# Determination of the size of the different sepsis categories presenting to a UK teaching hospital emergency department

M Majuran,[1] M Clancy[2]

[1] University of Southampton, Southampton, UK; [2] Emergency Department, Southampton General Hospital, Southampton, UK

Correspondence to: M Clancy, Emergency Department, Southampton General Hospital, Tremona Road, Southampton SO16 6YD, UK; mike.clancy@suht.swest.nhs.uk

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## ABSTRACT

**Aim:** To establish the size of the population of patients presenting to a UK emergency department (ED) with systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis and septic shock and to determine their mortality and length of stay.

**Setting:** Southampton General Hospital Emergency Department, a teaching hospital treating 90 000 patients per annum.

**Method:** A retrospective audit of all patients attending the ED for a 1-month period was undertaken in order to classify them into the different sepsis groups. Length of stay and mortality data were abstracted from the Patient Administration System, a computerised database.

**Results:** 137 (SIRS), 123 (sepsis) and 50 (severe sepsis or septic shock) patients were classified from 5832 new patients attending. The median length of stay was 5, 3 and 7.5 days, respectively, and the mortality was 6.6%, 4.1% and 26%, respectively. The incidence of severe sepsis or septic shock was 30 per 1000 patients admitted.

**Conclusion:** The high incidence of severe sepsis and septic shock with its attendant high mortality and length of stay is highlighted. If the figures are annualised, this would equate to 650 cases of severe sepsis or septic shock, of which 169 would die. The ED is well placed to improve this outcome by earlier detection and the use of goal directed therapy.

The mortality from severe sepsis still remains "unacceptably high",[1] with only a "slight reduction" in the mortality from septic shock over the years.[2] A comprehensive analysis of the epidemiology of severe sepsis in the USA during 1995 reported a mortality rate of 28.6%, amounting to 215 000 deaths nationally, estimated to be 9.3% of all the deaths in the USA that year and equivalent to the number of deaths following acute myocardial infarction.[3] Among the reasons suggested for the high mortality rate from severe sepsis were late recognition of the disease and inappropriate treatment prior to admission to the intensive care unit (ICU).[4] In order to tackle these and other possible causes for the high mortality rate, the Surviving Sepsis Campaign undertook to produce a set of evidence-based guidelines for the management of sepsis as "a first step toward a global strategy that can be adapted to local use".[5] Our aim was to establish the size of the population presenting at the Southampton General Hospital Emergency Department with systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis and septic shock, and to determine the mortality and length of stay in the hospital.

The definitions for the different sepsis categories[5] and how they were operationalised in this audit are given in table 1.

A recent study in the USA showed that half the patients admitted to hospital with sepsis came through the emergency department (ED),[6] and a retrospective observational study of severe sepsis and septic shock in several Canadian ICUs found that 32% of patients were admitted via the hospital EDs.[7] Most studies retrospectively assessed the source of admissions only after patients had reached the ICU. It is thus difficult to establish the size of the problem as it presents to the ED, hence the need for this study.

With the Surviving Sepsis guidelines highlighting that, similar to acute myocardial infarction, outcome is probably affected by the "speed and appropriateness of therapy administered in the initial hours after the syndrome develops", and in putting particular emphasis on the importance of the first 6 h following presentation (the so-called "golden hours"), the role of the ED becomes crucial in determining outcome.[8]

## METHODS

The audit was discussed in detail with a Research and Development officer for Southampton University Hospitals Trust and deemed not to require submission to an ethics committee or R&D approval.

### Subjects and selection of cases

The available ED patient records for all patients attending the department within the 4-week period from 27 March to 23 April 2006 were audited. Patients were excluded from further study if they left before treatment, were discharged (either to home or outpatient clinic) or were aged under 18 years. The number of patients in these groups was, however, recorded to help determine incidence rates. For the remaining patients a SIRS score was calculated based on the number of SIRS criteria met during the stay in the ED. Patients were excluded if they failed to meet a score of at least 2 during their stay. SIRS criteria were as shown in table 1.

### Data abstraction

For the remaining patients (ie, those adults who were admitted to the hospital and had a SIRS score of 2 or more during their stay), we recorded data to classify the patients with the information being entered directly into the SPSS 14.0 statistical package. Data were verified by checking for

**Table 1** Definitions relating to sepsis as decided at the 1991 ACCP/SCCM Consensus Conference and how they relate to the groupings in our study

| 1991 ACCP/SCCM Conference definitions[8] | Definitions as used in our audit |
|---|---|
| SIRS: the presence of two or more of the following criteria:<br>Body temperature >38°C or <36°C<br>Heart rate >90 beats per minute<br>Tachypnoea manifested by respiratory rate >20 breaths per minute or hyperventilation as indicated by $Paco_2$ <32 mm Hg (4.3 kPa)<br>Alteration in white blood cell count, such as >12 000/mm$^3$, <4000/mm$^3$ or the presence of >10% immature neutrophils ("bands") | As in the 1991 ACCP/SCCM Conference with the exception that, as band cell count is not routinely recorded in Southampton General Hospital, this was not used as a criterion |
| Sepsis: SIRS resulting from an active infectious process | As discussed later, Rivers *et al*[9] used the presence of a "documented or presumed infectious cause" as the discriminator for sepsis in their EGDT study and we have done the same. |
| Severe sepsis: sepsis associated with one or more of:<br>Organ dysfunction<br>Hypoperfusion abnormalities (eg, lactic acidosis, oliguria, acute alterations of mental status)<br>Sepsis-induced hypotension (systolic blood pressure <90 mm Hg or reduction by 40 mm Hg or more from the baseline in the absence of other causes for hypotension) | The criteria used were those recommended by Rivers *et al*[9] for the patient to be managed with EGDT, that is:<br>Systolic blood pressure <90 mm Hg or deviation of >40 mm Hg from the baseline<br>Mean arterial pressure <65 mm Hg<br>Serum lactate >4 mmol/l<br>Any signs of hypoperfusion or organ dysfunction (eg, oliguria, acute confusion) |
| Septic shock: severe sepsis with sepsis-induced hypotension that persists despite adequate fluid resuscitation | Due to difficulty in acquiring and analysing these data retrospectively, we allocated patients with severe sepsis and those with septic shock to one group: "severe sepsis or septic shock" |

ACCP/SCCM, American College of Chest Physicians/Society of Critical Care Medicine; $Paco_2$, arterial carbon dioxide tension; EGDT, early goal-directed therapy

anomalous results at the end of each session. Age and sex were recorded, together with values for the variables relating to SIRS criteria that could be derived from the notes (heart rate, respiratory rate and temperature). Baseline values were taken from the initial recording on the observation or resuscitation charts. Where these were not available, they were abstracted from the earliest set of recordings that could be found in either the triage or clerking notes. The central laboratory database was interrogated to provide a list of patients attending during the target period who had white blood cell counts in the SIRS range (<4000/mm$^3$ or >12 000/mm$^3$) and these values were also added to our results database. As well as the initial values, the most deranged values (ie, the most positively indicative of SIRS) during the stay were also recorded. Any missing values were noted as such and assumed to be normal.

To distinguish the sepsis group we applied the discriminator used by Rivers *et* al[7] of a "presumed or documented infection", which was taken to mean either a recent diagnosis with infection or clinical suspicion of such by the attending medical officer. Using microbial culture data to provide a pathological gold standard was considered, but as this information would not be available at the time of presentation and thus would not influence any clinical allocation to one of the groupings or subsequent management in the ED, this was rejected in line with other researchers.[10]

To examine the progression to severe sepsis, systolic blood pressure and mean arterial pressure were recorded to determine if hypotension was present, and serum lactate was noted as an indicator of organ dysfunction. Both the initial and most deranged values were recorded. Other signs of organ dysfunction or hypoperfusion were also noted, with any oliguria or acute changes in mental state being particularly sought. Severe sepsis was recorded in line with the definition in table 1.

While the intention was also to categorise separately the group who had progressed to septic shock, as mentioned previously this requires data on whether hypotension persisted despite adequate fluid resuscitation which were not reliably available, so we analysed the severe sepsis and septic shock groups as one ("severe sepsis or septic shock"). Length of stay (derived from date of attendance and date of discharge) and survival data were obtained from the PAS patient database using the patient number and date of birth.

### Analysis of data

Data were analysed using the SPSS Version 14.0 package. As the data were found not to fit the normal distribution, median values and interquartile ranges (IQR) were used and statistical analysis was undertaken using non-parametric testing. Specifically, contingency table-based $\chi^2$ analysis was used to determine any statistical significance between the distributions of categorical variables (ie, mortality and sex) among the groups. Kruskal-Wallis analysis was undertaken to determine

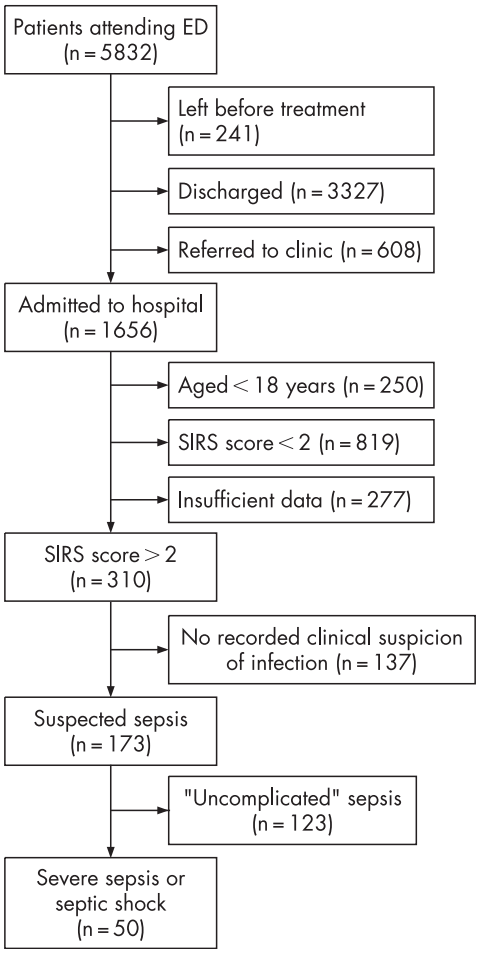


**Figure 1** Flow chart of numbers of patients in the study. SIRS, systemic inflammatory response syndrome.

**Table 2** Characteristics of the audit population (n = 310)

| | Total | SIRS without infection | "Uncomplicated" sepsis | Severe sepsis or septic shock | p Value |
|---|---|---|---|---|---|
| N (%) | 310 (100) | 137 (44.2) | 123 (39.7) | 50 (16.1) | |
| Male, n (%) | 152 (49.0) | 65 (47.4) | 65 (52.8) | 22 (44.0) | NS |
| Female, n (%) | 158 (51.0) | 72 (52.6) | 58 (47.2) | 28 (56.0) | NS |
| Age (years)* | 68 (45–83) | 64 (46–81.5) | 65 (38–80) | 78 (60.75–87.25) | 0.002 |
| Treated in ICU, n (%) | 9 (2.9) | 5 (3.6) | 1 (0.8) | 3 (6.0) | NS |
| Worst SIRS score during stay* | 2 (2–3) | 2 (2–2) | 2 (2–3) | 2.5 (2–3) | <0.001 |

*Data presented as median (IQR).
SIRS, systemic inflammatory response syndrome; ICU, intensive care unit; NS, not significant.

the same for interval variables (eg, age, length of stay) where the number of groups was >2, and the Mann-Whitney U test was used to compare a pair of groups. To further analyse our outcome measures (ie, length of stay and mortality), we performed survival analyses using the Kaplan-Meier method, censoring those discharged when analysing mortality and those who died when analysing length of stay, technique. These were then repeated using the Cox regression method and age as a covariant to determine if any significant difference between the groups persisted after accounting for age; p values <0.05 were considered statistically significant.

## RESULTS

During the 4-week period between 27 March and 23 April 2006, 5832 patients attended the ED at Southampton General Hospital. Of these, 241 left before treatment, 3327 were discharged home and 608 were discharged to various outpatient clinics. Of those admitted, 250 were excluded from the study as they were aged under 18, 819 because they did not display at least two clinical manifestations of SIRS and 277 because there were insufficient data recorded in the notes to determine if they met two or more of the SIRS criteria with any missing values assumed to be normal. This left a cohort of 310 patients for detailed analysis. Using the discriminators noted above and the most deranged measurements recorded during the patients' stay in the ED, we were able to divide the cohort into the following three groups: (1) SIRS (without infection), n = 137; (2) "uncomplicated" sepsis (ie, sepsis without signs of hypotension, hypoperfusion or organ dysfunction), n = 123 and (3) severe sepsis or septic shock, n = 50.

The overall grouping is depicted in fig 1. These results indicate that the incidence of patients with severe sepsis or septic shock is nearly 9 (50/5832) per 1000 patients attending the ED and 30 (50/1656) per 1000 patients admitted to the hospital via the ED.

### Patient characteristics

The characteristics of the patient cohort are shown in table 2; 49% were men and the median age was 68 years (IQR 45–83). Age was found to be significantly different between the three groups, and further analyses showed a significant difference in age between the group with severe sepsis or septic shock and the rest of the cohort (p = 0.001). There was also a significant difference between the three groups in the worst recorded SIRS score (p<0.001).

### Outcomes

Median hospital stay was 4.5 days for the whole cohort (IQR 2–11), with a significant difference between the three groups (SIRS alone: 5.0 days (2–11); uncomplicated sepsis: 3.0 days (2–8); severe sepsis or septic shock: 7.5 days (4–14.5), p = 0.004, table 3) and a more significant difference between the group with severe sepsis or septic shock and the rest of the cohort (p = 0.002, table 3). The mortality rate for the whole cohort was 8.7% (283 survivors and 27 deaths). There was a significant difference between the categories (mortality 6.6% for SIRS alone, 4.1% for uncomplicated sepsis and 26% for severe sepsis or septic shock, p = 0.001), with a more significant difference between the severe sepsis or septic shock group and the rest of the cohort (p<0.001). To analyse these outcome measures better we performed a Kaplan-Meier analysis which enabled us to adjust for those discharged when assessing mortality and those who died when assessing length of stay. Significant differences were found when comparing the mortality (p = 0.003) and length of stay (p = 0.001) between all three groups, which was enhanced when the group with severe sepsis or septic shock was compared with the rest of the cohort (mortality p = 0.001, length of stay p = 0.001). As noted above, the severe sepsis or septic shock group were significantly older than the rest of the cohort, so survival analyses were repeated using the Cox regression method using age as a covariant to determine if the statistical difference between the groups persisted once this was accounted for. It revealed that there was still a significant difference between the categories even after accounting for age for both length of stay (p = 0.022) and mortality (p = 0.025), and these were again more significant when the group with severe sepsis was compared with the rest of the cohort (mortality p = 0.008, length of stay p = 0.017, table 4).

When the mortality rate from severe sepsis was combined with the incidence rate given above, the overall mortality from severe sepsis or septic shock is nearly 8 cases/1000 patients admitted to the hospital via the ED (0.26×30).

**Table 3** Outcome measures

| | Total | SIRS without infection | "Uncomplicated" sepsis | Severe sepsis or septic shock | p Value | p Value (age adjusted) |
|---|---|---|---|---|---|---|
| Median (IQR) length of stay (days) | 4.5 (2–11) | 5 (2–11) | 3 (2–8) | 7.5 (4–14.5) | 0.004 | 0.022 |
| Mortality, n (%) | 27 (8.7) | 9 (6.6) | 5 (4.1) | 13 (26.0) | <0.001 | 0.025 |

SIRS, systemic inflammatory response syndrome.

**Table 4** Comparison of the characteristics of those with severe sepsis and the rest of the cohort

| | Severe sepsis or septic shock | SIRS without severe sepsis or septic shock | p Value | p Value (age adjusted) |
|---|---|---|---|---|
| n (%) | 50 (16.1) | 260 (83.9) | | |
| Male, n (%) | 22 (44.0) | 130 (50) | NS | |
| Female, n (%) | 28 (56.0) | 130 (50) | NS | |
| Age (years)* | 78 (60.75–87.25) | 65 (42–81) | 0.001 | |
| Treated in ICU, n (%) | 3 (6.0) | 6 (2.3) | NS | |
| Worst SIRS score during stay* | 2.5 (2–3) | 2 (2–3) | 0.019 | |
| Length of stay (days)* | 7.5 (4–14.5) | 4 (2–10) | 0.002 | 0.017 |
| Mortality, n (%) | 13 (26.0) | 14 (5.4) | <0.001 | 0.008 |

*Data presented as median (IQR).
SIRS, systemic inflammatory response syndrome; NS, not significant.

## DISCUSSION

This audit has revealed that the incidence of severe sepsis or septic shock in patients admitted to Southampton General Hospital via its ED is approximately 30 cases per 1000. This group was also associated with a significantly higher mortality rate of 26%. Length of stay was found to be significantly longer than for patients classified as having SIRS without infection and "uncomplicated" sepsis.

Extrapolating from our figures and assuming our study period was typical of the year and with no seasonal variation in the incidence of severe sepsis, we can estimate that Southampton General Hospital admits approximately 650 people with severe sepsis or septic shock per year from the ED and that, of those, 169 will not survive their stay in hospital.

The mortality rate calculated is similar to other reports,[3] and the recent analysis of the epidemiology of severe sepsis in England, Wales and Northern Ireland (the ICNARC analysis) found a rate of 30.8% in 2004.[11] Incidence data are more difficult to assess as we were not able to find any ED studies with which to compare it.

One limitation of this study is that the absence of resuscitation charts for many patients from their ED case notes and the lack of nursing protocols standardising the frequency for recording vital signs is likely to lead to an underestimate of our already sizeable numbers of patients with sepsis.

## CONCLUSION

Severe sepsis is a growing problem in the UK. While the overall mortality rates have been decreasing slowly over the past years,[11] as the population grows older the incidence of the disease is increasing and with it the actual number of deaths per year. Central to the Surviving Sepsis Campaign is the early identification and treatment of the disease in the ED. We have shown that there is a high incidence of cases presenting with severe sepsis or septic shock to the ED with a high rate of mortality.

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