Sepsis Study
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Introduction

Sepsis is an overwhelming systemic response to infection in which the immune system mediates a potentially damaging inflammatory response. Severe sepsis is defined as sepsis leading to dysfunction of one or more organ systems according to international consensus criteria. Successful management requires prompt recognition, appropriate interventions to identify and control the micro-organism(s) and restore oxygen delivery to tissues (with support of organ failure), and appropriate escalation for decisive medical management. Estimates of incidence of severe sepsis are dependent on coding and reliability of recognition, but are around 300/100,000 of the population: more common than myocardial infarction [1].

A large recent European study found mortality from sepsis to be 36% [2]. In the UK, ICNARC data (which only identifies cases occurring in ICU settings during the first 24 hours of admission to ICU) estimate 102,000 sepsis cases per year, with around 36,000 deaths [3]. Around 70% of patients with sepsis are managed in critical care hospital settings, with typical bed costs of around £1500/day. This equates to direct costs to the NHS of over £2.5 billion per year [4].

Sepsis may develop either in the community (from where patients requiring hospital care may be admitted through Emergency Departments/ Admissions Units) or in hospital inpatients whose condition deteriorates. Over 70% of cases arise in the community [5]. In 2011, the College of Emergency Medicine conducted an HQIP-funded audit of compliance with sepsis management standards in Emergency Departments (the Sepsis 6): compliance was suboptimal at 27-47% [6]. Ambulance and other pre-hospital services such as 111 present another key opportunity for prompt recognition and intervention, but it is unknown how many missed opportunities present, nor the frequency of presentation to Primary Care practitioners.

An estimated 65,000 people in the UK per year survive episodes of severe sepsis, often with serious long-term sequelae: amputation, muscular contraction, irreversible damage to lungs, heart and kidneys, psychiatric disorders such as cognitive dysfunction and PTSD. Consequences to continuing health and social care are considerable [7].

In 2010, the Centre for Maternal & Child Enquiries (CMACE) published the most recent triennial report of the UK Confidential Enquiry into Maternal Deaths (2006-2008). This report found sepsis to be the commonest cause of direct maternal death for this time period [8]. MBRRACE-UK have just started to undertake their first themed confidential enquiry., which will look at maternal mortality and morbidity due to sepsis and is due for publication in December 2014.. A contemporary analysis of avoidable and remediable factors in the process of care of adults with sepsis will therefore be a powerful adjunct to this work.

In 2010, the international Surviving Sepsis Campaign (SSC) published results in over 15,000 episodes showing that delivery of early antibiotics (at that stage within 3 hours) was independently associated with survival in a risk-adjusted model (odds ratio 0.86), but was achieved in only 67% of cases [9]. The recommendation has since been changed to delivery of antibiotics within 1 hour of sepsis being identified [10].

In 2010, the Scottish Trauma Audit Group (STAG) conducted an audit of sepsis within acute hospital settings. 1.7% of new admissions developed criteria for sepsis

within 2 days of attendance. 34% of these patients met the criteria for Severe Sepsis, with mortality of 24% in this group [11].

Recently, the parliamentary ombudsman published a detailed report identifying common themes in 10 case studies of patients that died following sepsis, This report identified failings throughout the patient pathway: from carrying out a timely initial assessment and identifying the source of infection to adequate monitoring and timely initiation of treatment [12]
Sepsis is therefore a major cause of avoidable mortality, morbidity and avoidable NHS expenditure and despite the wealth of research in this area there remains a need for a study to identify, in greater detail, remediable factors which if addressed could improve the quality of care of patients with sepsis.

The National Confidential Enquiry into Patient Outcome and Death (NCEPOD) has, over a 25 year period, undertaken 37 enquiries into the care received by patients. NCEPOD has an established method of reviewing care pathways involving organisational and clinician questionnaires together with a peer review of cases by Reviewers who are clinicians in everyday practice. These clinicians review and rate the care received by selected patients throughout the whole pathway from admission to discharge or death and categorise the standard of care. Themes emerge from these reviews from which NCEPOD is able to make recommendations. Clinician and organisational questions also allow care processes to be mapped and compared with established clinical standards. The thematic analysis resulting from this study will contribute to the evidence base for alterations in practice to reduce the avoidable mortality and morbidity associated with sepsis, and the overall quality of care provided to this group of patients.

References

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Aims and objectives

Aim:
To identify and explore avoidable and remediable factors in the process of care for patients with sepsis.

Objectives:

- To examine organisational structures, processes, protocols and care pathways for sepsis recognition and management in hospitals from admission through to discharge or death.

- To identify avoidable and remediable factors in the management of the care for a sample of adult patients with sepsis, throughout the patient pathway from presentation to primary care (if applicable), throughout secondary care to discharge or death, focusing on the following areas of care:
    - Evaluation of systems and processes that are in place to facilitate timely identification, escalation and appropriate treatment of infection, including transfer to high dependency and intensive care units where appropriate;
    - Examining the recognition of sepsis and early signs of septic shock across the entire patient pathway Investigating the appropriate management of sepsis
    - Reviewing whether there was a multidisciplinary team approach
    - Communication:
        - Between primary and secondary care
        - Between healthcare professionals; Documentation of sepsis-
        - With families and carers
    - Examining the management of the end of life pathway and ceilings of treatment

Methodology

Population
Adult patients (≥16 years old) who are seen by the critical care outreach team (or equivalent) or that are admitted directly to critical care during the study period with a diagnosis of sepsis*

** As defined by the surviving sepsis campaign (see appendix I on page 9 for detail).*

Exclusions
- Immunosuppressed neutropaenic patients on chemotherapy, immunosuppressant drugs for transplant programmes
- Pregnant women up to 6 weeks post-partum (covered by MBRRACE-UK maternal sepsis morbidity study)
- Patients on end of life care pathway at time of diagnosis or consultant-led decision made not to escalate (prior to entry into the study)
- Patients that develop sepsis after 48 hours on ICU/HDU
- Children <16 years

Sample period

Cases will be identified for the study during a 2 week period: 6th-20th May 2014.

Case identification

Cases will be identified prospectively through the completion of a 'SEPSIS case ID' spreadsheet every time a patient meets the criteria for the study during the 2 week data collection period. This process will be coordinated by specially appointed study contacts in ICU/HDU and on the critical care outreach team, together with the NCEPOD Local Reporters.

Sample size

On the basis of ICNARC data (identifies patients that develop sepsis within 24 hours of admission to ICU only), it is estimated that 2 weeks of data collection should yield identification of at least 1400 cases. Adding to this estimates of cases identified by the critical care outreach team we can expect a sample of at least 2000-2500 cases.

From the cases identified, a sample of 700 cases will be randomly selected for review.

Method of data collection

During the study data collection period limited, key data on selected aspects of care not recorded in the case notes will be collected via the prospective 'Sepsis case ID' spreadsheet.

After waiting 30 days for the outcome, spreadsheets will be passed to the NCEPOD Local Reporter in each hospital who from the PAS records, will be asked to collect additional data on dates of admission, discharge, discharge destination plus ICD10 coding data on patients included in the study.

Having identified the initial sample, a group of around 700 patients will be randomly selected for the peer review aspect of the study. Cases will be limited to 5 per hospital and a maximum of 3 per clinician. For these patients, the following data will be collected:

Clinician questionnaire
A clinician questionnaire will be sent for completion to the consultant responsible for each patient for the finished consultant episode prior to the entry into the study (Date admitted to critical care or seen by the outreach team (for patients that are admitted directly to critical care on arrival in hospital, this will be the admitting clinician)). The clinician questionnaire will collect data on the care of the patient from presentation with sepsis to death/discharge or 30/days after admission.

Case notes
Copies of the case notes will be requested from arrival in hospital (or up to 2 weeks before entry into the study for patients in hospital for more than 2 weeks prior to diagnosis with sepsis) up to death/discharge/30 days after admission. Requested extracts will include: Copies of the Ambulance Service Patient Report Form, Clinical annotations, emergency department notes, nursing notes, microbiology, biochemistry, radiology reports, DNA-CPR forms, surgical/anaesthetic charts,

acute/sepsis care pathways, rehabilitation notes, ICU charts and a copy of the death certificate and autopsy report (if applicable/available)

GP notes
Copies of General Practitioner (GP) notes will be requested in cases where the GP saw the patient in relation to the hospital admission (identified by the clinician questionnaire) for 2 weeks prior to the hospital admission.

Reviewer Assessment form (RAF)
A multidisciplinary group of Reviewers will review case-notes and clinician questionnaires and give their opinion on quality of care via completion of the RAF in the NCEPOD office. A separate GP RAF will be used to review the GP notes at GP reviewer meetings.

Organisational questionnaire
The organisational questionnaire will be disseminated to all participating sites and collect data on organisational aspects of care of patients with sepsis. Additional organisational data will be collected from Ambulance Services and from NHS England with respect to 111 service and emergency care commissioning.

Participating sites

For the organisational aspect of the study, all hospital providers that deal with patients with sepsis will be able to participate, including: acute hospitals, specialist hospitals, community/ 'cottage' hospitals, independent hospitals, treatment centres etc.

For the patient data part of the study, hospitals that have an ICU, HDU and/or critical care outreach team will be able to participate.

Pilot Study

A pilot study will be performed to test the method of data collection (including the feasibility of accessing primary care data) and the data collection materials and ensure that they are robust.

Analysis and Review of Data

Reviewers (peer review)
A multidisciplinary group of Reviewers will review the data collected and provide opinion on the care received by this group of patients, from admission to discharge. The advisor group will be made up of intensivists, critical care nurse specialists, general physicians, acute physicians, emergency department physicians, general surgeons and general practitioners (for the review of GP notes).

Data Entry
All clinician questionnaire data will be electronically scanned and combined with data from the assessment form completed by the Advisors. Quantitative data analysis will be undertaken using Excel and qualitative analysis will be undertaken by reviewing the themes arising from the Advisor meetings.

Confidentiality and data protection

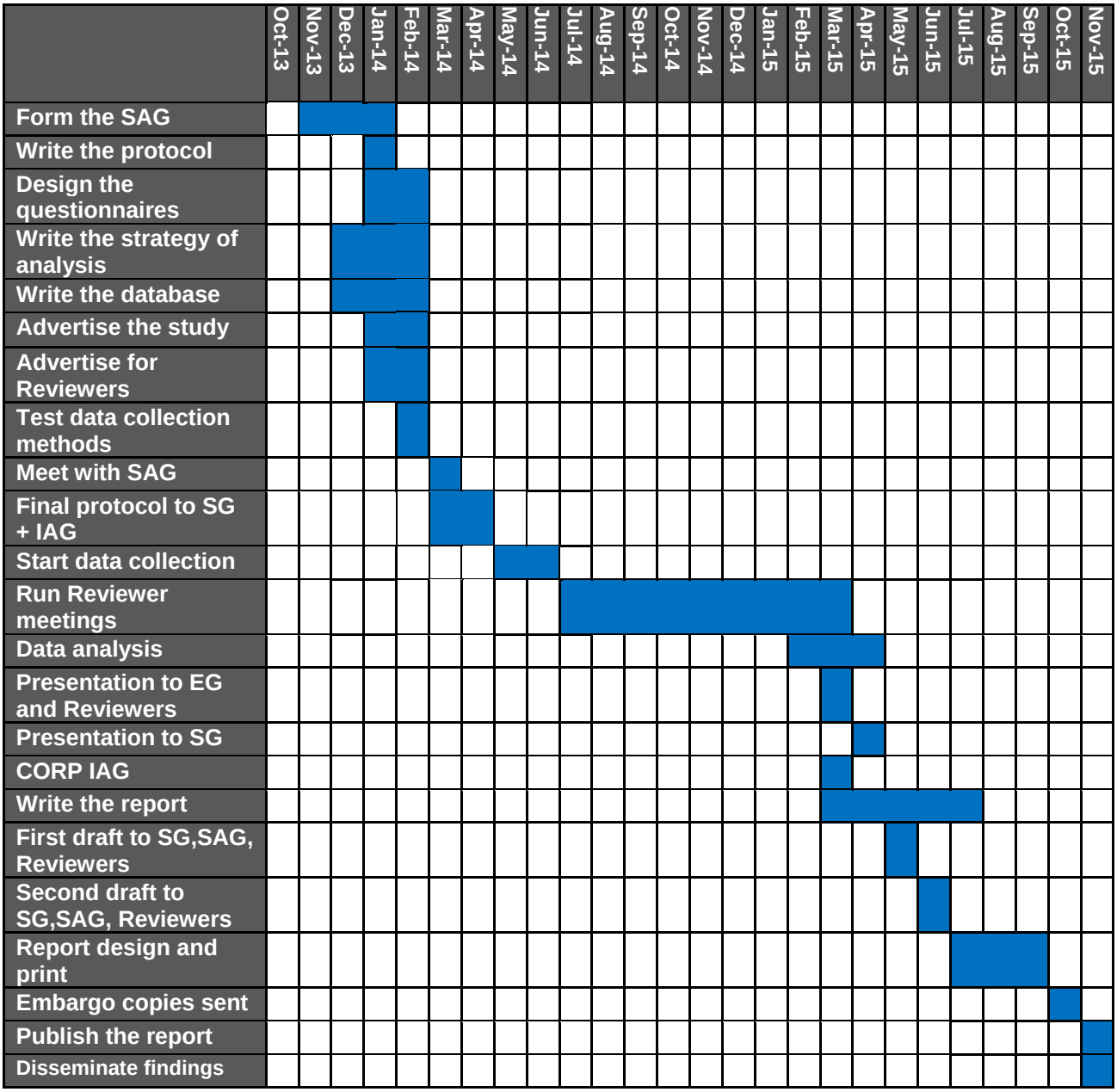
Once the data have been extracted by the NCEPOD researchers, the questionnaires and casenotes will be anonymised to remove patient identifiers prior to review by the Advisors.

All electronic data are held in password protected files and all paper documents in locked filing cabinets. As soon as possible after receipt of data NCEPOD will encrypt electronic identifiers and anonymise paper documents. Section 251 approval has been obtained to perform this study without the use of patient consent.

Dissemination

On completion of the study a report will be published and widely disseminated.

Timescale



Appendix 1: Modified SIRS Criteria- Diagnostic for Sepsis

Infection, documented or suspected, and more than one of the following:

- Fever (> 38.3°C)/Hypothermia (core temperature < 36°C)
- Heart rate > 90/min–1 or more than two sd above the normal value for age
- Tachypnea (RR>20 breaths/minute)
- Acutely altered mental statusArterial hypotension (SBP < 90 mm Hg, MAP < 70 mm Hg, or an SBP decrease > 40 mm Hg in adults or less than two sd below normal for age)
- Hyperglycemia (plasma glucose > 140 mg/dL or 7.7 mmol/L) in the absence of diabetes
- Leukocytosis (WBC count > 12,000 µL–1) or Leukopenia (WBC count < 4000 µL–1) (or normal WBC count with >10% immature forms)
- Significant edema or positive fluid balance (> 20 mL/kg over 24 hr)
- Plasma C-reactive protein more than two sd above the normal value
- Plasma procalcitonin more than two sd above the normal value
- Arterial hypoxemia (Pao2/Fio2 < 300)
- Acute oliguria (urine output < 0.5 mL/kg/hr for at least 2 hrs despite adequate fluid resuscitation)
- Creatinine increase > 0.5 mg/dL or 44.2 µmol/L
- Coagulation abnormalities (INR > 1.5 or aPTT > 60 s)
- Ileus (absent bowel sounds)
- Thrombocytopenia (platelet count < 100,000 µL–1)
- Hyperbilirubinemia (plasma total bilirubin > 4 mg/dL or 70 µmol/L)
- Hyperlactatemia (> 1 mmol/L)
- Decreased capillary refill or mottling

(WBC = white blood cell) Adapted from: Signs & symptoms of infection highlighted in Surviving Sepsis Campaign Sepsis Screening Tool: http://www.survivingsepsis.org/SiteCollectionDocuments/ScreeningTool.pdf and R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Andrew Rhodes, MB BS; et al: 2001 Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012 Critical Care Medicine Journal, February 2013; 41(2)pp580-637