A real-world evaluation of a Case-Based Reasoning algorithm to support antimicrobial prescribing decisions in acute care

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**Running Title:** Case-Based Reasoning decision support

**Summary:** A case-based-reasoning algorithm was evaluated in the real-world against prescriber decisions. The algorithm provided appropriate antibiotic recommendations that were significantly narrower in spectrum compared to choices being made in current clinical practice.

**Search terms:** Artificial intelligence, Machine Learning, Case-based Reasoning, Sepsis, Antimicrobial Stewardship, Clinical Decision Support Systems

**Abstract**

**Background:** A locally developed Case-Based Reasoning (CBR) algorithm, designed to augment antimicrobial prescribing in secondary care was evaluated.

**Methods:** Prescribing recommendations made by a CBR algorithm were compared to decisions made by physicians in clinical practice. Comparisons were examined in two patient populations. Firstly, in patients with confirmed *Escherichia coli* blood stream infections (‘*E.coli* patients’), and secondly in ward-based patients presenting with a range of potential infections (‘ward patients’). Prescribing recommendations were compared against the Antimicrobial Spectrum Index (ASI) and the WHO Essential Medicine List *Access*, *Watch*, *Reserve* (AWaRe) classification system. Appropriateness of a prescription was defined as the spectrum of the prescription covering the known, or most-likely organism antimicrobial sensitivity profile.

**Results:** In total, 224 patients (145 *E.coli* patients and 79 ward patients) were included. Mean (SD) age was 66 (18) years with 108/224 (48%) female gender. The CBR recommendations were appropriate in 202/224 (90%) compared to 186/224 (83%) in practice (OR: 1.24 95%CI:0.392-3.936;*p=0.71*). CBR recommendations had a smaller ASI compared to practice with a median (range) of 6 (0-13) compared to 8 (0-12) (*p<0.01*). CBR recommendations were more likely to be classified as *Access* class antimicrobials compared to physicians’ prescriptions at 110/224 (49%) vs. 79/224 (35%) (OR: 1.77 95%CI:1.212-2.588 *p<0.01).* Results were similar for *E.coli* and ward patients on subgroup analysis.

**Conclusions:** A CBR-driven decision support system provided appropriate recommendations within a narrower spectrum compared to current clinical practice. Future work must investigate the impact of this intervention on prescribing behaviours more broadly and patient outcomes.

**Abstract: 248**

**Words: 2999**

**Background**

Antimicrobial resistance (AMR) is a growing threat to patient safety. A major driver of AMR is the inappropriate use of antimicrobials.[1] A core challenge to optimising antimicrobial prescribing is addressing the variable use of antimicrobials across the hospital.

Most infections within hospitals are managed by non-infection specialists. To promote evidence-based practice of prescribing and therefore appropriate use, the physician is encouraged to follow local antimicrobial guidelines and policy. However, evidence demonstrates that adherence to prescribing policy tends to be poor, with a range of human and behavioural factors influencing prescribing decisions.[2–4]

With the global increase in the use of electronic health record and computerised-prescriber-order-entry systems,[5–7] development of electronic clinical decision support systems (CDSS) for antimicrobial prescribing has increased. CDSS have been demonstrated to enhance knowledge by providing person-specific and population level data to healthcare professionals to support their decision making.[8] This can improve the quality and safety of the healthcare provided.[8] Despite a wealth of literature surrounding CDSS for antimicrobial prescribing,[9–13] a number of significant gaps remain in their development, implementation, and evaluation.[13] Current CDSS do not utilise available data in an intelligent way to support decision making. They are predominantly rule-based systems that adhere to guidelines and policy.[13] These tend to provide inflexible, population level recommendations to prescribers.

The development of powerful processing capabilities and artificial intelligence provides an opportunity to utilise available data in a more precise manner.[14] This could potentially facilitate better decision making around antimicrobial selection, through the delivery of individualised, evidence-based recommendations utilising real-time patient data.

Withinthe field of infection management, the role of artificial intelligence has been previously explored.[15–27] Case-Based Reasoning (CBR), a type of artificial intelligence, has been used widely in the field of medical decision making including antibiotic decision making in intensive care,[25–28] radiology,[29,30] psychiatry,[31] chronic disease management,[32–35] hepatology,[36] diabetes,[37] and cancer [38].

Given the existing success of CBR in other areas of healthcare, we developed a CBR-driven CDSS using locally sourced data and designed for use in general medical and surgical settings within three London NHS hospitals, UK. This system was integrated into the hospitals electronic health record system and was evaluated using real-world patient data to explore the potential impact of the system on antimicrobial prescribing.

**Methods**

*Study design*

This study was a real-world evaluation of the potential of a CBR-driven CDSS to support antimicrobial prescribing decisions in the general medical setting. An in-house CBR algorithm was integrated into a CDSS and tested between July 2017 and February 2019. The first phase of the evaluation involved input of data from patients with confirmed *Escherichia coli* (*E.coli*) blood stream infections (“*E.coli* patients”). This was to allow evaluation of the CBR algorithm against confirmed infections, with known antimicrobial susceptibility profiles. *E.coli* was selected as the target organism given concerns over the rising global burden of *E.coli* blood stream infections on healthcare.[39,40] This includes their increasing prevalence and association with drug-resistance.[39,40] The second phase of testing evaluated use of the CDSS for a range of potential infections in ward-based patients who were identified on inpatient wards during general medical on-calls (“ward patients”). In the UK, general medical on-calls involve a doctor being responsible for a range a medical and surgical wards out-of-hours. They will respond to any unwell patients, often being required to initiate empirical antimicrobial therapy. This was designed to mimic real-world usage of the CDSS during the empirical phase of treatment.

The aim of the study was to evaluate the potential impact on antimicrobial prescribing if the system was implemented and used to support decision making in practice. Given that the CDSS aims to shift from static guideline based prescribing to a more dynamic and individualised means of supporting decision making; primary outcome measures selected were antimicrobial spectrum, determined by the Antimicrobial Spectrum Index (ASI) [41–45] and the WHO Essential Medicines List *Access*, *Watch*, *Reserve* (AWaRe) classification system.[46] This study was approved by London-Chelsea Regional Ethics Committee (ref: 17/LO/0047) and met all required data protection requirements in place during the study period.

*Study setting*

The study took place at a large London NHS Trust, with 1500 beds, serving a population of over 2 million people and comprising three major hospital sites that contain both medical and surgical specialties. The CDSS was implemented across the unified information technology infrastructure and was used by six members of specialist medical staff. These members were infection trained and received training prior to using the system. Training was standardised, using six off-line cases that the members of staff worked through with supervision from a member of the research team (BH).

*Clinical decision support system*

The CDSS used within this study is an in-house designed, Conformité Européene (CE) certification marked device. CE marking indicates that the device conforms with health, safety, and environmental protection standards of the European Economic Area. The interface was designed to run across all internet browsers and is responsive to changes in screen size. Data stored within the CDSS resides only on the server side. Data is stored with patient name and hospital numbers replaced using a SHA#256 pseudo-anonymisation protocol.

**Figure 1** outlines the core features of the CDSS graphical user interface. The interface was designed based on clinicians’ routine workflow. It is divided into two frames. The main frame facilitates input and review of real-time patient information and comparison to previous cases. This includes clinical examination findings, pathology and microbiology results, as well as antimicrobial prescribing information, which are input and automatically populated on the device in real-time. A supervised machine learning tool also provides support on the likelihood of infection being present.[47,48]

Within the CDSS server, a CBR algorithm was developed and integrated. CBR aims to solve a new problem by reusing, and if necessary, adapting, the solutions to similar problems that were solved in the past.[49] The CBR cycle, is dependent on the case-base to provide prior knowledge from which it assesses and adapts previous knowledge to make recommendations for the current, new cases.[50] The core variables available within the CBR algorithm are described in **Table 1**.

*Participant inclusion*

For initial testing, patients with confirmed *E.coli* blood stream infection identified through positive blood culture were identified and input into the CDSS. Following this, physicians used the CDSS prospectively inputting patient information during general medical on-calls. Physicians were recruited if they had training in infectious diseases and were available on the on-call rota within the study period. Any patient reviewed by the clinician were eligible for inclusion providing that they were admitted to one of the three hospitals evaluated, were 18-years of age or older, and were suspected of having an infection requiring the prescription of antimicrobial therapy. As this was an observational study, physicians were not required to follow the recommendations made by the CDSS and were expected follow their standard practice and to access Trust guidelines or specialist advice when required.

*Outcome measures*

Given concerns over current methods of defining appropriateness of antimicrobial therapy [51] and the need for dynamic decision support moving away from more static guideline driven prescribing,[13] we opted to compare the Antimicrobial Spectrum Index (ASI) [41–45] and WHO AWaRe classification [46] of recommendations provided by the CBR algorithm to prescriptions made in practice.

The ASI aims to classify agents based on activity against important pathogens, providing a metric that describes the spectrum of antimicrobial rather than simply deeming it as appropriate / inappropriate. Therefore, this provides the opportunity to quantify and compare the broadness of a prescribed antimicrobial, whilst also evaluating its coverage of important pathogens for which it is being used.[41–45]

ASI for individual agents was developed based on Gerber and colleagues prior work.[41] Two clinicians with experience in infectious diseases (TMR & LSPM) independently reviewed prescriptions and selected CBR recommendations determining the ASI and whether or not the spectrum of agent prescribed covered the pathogen (or likely causative pathogen in empirical therapy) that was being targeted. As an example, ASI values for single agents can range from 1 to 14. An ASI of 1/14 indicates a narrow spectrum agent, such as flucloxacillin. This is compared to tigecycline, which has an ASI of 13/14 due to is broad spectrum of activity, including against multi-drug resistant organisms. For combination therapy, the maximum ASI achievable remains 14, given that spectrums can overlap and would not be counted twice.

The WHO AWaRe classification system is a tool the classifies antimicrobials into three core groups.[46] *Access* antimicrobials are narrow spectrum agents, commonly used as first- and second-line agents for common infections and have a lower potential to select resistance than other groups. *Watch* antimicrobials are those that have a greater potential for the selection of antimicrobial resistance and therefore must be judiciously used in practice. *Reserve* antimicrobials are agents that should be held back for the treatment of multi-drug-resistant organisms, being used as last line treatments.[46] This classification provides a framework for standardised reporting of stewardship interventions and has been adopted internationally by policy makers and healthcare systems. The full table is available in ***supplementary document 1***. Where more than one antimicrobial was prescribed / recommended, the highest classification was chosen as the final outcome.

Additionally, the overall appropriateness of therapy was determined by two clinicians (TMR & LSPM) who independently reviewed both physician antibiotic decision and the CBR recommendations. For the purpose of this study, appropriateness was defined as when the spectrum of the antimicrobial prescribed or recommended, determined using the ASI, would cover the organism being targeted by therapy. For empirical prescribing, a local institution antibiogram was used to infer appropriateness. When subsequent culture had yielded a pathogen, individual sensitivity data were used.

*Sample size*

The study was powered to demonstrate a mean difference in ASIof greater than or equal to 1 unit with a power of 80% and significance of p=0.05, for a paired, two-tailed test. To achieve this, it was estimated that at least 74 patients would need to be included.

*Statistical analysis*

Data were analysed using SPSS 23.0 (IBM statistics, USA). Normality of distributions was evaluated using Shapiro-Wilks test for normality. Where normality was demonstrated paired t-testing was performed. Where data were non-parametric, Wilcoxon signed-rank test was used. For comparison of dichotomous outcomes, Pearson *X2* testing were used. All data were analysed as an intention-to-treat (ITT) analysis including both appropriate and inappropriate prescriptions. Per-protocol (PP) was also performed on patients where CBR recommendation spectrum covered the target pathogen being treated.

**Results**

*Descriptive data*

In total, 224 individual patients were included in the complete study.

Firstly, 145 *E.coli* patients were input into the CBR algorithm. Mean (SD) age was 66 (19) years with 77/145 (53%) female. All 145 patients had received antibiotic treatment. No individual patients were excluded.

Secondly, 89 ward patients were input into the CBR algorithm. Of these, 79/89 (89%) were included in the analysis. Ten cases were excluded as patients were treated for *Clostridium difficile* infection (3/10; 30%) or neutropenic sepsis (7/10; 70%), which was beyond the scope of this study. Mean (SD) age was 68 (16) years with 31/79 (39%) female. Of the 79 patients, 14 (18%) did not have clinical, biochemical, or microbiological evidence of infection. Pneumonia was the most common empirical diagnosis with 22/79 (28%) patients treated for this. Other empirical diagnoses made were intra-abdominal infection (11/79; 14%), blood stream infection (8/79; 10%), urinary tract infection (8/79; 10%), skin and soft tissue infection (8/79; 10%), and other infection (6/79; 8%).

*Case-Based Reasoning performance*

Of the 224 individual patients included, 202 (90%) of the CBR recommendations were deemed appropriate based on the spectrum of antimicrobial activity required. This was compared to 186/224 (83%) of prescriptions made by physicians. There was no statistical difference between physicians and CBR recommendations (OR:1.24 95%CI:0.392-3.936; *p=0.71*). Results were similar in the specific analysis of *E.coli* and ward patients, individually.

Comparison of the ASI for physicians and CBR recommendations is summarised in **Table 2**. Overall, the CBR algorithm was associated with significantly narrower spectrum of antibiotic prescribing with a median (range) ASI of 6 (0-13) for CBR, versus 8 (0-12) in practice (*p<0.01*). On subgroup analysis, ASI was found to be similar for prescribers and CBR algorithm in *E.coli* patients (*p=0.16*) and significantly lower from CBR recommendations in ward patients (*p=0.02*).

**Table 3** summarises WHO AWaRe classification of antimicrobial selections made by prescribers and the CBR algorithm. Overall, CBR recommendations were significantly more likely to be in the *Access* category of agents compared to *Watch* category when compared to physicians’ choices (**Figure 2**). Overall, physician prescriptions were classified as *Access* in 79/224 (35%) of cases compared to 110/224 (49%) of cases in the CBR recommendations (OR:1.77 95%CI:1.212-2.588; *p<0.01*). Results were similar for *E.coli* and ward patients on subgroup analysis. In the ward patient analysis, the CBR algorithm and physicians prescribed no therapy in 15/224 (7%) and 16/224 (7%) of cases, respectively (*p=0.83*).

**Discussion**

In this evaluation of a CBR algorithm, the CDSS made antibiotic recommendations at a similar level of appropriateness to physicians, whilst recommending a significantly narrower spectrum of therapy and increasing the rate of *Access* antimicrobial recommendations.

Unnecessary antibiotic exposure is a leading modifiable driver of AMR.[1] A major aspect of unnecessary exposure is the inappropriate prescribing of broad spectrum antimicrobials. A large focus of antimicrobial guidelines, prescribing policies, and antimicrobial stewardship programmes are promoting the appropriate use of narrow spectrum agents to reduce selection pressure placed on micro-organisms. Adherence to these interventions has been demonstrated to significantly reduce the selection pressure placed on micro-organisms, having a significant impact on rates of AMR.[52]

In line with antimicrobial stewardship policies, the WHO AWaRe criteria have been designed to support sustainable access to first- and second-line antimicrobials, whilst reducing the use of *Watch* and *Reserve* agents. *Watch* and *Reserve* agents are a concern as they promote the development of AMR and should be held back for the management of multi-drug resistant infection, respectively.[53] With financial incentives being placed on hospitals in the UK to demonstrate significant reductions in the use of *Watch* and *Reserve* agents, new interventions are required to support physician decision making to increase rates of *Access* prescriptions and reduce use of *Watch* and *Reserve* agents.

Antimicrobial prescribing guidelines are often developed based on expert opinion, national surveillance, and local microbiological data. These provide population level estimates of therapy that is likely to be successful for the treatment of a range of infections. Guidelines fail to allow flexibility for individual variations in clinical practice and face the challenge of needing to be regularly updated and responsive to shifting organism epidemiology and to drug availability and shortages. This may lead to failures with guideline compliance and inappropriate empirical treatment being initiated. This is a particular problem in multi-morbidity and polypharmacy, which now effects one in three patients admitted to hospital over the age of 65 years.[54]

The development of intelligent CDSS, that are able to provide personalised recommendations based on individual patient data may help address the problem of guideline based antimicrobial prescribing.[14] Intelligent CDSS designed to support antimicrobial prescribing have been reviewed extensively elsewhere.[13,55] The most notable example, with high quality data is the TREAT system. TREAT is a CDSS incorporating Causal-Probabilistic Networks. Using this approach, TREAT demonstrated a 9% improvement in appropriateness of prescribing [56] and a trend towards improved survival using this type of system.[19] However, Causal-Probabilistic networks require the construction of hugely complex decision maps. This leads to problems translating these solutions into clinical practice given the wide heterogeneity in practice and data availability.[57] It makes these systems challenging to develop, implement, and requires a large amount of information and technical skill to maintain.[49]

CBR is an alternative approach to the use of knowledge-based systems. CBR aims to solve a new problem by adapting a previously successful solution to the current problem encountered.[49] CBR aims to address many of the challenges associated with knowledge-based systems. For example, CBR does not require a defined model. Therefore, CBR simply relies on the extraction of case histories. Implementation of CBR requires the identification of significant features describing a particular problem, as opposed to creating an explicit model. Finally, CBR learns overtime through cases that it acquires, which makes maintenance easier than model-based systems.

Within this study, a CBR algorithm provided recommendations that were appropriate, but narrower in spectrum when compared to clinical practice. This was without direct weighting of recommendations to focus on narrower spectrum agents. A possible reason for this observation includes prescriber bias towards broader spectrum agents, particularly when making empirical treatment decisions and when the clinical picture does not fit with guidelines.[2,4] The acceptability of recommendations by physicians must be evaluated to explore the impact of individualised prescribing recommendations on prescriber behaviours in similar situations.

*Study limitations*

As an observational study it was not possible to control for all confounders within the study population. The study also did not evaluate the impact of the CDSS on prescribing behaviour, including the acceptability of the device to prescribers on implementation. This will be prospectively explored following the successful demonstration of proof-of-concept within this study. In addition, whilst the ASI and the WHO AWaRe classification system are validated approaches to assess spectrum of antimicrobial activity, they are based on historical data, which may not be entirely generalizable to the local environment and epidemiology within this study. The financial impact of implementing such a system was not the focus of this study. Robust economic analysis will be incorporated into future prospective evaluation of the CDSS in practice. Finally, this study was not designed to evaluate potential unintended consequences of implementing a CBR-drive CDSS, however the results have demonstrated that CBR performed similar to current real-world clinical decision making, with initial evaluation deeming them to be appropriate and safe.

**Conclusion**

A CBR algorithm provided antimicrobial recommendations that were in line with physician decisions, but also shifted recommendations towards narrower spectrum antimicrobial prescribing. CBR-based CDSS provides a flexible, intelligent method of augmenting individuals’ antimicrobial prescribing. Future work is now underway to explore the impact of integration of CBR with other methods for optimisation of antimicrobial prescribing, including dose optimisation platforms and patient-facing applications.

**Notes**

**Transparency declarations**

All authors have no conflicts of interest to declare.

**Ethics approval and consent to participate**

The study protocol for Enhanced, Personalized and Integrated Care for Infection Management at Point of Care (EPIC IMPOC) was reviewed and approved by the Chelsea Regional Ethics Committee (REC) REF: 17/LO/0047.

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**Availability of data and material**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request where not presented in the manuscript or figure.

**Author contributions**

TMR, LSPM, and AH conceived and designed the study. TMR, LSPM, and OB led clinical data collection. BH and PH led development and validation of the Case-Based Reasoning algorithm. TMR led data analysis with all authors contributing significantly to data interpretation and presentation. TMR drafted the first draft of the manuscript. All authors contributed significantly to revisions of the manuscript and consented for its submission in its final form.

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**Table 1.** Variables used within the clinical decision support system for antimicrobial selection.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Category** | **Variable** | **Data type** | **Currently available in CDSS** | **Label / Range** | **Included** |
| **Patient information** | Age | Extract | Yes | 0-110 | Yes |
|  | Gender | Extract | Yes | Male / Female | Yes |
|  | Ethnicity | Extract | Yes | <String> | No |
|  | Name | Extract | Yes | <String> | Yes |
|  | Admission date | Extract | Yes | DD/MM/YYYY | Yes |
|  | Current date | Extract | Yes | DD/MM/YYYY | Yes |
|  | Allergies | Drop down OR  Free text | Yes | Antibiotic name  <String> | Yes |
| **Physiological parameters** | Oxygen saturation | Number | No | 0-100 | Yes |
|  | Temperature | Number | Yes | 25-43 | Yes |
|  | Heart Rate | Number | Yes | 0-250 | Yes |
|  | Blood Pressure | Number | Yes | Systolic / 0-250  Diastolic / 0-150 | Yes  No |
|  | Respiratory Rate | Number | Yes | 0-50 | Yes |
|  | Glasgow Coma Scale | Number | No | 3-15 | No |
|  | Fluid balance | Number | No | -5000 - + 5000 | No |
| **Localising infection** | Clinical symptoms | Free text | No | <String> | No |
|  | Signs on examination | Drop down for:  i) Chest auscultation  ii) Abdominal palpation  iii) Heart sounds | Yes | 1. Crackles / Crepitations / Dull / Clear / Wheeze 2. SNT / Tender / Rigid / Ascites 3. Normal / Murmur (new) / Murmur (old) | Yes  Yes  No |
|  | Likely infection site | Drop down OR Free text | Yes | <String> | Yes |
| **Investigation results** | C-Reactive Protein | Extract | Yes | 0-550 | Yes |
|  | White Cell Count | Extract | Yes | 0-55 | Yes |
|  | Full blood count | Extract | Yes | 0-210 | Yes |
|  | Liver Function | Extract | Yes | ALT: 0-10000  ALP: 0-2000 | Yes  Yes |
|  | Renal Function | Extract | Yes | Cr: 0-1000 | Yes |
|  | Lactate | Number | Yes | 0-12 | Yes |
|  | Microbiology | Extract | Yes | Organism  Susceptibility profile  Site of culture | Yes  Yes  Yes |
|  | Radiology | Drop down - CXR | Yes | Clear / Consolidation / Effusion / Oedema | Yes |
| **Determining severity** | SIRS criteria\* | Extract | No | 0-6 | No |
|  | In-vitro susceptibility profiles | Extract | Yes | See above | Yes |
| **Miscellaneous parameters** | Indwelling lines | Tick box | Yes | Urinary catheter  CVC line | Yes  Yes |
| **(not identified** | Airway management | Drop down | Yes | Own / Trachy / Intubated / NIV | Yes |
| **in chapter** | HIV status | Tick box | Yes | HIV positive | Yes |
| **two)** | Diabetes | Tick box | Yes | Diabetic | Yes |
|  | Pregnant | Tick box | Yes | Pregnant | Yes |
|  | Renal support | Drop down | Yes | None / Dialysis / Transplant / CVVH | Yes |
|  | Inotropic support | Tick box | Yes | Yes | No |
|  | Hospital No. | Extract | Yes | <String> | Yes |
|  | NHS No. | Extract | Yes | <String> | Yes |
|  | Ward name | Extract | Yes | <String> | Yes |
| **Outcome** | Antibiotic prescription | Drop down | Yes | Antibiotic selection | Yes |
|  | Successful? | Drop down | Yes | No / No – escalated / Yes – completed / Yes – de-escalated / Unknown | No |
|  | Death | Tick box | Yes | Yes | No |
|  | Reason for death | Free text | No | <String> | No |

**Legend:** CXR = chest x-ray; SIRS = systemic inflammatory response syndrome; SNT = soft, non-tender; CVC = central venous catheter; Trachy = tracheostomy; CVVH = continuous veno-venous haemofiltration; NIV = non-invasive ventilation; HIV = human immunodeficiency virus

**Table 2. Comparison of prescriber and CBR antimicrobial spectrum index**

**Legend:** ASI = Antimicrobial Spectrum Index (range: 0-14); CBR = Case-Based Reasoning;E.coli = Escherichia coli; BSI = Blood stream infection

|  |  |  |  |
| --- | --- | --- | --- |
|  | Prescriber ASI  (range) | CBR ASI  (range) | p-value |
| Intention-to-treat |  |  |  |
| Total (n = 224) | 8 (0-12) | 6 (0-13) | ***0.009*** |
| E.coli BSI (n=145) | 8 (2-12) | 8 (2-12) | *0.158* |
| Ward cases (n = 79) | 6 (0-12) | 5 (0-13) | ***0.015*** |
| Per Protocol |  |  |  |
| Total (n = 202) | 8 (0-12) | 7 (0-12) | ***0.006*** |
| E.coli BSI (n = 138) | 8 (2-12) | 8 (2-12) | *0.188* |
| Ward cases (n=64) | 6 (0-12) | 5 (0-12) | ***0.030*** |

**Table 3.** Comparison of prescriber and CBR recommendations using WHO Access, Watch, Reserve classification system.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Prescriber** | **CBR** | **p-value** |  | **Prescriber** | **CBR** | **p-value** |
| **Intention-to-treat** |  |  |  | **Per Protocol** |  |  |  |
| **Total (n = 224)** |  |  | ***<0.001*** | **Total (n = 202)** |  |  | ***<0.001*** |
| *No treatment* | 16 (7) | 15 (7) |  | *No treatment* | 15 (7) | 15 (7) |  |
| *Access* | 79 (35) | 110 (49) |  | *Access* | 72 (36) | 99 (49) |  |
| *Watch* | 127 (57) | 97 (43) |  | *Watch* | 114 (56) | 88 (44) |  |
| *Reserve* | 2 (1) | 2 (1) |  | *Reserve* | 1 (1) | 0 (0) |  |
| ***E.coli* patients\* (n=145)** |  |  | ***<0.001*** | ***E.coli* patients**  **(n = 138)** |  |  | ***0.031*** |
| *No treatment* | 0 (0) | 0 (0) |  | *No treatment* | 0 (0) | 0 (0) |  |
| *Access* | 54 (37) | 74 (51) |  | *Access* | 53 (38) | 70 (51) |  |
| *Watch* | 90 (62) | 71 (49) |  | *Watch* | 84 (61) | 68 (49) |  |
| *Reserve* | 1 (1) | 0 (0) |  | *Reserve* | 1 (1) | 0 (0) |  |
| **Ward patients\*\***  **(n = 79)** |  |  | ***<0.001*** | **Ward patients (n=64)** |  |  | ***<0.001*** |
| *No treatment* | 16 (20) | 15 (19) |  | *No treatment* | 15 (23) | 15 (23) |  |
| *Access* | 25 (32) | 36 (46) |  | *Access* | 19 (30) | 29 (45) |  |
| *Watch* | 37 (47) | 26 (33) |  | *Watch* | 30 (47) | 20 (31) |  |
| *Reserve* | 1 (1) | 2 (3) |  | *Reserve* | 0 (0) | 0 (0) |  |

**Legend:** CBR = Case-Based Reasoning;E.coli = Escherichia coli; BSI = Blood stream infection

\*= Patients identified with confirmed Escherichia coli blood stream infections

\*\* = Patients identified on inpatient wards presenting with suspected infection

**Figure 1.** Clinical Decision Support System graphical user interface examples.

A screenshot of a computer

Description generated with very high confidence

**Legend:** *Top row main panel*: Example of the opening page of main and side panel with a summary of current patient information. Most similar cases within the case-base are also available for comparison in the side panel. *Top row side panel:* CBR results matching the current patient case to most similar cases identified within the case-base. *Bottom row main panel:* Blood test result data can be graphically displayed allowing the user to monitor trends in blood parameters commonly considered during antimicrobial prescribing. *Bottom row side panel:* CBR results providing the most common antimicrobials in similar cases (grouped antimicrobials) with likelihood of success. This panel also highlights drugs that have been unsuccessful in similar cases.

CBR = Case-Based-Reasoning

**Figure 2.** Comparison of prescriber and Case-Based Reasoning prescriptions using the WHO Access, Watch, Reserve classification system

![A screenshot of a computer

Description automatically generated]()