Sepsis and health inequalities: a summary of the evidence

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1 Summary

This report outlines what is known about sepsis and health inequalities, with particular emphasis on findings relevant to the UK. It explores prevalence of sepsis in different groups and what is known about access, experience and outcomes of healthcare for sepsis. It does this as a first step in understanding how sepsis might impact on different groups and to provide a jumping off point for anyone with a specific interest in a particular group, or looking to understand where the major gaps are in the current literature.

Although sepsis is believed to be a leading cause of mortality and critical illness worldwide, definitions have changed over time and vary between countries meaning it is challenging to study through health data (see 3.1.1). Also, sepsis can be caused by a number of different infections and can lead to different organs failing. According to NHS England *"Sepsis is a life-threatening reaction to an infection. It happens when your immune system overreacts to an infection and starts to damage your body's own tissues and organs."* This is based on the Sepsis-3 definition: life-threatening organ dysfunction caused by a dysregulated host response to infection *(see section 2.1)*.

Within the NHS, an aggregate scoring system called NEWS2 uses a basket of six physiological measurements to trigger treatment of suspected sepsis. There is NICE guidelines which seeks to standardise the interventions people receive once sepsis is suspected, including treatment with broad spectrum antibiotics (until source infection is identified), fluids and oxygen (see section 2.3).

The impact of sepsis can be significant, it not only has a high mortality rate (see section 3.1.2) but people who survive often have long-term physical, psychological, and cognitive disabilities (see section 3.1.4). However, in the literature and within NHS datasets, much more is known about mortality and length of hospital stay than the other potential outcomes. Sepsis has a high readmission rate and appears to increase mortality risk after discharge from the first occurrence.

Most of the papers identified in the review were not based on UK data. While there were extensive studies into potential prevalence (noting significant issues with definitions) and mortality, there was significantly less insight into the access and experiences of different populations. An overview of the findings is included in Table 1 below and are colour coded to indicate the strength of evidence: this review found limited high-quality evidence, particularly beyond age and gender.

There are known risk factors which lead to greater incidence of sepsis, some of which contribute to greater severity and mortality. These include:

- Age (very young and very old): typically, sepsis can be harder to identify quickly in these groups and mortality increases with age. This is a common finding and there is UK evidence supporting it.
- Frailty and comorbidities: these factors both increase incidence and mortality. Additionally, functional disabilities often increase after sepsis and may never return to previous levels. Again, this finding is replicated across many studies, although evidence about outcomes beyond mortality is limited.
- Recent surgery or cancer treatment: surgery can be a cause of infection, while cancer treatment can impact directly on the immune system leading to an increased risk of

sepsis. This is a commonly identified risk factor, and the NHS has specific guidance in place for people receiving cancer treatment.

- Learning disabilities: sepsis is considered to be one of the reasons why people with learning disabilities have significantly shorter life expectancies. Sepsis can be difficult to identify, especially if there are communication difficulties, leading to worse outcomes and mortality. Some UK-based evidence has been found for this.
- Living in more deprived areas: there are several lifestyle factors believed to contribute to sepsis incidence, many of which are more common in deprived areas. However, the literature searches found very limited research on this topic, except to confirm higher sepsis prevalence but not mortality in more deprived areas of the UK.
- Pregnancy: although a small proportion of the sepsis population, pregnancy is associated with a higher risk of sepsis. However, there is limited evidence on whether this leads to higher mortality.
- Birth sex: does not appear in the UK-based studies but other studies have identified a higher incidence in males.
- Ethnicity/race: in the USA there is extensive research into the impact of ethnicity and race. There are mixed findings largely due to a high correlation between ethnicity/race and other risk factors including comorbidities and poverty and it is unlikely the findings are directly transferrable to the UK context. The review did not identify any UK based evidence relating to ethnicity.

Across the world, it is generally agreed that sepsis must be treated rapidly to achieve the best outcomes. However, as one of the main elements of treatment is broad spectrum antibiotics there is a tension between early treatment and contributing to antimicrobial resistance (see 2.3.2). Consequently, over time the guidance is becoming more nuanced. Nonetheless, having timely access to healthcare is important, especially as patients do not initially recognise the potential severity of their symptoms. According to survey data, awareness of sepsis in the UK is high, although the nebulous and variable nature of the symptoms may still lead to delays seeking help (see 4.1).

The review did not find any literature that explored in detail how access could vary in the UK by the different groups, except to discuss how difficult sepsis is to identify in some patients. There are bespoke NICE guidelines for children, pregnant women and for health services based in rural areas where it can take longer to reach a hospital (see chapter 4).

Similarly, the review found very limited data about people's experiences of care for sepsis in the UK, and their route to recovery. Due to the high level of comorbidities and potential for long term impacts for those who survive, there is some discussion about the extent to which treatment in an Intensive Care Unit (ICU) is appropriate. This highlights the importance of having informative conversations with the patient and their family.

In conclusion, sepsis can be caused by a number of different infections and can be difficult to identify. Some health inequalities have been identified but often the strength of evidence is weak, or relevant research was not identified. Existing literature is focussed on quantitative outcomes, namely mortality, hospital length of admission, hospital readmission, leaving a gap in existing evidence of a qualitative nature that would give insight into the experiences of different people including their experiences of life after sepsis. Additionally, further research could usefully use NHS data to explore prevalence and outcomes for health inequality groups identified in the table below as having limited evidence currently.

The table below sets out the key evidence identified and is colour coded based on the strength of the evidence, and relevance to the UK context. Grey background means no evidence identified, red is low confidence or conflicting, amber moderate confidence and green is high confidence.

Table 1: Key evidence for each group included in the review.

	Prevalence/outcomes	Access	Experience
Older patients (especially those aged 80+ years)	Higher prevalence, higher mortality, especially with frailty and comorbidities.	Variation in presentation can make identification difficult.	Due to potential for poor outcomes literature highlights importance of discussing appropriate treatment pathway.
Younger patients (especially children aged under 4 years old)	Higher mortality in youngest children.	Symptoms particularly hard to identify in young children (and may be different).	NHS has developed differentiated approach for children (PEWS instead of NEWS2). However, limited information on outcomes and support if child lives.
Physical disability	Frailty and cancer are both risk factors for sepsis and frailty leads to higher mortality.	No information identified.	No information identified.
Learning disability	People with LD have shorter life-expectancy and in part this is attributed to sepsis.	Symptoms can be particularly hard to identify.	Risk that may not get the same treatment as people without LD.
Sex/Gender/Gender reassignment / Sexual orientation	Mixed evidence. Being male *may* increase risk. No evidence on sexual orientation.	Physiological differences are not taken into consideration in NEWS2 score.	No UK information identified.
Marriage / civil partnership	No information identified.	No information identified.	No information identified.
Pregnancy/maternity	Maternal sepsis during / after pregnancy is an important cause of mortality in women.	Physiological differences in pregnancy mean that maternity score has been developed for NHS.	No information identified.

Race / ethnicity	Mixed evidence including one UK study conducted during the COVID-19 pandemic which found white people may have worse mortality rates.	No UK information identified. Higher risk of misinformation and lower sensitivity of blood oxygen saturation measurement may impact.	No UK information identified.
Religion / belief	No information identified.	No information identified	No information identified.
English not first language / Poor health literacy	Limited direct evidence but difficulty communicating and potential for lower vaccine uptake hypothesised to increase prevalence / mortality.	May impact on ability to describe symptoms.	No UK information identified.
Asylum seeker / refugee	No UK information identified.	No information identified.	No UK information identified.
Rural / urban / coastal	No UK information identified.	For remote locations, NICE requires GPs to be able to administer antibiotics for sepsis.	No information identified.
Deprivation / employment / poverty	Some evidence of higher prevalence in areas with higher deprivation, but not necessarily higher mortality. No evidence found relating to employment or poverty specifically.	No UK information identified.	No UK information identified.
Criminal justice	No UK information identified but risk factor according to an American study.	Limited evidence, delayed access due to security may be an issue.	No information identified.
Mental health and substance use	Limited evidence identified, except smoking as a potential risk factor.	No information identified.	No information identified.
Homelessness	No information identified.	Limited information. May be risk of delayed access, as community can delay seeking care.	No information identified.

2 Introduction

This report summarises a review of the literature about sepsis and health inequalities. Where possible it focusses on the UK context, although much of the literature identified is based on American data. The review is made more challenging because the literature suggests sepsis is not consistently recorded in medical data[1].

As there is not extensive research available into sepsis and health inequalities, we have included potentially lower quality data but have included caveats where findings should be treated with extra caution. Where relevant, sample sizes are included as endnotes to each chapter. The main text also identifies where research had a small sample size or focussed on a specific subset of people which might not be generalisable to the UK context. However, we have not undertaken a full assessment of the quality of evidence as the aim was to undertake a pragmatic review to identify what evidence exists, enabling people to deep dive into the audiences that are most relevant to them.

Full details of the approach to the literature searches and inclusion criteria are included in Appendix 1.

The main report body is split into the following chapters:

- Introduction including important definitions
- Sepsis prevalence, incidence and outcomes
- Access to healthcare for sepsis (including speed of access to a diagnosis)
- Experiences of care for sepsis (including experiences after discharge)

Each chapter has an overview and then takes the evidence for health inequality group in turn where information was available. At the end of each chapter there is a summary of the 'missing' health inequality groups for which no evidence was identified in the literature searches. Finally, in Appendix 2 the same data is restructured by inequality group (i.e. prevalence/outcomes, access, and experience for each group) for readers interested in a particular group.

2.1 What is Sepsis?

"Sepsis is one of Britain's biggest killers; tens of thousands of people die in the UK every year, and for those who survive, the consequences can be devastating with organ failure, mental health issues and limb loss. There is evidence of huge variation in the recognition and treatment of sepsis across the country and the need for focused improvements cannot be overestimated."

Celia Ingham Clark MBE, SFFMLM, MChir, FRCS, FRCA Medical Director for Clinical Effectiveness, NHS England[2]

Sepsis is believed to be a leading cause of mortality and critical illness worldwide, but it exists in a spectrum and has changed over time and therefore it is not consistently and accurately captured in health data[3]. The impact of sepsis is significant, it not only has a high mortality rate but people who survive often have long-term physical, psychological, and cognitive disabilities[4].

According to NHS England *"Sepsis is a life-threatening reaction to an infection. It happens when your immune system overreacts to an infection and starts to damage your body's own tissues and organs."*[5]. Sepsis is not a specific illness but rather a syndrome, identified by a collection of clinical signs and symptoms which is what makes it difficult to identify and record accurately in health records. The NHS definition is based on Sepsis-3.

Sepsis-3 – defines sepsis as *"life-threatening organ dysfunction caused by a dysregulated host response to infection. For clinical operationalisation, organ dysfunction can be represented by an increase in the Sequential* [*Sepsis-related] Organ Failure Assessment (SOFA) score..."*[3]. This definition was developed by a task force with expertise in sepsis pathobiology, clinical trials, and epidemiology which was convened by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine. This work sought to develop a definition that could be operationalised in the absence of a standard diagnostic test, and which resulted in fewer errors in classifying sepsis.

This task force also defined septic shock: *"Septic shock should be defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. Patients with septic shock can be clinically identified by a vasopressor requirement..."*[3].

2.2 What are health inequalities?

According to NHS England *"Health inequalities are unfair and avoidable differences in health across the population, and between different groups within society. These include how long people are likely to live, the health conditions they may experience and the care that is available to them."*[6].

This review sought evidence relating to the following characteristics, chosen as they include the protected characteristics as stated in the equality act (2010). They also focus on the Government guidance on health disparities and health inequalities (Oct 2022):

- Age
- Sex
- Deprivation/employment/poverty
- Literacy/education and English not first language
- Gender / sexual orientation
- Pregnancy/marriage
- Race and ethnicity
- Religion / belief
- Asylum seekers / refugees
- Disability
- Mental illness & substance use
- Geography – urban/rural
- Homeless
- Criminal Justice system

There are two important considerations when reading this report: firstly, that these characteristics are often found in combination, and this intersectionality can exacerbate health inequalities further. The report addresses each one separately, but it is important to note this might understate the inequalities experienced by some individuals.

Secondly, the ability to report on health inequalities relies on these characteristics being captured in the relevant datasets. NHS coding of demographic information, specifically race, is

not consistent and therefore has the potential to introduce error into patient's records. Recent work by the Office for National Statistics has demonstrated that of those recorded as white British in health admin data sources, more than 96% reported the same ethnicity in the National Census. However for black and mixed ethnicity records the level of congruence was significantly lower[7]. Missing or incorrect data might also apply for other demographic information, including disability[8] and other social determinants of health[9].

2.3 Sepsis in the UK

According to an NHS report[2], approximately 70% of sepsis cases arise in the community, highlighting that sepsis is both a community and hospital issue. Identifying and treating sepsis quickly, through prompt administration of sepsis therapies, such as intravenous antimicrobials and fluid resuscitation, is associated with both better patient outcomes and lower health care–related costs[10]. Consequently, it is important that community services as well as hospitals are equipped to quickly identify sepsis and ensure timely access to treatment.

A recent large-scale study of NHS data[11] suggested that even more cases of sepsis (79.8%) were community-acquired (defined as a sepsis diagnosis within the first two days of hospital admission) while 20.2% were hospital acquired[a].

2.3.1 NHS response to sepsis

In the past decade, the NHS has established a cross-system sepsis programme drive to improve awareness and support early identification and treatment of sepsis. They concluded that if sepsis was identified and treated earlier it would both improve patient outcomes and save the NHS a significant amount of money and resource[2].

The NHS uses the National Early Warning Score (NEWS), and more recently NEWS2 as a validated approach for detecting patients with infection at risk of sepsis[12]. This approach is not appropriate for children or pregnant women, for whom Paediatric and Maternity Early Warning Scores (PEWS and MEWS) have been developed[13]. Outside of an acute health setting, early warning scores can be used to support decision-making – an approach that can be adapted for use with children, people who are or have recently been pregnant and those in custodial or community settings[14]. There is some discussion about whether or how machine learning might support better clinical decision-making for sepsis, including improving the accuracy of both short and long-term prognosis, developing a more sophisticated approach than tools such as NEWS2[15].

In the UK at the time of suspected sepsis diagnosis, the treatment expectation is labelled as the 'sepsis 6'[16] and continues to evolve. The main elements included in the NICE guidance are senior review, rapid antibiotic delivery , administration of oxygen, intravenous (IV) fluids, taking of bloods and cultures and monitoring[14].

2.3.2 Balancing timely treatment and anti-microbial resistance

Recently, NICE guidelines[8] have been updated to balance two risks: the risk of delaying treatment for sepsis and the risk of over-prescribing broad spectrum antibiotics which can have negative outcomes for the individual and contribute to antimicrobial resistance more generally. While the NICE guidelines still advise that people at high risk based on their NEWS2 score are treated with broad spectrum antibiotics within an hour, in line with a statement by the Academy of Medical Royal Colleges (AMORC) [17] it now recommends a wait of 3-6 hours for moderate or low risk cases, while awaiting results from diagnostic tests so that treatment can be tailored appropriately (unless there are signs of rapid deterioration) [14].

In addition to history, examination and laboratory results, this AMORC paper[17] suggests considering the influence of comorbid disease, frailty and ethnicity but does not explain how ethnicity should impact. Finally, there is discussion of moving to narrow spectrum drugs, if the patient is seen to be improving[17].

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[a] This study used NHS data. included 224,361 (10.2%) cases with non-COVID-19 sepsis and 1,346,166 matched controls. Records between 1st January 2019 and 30th June 2022 were included.

3 Prevalence, incidence, mortality and long-term impact

3.1 Overview

Before examining how sepsis impacts on different groups within the population, this section presents data for the UK overall and compares this with global data. It also highlights measurement challenges which impact on how all data on sepsis can be interpreted.

3.1.1 Measurement challenges

As noted above (2.1) it is difficult to establish the prevalence or incidence of sepsis with much certainty, because it can present in different ways and there is not a single test that confirms the diagnosis[1]. Similarly, estimates of mortality rates may differ, because the cause of death may be recorded as organ failure rather than sepsis[18], not least because many of the people who die with sepsis are of advanced age, frail and have comorbidities[19]. A US study showed that using administrative claims data, sepsis-related mortality estimates were 15% to 140% higher than death certificate data[20].

Some researchers[1] believe that it is more useful to break down the broad definition of sepsis into different subtypes, reflecting that the prognosis varies significantly depending on the cause and health of the patient before onset. For example, research shows that mortality can vary depending on the original infection site, and people with pre-existing conditions (e.g. COPD, cardiovascular diseases, etc) are at a higher risk of contracting sepsis that requires ICU admission[1].

Before trying to estimate the prevalence of sepsis in England, it is important to consider the findings of Rezel-Potts et al[21] who looked at the relationship between Office for National Statistics (ONS mortality records), GP Electronic Health Records (EHR) and Hospital Episode Statistics (HES). They found, among the 13,972 deceased patients with sepsis listed as any cause of death, only 2,438 (17%) had an incident sepsis event recorded in their GP EHRs and only 3,397 (24%) had incident sepsis events recorded in HES in the same period. Significantly, only 614 patients had index sepsis events recorded across all three data sources within 30 days of the date of event or date of death.

The methodological approach and definitions used in the studies identified vary significantly. This issue has been identified by other people seeking to review the available literature relating to sepsis and social determinants of health[22].

3.1.2 Numbers of sepsis cases and mortality in the UK

NHS data[23] relating to hospital admitted episodes of sepsis shows there were 489,000 sepsis cases in 2023-24 and in approximately half of those cases it was the main diagnosis[b]. Over half (54%) of the cases were male, 7% were in children aged less than 1 and 45% were in adults aged over 75. Rates of sepsis appear to have declined since the new Sepsis-3 definition was introduced, although since 2021 they appear to be relatively steady. However, according to ONS the number of deaths in England and Wales where sepsis was the underlying cause has risen from 2,630 in 2018 to 4,276 in 2023[24].

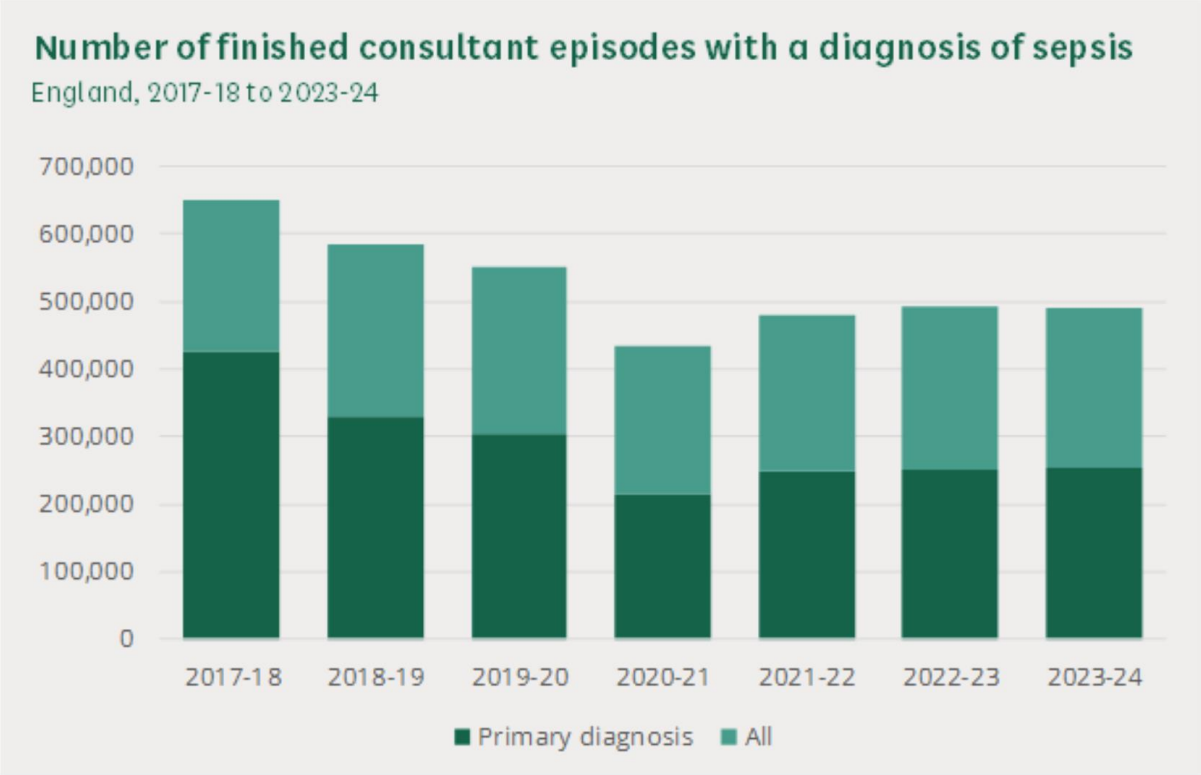

Figure 1: Sepsis diagnosis in hospital admissions[24]

The UK-based Sepsis Trust estimates that there are at least 245,000 cases of Sepsis in the UK every year[25], based on their own analysis of Hospital Episode Statistics (HES) data in 2017 and which they say is corroborated by a global study by Institute for Health Metrics and Evaluation (IHME)[26]. The changing definitions, and different incentives for recording cases, make it difficult to establish whether or not the number of cases is changing over time[27].

In their 2020 report, the Academy of Medical Royal Colleges[17] suggest sepsis could be more common. They state *"It is estimated that there are in the region of 918,000 adult sepsis admissions per year, and 66,096 deaths in the UK."* which is a higher incidence but lower rate of mortality than other sources. They go on to say *"In high- and middle-income countries, deaths from sepsis afflict primarily the elderly, frail, those with comorbid diseases, and the immunocompromised, many of whom are at or near the end of life. In children, sepsis occurs in fewer than a quarter of those presenting to hospital with infection, and mortality rates are low."*

National data from England in 2017–2018 (population 55.6 million) identified 1.73 million emergency hospital admissions with a discharge code indicating either bacterial infection or sepsis as the reason for admission[19], while data on UK critical care admissions with an ICU discharge diagnosis of sepsis based on data from 2015 numbered 44,115 (including admissions for hospital-acquired sepsis), of whom 13,455 died[19].

According to the source paper for these statistics[28], *"Sepsis-3 sepsis accounted for a third of admissions to adult general ICUs in England between 2011 and 2015"*. They calculated that the extrapolated population incidence increased from 88 to 102 per 100,000 person-years and that people with Sepsis-3 septic shock were around one-fifth of the sepsis population (approximately 19 per 100,000 person-years). The calculated acute hospital mortality for Sepsis-3 sepsis was 30% in 2015 and the acute hospital mortality for Sepsis-3 septic shock was 56% in 2015.

3.1.3 Worldwide sepsis mortality

A systematic review[29] of 170 studies published between 2009 and 2019 focussed on sepsis mortality and identified a 90-day sepsis mortality of 32.2% (95% CI: 27.0–37.5%) and 90-day septic shock mortality of 38.5% (95% CI: 35.4–41.5%). Rates varied between regions, with slightly lower mortality rates in Europe compared with North America. A smaller scale review of 51 studies published between 2015 and 2019 (which included 4 studies from low/middle income countries published from 1979 to 2019 to improve coverage of these countries), found incidence was 189 per 100,000 person-years and found an estimated 26.7% mortality [30]. As the incidence and mortality rates vary considerably between studies[31], depending on assumptions made, it is difficult to draw meaningful conclusions about the UK and how it is performing.

A Dutch study (2021)[18] looking at cause of early mortality on admission to an Intensive Care Unit (ICU) with sepsis (i.e. death within 48 hours of entering the ICU), found that early mortality occurs frequently in sepsis, mainly as a result of multiple organ failure, mesenteric ischaemia, and death after unsuccessful CPR. A retrospective review of the patient records by a panel of experts found that delayed or futile admission to ICU were frequently reported as the reason for early death, although the researchers note that their experts often disagreed. Cases of mesenteric ischaemia were often only identified in autopsies and otherwise may have been missed.

3.1.4 Other sepsis outcomes

While some people who have sepsis recover completely, it is not uncommon for sepsis survivors to experience long term impacts of their illness. A survey of American pensioners[c] showed self-rated health worsened initially after sepsis and only returned to the level of the control in year 6, and that sepsis survivors experienced lasting functional disabilities[32]. Sepsis survivors report both cognitive impairments, fatigue and lethargy[33], and new functional limitations (e.g. leading to reduced ability to exercise) as well as mental health impacts including depressive symptoms, anxiety and post-traumatic stress disorder[34]. Survivors may also live with long-term organ dysfunction, chronic pain and potentially amputation[35]. Following sepsis, people frequently experience a deterioration in overall health and are more likely to die than people who have not had sepsis[33].

Sepsis patients are at high risk of unplanned readmissions within 30 days, different reasons have been given to explain this including prolonged immunosuppression, physical weakness and deconditioning, impaired cough and swallowing and cognitive impairment[36]. In terms of demographics, a systematic review[37] showed that one in five sepsis patients are re-hospitalised, with an increased risk for older people, males, those with comorbidities, those discharged to somewhere other than home (e.g. a care home) and factors associated with their experience of sepsis such as infection and illness severity. It also found the main reason for rehospitalisation was infection (including sepsis)[37]. In the USA, social determinants such as low income, education, no healthcare insurance and lack of transportation have been shown to lead to higher readmission rates [36], [38].

A review looking specifically at Computerised Clinical Decision Support System use in the identification of sepsis noted that the studies tended to focus on patient outcomes such as mortality, sepsis identification, length of stay and admission to ICU, rather than longer term outcomes relating to life after sepsis[10].

Although not frequently mentioned, some papers reported that there is also potential for post-intensive care syndrome, anxiety and depression in family members of patients with severe sepsis, whether or not the patient died in ICU[39], [40], [41].

3.2 Epidemiology and risk factors

As noted above (3.1.3), it is difficult to compare data on sepsis between countries. However, the majority of published studies identified come from the USA and without them there would be limited data. Therefore, when this report draws on data from other countries, this is made clear in the text.

Starting with NHS data, there are known risk factors which lead to greater incidence of sepsis[17] [11] [42], some of which contribute to greater severity and mortality (see detailed sections below). These include:

- Age (very young and very old)
- Frailty and comorbidities
- Recent surgery or cancer treatment
- Learning disabilities
- Living in more deprived areas

Although sex does not appear in the UK-based studies, other studies[1],[43] have identified higher incidence among males, and one study[d] found the effect of high age was more than twice as high in men than in women[44].

There is some limited evidence that there are more sepsis cases in winter, perhaps due to higher rates of respiratory infections, and that mortality rates are higher in winter, even after controlling for severity[1]. Similarly, people admitted at the weekend may be more likely to die within both 7 and 30 days post admission[45].

A recent study[e] using NHS hospital data[11] found a number of factors that increase the risk of developing non-COVID-19 sepsis which are not directly covered in the sections below but which may be related to health inequalities, including:

- Patients living with underweight or obesity
- Smoking history
- Potential care home status
- Chronic kidney disease (CKD) or Renal Replacement Therapy (RRT) and organ transplantation
- Other diseases, including diabetes (not controlled), malignancy (haematological and non-haematological), chronic liver disease, cancer, other neurological diseases, immunosuppressive condition.

Another UK study examining community-acquired sepsis cases[f] found that strong predictors for sepsis included antibiotic exposure in prior 2 months and being house bound, in addition to confirming some of the factors listed above (cancer, diabetes). However, the findings also note that recent antibiotic users had lower rates of mortality[42].

A systematic review of community onset sepsis in high income countries (North America, Australasia, and North/Western Europe) supported many of these findings and also identified studies that demonstrated an excess risk for sepsis in participants with other clinical conditions (e.g. lung disease, and peripheral artery disease) and for those who are physically inactive[31]. A

Swedish study also found that low education was positively associated with sepsis[44] although it is not clear if this finding would apply in a UK context

An American study[g] concluded that *"previously healthy patients may be more likely to die when they seek treatment at the hospital with sepsis compared with patients with comorbidities."* [46]. There is no evidence of this in the UK-based studies identified, but the UK-based studies did not analyse their data in a way that would test this finding directly.

Preventing sepsis [47]

While this report mainly focusses on who gets sepsis and the impact that it has, it is also important to note that sepsis is caused by infections, so sepsis may be prevented by avoiding infections or treating them early. This can be achieved through good personal hygiene, having appropriate vaccines, eating a healthy diet and breastfeeding newborns. Some of these behaviours might be less common in some health inequality groups and therefore might contribute to higher rates of sepsis.

3.3 Age

Of all the demographic factors which are discussed relating to sepsis, age is one of the most frequently mentioned. Studies consistently show higher mortality in older people, especially the very old (i.e. 80+ years) and frail[11] [13], [42], [48].

The majority of hospital admissions are for older people and also for children under 4 years[1]. Studies differ on their assessments of rates of child mortality. One study of UK patients found that 77.5% of sepsis-related deaths occur in patients over 75 years with 150 deaths per year occurring in children between 0 to 18 years of age[1], while NICE evidence suggests that the rate in infants under one year is similar to that in people aged 60 years and over[13]. These statistics may not be contradictory but instead point the increased risk of mortality for the very youngest and oldest in society.

3.3.1 Older people

Different reasons are given for increased sepsis-mortality amongst older people. These reasons include potentially delayed treatment, as confusion may not be considered an indicator of an acute problem in the elderly[13], increased likelihood of co-morbidities or increased rates of Do Not Attempt Resuscitation (DNAR) instructions in place[49]. A study based on UK GP records[h] found that severely frail patients had both a higher risk of developing sepsis and a case fatality rate of 42.0% compared to 24.0% in non-frail patients (adjusted OR 1.53)[42]. As discussed below (5.2.1) higher mortality may also be recorded because it is not always appropriate to admit an old, frail patient with multiple comorbidities to intensive care, and therefore while sepsis is coded as the cause of death this will be in the context of other factors.

A study looking specifically at sepsis after appendectomies noted that, while cases are rare, being aged over 60 years increased the risk of sepsis and sepsis related morbidity and mortality[50]. Similarly, a secondary analysis of multinational data on adults with intra-abdominal infections[i] found mortality increased with age: 20.9% in middle-aged patients (aged 40-59), 30.5% in young-old patients (aged 60-69), 31.2% in middle-old patients (aged 70-79), and 44.7% in very old patients (aged ≥80 years)[49].

3.3.2 Children

While the evidence suggests that older adult mortality is higher than child mortality from sepsis, it remains one of the leading causes of morbidity and mortality in neonatal and paediatric age groups worldwide[51]. This is due to a combination of factors including changes that occur as the immune system develops, making the youngest children most vulnerable[51], and childhood comorbidities. In high income countries, these comorbidities commonly include chronic non-infectious conditions, such as malformations or impairments, neuromuscular conditions such as seizures, cerebral palsy and immune suppression (for example, as a result of chemotherapy) or immunodeficiency such as sickle cell disease[51]. An American study[j] found that more than two out of three children admitted with sepsis had at least one chronic disease, and that these children had higher mortality than previously healthy children [52].

The National Child Mortality Database programme found that across the entire cohort of infection related deaths in England[k] (n=1507) the clinical signs of sepsis were reported in 701 deaths. In 478 cases this was the only clinical condition/presentation identified. The review found that the highest risk of death from any infection was in children described as African (2.90 per 100,000 children), Pakistani (2.52 per 100,000 children), or having any other Asian (3.77 per 100,000 children) ethnic background. The report noted that these ethnic groups also have higher rates of early-onset neonatal sepsis due to Group B Streptococcus [53].

Studies from Netherlands[54] and America[55] focusing on neonatal cases, suggest that experience in hospital can impact on a child's length of stay. Specifically, having a single family room may lead to less late onset sepsis and a shorter length of stay with sepsis[54], while, as discussed further below (3.8) race can also lead to disparities in outcomes, especially for African American infants living in the USA[55]. The literature searches did not identify any UK evidence on this topic.

Children with developmental disabilities (e.g. impairments in communication, feeding and motor function) may also be at risk of poorer outcomes. A small-scale American study[l] found that children with developmental disabilities were more likely to have a sustained worse quality of life after discharge, than children with other conditions or who were healthy before sepsis[56]. Similarly, a study in Taiwan[57] found that surgical patients with an intellectual disability had an increased risk of postoperative sepsis and 30-day mortality, after controlling for demographic factors and comorbidities[m]. The authors suggest that reasons could include generally being in less good health, difficulties communicating, immune abnormalities, poor hand hygiene, and poverty.

Studies in low income countries have found that children with sepsis-associated liver injury (which occurred in one third of their sample) had a twofold higher risk of mortality than those without liver injury[58]. Another study in Argentina found that lower socioeconomic conditions were associated with higher prevalence of sepsis but similar outcomes[59]. Comorbidities such as malnutrition, HIV infection, tuberculosis, and chronic malaria are also associated with increased susceptibility to childhood sepsis in low income countries[51]. Neonatal sepsis may also be associated with cultural practices and beliefs relating to care for the umbilical cord, with some practices considered to potentially put children at increased risk[60]. Again, the literature searches did not identify any studies discussing these issues in the UK context.

3.4 Deprivation/employment/poverty

A NICE Equality Impact Assessment for Sepsis guidelines concluded *"Evidence suggests that there are increased barriers to care access for people with low socioeconomic status which*

include cost, transportation, poor health literacy and lack of social network which potentially contributes to the identified disproportionate impacts felt by this group." [13].

There is UK-based evidence[n] that the most socioeconomic deprived quintile of addresses, defined using the Index of Multiple Deprivation, are associated with higher odds of developing non-COVID-19 sepsis than the least deprived quintile (crude OR 1.80). However, deprivation was found to be only moderately associated with increased mortality[11]. A study using UK GP data[o] had similar findings [42], and again showed increase risk of sepsis but not necessarily higher rates of mortality for people living in areas classified as having high deprivation.

These findings are similar to those found worldwide. A scoping review also found evidence from other countries that socio-economic status is inversely related to the risk of sepsis[22] and an American review found that neighbourhoods with relatively low median income levels, low insurance rates, and low rates of higher education experience relatively higher sepsis related mortality[61]. Equally, these factors plus economic and housing instability have been identified as a predictor of unplanned hospital readmissions[36].

The literature searches did not find any data relating to employment and poverty and sepsis.

3.5 Literacy/health literacy/education/English not as first language

The literature searches found limited data on the topic of literacy, health literacy education and English not as a first language. As noted above (2.3.1) the NHS website warns that sepsis can be particularly hard to identify in people who have difficulty communicating and this could potentially include people who do not have English as a first language[5]. However, a relatively small American study[p] found that having limited English proficiency did not impact mortality odds overall, but did among white people with limited English proficiency (e.g. Russian, Arabic) which they hypothesised could be due to limited access to interpreters [62].

Throughout the literature there is an emphasis on the importance of recognising sepsis and seeking help, which might be less common amongst those with lower health literacy. This could have an indirect impact, as people with low health literacy may be less likely to have engaged in vaccination programmes so could be more vulnerable to developing sepsis[13].

As outlined above (3.4), lower rates of education have been associated with higher sepsis incidence in the USA, and also higher unplanned readmission rates [36] and a German study had similar findings [63]. The literature searches did not identify any UK studies that looked at education and sepsis.

3.6 Sex/Gender/sexual orientation

The evidence about whether sex (i.e. biological sex) impacts on prevalence or mortality is mixed [64] and no primary evidence relating to gender (i.e. social / cultural identity) or sexual orientation was identified. On balance, it appears that males may be more likely to develop sepsis [43] with some studies also indicating a higher risk of mortality compared with females[1]. However, not all studies have found this and some have found the reverse [65], [66].

As noted above, there may be a relationship between sex and age, with one study finding the effect of high age was more than twice as high in men than in women [44]. Suggested reasons for these differences between the sexes include genetic differences, the impact of oestrogen, prevalence of infections and behavioural differences as historically men may have been more likely to smoke or drink alcohol [43].

An American study also found that unexpected readmissions within 30 days of a sepsis diagnosis were more common among men [36].

The literature searches did not identify any research into sexual orientation and sepsis prevalence.

3.7 Pregnancy/marriage

Maternal sepsis is an important type of sepsis in women, and an important cause of mortality during and after pregnancy. As with all sepsis, estimates of incidence differ, ranging from 1 per 100,000 maternities (i.e. during pregnancy or within 42 days of the end of a pregnancy) to 4.9 per 10,000 live births, and cases of non-severe sepsis ranging from 198 per 100,000 maternities to 10 per 10,000 live births [67].

The most recent data on maternal deaths for the UK [68] (the MBRRACE maternal mortality 2021-23 report) found a rate of 0.5 per 100,000 maternities from pregnancy related sepsis and 0.75 per 100,000 indirect sepsis (e.g. from influenza or pneumonia).

An older UK based study[q] found pneumonia and genital tract infections were the most common sources of sepsis, and caesarean section was also a significant risk factor [69]. Young women (aged 16-19) had the highest ICU admission rates, both as a proportion of all ICU admissions for that age group, and as a proportion of all maternities in that age group, but had the lowest mortality rate [69]. Women aged over 40 also had elevated risk compared to those aged 20-39. Similarly, coming from an area with high deprivation led to higher risk. The absolute risk of mortality was 1.8 per 100,000 maternities [69]. Another UK study found that black pregnant or postpartum women were at higher risk of severe sepsis, along with women who had taken antibiotics in the fortnight before presenting with sepsis [70].

In line with sepsis risk factors, older age, increased BMI, black and other ethnic minority race, increased deprivation and pre-existing medical conditions were associated with higher risk, alongside risks associated with delivery by caesarean section [67]. There is some evidence that mortality in pregnancy associated severe sepsis may be lower than in non-pregnancy associated severe sepsis; mortality rates vary from 10.7% to 1.8 per 100,000, and one study found zero mortalities [67].

The review found no studies that explored whether marriage impacts sepsis prevalence or outcomes directly, although one study did suggest that while older men with sepsis may have a living wife who will advocate for their treatment, older women may be widows and their children might make different views about what is in their best interest [66].

3.8 Race and ethnicity

A recent study of NHS data[r] found that individuals of South Asian descent were observed to have a higher incidence of sepsis, while those categorised under the 'other' ethnic groups demonstrated a reduced incidence compared to individuals of white descent[11]. However, it also found that for community-acquired non-COVID-19 sepsis, the 30-day mortality rate was highest in patients of white ethnicity[11].

A recent systematic review [67], which mainly relied on data from the USA, found that there was no consistent pattern, and that sepsis incidence and mortality rates for black and white patients were different in each study with neither group consistently showing higher incidence or mortality. Some American studies have found sepsis mortality to be higher in black and Hispanic

patients, but suggest this might be a result of the quality of care in hospitals in different areas, rather than race[1], or due to health disparities based on lack of ambulatory care, socioeconomic factors and comorbidity rather than race [71], [72], [73]. Other studies suggest, ethnic minorities in the USA experience higher rates of infectious diseases[13], postoperative complications [74] [75] and smoking [75] which may lead to higher sepsis prevalence.

3.9 Asylum seekers/refugees

There is limited evidence in the UK about sepsis for asylum seekers or refugees. Evidence from Denmark suggests migrant status might be linked to a higher risk of bloodstream infections [76]. A NICE Equality Impact Assessment for Sepsis guidelines[13] stated *"These populations will often embark on arduous journeys and combined with often precarious living and housing circumstances may impact their nutrition and their immune system contributing to increased risk of developing sepsis and making infection source identification and control challenging."*. However, a small scale study[s] of maternal outcomes by asylum seeking status did not show a statistically significant difference in suspected sepsis [77].

3.10 Disability

3.10.1 Learning disabilities

People with learning disabilities die on average 16 years earlier than the general population in England, which at least in part has been attributed to sepsis [78]. A UK-based study[t] using GP data [42] found having a learning disability was strongly associated with the risk of developing community-acquired sepsis (crude odds ratio of 3.0) and also associated with higher hospital acquired sepsis. The 2022 Learning Disabilities Mortality Review (LeDeR) Annual Report [79] found that sepsis is a key contributor to premature mortality, with 14% of deaths being recorded as sepsis related – the second highest cause after pneumonia. A Taiwanese study of child surgical patients with learning disabilities[u] found them to be at increased risk of sepsis and 30-day mortality, and also longer hospital stays [57].

3.10.2 Frailty

While disability and frailty are not synonymous, as noted above (3.3.1) frailty is often listed as a risk factor for sepsis and sepsis mortality. For example, a UK-based study[v] using GP data [42] found severe frailty was strongly associated with the risk of developing sepsis (crude odds ratio of 14.9). Additionally, it found that severely frail patients had a case fatality rate of 42.0% compared to 24.0% in non-frail patients (adjusted odds ratio 1.53). A separate study showed that increased risk remained, even after controlling for age, sex, obesity, and other comorbidities [22].

3.10.3 Cancer

Similarly, while cancer is not a disability, cancer survivors are often identified in the literature as being at a heightened risk of sepsis, and cancer patients have higher odds of frailty (see 3.10.2). Even after controlling for the impact of frailty, an American study[w] found cancer survivors were more than twice as likely as patients with no cancer history to develop sepsis [80].

3.11 Mental illness and substance use

We identified very limited evidence relating to mental illness or substance use, noting that smoking is considered a risk factor (see 3.2 above). A study of cancer patients in Sweden[x] found that preexisting psychiatric disorders were associated with an increased risk of sepsis after

cancer diagnosis [81]. The positive association was consistently noted among patients with different demographic factors or cancer characteristics, for most cancer types, and during the entire follow-up after cancer diagnosis [81].

3.12 Geography - urban/rural/coastal

In Germany, distance to the nearest pharmacy has been associated with crude and age standardised sepsis incidence [63]. However, another study[y] found that living in a rural location in Germany was associated with both short- and long-term survival benefits for patients with community-acquired sepsis [82] and the authors hypothesise that this is due to environmental factors (e.g. higher stress in cities, higher levels of pollutants). In the USA, delay receiving medical care due to lack of transportation was strongly associated with 30-day readmission [38].

An American study[z] showed a relationship between exposure to small particulate matter ($PM_{2.5}$) and increased sepsis mortality risk, especially for older people living in urban areas [83]. However, other studies have not shown the same association [83].

UK literature appears to focus on deprivation but does not directly explore differences in outcome by geography.

3.13 Homeless

There was limited literature about the impact of sepsis for people who are homeless. NICE[13] concluded *"People experiencing homelessness are more likely to delay seeking care and there is non-UK evidence (USA) to suggest that they are more likely to die following an admission for severe sepsis which is linked to the increased likelihood of delayed presentation"* based on a paper by Shahryar et al [84]. A small Korean study[aa] found that homelessness did not impact on hospital and ICU mortality rates or length of stay.

3.14 Criminal justice system

The literature searches did not identify any information about people in the UK criminal justice system and sepsis. An umbrella review of mental and physical health morbidity in prison populations did not identify sepsis as a significant cause of mortality [85]. However, in the USA[bb], a small scale study found inmates were 2.8 times more likely to die from sepsis than non-inmates [86].

3.15 Missing evidence

The literature searches did not find any data about sepsis prevalence, incidence and mortality related to:

- Employment or poverty
- Sexual orientation
- Religion / beliefs
- Physical disability

The searches also did not find any relevant UK data about sepsis in the following groups:

- Literacy, health literacy, education or English not as a first language
- Mental illness and substance use
- Geography – urban/rural/coastal

- Marriage
- Homelessness
- Gypsy and Roma travellers
- Criminal justice system

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[b] Includes all episodes Admitted Patient Care activity in England for the financial year 2023-24. Codes: Streptococcal sepsis, Other sepsis, Puerperal sepsis and Bacterial sepsis of newborn

[c] 758 individuals were selected for inclusion in the sepsis cohort who were matched to 758 individuals who were not hospitalized. The survey was with people aged 65+ and was repeated every two years. Eight years after the baseline survey, 618 (81.5%) individuals in the sepsis cohort and 496 (65.4%) in the nonhospitalized cohort had died.

[d] A nationwide open-cohort study was conducted on all individuals ≥ 18 years of age during the period January 1, 1997, to December 31,2018, in Sweden. A total of 161,558 individuals were diagnosed with sepsis during the study period.

[e] This study used NHS hospital data. It included 224,361 (10.2%) cases with non-COVID-19 sepsis and 1,346,166 matched controls. Records between 1st January 2019 and 30th June 2022 were included.

[f] This study used NHS GP Electronic Patient Records data. It included 108,317 cases of community-acquired sepsis for patients aged 65-100 between Jan 1 2000 and July 1 2020.

[g] Sample was 6,715,286 hospitalized patients - adults with community-onset sepsis hospitalized in 373 US hospitals from 2009 through 2015 using clinical indicators of presumed infection and organ dysfunction

[h] The overall study population consisted of patients aged 65–100 years at any time during the observation period (from January 1, 2000, to summer 2020 who were registered at a GP practice in England. It included 108,317 cases classified as community-acquired sepsis.

[i] An observational study which included patients with intra-abdominal infection from 309 ICUs in 42 countries (January-December, 2016). The cohort included 2337 patients.

[j] This study used the 2013 Nationwide Readmissions Database (NRD) and included non-neonatal patients <19 years old hospitalized with sepsis. A total of 16,387 admissions, representing 14,243 unique patients, were included in the analysis.

[k] Data from April 2019 to March 2022

[l] Secondary analysis of Life after Paediatric Sepsis (LAPSE) investigation. Of 392 LAPSE participants, 137 were identified by their caregiver as having a severe developmental disability.

[m] Based on claims data from Taiwan's National Health Insurance programme from 2004 to 2013, which included 220,292 surgical patients aged 6 to 17 years. A propensity score matching procedure was used to select 2173 children with intellectual disability and 21,730 children without intellectual disability for comparison.

[n] This study encompassed 248,767 cases with non-COVID-19 sepsis from a cohort of 22.0 million individuals spanning January 1, 2019, to June 31, 2022.

[o] The overall study population consisted of patients aged 65–100 years at any time during the observation period (from January 1, 2000, to summer 2020 who were registered at a GP practice in England. It included 108,317 cases classified as community-acquired sepsis.

[p] A total of 2709 patients met the inclusion criteria in a large academic medical centre in New England, USA.

[q] Study used the Intensive Care National Audit & Research Centre (ICNARC) Case Mix Programme (CMP) database between 2008 and 2010. In 2008, 2009 and 2010, coverage of the database was 65.0%, 75.2% and 80.2% of critical care units in England, Wales and Northern Ireland. There were 646 pregnant or recently pregnant women who met the case definition for severe sepsis, which represented 14.4% of maternal critical care unit admissions.

[r] This study used NHS data. It included 224,361 (10.2%) cases with non-COVID-19 sepsis and 1,346,166 matched controls. Records were from between 1st January 2019 and 30th June 2022.

[s] Sample included 34 asylum seeking women with term born infants. compared to age- and ethnicity-matched controls delivering at the same hospital.

[t] The overall study population consisted of patients aged 65–100 years at any time during the observation period (from January 1, 2000, to summer 2020 who were registered at a GP practice in England. It included 108,317 cases classified as community-acquired sepsis.
[u] Among the 3,984,581 Taiwan residents who underwent major inpatient surgery (defined as procedures requiring general, epidural, or spinal anaesthesia) and who were hospitalized for more than 1 day in 2004 to 2013, we identified 220 292 surgical patients aged 6 to 17 years. Of these, there were 3294 children and adolescents with a history of intellectual disability before the index surgery.
[v] The overall study population consisted of patients aged 65–100 years at any time during the observation period (from January 1, 2000, to summer 2020 who were registered at a GP practice in England. It included 108,317 cases classified as community-acquired sepsis.
[w] 28,062 participants were included in study analysis of which 2,773 were categorized as cancer survivors
[x] A cohort study of 362,500 patients with newly diagnosed cancer during 2006–2014 in Sweden
[y] Study considered 118,893 hospitalized patients with community-acquired sepsis in 2013-2014 with direct hospital admittance.
[z] Based on enrolment data from the Centers for Medicare and Medicaid Services for 53 million Medicare beneficiaries (ages 65–120) living in the conterminous US between 2000 and 2008.
[aa] Data for a total of 5, 359 ICU admissions during the study period were retrieved. This final propensity-matched sample comprised 56 homeless and 112 non-homeless patients.
[bb] The study cohort included 8,568 cases of sepsis, of which 8,448 were non-inmates and 120 were inmates.

4 Access to healthcare

4.1 Introduction

Sepsis can be difficult to identify, and decline can happen quickly. As noted above (2.3) access to rapid treatment is considered essential. While approximately one in five sepsis cases start in hospital, the majority occur in the community. Therefore, it is important that people recognise the potential severity of their condition and seek help quickly. A recent survey by YouGov for the Sepsis Trust[cc] found 94% of people in the UK are aware of sepsis, with 91% recognising it as a medical emergency; an increase from 76% in 2019 and baseline levels 27% in 2012 [87]. However, only 31% thought they would be confident recognising if they or someone else had sepsis [87].

As discussed above, the symptoms of sepsis can be varied and difficult to spot. However, there are some circumstances in which sepsis is more likely (e.g. after surgery, during and after pregnancy and when immunosuppressed, for example when receiving cancer treatment). Therefore, the NICE guidelines suggest that extra effort should be made to make these patients aware of the signs, symptoms and potential severity of sepsis [88] with additional guidance in place specifically for people receiving treatment for cancer [89]. Work by The Sepsis Trust in the UK is identified as good practice in increasing awareness [90].

According to the NHS[5], sepsis can be especially hard to spot in the following groups:

- babies and young children
- people with dementia
- people with a learning disability
- people who have difficulty communicating

Each of these groups are likely to have more difficulty communicating, and any cognitive decline may be harder to identify. As such, it is possible it will take people form these groups (or their carers) longer to realise they may have sepsis.

The literature searches did not find any information about health beliefs and any impact this might have on sepsis.

Evidence from the USA[dd] suggests that emergency healthcare professionals (paramedics and emergency physicians) rarely documented a suspicion of sepsis, and vital signs measurements, in particular temperature, were often absent [91]. There is potential for computerised clinical decision support systems[10] or AI (Artificial Intelligence) models [92] to improve this, although they will still need to fit within the healthcare environment in order for them to be used effectively. There is some evidence that implementing standardised tools can improve the identification and escalation of sepsis, and improves outcomes as a result[16].

4.2 Age

4.2.1 Older people

The literature searches did not identify any information about access to healthcare for older people with sepsis. As noted above, some of the impacts of sepsis on cognitive function may be harder to identify in older people, which might delay access to healthcare. Additionally, older people may not develop a raised temperature, or increased heart rate but may develop a new

heart arrhythmia [93]. It is also possible they may struggle with health literacy due to cognitive decline, lack of familiarity with digital tools, and complex health information [94].

4.2.2 Children

It can be difficult to identify sepsis in children, and there are gaps in evidence around sepsis care for children [51]. Sepsis is particularly common in children aged under 1 year, and initially symptoms may look like other common illnesses or teething which may delay parents seeking help, especially if they are not aware of the risk of sepsis [95]. A review of child deaths[ee] from infection found that in 18% of deaths the recognition of suspected sepsis was not timely and in 12% of cases the child did not receive broad spectrum antibiotics within an hour. In most cases (85%) there were one or more red flags for sepsis when the child reported to hospital, and these were recognised in 77% of deaths. However, in 8% of cases, red flag symptoms were present but not recognised [53].

The NEWS2 assessment is not appropriate for children as they may present differently; they may not have a high temperature, may have a lower baseline heart rate so that an increase is harder to identify, and changes in their cognitive state may present as changes in behaviour and irritability [93]. Consequently, there are separate guidelines for assessing children [96] using the national Paediatric Early Warning Score (PEWS).

4.3 Sex/Gender/sexual orientation

In the NHS, most regions use the NEWS2 to identify sepsis and the appropriate treatment pathway. However, neither NEWS2 or the Sequential Organ Failure Assessment (SOFA) score take into consideration the different physiology of men and women.

A study using Swiss ICU data[ff] found a statistically significant difference of the total SOFA score on admission between women and men, driven by differences in the coagulation, liver and renal SOFA (laboratory-based) components [97]. Differences between sexes were more prominent in younger patients (aged 52 and under) [97]. Despite the differences in SOFA score, the women did not have better short-term outcomes and the paper suggests that differences in physiology mean that differences in laboratory scores for men and women need to be better understood [97].

4.4 Deprivation/employment/poverty

A committee meeting about the NICE guidelines for sepsis[13] discussed that socio-economic factors may have an impact on the recognition, diagnosis, and early management of sepsis. The Local Government Association also state in a recent report [94] *"People with lower income and education levels often have limited access to health information and resources, making it harder for them to make informed health decisions."* However, no further evidence was identified to support this perspective.

4.5 Literacy/health literacy/education/English not as first language

According to the equality impact assessment (EIA), the NICE committee reviewing the guidance considered that because 'history taking' is very important in the process of identifying sepsis, and that people with communication difficulties or those who do not speak English may not be able to give a history, this could lead to differences in access [13]. This could be true across the population as a whole, but the committee noted that it might be a particular issue where information leaflets were being used to raise awareness among those at higher risk of sepsis[13].

4.6 Pregnancy/marriage

The standard tools for diagnosing sepsis (including NEWS2) are not appropriate for people who are pregnant or who have recently been pregnant[14]. For example, baseline heart rate in pregnancy can be 10 to 15 beats more per minute [93]. Consequently, NICE has developed different guidance for risk factors for people who are pregnant or who have recently been pregnant (MEWS) [98]. Evidence from the USA suggests that death by sepsis in pregnancy is preventable up to 73% of the time, with early detection and prompt care. The relatively high mortality is attributed to delays in identification and non-standardised management [99].

4.7 Race and ethnicity

The review did not identify any literature relating to race and ethnicity and access to healthcare services in the UK for sepsis. An international study suggested that negative healthcare experiences and poor communication from providers can deter marginalised ethnic groups from seeking timely medical attention, thereby increasing their risk of deterioration while at home [100]. Recent UK research by the Patient Information Forum[gg] suggests that adults from ethnic minority groups are more likely to think they have seen health misinformation (19% compared with 9% of white adults), while a quarter of people from ethnic minority groups do not feel listened to compared with 15% of white people [101].

Unlike some of the other groups listed above (children, older people, pregnant women), white people and other ethnic groups appear to be similar clinically[hh] in terms of temperature, respiratory rate, oxygen saturation, and lactate values, although black people were more likely to report an altered mental state as their chief complaint [102].

Once help has been sought, blood oxygen saturation is one of the metrics used by NEWS2 to calculate sepsis risk, and pulse oximeters may work less well with dark skin [103]. Similarly, an American study noted that black patients are noted to often have higher creatinine levels than white patients with the same level of kidney function [33].

Most of the literature identified related to sepsis in America. These have shown prehospital sepsis recognition was similar across different races and ethnicities [104], that having an electronic sepsis alert system reduces racial differences in treatment of sepsis, compared to clinical judgement alone [105]. No genetic basis for sepsis susceptibility by race or ethnic grouping has been found [33], although some authors believe that one could be found in the future, and emphasise that genetic factors which lead to comorbidities that increase sepsis risk can be genetic and more common in black people [106].

According to an American review *"Differences in accessibility to health care such as preventive health services, primary care, and behaviours that promote health [such as healthy affordable food options] has been identified as a contributing factor to racial health disparities."* [106]. Generally, many agree that in the USA the high correlation between socioeconomic status and ethnicity mean it is difficult to disentangle the impact of ethnicity or race [106]. In the USA, lack of insurance, which is more common among the black population, can also impact how long it takes a person to decide to seek medical assistance [106].

4.8 Disability

4.8.1 Learning disabilities

The literature searches did not find papers relating to access for people with physical disabilities, frailty or cancer. The focus was on people with a learning disability or cognitive impairment who may face difficulties when describing symptoms and for whom cognitive decline may be harder to identify[13]. Providing easy-read information to inform people with learning disabilities about sepsis has been suggested as a way to increase awareness [35].

A Swedish qualitative study found that knowledge of the onset of sepsis is limited among patients and their families which makes early recognition of sepsis difficult, especially as symptoms are initially described as vague, potentially before rapid decline [107]. It demonstrated that often it was the carer rather than the person with cognitive impairments who would realise that the condition was serious, but that this could take time [107].

4.9 Geography

The NICE guidelines for sepsis [98] states *"In remote and rural locations where transfer time to emergency department is routinely more than 1 hour, ensure GPs have mechanisms in place to give antibiotics to people aged 16 or over with suspected sepsis who are or have recently been pregnant and meet high risk criteria in pre-hospital settings."* It also states that ambulance services should consider whether they need to put in place mechanisms to administer antibiotics. However, the literature searches found no data about whether this guidance is being implemented.

4.10 Homeless

The Equality Impact Assessment of NICE guidelines on sepsis states that *"People experiencing homelessness are more likely to delay seeking care. More generally those experiencing homelessness are more likely to have poor physical and mental health, be more vulnerable to issues associated with alcohol and drug use and can experience significant barriers to accessing health services which given the need for timely management if sepsis is suspected can result in greater adverse outcomes."* [13] No other literature was identified on the topic of homelessness and access to care for sepsis.

4.11 Criminal justice system

In a small-scale qualitative study of prisoners in England[ii] that looked at experiences accessing any hospital services, delayed access due to security arrangements and transport requirements was raised as a concern [108]. However, as the study did not specifically explore experiences of sepsis or other urgent care needs it is not clear whether this finding only relates to non-urgent care.

4.12 Missing evidence

The literature searches found very limited or no information about access to healthcare for:

- Older people
- Sexual orientation
- Gypsy and Roma travellers
- Religion / belief

- Physical disabilities
- Asylum seekers and refugees
- Geography – urban/rural/coastal
- Mental illness and substance use
- Criminal justice system

Even for the topics where some evidence was identified, the evidence was limited and predominantly did not relate to the UK specifically. Therefore, information about the role access plays in the inequalities in sepsis outcomes described in Chapter 3 is limited.

[cc] Survey of 2,087 respondents – no further data available

[dd] Retrospective cohort study of claims data from health insurances (n = 221,429 EMS cases), and paramedics' and emergency physicians' EMS documentation (n = 110,419);

[ee] The child death review process supplementary reporting form for infection asks questions about the recognition of suspected sepsis. Statistics are based on cases where this information was applicable and provided (131 cases in total)

[ff] Based on the Swiss ICU-registry - a mandatory database containing prospectively collected and validated information about all patients admitted to the 85 certified ICUs in Switzerland. Patients aged ≥ 16 years admitted to one of the 85 certified ICUs in Switzerland between 1st January 2021 and 31st December 2022 were included in the study. 5078 patients were included in the analysis.

[gg] Survey with 2003 participants, weighted to be nationally representative of the UK population.

[hh] Analysis based on all complete ICU patient records from an American hospital with sepsis discharge claims from 2001 to 2012 who were Black (2,532) or White (14,902)

[ii] Focus groups (n = 5) and 1:1 interviews (n = 17) were undertaken by peer researchers. 45 people took part in total.

5 Experience of care

5.1 Introduction

There are clear protocols set out in NICE guidelines which explain how patients should be treated if sepsis is suspected. Over time these have developed and have become more nuanced, considering the need to balance the benefits and risks of using broad spectrum antibiotics (see section 2.3.2). In low income countries, sepsis protocols have been demonstrated to lead to reduced mortality rates, even with partial implementation of protocols, although they did not necessarily reduce length of stay [109].

The literature searches found very limited information about people's experiences after discharge from hospital, except to note readmissions where applicable. The literature searches found very limited qualitative literature about sepsis and sepsis experiences, instead focussing mainly on quantitative measures.

Learning from sepsis deaths (2024)

A review of Coroners' Prevention of Future Deaths reports [110] found that between 2013 and 2022, six percent of these reports involved sepsis related deaths[jj], and the most common cause of death in these reports was 'sepsis without shock' (42%). The site of infection included the respiratory system (18%), gastrointestinal system (16%) and skin (13%). A quarter (26%) of the patients had experienced surgery recently. Paediatric cases frequently reported issues with sepsis screening tools (26%). For adult cases, the most frequent recommendations related to:

- a failure to keep accurate records or notes (28%),
- failure in communication or handover (27%) or
- failure to recognise risk factors or comorbidities (20%).

5.2 Age

5.2.1 Older people

As outlined above (section 3.1.4) there can be a number of life-changing outcomes for patients, even when sepsis is not fatal. A small scale piece of research[kk] suggested that older patients experience substantially higher 12-month mortality and also significantly worse and more sustained reductions in functional and cognitive skills[111].

As outlined above, older people with sepsis often have comorbidities. A UK study of suspected sepsis cases[ll] in a regional hospital found that 22% of patients had a Do Not Attempt Resuscitation (DNAR) in place when they came into the hospital with sepsis, although few of those who died in hospital had a documented escalation plan. The study concluded that it was important to have conversations about escalation and set realistic expectations about outcomes, as well as meeting the 1 hour target for intervention[112].

A small-scale survey[mm] of patients aged over 70 in the Netherlands considered whether treatment in ICU will always be the most appropriate cause of action and concluded that while 11 of their sample returned to their baseline functioning, 18 did not (with the most common impacts being on mobility and self-care). Nonetheless, all but one of their survey respondents were willing to

return to the ICU, which led them to conclude that *"Anticipated loss of functional outcome, and lost quality of life should be used with caution as an argument in shared decision-making regarding ICU-admission in elderly sepsis patients"* [113].

5.2.2 Children

As with adults, there is evidence that rapid administration of a sepsis bundle (agreed way to recognise, quick administration of fluids and antibiotics) reduced mortality, and where studies have not shown improvement, this has been attributed to differences in how time zero (ie the time at which the clock starts) is defined [90]. In the UK, the introduction of the Paediatric Early Warning Score (PEWS) into NICE guidelines is designed to help standardise recognition of sepsis in children [90].

It is noted that much of the worldwide quality improvement work to improve child experiences of care are focussed in specialist paediatric facilities, while children may be more likely to be initially brought to a facility working with adults and children [90]. This means it is important that all healthcare workers are familiar with paediatric sepsis alongside adult sepsis.

Worldwide, there are significant gaps in post-discharge support for children and a lack of information about which children will benefit from rehabilitation and what services they would benefit from [90].

A panel of 49 international experts seeking to develop evidence based recommendations for clinicians caring for children with septic shock and other sepsis-associated organ disfunction, found that a literature review failed to identify sufficient data to develop strong (or even weak in some instances) recommendations for critically ill children with septic shock or other sepsis-associated organ dysfunction although they achieved consensus on a number of recommendations[114].

Similarly, there is limited information about further intersectionality in sepsis experiences for children, although there is some evidence of a relationship between race/ethnicity and poverty and sepsis length of stay and mortality [115], [116].

5.3 Sex/Gender/sexual orientation

There are some documented differences in experiences of sepsis care by gender. Specifically, a Swedish study[nn] found that a higher proportion of men had all vital signs recorded, completed 1 hour sepsis bundles and a shorter time to antibiotics than women[117], although the study had some weaknesses [66]. An American study[oo] also found that women had a longer median time to antibiotics when presenting with sepsis or septic shock[118]. In both these studies, women had higher mortality from suspected septic shock, even after controlling for time to antibiotics.

A paper by Galiatsatos et al states there are differences in ICU care by gender across different conditions including sepsis, and women are less likely to be admitted to ICU[116], while a small Canadian cohort study showed women received less advanced life support measures [66]. It is not known why these differences occur, and whether they reflect different actual or assumed preferences of men and women who need ICU treatment, or the bias of medical practitioners [66].

5.4 Deprivation/employment/poverty

The only evidence relating to experience of care and deprivation related to America. These studies typically showed that some of the observed differences in length of stay and mortality

measures which appear to be driven by race can be explained instead by socioeconomic variables and ZIP code (i.e. an American postcode) [73]. Other studies demonstrate that apparently racial differences can be explained by which hospital a patient was treated in, with hospitals with majority black populations less likely to consistently follow sepsis guidelines (see 5.6 below). A further American study[pp] found that patients who reside in more disadvantaged neighbourhoods have a significantly higher risk for 30-day readmission following a hospitalisation for sepsis[119].

5.5 Literacy/health literacy/education/English not as first language

Only one American study[qq] addressed literacy or language and its impact on sepsis experiences, which showed central-line associated bloodstream infections were higher in patients who spoke a language other than English[120].

5.6 Race and ethnicity

There is also limited data on patient experiences of sepsis by race or ethnicity. In the USA, some studies demonstrate racial differences such as delays for black patients receiving antibiotics compared to white patients[118] and lower use[rr] of invasive mechanical ventilation and vasopressors[121]. Another small-scale study[ss] found African American patients with septic shock were treated with higher doses of norepinephrine (a vasopressor) and for a longer duration.

Some authors attribute these differences to the hospitals black people typically use[118], [122] which might have limited resources [106] or may be less likely to follow recommended protocols[117]. Not all studies found any racial differences after adjusting for confounding variables[123].

Some propose that any observed differences can be explained by a combination of social determinants, pre-existing co-morbidities and other factors such as attitude towards ICU usage and insurance [106]. However, other authors suggest that there is a need to adjust test results to take into account racial differences, such as the issue raised above (section 4.7) about overestimating oxygen saturation levels, or difficulties seeing a rash in people with darker skin [13].

As noted above (5.2.2), more research is needed into intersectionality of these characteristics, for example age and race, as there are some indications from the USA that young black children may have longer length of stay than white children[124].

5.7 Asylum seekers/refugees

A scoping review of migration health research in the UK[125] concluded there are growing numbers of studies into migrant heath, but that more research is needed. It found the focus of existing research tends to be infectious diseases (specifically HIV and TB) and mental health. It did not mention sepsis.

5.8 Disability

5.8.1 Physical disabilities

As noted above (section 5.2.1), many people entering hospital with sepsis already have a number of comorbidities and may be frail. In one UK study which looked at emergency department admissions treated for suspected sepsis[tt], less than half of the patients were living at home independently (42.5%) or could walk independently (41.5%) before admission and 19.3% were care home residents. Therefore, physical disabilities are very common among sepsis patients,

but there is currently limited or no guidelines about escalation of care for people with physical disabilities[112].

5.8.2 Learning disabilities

According to Lee et al (2024) [78] there are a number of issues that impact the experiences of people with learning disabilities using healthcare in the UK, which will be relevant to their experiences with sepsis:

- Healthcare staff often lack the awareness, expertise and experience to interact with and optimally manage patients with learning disabilities.
- People with learning disabilities may experience discriminatory attitudes from healthcare staff, some of which reflect unconscious bias.
- Health information and advice may be inaccessible to people with learning disabilities who often struggle to read or understand standard advice leaflets.
- Discriminatory attitudes may also be, at least in part, to blame for the high rate of inappropriate Do Not Attempt Cardiopulmonary Resuscitation (DNACPR) forms.
- The risk of diagnostic overshadowing, with symptoms assumed to be related to the learning disability meaning that other diagnoses are not considered.

While patients have a right to reasonable adjustments, there is limited information about whether these are being made [78]. A Canadian study found that providing individualised nursing care can help improve the experiences and outcomes of sepsis patients with a learning disability[126].

5.9 Missing evidence

The review did not find evidence about different experiences of sepsis care for the following groups:

- Sexual orientation
- Deprivation / employment / poverty outside the USA
- Ethnicity / race outside the USA
- Religion/belief
- Pregnancy/marriage
- Mental illness and substance use
- Geography - urban/rural/coastal
- Homelessness
- Criminal justice system

[jj] The study team acquired 4,305 PDFs from between July 2013 and November 2022.
[kk] Based on follow-up research with 328 adult surgical intensive care unit (ICU) sepsis patients.
[ll] A total of 1750 patients were randomly selected from the blood culture list and reviewed, resulting in 509 patients treated as suspected sepsis for the purpose of the study
[mm] Between 2012 and 2017, 144 patients had an unplanned ICU-admission due to abdominal sepsis. Seventy-two patients (50%) did not survive up to hospital discharge, 17 (24% of the hospital survivors) died within the first year after ICU-admission and 7 died later during follow up. This left a potential sample of 48, of whom 16 declined to participate and 3 were unable to answer. The survey was completed by 29 people.
[nn] 3240 patients were recorded in National Quality Sepsis Register (admitted to ICU with diagnosis of community acquired sepsis / septic shock). Of these, 520 were excluded, mostly due to missing data,

yielding 2720 in the final cohort. Patients were admitted via 32 EDs to 42 ICUs; 904 in 7 university hospitals and 1816 patients in 25 county hospitals

[oo] The cohort included 23,619 patients with suspected sepsis and 25,990 patients with suspected septic shock, of whom 23,259 (98%) had data recorded for sex.

[pp] There were 1,007 patients discharged with an ICD-10 code of sepsis. After a manual audit of the data, 647 patients (64.3%) met criteria for sepsis or septic shock per the Sepsis-3 definition. Of the 647 patients, 116 (17.9%) either died in hospital or were discharged to hospice. These patients were excluded from further analysis, resulting in 531 patients remaining in the study cohort.

[qq] This cohort study was performed at Seattle Children's, a 407-bed freestanding children's hospital in the Pacific Northwest. From October 1, 2012, to September 30, 2019, there were 232 228 eligible central catheter days and 344 Central line–associated bloodstream infections.

[rr] The database comprised of 73,140 ICU stays, of which 32,971 met the Sepsis-3 criteria. Following the inclusion and exclusion criteria, the final cohort consists of 23,914 ICU admissions

[ss] The study included 159 septic shock patients of whom 96 were African American.

[tt] A total of 1750 patients were randomly selected from the blood culture list and reviewed, resulting in 509 patients treated as suspected sepsis for the purpose of the study

6 Conclusion

The literature identified in the searches illustrates potential differences in access, experience and outcomes for different groups although the studies have many limitations. Existing research uses largely hospital-based data, focusses on quantitative outcomes and focusses predominantly on age-related factors. The evidence is sufficient to indicate that further inequalities may be identified with more analysis, although the data might be lacking to undertake high quality quantitative analysis on the groups which may be of interest.

There are significant gaps in the literature. Gaps include:

- UK-based studies (there are some but not many of these)
- Studies looking at specific groups identified in other studies as potentially at higher risk (insufficient confidence to draw conclusions for UK settings)
    - Sex/Gender/Gender reassignment / Sexual orientation
    - Race / ethnicity
    - English not first language / Poor health literacy
    - Criminal justice
    - Mental health and substance use
- Studies looking at specific groups about which we found limited/no data
    - Asylum seeker / refugee
    - Marriage / civil partnership
    - Religion / belief
    - Rural / urban / coastal
    - Homelessness
    - Sexual orientation
- Research into community-based sepsis / what happens before a person with sepsis reaches hospital
- Post-discharge outcomes
- Qualitative data about access to and experiences of sepsis care

The only area that feels well-researched in the UK is age and mortality outcomes due to sepsis. The NHS appears to have data on ethnicity and sepsis mortality, but this is not published and the last study identified used data from the COVID pandemic where other factors may have influenced the findings.

Appendix 1: Glossary

DNAR / DNACPR: A form kept in medical records to instruct medical staff not to Attempt [Cardiopulmonary] Resuscitation (different terms are used but they have the same meaning)

Invasive mechanical ventilation: having a tube inserted into the airway that is connected to a ventilator

NEWS2: an aggregate scoring system which uses a basket of six physiological measurements to trigger treatment of suspected sepsis.

SOFA: Sequential Organ Failure Assessment (SOFA) score, used to track a person's condition.

Vasopressor: drugs used to raise blood pressure in people whose blood pressure is very low

Appendix 2: Methodology and search

The literature searches for this report utilised PubMed, Embase and Google Scholar. The search terms outlined below were used to find initial relevant papers. Then a citation chaining technique was used which involved looking at their reference lists, Cited by, and Similar Articles in PubMed and Google Scholar. Each article found then went through that process.

This was supplemented with general Google searching looking for relevant reports (e.g. government, NHS or charity reports) and also looked any papers cited in those. The articles were collated then deduplicated.

The following terms were combined with “sepsis”.

("addict*" OR "adolescen*" OR "Aged" OR "Aging" OR "Asian" OR "asylum seek*" OR "At-risk group*" OR "belief*" OR "bisexual*" OR "Black*" OR "Ethnicity" OR "carer*" OR "child*" OR "Chronic illness patients" OR "civil partnership*" OR "communit*" OR "criminal justice" OR "depriv*" OR "disabilit*" OR "disable*" OR "Disadvantaged communities" OR "discriminat*" OR "domestic violence" OR "Economically disadvantaged" OR "Elderly" OR "Ethnic minorit*" OR "exclude*" OR "exclusion*" OR "families" OR "family" OR "gay" OR "Gender" OR "Gyps*" OR "Health disparities" OR "HIV" OR "AIDS" OR "homeless*" OR "homosexual" OR "immigra*" OR "Incarcerated" OR "inequalit*" OR "Inequity" OR "Intimate partner" OR "Lesbian" OR "LGBT*" OR "Linguistic" OR "Language" OR "english" OR "literacy" OR "Low-income" OR "marginali*" OR "marriage*" OR "maternity" OR "mental health" OR "Migrant workers" OR "minorit*" OR "Non-binary" OR "older" OR "paediatric*" OR "pediatric*" OR "poor" OR "popula*" OR "poverty" OR "pregnan*" OR "protected charact*" OR "queer" OR "race" OR "racial" OR "refugee*" OR "Religi*" OR "Roma" OR "rural" OR "Sexual Identit" OR "sexual orientation" OR "Sexual violence" OR "Social determinants of health" OR "Socially excluded" OR "substance abuse" OR "Substance use" OR "teenager*" OR "Trafficking victim*" OR "transgender*" OR "transsex*" OR "traveling" OR "Traveller*" OR "travelling" OR "undercounted" OR "underrepresent*" OR "underserved" OR "Undocumented" OR "Unemployed" OR "Victims of Violence" OR "vulnerable" OR "Women" OR "Working poor" OR "Young adults" OR "young people" OR "young person*" OR "youth*" OR "detention" OR "detained" OR "criminal record*" OR "parole*" OR "probation*" OR "ex-offender*" OR "offender*" OR "prison*" OR "inmate*" OR "custody" OR "faith*" OR "Christian*" OR "jew" OR "jewish" OR "jews" OR "judaism" OR "islam" OR "muslim*" OR "hindu*" OR "buddh*" OR "deaf" OR "hearing" OR "speech disorder*" OR "speech and language" OR "illiter*" OR "communication problem*")

Appendix 3: Findings by health inequality group

This section takes the evidence from Chapters 3-5 and reorganises it by characteristics.

7.1 Age

7.1.1 Prevalence and outcomes

Of all the demographic factors which are discussed relating to sepsis, age is one of the most frequently mentioned. Studies consistently show higher mortality in older people, especially the very old (i.e. 80+ years) and frail[11] [13], [42], [48].

The majority of hospital admissions are for older people and also for children under 4 years[1]. Studies differ on their assessments of rates of child mortality. One study of UK patients found that 77.5% of sepsis-related deaths occur in patients over 75 years with only 150 deaths per year occurring in children between 0 to 18 years of age[1], while NICE evidence suggests that the rate in infants under one year is similar to that in people aged 60 years and over[13]. These statistics may not be contradictory, but instead point the increased risk of mortality for the very youngest and oldest in society.

7.1.1.1 Older people

Different reasons are given for increased sepsis-mortality amongst older people. These reasons include potentially delayed treatment, as confusion may not be considered an indicator of an acute problem in the elderly[13], increased likelihood of co-morbidities or increased rates of Do Not Attempt Resuscitation (DNAR) instructions in place[49]. A study based on UK GP records[uu] found that severely frail patients had both a higher risk of developing sepsis and a case fatality rate of 42.0% compared to 24.0% in non-frail patients (adjusted OR 1.53)[42]. As discussed below (5.2.1) higher mortality may also be recorded because it is not always appropriate to admit an old, frail patient with multiple comorbidities to intensive care, and therefore while sepsis is coded as the cause of death this will be in the context of other factors.

A study looking specifically at sepsis after appendectomies noted that, while cases are rare, being aged over 60 years increased the risk of sepsis and sepsis related morbidity and mortality[50]. Similarly, a secondary analysis of multinational data on adults with intra-abdominal infections[vv] found mortality increased with age: 20.9% in middle-aged patients (aged 40-59), 30.5% in young-old patients (aged 60-69), 31.2% in middle-old patients (aged 70-79), and 44.7% in very old patients (aged ≥80 years)[49].

7.1.1.2 Children

While the evidence suggests that older adult mortality is higher than child mortality from sepsis, it remains one of the leading causes of morbidity and mortality in neonatal and paediatric age groups worldwide[51]. This is due to a combination of factors including changes that occur as the immune system develops, making the youngest children most vulnerable[51], and childhood comorbidities. In high income countries, these comorbidities commonly include chronic non-infectious conditions, such as malformations or impairments, neuromuscular conditions such as seizures and cerebral palsy and immune suppression (for example, as a result of chemotherapy) or immunodeficiency such as sickle cell disease[51]. An American study[ww] found that more than two out of three children admitted with sepsis had at least one chronic disease, and that these children had higher mortality than previously healthy children[52].

The National Child Mortality Database programme found that across the entire cohort of infection related deaths in England[xx] (n=1507) the clinical signs of sepsis were reported in 701 deaths. In 478 cases this was the only clinical condition/presentation identified. The review found that the highest risk of death from any infection was in children described as African (2.90 per 100,000 children), Pakistani (2.52 per 100,000 children), or having any other Asian (3.77 per 100,000 children) ethnic background. The report noted that these ethnic groups also have higher rates of early-onset neonatal sepsis due to Group B Streptococcus[53].

Studies from Netherlands[54] and America[55] focusing on neonatal cases, suggest that experience in hospital can impact on a child's length of stay. Specifically, having a single family room may lead to less late onset sepsis and a shorter length of stay with sepsis[54], while, as discussed further below (3.8) race can also lead to disparities in outcomes, especially for African American infants living in the USA[55]. The literature searches did not identify any UK evidence on this topic.

Children with developmental disabilities (e.g. impairments in communication, feeding and motor function) may also be at risk of poorer outcomes. A small-scale American study[yy] found that children with developmental disabilities were more likely to have a sustained worse quality of life after discharge, than children with other conditions or who were healthy before sepsis[56]. Similarly, a study in Taiwan[57] found that surgical patients with an intellectual disability had an increased risk of postoperative sepsis and 30-day mortality, after controlling for demographic factors and comorbidities[zz]. The authors suggest that reasons could include generally being in less good health, difficulties communicating, immune abnormalities, poor hand hygiene, and poverty.

Studies in low income countries have found that children with sepsis-associated liver injury (which occurred in one third of their sample) had a twofold higher risk of mortality than those without liver injury[58]. Another study in Argentina found that lower socioeconomic conditions were associated with higher prevalence of sepsis but similar outcomes[59]. Comorbidities such as malnutrition, HIV infection, tuberculosis, and chronic malaria are also associated with increased susceptibility to childhood sepsis in low income countries[51]. Neonatal sepsis may also be associated with cultural practices and beliefs relating to care for the umbilical cord, with some practices considered to potentially put children at increased risk[60]. Again, the literature searches did not identify any studies discussing these issues in the UK context.

7.1.2 Access

7.1.2.1 Older people

The literature searches did not identify any information about access to healthcare for older people with sepsis. As noted above, some of the impacts of sepsis on cognitive function may be harder to identify in older people, which might delay access to healthcare. Additionally, older people may not develop a raised temperature, or increased heart rate but may develop a new heart arrhythmia[93]. It is also possible they may struggle with health literacy due to cognitive decline, lack of familiarity with digital tools, and complex health information[94].

7.1.2.2 Children

It can be difficult to identify sepsis in children, and there are gaps in evidence around sepsis care for children[51]. Sepsis is particularly common in children aged under 1 year, and initially symptoms may look like other common illnesses or teething which may delay parents seeking help, especially if they are not aware of the risk of sepsis[95]. A review of child deaths[aaa] from infection found that in 18% of deaths the recognition of suspected sepsis was not timely and in

12% of cases the child did not receive broad spectrum antibiotics within an hour. In most cases (85%) there were one or more red flags for sepsis when the child reported to hospital, and these were recognised in 77% of deaths. However, in 8% of cases, red flag symptoms were present but not recognised[53].

The NEWS2 assessment is not appropriate for children as they may present differently; they may not have a high temperature, may have a lower baseline heart rate so that an increase is harder to identify, and changes in their cognitive state may present as changes in behaviour and irritability[93]. Consequently, there are separate guidelines for assessing children[96] using the national Paediatric Early Warning Score (PEWS).

7.1.3 Experience of care

7.1.3.1 Older people

As outlined above (section 3.1.4) there can be a number of life-changing outcomes for patients, even when sepsis is not fatal. A small scale piece of research[bbb] suggested that older patients experience substantially higher 12-month mortality and also significantly worse and more sustained reductions in functional and cognitive skills[111].

As outlined above, older people with sepsis often have comorbidities. A UK study of suspected sepsis cases[ccc] in a regional hospital found that 22% of patients had a Do Not Attempt Resuscitation (DNAR) in place when they came into the hospital with sepsis, although few of those who died in hospital had a documented escalation plan. The study concluded that it was important to have conversations about escalation and set realistic expectations about outcomes, as well as meeting the 1 hour target for intervention[112].

A small-scale survey[ddd] of patients aged over 70 in the Netherlands considered whether treatment in ICU will always be the most appropriate cause of action, and concluded that while 11 of their sample returned to their baseline functioning, 18 did not (with the most common impacts being on mobility and self-care). Nonetheless, all but one of their survey respondents were willing to return to the ICU, which led them to conclude that *"Anticipated loss of functional outcome, and lost quality of life should be used with caution as an argument in shared decision-making regarding ICU-admission in elderly sepsis patients"* [113].

7.1.3.2 Children

As with adults, there is evidence that rapid administration of a sepsis bundle (agreed way to recognise, quick administration of fluids and antibiotics) reduced mortality, and where studies have not shown improvement, this has been attributed to differences in how time zero (ie the time at which the clock starts) is defined[90]. In the UK, the introduction of the Paediatric Early Warning Score (PEWS) into NICE guidelines is designed to help standardise recognition of sepsis in children[90].

It is noted that much of the worldwide quality improvement work to improve child experiences of care are focussed in specialist paediatric facilities, while children may be more likely to be initially brought to a facility working with adults and children[90]. This means it is important that all healthcare workers are familiar with paediatric sepsis alongside adult sepsis.

Worldwide, there are significant gaps in post-discharge support for children and a lack of information about which children will benefit from rehabilitation and what services they would benefit from[90].

A panel of 49 international experts seeking to develop evidence based recommendations for clinicians caring for children with septic shock and other sepsis-associated organ disfunction, found that a literature review failed to identify sufficient data to develop strong (or even weak in some instances) recommendations for critically ill children with septic shock or other sepsis-associated organ dysfunction although they achieved consensus on a number of recommendations[114].

Similarly, there is limited information about further intersectionality in sepsis experiences for children, although there is some evidence of a relationship between race/ethnicity and poverty and sepsis length of stay and mortality [115], [116].

7.2 Religion / belief

No information about sepsis and religion or beliefs was identified in our literature searches.

7.3 Sex / Gender / Sexual orientation

There was limited data about any of these groups and sometimes it is not clear whether sex or gender was being used.

7.3.1 Prevalence and outcomes

The evidence about whether sex (i.e. biological sex) impacts on prevalence or mortality is mixed [64] and no primary evidence relating to gender (i.e. social / cultural identity) or sexual orientation was identified. On balance, it appears that males may be more likely to develop sepsis [43] with some studies also indicating a higher risk of mortality compared with females[1]. However, not all studies have found this and some have found the reverse [65], [66].

As noted above, there may be a relationship between sex and age, with one study finding the effect of high age was more than twice as high in men than in women [44]. Suggested reasons for these differences between the sexes include genetic differences, the impact of oestrogen, prevalence of infections and behavioural differences as historically men may have been more likely to smoke or drink alcohol [43].

An American study also found that unexpected readmissions within 30 days of a sepsis diagnosis were more common among men [36].

The literature searches did not identify any research into sexual orientation and sepsis prevalence.

7.3.2 Access

In the NHS, most regions use the NEWS2 to identify sepsis and the appropriate treatment pathway. However, neither NEWS2 or the Sequential Organ Failure Assessment (SOFA) score take into consideration the different physiology of men and women.

A study using Swiss ICU data[eee] found a statistically significant difference of the total SOFA score on admission between women and men, driven by differences in the coagulation, liver and renal SOFA (laboratory-based) components [97]. Differences between sexes were more prominent in younger patients (aged 52 and under) [97]. Despite the differences in SOFA score, the women did not have better short-term outcomes and the paper suggests that differences in physiology mean that differences in laboratory scores for men and women need to be better understood [97].

7.3.3 Experience of care

There are some documented differences in experiences of sepsis care by gender. Specifically, a Swedish study[fff] found that a higher proportion of men had all vital signs recorded, completed 1 hour sepsis bundles and a shorter time to antibiotics than women[117], although the study had some weaknesses [66]. An American study[ggg] also found that women had a longer median time to antibiotics when presenting with sepsis or septic shock[118]. In both these studies, women had higher mortality from suspected septic shock, even after controlling for time to antibiotics.

A paper by Galiatsatos et al states there are differences in ICU care by gender across different conditions including sepsis, and women are less likely to be admitted to ICU[116], while a small Canadian cohort study showed women received less advanced life support measures [66]. It is not known why these differences occur, and whether they reflect different actual or assumed preferences of men and women who need ICU treatment, or the bias of medical practitioners [66].

7.4 Asylum seekers / refugees

7.4.1 Prevalence and outcomes

There is limited evidence in the UK about sepsis for asylum seekers or refugees. Evidence from Denmark suggests migrant status might be linked to a higher risk of bloodstream infections [76]. A NICE Equality Impact Assessment for Sepsis guidelines[13] stated *"These populations will often embark on arduous journeys and combined with often precarious living and housing circumstances may impact their nutrition and their immune system contributing to increased risk of developing sepsis and making infection source identification and control challenging."*. However, a small scale study[hhh] of maternal outcomes by asylum seeking status did not show a statistically significant difference in suspected sepsis [77].

7.4.2 Access

Not identified through our literature searches which focussed on sepsis.

7.4.3 Experience of care

A scoping review of migration health research in the UK[125] concluded there are growing numbers of studies into migrant heath, but that more research is needed. It found the focus of existing research tends to be infectious diseases (specifically HIV and TB) and mental health. It did not mention sepsis.

7.5 Deprivation/employment/poverty

7.5.1 Prevalence and outcomes

There is UK-based evidence[iii] that the most socioeconomic deprived quintile of addresses, defined using the Index of Multiple Deprivation are associated with a higher odds of developing non-COVID-19 sepsis than the least deprived quintile (crude OR 1.80 [95% CI 1.77–1.83]), but found that deprivation was only moderately associated with increased mortality[11]. A study using UK GP data[jjj] had similar findings [42], and again showed increase risk of sepsis but not necessarily higher rates of mortality for people living in areas classified as having high deprivation.

These findings are similar to those found worldwide. A scoping review also found evidence from other countries that socio-economic status is inversely related to the risk of sepsis [22] and an American review found that neighbourhoods with relatively low median income levels, low insurance rates, and low rates of higher education experience relatively higher sepsis related mortality [61]. Equally, these factors plus economic and housing instability have been identified as a predictor of unplanned readmissions [36].

A NICE Equality Impact Assessment for Sepsis guidelines concluded *"Evidence suggests that there are increased barriers to care access for people with low socioeconomic status which include cost, transportation, poor health literacy and lack of social network which potentially contributes to the identified disproportionate impacts felt by this group."* [13].

The literature searches did not find any data relating to employment and poverty and sepsis.

7.5.2 Access

A committee meeting about the NICE guidelines for sepsis[13] discussed that socio-economic factors may have an impact on the recognition, diagnosis, and early management of sepsis. However, no further evidence was identified to support this perspective.

7.5.3 Experience of care

The only evidence relating to experience of care and deprivation related to America. These studies typically showed that some of the observed differences in length of stay and mortality measures which appear to be driven by race can be explained instead by socioeconomic variables and ZIP code [73]. Other studies demonstrate that apparently racial differences can be explained by which hospital a patient was treated in, with hospitals with majority black populations less likely to consistently follow sepsis guidelines (see 5.6). A further American study[kkk] found that patients who reside in more disadvantaged neighbourhoods have a significantly higher risk for 30-day readmission following a hospitalization for sepsis[119].

7.6 Disability

7.6.1 Prevalence and outcomes

7.6.1.1 Learning disabilities

People with learning disabilities die on average 16 years earlier than the general population in England, which at least in part has been attributed to sepsis [78]. A UK-based study[lll] using GP data [42] found having a learning disability was strongly associated with the risk of developing community-acquired sepsis (crude odds ratio of 3.0) and also associated with higher hospital

acquired sepsis. The 2022 Learning Disabilities Mortality Review (LeDeR) Annual Report [79] found that sepsis is a key contributor to premature mortality, with 14% of deaths being recorded as sepsis related – the second highest cause after pneumonia. A Taiwanese study of child surgical patients with learning disabilities[mmm] found them to be at increased risk of sepsis and 30-day mortality, and also longer hospital stays [57].

7.6.1.2 Frailty

While disability and frailty are not synonymous, as noted above (3.3.1) frailty is often listed as a risk factor for sepsis and sepsis mortality. For example, a UK-based study[nnn] using GP data [42] found severe frailty was strongly associated with the risk of developing sepsis (crude odds ratio of 14.9). Additionally, it found that severely frail patients had a case fatality rate of 42.0% compared to 24.0% in non-frail patients (adjusted odds ratio 1.53). A separate study showed that increased risk remained, even after controlling for age, sex, obesity, and other comorbidities [22].

7.6.1.3 Cancer

Similarly, while cancer is not a disability, cancer survivors are often identified in the literature as being at a heightened risk of sepsis, and cancer patients have higher odds of frailty (see 3.10.2). Even after controlling for the impact of frailty, an American study[ooo] found cancer survivors were more than twice as likely as patients with no cancer history to develop sepsis [80].

7.6.2 Access

7.6.2.1 Learning disabilities

The literature searches did not find papers relating to access for people with physical disabilities, frailty or cancer. The focus was on people with a learning disability or cognitive impairment who may face difficulties when describing symptoms and for whom cognitive decline may be harder to identify[13]. Providing easy-read information to inform people with learning disabilities about sepsis has been suggested as a way to increase awareness [35].

A Swedish qualitative study found that knowledge of the onset of sepsis is limited among patients and their families which makes early recognition of sepsis difficult, especially as symptoms are initially described as vague, potentially before rapid decline [107]. It demonstrated that often it was the carer rather than the person with cognitive impairments who would realise that the condition was serious, but that this could take time [107].

7.6.3 Experience of care

7.6.3.1 Physical disabilities

As noted above (section 5.2.1), many people entering hospital with sepsis already have a number of comorbidities and may be frail. In one UK study which looked at emergency department admissions treated for suspected sepsis[ppp], less than half of the patients were living at home independently (42.5%) or could walk independently (41.5%) before admission and 19.3% were care home residents. Therefore, physical disabilities are very common among sepsis patients, but there is currently limited or no guidelines about escalation of care for people with physical disabilities[112].

7.6.3.2 Learning disabilities

According to Lee et al (2024) [78] there are a number of issues that impact the experiences of people with learning disabilities using healthcare in the UK, which will be relevant to their experiences with sepsis:

- Healthcare staff often lack the awareness, expertise and experience to interact with and optimally manage patients with learning disabilities.
- People with learning disabilities may experience discriminatory attitudes from healthcare staff, some of which reflect unconscious bias.
- Health information and advice may be inaccessible to people with learning disabilities who often struggle to read or understand standard advice leaflets.
- Discriminatory attitudes may also be, at least in part, to blame for the high rate of inappropriate Do Not Attempt Cardiopulmonary Resuscitation (DNACPR) forms.
- The risk of diagnostic overshadowing, with symptoms assumed to be related to the learning disability meaning that other diagnoses are not considered.

While patients have a right to reasonable adjustments, there is limited information about whether these are being made [78]. A Canadian study found that providing individualised nursing care can help improve the experiences and outcomes of sepsis patients with a learning disability[126].

7.7 Literacy/education and English not first language

7.7.1 Prevalence and outcomes

The literature searches found limited data on the topic of literacy, health literacy education and English not as a first language. As noted above (2.3.1) the NHS website warns that sepsis can be particularly hard to identify in people who have difficulty communicating and this could potentially include people who do not have English as a first language[5]. However, a relatively small American study[qqq] found that having limited English proficiency did not impact mortality odds overall, but did among white people with limited English proficiency (e.g. Russian, Arabic) which they hypothesised could be due to limited access to interpreters [62].

Throughout the literature there is an emphasis on the importance of recognising sepsis and seeking help, which might be less common amongst those with lower health literacy. This could have an indirect impact, as people with low health literacy may be less likely to have engaged in vaccination programmes so could be more vulnerable to developing sepsis[13].

As outlined above (3.4), lower rates of education have been associated with higher sepsis incidence in the USA, and also higher unplanned readmission rates [36] and a German study had similar findings [63]. The literature searches did not identify any UK studies that looked at education and sepsis.

7.7.2 Access

According to the equality impact assessment (EIA), the NICE committee reviewing the guidance considered that because 'history taking' is very important in the process of identifying sepsis, and that people with communication difficulties or those who do not speak English may not be able to give a history, this could lead to differences in access [13]. This could be true across the population as a whole, but the committee noted that it might be a particular issue where information leaflets were being used to raise awareness among those at higher risk of sepsis[13].

7.7.3 Experience of care

Only one American study[rrr] addressed literacy or language and its impact on sepsis experiences, which showed central-line associated bloodstream infections were higher in patients who spoke a language other than English[120].

7.8 Mental illness & substance use

7.8.1 Prevalence and outcomes

We identified very limited evidence relating to mental illness or substance use, noting that smoking is considered a risk factor (see 3.2 above). A study of cancer patients in Sweden[sss] found that preexisting psychiatric disorders were associated with an increased risk of sepsis after cancer diagnosis [81]. The positive association was consistently noted among patients with different demographic factors or cancer characteristics, for most cancer types, and during the entire follow-up after cancer diagnosis [81].

7.8.2 Access

No evidence identified in our literature searches.

7.8.3 Experience of care

No evidence identified in our literature searches.

7.9 Geography – urban/rural

7.9.1 Prevalence and outcomes

In Germany, distance to the nearest pharmacy has been associated with crude and age standardised sepsis incidence [63]. However, another study[ttt] found that living in a rural location in Germany was associated with both short- and long-term survival benefits for patients with community-acquired sepsis [82] and the authors hypothesise that this is due to environmental factors (e.g. higher stress in cities, higher levels of pollutants). In the USA, delay receiving medical care due to lack of transportation was strongly associated with 30-day readmission [38].

An American study[uuu] showed a relationship between exposure to small particulate matter ($PM_{2.5}$) and increased sepsis mortality risk, especially for older people living in urban areas [83]. However, other studies have not shown the same association [83].

UK literature appears to focus on deprivation but does not directly explore differences in outcome by geography.

7.9.2 Access

The NICE guidelines for sepsis [98] states *"In remote and rural locations where transfer time to emergency department is routinely more than 1 hour, ensure GPs have mechanisms in place to give antibiotics to people aged 16 or over with suspected sepsis who are or have recently been pregnant and meet high risk criteria in pre-hospital settings."* It also states that ambulance

services should consider whether they need to put in place mechanisms to administer antibiotics. However, the literature searches found no data about whether this guidance is being implemented.

7.9.3 Experience of care

No evidence identified in our literature searches.

7.10 Pregnancy/marriage

7.10.1 Prevalence and outcomes

Maternal sepsis is an important type of sepsis in women, and an important cause of mortality during and after pregnancy. As with all sepsis, estimates of incidence differ, ranging from 1 per 100,000 maternities (ie during pregnancy or within 42 days of the end of a pregnancy) to 4.9 per 10,000 live births, and cases of non-severe sepsis ranging from 198 per 100,000 maternities to 10 per 10,000 live births [67].

The most recent data on maternal deaths for the UK [68] (the MBRRACE maternal mortality 2021-23 report) found a rate of 0.5 per 100,000 maternities from pregnancy related sepsis and 0.75 per 100,000 indirect sepsis (e.g. from influenza or pneumonia).

An older UK based study[vvv] found pneumonia and genital tract infections were the most common sources of sepsis, and caesarean section was also a significant risk factor [69]. Young women (aged 16-19) had the highest ICU admission rates, both as a proportion of all ICU admissions for that age group, and as a proportion of all maternities in that age group, but had the lowest mortality rate [69]. Women aged over 40 also had elevated risk compared to those aged 20-39. Similarly, coming from an area with high deprivation led to higher risk. The absolute risk of mortality was 1.8 per 100,000 maternities [69]. Another UK study found that black pregnant or postpartum women were at higher risk of severe sepsis, along with women who had taken antibiotics in the fortnight before presenting with sepsis [70].

In line with sepsis risk factors, older age, increased BMI, black and other ethnic minority race, increased deprivation and pre-existing medical conditions were associated with higher risk, alongside risks associated with delivery by caesarean section [67]. There is some evidence that mortality in pregnancy associated severe sepsis may be lower than in non-pregnancy associated severe sepsis; mortality rates vary from 10.7% to 1.8 per 100,000, and one study found zero mortalities [67].

The review found no studies that explored whether marriage impacts sepsis prevalence or outcomes directly, although one study did suggest that while older men with sepsis may have a living wife who will advocate for their treatment, older women may be widows and their children might make different views about what is in their best interest [66].

7.10.2 Access

The standard tools for diagnosing sepsis (including NEWS2) are not appropriate for people who are pregnant or who have recently been pregnant[14]. For example, baseline heart rate in pregnancy can be 10 to 15 beats more per minute [93]. Consequently, NICE has developed different

guidance for risk factors for people who are pregnant or who have recently been pregnant (MEWS) [98]. Evidence from the USA suggests that death by sepsis in pregnancy is preventable up to 73% of the time, with early detection and prompt care. The relatively high mortality is attributed to delays in identification and non-standardised management [99].

7.10.3 Experience of care

The standard tools for diagnosing sepsis (including NEWS2) are not appropriate for people who are pregnant or who have recently been pregnant[14]. For example, baseline heart rate in pregnancy can be 10 to 15 beats more per minute [93]. Consequently, NICE has developed different guidance for risk factors for people who are pregnant or who have recently been pregnant (MEWS) [98]. Evidence from the USA suggests that death by sepsis in pregnancy is preventable up to 73% of the time, with early detection and prompt care. The relatively high mortality is attributed to delays in identification and non-standardised management [99].

7.11 Homeless

7.11.1 Prevalence and outcomes

There was limited literature about the impact of sepsis for people who are homeless. NICE[13] concluded *"People experiencing homelessness are more likely to delay seeking care and there is non-UK evidence (USA) to suggest that they are more likely to die following an admission for severe sepsis which is linked to the increased likelihood of delayed presentation"* based on a paper by Shahryar et al [84]. A small Korean study[www] found that homelessness did not impact on hospital and ICU mortality rates or length of stay.

7.11.2 Access

The Equality Impact Assessment of NICE guidelines on sepsis states that *"People experiencing homelessness are more likely to delay seeking care. More generally those experiencing homelessness are more likely to have poor physical and mental health, be more vulnerable to issues associated with alcohol and drug use and can experience significant barriers to accessing health services which given the need for timely management if sepsis is suspected can result in greater adverse outcomes."* [13] No other literature was identified on the topic of homelessness and access to care for sepsis.

7.11.3 Experience of care

No evidence identified in our literature searches.

7.12 Race and ethnicity

7.12.1 Prevalence and outcomes

A recent study of NHS data[xxx] found that individuals of South Asian descent were observed to have a higher incidence of sepsis, while those categorised under the 'other' ethnic groups demonstrated a reduced incidence compared to individuals of white descent[11]. However, It also found that for that for community-acquired non-COVID-19 sepsis, the 30-day mortality rate was highest in patients of white ethnicity[11].

A recent systematic review[67], which mainly relied on data from the USA, found that there was no consistent pattern, and that sepsis incidence and mortality rates for black and white patients were different in each study with neither group consistently showing higher incidence or mortality. Some American studies have found sepsis mortality to be higher in black and Hispanic patients, but suggest this might be a result of the quality of care in hospitals in different areas, rather than race[1], or due to health disparities based on lack of ambulatory care, socioeconomic factors and comorbidity rather than race[71], [72], [73]. Other studies suggest, ethnic minorities in the USA experience higher rates of infectious diseases[13], postoperative complications [74] [75] and smoking[75] which may lead to higher sepsis prevalence.

7.12.2 Access

The review did not identify any literature relating to race and ethnicity and access to healthcare services in the UK for sepsis. An international study suggested that negative healthcare experiences and poor communication from providers can deter marginalised ethnic groups from seeking timely medical attention, thereby increasing their risk of deterioration while at home[100]. Recent UK research by the Patient Information Forum[yyy] suggests that adults from ethnic minority groups are more likely to think they have seen health misinformation (19% compared with 9% of white adults), while a quarter of people from ethnic minority groups do not feel listened to compared with 15% of white people[101].

Unlike some of the other groups listed above (children, older people, pregnant women), white people and other ethnic groups appear to be similar clinically[zzz] in terms of temperature, respiratory rate, oxygen saturation, and lactate values, although black people were more likely to report an altered mental state as their chief complaint [102].

Once help has been sought, blood oxygen saturation is one of the metrics used by NEWS2 to calculate sepsis risk, and pulse oximeters may work less well with dark skin[103]. Similarly, an American study noted that black patients are noted to often have higher creatinine levels than white patients with the same level of kidney function[33].

Most of the literature identified related to sepsis in America. These have shown prehospital sepsis recognition was similar across different races and ethnicities[104], that having an electronic sepsis alert system reduces racial differences in treatment of sepsis, compared to clinical judgement alone[105]. No genetic basis for sepsis susceptibility by race or ethnic grouping has been found [33], although some authors believe that one could be found in the future, and emphasise that genetic factors which lead to comorbidities that increase sepsis risk can be genetic and more common in black people[106].

According to an American review *"Differences in accessibility to health care such as preventive health services, primary care, and behaviours that promote health [such as healthy affordable food options] has been identified as a contributing factor to racial health disparities."* [106]. Generally, many agree that in the USA the high correlation between socioeconomic status and ethnicity mean it is difficult to disentangle the impact of ethnicity or race[106]. In the USA, lack of insurance, which is more common among the black population, can also impact how long it takes a person to decide to seek medical assistance[106].

7.12.3 Experience of care

There is also limited data on patient experiences of sepsis by race or ethnicity. In the USA, some studies demonstrate racial differences such as delays for black patients receiving antibiotics compared to white patients[118] and lower use[aaaa] of invasive mechanical ventilation and vasopressors[121]. Another small-scale study[bbbb] found African American patients with septic shock were treated with higher doses of norepinephrine (a vasopressor) and for a longer duration.

Some authors attribute these differences to the hospitals black people typically use[118], [122] which might have limited resources [106] or may be less likely to follow recommended protocols[117]. Not all studies found any racial differences after adjusting for confounding variables[123].

Some propose that any observed differences can be explained by a combination of social determinants, pre-existing co-morbidities and other factors such as attitude towards ICU usage and insurance [106]. However, other authors suggest that there is a need to adjust test results to take into account racial differences, such as the issue raised above (section 4.7) about overestimating oxygen saturation levels, or difficulties seeing a rash in people with darker skin [13].

As noted above (5.2.2), more research is needed into intersectionality of these characteristics, for example age and race, as there are some indications from the USA that young black children may have longer length of stay than white children[124].

7.13 Criminal Justice system

7.13.1 Prevalence and outcomes

The literature searches did not identify any information about people in the UK criminal justice system and sepsis. An umbrella review of mental and physical health morbidity in prison populations did not identify sepsis as a significant cause of mortality [85]. However, in the USA[cccc], a small scale study found inmates were 2.8 times more likely to die from sepsis than non-inmates [86].

7.13.2 Access

In a small-scale qualitative study of prisoners in England[dddd] that looked at experiences accessing any hospital services, delayed access due to security arrangements and transport requirements was raised as a concern [108]. However, as the study did not specifically explore experiences of sepsis or other urgent care needs it is not clear whether this finding only relates to non-urgent care.

7.13.3 Experience of care

No evidence identified in our literature searches.

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[uu] The overall study population consisted of patients aged 65–100 years at any time during the observation period (from January 1, 2000, to summer 2020 who were registered at a GP practice in England. It included 108,317 cases classified as community-acquired sepsis.

[vv] An observational study which included patients with intra-abdominal infection from 309 ICUs in 42 countries (January-December, 2016). The cohort included 2337 patients.

[ww] This study used the 2013 Nationwide Readmissions Database (NRD) and included non-neonatal patients <19 years old hospitalized with sepsis. A total of 16,387 admissions, representing 14,243 unique patients, were included in the analysis.

[xx] Data from April 2019 to March 2022

[yy] Secondary analysis of Life after Paediatric Sepsis (LAPSE) investigation. Of 392 LAPSE participants, 137 were identified by their caregiver as having a severe developmental disability.

[zz] Based on claims data from Taiwan's National Health Insurance programme from 2004 to 2013, which included 220,292 surgical patients aged 6 to 17 years. A propensity score matching procedure was used to select 2173 children with intellectual disability and 21,730 children without intellectual disability for comparison.

[aaa] The child death review process supplementary reporting form for infection asks questions about the recognition of suspected sepsis. Statistics are based on cases where this information was applicable and provided (131 cases in total)

[bbb] Based on follow-up research with 328 adult surgical intensive care unit (ICU) sepsis patients.

[ccc] A total of 1750 patients were randomly selected from the blood culture list and reviewed, resulting in 509 patients treated as suspected sepsis for the purpose of the study

[ddd] Between 2012 and 2017, 144 patients had an unplanned ICU-admission due to abdominal sepsis. Seventy-two patients (50%) did not survive up to hospital discharge, 17 (24% of the hospital survivors) died within the first year after ICU-admission and 7 died later during follow up. This left a potential sample of 48, of whom 16 declined to participate and 3 were unable to answer. The survey was completed by 29 people.

[eee] Based on the Swiss ICU-registry - a mandatory database containing prospectively collected and validated information about all patients admitted to the 85 certified ICUs in Switzerland. Patients aged ≥ 16 years admitted to one of the 85 certified ICUs in Switzerland between 1st January 2021 and 31st December 2022 were included in the study. 5078 patients were included in the analysis.

[fff] 3240 patients were recorded in National Quality Sepsis Register (admitted to ICU with diagnosis of community acquired sepsis / septic shock). Of these, 520 were excluded, mostly due to missing data,

yielding 2720 in the final cohort. Patients were admitted via 32 EDs to 42 ICUs; 904 in 7 university hospitals and 1816 patients in 25 county hospitals

[ggg] The cohort included 23,619 patients with suspected sepsis and 25,990 patients with suspected septic shock, of whom 23,259 (98%) had data recorded for sex.

[hhh] Sample included 34 asylum seeking women with term born infants. compared to age- and ethnicity-matched controls delivering at the same hospital.

[iii] This study encompassed 248,767 cases with non-COVID-19 sepsis from a cohort of 22.0 million individuals spanning January 1, 2019, to June 31, 2022.

[jjj] The overall study population consisted of patients aged 65–100 years at any time during the observation period (from January 1, 2000, to summer 2020 who were registered at a GP practice in England. It included 108,317 cases classified as community-acquired sepsis.

[kkk] There were 1,007 patients discharged with an ICD-10 code of sepsis. After a manual audit of the data, 647 patients (64.3%) met criteria for sepsis or septic shock per the Sepsis-3 definition. Of the 647 patients, 116 (17.9%) either died in hospital or were discharged to hospice. These patients were excluded from further analysis, resulting in 531 patients remaining in the study cohort.

[lll] The overall study population consisted of patients aged 65–100 years at any time during the observation period (from January 1, 2000, to summer 2020 who were registered at a GP practice in England. It included 108,317 cases classified as community-acquired sepsis.

[mmm] Among the 3,984,581 Taiwan residents who underwent major inpatient surgery (defined as procedures requiring general, epidural, or spinal anaesthesia) and who were hospitalized for more than 1 day in 2004 to 2013, we identified 220 292 surgical patients aged 6 to 17 years. Of these, there were 3294 children and adolescents with a history of intellectual disability before the index surgery.

[nnn] The overall study population consisted of patients aged 65–100 years at any time during the observation period (from January 1, 2000, to summer 2020 who were registered at a GP practice in England. It included 108,317 cases classified as community-acquired sepsis.

[ooo] 28,062 participants were included in study analysis of which 2,773 were categorized as cancer survivors

[ppp] A total of 1750 patients were randomly selected from the blood culture list and reviewed, resulting in 509 patients treated as suspected sepsis for the purpose of the study

[qqq] A total of 2709 patients met the inclusion criteria in a large academic medical centre in New England, USA.

[rrr] This cohort study was performed at Seattle Children's, a 407-bed freestanding children's hospital in the Pacific Northwest. From October 1, 2012, to September 30, 2019, there were 232 228 eligible central catheter days and 344 Central line–associated bloodstream infections.

[sss] A cohort study of 362,500 patients with newly diagnosed cancer during 2006–2014 in Sweden

[ttt] Study considered 118,893 hospitalized patients with community-acquired sepsis in 2013-2014 with direct hospital admittance.

[uuu] Based on enrolment data from the Centers for Medicare and Medicaid Services for 53 million Medicare beneficiaries (ages 65–120) living in the conterminous US between 2000 and 2008.

[vvv] Study used the Intensive Care National Audit & Research Centre (ICNARC) Case Mix Programme (CMP) database between 2008 and 2010. In 2008, 2009 and 2010, coverage of the database was 65.0%, 75.2% and 80.2% of critical care units in England, Wales and Northern Ireland. There were 646 pregnant or recently pregnant women who met the case definition for severe sepsis, which represented 14.4% of maternal critical care unit admissions.

[www] Data for a total of 5, 359 ICU admissions during the study period were retrieved. This final propensity-matched sample comprised 56 homeless and 112 non-homeless patients.

[xxx] This study used NHS data. It included 224,361 (10.2%) cases with non-COVID-19 sepsis and 1,346,166 matched controls. Records were from between 1st January 2019 and 30th June 2022.

[yyy] Survey with 2003 participants, weighted to be nationally representative of the UK population.

[zzz] Analysis based on all complete ICU patient records from an American hospital with sepsis discharge claims from 2001 to 2012 who were Black (2,532) or White (14,902)

[aaaa] The database comprised of 73,140 ICU stays, of which 32,971 met the Sepsis-3 criteria. Following the inclusion and exclusion criteria, the final cohort consists of 23,914 ICU admissions

[bbbb] The study included 159 septic shock patients of whom 96 were African American.

[cccc] The study cohort included 8,568 cases of sepsis, of which 8,448 were non-inmates and 120 were inmates.

[dddd] Focus groups (n = 5) and 1:1 interviews (n = 17) were undertaken by peer researchers. 45 people took part in total.