Clinical Decision Support Software for Empirical Antibiotic Prescribing in Hospital: A Systematic Review

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Background: Antibiotics are frequently prescribed in hospital, yet roughly one third of prescriptions are inappropriate. Some inappropriately prescribed antibiotics cause patient harm. The optimal choice of antibiotic aims to balance the risk of adverse effects with the likelihood of effectively treating infection. Clinical decision support software (CDSS) utilises individual patient data to provide patient-specific assessments or recommendations to support clinical decision making. This systematic review aimed to identify CDSS implemented in the hospital setting to influence empirical antibiotic prescribing, and to establish their impact on antibiotic prescribing and clinical outcomes.

Research Question: Does the implementation of CDSS in hospital influence antibiotic prescribing or clinical outcomes?

Methods: Medline, CENTRAL, and Embase were searched to identify studies that evaluated the impact of CDSS which were designed to influence initial empirical antibiotic prescribing in hospital. Risk of bias was assessed using ROBINS-I for non-randomised studies and Cochrane Risk of Bias 2 for randomised studies. Clinical outcomes (mortality, length of stay, readmission to hospital, time to antibiotics), outcomes related to antibiotic appropriateness (guideline adherence, coverage of causative organism), and outcomes related to antimicrobial stewardship (overuse of antibiotics likely to contribute to antimicrobial resistance, total antibiotic use) were extracted. A random effects meta-analysis was performed for outcomes with sufficient data.

Results: Fifteen full texts met eligibility criteria after screening 7,984 unique articles. The implementation of CDSS was associated with improvements in guideline adherence (OR 1.75, 95% CI 1.26 – 2.43), and a trend towards reduced mortality (OR 0.76, 95% CI 0.57 – 1.01). However, studies reporting clinical outcomes and outcomes related to antibiotic appropriateness were at high risk of bias. Outcomes related to antimicrobial stewardship were too heterogeneous to justify meta-analysis but there was high quality evidence to suggest that CDSS implementation can reduce the prescribing of broad spectrum antibiotics whilst maintaining safety.

Conclusion: CDSS can safely reduce the overprescribing of broad spectrum antibiotics and positively contribute to antimicrobial stewardship. Further high quality studies are required to determine if the implementation of CDSS also results in improvements in clinical outcomes.

Clinical Decision Support Software and Empirical Antibiotic Prescribing: A Systematic Review & Meta-Analysis

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Introduction

- Antibiotics are the cornerstone of effective treatment for acute infections caused by bacteria. However, suboptimal choice of antibiotics is common in hospital.
- The optimal choice of initial antibiotic is dependent upon the cause of infection, severity of illness, the likely causative organism, and patient physiology. These factors have to be balanced against adverse effects of antibiotics and the risk of antimicrobial resistance.
- Clinical Decision Support Software (CDSS) are defined as software that utilise patient-specific data to provide individualised assessments or recommendations about patient care.
- They have been proposed to help prescribers balance these competing risks and benefits to optimise antibiotic prescribing.

Methods

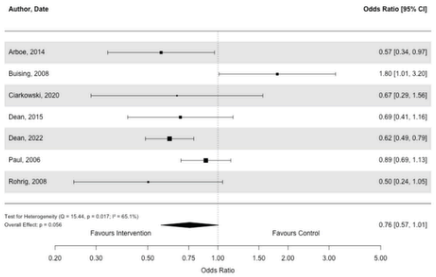
- Medline, CENTRAL, and Embase were searched to identify studies published before February 2024 that evaluated the impact of CDSS intended to influence initial empirical antibiotic prescribing.
- Data were extracted into core outcome groups including clinical outcomes, appropriateness of antibiotics, and antimicrobial stewardship.
- Risk of bias of included studies was assessed using ROBINS-I for non-randomised studies and Cochrane Risk of Bias 2 (ROB2) for randomised studies.
- A random effects meta-analysis was performed where sufficient data existed, and where results could be combined.

Results

- Fifteen full texts met eligibility criteria after review of 7,984 articles.
- The CDSS were implemented across emergency departments, hospital wards, and intensive care units.
- The CDSS aimed to influence specific infections such as pneumonia, soft tissue infection, and urinary tract infection in 8 studies, and antibiotic prescribing more broadly in 7 studies.
- 11 studies were non-randomised, 4 were cluster randomised controlled trials.

Clinical Outcomes

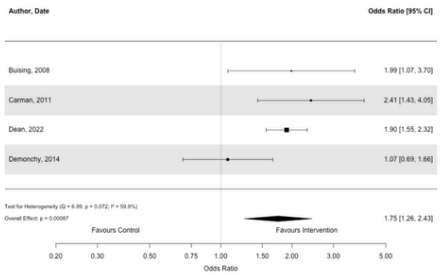
Meta-analysis for mortality outcomes



- There was a 24% reduction in mortality following the introduction of CDSS, on average across 7 studies that reported this outcome (OR 0.76, 95% CI 0.57 – 1.01, *p = 0.056*).
- There was no consistent change in readmission rates or length of stay following CDSS implementation.

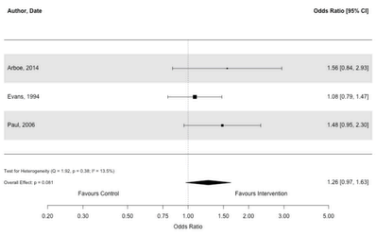
Antibiotic Prescribing

Meta-analysis for outcomes related to guideline adherent antibiotic prescribing



- Guideline adherent antibiotic prescribing was reported in 4 studies and improved following the implementation of CDSS (OR 1.75, 95% CI 1.26 – 2.43, *p < 0.001*).

Meta-analysis for outcomes related to coverage of the causative organism



- Coverage of the causative organism was reported in 3 studies and was similar before and after CDSS implementation (OR 1.26, 95% CI 0.97 – 1.63, *p = 0.081*)

Antimicrobial Stewardship

- Outcomes relevant to antimicrobial stewardship were reported in 6 studies.
- These included outcomes related to total antibiotic use, length of antibiotic use, the use broad-spectrum antibiotics, the frequency of antibiotic resistant organisms, and *Clostridium Difficile.*
- The implementation of CDSS was consistently associated with a reduction in broad-spectrum antibiotic prescribing.
- Two large cluster randomised controlled trials with approximately 100,000 patients in each demonstrated a reduction in broad-spectrum antibiotic prescribing of 28% in pneumonia, and 17% in UTI.

Discussion

- Whilst a reduction in mortality was observed following CDSS implementation, studies were at high risk of bias, and it is unlikely that the relationship was causal.
- High-quality evidence demonstrated that CDSS could be used effectively to reduce the overprescribing of broad-spectrum antibiotics safely.
- CDSS implementation is also associated with improved adherence to antibiotic prescribing guidelines.

Next Steps...

Background

- The data presented above suggest that CDSS can be used to positively influence antibiotic prescribing for antimicrobial stewardship.
- Community-acquired pneumonia (CAP) is a common cause of hospital admission and is associated with considerable morbidity and mortality.
- Antibiotics are the cornerstone of effective management, yet guideline adherence is sub-optimal.
- Fluoroquinolones are recommended for the treatment of severe CAP for people with a penicillin allergy; however, they are used more widely than this indication.
- Fluoroquinolones are associated with disabling and potentially long-lasting or irreversible side effects. As a result, they have been subject to regulatory restriction by the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK and also across Europe.

Aims

- The overall aim of this project is to establish prescribing practices across Birmingham, particularly related to guideline adherence and prescribing of fluoroquinolones.
- This will be accompanied by qualitative work to understand how decisions surrounding antibiotics are made.
- Together, this data will be used to inform the co-design of a CDSS aiming to improve prescribing safety in Birmingham if areas of suboptimal practice are identified.

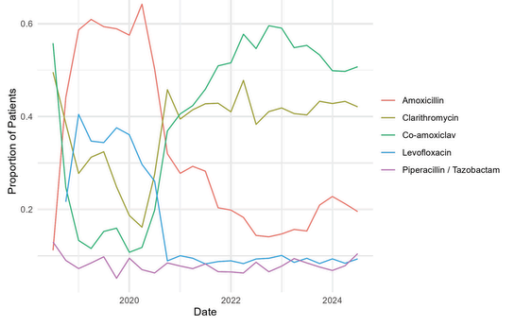
Quantitative Methods

- Routinely collected healthcare data were extracted from the electronic health record (EHR) of three hospital sites across Birmingham via PIONEER, the Health Data Research Hub for Acute Care.
- Digital maturity varied across the hospital sites, and consistent recording of data started between 2018 – 2022 at each site. Data were extracted from this point onwards.
- Patients were included if they had a primary diagnosis of pneumonia using ICD-10 and SNOMED codes and thoracic imaging requested within 48 hours of admission. Patients were excluded if they had a diagnosis code of hospital-acquired pneumonia or were in hospital in the 10 days prior to admission
- Pneumonia severity was stratified using CURB-65 scores from patient observations and demographics, or CRB-65 scores if urea was not recorded at the time of first antibiotic prescribing.
- Antibiotics were grouped into 24-hour intervals, to represent that antibiotics administered each day of admission. The primary outcome was antibiotics prescribed on day 2. Day 2 was chosen patients as it was felt to most accurately represent initial empirical antibiotics. Often at the point of admission diagnoses or source of infection may be uncertain, leading to more variable antibiotic prescription.
- The proportion of patients who received one of the 5 most commonly administered antibiotics was plotted as a line graph, showing prescribing patterns over time with data grouped by quarter.
- An interrupted time series design will be used to establish whether MHRA regulatory action influenced prescribing practice in the region.

Results

- The cohort included 2297 patients with mild CAP, 8411 with moderate CAP, 1401 with severe CAP, and 2244 with unknown severity due to missing data. Only patients without a recorded penicillin allergy were included.

Figure 1 – The proportion of non-penicillin allergic patients administered the five most commonly prescribed antibiotics for CAP over time



- There have been significant changes in the proportion of patients prescribed common antibiotics in CAP, which appear to coincide temporally with the Covid-19 pandemic.
- There has been a reduction in administration of levofloxacin since 2018. However, around 10% of patients are still administered levofloxacin on day 2 and prescribing behaviour has not changed in response to recent MHRA regulatory action in 2024.

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PIONEER Health Data Research Hub

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