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Recognition, response and outcomes of sepsis: A dual site retrospective observational study

Julia Crilly[a,b,*], Jemma Robinson[c], Vicki Sharman[c], Jack Cross[c], Bernadine Romero[a], Trudy Teasdale[c], Gerben Keijzers[a,b,d]

[a] Department of Emergency Medicine, Gold Coast Health, 1 Hospital Blvd, Southport 4215, QLD, Australia
[b] Menzies Health Institute Queensland, Griffith University, Parklands Drive, Parkwood 4222, QLD, Australia
[c] Pharmacy Department, Gold Coast Health, 1 Hospital Blvd, Southport 4215, QLD, Australia
[d] School of Medicine, Bond University, 14 University Dr, Robina 4226, QLD, Australia

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ABSTRACT

Objectives: To describe clinical recognition, response and outcomes of patients with sepsis.
Methods: A retrospective, observational study was undertaken at two hospitals. Inclusion criteria were: adult patients admitted via the Emergency Department (ED) between 1 January and 30 April 2014 allocated a primary ICD-10-AM discharge from hospital code related to sepsis. Recognition of sepsis was considered based on the presence of clinical documentation that reflects the Sepsis Kills criteria being met. Response to sepsis was considered based on the presence of clinical documentation where the patient received a response consistent with the 'Sepsis Six' strategies. Outcomes pertained to response to sepsis (e.g. time to antibiotics) and ED measures (e.g. time to be seen, ED length of stay). Sub-group analysis considered location where sepsis was recognised (ED/ward).
Result: In total, 96 patients met the inclusion criteria; most were admitted under general medicine (37%) followed by intensive care (18%). Sepsis was recognised in the ED for most patients (n = 64), with a history of fevers/rigors the most common (60%) indication of infection. Regarding response and ED outcomes for this group, the median time from triage nurse assessment i) to being seen by the treating clinician was 19 min; ii) to sepsis recognition was 27 min; and iii) to antibiotics was 181 min; 35% received antibiotics within 60 min from recognition. Those recognised in the ED had a longer ED stay than those where sepsis was recognised on the ward (336 min vs. 225 min, p = 0.013).
Conclusions: Sepsis can develop at various stages throughout the patient's journey. In this small sample, ED recognition was associated with longer ED stay, likely due to more interventions. Whilst guidelines recommend antibiotics be administered within 60 min of triage, this was not achieved for most patients. Given the dynamic nature of sepsis, future indicators may focus on time from recognition rather than time from triage.

1. Introduction

There are an estimated 18 million cases of sepsis per year worldwide [1]. In 2016, the third international consensus (sepsis-3) defined sepsis as a life-threatening organ dysfunction due to a dysregulated host response to infection [2]. Prior to then, the Surviving Sepsis Campaign (SSC) used different definitions which included: i) Systemic Inflammatory Response Syndrome (SIRS), ii) sepsis, iii) severe sepsis and iv) septic shock; each carrying progressively higher mortality rates [1]. Newer assessments consider the clinical criteria as an increase of two or more points in the Sequential Organ Failure Assessment (SOFA) score where, for patients with infection, there is an overall mortality of 10% [2]. The SOFA score has not been validated outside the Intensive Care Unit (ICU), likely due to the underpinning clinical criteria (e.g. Mean Arterial Pressure, Vasopressors, PaO_2/FiO_2) that are not easily/routinely measured outside the ICU setting. The quickSOFA (qSOFA) is a screening tool that identifies patients with suspected infection who are likely to have a prolonged ICU length of stay or to die in hospital. The qSOFA can be used at the bedside (not specific to ICU) to promptly identify two or more of: hypotension: systolic blood pressure:

* Corresponding author at: Department of Emergency Medicine, Gold Coast University Hospital, 1 Hospital Blvd, QLD 4215, Australia.
E-mail addresses: Julia.Crilly@health.qld.gov.au (J. Crilly), Jemma.Robinson@health.qld.gov.au (J. Robinson), Vicki.Sharman@health.qld.gov.au (V. Sharman), Jack.Cross@health.qld.gov.au (J. Cross), Bernadine.romero@health.qld.gov.au (B. Romero), Trudy.Teasdale@health.qld.gov.au (T. Teasdale), Gerben.Keijzers@health.qld.gov.au (G. Keijzers).

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≤100 mmHg, altered mental status: any Glasgow Coma Score < 15, tachypnoea: respiratory rate ≥22 [2]. The qSOFA has not, as far as we are aware, been validated in multiple sites. Due to the varied presentations of sepsis, there is a need for ongoing research into the recognition of and response to sepsis that incorporates the clinical utility of current definitions used.

The mortality rate in sepsis can be as high as 46% [3–5]. A number of studies have thus been devised in an effort to provide an evidence-based approach to improve sepsis-related process and outcome measures [6–11]. The SSC was established to provide consensus, evidenced-based guidelines for care designed to improve survival in patients with sepsis [6]. SSC bundles consist of seven aspects (measure lactate; obtain blood cultures; administer broad spectrum antibiotics; administer fluids, as required; apply vasopressors, as required; re-assess volume status and tissue perfusion; re-measure lactate, as indicated) required to be completed within 6 h of recognition (the first four within the first 3 h). Large studies on sepsis bundles have had variable results. One international study that involved 29,470 patients from 218 hospitals across USA, South America and Europe found that facilities that complied with the SSC bundle were noted to have a lower mortality rate than those that were less compliant with the SSC bundle (29% vs. 39%; $p < 0.001$) [7]. Other aspects noted to improve when using the SSC bundle include improved frequency of blood culture testing before antibiotic administration and improved time to antibiotic treatment [7]. The impact of improvements from these (or other) process measures (singularly or in certain combination) on patient outcomes are not clear. Seymour et al. (2017) [8] assessed similar bundled care in almost 50,000 patients in 149 hospitals and found a much smaller effect on mortality and no effect from certain components (such as fluid administration) of the bundle.

Noted studies [6–8] provide comprehensive insight on patients who are diagnosed with sepsis. There is a considerable emerging focus in the literature on the more immediate recognition and management of the potential for sepsis in the unpredictable environment when the patient first arrives at the ED or in the hospital ward environment where early signs of deterioration can be detected and acted upon. Within Australia, the New South Wales (NSW) Clinical Excellence Commission (CEC) has produced the 'Sepsis Kills' (SK) program which aims to reduce preventable harm to patients through improved recognition and management of sepsis throughout 97 hospitals in NSW [9]. The key elements of the improvement initiative were: *Recognition* of risk factors, signs and symptoms of sepsis; *Resuscitation* with appropriate intravenous fluids and administration of appropriate antimicrobials within the first hour of triage/diagnosis of sepsis; and *Referral* to appropriate senior clinicians and teams and retrieval if appropriate. Results from this program indicated that the proportion of patients receiving antibiotics within 60 min of triage increased from 10.6% to 27.5% and mortality declined from 19.3% to 14.1% between 2009 and 2013 [10]. Another study [11] evaluating the impact of the SK guideline in one Australian ED in a 12-month pre-post study, demonstrated an increase in the allocation of more urgent triage categories for patients presenting with sepsis and a 230 min reduction in mean time to antibiotics after the implementation of the guideline into the ED. The change in triage allocation, reduction in time to antibiotics and improved mortality is likely a combined effect of improved recognition, early appropriate treatment and temporal trends. The aim of this study was to describe clinical recognition of sepsis, response strategies to sepsis and outcomes of patients with sepsis. The findings generated from this study may assist to further inform if and where improvements in care delivery and outcomes for patients subsequently diagnosed with sepsis are needed within one Australian health service.

2. Methods

2.1. Design and setting

This was a retrospective observational study. At the time of the study, the health service comprised two regional public teaching hospitals with a combined total of over 800 acute care beds. In 2014 there were more than 146,000 patient presentations to the two EDs, with over 41,000 (28%) of those requiring hospital admission. These two public EDs along with three private EDs serve a surrounding community of around 500,000 people.

2.2. Study sample

Study inclusion criteria were: patients admitted to one of the two hospitals located within the health service, via the ED between 1 January 2014 and 30 April 2014, aged 18 years or older and allocated a primary ICD-10-AM discharge from hospital code related to one of five definite sepsis illnesses: Systemic Inflammatory Response Syndrome (SIRS); Sepsis; Severe Sepsis; Severe Sepsis with Septic Shock and Sepsis with Organ Dysfunction. These correspond to the ICD-10 codes shown in Table 1 and reflect previous literature using similar codes. Patients

Table 1
ICD-10 codes used to inform inclusion criteria for sepsis diagnosis.

Sepsis ICD-10 Codes	ICD-10 code description	Reference for code use
A02.1	Salmonella sepsis	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A22.7	Anthrax Sepsis	Jolley et al. (2015) [13]
A26.7	Erysipelothrix Sepsis	Jolley et al. (2015) [13]
A32.7	Listerial Sepsis	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A40.0	Sepsis due to Streptococcus, group A	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A40.1	Sepsis due to Streptococcus, group B	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A40.2	Sepsis due to Streptococcus Group D	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A40.3	Sepsis due to Streptococcus Pneumoniae	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A40.8	Other Streptococcal Sepsis	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A40.9	Streptococcal sepsis, unspecified	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A41.0	Sepsis due to Staphylococcus Aureus	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A41.1	Sepsis due to Other Spec Staphylococcus	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A41.2	Sepsis due to Unsp Staphylococcus	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A41.3	Sepsis due to Haemophlius influenzae	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A41.4	Sepsis due to Anaerobes	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A41.5	Sepsis due to other Gram-negative organisms	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A41.8	Other Specified Sepsis	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A41.9	Sepsis, Unspecified	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
A42.7	Actinomycotic sepsis	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
B37.7	Candidal Sepsis	Huggan et al. (2017) [12]; Jolley et al. (2015) [13]; Sundararajan et al. (2005) [14]
O85	Puerperal Sepsis	No ref identified

Table 2
Data collected and source.

Data Source	Data collected
EDIS data	Campus, Medical Record Number, Encounter Number, First and Last Name, Date of Birth, Sex, Date & time of ED presentation, Mode of arrival, Australasian Triage Scale (ATS), Reason for presentation, Date & time of ED triage, Date & time seen by clinician, Date & time of departure from ED, ED ICD code and description, Discharge disposition from ED
HBCIS data	Campus, Medical Record Number, Encounter Number, First and Last Name, Date of Birth, Sex, Date & time of hospital admission, Date & time of hospital departure, ICD code and description (HBCIS), Discharge destination from hospital
EMR data	Campus, Medical Record Number, Encounter Number, Last Name, First Name, Date Of Birth, Age > 65 years (yes/No), Sex, Triage category, Date and time of antimicrobial administration, Antimicrobial prescribed, dose and method of administration, Time between triage and administration of antimicrobial (min), Staff type prescribing treatment (registrar, consultant, NP), Allergy Status, Immunocompromised – Yes/No, Indwelling medical device – Yes/No, Recent surgery/ invasive procedure – Yes/No, History of fevers/rigors – Yes/No, Re-presentation within 48 h – Yes/No, Fall not related to mechanism of injury – Yes/No, Abdominal pain/peritonitis – Yes/No, Cough/SOB – Yes/No, Altered LOC, new onset confusion, neck stiffness, headache – Yes/No, Cellulitis, skin wound – Yes/No, Infection – Yes/No, Other medications given in ED (type/dose/route), Other fluids given in ED (type/dose/ route), Urine frequency, odour, dysuria – Yes/No, Respiration Rate < =10/min – Yes/No, Respiration Rate > =25/min – Yes/No, Oxygen Saturation < 95% – Yes/No, Systolic Blood pressure < =100 mmHg – Yes/No, HR < =50/min – Yes/No, HR > =120/min – Yes/No, Altered LOC or new onset of confusion – Yes/ No, Temperature < 35.5 – Yes/No, Temperature > 38.5 – Yes/No, Systolic Blood pressure < 90 mmHg – Yes/No, Lactate > = 4 mmol/L – Yes/No, Base excess < −5.0 – Yes/No, Advanced care directive Yes/No, Blood cultures taken? – Yes/No, If yes, time, Blood cultures taken prior to administration of antibiotic – Yes/ No, Is sepsis likely – Yes/No, If sepsis likely, Oxygen administered to maintain oxygen saturation > 95%– Yes/No, If sepsis likely, 2 anaerobic and 2 aerobic cultures, FBC, EUC, LFTs, coags, glucose, +/− wound, urine, sputum or other cultures – Yes/No, If sepsis likely, formal lactate or VBG taken – Yes/No, If sepsis likely, administered 0.9% NaCl fluid challenge STAT – Yes/No, Review of antibiotic choice when cultures available – Yes/No, Admitting Team (Medical/Surgical/ Specialty), Readmission with 28 days – Yes/No, If infection – site of infection, Hospital acquired – Yes/No/NA/unsure, Presumptive source of sepsis, Abdomen/CNS/Lung/Orthopaedic/Skin or soft tissue/Urinary tract/Vascular device/Other/ Unknown

Data collected based on the NSW 'Sepsis Kills' worksheet [10] and Sepsis Six [18].

were excluded if they were < 18 years old, transferred from an external facility, were directly admitted to the ward (i.e. did not have a corresponding ED record), or had another ICD-10 code (e.g. those pertaining to pyelonephritis, cellulitis, pneumonia) that may not have resulted in organ dysfunction.

2.3. Data collection

Data collected for this study was guided by previous research [15–17] and expert clinical advice. A data collection template was developed by the research team prior to study commencement to guide data collection. Routinely collected data (Table 2) were extracted from the hospitals health information systems by a member from the Hospital Health Informatics Directorate to inform patient and clinical descriptors and outcomes. Additional clinical and care delivery data were extracted from the electronic medical record (Table 2) by two study investigators to inform care delivered and the extent to which current practice within the health service corresponded with the NSW CEC SK Pathway. The consistency of data extraction between the two investigators was checked; the percentage of agreement (concordance) was 78.1%, based on 215 data collection points from a computer generated randomly selected sample of 5% of patients.

2.4. Outcome measures

Recognition of sepsis was considered based on the presence of clinical documentation that reflects the CEC SK criteria (2014 Version for Emergency Departments) being met (i.e. any of the risk factors, signs or symptoms of infection noted in Tables 5 and 6). Response to sepsis was considered based on the presence of clinical documentation where the patient received a response consistent with the 'Sepsis Six' strategies: 1) oxygen administered if $SpO_2 \leq 95\%$, 2) blood cultures taken, 3) venous blood gas taken (for Lactate), 4) intravenous (IV) fluid challenge, 5) antibiotics prescribed and administered within 60 min of triage or within 60 min of diagnosis, and 6) monitoring of observations [10,18]. Outcomes measured predominantly pertained to response to sepsis (e.g. time to antibiotics) and ED measures (e.g. time to be seen, ED length of stay). The primary outcome measure for this study was time to initial antibiotic administration (as documented on the patients National Inpatient Medication Chart) following triage in the ED. The CEC SK criteria recommend the administration of antibiotics within 60 min of triage or diagnosis. Given this definition, the decision was made to measure time from triage to antibiotic administration. Secondary measures included: time of initial antibiotic administration from recognition, where sepsis was recognised (ED or ward), time sepsis was recognised, ED length of stay (LOS), hospital LOS, in hospital mortality, and hospital re-admission within 28 days. Data collected for this study (Hypotension: SBP ≤ 100 mmHg, altered mental status: any GCS < 15, tachypnoea: RR ≥ 25) were also used to relate to contemporary qSOFA criteria (i.e. qSOFA: 2 or more of: Hypotension: SBP ≤ 100 mmHg, altered mental status: any GCS < 15, tachypnoea: RR ≥ 22 [2], although this was not a key objective for this study.

2.5. Statistical analysis

Statistical analysis was performed using SPSS version 23 (IBM Corporation, Armonk, NY, USA). Descriptive statistics (median, interquartile range, frequencies and percentages) were used to summarize demographic, ED, outcome and care delivery data. Inferential statistics (chi square test for categorical data and Mann-Whitney *U* test for non-parametric continuous data) were used to compare groups (i.e. sepsis criteria met in ED vs. ward). A p-value of < 0.05 was considered statistically significant. Missing data were not included in the analysis.

2.6. Ethics

Human Research Ethics Committee approval (HREC/15/QGC/11) was obtained to undertake this study.

3. Results

A total of 8500 hospital admissions from adults (aged ≥18) were made via the two EDs over the 4-month period. Of those, 96 met our study inclusion criteria (Fig. 1). Assessment of the geographical location of sepsis detection was possible for 87 patients (63 in ED, 24 on ward). The other 9 patients for whom location was unable to be identified were younger, more likely to be female, and less likely to arrive by ambulance. Due to these differences and given our primary outcome, subsequent analysis was based on the 87 patients for whom location could be detected.

Patient demographics, clinical characteristics and outcomes for patients with sepsis are presented in Table 3. Most patients were male (n = 57, 65.5%) and the median age was 69 years (IQR: 50.3–79.0). Almost two-thirds arrived by ambulance (n = 65, 74.7%), and over half

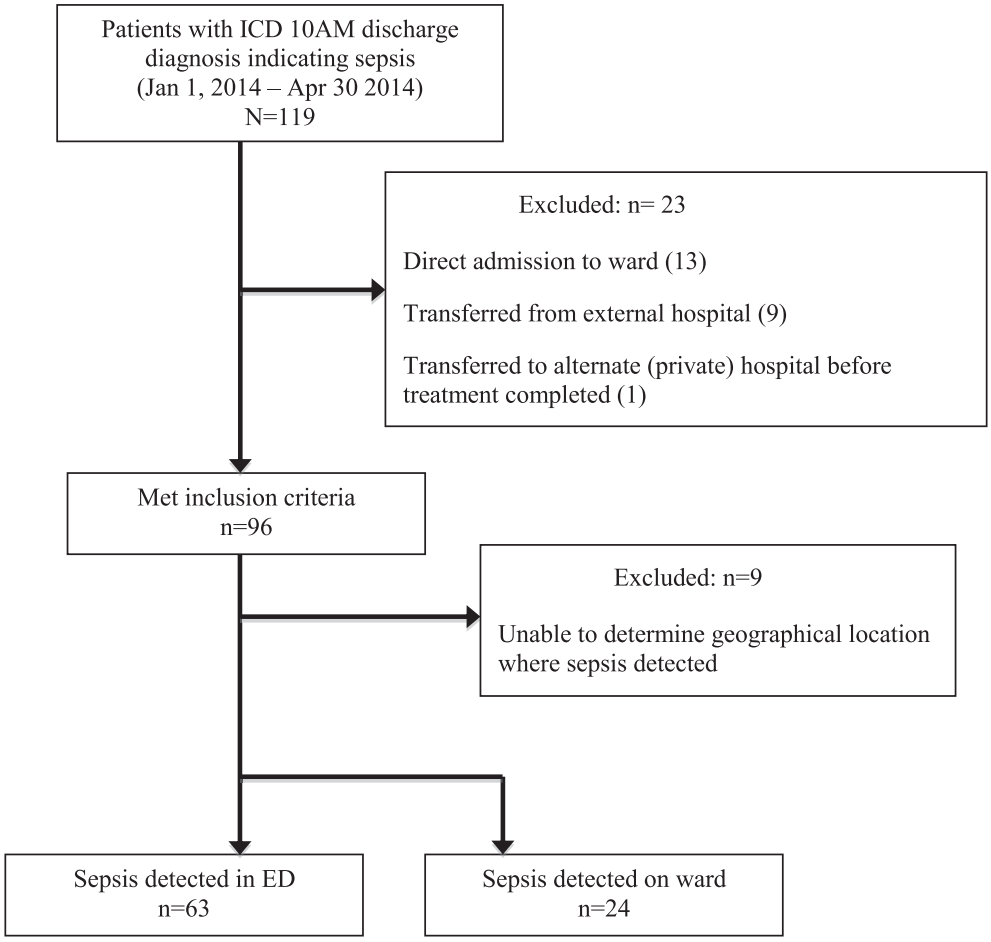

Fig. 1. Sample inclusion flow diagram.

were allocated with an Australasian Triage Scale (ATS) of 3 (n = 48, 55.2%). Those who met SK criteria in ED differed significantly from those who met SK criteria on a ward in terms of gender (more males in the ED group) and ATS (higher proportion of more urgent cases in the ED group) and admitting specialty team (more to ICU in the ED group).

Regarding outcomes for the 87 patients with sepsis, the median time to see a clinician was 23 min and the median ED LOS was 280 min. Less than half (n = 41, 48%) were seen within the recommended triage timeframe, and more than half (n = 49, 56%) had an ED LOS of > 4 h. The median hospital LOS was 10 days; 17% were readmitted within 28 days and the in-hospital mortality was 18%. Those who met SK criteria in ED differed significantly from those who met SK criteria on a ward in terms of ED LOS (longer in the ED group). For the 63 patients who met the SK criteria in the ED, around a quarter (n = 17, 27%) met the qSOFA(close) criteria, indicating a subgroup at risk of poorer prognosis.

Antibiotic therapy for patients diagnosed with sepsis is displayed in Table 4. The median time from triage to recognition (i.e. meeting SK criteria) was 73 min, time from recognition to antibiotic administration was 121 min and from triage to antibiotic administration 256 min. Numbers included in each of these outcome analyses varied for reasons including the administration of antibiotics prior to evidence of meeting SK criteria (this and other reasons noted in Table 4). One in ten (n = 9) patients received antibiotics within 60 min of triage and 35% (n = 23) received antibiotics within 60 min of meeting the SK criteria. Most patients had blood cultures taken (91%); for most of these cases, this occurred prior to antibiotic administration (70%, n = 54). As would be expected, those who met SK criteria in ED differed significantly from those who met SK criteria on a ward in terms of time from triage to meeting the SK criteria (shorter in the ED group) and time from triage to antibiotic administration (shorter in the ED group).

For those where SK criteria was met in the ED, all patients had at least one documented indication of infection, most commonly a history of fevers or rigors (n = 38, 60.3%) (Table 5). The majority of patients who met SK criteria in the ED (n = 55, 87%) met 'yellow criteria', indicating they had at least two signs indicating potential sepsis. The most of which were SpO_2 < 95%, systolic blood pressure ≤100 mmHg and temperature < 35.5 °C or > 38.5 °C. Just over half (n = 32, 50.8%) met the 'red criteria', indicating likely severe sepsis or septic shock; the most common of which were age > 65 years, lactate ≥4 mmol/L and base excess ≤ −5 (Table 6). In response to recognition of sepsis, each of the 'Sepsis Six' responses were provided in more than 65% of patients (Table 7).

4. Discussion

4.1. Recognition of sepsis

Patients with sepsis displayed SK criteria at varying stages throughout their hospital episode of care. At the point of triage all patients who present to the study site ED undergo a brief, limited assessment by a qualified triage registered nurse where the nurse assigns a triage category. At this point, the patient may not be displaying clear signs of sepsis; hence the potential allocation of other less urgent triage categories. The median time from triage to see the treating clinician for the entire sample was 22.5 min; 19 min for those who met the sepsis criteria in the ED and 37 min for those who did not meet the sepsis criteria until they were on an in-patient ward. As the majority of

Table 3
Demographic, ED characteristics and outcomes of patients based on whether sepsis criteria met in ED vs. on ward.

Variable	Total N = 87	Sepsis criteria met in ED (n = 63)	Sepsis criteria met on ward (n = 24)	P value
Demographic Characteristics				
Median (IQR) Age, yrs	69 (54–80)	69 (54–80)	71.0 (51.8–81.5)	0.898
Gender				0.017
Male	57 (65.5%)	46 (73.0%)	11 (45.8%)	
Female	30 (34.5%)	17 (27.0%)	13 (54.2%)	
ED Characteristics				
ED Australasian Triage Scale				0.025
1	10 (11.5%)	10 (15.9%)	0 (0.0%)	
2	24 (27.6%)	20 (31.7%)	4 (16.7%)	
3	48 (55.2%)	31 (49.2%)	17 (70.8%)	
4	5 (5.7%)	2 (3.2%)	3 (12.5%)	
5	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Arrival Mode				0.106
Ambulance	65 (74.7%)	50 (79.4%)	15 (62.5%)	
Other	22 (25.3%)	13 (20.6%)	9 (37.5%)	
Admitting Specialty				0.021
General Medicine	32 (36.8%)	18 (28.6%)	14 (58.3%)	
Intensive Care	16 (18.4%)	15 (23.8%)	1 (4.2%)	
Surgical	5 (5.7%)	5 (7.9%)	0 (0.0%)	
Other	34 (39.1%)	25 (39.7%)	9 (37.5%)	
Outcomes				
Time to see clinician (median, IQR) min[†]	22.5 (6.8–59.0)	19.0 (4.0–59.0)	37.0 (12.0–63.0)	0.087
Seen by doctor within recommended ATS timeframe				0.338
Yes	41 (47.7%)	32 (50.8%)	9 (37.5%)	
No	45 (52.3%)	31 (49.2%)	14 (58.3%)	
Median (IQR) ED length of stay (min)	280.0 (185.0–474.0)	336.0 (197.0–488.0)	225.0 (137.0–309.3)	0.013
ED length of stay				0.089
≤ 4 h	38 (43.7%)	24 (38.1%)	14 (58.3%)	
> 4 h	49 (56.3%)	39 (61.9%)	10 (41.7%)	
Median (IQR) hospital length of stay (days)	10 (5.0–17.0)	10 (4.0–23)	9 (6.0–14.8)	0.614
Discharge disposition from hospital				0.265
Home/Usual Residence	61 (70.1%)	46 (73.0%)	15 (62.5%)	
Died in hospital	16 (18.4%)	9 (14.3%)	7 (29.2%)	
Other[‡]	10 (11.5%)	8 (12.7%)	2 (8.3%)	
Hospital readmission within 28 days				0.584
Yes	15 (17.2%)	10 (15.9%)	5 (20.8%)	
No	72 (82.8%)	53 (84.1%)	19 (79.2%)	

Sepsis criteria met based on when documentation in patient notes reflected meeting Sepsis Kills criteria, [†]n = 86, [‡]'Other' category includes patients who discharged at own risk, had an episode change or required hospital transfer.

Table 4
Antibiotic therapy for patients with sepsis.

Variable	Total N = 87	Sepsis criteria met in ED (n = 63)	Sepsis criteria met on ward (n = 24)	P value
Median (IQR) time from triage to recognition[†]	73 (16–490)	27 (6–121)	867 (503–2403)	< 0.001
Median time from recognition (IQR) to antibiotic administration[‡]	121 (53.3–279.0)	117 (51.5–254.0)	265 (42.5–3567.5)	0.239
Median time from triage to antibiotic administration (IQR)[§]	256.0 (91.0–479.0)	181 (71.0–317.0)	413.0 (167.0–1132.5)	0.001
Antibiotics administered within 60 min of triage to ED (if prescribed)				0.212
Yes, ≤ 60 min	9 (10.8%)	8 (13.6%)	1 (4.2%)	
No, > 60 min	74 (89.2%)	51 (86.4%)	23 (95.8%)	
Antibiotics administered within 60 min of recognition (if prescribed)[‡]				0.918
Yes, ≤ 60 min	23 (34.8%)	20 (35.1%)	3 (33.3%)	
No, > 60 min	43 (65.2%)	37 (64.9%)	6 (66.7%)	
Blood cultures taken				0.137
Yes	79 (90.8%)	59 (93.7%)	20 (83.3)	
No	8 (9.2%)	4 (6.3%)	4 (16.7)	
Blood cultures taken prior to administration of antimicrobial				0.086
Yes	54 (70.1%)	43 (75.4%)	11 (55.0)	
No	23 (29.9%)	14 (24.6%)	9 (45.0)	
Median (IQR) number of antibiotics prescribed	1 (1–2)	2 (1–2)	1 (1–2)	0.389
Number of antibiotics prescribed				0.284
0	4 (4.6%)	4 (6.3%)	0 (0.0)	
1	42 (48.3%)	27 (42.9%)	15 (62.5)	
2	29 (33.3%)	22 (34.9%)	7 (29.2)	
3,4 or 5	12 (13.8%)	10 (15.9%)	2 (8.3)	

Sepsis recognition defined as documentation in patient notes reflected meeting SK criteria.
[†] 3 cases where criteria met pre-hospital with QAS coded as 0 min.
[‡] Analysis based on 66 patients (excludes 18 cases where antibiotics administered prior to meeting criteria and 5 cases where no antibiotics administered).
[§] Analysis based on 83 patients.

Table 5
Risk factors, signs or symptoms of infection.

Indication of infection	N = 63
History of fevers or rigors	38 (60.3%)
Cough/sputum/breathlessness	21 (33.3%)
New onset of confusion/altered LOC/neck stiffness/headache	21 (33.3%)
Abdominal pain/distension/peritonism	13 (20.6%)
Immunocompromised/chronic illness	12 (19.0%)
Dysuria/frequency/colour/odour	11 (17.5%)
Recent surgery or invasive procedure	10 (15.9%)
Cellulitis/wound infection	9 (14.3%)
Indwelling medical device	8 (12.7%)
Fall not related to mechanism of injury	6 (9.5%)
Re-presentation within 48 h	4 (6.3%)

NB. Analysis based on cases where sepsis criteria met in ED and considers that more than one indication of infection possible.

Table 6
Signs or symptoms of sepsis/severe sepsis.

Indication of sepsis	N = 63
Yellow criteria	
O_2 saturation < 95%	34 (54.0%)
Systolic blood pressure ≤100 mmHg	32 (50.8%)
Temperature < 35.5 °C or > 38.5 °C	29 (46.0%)
Heart rate ≤50 or ≥120 beats per minute	26 (41.3%)
Respirations ≤10 or ≥25 per minute	22 (34.9%)
New onset of confusion/altered LOC/neck stiffness/headache	19 (30.2%)
TWO or more yellow zone criteria present in ED (potential sepsis)	55 (87.3%)
Red criteria	
Age > 65	37 (58.7%)
Lactate ≥ 4 mmol/L[†]	20 (40.8%)
Base excess ≤ −5[‡]	17 (34.0%)
Systolic BP < 90 mmHg	20 (31.7%)
Immunocompromised	12 (19.0%)
At least ONE red zone criteria present in ED (severe sepsis/septic shock)	32 (50.8%)

NB. Analysis based on cases where sepsis criteria met in ED.
[†] Analysis based on 49 cases where lactate was measured.
[‡] Analysis based on 50 cases where base excess was measured.

Table 7
Response to patients with sepsis, based on Sepsis Six [18] and Sepsis Kills criteria [10].

Response	N = 63
1. Oxygen administered if SpO_2 ≤ 95%[†]	31 (86.1%)
2. Blood cultures taken	59 (93.7%)
3. Venous blood gas taken (for Lactate)	49 (77.8%)
4. Intravenous fluid challenge required	42 (66.7%)
5. Antibiotics prescribed and administered within 60 min of triage [within 60 min of diagnosis]	8 (13.6%) [37, 64.9%]
6. Monitoring of observations	[Not specifically collected]

More than one response possible for each patient.
[†] Analysis based on 36 cases where SpO_2 ≤ 95%.

patients were triaged an ATS of 3 (55%) or 2 (28%), this median time to seen by a treating clinician is reflective of this.

For most patients, sepsis was detected in the ED however there were some where criteria were not evident until after they were admitted to a hospital ward. The ability to recognise and diagnose sepsis in the ED, particularly in its early stages can be challenging as some patients can display signs and symptoms that could be attributed to other common conditions [5,19]. Furthermore, recognition and diagnosis in the most vulnerable patients such as the elderly and those with pre-existing organ dysfunction can be even more difficult as they may present with confusion or agitation, be afebrile and have a limited endogenous stress response with relatively normal vital signs [5,20]. The importance of taking a good clinical history should not go unnoticed. In our sample, the most common symptom of infection identified in ED was a history of fevers or rigors (over 50%) followed by recent surgery/cellulitis or wound infection. As there is no gold standard laboratory test or assay to detect sepsis, physicians must draw on their knowledge and experience to ensure the diagnosis of sepsis in its early stage is not delayed or missed.

The emergence of more recent literature with updated definitions and clinical scoring qSOFA for recognising patients at risk of poor outcomes may be useful in the adult population with suspected infection. qSOFA involves assessment of respiratory rate, altered mentation and systolic blood pressure [2]; assessments that can be easily performed by all clinical staff. Whilst recent research indicates the qSOFA has greater prognostic accuracy when compared to other criteria measures such as systematic inflammatory response syndrome (SIRS) and severe sepsis [21], there is still variation in the acceptance of these criteria [22]. In our study approximately 1 in 4 (n = 17, 27%) patients who met the SK criteria met the qSOFA(close) criteria. Thus, there is potential to use these more contemporary criteria in the study site ED to assist with prognosticating those with sepsis.

4.2. Response to patients with sepsis

Once recognised, most patients who displayed SK criteria received a response consistent with the 'Sepsis Six' strategies which include oxygen; blood cultures; IV Antibiotics; IV fluids; lactate and monitoring [18]. Regarding blood cultures, whilst 90% of the sample had blood cultures taken, in one third of these cases, cultures were not taken prior to antibiotic administration. This is important to guide the use of the most appropriate antibiotic type, dose and duration for the pathogen [23]. The taking of cultures before antibiotics was better adhered to in the ED and perhaps further education to ward staff regarding the importance of this is required. It is recognised that this may not have been adhered to due to critical nature of cases, and sometimes intravenous access can be challenging in patients with severe sepsis.

Performing a blood lactate test primarily helps to determine if someone is at risk for poorer outcomes and is used as part of an initial evaluation of sepsis [23,24]. There is a high association of elevated lactate levels and an increase in in-hospital mortality. It is particularly significant for patients with lactate levels > 4 mmol/L [25]. In one third of patients in our sample, a lactate test was not undertaken, possibly delaying or hampering the ability to detect and diagnose sepsis. Whilst we are not advocating for routine lactate tests on everyone who arrives to the ED, for those with signs of sepsis this test should be performed as clinically indicated, since it has prognostic value and can be used to guide resuscitation [23,24].

In two thirds (66%) of our sample, an IV fluid challenge was part of the response to sepsis. Guidelines and sepsis pathways recommend an initial IV fluid bolus of 30 ml/kg isotonic crystalloid for patients with sepsis and hypotension. However, there is a lack of evidence from clinical trials to support this. Both observational data as well as randomized studies suggest harm associated with injudicious use of fluids in sepsis [26–32]. Ongoing research is comparing early vasopressors with standard care [33] and will help further inform care bundles for this group of patients.

Most patients (n = 83/87) in our study were administered antibiotics. The delivery of antibiotics in a timely fashion has been a noted recommendation in the sepsis literature [23,34], although various definitions of 'timely' exist and include within 60 min of triage or time of diagnosis [10]; within 3 h of presentation [23], immediately after recognition or within one hour of identification of severe sepsis or septic shock [34] and within an hour of hypotension [35]. Whilst findings from studies indicate improved survival to hospital discharge for those with septic shock administered appropriate antimicrobials within an

hour of documented hypotension [35], no association between time to antibiotic and outcome was found in other studies of patients with sepsis in the ED [36], bacteraemia [37], and neutropenia [38]. The participating sites in our study did not have a sepsis guideline or bundle in place at the time of this study, therefore triage time was used as time zero. If sepsis was detected in the ED, the average time taken for patients to receive antibiotics was 3hrs from triage. Fourteen percent of patients received antibiotics within 60 min of triage and 35% received antibiotics within 60 min of recognition. Our findings are similar to those noted elsewhere in that, following the introduction of the SK program, the proportion of patients receiving antibiotics within 60 min of triage increased from 10.6% to 27.5%, between 2009 and 2013 [10].

The primary outcome for this study was time to antibiotic administration from triage. However, it should be noted that not all patients met the SK criteria at triage. Therefore, administration of antibiotics would have been longer in patients who met SK criteria after triage. A more appropriate reflection of administration time would thus be to measure time from recognition. The retrospective nature of the study means that determining the exact time of recognition was not possible. As such a surrogate marker (i.e. the presence of clinical documentation that reflects SK criteria (2014 Version for Emergency Departments) being met) was used and indicated that time from recognition (if in ED) to antibiotic administration was 117 min. This time may reflect, in part, the time taken to collect blood cultures (recommended prior to administering antibiotics) as well as for the prescription, preparation and administration of antibiotics. It also highlights an opportunity for clinical practice improvement.

The study also demonstrated a difference of time to recognition and time to administration of antibiotics from triage between the ED and the ward. Although this was statistically significant it's significance within the clinical setting is questionable. Patients must arrive through the ED prior to admission to the ward, therefore by the nature of the process it may be clinically expected that recognition on the ward and administration of antibiotics on the ward would be longer than in the ED. Despite the difference in administration of antibiotics within 60 min of recognition between ED and the ward, this was not statistically significant. This may have been a result of the small sample size. Further research needs to be conducted to determine whether clinical practice is different between the ED and ward from when sepsis is recognised.

Not all patients received a 'Sepsis Six' response. This may reflect aspects of the patient's condition (i.e. allergies, not for resuscitation order, stage of sepsis, not clinically indicated) and aspects of the care process (i.e. time taken to take blood samples/investigations, send and receive results from pathology, other confounding departmental factors). Along with the Sepsis Six response strategies, we also considered other patient and service delivery measures and outcomes (such as timeliness of care in ED, hospital LOS, mortality) that may reflect response efficacy. For all patients included in this study, timely and appropriate care delivery was provided in the ED. The median time to see a clinician was 22 min and just over half (51%) were seen within their recommended triage time. These outcomes differ slightly to national figures where time to see clinician is 18 min and 75% of all ED presentations were seen within their recommended triage timeframe in 2013–14 [39]. The median ED LOS was 280 min (4.5 h) with 44% of patients having an ED LOS of ≤ 4 h. Nationally, the median ED LOS was 160 min with 73% of all ED presentations having an ED LOS of ≤ 4 h in 2013–14 [39]. Patients recognised in the ED had a longer ED stay (of almost 2 h) than those where sepsis was recognised on the ward. These differences may reflect case acuity and complexity resulting in the need for more time intensive specialised emergency care, stabilisation of the patient before transferring to a ward or ICU, or broader hospital admission access block issues.

The management of sepsis is resource intensive and can have a considerable impact on the overall hospital LOS. The average hospital LOS for patients in our study was 10 days; shorter than the 13.5 days noted in other research on patients with severe sepsis [3], but much longer than the average hospital LOS of 5.6 days in 2013–14 [39] and 2.8 days in 2015–16 for most Australians [40]. In our study, 18.4% (n = 16) of patients were admitted to the Intensive Care Unit; a figure higher than a previous study where severe sepsis accounted for approximately 11% of patients admitted to Intensive Care Units [3]. Differences perhaps are reflective of our sample, where criteria indicated they had a firm discharge diagnosis of sepsis, or may reflect good recognition and admission processes in that patients needing ICU services are able to access ICU services.

The mortality rate for all patients in our study was 18%; 14% for those where sepsis was detected in ED and 29% for those where sepsis was detected on the ward. Within the broader literature, the mortality rate from sepsis varies from 14% to 46% [3–5,10], depending on factors such as the stage of sepsis, treatment modalities available to the patient, and underlying patient factors (e.g. age, other co-morbidities). Included in our sample were patients with sepsis related ICD 10 disease codes that were most likely on the more severe end of the spectrum. Most patient who only had infection but no organ dysfunction were likely not included. These inclusion criteria may be reflected in the mortality rate. Our results are however, in line with an Australia sepsis study [10], and outline the high mortality compared with the average in-hospital mortality rate of 0.7% reported in Australian public hospitals [41]. We used the Sepsis Kills criteria to determine sepsis detection, and outcomes may have varied, based on criteria used. When we applied qSOFA criteria, mortality rate for the ED group was 17%, suggesting a fair consistency between definitions.

4.3. Implications

There are several implications for clinical practice arising from this study. First, it is important that implementing sepsis detection and management guidelines in the ED and broader health service be considered as part of an appropriately tailored care pathway. Careful consideration is required, since certain facets of pathways have a changing evidence-base and as such may need ongoing adjustment to reflect best contemporary knowledge. Emphasis on areas with strongest evidence is essential to achieve and maintain high rates of compliance with treatment guidelines [42,43]. Second, targeted training is suggested for front end ED staff (i.e. those working at triage and early assessment areas) where time is critical for an undifferentiated patient in the recognition and response to sepsis. Given the risk assessment of sepsis is reliant on general observations (including respiratory rate, blood pressure, level of consciousness), the importance of i) performing, ii) accurately recording and iii) responding to variations in these is paramount. This information should inform the allocation of a triage category and escalation to senior staff, in order to achieve timely appropriate interventions (i.e. administration of timely antibiotics) for the sickest subgroups. Third, the same principles should apply to staff working in the ward as they do in the ED. That is, an inherent understanding that i) performing, ii) accurately recording and iii) responding to variations in routinely performed observations for all patients is required, especially since sepsis can develop gradually. Fourth, there is room for improvement in the rate of blood culture collection prior to the administration of antibiotics [44]. Once the diagnosis of suspected sepsis is made, the collection of blood cultures prior to antibiotic administration is strongly supported in clinical practice to inform the most appropriate antibiotic type, dose and duration for the pathogen [23].

4.4. Limitations

Routinely collected health data from patients allocated a primary discharge from hospital code related to sepsis over a 4-month period was used for this study. As such, our sample may be considered small and not entirely representative as some patients with sepsis may have received other primary disease/illness codes. As a retrospective,

observational study, we were not able to capture when a 'true' diagnosis of sepsis was made, grade the degree of sepsis or prove causation and there may be confounding factors not considered in our study. Although this study was undertaken at two sites within the same health service, we cannot determine the extent to which our findings are generalisable to other sites. For some patients, documentation regarding the recognition and response to sepsis was not found/reported. Thus, this missing data meant that our ability to comprehensively inform where sepsis was detected and what further response actions were undertaken was limited in a few cases. Despite these limitations, the key strength of this study is that it identified specific clinically important areas for practice improvement.

5. Conclusion

Findings from our study indicate that sepsis was detected at various stages throughout the patient's journey. As such, early warning systems need to be considerate of the dynamic nature of sepsis. Whilst guidelines exist that indicate antibiotics be administered early, this was difficult to achieve for most patients in clinical practice. Analysis incorporating additional outcomes based on response (e.g. whether antibiotics were administered within 60 min of meeting SK criteria) should be considered in future research with larger samples. Future research that is prospective and longitudinal in design is also required to inform aspects of sepsis care bundles with most impact on patient outcomes.

Ethical statement

This study received ethical approval from the Gold Coast Hospital and Health Service (HREC/15/QGC/11) Human Research Ethics Committee.

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Declaration of Competing Interest

The authors have no conflict of interest to report.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ienj.2019.06.005.

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