

## Outcomes 30 days after ICU admission: the 30DOS study

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**Background:** The spectrum of illness and long-term outcome of critically ill patients admitted to intensive care units (ICUs) in South Africa remains largely unknown.

**Objectives:** This study was designed to provide data on ICU outcomes and disease burden in public sector ICUs in KwaZulu-Natal. The primary objective was to describe 30-day mortality of all patients admitted to participating sites. Secondary objectives included clinical demographics and spectrum of illness amongst these patients, and testing a template to demonstrate feasibility of such data collection.

**Methods:** 30DOS was a multicentre, prospective, observational cohort study conducted over 30 days. An a priori decision was made to report study results separately for adults and paediatric patients. This article reports the results for adult patients. The complete 30-DOS study included 11 ICUs in six hospitals. All adult patients admitted to study ICUs were included. Patients were followed up telephonically by a research assistant. Data on patient demographics, preadmission functional scoring, injury severity scoring, co-morbidities, admission diagnosis/es, organ support, and outcome were collected.

**Results:** A total of 228 adults were included. The majority of admissions (73.7%) occurred on an emergency basis, with 68.4% occurring in the postoperative period. Approximately half were for non-communicable disease (49.6%), followed by trauma (29.0%) and infectious disease (21.5%). There were a total of 59 (25.9%) deaths within the first 30 days after admission. In-ICU mortality was 19.7%. There were 12 (5.3%) in-hospital deaths following discharge and two (0.9%) out-of-hospital deaths. Thirty-day survival was known for 174 (76.3%) admissions with a 33.9% mortality rate.

**Conclusion:** Overall in-ICU mortality was 19.7% with a large trauma burden in a young population. Thirty-day mortality was 33.9%. Information pertaining to patient demographics and spectrum of illness provided novel information to further the understanding of the demand placed on critical care resources within South Africa.

**Keywords:** critical care, 30-day mortality, Outcome, South Africa

### Introduction

Critical care in South Africa, despite its rapid growth and development, still faces considerable challenges, chief among these being a scarcity of resources.<sup>1–3</sup> As of 2008–2009 there were

only 4 719 critical care beds for a population of 49 million.<sup>2</sup> Only 25% of these were in the public sector, which provides medical care for 84% of the population.<sup>4</sup>

High-income countries are able to collect and report intensive care demographic and outcome data, often using a national database,<sup>5–10</sup> thereby allowing for disease surveillance and outcome improvement. South Africa has yet to develop this capacity. As a result the spectrum of illness and long-term outcome of critically ill patients admitted to intensive care units (ICU) in South Africa remains largely unknown. Yet, the rational utilisation and development of ICU resources in South Africa requires a sound knowledge of the burden of disease and the outcomes of critically ill patients.<sup>1–4</sup>

In the absence of an established national or regional database, multicentre collaborative studies offer the best possibility of collecting these data. It is with this background that the 30-Day Outcome Study (30DOS) was designed to provide data on ICU outcomes and disease burden in public sector ICUs in KwaZulu-Natal, South Africa. KwaZulu-Natal is the second most populated province of South Africa, accounting for 19.9% of the country's total population.<sup>11</sup> ICU data from this province are thus of importance for any further national discourse on intensive care services in South Africa. This study may also provide a template for future national critical care studies.

### Objectives

This study aimed to: (1) describe the 30-day mortality of all patients admitted to participating sites in KwaZulu-Natal; (2) describe the clinical demographics and spectrum of illness amongst these critical care patients; and (3) demonstrate the feasibility of, and provide a template for, the collection of such data. The study was reported according to the STROBE guidelines for the reporting of observational studies.<sup>12</sup>

### Methods

#### Design

The 30-Day Outcome Study (30DOS) was a multicentre, prospective, observational cohort study to determine the 30-day outcome of patients admitted to public sector ICUs in KwaZulu-Natal, South Africa. An a priori decision was made to report study results separately for adults and paediatric patients. The current paper reports the results for the adult patients. The complete 30DOS study included 11 ICUs in six hospitals. Of these, three were dedicated paediatric ICUs and this paper thus presents findings from eight ICUs in six hospitals. Of the eight ICUs there were three general ICUs in regional hospitals; two general ICUs in tertiary hospitals; a surgical ICU, a trauma ICU, and a cardiothoracic ICU in the provincial central hospital. There were a total of 60 adult ICU beds in the included study ICUs.

#### Sampling and process

All adult patients admitted to the study ICUs from 07h00 on October 20, 2014 to 06h59 on November 19, 2014 were included. An adult was defined as a patient 18 years or older. Patients were followed up by the admitting ICU team until death or discharge from ICU, if this occurred before 30 completed days in ICU, or until day 30 in ICU. Patients who were discharged from ICU before day 30 were followed up by a research assistant, who contacted either the patient or family telephonically to determine the patient's 30-day outcome. At least three attempts were made to contact the patient or relatives.

The data-collection tool was a paper-based case report form that collected data on each patient's demographics, preadmission functional scoring, injury severity scoring, co-morbidities,

admission diagnosis/es, organ support in ICU, and outcome. Functional assessment was conducted using the Barthel Index of Activities of Daily Living.<sup>13</sup> This index establishes the degree of independence from help for 10 activities of daily living, giving a score which ranges from 0 to 20. A score of zero represents complete dependence for all activities of daily living and 20 represents complete independence. Barthel scores were conducted on admission, using the patient's reported baseline function prior to critical illness, and then again at day 30 to represent the patient's functional outcome. Disease severity was determined using the APACHE II score for all patients, and in addition the Injury Severity Score (ISS) for trauma patients.<sup>14–17</sup> The primary study outcomes of interest were ICU mortality, ICU length of stay, 30-day mortality, and 30-day functional outcome.

#### Data analysis

Once each case report was completed, data were entered into the Research Electronic Data Capture (REDCap) database (a free, secure, web-based, electronic data capture system available at <https://redcap.health.uq.edu.au>) by site investigator(s). Completed study data were exported to an Excel® spreadsheet (Microsoft Corp, Redmond, WA, USA). Statistical analysis was performed using IBM SPSS® Statistics version 23.0 (IBM Corp, Armonk, NY, USA). Categorical variables were described as percentages and compared using chi-square or Fisher's exact tests, where appropriate. Continuous, normally distributed data were described using mean and standard deviation and analysed using Student's t-test. Non-parametric data were described using median and interquartile range (IQR) and analysed using Mann-Whitney U or Kruskal-Wallis tests as appropriate.

Approval for the study was obtained from the University of KwaZulu-Natal (BE210/14), the hospital management of each institution, and the Provincial Health and Research Ethics Committee of the KwaZulu-Natal Department of Health. Funding was supported by the Discipline of Anaesthesiology and Critical Care (University of KwaZulu-Natal) and the Pietermaritzburg Research Collaborative.

#### Results

A total of 228 adults were admitted to the study ICUs. The median age was 38.0 years (IQR 28.5–58.0 years), with 55.3% of admissions being male (Table 1). The majority of admissions (73.7%) occurred on an emergency basis, with 68.4% of all admissions occurring in the postoperative period. Only 12 (5.3%) patients were readmitted to ICU. The major referring disciplines were general surgery (26.8%), cardiothoracic surgery (20.2%), trauma surgery (17.1%), medicine (13.2%), and obstetrics and gynaecology (11.0%). Approximately half of the admissions were for non-communicable disease (49.6%), followed by trauma (29.0%) and infectious disease (21.5%).

All patients were reported to have excellent premorbid functioning prior to ICU admission, with a median Barthel score of 20 (range 5–20). The median APACHE II score was 17 (IQR 13–23, range 4–43) with the median ISS in the trauma patients being 21 (IQR 10–34, range 1–59). Overall 135 (59.2%) patients had at least one co-morbidity. The most common co-morbidity was cardiovascular disease (30.7%), followed by infectious disease (21.9%), HIV (19.3%), metabolic disease (15.4%), and respiratory disease (9.2%). Cancer, chronic kidney disease and neurological disorders were uncommon co-morbidities, with an incidence of less than 5%. Ventilation was provided to 74.1% of patients, with 55.7% receiving inotropic support. Only 10.1% of patients received renal replacement therapy.

**Table 1:** Demographic data for entire cohort comparing elective vs. emergency admissions (*p*-values for comparison of elective and emergency admission)

Factor	Entire cohort		Elective		Emergency	
	n (%) or median (IQR)	n (%) or median (IQR)	n (%) or median (IQR)	n (%) or median (IQR)	n (%) or median (IQR)	<i>p</i> -value
<i>Demographic data</i>						
Age (years)	38 (28.5–58.0)	53.5 (31.0–61.0)	35.0 (27.0–53.0)			0.002
Male	126 (55.3)	30 (50.0)	96 (57.1)			0.339
Nature of admission	Emergency	168 (73.7)				
	Elective	60 (26.3)				
Readmission	12 (5.3)	2 (3.3)	10 (6.0)			0.435
Pre-ICU hospital LOS (days)	1.0 (0.0–4.0)	3.5 (1.0–9.0)	0.0 (0.0–2.0)			< 0.001
Admitting discipline (where <i>n</i> > 5)	Cardiothoracic Surgery	46 (20.2)	38 (63.3)	8 (4.8)		< 0.001
	General Surgery	61 (26.8)	8 (13.3)	53 (31.6)		
	Medicine	30 (13.2)	0	30 (17.9)		
	O and G	25 (11.0)	1 (1.7)	24 (14.3)		
	Orthopaedics	8 (3.5)	5 (8.3)	3 (1.8)		
	Trauma	39 (17.1)	0 (0.0)	39 (23.2)		
	Urology	7 (3.1)	4 (6.7)	3 (1.8)		
Primary reason for admission	Infectious	49 (21.5)	7 (11.7)	42 (25.0)		< 0.001
	Non-communicable	113 (49.6)	51 (85.0)	62 (36.9)		
	Trauma	66 (29.0)	2 (3.3)	64 (38.1)		
Admitted from	Emergency department	47 (20.5)	0	47 (28.0)		< 0.001
	Theatre	144 (63.2)	60 (100)	84 (50.0)		
	Other	4 (1.8)	0	4 (2.4)		
	Ward	33 (14.5)	0	33 (19.6)		
Postoperative	156 (68.4)	60 (100)	96 (57.1)			< 0.001
Emergency surgery	93 (40.8)	0	91 (54.2)			
<i>Disease severity</i>						
APACHE score	17.0 (13.0–23.0)	15 (11–17)	20.0 (14.0–26.0)			< 0.001
ISS	21.0 (10.0–34.0)					
<i>Co-morbidities</i>						
Any comorbidity	135 (59.2)	51 (85.0)	84 (50.0)			< 0.001
Cardiovascular	70 (30.7)	35 (58.3)	35 (20.8)			< 0.001
HIV	44 (19.3)	10 (16.7)	34 (20.2)			0.547
Metabolic	35 (15.4)	20 (33.3)	15 (8.9)			< 0.001
Respiratory	21 (9.2)	8 (13.3)	13 (7.7)			0.198
Cancer	11 (4.8)	5 (8.3)	6 (3.6)			0.140
Renal	10 (4.4)	3 (5.0)	7 (4.2)			0.787
Neurologic	7 (3.1)	2 (3.3)	5 (3.0)			0.891
GIT	5 (2.2)	2 (3.3)	3 (1.8)			0.482

Notes: IQR = interquartile range; ICU = intensive care unit; LOS = length of stay; O and G = Obstetrics and Gynaecology; APACHE = acute physiology and chronic health evaluation score II; ISS = injury severity score; HIV = human immunodeficiency virus; GIT = gastrointestinal tract.

There were a total of 59 (25.9%) deaths within the first 30 days after admission. In-ICU mortality was 45 (19.7%). There were 12 (5.3%) in-hospital deaths following ICU discharge and two (0.9%) out of hospital deaths. Thirty-day survival was known for 174 (76.3%) admissions (see Figure 1 for flow-chart illustrating outcomes of study patients) with a 33.9% mortality rate. There was a short median ICU length of stay (LOS) of 3.0 days (IQR 1.0–6.0 days, range 0–59.0 days). In terms of functional outcome, the median 30-day Barthel score was 20 (range 7–20), reflecting excellent functional status.

There were a number of significant differences noted between the elective and emergency admissions. Elective admissions were older with a median age of 53.5 years as opposed to 35.0 years in emergency admissions (*p* = 0.002). The primary indication for admission differed between the elective and emergency groups, with 85.0% of elective admissions being due to non-communicable disease. There was a significantly higher proportion of trauma and infectious disease in the emergency admission group. The burden of non-communicable disease in the emergency group remained high at 36.9%.

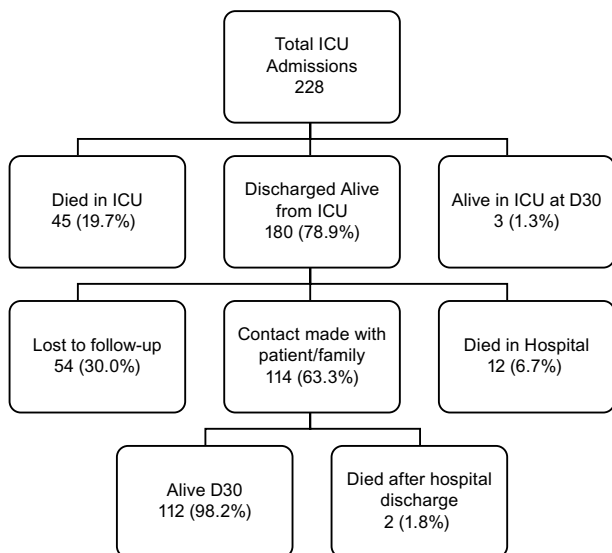


Figure 1: Flow diagram of inclusion and results of the 30-day outcome study. D30 = day 30.

Elective admissions were significantly more likely to have a co-morbidity (85.0% vs. 50.0%;  $p < 0.001$ ), cardiovascular disease (58.3% vs. 20.8%;  $p < 0.001$ ), and metabolic disease (33.3% vs. 8.9%,  $p < 0.001$ ). The median APACHE II score was, however, significantly higher in the emergency group (20 vs. 15,  $p < 0.001$ ). While there was no significant difference in mechanical ventilation or inotropic support between the emergency and elective admissions, emergency admissions were more likely to receive renal replacement therapy (13.1% vs. 1.7%,  $p = 0.012$ ) and less likely to receive nutritional support (53.6% vs. 71.7%,  $p = 0.015$ ).

In-ICU mortality was significantly higher in the emergency admission group than in the (elective admission group 24.4% vs. 6.7%;  $p = 0.003$ ). Overall 30-day mortality was similarly significantly higher in the emergency group (43.2% vs. 10.2%;  $p < 0.001$ ). ICU LOS was significantly shorter in the elective admission group (2.0 days vs. 3.0 days;  $p < 0.001$ ).

Both pre-admission and 30-day Barthel scores did not differ between elective and emergency admissions.

## Discussion

### Principal findings

The in-ICU and 30-day mortality of a representative sample of public hospitals in KwaZulu-Natal, South Africa was 19.7% and 33.9% respectively. The majority of the mortality was secondary to emergency admissions to ICU. Despite poor infrastructure, lack of transport and communication problems commonly experienced in this poorly resourced setting, the loss to follow-up was only 54 patients (23.7%).<sup>2-4</sup> However, this number may be inaccurate and we were unable to determine how many of the patients lost to follow-up had subsequently died. Future similar studies need to focus on identifying methods to decrease the proportion of patients lost to follow-up, even though similar challenges will most likely be faced.

The functional outcome of survivors was excellent (median 30-day Barthel score of 20) in a young population comprising nearly 30% trauma patients. In addition, the study was successful in

coordinating data capture and 30-day follow-up across six hospitals and 11 ICUs. We were able to describe the spectrum of disease and the demographic and clinical details of those admitted using the tools developed.

### Interpretation and implications

The results of this study need to be interpreted in the light of the disciplines and populations the study sites served. Half of the sites were general ICUs, admitting patients from a variety of medical and surgical disciplines. The other four ICUs were surgical disciplines (cardiothoracic, trauma, and two general surgical ICUs). The results of this study may be considered skewed and do not represent the national disease profile, which includes a significant infectious burden of disease. Importantly, three of the general ICUs represent regional hospitals, with two located in tertiary hospitals, while the other three ICUs are found in tertiary or quaternary teaching hospitals. The study population demographics reflect this distribution with the ICU population being young (mean age: 43 years) in comparison with high-income countries.<sup>6-8,10</sup>

With nearly three-quarters of admissions coming from emergency cases, 30% of cases resulting from trauma, and close on 60% of surgical ICU admissions occurring postoperatively, the tremendous burden of unplanned admissions is evident. Data from this study have been significantly influenced by the inclusion of a cardiothoracic ICU where the vast majority of work was elective. Without these data, figures would demonstrate even greater pressure exerted by emergency cases. The resources occupied by these emergency cases may prevent the completion of elective surgical cases and should be examined in a future study. This should be considered in future planning and development of critical care in KwaZulu-Natal and South Africa.

The difference between elective and emergency admissions in terms of disease classification is predictable, with 85% of elective admissions for non-communicable disease. However, with 25% and 38% of emergency admissions being accounted for by infectious disease and trauma respectively, this study highlights priorities where public health initiatives can play a role in decreasing the burden on critical care resources.<sup>4,6,18</sup>

Considering that the majority of the cases were emergency admissions, the in-ICU mortality rate in the study sample (19.7%) is in keeping with international trends.<sup>7-10</sup> The mortality rate of 24.4% at 30 days for emergency admissions may be considered high when reflecting on the pressure on available but limited resources. Resource-poor settings need to maintain strict triage criteria in order to maximise benefit from limited ICU beds. Future studies should look at appropriate timing of ICU discharges to determine whether discharges are influenced by high numbers of referrals and pressure to admit, decisions regarding non-beneficial care or triage, and whether these events influence outcomes following discharge.

The difference in length of ICU stay between elective and emergency admissions of one day may be due to differences in severity of illness, or the nature of the admission, or maybe a surrogate marker of the ICU bed pressure. Ventilation and inotropic support was common and represents a large clinical and financial burden. The low rate of RRT is surprising considering the high potential for acute kidney injury in the large emergency group. This may be explained by the lack of facilities to provide renal replacement therapy and again reflects the challenges of a resource-poor environment and deserves future investigation.<sup>2,3</sup>



**Table 2:** Organ support delivered for entire cohort and comparing elective vs. emergency admissions

Organ support	Entire cohort	Elective	Emergency	p-value
	n (%) or median (IQR)	n (%) or median (IQR)	n (%) or median (IQR)	
Mechanical ventilation (invasive)	169 (74.1)	43 (71.7)	126 (75.0)	0.613
Inotropic support	127 (55.7)	39 (65.0)	88 (52.4)	0.091
RRT	23 (1)	1 (1.7)	22 (13.1)	0.012
Nutritional support	133 (58.3)	43 (71.7)	90 (53.6)	0.015

Note: RRT = renal replacement therapy.

With an overall mean APACHE score of 18.8, the expected mortality rate was 25%.<sup>14</sup> According to APACHE severity scoring in the elective admissions, actual mortality of 6.7% was better than the predicted 15%. Similarly, emergency admissions had an actual mortality of 24.4% compared with the predicted mortality of 40%. These better than expected outcomes may be a result of careful patient selection in a resource-constrained system, a population that performs better than predicted, or scoring systems which may not be valid in the environment studied.<sup>14–16</sup>

Despite the young age of the 30DOS cohort there was a high prevalence of co-morbidities, with 59.2% of patients having at least one co-morbidity. In contrast, the ICON audit of 10 069 ICU patients worldwide reported that 45.3% of patients in their cohort had at least one co-morbidity.<sup>19</sup> The mean age of the ICON cohort was 60 years, and thus represented an older population that would be expected to have a higher prevalence of co-morbidities. This disparity may have been driven by differences in the definition of co-morbidities but may also be a result of an increased burden of HIV in South Africa. There was a significant difference in co-morbidities between the elective and emergency cohorts, with 85% of elective patients having at least one co-morbidity as opposed to 50% of emergency patients. This was driven by a significantly higher prevalence of cardiovascular disease and metabolic disease (mostly diabetes mellitus) in the elective cohort, which is expected as most of these patients were undergoing coronary artery bypass grafting. HIV disease was the second most common co-morbidity in the entire cohort (19.3%). In the emergency population the prevalence of cardiovascular disease (20.8%) and HIV disease (20.2%) was similar, highlighting the burden of HIV disease in KwaZulu-Natal. In contrast, international studies report a prevalence of HIV of 0.3–1.0%.<sup>19–21</sup> The study design required the admitting doctor to report if the patient was known to be HIV positive and did not note if the

patient was HIV negative or if the patient's HIV status was unknown. The prevalence of HIV in KwaZulu-Natal may be as high as 16.9%,<sup>22</sup> and unpublished audit data from one of the participating study ICUs has shown that in 65.9% of ICU admissions the patient's HIV status is unknown (unpublished data). The incidence of HIV reported in this study is thus likely to significantly underestimate the prevalence of HIV in patients admitted to intensive care units in the province. While the high prevalence of HIV disease is of concern as a potentially preventable burden on ICU resources, the clear willingness of the study ICUs to accept patients who are HIV positive represents a positive move towards the acceptance of HIV as a chronic co-morbidity to be staged and triaged like any other co-morbidity (Table 2).

### Limitations

Site selection was on a voluntary basis and does not reflect the entire province or private health care. However, the public hospitals serve the majority of the population. Sampling for this study took place over a 30-day period and may not reflect the burden over an entire year, as there are seasonal and monthly variations in the number of referrals. We did, however, schedule data collection for a period to reflect wider daily function. Patients were lost to follow-up due to communication difficulties or possibly death and thus not recorded as such. Attempts were made to avoid this by having at least two contact numbers for each patient, including those of their next-of-kin. However, those lost to follow-up may reflect a larger 30-day mortality. This remains unknown and will need further investigation.

Accurate data collection was dependent on the clinicians working in ICU. In addition, data on referral patterns, number of referrals, number of patients declined admission, and potential early discharges were not recorded, but these were not included in the objectives of this study. The Barthel scores were high on both admission and follow-up at 30-days with no significant changes. Again, the number of cases was probably too small to detect changes and we did not have a large enough cohort of traumatic brain injury cases to determine inclusion or exclusion criteria based on this pattern of pathology.

### Future research

This study highlighted various starting points for future research—specifically the need for further data capture on a national level in South African critical care. Both public and private ICUs should gather information on their patient demographics and outcomes and ideally a centralised database should be established. This will allow more appropriate critical care resource management and future development. Specific points of interest identified in this study including the limited demand for RRT and the burden of emergency cases on local units should be reviewed in more depth (Table 3).

**Table 3:** Outcome data for entire cohort comparing elective vs. emergency admissions

Outcome data	Entire cohort	Elective	Emergency	p-value
	n (%) or median (IQR)	n (%) or median (IQR)	n (%) or median (IQR)	
ICU mortality (30-day; n = 228)	45 (19.7)	4 (6.7)	41 (24.4)	0.003
Overall 30-day mortality (where outcome known; n = 174)	59 (33.9)	5 (10.2)	54 (43.2)	< 0.001
ICU LOS (days)	3.0 (1.0–6.0)	2.0 (1.0–4.0)	3.0 (1.0–8.0)	0.015
Barthel score (Admission)	20.0 (20.0–20.0)	20.0 (20.0–20.0)	20.0 (20.0–20.0)	0.585
Barthel score (Follow-up)	20.0 (20.0–20.0)	20.0 (20.0–20.0)	20.0 (20.0–20.0)	0.255
Patient lost to follow-up	54 (23.7)	10 (16.7)	44 (26.2)	0.136

Notes: ICU = intensive care unit; LOS = length of stay.

Furthermore, the hypothesis that several patient groups may derive limited outcome benefit beyond 30 days by admission to ICU should be examined. Identification of such groups may allow more rational decision-making with respect to entry criteria, thus minimising futility and maximising bed usage in the presence of scarce resources.

### Conclusion

The 30DOS study was successful in establishing a template for the data collection of mortality and 30-day outcome in eight adult ICUs in KwaZulu-Natal. Overall in-ICU mortality was 19.7% with a large trauma burden in a young population. The 30-day mortality was 33.9%. Information pertaining to patient demographics and spectrum of illness provided novel information to further the understanding of the demand placed on critical care resources within the local context. The study illustrated that quality data collection and integration is possible with collaboration by various ICUs at different sites. It highlights the possibility of, and need for, a national critical care database in order to recognise local and national burden of illness, foster research in a South African setting, and more efficiently manage our scarce ICU resources.

*Disclosure statement* – No potential conflict of interest was reported by the authors.

*Acknowledgements* – The authors would like to thank and acknowledge the Anaesthetic Network for South Africa ([www.ansa.org.za](http://www.ansa.org.za)) for providing the facility and funding to use the REDCap data capture system, Mr Simphiwe Gumede for his contribution, and the Pietermaritzburg Research Collaborative for funding the research assistant.

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Received: 01-08-2017 Accepted: 06-11-2017