Title: Advancing Quality in sepsis management: A large-scale programme for improving sepsis recognition and management in the North West region of England

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NP extracted the data

ABI-P performed the analysis

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**ABSTRACT:**

**Objective:** To evaluate the impact of a collaborative program for the early recognition and management of patients admitted with sepsis in the northwest of England.

**Setting:** 14 hospitals in the northwest of England.

**Intervention:** A quality improvement program (AQ sepsis) that promoted a sepsis care bundle including time-based recording of early warning scores, documenting SIRS criteria and suspected source of infection, taking of blood cultures, measuring serum lactate levels, administration of intravenous antibiotics, administration of oxygen, ﬂuid resuscitation, measurement of fluid balance and senior review.

**Main outcome measures:** Inpatient mortality, 30 day readmission rates and duration of hospital ≥ 10 days.

**Results:** Data for 7776 patients were included in this study between 1st July 2014 and 29th December 2015.Participation in the AQ sepsis program was associated with a reduction in readmissions within 30 days (OR 0.81 [0.69-0.95]) and hospital stays over 10 days (OR 0.69 [0.60-0.78]). However there was no reduction in mortality. Administration of a second litre of intravenous fluid within 2 hours, oxygen therapy and review by a senior clinician were associated with increased mortality. Starting a fluid balance chart within 4 hours was the only clinical process measure which did not affect mortality. Taking a blood culture sample, administering antibiotic therapy and measuring serum lactate within 3 hours of hospital arrival were all associated with reduced mortality (OR 0.69 [0.59-0.81], OR 0.77 [0.67-0.89] and OR 0.64 [0.54-0.77] respectively) and shorter hospitalizations (OR 0.58 [0.49-0.69], OR0.81 [0.70-0.94] and OR 0.54 [0.45-0.66] respectively). However, none of these measures had an impact on the risk of readmission to hospital within 30 days.

**Conclusions**: The AQ Sepsis collaborative in northwest of England improved readmission and length of stay for patients admitted with sepsis but did not affect mortality.Further cost-effectiveness evaluation of the program is needed.

Section 1: What is already known on this subject

* Sepsis is a significant cause of mortality and healthcare costs. Most patients with sepsis are admitted to hospital via the Emergency Department.
* Multiple observational studies have shown that sepsis improvement programs improve mortality however the impact on length of stay and readmissions is not well described
* Controversy also exists about how rapidly sepsis should be treated and which interventions improve outcomes

Section 2: What this study adds

* A regional sepsis improvement program focusing on patients admitted with sepsis in the northwest of England improved length of stay and readmissions but not mortality
* Our study suggests that sepsis quality improvement projects should assess hospital length of stay and readmission rates as well as mortality
* Taking a blood culture sample, administering antibiotic therapy and measuring serum lactate within 3 hours of hospital arrival were all associated with reduced mortality and shorter hospitalizations. Our study adds to the body of evidence supporting timely treatment for patients with sepsis.

**INTRODUCTION**

Sepsis is a significant cause of morbidity and mortality. In the UK, the estimated in hospital mortality is 30% (1). There are an estimated 150,000 sepsis admissions of sepsis in the UK, resulting in over 44,000 deaths (2). Over the past 40 years the incidence of sepsis has substantially increased, partly because of improved ascertainment and hospital coding but importantly as a consequence of increasing age of the population and greater prevalence of comorbidities(3,4). Early recognition and management through use of care bundles can reduce mortality (1)(5)(6) however multiple national audits have demonstrated inadequate management (7)(8). A number of international, national and regional sepsis improvement collaborative programs have reported on their outcomes (9)(10) (11). However most of these programs have focused on assessing the impact on sepsis mortality. Controversy also exists about how rapidly sepsis should be treated and which interventions improve outcomes (12).

Advancing Quality (AQ) is an established approach to reducing variation and improving outcomes for patients in the northwest of England. It aims to improve clinical care by producing and implementing evidence-based care bundles (measure sets) across a collaborative network of hospitals.

The aim of the AQ Sepsis programme is to improve early identification, diagnosis and treatment of patients presenting to hospital with sepsis and thereby improve outcomes. The project only includes patients admitted with sepsis and therefore patients who develop sepsis more than 48 hours after admission are excluded. Evaluation of the AQ sepsis program and use of its measure set in routine care had not been done.

We report the results of the evaluation of the AQ sepsis programme in 14 hospitals in the northwest of England. We assessed the association with specific AQ measures and mortality, length of stay and readmissions within 30 days. In addition, by using a before and after design we measured the impact of the formal introduction of this bundle into care on in-patient mortality, readmission and length of hospital stay.

**METHODS**

**Study design and sites**

This was a retrospective assessment of a quality improvement initiative carried out in 14 acute care hospitals in the northwest region of England that used the AQ sepsis measure set. The AQ measure set was developed by a local Clinical Expert Group and is based on evidence provided by a team from the British Medical Journal Evidence Centre. The AQ sepsis measure set was developed and launched in September 2014 and is consistent with recommendations from the International Surviving Sepsis Campaign, 2012 (13) -(Table 1) .

Table 1: AQ Sepsis Measure set (care bundle)

|  |  |
| --- | --- |
| SEPS-01 | Early Warning Score recorded within 60 minutes of hospital arrival |
| SEPS-02 | Evidence of 2 or more SIRS & documentation of suspected sepsis source within 2 hours of hospital arrival |
| SEPS-03 | Blood cultures taken within 3 hours of hospital arrival |
| SEPS-04 | Antibiotics administered within 3 hours of hospital arrival |
| SEPS-05 | Serum lactate taken within 3 hours of hospital arrival |
| SEPS-06 | Second litre of IV fluids commenced within 4 hours of hospital arrival if systolic BP < 90 mmHg or Lactate ≥ 4 mmol/l |
| SEPS-07 | Oxygen therapy administered within 4 hours of hospital arrival if SpO2 < 94% |
| SEPS-08 | Fluid Balance Chart commenced within 4 hours of hospital arrival if IV fluids commenced |
| SEPS-09 | Senior Review or assessment by Critical Care Team within 4 hours of hospital arrival if lactate > 4 mmol/l |

Hospitals were encouraged to share ideas and best practice. Regular learning and networking events were arranged as well as virtual networks. Hospitals were set specific targets to meet and data published publicly hence generating an element of competition. In addition some commissioners set local pay for performance targets for participating hospitals. Quality improvement was supported by feeding back data on performance and support to standardise data collection after the pilot phase. Mentoring and coaching support for participating hospitals was also provided to improve organisational aspects such as leadership, clinical pathway development and data collection. Subscription of hospitals participating in the collaborative is funded by local commissioners to improve quality of care and outcomes.

**Population**

Non-elective patients who developed sepsis within 48 hours of arrival were included. Patients who developed sepsis more than 48 hours after admission, pregnant women and patients who had a decision to palliate within 4 hours of admission were excluded. For the purpose of this study, sepsis was defined as a patient with a suspected infection, a documented source of infection, presenting an elevated early warning score (EWS) of 1 or more (and two of more systemic inflammatory response syndrome (SIRS) criteria. Early warning scores used were either the Modified Early Warning Score (MEWS) or National Early Warning Score (NEWS). SIRS criteria consisted of respiratory rate, heart rate, temperature, white cell count, acute confusion and hypotension.

**End-points**

The outcomes of interest were inpatient mortality, readmission within 30 days, and hospitalization longer than 10 days. Information on the compliance with the time-based care bundle was available from 1st July 2014. The bundle was published in July 2014, implemented in a pilot phase from 1st September 2014 across all participating NHS trusts, and officially rolled out on 1st December 2014. For the purposes of the study, we considered 1st July 2014-30th November 2014 as “before” the implementation of the bundle, and 1st December 2014-29th December 2015 as the “after implementation” period.

**Data collection**

Identification of the sepsis cohort was done using the national Secondary Uses Services Payment by Results dataset. These extracts were evaluated for Sepsis ICD 10 codes and an algorithm used to determine whether the patient should be included in the population. Inclusion and exclusion criteria were developed and published before data collection. Patients who did not have suspected infection within 48 hours of admission, pregnant women or patients who were on a palliative care pathway within 4 hours of admission were excluded. In addition, if there was a clinically documented reason why the patient was not eligible for an intervention, the patient was excluded from being eligible for the intervention. The data dictionary and algorithms used are available as an online appendix.

Retrospective case note review of patients fulfilling the inclusion criteria was undertaken by designated clinical or administrative staff. Hospitals determined who did the data extraction however training for all data extractors was provided by Advancing Quality through Webinars, face-to-face training, a data dictionary and collaborative events. A standard data collection form, coding rules and definitions were outlined in a data dictionary. Clinical processes included in the bundle of care measures are displayed in Table 1. Clinical information was transcribed onto web based data collection forms or via automated e-data transfer.

Data completeness was monitored on a hospital-level basis and reported to hospitals on a monthly basis. A threshold of 95% was set for all participating organisations to achieve cumulatively over the 12 month period, to ensure that the majority of patient case records are reviewed and recorded. The 95% threshold was set to allow for missing case notes. All hospitals submitted data for at least 95% of patients identified.

Quality control of the data transcription was ensured by local hospital teams however Advancing Quality used regular audits to assess data accuracy.

**Statistical tests**

Statistical tests were conducted using STATA 12 for MacOS. Categorical variables are reported as proportions, and univariable logistic regression was used to evaluate differences in regard of the outcomes of mortality, readmission within 30 days, and hospital stays longer than 10 days. Multivariable logistic regression was used to evaluate the different clinical measures of the bundle against the outcomes. Odds-Ratios (OR) and 95% confidence intervals were adjusted for age, Charlson Comorbidity Index (CCI), and lactate levels >4 mmol/L. Models included other variables with univariable significance of <0.1 Statistical significance for the evaluation of the clinical measures was set at a p value of 0.05. For analysis of the endpoint mortality, all participants were included. For the analysis of readmissions and length of hospital stay only those individuals who survived their hospital stay were included.

**RESULTS**

From 1st July 2014 to 31st December 2015, 16,210 cases with an ICD-10 code of sepsis were recorded on the databases from all participating hospitals. Of those, 7,776 cases complied with the AQ sepsis definition and were included in the analyses. In-hospital mortality within the study population was 26.86% (2089 patients), 30-day readmission rate 13.81% (1074 patients) and 38.04% (2958) of patients had a hospital stay > 10 days. A comparison of the patients’ characteristics and crude ORs for the outcomes of mortality, readmission within 30 days, and hospitalization longer than 10 days are shown in Table 2a and 2b. Of the 7,776 cases of sepsis recorded during the study period, 1520 (19.6%) were collected before the official roll-out of the bundle of care, and 6256 (80.5%) after. A total of 3993 (50.6%) were female, and 3842 (49.4%) were male. There was no significant difference in the gender distribution between the two periods. Ages were categorised in four groups ranging from 15 to over 85 years, with the smallest group, 15-44 years, containing 605 (7.8%) cases, and those within the 65-84 range representing the largest group with 3837 (49.3%) patients. A total of 6948 (96.9%) of cases were white and 189 (3.1%) from other ethnic groups.

Table 2a: Univariable association between baseline parameters and mortality (\* indicates p<0.05)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **TOTAL**  | **%** | **OR mortality** |
| **AGE (n=7776)** |  |  |   |
| **15-44** | **605** | **7.78** | 1 |
| **45-64** | **1767** | **22.72** | 3.26 [2.28-4.66]\* |
| **65-84** | **3837** | **49.34** | 6.22 [4.41-8.78]\* |
| **85+** | **1567** | **20.15** | 11.71 [8.24-16.65]\* |
|   |  |  |   |
| **GENDER (n=7775)** |  |  |   |
| **Female** | **3933** | **50.59** | 1 |
| **Male** | **3842** | **49.41** | 0.95 [0.86-1.05] |
|   |  |  |   |
| **CCI (n=7776)** |  |  |   |
| **0** | **1992** | **25.62** | 1 |
| **1-15** | **3534** | **45.45** | 1.61 [1.40-1.86]\* |
| **16-30** | **1855** | **23.86** | 3.34 [2.87-3.89]\* |
| **31-45** | **365** | **4.69** | 5.67 [4.47-7.19]\* |
| **45+** | **30** | **0.39** | 12.19 [5.53-26.86]\* |
|   |  |  |   |
| **ETHNIC GROUP (n=7169)** |  |  |   |
| **White** | **6948** | **96.92** | 1 |
| **Mixed** | **20** | **0.28** | 0.30 [0.07-1.29]  |
| **Asian** | **168** | **2.34** | 0.47 [0.31-0.72]\* |
| **Black** | **33** | **0.46** | 0.48 [0.18-1.25] |

Table 2b: Univariable association between baseline parameters and readmission and length of stay>10 days (\* indicates p<0.05)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **TOTAL\*** | **%** | **OR readmission** | **OR hospitalization >10 days** |
|  |  |  |  |  |
| **AGE (n=5687)** |   |   |   |   |
| **15-44** | **569** | **10.01** | 1 | 1 |
| **45-64** | **1465** | **25.76** | 1.38 [1.07-1.80]\* | 1.84 [1.47-2.31]\* |
| **65-84** | **2753** | **48.41** | 1.30 [1.02-1.67]\* | 2.81 [2.27-3.49]\* |
| **85+** | **900** | **15.83** | 1.18 [1.15-0.23]\* | 4.35 [3.42-5.52]\* |
|   |  |  |   |   |
| **GENDER (n=5686)** |  |  |   |   |
| **Female** | **2856** | **50.23** | 1 | 1 |
| **Male** | **2830** | **49.77** | 0.97 [0.86-1.12] | 0.91 [0.82-1.01] |
|   |  |  |   |   |
| **CCI (n=5687)** |  |  |   |   |
| **0** | **1672** | **29.40** | 1 | 1 |
| **1-15** | **2700** | **47.48** | 1.10 [0.93-1.29] | 1.31 [1.15-1.49]\* |
| **16-30** | **1131** | **19.89** | 1.46 [1.21-1.77]\* | 2.10 [1.80-2.45]\* |
| **31-45** | **175** | **3.08** | 1.46 [1.00-2.13]\* | 3.46 [2.50-4.79]\* |
| **45+** | **6** | **0.11** | 0.62 [0.08-4.95] | 3.99 [-.99-16.02] |
|   |  |  |   |   |
| **ETHNIC GROUP (n=5256)** |  |  |   |   |
| **White** | **5067** | **96.40** | 1 | 1 |
| **Mixed** | **18** | **0.34** | 0.52 [0.12-2.25] | 0.71 [0.28-1.79] |
| **Asian** | **143** | **2.72** | 0.96 [0.63-1.47] | 1.83 [1.27-2.65]\* |
| **Black** | **28** | **0.53** | 0.50 [0.15-1.64] p=0.251 | 2.13 [0.91-5.03] |

**Severity Indicators**

Gender did not predict mortality, readmission or prolonged hospital stay. However, older age showed a statistically significant association with all three evaluated outcomes. High CCI scores were associated with higher mortality and shorter hospitalizations (Table 2a & 2b). Information on lactate levels, blood pressure, and oxygen saturation was available (Table 3). We observed a strong association between elevated lactate levels and increased mortality (OR:3.10; CI [2.73-3.52]), and an extended hospital stay (OR: 1.89; CI [1.59-2.24]). Similarly, a systolic blood pressure <90mmHg was associated with poor outcome in all three outcomes analysed. Oxygen saturation <94% was associated with an 82% increase in mortality (1.82 [1.65-2.10]), and a 46% increase in hospitalizations >10 days (1.46 [1.31-1.64]) (Table 3).

Table 3: Association of outcomes with medical indicators of disease severity (\* indicates p<0.05)

 **Lactate >4mmol/L Blood pressure <90mmHg Oxygen saturation <94%**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Total included** | **Total** | **%** | **Odds ratio** | **Total included** | **Total** | **%** | **Odds ratio** | **Total included** | **Total** | **%** | **Odds ratio** |
| **Mortality** | 6428 | 607 | 9.44 | 3.10 [2.73-3.52]\* | 6554 | 405 | 6.18 | 1.58 [1.38-1.81]\* | 7774 | 1018 | 13.09 | 1.82 [1.65-2.10]\* |
| **Readmission**  | 4620 | 108 | 2.34 | 0.82 [0.66-1.03] | 5054 | 219 | 4.33 | 1.32 [1.11-1.56]\* | 5385 | 358 | 6.65 | 0.95 [0.83-1.10] |
| **hospitalization >10 days** | 4620 | 358 | 7.75 | 1.89 [1.59-2.24]\* | 5054 | 420 | 8.31 | 1.28 [0.57-0.65]\* | 5385 | 915 | 16.99 | 1.46 [1.31-1.64]\* |

**Outcomes before and after the implementation of the sepsis bundle**

The use of the bundle of care for the identification and management of sepsis patients was associated with a 19% reduction in readmissions within 30 days (aOR: 0.81; CI [0.69-0.95]; and a 31% reduction in hospital stays over 10 days (aOR: 0.69; CI [0.60-0.78]; p<0.0001). However, mortality was not altered (Table 4).

Table 4: Comparison of key endpoints before and after the introduction of the sepsis bundle for care (\* indicates p<0.05)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|   |   |   | **Before** | **After**  |   |
|   | **Total Before** | **Total After** | **Total** | **%** | **Total** | **%** | **Odds ratio [CI]** |
| **Mortality** | **1520** | **6256** | 405 | 26.64 | 1684 | 26.92 | 1.01 [0.89-1.15]  |
| **Readmission** | **1115** | **4572** | 241 | 21.61 | 833 | 18.22 | 0.81 [0.69-0.95]\* |
| **Hospitalization over 10 days** | **1115** | **4572** | 538 | 48.25 | 1786 | 39.06 | 0.69 [0.60-0.78]\* |

Before: 1st July-30th November 2014

After: 1st December 2014-29th December 2015

**Impact of the time-based bundle of care**

The different elements of the bundle were evaluated against the three outcomes of interest over the whole study period. All calculations were adjusted for age, CCI, and the presence of serum lactate levels >4mmol/L, as these are accepted indicators of disease severity (Table 5). Administration of a second litre of intravenous fluid within 2 hours, oxygen therapy and review by a senior clinician were all associated with an increase in mortality. Starting a fluid balance chart within 4 hours was the only clinical process measure which did not have a statistically significant effect on mortality. The implementation of all other individual measures was associated with a reduction in mortality. Taking a blood culture sample, administering antibiotic therapy and measuring serum lactate within 3 hours of hospital arrival were all associated with reduced mortality and shorter hospitalizations; however, the risk of readmission to hospital within 30 days was not altered by any of the measures.

Administration of intravenous fluid in patients with systolic blood pressure < 90 mmHg or lactate > 4 mmol/l did not appear to affect mortality (aOR 1.49 [1.07-2.06]), readmission (aOR 0.94 [0.64-1.39]) or length of stay ≥ 10 days (aOR 0.96 [0.69-1.34])

Table 5: Multivariable analysis of key endpoints of mortality, readmission and hospitalizations longer than 10 days and the eight steps included on the time-based bundle of care. All OR are adjusted for age, elevated lactate, and CCI (\* indicates p<0.05)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **TOTAL INCLUDED** | **OR\* Mortality** | **TOTAL INCLUDED** | **OR\* Readmission within 30 days** | **OR\* Hospitalization >10 days** |
| **Screening** | **7776** | 0.86 [0.73-1.00]\* | **5687** | 0.95 [0.79-1.16]  | 0.85 [0.73-1.00] |
| **Blood culture** | **6736** | 0.69 [0.59-0.81]\* | **5059** | 1.03 [0.83-1.27]  | 0.58 [0.49-0.69]\* |
| **Antibiotic** | **7592** | 0.77 [0.67-0.89]\* | **5555** | 1.11 [0.92-1.34]  | 0.81 [0.70-0.94]\* |
| **Lactate** | **6369** | 0.64 [0.54-0.77]\* | **4581** | 0.96 [0.75-1.22] | 0.54 [0.45-0.66]\* |
| **IV fluids(1)** | **2385** | 1.49 [1.07-2.06]\* | **1504** | 0.94 [0.64-1.39] | 0.96 [0.69-1.34] |
| **Oxygen**(2) | **2788** | 1.92 [1.40-2.62]\* | **1812** | 0.98 [0.67-1.43] | 1.12 [0.83-1.51] |
| **Fluid balance chart** | **6493** | 1.01 [0.89-1.16] | **4721** | 0.93 [0.79-1.10] | 1.12 [0.97-1.29] |
| **Senior review**(3) | **1254** | 1.85 [1.33-2.56]\* | **647** | 0.60 [0.36-0.99]\* | 1.01 [0.67-1.52] |

(1) applies to cases with either elevated serum lactate or low blood pressure

(2) applies to cases with either elevated serum lactate or low blood pressure

(3) applies to those with elevated serum lactate

**Discussion**

This study highlights the fact that sepsis is associated with high mortality. Mortality in our study is consistent with sepsis mortality in the UK (1). Sepsis also results in high rates of readmission and prolonged hospital stay and is estimated to cost up to £7.76 billion a year in the UK in terms of healthcare costs (14). Our study suggests that the AQ sepsis program was associated with reduced length of stay and readmission. Although mortality did not appear to improve, improvements in duration of hospital admission and readmission are important outcomes with significant resource implications. We are unable to make any strong conclusions about whether the improvement in outcomes were directly as a result of our program as we do not have similar data before the program started to do an interrupted time series analysis. We therefore acknowledge that despite being unlikely, temporal trends may be an alternative explanation for the improvements in outcomes. This notwithstanding our study is one of the first sepsis improvement programs to report length of stay and readmission rates as well as mortality data. Readmission following an episode of sepsis is as important because some studies have reported up to 30% of patients with sepsis developing another episode within 90 days (15) and it is associated with high healthcare utilisation and costs. Further cost-effectiveness evaluation of this program is needed. We recognise that process measures and provider-centred outcomes such as clinical and nursing workload are also useful outcomes to assess. However we were unable to compare these because we did not have such data for all the hospitals before the collaborative. We also acknowledge that it would have been useful to explore whether there was a dose-response relationship with greater adoption of elements of the sepsis bundle resulting in better outcomes. We intend to assess this as a separate study.

We found that elevated lactate levels, increasing age, hypoxia, hypotension, Charlson Comorbidy Index (CCI) predict worse outcomes such as mortality and prolonged hospital stay. However these variables did not predict readmission rates maybe because risk of readmission is determined by social as well as medical factors(16). Information on other recognised prognostic criteria such as Sequential Organ Failure Assessment Score (SOFA) were not available(17). However the quick SOFA score is currently being collected and its prognostic value should be assessed in future evaluation of the collaborative.

We also found that some time dependent variables such as senior review and administration of supplemental oxygen or second litre of intravenous fluid with 2 hours showed an inverse association with mortality.. Further analysis to assess whether patients who received these elements of the bundle had a higher median age, lower blood pressure, higher lactate or Charlson Comordity Index was not possible because the variables were recorded as categorical variables. Although this limited the analysis, we hypothesise that fluid resuscitation; senior review and need for supplemental oxygen are markers of severity of illness. In fact the AQ sepsis program recommended fluid resuscitation and senior review for hypotensive patients and patients with hyperlactemia because of the known association with severity of illness. We made a pragmatic decision to recommend starting a second litre of fluid within 4 hours for patients who had hypotension or hyperlactatemia. This equated to approximately 30ml/kg/hour over 3 hours and was consistent with surviving sepsis campaign guidelines for an average adult patient weighing 70 kg. We made this decision in order to ensure our fluid resuscitation bundle was easy to understand, implement and measure.

Timely collection of blood culture, measurement of lactate and administration of antibiotics were associated with improved mortality. Although we are unable to make statements about causality, the findings are similar to findings from the International Surviving Sepsis Campaign and other observational studies (11) (18)(19). In addition, we did not have sufficient data before the collaborative to assess whether there was a difference before and after.

Our study has several limitations. First, the observational design means that we can make statements about association rather than causation. Whilst our study suggests that the AQ sepsis collaborative has led to improvements in sepsis outcomes in the northwest of England, we cannot be certain that the improvements are purely as a result of the project. Secondly, although the “before implementation” period used in the analysis was not ideal, this was the only practical means of comparing outcomes before and after the program. We acknowledge that the short duration does not allow us to investigate trends that might inform the simple before and after comparison. We also acknowledge that since the “before” period was a short preparatory period, there are limitations in using this as a pre-intervention period. Ideally we would have wanted at least a year of data before the program to run an interrupted time series however this was not possible. We therefore cannot be certain that improvements were already occurring before the program. Lastly, although we used coded data, reviewing the outcomes of patients with an ICD-10-code for sepsis is an accepted approach. The fact that patient case notes were reviewed makes it likely that we included and therefore reviewed outcomes of patients with a true diagnosis of sepsis. We did not do a subgroup analysis comparing outcomes for patients with sepsis, severe sepsis and shock because patients were identified based on coding data. Coding data can be unreliable in differentiating severity of sepsis. For example, we found that some hospitals only a handful of patients with septic shock despite having busy intensive care units with severe sepsis and shock being one of the most common reasons for admission to critical care.

Despite these limitations, this study is large, comprehensive and representative of patients admitted to hospitals in the northwest region of England with sepsis. There was no attempt to select for high or low risk patients and as such our study includes the majority of patients admitted with sepsis rather than a small sample of patients.

A new consensus definition for sepsis was published in February 2016. Use of SIRS criteria is no longer recommended and the international taskforce redefined sepsis as patients with infection who are significantly more likely to die or be admitted to intensive care as a result of infection (17). The AQ collaborative is currently in the process of incorporating these changes in the definition of sepsis and is likely to increase the early warning score required for patients to be included in the project in order to reflect the new definition of sepsis. A recent study suggested that an aggregate NEWS score of  ≥ 5 may be more accurate at predicting mortality or admission to intensive care compared to SIRS criteria(20).

Our study fits with published data from other sepsis collaborative programs suggesting that regional collaborative programs can improve outcomes(10)(9). However our study highlights the importance of also using outcomes such as prolonged hospital stay and readmissions to also assess outcomes of sepsis improvement programs. The fact that we did not find an effect on mortality is interesting and not consistent with other studies(10)(9) (18). This may be due to the before and after design of our study and limitations already highlighted. This may also be due to variation in levels of adherence to the bundle across the participating hospitals. We are aware that some hospitals which are part of the collaborative have seen a reduction in sepsis mortality during the same period. Higher levels of compliance with the bundle across the region may be necessary to observe an impact on mortality. Our findings should not be interpreted as evidence to abandon sepsis improvement programs because they may not have an impact on mortality.

The use of a measure set for sepsis within a collaborative in the northwest of England was associated with a reduction in length of stay and readmission for sepsis. Lower mortality was associated with timely investigations and administration of antibiotics and there are strong clinical reasons to believe these associations are beneficial for patients. We would recommend the use of a similar approach in other settings.

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