35).

A high score may not always mean a high mortality either because the disease is self-limiting, or it can be treated rapidly and adequately. An example of this is diabetic ketoacidosis. Although patients with diabetic ketoacidosis present with a high score, with appropriate management, they can return to a normal physiological status quickly (8) and thus do not necessarily have a high mortality. The score is also not a linear scale, meaning there is not a linear relation between score and predicted mortality. If one doubled the score given by the scoring system, for example, from 10 to 20 the patient does not stand twice as high a risk of dying (8).

ICU case-mix is another important, influential factor; it refers to the characteristics of patients admitted to an ICU, and the case-mix may be different from the one used during the development and validation of the scoring system (5,9). Different ICUs admit patients with a variety of clinical conditions from different specialties and with varying severity of illness. As a result, the patient population in an ICU in a large tertiary centre varies from that of a unit in a district general hospital ICU. It has been noted that university-affiliated ICUs tend to admit sicker patients

compared to their regional or local counterparts (5). The predictive value of the scoring systems has been shown to deteriorate with differences in patient risks (36).

1.3.4 The APACHE scoring system

The APACHE score is a physiologically based scoring system originally developed in 1981 by Knaus et al (37). It comprises of a score and a calculated percentage probability of mortality. The initial APACHE score was divided into two sections; a physiological score to determine the acute illness status of the patient and a pre-admission evaluation to determine the chronic health status of the patient (37).

Thirty-four deranged physiological measurements from the seven major physiological systems (neurological, cardiovascular, respiratory, gastrointestinal, renal, metabolic, and haematological) are used to determine the physiological score and this is then reflected as a numerical sum. The pre-admission health status is allocated according to the patients' medical history it is then reflected as a letter (A, B, C, or D) representing a range, A representing excellent health to D representing chronic organ dysfunction (37).

In 1985 the APACHE II scoring system was developed as an upgrade from APACHE I by Knaus et al (7). The changes made to the score included a reduction in the number of variables from 34 to 12, some were reweighted, additional weightings were added for end-organ dysfunction, and emergency or non-operative admission (7). In addition to the acute physiology variables, age and the presence of severe chronic organ dysfunction or immune suppression were also incorporated (7).

The physiological variables in the APACHE II score are; rectal temperature, mean arterial pressure, heart rate, respiratory rate, oxygenation, arterial pH, serum sodium, potassium, creatinine, bicarbonate, hematocrit, white blood count, and Glasgow Coma Scale. The sum of these variables indicates the total Acute Physiology Score, points are then given for age, and lastly, for chronic health status (7). The APACHE II scoring methodology is summarised in Table 2.

Table 1: The APACHE II Severity of Disease scoring system (7)

Physiological Variable	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature rectal (C)	>41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	<29.9
Mean Arterial Pressure (mmHg)	>160	130-159	110-129		70-109		50-69		<49
Heart Rate	>180	140-179	110-139		70-109		55-69	40-54	<30
Respiratory Rate (nonventilated or ventilated)	>50	35-49		25-34	12-24	10-11	6-9		<5
Oxygenation (mmHg) a. FIO_2 >0.5 use A-a DO_2	>500	350-499	200-349		<200				
b. FiO_2 < 0.5 use PaO_2					>70	61-70		55-60	<55
Arterial pH	>7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7.15
Serum Sodium (mmol/l)	>180	160-179	155-159	150-154	130-149		120-129	111-119	<110
Serum Potassium (mmol/l)	>7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
Serum Creatinine (mg/l Double point score for acute renal failure)	>3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
Hematocrit (%)	>60		50-59.9	46-49.9	30-45.9		20-29.9		<20
White Blood Count (in 1000/mm3)	>40		20-39.9	15-19.9	3-14.9		1-2.9		<1
Glasgow Coma Scale	Score = 15 minus actual GCS								
Serum HCO_3 (venous, mmol/l, use if no ABGs)	>52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	<15
A= total Acute Physiology Score APS	Sum of the 12 individual variable points								
B = Age Points	**C = Chronic Health Points**								
<44 years 0 points	If the patient has a history of severe organ system insufficiency or is immunocompromised assign points as follows:								
45-54 years 1 points	a. For nonoperative or emergency postoperative patients = 5 points								
55-64 years 2 points	b. For elective postoperative patients = 2 points								
65-74 years 3 points									
>75 years 5 points									
APACHE II Score = Sum of A (APS points) + B (Age points) + C (Chronic Health points)									

Each variable is rated from 0 to 4, the higher the score the higher the deviation from normal. The maximum score is 71. A score of 25 represents a 50% predicted mortality, and a score of 35 represents a predicted mortality of 80%. Only the worst values recorded in the first 24 hours of ICU admission are considered and used to calculate the score (7).

APACHE III was developed in 1991 by Knaus et al (38) using data collected from North American databases; physiological variables, as well as chronic health items, were selected via logistic regression analysis. It was then updated in 1998 due to its declining prognostic performance (38), but the use of the APACHE III

score has been limited because the equations used are owned by a commercial company (5).

The APACHE IV was developed in 2006 by Zimmerman et al (9), using 104 ICUs in the United States of America (USA). It includes a separate scoring system for coronary artery bypass patients and can be used to predict the length of hospital stay as well as the duration of mechanical ventilation (9).

1.4 Validation of scoring systems

1.4.1 Discrimination and calibration

For one to reliably use the correct scoring system in any ICU and patient population, a performance evaluation or validation is necessary. This is done using methods such as calibration and discrimination. The sample of patients used to validate a model needs to either be a new cohort of patients or an already existing database randomly split into two, one portion to develop the model and the other to validate it (23).

Model discrimination is the ability of the model to distinguish between groups of patients who survive and those who do not, therefore, the model should assign a higher probability of death to those who will die (5). This is done by calculation of the area under the receiver operating characteristic (AUROC) curve created using the number of actual deaths versus predicted deaths. An AUROC of 1 is considered perfect discrimination (39); and 0.80 is considered a good fit. An AUROC of greater than 0.7 is preferred for a good prediction model (40).

The receiver operating characteristic (ROC) developed from these values allows a graphical representation of the results (5). The ROC plots the sensitivity of a test against 1 minus specificity with the AUROC representing the combined performance (5).

Model calibration refers to the degree of correspondence between estimated probabilities and actual observation. It is documented either quantitatively using a goodness of fit test (commonly the Hosmer-Lemeshow statistic) or graphically using calibration curves where the distribution of observed to expected mortality

rates are plotted on a graph (40). If the number of deaths in the actual population is close to that which was predicted, then the model is well calibrated (8). A model with good fit should have a p-value >0.05 for the Hosmer-Lemeshow Statistic (40).

1.4.2 Validation of the APACHE II score

Validation studies of critical care scoring systems are necessary as the predictive value of the score varies from population to population (40).

International validation of APACHE II

APACHE II has been validated extensively in comparison to other models (10 – 13). However, not all studies have demonstrated population-specific validity. A study conducted in Greece comparing APACHE II and SAPS II scores (41) showed that both models underestimated mortality, therefore, having poor calibration, although both had a good discrimination ability (AUROC 0.83 and 0.86 respectively) for that population. Similar results were seen in a large ICU study in Singapore where APACHE II was shown to have good discrimination AUROC 0.76 and poor calibration $p < 0.001$ (10). In a Korean study done in nine ICUs, the APACHE II showed poor calibration ($p < 0.001$), with modest discrimination (AUROC 0.729) (13).

All the current critical care scoring systems were created in developed countries under first-world conditions (5). Developing countries such as South Africa face different challenges with regards to healthcare, thus impacting the disease profile and consequently, the case-mix of patients admitted to ICU (17).

Validation of APACHE II in South Africa

The APACHE II has been validated locally in a prospective study conducted in Tygerberg hospital, a hospital affiliated to Stellenbosch University in SA (42). In this study, the APACHE II score was found to have good discrimination with an AUROC of 0.83. It also showed a good fit with the predicted mortality, being within the 95% confidence interval of the actual mortality, proving that for that ICU population, the APACHE II score was well-calibrated (42).

The Tygerberg Hospital study had limitations that affected the accuracy of the results. All patients admitted to the ICU were included in the calculation of mortality risk prediction, even those who died within the first four hours of admission. This is traditionally an exclusion criterion as the mortality in the ICU may be overrepresented in this case. Secondly, it is not clear whether the study was powered to determine the sample size. Lastly, the study was designed only to assess ICU mortality as opposed to hospital mortality, as predicted by the APACHE II score, as an outcome (42).

1.5 The burden of HIV in South Africa

The disease profile in the South African intensive care population is different as compared with the rest of the world (17). The high HIV disease burden puts additional strain on already scarce ICU resources in SA (17). In 2019, of the 58,78 million people in SA, 7,97 million are estimated to be HIV positive (13,5% of the population) (43). There were 240 000 new HIV infections documented in 2018, with 71 000 South Africans dying from AIDS-related illnesses (44).

SA also has the most extensive anti-retroviral treatment (ART) program in the world, with 4.8 million South Africans being estimated to be on ARTs in 2018 (44) . The success of the ART rolled out in the country has seen the number of those living with HIV increase (44).

Among the most common indications for ICU admission in this HIV positive group of patients are respiratory failure, sepsis, and neurological disease (45). These patients present a distinct set of challenges. For example, they are susceptible to opportunistic fungal infections such as pneumocystis carinii pneumonia (46). They are also at a higher risk for immune reactions such as Immune reconstitution syndrome (46).

The study by Bhagwanjee et al (47) in 1997, showed 13% of the patients admitted to ICU were HIV positive. They described the outcome of HIV positive patients in an intensive care population and showed that there was no difference in mortality between HIV positive and HIV negative patients. However, this study was done 20 years ago. Another study done in 2016 by Kwizera et al (48) in Uganda showed that HIV positive patients have a higher mortality compared to HIV negative

patients (48), the mortality rate in HIV positive group of patients was 57% and 28% in the negative group. A hosmer Lemeshow statistic was done p 0.258 showing good calibration of APACHE II in this population, a model discrimination wasn't done (48).

The Tygerberg study done by van der Merwe et al (42) study showed that the APACHE II score demonstrates a high ICU mortality in the immunocompromised patient group. However, this group was not exclusive to HIV positive patients, other patients with immune-suppressing conditions (such as organ transplant patients and leukaemia patients) were included in the group (42).

1.6 Summary

Critical care is an important part of every healthcare system. Equally important is the use of critical care scoring systems to define the ICU population and to monitor the standard of care (14). These scoring systems need to be updated periodically for them to remain useful amid changing ICU populations, disease prevalence, and ICU practices (22). Hence, various upgraded versions of the scoring systems are seen, for example, APACHE II, III, and IV (2).

There is a need for these scoring systems to be validated for every population that they are used in (5). SA has a different ICU case mix to that of developed countries, with a greater number of HIV positive patients admitted to the ICU (17). ART availability has markedly improved the survival of patients in the ICU (46).

The APACHE II scoring system is being used at the Charlotte Maxeke Johannesburg Academic Hospital multidisciplinary ICU. However, it has not been validated for this population, and the calibration and discrimination of the APACHE II scoring system in this context is unknown. Therefore, it is important to validate this critical care scoring system in this ICU. This will assist with quantifying what impact the HIV pandemic and the consequent use of ART has had on the performance of this critical care scoring system scores in this ICU population.

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Section 2: Author's guidelines

Southern African Journal of Critical Care (SAJCC)

Scope of the Journal.

This Journal publishes scientific articles related to multidisciplinary critical and intensive medical care and the emergency care of critically ill humans.

To submit a manuscript, please proceed to the *SAJCC* Editorial Manager website:

www.editorialmanager.com/sajcc

Please view the Author Tutorial for guidance on how to submit on Editorial Manager.

Authorship

Named authors must consent to publication. Authorship should be based on: (*i*) substantial contribution to conceptualisation, design, analysis and interpretation of data; (*ii*) drafting or critical revision of important scientific content; or (*iii*) approval of the version to be published. These conditions must all be met for an individual to be included as an author (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org)

If authors' names are added or deleted after submission of an article, or the order of the names is changed, all authors must agree to this in writing.

Please note that co-authors will be requested to verify their contribution upon submission. Non-verification may lead to delays in the processing of submissions. Author contributions should be listed/described in the manuscript.

Conflicts of interest

Conflicts of interest can derive from any kind of relationship or association that may influence authors' or reviewers' opinions about the subject matter of a paper. The existence of a conflict – whether actual, perceived or potential – does not preclude publication of an article. However, we aim to ensure that, in such cases, readers have all the information they need to enable them to make an informed assessment about a publication's message and conclusions. We require that both authors and reviewers declare all sources of support for their research, any personal or financial relationships (including honoraria, speaking fees, gifts received, etc) with relevant individuals or organisations connected to the topic of the paper, and any association with a product or subject that may constitute a real, perceived or potential conflict of interest. If you are unsure whether a specific relationship constitutes a conflict, please contact the editorial team for advice. If a conflict remains undisclosed and is later brought to the attention of the editorial team, it will be considered a serious issue prompting an investigation with the possibility of retraction.

Research ethics committee approval

Authors must provide evidence of Research Ethics Committee approval of the research where relevant. Ensure the correct, full ethics committee name and reference number is included in the manuscript an accompanying documentation. A copy of the ethics approval letter must be uploaded as a supplementary file.

If the study was carried out using data from provincial healthcare facilities, or required active data collection through facility visits or staff interviews, approval should be sought from the relevant provincial authorities. For South African authors, please refer to the guidelines for submission to the National Health Research Database. Research involving human subjects must be conducted according to the principles outlined in the Declaration of Helsinki. Please refer to the National Department of Health's guideline on Ethics in Health research: principles, processes and structures to ensure that the appropriate requirements for conducting research have been met, and that the HPCSA's General Ethical Guidelines for Health Researchers have been adhered to.

Protection of rights to privacy

Research Participants

Information that would enable identification of individual research participants should not be published in written descriptions, photographs, radiographs and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) has given informed written consent for publication and distribution. We further recommend that the published article is disseminated not only to the involved researchers but also to the patients/participants from whom the data was drawn. Refer to Protection of Research Participants. The signed consent form should be submitted with the manuscript to enable verification by the editorial team.

Other individuals

Any individual who is identifiable in an image must provide written agreement that the image may be used in that context in the *SAJCC.*

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Ethnic/race classification

Use of racial or ethnicity classifications in research is fraught with problems. If you choose to use a research design that involves classification of participants based on race or ethnicity, or discuss issues with reference to such classifications, please ensure that you include a detailed rationale for doing so, ensure that the categories you describe are carefully defined, and that socioeconomic, cultural and lifestyle variables that may underlie perceived racial disparities are appropriately controlled for. Please also clearly specify whether race or ethnicity is classified as reported by the patient (self-identifying) or as perceived by the investigators. Please note that it is not appropriate to use self-reported or investigator-assigned racial or ethnic categories for genetic studies.

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, submissions may include an anonymized version of the manuscript.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:

- An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.
- Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.
- Mask self-citations by referring to your own work in third person.

General article format/layout

Submitted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction prior to being sent for review, which will delay publication.

General:

- Manuscripts must be written in UK English (this includes spelling).
- The manuscript must be in Microsoft Word or RTF document format. Text must be 1.5 line spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes). Pages and lines should be numbered consecutively.
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- Medical drugs should be referred to by their generic name although the trade name may be used in brackets in the text once if unique.

If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

Preparation notes by article type

Research

Guideline word limit: 3 000 words (excluding abstract and bibliography)

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The title of the manuscript should concisely describe the study but should not include the outcome. The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. At the end of the introduction clearly state the aim or objective of the study. The primary and secondary outcomes should be specified.

In the Methods section describe in sufficient detail so that others would be able to replicate the study should they need to. Sections of the methods that have been

described in previous publications need only be referenced. The statistical methods should be described. Where appropriate, sample size calculations should be included to demonstrate that the study is not underpowered.

Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

The discussion should be confined to an interpretation of your results with respect to your stated aim and if applicable, a comparison to the results of similar studies. The strengths and weaknesses of your study should be discussed.

The conclusion should be confined to an interpretation of the results of the study and a recommendation if applicable.

- May include up to 6 illustrations or tables.
- References should only include the most recent and relevant articles. A maximum of 30 references is advised.

Structured abstract

- This should be no more than 250 words, with the following headings:
  - **Background:** why the study is being done and how it relates to other published work.
  - **Objectives:** what the study intends to find out
  - **Methods:** must include study design, number of participants, description of the research tools/instruments, any specific analyses that were done on the data.
  - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
  - **Conclusion:** must be supported by the data, and be aligned with the conclusion in the main text.
  - Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors. It should be able to be intelligible to the reader without referral to the main body of the article.
  - Do not include any references in the abstracts.

Here is an example of a good abstract.

***Scientific letters*/short reports**

These are shorter length, scholarly research articles of no more than 1500 words, and include case reports.

Guideline word limit: 1500 words

- Abstract: Structured, maximum 250 words, with the following headings: Background, Objectives, Methods, Results, and Conclusion.
- May include only one illustration or table
- A maximum of 15 references

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.

Please make clear the type of evidence that supports each key statement, e.g.:

- expert opinion
- personal clinical experience
- observational studies
- trials
- systematic reviews.

Review articles

Narrative review articles should always be discussed with the Editor prior to submission. (Structured reviews or meta-analyses' need not be).

Guideline word limit: 4 000 words

These are welcome, but should be either commissioned or discussed with the Editor before submission. A review article should provide a clear, up-to-date account of the topic and be aimed at non-specialist hospital doctors and general practitioners. They should be aligned to practice in South and/or sub-Saharan Africa and not a précis of reviews published in the international literature

Please ensure that your article includes:

- Abstract: unstructured, of about 100-150 words, explaining the review and why it is important
- Methods: Outline the sources and selection methods, including search strategy and keywords used for identifying references from online bibliographic databases. Discuss the quality of evidence.
- When writing: clarify the evidence you used for key statements and the strength of the evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this is opinion. Avoid specialist jargon and abbreviations, and provide advice specific to southern Africa.
- Personal details: Please supply your qualifications, position and affiliations address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Correspondence (Letters to the Editor)

Guideline word limit: 400 words

Letters to the editor should relate either to a paper or article published by the SAJCC or to a topical issue of particular relevance to the journal's readership

- May include only one illustration or table
- Must include a correspondence address.

Obituaries

Guideline word limit: 400 words

Should be offered within the first year of the practitioner's death, and may be accompanied by a photograph.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide evidence of consent to republication obtained from the copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.
- Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.
- All illustrations (graphs, diagrams, charts, etc.) must be in PDF form.
- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.
- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.
- Number each table in Arabic numerals (Table 1, Table 2, etc.) consecutively as they are referred to in the text.
- Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.
- Ensure each table has a concise title and column headings, and include units where necessary.
- Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

References

NB: *Only complete, correctly formatted reference lists in Vancouver style will be accepted. If reference manager software is used, the reference list and citations in text are to be unformatted to plain text before submitting.*

- Authors must verify references from original sources.
- Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]
- All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).
- Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.
- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 **not** 1215-17.
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  - On the Crossref homepage, paste the article title into the 'Metadata search' box.
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Some examples:

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- *Book references:* Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101.
- *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.
- *Internet references:* World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: WHO, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).
- Legal references
- Government Gazettes:

  National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116 of 1990). Free primary health care services. Government Gazette No. 17507:1514. 1996.

  In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the notice number in this Gazette.

- Provincial Gazettes:

  Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment and Land Affairs. Publication of the Gauteng health care waste management draft regulations. Gauteng Provincial Gazette No. 373:3003, 2003.

- Acts:

South Africa. National Health Act No. 61 of 2003.

- Regulations to an Act:

  South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicine services. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

- Bills:

  South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

- Green/white papers:

  South Africa. Department of Health Green Paper: National Health Insurance in South Africa. 2011.

- Case law:

  Rex v Jopp and Another 1949 (4) SA 11 (N)
  Rex v Jopp and Another: Name of the parties concerned
  1949: Date of decision (or when the case was heard)
  (4): Volume number
  SA: SA Law Reports
  11: Page or section number
  (N): In this case Natal - where the case was heard. Similarly, (C) woud indicate Cape, (G) Gauteng, and so on.
  NOTE: no . after the v

- *Other references (e.g. reports) should follow the same format:* Author(s). Title. Publisher place: Publisher name, year; pages.
- Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.
- Unpublished observations and personal communications in the text must **not** appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.

From submission to acceptance

Submission and peer-review

To submit an article:

- Please ensure that you have prepared your manuscript in line with the SAJCC requirements.
- All submissions should be submitted via Editorial Manager

- The following are required for your submission to be complete:
  - Anonymous manuscript (unless otherwise stated)
  - Author Agreement form
  - Manuscript
  - Ethics Approval form (for research articles)
  - Any supplementary files: figures, datasets, patient consent form, permissions for published images, etc.
  - Once the submission has been successfully processed on Editorial Manager, it will undergo a technical check by the Editorial Office before it will be assigned to an editor who will handle the review process. If the author guidelines have not been appropriately followed, the manuscript may be sent back to the author for correcting.

Peer Review Process

All manuscripts are reviewed initially by two of the editors and only those that meet the scientific and editorial standards of the journal, and fit within the aims and scope of the journal, will be sent for external peer review. Each manuscript is reviewed by two reviewers selected on the basis of their expertise in the field.

A double blind review process is followed at SAJCC. The time period of the entire review process may vary however depending upon the quality of the manuscript submitted, reviewers' responses and the time taken by the authors to submit the revised manuscript.

Manuscripts from review may be accepted, rejected or returned to the author for revision or resubmission for review. Authors will be directed to submit revised manuscripts within two months of receiving the editor's decision, and are requested to submit a point by point response to the reviewers' comments. Manuscripts which authors are requested to revise and resubmit will be sent for a second round of peer review, often to the original set of reviewers. All final decisions on a manuscript are at the Editor's discretion

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Production process

The following process should usually take between 4 - 6 weeks:

1. An accepted manuscript is passed to a Managing Editor to assign to a copyeditor (CE).
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Section 3: Draft article

Retrospective evaluation of the APACHE II critical care scoring system in a multidisciplinary intensive care unit

Kenalemodisa Lindiwe Mogotsi, MBChB, DA (SA)

Juan Scribante, PhD

Helen Perrie, MSc

Ahmad Alli, MBBCh, MMed, FCA(SA), Cert Crit Care (SA)

Department of Anaesthesiology, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand

Corresponding Author

KL Mogotsi

Department of Anaesthesiology
Chris Hani Baragwanath Academic Hospital
26 Chris Hani Rd
Diepkloof, Soweto
Johannesburg
1860

mogotsikl@yahoo.com

011 93309334

Key words: APACHE II score, discrimination, calibration, multidisciplinary ICU

Abstract

Background

APACHE II is one of the oldest scoring systems and it is still used globally due to its availability and ease of use. A performance evaluation is necessary when using a critical care scoring system in any particular ICU and patient population.

Objective

The aim of this study was to evaluate the performance of the APACHE II scoring systems in a multidisciplinary ICU at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

Methods

A retrospective evaluation of ICU patients' records between February and May 2018 was conducted. Follow-up was until death or hospital discharge.

Results

Of the 256 records included, 44.1% were medical and 55.9% were surgical admissions. The mean (SD) age of the patients was 43.7 (18.3) years and for the APACHE II score was 20.3 (8.4). The mean (SD) predicted mortality rate was 39.2% (23.9%) and the actual mortality rate was 33.0%. The standardised mortality ratio was 0.84, and the correct classification rate was 71%. Discrimination was good (AUROC = 0.8087), as was calibration at 10.55 (p=0.2284) for ICU mortality and 9.95 (p=0.2684) for mortality at hospital discharge. The median (IQR) APACHE II score for the HIV negative and positive groups was 19.0 (13.0 – 25.0) and 23.5 (17.5 – 30.0), respectively. The predicted mortality rate was 36.3% and 49.4% and the actual mortality rate was 32.3% and 40.0% in the HIV negative and positive groups, respectively.

Conclusion

This study found good discrimination and calibration of the APACHE II score in the multidisciplinary ICU at CMJAH.

Introduction

Intensive care is a fast-growing specialty, and it is an essential part of the global health care system (1). There is an increase in demand for intensive care services, therefore efficacious allocation of this scarce resource is imperative (2). A variety of factors are taken into consideration when allocating intensive care resources (3), and critical care scoring systems can facilitate this process (4).

Critical care scoring systems predict mortality of patients admitted to the intensive care unit (ICU), based on the severity of disease and other variables (4). They can be used as audit tools to assess the performance of an individual ICU over time and in comparison to other ICUs (5). There are many critical care scoring systems, for examples, the Acute Physiology and Chronic Health Evaluation (APACHE) II, APACHE IV, Simplified Acute Physiological score (SAPS) III, and Sequential Organ Function Assessment (SOFA) are among the most commonly used scoring systems worldwide and have been widely validated for different intensive care populations (6). The APACHE II was the focus of this study. It is a physiological scoring system (7) that was initially developed by Knaus et al (8) in 1981 and assesses the severity of disease and provides an estimate of in-hospital mortality (7). The APACHE II is one of the oldest scoring systems and is still used globally due to its availability and ease of use (9-12). However, the accuracy of critical care scoring systems is dynamic, and they need to be updated periodically when the accuracy is questioned (13). To reliably use a critical care scoring system in any particular ICU and patient population, a performance evaluation or validation is necessary (5). As the patient case mix may be different from the one used during the development and validation of the scoring system, this may affect the accuracy of the critical care scoring system in different populations (5, 13).

The disease profile of the South African intensive care population differs from the rest of the world. The high human immunodeficiency virus (HIV) disease burden puts additional strain on already scarce ICU resources in South Africa (SA) (14). In 2019 there were 7.97 million HIV positive people in SA, which is 13.5% of the population (15). More HIV positive patients are being admitted to ICU (14) and a study has shown they have a higher mortality compared to HIV negative patients,

especially in low-income country ICUs (16). The APACHE II scoring system is being used in the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) multidisciplinary ICU. It has not been validated for this population, and the calibration and discrimination in this context are unknown. The aim of this retrospective study was to evaluate the performance of the APACHE II scoring system in a multidisciplinary ICU at CMJAH over a four-month period.

Methods

Approval to conduct the study was obtained from the Human Research Ethics Committee (Medical) and other relevant authorities. A retrospective, contextual, descriptive research design was followed.

The study population was the records of patients admitted to the multidisciplinary ICU at CMJAH over four months between February and May 2018. A consecutive convenience sampling method was used and the sample size was realised by the number of records of patients admitted during the study period. Illegible and incomplete records, records of patients who died within three hours of admission to ICU or with an ICU length of stay of less than eight hours were excluded from the study.

Actual mortality in this study included ICU and hospital mortality. Hospital mortality was determined by the status of the patient at hospital discharge. One of the groups of ICU patients in which the APACHE II scoring system was evaluated was HIV positive patients. In the ICU where the study was conducted, HIV status is confirmed on serum ELISA or PCR testing and was recorded retrospectively from patient records.

The number of admissions, ICU deaths and hospital deaths were recorded from the admission book and electronic hospital records. Based on anecdotal data from the ICU management, the ICU case mix is not influenced by seasonality and therefore, the period February to May 2018 was chosen. Data capturing was done by one author (KLM).

Variables from the APACHE II scoring system (7) were collected from ICU charts and electronic laboratory results. The APACHE II mortality predictions for every patient were calculated and recorded. The following statistical programs were used, Stata 16.0 (StataCorp, Texas, USA) and SAS University Edition (Version 3.8, SAS, North Carolina, USA). Categorical variables were described using frequencies and percentages, and continuous variables using mean (SD) or median (IQR) depending on the distribution of the data. A standardised mortality ratio (SMR) and correct classification rate were calculated, and a Chi square test was used to compare the mortality between HIV^- and HIV^+ patients. Calibration and discrimination were assessed for all patients, the HIV negative as well as the HIV positive groups of patients. In this study, calibration was determined using the Hosmer-Lemeshow H statistic. If the number of deaths in the actual population is close to that which was predicted, then the model is considered to be well-calibrated (17). A p-value of >0.05 is considered good calibration (18).

Discrimination is the ability of the model to distinguish between groups of patients who survive and those who do not survive (17). Specificity and sensitivity of the APACHE II score were used as an assessment of discrimination. A set of receiver operating characteristic (ROC) curves was developed from these values, and the area under the receiver operating characteristic (AUROC) for each curve was then calculated. An AUROC of 1 is considered perfect discrimination and an AUROC of greater than 0.7 is preferred for a good prediction model (17).

Results

The trajectory of the 309 patients admitted to the ICU during the study period is shown in Figure 1. The characteristics of the 256 (82.8%) patients included are shown in Table 1. Only the 10 most common admission diagnoses and the 4 most common comorbidities are shown.

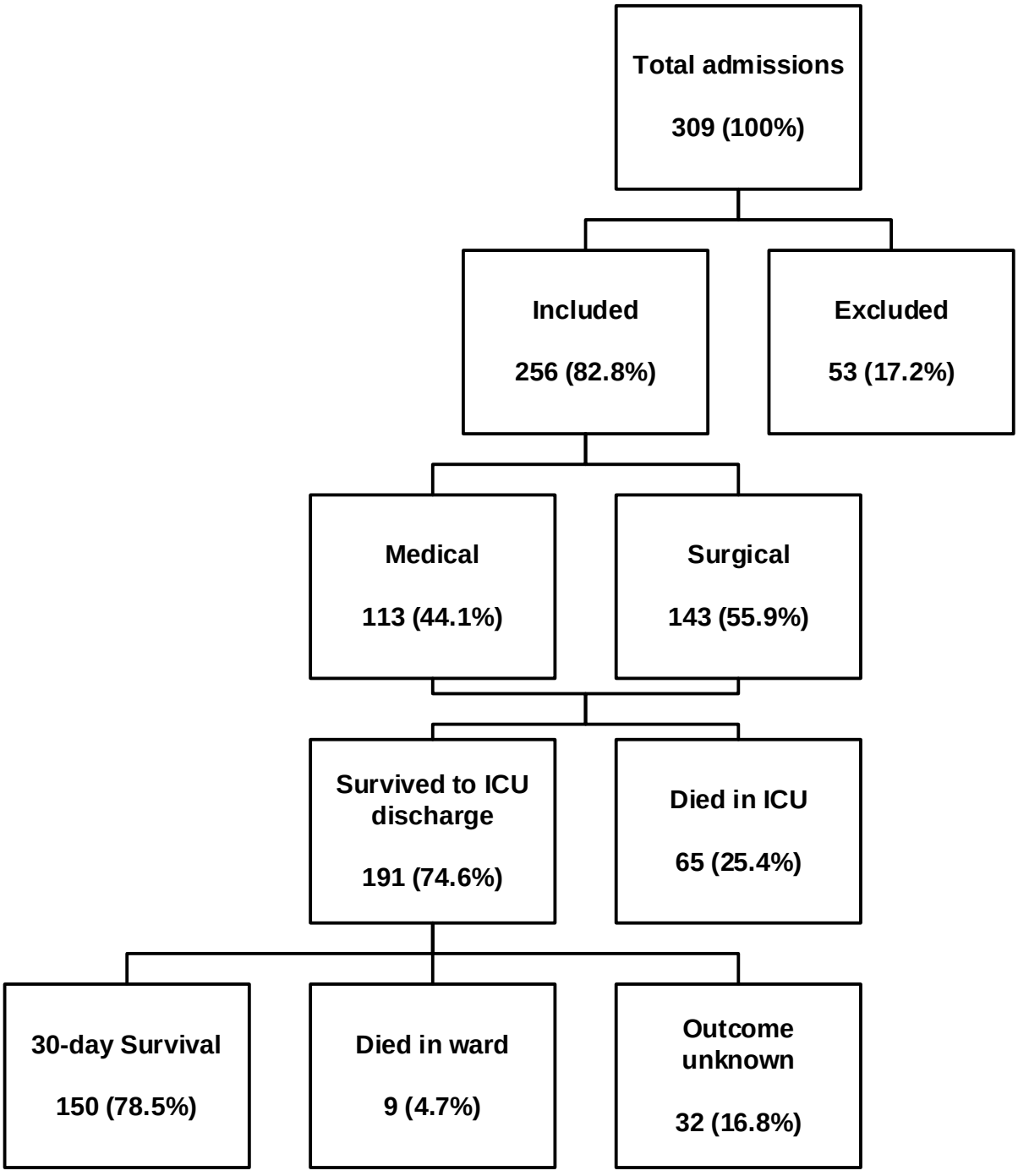

Figure 1: Study flow diagram

Table1: Characteristics of patients

Characteristic	Mean	SD
Age (years)	47.3	18.3
	Number	**Percentage**
Comorbidities		
Hypertension	63	24.6
Diabetes mellitus	29	11.3
Malignancies	55	21.5
Renal disease	45	17.6
None	58	22.7
Admission		
Emergency	194	75.8
Elective	62	24.2
HIV status		
HIV^-	191	74.6
HIV^+ on treatment	40	15.6
HIV^+ not on treatment	3	1.2
HIV^+ treatment unknown	7	2.7
Not documented	15	5.9
Diagnoses		
Pneumonia	19	7.4
Perforated viscus	19	7.4
Poisoning	17	6.6
Upper gastrointestinal bleed	9	3.5
Diabetic keto acidosis	8	3.1
Hysterectomy post caesareans delivery	7	2.7
Renal failure	6	2.3
Thyroidectomy	6	2.3
Arthroplasty	6	2.3
Nephrectomy	5	2.0
Other	154	60.2

The mean (SD) APACHE II score for the whole group was 20.3 (8.4), with a minimum and maximum of 5 and 44, respectively. The mean (SD) predicted mortality rate was 39.2% (23.9%), with a minimum and maximum of 5.8% and 94.8%, respectively. The predicted mortality rate in the HIV positive group was 49.4%, and 36.3% in the HIV negative group. The actual mortality rate for the 224 patients whose hospital outcome was known was 33.0%, while the actual mortality rate in the HIV positive group was 40.0%, and 32.3% in the HIV negative group. The was no significant difference between the mortality rate of the HIV – and HIV + patients p = 0.32. The overall SMR was 0.84, and the overall correct classification rate was 71% for the 224 patients whose outcome was known.

Table 2. shows the APACHE II score distribution, the predicted and actual mortality scores, and lastly where applicable the SMR among the HIV negative, HIV positive, and HIV unknown patients, for those who died in ICU, died in the ward, survived to hospital discharge, and lastly, those who were lost to follow up (outcome unknown).

Table 2: APACHE II score distribution in different patient groups

Outcome	Number	Median (IQR)	*Predicted mortality	*Actual mortality (SMR)
Known HIV $^{-}$	191	19.0 (1.03 – 25.0)	35.5	32.3 (0.91)
Known HIV $^{+}$	50	23.5 (17.5 – 30.0)	42.4	40.0 (0.94)
HIV unknown	15	21.0 (16.5 – 27.5)	37.2	33.3 (0.90)
Died ICU	65	28.0 (22.0 – 30.0)	63.9	100.0 (1.56)
Died in ward	9	20.0 (16.0 – 22.0)	35.5	100.0 (2.81)
30-day survival group	150	17.0 (11.0 – 24.0)	26.2	n/a
Outcome unknown	32	18.5 (14.0 – 22.8)	n/a	n/a

*The predicted and actual mortality is for patients whose outcome is known.

The diagnostic performance of the APACHE II score in the group overall (n = 256), known HIV negative (n = 191), and known HIV positive (n = 50) group was evaluated. The AUROC was 0.8087 in the overall group (Figure 2a), 0.8113 in the known HIV negative group (Figure 2b), and 0.7705 in the known HIV positive group (Figure 2c).

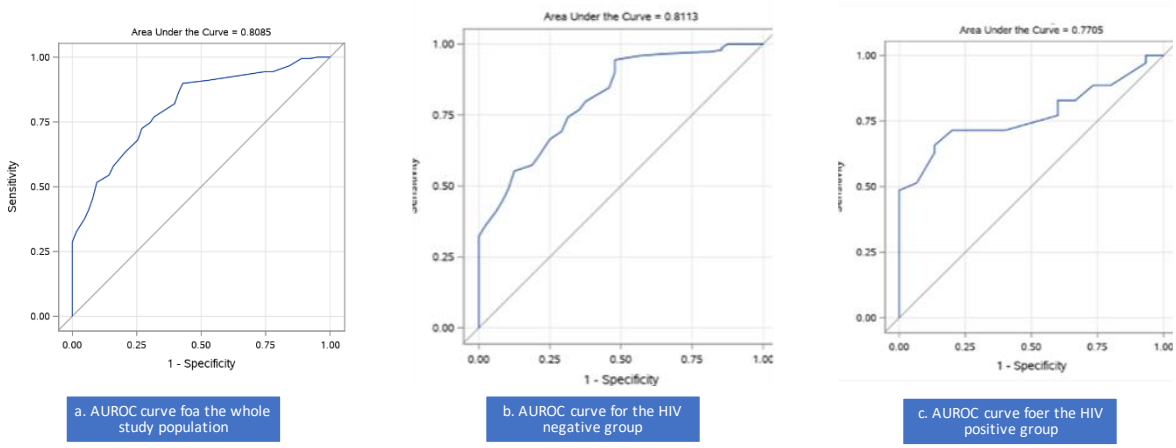

Figure 2: The diagnostic performance of the APACHE II score

The Hosmer-Lemeshow H statistic was 10.55 (p=0.2284) for detecting those who survived to ICU discharge (n=191) and those who died in ICU (n=65), and was 9.95 (p=0.2684) for those who survived to hospital discharge (n=150) and those who died in the ward (n=9)

Discussion

In this study we found that the APACHE II score showed good overall discrimination and calibration ability in the CMJAH ICU population. We also sought to describe the effect, if any, of underlying HIV disease in our patient population. Although marginally inferior to patients without HIV, we found that the APACHE II score had reasonable diagnostic accuracy in patients with HIV. Of note is that the mortality rate of patients with HIV in the ICU was higher than those without HIV, but the difference was not significant.

HIV prevalence is very high in low to middle-income countries, especially in SA, in 2019 the adult HIV prevalence in South Africa was 19.07%, the HIV prevalence in this study was 19.5% (19). HIV positive patients are thought to have a poorer outcome in ICU (16). This was challenged by Bhagwanjee et al (20) in 1997 before the rollout of antiretroviral therapy (ART), where the authors found that the HIV positive patients in ICU did not have higher mortality in comparison to the HIV negative group. HIV prevalence in that study was 13,0%, the mean APACHE scores were 9 and 8 with a hospitality mortality of 6% and 3% for the HIV- and

HIV+ groups, respectively. Nonetheless, in this study the HIV positive group had higher median APACHE II scores and actual mortality rates than patients without HIV.

The impact of ART on the outcome of HIV positive patients has been a topic of much discussion (21-23). Some studies make an argument that the severity of the acute illness (22) as well as better access and treatment in ICU (21), had more to do with ICU outcomes rather than ARTs (21, 22), while in another study it was argued that ARTs had a direct effect on ICU outcomes (23). A large proportion of this study's sample was on ARTs (80%), subdividing the HIV positive group into those on treatment and not on treatment might have been beneficial to assess the impact of ART. This was not possible due to the limited sample size of the HIV positive patients not on treatment and was not in the scope of the study.

Despite these findings supporting APACHE II use in our population, there is evidence of declining accuracy of the APACHE II score, especially in high-income countries. This could predict the future trajectory of the diagnostic accuracy of the score in our institution. Initial validation of the APACHE II score showed good discrimination and calibration in high-income countries (24-26). Thereafter in the 2000s, the APACHE II started showing a decline in discrimination and calibration ability in high-income countries (9, 10, 27). This has been attributed to reasons such as differences in case-mix to the initial APACHE II population (27), changes in disease prevalence (10), and advances in diagnostic and therapeutic interventions (9, 10).

A systematic review done in 2018 in low to middle-income countries showed that prognostic scoring systems, such as the APACHE II, still performed well (28) with AUROC values ranging from 0.6 to 0.93, it is interesting to note that in this study the AUROC value was within this range. According to the World Bank 2020 country classification (29), SA is classified as an upper-middle-income country.

However, the ICU in which this study was conducted was at an academic hospital, with diagnostic and therapeutic interventions in keeping to those in high-income countries. The Tygerberg Hospital ICU in the Western Cape had similar results

(30), the APACHE II scoring system was validated with a ROC value of 0.83, and the study was also conducted at an academic hospital with a similar sample size and a mean APACHE score of 17.4.

The sample size in this study was small, and that could be the reason the APACHE II performed well and was validated in the CMJAH population. Zhu et al (31) showed that the goodness of fit test produced poor results as the ICU mortality differed from the original group, but a smaller sample size improved the performance of the scoring system in spite of this. The p-value may indicate good calibration even though the fit is not good. This is also believed to be part of the reason for good calibration in some of the articles in the systematic review (28). The AUROC values in the systematic analysis ranges from 0.6 to 0.93, it is interesting to note that this study's AUROC value was within this range.

Although anecdotally, it was thought that HIV status would be one of the possible confounders to this study's analysis, this was not found to be the case. However, this conclusion also may be biased by a small sample size.

Other limitations of this study were that it was a contextual single centre study, therefore, the results may not be generalised to other ICUs. It was also a retrospective study and dependent on the quality of the completed records. The study period is a limitation as it may exclude any possible seasonal influence to ICU case mix. A further limitation was that 27.5% of patient records were excluded due to missing data and unknown outcomes.

Furthermore, other patient populations were not included in this study such as cardiac, trauma and neurosurgery patients. This study evaluated the APACHE II scoring system, and further research needs to be conducted in CMJAH assessing its performance against more modern scoring systems such as APACHE IV, SOFA and SAPS. We also recommend that future studies need to include larger sample sizes and be conducted prospectively.

Conclusion

The APACHE II score is a convenient and cost-effective way to benchmark ICUs, especially within the resource constraints faced in the developing world. Armed with this APACHE II information, hospital administrators and physicians can implement measures to align measured mortality with expected mortality and therefore improving patient outcomes. This study found that the APACHE II score has good discrimination and calibration in the mixed surgical and medical ICU at CMJAH. More work needs to be done to understand the effect of untreated HIV on scoring system accuracy.

Conflict of interest

The authors declare that we have no financial or personal relationships which may have inappropriately influenced us in writing this paper.

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Section 4: Proposal

Retrospective evaluation of the APACHE II critical care scoring system in a multidisciplinary intensive care unit

Kenalemodisa Lindiwe Mogotsi

1725851

Clearance certificate no: M180605

Supervisor:	Juan Scribante
	Department of Anaesthesiology
Co-supervisor:	Helen Perrie
	Department of Anaesthesiology
Co-supervisor:	Ahmad Alli
	Department of Anaesthesiology

4.1 Introduction and problem statement

Intensive care is a fast-growing specialty, and it is an essential part of global health care system (1), there is an increase in demand for intensive care services, therefore efficacious allocation of this scarce resource is imperative (2). A variety of factors are taken into consideration when allocating intensive care resources (3), and critical care scoring systems facilitate this process (4).

Critical care scoring systems predict mortality of patients admitted to the Intensive care unit (ICU), based on the severity of disease and other variables (4). They can be used as audit tools to assess the performance of an individual ICU over time, and in comparison, to other ICUs. They can also assist in the appropriate allocation of this resource to intensive care patients (4, 5).

There are many critical care scoring systems, for examples, Acute Physiology And Chronic Health Evaluation II (APACHE), APACHE IV, Simplified Acute Physiology Model III (SAPS) and Sequential Organ Function Assessment (SOFA) are among the most commonly used scoring systems worldwide and they have been widely validated for different intensive care populations (5,6). APACHE II will be the focus of this research.

The APACHE II scoring system assesses the severity of disease and provides an estimate of in-hospital mortality (7). It is a physiological scoring system that was initially developed by Knaus et al (8) in 1981. It comprises of a score and a calculated percentage probability of mortality. The initial APACHE I score was divided into two sections; a physiological score to determine the acute illness status of the patient and a pre-admission evaluation to determine the chronic health status of the patient (8). In 1985 the APACHE II scoring system was developed as an upgrade from the APACHE I scoring system (7).

In the APACHE II scoring system, the physiological variables used to calculate the score were reduced, some were reweighted, and additional weightings were added for end organ dysfunction and emergency or non-operative admissions (7).

In addition to the acute physiology variables, age and the presence of severe chronic organ dysfunction or immune suppression were also incorporated (7). Only the worst value recorded in the first 24 hours of ICU admission is taken into account and used to calculate the score (7,8). The maximum score is 71 (7). The scoring template is summarised in Appendix A1 and 2.

APACHE II is one of the oldest scoring systems and it is still used globally due to its availability and ease of use (5, 9, 10, 11). However, the accuracy of critical care scoring systems is dynamic, and they need to be updated periodically when the accuracy is questioned (12).

In order to reliably use a critical care scoring system in any particular ICU and patient population, a performance evaluation or validation is necessary (5). As the patient case mix may be different from the one used during the development and validation of the scoring system, this may affect the accuracy of the critical care scoring system in different populations (5, 12).

The disease profile in the South African intensive care population is different as compared with the rest of the world. The high human immunodeficiency virus (HIV) disease burden puts additional strain on already scarce ICU resources in South Africa (13). In 2019 there were 7.97 million HIV positive people in South Africa, which is 13.5% of the population (14). More HIV positive patients are being admitted to ICU (13) and they have a higher mortality compared to HIV negative patients especially in low income country ICUs (15).

Bhagwanjee et al (16) in 1997, showed 13% of the patients admitted to ICU were HIV positive. They described the outcome of HIV positive patients in an intensive care population and showed that there was no difference in mortality between HIV positive patients and HIV negative patients (16). However, this study was done more than 20 years ago.

The performance of the APACHE II has been evaluated in a South African general ICU by van der Merwe et al (17) in Tygerberg Hospital. The study concluded that

APACHE II was validated for use in a developing country (17), however, this study was done in 2005 and it only focused on ICU mortality.

The APACHE II scoring system is being used in the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) multidisciplinary ICU, however, it has not been validated for this population, and the calibration and discrimination in this context is unknown.

4.2 Aim and objectives

4.2.1 Aim

The aim of this retrospective study is to evaluate the performance of the APACHE II scoring systems in a multidisciplinary ICU at CMJAH over a four-month period.

4.2.2 Objectives

The objectives of this study are to**:**

- describe principal admission diagnosis
- determine the APACHE score (overall, HIV negative and HIV positive)
- determine and document the predicted mortality rate for the study group (overall, HIV negative and HIV positive)
- measure the actual mortality rate (overall, HIV negative and HIV positive)

compare the actual mortality rate versus the predicted mortality rate in patients admitted to the multidisciplinary ICU over the study period.

in the group of patients admitted to the multidisciplinary ICU over the study period.

4.3 Research assumptions

The following definitions will be used in this study.

Actual mortality: in this study included ICU and hospital mortality. Hospital mortality was determined by the status of the patient at hospital discharge.

HIV positive patients: will be patients with confirmed HIV on blood results, because a CD4 count is unreliable in critically ill patients (18). Information about HIV status will be obtained from the patients' records as this is a retrospective study.

Incomplete record: will be any record that does not have all the variables required to calculate the APACHE II score.

4.4 Demarcation of study field

The study will be conducted at CMJAH, a 1 200-bed central hospital, affiliated to the University of the Witwatersrand. The hospital has six ICUs, with a total of 57 beds. This study will take place in the multidisciplinary ICU, a 12-bed unit, which admits on average 1 200 patients per.

4.5 Ethical considerations

Approval to conduct the study was obtained from the Human Research Ethics Committee (Medical), the Graduate Studies Committee of the University of the Witwatersrand, the CEO of CMJAH (Appendix B) and the Director of the multidisciplinary ICU (Appendix C) who is also the gatekeeper of the ICU records.

This will be a retrospective study. There will be no identifiable information recorded on the data collection sheet, only a study number. A list with the patients' names, hospital numbers and study numbers will be generated and filed separately. The raw data will only be accessed by the researcher and the supervisors, therefore, confidentiality will be maintained. The data collected will be stored securely on a password-protected electronic database for six years after completion of the study.

This study will be conducted according to the principles of the Declaration of Helsinki (19) and the South Africa Guidelines for Good Clinical Practice (20).

4.6 Research methodology

4.6.1 Research design

A retrospective, contextual, descriptive research design will be followed in this study.

In a retrospective study variables that occurred in the past are measured (21). In this study, data will be obtained from ICU charts that have already been completed

A contextual study is one that refers to a specific group also defined as a “small scale world” by De Vos et al (22). This study will be conducted contextually in the multidisciplinary ICU at CMJAH.

A descriptive study, according to Brink et al (21), is concerned with gathering information from a representative sample of the population to answer a specific question about the population, without attempting to establish a causal link. This study will describe how an internationally developed scoring system performs in an intensive care population at CMJAH

4.6.2 Study population

The study population will be records of patients admitted to the multidisciplinary ICU at CMJAH, over the period of four months between February and May 2018.

4.6.3 Study sample

Sample size

The sample size will be realised by the number of records of patients 18 years and older admitted over the four-month study period. This is estimated to be approximately 300 records.

Sampling method

In this study, a consecutive convenience sampling method will be used. According to Endacott and Botti (23), convenience sampling is “the use of the most readily accessible individuals or units in a study” and consecutive sampling is “a version

of convenience sampling where every available individual or event within an accessible population is chosen.

Inclusion and exclusion criteria

The inclusion criterion in this study is all the records of patients 18 years and older who are admitted to the ICU during the study period.
The exclusion criteria in this study will be:

- illegible and incomplete records
- patients who died within three hours of admission to ICU
- patients with an ICU length of stay of less than eight hours

4.6.4 Data collection

The ICU admissions book will be used to determine the number of admissions during the period of the study. The names and hospital numbers of the patients will be recorded on a separate Microsoft Excel ® spreadsheet and each record will be assigned a study number.

The time period February to May 2018 was chosen because it was convenient, the ICU case mix is not influenced by seasonality, and therefore our evaluation will not be affected by the time period of the study.

The ICU charts of the identified patients will be retrieved from storage. The relevant data will be collected according to the data collection sheet (Appendix D), only the worst value recorded in the first 24 hours of ICU admission will be taken into account and used to calculate the APACHE II score (7,8). The data will then be scored according to the scoring system. The scoring template is summarised in Appendix A1.

Data capturing will be done in the multidisciplinary ICU at CMJAH, and records will not be removed from the hospital.

4.6.5 Data analysis

The data will be captured onto spreadsheets using Microsoft Excel ® 2016. The APACHE II mortality predictions for every patient will be calculated and then recorded.

The ICU death book will be used to document the actual mortality in ICU and the hospital records will be used to document observed 30 day in-hospital mortality. Calibration and discrimination will be done for all the groups. Calibration refers to the degree of correspondence between estimated probabilities and actual observation (24), a goodness of fit test is used. In this study for calibration, the Hosmer-Lemeshow statistic will be used. If the number of deaths in the actual population is close to that which was predicted, then the model is considered to be well calibrated (25).

Discrimination is the ability of the model to distinguish between groups of patients who survive and those who do not survive (5). Specificity and sensitivity will be used in this study, a receiver operating characteristic curve (ROC) curve will be developed from these values, and the area under the receiver operating characteristic (AUROC) will then be calculated. An AUROC of 1 is considered perfect discrimination; and less than 0.60 is considered to be a poorly discriminating model. An AUROC of greater than 0.7 is preferred for a modest prediction model (24).

4.7 Significance of the study

Due to the increase in the demand for intensive care services, the need for efficacious allocation of this scarce resource is of paramount importance (1). Critical care scoring systems are used to facilitate this process (4,5).

It is important that critical care scoring systems be validated in the population in which they are used (25). South Africa has a different ICU case mix to that of developed countries, with a greater number of HIV positive patients admitted to the ICU (13).

Evaluation of the APACHE II scoring systems in the CMJAH multidisciplinary ICU will assist in determining whether this is the best scoring system to be used in this intensive care population.

4.8 Validity and reliability of the study

The validity of the study refers to the degree to which a measurement represents a true value and the reliability is the consistency of the measure achieved (26).

Measurements to ensure the validity and reliability of this study are:

- using an appropriate study design
- a standardised data collection sheet being used
- a single researcher collecting all the data
- data analysis being done in consultation with a biostatistician.

4.9 Potential limitations

Limitations are defined as restrictions or problems that may decrease the application of the findings to the general population (21).

The limitations of this study are that the study is done contextually, therefore the results of this study may not be generalisable to other intensive care patient populations.

Some patients may be excluded from the study due to incomplete data.

As this is a retrospective study, the information on the ICU charts will have been collected by other individuals, the researcher, therefore, relies on others to have recorded this data accurately.

4.10 Project outline

4.10.1 Time frame

Activity	July 2018	Sep 2018	Mar 2019	Apr 2019	May 2019	Jun 2019	July 2020	Aug 2020	Sep 2020	Nov 2020
Proposal preparation										
Literature review										
Proposal submission										
Ethics approval										
Postgraduate approval										
Data collection										
Data analysis										
Draft article										
Submission										

4.10.2 Budget

Item	Price per page	Number of pages	Copies	Total
Proposal	1	20	10	R 200
Ethics	1	10	25	R 250
Post graduate form	1	1	6	R 6
Complete report	1	100	4	R 400
Grand total		R 131		**R 856**

The Wits Department of Anaesthesiology will incur the costs of paper and printing.

4.11 References

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4.12 Appendices

Appendix A1: APACHE II scoring system

The APACHE II Severity of Disease Classification System

Physiologic Variable	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature - rectal (°C)	≥41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9
Mean Arterial Pressure (mm Hg)	≥160	130-159	110-129		70-109		50-69		≤49
Heart Rate	≥180	140-179	110-139		70-109		55-69	40-54	≤39
Respiratory Rate (nonventilated or ventilated)	≥50	35-49		25-34	12-24	10-11	6-9		≤5
Oxygenation (mmHg) a. $FiO_2 > 0,5$ use A-aDO_2 b. $FiO_2 < 0,5$ use PaO_2	a ≥500	350-499	200-349		<200				
	b				> 70	61-70		55-60	<55
Arterial pH	≥7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7.15
Serum Sodium (mmol/l)	≥180	160-179	155-159	150-154	130-149		120-129	111-119	≤110
Serum Potassium (mmol/l)	≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
Serum Creatinine (mg/dl, Double point score for acute renal failure)	≥3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
Hematocrit (%)	≥60		50-59.9	46-49.9	30-45.9		20-29.9		<20
White Blood Count (in 1000/mm³)	≥40		20-39.9	15-19.9	3-14.9		1-2.9		<1
Glasgow-Coma-Scale (GCS)	Score = 15 minus actual GCS								
Serum HCO_3 (venous, mmol/l, use if no ABGs)	≥52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	<15
A = Total Acute Physiology Score APS	Sum of the 12 individual variable points								

B = Age Points		**C = Chronic Health Points**
≤44 years	0 points	If the patient has a history of severe organ system insufficiency or is immunocompromised assign points as follows:
45-54 years	2 points	a. For nonoperative or emergency postoperative patients – 5 points
55-64 years	3 points	b. For elective postoperative patients – 2 points
65-74 years	5 points	
≥75 years	6 points	

APACHE II Score = Sum of A (APS points) + B (Age points) + C (Chronic Health points)

(From: Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med 1985;13(10):818-29)

Appendix A2: APACHE II scoring system

PHYSIOLOGIC VARIABLE	HIGH ABNORMAL RANGE				LOW ABNORMAL RANGE				
	+4	+3	+2	+1	0	+1	+2	+3	+4
TEMPERATURE — rectal (°C)	≥41°	39°–40.9°		38.5°–38.9°	36°–38.4°	34°–35.9°	32°–33.9°	30°–31.9°	≤29.9°
MEAN ARTERIAL PRESSURE — mm Hg	≥160	130–159	110–129		70–109		50–69		≤49
HEART RATE (ventricular response)	≥180	140–179	110–139		70–109		55–69	40–54	≤39
RESPIRATORY RATE (non-ventilated or ventilated)	≥50	35–49		25–34	12–24	10–11	6–9		≤5
OXYGENATION: A-aDO_2 or PaO_2 (mm Hg) a. FiO_2 ≥0.5 record A-aDO_2 b. FiO_2 <0.5 record only PaO_2	≥500	350–499	200–349		<200 PaO_2 > 70	PaO_2 61–70		PaO_2 55–60	PaO_2 < 55
ARTERIAL pH	≥7.7	7.6–7.69		7.5–7.59	7.33–7.49		7.25–7.32	7.15–7.24	<7.15
SERUM SODIUM (mMol/L)	≥180	160–179	155–159	150–154	130–149		120–129	111–119	≤110
SERUM POTASSIUM (mMol/L)	≥7	6–6.9		5.5–5.9	3.5–5.4	3.3–3.4	2.5–2.9		<2.5
SERUM CREATININE (mg/100 ml) (Double point score for **acute** renal failure)	≥3.5	2.0–3.4	1.5–1.9		0.6–1.4		<0.6		
HEMATOCRIT (%)	≥60		50–59.9	46–49.9	30–45.9		20–29.9		<20
WHITE BLOOD COUNT (total/mm3) (in 1,000s)	≥40		20–39.9	15–19.9	3–14.9		1–2.9		<1
GLASGOW COMA SCORE (GCS) Score = 15 minus actual GCS									
A Total ACUTE PHYSIOLOGY SCORE (APS) Sum of the 12 individual variable points									
Serum HCO_3 (venous mMol/L) (Not preferred, use if no ABG's)	≥52	41–51.9		32–40.9	22–31.9		18–21.9	15–17.9	<15

B AGE POINTS: Assign points to age as follows:

AGE(yrs)	Points
≤44	0
45–54	2
55–64	3
65–74	5
≥75	6

C CHRONIC HEALTH POINTS
If the patient has a history of severe organ system insufficiency or is immuno-compromised assign points as follows:
a. for nonoperative or emergency postoperative patients — 5 points
or
b. for elective postoperative patients — 2 points

DEFINITIONS
Organ insufficiency or immuno-compromised state must have been evident **prior** to this hospital admission and conform to the following criteria:
LIVER: Biopsy proven cirrhosis and documented portal hypertension; episodes of past upper GI bleeding attributed to portal hypertension; or prior episodes of hepatic failure/encephalopathy/coma.
CARDIOVASCULAR: New York Heart Association Class IV.
RESPIRATORY: Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction, i.e., unable to climb stairs or perform household duties; or documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension (>40mmHg), or respirator dependency.
RENAL: Receiving chronic dialysis.
IMMUNO-COMPROMISED: The patient has received therapy that suppresses resistance to infection, e.g., immuno suppression, chemotherapy, radiation, long term or recent high dose steroids, or has a disease that is sufficiently advanced to suppress resistance to infection, e.g., leukemia, lymphoma, AIDS.

APACHE II SCORE

Sum of [A] + [B] + [C]

[A] APS points
[B] Age points
[C] Chronic Health points
Total APACHE II

Appendix B: Letter requesting permission from the CEO of Charlotte Maxeke Johannesburg Academic Hospital

Dr Kenalemodisa Mogotsi

Department of Anaesthesiology

The University of the Witwatersrand

22 May 2018

Attention: The CEO of Charlotte Maxeke Johannesburg Academic Hospital

Dear Ms Gladys Bogoshi

I am a registrar in the Department of Anaesthesiology, I'm currently doing my research for my Master of Medicine in Anaesthesiology. My research is on the evaluation of the Acute Physiology and Chronic Physiology Evaluation II (APACHE II) scoring system in the multidisciplinary ICU at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

The study has been approved by the Human Research Ethics Committee, and the Graduate studies committee at the University of wits.

I am requesting permission to investigate the objectives of my research. There will be no cost to the hospital as a result of this study, the data will be collected on site, no records will be removed from the hospital premises and the report of this study will be available to you should you wish to see it.

Thank You

Kind regards

Kenalemodisa Mogotsi

0835166255

Appendix C: Letter to the Director of the Multidisciplinary ICU

Appendix C: Letter to the Director of the Multidisciplinary ICU

Dr Kena Mogotsi

Department of Anaesthesiology

University of the Witwatersrand

22 May 2018

Dear Prof Richards

I am currently doing my research for the Master of Medicine in Anaesthesiology. My research is on the validation of the Acute Physiology and Chronic Physiology Evaluation II (APACHE II) scoring system in the multidisciplinary ICU at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

The study will be submitted for approval to the Human Research Ethics Committee at CMJAH, and the Graduate Studies Committee of the University of the Witwatersrand.

I am requesting permission to investigate the objectives of my research, please allow me to review the charts. There will be no cost to the hospital as a result of this study, the data will be collected on site, no records will be removed from the hospital premises and the report of this study will be available to you should you wish to see it.

Thank You

Kind regards

Kena Mogotsi
0835166255

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Appendix D: Data collection sheet

Study No:	
Age (in years)	
Comorbidities	
Admission diagnosis	
Planned or unplanned admission	
Emergency / elective surgery	
Immune compromised or severe organ dysfunction	
HIV status	
ARV treatment	
Oxygenation (mmHg) a) FiO_2 b) PaO_2 c) $PaCO_2$	
Heart rate (Bpm)	
Mean arterial pressure (mmHg)	
Respiratory rate (nonventilated or ventilated)	
Glasgow Coma Scale	
Serum Creatinine (mg/dl)	
Presence of Acute Renal Failure	
Serum Sodium (mmol/l)	
Serum Potassium (mmol/l)	
Serum HCO_3 (venous, mmol/l if no ABG)	
Arterial pH	
Temperature (rectal) (**°C)**	
White blood count (x1000)	
Haematocrit (%)	
Principle diagnostic category	

Section 5: Annexures

5.1 Ethics approval

UNIVERSITY OF THE
WITWATERSRAND
JOHANNESBURG

R14/49 Dr Kenalemodisa Lindiwe Mogotsi et al

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M180605

NAME: (Principal Investigator)	Dr Kenalemodisa Lindiwe Mogotsi et al
DEPARTMENT:	Anaesthesiology Chris Hani Baragwanath Academic Hospital Multidisciplinary Intensive Care Unit
PROJECT TITLE:	Retrospective evaluation of the APACHE II critical care scoring system in a multidisciplinary intensive care unit
DATE CONSIDERED:	29/06/2018
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof Juan Scribante
APPROVED BY:	Dr CB Penny, Chairperson HREC (Medical)
DATE OF APPROVAL:	26/09/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in June and will therefore be due in the month of June each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date 17/10/18

5.2 Graduate studies approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

12 September 2018
Person No: 1725851
PAG

Dr KL Mogotsi
No 32 Barbadas Island Villas
9 Wisbeck Road
2091
South Africa

Dear Dr Kenalemodisa Mogotsi

Master of Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *Retrospective evaluation of the APACHE II critical care scoring system in a multidisciplinary intensive care unit* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

5.3 CEO approval

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

Enquiries:
Ms. N. Mzila
Office of the Clinical Director
Tell: (011): 488-4812
Email: Nolwazi.Mzila@gautemg.gov.za
19 October 2018

GP_201810_027

Dear Dr. K. Mogotsi

STUDY TITTLE: Retrospective Evaluation of the APACHE II Critical Care Scoring System in a Multidisciplinary Intensive Care Unit.

Permission is granted for you to conduct the above recruitment activities as described in your request provided:

1. Charlotte Maxeke Johannesburg Academic Hospital will not anyway incur or inherit costs as result of the said study.
2. Your study shall not disrupt services at the study sites.
3. Strict confidentiality shall be observed at all times.
4. Informed consent shall be solicited from patients participating in your study.

Please liaise with the HOD and Unit Manager or sister in charge to agree on the dates and time that would suit all parties.

Kindly forward this office with the results of your study on completion of the research.

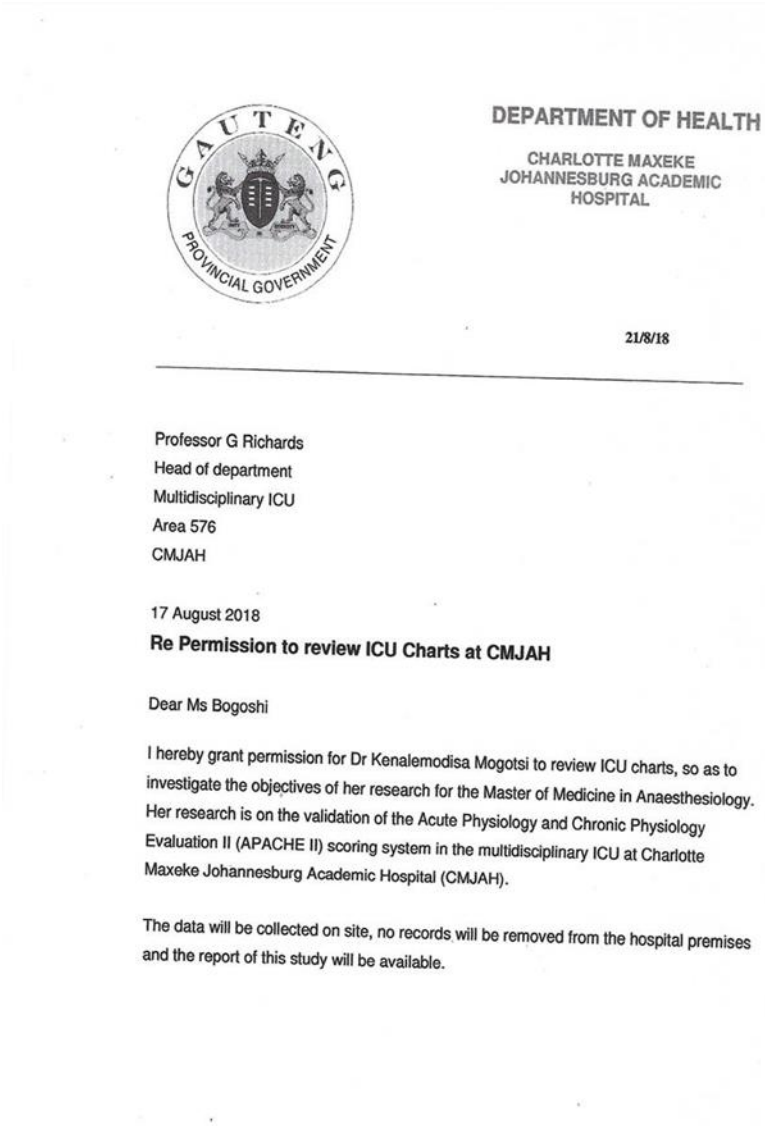
Supported / ~~not supported~~

Dr. M.I. Mofokeng
Clinical Director
DATE: 19/10/2018

Approved/not approved

Ms. G. Bogoshi
Chief Executive Officer
Date: 13.11.2018

5.4 ICU approval



DEPARTMENT OF HEALTH

CHARLOTTE MAXEKE
JOHANNESBURG ACADEMIC
HOSPITAL

21/8/18

Professor G Richards
Head of department
Multidisciplinary ICU
Area 576
CMJAH

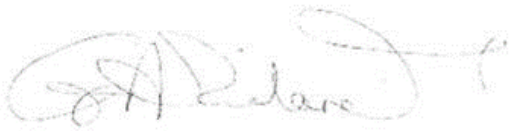
17 August 2018

Re Permission to review ICU Charts at CMJAH

Dear Ms Bogoshi

I hereby grant permission for Dr Kenalemodisa Mogotsi to review ICU charts, so as to investigate the objectives of her research for the Master of Medicine in Anaesthesiology. Her research is on the validation of the Acute Physiology and Chronic Physiology Evaluation II (APACHE II) scoring system in the multidisciplinary ICU at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

The data will be collected on site, no records will be removed from the hospital premises and the report of this study will be available.



GA Richards

MBBCh PhD FCP (SA) FRCP FCCP

Academic Head Division of Critical Care University of the Witwatersrand

Director Critical Care Charlotte Maxeke Johannesburg Academic Hospital and

Chief Physician Departments Medicine and Pulmonology University of the Witwatersrand

5.5 Turnitin report

1725851:turn it in document.docx

ORIGINALITY REPORT

5%	%	7%	2%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Khosro Hekmat, Axel Kroener, Hartmut Stuetzer, Robert H.G. Schwinger, Sandra Kampe, Gerardus B.W.E. Bennink, Uwe Mehlhorn. "Daily Assessment of Organ Dysfunction and Survival in Intensive Care Unit Cardiac Surgical Patients°, The Annals of Thoracic Surgery, 2005 Publication	2%
2	ceaccp.oxfordjournals.org Internet Source	0%
3	K. STRAND. "Severity scoring in the ICU: a review", Acta Anaesthesiologica Scandinavica, 04/2008 Publication	0%
4	Hekmat, K.. "Daily Assessment of Organ Dysfunction and Survival in Intensive Care Unit Cardiac Surgical Patients", The Annals of Thoracic Surgery, 200505 Publication	0%
5	"ESICM LIVES 2017", Intensive Care Medicine	

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | FACULTY OF HEALTH SCIENCES

10 November 2020

The Chairperson
Graduate Studies Committee
Faculty of Health Sciences
University of the Witwatersrand

Dear Professor Papathanasopoulos

Re: M Med: **Retrospective evaluation of the APACHE II critical care scoring system in a multidisciplinary intensive care unit**

Dr Kenalemodisa Mogotsi, student number: 1725851, has submitted her research report to Turnitin, which revealed a similarity index of 5%. These similarities appear not to be plagiarism but mainly the use of common terminology and phrases specific to the research topic.

Yours sincerely,

Juan Scribante
Supervisor