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Published in:
Acta Anaesthesiologica Scandinavica

DOI:
10.1111/aas.13777

Publication date:
2021

Document version:
Accepted manuscript

Citation for pulished version (APA):
Mikkelsen, V. S., Gregers, M. C. T., Justesen, U. S., Schierbeck, J., & Mikkelsen, S. (2021). Prehospital Antibiotic Therapy preceded by Blood Cultures in a Physician-manned Mobile Emergency Care Unit. *Acta Anaesthesiologica Scandinavica*, *65*(4), 540-548. https://doi.org/10.1111/aas.13777

Prehospital Antibiotic Therapy preceded by Blood Cultures in a Physician-manned Mobile Emergency Care Unit

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Word count: Abstract: 250; Main body of manuscript: 2971

Short title: Prehospital antibiotics

Conflicts of interest: None of the authors declare any conflicts of interest

The study was registered at ClinicalTrials.gov (ClinicalTrials.gov Identifier: NCT03919851)

Abstract

Background

Rapid recognition and antibiotic treatment, preferably preceded by blood cultures (BCs), is a mainstay in sepsis therapy. The objective of this investigation was to determine if prehospital BCs were feasible and drawn with an acceptably low level of contamination. Another objective was to investigate whether prehospital antibiotics were administered on correct indications.

Methods

We performed a register-based study in a prehospital physician-manned mobile emergency care unit (MECU) operating in a mixed urban/rural area in Denmark. All patients who received prehospital antibiotics by the MECU from November 2013 – October 2018 were reviewed. Outcome measures were characterisation of microbial findings and the confirmation of the prehospital indication for antibiotics following in-hospital examination.

Results

One-hundred-and-nineteen patients received antibiotics prehospitally. Six patients were excluded. One-hundred-and-thirteen patients were included in the study.

BCs were drawn in 107 of the 113 patients (94.7% (88.8% - 98.0%)). We found a true pathogen of sepsis in 29 (27.1% (19.0% - 36.6%)) of these 107 patients. Nine (8.4% (3.9% - 15.4%)) patients had contaminated prehospital BCs.

Forty-nine of all patients (36.3% (27.4% - 45.9%)) had causative pathogens in either their BCs or other samples confirming the prehospital tentative diagnosis. Eighty-two (72.6% (63.4% - 80.5%)) patients received antibiotic therapy in-hospitally, while 27 (23.9% (16.4% - 32.8%)) were assigned an in-hospital diagnosis not associated with infection. Four (3.5% (1.0% - 8.8%)) patients died in hospital before a diagnosis was established.

Conclusions

Prehospital administration of antibiotics preceded by BCs is feasible. Antibiotics are administered on reasonable indications.

No external funding was obtained in this study.

Competing interests:

Vibe Sommer Mikkelsen: None

Mads Christian Tofte Gregers: None

Ulrik Stenz Justesen: None

Jens Schierbeck: None

Søren Mikkelsen: None

INTRODUCTION

Sepsis is defined as a life-threatening condition where a dysregulated host response to infection leads to organ dysfunction [1]. It is estimated that sepsis affects more than 30 million people globally leading to 6 million deaths [2] with a mortality up to 50% of patients with septic shock [3]. Globally, the number of patients with sepsis is increasing [4-7]

Early treatment of sepsis is associated with better survival rates and outcome [3,8-14]. With every one-hour delay of antibiotic treatment mortality has been reported to increase by three to seven per cent [4-6].

This emphasises the need for rapid recognition and treatment of sepsis and requires both the ability of the prehospital personnel to recognise sepsis but also, ideally, the ability to obtain BCs before administration of antibiotics [15].

Despite the existence of several sepsis scoring systems, recognising sepsis is difficult. Different scoring systems have shown considerable variability in prehospital recognition of sepsis. The sensitivity has been reported as ranging from 10% to 87% [4,6,9-11,16]. This uncertainty might affect patients in critical need of antibiotic therapy.

In Denmark, the Emergency Medical System (EMS) consists of not only ambulances operated by paramedics (PMs) and emergency technicians (EMTs) but also of Mobile Emergency Care Units (MECU) staffed with a specialist in anaesthesiology [17,18]. Administration of antibiotics does not lie within the curriculum of the PM or the EMT. Prehospitally, the decision to administer antibiotics in patients with sepsis or severe infections is thus made at the discretion of the attending anaesthesiologist.

We speculated whether a prehospital physician-manned system in which the blood cultures (BC) were obtained prehospitally before prehospital administration of antibiotics could provide BCs with an acceptable low level of contamination – in our case an estimated contamination rate of 5% - or whether attempts at procuring reliable prehospital BCs were futile.
We further speculated whether prehospital antibiotics were administrated on correct indications.

The primary purpose was thus to investigate the feasibility and quality of the BCs obtained by assessing the level of contamination. Furthermore, in order to assess whether the prehospital antibiotics were administered on correct indications, we compared the diagnoses assigned prehospitally according to the WHO ICD-10 classification system [19] with the diagnoses assigned to the patient following full in-hospital diagnostic work-up. We further performed an assessment whether the prehospital antibiotics were continued once the patients were admitted to hospital.

METHODS

Study setting and population

In Denmark, the EMS is regulated by law and is a publicly funded system of three tiers in which the basic resource is an ambulance manned by two EMTs [17,18,20,21]. Our study was carried out in Odense in the region of Southern Denmark. The MECU in Odense consists of one rapid-response car operating all year. The MECU in Odense covers approximately 2.500 km^2 and services approximately 250.000 citizens [17]. The specialist in anaesthesiology treats the patients according to international guidelines including the guidelines in the Surviving Sepsis Campaign [15]. On suspicion of severe infection but before administering antibiotics, the physician draws BCs, one 10 mL aerobic and one 10 mL anaerobic blood culture bottle. These BCs are subsequently brought to the Emergency Department and sent to the department of clinical microbiology for analysis.
The MECU administers meropenem, a broad spectrum carbapenem, in most infections prehospitally. This treatment is chosen on an empirical basis and coincides with the drug of choice administered at the intensive care unit at Odense University Hospital (the primary referral hospital of the MECU) in cases of sepsis or severe infection of unknown origin.

After concluding the emergency run the anaesthesiologist documents the details of the mission in a MECU database containing the findings, the tentative diagnosis assigned to the patients and the treatments administered prehospitally. Furthermore, the physician documents the emergency run with a discharge summary [17] . Each patient is individually identified via the unique Civil Personal Registration number [22] .

Study design

This study was a retrospective register study of all patients given prehospital antibiotic therapy in a period of five-years. The study was approved as a quality control study to ensure that the current practice regarding prehospital antibiotic therapy is within current recommended guidelines. Based on this approval, data from the preceding five years could be analysed.
The study was registered at ClinicalTrials.gov (ClinicalTrials.gov Identifier: NCT03919851)

Data sources

The data sources consisted of prehospital medical records, microbiology records and in-hospital medical records.

Inclusion criteria

- All patients that received prehospital antibiotic therapy by the MECU in Odense in the period from 1st November 2013 – 30th October 2018 were screened for inclusion.

Exclusion criteria

- Patients lost to follow-up
- Patients receiving prophylactic antibiotics (e.g. following major trauma)
- Patients without a tentative prehospital diagnosis

Definitions

The international definition of sepsis changed within our observation period. However, we have used a pragmatic approach to assess the accuracy of the diagnoses – and as such – the confirmation of indication

for antibiotics. When confirming prehospital diagnoses with in-hospital diagnoses, we decided to use the ICD-10 diagnosis given by the dismissing ward as confirmation. Thus, a formal calculation of sepsis-criteria was not performed.

The following variables were registered

- The prehospital tentative diagnosis according to ICD-10 classification[19]
- The diagnosis assigned to the patient following complete in-hospital examination
- Results from prehospital BCs
- Results from other in-hospital microbiology samples

Other variables included age, sex, and the first set of prehospitally obtained vital parameters (Heart rate (HR), Blood Pressure (BP), Respiratory Rate (RR), Oxygen saturation (SAT), Glasgow Coma Score (GCS), Temperature (TP), Blood lactate), and National Advisory Committee on Aeronautics' severity score (NACA)) [23]. Post-Hoc, the qSOFA score was calculated [24]. Furthermore, the time that elapsed from first MECU contact with the patient to the arrival at the ED was recorded. A clinical microbiologist (Author USJ) assessed the BCs for contamination and compared the initial treatment with the in-hospital treatment and diagnosis to assess the decision to initiate prehospital treatment with antibiotics. This assessment was then revised with authors VSM and SM and compared to in-hospital medical records in cases of doubt.

Descriptive analysis and statistical methods

All information from the prehospital medical records was extracted electronically. All variables from the microbiology records and in-hospital medical records were manually extracted by author VSM. Blood cultures were carried out using BacT/ALERT (bioMerieux, Marcy l'Etoile, France).
Excel (Microsoft Corp. Redmond, Washington, USA) and STATA 16.0 (StataCorp, College Station, Texas, USA) were used for statistical analyses. Data are presented as proportions (with 95% confidence intervals (CI) based on a binomial distribution), median and quartiles or range (where appropriate).

Ethical issues, data handling and storage
According to the Danish Legislation, quality control follow-up studies require approval from the local hospital board of directors at the treating facility [25]. This study was approved as a quality control study by the hospital board of directors at Odense University Hospital (Ref. No. 18/63141). All data were anonymised and stored on an encrypted SharePoint.

Trial registration
The study was registered at ClinicalTrials.gov (Identifier: NCT03919851)

Patient and public involvement
The study was performed as a register-based project. No patient or public were involved in the planning or execution of this study.

RESULTS

Demographic data

A total of 113 patients were included in the study after exclusions. Of these, 65 (57.5%) were male. The median age was 72 years. Most of the patients exhibited vital parameters outside of the normal range. Likewise, both the NACA-score and the qSOFA score indicated that the patients were deranged.
The median time from the first contact with the patient to the arrival at the Emergency Department was 35.5 minutes.
For baseline characteristics, see table 1.

(Table 1 near here)

Microbiological findings

Pathogens

Of the 107 BCs drawn prehospitally, 29 (27.1% (19.0% - 36.6%)) were assessed to have true pathogens (see Table 2).

(Table 2 near here)

After reviewing the in-hospital medical records and other microbiological samples, based on other findings than the prehospitally drawn BCs, a possible cause of sepsis was established in another 12 patients (11.2% (5.9% - 18.8%)). Seven patients had enterobacteria in urine samples, four patients had *S. pyogenes*, *S. pneumoniae*, *Mycoplasma pneumoniae* and Influenza virus from the upper respiratory tract samples and one patient had *S. aureus* from a leg ulcer.
As a result of this review, the total number of patients that were found to have a causative pathogen associated to their diagnosis (MECU or hospital discharge diagnosis) was adjusted to 41 (38.3% (29.1% - 48.2%)).

Blood culture contamination

Nine patients (8.4% (3.9% - 15.4%)) had positive BCs that were regarded as contaminants (different coagulase negative staphylococci, viridans streptococci and corynebacteria).

Diagnostic accuracy

Prehospitally, 72.6% (63.4% - 80.5%) of the patients were assigned a prehospital tentative diagnosis of sepsis. Other prehospital diagnoses that resulted in antibiotic therapy included suspicion of meningitis or other severe infections.
At discharge from hospital, 41 patients (36.3% (27.4% - 45.9%)) had been assigned the diagnosis sepsis. In 24 of these 41 patients, (58.5% (42.1% - 73.7%)) this diagnosis was based on microbiological findings while in 17 patients 41.5% (26.3% - 57.9%) the diagnosis was based on clinical findings alone. Of the 24 diagnoses confirmed by microbiological findings, 79.2% (19/24) were based on BCs drawn prehospitally; the remaining based on other in-hospital samples.
The discharge diagnosis, “Other severe infection”, were assigned to another 41 patients (36.3% (27.4% - 45.9%)) and was confirmed by microbiological findings in 14 (34.1% (20.1% - 50.6%)) of the cases. In 27 patients, (65.8% (49.4% - 79.9%)) diagnosed with a severe infection, this diagnosis was based solely on clinical findings. Of the 14 discharge diagnoses confirmed by microbiological findings, 11 (78.6% (49.2% -

95.3%)) were based on BCs drawn prehospitally, the remaining based on other in-hospital samples. Of the prehospitally drawn BCs causative pathogens were found in 19/41 (46.3%) of the patients who received the diagnosis “sepsis”, while the number was 11/41(26.8%) for the patients who received the diagnosis of “Other severe infection”. Twenty-seven (23.9% (16.4% - 32.8%)) of all patients treated with prehospital antibiotics were discharged from the hospital with a diagnosis not associated with an infection. Of these 27 patients, a causative pathogen was found in two patients when reviewing other microbiological findings, possibly suggesting more than one cause of admission to the hospital. Four patients died before a diagnosis could be established. See Figure 1 for the distribution among the different groups.

(Figure 1 near here)

Hospital ICD-10 discharge diagnoses are listed in table 3.

(Table 3 near here)

DISCUSSION

The primary aim of this study was to investigate whether prehospital BCs could be drawn with an acceptable level of contamination. In order to do so, we characterised the microbiological findings in all BCs. Of all BCs drawn prehospitally, 8.4% were considered contaminated. The inclusion criterion for all patients was prehospital antibiotic therapy. When all prehospital BCs and other microbiological samples and in-hospital clinical findings were taken into consideration, three-quarter of the patients who had antibiotic therapy initiated prehospitally received further antibiotics in-hospitally. In one patient in four, the prehospital antibiotic therapy was discontinued once the patient arrived at the ED, while 3.5% died before a full diagnostic examination could be performed.

Blood Cultures

In a physician-based prehospital system, there is a potential for early administration of antibiotics in severe infections. This may be relevant when treating patients suspected of having sepsis or other severe infections [15]. The administration of antibiotics, however, reduces or eliminates the ensuing ability to perform assessments of the sensitivity of the microorganisms towards antibiotics. BCs should therefore ideally be drawn before antibiotic therapy is initiated. Contamination of BCs, most often caused by *S. epidermidis* or other coagulase-negative staphylococci, may, however, blur the findings in the acutely ill patients. A previous study found that out of 69 positive BCs from 432 patients, 19 of the positive BCs contained pathogens that were considered to constitute contamination [26].

When working prehospitally in less than optimal conditions it is often easiest to draw BCs from the peripheral venous catheter as this is being inserted. This, however, has proven to be associated with higher contamination rates [27].

The contamination rate in our study was 8.4%. At the Department of Clinical Microbiology, Odense University Hospital, the general BC positivity rate in in-hospital BCs has been approximately 7% to 8% from 2013 to 2017, including contaminants. The in-hospital contamination rate at Odense University Hospital has been estimated to amount to approximately 2%. In other studies, the in-hospital contamination rates have been reported to be between 0.6% to 17% but it is recommended by the US Clinical and Laboratory Standards Institute that it should not exceed 3% [28]. Contaminated BCs may lead to inappropriate antibiotic treatment and decreasing the contamination rates should thus be prioritised. The contamination rate of the BCs drawn prehospitally in our study was thus higher than the in-hospital rates. It was also higher than the 5 % that we hypothesised when planning the study. The positivity rate of true pathological findings from the BCs drawn prehospitally was 27.1%. This is higher than the similar rate from in-hospital BCs at Odense University Hospital, which has been estimated to be 7%-8% including contaminants. Despite the high number of contaminated prehospital BCs, we believe that the high number of true positive findings in the material confirms that there is valuable information in the prehospital BCs. This higher positivity rate further supports the MECUs ability to recognise sepsis or severe infections prehospitally. It must be considered, though, that in comparison to the prehospital conditions, the clinical threshold for drawing BCs in-hospitally is low; the in-hospital BCs often being drawn with little or no suspicion of infection. Further supporting the finding that the positivity rate should be higher in the prehospital setting are the treatment principles that prehospital BCs are not drawn unless there is a suspicion of severe infection great enough to elicit prehospital antibiotic therapy. Thus, the truly ill patients, who may be expected to have a higher rate of positive BCs may be more frequent among the patients treated by the MECU than those treated at the ED.

Early antibiotic treatment

Early recognition and treatment of sepsis are crucial elements for survival and improvement in outcome [3,8,9,10-14,29-31] and mortality may increase with three to seven per cent with every one hour delay of antibiotic treatment [10,12].
Many studies have found that training in recognition of sepsis by the EMS personnel reduces the time that elapses from arrival at the emergency department to first administration of antibiotics [10,12,29-32]. One study found that patients with bacterial meningitis diagnosed upon arrival had a median time to antibiotic therapy of 1.3 hours compared to 8.5 hours when diagnosed after arrival [31]. The difference in diagnosing bacterial meningitis on admission or later and the subsequent time to antibiotics (TTA) was considered of significance regarding in-hospital mortality (14% vs 30%) [31]. These reductions in TTA may be a result of the increased awareness of a critical disease when a tentative diagnosis of sepsis or other infections is mentioned explicitly. With that purpose in mind, an array of screening tools regarding sepsis has been employed [4,5,11,12].

However, while early antibiotic therapy is regarded as the gold standard, some studies have found no significant change in mortality when TTA was reduced [12,13,33]. A Dutch intervention trial sought to determine whether antibiotics administered prehospitally by EMTs would have a positive effect on mortality, but found no significant difference in neither mortality, ICU admissions, nor the length of admission [12]. Another study carried out by the EMS in Sweden also reported that although suspicion of sepsis by the EMS personnel at the scene was significantly associated with survival, there were no significant associations between mortality and prehospital time to antibiotics [33]. In the Dutch study [12], EMTs were trained in sepsis recognition using a set of predefined criteria, while in our study the recognition of sepsis was made by an experienced prehospital anaesthesiologist using no explicitly defined criteria for sepsis but rather a clinical evaluation.
Both EMTs and patients themselves may have problems identifying severe infections. In a Danish study, it was found that in a group of severe sepsis patients, 62.8% arrived at the ED without the use of ambulances, 28.2% were transported by ambulance, and in only 9.0% of patients, a MECU was involved in the treatment [34].
One study found that one-third of acute patients with bacteraemia presented at the emergency department with normal body temperature [35]. This finding underscores the difficulty of detecting infection and correlates well with another study seeking to find an association between body temperature and bacteraemia [26]. In many cases of bacteraemia in our study, there were no changes in body temperature.

Early prehospital antibiotics may mitigate other time-critical infections than sepsis. In one study in the Region of Southern Denmark, the median MECU response time was 8 minutes [17]. This, along with the median time of 35.5 min from initial contact with the patient to the arrival at the ED, reduces TTA significantly. This may have implications for survival in meningitis as a risk ratio of in-hospital mortality of 1.1 per hour of delay has previously been demonstrated [31].

Another important factor in the prehospital antibiotic therapy in association with antibiotic stewardship is the timely, in-hospital de-escalation at the earliest possible time when sensitivity/resistance-tests have been concluded. As the diagnostic tools of the MECU are limited, it is necessary to initiate prehospital antibiotic therapy on indication of the life-threatening condition of sepsis on a broad-spectrum basis and rely on in-hospital diagnostics to de-escalate appropriately. As this study did not focus on the antimicrobial sensitivity of the causative pathogens, it is not possible to determine in how many cases the prehospital antibiotic therapy may have been too aggressive.

With antimicrobial stewardship and the in-hospital appropriate de-escalation in mind, we believe our results suggest that prehospital antibiotic therapy is initiated on correct indication, and that prehospital treatment of sepsis or severe infections is reasonable.

Application to countries outside of Denmark

The setup in Denmark with the physician manned Mobile Emergency Care Unit [18] is comparable with most other Scandinavian countries [36]. As some studies have shown benefit in early antibiotic therapy [3,10-13,29-31]; in emergency medical systems with longer response or transportation times, prehospital administration of antibiotics could lead to an improvement in outcome.

Strengths of the study

Because of the unique Danish Civil Registry including all Danish inhabitants, only four patients were lost-to-follow-up.
All BCs and other microbiology samples were assessed by an expert in clinical microbiology and have undergone thorough considerations regarding true pathogenicity.

Limitations

The relatively low number of patients and the short study period is a limitation. The ethical approval obtained for this study, however, limited the observation period to five years.
The study is a single-centre study performed in the Region of Southern Denmark and may thus only reflect patterns relevant to this particular centre.
A further limitation in this study was that we only investigated patients that did receive prehospital antibiotics. This makes it impossible to draw any conclusions whether the MECU recognises and diagnoses patients with sepsis accurately in the prehospital setting. However, the study was planned with two research questions: 1) Is it possible to acquire prehospital BCs with an acceptable level of contamination and 2) Are prehospital antibiotics administered too liberally.
In order to reduce bias, it would have been beneficial to the study if pathogenicity/contamination was secondarily assessed by another clinical microbiologist.
If the research question had been to elucidate both sensitivity and specificity of the MECU physicians´ ability to diagnose prehospital sepsis or severe infections, a larger study would have been required. In this larger study, all patients seen by the MECU in the observation period should have been included, not only the patients who received antibiotics prehospitally.
Further limitations are that in some patients while establishing an intravenous line was possible, it was not possible to obtain enough blood for blood cultures to be analysed. Thus, the number of patients receiving prehospital antibiotics does not equal the number of patients having prehospital blood cultures obtained.

CONCLUSION

In this study, we found an acceptably low level of contamination in view of a high level of true pathogens in BCs drawn before prehospital administration of antibiotics on the indication presumed sepsis or severe infection. The ensuing in-hospital diagnoses confirmed the indication for antibiotics to such an extent that we believe that over-use of antibiotic therapy was not an issue prehospitally. We conclude that the practice of drawing BCs and initiating antibiotic therapy in suspected cases of sepsis or severe infections is feasible.

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Author statement:

VSM conceived the idea and the study design and reviewed the data. VSM drafted the manuscript. VSM critically revised the manuscript and approved the manuscript prior to submission.

MCG participated in conceiving the idea and the study design. MCG critically revised the manuscript and approved the manuscript prior to submission.

USJ conceived the idea and the study design and reviewed the data. USJ critically revised the manuscript and approved the manuscript prior to submission.

JS participated in conceiving the idea and the study design. JS critically revised the manuscript and approved the manuscript prior to submission.

SM conceived the idea and the study design and reviewed the data. SM critically revised the manuscript and approved the manuscript prior to submission.

Funding: No funding was received

Declaration of interests: None of the authors has any competing interests to declare

A data sharing statement: Anonymized data are available upon individual request

Legends to figure and tables:

Figure 1: Flowchart of included patients who received prehospital antibiotics

Table 1: Demographics and selected vital parameters and characteristics of the study population

Table 2: Distribution of microbiological species isolated in the study population

Table 3: Distribution of discharge diagnoses following admission to hospital

Table 1

Patient characteristics: Initial variables recorded by the MECU
(Distribution between sexes described as percentage. Other variables described as medians and quartiles)

Variable	Median (Quartiles)
Age (y)	72 (56, 81)
Male	65 (57.5%)
Female	48 (42.5%))
Systolic BP (mmHg) (Median (Quartiles))	120 (94, 140)
Temperature (Celcius) (Median (Quartiles))	38.6 (37.3, 39.6)
Respiratory rate (breaths/min) (Median (Quartiles)	25.5 (20, 36)
Heart rate (beats/min) Median (Quartiles)	110 (96, 128)
Glascow Coma Score Median (Quartiles)	12 (6.8, 14)
SpO2 (%) Median (Quartiles)	93 (84, 97)
Lactate mmol/liter Median (Quartiles)	3.6 (2.6, 7.4)
Q-sofa score Median (Quartiles)	2 (1, 2)
NACA-score Median (Quartiles)	5 (4, 5)
Time from the first contact with the patient to the arrival at the ED (Minutes) Median (Quartiles)	35.5 (29.8, 44)

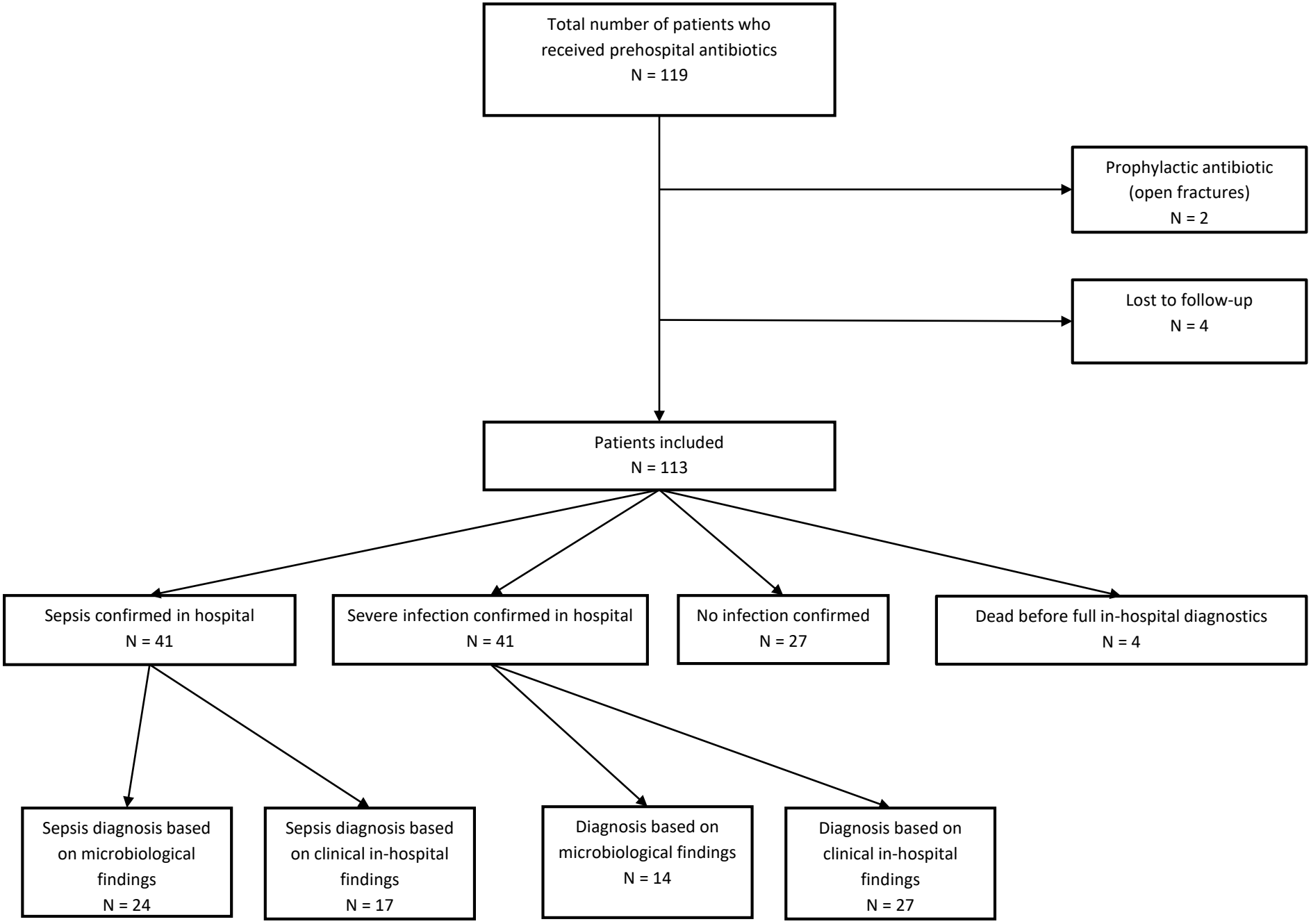
Table 2. Distribution of species isolated from blood cultures in 29 patients*

Species	n
- Gram negative	
Escherichia coli	11
Klebsiella pneumoniae	4
Klebsiella oxytoca	1
Enterobacter cloacae	1
Citrobacter freundii	1
Serratia marcescens	1
Pseudomonas aeruginosa	1
Haemophilus influenzae	1
Neisseria meningitidis	1
- Gram positive	
Staphylococcus aureus	5
Streptococcus pneumoniae	2
Streptococcus pyogenes	1
Streptococcus anginosus	1
Enterococcus faecalis	3
Enterococcus faecium	1
Clostridium perfringens	1

* Two species were isolated from the BCs in seven patients

Table 3

ICD-10 chapter	Diagnosis group		N	(% (95% CI))
Chapter I	Certain infectious and parasitic diseases	(A00-B99)	41	(36.3 (27.4 – 45.9))
Chapter II	Neoplasms	(C00-D48)	1	(0.9 (0.0 – 4.8))
Chapter III	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	(D50-D89)	1	(0.9 (0.0 – 4.8))
Chapter IV	Endocrine, nutritional and metabolic diseases	(E00-E90)		
Chapter V	Mental and behavioural disorders	(F00-F99)		
Chapter VI	Diseases of the nervous system	(G00-G99)	5	(4.4 (1.5 – 10.0))
Chapter VII	Diseases of the eye and adnexa	(H00-H59)		
Chapter VIII	Diseases of the ear and mastoid process	(H60-H95)		
Chapter IX	Diseases of the circulatory system	(I00-I99)	11	(9.7 (5.0 – 16.8))
Chapter X	Diseases of the respiratory system	(J00-J99)	22	(19.5 (12.6 – 28.0))
Chapter XI	Diseases of the digestive system	(K00-K93)	5	(4.4 (1.5 – 10.0))
Chapter XII	Diseases of the skin and subcutaneous tissue	(L00-L99)	1	(0.9 (0.0 – 4.8))
Chapter XIII	Diseases of the musculoskeletal system and connective tissue	(M00-M99)		
Chapter XIV	Diseases of the genitourinary system	(N00-N99)	4	(3.5 (0.9 – 8.8))
Chapter XV	Pregnancy, childbirth and the puerperium	(O00-O99)		
Chapter XVI	Certain conditions originating in the perinatal period	(P00-P96)		
Chapter XVII	Congenital malformations, deformations and chromosomal abnormalities	(Q00-Q99)		
Chapter XVIII	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	(R00-R99)	15	(13.3 (7.6 – 20.9))
Chapter XIX	Injury, poisoning and certain other consequences of external causes	(S00-T98)	7	(6.2 (2.5 – 12.3))
Chapter XX	External causes of morbidity and mortality	(V01-Y98)		
Chapter XXI	Factors influencing health status and contact with health services	(Z00-Z99)		
Chapter XXII	Codes for special purposes	(U00-U85)		
Total			113	(100)


Total number of patients who received prehospital antibiotics N = 119
Prophylactic antibiotic (open fractures) N = 2
Lost to follow-up N = 4
Patients included N = 113
Sepsis confirmed in hospital N = 41
Severe infection confirmed in hospital N = 41
No infection confirmed N = 27
Dead before full in-hospital diagnostics N = 4
Sepsis diagnosis based on microbiological findings N = 24
Sepsis diagnosis based on clinical in-hospital findings N = 17
Diagnosis based on microbiological findings N = 14
Diagnosis based on clinical in-hospital findings N = 27