

Correlation of Clinical Sepsis Definitions with Microbiological Characteristics in Patients Admitted Through a Sepsis Alert System; A Prospective Cohort Study

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Abstract

Background: Sepsis was recently redefined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. With this redefinition (Sepsis-3), clinical and microbiological characteristics of patients with sepsis may differ from the patients fulfilling the previous described definition (Sepsis-2).

Purpose: To describe differences in clinical and microbiological characteristics of sepsis episodes between Sepsis-3 and Sepsis-2. The secondary aim was to compare blood culture outcomes between episodes fulfilling Sepsis-3 and Sepsis-2 criteria, respectively.

Methods: A prospective study design was used to include patients presenting with clinically suspected sepsis in the emergency department. Six blood culture bottles were collected from each patient. Blood cultures were described as having clinically relevant growth, contaminant growth, or no growth. Clinical and laboratory data were collected from medical records and the laboratory information system.

Results: The analysis included 549 episodes. There were 387/549 (70.5%) Sepsis-3 and 443/549 (80.7%) Sepsis-2 episodes. In total, 369/549 (67.2%) episodes fulfilled both Sepsis-3 and Sepsis-2 criteria. Blood cultures were positive for clinically relevant growth in 140/387 (36.1%) and 155/443 (35.0%) episodes in Sepsis-3 and Sepsis-2, respectively. Other clinical and microbiological characteristics did not differ between Sepsis-3 and Sepsis-2.

Conclusions: A high proportion of patients included through a sepsis alert system fulfilled both Sepsis-3 and Sepsis-2 criteria. The performance of blood cultures in detection of microorganisms was poor and were similar in Sepsis-3 and Sepsis-2 patients.

Introduction

Background:

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection [1, 2]. The clinical definition of sepsis has varied over time, and the current definition was introduced in 2016 as Sepsis-3 [2, 3]. The major change was the use of parameters related to organ dysfunction as a consequence of infection, in contrast to the systemic inflammatory response syndrome (SIRS) used in the previous definition (Sepsis-2). Early optimal blood culture sampling is a cornerstone of sepsis management [4, 5], and blood culture is widely accepted as the gold standard for microbiological diagnostics in sepsis [6].

The microbiological findings in sepsis according to the previous definition have been well studied. In particular, the proportion of positive blood cultures in cases fulfilling Sepsis-2 criteria is reported to be around 30% in several studies [1, 7-9].

Importance:

In contrast to Sepsis-2, the microbiological characteristics in Sepsis-3 cases has scarcely been studied, two separate studies have reported the rate of blood culture positivity to be 22% and 48.2% [10, 11]. Sepsis treatment recommended by current guidelines relies on data originally from Sepsis-2 data [3]. However, it is possible that differences in the microbiological spectrum between Sepsis-3 and Sepsis-2 have an impact on the approach to the diagnosis and treatment of sepsis in future guidelines. Therefore, there is a need to characterize clinical and microbiological features in patients with Sepsis-3 and compare to those with Sepsis-2.

Goals of this investigation:

The primary aim of the study was to analyze clinical and microbiological characteristics in patients with suspected sepsis, according to both Sepsis-3 and Sepsis-2 definitions.

Materials And Methods

Study design and setting

This prospective clinical study was performed at Karolinska University Hospital Huddinge, Stockholm, Sweden. The hospital has 760 beds and the ED had 53,508 visits in 2019 [12]. In the Emergency Department, all patients are routinely subjected to triage with the Rapid Emergency Triage and Treatment System [13], and a sepsis alert was triggered for triage signs of organ dysfunction combined with signs of infection, i.e. fever, history of fever, or clinical suspicion of infection, as we have previously described [14]. Patients who triggered the sepsis alert were subjected to a multidisciplinary bedside assessment by physicians from the Emergency Department, the Department of Infectious Diseases and the Intensive Care Unit within fifteen minutes, to optimize clinical assessment and treatment.

Selection of Participants:

Consecutive adult patients who triggered the sepsis alert from September 2017 to February 2019 were included in the study. Patients with suspected sepsis accorded to the sepsis alert were included prospectively, thus patients with a final diagnosis other than sepsis and/or infection were also included in the study. A suspected sepsis episode, here referenced as an “episode,” was defined as a patient who triggered the sepsis alert system. Two or more episodes from the same patient could be included if they occurred more than 72 h apart as described previously [14]. Episodes were excluded if fewer than six blood culture bottles were collected, or if there was uncertainty that the collection of blood was performed in accordance with the study protocol.

Blood culture collection and transportation

Three blood culture sets, each one consisting of an aerobic (BactAlert FA Plus) and an anaerobic (BactAlert FN Plus) blood culture bottle, were sampled from each patient who triggered the sepsis alert system. The blood culture bottles were transported to the Department of Clinical Microbiology, Karolinska University Hospital according to routine practice, and were analyzed according to the standard routine. From the beginning of the study in September 2017 until September 20, 2018, the blood culture bottles were incubated in BacT/ALERT 3D (Bio-Merieux, France). Beginning on September 20, 2018, the clinical microbiology laboratory changed its blood culture system to BacT/ALERT Virtuo (Bio-Merieux, France). The BactAlert FA Plus and BactAlert FN Plus blood culture bottles were used throughout the study. Blood cultures were incubated in the system until they signaled positive or for a total of five days. In positive blood cultures, samples were Gram stained and then subcultured on agar plates. Colonies that grew on agar were subjected to species identification by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonik, Bremen, Germany) and were subjected to antibiotic susceptibility testing by standard laboratory procedures.

Definition of clinically relevant growth and contaminant growth

Information regarding blood culture results in terms of isolate identification and time to detection was collected from the laboratory information system. Detected isolates were defined as clinically relevant growth or contaminant growth, according to an improved version of the methods used in previously published reports [14, 15]. Clinically relevant growth was defined as growth of pathogenic microorganisms in at least one blood culture bottle. Contamination was defined as such if two criteria (A and B) were fulfilled. First (A), isolates commonly regarded as contaminants (coagulase-negative staphylococci, *Corynebacterium* spp., *Micrococcus* spp., *Micrococcus* spp., and *Facklamia* spp.), as described by previous studies and guidelines, were considered to be potentially contaminant if they grew in three or fewer of the six bottles. Second (B), the potential contaminants had to show no growth in any other relevant microbiological sample (urine, skin/soft tissue, lower respiratory tract, cerebrospinal fluid, pleural/ascitic drainage) within ± 5 days of blood culture sampling.

Data collection and analysis

Clinical and microbiological data were collected using the hospital's electronic record system and the electronic laboratory information system, respectively. Sepsis-3 was considered to be present if two criteria (A and B) were fulfilled: A) infection was clinically suspected at admission to the ED; B) organ dysfunction corresponding to an increase in sequential organ failure assessment (SOFA) score ≥ 2 from baseline was present. Baseline SOFA score was determined by the best (i.e. most physiological) data points during a 3-month period before inclusion in the study. In case of missing baseline data, the score for that data parameter was assumed to be zero. In the present study, (A) was defined as present if broad spectrum antibiotics were initiated within 48 hours after time of blood culture sampling and ongoing for at least 4 days afterwards as described in previous epidemiological studies [16].

Sepsis-2 was considered to be present if two criteria (A and C) were fulfilled. First (A), defined as above. Second (C), two or more SIRS criteria were present.

Statistical analysis

Frequencies and percentages were used to summarize categorical variables, while means and standard deviations, together with medians and interquartile ranges, were used to summarize numerical variables. Statistical analyses were carried out using SPSS (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.)

Results

In total, 652 episodes triggered the sepsis alert system during the study period. Fig. 1 depicts the study flow chart and reasons for exclusion. After exclusion, 549 episodes from 514 unique patients were included in the final analysis. Of the 31 patients who had more than one episode included in the study, 27 patients had two episodes and four had three. The mean patient age was 69.5 (SD \pm 17) and 61% were male. In total, 1647 blood culture sets (3294 blood culture bottles) were collected, each consisting of one BacT/Alert FA Plus and one FN Plus bottle.

Characterization of study subjects

Overall, 387/549 (70.5%) episodes fulfilled Sepsis-3 criteria (from here on called Sepsis-3 positive episodes) and 443/549 (80.7%) episodes fulfilled Sepsis-2 criteria (from here on called Sepsis-2 positive episodes). In total, 369/549 (67.2%) episodes fulfilled both Sepsis-3 and Sepsis-2 criteria. The number and proportion of episodes fulfilling either, both or none of the two studied criteria for sepsis (Sepsis-3 and Sepsis-2) is shown in Fig.2. The clinical characteristics of episodes that fulfilled none, one or both sepsis definitions are described in detail in Table 1. Median (IQR) SOFA score was 3 (2-5) in the Sepsis-3 positive group, as well as in the Sepsis-2 positive group. 28-day mortality was 60/387 (15.5%) and 64/443 (14.4%) in Sepsis-3 and Sepsis-2 group, respectively.

Table 1. Clinical characteristics of the episodes (N = 549 episodes).

<i>Characteristic</i>	<i>Sepsis-3 positive*/Sepsis-2 positive (n=369)</i>	<i>Sepsis-3 negative/Sepsis-2 positive (n=74)</i>	<i>Sepsis-3 positive/Sepsis-2 negative (n=18)</i>	<i>Sepsis-3 negative/Sepsis-2 negative (n=88)</i>
Demographics		-		
- Male - n (%)	231 (62.6)	45 (60.8)	11 (61.1)	51 (58.0)
- Age – years **	73 (13.6)	61 (19.2)	71 (15.6)	61 (20.2)
- 28-day mortality n (%)	59 (16.0)	5 (6.8)	1 (5.6)	8 (9.1)
- Admission to intensive care unit during hospital stay, n (%)	40 (10.8)	1 (1.4)	3 (16.7)	2 (2.3)
- SOFA score†	3 (3-5)	1 (1-2)	3.5 (2-6)	2 (1-3)
Co-morbidities, n (%)				
- Congestive heart failure	73 (19.8)	8 (10.8)	4 (22.2)	10 (11.4)
- Diabetes mellitus	113 (30.6)	17 (23.0)	4 (22.2)	32 (36.4)
- Ischemic heart disease	57 (15.4)	5 (6.8)	2 (11.1)	7 (8.0)
- Peripheral vascular disease	42 (11.4)	4 (5.4)	0 (0.0)	5 (5.7)
- Cerebrovascular disease	80 (21.7)	12 (16.2)	3 (16.7)	12 (13.6)
- Malignancy	99 (26.8)	11 (14.9)	6 (33.3)	14 (15.9)
- Chronic kidney failure (GFR <60)	107 (29.0)	8 (10.8)	4 (22.2)	16 (18.2)
- Chronic pulmonary disease	58 (15.7)	19 (25.7)	2 (11.1)	10 (11.4)
- Chronic liver failure	11 (3.0)	2 (2.7)	1 (5.6)	3 (3.4)
Source of infection††				
- Respiratory tract	138 (37.4)	26 (35.1)	7 (38.9)	3 (3.4)
- Urinary tract	83 (22.5)	15 (20.3)	4 (22.2)	0 (0.0)
- Abdominal	30 (8.1)	7 (9.5)	0 (0.0)	2 (2.3)
- Soft tissue/skin/skeletal/joint	25 (6.8)	10 (13.5)	2 (11.1)	0 (0.0)
- Central nervous	2 (0.5)	0 (0.0)	1 (5.6)	1 (1.1)

system					
-	Endocarditis	6 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)
-	Other/unknown	93 (25.2)	16 (21.6)	4 (22.2)	1 (1.1)
-	No suspected infection	N/A	N/A	N/A	81 (92.0)

SOFA: Sequential Organ Failure Assessment. GFR: Glomerular filtration rate.

*Sepsis-3 positive episodes were defined as present if there was an increase in SOFA score by 2 compared to baseline, as well as evidence of infection. Infection in this study was defined as present if the patient was administered intravenous antibiotic therapy within 48 hours from admission and during at least 4 days.

Sepsis-2 positive episodes were defined as present if there were 2 or more SIRS criteria in combination with infection.

**Denotes mean \pm standard deviation.

†Denotes median (interquartile range).

††Two or more sources of infection were found in 9 episodes, so total percentage exceeds 100%.

Microbiological findings

Growth in blood culture was noted in 209/549 (38.1%) episodes (in 200 unique patients). Clinically relevant growth was found in 170 episodes (31.0), of which 11 concomitantly had contaminant growth. A total of 39 episodes (7.1%) had only contaminant growth. Among 170 episodes with relevant growth, monomicrobial growth was detected in 140 cases (82.4%) and polymicrobial growth in 30 (17.6%). The microbiological findings in episodes that fulfilled none, one or both sepsis definition is described in detail in Table 2 and Fig 2. When Sepsis-3 positive episodes were analyzed, 140/387 (36.2%) episodes had clinically relevant blood culture growth. For Sepsis-2 positive episodes, 155/443 (35.0%) episodes had clinically relevant blood culture growth. Contaminations were found in 35/387 (9.0%) of Sepsis-3 positive episodes, and 41/443 (9.3%) of Sepsis-2 positive episodes. In patients who did not fulfill any of the sepsis definitions, 8/88 (9.1%) episodes had clinically relevant growth, and 8/88 (9.1%) episodes had contaminant growth. The clinically relevant growth in blood culture in relation to clinical sepsis diagnosis is depicted in Fig. 2.

Table 2. Microbiological characteristics of the episodes (N = 549 episodes).

<i>Characteristic</i>	<i>Sepsis-3 positive*/Sepsis-2 positive (n=369)</i>	<i>Sepsis-3 negative/Sepsis-2 positive (n=74)</i>	<i>Sepsis-3 positive/Sepsis-2 negative (n=18)</i>	<i>Sepsis-3 negative/Sepsis-2 negative (n=88)</i>
Microbiological findings				
- BSI episodes with clinically relevant growth	133 (36.0)	22 (29.7)	7 (38.9)	8 (9.1)
- Contaminated episodes	34 (9.2)	7 (9.5)	1 (5.6)	8 (9.1)
- Episodes with G+ isolates	62 (16.8)	7 (9.5)	5 (27.8)	3 (3.4)
- Episodes with G- isolates	85 (23.0)	15 (20.3)	2 (11.1)	4 (4.5)
- Fungal isolates	1 (0.3)	• 0 (0.0)	0 (0.0)	0 (0.0)
- Episodes with anaerobic isolates	7 (1.9)	3 (4.1)	0 (0.0)	1 (1.1)
- Time to Detection (h)**	17 (11.5)	25 (21.9)	15 (5.8)	25 (13.1)

BSI: blood stream infection

*Sepsis-3 positive episodes were defined as present if there was an increase in SOFA score by 2 compared to baseline, as well as evidence of infection. Infection in this study was defined as present if the patient was administered intravenous antibiotic therapy within 48 hours from admission and during at least 4 days. Sepsis-2 positive episodes were defined as present if there were 2 or more SIRS criteria in combination with infection.

**Denotes mean \pm standard deviation.

The rank order of clinically relevant and contaminant microorganisms is found in detail in Table 3. Escherichia coli was the most common microorganism in both Sepsis-3 positive as well as Sepsis-3 negative episodes. Overall, contaminant microorganisms in both Sepsis-3 positive and Sepsis-3 negative episodes consisted of coagulase negative staphylococci, 21/39 (53.8%) and 8/17 (47.1) respectively.

Table 3. Rank order of microorganisms in sepsis-3 positive and sepsis-3 negative episodes.

<i>Sepsis-3* positive episodes</i>		<i>Sepsis-3* negative episodes</i>	
Clinically relevant microorganisms			
Microorganism	n (%)	Microorganism	n (%)
<i>Escherichia coli</i>	45 (25.9)	<i>Escherichia coli</i>	10 (28.6)
<i>Staphylococcus aureus</i>	21 (12.1)	<i>Streptococcus pneumoniae</i>	2 (5.7)
<i>Klebsiella pneumoniae</i>	14 (8.0)	<i>Streptococcus anginosus (milleri)</i> group	2 (5.7)
<i>Staphylococcus epidermidis</i>	11 (6.3)	<i>Bacteroides fragilis</i>	2 (5.7)
<i>Enterococcus faecalis</i>	9 (5.2)	<i>Parvimonas micra</i>	2 (5.7)
<i>Pseudomonas aeruginosa</i>	8 (4.6)	<i>Klebsiella pneumoniae</i>	1 (2.9)
<i>Klebsiella oxytoca</i>	7 (4.0)	<i>Pseudomonas aeruginosa</i>	1 (2.9)
<i>Enterococcus faecium</i>	6 (3.4)	<i>Klebsiella oxytoca</i>	1 (2.9)
<i>Streptococcus agalactiae</i>	5 (2.9)	<i>Enterobacter cloacae</i>	1 (2.9)
Group A streptococci	5 (2.9)	<i>Moraxella (Branhamella) catarrhalis</i>	1 (2.9)
<i>Streptococcus pneumoniae</i>	4 (2.3)	<i>Acinetobacter</i> species	1 (2.9)
<i>Enterobacter cloacae</i>	3 (1.7)	<i>Campylobacter</i> species	1 (2.9)
<i>Serratia marcescens</i>	3 (1.7)	<i>Haemophilus influenzae</i>	1 (2.9)
<i>Proteus mirabilis</i>	3 (1.7)	<i>Enterobacter aerogenes</i>	1 (2.9)
<i>Pantoea</i> species	2 (1.1)	<i>Staphylococcus aureus</i>	1 (2.9)
<i>Citrobacter freundii</i>	2 (1.1)	<i>Staphylococcus epidermidis</i>	1 (2.9)
<i>Streptococcus mitis</i> group	2 (1.1)	<i>Enterococcus faecalis</i>	1 (2.9)
Group B streptococci	2 (1.1)	<i>Enterococcus faecium</i>	1 (2.9)
Others	22 (12.6)	Others	4 (11.4)
Total clinically relevant microorganisms	174	Total clinically relevant microorganisms	35
Contaminant microorganisms			
Coagulase negative staphylococci	21 (53.8)	Coagulase negative staphylococci	8 (47.1)
<i>Staphylococcus epidermidis</i>	13 (33.3)	<i>Staphylococcus epidermidis</i>	7 (41.2)
<i>Corynebacterium</i> species	4 (10.3)	<i>Macroccoccus</i> species	1 (5.9)

<i>Micrococcus luteus</i>	1 (2.6)	<i>Facklamia</i> species	1 (5.9)
Total contaminant microorganisms	39	Total contaminant microorganisms	17
Total microorganisms	213	Total microorganisms	52

* Sepsis-3 positive episodes were defined as present if there was an increase in SOFA score by 2 compared to baseline, as well as evidence of infection. Infection in this study was defined as present if the patient was administered intravenous antibiotic therapy within 48 hours from admission and during at least 4 days.

** *Stenotrophomonas maltophilia*, *Proteus vulgaris*, *Pseudomonas* species, *Enterococcus* species, *Globicatella* species, *Lactobacillus* species, *Micrococcus luteus*, *Enterococcus casseliflavus*, *Actinotignum schaalii*, *Helcococcus* spp, *Eggerthella lenta*, *Clostridium perfringens*, *Prevotella* species, Unidentified gram negative anaerobe coccus, *Peptoniphilus* species, *Peptostreptococcus anaerobius*, *Candida parapsilosis*, *Micrococcus luteus* (all n = 1).

Discussion

The present prospective study showed that most patients who triggered the sepsis alert in our emergency department fulfilled both Sepsis-3 and Sepsis-2 criteria, and the rate of blood culture positivity was similar but poor in both Sepsis-3 and Sepsis-2.

In the present study, episodes fulfilling Sepsis-3 criteria had a bacteremia rate of 36.2% and episodes fulfilling Sepsis-2 criteria had similar bacteremia rate of 35.0%. One previous study reports 22% bacteremia in patients with Sepsis-3 [10], and in another study, 48.4% patients presenting with Sepsis-3 had positive blood cultures, however it was not stated if they consisted of only clinically relevant growth [11]. At least in the case of the higher reported rate of 48.2% only patients admitted to the ICU were studied, and probably does not reflect the frequency of bacteremia in the vast majority of patients with sepsis in the ED. In addition, previous data on patients with Sepsis-2 has shown bacteremia rates of around 30% [7-9, 17].

In the present study, the bacteremia rate was generally higher than previously reported. The reason for this discrepancy is unknown, however it might be related to differences in study design. In the present study, patients were included prospectively in the ED and there were no patients that received intravenous antibiotic treatment immediately prior to blood culture sampling. In addition, all included episodes had six blood culture bottles compared to four bottles that were used in the previous studies. As it is well known that blood culture yield correlates with sampled volume [6, 18, 19], this may have increased sensitivity by increasing the blood culture sample volume. We also employed a previously published method [14, 15] to define clinically relevant growth and contaminant growth. Notably, previous studies in both Sepsis-3 and Sepsis-2 patients included mostly retrospectively identified patients with sepsis [7, 20] or did not specify whether contaminants were excluded in the blood culture positivity analysis [7, 9, 20, 21].

The microbiological findings in Sepsis-3 and Sepsis-2 positive episodes were similar regarding both clinically relevant pathogens, contaminants and microbiological spectrum. It is reasonable to suggest that

the underlying reason for this might be the large overlap between the two groups in the present study. However, in the 88 episodes that had discrepant sepsis categorizations (Table 2), there were more episodes with clinically relevant growth and fewer contaminations in the Sepsis-3 positive group compared to the Sepsis-2 positive group. As the sample size of episodes with discrepant sepsis categorization was small, it was not possible to exclude a difference in blood culture results in this group.

The microorganisms implied in community acquired sepsis has previously been well studied, and the most common pathogens consist of *E. coli*, other *Enterobacterales* and *S. aureus* [8]. In the present study, the rank order of microorganisms in Sepsis-3 positive episodes is consistent with the findings in previous studies. However, in episodes that did not fulfill Sepsis-3 criteria, *Enterobacterales* other than *E. coli* as well as *S. aureus* was not as commonly isolated as in the Sepsis-3 positive episodes. It is possible that this difference reflects the importance of certain microbial virulence factors and interplay with immunological mechanisms as a major cause of organ dysfunction in sepsis [22].

There is a significant overlap between patients fulfilling Sepsis-3 and Sepsis-2 criteria. In the present results, 80% of patients fulfilling criteria for either sepsis criteria also fulfilled the other criteria. This contrasts to a recently published large study by Engoren et al [23] which included 18,183 patients who had either Sepsis-3 or Sepsis-2, where only 6,841 (37.6%) fulfilled criteria for both definitions. Additionally, our results contrast with another study by Todorovic et al. in which 24% of patients fulfilled both definitions of sepsis [24]. All patients included in the present study had a clinical suspicion of sepsis and were admitted to the ED at the time of inclusion. The discrepancy between the present results and previously published data is significant and may therefore be a result of patient selection criteria. In the previous study by Engoren et al, patients were screened retrospectively for sepsis, whereas in the present study, patients with suspected sepsis were included prospectively using a sepsis alert system. As trigger parameters for the sepsis alert system included components also present in SOFA (e.g. altered mental status, oxygen saturation) it is probable that the use of a sepsis alert system increased the likelihood that patients who fulfilled Sepsis-3 also fulfilled Sepsis-2 in our study.

The main strength of this study is its prospective design, using a clinical screening tool to select patients with suspected sepsis at presentation to the ED. The prospective design allowed for inclusion of patients with a “a priori” high likelihood of sepsis, regardless of the final diagnosis. The present results reflect the real-world scenario, where the final diagnosis is not available to the health care provider in the emergency department. Also, due to the prospective design, the blood culture sampling process was standardized, requiring 6 blood culture bottles to be sampled before initiation of antibiotic therapy in all patients included in the study.

The present study has several limitations. First, our study included only patients with a suspected infection upon presentation to the ED. This might introduce a bias in patient selection. However, the patients were carefully evaluated and represent a well-defined cohort for sepsis. Second, most patients included in the study had community acquired sepsis. However, the clinical criteria for Sepsis-3 and Sepsis-2 is general and applies for both community acquired sepsis and hospital acquired sepsis.

Conclusions

As the clinical definition of sepsis has changed, the performance of blood cultures and microbiological findings in sepsis may now be different. The present study showed that a high proportion of patients included through a sepsis alert system fulfilled both Sepsis-3 and Sepsis-2 criteria. The performance of blood cultures in detection of microorganisms was poor and were similar in Sepsis-3 and Sepsis-2 patients.

Abbreviations

SIRS: systemic inflammatory response syndrome

ED: emergency department

SD: standard deviation

IQR: interquartile range

SOFA: sequential organ failure assessment

GFR: glomerular filtration rate

BSI: blood stream infection

Declarations

Ethics approval and consent to participate: Ethical approval for the study was granted by the Regional Ethical Committee in Stockholm (reference number 2017/1358-31). Consent to participate was waived for this study.

Consent for publication: Consent for publication was not needed for the present study.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors states that no conflicts of interest are present.

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Authors' contributions: VÖ, DY and and DU conceived the study design and were responsible for collecting and curating the data. CU, ÅP, JSC and KS provided input in the study design prior to commencing the study, as well as interpretation and discussion of collected data. DY drafted the manuscript, and all authors contributed continuously to its revision. VÖ takes responsibility for the study.

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Figures

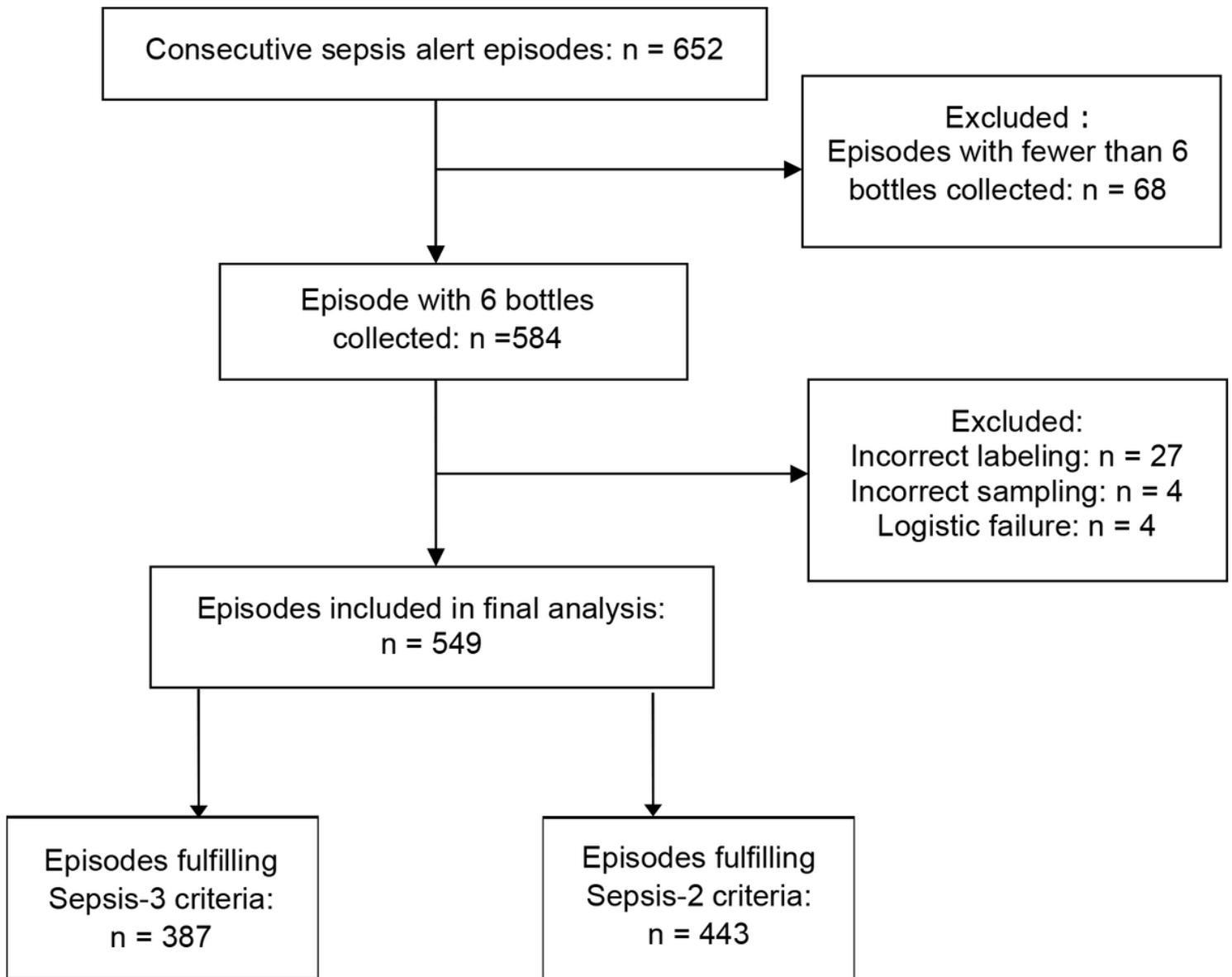


Figure 1

Flow chart of the study population.

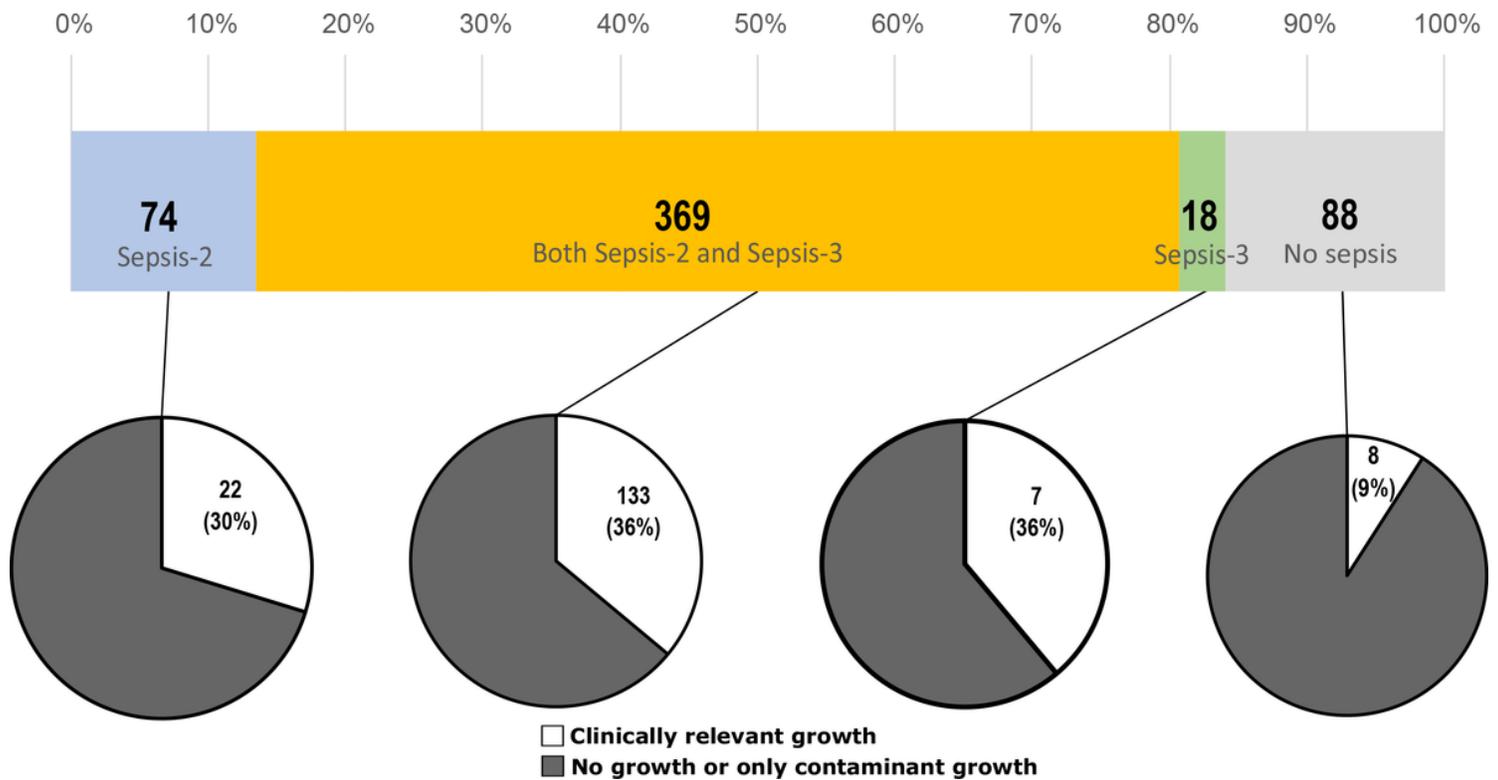


Figure 2

Clinical classification of suspected sepsis episodes and blood culture results. Numbers inside the horizontal bar denote episodes fulfilling criteria for clinical classification of Sepsis-3, Sepsis-2, both, or none. Percentages above the bar denotes the cumulative percentage of all included episodes. Numbers inside circles denote episodes with clinically relevant growth, and percentages in parenthesis denote percentage of all episodes in the associated clinical classification.

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