**Quantifying the impact of a digital sepsis alert on key patient outcomes and process measures.**

*We will use interrupted time series with a control to determine the impact of the introduction of alerts on patient outcomes and process measures*

*Main cohort: patients (18+) with an SoS ICD-10 code (intervention group) at discharge OR a falls ICD-10 code (control group).*

*Time period: April 2010 to March 2021*

*General data description: patient information, admission & discharge information, A&E information and ICU admission if possible*

## 1.Introduction

### 1.1 Background/rationale

To improve care for patients with sepsis, comply with national financial incentive programmes, and make best use of the introduction of electronic health records hospitals in England have introduced digital sepsis alerts. A variety of algorithms have been used, with different workflows and with different implementation strategies.

A variety of studies have demonstrated that digital sepsis alerts, and more general deteriorating early warning scores such as NEWS2, have high predictive power for mortality.[1] A small number of studies have shown that introducing digital alerts to identify patients at risk of deterioration have had an impact on patient outcomes.[2-3]

Although randomised control trials are considered the gold standard for evidence, digital alerts have generally been introduced across hospitals without randomisation or phased across the hospital. In ICHT sepsis alerts were introduced in a phased approach and we used a propensity score based causal inference method (inverse probability of treatment weighting), common in the analysis of natural experiments, to emulate as much as possible a RCT using real world healthcare data. In ICHT the introduction of digital sepsis alerts was associated with a 23% lower risk of death within 30 days.[4]

In this study we aim to analyse the impact of the introduction digital alerts across five NHS Trusts. With the exception of ICHT the introduction of alerts was part of the introduction of electronic health records (EHR). This presents challenges, for example:

- Data availability prior to the introduction of EHRs is limited to data routinely collected for administrative purposes. This includes admission, discharge and formal diagnosis information, but excludes detailed microbiology information and detailed patient treatment information such as the administration of antibiotics.
- The impact of the alerts on patient outcomes will be confounded by the introduction of EHRs, a major change in the hospital system.

Although we would expect digital sepsis alerts to have the main impact on patients with sepsis, and this is the stated aim of many commercial sepsis alerts, administrative data may not be sufficient to identify patients with sepsis, particularly as national guidance on sepsis coding changed in 2014, effectively increasing the number of patients with an official diagnosis of sepsis.[5] In addition, efficient clinical response to digital sepsis alerts may result in a decrease in disease progression to sepsis. We have therefore decided to focus on outcomes of patients with an ICD-10 Suspicion of Sepsis code.[6]

We will use interrupted time series with a control to determine the impact of the introduction of alerts on patient outcomes and process measures. Interrupted time series is an important methodology which allows before and after comparisons whilst taking trends prior to the intervention into account and is considered a robust methodology for analysing natural experiments. However, confounding due to other 'interventions' occurring at the same time as the intervention of interest can confound interpretation. A control is an appropriate method to take this type of confounding into account.[7]

For the control we have selected patients with an ICD-10 code included in the category gastrointestinal bleeding. This is a suitable control as we would not expect these patients to trigger a sepsis alert and outcomes should not be impacted by patients being identified as having sepsis. The ICD-10 codes included in this indicator are shown in Table 1.

**Objective - Quantify the impact of a digital alert on the key patient outcomes and process outcomes**

**Primary outcome:** in-hospital mortality within 30 days
**Secondary outcome:** length of stay
ICU admission

**2.Methods**

**2.1Study design**

**Setting - Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection**

This is a time series analysis across five NHS Trusts in England and one NHS Trust in Wales. The period of study is 1st April 2010 to 31st March 2020.

**2.2 Participants - the eligibility criteria, and the sources and methods of selection of participants**

All adult (18+) inpatients admitted as emergency patients between 01/04/10 and 31/03/2 are initially eligible for inclusion in the study.

Intervention group: patients with a discharge diagnosis including one of the SoS sepsis codes at any place in the diagnosis.

Control group: patients with a discharge diagnosis which is use by the NHS to identify patients with a 'Fall' code.

**2.3 Variables - Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable**

**Primary outcome**: in-hospital mortality within 30 days of admission

**Secondary**:

- In-hospital mortality within 7 days of admission
- Length of stay
- ICU admission

**Intervention:** Introduction of digital alerts or changes in screening programmes

**Potential confounders:**

- Age
- Sex
- Comorbidities which increase the risk of poor patient outcomes
- Ethnicity
- Season

**Sub-group analysis**

Age-groups

Patients who are immune-compromised

**2.4 Data sources/ measurement - For each variable of interest, give sources of data and details of methods of assessment (measurement).**

Data are routinely collected data to comply with NHS requirements for Secondary Users Service. Data is quality checked by individual Trust before it is submitted to the NHS, and is compiled into Hospital Episode Statistics which have been widely used for research in the UK.

As part of the NIHR-Health Informatics Collaborative data managers at each trust shared data through a secure data platform. All data was quality checked and processed by the data warehouse team at ICHT.

**Bias – Describe any efforts to address potential sources of bias**

We are using a control intervention group to address the main source of bias – that is that for four of the six Trusts alerts were introduced at the same time as digital alerts.

**Study size**

Six NHS Trusts were recruited to take part in the study. The number of patients included in the study is determined by the number of patients who were discharged with an SoS ICD-10 code. The power to detect differences will be determined post-hoc.

**Quantitative variables - Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why**

Ethnicity – ethnicity coding is based on recorded ethnicity using NHS ethnicity codes. Due to small groups of some ethnic groups we will combine into standard combinations for statistical comparisons. Full details of ethnic groups are included in the supplementary materials.

Age – We broke age into 10-year age groups. For statistical comparisons we combined smaller groups. Full details are included in the supplementary materials.

Length of stay - length of stay, measured in hours, was determined from the date and time of admission and discharge recorded in the patient record. For this descriptive study we will quantify length of stay for patients who are discharged alive.

Mortality – mortality was based on discharge destination recorded. For the purposes of this study only in-hospital mortality was available for all NHS trusts.

**Missing data**

Patient admissions will not be excluded if patient data is missing, an additional category of missing will be included for age, gender, ethnicity and deprivation. As part of quality checks we will confirm whether there are any patterns in missing data.

**Statistical methods**

***(*a) Describe all statistical methods, including those used to control for confounding**

*Descriptive analysis*

We will describe trends in patient mix over time using graphical methods, we will use time series to determine if there were changes in patient mix, including sub-groups of patients, patients with SoS and falls patients.

We will use break point approaches to identify potential key points in time where changes occurred. This will aid in interpretation of results.

*Comparative analysis*

We will use interrupted time series with a control, adjusted for patient case mix and season. Each Trust will be modelled separately as the introduction of sepsis alerts and electronic health records is different for each Trust. Comparisons will be made between the change in slope and step change in counts.

**(*b*) Describe any methods which will be used to examine subgroups and interactions**

Within each model we will separately consider subgroups when we perform our analysis. We will consider a priori interactions.

**(*c*) Explain how missing data will addressed**

Missing data will be included as a category on its own for factors such as ethnicity and deprivation. We will inspect data to identify periods of missing data, and consider imputation.

| ICD-10 Code | ICD-10 Description |
|---|---|
| I850 | Oesophageal varices with bleeding |
| K226 | Gastro-oesophageal laceration - haemorrhage syndrome K228 Other specified diseases of oesophagus |
| K250 | Gastric ulcer, acute with haemorrhage |
| K252 | Gastric ulcer, acute with both haemorrhage and perforation |
| K254 | Gastric ulcer, chronic or unspecified with haemorrhage K256 Chronic or unspecified Gastric ulcer with both haemorrage and perforation |
| K260 | K260 Duodenal ulcer, acute with haemorrhage |
| K262 | K262 Duodenal ulcer, acute with both haemorrhage and perforation |
| K264 | K264 Duodenal ulcer, chronic or unspecified with haemorrhage K266 Chronic or unspecified Duodenal ulcer with both haemorrage and perforation |

| | |
|---|---|
| K270 | K270 Peptic ulcer, acute with haemorrhage |
| K272 | Peptic ulcer, acute with both haemorrhage and perforation |
| K274 | Peptic ulcer, chronic or unspecified with haemorrhage |
| K276 | Chronic or unspecified peptic ulcer with both haemorrhage and perforation |
| K280 | Gastrojejunal ulcer, acute with haemorrhage |
| K282 | Gastrojejunal ulcer, acute with both haemorrhage and perforation |
| K284 | Gastrojejunal ulcer, chronic or unspecified with haemorrhage |
| K286 | Chronic or unspecified Gastrojejunal ulcer with both haemorrhage and perforation |
| K290 | Acute haemorrhagic gastritis |
| K920 | Haematemesis |
| K921 | Melaena |
| K922 | Gastrointestinal haemorrhage, unspecified |

Table 1: ICD-10 codes for gastrointestinal bleeding [8]

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