THE UNIVERSITY OF SHEFFIELD

What factors affect survival in critically ill older people?

Using a CriSTAL scoring system to identify premorbid conditions associated with a poor outcome after admission to Intensive Care in people 70 years or older

Kieran Jankowski

Contents

Abstract

Introduction. More frail, elderly individuals are being referred for access to higher levels of medical services leading to increased demand for Intensive Care services. Identifying those individuals with the best chances of survival means there is less risk of subjecting people to treatments with no overall benefit or potential harm and maximising the individual's knowledge of their potential for recovery. To date, there is no objective prognostic scoring system for use at the point of admission to the ICU to inform these considerations and provide information to patients on their likely chances of survival after ICU admission.

Methods. An adapted version of a previously published CriSTAL study combining degree of frailty with ten chronic disease variables and four markers of health was used to create a 15 item screening tool (Cardona-Morrell and Hillman, 2015). The CriSTAL dataset was designed to identify individuals nearing the end of their life. A retrospective epidemiological database analysis of admission and outcome data was collected from the electronic patient data management system at Sheffield Teaching Hospitals (Metavision). The aim was to examine the prognostic ability of chronic health indicators using an adapted CriSTAL model (Cr1) on the first half of the dataset which would then allow identification and weighting of the variables of those significantly associated with mortality and create an adapted CriSTAL model (Cr2). Cr2 was used to predict likely outcomes at a population and individual level for the second half of the dataset.

Results. Data were obtained between the period 1st March 2015 – 31st December 2016 for a total 1000 elderly (≥ 70years) patients with a mean age of 77.50 years (± 5.83 SD; Range: 70-101years). This sample was split randomly into two comparable groups termed *Training* (Mean age: 77.34 ± 5.83 SD; Total mortality: 29.2%) & *Test* (Mean age: 77.67 ± 5.83 SD; Total mortality: 25.2%) for different analyses. Analysis of the *Training* sample with the Cr1 model identified 8 variables to be clinically important in predicting mortality (P≤0.1) including: recent MI, an abnormal ECG, Congestive cardiac failure (NYHA≥2), Chronic obstructive pulmonary disease, Chronic liver disease, Metastatic cancer, Stay in hospital ≥ 5 days preceding ICU admission, and Frailty (CFS≥4). Results showed that both models were able to predict population based outcome to a reasonable degree (Cr1 - 76.6% vs Cr2 - 79.6). Of these results specificity was high, whilst sensitivity was comparatively low (98.3% & 38.4% vs 96.2% & 28.2%). ROC curve analysis indicated significant calibration of both models and moderate predictive capabilities of both models (AUC: Cr1=0.67; Cr2=0.72). The most appropriate cut off for Cr2 was found to be a CriSTAL score >4 which had sensitivity and specificity of 73.0% and 36.1%, respectively.

Conclusion. This study identified 8 statistically significant variables that predicted patient mortality, including two variables (Abnormal ECG & Stay in hospital ≥ 5 days preceding ICU admission) not previously studied. Cr2 showed consistent improvements on Cr1 and exhibited competitive AUC results to other ICU prognostic models not designed for use at the point of admission to ICU. However, the relative lack of sensitivity and specificity in the ROC curve results means neither model is able to provide definitive outcome predictions. Despite this, the results found here meet one of our initial objectives in that identifying the presence of one or more of our significant variables in an elderly patient could be used to inform clinical discussions with patients and relatives as to whether or not intensive care admission may be desirable.

1. Introduction

1.1 Predicting Outcomes from Intensive Care: rationale for the study

Intensive care (in many countries known as critical care) is a medical speciality responsible for the management of acutely unwell patients and those with the potential to become critically unwell. Patients can suffer from, or be at risk of developing single or multiple organ failures: they may present after surgery, on a hospital ward after deterioration, after presenting to the emergency department and from other smaller hospitals that cannot provide the specialist care, investigations and greater degree of supervision that intensive care units (ICUs) in larger hospitals can offer.

Developments in medical practice also bring many challenges for providing intensive care services. The National Health Service (NHS) offers more treatments than ever before, and whist this is undoubtedly beneficial to the population, it is accompanied by a rising expectation for the service it provides for patients. Social and medical progress has led to a growth in the population and rising levels of chronic diseases. Since mid-2005, the UK population aged 65 and over has increased by 21% and the population aged 85 and over has increased by 31% (Levine et al., 2007; Office of National Statistics (ONS), 2015a). The combination of an older, frailer population who are undergoing major surgery and novel treatment options is resulting in an increased demand for healthcare.

The UK's current provision for adult critical care beds stands at 4022: in January, February, and March of 2016 capacity was surpassed by 1.2%, 2.5% and 0.4%, respectively. Analyzing the accompanying admission trends, older patients generally occupied more critical care beds than younger patients, with 65 to 69 year-old men and 75 to 79 year-old women being recorded more than any other age groups (NHS England, 2016).

Providing critical care treatment to patients is accompanied by huge emotional and physical burdens for both patients and relatives, particularly as there are relatively little long term outcome data on the functioning of older patients after they have recovered from a critical care

stay and gone home. Admission to intensive care can be a life changing event for any individual: loss of financial stability, ongoing poor health, or inability to live independently are all significant outcomes for those who may have apparently achieved a 'good' recovery and outcome. Furthermore, bed days on ICU are one of the most expensive in healthcare, costing between €1168 and €2025 per day, (depending on the number and types of organs supported) with a mean length of stay of approximately 6 days (Tan et al., 2012). Due to an ability to support multiple organs at once, and the personal and societal cost that comes with these organ supports, huge expectation is placed on the intensive care unit to help an individual recover to full pre-morbid status. However, despite best efforts to help patients recover, some interventions e.g. invasive mechanical ventilation and renal support have been associated with causing considerable additional morbidity and a long term (15 years or more) ongoing health burden. Having conversations with patients and families as to the likely benefits and burdens of providing such treatments is necessary to enable realistic and informed decisions to be made whenever possible.

Identifying those patients who are likely to have poor outcomes as they come to the end of their lives is essential so as not to subject individuals to treatment burdens that may be of no overall benefit to them, and may end up causing unnecessary suffering and distress.

Responsibility for decisions regarding the appropriate treatments ultimately falls on the attending clinician whose role it is to take into consideration the acute physiology of the patient in combination with pre morbid factors and predict that individual's likely outcome and longer term recovery. This can then be used to discuss the benefits and burdens of treatment with the patient, their family and referring medical teams. The heterogeneity in any given condition can be vast, which is often reflected in differing views from specialists in different teams. Further problems occur when patients are deteriorating acutely, as delayed admission to ICU is strongly linked with poorer outcomes (Chalfin et al., 2007). One method of assisting the admission decision making process has been the creation of outcome predictor scoring systems. Pre-morbid factors are combined with acute physiology values to calculate a standardised numerical value which represents the predicted outcome from that set of circumstances. A variety of scoring systems are currently being used in clinical practice however, all have shortcomings most notably that they are not designed for use at the point of deciding whether or not to admit to critical care.

Understanding the complex relationship between pre-morbid factors and outcomes in the intensive care population carries huge significance for optimising good patient outcomes and giving patients and families useful, relevant information, particularly as they get older. A published CriSTAL (Criteria for Screening and Triaging to Appropriate aLternative care) scoring system (Cardona-Morrell and Hillman, 2015) has been created to identify elderly patients on the wards at the end of their lives and quantify the risk of death in hospital or soon after discharge. A previous pilot in Sheffield of an adapted CriSTAL model at the point of admission to critical care, recognised some potential for it to be used to identify those patients who subsequently had a poor outcome after admission (Yogasundaran et al., 2016).

My study investigated an adapted CriSTAL scoring system's full clinical potential by analysing retrospective data collected from all non elective elderly admissions to the Sheffield Critical Care Department.

1.2 The ageing population and Treatment Burdens of Intensive Care

The number of people worldwide aged 60 years or over is projected to grow by 56% between 2015 and 2030 and is projected to accelerate further beyond 2030 (Nations, 2015).

The Office of National Statistics (ONS) estimated in June 2015 that the UK's population stood at just over 65 million. Whilst the population as a whole continues to grow steadily, the older portion of the population is growing at a much quicker rate (ONS, 2016). These trends are likely to continue and estimates for midyear 2039 population suggest that 18 million (24.3%) of the population will be 65 and over, and 3.56 million (4.8%) will be aged 85 and over (ONS, 2015b).

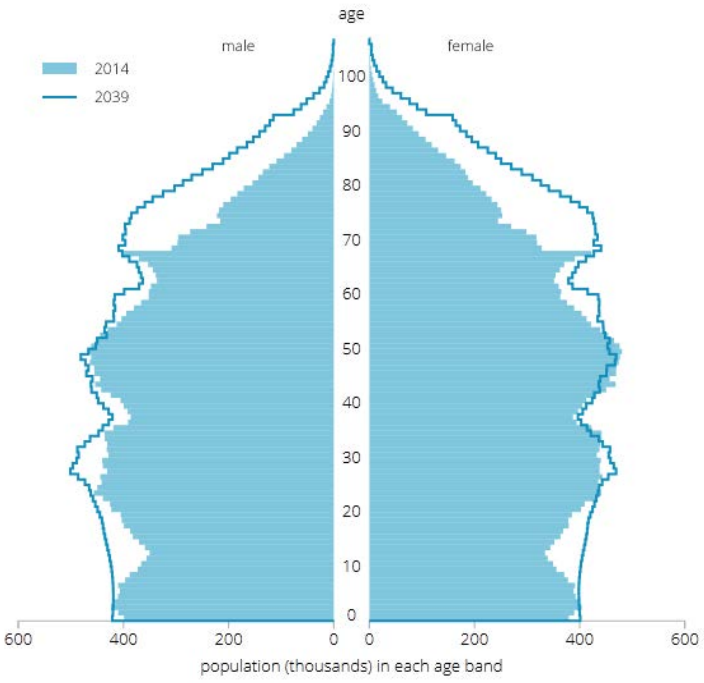


Figure 1. Age structure of UK population, mid-2014 and predicted mid-2039; National Population Projections: 2014-based Statistical Bulletin (ONS, 2015a).

For some individuals, medical interventions offered by intensive care treatments may not result in survival and can create significant ongoing burdens for those who do survive. UK reported mortality is between 20-25% whilst Fuchs et al reported a 11% - 14.6% on unit, and a further 18.8% -27.9% in hospital mortality post discharge for the US population (Fuchs et al., 2012). For patients who survive beyond hospital discharge many challenges await them in their recovery. Post–intensive care syndrome (PICS) encompasses new or worsening impairments in a person's physical, cognitive, or mental status arising after critical illness (Mikkelsen et al., 2015). It is estimated that 25% to 75% of ICU survivors have challenges with depressive symptoms, anxiety, cognitive impairment, and/or posttraumatic stress disorder in addition to an ongoing burden of new of worsened physical illness (Wolters et al., 2016). 31% of patients report reduced physical activity in one study, while social life had worsened in 32% and functional limitation increased in 30% (Capuzzo et al., 1996).

It is well documented that differences in elderly patient's baseline functional status preceding and post stay on intensive care is vast. For example, elderly patients who were deemed to have good baseline functional status, 40% of them were dependent at hospital discharge and 24.4% had moderate to severe disability at 1-year follow-up. For the majority of patients significant recovery was observed during the first 3 months after discharge, however further recovery slowed or even stopped all together beyond 3 months up to one year (Villa et al., 2016). This indicates that even the patients with largest physiological reserves it can be months before they reach an acceptable health and functional status. As a result, ICU survivors report lower QOL for all domains (except bodily pain) at baseline and at 6 months to 14 years after discharge (Dowdy et al., 2005). This is of particular concern for the large number of elderly patients admitted to intensive care as they realistically cannot expect another 14 years of life to overcome health burdens caused by intensive care.

Identifying individuals who are unlikely to survive their ICU stay or are coming to the end of their life irrespective of ICU treatment is vital to allow a proper and informed discussion as to the person's likely quality of life should they survive. The aim should be to avoid treatments that produce outcomes that are unacceptable to individual patients e.g. an inability to wash and dress or mobilise may be unacceptable so some older person who would not consider treatment that resulted in survival but them becoming dependent to be a 'success'. As the elderly are the greatest users of intensive care, and also those associated with poorer overall outcomes, predicting how these patients are likely to fair before embarking on treatment is hugely important

for them and for the NHS.

1.3 How important is age as a prognostic variable?

The role of advancing age as a significant factor in intensive care outcomes lacks clarity. Many studies have examined this and have found that compared to younger age groups, mortality during and after intensive care treatment was significantly higher for patients aged ≥ 80years (Bagshaw et al., 2009). Older patients had comparably greater ICU and hospital-adjusted odds of death (Boumendil et al., 2005) and beyond the age of 75 years, age becomes a significant independent risk factor for mortality (Fuchs et al, 2012). For these reasons, in some studies older patients have been found to have a lesser chance of admission to the ICU and greater chance of receiving do-not-attempt resuscitation orders (DNAR) or decisions to withhold life-sustaining therapies (Soares et al., 2006).

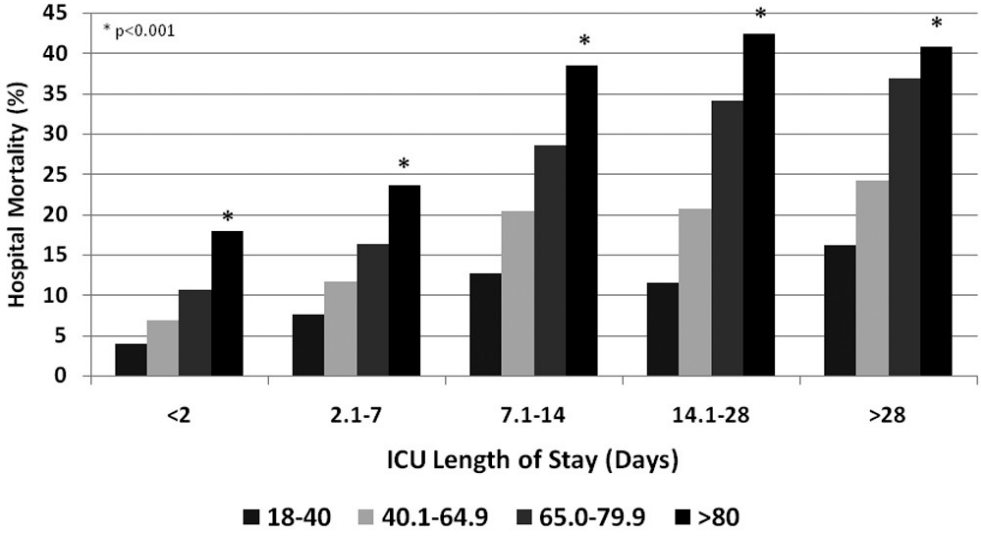


Figure 2. Hospital mortality and ICU length of stay by age category; Very old patients admitted to intensive care in Australia and New Zealand: a multi-centre cohort analysis (Bagshaw et al., 2009)

Whilst increasing age is undeniably a major determinant of mortality, many studies argue that the correlation between advancing age and mortality is not due to age alone and find factors commonly associated with advancing age such as severity of illness, co-morbidities and prior functional status to be more reliable in predicting mortality.

Co morbidity, defined as the presence of one or more diseases, is a good predictor of general

wellbeing. Charlson and coworkers found that increased morbidity was considerably linked with increased risk of mortality at 1 year post ICU discharge (Charlson et al., 1987). More recently Groll and colleagues specifically studied the effect of multimorbidity on functional outcome and found again a greater degree of chronic illness was associated with greater deterioration in physical function (Groll et al., 2005).

Hofhuis' study, however, demonstrated that pre-admission health-related quality of life (HRQOL) measured with either the one-item general health question or the complete SF-36 (Short Form Health Survey) had good results in predicting survival/mortality in ICU patients (Hofhuis et al., 2007) whilst Bo and colleagues found mortality was 30% in patients who had an activities of daily living score of 1–6 (dependent), as compared with 7.8% in patients with a score of 0 (independent).

1.4 Frailty

One medical concept that supports the theory that co-morbidity combined with functional status bears more significance outcome than age alone, is frailty. The term represents the decline in health, energy, physical ability, and cognition towards the end of life and is often associated with many adverse events such as falls, susceptibility to acute illness, perioperative complications, unplanned hospital admissions, and mortality. Pathologically, frailty is characterized by non specific widespread inflammation and elevated markers of blood clotting resulting in an impaired homeostatic reserve and a reduced capacity of the individual to withstand stress which is illustrated in figure 5 (Lang et al., 2010). The disease process is outlined in figure 6 where by the accumulative effects of lack of physical exercise, inadequate nutrition, unhealthy environment, immunosenescence, injuries, disease and drug use cause a down regulation of physiological systems and result in sarcopenia, osteopenia, decreased exercise tolerance and reduced metabolism (Lang et al., 2009). It therefore stands, that identifying this cohort of vulnerable patients are very important, however clinical identification of frailty by definition is impractical, and there is no one universal definition.

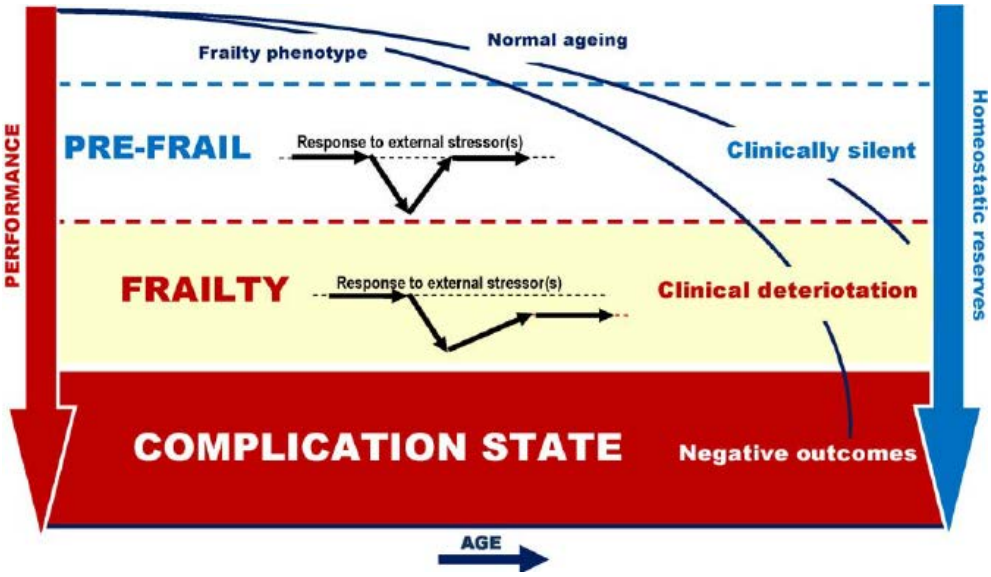


Figure 5. The Development of frailty with advancing age (Lang et al., 2010).

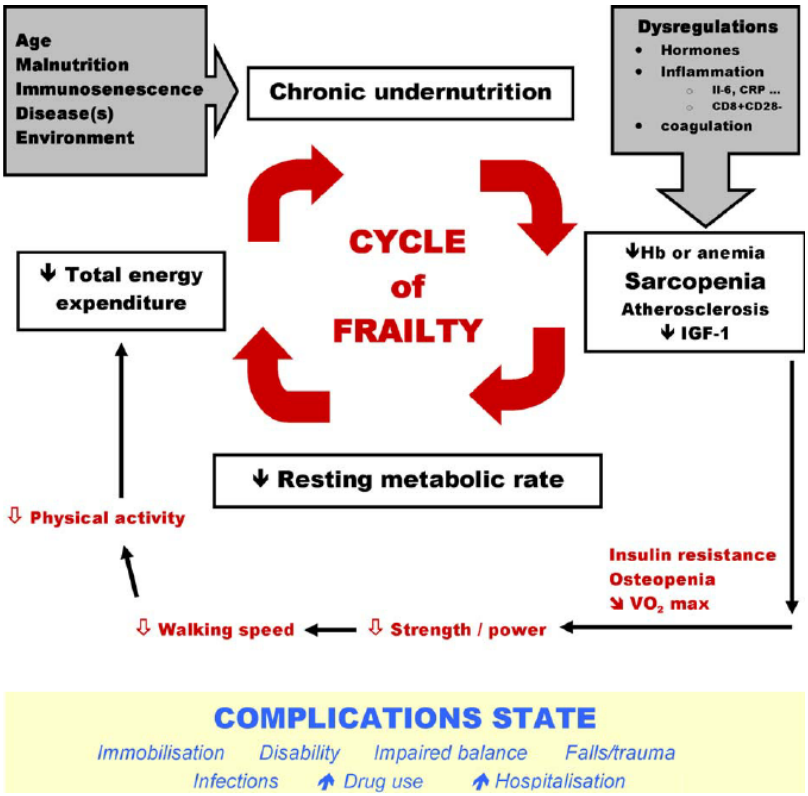


Figure 6. The cycle of frailty (Lang et al., 2010)

Frailty is not routinely assessed or recorded in a critical care setting. Currently, the most frequently used measure of frailty in a clinical intensive care setting is derived from scoring systems that stratify patients into groups based on the degree of frailty. The Clinical Frailty Scale (CFS) is an example of this (Rockwood et al., 2005) (Appendix 7.1). The score ranges from 1 (robust health) to 9 (terminally ill). This method of classifying frailty is much more clinically appropriate for ICU use due to its simplicity. In its initial trial the CFS identified that those with higher scores were older, more likely to be cognitively impaired, had impaired mobility and function, had more co morbidity and ultimately found that frailty is an independent risk factor for mortality. Bagshaw's study found large portions (32.8%) of the older intensive care population (>50 years) to have higher CFS scores (≥4) who in turn had higher in-hospital mortality rates (32%) compared to those not deemed as frail (16%). The Kaplan Meier plot illustrated in figure 7 represents the data from this study and identifies increasing severity of frailty as a predictor of death. Furthermore, those who survived were associated with significantly longer durations of stay in both ICU and hospital, had a greater rate of hospital readmission, were less likely to be living at home independently after 12 months and health-related quality of life was generally lower at 6 and 12 months (Bagshaw et al., 2014).

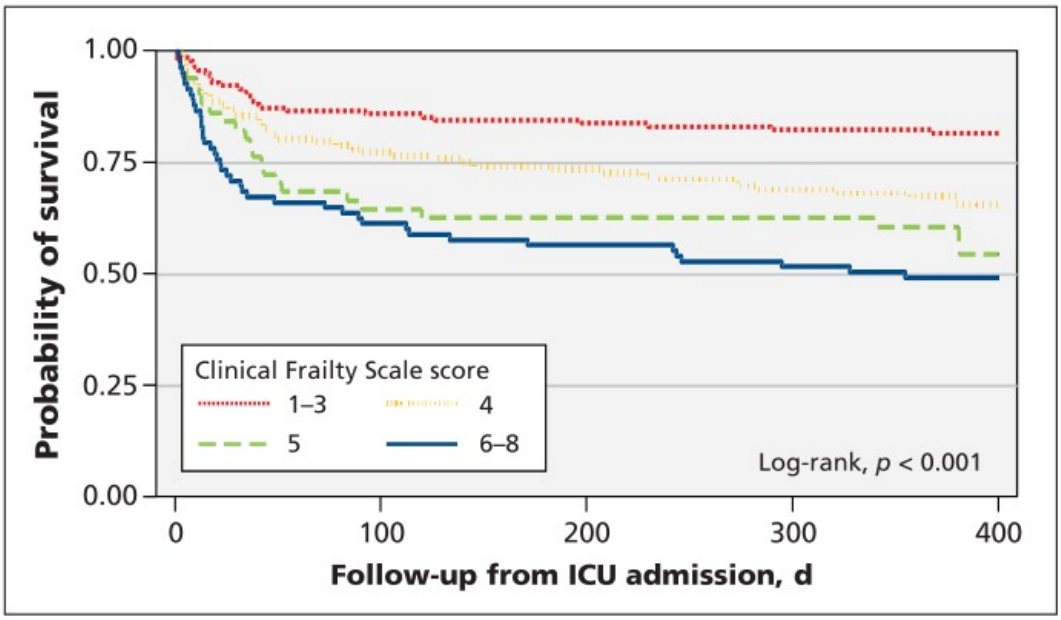


Figure 7. Kaplan–Meier survival curves stratified by Clinical Frailty Scale score; Association between frailty and short- and long-term outcomes among critically ill patients: a multicentre prospective cohort study (Bagshaw et al., 2014)

Mortality and degree of frailty are undoubtedly inversely associated which makes identifying the degree of frailty at the point of admission vital in order to aid clinical discussion of prognosis and treatment options. It is also hugely important to identify those with considerable degrees of frailty because the physical and psychological demands of intensive care are likely to result in much poorer outcomes and cause unnecessary suffering for them. Alternatively, the ability to identify even very elderly patients with minimal degrees of frailty may remove age as a direct discriminatory factor for decisions regarding provision of care.

1.5 Chronic disease

Chronic morbidity in the population is becoming increasingly evident. Comparing population morbidity from 1990 to 2010, proportions of all aged deaths attributed to cardiovascular and circulatory diseases, diabetes, urogenital, blood, and endocrine diseases, cirrhotic liver diseases, mental and behavioural disorders, neurological disorders and neoplasms have increased (Lozano et al., 2012). Identifying the morbidities that are known to each increase mortality risk in patients admitted to intensive care allows for better informing of conversations with patients about the benefits and burdens of a proposed treatment by enabling better individual outcome prediction.

Cardona et al realised the importance of both chronic disease and its effect on the elderly population, and a need to assist and standardise clinicians, and help carers and families in decision-making regarding the most sustainable model for appropriate and best quality care. Their study reports the development of a clinical decision aid: CriSTAL (Criteria for Screening and Triaging to Appropriate aLternative care) to identify patients at the end of their life. The variables and thresholds explored for the screening tool were adopted from existing scales that demonstrated association with either in-hospital or 30-day mortality, or survival to 12 weeks (Cardona-Morrell and Hillman, 2015). Variables are chronic kidney disease, previous myocardial infarction, abnormal ECG at presentation, congestive cardiac failure, chronic pulmonary disease, cerebrovascular disease, dementia/cognitive impairment, long term psychiatric disorder, chronic liver disease, solid tumour(s), length of stay in hospital, previous hospitalisation in the past year, ICU readmissions, marked weight loss and frailty.

My project adopted criteria from the original CriSTAL model believed to be suitable for predicting the end of life in an intensive care patient population according to other relevant literature and applied them to a retrospective database of patients admitted to intensive care units in hospitals in Sheffield.

2. Methodology

Ethical approval was sought from the University of Sheffield for a student BMedSci project. The project was also registered (CEU project number 7710) as an extension of a previous service review registered and conducted at Sheffield Teaching Hospitals (CEU project number 6825).

Included patients were:

- Adults admitted as an emergency to critical care units at the Northern General Hospital (NGH) or the Royal Hallamshire Hospital (RHH) in Sheffield.
- Age ≥ 70 years at the point of admission
- Any elective admission to critical care was excluded from analysis
- All patients in this study have been selected as meeting the above criteria and admitted between 1st March 2015 and 31st December 2017.
- As the study is retrospective, it had no effect on patient management or exposed them to any additional risks during their admission which had been completed by the time of my analysis..
- Informed consent was not obtained from or on behalf of the participants as all data used in the study was routinely collected during their stay on intensive care.

2.1 Confidentiality

Patient confidentiality was maintained using appropriate information governance procedures e.g. all patient detail containing patient identifiable data were stored on only my trust domain and patients were then given audit IDs so patient identities were protected when undertaking statistical analysis of their CriSTAL scores

2.2 Previous work

The CriSTAL scoring system originally created by Cardona and Hillman (Cardona-Morrell and Hillman, 2015), is aimed at predicting individual outcome and so could be helpful in assisting clinicians with decisions regarding elderly patients at the point of admission or as a quantifiable outcome figure for the STH patient population to aid conversations with families. Adapting the original CriSTAL model STH developed a simplified CriSTAL scoring system using only frailty and chronic disease related variables. The result of this was a 15 item scoring tool (Figure 8) which underwent a retrospective pilot study for 3 months between January and March 2014. The sample included 125 patients with a median age of 79 years. Patients would either be given a score of one or zero depending on the presence of absence of a variable meaning the maximum score was 15. The results of the Mann Whitney U test can be seen in table 1 (Yogasundaran et al., 2016).

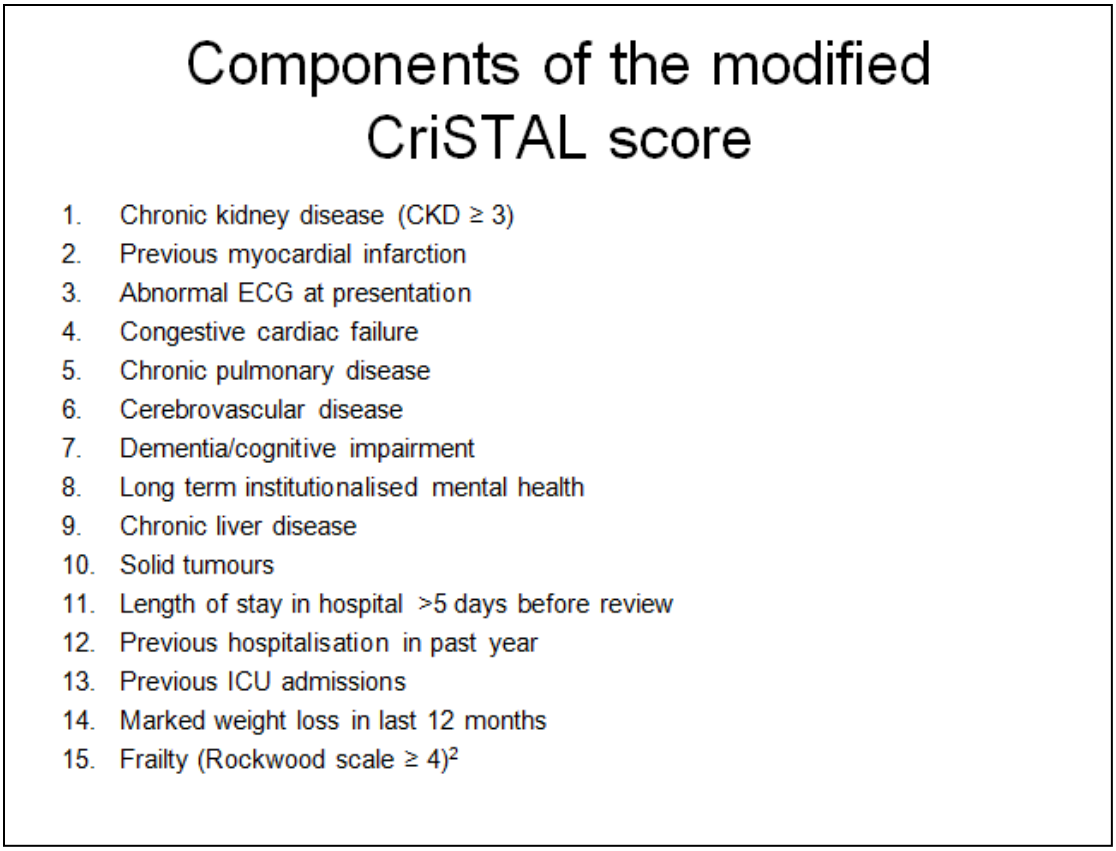


Figure 8. STH's modified CriSTAL criteria – Final model (Yogasundaran et al., 2016).

Median modified CriSTAL score across subgroups

	n	Overall	Survivors	Non-survivors	p-value
Total	125	2.0 (0-7)	2.0 (0-7)	3.0 (1-6)	0.001
Level 3 patients	56	3.0 (0-6)	2.5 (0-6)	3.0 (1-6)	0.024
Level 2 patients	69	2.0 (0-7)	2.0 (0-7)	3.5 (1-5)	0.041

Table 1. Results from the STH pilot CriSTAL study under taken by Yogasundaran et al. (Yogasundaran et al., 2016).

2.3 Statistical Analysis

2.3.1 Primary Analysis

My initial analysis studied summary statistics associated with each of the individual CriSTAL criteria based on the entire 1000 patients including the incidence in the sample population compared to similar studies and the associated mortality rates. The sample was then divided randomly into two equal sized groups (*Training* & *Test*) for two different retrospective analyses and each group's demographics compared.

2.3.2 Secondary Analysis

The first half of the data was analysed on the *Training* sample using the original modified CriSTAL scoring system (Cr1) used by Yogasundaran et al. This model contained 15 independent variables, of which 6 (CKD, MI, CCF, Cerebrovascular Disease, Cancer and Frailty) were sub divided into severity groups with group (1) being the least severe. In this model the absence of a predictor scored 0 points whilst the presence of a predictor scored 1 point totaling a maximum score of 15. This sample underwent a binary logistic regression using using IBM SPSS Statistics 23 software which was used to determine the mortality odds ratios, along with the degree of significance of each CriSTAL variable on outcome. This analysis was then used to create the new modified CriSTAL model (Cr2) which was then applied to the *Test* sample.

2.3.3 Creation of the Cr2 model

Performing a "Backwards LR" in binary logistic regression function to the training sample non significant criteria were eliminated in a stepwise manner and the associated impact on the model's predictive power calculated. Using mortality odds ratios as a guide, the remaining criteria were weighted appropriately and formed the new modified CriSTAL model (Cr2).

2.3.4 Tertiary analysis

Final analysis focused on comparing the predictive power of each model and its clinical appropriateness. Statistical tests used to do this included a T test to assess the scoring difference

between alive and deceased patients for both models, and receiver operator characteristic (ROC) curves used to assess the model as a predictor of outcome.

3. Results

3.1 Research Subjects

During the study period of 1st March 2015 – 31st December 2016 1000 patients aged ≥70yearswere selected for analysis due to non elective stays in intensive care units in Sheffield. Patients admitted to the unit from the neurosciences critical care unit were excluded due to a lack of Clinical Farilty Score as part of their routine data collection and 2 patients were excluded due to having no medical history details available. The mean age of the entire sample was 77.50 years ± 5.83 SD. There were 728 (72.8%) patients alive at discharge and the remaining 272 (27.2%) died on the unit. The distribution in levels of care was approximately 3:1 for level 2 and level 3 organ supports, respectively (755 level 2 patients and 245 level 3 patients – See figure 9 for definitions).

Level 0	Patients whose needs can be met through normal ward care in an acute hospital
Level 1	Patients at risk of their condition deteriorating, or those recently relocated from higher levels of care, whose needs can be met on an acute ward with additional advice and support from the Critical Care team
Level 2	Patients requiring more detailed observation or intervention including support for a single failing organ system or post-operative care and those 'stepping down' from higher levels of care
Level 3	Patients requiring advanced respiratory support alone, or basic respiratory support together with support of at least two organ systems. This level includes all complex patients requiring support for multi-organ failure.

Figure 9. Level of care definitions (The Faculty of Intensive care medicine, 2015)

The total sample was randomly assigned to one of two groups named '*Training*' sample and '*Test*' sample for the purposes of two different analyses. Both groups had statistically identical baseline characteristics.

N.B. Complete tables containing summary statistics, odds ratios and significance values can be found in Appendix 2 & .3

3.2 Frailty

A clinically relevant degree of frailty was deemed as a Rockwood CFS score of 3 or above. Each score was collected as individual variables. In total frailty was found in 699 (69.9%) of the population. The most commonly encountered score was 4 (vulnerable) representing 35.6% of all significant frailty scores. As expected, as the severity of frailty increased, the population assigned to each score fell periodically. Of the patients deemed to have no significant frailty, survival likelihood was high (83.7%). However, as the degree of frailty increased the mortality risk also rose to such extent that 44.7% of stage 7 patients (severely frail) died.

Logistic regression indicated that all scores of 3 or above had an increased risk of mortality however results and significance varied. Compared to patients with no frailty, scores of 4 (*OR 1.86; 95%CI 0.99-3.48; P=0.054*), 5 (*OR 2.21; 95%CI 1.16-4.24; P=0.016*), 6 (*OR 1.25; 95%CI 0.59-2.63; P=0.56*), and 7 (*OR 4.1; 95%CI 1.30-12.65; P=0.016*), all resulted in a higher risk of mortality however statistical significance was only exhibited in scores of 5 and 7 where P=0.016 in both cases.

3.3 Elimination and Weighting

Using the Backwards LR function in IBM SPSS logistic regression with stepwise removal it was possible to alter the CriSTAL model removing individual insignificant criteria to determine the most efficient and accurate predictive model. The removal probability statistic was set to 0.1 to formulate a model which included clinically meaningful as well as statistically significant variables. Variables removed from the model in sequential order from step 2 were: Weight loss, psychiatric history, CKD, Previous Hospitalisation, Dementia, CVD and ICU re admission. The result of removing these 8 variables from the model resulted in a net decrease in predictive power to 76.6% (-1.0%) however this difference was not significantly different from the predictive power of the Cr1 dataset (P=0.802).

The backwards LR could not eliminate insignificant sub criteria and so needed to be eliminated manually. These sub variables were: MI >6 months, congestive heart failure (NYHA class 1), presence of solid tumours and local metastasis. The weighting of individual clinically meaningful criteria was altered based on the associated odds ratios to create a new model with a maximum score of 30.

3.4 Tertiary Analysis – Analysis of CriSTAL

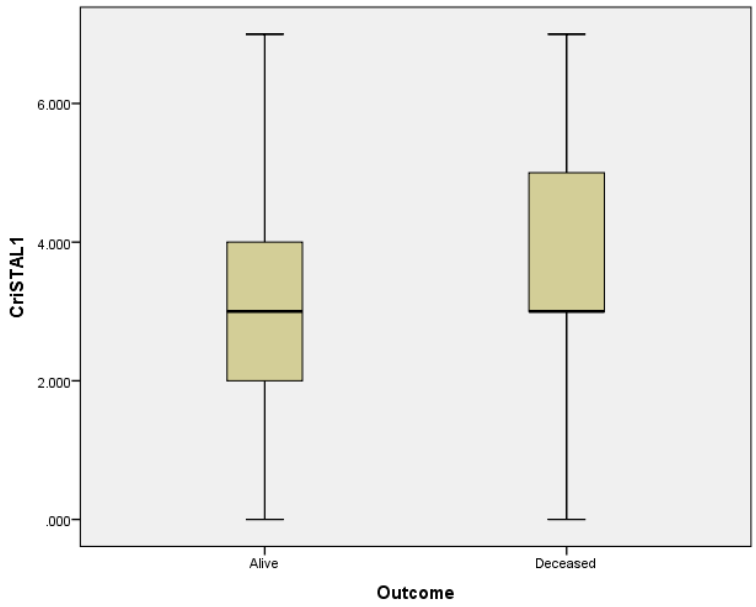
3.4.1 Group baseline characteristics

Training

CriSTAL scores for the original model (Training sample) ranged from 0-7. The mean and median CriSTAL scores for the total sample were 2.97 ± 1.57 SD (95%CL 2.83-3.11) and 3 (IQR 2.0-4.0). The majority of patients scored either 2 (21.6%) or 3 (26.2%) whilst both scoring extremes were encountered much less often (0=4.8% & 7=2.0%).

		CriSTAL									
		Outcome									
		Alive					Deceased				
		Mean	Median	Max	Min	Standard Deviation	Mean	Median	Max	Min	Standard Deviation
Bed Lev	2	2.762	3.000	7.000	.000	1.492	3.753	4.000	7.000	1.000	1.408
	3	2.429	2.000	7.000	.000	1.593	3.491	3.000	7.000	.000	1.627

Table 2. Summary statistics of Cr1 Cristal Scores by Bed level and Outcome.



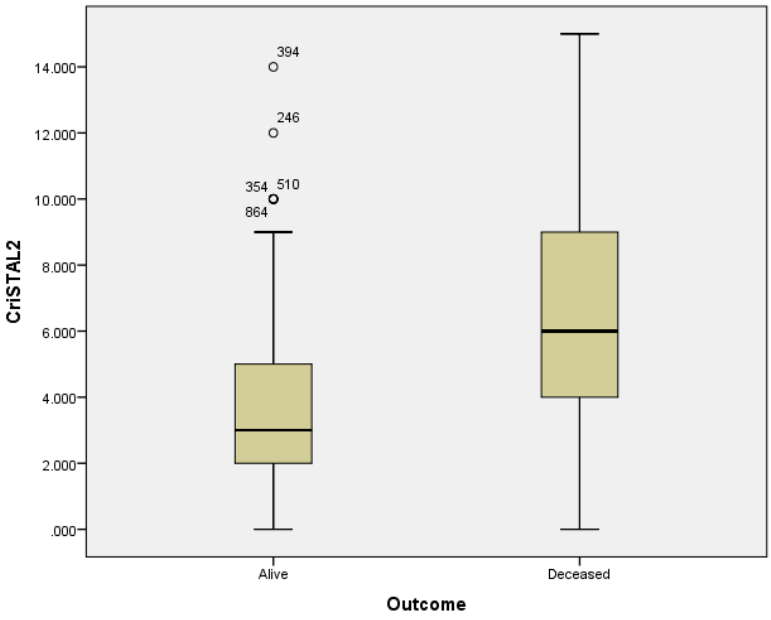
Graph 1. Box plot showing the spread of Cr1 scoring for each outcome.

Test

CriSTAL scores for the modified model (*Test* sample) ranged from 0-15. The mean and median CriSTAL scores were 3.85 ± 2.82 SD (95%CL 3.60-4.10) and 4 (IQR 2.0-6.0). Predictably, as the range of scores increased by over 2 fold, the spread of the data was greater with the most elicited score = 2 (16.6%) followed by scores of 5 (12.8%) and 3 (12.6%). Higher scores were much less common with scores of 11-15 representing only 1.4% of the sample.

		CriSTAL									
		Outcome									
		Alive					Deceased				
		Mean	Median	Min	Max	Standard Deviation	Mean	Median	Min	Max	Standard Deviation
Bed Lev	2	3.659	3.000	.000	12.000	2.512	6.646	6.000	.000	15.000	3.355
	3	4.017	4.000	.000	14.000	2.600	5.447	5.000	.000	11.000	3.140

Table 3. Summary statistics of Cr2 Cristal Scores by Bed level and Outcome.



Graph 2. Box plot showing the spread of Cr2 scoring for each outcome including outliers.

3.4.2 Comparisons of means

Studying the distribution of the data through the use of histograms, CriSTAL scores followed a normal distribution, therefore an independent T test was selected to compare the difference in CriSTAL scores based on outcome. Cr1 revealed a statistically significant difference between the lower scoring survival group (Mean 2.79; SD 1.52; N=354) and the deceased, (Mean 3.65; SD 1.50 N=156) P<0.001. The magnitude of the difference in means (Mean difference -0.96; 95%CI -1.25--0.67) was moderate (eta squared = 0.77).

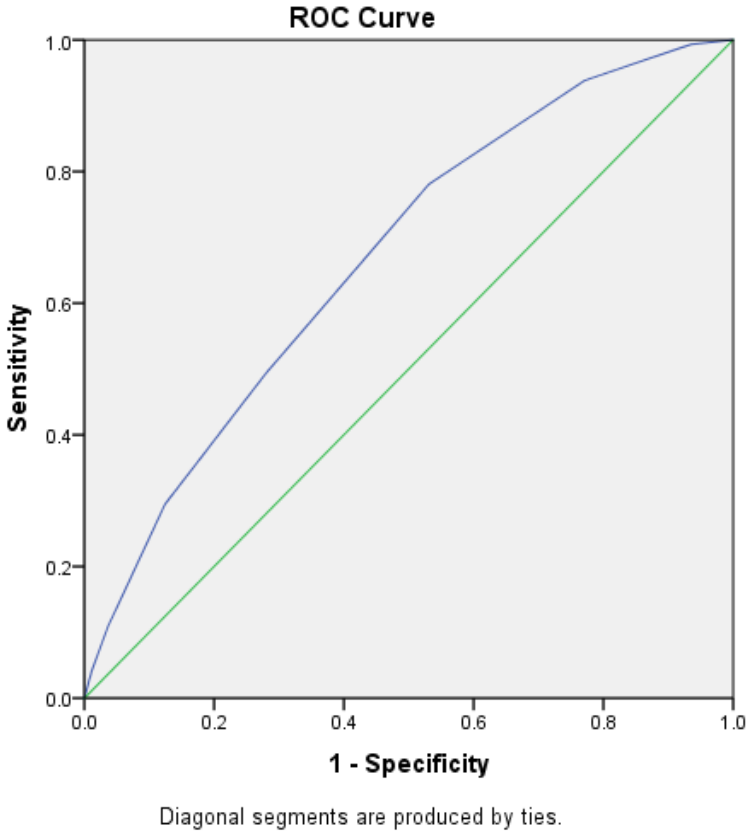
Cr2 also revealed a statistically significant difference between the lower scoring survival group (Mean 3.72; SD 2.53; N=374) and deceased patients, (Mean 6.20; SD 3.32; N=126) P<0.001. The magnitude of the difference in means (Mean difference -2.48; 95%CI -3.29—1.84) was moderate (eta squared = 0.12) however is notably larger than the original model.

Both models show that scores in CriSTAL differed significantly depending on outcome. Whilst both elicit statistical significance, the original model's mean difference of 0.96 means it cannot be a clinically significant result as the model does not separate the sample by enough of a margin to categorize mortality and survival. The modified model has a greater mean difference which improves its usability in clinical settings however an even larger mean difference would be preferable. Nonetheless the modified model has statistical and clinical potential.

3.4.3 Receiver Operator Characteristic (ROC) curve analysis.

A ROC curve was used to test whether the model is a good predictor of population or individual outcomes. The ROC curve and its associated area under the curve (AUC) are a reliable measure of model accuracy. If the total area under the curve (AUC) is equal to 1 it implies the model is 100% accurate however, an AUC of 0.5 indicates the model has no better discrimination than random choice. From Graphs 1 & 2 both models have ROC lines displaced up and to the left of the 45^{o} line of random discrimination implying both models have significantly better predictive ability than random choice which is agreeable with the logistic regression outputs. AUC results for Cr1 (*AUC 0.67; 95%CI 0.62-0.72; P<0.001*) and Cr2 (*AUC 0.72; 95%CI 0.66-0.77; P<0.001*) indicate that whilst both are predictive of mortality Cr1 would be classified as poor predictive model (AUC 0.6-0.7) whereas Cr2 would be classified a fair prediction model (AUC=0.7-0.8).

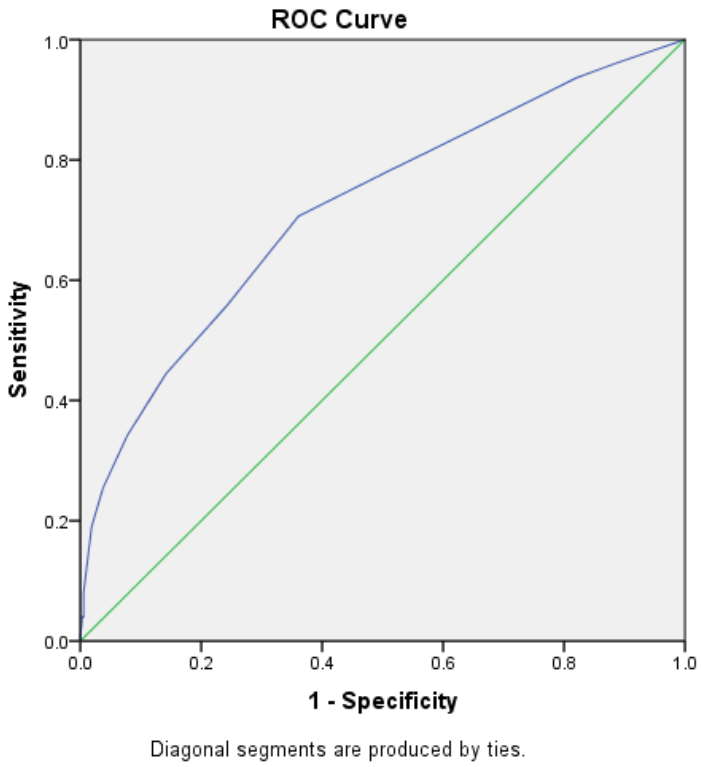
Studying the ROC curve of Cr1 (Graph 1) it is apparent that finding a point which has a good compromise between sensitivity and specificity is difficult. Using the coordinates of the graph the most appropriate point to make the cut off point lies at (0.6, 0.4) however studying the accompanying table the most appropriate sensitivity is 0.493 therefore implying a modified CriSTAL score of 3 or greater would correctly identify 49.3% of dying patients. The trade off from this result is a comparably high sensitivity of 72%. Given that random identification would result in a sensitivity of 50% this model does not perform well with regards to predicting mortality however it is able to correctly identify patients who will survive at a much better rate.



Graph 3. ROC Curve used to assess sensitivity and specificity for Cr1 (Blue). AUC=0.5 reference line (green).

The Cr2 ROC curve exhibited a slightly different curve with a notable appropriate point of compromise at (0.73, 0.36) indicating that at a proposed score of 4 or greater the modified CriSTAL model is able to correctly identify 73% of dying patients however the associated sensitivity trade off suggests that 36.1% of dying patients would be incorrectly classified These results show that the adjustments to the model have improved its sensitivity to mortality whilst only compromising its specificity slightly.

CriSTAL score in both models has shown to be predictive of mortality however despite improvements to the model, clinically meaningful sensitive and specificity statistics were not achieved. Therefore indicating the model cannot accurately predict mortality at an individual level however it can be used to provide better information to Sheffield patients and relatives about their chances of survival if admitted to intensive care.



Graph 4. ROC Curve used to assess sensitivity and specificity for Cr2 (Blue).
AUC=0.5 reference line (green).

4. Discussion

4.1 Interpretation of demographics

4.1.1 Mortality

The primary outcome of the study was mortality which occurred in 27.2% of admissions, a figure which appears relatively low considering the elderly patient cohort and high severity of chronic morbidity. ICU mortality rates are known to fluctuate widely in the published literature depending on differing patient cohorts and individual policy regarding admission and treatment withdrawal from unit to unit. However, for a total cohort in a general ICU mortality rates are estimated to be between 13.8%-22% (Higgins et al., 2007; Luyt et al., 2007). When excluding "young" patients (<65 years) from these statistics our results become much more comparable (18.8%-28% (Boumendil et al., 2005; Fuchs et al., 2012)) indicating raw data for outcomes in Sheffield are similar to other ICU populations. Ideally, to ensure mortality figures are not favorably altered by discharging dying patients, data on post discharge mortality would have been collected and compared, but this was not viewed as part of the service review element of this study so was not compared.

4.1.2 Frailty

Of the total sample, a notable degree of frailty (≥CFS 4) was evident in the majority of the sample (69.9%). Whilst this number initially seems extremely high this was anticipated as the sample population is of acutely unwell elderly patients many of whom are much more likely to be frail than younger fitter populations. When compared to the best comparative studies our results suggest our population was significantly frailer than Bagshaw et al's (32.8%≥CFS 4 (-37.1%)) and Maguet et al's (23.0%≥CFS 5 (-22.2%) findings (Bagshaw et al., 2014; Le Maguet et al., 2014). These results imply that frailty could be over diagnosed in ICU or that frailty is genuinely more prevalent in a Northern English single city population than in a Canadian one. (Arblaster, 2012).

Despite the large samples of frailty in each grade, all degrees of frailty ≥CFS4 elicited clinical significance. Statistical significance was only seen in scores 5 and 7 however a score of 4 was

included in Cr2 as its P value was deemed low enough to have a clinically significant influence. In conclusion we found that all degrees of frailty are clinically significant at predicting mortality – a finding which is in agreement with the literature (Bagshaw et al., 2014; Le Maguet et al., 2014).

4.2 Predicting outcomes: Clinical significance vs Statistical significance

Three different statistical tests were chosen to assess the accuracy and the usability of both CriSTAL scoring models. Both outcomes of the Independent T test resulted in statistically significant P values meaning CriSTAL scores for patients who survived and died were proven to have absolute differences indicating both models were able to differentiate each outcome. However in the Cr1 cohort statistically significant mean difference, was a mean difference of 0.96 of a point, which could not be used clinically as it would not effectively separate those who are likely to survive and those who are likely to die. This was improved upon in the Cr2 analysis which produced a mean difference of 2.48 indicating likely outcome would separated by at least 2 points. Whilst both models are statistically appropriate neither can be suggested as clinically appropriate simply due to the minimal separation in score for each outcome.

Secondly, logistic regression outputs were able to calculate the ability to predict population outcome based on the variables in the scoring system. Both models were calculated to be statistically significant improvements on the assumption of unanimous survival however both models seemed to lack capabilities to correctly predict patients likely to die (Percentage correct - Cr1 38.4% Cr2 30.2%) with the later model able to do this notably more poorly which indicates the elimination of 8 variables whilst classed as insignificant, did contribute to better mortality prediction. Conversely, both models' ability to predict survival was extremely high (Percentage correct Cr1-93.8% Cr2-96.3) with Cr2 boasting the higher percentage correct. In summary, logistic regression found that both models were clinically appropriate in the use of predicting mortality and although eliminating insignificant variables improves the model's usability and reduces completion time, it does sacrifice accuracy of mortality prediction. However the high percentage of correct results for survival indicate that patients with no or very few variables of morbidity are extremely likely to survive suggesting that both models can serve well as a survival predictor.

Finally ROC and associated AUC analysis was performed to assess the model's ability to predict outcomes at an individual level which would answer the initial outcome of our study as to a CriSTAL model's predictive capability of outcome prediction at the point of admission. Once

again results from both models were statistically significant improvements on random choice however the calculated predictive capacities of Cr1 and Cr 2 were deemed to be poor (AUC=0.67) and fair (AUC=0.72), respectively. Comparatively recognised ICU scoring system, APACHE IV (AUC=0-86-0.89), ICNARC (AUC=0.87) and SAPS III (AUC=0.80) are all classed as good predictors and possess notably better predictive capabilities than Cr2. However as previously mentioned these systems take 24 hours to complete, involve a huge number of variables and are only designed for assessment of population mortality. When comparing the Cr2 to the most comparable model MPMIII (AUC=0.721-0.80) our results are comparable whilst containing half the variables, all of which are available at the point of admission. The comparability of our Cr2 model and the clinically accepted model MPMIII indicates that the CriSTAL model does still have very significant potential as a clinical discussion aid.

4.3 Future work

Having established significant and insignificant mortality predictors in elderly patients many of the results for individual variables require no further work as they can reliably inform clinical decisions at the point of admission.

However, With regards to the CriSTAL model for quantifying an individual's risk of mortality, important and necessary advancements from Cr1 have been achieved. However to further advance Cr2s predictive capacity, variables such as Polytrauma, Sepsis, presence of a DNAR and haematological cancers should be investigated and results should be significant variables added to the scoring system or in respect of Polytrauma, the model should exclude such patients as there is usually no discussion around admission for these patients. Besides investigating these variables, alterations to the definition of the Stroke variable should be made to investigate the significant influence the literature suggests acute stoke has on outcome.

Further testing suggestions would include: testing the scoring system using a prospective population at the point of admission as this would likely eliminate many of the data collection issues encountered in our retrospective analyses, expanding the sample geographically to see how well the model created in Sheffield can be applied to other ICUs across the country and to collect data on 30 day or even in hospital outcomes which would assess the model's true capabilities to predict all forms of short term outcomes.

5. Conclusion

The ageing population is currently, and is expected to continue to place increasing demands on intensive care services. As a result the last decade has seen a drive for prognostic models with the aim to improve medical service allocation by better selecting patients who are more likely to benefit from treatment escalation. These models have all exhibited strong predictive capabilities however all have shortcomings with regard to their clinical applicability. First to note is that all previously accredited models are for predicting population based outcome rather than case based. Secondly, the majority of these models require 24 hours to collect data on all the variables meaning they cannot possibly be used at the point of admission for informing discussions on individual cases. And finally no model is yet to experiment with the use of frailty as a variable, despite its proven association with adverse outcomes in elderly patients in and out of intensive care.

The study hypothesis that our final model (Cr2) would accurately predict ICU mortality in a retrospective cohort was not proven to be true. However, the results from the ROC indicate that scoring above a 4 would correctly identify almost 3 quarters of patients likely to die which implies it does have a reasonable level of mortality prediction which could usefully inform conversations with referring teams, patients and relatives. Further to this, when compared to the MPM_oIII model, Cr2 exhibited competitive results whilst only containing half the number of variables and unlike the MPM_oIII is available for use at the point of admission. It is predicated that with further investigation once the limitations of this study have been addressed the accuracy of Cr2 will be improved upon, making it much more competitive with other establish prognostic models.

In regards to our secondary objective, we identified 8 variables significantly predictive of mortality including moderate to severe degrees of frailty - indicating that the reasoning behind incorporating frailty into the model was well founded. Two novel parameters of any ECG abnormality and Hospital stay ≥5 days preceding admission were identified as statistically significant in predicting mortality. Although all these significant factors when combined failed to achieve strong prognostic sensitively and specificity, these results undoubtedly still have clinical importance. For example, clinicians finding the presence, or equally the absence of these

variables in a patient at the point of admission will likely be able to consider admission decisions and also will likely be able to use them to explore patient and family expectations of survival during their conversations.

This study demonstrates that using only a few simple chronic disease markers at the point of admission has the potential to predict short term mortality. As a result, chronic morbidity will need to become central to clinical decisions and treatment plans for critically ill elderly patients rather than just chronological age. Although results from the study were not conclusive enough to reject the null hypothesis our final model did exhibit similar results to a 16 item, clinically accepted model (MPM_oIII) and to an extent, our objectives of the study were achieved. Furthermore, the discovery of new significant variables which to date have not been tested on the wider intensive care population is a finding of great importance and should be explored further.

6. Bibliography

Arblaster, L. (2012). Accuracy and Precision of Critical Care medical staff using the Clinical Frailty Scale (BMedSci thesis), pp. 120-133.

American HeartAssociation. (2017). Classes Of Heart Failure.

Bagshaw, S.M., Stelfox, H.T., McDermid, R.C., Rolfson, D.B., Tsuyuki, R.T., Baig, N., Artiuch, B., Ibrahim, Q., Stollery, D.E., Rokosh, E., *et al.* (2014). Association between frailty and short- and long-term outcomes among critically ill patients: a multicentre prospective cohort study. Canadian Medical Association Journal *186*, E95-E102.

Bagshaw, S.M., Webb, S.A.R., Delaney, A., George, C., Pilcher, D., Hart, G.K., and Bellomo, R. (2009). Very old patients admitted to intensive care in Australia and New Zealand: a multi- centre cohort analysis. Critical Care *13*, R45-R45.

Boumendil, A., Aegerter, P., Guidet, B., and Network, C.U.-R. (2005). Treatment intensity and outcome of patients aged 80 and older in intensive care units: A multicenter matched-cohort study. Journal of the American Geriatrics Society *53*, 88-93.

Capuzzo, M., Bianconi, M., Contu, P., Pavoni, V., and Gritti, G. (1996). Survival and quality of life after intensive care. Intensive Care Medicine *22*, 947-953.

Cardona-Morrell, M., and Hillman, K. (2015). Development of a tool for defining and identifying the dying patient in hospital: Criteria for Screening and Triaging to Appropriate aLternative care (CriSTAL). Bmj Supportive & Palliative Care *5*, 78-90.

Chalfin, D.B., Trzeciak, S., Likourezos, A., Baumann, B.M., Dellinger, R.P., and grp, D.-E.s. (2007). Impact of delayed transfer of critically ill patients from the emergency department to the intensive care unit. Critical Care Medicine *35*, 1477-1483.

Charlson, M., Pompei, P., Ales, K., and MacKenzie, C. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: development and validation., pp. 373-383.

Dolgin, M.N.Y.H.A.C.C. (1994). Nomenclature and criteria for diagnosis of diseases of the heart and great vessels / the Criteria Committee of the New York Heart Association., pp. 253–256.

Dowdy, D.W., Eid, M.P., Sedrakyan, A., Mendez-Tellez, P.A., Pronovost, P.J., Herridge, M.S., and Needham, D.M. (2005). Quality of life in adult survivors of critical illness: A systematic review of the literature. Intensive Care Medicine *31*, 611-620.

Fuchs, L., Chronaki, C.E., Park, S., Novack, V., Baumfeld, Y., Scott, D., McLennan, S., Talmor, D., and Celi, L. (2012). ICU admission characteristics and mortality rates among elderly and very elderly patients. Intensive Care Medicine *38*, 1654-1661.

Groll, D.L., To, T., Bombardier, C., and Wright, J.G. (2005). The development of a comorbidity index with physical function as the outcome. Journal of Clinical Epidemiology *58*, 595-602.

Higgins, T.L., Teres, D., Copes, W.S., Nathanson, B.H., Stark, M., and Kramer, A.A. (2007). Assessing contemporary intensive care unit outcome: An updated Mortality Probability Admission Model (MPM0-III). Critical Care Medicine *35*, 827-835.

Hofhuis, J.G., Spronk, P.E., Van Stel, H.F., Schrijvers, A.J., and Bakker, J. (2007). Quality of life before intensive care unit admission is a predictor of survival. Critical Care *11*, 7.

KDOQI (2002). Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification.

Lang, P.O., Michel, J.P., and Zekry, D. (2009). Frailty Syndrome: A Transitional State in a Dynamic Process. Gerontology *55*, 539-549.

Lang, P.O., Mitchell, W.A., Lapenna, A., Pitts, D., and Aspinall, R. (2010). Immunological pathogenesis of main age-related diseases and frailty: Role of immunosenescence. European Geriatric Medicine *1*, 112-121.

Le Maguet, P., Roquilly, A., Lasocki, S., Asehnoune, K., Carise, E., Saint Martin, M., Mimoz, O., Le Gac, G., Somme, D., Cattenoz, C., *et al.* (2014). Prevalence and impact of frailty on mortality in elderly ICU patients: a prospective, multicenter, observational study. Intensive Care Medicine *40*, 674-682.

Levine, S.K., Sachs, G.A., Jin, L., and Meltzer, D. (2007). A prognostic model for 1-year mortality in older adults after hospital discharge. American Journal of Medicine *120*, 455-460.

Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., Abraham, J., Adair, T., Aggarwal, R., Ahn, S.Y., *et al.* (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet *380*, 2095-2128.

Luyt, C.E., Combes, A., Aegerter, P., Guidet, B., Trouillet, J.L., Gibert, C., Chastre, J., and Network, C.U.-R. (2007). Mortality among patients admitted to intensive care units during weekday day shifts compared with "off" hours. Critical Care Medicine *35*, 3-11.

Mikkelsen, M., Iwashyna, T., and Thompson, C. (2015). Why ICU Clinicians Need to Care about Post-Intensive Care Syndrome (Society of Critical Care Medicine).

NHS England. (2016). Critical Care bed capacity and urgent operations cancelled 2016/2017 data.

Rockwood, K., Song, X.W., MacKnight, C., Bergman, H., Hogan, D.B., McDowell, I., and Mitnitski, A. (2005). A global clinical measure of fitness and frailty in elderly people. Canadian Medical Association Journal *173*, 489-495.

Soares, M., Carvalho, M.S., Salluh, J.I.F., Ferreira, C.G., Luiz, R.R., Rocco, J.R., and Spector, N. (2006). Effect of age on survival of critically ill patients with cancer. Critical Care Medicine *34*, 715-721.

Tan, S.S., Bakker, J., Hoogendoorn, M.E., Kapila, A., Martin, J., Pezzi, A., Pittoni, G., Spronk, P.E., Welte, R., and Hakkaart-van Roijen, L. (2012). Direct Cost Analysis of Intensive Care Unit Stay in Four European Countries: Applying a Standardized Costing Methodology. Value in Health *15*, 81-86.

The faculty of intensive care medicine. (2015). Guidelines for the Provision of Intensive Care Services, T.i.c. society, ed

The Office of National Statistics. (2015a). National Population Projections: 2014-based Statistical Bulletin.

The Office of National Statistics. (2015b). Past and projected data from the period and cohort life tables, 2014- based, UK, 1981 to 2064.

The Office of National Statistics. (2016). Overview of the UK population: February 2016.

Villa, P., Pintado, M.C., Lujan, J., Gonzalez-Garcia, N., Trascasa, M., Molina, R., Cambronero, J.A., and de Pablo, R. (2016). Functional Status and Quality of Life in Elderly Intensive Care Unit Survivors. Journal of the American Geriatrics Society *64*, 536-542.

United Nations. (2015). World Population ageing report.

Wolters, A.E., Peelen, L.M., Welling, M.C., Kok, L., de Lange, D.W., Cremer, O.L., van Dijk, D., Slooter, A.J.C., and Veldhuijzen, D.S. (2016). Long-Term Mental Health Problems

After Delirium in the ICU. Critical Care Medicine *44*, 1808-1813.

Yogasundaran, A., Wheeler, A., Bauchmuller, K., and Bryden, D. (2016). 36th International Symposium on Intensive Care and Emergency Medic ine. In Use of a modified cristal score to predict futility of critical care in the elderly (Brussels, Belgium), pp. 443.

7. Appendix

Appendix 7.1. The Canadian Study on Health and Ageing Clinical Frailty Scale; A global clinical measure of fitness and frailty in elderly people (Rockwood et al., 2005).

Clinical Frailty Scale

1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 Well – People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.

3 Managing Well – People whose medical problems are well controlled, but are not regularly active beyond routine walking.

4 Vulnerable – While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up", and/or being tired during the day.

5 Mildly Frail – These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 Moderately Frail – People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.

7 Severely Frail – Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9 Terminally Ill – Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia,** recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia,** they cannot do personal care without help.

Appendix 7.2 Summary Statistics for all CriSTAL variables over the entire sample detailing total prevalence of each variable and the proportion of patients alive and deceased with that variable.

		Outcome					
		Alive		Deceased		Total	
		Count	Row N %	Count	Row N %	Count	Column N %
CKD	No CKD	626	73.0%	231	27.0%	857	85.7%
	Stage 3	83	72.8%	31	27.2%	114	11.4%
	Stage 4	10	83.3%	2	16.7%	12	1.2%
	Stage 5	9	52.9%	8	47.1%	17	1.7%
MI	No MI	603	74.6%	205	25.4%	808	80.8%
	MI ≥6 Months	92	74.2%	32	25.8%	124	12.4%
	MI < 6 Months	33	48.5%	35	51.5%	68	6.8%
ECG	Normal	408	79.8%	103	20.2%	511	51.1%
	Abnormal	320	65.4%	169	34.6%	489	48.9%
CCF	No CCF	634	75.1%	210	24.9%	844	84.4%
	NYHA 1	46	80.7%	11	19.3%	57	5.7%
	NYHA 2	30	65.2%	16	34.8%	46	4.6%
	NYHA 3	18	48.6%	19	51.4%	37	3.7%
	NYHA 4	0	0.0%	16	100.0%	16	1.6%
COPD	No COPD	575	75.9%	183	24.1%	758	75.8%
	COPD	153	63.2%	89	36.8%	242	24.2%
CVD	No CVD	604	72.6%	228	27.4%	832	83.2%
	TIA	46	78.0%	13	22.0%	59	5.9%
	Stroke	78	71.6%	31	28.4%	109	10.9%
Dementia	No Cog Impairment	690	73.2%	253	26.8%	943	94.3%
	Cog Impairment	38	66.7%	19	33.3%	57	5.7%
Psychiatric	No Psychiatric treatment	718	72.7%	270	27.3%	988	98.8%
	Psychiatric treatment	10	83.3%	2	16.7%	12	1.2%
CLD	No Liver disease	711	73.8%	253	26.2%	964	96.4%
	Liver disease	17	47.2%	19	52.8%	36	3.6%
Cancer	No Cancer	582	71.9%	228	28.1%	810	81.0%
	Solid Tumour	113	83.7%	22	16.3%	135	13.5%

	Local Metastasis	11	73.3%	4	26.7%	15	1.5%
	Metastatic Disease	22	55.0%	18	45.0%	40	4.0%
Stay	<5days	617	75.5%	200	24.5%	817	81.7%
	≥5days	111	60.7%	72	39.3%	183	18.3%
Hospitalisation	No Previous Hospitalisation	507	75.2%	167	24.8%	674	67.4%
	Previous Hospitalisation	221	67.8%	105	32.2%	326	32.6%
ICU	No admission to ICU	690	72.6%	260	27.4%	950	95.1%
	Repeat admission to ICU	37	75.5%	12	24.5%	49	4.9%
Weight loss	No Weight Loss	714	73.5%	257	26.5%	971	97.1%
	Significant Weight Loss	14	48.3%	15	51.7%	29	2.9%
Frailty	Rockwood <4	252	83.7%	49	16.3%	301	30.1%
	Rockwood 4	177	71.1%	72	28.9%	249	24.9%
	Rockwood 5	162	68.1%	76	31.9%	238	23.8%
	Rockwood 6	116	66.7%	58	33.3%	174	17.4%
	Rockwood 7	21	55.3%	17	44.7%	38	3.8%

Appendix 7.3. Cr1 Logistic regression output presenting each variable and its relationship with mortality including odds ratios (ExpB) and 95%CI, P values (Sig) and standard error (SE).

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	CKD			1.322	3	.724			
	CKD(1)	-.165	.363	.206	1	.650	.848	.417	1.727
	CKD(2)	.566	.984	.331	1	.565	1.761	.256	12.113
	CKD(3)	.851	.998	.728	1	.394	2.342	.331	16.552
	MI			7.721	2	.021			
	MI(1)	-.256	.389	.435	1	.510	.774	.361	1.658
	MI(2)	.981	.377	6.796	1	.009	2.668	1.276	5.581
	ECG(1)	.824	.243	11.475	1	.001	2.279	1.415	3.672
	CCF			9.282	4	.054			
	CCF(1)	-1.390	.624	4.960	1	.026	.249	.073	.846
	CCF(2)	.889	.501	3.141	1	.076	2.432	.910	6.498
	CCF(3)	.395	.536	.543	1	.461	1.484	.519	4.243
	CCF(4)	21.650	11202.060	.000	1	.998	2525089882.903	.000	.
	COPD(1)	.605	.271	4.975	1	.026	1.831	1.076	3.116
	CVD			2.478	2	.290			
	CVD(1)	.424	.475	.796	1	.372	1.528	.602	3.875
	CVD(2)	.456	.330	1.912	1	.167	1.578	.827	3.013
	Dementia(1)	.377	.447	.713	1	.399	1.459	.607	3.504
	Psychiatric(1)	-.284	1.150	.061	1	.805	.753	.079	7.169
	CLD(1)	2.544	.714	12.689	1	.000	12.733	3.140	51.624
	Cancer			6.441	3	.092			
	Cancer(1)	-.029	.371	.006	1	.937	.971	.470	2.008
	Cancer(2)	-1.130	1.158	.952	1	.329	.323	.033	3.127
	Cancer(3)	1.242	.537	5.344	1	.021	3.463	1.208	9.926
	Stay(1)	1.041	.287	13.198	1	.000	2.833	1.615	4.969

	Hospitalisation(1)	.105	.252	.174	1	.677	1.111	.678	1.820
	ICU(1)	-.846	.661	1.638	1	.201	.429	.118	1.567
	Weightloss(1)	-.021	.717	.001	1	.977	.980	.240	3.991
	Frailty			10.197	4	.037			
	Frailty(1)	.618	.320	3.725	1	.054	1.855	.990	3.475
	Frailty(2)	.795	.331	5.771	1	.016	2.214	1.158	4.235
	Frailty(3)	.222	.379	.343	1	.558	1.249	.594	2.625
	Frailty(4)	1.401	.580	5.844	1	.016	4.060	1.304	12.646
	Constant	-2.517	.315	63.792	1	.000	.081		