Pan-European early switch/early discharge opportunities exist for hospitalised patients with methicillin-resistant Staphylococcus aureus complicated skin and soft-tissue infections

Nathwani, D.; Eckmann, C.; Lawson, W.; Stephens, J.M.; Macahilig, C.; Solem, C.T.; Simoneau, D.; Chambers, R.; Li, J. Z.; Haider, S.

Published in:
Clinical Microbiology and Infection

DOI:
10.1111/1469-0691.12632

Publication date:
2014

Document Version
Publisher's PDF, also known as Version of record

Pan-European early switch/early discharge opportunities exist for hospitalized patients with methicillin-resistant *Staphylococcus aureus* complicated skin and soft tissue infections

D. Nathwani[1], C. Eckmann[2], W. Lawson[3], J. M. Stephens[4], C. Macahilig[5], C. T. Solem[4], D. Simoneau[6], R. Chambers[7], J. Z. Li[8] and S. Haider[9]

1) *Ninewells Hospital & Medical School, Dundee, UK,* 2) *Klinikum Peine & Medical University Hannover, Peine, Germany,* 3) *Imperial College Healthcare NHS Trust, London, UK,* 4) *Pharmerit International, Bethesda, MD,* 5) *Medical Data Analytics, Parsippany, NJ, USA,* 6) *Pfizer IO, Paris, France,* 7) *Pfizer Inc., Collegeville, PA,* 8) *Pfizer Inc., La Jolla, CA and* 9) *Pfizer Inc., Groton, CT, USA*

Abstract

The objective of this study was to document pan-European real-world treatment patterns and healthcare resource use and estimate opportunities for early switch (ES) from intravenous (IV) to oral antibiotics and early discharge (ED) in hospitalized patients with methicillin-resistant *Staphylococcus aureus* (MRSA) complicated skin and soft tissue infections (cSSTIs). This retrospective observational medical chart review study enrolled 342 physicians across 12 European countries who collected data from 1542 patients with documented MRSA cSSTI who were hospitalized (July 2010 to June 2011) and discharged alive (by July 2011). Data included clinical characteristics and outcomes, hospital length of stay (LOS), MRSA-targeted IV and oral antibiotic use, and ES and ED eligibility according to literature-based and expert-validated criteria. The most frequent initial MRSA-active antibiotics were vancomycin (50.2%), linezolid (15.1%), clindamycin (10.8%), and teicoplanin (10.4%). Patients discharged with MRSA-active antibiotics (n = 480) were most frequently prescribed linezolid (42.1%) and clindamycin (19.8%). IV treatment duration (9.3 ± 6.5 vs. 14.6 ± 9.9 days; p <0.001) and hospital LOS (19.1 ± 12.9 vs. 21.0 ± 18.2 days; p 0.162) tended to be shorter for patients switched from IV to oral treatment than for patients who received IV treatment only. Of the patients, 33.6% met ES criteria and could have discontinued IV treatment 6.0 ± 5.5 days earlier, and 37.9% met ED criteria and could have been discharged 6.2 ± 8.2 days earlier. More than one-third of European patients hospitalized for MRSA cSSTI could be eligible for ES and ED, resulting in substantial reductions in IV days and bed-days, with potential savings of €2000 per ED-eligible patient.

Keywords: Antibiotic treatment, clinical criteria, economics, IV-to-oral switch, length of stay
Original Submission: 22 December 2013; **Revised Submission:** 16 March 2014; **Accepted:** 22 March 2014
Editor: M. Paul
Article published online: 27 March 2014
Clin Microbiol Infect 2014; **20**: 993–1000
10.1111/1469-0691.12632

Corresponding author: J. M. Stephens, Pharmerit International, 4350 East West Highway, Suite 430, Bethesda, MD 20814, USA
E-mail: jstephens@pharmerit.com

Introduction

Hospitalization for complicated skin and soft tissue infections (cSSTI) caused by methicillin-resistant *Staphylococcus aureus* (MRSA) represents a substantial clinical and economic burden [1,2]. The standard treatment option for MRSA cSSTI is the administration of intravenous (IV) antibiotics (frequently vancomycin), often involving hospitalization.

Decreasing hospital capacity (http://www.hope.be/03activities/quality_eu-hospitals/eu_country_profiles/00-hospitals_in_europe-synthesis_vs2011-06.pdf) and increasing economic pressure underscore the importance of optimizing care. One key antibiotic stewardship strategy with the potential to improve efficiency is promoting IV-to-oral (PO) switch treatment to facilitate hospital discharge while maintaining equivalent outcomes [3]. PO antibiotic use can help to optimize inpatient bed use, and IV-to-PO switch treatment is not a

resource-intensive core stewardship strategy (it is implementable in resource-limited settings) [4].

European hospitals should observe and document current practice to identify opportunities for early switch (ES) from IV to PO antibiotic treatment, and early discharge (ED) from inpatient to outpatient IV or PO antibiotic treatment, to improve the delivery of effective and fiscally prudent management of infections. Throughout Europe, inpatient IV vancomycin therapy is used for MRSA cSSTI throughout treatment, although PO antibiotic options are available. We therefore conducted a pan-European real-world study of treatment patterns, healthcare resource use and criteria-based assessment of ES/ED opportunities in patients with MRSA cSSTI.

Methods

This retrospective observational medical chart review study enrolled patients from 12 European countries (the UK, Ireland, France, Germany, Italy, Spain, Portugal, Austria, Greece, Poland, Slovakia, and the Czech Republic). An observational study design was chosen to determine real-world treatment patterns and resource use. Medical charts of hospitalized patients with MRSA cSSTI (admitted from 1 July 2010 to 30 June 2011, and discharged alive by 31 July 2011) were randomly sampled for data on clinical and resource utilization outcomes. Patients prescribed IV-to-PO switch antibiotic treatment for MRSA cSSTI were non-randomly oversampled (after random sample quotas were achieved) to allow a sufficient sample size to compare IV-only and IV-to-PO switch MRSA-targeted treatment. The protocol did not specify which antibiotics to select in the random sample or oversample, and site investigators were blinded to the sponsor to minimize bias in the selection of medical charts. Real-world treatment patterns and outcomes were documented, and ES/ED eligibility criteria (Table 1) were identified.

Patient inclusion and exclusion criteria

Patients were identified by hospital-based infectious disease specialists, internal medicine specialists (with infectious disease subspecialties), and medical microbiologists. Patients had a new, microbiologically confirmed MRSA cSSTI (e.g. deep/extensive cellulitis, infected wound or ulcer, major abscess, or other soft tissue infections requiring substantial surgical intervention) and received $\geq$3 days of IV anti-MRSA antibiotics.

Exclusion criteria included: treatment for the same cSSTI within 3 months of hospitalization (to assess re-hospitalizations resulting from an initial cSSTI, without including recurrent infections); suspected/proven diabetic foot infections, osteomyelitis, infective endocarditis, meningitis, joint infections, necrotizing soft tissue infections, gangrene, prosthetic joint infection, or prosthetic implant/device infection; significant concomitant infection at other sites; immunosuppression; pregnancy/lactation in women; or enrolment in another cSSTI-related clinical trial.

Study populations and subgroups

The primary study population included patients whose medical charts were randomly selected for the purpose of describing MRSA cSSTI patient characteristics, clinical management patterns, and ES/ED eligibility across Europe.

Antibiotic treatment patterns were described for a confirmed MRSA-active treatment subgroup (labelled indication for MRSA treatment or with confirmatory culture susceptibility). A second subgroup was compared for IV days and hospital length of stay (LOS) between patients switched from IV to PO treatment and those receiving IV-only treatment.

Key outcomes

The key study endpoints and ES/ED criteria utilized included both IV-related and LOS-related outcomes (Table 1).

Actual LOS and medical treatment patterns were determined from the primary study population. Time to MRSA-active treatment, number of lines of MRSA-active treatment, length of inpatient MRSA-active IV treatment, frequency of antibiotic changes, first and last MRSA-active antibiotics used and frequency of MRSA-targeted antibiotics at hospital discharge were determined for the subgroup receiving MRSA-active treatment.

ES/ED eligibility criteria for use in real-world clinical settings were created from literature review [5–13] and expert consensus opinion (Table 1). Patients meeting ES/ED criteria were identified within the primary study population. A hypothetical length of IV treatment (days between the start of initial MRSA-targeted IV treatment and the date when the last key ES criterion was met) and hypothetical LOS (days between hospital admission for cSSTI or the date on which cSSTI was diagnosed and the date when the last ED criterion was met) were then calculated (Table 1).

To determine the potential economic impact of ED, bed-days saved for ED-eligible patients were multiplied by unit costs of providing a hospital bed in the year 2008 (http://www.who.int/choice/country/country_specific/en/index.html), in international dollars, adjusted for inflation to 2012 and converted to Euros (http://epp.eurostat.ec.europa.eu/tgm/table.do?tab=table&language=en&pcode=tec00118&tableSelection=1&footnotes=yes&labeling=labels&plugin=1). Costs included the 'hotel' component of hospital costs, and not drug/diagnostic test costs. To provide a cost reflective of the patient distribution among the countries sampled, a cross-country average was calculated (Appendix S1).

TABLE 1. Definitions of study endpoints and early switch (ES)/early discharge (ED) criteria

IV-related endpoints	
Actual length of IV usage	Time between initiation of MRSA-targeted IV therapy and last day of MRSA-targeted IV therapy (for patients switched from IV to PO) or discharge (IV-only patients)
ES eligibility	At minimum, the following key criteria needed to be met prior to actual IV discontinuation: • Stable clinical infection • Afebrile/temperature of <38°C for 24 h • WBC count normalizing, WBC count not $<4 \times 10^9$/L or $>12 \times 10^9$/L • No unexplained tachycardia • Systolic blood pressure of ≥100 mm Hg • Patient tolerates PO fluids/diet and able to take PO medications with no gastrointestinal absorption problems Additional criteria related to ES that were assessed, but not required to be documented, included: • Available bacteriology for cSSTI caused by MRSA that is sensitive to PO treatment • Available bacteriology for cSSTI caused by MRSA that is sensitive to OPAT • No surgery scheduled within the next 36 h • No requirement for IV line other than administration of IV antibiotic therapy
Hypothetical IV days	Days between the day of initial MRSA-targeted IV antibiotic administration and the date when the patient satisfied the last of the key ES criteria listed above
Potential reduction in IV days	Difference in days between actual and hypothetical IV days among ES-eligible patients
LOS-related endpoints	
LOS (from beginning of cSSTI episode)	Number of days from cSSTI index[a] and hospital discharge
ED eligibility	At minimum, the following criteria needed to be met prior to discharge: • All key ES eligibility criteria listed above • No other reason to stay in hospital except infection management Additional criteria related to ED that were assessed, but not required to be documented, included: • Stable mental status • Stable comorbid illnesses • Stable social situation
Hypothetical LOS	Number of days from cSSTI index[a] to the date when the patient satisfied all key required criteria and actual LOS
Potential reduction in LOS (bed-days saved)	Difference in days between actual and hypothetical LOS among ED-eligible patients

cSSTI, complicated skin and soft-tissue infection; IV, intravenous; LOS, length of stay; MRSA, methicillin-resistant *Staphylococcus aureus*; OPAT, outpatient parenteral antibiotic therapy; PO, oral; WBC, white blood cell.
[a]Date of admission for patients admitted for cSSTI; cSSTI diagnosis date otherwise. In cases where the cSSTI diagnosis date was earlier than the admission date, the admission date was used.

Statistical analysis

Descriptive analyses were conducted for all study populations. Within the MRSA-active treatment subgroup, patients were stratified by antibiotic administration pattern (IV only or IV-to-PO switch). For categorical or ordinal outcomes, Pearson's chi-square tests were used for bivariate statistical testing. For continuous outcomes, Student's *t*-tests and one-way analysis of variance tests were used. All inferences were made on the assumption of a two-sided test with alpha = 0.05.

Results

The primary study population comprised 1502 patients randomly selected by 342 physicians for chart abstraction. The MRSA-active treatment subgroup included 1468 patients who received at least one medication with confirmed anti-MRSA activity. The subgroup for IV-only vs. IV-to-PO switch comparisons included 1508 patients (1468 receiving MRSA-active treatment plus 40 oversampled patients who received MRSA-active IV-to-PO switch treatment).

Patient and clinical characteristics

Most patients were white males, with an average age at hospital admission of 60.9 years (Table 2). The primary reason for hospitalization was MRSA cSSTI (80.8%); the most common infections were deep/extensive cellulitis (26.1%), surgical site infections of post-traumatic wounds (26.0%), and infected ulcers (24.7%). Of the patients, 38.7% required surgical intervention for cSSTI management. Among the main sample, 1475 (98.2%) patients had at least one cSSTI wound

TABLE 2. Patient and disease characteristics

	Primary study population (*N* = 1502)
Demographic and clinical characteristics	
Age (years), mean ± SD	60.9 ± 16.5
Male, *n* (%)	917 (61.1)
White, *n* (%)	1395 (92.9)
Charlson Comorbidity Index, mean ± SD	2.3 ± 2.2
Infection characteristics	
Primary reason for hospitalization is treatment of MRSA cSSTI, *n* (%)	1214 (80.8)
Timing of cSSTI index diagnosis, *n* (%)	
At hospital admission	1246 (83.0)
1–3 days after admission	48 (3.2)
≥4 days after admission	208 (13.8)
Type of cSSTI, *n* (%)	
Surgical site infection or post-traumatic wound	390 (26.0)
Major abscess	265 (17.6)
Infected ulcer	371 (24.7)
Deep/extensive cellulitis	392 (26.1)
Other (including infected burn)	84 (5.6)
cSSTI location, *n* (%)	
Head/skull/neck	62 (4.1)
Torso/abdomen	456 (30.4)
Upper extremity	224 (14.9)
Lower extremity	760 (50.6)
Sepsis, defined as severe sepsis or septic shock during cSSTI episode, *n* (%)	258 (17.2)
Procedures and treatments	
Surgical procedures for cSSTI treatment, *n* (%)	582 (38.7)
Total number of procedures, mean ± SD	0.4 ± 0.6
Patient switched from IV to PO inpatient MRSA-active treatment, *n* (%)	161 (10.7)
Patient received MRSA-targeted treatment at discharge, *n* (%)	483 (32.2)

cSSTI, complicated skin and soft tissue infection; IV, intravenious; MRSA, methicillin-resistant *Staphylococcus aureus*; PO, oral; SD, standard deviation.

culture performed; among these, susceptibility testing was performed in 1319 (89.4%).

Most patients had one or more comorbidities at admission (most commonly: diabetes, 31.3%; and peripheral vascular disease, 23.8%). Many patients (17.2%) had sepsis. Patient demographic and clinical characteristics of the main study population were similar to those of the subgroups. However, diabetes and cerebrovascular comorbidities and infected ulcer and infected burn cSSTI diagnoses were more common in patients with IV-only treatment than in those with IV-to-PO switch treatment.

Actual treatment patterns and healthcare resource utilization

Within the primary study population, 1224 patients (81.5%) received only IV MRSA-active treatment; 161 (10.7%) were switched from IV to PO MRSA-active treatment while hospitalized; 83 (5.6%) had other MRSA-active treatment patterns (e.g. concomitant use of PO and IV antibiotics through discharge or switch from IV to PO to IV); and 34 (2.3%) received antibiotic treatment not confirmed to be MRSA-active. The mean (± standard deviation (SD)) LOS from cSSTI diagnosis to discharge was 20.6 ± 17.4 days. Other resource utilization included surgical procedures (debridement/incision/drainage) in 38.7% of patients.

MRSA-active treatment subgroup. The mean (±SD) time to administration of MRSA-active treatment was 1.2 ± 2.7 days following MRSA cSSTI diagnosis. The mean (±SD) length of MRSA-active treatment by any route (i.e. IV, intramuscular, or PO) was 14.8 ± 9.9 days, and the mean length of MRSA-active IV treatment was 14.0 ± 9.7 days. One thousand one hundred and eighty-nine patients (81.0%) were treated with a single MRSA-active antibiotic regimen, 261 patients (17.8%) changed at least one MRSA-active regimen and 18 patients (1.2%) modified their antibiotic regimen twice while in the hospital (changes from IV to PO formulations of the same medication were not counted as a regimen change). Reasons for the change of antibiotic or dosing were not always documented in medical charts. The most common reason for vancomycin dose change was drug-level maintenance (38.6%), and those for teicoplanin dose change were protocol/guidelines (27.4%) and loading dose (19.2%). Among 161 (11.0%) patients who switched to PO treatment during their hospital stay, the most common reasons for switching included improvement of symptoms (50.9%), convenience (5.6%), and lack of drug resistance (5.6%).

The most frequently prescribed initial MRSA-active antibiotic was vancomycin, followed by linezolid, clindamycin, and teicoplanin (Table 3). Analysis of final inpatient MRSA-active antibiotic regimens showed that, during the course of treatment, the proportion of inpatients receiving vancomycin decreased, and the proportion of inpatients receiving linezolid increased. In the MRSA-active treatment subgroup, 480 patients (32.7%) were discharged on either parenteral (7.3%) or PO (92.7%) MRSA-active antibiotics. Linezolid was the most frequently prescribed antibiotic (42.1%, with >98% receiving PO linezolid) at discharge.

IV-to-PO switch MRSA-active oversampled subgroup. The duration of IV therapy was significantly shorter and hospital LOS was numerically shorter for patients switched from IV to PO treatment (*n* = 197) than for patients receiving IV treatment throughout (*n* = 1228). The mean (±SD) duration of IV treatment for patients switched from IV to PO treatment was 9.3 ± 6.5 days, and that for patients receiving IV-only treatment was 14.6 ± 9.9 days (p <0.001). Mean (±SD) hospital LOS was 19.1 ± 12.9 days for patients switched from IV to PO treatment and 21.0 ± 18.2 days for patients receiving IV-only treatment (p 0.162).

Actual and hypothetical outcomes based on ES and ED eligibility

Five hundred and four (33.6%) patients met all of the ES criteria listed in Table 1 prior to IV discontinuation. Among these 504 ES-eligible patients, the actual mean (±SD) length of

TABLE 3. Targeted methicillin-resistant *Staphylococcus aureus* (MRSA) antibiotic selection by line of treatment during hospitalization and at discharge[a]

	First MRSA-active antibiotic (*N* = 1468)		Last inpatient MRSA-active antibiotic (*N* = 1468)		Discharge MRSA-active antibiotic (*N* = 480)	
	n	%[a]	*n*	%	*n*	%
Vancomycin	737	50.2	609	41.5	11	2.3
Linezolid	222	15.1	310	21.1	202	42.1
Clindamycin	159	10.8	141	9.6	95	19.8
Teicoplanin	153	10.4	158	10.8	14	2.9
Ciprofloxacin	101	6.9	105	7.2	58	12.1
Daptomycin	87	5.9	98	6.7	1	0.2
Rifampicin	62	4.2	60	4.1	34	7.1
Tigecycline	48	3.3	54	3.7	2	0.4
TMP-SMX	45	3.1	56	3.8	57	11.9
Fusidic acid	21	1.4	26	1.8	16	3.3
Doxycycline	14	1.0	25	1.7	21	4.4

TMP-SMX, trimethoprim–sulfamethoxazole.
[a]Data presented for the subgroup of patients in the random MRSA-active treatment cohort. Because the listed medications may have been used together and these categories are not mutually exclusive, the sum of percentages is >100%.

IV treatment was 15.4 ± 9.2 days, but hypothetically could have been 9.4 ± 7.7 days if days after all ES criteria had been met were removed, suggesting a potential reduction in IV treatment duration of 6.0 ± 5.5 days (Fig. 1).

A total of 569 (37.9%) patients met all of the ED criteria listed in Table 1 prior to hospital discharge. The actual and hypothetical mean LOS for these 569 ED-eligible patients were 20.8 ± 14.8 and 14.6 ± 11.9 days, respectively, suggesting a potential reduction in LOS of 6.2 ± 8.2 days (Fig. 1).

On the assumption of an average cost of €345 per bed-day (Appendix S1), the total savings for the randomly selected population would be over €1.2 million, with more than €2000 in bed-day cost savings being realized per ED-eligible patient.

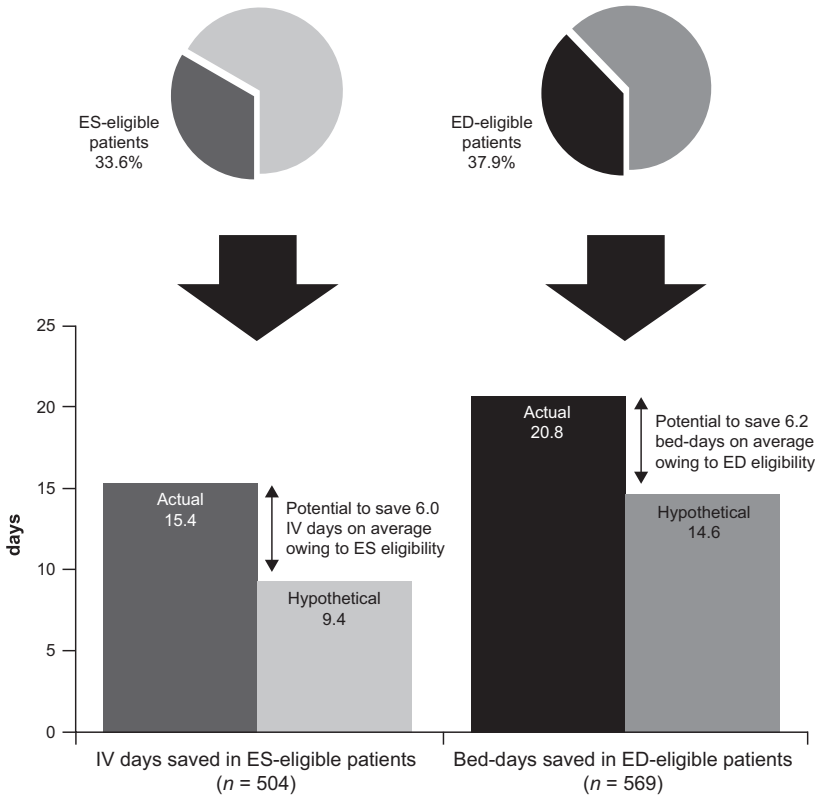

FIG 1. Comparison of actual and hypothetical intravenous (IV) days and bed-days in early switch (ES)-eligible and early discharge (ED)-eligible patients.

Discussion

This is the first pan-European study evaluating actual real-world clinical practice and ES and ED opportunities in hospitalized patients with MRSA cSSTI. More than one-third of patients met ES (33.6%) or ED (37.9%) criteria. Wide variability in ES and ED eligibility was found across countries, which may reflect local policies or guidelines. A potential 6.2-day reduction in LOS (~€2000 reduction in bed-day costs) per ED-eligible patient suggests missed opportunities, because the observed reduction was only 2 days for IV-to-PO switch patients. More consistent use of a criteria-based ES and ED protocol could further shorten LOS by 4 bed-days for eligible patients.

A growing demand exists for real-world comparative effectiveness data in many countries, as clinical trial populations are often not reflective of a typical patient population seen in clinical practice. Our study provides a snapshot of treatment patterns by using consistent methodology across 12 countries, making this analysis unique, as few databases in Europe have both clinical and resource utilization details.

The low frequency of use of co-trimoxazole was surprising in this real-world study; however, it is possible that initial treatment with IV co-trimoxazole is less likely to be used when patients are first admitted, are more unstable, and microbiological diagnosis is less certain. Evidence to support the use of co-trimoxazole in cSSTI is old and weak, with no clinical trials for this indication. Furthermore, oral co-trimoxazole is recommended for community-acquired MRSA in ambulatory settings [14]. Once patients have stabilized and microbiology has confirmed susceptibility, its use for PO switch is more likely to occur, which was reflected by its greater use as a discharge antibiotic in our study.

Our study results are similar to those of published studies enrolling patients with various infectious diseases in several European countries and the USA, which suggest that ~30% to >50% of patients could be switched from IV to PO treatment [7,10,15–18] and that 20–30% of patients could be discharged home sooner when on PO antibiotics [7,10,17]. Most of these studies were conducted in one institution [7,10,16,18] and enrolled patients with various infections; some studies provided aggregated economic projections based on single countries [7,19].

Our study is unique, as the patient population is large and captures real-world practice data and potential opportunities across Europe specifically for MRSA cSSTI. Approximately 17% of our study population had sepsis, which was a higher proportion than observed in a randomized study that compared linezolid and vancomycin for MRSA cSSTI [20], suggesting that potential ES/ED opportunities may be even greater in patients with non-MRSA-confirmed cSSTI.

As this study was a retrospective medical chart review, some study design limitations are inherent. Information was dependent on or was estimated on the basis of medical records (e.g. dates on which patients met the criteria for ES/ED). When prescribed medications were not indicated for MRSA but were potentially MRSA-active, susceptibility information was only available if documented in medical charts. As this was a retrospective study, not all ES/ED criteria could be applied at inclusion to determine actual (rather than potential) cost savings. For this reason, patients switched from IV to PO antibiotics were compared with those receiving IV-only treatment. The results could be influenced by a disease severity bias in those receiving IV-to-PO switch treatment vs. IV-only treatment; the latter's potentially less severe disease and better health status may result in a shorter LOS. Although IV-only treatment was associated with significantly higher rates of diabetes and cerebrovascular disease than switch from IV to PO treatment, the incidence of sepsis was similar between treatment groups.

Patients hospitalized with cSSTI were selected according to prespecified definitions. Furthermore, the study design masked the identities of the study sponsor from recruited physicians. The investigators created a design and robust application of ES/ED criteria with a systematic approach that was effective elsewhere [17]. The applicability of the ES/ED criteria in this study needs to be validated prospectively. However, awareness of prospective evaluation of ES/ED criteria might influence the participating centres, potentially jeopardizing the results.

The medical literature identifies several cost drivers for the treatment of serious multidrug resistant bacteria that are dependent on the type and severity of the infections (e.g. for cSSTI: drug acquisition costs; hospital LOS; need for patient isolation; and development of complications, such as abscess or the requirement for surgery) [21,22]. Increased LOS is the key cost driver [23]. Identification of ES/ED opportunities for patients with MRSA cSSTI hospitalized in Europe could lead to significant reductions in LOS, thereby providing a mechanism for improving throughput and increasing efficiency. This cost-efficiency strategy is recognized as an approach whereby more patients can receive healthcare with the same investment in fixed costs [24]. ES/ED will not only provide resource advantages, but will also underpin the premise of safe, effective and high-quality, patient-centred care—a core European healthcare delivery strategy (http://www.euro.who.int/__data/assets/pdf_file/0007/98233/E91397.pdf). These data could provide the stimulus for the development of effective implementation strategies (e.g. care pathways) for managing cSSTI within European hospitals and the outpatient setting [25].

Conclusions

Our data suggest that a substantial number of patients with MRSA cSSTI could be switched to PO therapy and discharged earlier from hospital, resulting in cost savings across European healthcare systems. The development and implementation of a pragmatic care pathway for patients with MRSA cSSTI enabling early identification, ES and, ultimately, ED of patients safely treatable for MRSA cSSTI is warranted.

Acknowledgements

Editorial/medical writing support was provided by B. Lesher of AGW Communications, and was funded by Pharmerit International. The support provided by R. Beck, Jr of Engage Scientific Solutions consisted solely of manuscript formatting, with no contribution to editorial content, and was funded by Pfizer Inc. The authors thank M. Li of Pharmerit International for her support with manuscript formatting.

Clinical experts involved in the original study design: UK—D. Nathwani and W. Lawson; Germany—C. Eckmann; France—E. Senneville; Spain—E. Bouza; Italy—G. Ippolito; Austria—A. Wechsler Fördös; Portugal—G. do Carmo; Greece—G. Daikos; Slovakia—P. Jarcuska; Czech Republic—M. Lips and M. Pelichovska; and Ireland—C. Bergin.

The results from this study were presented in part as a poster presentation at the 23rd European Congress of Clinical Microbiology and Infectious Diseases, held in Berlin, Germany, 27–30 April 2013.

Funding

This study was sponsored by Pfizer Inc.

Transparency Declarations

D. Nathwani has received no financial support for the production of this manuscript. D. Nathwani has received lecture fees, travel support for attending meetings and fees for advisory boards from Bayer, Astellas, AztraZeneca, Durata, and Pfizer. C. Eckmann has received lecture fees, travel support for attending meetings and fees for advisory boards from Bayer, AstraZeneca, Cubist, Durata, and Pfizer. W. Lawson has received support for attending meetings, travel support and fees for advisory boards from Astellas and Pfizer. J. M. Stephens and C.T. Solem are employees of Pharmerit International, who were paid consultants to Pfizer in connection with this study. C. Macahilig is an employee of Medical Data Analytics, a subcontractor to Pharmerit International for this project. D. Simoneau, R. Chambers, J. Z. Li and S. Haider are employees of Pfizer.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Cost per bed-day assumptions.

References

1. Edelsberg J, Berger A, Weber DJ, Mallick R, Kuznik A, Oster G. Clinical and economic consequences of failure of initial antibiotic therapy for hospitalized patients with complicated skin and skin-structure infections. *Infect Control Hosp Epidemiol* 2008; 29: 160–169.
2. Hatoum HT, Akhras KS, Lin SJ. The attributable clinical and economic burden of skin and skin structure infections in hospitalized patients: a matched cohort study. *Diagn Microbiol Infect Dis* 2009; 64: 305–310.
3. Dellit TH, Owens RC, McGowan JE Jr *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.
4. Goff DA, Bauer KA, Reed EE, Stevenson KB, Taylor JJ, West JE. Is the 'low-hanging fruit' worth picking for antimicrobial stewardship programs? *Clin Infect Dis* 2012; 55: 587–592.
5. Chapman AL, Dixon S, Andrews D, Lillie PJ, Bazaz R, Patchett JD. Clinical efficacy and cost-effectiveness of outpatient parenteral antibiotic therapy (OPAT): a UK perspective. *J Antimicrob Chemother* 2009; 64: 1316–1324.
6. Cunha BA. Oral antibiotic therapy of serious systemic infections. *Med Clin North Am* 2006; 90: 1197–1222.
7. Desai M, Franklin BD, Holmes AH *et al.* A new approach to treatment of resistant gram-positive infections: potential impact of targeted IV to oral switch on length of stay. *BMC Infect Dis* 2006; 6: 94.
8. Matthews PC, Conlon CP, Berendt AR *et al.* Outpatient parenteral antimicrobial therapy (OPAT): is it safe for selected patients to self-administer at home? A retrospective analysis of a large cohort over 13 years. *J Antimicrob Chemother* 2007; 60: 356–362.
9. Nathwani D, Moitra S, Dunbar J, Crosby G, Peterkin G, Davey P. Skin and soft tissue infections: development of a collaborative management plan between community and hospital care. *Int J Clin Pract* 1998; 52: 456–460.
10. Parodi S, Rhew DC, Goetz MB. Early switch and early discharge opportunities in intravenous vancomycin treatment of suspected methicillin-resistant staphylococcal species infections. *J Manag Care Pharm* 2003; 9: 317–326.
11. Seaton RA, Bell E, Gourlay Y, Semple L. Nurse-led management of uncomplicated cellulitis in the community: evaluation of a protocol incorporating intravenous ceftriaxone. *J Antimicrob Chemother* 2005; 55: 764–767.
12. Tice AD, Rehm SJ, Dalovisio JR *et al.* Practice guidelines for outpatient parenteral antimicrobial therapy. IDSA guidelines. *Clin Infect Dis* 2004; 38: 1651–1672.

13. Lee SL, Azmi S, Wong PS. Clinicians' knowledge, beliefs and acceptance of intravenous-to-oral antibiotic switching. Hospital Pulau Pinang. *Med J Malaysia* 2012; 67: 190–198.
14. Napolitano LM. Early appropriate parenteral antimicrobial treatment of complicated skin and soft tissue infections caused by methicillin-resistant *Staphylococcus aureus*. *Surg Infect (Larchmt)* 2008; 9(suppl 1): s17–s27.
15. Buyle FM, Metz-Gercek S, Mechtler R *et al.* Prospective multicentre feasibility study of a quality of care indicator for intravenous to oral switch therapy with highly bioavailable antibiotics. *J Antimicrob Chemother* 2012; 67: 2043–2046.
16. Di Giammarino L, Bihl F, Bissig M, Bernasconi B, Cerny A, Bernasconi E. Evaluation of prescription practices of antibiotics in a medium-sized Swiss hospital. *Swiss Med Wkly* 2005; 135: 710–714.
17. Dryden M, Saeed K, Townsend R *et al.* Antibiotic stewardship and early discharge from hospital: impact of a structured approach to antimicrobial management. *J Antimicrob Chemother* 2012; 67: 2289–2296.
18. Mertz D, Koller M, Haller P *et al.* Outcomes of early switching from intravenous to oral antibiotics on medical wards. *J Antimicrob Chemother* 2009; 64: 188–199.
19. Gray A, Dryden M, Charos A. Antibiotic management and early discharge from hospital: an economic analysis. *J Antimicrob Chemother* 2012; 67: 2297–2302.
20. Itani KM, Dryden MS, Bhattacharyya H, Kunkel MJ, Baruch AM, Weigelt JA. Efficacy and safety of linezolid versus vancomycin for the treatment of complicated skin and soft-tissue infections proven to be caused by methicillin-resistant *Staphylococcus aureus*. *Am J Surg* 2010; 199: 804–816.
21. Itani KM, Weigelt J, Li JZ, Duttagupta S. Linezolid reduces length of stay and duration of intravenous treatment compared with vancomycin for complicated skin and soft tissue infections due to suspected or proven methicillin-resistant *Staphylococcus aureus* (MRSA). *Int J Antimicrob Agents* 2005; 26: 442–448.
22. Zilberberg MD, Shorr AF, Micek ST *et al.* Epidemiology and outcomes of hospitalizations with complicated skin and skin-structure infections: implications of healthcare-associated infection risk factors. *Infect Control Hosp Epidemiol* 2009; 30: 1203–1210.
23. Nathwani D. Impact of methicillin-resistant *Staphylococcus aureus* infections on key health economic outcomes: does reducing the length of hospital stay matter? *J Antimicrob Chemother* 2003; 51(suppl 2): ii37–ii44.
24. Ward WJ Jr, Spragens L, Smithson K. Building the business case for clinical quality. *Healthc Financ Manage* 2006; 60: 92–98.
25. Eron LJ, Lipsky BA, Low DE, Nathwani D, Tice AD, Volturo GA. Managing skin and soft tissue infections: expert panel recommendations on key decision points. *J Antimicrob Chemother* 2003; 52(suppl 1): i3–i17.