Feasibility study of hospital antimicrobial stewardship analytics using electronic health records

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Research

Keywords: antimicrobial stewardship, medical informatics applications, electronic health records, electronic prescribing, public health surveillance, epidemiological monitoring, health information systems, bacterial infections and mycoses

DOI: https://doi.org/10.21203/rs.3.rs-33072/v2

Abstract

Background: Hospital antimicrobial stewardship (AMS) programmes are multidisciplinary initiatives to optimise the use of antimicrobials. Most hospitals depend on time-consuming manual audits to monitor clinicians' prescribing. But much of the information needed could be sourced from electronic health records (EHRs).

Objectives: To develop an informatics methodology to analyse characteristics of hospital AMS practice using routine electronic prescribing and laboratory records.

Methods: Feasibility study using electronic prescribing, laboratory and clinical coding records from adult patients admitted to six specialties at Queen Elizabeth Hospital, Birmingham, UK (September 2017–August 2018). The study involved: (1) a review of antimicrobial stewardship standards of care; (2) their translation into concepts measurable from commonly available EHRs; (3) pilot application in an EHR cohort study (n=61,679 admissions).

Results: We developed data modelling methods to characterise the use of antimicrobials (antimicrobial therapy episode linkage methods, therapy table, therapy changes). Prescriptions were linked into antimicrobial therapy episodes (mean 2.4 prescriptions/episode; mean length of therapy of 5.8 days) enabling production of several actionable findings. For example, 22% of therapy episodes for low-severity community acquired pneumonia were congruent with prescribing guidelines, with a tendency to use antibiotics with a broader spectrum. Analysis of therapy changes revealed a delay in switching from intravenous to oral therapy by an average 3.6 days [95% CI: 3.4; 3.7]. Performance of microbial cultures prior to treatment initiation occurred in just 22% of antibacterial prescriptions. The proposed methods enabled fine-grained monitoring of AMS practice all the way down to specialties, wards, and individual clinical teams by case mix, enabling more meaningful peer comparison.

Conclusions: It is feasible to use hospital EHRs to construct rapid, meaningful measures of prescribing quality with potential to support quality improvement interventions (audit/feedback to prescribers), engagement with front-line clinicians on optimising prescribing, and AMS impact evaluation studies.

1 Introduction

The aims of antimicrobial stewardship (AMS) are 'first, to ensure effective treatment of patients with infection, and second, to minimise collateral damage from antimicrobial use'.[1] Hospital AMS guidelines[2–7] recommend regular clinical audits of prescriptions and feedback of results to prescribers by infection specialists. Yet, doing so is labour-intensive and dependent on specialist expertise,[8] as it involves reviewing what diagnostic tests were performed and assessing the compliance with local prescribing guidelines. Similarly, point prevalence surveys conducted for infection surveillance[9] can be prohibitive both in terms of professional time and methodological skill. This hinders hospitals' capacity to monitor prescribing on a large scale.[8,10,11]

Electronic health records (EHRs) collected routinely by hospital information systems offer potential solutions to this problem. King *et al.*[12] and Hand *et al.*[13] scoped the potential role of electronic prescribing software in supporting prescribers across the full antibiotic lifecycle (prescription initiation; review; discontinuation and dispensing of discharge medications). Other studies have demonstrated the feasibility of using computerised laboratory results, including microbial cultures and sensitivities, to guide the choice of antimicrobial agent in empirical therapy[14] and increase the proportion of cases treated with effective antimicrobials.[15]

EHRs thus have the potential to enable a range of functions recommended in AMS guidelines,[2] particularly: audit of practice, feedback to prescribers, and infection surveillance (tracking syndromes, pathogens and susceptibility). Despite this, the use of EHRs to drive AMS programmes remains 'underexploited'.[16:56] Extraction of records is challenging,[17]

resulting in very limited secondary use for evidence-based medicine.[18] In response, the UK's Antimicrobial Resistance National Action Plan set goals for a comprehensive use of EHRs to 'support and drive good antimicrobial stewardship by coding, auditing and providing feedback for surveillance' by 2025.[16:p.56]

The aim of the present paper was to assess the feasibility of auditing antimicrobial stewardship practices using routinely-collected EHRs in order to provide relevant information to different AMS stakeholders including clinicians, hospital managers and policy-makers. Key objectives were to:

1. infer the indication of antibiotics prescribed to inpatients
2. assess the congruence of individual prescriptions with local prescribing guidelines, particularly in relation to empirical therapy
3. compute metrics of stewardship beyond consumption of antibiotics
4. compare these metrics between specialties and between consultant teams within specialities.

This feasibility study followed the three steps. First, we synthesised concepts relevant to antimicrobial stewardship performance from clinical guidelines and infection surveillance protocols, and translated them into operational definitions applicable to EHRs. Second, we modelled and visualised records to refine definitions that could be applied to data from one specialist hospital in Birmingham, UK. Third, we computed AMS metrics and reviewed compliance of clinical practices with AMS guidelines.

2 Materials And Methods

2.1 Ethics

This research was approved by University College London's Research Ethics Committee (REC reference 16765/002). Informed consent was not sought for the secondary analysis of pseudonymised electronic health records.

2.2 Study design and population

We conducted a retrospective cohort study of records corresponding to episodes of care in six specialties (general medicine, respiratory medicine, geriatric medicine, cardiology, general surgery, urology) at Queen Elizabeth Hospital Birmingham (QEHB) for adult inpatients admitted between 1 September 2017 to 31 August 2018 (n=61,679 admissions). QEHB is a specialist teaching hospital in Birmingham, UK with over 1,000 general and acute inpatient beds.

2.3 Variables

Pseudonymised EHRs consisted of patient demographics, clinical diagnosis codes (ICD-10, reclassified as shown in Table S5),[19] clinical procedure codes (OPCS-4),[20] episodes of care (pseudonymised consultant code, consultant specialty), ward movements, and key investigation results (blood counts, vital signs, blood pressure, organ function).

Antibacterial drug prescription and administration records were extracted from QEHB's locally-developed Prescribing, Information and Communication System (PICS).[21] PICS follows the common UK 'dose-based' prescribing approach,[22] in which prescribers issue a request containing one or more drug names (Trade Family), dose, route and frequency.

Microbial culture results, including no growth results and cultures ordered by general practitioners were extracted from PICS. We applied EUCAST interpretative criteria,[23] and classified bacterial isolates by multi-drug resistance profile (multiple, extensive, and pan-drug resistance) according to rules set out by Magiorakos *et al.*[24] CURB-65,[25] an important

risk stratification score for community-acquired pneumonia, was computed without the confusion score due to lack of reliable data.

2.4 AMS metrics

Relevant definitions and standards of care were identified from international hospital antimicrobial stewardship and infection treatment guidelines using a list systematically compiled in 2018,[26] alongside four UK-specific reference sources.[2,9,27,28] We narrowed down a list of measures (Table 1) on the basis of (a) their relevance to inform a hospital AMS strategy, and (b) the availability of sufficient information to measure them within commonly-encountered EHRs. These measure characterise:

- **Antimicrobial consumption (dose and duration)**. Defined daily doses, days of therapy, and length of therapy (duration of the episode, irrespective of the number of antimicrobials administered concurrently) were calculated and aggregated by ward, specialty, consultant teams, and clinical indication as per definitions by Ibrahim *et al.*[29]
- **Changes of therapy** as part of a 'therapy episode' (section 2.5), by tracking changes in antibacterial treatment choices and their timing relative to microbiological outcomes and clinical progression. One such change, de-escalation, is recommended when microbial culture and susceptibilities are available, or when there is limited evidence of infection. It is most easily measured in antibiotics with the broadest spectrum of activity, where only a small number of other drugs would have equivalent spectrum. Conversion from intravenous therapy to oral therapy is another commonly recommended change of therapy intervention, which can facilitate discharge and reduce some adverse effects of injections.[30] We computed the time by which criteria for switching from intravenous to oral regimes were met, based on a set of 'ABCD' criteria listed in QEHB's antimicrobial prescribing guidelines (Table 3), some of which are shared with the Glasgow Audit Tool.[28] Out of these, ability to take oral medication (criterion B) could not be assessed from records, but other criteria could be measured continuously
- **Congruence of practice with prescribing guideline.** Prescriptions starting a therapy episode were compared with first-line choice of therapy recommended in local prescribing guidelines.
- **Adherence to microbial sampling guidelines** recommending submission of bacterial cultures prior to initiation of empirical treatment.[27] We computed the proportion of prescriptions with a microbial sample taken in the three days leading up to antibacterial therapy initiation.

Underlying concepts are further characterised in detail and mapped onto relevant SNOMED-CT concept codes[31] in supplementary Table S1.

2.5 Data modelling

Graph theory principles were used to construct periods of uninterrupted antibiotic therapy (therapy episodes) by linking related prescription records. Rule definitions underpinning this linkage are available along with this paper (appendix S2, supplementary Table S3). This enabled identification of sequences of drug administration making up therapy episodes, particularly transition from one class of antimicrobials to another.

For each antimicrobial therapy episode, a dynamic table could be constructed with an hourly resolution capturing changes in therapy in relation to clinical parameters (Table 2) as the basis for analysing changes of therapy in relation to clinical response to treatment (including tracking the timing of conversion from intravenous to oral therapy administration).

Data processing software was written in Structured Query Language (SQL), R and tidyverse.[32–34] and served as a prototype for the Ramses package.[35,36]

2.6 Prescribing indication inference (supervised classification)

PICS captures drug prescription indications as free text. Such information was not made available to researchers due the data containing identifiable information and the high prevalence of missing data (in the region of 50%). In order to demonstrate our approach, drug indications were instead classified retrospectively using a training dataset that had been collected during an audit of antibacterial prescribing conducted by pharmacists between 2012 and 2017. This dataset included 4200 prescriptions issued for 2,712 patients in the following specialties: general medicine, respiratory medicine, geriatric medicine, and general surgery. Pharmacists classified each prescription into 21 possible indications including 'Not specified' and 'Other' using data in PICS and paper medical records. 463 prescriptions did not have a valid clinical indication, and 364 could not be linked to electronic prescription records, restricting the analysis to a total of 3,228 prescriptions corresponding to 2,901 therapy episodes. Indication categories with fewer than 50 episodes (endocarditis, bronchiectasis, diabetic foot and/or osteomyelitis, surgical prophylaxis) were reclassified as 'Other'. These records were used as training data to predict the clinical indication across all antimicrobial prescriptions, using random forest classification with a moderate-to-low balanced accuracy of 59% overall. Predictive analytics were estimated using repeated 5-fold stratified cross-validation and are reported in appendix S6-S7.

3 Results

3.1 Antimicrobial consumption descriptive characteristics

A basic characterisation of prescribing requires linking prescriptions into episodes of therapy, to describe their duration in relation to patient demographics or type of infection treated. Between 1 September 2017 and 31 August 2018, there were 61,679 adult admissions (46,853 distinct patients) across the six specialties. Table 4 presents key metrics characterising antibacterial use (prevalence, duration, quantity) by age group. The mean length of admission was 4.2 days, and 21,757 admissions (35%) contained at least one antibacterial prescription. A total of 59,884 antibacterial prescriptions were issued, corresponding to 24,511 antibacterial therapy episodes, 141 of which spanned more than one admission. The mean length of antibacterial therapy episodes (LOT) was 5.8 days, equivalent to a mean 8.7 days of therapy (DOT) per admission. The mean days of therapy increased with age and was significantly higher (9.9 days) in emergency admissions than in elective admissions (4.3 days, Figure 1).

3.2 Changes of therapy

Changes of therapy could be analysed from the structure of therapy episodes to identify escalation or de-escalation. For instance, therapy episodes initiated with meropenem (n=969) were most commonly:

(a) stopped (33%), after a mean duration of 3.0 days;

(b) continued (28%), after a mean duration of 2.0 days;

(c) switched to piperacillin/tazobactam (12%), after a mean duration of 1.1 days;

(d) switched to co-amoxiclav (9.1%), after a mean duration of 1.9 days;

Outcomes (a), (c) and (d) can be regarded as de-escalation in this particular instance.

3.3 Switch from intravenous to oral therapy

Within 16,688 out of the 24,510 antibacterial therapy episodes, we identified 17,614 episodes consisting of one or more intravenous prescriptions. Overall, 6,404 (36%) of such the intravenous episodes were converted to oral therapy, with a median and mean duration of intravenous treatment of 2.4 days and 3.5 days respectively. On the contrary, 11,210 intravenous episodes (64%) continued with injections until end of therapy, with a median duration of 1.3 days and a mean duration of 3.5 days. As shown in Figure 3, variation in the conversion to oral therapy across clinical teams and specialties was evident and can be attributed, at least in part, to case mix. For instance, a likely explanation for cardiology's lower conversion rate (8%) is that prolonged intravenous therapy is recommended for deep-seated infections such as endocarditis.

We sought to analyse the timeliness of conversion from intravenous to oral therapy based on ABCD criteria (Table 3). Out of 6,404 intravenous episodes successfully switched, 2,670 (42%) met A, C and D criteria before oral conversion occurred. Out of 11,210 sequences never switched, 2,682 (21%) met A, C and D criteria before end of therapy. Across both sets, the delay between criteria being met and end/conversion of therapy had a median of 2.1 days, a mean of 3.6 days [95% CI: 3.4; 3.7], and a standard deviation of 5.7 days, suggesting considerable variation. Figure 4 presents team- and specialty-level mean delays, suggesting once again some differences between consultant teams within specialties.

3.4 Congruence with prescribing guidelines

We take the example of community-acquired pneumonia (CAP). In addition to being the most common indication for therapy initiation, CAP prescribing guidelines revolved around a widely-adopted risk stratification score (CURB-65) which could be measured from EHRs. Of 4,222 therapy episodes initiated for CAP, 4,109 (97%) could be linked with a CURB-65 severity score in the 48 hours before or after antibiotic initiation (assuming a mental confusion score of 0 due to as this information was not recorded electronically). At the time of prescribing, QEHB guidelines recommended:

- CURB-65 score 0 or 1: amoxicillin; doxycycline (penicillin allergy)
- CURB-65 score 2: amoxicillin/clarithromycin; benzylpenicillin/clarithromycin; moxifloxacin (penicillin allergy)
- CURB-65 score 3+: co-amoxiclav/clarithromycin; moxifloxacin (penicillin allergy).

4 Discussion

4.1 Principal findings

This single-site study demonstrates a pragmatic approach to computing meaningful measures of AMS from electronic prescription, laboratory and hospital care records to support stewardship teams in rapidly identifying areas of prescribing behaviour where there is scope for improved stewardship. In addition to measuring variation in antibiotic use, we demonstrate the feasibility of using routine data to assess overall compliance with guidelines (using the example of CAP), and show how these datasets can be used to compute a range of prescribing metrics (Table 1) built around international AMS recommendations. This can be used to monitor performance; inform the design of stewardship interventions; evaluate their impact; and engage clinical teams in audit and feedback interventions to optimise their prescribing.[16]

4.2 Study strengths and limitations

This study is novel in attempting to measure clinical constructs that normally require manual audits or point prevalence surveys using routinely collected data.[28,37] We outlined ways of measuring stewardship performance in clinical practice beyond antimicrobial consumption, the main indicator currently used in stewardship surveillance.[38] National surveillance systems for prescribing and resistance in secondary care provide high-quality measures of resistance and prescribing for

policy-makers, but they do not address the needs of front-line clinicians who require more detailed metrics to identify opportunities to improve their performance. This feasibility study demonstrates the potential for locally-developed analytics to address the local needs and stewardship priorities of clinicians using routinely-collected EHRs. Future iterations of our approach could be expanded to report on the effective and timely use of surgical prophylaxis (and its congruence with guidelines), timely initiation of antimicrobial therapy, and adequate empirical therapy coverage of microbial isolates.

Outside of intensive care research, existing literature contains few examples of EHR research simultaneously analysing electronic prescribing, laboratory and care records. To our knowledge, only large bespoke data engineering platforms have achieved this.[39–41] Unlike the present study, such platforms exploit health messages streaming from hospital information systems in real-time: these contain dynamic information, unlike the retrospective view provided from EHRs commonly curated in hospital warehouses. This noteworthy difference has implications: the structure and content of dynamic health messages tends to be system-specific, and require significant investment into developing dedicated data and analytical models. Such platforms are neither feasible in most hospitals, nor justified for simple surveillance of antibiotic use, stewardship performance, and pathogen susceptibility. The pragmatic approach described in the present paper would be accessible to a wider range of hospitals, particularly if interoperable software[35,36] and codelists/vocabularies are made widely available. In those conditions, a modest proportion of an information analyst's time would be sufficient to validate and map local data to standardised vocabularies and generate comprehensive reports. Metrics specified in Table 1 are designed to be feasible independently of variation in EHRs and vocabularies across hospitals.

This feasibility study reveals the challenges associated with assessing congruence with local prescribing guidelines and the complexity of prescribing decisions. This is partly due to limitations of routine data, but it also reflects lack of consensus around when it is appropriate to de-escalate antibiotics. Manual review of individual prescribing records led authors to conclude that there is too much ambiguity in electronic health records to confidently assess the appropriateness of individual prescribing decisions. Prescribing indication data were not available, and made it necessary to rely upon statistical classification. This introduced error into the findings: for example, the classifier precision for CAP was 80% (supplementary Table S7), indicating that one in five episodes classified as CAP were likely to have a different indication. However, it is increasingly common for prescribing indication to be recorded in electronic prescribing systems which may make it feasible to assess congruence with prescribing using electronic health records alone. Similarly, the lack of access to dispensing records prevented analysis of "to take away" medications issued at discharge, which can significantly prolong the total length of therapy. Finally, prescription records obtained from a snapshot source did not include a history of changes made to prescriptions' intended duration. This prevented analysis of how frequently prescriptions were stopped early. All analyses were restricted to structured data, and did not attempt to derive information which may have been recorded in free text in medical notes.

4.3 Implications

Findings from this feasibility study are now informing the development of an open-source software package[35] designed to enable hospitals to build their own stewardship analytics using routinely-collected EHRs. This has the potential to transform the delivery of stewardship in hospitals by making detailed information on prescribing patterns and resistance widely available in the context of increasing use of electronic prescription, laboratory and hospital care record systems in high-income nations. As of 2020, half of England's acute hospitals had adopted electronic prescribing.[42] International guidelines[2–7] recommend local investment into surveillance and analytics to rationalise the use of antimicrobials. In particular, the UK's Antimicrobial Resistance National Action Plan[16] aims to complete the introduction of electronic prescribing systems across England by 2025, alongside the adoption of international clinical terminology in computerised laboratory systems.[43] Strong evidence supports the use of feedback to prescribers,[2,44] but feedback needs to be relevant,

targeted (team- or individual-level), reliable and timely to influence prescribing behaviour.[45] Further research is needed to statistically adjust those measures for case mix in the same way as consumption measures.[46] User-centred research[47] is also needed to tailor these measures to individual clinical teams, or to enable AMS teams or hospital managers to monitor specific prescribing behaviours across hospitals. There is also a need for research to develop evidence-based standards of care for antimicrobial stewardship, for instance to support decisions around de-escalation.[48] This could be facilitated by observational studies of routine care records.

5 Conclusions

This study shows it is feasible to draw on electronic prescription, laboratory and hospital care records to provide meaningful measures of AMS, by:

1. **Reconstructing 'therapy episodes'**, which link all relevant prescription records and enable analyses of the length, changes and discontinuation of antimicrobial therapy.
2. **Inferring the clinical intent and indication of prescriptions** (for both monotherapy and combination therapy). We have illustrated the use of supervised classification in general medicine specialties with moderate accuracy for the most common infection categories.
3. **Computing stewardship performance and quality metrics**. Examples include conversion of intravenous therapy to oral therapy when patients show signs of resolution, microbial culture sampling and congruence with guidelines.

However, one of the most significant obstacles hindering hospitals' stewardship efforts lies the difficulty in extracting and analysing EHRs from a range of diverse systems.[18] Reproducible analytical tools are now available to assist microbiology culture and susceptibility analytics.[49] Software development is underway to support other hospitals in adopting the approach tested in the present study.

Abbreviations

AMS	antimicrobial stewardship
CAP	community-acquired pneumonia
CRP	C-reactive protein
DOT	days of therapy
EHR	electronic health record
IV	intravenous
LOT	length of therapy
PICS	Prescribing, Information and Communication System
QEHB	Queen Elizabeth Hospital Birmingham
UK	United Kingdom
WBC	white blood cell count

Declarations

Acknowledgements

This work uses pseudonymised data provided by patients and collected by the NHS as part of their care and support. The authors also acknowledge the contribution of staff of the Pharmacy Department at University Hospital Birmingham NHS Foundation Trust, who collected high-quality antimicrobial review outcome data.

This paper was published on behalf of the PASS research group: Niall Anderson, Elise Crayton, Gillian Forbes, Arnoupe Jhass, Emma Richardson, Michelle Richardson, Patrick Rockenschaub, Catherine Smith, Elizabeth Sutton, Rosanna Traina (Investigation); Lou Atkins, Anne Conolly, Spiros Denaxas, Ellen Fragaszy, Rob Horne, Patty Kostkova, Fabiana Lorencatto, Susan Michie, Jennifer Mindell, John Robson, Claire Royston, Carolyn Tarrant, James Thomas, Jonathan West (Conceptualisation, Funding Acquisition and Resources); Haydn Williams (Resources); Nadia Elsay, Chris Fuller (Project Administration).

Funding

This study was carried out as part of Preserving Antibiotics through Safe Stewardship (PASS), a programme grant funded by the Economic & Social Research Council (grant reference ES/P008321/1).

AH is a National Institute for Health Research (NIHR) Senior Investigator. LS is funded by a NIHR Clinician Scientist Award (CS-2016-007). The views expressed in this article are those of the authors and not necessarily those of the NIHR, or the Department of Health and Social Care.

Transparency declarations

None to declare.

Authors' contributions: DMcN extracted data for the study team. MJG extracted and classified microbial culture and susceptibility records. GS led the collection of the prescription review data. PDM programmed and conducted analyses, and drafted the manuscript. MJG, LS, AH and PDM reviewed visualisations of results and interpreted the findings. All authors have read and approved the submitted manuscript.

References

1. Davey P, Sneddon J, Nathwani D. Overview of strategies for overcoming the challenge of antimicrobial resistance. *Expert Rev Clin Pharmacol* 2010; **3**: 667–686. Epub ahead of print 2010. DOI: 10.1586/ecp.10.46.

2. National Institute of Health and Care Excellence. Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use. NICE guideline NG15, https://www.nice.org.uk/guidance/ng15 (2015, accessed 24 October 2018).

3. SARI Hospital Antimicrobial Stewardship Working Group. *Guidelines for Antimicrobial Stewardship in Hospitals in Ireland*. Dublin, Ireland, https://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/infectioncontrolandhai/guidelines/File,4116,en.pdf (2009, accessed 11 November 2019).

4. Haute Autorité de Santé. *Antibiotic therapy and prevention of bacterial resistance in healthcare organisations. Clinical practice guideline April 2008*. Saint-Denis La Plaine, France, https://www.has-sante.fr/jcms/c_665169/fr/strategie-

d-antibiotherapie-et-prevention-des-resistances-bacteriennes-en-etablissement-de-sante (2008, accessed 11 November 2019).

5. Pulcini C, Binda F, Lamkang AS, et al. Developing core elements and checklist items for global hospital antimicrobial stewardship programmes: A consensus approach. *Clin Microbiol Infect* 2019; **25**: 20–25. Epub ahead of print January 2019. DOI: 10.1016/j.cmi.2018.03.033.

6. Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship. *Clin Infect Dis* 2007; **44**: 159–177. Epub ahead of print 15 January 2007. DOI: 10.1086/510393.

7. Stichting Werkgroep Antibiotica Beleid. *A Teams Practical Guide. Antimicrobial Stewardship in the Netherlands*, https://web.archive.org/web/20201201132724/https://swab.nl/en/download-practice-guide (2018, accessed 1 December 2020).

8. Chung GWW, Wu JEE, Yeo CLL, et al. Antimicrobial stewardship: A review of prospective audit and feedback systems and an objective evaluation of outcomes. *Virulence* 2013; **4**: 151–157. Epub ahead of print 15 February 2013. DOI: 10.4161/viru.21626.

9. European Centre for Disease Prevention and Control. *Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals – protocol version 5.3*. Stockholm, https://ecdc.europa.eu/en/publications-data/point-prevalence-survey-healthcare-associated-infections-and-antimicrobial-use-3 (2016, accessed 15 May 2019).

10. Howard P, Pulcini C, Levy Hara G, et al. An international cross-sectional survey of antimicrobial stewardship programmes in hospitals. *J Antimicrob Chemother* 2014; **70**: 1245–1255. Epub ahead of print 18 December 2014. DOI: 10.1093/jac/dku497.

11. Van Gastel E, Costers M, Peetermans WEE, et al. Nationwide implementation of antibiotic management teams in Belgian hospitals: a self-reporting survey. *J Antimicrob Chemother* 2010; **65**: 576–580. Epub ahead of print 1 March 2010. DOI: 10.1093/jac/dkp470.

12. King A, Cresswell KM, Coleman JJ, et al. Investigating the ways in which health information technology can promote antimicrobial stewardship: a conceptual overview. *J R Soc Med* 2017; **110**: 320–329. Epub ahead of print 21 August 2017. DOI: 10.1177/0141076817722049.

13. Hand KS, Cumming D, Hopkins S, et al. Electronic prescribing system design priorities for antimicrobial stewardship: a cross-sectional survey of 142 UK infection specialists. *J Antimicrob Chemother* 2017; **72**: 1206–1216. Epub ahead of print 20 December 2017. DOI: 10.1093/jac/dkw524.

14. Cánovas-Segura B, Campos M, Morales A, et al. Development of a clinical decision support system for antibiotic management in a hospital environment. *Prog Artif Intell* 2016; **5**: 181–197. Epub ahead of print 2016. DOI: 10.1007/s13748-016-0089-x.

15. Curtis CE, Al Bahar F, Marriott JF. The effectiveness of computerised decision support on antibiotic use in hospitals: A systematic review. *PLoS One* 2017; **12**: e0183062. Epub ahead of print 24 August 2017. DOI: 10.1371/journal.pone.0183062.

16. UK Department of Health and Social Care. *Tackling antimicrobial resistance 2019-2024. The UK's five-year national action plan*, https://www.gov.uk/government/publications/uk-5-year-action-plan-for-antimicrobial-resistance-2019-to-2024

(2019, accessed 8 April 2019).

17. Baysari MT, Lehnbom EC, Li L, et al. The effectiveness of information technology to improve antimicrobial prescribing in hospitals: A systematic review and meta-analysis. *Int J Med Inform* 2016; **92**: 15–34. Epub ahead of print 2016. DOI: 10.1016/j.ijmedinf.2016.04.008.

18. Micallef C, Chaudhry NT, Holmes AH, et al. Secondary use of data from hospital electronic prescribing and pharmacy systems to support the quality and safety of antimicrobial use: a systematic review. *J Antimicrob Chemother* 2017; **72**: 1880–1885. Epub ahead of print 1 July 2017. DOI: 10.1093/jac/dkx082.

19. World Health Organisation. *The ICD-10 Classification of Mental and Behavioural Disorders. Clinical descriptions and diagnostic guidelines*. Geneva, https://www.who.int/classifications/icd/en/bluebook.pdf (1993, accessed 26 November 2018).

20. Health and Social Care Information Centre. *OPCS Classification of Interventions and Procedures Version 4.8 (SCCI0084 Amd 105/2015)*, https://digital.nhs.uk/data-and-information/information-standards/information-standards-and-data-collections-including-extractions/publications-and-notifications/standards-and-collections/scci0084-opcs-classification-of-interventions-and-procedures (2016, accessed 5 April 2019).

21. Nightingale PGG, Adu D, Richards NTT, et al. Implementation of rules based computerised bedside prescribing and administration: intervention study. *BMJ* 2000; **320**: 750–753. Epub ahead of print 18 March 2000. DOI: 10.1136/bmj.320.7237.750.

22. UK Health and Social Care Information Centre. *dm+d Implementation Guide (Secondary Care) V5.0*, https://www.nhsbsa.nhs.uk/sites/default/files/2017-02/Secondary_Care_Electronic_Prescribing_Implementation_Guidance_5_0.pdf (2015, accessed 15 April 2019).

23. European Committee on Antimicrobial Susceptibility Testing. *EUCAST Expert Rules Version 3.1. Intrinsic Resistance and Exceptional Phenotypes Tables. 26 September 2016*, http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Expert_Rules/Expert_rules_intrinsic_exceptional_V3.1.pdf (2016, accessed 1 May 2019).

24. Magiorakos A-P, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect* 2012; **18**: 268–281. Epub ahead of print March 2012. DOI: 10.1111/j.1469-0691.2011.03570.x.

25. Lim WS. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003; **58**: 377–382. Epub ahead of print 1 May 2003. DOI: 10.1136/thorax.58.5.377.

26. EU-JAMRAI. *Work Package 7. List of revised guidelines; tools and implementation methods for antibiotic stewardship: Hospital care*, https://web.archive.org/web/20201201115136/https://eu-jamrai.eu/wp-content/uploads/2019/04/EUjamrai_D7.1_RevisedGuidelinesATBS_HOSPITALCare_WP7_2018.10.31_Rev01.pdf (2018, accessed 1 December 2020).

27. Public Health England. *Start Smart–Then Focus. Antimicrobial Stewardship Toolkit for English Hospitals*, https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus (2015, accessed 13 November 2018).

28. Seaton RA, Nathwani D, Burton P, et al. Point prevalence survey of antibiotic use in Scottish hospitals utilising the Glasgow Antimicrobial Audit Tool (GAAT). *Int J Antimicrob Agents* 2007; **29**: 693–699. Epub ahead of print June 2007.

DOI: 10.1016/j.ijantimicag.2006.10.020.

29. Ibrahim OM, Polk RE. Antimicrobial use metrics and benchmarking to improve stewardship outcomes: Methodology, opportunities, and challenges. *Infect Dis Clin North Am* 2014; **28**: 195–214. Epub ahead of print 2014. DOI: 10.1016/j.idc.2014.01.006.

30. Athanassa Z, Makris G, Dimopoulos G, et al. Early Switch to Oral Treatment in Patients with Moderate to Severe Community-Acquired Pneumonia. *Drugs* 2008; **68**: 2469–2481. Epub ahead of print 2008. DOI: 10.2165/0003495-200868170-00005.

31. UK Health and Social Care Information Centre. UK SNOMED CT Drug Extension, RF2: Full, Snapshot & Delta, https://isd.digital.nhs.uk (2018).

32. R Core Team. R: A Language and Environment for Statistical Computing, https://www.r-project.org/ (2018).

33. Wickham H. tidyverse: Easily Install and Load the 'Tidyverse', https://cran.r-project.org/package=tidyverse (2017).

34. Wickham H, François R, Henry L, et al. dplyr: A Grammar of Data Manipulation, https://cran.r-project.org/package=dplyr (2019).

35. Dutey-Magni PF, Shallcross L. Ramses: R package for Antimicrobial Stewardship & Surveillance. [software programme] 2021. DOI: 10.5281/zenodo.4428900.

36. Dutey-Magni PF, Shallcross L. Ramses: R package for Antimicrobial Stewardship & Surveillance, [software documentation website] https://ramses-antibiotics.web.app/ (2021, accessed 13 January 2021).

37. Charani E, de Barra E, Rawson TM, et al. Antibiotic prescribing in general medical and surgical specialties: a prospective cohort study. *Antimicrob Resist Infect Control* 2019; **8**: 151. Epub ahead of print 13 December 2019. DOI: 10.1186/s13756-019-0603-6.

38. Vlahović-Palčevski V, Gyssens IC. Quality Indicators and Quantity Metrics of Antibiotic Use. In: Pulcini C, Ergönül Ö, Can F, et al. (eds) *Antimicrobial Stewardship*. Elsevier, pp. 29–37. Epub ahead of print 2017. DOI: 10.1016/B978-0-12-810477-4.00003-9.

39. Beaudoin M, Kabanza F, Nault V, et al. An Antimicrobial Prescription Surveillance System that Learns from Experience. *AI Mag* 2014; **35**: 15. Epub ahead of print 21 March 2014. DOI: 10.1609/aimag.v35i1.2500.

40. Lovis C, Colaert D, Stroetmann VNN. DebugIT for patient safety - improving the treatment with antibiotics through multimedia data mining of heterogeneous clinical data. *Stud Health Technol Inform* 2008; **136**: 641–6, http://www.ncbi.nlm.nih.gov/pubmed/18487803 (2008).

41. Morales A, Cánovas-Segura B, Campos M, et al. Proposal of a Big Data Platform for Intelligent Antibiotic Surveillance in a Hospital. In: Luaces O, Gámez JA, Barrenechea E, et al. (eds) *Advances in Artificial Intelligence. 17th Conference of the Spanish Association for Artificial Intelligence, CAEPIA 2016, Salamanca, Spain, September 14-16, 2016*, pp. 261–270. Epub ahead of print 2016. DOI: 10.1007/978-3-319-44636-3_24.

42. Wilkinson E. 'A blessing and a curse': the struggle to introduce e-prescribing. *The Pharmaceutical Journal*, https://www.pharmaceutical-journal.com/news-and-analysis/features/a-blessing-and-a-curse-the-struggle-to-introduce-e-prescribing/20206818.article (2019, accessed 12 August 2020).

43. NHS Digital. *Clinical Information Standards (beta). 21 January 2019*, https://digital.nhs.uk/about-nhs-digital/our-work/nhs-digital-data-and-technology-standards/clinical-information-standards (2019, accessed 8 November 2019).

44. Ivers N, Jamtvedt G, Flottorp S, et al. Audit and feedback: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev*. Epub ahead of print 13 June 2012. DOI: 10.1002/14651858.CD000259.pub3.

45. Brehaut JC, Colquhoun HL, Eva KW, et al. Practice Feedback Interventions: 15 Suggestions for Optimizing Effectiveness. *Ann Intern Med* 2016; **164**: 435. Epub ahead of print 15 March 2016. DOI: 10.7326/M15-2248.

46. van Santen KL, Edwards JR, Webb AK, et al. The Standardized Antimicrobial Administration Ratio: A New Metric for Measuring and Comparing Antibiotic Use. *Clin Infect Dis* 2018; **67**: 179–185. Epub ahead of print 2 July 2018. DOI: 10.1093/cid/ciy075.

47. Yardley L, Morrison L, Bradbury K, et al. The Person-Based Approach to Intervention Development: Application to Digital Health-Related Behavior Change Interventions. *J Med Internet Res* 2015; **17**: e30. Epub ahead of print 30 January 2015. DOI: 10.2196/jmir.4055.

48. Tabah A, Bassetti M, Kollef MH, et al. Antimicrobial de-escalation in critically ill patients: a position statement from a task force of the European Society of Intensive Care Medicine (ESICM) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Critically Ill Patient. *Intensive Care Med* 2020; **46**: 245–265. Epub ahead of print 28 February 2020. DOI: 10.1007/s00134-019-05866-w.

49. Berends MS, Luz CF, Friedrich AW, et al. AMR – An R Package for Working with Antimicrobial Resistance Data. *bioRxiv* 2019; 810622. Epub ahead of print 1 January 2019. DOI: 10.1101/810622.

Tables

Table 1. Overview of antimicrobial stewardship metrics

Domain	Measures
Antimicrobial consumption	Proportion of hospital admissions with at least one antimicrobial prescription Mean DOT (total duration of all prescriptions, including where there is overlap, eg. combination therapy) Mean LOT (time elapsed between the first and the last drug administration in an episode) Rate of DOT and LOT per 1,000 admissions[29]
Change of therapy (stop, switch, continue)	Proportion of first-line monotherapy or combination therapy leading to a different choice of therapy, continuation, or discontinuation
Intravenous to oral administration switch	Proportion of antimicrobial therapy episodes initiated by intravenous route being subsequently converted in full to oral route Mean time elapsed between intravenous therapy initiation and its complete conversion to oral therapy
Congruence with guidelines	Proportion of antimicrobial therapy episodes initiated with one of the first-line treatment options listed in the local empirical prescribing guidelines.
Microbial culture taking	Proportion of prescriptions belonging to a therapy episode initiated within 3 hours of a blood, urine, skin or sterile site microbial sample being taken

Notes: DOT: days of therapy; LOT: length of therapy

Table 2. Example structure of a therapy table

patient	time	mode	last WBC	WBC trend 72h	peak CRP in last 72 hours	Last CRP	...	ABCD criteria met?
X	2018-07-31 18:49:51	IV	11.0	-0.05	151	100	...	Yes
X	2018-07-31 19:49:51	IV	8.2	-0.02	151	100	...	Yes
X	2018-07-31 20:49:51	oral	8.2	-0.02	151	40	...	Yes
...	...	...	...	...	...	...	...	...

Notes: IV: intravenous; WBC: white blood cell count; CRP: C-reactive protein concentration.

Table 3. ABCD criteria: Considerations for intravenous to oral switch (see detailed criteria in appendix S8)

	Criteria	Markers
A	Afebrile for at least 24 hours	• temperature 36-38°C for 48 hours
B	Able to take oral medication *(not measured)*	• functional gastrointestinal tract • no malabsorption • no interaction with other medications • enteral drug form available • patient can swallow and tolerate oral fluids via a tube
C	Clinically improving	• no unexplained tachycardia (heart rate less than 90 beats/minute in the past 12 hours) • blood pressure stable in the past 24 hours • respiratory rate less than 20 breaths/minute in the past 24 hours • white cell count 4-12 x 10^9/L OR a high white cell count that is falling • falling C-reactive protein
D	Not suffering from certain deep-seated/high-risk infections	• Liver abscess • Osteomyelitis, Septic arthritis • Inadequately drained abscesses or empyema • Cavitating pneumonia • *Staphylococcus aureus* bacteraemia • Severe necrotising soft tissue infections • Severe infections during chemotherapy related neutropenia • Infected implants/prosthesis • Meningitis/encephalitis • Intracranial abscesses • Mediastinitis • Endocarditis • Exacerbation of cystic fibrosis/bronchiectasis

Table 4. Characteristics of admissions and antibacterial therapy by age group in six selected specialities (September 2017–August 2018)

	ALL ADMISSIONS					ADMISSIONS WITH ≥1 PRESCRIPTION(S)						
Age group (years)	Unique patients *N*	Admissions *N*	Mean LOS (SD)	LOS IQR	DOT per 1,000 bed-days [95% CI]	Admissions *N* (% total admissions)	Mean LOS (SD)	LOS IQR	Prescriptions *N*	Therapy episodes *N*	Mean LOT (SD)	LOT IQR	Mean DOT (SD)
18-24	3,088	3,937	1.9 (6.0)	0.2–1.7	788 [787–788]	1,020 (26)	4.6 (10.6)	0.8–4.7	2,294	1,069	4.1 (7.5)	1.0–4.4	5.7 (15.5)
25-34	4,455	5,626	2.2 (6.8)	0.2–1.8	789 [789–790]	1,439 (26)	5.8 (12.0)	0.9–5.9	3,523	1,541	5.1 (10.5)	1.0–5.2	6.9 (16.2)
35-44	5,056	6,389	2.5 (6.9)	0.2–2.0	795 [794–795]	1,617 (25)	6.6 (11.7)	1.0–7.4	4,176	1,748	5.7 (9.8)	1.0–6.4	7.8 (15.2)
45-54	6,596	8,423	2.7 (7.2)	0.2–2.3	827 [827–827]	2,307 (27)	7.1 (12.0)	1.2–8.2	5,965	2,523	5.8 (11.7)	1.0–6.3	8.3 (21.1)
55-64	7,627	9,977	3.6 (8.4)	0.2–3.5	834 [833–834]	3,281 (33)	8.5 (12.5)	1.6–9.8	8,989	3,707	6.2 (10.9)	1.1–7.0	9.2 (18.0)
65-74	8,448	11,230	4.4 (9.5)	0.2–4.7	740 [740–740]	4,277 (38)	8.9 (13.2)	1.8–10.3	11,620	4,868	5.6 (7.8)	1.3–7.0	8.5 (15.1)
75-84	7,196	9,815	6.3 (11.6)	0.4–7.4	674 [674–674]	4,440 (45)	10.7 (14.8)	2.1–13.5	12,900	5,164	5.9 (7.1)	2.0–7.4	9.4 (12.9)
85-94	4,082	5,668	8.6 (13.1)	0.8–11.0	618 [617–618]	2,986 (53)	12.9 (15.4)	2.8–17.0	9,196	3,558	6.2 (6.1)	2.0–8.1	10.1 (12.2)
95+	464	614	10.2 (13.5)	1.0–14.7	607 [606–608]	390 (64)	13.4 (14.9)	2.6–19.0	1,221	475	5.8 (5.3)	2.0–7.3	9.7 (11.2)
All ages	**46,853***	**61,679**	**4.2 (9.5)**	**0.2–4.1**	**726 [726–726]**	**21,757 (35)**	**9.1 (13.6)**	**1.6–10.7**	**59,884**	**24,653**	**5.8 (8.8)**	**1.3–7.0**	**8.7 (15.6)**

Notes: CI: confidence interval; DOT: days of therapy; IQR: interquartile range; LOS: length of stay (days); LOT: total length of therapy per admission (days); SD: standard deviation; *column does not add up to total as patients may change age group during the year.

Table 5. First-line therapy choice in CAP episodes in patients with a CURB-65 score of 0 or 1

	Therapy episodes n (% column total)	
First-line therapy	URB65=0	URB-65=1
Amoxicillin	205 (22.1)	249 (15.5)
Amoxicillin, clarithromycin	56 (6.0)	104 (6.5)
Azithromycin	4 (0.4)	6 (0.4)
Benzylpenicillin	2 (0.2)	3 (0.2)
Benzylpenicillin, clarithromycin	14 (1.5)	31 (1.9)
Benzylpenicillin, metronidazole	1 (0.1)	0 (0.0)
Ciprofloxacin	2 (0.2)	9 (0.6)
Clarithromycin	76 (8.2)	75 (4.7)
Clarithromycin, co-amoxiclav	261 (28.2)	541 (33.8)
Co-amoxiclav	104 (11.2)	211 (13.2)
Meropenem	9 (1.0)	24 (1.5)
Piperacillin/tazobactam	2 (0.2)	2 (0.1)
Ceftriaxone	10 (1.1)	2 (0.1)
Clarithromycin, moxifloxacin	2 (0.2)	4 (0.2)
Clarithromycin, piperacillin/tazobactam	4 (0.4)	9 (0.6)
Meropenem, vancomycin	7 (0.8)	10 (0.6)
Other	168 (18.1)	322 (20.1)
Total	**927 (100)**	**1,602 (100)**

Note: URB65: severity score based on CURB-65,[25] with mental confusion item set to zero: urea (blood urea nitrogen>7 mmol/L) (1 point), respirations per minute>30 (1 point), systolic blood pressure<90 mmHg (1 point), age≥65 years (1 point).