

## **Sepsis: A global review**

Sepsis is currently one of the most significant challenges that nurses face when caring for patients. This paper discusses the global impact of sepsis and its implications, and highlights the importance of identifying sepsis and what treatment options are available in the United Kingdom (UK).

Daniels (2015) asserts that globally sepsis is perhaps the most pressing of public health issues. The UK National Confidential Enquiry into Patient Outcome and Death (NCEPOD, 2015) highlighted sepsis as being a leading cause of avoidable death that kills more people than breast, bowel and prostate cancer combined. Sepsis is a common and potentially life-threatening condition triggered by an infection (NHS England, 2015). Sepsis can be caused by a number of infections, but the most common sources are generally deemed to be the lung, the urinary tract and the abdominal organs. Sepsis can be triggered by introducing bacteria into blood via medical devices (UK sepsis trust, 2016). When people suffer from sepsis, the body's immune system has an unregulated response to infection, setting off a series of reactions, including widespread inflammation, swelling and blood clotting (NHS England, 2015). These can lead to a significant decrease in blood pressure, reducing the blood supply to vital organs, starving them of oxygen. If not treated quickly, sepsis can progress to severe sepsis which can lead to organ failure collective organ failure and/or fatality. While sepsis can affect anyone, it is most common in the elderly and the very young (World Sepsis Day, 2015). Chronic illnesses, including Diabetes Mellitus, Cancer, AIDS, Kidney or Liver disease increase the risk of sepsis, as does pregnancy or the occurrence of severe burns or physical injury (World Sepsis Day, 2015).

### Definitions of Sepsis

Definitions of sepsis are currently under review and new international consensus definitions are imminent (NICE, 2016). Bateson and Patton (2014) argued that sepsis has a spectrum of severity from uncomplicated sepsis, to severe sepsis, considered as sepsis and sepsis-related organ dysfunction or tissue hypoperfusion through to the most severe form of sepsis: septic shock, which is diagnosed in the presence of sepsis-related hypotension that persists even despite sufficient fluid resuscitation.

The definitions have formed the basis of research and guidance by leading campaign groups, such as the Surviving Sepsis Campaign (SSC) and the Global Sepsis Alliance (McClelland and Moxon, 2014). A review of the literature indicates there is general agreement (Cohen et al, 2015; Levy et al, 2003; Kaukonen et al, 2015; Balk, 2014) that these definitions lack sensitivity (the ability of the criteria to correctly identify sepsis) and specificity (the ability to correctly identify people without sepsis). The SSC currently explains sepsis as the existence of infection together with systemic indications of infection (Dellinger, 2013).

The NICE guidelines (NICE, 2016) acknowledge that new international consensus definitions are imminent and thus do not use the terms SIRS or severe sepsis, but instead use the term 'sepsis', recommending actions according to clinical parameters. Daniels (2015) argues that both a pragmatic definition (aimed at early identification) and an epidemiological definition (designed for public health surveillance and clinical trial design) are needed.

### Global impact

A review of the literature shows general agreement on the global burden of sepsis, including the growth in the number of cases, the high level of mortality coupled with a reduction in case fatality rates, and the underestimation of the problem due to inconsistencies in the way data is collected.

The first crude estimate of worldwide incidence of sepsis was 15-19 million (Adhikari et al, 2010). To provide a more refined estimate for the Lancet Infectious Diseases Commission, Fleischmann et al (2015) identified 33 studies providing population-level data incidence of hospital-treated sepsis. Based on these studies, Fleischmann et al (2015) estimated the annual incidence was up to 31 million cases of sepsis (similar to the SSC estimate of 30 million people worldwide each year (World Sepsis Day, 2015)) and 24 million cases of severe sepsis, with about 6 million death rates.

Estimates of the occurrence of severe sepsis in the general population are hard to obtain but annual figures are cited as 38/100 000 in Finland (Karlsson et al, 2007), 25/100 000 in Spain (Blanco et al, 2008), and 95 / 100 000 in those under 65 years of age in the U.S. but rising to 1,220/ 100 000 in over 65s (Richards 2013) indicating that sepsis becomes a growing health issue as the population ages (Hall et al, 2011). Many studies, at least from wealthier countries, report the occurrence of rising incidence and falling case of death (Cohen et al, 2015). Data for sepsis hospitalisations is available in countries including Australia, New Zealand, Taiwan and the US, the number of cases has risen steadily (Kaukonen et al, 2014; Shen et al, 2010; Hall et al, 2011 and Lagu et al, 2012)

Information collected for debt purposes by the US National Centre for Health Statistics estimates that there was an increase in the hospitalisations for sepsis elevated from 621,000 in the year 2000 to 1,141,000 in 2008 (Hall et al, 2011). It was also noted that there was an increase of up to three-fold in the number of hospital admissions for health care related community acquired infections over the last decade. Over the same period comparing stroke and myocardial infarction admissions remained stable (Seymour et al, 2012), resulting in the numbers of hospitalisations with sepsis overtaking those for myocardial infarction.

While sepsis cases may be increasing, mortality rates nonetheless appear to be decreasing through time, at a rate of 3-5% over the past 20 years (Stevenson et al, 2014). It could be argued that the falling mortality rate is due to improvement in care or a decreased effect through increased recognition of patients that are not as ill as those who would have previously been detected. Within the UK, ICNARC (2011) estimates (relating only to cases recorded within ICU settings during 24 hours of admission) are of 102,000 sepsis cases a year causing 36,000 deaths (Daniels, 2009). Daniels (2011) also cites sepsis as causing 37,000 deaths annually.

Internationally, sepsis continues to be a dominant cause of fatality due to infection despite leading modern medicine including vaccines, antibiotics and acute care (World Sepsis Day, 2015). Vincent et al (2014) through a worldwide appraisal of the mortality rate found that one third of patients with sepsis treated in an ICU setting died without leaving hospital, with mortality rates of up to 40-50% when septic shock is present. Liu et al (2014) also state that sepsis remains an outstanding cause of overall fatality, contributing from a third to a half of all hospital mortalities. This is supported by European research (Vincent, 2006) findings that 36% of deaths in ICUs were due to sepsis.

In terms of the developing world, the review of 33 studies by Fleischmann et al (2015) noted the absence of population-based data on sepsis incidence from poor-income and middle-income countries (LMICs). However, it is claimed that overall in the developing countries sepsis is the cause 60-80% of fatalities per year, which affects greater than 6 million babies and children each year with more than 100,000 woman acquiring sepsis through the course of pregnancy and childbirth (Kissoon et al, 2011). Say et al (2014) state that while globally an estimated 11% of maternal deaths are caused by sepsis, the vast majority of these occur in developing regions. Maternal sepsis is recognised as a challenge in both low- and high-resource settings with figures indicating that one-quarter of women who die within the 6 weeks after pregnancy in the UK die from sepsis (Knight et al, 2014).

### Accuracy of estimates

While the existing data points to a significant global problem, the literature reveals a consensus of opinion that the current sepsis figures underestimate the size of the problem. The Lancet Commission (Cohen et al, 2015) highlights the fact that sepsis does not have a single diagnostic test and thus measurements of sepsis can differ across, and even within, countries.

Three general approaches to the measurement exist: “clinically defined sepsis in prospective clinical registries, administrative coding of sepsis in hospital discharge databases, and causes of death from vital statistics records” (Cohen et al, 2015). Each of these approaches is unique and has its limitations. Clinical registries, for example, cannot capture all ICUs; hospital discharge databases only capture those people treated in hospital and death records mostly assign infectious diseases to the underlying infection. While there is a vast literature on sepsis, it is notable that much of the evidence is based on data collected in ICUs and Cohen et al (2015) highlighted the fact that very little is noted about sepsis outside the context of clinical practice in main critical care centres in developed countries.

Due to the data collection methods, many researchers point to the figures as underestimates. The SSC claims that the hospital treatment of sepsis is up to seven fold higher in resource rich countries (World Sepsis Day, 2015). Bateson & Patton (2015), emphasise that 37000 deaths in the UK is a conservative estimate, as this includes only those patients diagnosed with severe sepsis within 24 hours of admission to ICUs. A study of information recorded on death certificates in England, for the period 2001–2010 (McPherson et al, 2013), revealed that 1 in 20 deaths was associated with sepsis. Importantly, these deaths occur across a wide range of specialty areas and 15,000 (7%) deaths definitely associated with sepsis in 2001-10 did not occur in hospital. This finding again suggests estimates of sepsis are low, since much of the research has been based on data collected from ICUs, thus ignoring deaths occurring outside of hospital. Dr Alex Goodwin (NCEPOD, 2015) claims that the reported incidence in the UK is likely to be an underestimate as the clinician coding system prioritises the source of infection. Overall, he estimates that there could be as many as 200,000 cases of sepsis in the UK, and up to 60,000 deaths a year (NCEPOD, 2015) – much higher than the current reported figures.

### Implications of sepsis

Research on sepsis outcomes has traditionally focused on mortality as an end point (Bateson and Patton, 2015). Increasingly, however, the costs and long-term consequences of survival from sepsis are being documented and these are likely to be substantial (Winters et al, 2010; McPherson et al, 2013; Iwashyna et al, 2010; Goodwin et al, 2015). Daniels (2015) states that patients with sepsis spend more time in hospital, and also in ICUs, than do patients admitted for other reasons. Goodwin et al (2015) claim that around 65,000 people within the UK per year survive sepsis, but often with serious long-term effects that result in amputation, muscular contraction, damage to lungs that cannot be reversed, damage to the heart and kidneys and also cognitive disorders. When these factors are considered together with the statistics on death, Daniels (2015) argues that the true human and fiscal costs of sepsis become “frightening”.

According to McPherson et al (2013), in 1995-1996 in a UK hospital the average cost of treating a patient who had sepsis was six times the cost of treating a patient who did not have sepsis. Around 70% of patients who suffer from severe sepsis will need to be moved to intensive care units and, in the UK, it is estimated that the costs of a bed within the ICU is around £1500 a-day, the cost can be higher depending on the severity of the condition and the treatment required (Richards, 2013).

According to Frost et al (2010) this represents a total cost of over £2.5 billion per year to the NHS. It is generally agreed that early recognition and treatment will have great economic benefits. The Agency for Healthcare Research and Quality lists sepsis as the mostly costly condition treated in US hospitals, equating more than \$20 billion in 2011 rising the average annually by 11.9% (Pfuntner et al, 2011). Estimations also show that the US collaboratively detected earlier sepsis recognition evidenced based treatment (Pfuntner et al, 2011). Therefore relating to 92,000 fewer mortalities per year, 1.25 million fewer hospital days, and cuts in hospital expense of over \$1.5 billion (Shorr et al, 2007).

The UK Sepsis Trust has estimated that a typical medium-sized general hospital could save £1.25 million annually through improved management of sepsis, and that achieving 80% delivery of the basic standards of care is likely to save 10,000 lives per year and around £170 million annually for the National Health Service (UK Sepsis Trust Briefing, 2013). The longer term economic benefits are likely to be even greater. This would suggest that early diagnosis and treatment of sepsis is essential as it will lead to significant economic benefits and a reduction in the long-term costs for the NHS.

#### The importance of identifying sepsis and commencing treatment

A review of the literature suggests that there is general agreement that increased recognition and active management of patients with sepsis have improved outcomes over the past 15 years (Cohen et al, 2015; Yealy et al, 2015; Daniels, 2015). However, there is much evidence to suggest that there is significant room for improvement in both recognition and management (Cohen et al, 2015; NHS England, 2015; NCEPOD, 2015; Dellinger, 2013; PHSO, 2013; Yealy et al, 2015) and nurses can play a significant role in the improvement process.

McClelland and Moxon (2014) argue that 'nurses play a key role in spotting patients who are unwell or deteriorating, and initiating life-saving treatments'. It is essential, therefore, that nurses develop a culture of suspicion of sepsis and respond quickly to detect, manage and escalate patients suffering from sepsis, particularly those patients in the community where over 70% of cases arise (NCEPOD, 2015), where early intervention can prevent harm and significantly reduce mortality. This suspicion accords with the arguments of Daniels (2015), who claims that without an understanding among health professionals regarding the symptoms in patients signifying sepsis opportunities to recognise and treat will continued to be missed. Nurses are often the first to suspect that a patient may have sepsis and are often the first to initiate treatments are prescribed. Equally, it is up to nurses to assist in the combating of sepsis and ensure that infection control practices are adhered to. The role of the nurse is pivotal in relation to sepsis.

The SSC recommends the use of two care bundles in the management of sepsis (Dellinger, 2013); the first bundle must be completed within 3 hours and the second within 6 hours. While research demonstrates that compliance with these bundles is associated with a reduction in hospital deaths (Levy et al, 2015), it is clear that there is significant room for improvement in compliance rates (NCEPOD, 2015) and the reliable delivery of the basics of care (Daniels, 2015). In addition to this the NICE (2016) should also be utilised by nursing staff and medics in addition to the sepsis six to ensure that patients receive the care they need. Whilst there are similarities between the sepsis six and NICE guidance (2016), in practice many trusts do advocate the use of the NICE guidance (2016). Many UK trusts have now also revised their protocols in light of the new NICE NG51 guidance (2016), and as such nurses in practice should be utilising this more and adhering to it.

In the UK, the Sepsis Six care bundle, developed by Daniels (2011), is often used for the initial management of sepsis and, while it is similar to the SSC 3-hour bundle, it should instead be

completed within the first hour of sepsis identification (Bateson and Patton, 2015). This bundle as a whole has been shown to reduce the relative risk of death by 46.6% (Daniels et al, 2010) when delivered to patients with severe sepsis within one hour. Close monitoring and regular review can identify patients who do not improve with the Sepsis Six, prompting urgent referral to critical care. Nurses play a vital role in the administration of these bundles and thus in improving compliance rates and ultimately patient outcomes. Finally, it is important to note that the NCEPOD (2015) report highlights that many basic elements of good nursing practice, including effective hand-washing, recording of basic vital signs, adherence to hospital protocols and good documentation are fundamental remedial factors, which if properly addressed, would improve the quality of care of patients with sepsis.

### Conclusion

This article examined the global impact of sepsis and its associated implications. It highlights the importance of identifying sepsis and the treatments advocated within the UK. It is essential to raise awareness of this as a nursing issue, to ensure that patients are kept safe and to prevent more patients from dying from this. As nurses it is essential that the NICE guidance NG51 (2016) is adhered to and implemented in an attempt to prevent more lives being lost.

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