University of Dundee

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Nathwani, D.; Lawson, W.; Dryden, M.; Stephens, J.; Corman, S.; Solem, C.; Li, J.; Charbonneau, C.; Baillon-Plot, N.; Haider, S.; Eckmann, C.

Implementing criteria-based early switch/early discharge programmes: a European perspective

D. Nathwani[1], W. Lawson[2], M. Dryden[3], J. Stephens[4], S. Corman[4], C. Solem[4], J. Li[5], C. Charbonneau[6], N. Baillon-Plot[6], S. Haider[7] and C. Eckmann[8]

1) Ninewells Hospital and Medical School, Dundee, 2) Hammersmith Hospital, Imperial College Healthcare NHS Trust, London, 3) Hampshire Hospitals NHS Foundation Trust, Winchester, Hampshire, UK, 4) Pharmerit International, Bethesda, MD, 5) Pfizer Inc., San Diego, CA, USA, 6) Pfizer Inc., Paris, France, 7) Pfizer Inc., Groton, CT, USA and 8) Klinikum Peine, Academic Hospital of Medical University Hannover, Peine, Germany

Abstract

Early switch (ES) from intravenous (IV) to oral antibiotic therapy programmes is increasingly included as a component of hospital antimicrobial stewardship initiatives that aim to optimize antimicrobial therapy while limiting toxicity and resistance. In terms of prioritizing the most cost-effective stewardship interventions, ES has been seen as a 'low-hanging fruit', which refers to selecting the most obtainable targets rather than confronting more complicated issues. Administration of highly bioavailable oral antibiotics should be considered for nearly all non-critically ill patients and has been recommended as an effective and safe strategy for over two decades. However, to accrue the most benefit from ES, it should be combined with an early discharge (ED) plan, protocol, or care pathway. Benefits of this combined approach include improved patient comfort and mobility, reduced incidence of IV-line-related adverse effects, reduced IV antimicrobial preparation time, decreased hospital stays, reduced antimicrobial purchasing and administration costs, decreased patient deconditioning, and shortened recovery times. Results from published studies document decreases in healthcare resource use and costs following implementation of ES programmes, which in most studies facilitate the opportunity for ED and ED programmes. Barriers to the implementation of these programmes include clinician misconceptions, practical considerations, organizational factors, and a striking lack of awareness of IV to oral switch guidance. These and other barriers will need to be addressed to maximize the effectiveness of ES and ED programmes. As national antimicrobial stewardship programmes dictate the inclusion of ES and ED programmes within healthcare facilities, programmes must be developed and success must be documented.
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Corresponding author: J. Stephens, Pharmerit International, 4350 East West Highway, Suite 430, Bethesda, MD 20814, USA
E-mail: jstephens@pharmerit.com

Introduction

Intravenous (IV) antibiotics are typically prescribed for hospitalized patients with serious, often life-threatening, infections. Results from a European point prevalence survey in acute-care hospitals showed that the majority of patients with hospital-acquired infections (70%) received IV antibiotic therapy, although the rate ranged from a low of 50% in Scotland and Wales (UK) and Sweden to a high of 90% in Greece and Romania [1]. The duration of IV antibiotic therapy and hospital stays also varied widely among European countries [2,3]. Results from a study evaluating the treatment of patients with methicillin-resistant *Staphylococcus aureus* (MRSA) complicated skin and soft-tissue infections (cSSTIs) showed that duration of IV antibiotic therapy ranged from a low of 10.1 days in the UK to a high of 18.6 days in Poland. Mean hospital length of stay

ranged from a low of 15.2 days in the UK to a high of 25.0 days in Portugal [2].

In many cases, patients remain hospitalized for the full duration of IV antibiotic therapy. Although outpatient parenteral antibiotic therapy (OPAT) may be an option to reduce length of stay for some patients, these programmes are much more suited to areas where protracted parenteral antibiotic treatment is required (e.g. in bone and joint infections) or the availability of an effective, well-tolerated oral agent is limited. Furthermore, these programmes are not uniformly available throughout Europe [4], and evidence suggests that many patients who require home antibiotic therapy can be treated with an oral agent at hospital discharge, particularly where the course of antibiotic therapy is not prolonged [5]. Additionally, the burden of OPAT for both the patient and medical professional can be high. Patients require a line *in situ* which increases their risk of IV-line-related infections and, depending on OPAT model (e.g. OPAT centre, hospital unit administration), transportation to an outpatient infusion centre [6]. The impact of emerging novel single-dose or two-dose infusion therapies on the need for such OPAT infrastructure remains to be seen.

With the availability of potent, highly bioavailable oral antibiotics, there is an opportunity to promote switching from IV to oral therapy earlier and potentially reduce length of stay as a result. The availability of potent, highly bioavailable agents such as oral quinolones, macrolides and cephalosporins over the last two decades has transformed our ability to safely and effectively manage patients with a range of infections [7]. However, conversion from IV glycopeptides to oral therapy when treating serious, resistant Gram-positive infections remained a challenge until the introduction of linezolid in the early part of the last decade [2].

In this narrative review we discuss from a hospital standpoint the evidence to support the criteria for early switch (ES) and early discharge (ED), the value of these clinical programmes from a European perspective, and their implementation.

Early switch/early discharge criteria: defined

Many hospitals are including ES and ED criteria as part of their antimicrobial stewardship programmes. Antimicrobial stewardship is defined as

"coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administrations. The major objectives of antimicrobial stewardship are to achieve best clinical outcomes related

to antimicrobial use while minimizing toxicity and other adverse events, thereby limiting the selective pressure on bacterial populations that drives the emergence of antimicrobial-resistant strains. Antimicrobial stewardship may also reduce excessive costs attributable to suboptimal antimicrobial use" [8].

Such stewardship programmes aim to promote the appropriate use of antibiotics through the use of standards and guidelines, education, communication and audit [9]. Early switch programmes focus on optimizing drug regimens and should be used in conjunction with other stewardship programmes that focus on minimizing antibiotic resistance.

Although criteria to use in ES programmes for patients with community-acquired pneumonia are provided in national guidelines [10,11], guidance for patients with other types of infections is less clearly defined. Numerous criteria were evaluated in studies evaluating ES and ED programmes in patients with various types of infections including lower respiratory tract infections, urinary tract infections, SSTIs, intra-abdominal infections (Table 1) [7,9,12–25]. Most programmes assessed ES and ED eligibility 2–4 days following initiation of IV antibiotic therapy. Typically at this time, culture and sensitivity results are available and the decision to continue or change treatment course can be made. Intravenous antibiotic therapy is only recommended for patients who are severely ill, are unable to tolerate oral antibiotic therapy, or need antimicrobial coverage or tissue penetration not obtainable with oral antibiotic therapy [26].

Intravenous to oral switch programmes are described in detail in the medical literature [9,12,14,16,17,19–21,23,24,27]. Although various criteria are included in these programmes, in general, criteria can be divided into those that assess available oral therapies, the patient's clinical status, and the patient's ability to adequately absorb orally administered therapy. Examples of IV antibiotics that have an oral equivalent include many penicillins, fluoroquinolones and linezolid. Examples of

TABLE 1. Criteria used to determine patient eligibility for intravenous to oral antimicrobial switch therapy

Criteria
Temperature <38°C or >36°C for 24–48 h; normalizing body temperature; afebrile for at least 8–24 h [5,9,12,14,16–18,20,21,23,25]
No unexplained tachycardia, haemodynamic instability [7,9,14,16,21,23,25]
Clinical improvement, no clinical indication for intravenous therapy [5,7,9,12,17–20,23,25]
Oral fluids/food tolerated, no reason to believe oral absorption of antimicrobials may be poor; may be by nasogastric/gastric feeding tube [5,7,9,12,14–20,22,23,25]
Improving white blood cell count [5,9,12,14,16,17,20,23,25]
Improving C-reactive protein [5,9]
Suitable oral antimicrobial therapy [9,12,23,24,33]
No surgery scheduled within next 24–36 h [16,25]

TABLE 2. Patients with methicillin-resistant *Staphylococcus aureus* complicated skin and soft-tissue infections (n = 1502) meeting early switch criteria before intravenous discontinuation

Early switch criteria[a]	Patients		Days from start of IV antibiotic therapy to meeting criteria
	n	%	Median (Range)
Stable clinical infection	663	44.1	7.0 (0–98)
Afebrile/temperature <38°C for 24 h	839	55.9	5.0 (0–98)
White cell count normalizing (>4 × 10^9 but <12 × 10^9 cells/L)	734	48.9	7.0 (0–98)
No unexplained tachycardia	789	52.5	4.0 (0–98)
Systolic blood pressure ≥100 mmHg	815	54.3	3.0 (0–98)
Tolerates oral fluids/diet and able to take oral medication with no gastrointestinal absorption problems	804	53.5	3.0 (0–98)
Available bacteriology for MRSA cSSTIs sensitive to oral antibiotic treatment	970	64.6	2.0 (0–43)
Available bacteriology for MRSA cSSTIs sensitive to OPAT antibiotic treatment	1043	69.4	2.0 (0–43)
No surgery scheduled for next 36 h	530	35.3	4.0 (0–98)
No requirement for IV line except IV antibiotic therapy	465	31.0	4.0 (0–45)

cSSTI, complicated skin and soft-tissue infection; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; OPAT, outpatient parenteral antimicrobial therapy.
[a]Criteria must be met before actual MRSA active IV antibiotic discontinuation.

criteria used to assess a patient's clinical status include temperature, white blood cell count and C-reactive protein as well as general overall clinical improvement. Examples of criteria used to assess a patient's ability to tolerate oral therapy include the ability to tolerate oral food or fluids and no reason to believe that oral therapy will be poorly absorbed.

We evaluated the likelihood and timing of meeting standard ES and ED criteria in a chart review study that captured data on 1502 randomly selected patients with MRSA cSSTI in 12 European countries [2,25]. Data were obtained from hospital records of patients aged 18 years or older who were hospitalized with a documented MRSA cSSTI between 1 July 2010 and 30 June 2011 and discharged alive by 31 July 2011. Study investigators determined whether patients met each ES and ED criterion before discontinuation of IV therapy (either switching from IV to oral antibiotics or discharge) and discharge, respectively, and the number of days from cSSTI diagnosis to meeting criteria. Results of the evaluation are shown in Tables 2 and 3. Less than half of patients were identified as having a normalizing white blood cell count or stable clinical infection before discontinuation of IV therapy, with a median of 7 days from initiation of IV therapy to meeting these criteria. Patients were more likely to be afebrile, without tachycardia or hypotension, and to tolerate oral fluids/diet before discontinuation of IV therapy, and met these criteria earlier. With respect to early discharge criteria, over two-thirds of patients had stable clinical infections and improving white blood cell counts before discharge, but the median time to meeting these criteria (9 days) was longer than any other. Patients had other reasons to be hospitalized for a median of 8 days after cSSTI diagnosis, and less than half of patients met this criterion before discharge. Hence, it appears that the physician's assessment of clinical improvement and normalizing white blood cell counts would be important determinants of length of IV therapy and hospital stay

TABLE 3. Patients with methicillin-resistant *Staphylococcus aureus* complicated skin and soft-tissue infections (n = 1502) meeting early discharge criteria before actual discharge

Early discharge criteria	Patients		Days from diagnosis to meeting criteria
	n	%	Median (range)
No other reason to stay in the hospital except infection management	716	47.7	8.0 (0–122)
Stable mental status	796	50.3	2.0 (0–122)
Stable comorbid illness	755	50.3	4.0 (0–269)
Stable social situation	709	47.2	1.0 (0–122)
Stable clinical infection	1004	66.8	9.0 (0–138)
Afebrile/temperature <38°C for 24 h	1091	72.6	6.0 (0–138)
White cell count normalizing (>4 × 10^9 but <12 × 10^9 cells/L)	1032	68.7	8.0 (0–138)
No unexplained tachycardia	1007	67.0	5.0 (0–138)
Systolic blood pressure ≥100 mmHg	1028	68.4	4.0 (0–138)
Tolerates oral fluids/diet and able to take oral meds with no gastrointestinal absorption problems	1043	69.4	4.0 (0–138)
Available bacteriology for MRSA cSSTIs sensitive to oral antibiotic treatment	1101	73.3	2.0 (0–94)
Available bacteriology for MRSA cSSTIs sensitive to OPAT antibiotic treatment	1157	77.0	2.0 (0–94)
No surgery scheduled for next 36 h	658	43.8	5.0 (0–94)
No requirement for IV line except IV antibiotic therapy	626	41.7	6.0 (0–77)

if these criteria were applied prospectively. This finding is consistent with other studies, which suggest that the most common reason for not switching patients from IV to oral therapy is lack of clinical improvement [9,19].

Benefits of ES and ED programmes

In terms of prioritizing the most cost-effective stewardship interventions, ES has been seen as a 'low-hanging fruit', which in reference to stewardship, refers to selecting the most obtainable targets rather than confronting more complicated management issues [28]. These strategies require fewer resources and less effort than other stewardship activities; however, they are applicable to a variety of healthcare settings, including limited-resource hospitals, and have demonstrated significant financial savings.

The goals of an ES and ED programme are to decrease both the duration of IV antimicrobial therapy and the length of hospitalization while maintaining equivalent effectiveness. Benefits of ES programmes that facilitate switching from IV to oral antimicrobial therapy include the following: improved patient comfort and mobility [5,17], reduced incidence of IV-line related adverse effects such as catheter-related bacteraemia and phlebitis [5,16,29], reduced nursing or pharmacy time spent preparing IV antimicrobials [5,17,30], decreased hospital length of stay [2,5,17,18,20,24,29,31] and reduced antimicrobial purchasing and administration costs [17,24]. Additionally, when clinical outcomes are equivalent, patients prefer oral therapy to IV therapy [32]. Benefits of ES followed by ED programmes include a lower risk of line-related infections [29], less patient deconditioning [5,23], and a shorter recovery time [23].

The benefits of ES programmes are well recognized in patients with community-acquired pneumonia. Guidelines for IV to oral switch therapy in patients with community-acquired pneumonia are included in national guidelines published by the British Thoracic Society [10] and the Infectious Diseases Society of America/American Thoracic Society [11]; the latter additionally includes criteria for ED. The actual or potential benefits of ES and ED programmes were demonstrated in numerous studies enrolling patients with various types of infections including those caused by bacteria and fungi [7,9,12–25,29,33]. Indeed, in children with pyelonephritis early IV to oral switch was deemed non-inferior to IV therapy only, thereby providing further evidence to support this intervention [34].

Impact on healthcare resource use

Results from a 2003 Canadian study suggested a potential decrease in both IV treatment and hospitalization length for patients hospitalized with an MRSA SSTI and treated with vancomycin [15]. Study results showed the potential for a saving of 14.5 IV-therapy-days for patients who met ES criteria, had they been switched to a suitable oral agent. The most frequently cited reason for not switching to oral therapy was the lack of an effective oral treatment as the study was conducted before the availability of linezolid. Twelve years later, the significant potential for reduction in length of IV treatment and hospitalization has been identified for patients hospitalized with an MRSA cSSTI in Europe [25]. In this real-world study, 504 of the 1502 enrolled patients (33.6%) met ES and ED criteria. Administration of an oral therapy active against MRSA had the potential to decrease the IV therapy duration by 6.0 ± 5.5 days and hospital length of stay by 6.2 ± 8.2 days. Another study from the UK including 211 patients within the same disease context found that 29% of patients receiving at least 5 days of IV glycopeptide therapy were eligible for ES and ED, saving 649 inpatient days over a 6-month period. An additional 247 IV antibiotic therapy days were saved by patients meeting ES but not ED criteria [16].

Results from a study conducted in Norway, across a range of infections, showed a significant decrease in IV therapy duration and hospital length of stay following implementation of ES guidelines [24]. Unnecessary IV therapy decreased in duration from 3.4 to 1.4 days and hospital stay from 7.0 to 6.3 days following implementation of ES guidelines. Importantly, no difference in mortality, need to restart IV therapy, or readmission rate was found.

The impact of a three-step critical pathway among patients hospitalized with community-acquired pneumonia was evaluated in a randomized trial conducted in two tertiary care hospitals in Spain. Recommendations for early mobilization of patients, use of objective criteria for switching from IV to oral antibiotics, and specific criteria for hospital discharge were implemented using a printed checklist placed in the chart of patients randomized to the critical pathway arm, with the control group receiving usual care. Use of the critical pathway was associated with a 2-day reduction in median length of IV therapy and a 2-day reduction in length of stay, with no detriment to safety measured by adverse events, hospital readmission and mortality [29].

Impact on costs

Costs appear to be decreased in patients switched from IV to oral therapy. In a UK-based study conducted in medical and surgical wards across five UK hospital trusts, it was estimated that an ES and ED programme could save £363 per patient in total costs, of which £32 was attributable to switching from IV to oral antibiotic therapy alone [31]. Additional savings from

shorter hospital stays was also reported. Application of ES and and ED criteria retrospectively to patients with MRSA cSSTIs in a pan-European chart review study suggested potential savings of more than €2000 in bed-day costs per ED eligible patient [25].

Cost savings may be even greater if indirect costs for drug administration are included in calculations. In a Dutch study, the average time required for drug administration by volumetric pump, syringe pump, 'unaided' infusion bag, and direct IV injection represented between 11% and 53% of the total antibiotic therapy daily costs [30]. These indirect costs ranged from 13% to 113% of antibiotic acquisition costs. The cost to insert an IV catheter was not included in this cost calculation, but was estimated at €9.17. In a separate study of 694 patients with various infection types, application of an ES checklist was estimated to reduce nurse workload by 350 hours per year [19].

Implementation

Country-specific programmes
Many countries are starting to include IV to oral switch therapy initiatives as a component of their national antimicrobial stewardship programmes. However, antimicrobial stewardship programmes are not consistently used among European nations. Evidence from the European Society of Clinical Microbiology and Infectious Disease (ESCMID) Study Group for Antibiotic Policies (ESGAP) global survey of antimicrobial stewardship shows that 81% of European countries and 73% of European hospitals have antimicrobial stewardship standards; 66% of hospitals have antimicrobial stewardship programmes in place [35]. Various strategies are used by these stewardship programmes, with approximately 82% of European hospitals with stewardship programmes participating in this survey having an IV to oral switch programme [35].

The UK, Belgium, Austria and Germany all have antimicrobial stewardship initiatives that incorporate IV to oral switch therapy programmes. For example, the Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infections in England initiated the 'Start Smart—then Focus' programme. This national antimicrobial stewardship programme contains an IV to oral switch component (Fig. 1) [26]. This initiative focuses on a review of antimicrobial therapy 48 h after treatment initiation. The best practice standard for IV to oral switch therapy is that IV antibiotics be switched to oral therapy within 24 h of the patient meeting local switch criteria. Recommendations are to audit IV to oral switch programmes annually or monitor the consumption of IV compared with oral antimicrobial therapy.

The Scottish Antimicrobial Prescribing Group (SAPG) is responsible for implementation of the Scottish Management of

Antimicrobial Resistance Action Plan (ScotMARAP) [36]. The ScotMARAP includes IV to oral switch guidance for patients receiving empirical antimicrobial therapy.

Sequential IV to oral therapy is also a component of the majority of antimicrobial stewardship programmes supported by the Belgian Antibiotic Policy Coordination Committee (BAPCOC) [37]. The BAPCOC supports the development of antibiotic management teams through policy guidance and federal funding for antibiotic managers. Sequential IV to oral therapy guidelines are used by approximately 79% of the antibiotic management teams.

Intravenous to oral switch programmes are core activities of antimicrobial stewardship programmes in Austria and Germany [38]. The quality indicator states that hospitals should have written recommendations for parenteral-to-oral switch antimicrobial therapy available and that they are updated every 2 years. Similarly, a quality indicator was developed and proposed for assessing the appropriate IV to oral switch of bioavailable antibiotics. This is believed to be a feasible and clinically relevant approach to measuring the implementation of the interventions and may provide the quality improvement leverage within healthcare systems [14].

Lastly, to ensure greater consistency of stewardship indicators, the Transatlantic Taskforce on Antimicrobial Resistance [TATFAR] group has developed through a formal Delphi process structural and process indicators for stewardship; the availability of IV to oral switch guidance is a key supplementary indicator (D. Nathwani, personal communication). Such international guidance again supports the value of this stewardship strategy.

Hospital-specific programmes
Numerous examples of hospital-specific ES and ED programmes are available in the published medical literature [7,9,12–24]. Most programmes evaluate a patient's ability to take oral therapy 2–3 days after initiation of IV therapy (Fig. 2). Although different approaches to programme implementation are used, most of these programmes through the use of policies, treatment guidelines, surveillance data, educational resources, targeted intervention and audit aim to reduce the number of IV inpatient antibiotic days. Successful programmes typically include immediate feedback, which is directed to the physician-in-charge and contain patient-specific, clear, unambiguous advice [7].

Barriers to implementation

Country level
Several barriers to implementation of ES and ED programmes at a national level are described in the medical literature. The inclusion of an IV to oral switch programme in a national antimicrobial stewardship initiative does not guarantee the
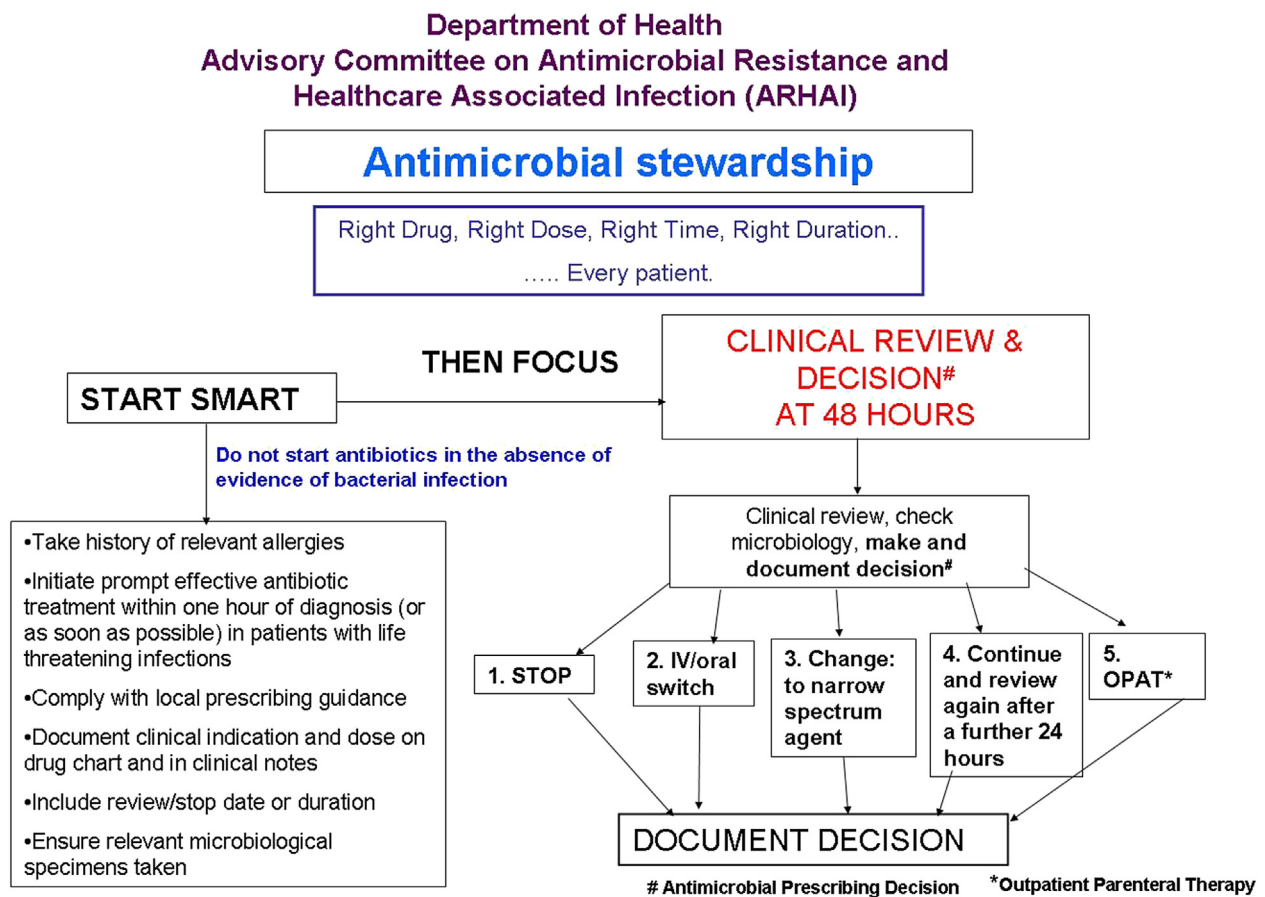
FIG. 1. Antimicrobial Stewardship in Secondary Care, Antimicrobial Stewardship Algorithm [26].

acceptance or success of the programme at a hospital level [39]. Evidence from England suggests that acceptance of nationally or centrally developed programmes is slow. Prescribing appears to be influenced by the cultural beliefs of the patient and the prescriber, patient demand, socio-economic factors, and clinical autonomy, not national guidelines [40,41]. To improve uptake of national guidelines, recommendations are to develop consensus documents through collaboration of key stakeholders at the national level and disseminate these recommendations at a local level through the identification and professional development of local leaders [42].

Unit/hospital level

Barriers to ES and ED at a unit/hospital level include staffing time constraints, staffing changes and prescribing etiquette [43,44]. Reassessment of antimicrobial therapy after 48–72 h of treatment is often neglected because of time constraints and changes in staffing [19]. Information on why the antimicrobial was started and the goal of therapy may not be communicated among clinical teams resulting in the unnecessary continuation of antibiotic therapy including unnecessary IV therapy. In many

institutions, prescribing etiquette, or the reluctance of junior medical staff members to change the prescribing habits of more senior staff members, determines or influences treatment patterns [43]. Changes to antibiotic regimens are often made by more senior medical staff, who typically review patient medical charts less frequently than junior staff members.

Prescriber level

Prescribers are often hesitant to modify an apparently efficacious empirical therapy, especially if there is no direct oral equivalent for the IV formulation [45]. To overcome this barrier, precise recommendations should be offered when requesting a change from an IV antibiotic with no direct oral equivalent formulation. Potentially, ES and ED programmes may benefit by administration of IV antibiotics with highly bioavailable oral formulations, by offering precise guidelines regarding which oral antibiotics can be substituted for IV antibiotics or be used to treat specific conditions, or by providing an infectious disease consult [46]. Other prescriber-specific barriers identified include time constraints, rapid rotation of physicians in charge of patients, and the belief that IV therapy is superior to oral therapy [22,44].

FIG. 2. Example of intravenous to oral switch policy [9]. Reproduced from McCallum *et al.* [9] with permission from the authors.

Conclusions

The benefits of ES and ED programmes to patients and providers are many. Patient benefits include increased comfort and mobility, decreased risk of IV-line related adverse effects, and improved recovery times. Provider benefits include decreased IV preparation time, potential for reduced hospital length of stays, and decreased antimicrobial purchasing and administration costs. Therefore, ES and ED programmes have the potential to offer improved quality of care at reduced total cost, thereby providing a powerful and persuasive argument for adoption and implementation [47].

Antimicrobial stewardship programmes should incorporate not only ES and ED initiatives that focus on optimizing drug regimens but additional initiatives that focus on minimizing drug resistance.

Recommendations for implementing ES and ED programmes in hospitals are shown in Table 4. It is important for hospitals to engage key stakeholders early in the planning process, in order to identify and respond to potential barriers to adherence. Multi-pronged approaches that provide clear and explicit feedback are the most likely to succeed in altering prescribing behaviour. Measuring and feeding back the benefits of these programmes will also be instrumental in generating continued buy-in from practitioners and administrators [48].

TABLE 4. Recommendations for implementing early switch/early discharge programmes for antibiotics

- Identify the size of the problem locally and opportunities for early switch/early discharge through audit and harness local support from clinicians and administrators
- Outline an evidence-based plan of implementation with measurable criteria for success for implementation
- Engage a multidisciplinary team in the design of the programme, including key stakeholders from the clinical service and infection specialists (e.g Infectious Diseases, Microbiology, and Pharmacy and Nursing departments). Identify clinician champions where possible
- Use multiple intervention tools to promote good antibiotic prescribing practices, including educational activities and materials, audit and feedback, and reminders. Ensure these tools are tested/piloted before spread to all parts of the hospital; prevent duplication of process—embed or integrate into similar existing work such as review of need for peripheral venous cannulae
- Provide prescribers with timely and regular feedback that is clear and directive, and deliver specific recommendations for improved prescribing (e.g. antibiotic dose, route and frequency)
- Evaluate the programme performance regularly to demonstrate its value and benefits to key stakeholders

Transparency declaration

Acknowledgement

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