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Hospital Acquired Pneumonia- What's the Score? A scoping review and original case study investigating the role of severity scoring indices in Hospital Acquired Pneumonia in the UK

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Hospital Acquired Pneumonia- What's the Score?

A scoping review and original case study

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Declaration:

'Yr wyf drwy hyn yn datgan mai canlyniad fy ymchwil fy hun yw'r thesis hwn, ac eithrio lle nodir yn wahanol. Caiff ffynonellau eraill eu cydnabod gan droednodiadau yn rhoi cyfeiriadau eglur. Nid yw sylwedd y gwaith hwn wedi cael ei dderbyn o'r blaen ar gyfer unrhyw radd, ac nid yw'n cael ei gyflwyno ar yr un pryd mewn ymgeisiaeth am unrhyw radd oni bai ei fod, fel y cytunwyd gan y Brifysgol, am gymwysterau deuol cymeradwy.'

Rwy'n cadarnhau fy mod yn cyflwyno'r gwaith gyda chytundeb fy Ngrichwyliwr (Goruchwylwyr)'

'I hereby declare that this thesis is the results of my own investigations, except where otherwise stated. All other sources are acknowledged by bibliographic references. This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree unless, as agreed by the University, for approved dual awards.'

I confirm that I am submitting the work with the agreement of my Supervisor(s)'

Thesis Abstract:

The NHS serves an aging population and is world renowned for providing high quality health care. However, hospitals are not intrinsically safe places to stay, especially for the elderly, with nosocomial, antibiotic resistant infections a particularly headline-inducing concern. One of the most prevalent nosocomial infections is Hospital Acquired Pneumonia (HAP). Hospital Acquired Pneumonia has a high mortality, tends to affect an elderly population and is more likely to be secondary to an antibiotic resistant micro-organism than it's community-acquired neighbour.

Despite these facts, HAP has had much less research into it than Community Acquired Pneumonia (CAP). One of the major international success stories in CAP research in recent years has been the development of severity scoring indices at diagnosis to help guide treatment decisions, place of therapy and intensive care review when necessary. Prior to this study, the author was not aware of any such score for HAP, and the overarching aim of this thesis is to investigate if there are any applicable HAP severity scores, if the evidence supports their use in the UK HAP population and whether or not they are currently recommended.

The thesis takes the form of an introduction to the topic, a scoping review into severity scoring indices in HAP- looking at both guidelines and original research, a case study original piece of research and finally recommendations for further research in the area. The outcomes of the scoping review concluded that the research into the area is currently inadequate. The case study, however, supported the notion that severity scoring indices may have a useful role in prognostication at diagnosis. Further research is desperately needed and the case for this and focus for this is set out in detail in the conclusion of this thesis. The broad suggestion, however, is for a large multi-centre study applying scoring indices to UK HAP population to assess prognostication, involvement of a stakeholder group to ensure appropriate metrics are reviewed, and two scores are suggested to use in this study following promising results at prognosticating in the case study- the I-ROAD score, and the PSI.

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Chapter One

Introduction

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1. Introduction

Hospitals are not intrinsically safe places in which to stay; hospital residents are at increased risk of multiple disease processes including venous thromboembolism, pressure sores and infections (Lagoe & Wester, 2010; Vincent et al., 2001). Over the past few years increasing pressures in social care have resulted in increased amount of hospital stays in the elderly and co-morbid population (National Audit office, 2016; Oliver, 2017). These patients are already at a higher risk of developing hospital related illness as well as being at a higher risk of succumbing to them.

Much work has gone into minimising the risks associated with hospital admission. Such as thromboembolism prophylaxis guidelines aiming to minimise the risk of deep vein thromboses and pulmonary embolisms, as well as schemes aiming to reduce musculoskeletal deconditioning in inpatients- known as 'PJ Paralysis' (NICE, 2010; Health service 360, 2020). Hospital acquired infection is an area in which many changes have been implemented to reduce disease burden. Approximately 300000 hospital acquired infections are estimated to occur per year in England associated with NHS care (NICE, 2013). The changes which have been brought in to address this include 'bare below the elbow' policies, handwashing audits, aseptic procedure documentation and infection control teams in hospitals (NICE, 2013).

MRSA (Methicillin resistant Staphylococcus Aureus), VRE (Vancomycin resistant Enterococcus) and Clostridium Difficile (C.Diff) have been focus areas for a significant amount of work as antibiotic resistance and its potential effects have gained publicity. Screening now takes place for MRSA in

hospital inpatients and VRE screening for out of area patients (Department of Health expert advisory committee on Antimicrobial Resistance and Healthcare Associated Infection, 2014; Liverpool Heart and Chest Hospital, 2016). Screening allows early recognition of these organisms which is both therapeutically helpful should the patient require antimicrobial agents as well as being helpful for isolation and preventing spread. Thankfully, rates of severe hospital associated infection such as MRSA and C.Diff have been reducing in recent years (NICE, 2014).

Despite the significant efforts into reducing hospital associated pathology and infection, in particular nosocomial infection remains a common and serious occurrence. Prevalence of nosocomial infection is estimated at 8.2% with a significant mortality (NICE, 2013). The largest burden of nosocomial infections are urinary tract infections (17.2%) and respiratory infections-, such as hospital acquired pneumonia (22.8%) (NICE, 2014). The mortality from hospital acquired pneumonia (HAP) is significantly higher than that of community acquired pneumonia (CAP) (NICE, 2016). This may be due to the patient population, a generally older and more comorbid population, and the organisms involved- often 'atypical organisms' with a higher level of resistance to the first line antimicrobial agents used in the community. As well as a high level of mortality, HAP increases hospital stay significantly and can lead to significant deconditioning of patients already at risk due to their underlying frailty (NICE, 2016; Russel et al., 2015).

In this thesis the researcher will investigate HAP further. Specifically looking at an area which has had significant international attention in community acquired pneumonia in recent years- severity scoring indices. The researchers are aware that severity scoring has become integral to initial assessment of CAP in the UK, whereas this is not the case for HAP. This thesis will investigate if this is true and why. Chapter one introduces HAP, differentiating it from and considering other non-CAP pneumonias and severity indices- where they're used and what they achieve. Chapter two consists of a scoping review looking into HAP and severity indices, painting the full picture of research and international guidelines in the area. Chapter three is a piece of original research, using case study

design to assess the use of severity indices in HAP. Finally, Chapter four draws together a synthesis of the preceding chapters, concluding in learning points and recommendations for further research and policy.

1.1 Defining Hospital Acquired pneumonia

A HAP is defined as a pneumonia which develops 48 or more hours following hospital admission, which was not incubating at admission. This is usually confirmed on chest x-ray. HAP can include pneumonia which occurs 48 or more hours following intubation- a subgroup known as Ventilator associated pneumonia (VAP). For the purposes of this document, HAP will not include VAP as they are clinically different entities (NICE, 2019).

As well as CAP, HAP and VAP, there are other classifications of pneumonia which are either historical, or contemporary but not used within the UK/USA. These include Nursing home acquired pneumonia (NHAP), Healthcare associated pneumonia (HCAP) and psychiatric hospital acquired pneumonia (PHAP) (Anand & Kollef, 2009; Haga Et al., 2018). The underlying theme being that these populations have been thought more likely to be infected with an atypical pathogen and subsequently to require broader spectrum antibiotics. These definitions are not in use in the UK or USA as it is felt the definitions are not specific enough to effect different treatment to that prescribed for CAP according to the severity of the pneumonia (NICE, 2014).

It is worth noting at this point that all subgroups of pneumonia are subject to international variance. That is to say that although 'HAP' may be considered under the same definition in two countries, they may in fact be describing different disease entities due to the hospital system in which the diagnosis was made. For example, there is a much higher proportion of low acuity community hospitals in Japan compared to America and therefore a HAP in japan from a community hospital may be more comparable to a CAP in America (Japanese Respiratory Society, 2009). This is before

we consider that lung disease is known to affect patients differently based on their ethnic background.

The outcome of these three factors- the different subgroup use, the different hospital systems and the different disease characteristics in different ethnic groups- form an important limitation on the applicability of any HAP study not performed in the healthcare setting for which its results are being considered. That is to say that a HAP study in Japan is severely limited as research to guide management in the American or British HAP population.

Despite the high incidence, severity and wider effects of HAP as described above, the amount of research into the disease process is a long way behind similar disease processes such as CAP. Community acquired pneumonia is a thoroughly well researched topic, with over seven times as many results for "*Community acquired pneumonia*" on Pubmed than "*Hospital acquired pneumonia*" (9776 and 1325 respectively) (Pubmed, 2020). Indeed, the British Thoracic Society does not have a guideline set for Hospital Acquired pneumonia, whereas there is a Community acquired set of guidelines (British Thoracic Society, 2009). One area where HAP research has lagged behind CAP in particular is in scoring system analysis.

1.2 Scoring Systems

One of the most significant changes to CAP management over the past 20 years has been the introduction of severity scoring at admission. This takes different forms around the world, with the UK using the CURB-65 score, and the USA using the PSI score for example (NICE, 2014; Metlay et al., 2019). Despite different scores being used, the objectives remain the same. Scoring systems inform the admitting doctor's decision regarding place of care (home/hospital/ICU), initial treatment (narrow or broad-spectrum antibiotics) and the scores are prognostically helpful. Scoring systems in CAP have been well validated (NICE, 2014; Capelastegui et al., 2006). Outside of CAP, scoring severity systems are used more broadly for prognostication, treatment and consideration of ITU admission. These are both disease specific scores (e.g. Glasgow and Ranson for pancreatitis) and general

physiological scores (e.g. APACHE II, SOFA). Physiological scores can be used to escalate to critical care and to monitor a patient's progress during their critical care admission (Vincent et al., 1996; Knaus et al., 1985).

Despite the wide and successful use of scoring systems in CAP, the use of scoring systems in other illnesses and in the critically unwell patient, there has not been a wide adoption of a scoring system for HAP in the UK. Furthermore, neither UK, American nor European guidelines encourage the use of scoring systems in HAP (NICE, 2019; Kalil et al., 2016; Torres, 2017). Where there is a reason for this, it is stated that the committee making the guidelines is not aware of enough evidence for the use of scoring systems in HAP. There is, however, a scoring system which is recommended by Japanese Guidelines, the I-ROAD scoring system (Seki et al., 2008). This was developed using analysis of a large database of HAP patients in Japan, formulating a scoring system with the prognostic indicators for mortality. A similar method was initially used to develop the CURB-65 index, with retrospective analysis of a large number of community acquired pneumonia cases.

Given the successful use of scoring systems in community acquired pneumonia, the successful use of scoring systems in the critically ill and the adoption of a HAP scoring system in Japan, the possibility of a HAP scoring system having utility in the UK warrants review. As mentioned above CAP scoring systems are used to indicate location of care (home/hospital/ITU), select antibiotic therapy and prognosticate mortality. While physiological scores are used to predict ITU admission and monitor progress in critical care. HAP patients often fit into both the pneumonia group and the critically unwell group- as such it may be that CAP scoring systems are useful in this population, or it may be that physiological scoring systems are more appropriate. A successful scoring system in HAP would help in three ways; it would aid selection of an appropriate antimicrobial agent by predicting drug resistant pathogens, indicate whether a patient was likely to be able to be cared for on a ward or require ITU transfer and finally it would prognosticate for mortality. In the elderly and co-morbid population understanding the possible need for ITU early is especially useful to allow early

discussions regarding limits of care according to the patient and their families wishes, as well as allowing the early involvement of critical care. In CAP, scoring systems allow consistency of treatment depending on severity of pneumonia with increased accuracy than purely clinical judgement, they allow early referral to intensive care where this is likely to be needed and they facilitate home management of mild pneumonia in appropriate cases, all of which are directly beneficial to the patients (Capelastegui et al., 2006). The clinical utility & benefit has been demonstrated by their international uptake & recommendation by multiple different respiratory societies.

The first steps in evaluating HAP scoring systems is to review all current evidence looking at HAP prognostication scores in a literature review. It may be that there is enough evidence already to suggest that the use of scoring systems is appropriate or is not appropriate in this population. However it may be that there is little or no evidence to support either argument, at which point it may be worth considering evidence for scoring systems in other non-CAP pneumonia groups as an indication as to whether or not they are likely to work in HAP. For example, if the evidence suggests NHAP patients can be accurately triaged by an existing scoring system, it is worth considering that this scoring system may be transferable to HAP patients. This assumption would be based on the higher assumed prevalence of atypical pathogens and a more elderly, comorbid population in both NHAP and HAP compared to CAP. If no strong evidence emerges, small pilot trials to review the application of currently existing scoring systems would be an appropriate step to take prior to larger studies on promising scoring systems.

An alternative approach would be to mirror that taken by the Japanese Respiratory Society in the past- curating a large database of HAP episodes and using logistic regression to find independent predictors of mortality/ITU admission/drug resistant organisms, and formulating a scoring index with the results. This would be very time consuming but has potential to develop a tool of high clinical use, as has been shown in Japan with the I-Road scoring system, and in the UK with CURB-65.

It is worth noting that although in CAP there are multiple scoring systems which have been well validated and adopted into clinical use, HAP is- as described above- a different clinical entity. HAP effects a different population, has a different microbial basis and a different prognosis. As such, although it may be that a CAP severity score appropriately stratifies HAP severity, it would be inappropriate to assume this prior to validation within this cohort of patients.

1.3 Scoping the thesis: Exploring HAP scoring

In conclusion, despite the high prevalence and mortality associated with hospital acquired pneumonia, and the large steps that have been taken in recent years to reduce the multiple risks of hospital admission, HAP remains poorly researched relative to its community acquired compatriot. The evidence behind severity scoring in CAP is strong, with wide international uptake of one system or another. However, there is much less consensus behind HAP scoring and the evidence appears to be sparse. Given the utility of scoring systems in both CAP and the critically unwell patient, it follows that investigating scoring systems in HAP has potential to be clinically useful.

This thesis seeks to develop this area of inquiry through a process initially focused on a scoping review of the literature, followed by pilot study centred on exploring HAP scoring indices within the context of a single case study, focused on a District General Hospital.

The questions this study aims to address, are whether there is currently any evidence to support the use of severity scoring indices in HAP in the UK. And if this evidence exists, are the scoring systems of clinical and prognostic value. If the evidence is not present, the study will aim to address whether a pilot study into HAP severity scoring would support further research in the area.

Chapter two of the thesis will centre on the scoping review into HAP severity scoring, looking at the pre-existing evidence for their use. Chapter three will focus on the empirical pilot study, taking the information gathered from the scoping review and synthesising it into an original piece of research to further address the utility of these scores in the UK population. Finally, chapter four will consider

the findings of the scoping review and the pilot study, their relative strengths and weaknesses and contextualise the findings with the current literature. During this section the thesis will also reflect on next steps for research in this area, and how the approaches and research methods used influenced chapters one and two.

Chapter Two

Mapping the evidence for Severity Index use in Hospital Acquired Pneumonia: An exploratory Scoping Review

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2.1 Introduction:

The scoping review aimed to examine the current evidence supporting or refuting the use of severity scoring indices to aid treatment decisions and prognostication in Hospital acquired pneumonia (HAP). Preliminary searches demonstrated limited research into the area, this scoping review aims therefore to provide a clear narrative to the topic including a broad inclusion of relevant material. The approach used a modified approach to Arksey and O'Malley (2005) framework. To allow utilisation of all available evidence- be that systematic review, guidelines or opinion pieces- a wide study technique was necessary, due to the limited number of studies in this area. The classic scoping review technique has been slightly modified to allow two streams of evidence during the charting and collating phases as described below. This is due to the main two distinct information sources in

HAP (Guidelines and literature). The conclusion of this study aims to address whether the evidence and guidelines currently support HAP severity scoring in clinical practice, if not, to address if there is evidence to support further research and if so, to direct areas for that research. If unable to answer the HAP severity index question, this scoping review will build the complete foundation for further research in the area.

Defining 'HAP':

Hospital acquired pneumonia can be defined as pneumonia developed in a hospital setting, occurring 48 hours or more following hospital admission, and not being incubated at time of admission (ATS/IDSA, 2005). HAP incidence has been estimated at 8-10% in the elderly inpatient population, with up to 50% of HAP patients suffering complications during admission, and mortality estimated at 26-29% (Burton et al., 2016; Sopena, et al., 2000; Kalil, et al., 2016). HAP is empirically treated with broader spectrum antibiotics compared to community acquired pneumonia (CAP) due to the pathogens which typically cause HAP and their antimicrobial resistance patterns being different from those in CAP (NICE, 2019a). CAP is a very common cause of hospital admission with CAP-admission incidence previously calculated at 20.6 cases per 10000 adults per year (Bjarnason et al., 2018). Overall, a significantly greater amount of research has been done into CAP compared to HAP, including into severity assessment at diagnosis. For instance, an initial 'Pubmed' search of "Community acquired pneumonia AND Severity index" returns 534 results, whereas "Hospital acquired pneumonia AND Severity index" did not return any matches.

HAP is not the only pneumonia which has been treated separately to CAP at diagnosis. In the past, and currently outside of the UK, further subgroups of pneumonia have been used to guide treatment based on the increased likelihood of drug resistant pathogens. Other pneumonia subgroups include healthcare associated pneumonia (HCAP) and nursing home acquired pneumonia (NHAP) (ATS/IDSA, 2005; El-Solh, 2011). The concept of HCAP was introduced in the 2005 American thoracic society guidelines, describing patients who are in frequent contact with healthcare but do not fit the criteria for HAP. These guidelines advocated the use of broad-spectrum antibiotics empirically in HCAP due to increased incidence of drug resistant pathogens (ATS/IDSA, 2005). Despite more recent ATS guidelines determining that in America HCAP is not a clinically relevant pneumonia subgroup, in some countries HCAP and NHAP remain treated with different empirical antibiotics to combat a different cohort of likely causative pathogens (Kalil, et al., 2016). Significantly, neither HCAP or NHAP are currently recognised by the British Thoracic Society as being a subgroup of pneumonia in the UK and these patients would be considered to have a CAP (Lim, et al., 2009). As well as there being pneumonia subgroups between CAP and HAP, HAP can also be split into ventilator associated

pneumonia (VAP) and non-VAP. VAP is typically associated with critically ill patients and there is a significant amount of research which has gone into the prevention, identification, and treatment of VAP as it is a disease in a very closely monitored patient group, and also VAP is associated with a high mortality and financial cost (Kalil, et al., 2016; Pugh, et al., 2015). For the purposes of this review, HAP will refer to non-VAP unless otherwise specified.

Severity Indices:

Severity assessment has become a vital part of the initial clinical management of CAP, with UK, American and European guidelines all supporting the use of a severity assessment tool at time of diagnosis (NICE, 2019b; Metlay, et al., 2019; Woodhead, et al., 2011). Severity indices are used to guide location of treatment, empirical antibiotic therapy, Intensive Treatment Unit (ITU) review and mortality prediction. Generally higher scores indicate patients are more likely to be treated in hospital, with broader antibiotic therapy, have early critical care review and are more likely to succumb to their illness. However, scoring indices are not as widely used in HAP. Neither UK or American guidelines recommend their use and a brief literature search shows little research into this area (Kalil, et al., 2016; NICE, 2019a). Given the ubiquity with which CAP severity indices are used and their clinical usefulness, it follows that a scoring system in HAP able to guide antibiotic choice, critical care review and indicate prognosis would be beneficial.

To fully evaluate the use of severity scoring systems in hospital acquired pneumonia, it is important to examine both the current best practice as defined by national guidelines and relevant bodies. And subsequently to review the evidence for these recommendations, and if recommendations are lacking, to review evidence which could be used to formulate guidelines or direct research in the future. The aim of this review was not to adhere strictly to inclusion and exclusion criteria of HAP clinical trials as in a systematic review. The aim was to gather all available evidence, current thinking, and background we have on the topic of HAP severity scoring to develop the full narrative, then use this to direct the next steps in HAP severity scoring research or implementation. The use of the scoping review format suited this flexible investigative approach well. We conducted preliminary searches which indicated that the evidence base for HAP severity scoring is likely to be limited. Consideration has therefore been given to increase the scope of this study; if little evidence is found, the review will widen to consider scoring system use in other non-CAP subgroups of pneumonia (HCAP/NHAP). This will indicate whether there may be a benefit to the use of severity scoring in pneumonia subgroups with a higher likelihood of having atypical pathogens. The study will highlight specific scoring indices which are shown to discriminate well in these patient groups. Following the collation and analysis of current evidence, areas for further research and an approach for this are

highlighted. The prevalent scoring systems found in the literature will also be described in more detail to inform the discussion concerning their use in HAP- for example how easy they would be to implement in a clinical setting.

2.2 Research Questions:

The study focused on two interrelated research questions:

1. Is there sufficient evidence to suggest severity scoring system use in patients diagnosed with Hospital Acquired Pneumonia in the UK would be clinically beneficial?
2. Do current international guidelines support severity scoring systems in patients with Hospital Acquired Pneumonia?

2.3 Aims and Objectives:

- To identify the current guidelines and their underlying research concerning the use of severity scoring systems in non-VAP hospital acquired pneumonia (HAP).
- To evaluate the evidence for prognostic scoring in HAP, and the quality and quantity of the evidence available for specific scoring indices.
- To review the severity scoring systems and their prognostic accuracy in HAP
- To suggest clinical best practice based on current evidence for HAP severity scoring if the evidence is strong enough or identify areas for further research if evidence is sub-optimal.

2.4 Method:

A preliminary search for HAP scoring systems was conducted and found limited studies. As conclusions drawn from reviews of purely HAP scoring system papers would therefore give limited information, the approach of this review was widened. We reviewed: HAP studies, wider non-cap pneumonia studies, guidelines and opinion pieces and collated the information, aiming to guide the HAP severity index conversation and direct further research. To bring all of this information together required a flexible study design allowing the inclusion of mixed methodology papers and a diversity of evidence.

Overall, the study adopted the form of a scoping review which, compared to a systematic review, focuses not on a defined question with inclusion and exclusion criteria but employs a broader approach to review all the subject matter concerning a topic (Arksey & O'Malley, 2005). As the aim of this review is to draw together different strands of information regarding HAP scoring systems

including guidelines, opinion, studies in HAP and studies in other non-CAP pneumonia groups- a scoping review is more appropriate than a systematic review (Arksey & O'Malley, 2005).

The structure for this review was developed from the scoping review methodology framework as described by Arksey and O'Malley (2005) and further revised by the Joanna Briggs Institute (2015). This review follows the five scoping review stages as laid out below and described by Arksey and O'Malley (2005) and Levac (2010) with an additional stage due to the subject matter. The original five stages are: defining the research question (see above), literature search, charting of data from all relevant literature, collating and summarizing themes from the charted data and finally reporting the outcomes. In addition to this literature 'stream', the researcher performed a review of the current relevant guidelines and fed the results from this into the synthesis to enhance the full narrative (Figure 1). This augmented the explanatory narrative gained from an analysis of selected papers, providing a key additional source of evidence as part of the 'grey literature'.

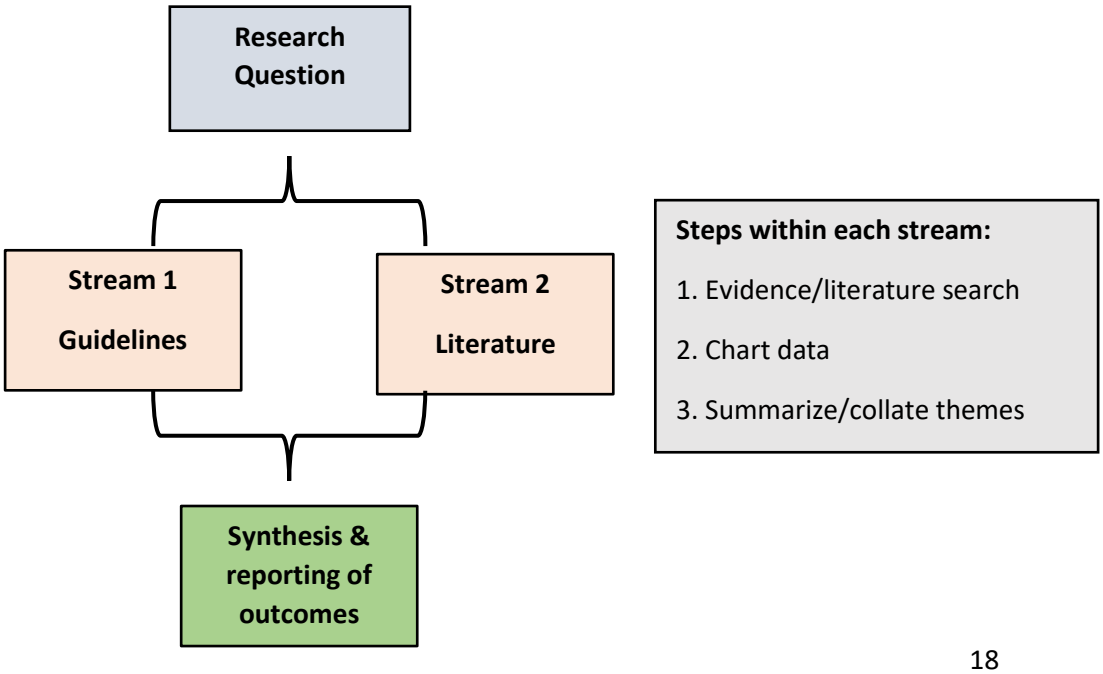


Fig 1. Study schematic

2.5 Stream 1- Current Guideline Review:

Guidelines: The British Thoracic Society, NICE, Diseases Society of America (IDSA)/American Thoracic Society (ATS), European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT), were all reviewed for guidance on HAP scoring indices as well as current understandings of HCAP as a separate pneumonia class from CAP or HAP. These guidelines either directly relate to UK practice or were widely mentioned in the literature found during this scoping review. In addition, Japanese guidelines were reviewed due to the significant amount of research into hospital acquired pneumonia and scoring indices conducted in Japan identified during this study.

2.6 Stream 2, Step 1 - Literature Search, inclusion and exclusion guidelines:

For the wider literature search PubMed, The Cochrane Library and Web Of Science were reviewed for articles containing “Hospital Acquired Pneumonia or HAP or Healthcare associated pneumonia or HCAP or Nosocomial Pneumonia” AND “Scoring System or Severity Index or Prognostic Index” (using the Field Tag TI- for title- on Web Of Science) (Pubmed, 2020; The Cochrane Library, 2020; Web of Knowledge, 2020). Articles were then reviewed by title, by abstract and by full text for relevance to the research question. For articles to be considered relevant they must apply at least one severity scoring system to a HAP patient group and discuss the prognostic accuracy of the score. Outcomes which were considered were mortality, ITU admission and presence of drug resistant pathogen causing pneumonia. However, following the initial review, the number of papers which fit this criterion was very small. Therefore, the scope of the review was widened, subsequently any paper from the above search criteria, which applied a scoring system to non-CAP pneumonia patients with the same outcomes measured was considered. This included studies which reviewed HAP, Nursing Home Acquired Pneumonia (NHAP), Healthcare Associated Pneumonia (HCAP), Ventilator associated pneumonia (VAP) and Psychiatric Hospital acquired Pneumonia (PHAP). In the UK, both HCAP and NHAP are not considered separate entities and are instead categorised as CAP. However, these studies were included as they are considered in different parts of the world (often where the studies

are performed) to be a separate entity due to patients presenting with an increased proportion of drug resistant pneumonia. As drug resistant pathogens are the primary reason for considering HAP as a different disease entity to CAP it was felt that, although there are clear limitations to including these patient groups, they demonstrate the use of severity scoring system in a pneumonia cohort not considered CAP in the locality of the study. The differences between pneumonia subgroups in the UK and abroad is often due to different healthcare systems. (Japanese Respiratory Society, 2009a) Given the limited information on HAP itself, this was considered an appropriate wider population to review within the bounds of the original search strategy.

Studies were excluded if there was no subgroup analysis excluding CAP patients, discussion articles (neither original research, systematic review or meta-analyses) were excluded from data analysis, articles which apparently duplicated information were not included in further analysis (information from one of the duplicate studies only would be included to avoid inappropriately weighting one set of data), and guidelines were not used for data analysis. Any relevant information from the papers not used in numerical analysis was tabulated and informed the discussion surrounding the review. Therefore all 26 studies appropriate for this review (figure 2), fed into the overall discussion if there was relevant information or themes.

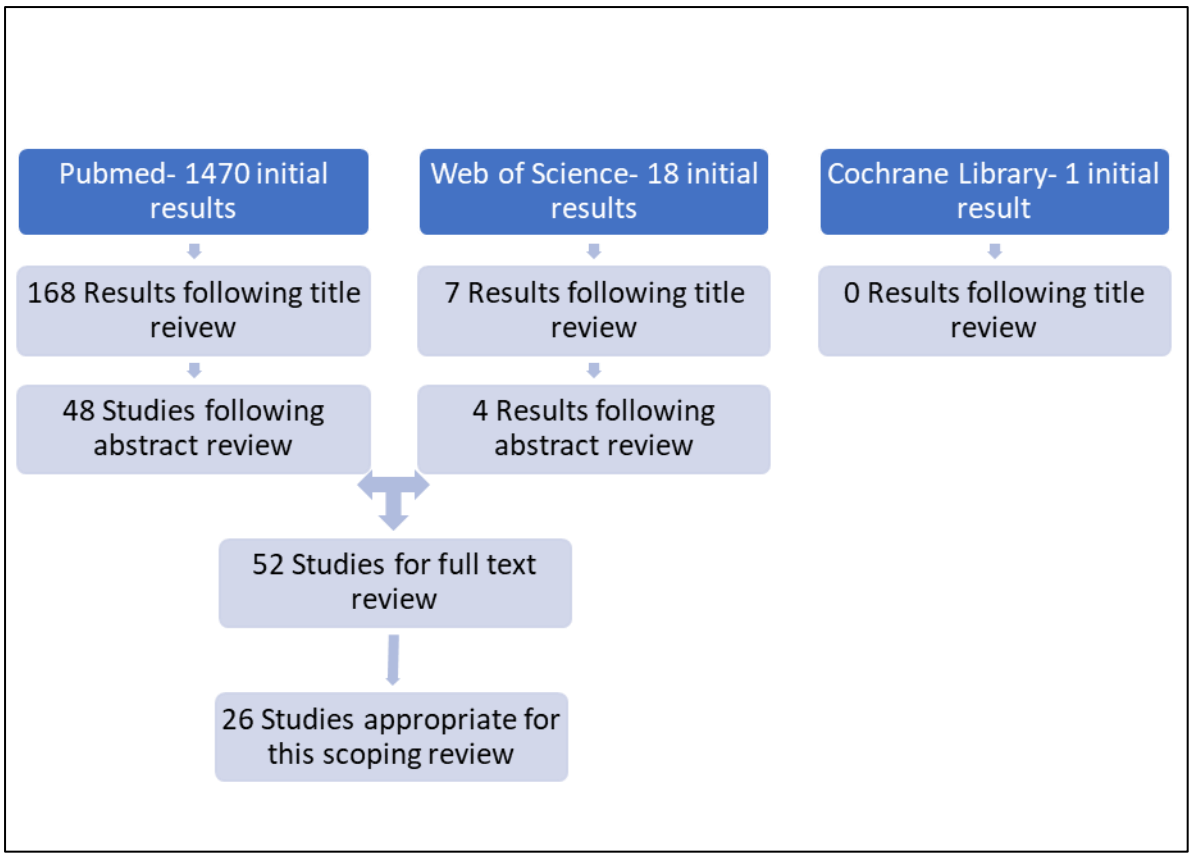


Fig 2. Modified Prisma Diagram of Literature stream: Search Strategy (Liberati et al., 2009)

2.7 Stream 2, Step 2 - Data Charting:

Following identification of appropriate studies, each study was reviewed and the outcomes relevant to this review were charted (Data Charting tables 1 and 2). Study objectives, population, study type and methodology were collected for analysis. Limitations of each study were noted, and important study findings were listed for further analysis. The limitations were not considered for formal weighting of included papers, but to demonstrate the limitations present in all the current research when applied to severity scoring in HAP in the UK. All 52 papers reviewed at the full text stage are included in the chart for transparency regarding the inclusion/exclusion, with explanation of why the study was not further studied or where a full text was not available for review.

2.8 Stream 2, Step 3- Summarizing/collating themes:

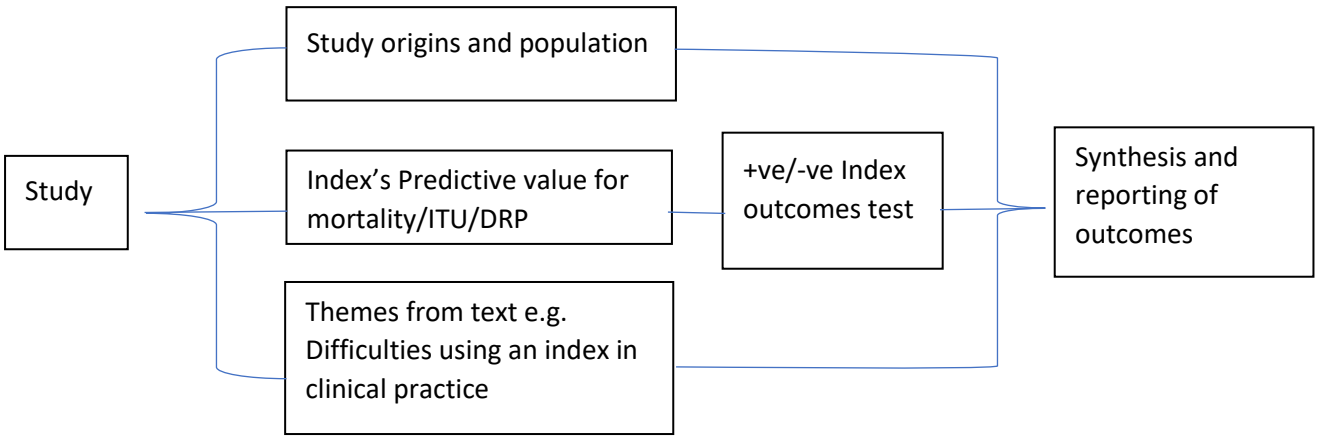


Fig 3 Step three protocol

This scoping review step has been slightly amended due to the nature of the studied material. Normally a thematic analysis may be performed at this stage (Arksey & O'Malley, 2005). However, as the studies had both qualitative and quantitative elements, a modified analysis was performed to better demonstrate the themes and results from the reviewed studies. This included a qualitative arm and two quantitative arms, feeding all results back into the overall synthesis as broad themes (Fig 3). As a consequence, the researcher utilised a discrete set of methods to the analysis of these different arms as part of the scoping review approach (Arksey & O'Malley, 2005).

The aim of the analysis was to define the origins of the study, their population, themes regarding a severity index's use and the findings regarding severity index's predictive value for three main outcomes (Mortality, ITU admission, Drug resistant pathogen culture). The analysis was carried out by reviewing the charted data looking at both the main outcomes and at themes as they emerged such as study limitations and scoring system limitations in practice. Outcomes were then defined for the scoring index and themes were fed into the synthesis. However, the studies identified within the review were clinically varied in terms of geography, size (some studies of less than 100 patients, some with over 17000), pathology (NHAP/PHAP/HCAP/VAP/HAP), outcomes (mortality/ microbial diagnosis/ ICU admission) and quality of the research. As a result, pooling all the quantitative data to demonstrate Severity Index performance would have been without merit and inappropriate.

Therefore the following quantitative analyses were carried out: number of studies considering each scoring system (novel systems and adjusted systems not included as each only used once in localised trials), number of studies reviewing each pneumonia population (NHAP/HCAP/PHAP), geographical origin of studies, for each scoring system number of positive and negative outcomes from review (defined below) for any of the three following outcomes: *Mortality, ITU admission* and *drug resistant*

pathogen identification. These quantitative analyses allowed thematic analysis as per the Arksey and O'Malley framework. To give context to the themes and outcomes from this analysis, several of the more prominent scoring systems are briefly described for background information prior to the results below to inform the dialogue of this review and the next steps in research.

2.9 Defining positive or negative study outcomes:

As the outcomes for each study were heterogenous and reported as such, positive or negative outcomes for accuracy for each of the three outcomes were considered the best way to review the scoring indices across the studies. Where a study reports area under the receiver operator curve analysis (AUC), a score of 0.7 or greater is considered positive for that outcome, if less than 0.7 it is considered negative. If there is no AUC mentioned, but the study reports a qualitive outcome as positive or negative, this is used. If the study neither uses AUC, nor qualitatively reports a scoring index's accuracy but compares one scoring system to another, the 'worst system' is classed as negative and the 'better systems' positive, unless all are defined as positive/negative. Where a study mentions a scoring system but does not report its results or describe its accuracy for a given outcome, neither positive nor negative accuracy are recorded.

The algorithm for explaining the above process by which scoring indices were classified as 'positive' or 'negative' for the prediction of a given variable can be viewed in Appendix 1.

2.10 Scoring Systems Overview:

Pneumonia Severity Index: PSI was developed in the 1990's in America as a risk stratification tool to identify patients with community acquired pneumonia who could be safely treated in the community. It uses 20 variables including patient demographics, comorbidities and physiological variables (Fine, et al., 1997). PSI is currently recommended for severity assessment in CAP by the American thoracic society and infectious diseases society of America (Metlay, et al., 2019).

CURB-65: CURB-65 is a scoring system derived from confusion, urea, respiratory rate, blood pressure and age over 65. The study was designed with data from the UK, Netherlands and New Zealand and stratifies patients into three risk groups which aims to identify patients suitable for community treatment, hospital treatment and patients who require early critical care review or admission (Lim, et al., 2003). CURB-65 Is currently recommended for CAP severity assessment by the British Thoracic society (NICE, 2019b).

A-DROP: The A-DROP classification is a derivative of CURB-65 adjusted for the Japanese population. It has shown similar results to CURB-65 in the Japanese population (Shindo, et al., 2008).

I-ROAD: A scoring system developed by the Japanese respiratory society to evaluate HAP severity. It was designed following analysis of a large Japanese HAP database and includes patient information and clinical assessment information (Japanese Respiratory Society, 2009b).

SOAR: Designed in the UK to better assess CAP severity in the elderly population, where confusion and high urea- features in CURB-65 scoring- are both common. Uses Systolic BP, Oxygenation, Age and Respiratory rate (British Thoracic Society, 2006).

APACHE II: This scoring system developed to assess severity in intensive care patients and monitor progress. This score is not a pneumonia specific scoring system but an indicator of wider physiological derangement (Knaus, et al., 1985).

SOFA and qSOFA: The SOFA score was designed to quantify the level of multiple organ failure a patient had sustained secondary to infection. qSOFA was developed as a rapid bedside test to indicate poor outcomes in patients with sepsis, it has been shown to be a better indicator of this than the SOFA score outside of the intensive care setting (Vincent, et al., 1996; Seymour, et al., 2016). Neither of these scoring indicies are pneumonia specific, both are based on non-specific physiological disturbance.

2.11 Results:

Overall, 'Stream One' found that no current guidelines support the use of HAP severity scoring indices in the UK/USA/Europe. The Japanese guidelines do suggest the use of a scoring system, but their HAP population is a very different cohort to the UK HAP population. HCAP and NHAP are not recognised as different from CAP in the contemporary UK or USA guidelines. In terms of 'Stream Two' there is a sparsity of HAP severity scoring index research, especially in the UK. In the evidence reviewed, mortality is the only outcome included in a large number of studies. However, the only scoring system which has been studied widely and has good results for mortality is PSI- a score which is recurrently described as clinically difficult to use in the literature.

The overall findings are that more research is needed in this area before clear recommendations can be made as to the use of severity scoring indices.

2.12 Stream One Results- Guidelines:

In the hospital acquired pneumonia antimicrobial prescribing guidelines published by NICE in September 2019, the recommendation is to base HAP severity assessment on clinical judgement and

not scoring indices (NICE, 2019a). In the evidence section of this guideline it is stated that the committee responsible for the guidelines knew of no validated severity scoring system in HAP. The British Thoracic society does not have any guidelines relating to hospital acquired pneumonia, only community acquired pneumonia (Lim, et al., 2009). Neither NICE or the British Thoracic society has HCAP guidelines or mentions HCAP as a separate entity in its guidelines, NICE classifies into only CAP or HAP.

The 2016 Infectious Diseases Society of America (IDSA)/American Thoracic Society (ATS) guidelines on the management of adults with HAP and VAP did not include HCAP (Kalil, et al., 2016). HCAP was included in the 2005 guidelines as referred to pneumonia acquired in health care facilities such as nursing homes, haemodialysis centres, outpatient clinics, or during hospitalization within the past three months (ATS/IDSA, 2005). However, it was felt to be too sensitive and not specific enough to identify a subgroup of patients with multi-drug resistant pathogens appropriately. Similarly, HCAP was not included in the combined 2017 European and Latin American guidelines (ERS/ESICM/ESCMID/ALAT) for the management of HAP and VAP (Torres, et al., 2017). Neither the 2005 or 2016 IDSA/ATS guidelines recommend the use of any scoring system in HAP- the only scoring system discussed in the 2016 IDSA/ATS guidelines is CPIS for diagnosis and the recommendation is not to use it. The International ERS/ESICM/ESCMID/ALAT 2017 guidelines for HAP/VAP management similarly do not advocate the use of a scoring system- there is no consideration of scoring systems within the guidelines.

Finally, the Japanese Respiratory Society guidelines have suggested the use of scoring systems since 2002 for HAP, these were updated in 2008 to the IROAD scoring system (Seki, et al., 2008). The necessity for the scoring system is drawn from the different population of patients to the US HAP population who almost all have severe disease, whereas in japan a significant variation in HAP patients exists (Japanese Respiratory Society, 2009a). This can be explained by different types of hospitals in the two countries and a markedly different healthcare system. In Japan HCAP and NHAP are considered separately to CAP and HAP, although there is an overlap in the HCAP group with both CAP and HAP. The differences between the healthcare systems in Japan and the US (where the HCAP definition arose in 2005) are such that there is heterogeneity between Japanese HCAP patient groups and HCAP patients previously described in the USA also. The healthcare system difference is equally applicable to the UK and Japan. As such the HAP and HCAP patients in Japanese studies within this scoping review are likely to be a very different population to the population the outcome of this study is aimed at (UK HAP patients). In summary, no contemporary European or North

American guidelines advocate the use of HAP severity scoring index or the use of the HCAP pneumonia subgroup. Where described the reason for not using a scoring index is a lack of evidence.

2.13 Stream Two Results- Literature Review:

The following two tables contain all relevant charted information from all 52 studies where full text review was attempted. This includes studies where the full text was not obtained and some studies which were not relevant on further reading, this is for transparency and also to ensure that the full narrative of this scoping review and the subject of it is covered. Leaving these studies in the table allows readers to appreciate the entire evidence base for the analysis and in future assess whether or not studies were overlooked by this scoping review or the reason for which they were not analysed further.

2.14 Table 1- Data Charting Table- Part 1 and 2, Full Charting summary, Stream Two Step 2

Table 1 part one and two are the full charting summaries of all texts chosen for full text review. Included are study aims, population, method, outcomes, and relevance to this scoping review. In the final column are significant findings and limitations on the use of the study with regard to the UK HAP population. The table has been divided into two due to space on the page. The study numbers across the two charts correlate such that study 1 on part 1 is study 1 on part 2 and so on.

Data Charting Table:

Table 1 Part 1

No.	Reference:	Study Type:	Study Aim:	Study Size:	Population/Location:
1.	Noguchi, S., Yatera, K., Naito, K., Hata, R., Kawanami, T., Yamasaki, K., Kato, T., Orihashi, T., Inoue, N., Sakamoto, N., Yoshii, C., & Mukae, H. (2019). Utility of the Quick Sequential Organ Failure Assessment in Japanese patients with nursing- and healthcare-associated pneumonia. *Geriatrics & gerontology international*, *19*(3), 177–183. https://doi.org/10.1111/ggi.13581	Retrospective observational study.	To clarify the role of severity scoring systems in Nursing home or Healthcare associated pneumonia (NHCAP) patients.	289 patients (352 identified, 63 excluded due to insufficient data).	Patients admitted with NHCAP over one-year period to 5 Japanese Teaching Hospitals.
2.	Xu, L., Ying, S., Hu, J., Wang, Y., Yang, M., Ge, T., Huang, C., Xu, Q., Zhu, H., Chen, Z., & Ma, W. (2018). Pneumonia in patients with cirrhosis: risk factors associated with mortality and predictive value of prognostic models. *Respiratory research*, *19*(1), 242. https://doi.org/10.1186/s12931-018-0934-5	Retrospective observational study.	To analyse risk factors and severity scores for mortality prediction in patients with cirrhosis and pneumonia.	203 Patients with cirrhosis and pneumonia (Community acquired or nosocomial).	Patients with liver cirrhosis and pneumonia over two-year period at the First Affiliated Hospital of Zhejiang University School of Medicine (China).

3.	Jiang, J., Yang, J., Jin, Y., Cao, J., & Lu, Y. (2018). Role of qSOFA in predicting mortality of pneumonia: A systematic review and meta-analysis. *Medicine*, *97*(40), e12634. https://doi.org/10.1097/MD.0000000000012634	Meta-analysis	To examine the role of qSOFA score in predicting pneumonia mortality.	17868 Patients with CAP or HCAP.	All patients included in a literature search pertaining to qSOFA and Pneumonia.
4.	Hamaguchi, S., Suzuki, M., Sasaki, K., Abe, M., Wakabayashi, T., Sando, E., Yaegashi, M., Morimoto, S., Asoh, N., Hamashige, N., Aoshima, M., Ariyoshi, K., Morimoto, K., & Adult Pneumonia Study Group – Japan (2018). Six underlying health conditions strongly influence mortality based on pneumonia severity in an ageing population of Japan: a prospective cohort study. *BMC pulmonary medicine*, *18*(1), 88. https://doi.org/10.1186/s12890-018-0648-y	Prospective observational study	To identify co-morbidities associated with mortality in pneumonia and analyse their impact on severity prediction.	1772 Patients with HCAP or CAP.	Patients admitted to four Japanese community hospitals with HCAP or CAP over two year period.
5.	Miyazaki, H., Nagata, N., Akagi, T., Takeda, S., Harada, T., Ushijima, S., Aoyama, T., Yoshida, Y., Yatsugi, H., Fujita, M., & Watanabe, K. (2018). Comprehensive analysis of prognostic factors in hospitalized patients with pneumonia occurring outside hospital: Serum albumin is not less important than pneumonia severity assessment	Retrospective observational study	To identify variables associated with mortality in patients admitted to hospital with pneumonia.	534 patients (217 NHCAP)	All patients admitted to single Japanese hospital with pneumonia over a six year period (2010-2016).

	scale. *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy*, *24*(8), 602–609. https://doi.org/10.1016/j.jiac.2018.03.006				
6.	Haga, T., Ito, K., Sakashita, K., Iguchi, M., Ono, M., & Tatsumi, K. (2018). Risk Factors for Death from Psychiatric Hospital-acquired Pneumonia. *Internal medicine (Tokyo, Japan)*, *57*(17), 2473–2478. https://doi.org/10.2169/internalmedicine.0435-17	Retrospective observational study	To identify risk factors for mortality in Psychiatric Hospital Acquired Pneumonia.	409 Patients with PHAP	All patients admitted to Tokyo Metropolitan Matsuzawa Hospital from psychiatric hospitals for PHAP treatment 2007-2017.
7.	Ranzani, O. T., Taniguchi, L. U., & Torres, A. (2018). Severity scoring systems for pneumonia: current understanding and next steps. *Current opinion in pulmonary medicine*, *24*(3), 227–236. https://doi.org/10.1097/MCP.0000000000000468	Evidence summary	To evaluate the use of scoring systems in CAP.	N/A	N/A
8.	Yan, S. T., Sun, L. C., Lian, R., Tao, Y. K., Zhang, H. B., & Zhang, G. (2018). Diagnostic and predictive values of procalcitonin in bloodstream infections for nosocomial pneumonia. *Journal of critical care*, *44*, 424–429. https://doi.org/10.1016/j.jcrc.2017.12.022	Retrospective observational study	To evaluate procalcitonin compared to PSI score for mortality predication and identifying organism type in Nosocomial Pneumonia (NP).	286 patients with nosocomial pneumonia. Using American guidelines definition of NP.	Patients in the China-Japan friendship hospital with nosocomial pneumonia, positive blood culture and no malignant tumour or rheumatological disease over a 30-month period.

9.	Asai, N., Watanabe, H., Shiota, A., Kato, H., Sakanashi, D., Hagihara, M., Koizumi, Y., Yamagishi, Y., Suematsu, H., & Mikamo, H. (2018). Could qSOFA and SOFA score be correctly estimating the severity of healthcare-associated pneumonia?. *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy*, *24*(3), 228–231. https://doi.org/10.1016/j.jiac.2017.10.004	Retrospective observational study.	To evaluate qSOFA and SOFA scores as prognostic severity indices in HCAP.	81 HCAP Patients	Patients with HCAP (defined by ATS/IDSA 2005 guidelines) attending Aichi Medical University hospital.
10.	Ahn, J. H., Lee, K. H., Chung, J. H., Shin, K. C., Lee, C. K., Kim, H. J., & Choi, E. Y. (2017). Clinical characteristics and prognostic risk factors of healthcare-associated pneumonia in a Korean tertiary teaching hospital. *Medicine*, *96*(42), e8243. https://doi.org/10.1097/MD.0000000000008243	Retrospective observational study	To assess if HCAP is a clinically relevant patient group in Korea.	1046 patients with pneumonia. 399 with HCAP. HCAP defined by 2005 ATS/IDSA guidelines.	Patients admitted to a Korean Teaching Hospital over a two-year period (2014-2016) with pneumonia.
11.	Murillo-Zamora, E., Medina-González, A., Zamora-Pérez, L., Vázquez-Yáñez, A., Guzmán-Esquivel, J., & Trujillo-Hernández, B. (2018). Performance of the PSI and CURB-65 scoring systems in predicting 30-day mortality in healthcare-associated pneumonia. Desempeño de los sistemas de	Cross Sectional study	To review PSI and CURB-65 scoring systems as 30-day mortality predictive tools in HCAP patients.	109 Patients	Non-immunocompromised adults with HCAP from three urban hospitals in Mexico. HCAP patients with radiographic features of pneumonia at least 48 hours

	puntuación PSI y CURB-65 para predecir la mortalidad a 30 días de la neumonía asociada a la asistencia sanitaria. *Medicina clinica*, *150*(3), 99–103. https://doi.org/10.1016/j.medcli.2017.06.044				post admission. Over a four month period in 2016.
12.	Koizumi, T., Tsukada, H., Ito, K., Shibata, S., Hokari, S., Tetsuka, T., Aoki, N., Moro, H., Tanabe, Y., & Kikuchi, T. (2017). A-DROP system for prognostication of NHCAP inpatients. *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy*, *23*(8), 523–530. https://doi.org/10.1016/j.jiac.2017.04.013	Retrospective observational study	To compare the usefulness of different severity indices (PSI, CURB-65, I-ROAD and A-DROP) in NHCAP for the purpose of prognostic prediction.	303 Patients. 144 with NHCAP.	Patient hospitalised with NHCAP or CAP in Respiratory Medicine of Niigata General City Hospital over two-year period.
13.	Noguchi, S., Yatera, K., Kawanami, T., Fujino, Y., Moro, H., Aoki, N., Komiya, K., Kadota, J. I., Shime, N., Tsukada, H., Kohno, S., & Mukae, H. (2017). Pneumonia Severity Assessment Tools for Predicting Mortality in Patients with Healthcare-Associated Pneumonia: A Systematic Review and Meta-Analysis. *Respiration; international review of thoracic diseases*, *93*(6), 441–450. https://doi.org/10.1159/000470915	Meta-analysis	To evaluate current evidence for the use of scoring systems in healthcare associated pneumonia. PORT and CURB-65 scores evaluated.	8 Studies, 2814 patients.	A mixture of HCAP patients and NHAP patients. Studies from Japan (x2), Korean (x2), Taiwan, Italy, Hong Kong and USA. Only two studies were prospective.

14.	Putot, A., Tetu, J., Perrin, S., Bailly, H., Piroth, L., Besancenot, J. F., Bonnotte, B., Chavanet, P., Charles, P. E., Sordet-Guépet, H., & Manckoundia, P. (2016). A New Prognosis Score to Predict Mortality After Acute Pneumonia in Very Elderly Patients. *Journal of the American Medical Directors Association*, *17*(12), 1123–1128. https://doi.org/10.1016/j.jamda.2016.07.018	Retrospective observational study	Application of a new scoring system using N-Terminal Pro-BNP plasmatic rate, uraemia and monocyte count to elderly patients with pneumonia to assess its prognostic usefulness.	217 Patients, 56 NHAP, 23 HAP.	All patients hospitalised with acute pneumonia aged over 75 during a 6-month period in 6 Clinical departments at Burgundy University Hospital France.
15.	Dhawan, N., Pandya, N., Khalili, M., Bautista, M., Duggal, A., Bahl, J., & Gupta, V. (2015). Predictors of mortality for nursing home-acquired pneumonia: a systematic review. *BioMed research international*, *2015*, 285983. https://doi.org/10.1155/2015/285983	Systematic Review	Review of the current evidence of risk stratification tools in NHAP, specifically with reference to mortality.	20 Articles. Each study contained between 73 and 2271 patients.	Studies looking at NHAP patients aged 65 or older. Countries of the study not mentioned in the article but are from all over the world.
16.	Shorr, A. F., & Zilberberg, M. D. (2015). Role for risk-scoring tools in identifying resistant pathogens in pneumonia: reassessing the value of healthcare-associated pneumonia as a concept. *Current opinion in pulmonary medicine*, *21*(3), 232–238. https://doi.org/10.1097/MCP.0000000000000159	Review paper	Review of the concept of HCAP and scoring systems for improving detection of drug resistant organisms.	N/A	N/A

17.	Lee, M. K., Kim, S. H., Yong, S. J., Shin, K. C., Park, H. C., Choi, J., Choi, Y. S., Seong, J. H., Jung, Y. R., & Lee, W. Y. (2015). Clinical and microbiological features of patients admitted to the intensive care unit with nursing and healthcare-associated pneumonia. *The Journal of international medical research*, *43*(2), 236–249. https://doi.org/10.1177/0300060514551188	Retrospective observational cohort study	To review characteristics of NHCAP patients admitted to a respiratory ICU and examination of clinical and microbiological features related to mortality at admission.	428 Patients with NHCAP	Patients admitted to a single respiratory ICU in a Korean Hospital with NHCAP over a 5-year period.
18.	Ottosen, J., & Evans, H. (2014). Pneumonia: challenges in the definition, diagnosis, and management of disease. *The Surgical clinics of North America*, *94*(6), 1305–1317. https://doi.org/10.1016/j.suc.2014.09.001	Review article	American review article on Pneumonia. Discusses current understanding of the disease.	N/A	N/A
19.	Matsunuma, R., Asai, N., Ohkuni, Y., Nakashima, K., Iwasaki, T., Misawa, M., & Norihiro, K. (2014). I-ROAD could be efficient in predicting severity of community-acquired pneumonia or healthcare-associated pneumonia. *Singapore medical journal*, *55*(6), 318–324. https://doi.org/10.11622/smedj.2014082	Retrospective observational study	Comparison of multiple prognostic tools to evaluate the usefulness of the I-ROAD scoring system as a severity index in HCAP.	302 Patients, 74 with HCAP.	Patients admitted to Kameda Medical Centre, Japan over 48-month period, diagnosed with pneumonia.

20.	Ma, H. M., Ip, M., Woo, J., & Hui, D. S. (2014). Development and validation of a clinical risk score for predicting drug-resistant bacterial pneumonia in older Chinese patients. *Respirology (Carlton, Vic.)*, *19*(4), 549–555. https://doi.org/10.1111/resp.12267	Two observational cohort studies.	Development and validation of a scoring system for predicting drug resistant pneumonia.	354 patients in derivation group and 96 in validation group.	Patients presenting to the teaching hospital of the Chinese University of Hong Kong (CUHK), over the age of 65 with pneumonia. Patients were excluded if hospital admission in previous 14 days or suspected nosocomial infection. Each study collected data over a one-year period.
21.	Ishibashi, F., Sunohara, M., & Kawagoe, S. (2015). Performance of severity scores for home care-based patients suffering from pneumonia. *Geriatrics & gerontology international*, *15*(3), 311–317. https://doi.org/10.1111/ggi.12274	Retrospective observational study	To examine whether current scoring systems, particularly PSI, can predict mortality in NHAP patients treated at home.	97 patients.	Patients diagnosed with pneumonia at Aozora Clinic in Kamihongo (Japan), in 2011.
22.	Ugajin, M., Yamaki, K., Hirasawa, N., Kobayashi, T., & Yagi, T. (2014). Prognostic value of severity indicators of nursing-home-acquired pneumonia versus community-acquired pneumonia in elderly	Retrospective observational study	Comparing the prognostic usefulness of scoring systems in NHAP compared to CAP	138 NHAP patients and 307 CAP patients.	Patients aged over 65 and hospitalised due to CAP or NHCAP over a three-year period in Ichinomiya-Nishi Hospital Japan.

	patients. *Clinical interventions in aging*, *9*, 267–274. https://doi.org/10.2147/CIA.S58682				
23.	Porfyridis, I., Georgiadis, G., Vogazianos, P., Mitis, G., & Georgiou, A. (2014). C-reactive protein, procalcitonin, clinical pulmonary infection score, and pneumonia severity scores in nursing home acquired pneumonia. *Respiratory care*, *59*(4), 574–581. https://doi.org/10.4187/respcare.02741	Prospective observational trial	To evaluate CPIS and procalcitonin in NHAP diagnosis and review pneumonia scoring system's inpatient mortality prediction value in NHAP patients.	58 Patients diagnosed with NHAP and 28 with other pulmonary disorders.	All nursing home residents admitted to Pulmonary Department at Nicosia General Hospital in Nicosia, Cyprus over 14-month period.
24.	Di Pasquale, M., Ferrer, M., Esperatti, M., Crisafulli, E., Giunta, V., Li Bassi, G., Rinaudo, M., Blasi, F., Niederman, M., & Torres, A. (2014). Assessment of severity of ICU-acquired pneumonia and association with etiology. *Critical care medicine*, *42*(2), 303–312. https://doi.org/10.1097/CCM.0b013e3182a272a2	Prospective observational study	To evaluate correlation between pneumonia severity and microbiological agent in ICU acquired pneumonia.	343 patients. 208 VAP, 138 HAPs (all ICU acquired pneumonia-ICUAP).	45 beds over 6 ICUS in a single university teaching hospital.
25.	Nakagawa, N., Saito, Y., Sasaki, M., Tsuda, Y., Mochizuki, H., & Takahashi, H. (2014). Comparison of clinical profile in elderly patients with nursing and healthcare-associated pneumonia, and those with community-acquired pneumonia. *Geriatrics & gerontology*	Retrospective observational study	To delineate the different clinical characteristics and risk factors for mortality in CAP compared to NHAP.	1020 patients, 960 eligible for this study 373 patients with CAP and 587 NHAP.	Patients aged 65 or older, admitted for pneumonia to the Division of Respiratory Medicine, Tokyo Metropolitan Geriatric

	international, *14*(2), 362–371. https://doi.org/10.1111/ggi.12110				Hospital in Tokyo, Japan over a 6-year period.
26.	Esperatti, M., Ferrer, M., Giunta, V., Ranzani, O. T., Saucedo, L. M., Li Bassi, G., Blasi, F., Rello, J., Niederman, M. S., & Torres, A. (2013). Validation of predictors of adverse outcomes in hospital-acquired pneumonia in the ICU. *Critical care medicine*, *41*(9), 2151–2161. https://doi.org/10.1097/CCM.0b013e31828a674a	Prospective observational study	To validate a previously defined set of adverse outcome predictors patients with ICU acquired pneumonia. CPIS and SOFA score performance was also analysed.	335 Patients with ICU acquired pneumonia (ICUAP). 200 VAP, 135 Non-VAP ICUAP.	45 beds over 6 ICUS in a single university teaching hospital.
27.	Lee, J. C., Hwang, H. J., Park, Y. H., Joe, J. H., Chung, J. H., & Kim, S. H. (2013). Comparison of severity predictive rules for hospitalised nursing home-acquired pneumonia in Korea: a retrospective observational study. *Primary care respiratory journal : journal of the General Practice Airways Group*, *22*(2), 149–154. https://doi.org/10.4104/pcrj.2013.00011	Retrospective observational study	To compare several severity indices (SOAR, PSI, CURB-65, NHAP score) for prediction of mortality and ICU admission in NHAP population of Korea.	208 NHAP Patients	Patients admitted over a three-year period to a single general hospital with NHAP. HAP excluded.
28.	Jeong, B. H., Koh, W. J., Yoo, H., Um, S. W., Suh, G. Y., Chung, M. P., Kim, H., Kwon, O. J., & Jeon, K. (2013). Performances of prognostic scoring systems in patients with healthcare-associated pneumonia. *Clinical infectious diseases : an*	Retrospective observational study with prospectively	To evaluate PSI and CURB-65 scores' 30-day mortality prediction in HCAP.	938 patients, 519 with CAP, 419 with HCAP.	Patients hospitalised with pneumonia over a two-year period at Samsung Medical Centre (South Korea). HAP patient excluded.

	official publication of the Infectious Diseases Society of America, *56*(5), 625–632. https://doi.org/10.1093/cid/cis970	collected data.			
29.	Park, S. C., Kang, Y. A., Park, B. H., Kim, E. Y., Park, M. S., Kim, Y. S., Kim, S. K., Chang, J., & Jung, J. Y. (2012). Poor prediction of potentially drug-resistant pathogens using current criteria of health care-associated pneumonia. *Respiratory medicine*, *106*(9), 1311–1319. https://doi.org/10.1016/j.rmed.2012.04.003	Retrospective observational study	To assess HCAP definition for prediction of drug resistant pneumonia. To develop improved scoring system for prediction of drug resistant pneumonia.	339 Patients, 172 CAP patients and 167 with HCAP.	Patients over 20 years old with culture positive pneumonia admitted to Severance hospital, South Korea, over a two-year period.
30.	Carrabba, M., Zarantonello, M., Bonara, P., Hu, C., Minonzio, F., Cortinovis, I., Milani, S., & Fabio, G. (2012). Severity assessment of healthcare-associated pneumonia and pneumonia in immunosuppression. *The European respiratory journal*, *40*(5), 1201–1210. https://doi.org/10.1183/09031936.00187811	Prospective observational study	To assess mortality prediction accuracy of CURB-65, CURB, CRB-65, SCAP and PSI in HCAP patients. To review clinical difference between CAP, HCAP and pneumonia in the immunocompromised patient.	629 patients, 322 with CAP, 307 with HCAP. 219 of the HCAP patients were immunocompromised, 88 were not.	Adult patients admitted to single hospital in Italy with pneumonia over a 5-year period. VAP, HAP and aspiration pneumonia were amongst the excluded population.
31.	Heppner, H. J., Sehlhoff, B., Niklaus, D., Pientka, L., & Thiem, U. (2011). Pneumonie-Schwere-Index (PSI), CURB-65 und Mortalität bei hospitalisierten	Retrospective observational study	Assessment of PSI and CURB-65 as prognostic	209 Patients with aspiration pneumonia	Elderly patients with aspiration pneumonia over four year period in a single

	geriatrischen Patienten mit Aspirationspneumonie [Pneumonia Severity Index (PSI), CURB-65, and mortality in hospitalized elderly patients with aspiration pneumonia]. *Zeitschrift fur Gerontologie und Geriatrie*, *44*(4), 229–234. https://doi.org/10.1007/s00391-011-0184-3		indicators in elderly patients with aspiration pneumonia.		centre (Marien hospital, Herne). Data from a comparable CAP group also gathered.
32.	Falcone, M., Corrao, S., Venditti, M., Serra, P., & Licata, G. (2011). Performance of PSI, CURB-65, and SCAP scores in predicting the outcome of patients with community-acquired and healthcare-associated pneumonia. *Internal and emergency medicine*, *6*(5), 431–436. https://doi.org/10.1007/s11739-011-0521-y	Multicentre prospective observational study	Comparison of PSI, CURB-65 and SCAP for adverse outcome prediction in HCAP.	313 patients with pneumonia, 223 with CAP and 90 with HCAP.	Patients admitted with HCAP or CAP to 55 Italian Hospitals.
33.	Fang, W. F., Yang, K. Y., Wu, C. L., Yu, C. J., Chen, C. W., Tu, C. Y., & Lin, M. C. (2011). Application and comparison of scoring indices to predict outcomes in patients with healthcare-associated pneumonia. *Critical care (London, England)*, *15*(1), R32. https://doi.org/10.1186/cc9979	Retrospective cohort study	To assess several scoring systems (SCAP, SOAR, SMART-COP, Modified ATS Criteria, PSI, CURB-65, SMART-CO and IDSA/ATS) for prediction of 30-day mortality, 3-day and 14-day	444 Patients	Adults with HCAP from 6 medical centres in Taiwan discharged over a one year period. HAP was one of the exclusion criteria.

			ITU admission in HCAP patients.		
34.	Man, S. Y., Graham, C. A., Chan, S. S., Mak, P. S., Yu, A. H., Cheung, C. S., Cheung, P. S., Lui, G., Lee, N., Chan, M., Ip, M., & Rainer, T. H. (2011). Disease severity prediction for nursing home-acquired pneumonia in the emergency department. *Emergency medicine journal : EMJ*, *28*(12), 1046–1050. https://doi.org/10.1136/emj.2010.107235	Prospective observational study	Evaluating the use of 5 predictive scores (PSI, CURB-65, M-ATS, R-ATS, España rule), for NHAP severity to identify patients for community management.	767 NHAP patients	Patients admitted to single hospital in Hong Kong over 18-month period with NHAP.
35.	Napolitano L. M. (2010). Use of severity scoring and stratification factors in clinical trials of hospital-acquired and ventilator-associated pneumonia. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, *51 Suppl 1*, S67–S80. https://doi.org/10.1086/653052	Discussion paper	Discussion paper, considering the difficulties in HAP and VAP trials. Includes section on scoring systems.	N/A	N/A
36.	El-Solh, A. A., Alhajhusain, A., Abou Jaoude, P., & Drinka, P. (2010). Validity of severity scores in hospitalized patients with nursing home-acquired pneumonia. *Chest*, *138*(6), 1371–1376. https://doi.org/10.1378/chest.10-0494	Retrospective analysis of prospectively collected data	To compare accuracy of CURB65, CRB-65, CURB and SOAR for 30-day mortality and ICU admission prediction in NHAP.	457 Patients with NHAP	Patients admitted to two US university hospitals with NHAP.

37.	Japanese Respiratory Society (2009). Establishment of new severity ratings based on analysis of hospital-acquired pneumonia. *Respirology (Carlton, Vic.)*, *14 Suppl 2*, S4–S9. https://doi.org/10.1111/j.1440-1843.2009.01571.x	Description of Guideline Creation	To describe the process of development of the Japanese HAP scoring system.	834 Patients.	Patients included in a national multicentre survey with HAP in Japan.
38.	Mylotte, J. M., Naughton, B., Saludades, C., & Maszarovics, Z. (1998). Validation and application of the pneumonia prognosis index to nursing home residents with pneumonia. *Journal of the American Geriatrics Society*, *46*(12), 1538–1544. https://doi.org/10.1111/j.1532-5415.1998.tb01539.x	Retrospective observational study	To assess prediction of pneumonia severity using PSI in NHAP patients. To compare inpatient and outpatient IV antibiotic treatment in NHAP.	158 patients with NHAP, 100 treated as inpatients, 58 treated in Nursing homes	Patients either from a single geriatric unit in a US hospital (from 1996) or from two nursing homes (between 1994 and 1997). All patients with NHAP.
39.	Mirsaeidi, M., Peyrani, P., Ramirez, J. A., & Improving Medicine through Pathway Assessment of Critical Therapy of Hospital-Acquired Pneumonia (IMPACT-HAP) Investigators (2009). Predicting mortality in patients with ventilator-associated pneumonia: The APACHE II score versus the new IBMP-10 score. *Clinical infectious diseases : an official publication of the*	Retrospective observational study	To create and assess a severity index for use in VAP which is more easily calculable than APACHE II.	178 VAP patients	Patients selected from IMPACT-HAP database in the America. Only VAP patient data collected from the database. Data from a one-year period.

	Infectious Diseases Society of America, *49*(1), 72–77. https://doi.org/10.1086/599349				
40.	Seki, M., Watanabe, A., Mikasa, K., Kadota, J., & Kohno, S. (2008). Revision of the severity rating and classification of hospital-acquired pneumonia in the Japanese Respiratory Society guidelines. *Respirology (Carlton, Vic.)*, *13*(6), 880–885. https://doi.org/10.1111/j.1440-1843.2008.01348.x	Description of Guideline Creation	To describe the process of development of the Japanese HAP scoring system.	834 Patients.	Patients included in a national multicentre survey with HAP in Japan.
41.	Kollef, K. E., Reichley, R. M., Micek, S. T., & Kollef, M. H. (2008). The modified APACHE II score outperforms Curb65 pneumonia severity score as a predictor of 30-day mortality in patients with methicillin-resistant Staphylococcus aureus pneumonia. *Chest*, *133*(2), 363–369. https://doi.org/10.1378/chest.07-1825	Retrospective observational study	To compare APACHE II, CURB-65 and CRB65 in MRSA pneumonia severity prognostication.	218 Patients with MRSA pneumonia	Patients with MRSA pneumonia at Barnes-Jewish teaching hospital, identified over a 3-year period.
42.	Committee for the Japanese Respiratory Society Guidelines in Management of Respiratory (2004). Severity rating of hospital-acquired pneumonia and classification. *Respirology (Carlton, Vic.)*, *9 Suppl 1*, S13–S15. https://doi.org/10.1111/j.1440-1843.2003.00544.x	Japanese Respiratory Society HAP guidelines	These are out of date guidelines for HAP. Studies 37 and 40 describe the creation of the new guidelines.	N/A	N/A

43.	Naughton, B. J., Mylotte, J. M., & Tayara, A. (2000). Outcome of nursing home-acquired pneumonia: derivation and application of a practical model to predict 30 day mortality. *Journal of the American Geriatrics Society*, *48*(10), 1292–1299. https://doi.org/10.1111/j.1532-5415.2000.tb02604.x	Retrospective observational study	To derive simple scoring system which can be applied by nursing home staff to patients to predict 30-day mortality in NHAP.	378 Episodes of NHAP.	All nursing home residents diagnosed with pneumonia from 11 nursing homes in Buffalo (USA). Data collected over two 5-month periods between 1997 and 1999.
44.	Rello, J., Rué, M., Jubert, P., Muses, G., Soñora, R., Vallés, J., & Niederman, M. S. (1997). Survival in patients with nosocomial pneumonia: impact of the severity of illness and the etiologic agent. *Critical care medicine*, *25*(11), 1862–1867. https://doi.org/10.1097/00003246-199711000-00026	Retrospective observational study	Assessing the effect of severity of Nosocomial Pneumonia on outcomes at various stages during the disease process.	62 Patients	Intubated patients admitted to a single ICU in Spain with nosocomial pneumonia in 1997.
45.	Keita-Perse, O., & Gaynes, R. P. (1996). Severity of illness scoring systems to adjust nosocomial infection rates: a review and commentary. *American journal of infection control*, *24*(6), 429–434. https://doi.org/10.1016/s0196-6553(96)90036-x	Literature review	Assessing literature for severity scores aiming to improve comparison of nosocomial infection between different ICUs.	11 Studies were found.	Articles from 1991 to 1996 considering severity of illness scoring systems.

46.	Almirall, J., Mesalles, E., Klamburg, J., Parra, O., & Agudo, A. (1995). Prognostic factors of pneumonia requiring admission to the intensive care unit. *Chest*, *107*(2), 511–516. https://doi.org/10.1378/chest.107.2.511	Prospective observational study	Assessment of prognostic factors for mortality in patients admitted to ICU with severe pneumonia.	127 patient, 58 CAP, 69 HAP- including 23 ICU acquired.	Patients admitted to single ICU in Barcelona between 1986 and 1989 with severe pneumonia or developing pneumonia in ICU.
47.	Petersen, I. S., Jepsen, O. B., Hartmann-Andersen, J. F., Toftegaard, M., Haumann, P., Knudsen, K. K., Jacobsen, K., Hasselstrøm, L., Engelsen, J., & Lauritsen, H. K. (1994). Pneumoni blandt patienter indlagt på intensiv terapiafsnit. Epidemiologisk multicenterstudie of APACHE II-score, incidens og forløb [Pneumonia among patients admitted to intensive care units. An epidemiological multicenter study of APACHE II score, incidence and course]. *Ugeskrift for laeger*, *156*(36), 5126–5130.	Unable to get full text access	Danish article	Not available	Not available
48.	Salemi, C., Morgan, J. W., Kelleghan, S. I., & Hiebert-Crape, B. (1993). Severity of illness classification for infection control departments: a study in nosocomial pneumonia. *American journal of infection control*, *21*(3), 117–126. https://doi.org/10.1016/0196-6553(93)90002-l	Case control study	To assess a subjective severity of illness score for nosocomial pneumonia prediction in inpatients.	128 patients with bacterial nosocomial pneumonia and 252 control patients without.	Patients with bacterial nosocomial pneumonia in Kaiser Permanente Hospital, California from 1987 to 1988.

49.	Al-Badaway, T. H., Abouelela, A. M., & Kawi, M. A. G. A. (2016). Predictive value of different scoring systems for critically ill patients with hospital acquired pneumonia.. *Egyptian Journal of Chest Disease and Tuberculosis*, 65 (4) pp. 757-763. https://doi.org/10.1016/j.ejcdt.2016.05.010.	Prospective cohort study	To assess the prognostic value of PSI, CURB-65, SOAR, Modified-ATS, IDSA/ATS, SMART-COP, SMRT-CO and SOAR scoring systems in HAP patients. The outcomes were 28-day mortality, ICU stay and number of days on mechanical ventilation.	60 Patients with HAP, including VAP.	Patients admitted to the critical care department of the Alexandria University Hospital in Egypt, over a one-year period with HAP.
50.	Roquilly, Antoine & Feuillet, Fanny & Launey, Yoann & Thioliere, L. & Cinotti, Raphaël & Nesseler, Nicolas & Rozec, Bertrand & Seguin, Philippe & Lasocki, Sigismond & Sébille, Véronique & Asehnoune, Karim. (2014. A bedside scoring system for the resistance to a limited spectrum antimicrobial therapy in 631 Brain-injured patients.. *Intensive Care Medicine.* 40 pp s51-s51. https://www.researchgate.net/publication/296071296_A_BEDSIDE_SCORING_SYSTEM_FOR_THE_RESISTANCE_TO_A_LIMITED_SPECTRUM_ANTIMICROBIAL_THERAPY_IN_631_BRAIN-INJURED_PATIENTS_WITH_HOSPITAL-ACQUIRED_PNEUMONIA	Prospective multi-centre observational study.	To design and validate a scoring system for the prediction of antibiotic resistant pathogens in patients with Brain Injury and HAP.	631 Brain-Injured patients with HAP. 379 for data collection and scoring system development, 252 in validation co-hort.	Patients admitted to three ICUs in France with HAP and brain-injury.

51.	Amin, Z. 2013. Validation of CURB-65 Scoring System in Patients with Hospital Acquired Pneumonia. *Respirology*. 18 (Sup4), pp 104-104. https://doi.org/10.1111/resp.12184_9	Retrospective observational study	To attempt validation of CURB-65 score in HAP.	171 HAP patients.	Indonesian HAP patients from a 6-year period.
52.	Kropec, A., Schulgen, G., Just, H., Geiger, K., Schumacher, M., & Daschner, F. (1996). Scoring system for nosocomial pneumonia in ICUs. *Intensive care medicine*, *22*(11), 1155–1161. https://doi.org/10.1007/BF01709329	Prospective cohort study	To develop scoring system for prediction of nosocomial pneumonia in ICU.	756 ICU patients with stays of >48 hours.	Single centre ICU over a two-year period in Germany.

Data Charting table:

Table 1 part 2:

No.	Methodology and Intervention:	Outcomes:	Findings relevant to my scoping review:
1.	Retrospective application of PSI, A DROP, I-ROAD and qSOFA to predict mortality in NHCAP patients. And risk factor analysis to predict potentially drug resistant pathogens in NHCAP patients.	289 patients included. Average age 85.2. Pneumonia related inpatient mortality 6.9%. The area under the curve (receiver operating characteristic curve) and 95% confidence interval [CI] for pneumonia-related mortality predicted using the PSI were 0.697 (95% CI 0.59–0.80), A-DROP 0.63 (95% CI 0.51–0.76), I-ROAD 0.61 (95% CI 0.52–0.70) and qSOFA 0.701 (95% CI 0.59–0.81). Risk factors for PDR pathogens were raised respiratory rate, orientation disturbance and hypoalbuminaemia. Addition of albumin improved AUC for mortality prediction in both PSI and qSOFA. There was no association between potentially drug resistant pathogens and mortality.	1. This was a small, single centre, retrospective study into NHCAP, not in a UK population. These are all limitations of the study for application to a UK HAP population 2.qSOFA was found to be the most useful mortality prediction tool in this NHCAP population. qSOFA had poor sensitivity and good specificity. 3. PSI performed the best of the other tested scores but predictive power found to be insufficient in this population. 4. PDR pathogen isolation was not associated with mortality
2.	Patients with liver cirrhosis and pneumonia were retrospectively reviewed with regards to risk factors and scoring systems to predict mortality.	Despite this study identifying the community and nosocomial pneumonia patient groups and their differences, there was no separation of the two for severity index analysis and as such the results cannot be applied to HAP specifically, especially given the specific (Liver cirrhosis) patient group. As this study was not used in any further analysis.	1. This study is not appropriate for further analysis regarding the purposes of this scoping review.
3.	Meta-analysis using data extraction and statistical analysis from included studies	This study used data extraction to examine the effectiveness of qSOFA in mortality prediction in pneumonia. It included CAP and HCAP patients, and although it demonstrated a CAP	1. This study is not appropriate for further analysis regarding the purposes of this scoping review.

	to assess qSOFA for mortality prediction in pneumonia.	subgroup, there was no HAP subgroup analysis. As this study was not used in any further analysis.	
4.	Prospective review of associations between co-morbidities and pneumonia mortality. Comparison of this with CURB and PSI for prediction.	This study reviewed co-morbidities of patients with pneumonia (CAP or HCAP) and found 6 which were associated with increase mortality in this population. These were then compared with CURB65 and PSI as prognostic tools. The paper concluded that an increasing number of comorbidities in an elderly population should be incorporated into scoring systems. The paper included CAP and HCAP patients, there was no HAP/HCAP subgroup analysis. As this study was not used in any further analysis.	1. This study is not appropriate for further analysis regarding the purposes of this scoping review.
5.	Retrospective chart and x-ray review, using logistical regression to assess individual factors and scoring methods for mortality prediction.	This study was a retrospective review of chart data and chest x-rays to identify variables associated with mortality in pneumonia admissions. Although the study reviewed two scoring systems and included NHCAP, it did not analyse these patients as a subgroup separate from CAP. As this study was not used in any further analysis.	1. This study is not appropriate for further analysis regarding the purposes of this scoping review.
6.	Retrospective clinical file review of patients admitted with PHAP. Reviewing the clinical difference between survivors and non-survivors and assessing	Age >65, bilateral infiltrates on x-ray and BMI were the factors most associated with mortality on logistic regression. Using the A-DROP classification as severity increased, mortality increased, area under the ROC was 0.699. They modified the A-DROP score with addition of other parameters which	1. This is a small, PHAP subgroup and is a Japanese population. There are therefore significant limitations to application of this data to a UK HAP population. 2. A-DROP, PSI and I-ROAD scores all correlated to mortality in a non-CAP pneumonia group. However, the

	prognostication using severity scoring systems in this population.	improved this. Both I-ROAD and PSI scores also correlated severity index scores with mortality but no ROC was included in the paper. The study did not compare the scoring systems.	A-DROP ROC curve was <0.7 and there was no number given for the other scores.
7.	On full text review, not applicable to HAP- no HAP consideration.	This study is not appropriate for further analysis regarding the purposes of this scoping review- no HAP subgroup.	1. This study is not appropriate for further analysis regarding the purposes of this scoping review.
8.	In patients diagnosed with NP, procalcitonin (PCT) and blood culture results were compared for correlation and diagnostic relevance. PSI and PCT were compared as 28 + 60 day mortality predictors in the same population.	This study showed that PSI was a better prognostic tool that procalcitonin for predicting 28- and 60-day mortality in nosocomial pneumonia patients. It showed a significant correlation between PSI and PCT scores. The area under the receiver operating curve values for 28-day mortality were 0.758 (95% CI, 0.701–0.815) for PSI and 0.620 (95% CI, 0.550–0.690) for serum PCT. This was very similar to 60 day mortality.	1. Limited study as retrospective study from one hospital in a significantly different population from the UK. Furthermore, patients with rheumatological disease and malignancy excluded. 2. However the study did demonstrate a good prognostic use of PSI for mortality prediction in Nosocomial pneumonia. 3. The discussion section of the study highlighted the limited use of PSI in clinical practice due to its complexity.
9.	Patients were scored using; Curb65, A-drop, PSI, I-ROAD and SOFA scores at time of diagnosis. These scores were then assessed for 30-day mortality prediction.	Regarding 30-day mortality prediction, the area under the receiver-operating characteristic (ROC) curve for A-DROP was 0.753, CURB-65 0.800, PSI 0.878 and SOFA score 0.930. I-road was 0.628. SOFA score of 4 or higher was the most sensitive and specific of all the scoring systems used, with a sensitivity of 20%, specificity of 100%, PPV 100% and NPV 68%.	1. Note that HAP patients were excluded from this study, in addition to the population being significantly different to the UK. It is also a small sample size. These are significant limitations for the application of this study results to a UK HAP population.

			2. This study shows good prognostic use of all scores used in a HCAP population, apart from I-road. 3. Despite this study looking into qSOFA, this is the only scoring system within the study not given a ROC score.
10	Demographics, disease severity and microbial profiles for different pneumonia subgroups were compared using multi-variable logistic analysis. The primary aim was to assess if the HCAP definition was useful for defining a different patient population from CAP.	PSI was measured in all patients, in the HCAP group it was found to be an independent risk factor for 28-day mortality. HCAP patients had a higher mortality and a higher prevalence of drug resistant pathogens than CAP, however HCAP was not an independent risk factor for mortality. The presence of drug resistant pathogens in the HCAP group was significantly higher than in the CAP group.	1. HAP patients were excluded from the study. 2. PSI was found to be a useful prognostic tool for mortality in HCAP patients. 3. This is a one centre retrospective study in Korea, with no HAP patients, and as such has severe limitations when applying findings to a UK population with HAP.
11	PSI and CURB-65 scores were measured for all patients and subsequently compared to 30-day mortality. The scores were calculated retrospectively from the notes.	At every pneumonia severity, PSI had a higher sensitivity and a lower specificity for mortality prediction. The area under the received operator curve for CURB-65 and PSI was 0.698 (95% CI: 0.600–0.797) and 0.737 (95% CI: 0.646–0.827) respectively. Mortality was 59.6%. The study concludes that both PSI and CURB-65 have moderate mortality prediction in HCAP patients. PSI had a higher sensitivity but a lower specificity that CURB-65 at all pneumonic severity levels.	1. This study definition of HCAP is very similar to HAP, as the diagnostic criteria include features after 48 hours of inpatient admission. 2. The study states that both CURB-65 and PSI are appropriate for mortality prediction in an HCAP population, however the study is limited when applied to UK HAP population- it is a small Mexican study with a possibly slightly broader range of patients that purely HAP. Furthermore, only PSI had a ROC >0.7.

			3. The mortality in this study was high.
12	The four scoring systems were applied to all patients, 30-day mortality and inpatient mortality were calculated, and the scoring systems were compared for predictive accuracy using a receiver operating characteristics curve. Each score was limited to a mild and a severe group only.	30 Day mortality in the NHCAP group increased with increasing severity score for each of the four prognostic indices. The area under the receiver operating curve for 30-day mortality prediction using the four scores were: A-drop- 0.7621, CURB-65- 0.8085, IROAD- 0.7596, PSI- 0.7456. Showing good predictive values for 30-day mortality in NHCAP using any of the four scoring systems. The study's outcome was that A-DROP was the most useful scoring system as it was simpler than PSI, faster to compile than IROAD, and more specific to the Japanese population than CURB-65. The results are consistent with non-inferiority of A-DROP but do not show superiority.	1. NHCAP is a classification developed specifically for a Japanese population and is therefore not necessarily comparable with a UK HAP population. 2. In addition this is a single centre, small, retrospective study, all of which are study limitations.
13	A Pubmed search was carried out for relevant articles; retrospective or prospective studies in HCAP/NHAP patients, applying severity scores and reporting mortality. Subsequently all of data from all studies was analysed for	8 Articles were selected for review, of which 7 reviewed the PORT score and 8 of which reviewed the CURB-65 score. In the PORT group, a score of 4 or more gave AUROC of 0.68 (95% CI: 0.64-0.72) and scores of five gave 0.71 (95% CI: 0.67-0.75). In the CURB-65 group, Using cut off values of ≥2 and ≥3, the AUCs were 0.65 (95% CI: 0.61-0.69) and 0.66 (95%CI: 0.62-0.70), respectively. This study found that whilst the PORT score is likely more accurate than CURB-65 in HCAP patients,	1. Study highlights difficultly in clinical application of complex scoring systems (PORT). 2. These patients had either HCAP or NHAP, not HAP. None of the studies are from the UK and most were retrospective. Only one study was described as 'good quality', all others were moderate or poor quality. 3. Further evidence that PORT and CURB-65 scores are useful in non-CAP patients, but not as effective as in CAP.

	mortality prediction accuracy using AUROC comparison.	it is difficult to apply clinically and neither score is sufficiently powered in HCAP compared to in CAP.	
14	No HAP/HCAP subgroup analysis was conducted so this study was not further analysed and will not be further used in this scoping review.	This study is not appropriate for further analysis regarding the purposes of this scoping review.	1. This study is not appropriate for further analysis regarding the purposes of this scoping review.
15	PUBMED, EMBASE and CINAHL all reviewed for articles looking at risk factors for mortality in NHAP. Scoring systems were reviewed as part of this study for both mortality and ICU admission prediction.	The study looked at assorted factors to ascertain risk factors for mortality in NHAP, including demographics and aetiology. The study showed PSI as the best evidenced predictive scoring system in NHAP, with CURB-65 also a useful, validated system. The third most useful study was SOAR. The study also suggested biomarkers may have a role to play in this area. The conclusion, however, was that more work needs to be done to delineate the most useful predictor or scoring system.	1. Further evidence in support of PSI and CURB-65 in the non-CAP pneumonia patient. 2. Non-UK studies and NHAP patients- not a UK HAP population. 3. This study also excluded other studies looking at multiple disease entities which may have provided further evidence.
16	N/A	This is a review article which looked at HCAP as a concept and its limitations- broadly that using HCAP as a screening tool for resistant pathogens is ineffective. It reviewed scoring systems used for predicting drug resistant pathogens in patients attending from the community, which it found had been validated. It did not subgroup analyse these by pneumonia	1. This study is not for further analysis in this scoping review.

		classification, and the study is therefore not applicable to this scoping review.	
17	Patients split into four groups depending on their NHCAP categorisation. Their demographics, microbiological diagnosis and clinical features (including CURB-65, PSI and APACHE II) were then reviewed and analysis of mortality predictors was carried out.	The study found that age, PSI score and ICU admission length were all significantly higher in the non-survivor group of patients. CURB-65 score was not significantly different between the two groups. Low bicarbonate levels and microbial diagnosis were also statistically significantly different between survivors and non-survivors. Mortality was not significantly different between the four different groups according to which NHCAP criteria they met.	1. This study is a single centre retrospective study in a Korean NHCAP population which is a significant limitation when applying findings to the UK HAP population. 2. This study shows PSI as a statistically useful prognostic index in non-CAP pneumonia. However, it finds CURB-65 not to be useful. APACHE II not compared but was calculated.
18	NA	Wide ranging article discussing various aspects of pneumonia. States scoring systems not used in HAP, no information applicable to this scoping review.	1. This study is not appropriate for further analysis in this scoping review.
19	Characteristics of all patients on admission were reviewed (baseline characteristics, lab findings, identified pathogens, clinical outcomes etc), and the following scores: CURB-65, PSI, A-DROP and I-ROAD, were calculated for all patients and	The study found higher pneumonia severity and mortality in the HCAP group than the CAP group. Mortality increased as severity increased as scores by PSI and I-ROAD scores in the HCAP group. However, in CURB-65 and A-DROP this was not the case in less severe disease. The number of patients in with less severe disease was however very small. I-ROAD and PSI had the highest sensitivity in the HCAP group, with the A-DROP score being the most specific. The AUROC were:	1. Limited study as single centre, small, retrospective study in Japanese population. As such applying findings to UK HAP population inappropriate. 2. Study found I-ROAD and PSI to be effective severity scoring indices in HCAP, however pointed out the difficulties in using PSI as a clinician due to its complexity.

	the results were analysed for significance in mortality prediction using AUROC analysis.	0.793,0.717, 0.798 and 0.745 for A-drop, CURB-65, I-ROAD and PSI respectively. The study concluded that I-ROAD was effective for severity scoring in HCAP, while CURB-65 and A-DROP underestimated severity. They found PSI to be comparable to I-ROAD.	3. Number of patients within the HCAP subgroup small, and the number with low severity pneumonia even lower, a further limitation.
20	This builds on previous work by the author demonstrating high CURB-65 score, bronchiectasis and recent hospital admission as being risk factors for drug resistant bacterial pneumonia. These risks were weighted into a scoring index based on statistical analysis from the deviation cohort and this was applied to the validation cohort to assess the index's usefulness in predicting drug resistant pneumonia compared to using the ATS HCAP definition.	The area under the receiver operating curve for the study's novel scoring system was 0.751 (95% confidence interval (CI): 0.703–0.795) compared to using the definition of HCAP to guide therapy which was 0.650 (95% CI: 0.597–0.699), when predicting drug resistant pneumonia in the derivation cohort. In the validation cohort, they were 0.782 (95% CI: 0.686–0.859) and 0.671 (95% CI: 0.568–0.764), respectively. The study found that by using their novel scoring system to predict drug resistant pathogens instead of initiating broad spectrum empirical antibiotics secondary to the patient meeting HCAP definition, the use of inappropriate antibiotics could be reduced.	1. This was a single centre study in Hong Kong looking at non-HAP patients. Furthermore, the scoring system used by the study was both developed based on their own research and on a similar patient group. These are all limitations of the study when applied to the UK HAP population. 2. The study showed the use of a scoring system to be better than the use of a pneumonic definition in guiding therapy in a non-CAP pneumonia group. 3. The study demonstrated a scoring system which can usefully detect drug resistant bacterial pneumonia. 4. As this study used a novel scoring system which only appears in the literature once, it is not included in the analysis tables for this article.
21	Each patient was scored using A-DROP, PSI and CURB-65 score	Using the scores as mortality predictors gave the following results for area under receiver operator curves; PSI 0.859, the	1. This was a small retrospective study in a single centre, outside of a hospital setting, using a

	and these were then compared with pneumonic severity. A modified PSI score without radiographic or lab results was also used (PSI-HC).	modified PSI score (PSI-HC) 0.856, A-DROP 0.778 and CURB-65 0.806 respectively. The study concluded that all the scoring systems were useful for predicting mortality in NHAP patients treated in the community, with PSI likely the most accurate (but no significant AUC difference). They proposed a large multi-centre trial would be helpful to assess the PSI-HC as a more pragmatic scoring system in this patient group.	compromised PSI score (due to lacking ABG/CXR/RR data) and not in a UK population. These are all limitations of the study for application to a UK HAP population. 2. This study demonstrates three commonly used scoring systems for CAP as being useful in mortality prediction in non-CAP pneumonia patients.
22	Patient notes were analysed, clinical and demographic data was collected, CURB-65, PSI and A-DROP was calculated for all patients from time of diagnosis. The scores were then assessed for prediction of 28-day mortality.	Patients in the NHAP group had a higher mortality rate, were older and had more comorbidities. Each scoring system was less effective in the NHAP group than in the CAP group. The area under the receiver operator curve for Curb-65, PSI and A-DROP were 0.69, 0.67 0.70 respectively.	1. This was a small, retrospective study in a non-HAP patient group in Japan. These are all limitations when applying the results to a UK HAP population. 2. This study demonstrated that scoring systems designed for CAP were more effective at predicting mortality in CAP than in an older, more co-morbid pneumonia group. 3. CURB-65, A-DROP and PSI were of similar use in NHAP patients, only A-DROP had an AUROC of ≥0.7
23	Clinical data, lab data and imaging for each patient was reviewed for calculation of CPIS score and severity scores (CURB-65, PSI, SMART-COP, NHAP index and SOAR). These	The AUROC for predicting inpatient mortality with CRP and Procalcitonin was 0.63 and 0.84 respectively. Of the pneumonia severity scores, CURB-65 performed best with an AUROC of 0.68 (95% CI: 0.53-0.84). With PSI, NHAP index, SMART-COP and SOAR scoring 0.65 (95% CI 0.49–0.82), 0.58	1. This was a small, single centre study of NHAP patients in Cyprus. These limitations need consideration before applying the result to UK HAP patients. 2. This study showed that CURB-65 and PSI were the best tested prognostic indices for NHAP, however neither had a high AUROC score.

	were then compared to inpatient mortality figures.	(95% CI 0.41–0.75), 0.57 (95% CI 0.36–0.78) and 0.62 (95% CI 0.42–0.82) respectively. The study concluded that CURB-65 and PSI performed best as prognostic scoring systems in pneumonia.	
24	APACHE II, SAPS, SOFA and CPIS all calculated for patients at diagnosis and at other times during admission. Scoring systems were then analysed for a correlation with presence or absence of multi-drug resistant pathogens as well as 28- and 90-day mortality.	Mortality was higher in patients with a SOFA score >8 or an APACHE II score >20. There was no correlation between pneumonia severity and multi-drug resistant pathogens.	1. This was a single centre, small study in an ICU as these limitations need to be considered when applying the findings to a UK non-ICU HAP population. 2. This study found no correlation between pneumonia severity and drug resistant pathogens in a non-CAP pneumonia patient group. 3. This study did not use common pneumonia specific scoring systems, rather using scoring systems which grade systemic inflammatory response.
25	Baseline characteristics, pneumonia severity, risk factors for mortality and outcomes were compared between CAP and NHAP patients. A-DROP score was used to assess severity.	NHAP patients were older, had more comorbidities and a worse performance status than CAP patients. Heart failure, CKD, malignancy and poor performance status were all associated with higher mortality in the NHAP patient group. Although overall A-DROP score was statistically significant for mortality prediction in NHAP, there was no significant difference between patients scoring 2,3 and 4 on the 5-point scale. A-DROP was a much better predictor in CAP patients.	1. Single centre, retrospective study in Japanese NHAP population, therefore significant limitations for application to UK HAP population. 2. This study showed that although a score of 5 or 1 on the A-DROP scale was helpful in prediction, a scores of 2/3/4 were not useful in mortality prediction.

26	CPIS and SOFA scores were calculated on day 1, 3 and 5 following diagnosis. Scores were compared to the outcomes of 28-day mortality and ventilator-free days and assessed for correlation.	This study found that at onset of pneumonia, SOFA scores were significantly higher in patients who died compared to those who survived. CPIS at diagnosis was not prognostically valuable for mortality. Both CPIS and SOFA scores declining during the admission were correlated with improved outcomes, this was of statistical significance in the SOFA score but not in CPIS. Other variables found to be associated with 28-day mortality included previous alcohol abuse, shock at diagnosis, inability to increase PaO2 at day three and a rising SOFA score from day one to three.	1. This is a single centre ICU based study including VAP patients in a non-UK population. These are all limitations to its application to UK HAP patients. 2. This study found that SOFA was superior to CPIS for mortality prediction in a non-CAP pneumonia population. 3. This study found that CPIS was not useful in prognosticating in this population. 4. This study showed value in measuring the progression of a scoring system over days compared to a single value at diagnosis.
27	Notes were reviewed for demographics, clinical parameters and outcomes (ICU admission/Mortality/etc). Scoring systems were then retrospectively applied to review prognostic value of each system. Scores and outcomes were then compared for correlation, including use of Youden index and AUROC.	All four scoring systems showed increased mortality, ICU admission and severe pneumonia with increasing scores, this was statistically significant. PSI and CURB-65 scored significantly more patients into the most severe category compared to NHAP score or SOAR. The AUROC for mortality for PSI, CURB-65, SOAR and NHAP score were 0.73, 0.69, 0.64 and 0.64 respectively. PSI had the highest Youden index (for a score of 5) for mortality, severe pneumonia and ICU admission. CURB-65 was second best in all outcomes in terms of Youden index. The study found that PSI had the best	1. This was a small, single centre, retrospective study in a NHAP population in Korea was HAP patients excluded. These are all limitations when considering the application of the outcomes with a UK HAP population. 2. This study showed PSI to be the best predictor of measured adverse outcomes in a non-CAP pneumonia population. 3. This study showed CURB-65 (a significantly shorter and more commonly used score in the UK to have better mortality prediction than either the SOAR or NHAP group in this population.

		discriminatory power of the scoring system with reference to the measured outcomes.	4. The study mentioned the difficult clinical use of PSI.
28	Patient data prospectively collected, scores retrospectively applied and prognostic accuracy of scoring systems compared for HCAP and CAP. Area under receiver operator curve compared for 30-day mortality between scoring systems.	There was a trend of worsening 30-day mortality as severity index score increased for both CAP and HCAP groups scored by either PSI or CURB-65. Mortality was higher at every severity score in HCAP group. Patients defined as low risk when scored by CURB-65 had a higher mortality than low risk PSI patients. At every severity, PSI had a higher sensitivity, but lower specificity compared to CURB-65. The AUROC were 0.679 and 0.599 for PSI and CURB-65 respectively in HCAP. Both systems performed better in CAP than HCAP.	1. This was a retrospective, single centre, HCAP trial in a South Korean population, limiting its application to a UK HAP population. 2. This study suggested that PSI was better at prognosticating mortality in HCAP than CURB-65. 3. This study concluded that for HCAP a new scoring system was required to improve prognostication.
29	Baseline characteristics, microbial data and outcomes were reviewed. Correlation between patients fulfilling the ATS HCAP definition and the culture of a potentially drug resistant pathogen was assessed. A new scoring system was developed following risk factor analysis for drug resistant pathogen and the score was	Potentially drug resistant pathogens were more prevalent in the HCAP group than the CAP group. HCAP patients had a significantly higher PSI score on diagnosis, but CURB-65 scores were similar across the two groups. Recent hospital admission, recent IV antibiotics and NG feeding tube use were all independent risk factors for drug resistant pathogens. The study combined these factors into a new scoring system and applied it to the same patient's group. The AUROC for potentially drug resistant pathogens for the new score was 0.711 and for the HCAP criteria 0.634. However, this analysis	1. This study shows that HCAP definition has a poor predictive value for identifying drug resistant pathogens in this patient group. 2. This study is limited in that it is a retrospective single centre study in Korea looking at HCAP and CAP. The use of this data in UK HAP patients would therefore be inappropriate. 3. The lack of subgroup analysis for the new scoring systems means that the data for it should not be used in analysis this scoping review.

	then assessed for predictive value.	includes CAP patients and as such is not appropriate for further analysis in this scooping review.	4. It is worth noting that the new scoring system was developed with and validated on the same patient population which reduces the value of the validation.
30	All 5 severity indices were calculated for patients based on their admission data. Other demographics/clinical data and mortality outcomes were recorded. Scoring indices were assessed for mortality prediction.	In the HCAP group, all 5 scoring systems showed increasing mortality as severity score increased. PSI and CURB-65 had the lowest proportion of 'low risk' patients, and the PSI low risk group had the lowest mortality of all the low risk groups. All scores performed better in CAP patients than in HCAP patients. PSI and SCAP both performed better than any of the CURB scores although this was not statistically significant. The AUROC for PSI, CURB, CURB-65, CRB-65 and SCAP were 0.68, 0.60, 0.62, 0.62 and 0.67 respectively. In non-immunocompromised HCAP patients all scores performed much better- similar to CAP. However in immunocompromised patients only PSI and SCAP were prognostic.	1. This is a single centre study in an Italian HCAP population with a significant number of immunocompromised patients. These limitations must be considered when applying the results to UK HAP populations. 2. This study found PSI to be the best tested scoring system for HCAP, although not statistically different from the others. 3. This study found a significant difference in severity score accuracy in immunocompromised and immunocompetent patients. 4. Again this study found that the scoring systems we currently have are more accurate in CAP prognostication than HCAP. 5. All scores were poorly predictive in HCAP with immunocompromise but good in the immunocompetent.

31	Patient's CURB-65 and PSI scores were calculated and compared to outcomes of morbidity and mortality. Score use in CAP patients was compared to use in aspiration.	Mortality was higher in patients with aspiration pneumonia than with CAP. PSI showed a trend of increasing score with increasing mortality, but the study concluded that there was no prognostic value for CURB-65 or PSI in aspiration pneumonia.	1. This is a single centre small study in aspiration pneumonia in Germany. These limitations need to be considered when the study is used in UK HAP patients. 2. This study showed no benefit to the use of CURB-65 or PSI in a non-CAP pneumonia group.
32	Patients with CAP and HCAP were scored using PSI, CURB-65 and SCAP. Their scores were compared to adverse outcomes of septic shock, ICU admission and inpatient mortality.	There was a higher incidence of adverse outcomes in the low risk HCAP patients compared to the low risk CAP patients. Mortality was higher in the HCAP patients than the CAP patients. High severity scores for all three scores were associated with increased risk of mortality (statistically significant). All three scoring systems performed well in CAP but were less useful in HCAP due to missing high risk patients and classifying them as low risk.	1. This is an Italian study with less than 100 HCAP patients and is not a HAP population, there is also limited data in the paper itself. These are limitations for its use in the UK HAP population. 2. This paper suggests that CAP scores are not useful in HCAP patients due to the higher severity of the disease and the inability of these scores to detect high risk patients. 3. This study found a higher proportion of multi drug resistant pathogens in HCAP than CAP.
33	Severity index scores were compared to clinical outcomes (30-day mortality, ITU admission at day 3 and day 14) for correlation. The correlations were then tested for statistical	Septic shock, altered mental status, high serum Urea and requirement for mechanical ventilation all predisposed to ITU admission and mortality. For all tested scoring systems, mortality, 3- and 14- day ITU admission and length of hospital stay increased as severity score increased. PSI and CURB-65 were the best mortality prediction tools, with AUROCs of 0.7	1. This is a HCAP study in a Taiwanese population. These limitations should be considered before applying the results to a UK HAP population. 2. This study found that SCAP performed well at both ITU admission and 30-day mortality prediction.

	significance using AUROC, PPV, NPV and 95% CI.	and 0.66 respectively. However, for ITU admission, Modified ATS, IDSA/ATS, SMART-COP and SCAP were significantly better at prediction than the other scores. The AUROC for 30-day mortality for the scores were: Modified ATS (0.683), IDSA/ATS (0.684), SOAR (0.584), SCAP (0.709), SMART-COP (0.686), SMRT-CO (0.672), CURB-65 (0.662) and PSI (0.703).	3. CURB-65 and PSI both performed poorly in the ITU admission prediction. 4. This is a very comprehensive review with many scores, a large population and several useful outcomes reviewed.
34	Patient data was collected, scoring systems were calculated and results were compared to the primary outcome of severe pneumonia (defined by ITU stay or 30-day mortality).	PSI, the España rule and CURB-65 stratified the patients in two groups with a significant difference in 30-day mortality, but not in ITU stay. Both the R-ATS and M-ATS stratified patients into significantly different groups for 30-day mortality, ITU admission and severe pneumonia. PSI and CURB-65 were better at identifying low risk patients than the other scores.	1. This is a single centre, NHAP study in Hong Kong. These limitations should be considered before applying the results to a UK HAP population. 2. This study aims to identify low risk pneumonia for home treatment, which is not the aim of this scoping review and less applicable to a HAP pneumonia subgroup. 3. This showed that PSI and CURB-65 were not useful indicators of ICU admission in a non-CAP pneumonia population.
35	N/A	This paper discusses the use of CURB-65 and PSI in CAP. It describes poor evidence for the use of CPIS as a severity indicator in pneumonia and advises that in all HAP/VAP trials a severity of illness score should be use, suggesting APACHE II/III.	1. This paper is not directly applicable to the analysis section of this scoping review.

36	Clinical and laboratory data collated and used to formulate all scoring systems for each patient. Scores then compared to patient outcomes for prediction accuracy.	The study found that the British thoracic society scoring systems all performed similarly, with CURB, CURB-65 and CRB-65 showing AUCs of 0.605 (95% CI, 0.559-0.650), 0.593 (95% CI, 0.546-0.638), and 0.592 (95% CI, 0.546-0.638), respectively. SOAR was found to be superior however at both 30-day mortality prediction- 0.765 (95% CI, 0.724-0.803), and ICU admission prediction.	1. This is a US paper looking at NHAP patients, both of which are limitations to be considered when applying the study's findings to a UK HAP population. 2. The study found CURB to be ineffective in a non-CAP pneumonia population, however SOAR was a useful prognostic index for both 30-day mortality and ICU admission.
37	A survey of HAP patients in Japan was carried out to identify independent risk factors for mortality. These were then combined into a scoring system.	This study describes the process by which the I-ROAD scoring system was developed. It explains the validity of the scoring system based on the same population as it was derived. There is no comparison to other scoring systems.	1. This is not an independent evaluation of a severity index but does provide rationale and validity (in a Japanese HAP population) for a HAP scoring system. 2. This is a large multicentre trial; however independent validation would improve the confidence we can have in the results. 3. This is not a UK population which is a limitation for the purposes of this scoping review.
38	Retrospective chart review- PSI was calculated for each patient at time of diagnosis. This was compared to 30-day mortality to determine PSI's mortality prediction accuracy in this population.	The study found that the PSI scores in this study were similar to the PSI scores from the original validation study for the severity index. Furthermore, they found that as PSI score increased, mortality increased. There was no significant difference in length of antibiotic treatment in the inpatient and the nursing home groups. The study concluded that the PSI score was applicable to nursing home residents.	1. This is a small American study in a NHAP population which was carried out over twenty years ago. These limitations need consideration before applying the results to a UK HAP population. 2. This study showed the PSI as being a useful predictive score in NHAP patients.

39	Data from HAP database reviewed (only VAP data collected), from a one-year period. 60 Variables were reviewed for independent mortality prediction, 5 easily clinically available variables were chosen to form a scoring system. The new score was calculated at time of diagnosis, with an APACHE II score and they were compared statistically for mortality prediction at 14 days.	Both scores had a low positive predictive value, and a high negative predictive value at all score points. The area under the receiver operator curve was 0.808 (95% CI: 0.721-0.895) for the new scoring system (IBMP-10) and 0.743; 95% CI, 0.628–0.857 for the APACHE II. These scores were significantly different. The new scoring system used the following measures: Immunosuppression, blood pressure, multi-lobar pneumonia, platelet count and admission length prior to VAP.	1. This is a small retrospective American study on VAP patients, with the data extracted from a database. These limitations are important when considering the implications for a UK HAP population. 2. This study showed a new, short scoring system which was effective at predicting mortality in a non-CAP pneumonia group. 3. This study also showed that APACHE II was effective at predicting mortality in these patients. 4. As the new score was a novel scoring system not described elsewhere in the literature, it will not be included in the analysis section of this scoping review. The APACHE II data will be included.
40	As for study number 37- this study describes the same process.	-	Study number 37 is identical.
41	Patients admitted with MRSA pneumonia and treated with vancomycin or linezolid were scored with APACHE II, CURB-65 and CRB65 with outcomes of	Patients dying within 30 days had a statistically higher APACHE II score, CURB-65 and CRB65 score than those who survived. APACHE II was more sensitive than the other scores at all risk levels. ROC Curves for the scores in the HCAP subgroup were: APACHE II 0.784, CURB-65 0.604 and CRB65	1. This is a small, single centre, MRSA pneumonia subgroup study from an American hospital. These are limitations which need to be considered when applying the findings of the study to the UK HAP population.

	30-day mortality compared to assess predictive accuracy of these scores in this patient group.	0.620. In addition, vasopressor use and decreasing PaO2 were found to be independent predictors of 30-day mortality.	2. This study showed APACHE II as being superior to CURB-65 and CRB-65 in prediction of 30-day mortality in HCAP patients with MRSA pneumonia.
42	N/A	N/A	N/A
43	Patient data was collected (comorbidities, demographics, recent blood tests, etc), and independent mortality risk factors were identified by logistic regression. These were turned into a severity scoring index. The score was validated on the same cohort from which it was derived.	Tachycardia, tachypnoea, dementia and altered mental state were all independent predictors of mortality. These formed the scoring system used to predict mortality. As the score increased, the mortality increased, the AUROC for the scoring system was 0.74.	1. This study looks at NHAP patients and does not use blood tests, radiographic features or oxygen saturations to severity assess patients. These all make its application to HAP patients less appropriate. The HAP population will uniformly have access to blood tests and radiographs. This scoring system may have applications in certain hospital situations, but it is not broadly appropriate to use in the inpatient management of HAP in the UK. 2. This study is twenty years old which is another limitation. 3. As the new score was a novel scoring system not described elsewhere in the literature, it will not be included in the analysis section of this scoping review.
44	Patients admitted to the ICU who had nosocomial pneumonia had their charts	There was a significant difference in mortality scores between survivors and non-survivors at diagnosis. However, there was not a significant difference at ICU admission time, or at 24	1. This study was a small single centre retrospective study in a Spanish ICU which excluded patients with drug resistant pneumonia. These are all limitations

	retrospectively reviewed and a Mortality Probability Model Score (MPM II) calculated at admission to ICU, diagnosis of nosocomial pneumonia and at 24 hours. These scores were compared to mortality.	hours post admission. The study also noted that Pseudomonas was an independent mortality predictor not included on the MPM II scoring system.	which need to be considered before it can be applied to a UK HAP population. 2. This study does review a scoring system for mortality prediction in nosocomial pneumonia and shows promising results, however the score is not compared to other scores, it is not well evaluated statistically in this study as a predictor and MPM II is a complicated scoring system, not specific to pneumonia and more focused on the ICU environment. 3. This study is twenty years old which is another limitation.
45	This study did not look into pneumonia specifically and did not review the scoring systems for clinical use, therefore it was not appropriate for further analysis in this scoping review.	This study is not appropriate for further analysis regarding the purposes of this scoping review.	This study is not appropriate for further analysis regarding the purposes of this scoping review.
46	All patients had data collected at diagnosis of pneumonia or admission to ICU (if diagnosed outside of ICU), including SAPS score, presence of septic shock,	There was no subgroup analysis of nosocomial pneumonia and SAPS score, as such this study is not appropriate for further analysis regarding the purposes of this scoping review.	This study is not appropriate for further analysis regarding the purposes of this scoping review.

	need for mechanical ventilation and other demographic information. These were compared using multivariable logistic regression for relationship to mortality.		
47	Not available as full text	Not available as full text	Not available as full text
48	All patients were given a severity score determined by their presenting illness, it's severity and the patient's likelihood of mortality due to this disease. This severity score was then compared to the patients development of nosocomial pneumonia.	A high severity score was significantly associated with development of nosocomial pneumonia. Other factors found to be significantly associated with development of nosocomial pneumonia included NG feeding, IV hyperalimentation and ventilator use. APAHE II score was not associated with development of nosocomial pneumonia. This study did not look at a scoring system with relation to outcomes in nosocomial pneumonia and as such is not appropriate for further analysis in this scoping review.	1. This study showed that scoring systems can be used to predict nosocomial pneumonia in hospital patients. 2. This was a single centre small study carried out a long time ago which are important factors to consider. 3. This study is not appropriate for further analysis in this scoping review.
49	Adults admitted to the critical care department with HAP or VAP had 7 severity scores complete at diagnosis, this was compared to mortality, ICU stay and mechanical ventilation to	All scoring systems had an AUROC of more than 0.7 for mortality prediction with SMART-COP having the best result, it was also the most specific score at 93%. The AUROC scores were: Smart-COP (0.820), SMRT-CO (0.807), PSI (0.806), IDSA/ATS (0.790), SOAR (0.734), CURB-65 (0.747), Modified ATS (0.772). SMART-COP was also the score most closely	1. This is a single centre ICU only study carried out in Egypt including both HAP and VAP patients. These are limitations for application generally to a UK HAP population. 2. This study showed superiority of SMART-COP to the other tested scoring systems, although all scores

	assess the prognostic value of each score. Predictive value assessed using ROC curve analysis.	correlated with days of mechanical ventilation and ICU stay length. All scores had a statistically significant relationship to mechanical ventilation length and ICU stay apart from PSI.	performed well at mortality prediction and apart from PSI, scored well for the other outcomes. 3. The demographics are not available, as such the number of VAP patients is uncertain.
50	Data was collected prospectively in 379 patients presenting with HAP with a background brain injury to three ICUs in France. The data was analysed to find variables associated with drug resistant pathogens. A scoring system was developed from these variables and was compared to ATS guidelines for predicting drug resistant pathogens in a second patient group.	Variables found to be associated with drug resistant pathogens were: >48 hours antibiotic therapy during previous hospitalisation and prior hospitalisation of ten days or greater. The new scoring system outperformed the ATS guidelines at predicting drug resistant pathogens (AUROC 0.822 for novel score, 0.735 for ATS guidelines).	1. Only the abstract was available for this study. 2. This study looks only at ICU patients with brain injuries in France and uses only a novel scoring system- not fully detailed in the abstract- and guidelines. These are significant limitations for application to a UK HAP population. 3. This study demonstrated that scoring systems can outperform conventional guidelines when considering antimicrobial resistance predictions. 4. As the new score was a novel scoring system not described elsewhere in the literature, it will not be included in the analysis section of this scoping review.
51	Retrospective observation of patient notes to compare CURB-65 score with mortality.	As CURB-65 score increased, mortality increase, although area under the ROC curve was only 0.376. There were no patients with a CURB-65 score of 5. This study showed poor discrimination between severe and non-severe HAP using CURB-65.	1. Conference abstract available only. 2. Small, retrospective, Indonesian study which limits the applicability of result to a UK population.

			3. This abstract appears to show very poor prognostic accuracy from CURB-65 in HAP, although it is difficult to assess with only the abstract available. 4. Full text not available
52	Data from ICU patients who developed who developed pneumonia was used to crease a scoring system to predict pneumonia in this patient group.	The review showed that thorax drainage, antacid use, no infection on admission, male gender and urgent surgery were amongst risk factors for nosocomial pneumonia. No scoring systems were used to assess severity. This study is not suitable for further analysis in this study.	1. This study is not applicable to this scoping review and will not be analysed further.

2.15 Table 2: Stream 2, Step 3: Study origin analysis

It was noteworthy that none of the papers screened to be included in the final data analysis were from the UK. Indeed, most of the studies were undertaken in Asian populations, with Japan studies significantly outnumbering any other nation (Table 2). Six studies were from Europe, half of these from Spain, and three were from the USA.

Origin of study:	**Number of studies:**
Japan	9
Korea	4
USA	3
Spain	3
China	2
Meta-analysis/ Systematic review	2
Mexico	1
Cyprus	1
Italy	2
Germany	1
Taiwan	1
Egypt	1

2.16 Table 3: Stream 2, Step 3: Pneumonia subgroup analysis

The most studied non-CAP pneumonia subgroup in the analysed studies was NHAP, followed by HCAP (Table 3). There were only 7 studies which looked at HAP, there were significant limitations to all these studies when applied to UK non-ventilator associated HAP as can be seen in Table 1.

Pneumonia Subgroup:	**Number of studies included:**
Nursing Home Acquired Pneumonia	13
Healthcare Associated Pneumonia	10
Hospital/Ventilator associated pneumonia (HAP/VAP)	7

Psychiatric Hospital acquired Pneumonia	1
Aspiration Pneumonia	1

2.17 Table 4: Stream 2, Step 3: Scoring system prevalence.

Significantly, the two scores that were most highly cited in the analysed studies were PSI and CURB-65. Of the other scores, only A-DROP, IROAD and SOAR were used in 5 or more studies. Overall, 21 different scoring indices were used in total (Table 4).

Scoring System:	**Number of studies included:**
PSI	23
CURB-65	21
A-DROP	8
SOAR	6
IROAD	5
SMART COP	3
SOFA	3
APACHE II	3
Modified ATS Score	3
NHAP Score	3
CRB 65	3
CURB	2
SMART CO	2
ATS/IDSA	2
qSOFA	2
CPIS	2
SAPS	2
SCAP	2
Espana Score	1
R-ATS	1
MPM II	1

All the scoring systems were analysed at least once as part of the analysis in the review for mortality prediction (where more than one mortality prediction was used in a single study, the researcher utilised the closest to 30-day mortality for consistency). Only 10 scores were assessed for ICU admission prediction and no score was found to have a statistically significant correlation to drug resistant pathogen isolation (Tables 5 i, ii, iii).

Significantly, of the scoring systems used five or more times for mortality, PSI had the best results, with CURB-65 scoring poorly despite being included in many studies. Scores assessing general physiological disturbance (SOFA, APACHE II, qSOFA) appeared to predict mortality better than the pneumonia specific scores (PSI, CURB-65, A-DROP, IROAD, SOAR), but the number of studies they were used in were so small as to limit any conclusions which can be drawn.

The small number of studies which focused on ITU admission severely limited any conclusions which could be drawn from the analysis. However, neither PSI nor CURB-65 performed well at ICU admission prediction across the studies they were included in. The modified ATS score appears to be a useful ICU admission predictor but this was only assessed in two studies.

Table 5 (i)

Scoring System:	**Effective Mortality prediction:**	**Ineffective Mortality prediction.**	**% 'effective':**
PSI	20	7	77%
CURB-65	8	13	40%
A-DROP	5	3	63%
IROAD	2	2	50%
SOAR	3	3	50%
SMART COP	1	2	33%
SOFA	3	0	100%
APACHE II	3	0	100%
Modified ATS Score	2	1	67%
qSOFA	2	0	100%
CRB 65	0	3	0%
CURB	0	2	0%
SMART CO	1	1	50%
ATS/IDSA	1	1	50%

NHAP Score	0	2	0%
CPIS	0	1	0%
SAPS	1	1	50%
SCAP	0	2	0%
Espana Score	1	0	100%
R-ATS	1	0	100%
MPM II	1	0	100%

Table 5 (ii)

Scoring System:	**'Effective' ICU admission prediction:**	**'Ineffective' ICU admission prediction.**	**% 'Effective':**
PSI	2	3	40%
CURB-65	2	3	40%
SOAR	1	2	33%
Modified ATS	2	0	100%
SMART COP	1	0	100%
SMART CO	1	0	100%
ATS-IDSA	1	0	100%
R-ATS	1	0	100%
NHAP Score	0	1	0%
Espana Score	0	1	0%
SCAP	0	1	0%

Table 5 (iii)

Scoring System:	**'Effective' DRP prediction:**	**'Ineffective' DRP prediction.**	**% 'Effective':**
PSI	0	1	0%
APACHE II	0	1	0%
SAPS	0	1	0%
SOFA	0	1	0%

2.19 Streams 1 and 2, Synthesis and reporting of outcomes:

The first aim of this study was to identify the current HAP scoring index guidelines and the underlying evidence for this. The guidelines section demonstrates that in the UK and abroad there are currently no guidelines which suggest the use of a severity scoring, apart from Japan- and this is likely explained by the differing healthcare systems and subsequently different pneumonia sub-populations.

The underlying evidence for the use of HAP severity scoring was severely limited, with only 7 unique studies identified looking at HAP at all. Of these seven HAP studies, four studies either included VAP or were entirely ICU based, limiting their application to ward based HAP. One of the remaining three was the derivation of a Japanese scoring system and its validation within the same cohort, one study was a small Chinese study looking only at the PSI score, and the final study was only a conference abstract and the researcher was unable to access or locate the full text of the study for analysis, in any case it was a very small study.

As the number of HAP studies was so low, the scope of the review was widened, and all studies from the initial search criteria investigating a non-community acquired pneumonia subgroup were reviewed. Although this does increase the amount of data available in non-CAP pneumonia severity scoring, it is a further introduction of population variance. Nursing home and healthcare associated pneumonia then became the most studied pneumonia subgroups. Subgroups which are not considered separately in the UK at all.

By far the country from which the most studies originated was Japan, which is a significant limitation on this study when applied to the UK population as explained above- the pneumonia subgroups in Japan are different to the UK due to the healthcare system, before considering the differing genetic makeup and disease burden across the two nationalities. Indeed, none of the studies were conducted in UK hospitals.

Only five scoring indices were reviewed five or more times for mortality prediction, with PSI and CURB-65 being reviewed greatly more so than the other studies. PSI was found to be a good predictor of mortality in 77% of the studies and it is the only scoring system reviewed more than three times which was considered ‘positive’ by more than 70% of the studies in which it was reviewed. Using 70% as a cut off, most of the scores in the review performed poorly. CURB-65, IROAD and SOAR were all studied more than five times and found to be ‘positive’ in no more than half of the studies in which they were studied. It is notable that three physiological scoring systems (SOFA, qSOFA and APACHE II) all scored 100%. While all three of these scores were only used a small

number of times, physiological scores appear to perform better than the classic pneumonia scoring systems.

It was noted by many of the studies that scores such as APACHE II and PSI with many inputs would be difficult to apply in a ward based clinical setting and that clinicians preferred shorter scoring systems such as CURB-65 or A-DROP.

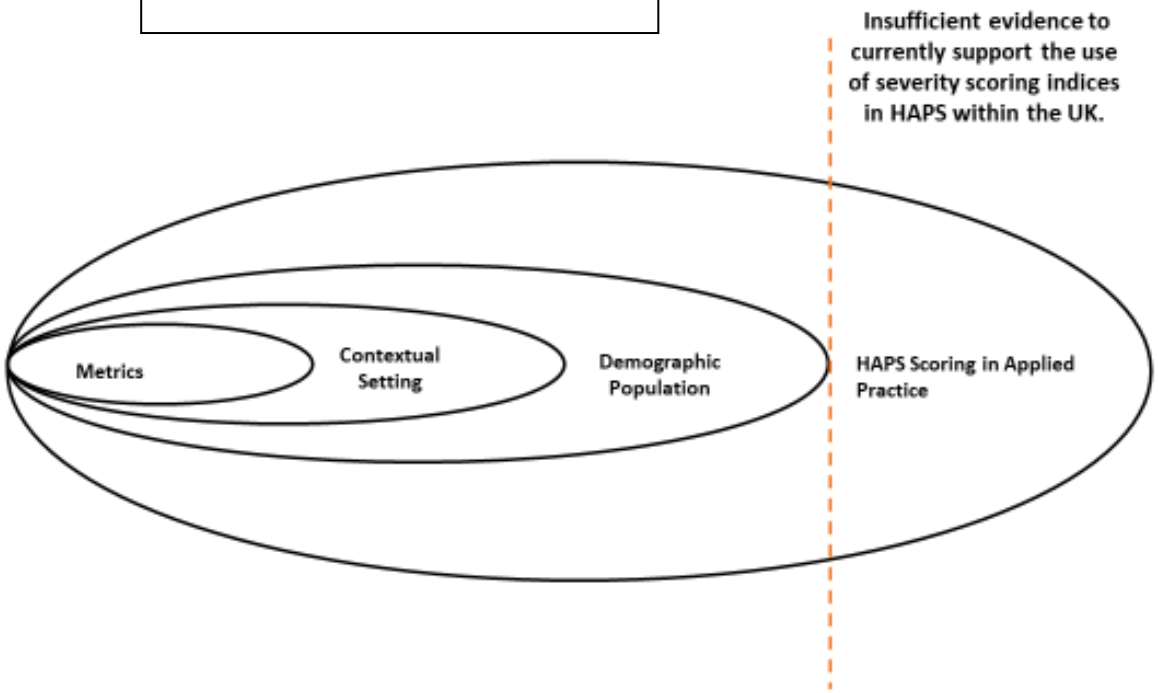
Ten scores were used to assess ICU admission prediction and the only score which was used more than once and had a greater than 50% 'positive' score was the modified ATS score. The two studies that found this were in Taiwan and China, in HCAP and NHAP populations. No scoring system was found to have good prognostication for ICU admission in HAP in more than a single study.

No pre-existing scoring system was shown to have useful prognostication for drug resistant pathogens, there was a paucity of evidence for this outcome from the data.

Overall, the literature review highlights the importance of metrics, contextual setting, demographic population and applied practice (Figure 4). As can be seen in the diagram, for a scoring index to be used in applied practice, the evidence needs to show that it is of good discriminative value, that it is applicable to the population in which it is to be used and that it is appropriate to use in that setting. In the case of UK HAP therefore, a scoring system would have to have evidence that it predicts useful outcomes, it would need to be validated in a UK HAP population and would need to be usable in a clinical setting (requirement for 30 variable input for example, would be inappropriate).

Therefore, the evidence does not exist to suggest any one score would accurately prognosticate the three main outcomes of this scoping review. The evidence which we do have has significant limitations when applied to the UK HAP demographic (e.g. nationality, pneumonia subtype). Therefore, there is not enough evidence to currently support the use of severity scoring indices in the UK. However, this is due to a lack of relevant evidence and not a presence of high-quality literature refuting the benefits of severity indices in these patients. More research in this area is subsequently required and there is some suggestion that general physiological indices may perform better than pneumonia specific scoring indices from the research already performed.

Figure 4- Synthesis of analysis



2.20 Discussion:

This study intended to address the limited use of severity scoring indices in HAP compared to CAP in the UK given the high burden of the disease and the benefits of scoring system use in CAP. However, the limited use is in accordance with national and international guidelines and the reason for this is a sparsity of evidence support HAP scoring- particularly in the UK. There is not currently the evidence base to change these recommendations or current practice. Whereas the evidence for severity scoring in CAP is strong and the guidelines already reflect this, the research has not been performed for HAP. The outcome of this study is to encourage research going forward to address the question which underlies this scoping review- Is there benefit to be gained from Severity Scoring Index use in HAP in the UK? An approach to answering this question follows:

A severity scoring index which was applicable to HAP for mortality prediction, ICU admission and drug resistant pathogen identification would be beneficial to physicians caring for this patient group. A large UK study applying currently existing severity scores to HAP patients to assess these outcomes would be beneficial, as using a pre-existing score would be relatively simple to apply to practice if predictive accuracy were good enough. This kind of study has not been done before now. In such a study it would be beneficial to assess PSI (as there is evidence it has good prognostic accuracy in non-cap pneumonia), physiological scores (such as APACHE II or SOFA) as there is some limited evidence that they may be more predictive than classic pneumonia scores, and finally include shorter scoring systems (e.g. A-DROP, qSOFA) as they are easier to use in clinical ward based practice.

If this prospective study did not clearly identify a scoring system with acceptable accuracy as agreed by a suitable stakeholder group (e.g. the British Thoracic Society), another approach could be that of the Japanese Respiratory Society with IROAD. That is to create a large HAP database/survey with clinical information and use logistic regression to identify independent predictors for mortality, and subsequently build a score using this information.

2.21 Conclusions:

In conclusion neither current UK nor other western guidelines recommend a severity scoring index in HAP. There is not currently enough evidence to suggest a pre-existing scoring system would usefully predict mortality, ICU admission and drug resistant pathogens in a UK population. There is currently not enough evidence to support severity scoring in UK HAP patients. Most of the evidence on non-CAP pneumonia and severity scoring has important limitations on its application to the UK HAP

population due to either the country of origin, the pneumonia subgroup or the number of patients in the studies. Further research is needed, but physiological scoring indices may predict mortality better than pneumonia specific scoring indices.

Chapter Three

Exploring the utility of prognostic Severity Scoring Indices in Hospital Acquired Pneumonia: a case study

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3.1 Abstract:

Background: Hospital acquired pneumonia (HAP) is a common nosocomial infection associated with a significant mortality, however HAP is poorly researched when compared to community acquired pneumonia (CAP) (Nair & Niederman, 2013). In CAP, severity scoring systems are internationally recommended to aid treatment decisions such as location of care and critical care input. However a preliminary scoping review has found this is not the case in HAP guidelines and there is a paucity of research into the use of scoring indices in HAP in the UK. (NICE, 2014)

Objectives: We aimed to evaluate whether scoring systems could be used to prognosticate for mortality, ITU admission or drug resistant pathogens in a UK HAP population. We hypothesized that scoring systems can be used in HAP patients to predict these variables at time of diagnosis.

Method: We carried out an observational study over two wards in a regional district general hospital in Wales looking at prospective and retrospective data in patients who developed HAP. A selection of scoring systems identified during a preliminary scoping review- PSI, CURB-65, SOAR, I-ROAD, Q-SOFA- were applied to each patient at time of diagnosis. These scores were reviewed for accuracy at prognosticating outcomes.

Results: 37 Patients were identified for this study, the mortality rate at 30 days was 19%. The results showed two scores-PSI and I-ROAD to have good mortality prediction ability in this patient cohort with area under the receiver operator curve (AUC) scores of 0.796 and 0.788 at 30 days, respectively. The other three studied scoring systems performed poorly. The low number of ITU admission and drug resistant pathogens in the population studied made useful analysis for these variables impossible.

Conclusions: This study encourages the notion that a scoring system may be beneficial in the UK HAP population and suggests PSI or I-ROAD may be useful for this. The study does not answer questions about drug resistant pathogen and ITU admission prediction, nor the wider validation of these scoring indices- larger studies are warranted to investigate this.

3.2 Introduction:

Hospital acquired pneumonia (HAP) is a common and serious nosocomial infection. HAP is defined as pneumonia presenting more than 48 hours following admission to hospital and not being incubated at time of admission (NICE, 2019). Compared to pneumonia acquired in the community (CAP), the population who present with HAP are typically older, have more comorbidities and are more likely to culture an 'atypical pathogen'. Subsequently antibiotic guidance favours a broader spectrum antibiotic empirically, and mortality in HAP is greater than that in CAP (NICE, 2016; Russel, et al., 2015). One of the most important innovations in CAP management in recent decades has been the international introduction and utilisation of severity scoring indices. Scores such as CURB-65, PSI and SOAR are used at diagnosis to aid treatment decisions (Fine, et al., 1997; Lim, et al., 2003; Myint, et al., 2006). For example, in the UK, NICE and the British Thoracic Society both recommend the use of CURB-65 at diagnosis to guide decisions in CAP (British thoracic society, 2009; NICE, 2014). A low CURB-65 score indicates the patient is likely to be able to be treated at home with narrow spectrum oral antibiotics. A slightly higher score at diagnosis indicates a hospital admission and broader spectrum intravenous antibiotics. With the highest scoring patients warranting early intensive care review to ensure optimal management, as well as indicating a higher mortality in this population.

It can be seen therefore that severity scoring indices in pneumonia are used to guide location of treatment, initial therapy based on likely pathogen, escalation of care and prognostication. However, no such systems or scores are currently advised for use in the UK for HAP. With the NICE committee for HAP management unaware of any validated scoring system (NICE, 2019). A preceding scoping review (Chapter 2) found that the international evidence base for HAP severity scoring systems was minimal, and the UK evidence base essentially non-existent. The scoping review also highlighted that in some non-CAP pneumonia studies (e.g. nursing home/healthcare/psychiatric hospital acquired pneumonia) scores which are used to indicate general physiological disturbance (e.g. APACHE II score) may perform better in HAP than scores classically designed for pneumonia.

Given the international adoption of CAP severity scoring systems, the lack of research into similar HAP scoring systems and the high mortality burden of HAP, the researcher believes HAP severity indexes required further research. The aim of this case study, therefore, is to indicate whether a pre-existing scoring system is likely to be accurate at predicting the treatments required and outcomes in

HAP, as predicted in CAP by CAP scoring indices. Namely whether they can predict mortality, ITU admission and drug resistant pathogen culture.

This case study aimed to inform a larger study/project aiming to either confirm prognostic accuracy in a larger cohort of an existing scoring index or design a new scoring index if none of the indices reviewed here shows any prognostic utility. The scoring indices chosen for this study were identified following the completion of a scoping review (Chapter Two) to represent CAP scoring systems, physiological scoring systems, HAP scoring systems and where possible easy to use scores- as to increase clinical ease of use. The outcomes of the scoping review were that there is not currently enough relevant evidence to evaluate HAP severity index use in the UK, that some scores may be able to prognosticate for mortality in non-CAP pneumonia (e.g. PSI) and that there is some limited evidence that scores assessing physiological disturbance may perform better in HAP than scores designed to assess pneumonia severity.

3.3 Method:

Approach:

The approach adopted uses an overarching case study design (Yin, 2018; Gerring, 2017; Baxter & Jack, 2008). In essence case study work is centred on an '*intensive study of a single case or small number of cases which draws on observational data and promises to shed light on a larger population'* (Gerring, 2017, p.28). This approach allows this study to apply the findings of the preceding scoping review (chapter 2) to a small population within two wards in a single hospital, to shed light on the wider implications within the UK HAP population. Although the results will not prove or disprove the utility of scoring indices within the entire population, the aim is to indicate whether larger scale research is appropriate and direct it, without using large amounts of resource. The context for this research is a resource limited health service, the use of case study in this way allows intense focus on a limited size population to ensure that larger research is not wasted and is directed, with lessons learnt from the initial case.

The initial scoping review has allowed the focus of the case study to be directed in the following ways: The independent variables have been adapted from those for which CAP severity indices are used. The scores used have been selected based on the outcomes from the scoping review (scores which have either been widely studied, scores found to be efficacious in non-CAP pneumonia, physiological severity scores, and scores which are short for ease of clinical use). The use of a respiratory and a care of the elderly ward allowed us to focus on areas of the hospital where HAP was likely to be seen.

Case study work also allows a diverse range of approaches across quantitative, qualitative and mixed methods designs, including the use of single and multiple cases. This gave theoretical scope to split the wards into different cases for sub-group analysis and allowed the option for qualitative data to be incorporated into the study if highlighted during the study. Neither of these options were used, but the flexibility was intentional in the design to ensure that important findings could be displayed in the study when and if found.

Study Population:

Data collection for this study was conducted between November 2019 and May 2020 using data collected from patients diagnosed with Hospital Acquired Pneumonia on two wards (one Respiratory and one Care of the Elderly) in a district general hospital serving a region of North Wales. Patients who were diagnosed with HAP between October and March (Inclusive) on one of these two wards were included for retrospective or prospective notes review for inclusion in this study. Notes were identified for review if the diagnosis of HAP had been recorded in the ward discharge book, on the patient's discharge letter or on the patient's death notification. Following initial identification, the diagnosis of HAP was checked against the definition for HAP below. Permission to carry out this observational data collection was sought and granted from both the hospital audit department and Bangor University research ethics team.

Data Collection:

Data was collected both retrospectively and prospectively to ensure that as large a percentage of HAP patients were included in the study as possible. In both cases data was taken exclusively from pre-recorded sources and no patient interaction or intervention was carried out. Although some data was collected following patient discharge (retrospective) and some during their admission and their illness (prospective) there was no material difference in the way the data was collected or influence of collection on patient care. Collected data was taken exclusively from the following pre-recorded sources: *Ward discharge lists, patient notes, discharge letters, blood test results, imaging and imaging reports, death notifications.* The data collected included patient demographics, and factors pertinent to the severity scoring systems in the study. All collected data was entered onto a standardised data-collection form (appendix 4), which was included in applications for both university and hospital audit approval.

Where clinical information was required for scoring systems, information which was most contemporaneous to the diagnosis of HAP was used. For example- the most recent documented observations either before diagnosis or at time of diagnosis, the blood tests closest to diagnosis

before initiation of treatment, imaging requested at time of diagnosis or just prior. Demographic and background data were mostly collected from the admission booklet, but where data was lacking here the notes were more forensically examined. The aim was to replicate the information which would be available to the clinician at time of diagnosis to best demonstrate the effectiveness of severity scoring at diagnosis. Where information was lacking, for example if no lactate blood test had been taken, that component was considered normal for the purpose of severity scoring. The rationale for this being the assumption that if the test was not considered clinically necessary it was more likely to be normal than to be abnormal and the information would not have contributed to the severity score if the clinical team had been using one at the time. This is of course a limitation on this study, but one which cannot be avoided in a study in which alterations to patient care, investigation or treatment is not undertaken. I.e., to remove this limitation would necessitate further investigations to be carried out on patients not felt clinically necessary by the clinical team and this is outside the scope of this study.

Definition of HAP and Severity scores used:

Hospital acquired pneumonia was defined in the data collection process as a pneumonia diagnosed at least 48 hours into a hospital admission, not being incubated at admission (NICE, 2019).

The researcher included all patients who were diagnosed and treated for a HAP at least 48 hours into their hospital admission (or at any time if readmitted from home less than a week following discharge). Some of these patients did not have a chest x-ray performed at time of diagnosis and some of the patients who did had their x-ray reported inconclusively (e.g. “Pneumonia can not be excluded”) and indeed some x-rays were reported as clear by the radiologist- sometimes in direct conflict with the interpretation of the doctor on the ward according to their documentation in the notes. To address this concern, radiographic findings were not required for inclusion as HAP in this study as all patients were diagnosed and treated as HAP by a hospital doctor. However, subgroup analysis was carried out depending on x-ray changes to account for this possible confounding variable. Again, this is a limitation on the study. Stricter criteria for diagnosis of HAP may be considered in a larger study, but it was felt that if the scoring systems were to be used in practice, they would be applied to all patients treated as HAP- although clearly best clinical practice would include an x-ray in all suspected HAPs at diagnosis.

The scoring systems used during this study were: PSI, CURB-65, I-ROAD, SOAR and qSOFA. These were chosen following analysis from a preliminary scoping review into severity scoring indices in HAP. The scoping review found that in non-CAP pneumonia, by far the most prevalent scoring systems reviewed were PSI and CURB-65. The only HAP specific scoring system which was identified

during the scoping review was the I-ROAD score from Japan. The scoping review suggested that physiological scoring systems may perform better in HAP than CAP scoring systems, qSOFA was therefore included as a physiological scoring system. The reason qSOFA was included over other physiological scoring systems was its ease of use- as explained below- which lead to qSOFA being chosen over SOFA and APACHE II score. Finally, SOAR was included as it was another commonly used, quick scoring system which was designed specifically for elderly patients- age being a significant risk factor for HAP. All the scoring systems aside from PSI are relatively short and quick to apply in clinical practice. Difficulty applying complete scoring indices in day to day medicine was a recurrent theme from the scoping review, as such this study aimed to find a score both easy to use and accurate. PSI however was so ubiquitous in the scoping review literature, and promising, it was felt it would be inappropriate to exclude it.

Pneumonia Severity Index: PSI was developed in the 1990's in America as a risk stratification tool to identify patients with community acquired pneumonia who could be safely treated in the community. It uses 20 variables including patient demographics, comorbidities and physiological variables. PSI is currently recommended for severity assessment by the American thoracic society and infectious diseases society of America. It showed promising results for mortality prediction in non-CAP pneumonia in the scoping review preceding this study, however it was regularly criticised in the literature as being long and difficult to use in clinical practice. (Fine, et al., 1997; Metlay et al., 2019)

CURB-65: CURB-65 is a scoring system derived from patient confusion, blood urea, respiratory rate, blood pressure and age over 65. The original study was designed with data from the UK, Netherlands and New Zealand and stratifies patients into three risk groups which aims to identify patients with CAP suitable for community treatment, hospital treatment and patients who require early critical care review or admission. CURB-65 Is currently recommended for CAP severity assessment by the British Thoracic society. (Lim, et al., 2003; British Thoracic Society, 2009)

I-ROAD: A scoring system developed by the Japanese respiratory society to evaluate HAP severity. It was designed following analysis of a large Japanese HAP database and includes patient demographic information and clinical assessment information. (Japanese Respiratory Society, 2009)

SOAR: Designed in the UK to better assess CAP severity in the elderly population, where confusion and high urea- features in CURB-65 scoring- are both common. Uses Systolic BP, Oxygenation, Age and Respiratory rate. (Myint, Et al., 2006)

SOFA and qSOFA: The SOFA score was designed to quantify the severity of multiple organ failure a patient had sustained secondary to infection, qSOFA was developed as a rapid bedside test to indicate poor outcomes in patients with sepsis, it has been shown to be a better indicator of this than SOFA score outside of the intensive care setting. Neither of these scoring systems are pneumonia specific, both are based on non-specific physiological disturbance. (Vincent, 1996; Seymour, 2016)

Data Analysis:

Demographic characteristics and descriptive statistics were tabulated as frequencies (%) or as the mean (±standard deviation) and median (range). Frequencies of survival for each severity level of each scoring index was presented by percentage for both 7- and 30-day mortality. These mortality measures were used as they were the most commonly found in the literature from the scoping review, therefore aiding any future comparison of data from this study with other studies caried out or to be carried out. This also allowed the reviewers to collect data for all appropriate patient, whereas survival to discharge would have significantly reduced the number of patients for whom full data sets could have been collected. For each scoring system sensitivities, specificities, positive predictive values and negative predictive values were calculated for at least one cut off score for both 7- and 30-day mortality. The Area Under the Receiver Operator Curve (AUC) was created for overall mortality prediction, with associated standard error, asymptotic significance and Asymptotic 95% confidence interval. P values <0.05 were considered statistically significant. AUC was used for both 7- and 30-day mortality in each scoring index. SPSS Software was used for AUC analysis, other analysis and calculations were performed using Microsoft Excel software.

Subgroup analysis of the 24 patients who had confirmed changes on x-ray was performed to compare with the overall cohort for the purposes of predictive accuracy.

3.4 Ethics

The study had ethical approval from Bangor University (application number 16689) and approval from the local NHS health board audit and effectiveness team (Project registration: 19/369). Data were collected from case notes and laboratory or radiological results using the hospital's adopted clinical computer systems. Data was collected by members of the clinical team in the hospital (Dr M Peirson and Dr P Kempster All data was stored securely and anonymously as per the ethical and research and development clearance.

3.5 Results:

Population Characteristics:

Thirty-seven patient episodes of HAP were identified during this study, 23 episodes with female patients and 14 with male. The mean age at diagnosis was 81±12 years old, with mean frailty score of 6±1.5, time from admission to diagnosis of 26±27 days and a background of 4 comorbidities. 27 Episodes were recorded on the respiratory ward, 10 on the care of the elderly ward. The mean age on the respiratory ward was 79, with a mean frailty score of 6. On the care of the elderly ward, the mean age was 87 and the mean frailty score also 6. The time from admission to diagnosis was highly variable, with a median time of 16 days, an interquartile range of 20 days and a total range of 4-120 days. 17 Patient episodes were associated with current or ex-smokers (7 and 10 respectively), 15 episodes had no smoking history and no smoking documentation could be found in 5 sets of patient notes. The most prevalent comorbidities in this population were COPD (15 episodes) and hypertension (12 episodes).

Presentation at diagnosis and mortality:

At time of diagnosis the mean early warning score (EWS) was 5±3, with a mean set of observations of: respiratory rate 23, heart rate 93, blood pressure 125/71 and a temperature of 37.25. EWS is a basic measure of physiological disturbance which is used as an indicator of clinical deterioration & need for patient assessment commonly used in the NHS (Baker, et al., 1974). At diagnosis, the mean results (and standard deviations) for White Cell Count, CRP and Urea were 14.1(5.1), 112.8(86) and 8.4(5.4) respectively. No patients had an accurate urine output measured. Survival at 7 days following diagnosis was 92% (34 patients), which dropped to 81% (30 patients) by 30 days following diagnosis. Only one of the 10 patients on the care of the elderly ward died, all other deaths were on the respiratory ward. No patients were transferred to intensive care for their HAP treatment. Only four patients cultured any micro-organisms, two of these were viruses, one patient cultured MRSA and Serratia and the last result was a Klebsiella species.

Chest x-rays were done in 34 patients, there were changes clearly compatible with pneumonia in 24 patients, the results were equivocal in 7 patients and the x-rays were reported as normal in 3 patients. The timing of the x-rays was variable, with some done at time of diagnosis, some done weeks later and as above- some not completed at all.

Scoring systems

Curb-65: When stratified by CURB-65 score, most patients scored in the less severe scoring bands- with no patients meeting the criteria for the highest score of five, and only three patients scoring four. Deaths were spread across the severity groups with 20%, 25%, 30% and 35% mortality at thirty days in groups 1, 2, 3 and 4 respectively. Using a score of three or

above as a mortality predictor gave poor positive predictive values (ppv)- 0.23 and 0.44 and sensitivities- 0.6 and 0.44 at 7 and 30 days respectively. In addition, CURB-65 showed poor predictive utility, with an area under the receiver operator curve (AUC) of 0.622 for 7 day mortality and 0.595 for 30 day mortality.

PSI: The median severity score by PSI was 4 or 'Moderately Severe'. Mortality increased as PSI score increased at both 7- and 30-days post diagnosis. PSI showed good predictive utility for mortality, with AUC scores of 0.878 and 0.796 for 7 and 30-day mortality. The asymptotic significance of these results was 0.007 and 0.008 respectively. However, using a score of 4 or greater as a cut off, the positive predictive value of PSI was only 0.16 for 7-day mortality, and the sensitivity just over 0.3 for both mortality prediction times. No patients with a PSI score below 4 died. PSI ≥4 as a predictor for mortality showed good negative predictive value and specificity.

I-ROAD: When scored by I-ROAD, 6 patients were classified as having mild pneumonia- none of these patients died within 30 days. 17 patients were classified as having moderate pneumonia, none of these died within a week, but 2 died within 30 days. 14 Patients were classified as having severe pneumonia, 5 of these had died within a week and half had passed away within 30 days. I-ROAD showed good predictive value for mortality with 7- and 30- day AUC scores of 0.859 and 0.788 respectively. The Asymptotic significance of these AUC scores was 0.011 and 0.010 respectively. Using severe pneumonia as a cut off score, I-ROAD had scores of more than 0.7 for sensitivity, specificity and negative predictive value at 30 days, with a positive predictive value of 0.5.

SOAR: Patients were concentrated into the two medium severity scores by SOAR with only 3 patients scoring 0, and 3 patients scoring 3 for severity. As severity score increased, mortality rate increased using this scoring system. However, SOAR's AUC scores for 7 and 30-day mortality were only 0.650 and 0.623 respectively. SOAR also had poor positive predictive values and sensitivity using either ≥2 or ≥3 as a cut off score for mortality prediction.

qSOFA: qSOFA was the worst scoring system in terms of AUC score with 7- and 30-day scores both <0.6. The mortality rate did not increase as the severity score increased, with no patients in the most severe group dying. qSOFA had extremely poor PPV and sensitivity scores. 31 out of 37 patients were classified into group 0 or 1. These groups are considered low risk for sepsis according to qSOFA's original purpose.

X-Ray Subgroup Analysis: Following exclusion of the patients who either had not had an x-ray, or who's x-ray did not show clear new signs of pneumonia, there remained 24 patients. The 7-day mortality in this group was 3/24 and the 30 day mortality was 6/24. In this subgroup, the AUC for PSI at 7- and 30-day mortality was 0.937 and 0.750 respectively and for IROAD was 0.810 and 0.759 respectively. Giving similar results to the entire cohort of patients who were treated as a HAP irrespective of x-ray presence and findings. The asymptotic significance was however greater in the x-ray subgroup for both high performing scoring systems at both 7- and 30- day mortality prediction. This is likely due to the smaller sample size in the x-ray subgroup.

Table 6, X-ray subgroup analysis:

	Whole Cohort:	X-ray Subgroup:
PSI 7 Day Mortality AUC	0.878	0.937
PSI 7 Day Asymptotic Significance	0.007	0.016
PSI 30 Day Mortality AUC	0.796	0.750
PSI 30 Day Asymptotic Significance	0.008	0.072
IROAD 7 Day Mortality AUC	0.859	0.810
IROAD 7 Day Asymptotic Significance	0.011	0.089
IROAD 30 Day Mortality AUC	0.788	0.759
IROAD 7 Day Asymptotic Significance	0.010	0.062

Summary:

The typical patient in this study was an octogenarian with a high frailty score, four comorbidities, a set of observations meeting the sepsis criteria and an approximately one-month hospital stay prior to diagnosis. When scoring systems were applied at diagnosis, two scores showed good predictive value for mortality, with the other three scores having poor sensitivity and AUC scores. The best positive predictive value for mortality of all the scores was 0.5 which was achieved by I-ROAD for 30-day mortality. The scores showed similar predictive accuracy irrespective of x-ray findings, although the significance of the prediction is reduced in the x-ray confirmed pneumonia group. Subgroup analysis according to ward of admission was not performed due to the small number of patients &

low incidence of mortality on the care of the elderly ward, this was not felt appropriate. Whether different wards or specialty affects outcome would be an important consideration in any future research with a bigger patient population.

3.6 Discussion:

Main Findings:

The cohort of patients in this group is striking. There is a significant amount of comorbidity and background frailty combined with a high length of admission prior to diagnosis. Given this, it is not surprising that the number who both required and were suitable for ITU admission was low. Unfortunately given the low numbers of ITU admissions and drug resistant pathogens cultured, it would be unhelpful to assess the scoring indices for their prediction for these variables.

Two scoring indexes performed well for predicting mortality at both 7- and 30- days, with PSI and I-ROAD having good AUC scores and low asymptotic significance <0.05. Of these two scores it is worth mentioning that PSI requires 20 variables to create a score, whereas I-ROAD requires consideration of a maximum of 7. Both scores performed well in the x-ray confirmed pneumonia group also, although larger sample sizes would be required to show statistical significance.

CURB-65, SOAR and q-SOFA all performed poorly and are unlikely to have any utility in the prognostication of HAP.

This study also identified the difficulties of applying well performing scoring indices to real world settings. That is to say that some variables which may well aid accuracy of a scoring system are not measured in a way to of be clinically helpful. Urine output for example was not measured accurately in a single patient, blood glucose was rarely contemporaneous with diagnosis and a significant number of patients did not have an x-ray despite a pneumonia diagnosis. Clearly then either a scoring system needs to be so easy in its components that these failings do not limit its accuracy, or so significant in its effect on patient management as to warrant the addition of suitable investigations to accurately predict outcomes.

Strengths and Limits of Study:

This is a novel study into an area poorly researched, with little background literature to guide the way. However, the study was based on the proven utility of scoring indices in a closely related pathology (CAP) and set in the context of improving outcomes in a disease with a significant mortality. The scoring systems used were chosen as they have been validated elsewhere for similar or associated conditions (CAP or Sepsis or HAP). Scores were chosen to cover both a diagnosis-based

(pneumonia) and physiological (qSOFA) approach and were selected following review into the available guiding literature. The demographics of the population is concordant with that described more widely for HAP in the literature- an elderly population with a high frailty score and a significant number of comorbidities. This implies that this is an appropriate sample in which to assess these scoring indices. None of the scores used in this study were designed for use in hospital acquired pneumonia in the UK- however no such scoring system exists that the study author is aware of.

This was a small, single centre, observational case study. It would be inappropriate therefore to conclude that the two best performing scoring indices are validated as prognostication tools for wide use in UK HAP patients. However, the study does indicate further research into PSI and I-ROAD for this purpose stands a good chance of achieving that validity. Whereas a study investigating CURB-65, SOAR or qSOFA is highly unlikely to recommend one of these as a HAP severity index. As a preliminary case study, the aims have therefore been achieved.

Not all patients in this study had x-rays to confirm their pneumonia, or x-ray changes where x-rays were performed. All patients were however treated clinically as hospital acquired pneumonia. In subgroup analysis x-ray confirmed pneumonia did not appear to affect the accuracy of the two well-performing scoring indices, although their statistical significance was reduced as a consequence, likely due to the reduction in sample size.

A significant amount of data was missing for the completion of the scoring systems, which may have significantly affected the accuracy of scoring systems. Urine output for example, was not measured on a single patient, Arterial Blood Gas' (ABG)s were variably performed at diagnosis and the most recent glucose was often not contemporaneous with diagnosis. However, it is worth considering that if this information is not collected in the routine clinical treatment of HAP, it could act as a barrier to the future use of a scoring system that required that information. As such, if a scoring system owed its accuracy to data which is normally not collected or available, it is an inappropriate scoring system to endorse. Therefore, although this may appear to be a weakness to the validation of scoring systems in this cohort, it is in fact a strength for their validation in the study setting of a UK District General Hospital in normal clinical practice.

Some of the missing data, however, would have been available at time of diagnosis- basic observations for example, and in some patients the observations which were recorded closest to time of diagnosis were hours before or after diagnosis. This is a limitation on accuracy, but one which is difficult to overcome unless the diagnostician is involved in data collection and carries it out prospectively at time of diagnosis.

This study was carried out over two medical wards in a single hospital, one being a respiratory ward and one being a care of the elderly general medical ward. This could be expected to increase the respiratory comorbidity, age and frailty of the patients selected. In future studies it may be appropriate to ensure wards of differing specialities are included to validate scoring indexes in a wider demographic.

Unfortunately, there was insufficient information available to assess these scoring systems for their prediction of drug resistant pathogens or ITU admission. Hopefully, these questions could be answered in a larger study with a higher number of ITU admissions and cultured pathogens.

Interpretation of findings in wider context:

The current research into scoring systems in HAP in the UK is minimal. This study's aim was to assess if there is likely to be any merit to using an existing scoring system for prognostication and to guide treatment in HAP. To see if a scoring system is likely to have utility in this group of patients and to see if the mammoth task of creating a new scoring system could be avoided. The three chosen outcomes for monitoring were ITU admission, drug resistant pathogen and mortality prediction. Having an index which accurately predicted all three outcomes would direct drug therapy, escalation of care and end of life discussions in the same way scoring indices are currently used for CAP.

This study was unable to address two of those three variables in any meaningful way. However, it does suggest that existing scoring systems could usefully be able to predict mortality in this patient group. And this may be achievable with the use of a simple scoring system in the I-ROAD score.

For either PSI or I-ROAD to be validated in this way, a much larger multicentre study would be required to confirm accuracy of prediction. This could concurrently assess for ITU admission and pathogen culture which would be likely be observed in a larger study.

Next steps for research:

Given the promising initial mortality prediction of both PSI and I-ROAD, it would be appropriate to follow this case study up with a large multicentre observational study to assess both of these scores for mortality (ideally both short term and up to a year), as well as drug resistant pathogen culture and ITU admission. If the results of the larger validation study were as promising as this case study, it would then be appropriate to involved stakeholder groups such as the British Thoracic Society and NICE to consider the recommendation of such scores as best practice in HAP for guiding treatment.

If the scores were found to have limited utility in a larger study, either for mortality prediction or the other variables, the next step could follow a similar path to that taken during the creation of the I-

ROAD and CURB-65 scores. This would be to create a large HAP database- collecting observational data on HAPS across the UK, using statistical analysis to identify independent predictors of mortality/drug resistant pathogens/ITU admission, and subsequently creating and validating a scoring system based on this.

4.7 Conclusion:

Both the PSI and I-ROAD scoring systems showed mortality prediction accuracy in this small case study. This requires further validation in a larger cohort observational study, during which their prediction accuracy of other outcomes should be assessed.

Chapter Four

Discussion and Recommendations

4.1 Introduction:

In the preceding three chapters, the researcher has explored the success of scoring systems in community acquired pneumonia (CAP) and the relative disparity in research between hospital acquired pneumonia (HAP) and CAP- particularly in relation to severity scoring. Subsequently a scoping review and case study work focused on assessing the utility of scoring indices in HAP. In this chapter the researcher will present an overview of the case for scoring index use in HAP, as well as reflecting on the methodology of both the scoping review (Chapter 2) and the original case study research (Chapter 3). It considers how the elements of both could be improved, discusses the need for future research in this area, and considers the clinical impact of these studies.

4.2 Overview of Results

4.2.1 Chapter One Review:

Hospital Acquired Pneumonia:

As previously described, hospital acquired pneumonia is a pneumonia developed more than 48 hours following admission to hospital, not being incubated at time of admission, and is usually confirmed with radiographic evidence of consolidation in the lungs. When compared to the CAP population, the HAP population is older, frailer and have more comorbidities (Burton, et al., 2016; Sopena, et al., 2014; Azmi, et al., 2016). In addition, when comparing the literature of HAP to the literature in CAP, there is a significant discrepancy, with CAP being researched a significantly greater amount- another example of this being Cochrane studies; when searching for record title "Community acquired pneumonia" finds eight times as many Cochrane reviews as "Hospital acquired pneumonia". Given the high prevalence, high mortality, and low research levels in HAP it stands to reason that more research to improve outcomes and clinical decision making is likely to have a significant impact on disease outcomes. With the elderly population a larger proportion of

the HAP patient group than the CAP, and an aging population, it is also concerning that this disease is going to become a greater burden to the healthcare system over the next years and decades.

Scoring Systems:

Scoring systems are used commonly in hospitals for a multitude of reasons and in increasing number over the past few years. Scores can be applied to different aspects of patient presentation- they may be disease specific such as Child-Pugh scoring in liver failure, organ system scoring such as with the SOFA score, physiological derangement scores such as in APACHE II scoring, anatomical scoring such as in the Injury Severity Score (ISS) or simple observation parameter scoring indices such as the National Early Warning score NEWS or Glasgow Coma score GCS (Baker, et al., 1974; Child & Turcotte, 1964; Smith, et al., 2013; Teasdale & Jennett, 1974). They are quick decision-making tools which help to build evidence-based medicine into daily practice. Some uses of scoring systems for examples are: in pancreatitis to guide intensive care input, in atrial fibrillation to guide decisions regarding anticoagulation and in some hospitals, they are used for all patients on admission to aid decisions concerning venous thromboembolism prophylaxis (Blamey, et al., 1984; Chopard, et al., 2006; Lip, 2010).

More relevant to HAP, however, is the use of scoring systems in both CAP and intensive care/critical illness. Scores such as CURB-65, PSI and SOAR are used internationally for CAP and are supported by international guidelines for best practice in CAP to guide place of care, antibiotic therapy and prognosticate outcomes. In addition, scores such as SOFA, qSOFA, APACHE II and SAPS are commonly used in the critically unwell patient to gauge organ failure, severity of sepsis and prognosticate. As HAP is a similar pathology to CAP, with worse mortality, the successful use of scoring systems in both CAP and critical illness indicates their use in HAP is likely to be possible and clinically beneficial.

Ideally a scoring system would be easy to use, highly discriminative, internationally valid, with good predictive value and apply accurately to patients from all countries and populations. Ease of use of scoring systems requires a relatively low number of parameters, the used parameters to be collected in routine care, not requiring additional tests or examinations and not to be subjective. The authors were not aware of any HAP scoring systems commonly used in the UK at the beginning of the study- nor indeed at the end.

4.2.2 Chapter Two Review- Scoping review:

As mentioned above, the two main reasons for investigating the use of scoring systems in HAP are the ubiquity with which scoring systems are successfully used in CAP- but not in HAP- and the

increased mortality in HAP in comparison to CAP. The increased mortality implies that there may be much to gain from introducing an accurate scoring system in terms of clinical outcomes. The aim of carrying out a literature review, was to identify the reason for scoring indices not being standard clinical practice in HAP- be that a lack of research, proven lack of utility or another reason- and to assess the current evidence for scoring systems in HAP in the UK if any was found. A preliminary search identified minimal trials investigating HAP scoring systems- especially in the UK population. The studies which were found demonstrated significant limitations when applied to the UK HAP population. We felt this made a systematic review inappropriate. If we had decided to carry out a systematic review, the following would have been the likely inclusion criteria:

1. UK based studies
2. Assessing scoring indices for accuracy of the following outcomes: Mortality, ITU admission, drug resistant pathogen culture.
3. Looking exclusively at HAP diagnoses
4. Search Terms: “Hospital Acquired Pneumonia or HAP or Healthcare associated pneumonia or HCAP or Nosocomial Pneumonia” AND “Scoring System or Severity Index or Prognostic Index”

This would have brought up zero results and as such concluded conclusively that there was no current evidence for scoring indices in the UK HAP population and more research is required.

Given the indication from the preliminary search that this would be the case, a different study method was decided upon. The method being a scoping review as described by Arksey and O’Malley (2005) and refined by the Joanna Briggs institute (2015). The study design is a five-step process: the definition of a research question, the literature search, charting of data from the literature, collating and summarising the themes from the charted data and finally reporting the outcomes.

While a systematic review aims to address a well-defined question, with a limited scope of included study types and a rigid inclusion/exclusion criterion, a scoping review is much broader in approach. A scoping review allows development of the research question during the study, allowing incorporation of multiple relevant information sources, for example: randomised control trials, expert opinion, stakeholder focus group answers or government policy. Owing to the limited results found in the preliminary search, a scoping review was chosen to include a suitable number of information sources as to fully paint the current picture of HAP scoring systems. It may be that in a few years when multiple RCT’s have taken place a systematic review is more appropriate, but at this point a scoping review to direct future RCT’s was felt a better place to start- identifying fully the foundations of research to come. The adaptations to the original question are fully explored below.

Step 1- Research Question: The overarching aim of the study was to address why HAP scoring systems are not commonly used in UK clinical practice. This was further broken down into the following two questions:

- Is there sufficient evidence to suggest severity scoring system use in patient diagnosed with Hospital Acquired Pneumonia in the UK would be clinically beneficial?
- Do current international guidelines support severity scoring systems in patients with Hospital Acquired Pneumonia?

The first question was defined using a PICO (Population, Intervention, Comparison, Outcome) model (table 1), to address whether there is supporting or refuting evidence for HAP scoring indices. The second question looks to more broadly investigate if scoring systems are currently in use anywhere in the world and whether international bodies responsible for pneumonia guidelines have investigated this in the past.

Step 2 – Question 1- Literature search: PubMed, The Cochrane Library and Web Of Science were reviewed for articles containing "Hospital Acquired Pneumonia or HAP or Healthcare associated pneumonia or HCAP or Nosocomial Pneumonia" AND "Scoring System or Severity Index or Prognostic Index" (using the Field Tag TI- for title- on Web Of Science). Following the initial search, articles were reviewed by title, abstract and full text- with irrelevant studies excluded at each stage. Following initial review, the number of papers which directly looked at severity scores in HAP was extremely limited in both number and in relevance to a UK HAP population. Therefore, the scope of the study was increased- using the same search criteria, all studies which applied a scoring system to non-CAP pneumonia patients with the same outcomes measured was considered. This included studies which reviewed HAP, Nursing Home Acquired Pneumonia (NHAP), Healthcare Associated Pneumonia (HCAP), Ventilator associated pneumonia (VAP) and Psychiatric Hospital acquired Pneumonia (PHAP). In the UK, both HCAP and NHAP are not considered separate entities and are instead categorised as CAP. However, these studies were included as they are considered in different parts of the world (often where the studies are performed) to be a separate entity due to patients presenting with an increased proportion of drug resistant pneumonia. As drug resistant pathogens are the primary reason for considering HAP as a different disease entity to CAP it was felt that, although there are clear limitations to including these patient groups, they demonstrate the use of severity scoring system in a pneumonia cohort not considered CAP in the locality of the study. This was considered an appropriate wider population to review within the bounds of the original search strategy.

Step 2 – Question 2- Guidelines from: The British Thoracic Society, NICE, Diseases Society of America (IDSA)/American Thoracic Society (ATS), European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT), were all reviewed for guidance on HAP scoring indices as well as current understandings of HCAP as a separate pneumonia class from CAP or HAP. These guidelines either directly relate to UK practice or were widely mentioned in the literature found during this scoping review. In addition, Japanese guidelines were reviewed due to the significant amount of research into hospital acquired pneumonia and scoring indices conducted in Japan identified during this study.

Step 3- Charting Data: All studies from the literature were collated into a single table, study objectives, population, study type and methodology were tabulated as well as study limitations. All studies reviewed in full text review were tabulated, whether they were included in the end analysis or not and whether or not the full text could be found. The reason for this, is that this scoping review's aim is to act as the foundation for all further HAP severity index work, therefore having all studies available which would be found at future searches and explaining their relevance or otherwise should aid future reviewers and enable the full narrative to be displayed.

Following review, the international recommendation of severity scoring indices was minimal and the information available equally so. As such the outcomes for this were documented descriptively in prose.

Step 4- Collating and summarising the themes from the charted data: There were three main elements to collate and summarise in relation to the literature review- the background of the individual papers (population, study type, limitations, etc), the outcomes we were reviewing for (Mortality prediction, ITU admission prediction, Drug resistant pathogen prediction) and finally themes from the text- for example, multiple studies mentioned the difficulties of applying the PSI score clinically as it had so many variables. The study background and the three reviewed outcomes could both be considered in quantitative ways, with the textual themes adding a third, qualitative arm to the data analysis. The study background gave country of origin, pneumonia subtype and scoring index used as totals- demonstrating a non-UK cohort of primarily non-HAP pneumonia studies. The three primary outcomes the study was assessing were categorised by scoring index into positive or negative based on Area under the receiver operator score or study reporting, to allow formation of an overview of the study findings despite heterogeneous reporting of outcomes across the different studies. Other themes were initially described in the chart, and common themes were

discussed following close review of the chart for commonality. Themes from the international guidance stream were also described from the second limb of the scoping review.

Step 5- Reporting Outcomes: Finally, the above results were collated to describe the overall picture which had been painted of the research and current use of scoring indices in hospital acquired pneumonia. The conclusions show the current standpoints of the UK, US, Japanese and European medicinal/respiratory societies as a demonstration of current international practice regarding HAP scoring indices. Where the information is available the conclusion also explains why this approach has been taken by the international societies. In addition, the entire international background of HAP severity scoring research is explained- with associated limitations discussed and difficulties of implementation noted. This concludes that currently western guidelines do not suggest the use of HAP severity scoring, that there is not the evidence currently to support HAP scoring indices in the UK and that there is no evidence that HAP scores have been validated for the three primary outcomes reviewed in this scoping study. The conclusion is broader than this however, as it also demonstrates the research in other non-HAP pneumonia groups, which gives an indication of how HAP scoring research may proceed going forward. Suggesting for example that scoring systems based on physiological disturbance may perform better than scoring indexes designed specifically for pneumonia, and that some scoring systems are difficult to use clinically as they are very detailed (e.g. PSI).

Strengths and Limitations

The positives to draw from this review include the inclusion of both current practice guidelines in HAP scoring, all available research in the field and the detailed charting table which allows readers to read further into the data if so desired. The fact all studies which made it to full text review were included in charting allows transparency in the research process, although this does add 'clutter' to the study. The scoping review's broad approach allows it to demonstrate a complete picture of HAP scoring compared to a systematic review of purely the literature or a review of simply current practice. However, more streams could have been included- for example, a stakeholder questionnaire to respiratory physicians on whether a HAP scoring index would be beneficial in their day to day work and which outcomes would be important to them. The broad approach to the study also limits the application to HAP directly as other pneumonia subgroups were included (despite the reasons for this being given). As the study was expanded to include other pneumonia groups, it could also be argued that the search terms should have been widened to possibly encounter more studies looking at non-HAP, non-CAP pneumonia to widen the dataset. The reason for not doing this

was that the initial study expansion was felt an appropriate balance between increasing the available data and shifting the scoping review to look at many tens of studies in pneumonia subgroups not considered clinically applicable in the UK. This allowed for a concise synthesis of the relevant take home messages from this scoping review in a simple easily digestible paragraph setting out both findings and research opportunities which was another strength of this scoping review. The addition of guidelines from different countries again broadens the study to allow a fuller picture to develop, but 3/4 guidelines included were from the west, despite most of the studies originating from Asia- including more guidelines from the rest of the world may have improved the study further.

Scoping review changes:

If we were to conduct the scoping review again, I would suggest the following changes

- Subgroup analysis of HAP- only studies
- Inclusion of stakeholder group stream of data
- Inclusion of wider range of international guidelines
- Widened search criteria to include more non-CAP pneumonia evidence and subgroup analysis of these different pneumonia groups
- Division of the charted data into 'included studies' and 'excluded studies' tables for ease of navigation

4.2.3 Chapter three review:

Study aims and design:

The aim of this study was to build on the work of the scoping review, and to add to the available literature regarding HAP scoring indices in the UK. This was to be a small case study to test the concept of HAP scoring indices in this population. The 'case' being two wards in a district general hospital in North Wales. Over a winter period, all patients identified on these wards as being treated for a HAP had multiple scoring systems applied as they would have scored at time of diagnosis. These scores were then statistically analysed for predicting mortality, ITU admission and culture of drug resistant pathogens. The study was designed as purely observational so as not to in any way interfere with patient treatment- this reduced the ethical implications of the study and allowed the study team to examine the implementation of scoring systems in a real world environment, with only the data which would normally be available to the clinician at time of diagnosis. The scores used were highlighted by the scoping review as likely to have utility in this population- either due to their utility in other non-CAP pneumonia, the patient demographic of HAP patients or high frequency in the literature in non-CAP pneumonia.

Results and Analysis:

37 patients were identified for the study, not all of these patients had radiographic evidence of pneumonia, but all were treated as HAP. The study showed the HAP population on these wards during this time was an elderly group of patients with a high background frailty, and multiple comorbidities. The mortality was not dissimilar to that seen in other HAP studies, although the number of admissions to ITU (0) and drug resistant pathogens cultured (1) meant that no useful analysis of these two outcomes could be performed. The scoring indices distributed patient's risk levels variably with some grouping all patients in moderate risk categories, some placing patients almost exclusively in the low risk categories and some distributing the patients throughout risk categories. The statistical analysis showed that two scoring indices performed well at predicting 7- and 30- day mortality, whereas the other three scoring indices did not. The well performing indices were the I-ROAD score and the PSI score. On subgroup analysis, both scoring indices continued to perform well in the patient group with radiographic features of pneumonia.

Strengths and Limitations:

The main strength of this study is its novelty- to the authors knowledge there are no studies looking at HAP scoring indices in the UK HAP population. This study is also informed by a wealth of information from the scoping review which preceded it, meaning that the scoring systems being used are selected based on all available research in the area of HAP and non-CAP pneumonia severity scoring as well as international HAP and CAP guidelines. The population of the study is both a strength in that it is exclusively a UK HAP population- with subgroup analysis of patients with radiographic evidence also, and also because the age and background of the patients is consistent with that seen in previous HAP studies. However, this is a small study in two specialist wards (one respiratory, one care of the elderly and general medicine), meaning the patient population is unlikely to be representative of entire the UK HAP population.

The nature of the study (prospective and retrospective observational study) has the positives of being real-world in that the scoring systems were applied only with the information available at time of diagnosis and required no additional examinations or investigations. However, the subsequent lack of full data may have impeded the accuracy of the tested scores. The benefit to this is the ability to review the scores in a real-world setting, the disadvantage being an accurate score may have been misclassified as inaccurate due to missing data. Similarly, the lack of timely x-rays in some of the patients questions the underlying disease process in some of the cohort, which would be a significant limitation on the results. We tried to overcome this by subgroup analysis, however in a larger prospective study it would be appropriate to x-ray all patients with HAP at diagnosis for

confirmation- this is a widely accepted clinical practice and should not therefore be a patient care issue. Missing data extends to the outcomes of ITU admission and drug resistant pathogen culture. This is an unfortunate consequence of the small study size and would be better addressed by a larger study.

In addition, although there was a good reason for using each of the 5 scoring systems used in the study, this is a relatively low number of scoring systems to investigate when there are so many which exist- both pathology and physiological insult-based scoring systems. In a future study it may be appropriate to review a larger number of scoring systems.

4.4 Synthesis of Research:

The scoping review is, to the authors knowledge, the most comprehensive review of severity scoring indices in Hospital Acquired Pneumonia in the UK currently carried out. The subsequent case study is the first UK HAP scoring index study the authors are aware of. Despite the relative limitations of both- the limited number of relevant papers and broad inclusion criteria in the scoping review, and the small size and limited reporting of two of the three outcomes in the case study- both pieces add value to the discussion surrounding HAP. To the authors knowledge there have been no further studies into the topic since the original work was carried out, leaving them as the current option for foundations of research in this area.

The scoping review allowed the researcher to focus the case study in terms of demographic and scores used, and demonstrated two scores (I-ROAD and PSI) giving impressive mortality risk stratification during the study. Unfortunately, as described the case study did not address two of the three outcomes for which it was intended, and this does have significant implications for the utility of any scoring system in future. This would need to be considered in future research.

Returning to the author's ideal scoring index, for this study the scoring index would be considered easy to use, highly discriminative in terms of all three study outcomes and internationally valid. This would allow widespread adoption of a quick tool which materially impacted patient care decisions and prognosis internationally. From the study, I-ROAD is most promising in this regard. I-ROAD was highly discriminative in terms of mortality, has already been validated in Japan and was easy to use. It needs wider validation in the UK population and the two variables other than mortality need further review, but it is promising. PSI is a much more complex scoring index and has less documented utility in HAP, but also warrants further investigation.

4.5 Recommendations: Wider Context and Next Steps:

The context for this research is an under-investigated pathology with high incidence, high mortality which affects a high-risk population. The aims were to investigate whether the use of simple scoring indexes at diagnosis could aid clinicians managing this pathology. The relevant research found was minimal, and the small size of the case report needs to be considered in this wider context- a spark, which hopefully could ignite a bonfire.

One element this study did not go consider at depth was the qualitative effect of scoring systems on patients & clinicians. It has been documented previously that multiple studies found some scoring systems too unwieldy clinically to be beneficial, using a scoring system does add work to clinicians treating patients also. However, scoring systems do aid incorporation of evidence-based medicine into daily practice and aid decision making. The best way to evaluate these contrasting points would be a piece of qualitative research into both clinician and patient opinions on scoring systems, how they should be used and what would prevent their use or make them less beneficial. This could take the form of a nationwide study of clinicians or specific stakeholder group interviews (senior respiratory clinicians and patient groups etc). This would be an area worth considering alongside the studies mentioned below.

This study is a starting point, the next steps in HAP scoring index research would ideally include a larger, multi-centre study looking to validate a scoring system. This case study highlights that this would not necessarily be a futile study. The learning points from this study to consider for the validation study would include a larger cohort to assess for all three main outcomes, to prospectively get a chest x-ray to confirm all diagnoses, incorporation of IROAD and PSI into the study and ideally the involvement of a stakeholder group in the study design to consider other outcomes which may be important. In summary the author would recommend the following next steps.

1. A wide validation study in the UK applying scoring indices to HAP patients, incorporating I-ROAD and PSI, ensuring that all investigations were caried out at diagnosis to complete the scoring indices in full.
2. A discussion with stakeholder groups (e.g. the British Thoracic society) to ensure that any additional outcomes they would consider important could be investigated in the wide study and to adapt the idea of a perfect scoring index to that felt important by the relevant specialists.
3. Currently no change in clinical practice or policy based on this research as the evidence is not yet sufficient to advise widespread change in clinical practice or policy.

4. Consideration of the building of a large UK HAP database which would incorporate details of patient demographics and presentation as well as outcomes. This may enable a UK specific score to be designed in future which would offer better clinical prediction, although the development would take a significant amount of work.
5. Finally, this study demonstrates the disparity of research between CAP and HAP. Given the severity of HAP, the high mortality and the aging population, the author would encourage research into HAP more widely to improve patient outcomes moving forwards.

If these steps were taken, hopefully a scoring system could be incorporated into widespread use in the UK leading to improved management of Hospital Acquired Pneumonia- incorporating evidence based medicine into daily practice without incurring an increased burden of work on clinicians.

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Appendices:

Chapter 1 Appendix 1:

PICO Approach:

Population	UK patients with HAP
Intervention	Application of severity scoring indices
Comparison	Compared to no severity score
Outcome	Enable treatment decisions, early ITU input and prognostication.

Chapter 3 Appendix 1- Demographic and Time of Diagnosis Data:

Baseline Characteristics:

Characteristic:	Mean (SD)/Median (Range) Or N (%)
Age	81 (12)/ 83 (44-98)
Gender (Female)	23 (62%)
Smoking Status Current-/Ex-/Non-Smoker/Undocumented	7(19%) / 10(27%) /15(41%) /5(14%)
Frailty Score	6 (1.5)/ 6 (3-8)
Number of documented comorbidities	4 (2)/ 1 (1-15)

Comorbidity Prevalence:

COPD	15 (41%)
Cancer	14 (38%)
Hypertension	12 (32%)
Other Lung Diseases	10 (27%)
Ischaemic heart disease	10 (27%)
Atrial fibrillation	8 (22%)
Osteo-arthritis	7 (19%)
Diverticular Disease	4 (11%)
Congestive cardiac failure	3 (8%)
Other Cardiac Conditions	3 (8%)
Type two diabetes	3 (8%)

Chronic kidney disease	3 (8%)
Cerebrovascular disease	2 (5%)
Other Comorbidities- assorted	70 (189%)

Observations at Diagnosis:

Observation:	Mean (SD):	Median (Range):
Respiratory rate	23 (7)	20 (16-40)
Heart rate	93 (16)	93 (52-126)
Systolic blood pressure	125 (22)	124 (93-160)
Diastolic blood pressure	71 (18)	70 (42-122)
Temperature	37.25 (1.03)	37.1 (34.1-39)
EWS	5 (3)	5 (2-10)

n.b Oxygen Saturations not included as patients all on variable amounts of oxygen at diagnosis- comparison of raw value not helpful.

Bloods at Diagnosis:

WCC	14.1 (5.1)
CRP	112.8 (86.0)
Urea	8.4 (5.4)

Chapter 3 Appendix 2: Severity Index Data:

Severity Index Score at Diagnosis:

Severity Index:	Score at diagnosis:	Frequency:	Median:
CURB-65	0 1 2 3 4 5	2 10 12 10 3 0	Median- 2
PSI	1 2	0 4	Median- 4

	3 4 5	7 16 10	
I-ROAD	Mild Moderate Severe	6 17 14	Median- Moderate.
qSofa	0 1 2 3	17 14 4 2	Median- 1
SOAR	0 1 2 3	3 19 12 3	Median- 1

Sensitivity, Specificity, Negative Predictive Value, Positive predictive value:

Scoring System:	Cut Off Score	PPV (7 day)	PPV (30 day)	NPV (7 day)	NPV (30 day)	Sensitivity (7 day)	Sensitivity (30 day)	Specificity (7 Day)	Specificity (30 day)
CURB-65	≥3	0.23	0.44	0.92	0.79	0.60	0.44	0.70	0.68
PSI	≥91 (class 4)	0.16	0.33	1.00	0.91	1.00	0.89	0.34	0.36
SOAR	≥ 2	0.20	0.33	0.91	0.82	0.6	0.56	0.63	0.64
	≥ 3	0.33	0.33	0.88	0.76	0.20	0.13	0.94	0.93
qSOFA	≥ 2	0.17	0.33	0.85	0.77	0.20	0.22	0.84	0.86
	≥ 3	0.00	0.00	0.86	0.74	0.00	0.00	0.93	0.93
I-ROAD	≥ Mod	0.16	0.29	1.00	1.00	1.00	1.00	0.19	0.21
	≥ Sev	0.36	0.50	1.00	0.91	1.00	0.78	0.72	0.75

Survival at 7 and 30 days by Initial Severity score:

	Severity index score:	Frequency at diagnosis:	Alive at 7 day:	Alive at 30 day:
CURB-65	0	2	2 (100%)	2 (100%)
	1	10	9 (90%)	8 (80%)

	2	12	11 (92%)	9 (75%)
	3	10	7 (70%)	7 (70%)
	4	3	3 (100%)	2 (67%)
	5	0	N/A	N/A
PSI	1	0	N/A	N/A
	2	4	4 (100%)	4 (100%)
	3	7	7 (100%)	7 (100%)
	4	16	15 (94%)	13 (81%)
	5	10	6 (60%)	4 (40%)
SOAR	0	3	3 (100%)	3 (100%)
	1	19	18 (95%)	16 (84%)
	2	12	9 (75%)	7 (58%)
	3	3	2 (67%)	2 (67%)
qSOFA	0	17	15 (88%)	14 (82%)
	1	14	12 (86%)	10 (71%)
	2	4	3 (75%)	2 (50%)
	3	2	2 (100%)	2 (100%)
I-ROAD	Mild	6	6 (100%)	6 (100%)
	Moderate	17	17 (100%)	15 (88%)
	Severe	14	9 (64%)	7 (50%)

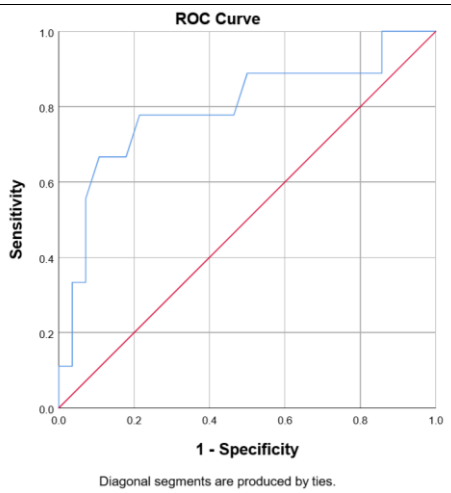
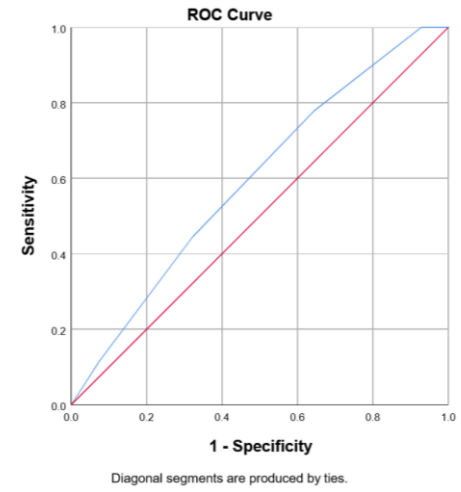
AUC Statistics- 7 Day Mortality:

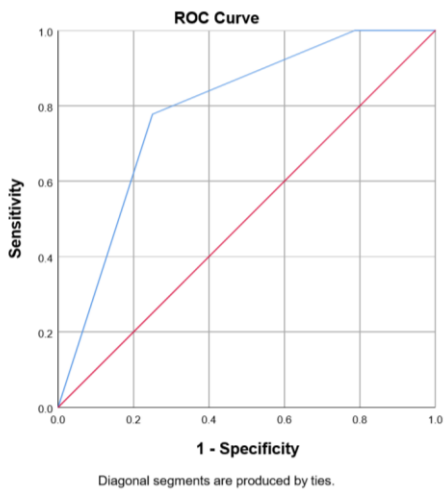
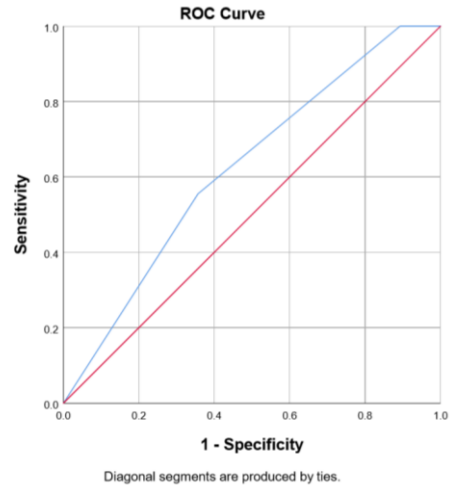
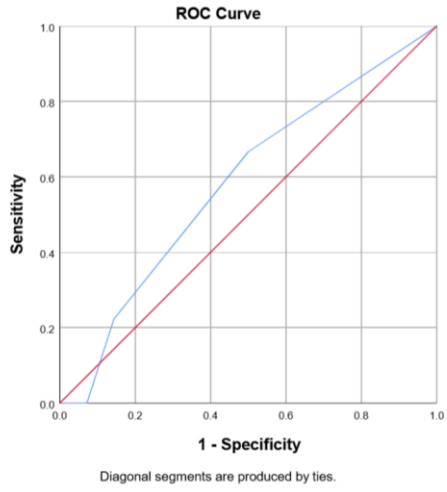
Scoring System:	AUC:	Standard Error:	Asymptotic Significance:	95% Asymptotic Significance Confidence Intervals:	
				Lower:	Upper:
CURB-65	0.622	0.126	0.386	0.375	0.869
PSI	0.878	0.057	0.007	0.766	0.990
I-Road	0.859	0.062	0.011	0.737	0.981
SOAR	0.650	0.132	0.286	0.390	0.910
qSOFA	0.534	0.138	0.807	0.263	0.805

AUC Statistics- 30 Day Mortality:

Scoring System:	AUC:	Standard Error:	Asymptotic Significance:	95% Asymptotic Significance Confidence Intervals:	
				Lower:	Upper:
CURB-65	0.595	0.106	0.396	0.387	0.803
PSI	0.796	0.098	0.008	0.604	0.987
I-Road	0.788	0.082	0.010	0.627	0.949
SOAR	0.623	0.104	0.272	0.419	0.827
qSOFA	0.583	0.108	0.457	0.371	0.796

Chapter 3 Appendix 3: Area Under the Receiver Operator Curves:

PSI 30 Day	
CURB-65 30 Day	

IROAD 30 Day	
SOAR 30 Day	
qSOFA 30 Day	

Chapter 3 Appendix 4: Data collection form:

Data field:	
Age	
Gender	

Comorbidities (Including Neoplastic, liver disease, renal disease, cerebrovascular disease or congestive heart failure)	
Smoking status	
Living status	
Nursing home status	
Frailty Score	
Time from admission to diagnosis	
Observations	
NEWS	
Mental status	
Most recent blood tests	
Results from most recent ABG/VBG	
Most recent blood glucose measurement	
X-ray Findings at diagnosis	
Urine output	
7 day and 30 day mortality	
ITU transfer	
Microbiology	
Severity scores: -CURB65 -PSI -I-ROAD -SOAR -qSOFA	