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Invited Review

Gram-negative bloodstream infections and sepsis: risk factors, screening tools and surveillance

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Abstract

Introduction and background: Incidence of gram-negative bloodstream infections (GNBSIs) and sepsis are rising in the UK. Healthcare-associated risk factors have been identified that increase the risk of infection and associated mortality. Current research is focused on identifying high-risk patients and improving the methods used for surveillance.

Sources of data: Comprehensive literature search of the topic area using PubMed (Medline). Government, professional and societal publications were also reviewed.

Areas of agreement: A range of healthcare-associated risk factors independently associate with the risk of GNBSIs and sepsis.

Areas of controversy: There are calls to move away from using simple comorbidity scores to predict the risk of sepsis-associated mortality, instead more advanced multimorbidity models should be considered.

Growing points and areas for developing research: Advanced risk models should be created and evaluated for their ability to predict sepsis-associated mortality. Investigations into the accuracy of NEWS2 to predict sepsis-associated mortality are required.

Key words: gram-negative, bloodstream infection, sepsis, mortality

Introduction

Gram-negative bloodstream infections (GNBSIs) are serious infections resulting from bacterial dissemination into the bloodstream and are associated with an increased risk of sepsis and mortality.[1] Incidence is rising globally and in the UK, attributed by an aging population, multimorbidity and increased medical and surgical interventions, along with improved detection.[2] Sepsis differs from bloodstream infections (BSIs), in that sepsis is defined as the life-threatening organ dysfunction caused by a dysregulated host immune response to infection.[3] Sepsis is a common cause of death, with ~123 000 cases and 37 000 deaths in the UK each year.[2] Recently published studies have reported on the multiple healthcare-associated risk factors for GNBSIs and sepsis, which have aided public health interventions.[4–6] This review will therefore provide an overview of the studies that have identified these risk factors.

With no biological test for sepsis currently available, generalized screening tools are used in the UK to aid sepsis detection.[7] Here, we will discuss the accuracy and the areas of debate for the use of the national early warning score (NEWS2) for sepsis detection.

As the incidence of GNBSIs and sepsis continue to increase, surveillance schemes have been established to monitor trends overtime, which rely on the International Classification of Diseases, Tenth Revision (ICD-10) codes to identify sepsis cases. This review will look at past issues with sepsis coding, the improvements made and the future for monitoring sepsis incidence. The search for relevant literature was conducted on the online database PubMed, focusing on relevant, peer-reviewed journals in addition to governmental and professional societal publications.

Pathway from infection to sepsis

During gram-negative infection, the progression from localized infection to GNBSI can result from bacterial translocation across epithelium into the bloodstream, induced by bacterial overgrowth or physical damage to the epithelium.[8,9] The progression from GNBSIs to sepsis occurs when the immune response to the gram-negative bacteria becomes dysregulated and induces organ dysfunction. This process involves multiple mechanisms, involving immune cell dysregulation, blood vessel endothelium and microvascular dysfunction as well as cellular metabolic reprogramming, occurring over an acute period.[10–12] Consequently, inadequate oxygen perfusion into cells can occur, along with cell hypoxia and ischemia. If left unchecked, sepsis can progress further into septic shock, multiple organ failure and death.

There are many factors that influence the likelihood of BSIs and for the development of sepsis, here we will discuss those identified by epidemiological studies.

Healthcare-associated GNBSIs

GNBSIs have seen a global increase in incidence over the last 20 years.[1] *Escherichia coli (E. coli), Klebsiella species* and *Pseudomonas aeruginosa* account for 72% of all GNBSIs, with *E.coli* representing 59% of all cases.[1] A growing number of GNBSI cases are said to be healthcare-associated, meaning, patients have received healthcare either in the community or hospital within the 28 days prior to the BSI episode.[1] The main healthcare interactions known to be risk factors for GNBSIs include but are not limited to those displayed in Figure 1.[1]

One of the risk factors for GNBSIs and sepsis are urinary tract infections (UTIs), with urinary catheterization being a main risk factor for healthcare-associated GNBSIs (Fig. 1). An epidemiological study by Abernethy et al.[4] identified that of 1731 *E. coli* BSIs investigated, 59% were healthcare-associated and 51% had a urogenital tract source. Of these cases, 84% were associated with urinary catheters. A study by Melzer et al.[13] investigated the association further, concluding that urinary catheterization was independently associated with severe sepsis (odds ratio, OR = 3.94) in addition, infections with a urinary source but non-catheter related also independently associated with severe

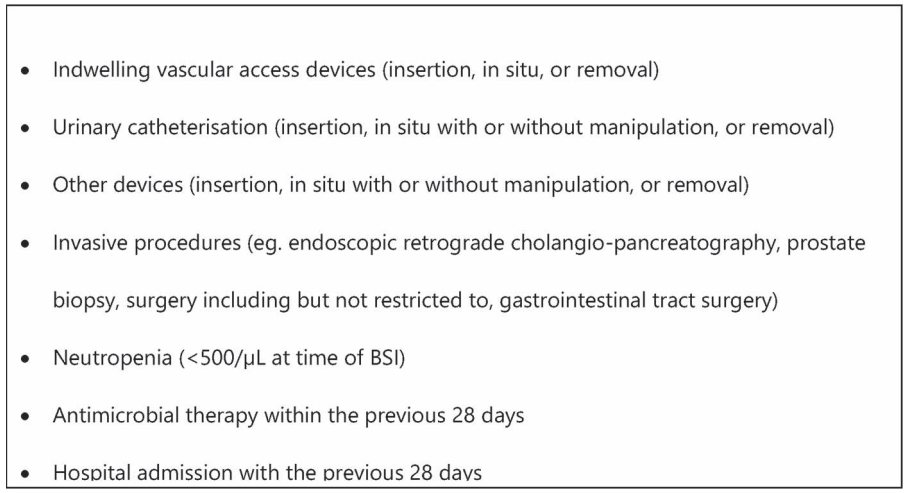

Fig. 1 Healthcare-associated risk factors for GNBSIs in the UK.[1]

sepsis (OR = 1.27). The results imply that UTIs are a considerable risk factor for sepsis, with urinary catheterization increasing the associated risk of GNBSIs further. It should be noted that since the study, according to the Third International Consensus Definitions for sepsis, the term severe sepsis has become redundant, with the new sepsis definition encompassing the terminology and symptoms of severe sepsis.[3]

One of the potential causes of initial catheter-associated infection is inadequate sterile techniques during insertion or removal,[14] specifically when care is delivered in the community and home setting. With the results from epidemiological studies identifying the link between urinary catheterization and GNBSIs, the National Institute for Health and Care Excellence (NICE) have recommended that novel qualitative investigations be carried out to understand whether correct aseptic techniques of urinary catheterization are followed. Results from such studies are predicted to identify barriers for infection prevention within the community and aid the development of public health interventions.[15]

Prior antibiotic treatment is an additional healthcare-associated risk factor for GNBSIs (Fig. 1). The Abernethy et al.[4] study found antibiotic use in the 4 weeks prior to the BSI was the most frequently reported healthcare exposure (32.4% of 1731 patients), with one third of antibiotics prescriptions used to treat UTIs. Antibiotic use can increase the risk of antimicrobial resistance, which can lead to treatment failures and poorer outcomes. Resistance levels are rising globally and within the UK, as a result incentives were introduced by the UK government in 2015 to reduce antibiotic prescribing in primary care by at least 1% from the previous year.[16] Antibiotic therapy for UTIs was reduced in-line with the incentives, with many patients receiving no or deferred antibiotic therapy in primary care settings. To assess what impact this incentive had on GNBSIs and sepsis, Gharbi et al.[17] conducted a retrospective population-based cohort study, focusing on elderly patients with UTIs within the community. The main finding indicated that patients over the age of 65 years with a UTI in the community setting were at a significantly higher risk of developing a BSI within 60 days and had poorer outcomes when antibiotic therapy was either not prescribed or deferred. The vulnerable population identified in the study deviates from the majority of patients with UTI, as no or deferred antibiotic prescription does not normally cause serious adverse outcomes. The Gharbi et al. study confirms the importance of novel investigations surrounding published guidelines, to ensure that patient care

remains at a high standard and adverse outcomes are limited for all individuals.

Despite the target for GNBSI incidence to be reduced by 50% by 2020 in UK, there are few substantial intervention guidelines published. This concern was raised by Bhattacharya et al.[18] who stated that due to the absence of necessary interventions, the rates of *E. coli* BSIs are predicted to continue rise, to 90.5 per 100 000 by 2020/21, a 22% increase in incidence since 2012/13. Suitable interventions aimed at reducing GNBSIs are particularly difficult to identify as many of the risk factors for GNBSI are complex and substantial evidence about community-based healthcare infection control measures are needed to make recommendations.

Sepsis risk in chronic disease and multimorbidity

An overriding theme of how chronic disease contributed to the increased risk of sepsis and poorer outcomes is that the pro-inflammatory, pro-oxidative and pro-coagulation processes observed in chronic disease contribute to impaired integrity of blood vessel endothelium, causing leakier blood vessels. Such processes have been observed in chronic obstructive pulmonary disease (COPD), cardiovascular disease and liver cirrhosis.[11] In addition, hypertension, diabetes mellitus and chronic renal disease have been shown to reduce the thickness and therefore protective ability of glycocalyx, a protein matrix that coats the luminal surface of the endothelium.

As mentioned earlier in the review, during infection the progression from localized infection to BSI can result from bacterial translocation across blood vessel endothelium. In individuals with chronic disease or multimorbidity, the leakier blood vessels allow for easier translocation, therefore increasing the risk of BSIs and sepsis. The damage ensured to the endothelium, as a result of sepsis-induced immune dysregulation and organ dysfunction, is exacerbated in those with impaired basal functionality, causing more severe physiological outcomes.[11]

A Swedish study by Holmbom et al.[19] found that comorbidity was independently associated with 30-day mortality in patients with healthcare-associated BSIs (relative risk, RR = 1.56 for one comorbidity and 1.89 for ≥2 comorbidities). Although the study confirmed that patients with more comorbidities have an increased risk of healthcare-associated BSIs, the study did not investigate to what extent specific chronic diseases had on the associated risk.

Another study investigating comorbidity and mortality was carried out by Fabbian et al.[20] in which a comorbidity score was calculated for each patient. Several comorbidity scores exist, all following the concept that an aggregated score is obtained from weighted scores given to commonly observed chronic conditions. The study observed that an increasing comorbidity score was independently associated with in-hospital mortality (OR = 1.07 per unit of increasing score). Both studies confirm the independent association of comorbidity on the risk of mortality. Aggregated comorbidity scores are commonly used in clinical practice in risk models to identify patients at higher risk of poorer outcomes, including in patients with GNBSIs and sepsis. Although valuable, emerging studies have begun to focus on producing advanced risk scores, using full patient history to understand the impact of multimorbidity (≥2 chronic diseases occurring in combination[21]) on the risk of sepsis-associated mortality.

A large Danish study focused on using full disease history obtained from electronic health records, to predict 30-day sepsis-associated mortality, using data from 120 000 patients diagnosed with an ICD-10 code A41 'other sepsis'.[5] Disease trajectories (defined as temporal sequences of consecutive diagnoses by Beck[5]) were constructed by combining commonly occurring diagnoses pairs with a temporal direction. Results identified that patients following at least one disease trajectory had an increased RR for sepsis-associated mortality compared to patients with no disease trajectory (RR = 1.32). The initial finding validates the results of the Holmbom et al.[19] and Fabian et al.[20] studies, confirming that the presence of multiple chronic

diseases increase the risk of mortality. Furthermore, alcohol abuse, diabetes mellitus and anaemia were found to be major diagnoses for increasing the RR for sepsis-associated mortality. The study highlights how common chronic diseases follow temporal disease trajectories that lead to increased sepsis-associated mortality. In addition, several subgroups of patients with particular chronic disease trajectories have been identified to have a heightened risk of sepsis-associated mortality. Findings from this study contribute to the evidence supporting the use of advanced risk scores in subsequent research and clinical practice. Follow-on studies should compare the ability of multimorbidity models and simple single-score comorbidity models to predict sepsis-associated mortality. Results from this would determine whether the more advanced score has any clinical benefit.

Within the Beck et al.[5] study, more detailed investigation into the relationship of diabetes and sepsis-associated mortality was conducted, as there is debate as to whether it increases or lowers the mortality risk. Diabetes mellitus diagnoses were categorized as insulin-dependent (IDDM) and non-insulin dependent (NIDDM). The study found that IDDM was associated with an increased risk of sepsis-associated mortality (RR = 1.13) whereas NIDDM had no effect (RR = 1.11, $P = 0.15$). This further highlights the importance of identifying the association of specific conditions and sepsis-associated mortality in order to obtain the most accurate risk score. The biological pathways involved in increasing and lowering the risk of sepsis-associated mortality is not fully understood. However, studies such as Beck et al. contribute to building a hypothesis as to why the observations occur, which could ultimately aid clinical therapies for and improve outcomes for patients with diabetes and sepsis.

Similarly, Zador et al.[6] investigated how multimorbidity and subgroups of specific disease combinations were associated with the risk of sepsis and mortality. There were six subgroups identified, with sepsis-associated mortality highest in the hepatic/addiction subgroup, followed by the cardiac, cardiopulmonary and complicated diabetes subgroups.

Both studies confirm that there are specific multimorbidity subgroups that increase the risk of sepsis-associated mortality. As a result, both provide evidence to support the shift away from currently used single-disease models that use simpler comorbidity scores and promote the multimorbid approach for risk modelling and clinical use.

As the population ages and the number of people living with chronic disease increases, frailty is also becoming a widespread public health problem. Frailty is a clinical syndrome that encompasses unintentional weight loss, self-reported exhaustion, weakness, slow walking speed and low physical activity. An American study by Mahalingam et al.[22] sort to determine the association of frailty and long-term risk of community-acquired sepsis within the REGARDS cohort. Frailty was found to be associated with first sepsis events (adjusted hazard ratio, HR 1.44) and 30-day mortality (adjusted odds ratio, OR 1.62). Additionally, the presence of 1, 2 or 3 frailty indicators was associated with first sepsis events (adjusted HR 1.23, 1.54 and 1.78, respectively) and 30-day sepsis mortality (adjusted OR 1.05, 1.53 and 2.03, respectively). The nature of the study meant that recall bias of reporting frailty was likely. Additionally, access to healthcare was not recorded and therefore not adjusted for analysis. This is likely to have influenced the observed association as people with frailty are more likely to have healthcare-associated risk factors including hospitalization and urinary catheters, which increase the risk of infection and sepsis.[23]

Screening tools for sepsis—the NEWS2

As no biological test for sepsis is available, detection relies on laboratory confirmed positive blood cultures, along with identifying patient deterioration and clinical judgement. As part of the Sepsis-3 update to the sepsis definition, the quick sepsis related organ failure assessment (qSOFA) and sequential organ failure assessment (SOFA) were introduced for sepsis-specific screening tools.[3,24]

Table 1 The NEWS2 scoring system. Reproduced with permission from Royal College of Physicians[3]

	Score						
Physiological parameter	3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25
SpO_2 scale 1 (%)	≤91	92–93	94–95	≥96			
SpO_2 scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse (per minute)	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			CVPU
Temperature (C°)	≤35.0		36.1–36.0	96.1–38.0	38.1–39.0	≥39.1	

These incorporated both routinely collected bedside information and tests for urine output as well as bilirubin, platelet and creatinine levels.[3,24] To enable detection using routinely collected patient observations, the UK adopted the use of the national early warning score (NEWS) for aiding sepsis detection.

NEWS

NEWS is a generalized deterioration screening tool, which was implemented to be used as a first line screening tool for sepsis. NEWS is based on a simple scoring system in which a score is allocated to six physiological measurements that are already taken in hospital (Table 1).[7] Indication of sepsis is through augmented scores, which prompts escalation of treatment by clinicians (Table 2).[7] Several studies have confirmed that NEWS has a good predictive ability for in-hospital mortality in patients with infection, with the screening tool having superior accuracy compared to qSOFA.[25,26] A study by Kovach et al.[27] found that NEWS and SOFA have similar predicative accuracy for non-intensive care unit mortality, but SOFA outperformed NEWS for predicting overall in-hospital and ICU mortality.

In contrast, a meta-analysis conducted by Hamilton et al.[28] concluded that early warning scores, including the NEWS and the modified EWS (MEWS), were not able to accurately predict sepsis mortality. The MEWS contains the same parameters as NEWS with the addition of urine output measures. Results identified that combining all six studies of NEWS (one study) and MEWS (five studies), the overall sensitivity and specificity was 62% and 66%, respectively, highlighting the low predictive value. Although an interesting meta-analysis, the low number of studies included highlights an important limitation, so significant conclusions should not be drawn from the study. A future meta-analysis including a greater number of studies would be appropriate and necessary in order to validate the findings.

NEWS2

In 2017, an update of NEWS (NEWS2) was published and introduced into hospital settings across the UK.[7] The update included two modifications of NEWS, aimed to improve the accuracy of detecting general deterioration, including sepsis. Firstly, it was clarified that any new confusion or delirium in patients should prompt a score[7] (Table 1). Secondly, the NEWS2 included an adapted SpO_2 weighting for patients with type II respiratory failure (T2RF) who had prescribed oxygen saturation of 88–92% (Scale 2) (Table 1).[7]

The Pimentel et al.[29] validation study compared NEWS and NEWS2 for predicting all-cause in-hospital mortality. The study found that the NEWS2 had a lower ability to predict in-hospital compared with NEWS, shown through receiver operator characteristic (ROC) curve analysis, for patients with documented T2RF (0.841 vs 0.862), at risk of T2RF (0.860 vs 0.881) and for patients at no risk of T2RF (0.891 vs 0.910). Conclusions from the study suggest that the modifications in NEWS2 do not improve the

Table 2 NEWS thresholds and triggers. Reproduced from Royal College of Physicians[3]

NEW score	Clinical risk	Response
Aggregate score 0–4	Low	Ward-based response
Red score	Low-medium	Urgent ward-based response*
Score of 3 in any individual parameter		
Aggregate score 5–6	Medium	Key threshold for urgent response
Aggregate score 7 or more	High	Urgent emergency response**

*Response by a clinician or team with competence in the assessment and treatment of acutely ill patients in recognizing when the escalation of care to a critical care team is appropriate.
**The response team must also include staff with critical care skills, including airway management.

detection of in-hospital mortality for patients with T2RF. The study focused on all-cause mortality, so conclusions cannot be drawn for sepsis-associated deaths only. Despite this, the results from the study are interesting and future research should compare NEWS and NEWS2 for the ability to predict sepsis-associated mortality.

The implementation of NEWS2 was also criticized by Hodgson et al.,[30] who conducted a retrospective analysis on 2361 patients with acute exacerbation COPD.[31] The NEWS2 was more likely to categorize high risk patients who went on to die (score ≥ 7) into lower risk thresholds compared to the original NEWS, reducing the sensitivity of NEWS2. The study argues that the development of NEWS2 is counter-intuitive to the reasoning of NEWS, as it introduces different scoring subsets for patients, therefore deviating from the original aim of it being a generalized screening tool. Moreover, the use of the adapted SpO_2 weighting relies on an accurate diagnosis of T2RF, which is often revised during the initial admission period. This could lead to an inappropriate use of the selected SpO_2 weighting.

Mohammed et al.[32] further critiqued NEWS2, suggesting that the addition of three points for new confusion or delirium would increase the number of escalation alerts by 21–26%, potentially leading to false alerts. Although an informative study, the effect this had on mortality rates was not investigated. This would have added the value needed to support the clinical benefits of the NEWS2 addition of scores for new confusion/delirium.

Some studies have, however, identified NEWS2 as having a good accuracy for predicting sepsis. In a study by Mellhammar et al.,[33] NEWS2 had a superior ability to predict sepsis-associated mortality compared with the qSOFA in both the data sets analysed (area under ROC curve, 0.80 vs 0.71 in the 2011/12 cohort and 0.70 vs 0.62 in the 2015/16 cohort). Results confirm that NEWS2, like the original NEWS, has a better predictive accuracy than qSOFA. Similarly, Fernando et al.[34] found that in 1708 patients with suspected infection, NEWS2 had good accuracy for predicting in-hospital mortality (area under ROC curve = 0.75). With similar results found within different cohorts, it is evident that NEWS2 is a good predictor for sepsis-associated mortality, similar to NEWS and superior to the qSOFA. From the research available the single, relatively cheap, generalized screening tool, NEWS2, is the most effective method to screen for sepsis. Continued research investigating NEWS2 is welcomed and will support improvements of the screening tool.

ICD-10 coding of sepsis

Monitoring the incidence and associated mortality of sepsis across and within countries is based on administrative data using the ICD-10 codes to establish sepsis cases (A40 and A41 codes). Adequate coding for sepsis is therefore vital to understand trends overtime and to assess whether targets for reducing incidence and mortality are achieved.[35–38] Due to the heterogeneity of sepsis infection source, symptoms, clinical documentation and the subjectivity of coders, the accuracy of ICD-10 codes to correctly identify sepsis has been questioned.[35–38]

A single centre study by Chin et al.[39] established that the term 'urosepsis' was frequently used by clinicians at the University Hospital of South Manchester, UK to document sepsis with a UTI source. Coding guidelines at the time of the study stated that 'urosepsis' may indicate sepsis or localized infection of an organ, which may have contributed to an under reporting of sepsis incidence.[40] As the study was confined to a single centre, it is not possible to determine whether this practice occurred elsewhere and what impact this had on published rate of sepsis incidence.

Another study that investigated the variability of sepsis coding was conducted by Fleischmann-Struzek et al.[38] Two strategies of ICD-10 coding were analysed to establish the impact on sepsis incidence and mortality rates. Using explicit strategies, which use coding approaches for ICD-10 codes for sepsis and septicaemia only, found that some sepsis cases were missed by 2.7-fold, although this strategy did have a good positive predictive power of sepsis. In contrast, the implicit strategy, which uses codes linked to infection and organ dysfunction that mirror clinical sepsis criteria, was found to overestimate sepsis incidence by 3-fold. The resulting differences in sepsis incidence ranged from 227–372 per 100 000 people. The study indicates that due to a lack of gold standard coding guidelines for sepsis, reported rates could vary. This is an important finding as published rates contributed to the development of public health interventions and evaluation of intervention programmes.

In the UK, official guidelines for sepsis coding were updated in April 2017 and 2019, with the aim to improve monitoring of sepsis outcome measures overtime. The changes arose from the numerous reports that varied documentation and coding resulted in inaccurate sepsis incidence and mortality rates, along with the update of the sepsis definition.[37–39,41] Updated guidelines specified that as standard, sepsis cases should be documented and coded as sepsis in the primary diagnosis position, using the A40/A41 codes, followed by the code for source of infection.[42]

Evaluation of how the updated guidelines have impacted on care and coding are yet to be carried out. However, incidence is predicted to rapidly increase as a result of the standard use of the A40/41 codes, as these may have been previously excluded from patient documentation.[2] Mortality trends for specific sepsis codes may require careful interpretation. It has been suggested that any falling trends in mortality for specific sepsis codes cannot be solely attributed to improved patient care. Rates may also be influenced by a diluting effect caused by an increase in coding of patients who are less sick than those who would have been previously included.[2] As a result, evaluation of how standardized coding effects sepsis trends requires assessment in the coming years once adequate levels of patient data have been obtained.

Recently, Inada-Kim et al.[36] developed methods to monitor the incidence and outcome of suspicion of sepsis (SOS) cases, defined as bacterial infections serious enough to warrant hospitalization. The study rationale describes that the sole use of the A40/41 sepsis codes may result in the under-reporting of sepsis incidence and mortality. This is a result of many UK clinicians not reporting sepsis as the primary diagnoses upon hospitalization, instead focusing on the source of infection. The Inada-Kim study therefore suggested that monitoring incidence and outcome measures, such as length of stay and mortality, for SOS cases is best practice to evaluate the success of sepsis prevention and improvement strategies. Results from the study identify that the most common SOS diagnoses include those for UTIs, pneumonia and infection following a procedure. Additionally, both UTIs and pneumonias are associated with the greatest number of deaths of all SOS codes investigated. Results show that it is possible to monitor outcome measures for SOS diagnoses using recorded patient data. Furthermore, SOS codes could be incorporated into risk scores for sepsis-associated mortality to better understand the patients at a higher risk of poorer outcomes.

Over the years, the lack of clarity of a gold standard method of documenting and coding sepsis has resulted in major disparities in reported sepsis

incidence and associated mortality. However, with recent updates, accuracy of both the documentation and coding of sepsis should improve, providing more valuable information on changes to incidence overtime. Furthermore, with the Inada-Kim study addressing the need to monitor SOS cases, there remains further potential to improve monitoring. It will be several years before the impact of these changes can be assessed; however, it can be postulated that more detailed and standardized coding practices will provide accurate and valuable evidence to support future policy recommendations and improvement strategies.

Conclusion

The research available on GNBSIs and sepsis is vast, as it continues to be a significant public health concern. As a result, this review does not exhaust the subject of sepsis risk factors, detection or surveillance systems. Nevertheless, this review gives an overview of the current understanding of the main risk factors associated with healthcare-associated GNBSIs and sepsis. Understanding the risk factors is vital in achieving the goals set out for reducing sepsis mortality. With the increasing epidemiological research into the risk factors, a more detailed and accurate picture of high-risk individuals is forming in order to aid infection prevention, early detection and prevention of sepsis mortality. As the number of individuals living with multimorbidity rises, it is important to further understand how this affects the risk of GNBSIs and sepsis and establish whether screening subsets for a minority of patients is the most beneficial method for accurate sepsis detection. Furthermore, substantial research is required to evaluate whether advanced risk scores can improve the ability to predict poorer outcome in patients with sepsis and establish how it could be incorporated into a clinical setting.

Importantly, but not addressed in this review, is the necessity of a definitive biochemical test for sepsis, which would improve the accuracy of diagnosis and documenting of sepsis. Until this, the ability for the NEWS2 screening tool to accurately predict sepsis-associated mortality requires further evaluation, including in subgroups of patients. Finally, continued improvement of sepsis documentation and coding is required to ensure accurate evaluation of incidence and mortality across the UK. It may be that surveillance programmes steer towards monitoring SOS codes in addition to sepsis codes in order to further evaluate infection prevention programmes.

Authors' biography

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Tony Roberts holds BA (Hons) and an MA in Philosophy and MSc in Health Services Research. He is an NHS measurement specialist with interests in Health Services Research, epidemiology and Statistical Process Control. He is Deputy Director (Clinical Effectiveness), South Tees Hospitals NHS Foundation Trust. Deputy Director, North East Quality Observatory Service. Patient Safety Lead, Academic Health Science Network, North East and North Cumbria.

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