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Economic evaluation of the treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSIs) from the national payer perspective: introduction of a new treatment to the patient journey. A simulation of three European countries

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ORIGINAL RESEARCH

Economic evaluation of the treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSIs) from the national payer perspective: introduction of a new treatment to the patient journey. A simulation of three European countries

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ABSTRACT

Background: The aim of this study was to develop a spending predictor model to evaluate the direct costs associated with the management of ABSSSIs from the National health-care provider's perspective of Italy, Romania, and Spain.

Methodology: A decision-analytic model was developed to evaluate the diagnostic and clinical pathways of hospitalized ABSSSI patients based on scientific guidelines and real-world data. A Standard of Care (SoC) scenario was compared with a dalbavancin scenario in which the patients could be discharged early. The epidemiological and cost parameters were extrapolated from national administrative databases (i.e., hospital information system). A probabilistic sensitivity analysis (PSA) and one-way sensitivity analysis (OWA) were performed.

Results: Overall, the model estimated an average annual number of patients with ABSSSIs of approximately 50,000 in Italy, Spain, and Romania. On average, the introduction of dalbavancin reduced the length of stay by 3.3 days per ABSSSI patient. From an economic perspective, dalbavancin did not incur any additional cost from the National Healthcare perspective, and the results were consistent among the countries. The PSA and OWA demonstrated the robustness of these results.

Conclusion: This model represents a useful tool for policymakers by providing information regarding the economic and organizational consequences of an early discharge approach in ABSSSI management.

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ABSSSIs; dalbavancin; economic evaluation; Italy; Spain; Romania

1. Introduction

In 2013, the US Food and Drug Administration (FDA) coined the acronym 'ABSSSIs' (Acute Bacterial Skin and Skin Structure Infections) to include all complicated infections of the skin and soft tissues [1]. ABSSSIs include severe skin and soft tissue infections, such as cellulitis, erysipelas, cutaneous abscesses, infected wounds, and ulcers, that usually require inpatient management, surgical procedures and parenteral antibiotic therapy.

Inpatient treatment of ABSSSIs imposes a significant economic burden on the health-care system. In the United States, over 750,000 patients per year are admitted to the hospital for ABSSSI, incurring an estimated cost of >6 billion dollars [2]. Nearly 10% of all US hospital admissions are attributed to ABSSSIs [3], while in Europe ABSSSIs may account up to 15% of all infections treated in hospitals [4].

ABSSSIs are primarily caused by Gram-positive pathogens, mainly *Staphylococcus aureus* and *Streptococcus pyogenes*, but are also caused by Gram-negative and anaerobic bacteria, particularly in polymicrobial infections [5].

S. aureus has historically been the leading cause of ABSSSIs, although its clinical relevance has rapidly increased over the previous 15 years due to the emergence of methicillin-resistant S. aureus (MRSA) [6]. *S. aureus* is considered the predominant pathogen in all regions across North America, Latin America, and Europe. The rates of MRSA vary among these continents, and the highest proportion is observed in the Americas [6–8]. *Staphylococcus aureus* is also the most common cause of complicated Skin and Soft Tissue infections (cSSTIs) in Europe. According to a study investigating more than 3000 cSSTI-associated isolates sampled from 19 countries in and around Europe between 2008 and 2009, nearly one-third of the isolates were *S. aureus*, and of these isolates, approximately one-half were MRSA [7,8].

In Europe, the incidence of MRSA has changed over the previous 10 years; however, in the European Union, MRSA

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accounts for 16.7% of all *Staphylococcus aureus* isolates. In 10 countries, the incidence of MRSA in infections sustained by *Staphylococcus aureus* was 10–25%. However, an incidence of MRSA >25% was reported in Italy and Spain, and accounted almost for 50% of *S. aureus* isolates in Romania [9].

Due to the emerging incidence of bacterial resistance to multiple antibiotics, ABSSSIs are increasingly challenging to treat [10]. Furthermore, the choice of treatment is often complicated by the urgency to treat with an antibiotic therapy before having obtained a confirmed microbiological diagnosis.

Due to the increasing incidence of MRSA, particularly in community-acquired infections, vancomycin, which is the standard therapy for documented MRSA infections, is often the treatment of choice if MRSA is suspected. However, the use of this agent might me associated with suboptimal outcomes [11–13].

The guidelines of the Infectious Diseases Society of America recommend therapy with β-lactam or clindamycin for mild/moderate ABSSSIs and non-purulent ABSSSI and vancomycin plus piperacillin/tazobactam for severe, non-purulent ABSSSI [5]. The empirical treatment of purulent ABSSSIs should cover MRSA with doxycycline or trimethoprim/sulfamethoxazole (TMP/SMX) in moderate cases and vancomycin, daptomycin, linezolid, telavancin, or ceftaroline in severe cases [14]. However, clinical MRSA isolates have progressively shown a decreasing susceptibility or resistance to these drugs [15]. Consequently, the treatment of ABSSSIs currently requires a greater need for hospitalization, which is associated with a net increase in costs [16].

Dalbavancin is a novel long-acting lipoglycopeptide that was approved by the FDA in May 2014 and the European Medicines Agency (EMA) in February 2015 for the treatment of ABSSSIs caused by susceptible Gram-positive organisms. It is active against gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), and minimum inhibitory concentrations (MICs) are consistently <0.125 μg/ml, lower than most other anti-MRSA agents. In vitro data against MRSA, suggest that dalbavancin is 4–8 times more potent than vancomycin. Moreover, dalbavancin has a β half-life (elimination half-life) of >8 days (~200 hours) and a terminal half-life of >14 days (~346 hours), allowing for clinical safety and efficacy assessment using a once-weekly dosing regimen of 1000 mg on day1 and 500 mg on day 8 or 1500 mg in one administration (3 vials) [17,18].

Due to its long-acting bactericidal activity and unique dosing schedule, dalbavancin allows clinicians to endorse early discharge (ED) programs, enabling patients to complete the treatment after hospital discharge. ED programs have been shown to significantly reduce the use of hospital resources [19] in the management of MRSA infections, particularly complicated skin and skin structure infections [19,20].

The first objective of this study was to develop a spending predictor model to evaluate the direct costs associated with the hospital management of ABSSSIs from the perspective of the National Healthcare provider. The second objective was to collect data on the direct costs of hospital management of ABSSSIs in three European countries, namely, Italy, Romania, and Spain. Finally, the third objective was to apply country-specific cost inputs to the spending predictor model to compare the estimated direct costs of the hospital treatment of ABSSSIs between patients treated with standard antibiotics therapy and those treated with dalbavancin.

2. Methods

Authors followed methodological indications of the ISPOR Budget Impact Analysis – Principles of Good Practice [21]. Due to the lack of data availability and as advised by the above-mentioned article, whenever data from the clinical trials and/or the official administrative databases were not accessible, clinical experts' opinions were used as data source [21].

2.1. Health-care systems and perspective

A decision-analytic model was built based on the current clinical practices in three European countries to simulate the hospital management of ABSSSI patients receiving empiric treatment with antibiotics (Figure 1).

The choice of the Countries was based on access to healthcare and public spending per capita data. Most of 28 Countries in the European Union have a publicly directly or indirectly funded National system that provides universal access to healthcare. However, national expenditures on healthcare widely vary around the EU28 mean value (€ 2,323 per capita) [22]. Based on the relevance of incremental costs/savings to the public budget, the simulation included the two EU28 countries closest to the mean (Italy, € 2,339, and Spain, € 2,199) and the country with the lowest per capita annual expenditure (Romania, € 809).

The model was generated from the perspective of the National health-care provider.

2.2. Eligible population

An algorithm consistent with the IDSA guidelines published in 2014 [14] was used to identify severe purulent and non-purulent patients requiring observation for over 72 h. The eligible patients were identified using the national administrative databases of each Country (Appendix A). The algorithm included all acute inpatient admissions. The longest data collection period per country was selected based on the available data as follows: between 1 January 2006 and 31 December 2010 in Italy, 1 January 2010 and 31 December 2013 in Romania, and 1 January 2006 and 31 December 2015 in Spain.

2.3. Intervention comparison and model structure

The decisional tree was designed to follow IDSA guidelines and as illustrated in Figure 1: In the model, all ABSSSI patients can be hospitalized for purulent or non-purulent ABSSSIs (first probabilistic node). The patients initially received an empirical antibiotic treatment to cover both Gram-positive and Gram-negative infections.

The model considers that the patients could receive vancomycin, intravenous linezolid, or teicoplanin as Gram-positive therapy plus piperacillin tazobactam as Gram-negative therapy (current intervention or Standard of Care, SoC) or the new intervention of dalbavancin as the Gram-positive therapy of choice in addition to piperacillin tazobactam. The choice of antibiotic combination therapy (antibiotic for gram-positive plus piperacillin tazobactam) was made according for the IDSA guidelines on the treatment of severe ABSSIs [5].

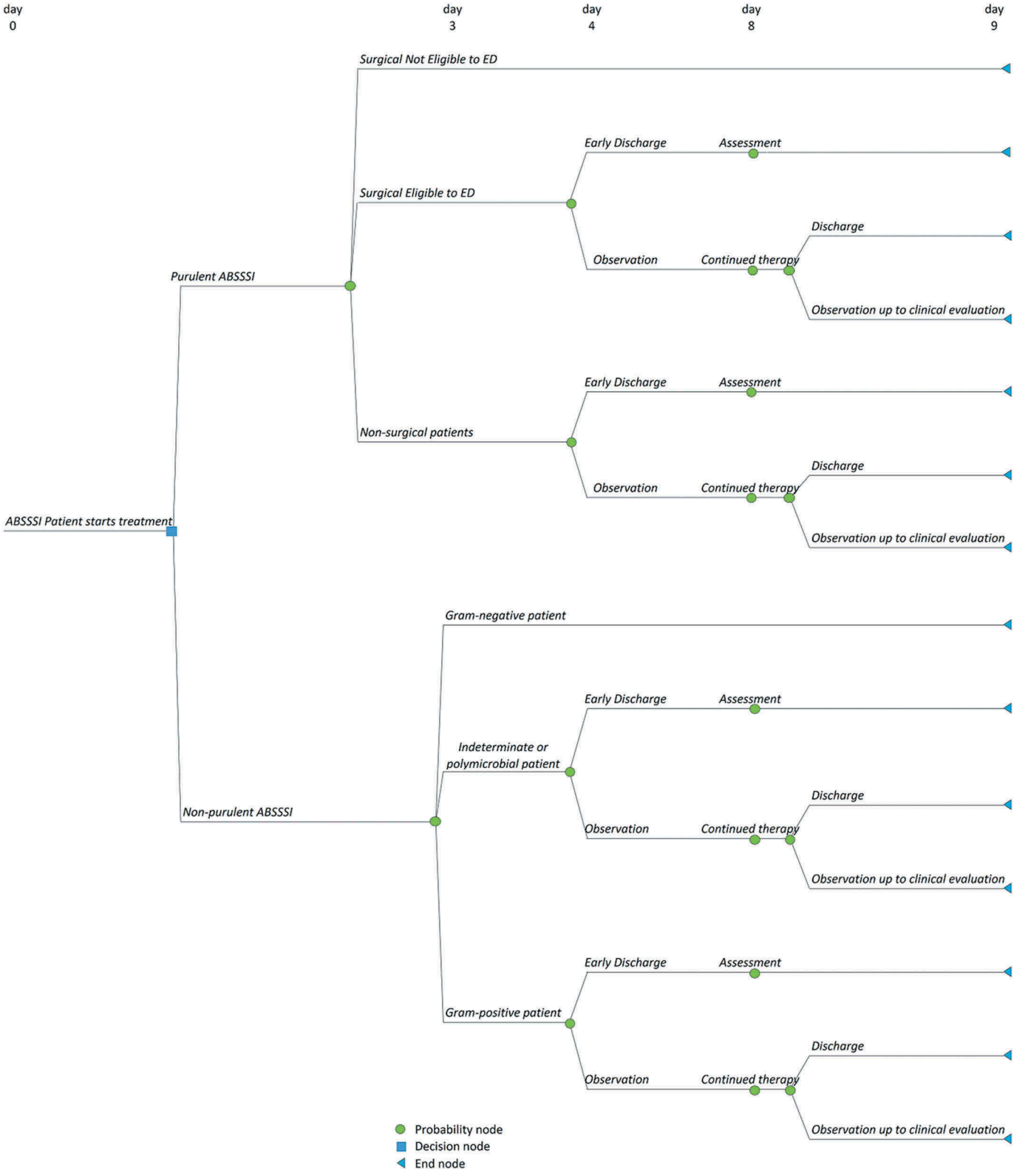

Figure 1. Decision tree model structure.

After receiving the first dose of the empirical antibiotic therapy, the patients may progress to one of the following treatment pathways (branch of possible events): purulent surgical eligible for early discharge (ED), purulent surgical not eligible for ED, purulent not surgical, non-purulent Gram-positive, non-purulent Gram-negative, non-purulent indeterminate or polymicrobial. Each pathway (except for purulent surgical not eligible for ED) includes the following states: discharge on day 4, observation up to day 8, discharge on day 9, or observation up to the clinical evaluation. Pathways were developed following IDSA guidelines and clinical expert opinion, and designed to retrace ABSSSI treatment pattern in the real practice: for patients with

severe infections, clinical reassessment is usually performed 72 h after the hospitalization (discharge on day 4 or prolonged observation until day 8), while treatment duration is indicated to be 7–14 days (discharge on day 8 or prolonged observation, corresponding to a hospitalization for more than 8 days). Dalbavancin allows the discharge at day 4, due to its half-life that permits an antibiotic coverage of 14 days. The transition probabilities change according to the treatment (SoC or dalbavancin) administered on day 0 (tree's decision node).

2.4. Non-monetary inputs to the model

The input value of the probabilistic nodes is reported in Table 1.

The purulent and non-purulent occurrence rates and the time to discharge in the SoC scenario were estimated based on data obtained from the real-world databases of each Country (details are provided in Appendix), while the discharge probabilities in the dalbavancin scenario were estimated based on the opinion consensus of experts (co-authors of this manuscript). However, the transition probabilities in Spain were assumed to be the same as those applied to Italy due to the lack of Country-specific data.

The cut-offs for the eligibility to early discharge (ED) were set based on the distribution of the length of stay of the included patients stratified as purulent or non-purulent. For both purulent and non-purulent infections, eligibility for early discharge was attributed to patients with a length of stay ≥4, considering the differences in medical treatments as suggested by clinical experts.

All purulent infections were considered sustained by *S. aureus*, while the distribution of the bacteria responsible for the non-purulent infections was estimated based on the consensus among the experts. The treatment patterns followed by the patients with purulent and non-purulent infections and the discharge probabilities in the SoC scenario, were based on real-world data obtained from the administrative databases of each Country. For the sake of avoiding an over-complication of the decisional tree, all the therapies included in the model were assumed to have 100% efficacy.

2.5. Cost inputs to the model

The inputs used to inform the model were based on a literature review and expert clinical opinion [23]. The following cost

Table 1. Transition probabilities: SoC (real-world data) vs. Dalbavancin (expert opinion)[a].

Number of patients with ABSSSIs	ITALY	ROMANIA	SPAIN	References
Non-purulent patients – Sort of bacteria		*Model value*		
Indeterminate	71%	18%	70%	Expert opinion
Polymicrobial	17%	18%	10%	
Gram-negative	7%	9%	7%	
Gram-positive	6%	56%	13%	
Purulent patients – Sort of origin		*Model value*		
Surgical	26%	95%	70%	Expert opinion
Non-surgical	74%	5%	30%	
Surgical eligible for ED	50%	30%	50%	
Surgicl not eligible for ED	50%	70%	50%	
Discharge distribution with dalbavancin				References
Non-purulent patients: Indeterminate or polymicrobial		*Model value*		
Discharge (4 day)	50%	60%	60%	Expert opinion
Discharge (8 day)	70%	70%	70%	
Non-purulent patients: Gram-positive		*Model value*		
Discharge (4 day)	70%	70%	70%	Expert opinion
Discharge (8 day)	80%	90%	90%	
Purulent patients: Surgical		*Model value*		
Discharge (4 day)	70%	70%	50%	Expert opinion
Discharge (8 day)	80%	80%	70%	
Purulent patients: Non-surgical		*Model value*		
Discharge (4 day)	70%	65%	40%	Expert opinion
Discharge (8 day)	80%	80%	70%	
Discharge distribution with standard therapy				References
Non-purulent patients: Indeterminate or polymicrobial		*Model value*		
Discharge (4 day)	11%	10%	11%	Data from administrative databases
Discharge (8 day)	42%	35%	42%	
Non-purulent patients: Gram-positive		*Model value*		
Discharge (4 day)	11%	31%	11%	Data from administrative databases
Discharge (8 day)	58%	55%	58%	
Purulent patients: Surgical		*Model value*		
Discharge (4 day)	11%	55%	11%	Data from administrative databases
Discharge (8 day)	50%	65%	50%	
Purulent patients: Non-surgical		*Model value*		
Discharge (4 day)	12%	33%	12%	Data from administrative databases
Discharge (8 day)	57%	67%	57%	

a in the table are shown the percentage of discharge at each decision point of the analytic model that has been used to describe patients' pathway. Each pathway (except for purulent surgical not eligible for ED) includes the following states: discharge on day 4, observation up to day 8 and discharge on day 9, or observation up to the clinical evaluation. Full distribution is shown in Appendix B in Table A2.

assumptions were used to inform the model based on a consensus of expert opinion.

- **Hospitalization cost**: Consistent with the perspective of the study, the hospitalization costs were determined exclusively based on National Diagnosis-Related Group (DRG) tariffs. Consequently, from the perspective of the payer, the patient's length of stay (LoS) at a hospital is irrelevant to the cost of hospitalization. However, a length of stay >8 days – as described in the treatment patterns suggested by the clinical experts – implies additional risks to the patient, which could bear incremental costs to the payer as follows:
  - **Additional risks**: The model assumes that if a patient is not discharged by day 8, an increased possibility of adverse events is associated with the length of hospital stay.
  - **Incremental costs**: The incremental costs were estimated as the difference between the direct costs associated with a patient LoS ≤8 days and the cost incurred by patients with a LoS >8 days.
- A systematic review of the existent literature was performed to identify the direct costs associated with each state of the model. Table 2 shows the inputs used to inform the cost estimate of each intervention. Consistent to Summary of Product Characteristics (SmPC) of each medicament included in the analysis and clinical practice, all the costs relative to treatments' adverse events were considered not sensitive, with the only exception to the renal adverse event concomitant to vancomycin administration that requires medical treatment in addition of therapy's withdrawal. The inputs used to evaluate the additional costs incurred with vancomycin are summarized in Appendix B.

2.6. Statistical analysis

The results are presented as the net difference between the direct costs incurred by the SoC treatment and those incurred by the dalbavancin treatment.

A probabilistic sensitivity analysis (PSA) and one-way deterministic sensitivity analysis (OSA) were performed to estimate the intrinsic variability in the inputs used to inform the model.

The probabilistic distribution used for the PSA was obtained by applying generally reported development of economic evaluation models and distinguishing between costs (gamma distribution) and epidemiological parameters (beta distribution) [30]; the details are provided in Appendix B.

In total, 5,000 Monte Carlo simulations were performed.

The uncertainty imposed by the inputs on the results of the analysis was estimated by performing an OSA. In this analysis, the inputs varied within an uncertainty range, and the impact on the final result was represented by a tornado graph.

In particular, the impact of the variation in the following parameters was analyzed:

(1) Efficiency of dalbavancin (−10% to +10%) – representing the efficacy of early discharging compared to the SoC;
(2) Frequency of adverse events (−10% to +10%);
(3) Additional hospitalization cost (−10% to +10%);
(4) Administration cost (PICC) (−10% to +10%);
(5) Daily cost in the hospital (€ 0-Max), where the maximum is equal to € 732 in Italy [31],€ 601 Spain [32] and € 100 in Romania [33]; and
(6) Length of stay (LoS) (−10% to +10%).

3. Results

The model included approximately 50,000 patients admitted annually with the main diagnosis of ABSSSI in Italy, Romania, and Spain. Figure 2 shows the number and stratification by the state of the ABSSSI patients in each country. In Italy, 19,034 patients were included in the analysis as follows: 79.5% (15,131) of the patients were affected by severe ABSSSIs, 54% of the patients had a diagnosis of non-purulent ABSSSIs and 46% of the patients had a diagnosis of purulent ABSSSIs. The average age of the patients with non-purulent ABSSSIs was 63.8 years, and that of the purulent ABSSSI patients was 59.4 years. In Romania, 30,997 patients were included, and 70.3% (21,793) of these patients were severe (61.2% had a diagnosis of non-purulent ABSSSIs, and 38.8% had a diagnosis of purulent ABSSSIs). The Romanian patients were on average 10 years younger than the Italian patients (average age of 56.0 years among the non-purulent patients and 47.5 among the purulent patients). In the Spanish cohort, determining the accurate stratification by severity, infection type and characteristics of the patients was impossible. This issue was resolved by applying the Italian stratification of the ABSSSI patients to the Spanish population as described in the 'Methods' section. In total, 17,997 ABSSSI patients were estimated, and 78% (14,027) of the patients were considered to have severe infections (54% with a diagnosis of non-purulent ABSSSI and 46% with a diagnosis of purulent ABSSSI).

On average, the dalbavancin treatment reduced the in-hospital length of stay by 4.15 days (95% CI: −4.57 to −3.74 days) per Italian ABSSSI patient, 2.5 days (95% CI: −2.78 to −2.23 days) per Romanian patient and 3.4 days (95% CI: −3.76 to −3.06) per Spanish patient (Table 3).

The estimated budget impact of the new intervention (dalbavancin) by Country and cost type (drug, hospitalization, specialist services and AE) is reported in Table 4. From the Italian NHS perspective, a total expenditure of € 25.33 million (PSA 95% CI: € 23.89–26.82 million) was estimated and included in the analysis. The new intervention (dalbavancin) increased the drug cost by 37% compared to SoC. However, the incremental cost of the drug was completely offset by the decrease in resources required for the treatment (−38.5%), and the total impact was approximately neutral (-€ 0.06 million).

In the Romanian setting, a total expenditure of € 26.9 million (PSA 95% CI: € 22.93–28.13 million) was estimated for the treatment of all ABSSSI patients with SoC. Dalbavancin reduces the in-hospital length of stay by approximately 2.5 days (PSA 95% CI: −2.78 to −2.23 days) per patient (Table 4). The increase in the cost of the drugs (+37.1%) was partially compensated for by the decrease in the other costs (−35.1%). Compared to SoC, the total impact of the new intervention on the hospital budget was a negligible increase of 0.1% (€ 0.26 million).

Table 2. Costs inputs for each country included in the analysis.

				References		
Drug therapy	ITALY	ROMANIA	SPAIN	Italy	Romania	Spain
Dalbavancin (1000mg)	€ 773	€ 670*	€ 844			
Dalbavancin (500mg)	€ 387	€ 335*	€ 422			
Vancomycin (daily cost of administration)	€ 19	€ 23	€ 14	[24]	[33]	[25]
Teicoplanin (daily cost of administration)	€ 45	€ 24	€ 22			
Linezolid (daily cost of administration)	€ 76	€ 50	€ 72			
% who received vancomycin	35%	59%	54%	Expert opinion	Expert opinion	Expert opinion
% who received teicoplanin	35%	11%	7%			
% who received linezolid	30%	30%	39%			
Gram-positive therapy (daily administration)	€ 45	€ 31	€ 37			
Piperacillin tazobactam	€ 23	€ 26	€ 5	[24]	[33]	[25]
Oral therapy (Amoxicillin Clavulanate)	€ 5	€ 3	€ 3			
Hospitalization						
Incremental cost due to an average length of hospital stay >8 days (purulent)	€ 884	€ 310	€ 884	Data from administrative databases	Data from administrative databases	Assumed to be equal to Italy
Incremental cost due to an average length of hospital stay >8 days (non-purulent)	€ 870	€ 654	€ 870			
Diagnostic tests						
Swab	€ 8.80	€ 3	€ 7	[26]	Database from The National Institute for Infectious Diseases Prof. dr. Matei Bals	[27]
Ultrasound	€ 50	€ 6	€ 20			
CAT	€ 48	€ 40	€ 86			
MRI	€ 160	€ 156	€ 126			
Specialist service						
Examination	€ 21	€ 5	€ 37	[26]	Database from The National Institute for Infectious Diseases Prof. dr. Matei Bals	[27]
Placement of PICC and other related costs						
Placement of peripherally inserted central catheter (PICC)	€ 383	€ 267	€ 495	[28]	Database from The National Institute for Infectious Diseases Prof. dr. Matei Bals	[27]
Thrombophlebitis	€ 306	€ 960	€ 498	[28]		[27]
Malposition	€ 236	€ 134	€ 248	[28]		[27]
Malfunction	€ 383	€ 267	€ 495	[28]		[27]
PICC-related infection	€ 1,263	€ 1,038	€ 945	Difference between DRG 277 (with CC) and DRG 278 (without CC)	Difference between DRG 277 (with CC) and DRG 278 (without CC)	Difference between DRG 277 (with CC) and DRG 278 (without CC)
PICC dressing patch costs	€ 6	€ 10	€ 7	Appendix B	Appendix B	Appendix B
Additional costs due to vancomycin						
EA dialysis	€ 6	€ 19	€ 13			
EA nephrotoxicity	€ 1	€ 3	€ 4	Appendix B	Appendix B	Appendix B
Monitoring	€ 50	€ 46	€ 185			
PICC Risk						
Risk of thrombophlebitis (daily)	0.8%	0.8%	0.8%	[29]	[29]	[29]
Risk of infection (daily)	0.2%	0.2%	0.2%			
Risk of malposition	9.3%	9.3%	9.3%			
Risk of malfunction (daily)	0.8%	0.8%	0.8%			

* *Estimated cost*.

From the Spanish NHS perspective, the model estimated a total expenditure of € 23.5 million (95% CI: € 22.16–24.84 million) for the treatment of all ABSSSI patients with SoC. Dalbavancin reduces the in-hospital length of stay by approximately 3.2 days (PSA 95% CI: −3.76 to −3.06 days) per patient (Table 4). The increase in the cost of the drugs (+42.3%) was partially compensated for by the decrease in the other costs (−41.4%). Compared to SoC, the total impact of the new intervention on the hospital budget was a negligible increase of 1% (€ 0.25 million).

Figure 3 shows the OWA results. In all three settings, the three most influential parameters were the assumptions considered for the daily cost of the hospital stay, the effectiveness estimated for dalbavancin and the cost of administration. If we consider the minimum cost in each country per hospitalization day (base-case analysis assuming the only DRG tariff is a unique cost parameter independent of the length of stay), dalbavancin could decrease the total economic burden by several million euros in Italy, Romania,

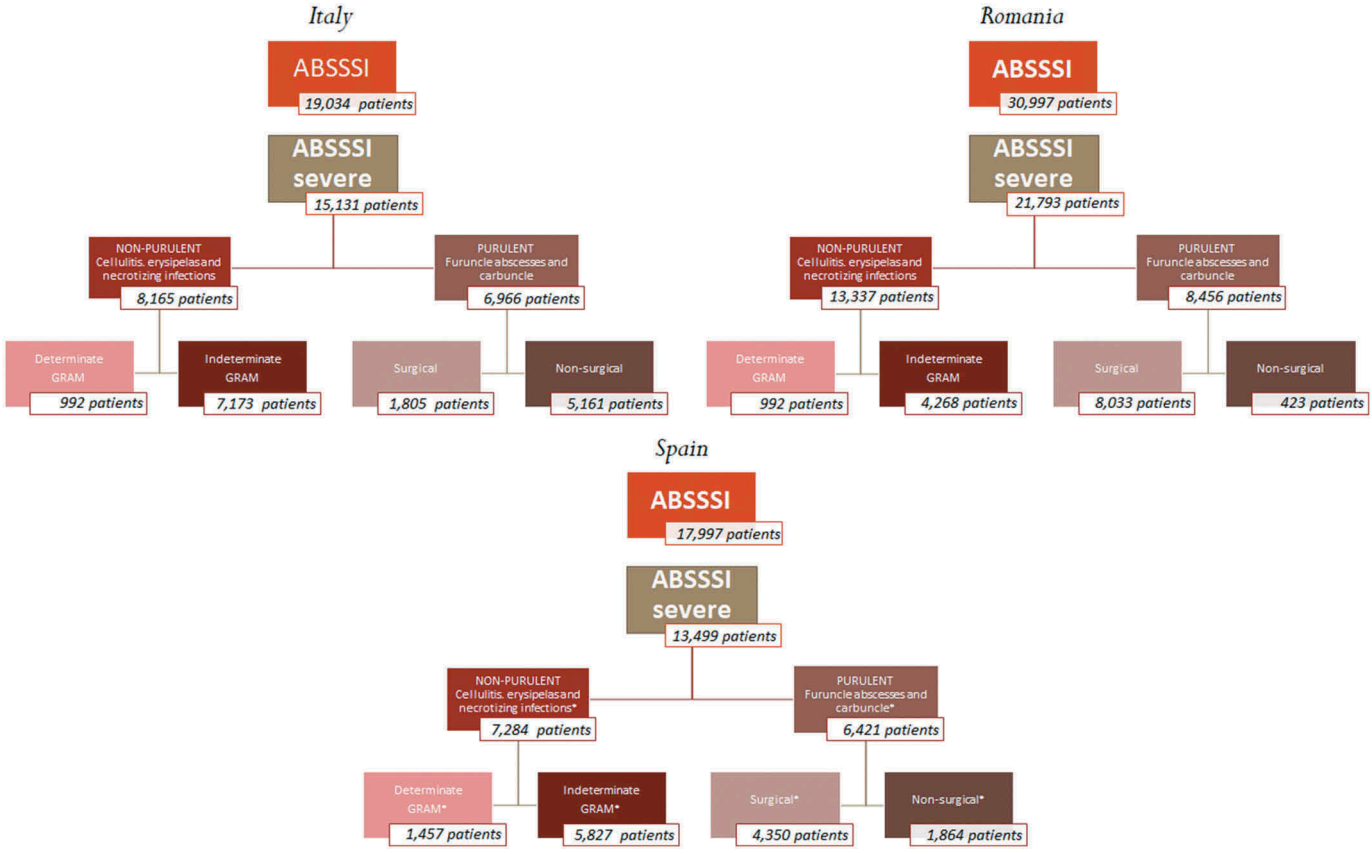

Figure 2. Average annual admissions due to severity and presence of purulence in Italy (2006–2010), Romania (2010–2013), and Spain (2006–2015).
* Assumed to have the same distribution as the Italian data.

and Spain. The efficiency of dalbavancin is the second most important parameter.

4. Discussion

Considering the costs from a hospital perspective (i.e., meals, laundry services, etc.), according to the probabilistic analysis, dalbavancin could decrease the total economic burden with a significant difference.

The advantages of the dalbavancin administration scheme and currently reported tolerability data may be represented by the following:

- Reduction in hospital LoS, and
- Reduction in the following risks:
  - *Peripherally inserted central catheter (PICC) related adverse events not necessary in the dalbavancin administration scheme, and*
  - *Reported drug-related adverse events compared to vancomycin.*

The reduction in the length of stay reduces the exposure to additional risks, such as Hospital Acquired Infections (HAIs), although these infections were not considered in the present analysis.

In performing pharmacoeconomic evaluations, only the direct price of purchasing medications is customarily considered. However, to assess the total costs of intravenous (IV) drug therapy, other costs associated with the preparation, administration, and monitoring of IV antibiotic therapy must be evaluated. Gaining insight into all factors that contribute to the actual total overall costs of drug therapy may help increase awareness of the drivers of the costs of hospital services and identify opportunities for cost savings [34].

Hospital LoS is commonly considered by several authors the most important variable driving total health-care costs in

Table 3. PSA results: length of stay (LoS) per patient.

LoS	SoC	Dalbabancin	Difference
Italy			
Non Purulent	11.4	7.9	−3.5
(Min-Max)	(10,89–11,84)	(7,41–8,29)	(−4,08 – −2,94)
Purulent	11.7	6.8	−4.9
(Min-Max)	(11,25–12,22)	(6,42–7,25)	(−5,47 – −4,33)
Total	**11.5**	**7.4**	**−4.15**
(Min-Max)	**(11,19–11,87)**	**(7,07–7,68)**	**(−4,56 – −3,74)**
Romania			
Non Purulent	10.3	6.6	−3.8
(Min-Max)	(10,03–10,66)	(6,28–6,84)	(−4,16 – −3,41)
Purulent	9.8	9.3	−0.5
(Min-Max)	(9,43–10,09)	(8,94–9,62)	(−0,68 – −0,27)
Total	**10.1**	**7.6**	**−2.5**
(Min-Max)	**(9,88–10,35)**	**(7,37–7,86)**	**(−2,78 – −2,23)**
Spain			
Non Purulent	11.4	7.1	−4.3
(Min-Max)	(10,91–11,82)	(6,7–7,54)	(−4,81 – −3,69)
Purulent	12.1	9.7	−2.4
(Min-Max)	(11,69–12,61)	(9,33–10,1)	(−2,78 – −2,08)
Total	**11.7**	**8.3**	**−3.4**
(Min-Max)	**(11,4–12,05)**	**(8–8,62)**	**(−3,76 – −3,06)**

Table 4. PSA results: annual costs (95% CI: min-max).

	SoC			Dalbavancine			Difference Dalbavancine – SoC		
Cost Items	Italy	Romania	Spain	Italy	Romania	Spain	Italy	Romania	Spain
Nonpurulent ABSSSI patients (€ milions)									
Drugs	€ 5.37	€ 5.77	€ 2.87	€ 10.82	€ 13.32	€ 9.26	€ 5.45	€ 7.54	€ 6.39
(Min-Max)	*(€4.76 – €6.01)*	*(€5.23 – €6.34)*	*(€2.48 – €3.29)*	*(€9.69 – €12.01)*	*(€12.09 – €14.6)*	*(€8.25 – €10.34)*	*(€4.53 – €6.37)*	*(€6.47 – €8.62)*	*(€5.47 – €7.32)*
Specialist service	€ 5.84	€ 7.10	€ 5.88	€ 3.09	€ 3.25	€ 2.49	-€ 2.75	-€ 3.85	-€ 3.39
(Min-Max)	*(€5.24 – €6.47)*	*(€6.45 – €7,78)*	*(€5.18 – €6.62)*	*(€2.76 – €3.44)*	*(€2.86 – €3.66)*	*(€2.05 – €2.97)*	*(€-2.77 – €-2.07)*	*(€-1.06 – €-0.73)*	*(€-2.59 – €-1.89)*
Hospitalization	€ 2.64	€ 3.72	€ 2.35	€ 1.14	€ 0.90	€ 0.80	-€ 1.50	-€ 2.82	-€ 1.55
(Min-Max)	*(€2.17 – €3.16)*	*(€3.22 – €4.27)*	*(€1.94 – €2.79)*	*(€0.87 – €1.45)*	*(€0.72 – €1.11)*	*(€0.61 – €1.02)*	*(€-1.95 – €-1.05)*	*(€-3.27 – €-2.38)*	*(€-1.94 – €-1.17)*
AE	€ 0.84	€ 1.73	€ 0.92	€ 0.15	€ 0.19	€ 0.14	-€ 0.68	-€ 1.54	-€ 0.79
(Min-Max)	*(€0.74 – €0.94)*	*(€1.56 – €1.91)*	*(€0.82 – €1.03)*	*(€0.12 – €0.18)*	*(€0.16 – €0.23)*	*(€0.11 – €0.16)*	*(€-0.77 – €-0.6)*	*(€-1.69 – €-1.38)*	*(€-0.88 – €-0.69)*
Total	**€ 14.69**	**€ 18.33**	**€ 12.02**	**€ 15.20**	**€ 17.66**	**€ 12.69**	**€ 0.51**	**-€ 0.67**	**€ 0.67**
(Min-Max)	***(€13.23 – €16.22)***	***(€16.9 – €19.82)***	***(€10.78 – €13.33)***	***(€13.69 – €16.79)***	***(€16.18 – €19.21)***	***(€11.34 – €14.1)***	***(€-0.56 – €1.59)***	***(€-1.8 – €0.46)***	***(€-0.28 – €1.61)***
Purulent ABSSSI patients (€ milions)									
Drugs	€ 3.42	€ 2.33	€ 2.79	€ 7.70	€ 4.51	€ 6.37	€ 4.28	€ 2.18	€ 3.58
(Min-Max)	*(€2.97 – €3.91)*	*(€2 – €2.69)*	*(€2.35 – €3.27)*	*(€6.77 – €8.7)*	*(€3.94 – €5.13)*	*(€5.58 – €7.21)*	*(€3.51 – €5.05)*	*(€1.77 – €2.59)*	*(€2.95 – €4.21)*
Specialist service	€ 5.00	€ 4.54	€ 5.05	€ 2.58	€ 3.64	€ 2.81	-€ 2.42	-€ 0.90	-€ 2.24
(Min-Max)	*(€4.42 – €5.61)*	*(€4 – €5.11)*	*(€4.38 – €5.77)*	*(€2.28 – €2.9)*	*(€3.19 – €4.12)*	*(€2.34 – €3.32)*	*(€-2.77 – €-2.07)*	*(€-1.06 – €-0.73)*	*(€-2.59 – €-1.89)*
Hospitalization	€ 2.64	€ 3.72	€ 2.35	€ 0.67	€ 0.65	€ 1.47	-€ 1.97	-€ 3.08	-€ 0.88
(Min-Max)	*(€2.17 – €3.16)*	*(€3.22 – €4.27)*	*(€1.94 – €2.79)*	*(€0.52 – €0.85)*	*(€0.52 – €0.78)*	*(€1.23 – €1.74)*	*(€-2.52 – €-1.42)*	*(€-3.65 – €-2.51)*	*(€-1.44 – €-0.32)*
AE	€ 0.84	€ 1.73	€ 0.92	€ 0.11	€ 0.74	€ 0.33	-€ 0.73	-€ 1.00	-€ 0.59
(Min-Max)	*(€0.74 – €0.94)*	*(€1.56 – €1.91)*	*(€0.82 – €1.03)*	*(€0.09 – €0.13)*	*(€0.62 – €0.86)*	*(€0.27 – €0.4)*	*(€-0.83 – €-0.62)*	*(€-1.21 – €-0.78)*	*(€-0.72 – €-0.45)*
Total	**€ 11.60**	**€ 8.61**	**€ 11.06**	**€ 11.07**	**€ 9.54**	**€ 10.98**	**-€ 0.53**	**€ 0.92**	**-€ 0.07**
(Min-Max)	***(€10.31 – €12.97)***	***(€7.65 – €9.63)***	***(€9.76 – €12.43)***	***(€9.82 – €12.4)***	***(€8.51 – €10.62)***	***(€9.73 – €12.31)***	***(€-1.34 – €0.28)***	***(€0.66 – €1.19)***	***(€-0.61 – €0.47)***
Total ABSSSI patients (€ milions)									
Drugs	€ 8.79	€ 8.11	€ 5.66	€ 18.52	€ 17.83	€ 15.63	€ 9.73	€ 9.72	€ 9.97
(Min-Max)	*(€8.13 – €9.48)*	*(€7.52 – €8.72)*	*(€5.02 – €6.33)*	*(€17.29 – €19.8)*	*(€16.62 – €19.08)*	*(€14.56 – €16.74)*	*(€8.35 – €11.11)*	*(€8.5 – €10.95)*	*(€8.77 – €11.17)*
Specialist service	€ 10.84	€ 11.64	€ 10.93	€ 5.67	€ 6.89	€ 5.30	-€ 5.17	-€ 4.75	-€ 5.63
(Min-Max)	*(€10.18 – €11.52)*	*(€10.86 – €12.45)*	*(€9.97 – €11.93)*	*(€5.31 – €6.04)*	*(€6.29 – €7.51)*	*(€4.54 – €6.11)*	*(€-5.68 – €-4.65)*	*(€-5.18 – €-4.32)*	*(€-6.15 – €-5.1)*
Hospitalization	€ 5.09	€ 4.46	€ 4.72	€ 1.81	€ 1.55	€ 2.27	-€ 3.27	-€ 2.91	-€ 2.45
(Min-Max)	*(€4.54 – €5.67)*	*(€3.97 – €4.98)*	*(€4.25 – €5.21)*	*(€1.51 – €2.14)*	*(€1.34 – €1.78)*	*(€1.99 – €2.57)*	*(€-3.82 – €-2.73)*	*(€-3.35 – €-2.47)*	*(€-2.85 – €-2.04)*
AE	€ 1.57	€ 2.74	€ 1.77	€ 0.26	€ 0.93	€ 0.47	-€ 1.30	-€ 1.81	-€ 1.30
(Min-Max)	*(€1.46 – €1.68)*	*(€2.53 – €2.95)*	*(€1.65 – €1.9)*	*(€0.23 – €0.3)*	*(€0.81 – €1.05)*	*(€0.4 – €0.54)*	*(€-1.4 – €-1.2)*	*(€-1.97 – €-1.65)*	*(€-1.4 – €-1.2)*
Total	**€ 26.29**	**€ 26.94**	**€ 23.08**	**€ 26.27**	**€ 27.20**	**€ 23.67**	**-€ 0.01**	**€ 0.26**	**€ 0.59**
(Min-Max)	***(€25.09 – €27.52)***	***(€25.75 – €28.16)***	***(€21.79 – €24.4)***	***(€24.88 – €27.7)***	***(€25.9 – €28.53)***	***(€22.32 – €25.06)***	***(€-1.69 – €1.66)***	***(€-1.09 – €1.6)***	***(€-0.78 – €1.97)***

Figure 3. DSA: tornado diagram (total burden).

patients with different health conditions [35–37]; even if national health-care providers usually pay hospitals through DRGs to standardize the financial contributions for the treatment of the same health conditions, an over threshold LoS frequently occur due to adverse events, contributing to a further increase in the economic healthcare burden [38]. The analysis presented in this manuscript predicted the possibility of an increased hospital LoS based on a statistical distribution of over threshold analysis to enhance our understanding of how in-dwelling can affect total health-care costs in a DRG-based system.

Intravenous drug infusion and catheter usage are important tools in in-hospital patient care but may be associated with serious catheter-related morbidity and discomfort. PICCs function as central catheters, allowing both drug infusion and blood sampling, and lessen the risk of central venous catheter insertion. Nevertheless, Periard and colleagues showed that even if PICCs are efficient and appreciated catheters in hospitalized patients, one-fifth of patients with PICC develop adverse events attributable to the inserted medical device, indicating that PICCs should not be used as the first-choice option in all hospitalized patients [39].

Vancomycin is active against Gram-positive bacteria, including MRSA, and is regularly used as an armamentarium for the treatment of ABSSSIs and other infectious diseases. The guidelines for vancomycin therapeutic monitoring by the IDSA suggest targeting vancomycin with concentrations of 10 mg/L to avoid the development of resistant strains and concentrations of 15–20 mg/L to improve tissue penetration, which increases the probability of achieving optimal target serum concentrations and improving clinical outcomes. Nephrotoxicity, which is usually reversible, is the most serious common adverse effect of vancomycin and is strictly linked to its plasma concentrations. While the average daily cost of vancomycin is relatively low, a comprehensive account of the cost of vancomycin use should include the direct costs associated with measuring the serum concentrations and those associated with the treatment of adverse reactions, such as nephrotoxicity [40]. Dalbavancin has a better potential tolerability profile than other therapies for ABSSSIs, and it has been recommended by a recently published meta-analysis [41].

Although not within the scope of the present analysis, cross-bacterial colonization can increase with prolonged LoS and is mainly caused by MRSA. Clinicians should consider colonization in assessments of discharging patients from the hospital, particularly if the clinical conditions are improved and stable [42,43].

Common to most economic models, this study has various limitations. First, the model was constructed by combining data obtained from multiple randomized clinical trials involving homogeneous populations, but heterogeneous populations existed among the studies considered. To date, the lack of sufficient information for performing an adequate meta-analysis and the inability to appropriately compare the data prevent achieving better estimates. However, all clinical information and modeling assumptions were validated and discussed with key opinion leaders, who identified adequate uncertainty parameters that were used to perform the deterministic sensitivity analysis.

Second, consulting with a panel of experts was the only way to identify the advantages associated with the dalbavancin treatment of patients suffering from ABSSSIs. However, for explanatory purposes, the constant rate of increases and decreases in the cost of items, is based on scenarios designated by the panel of clinical experts.

Moreover, in Italy and Spain, the tariffs can vary among the regions due to the delocalization of the NHS, but costs from only one region perspective were used, further limiting the analysis. Moreover, in Romania, hospitals purchase most antibiotic therapies directly from wholesalers, and the purchase price of dalbavancin used in the analysis was estimated.

Additionally, the assessment period for each country are not perfectly comparable due to the different data availability and the transition probabilities in Spain were assumed to be the same as those applied to Italy. However, all these limitations were considered in the deterministic and probabilistic SA.

Finally, in the model, the cost of a 4-day LoS hospitalization was assumed to be the same as the cost of an 8-day LoS hospitalization. This assumption is a methodological limitation that has a negligible impact on the final estimates since it represents a cost item that is constant in both considered scenarios.

The results of this analytic model are consistent with other published studies comparing SoC treatment for ABSSSIs with newer therapies, different therapeutic administration settings, such as outpatient parenteral antimicrobial therapy (OPAT), or avoiding PICC lines for treatment infusion. In a recent article, Browne, Muszbek [44] estimated the cost consequences of using daptomycin compared with those of using vancomycin as the first-line treatment in patients with proven MRSA-induced bacteremia-infective endocarditis. Daptomycin required fewer therapeutic switches and a shorter length of stay. When the length of stay was reduced from 42 days to 28 days, daptomycin saved £ 4037 per person compared with vancomycin. Stephens, Gao [45] compared the cost of oral linezolid therapy with the cost of vancomycin or daptomycin regimens and concluded that using linezolid has a potential economic benefit over traditional OPAT considering the total inpatient and outpatient medical costs. PICCs are commonly used to administer antibiotics or other medications, particularly in patients requiring hospital in-dwelling; in a study evaluating the cost offsets of treating Gram-positive ABSSSIs with varied hospital LoS, a sensitivity analysis comparing the inpatient and outpatient cost breakdown revealed that a key outpatient cost driver was the PICC cost, with an average per patient cost of $873 for placement and $205 for complications [46].

5. Conclusion

This economic analysis suggests that the use of dalbavancin could generate a significant reduction in the length of stay with no statistically significant incremental costs from a National health-care provider perspective. The validity of this conclusion should better be tested in a 'real-life' setting, though it has been further strengthened by the convergence of the results reported from all three European Countries with different discharge probabilities, cost inputs, and budget constraints. In conclusion, the use of dalbavancin would allow an early discharge approach in ABSSSI management, providing the option to significantly reduce patients' exposure to additional risks associated with prolonged hospitalization, at no incremental cost for the National health-care providers. This model could represent a useful tool for

clinicians and policymakers to inform their decision about the optimal treatment pattern of ABSSSIs in the hospital setting.

Key issues

- Acute Bacterial Skin and Skin Structure Infections (ABSSSI) impose a significant economic burden on the health-care systems due to the associated inpatient management, surgical procedures, and parenteral antibiotic therapy.
- The present study aimed to develop a predictor model to evaluate the direct costs associated with the management of ABSSSIs. We collected data of hospital management in three European countries namely, Italy, Romania and Spain and compared drug costs related to therapy-related adverse events, administration costs, diagnosis-related groups (DRG) and service-related resources associated with standard of care (SoC) and dalbavancin.
- the introduction of dalbavancin reduced the length of stay by 3.3 days per ABSSSI patient and from an economic perspective, dalbavancin did not incur in any additional cost from the National Healthcare perspective of all the included countries. Considering the costs from a hospital perspective according to the probabilistic analysis, dalbavancin could decrease the total economic burden with a significant difference.

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A reviewer on this paper has disclosed that their company (ICPD) was involved in the development of dalbavancin. They provided pharmacometric support for the US FDA submission and received grant support from the company that submitted the NDA (Durata). They do not currently have an ongoing financial relationship with the company that markets dalbavancin in the US (Allergan). Peer reviewers on this manuscript have no other relevant financial relationships or otherwise to disclose.

Ethics approval

Institutional ethics committee approval and informed consent were not required.

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Appendices

Appendix A.

Algorithm to identify the ABSSSI patients in Italy

The following algorithm was implemented on all acute inpatient admissions with discharge dates between January 1st, 2006 and December 31th, 2010 from Italian Hospital Information System (HIS).

In order to be defined SEVERE *purulent and nonpurelent* patients requiring observation over 72 hours, one of the following inclusion criteria had to be met:

All *acute inpatient* admissions with discharge
AND Main diagnosis of:

- 'Cellulitis and abscess of finger and toe' (ICD-9-CM 681.xx)
- 'Other cellulitis and abscess' (ICD-9-CM 682.x)
- 'Other local infections of skin and subcutaneous tissue' (ICD-9-CM 686.xx)
- 'Posttraumatic wound infection not elsewhere classified' (ICD-9-CM 958.3)
- 'Other postoperative infection' (ICD-9-CM 998.59)

OR

- Diagnosis Related Group (DRG) of:
  - 'Cellulitis, age >17 with complications' (DRG 277)
  - 'Cellulitis, age >17 without complications' (DRG 278)
  - 'Post-operative and post-traumatic infections' (DRG 418)

Exclusion criteria:

- hospitalizations of patients aged <17 years
- hospitalizations with length of stay <2 days
- main diagnosis of 'Infected postoperative seroma' (ICD-9-CM 998.51)

Definition of 'purulent' case:
All selected admissions with main or secondary diagnosis of:

- 'Carbuncle and furuncle' (ICD-9-CM 680.x)
- 'Cellulitis and abscess of finger, unspecified' (ICD-9-CM 681.00)
- 'Cellulitis and abscess of toe, unspecified' (ICD-9-CM 681.10)
- 'Cellulitis and abscess of unspecified digit' (ICD-9-CM 681.9)
- 'Other cellulitis and abscess' (ICD-9-CM 682.x)
- 'Pilonidal cyst with abscess' (ICD-9-CM 685.0)

Definition of 'Infection with drug-resistant microorganisms' case:
All selected admissions with main or secondary diagnosis of:

- 'Infection with drug-resistant microorganisms' (ICD-9-CM V09.xx)

Definition of 'severe' case:

All selected admissions with length of stay ≥4
AND main diagnosis not in:

- 'Felon' (ICD-9-CM 681.01)
- 'Onychia and paronychia of finger' (ICD-9-CM 681.02)
- 'Onychia and paronychia of toe' (ICD-9-CM 681.11)

AND Diagnosis Related Group (DRG) not in:

- 'Subtotal mastectomy for malignancy with CC' (DRG 259)
- 'Extensive procedure unrelated to principal diagnosis' (DRG 468)
- 'Ungroupable' (DRG 470)
- 'Prostatic procedure unrelated to principal diagnosis' (DRG 476)
- 'Non-extensive procedure unrelated to principal diagnosis' (DRG 477)
- 'Tracheostomy for face, mouth and neck diagnoses' (DRG 482)
- 'Tracheostomy except for face, mouth and neck diagnoses' (DRG 483)
- 'Extracorporeal membrane oxygenation or tracheostomy with mechanical ventilation ≥96 hours or principal diagnosis unrelated to the face, mouth and neck with major procedure' (DRG 541)
- 'Tracheostomy with mechanical ventilation ≥96 hours or principal diagnosis unrelated to the face, mouth and neck without major procedure' (DRG 542)

Algorithm to identify the ABSSSI patients in Romania

For mapping between ICD9-ICD10 codes is used the tool available 'ICD-9 to ICD-10 Code Search | ICD-10 Code Lookup & Crosswalk' and double-checked the correspondences.

Algorithm to identify the ABSSSI patients in Spain

Spanish official database (http://pestadistico.inteligenciadegestion.msssi.es/publicosns) -CIE-9 681, 682 and/or DRG APR 383.

Table A1. Parameters for estimating the additional costs due to vancomycin therapy.

Parameters	Description	Italy	Romania	Spain	Reference
Therapeutic Drug Monitoring TDM	Twice daily for 3 days	€ 24	€ 26	€ 57	Ref. Italy, Romania, Spain: tariffario QUAS 2017, expert opinion, tariffario Osakidetza 2015
PICC dressing patch costs	To be changed every 7 days	€ 6	€ 10	€ 7	PICC dressing costs (BioPatches) – all PICC population (ref. Pietro Zerla evalueting safty, efficacy, and cost-effectiveness of PICC securement. J Vasc Access 2017; 00 (00): 000–000)
CVC device for dialysis	Only if not included in the tariff	€ 350	€ 120	-	Ref. Italy, Romania, Spain: tariffario QUAS 2017, expert opinion, in Spain CVC cost is included in Hemofiltration tariff
Hemofiltration Cost/day	3 days	€ 104	€ 700	€ 260	Ref. Italy Romania, Spain: tariffario QUAS 2017, expert opinion, tariffario Osakidetza 2015
Nephrologist consultation Cost	Only for nephrotoxicity	€ 75	€ 61	€ 89	Ref. Romania, Spain: expert opinon, tariffario Osakidetza 2015; Ref Italy: Tariffario Nazionale FISDE 2016
% of Nephrologist consultation		35%	25%	35%	Expert opinion
% nephrotoxicity		24%	30%	24%	Italy and Spain: ref. van Hal Antimicrob Agents Chemother. 2013 Feb;57(2):734–44; Ref Romania: Expert opinion
% required dialysis		3%	1.50%	3%	Expert opinion
% treated with Vancomycin		35%	54%	54%	Expert opinion
Total cost for EA Dialysis (CVC device for dialysis + Hemofiltration)		€ 7	€ 17	€ 13	Calculation
Total costs for EA Nephrotoxicity	Only for patient with length of stay >4	€ 2	€ 2	€ 4	Calculation
Total costs for Monitoring Vancomycin		€ 25	€ 42	€ 92	Calculation

Table A2. Parameters used for implementation of the model and PSA.

Number of patients with ABSSSI	Base case	Min	Max	SD	DISTRIBUTION	ALPHA	BETA
Italian parameters and distribution							
Number of patients eligible to early discharge	15.131						
Purulent > 3 day	6.966						
Nonpurulent > 3 day	8.165						
Sort of infection (> 3 day)	Model value	Min	Max				
Purulent ABSSSI	46%	41,4%	50,6%	2,3%	BETA	207,29	241,95
Nonpurulent ABSSSI	54%	48,6%	59,4%	2,8%	BETA	176,87	149,91
Nonpurulent patient – Sort of bacteria	Model value	Min	Max				
Indeterminate	71%	64,0%	78,3%	3,6%	BETA	110,83	43,94
Polymicrobial	17%	15,0%	18,4%	0,9%	BETA	320,00	1.595,17
Gram-negative	7%	6,0%	7,3%	0,3%	BETA	358,64	5.038,75
Gram-positive	6%	5,0%	6,1%	0,3%	BETA	363,01	6.229,36
Purulent patient – Sort of origin							
Surgical	26%	23,3%	28,5%	1,3%	BETA	284,61	812,69
Non surgical	74%	66,7%	81,5%	3,8%	BETA	99,55	33,82
Surgical eligible to ED	50%	45,1%	55,1%	2,6%	BETA	191,70	189,93
Surgical No eligible to ED	50%	44,9%	54,9%	2,5%	BETA	192,46	192,23
Discharge distribution with dalbavancin	Mean	Min	Max				
Nonpurulent patient: Indeterminate or polymicrobial							
Discharge(4 day)	50%	45,0%	55,0%	2,6%	BETA	192,08	191,08
Observation(4 day)	50%	45,0%	55,0%	2,6%	BETA	192,08	191,08
Discharge(8 day)	70%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Observation up to clinical evaluation	30%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Nonpurulent patient: Gram-positive							
Discharge(4 day)	70%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Observation(4 day)	30%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Discharge(8 day)	80%	72,0%	88,0%	4,1%	BETA	76,83	18,21
Observation up to clinical evaluation	20%	18,0%	22,0%	1,0%	BETA	307,33	1.228,31
Purulent patient: surgical							
Discharge(4 day)	70%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Observation(4 day)	30%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Discharge(8 day)	80%	72,0%	88,0%	4,1%	BETA	76,83	18,21
Observation up to clinical evaluation	20%	18,0%	22,0%	1,0%	BETA	307,33	1.228,31
Purulent patient: nonsurgical							
Discharge(4 day)	70%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Observation(4 day)	30%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Discharge(8 day)	80%	72,0%	88,0%	4,1%	BETA	76,83	18,21
Observation up to clinical evaluation	20%	18,0%	22,0%	1,0%	BETA	307,33	1.228,31
Discharge distribution with standard therapy	Model value	Min	Max				
Nonpurulent patient: Indeterminate or polymicrobial							
Discharge(4 day)	11%	9,8%	11,9%	0,6%	BETA	342,51	2.815,61
Observation(4 day)	89%	80,2%	98,1%	4,5%	BETA	41,65	4,06
Discharge (8 day)	58%	52,6%	64,2%	3,0%	BETA	159,82	112,85
Observation up to clinical evaluation	42%	37,4%	45,8%	2,1%	BETA	224,34	313,92
Nonpurulent patient: Gram-positive							
Discharge(4 day)	11%	9,8%	11,9%	0,6%	BETA	342,51	2.815,61
Observation(4 day)	89%	80,2%	98,1%	4,5%	BETA	41,65	4,06
Discharge (8 day)	58%	52,6%	64,2%	3,0%	BETA	159,82	112,85
Observation up to clinical evaluation	42%	37,4%	45,8%	2,1%	BETA	224,34	313,92
Purulent patient: surgical							
Discharge(4 day)	11%	10,1%	12,4%	0,6%	BETA	340,92	2.686,75
Observation(4 day)	89%	79,9%	97,6%	4,5%	BETA	43,24	4,48
Discharge(8 day)	50%	45,1%	55,1%	2,6%	BETA	191,70	189,93
Observation up to clinical evaluation	50%	44,9%	54,9%	2,5%	BETA	192,46	192,23
Purulent patient: nonsurgical							
Discharge(4 day)	12%	10,9%	13,3%	0,6%	BETA	337,77	2.458,47
Observation(4 day)	88%	79,1%	96,7%	4,5%	BETA	46,39	5,37
Discharge(8 day)	57%	51,3%	62,6%	2,9%	BETA	165,38	124,01
Observation up to clinical evaluation	43%	38,7%	47,4%	2,2%	BETA	218,78	288,42
PICC risk							
Risk thrombophlebitis (per day)	0,8%	0,7%	0,9%	0,040%	BETA	381,16	48.353,04
Risk infection (per day)	0,2%	0,2%	0,2%	0,011%	BETA	383,30	170.089,84
Risk malposition(per day)	9,3%	8,3%	10,2%	0,472%	BETA	348,59	3.415,18
Risk malfunction (per day)	0,8%	0,7%	0,9%	0,040%	BETA	381,16	48.468,38
Costs parameter							

(*Continued*)

Table A2. (Continued).

Number of patients with ABSSSI	Base case	Min	Max	SD	DISTRIBUTION	ALPHA	BETA
Drug therapy	Model value	Min	Max				
Dalbavancin (1 + 1 dose)	€ 773	€ 696	€ 851	€ 39	GAMMA	€ 384,16	€ 2,01
Dalbavancin (3 dose)	€ 387	€ 348	€ 425	€ 20	GAMMA	€ 384,16	€ 1,01
Vancomycin (cost per day of administration)	€ 19	€ 17	€ 20	€ 1	GAMMA	€ 384,16	€ 0,05
Teicoplanin (cost per day of administration)	€ 45	€ 41	€ 50	€ 2	GAMMA	€ 384,16	€ 0,12
Linezolid	€ 76	€ 68	€ 83	€ 4	GAMMA	€ 384,16	€ 0,20
% use vancomycin	35%	32%	39%	1,8%	BETA	249,70	462,74
% use teicoplanin	35%	32%	39%	1,8%	BETA	249,70	462,74
% use linezolid	30%	27%	33%	1,5%	BETA	268,91	626,46
Gram-positive therapy (per day of administration)	€ 45	€ 41	€ 50	€ 2	GAMMA	€ 384,16	€ 0,12
Piperacillin tazobactam	€ 23	€ 21	€ 26	€ 1	GAMMA	€ 384,16	€ 0,06
Oral therapy (Amoxicillin Clavulanate)	€ 5	€ 4	€ 5	€ 0	GAMMA	€ 384,16	€ 0,01
Hospitalization							
Hospitalization purulent patient	€ 884,4	€ 796	€ 973	€ 45	GAMMA	€ 384,16	€ 2,30
Hospitalization nonpurulent patient	€ 870,0	€ 783	€ 957	€ 44	GAMMA	€ 384,16	€ 2,26
Cost per day of hospitalization	€ 650,0	€ 585	€ 715	€ 33	GAMMA	€ 384,16	€ 1,69
Diagnostic tests							
Swab	€ 8,80	€ 7,92	€ 20	€ 0,4	GAMMA	€ 384,16	€ 0,02
Ultrasound	€ 50	€ 45	€ 55	€ 3	GAMMA	€ 384,16	€ 0,13
CAT	€ 48	€ 43	€ 53	€ 2	GAMMA	€ 384,16	€ 0,12
MRI	€ 160	€ 144	€ 180	€ 10	GAMMA	€ 245,86	€ 0,65
Specialist service							
Examination	€ 21	€ 68	€ 83	€ 4	GAMMA	€ 384,16	€ 0,20
Installation PICC and other related costs							
Installation of Peripherally Inserted Central Catheter (PICC)	€ 383	€ 345	€ 422	€ 20	GAMMA	€ 384,16	€ 1,00
Thrombophlebitis	€ 306	€ 276	€ 337	€ 16	GAMMA	€ 384,16	€ 0,80
Infection PICC related	€ 1.263	€ 1.137	€ 1.389	€ 64	GAMMA	€ 384,16	€ 3,29
Malposition	€ 236	€ 212	€ 259	€ 12	GAMMA	€ 384,16	€ 0,61
Malfunction	€ 383	€ 345	€ 422	€ 20	GAMMA	€ 384,16	€ 1,00
PICC dressing patch costs (to be changed every 7 days)	€ 6	€ 5	€ 7	€ 0	GAMMA	€ 384,16	€ 0,02
Additional costs due to Vancomycin							
EA Dialysis (CVC device for dialysis + Hemofiltration)	€ 6	€ 5	€ 6	€ 0	GAMMA	€ 384,16	€ 0,02
EA Nephrotoxicity	€ 1	€ 1	€ 1	€ 0	GAMMA	€ 384,16	€ 0,00
Monitoring Vancomycin (twice daily for 3 days)	€ 50	€ 45	€ 55	€ 3	GAMMA	€ 384,16	€ 0,13
Length of hospital stay							
Average length of hospital stay purulent	11,6	10,4	12,8	0,59	GAMMA	€ 384,16	€ 0,03
Average length of hospital stay nopurulent	11,1	10,0	12,2	0,57	GAMMA	€ 384,16	€ 0,03
Average length of hospital stay purulent >11,7	17,2	15,5	18,9	0,88	GAMMA	€ 384,16	€ 0,04
Average length of hospital stay nopurulent >11,2	16,7	15,0	18,4	0,85	GAMMA	€ 384,16	€ 0,04
Additional day per purulent >11,7	8,2	7,4	9,0	0,42	GAMMA	€ 384,16	€ 0,02
Additional day per nopurulent >11,2	7,7	6,9	8,5	0,39	GAMMA	€ 384,16	€ 0,02
Romanian parameters and distribution							
Number of patients eligible to early discharge	21.793				GAMMA		
Purulent > 3 day	8.456				GAMMA		
Nonpurulent > 3 day	13.337				GAMMA		
Sort of infection (> 3 day)	Model value	Min	Max				
Purulent ABSSSI	39%	34,9%	42,7%	2,0%	BETA	235,10	369,79
Nonpurulent ABSSSI	61%	55,1%	67,3%	3,1%	BETA	149,06	93,51
Nonpurulent patient – Sort of bacteria	Model value	Min	Max				
Indeterminate	18%	15,8%	19,3%	0,9%	BETA	316,93	1.493,11
Polymicrobial	18%	15,8%	19,3%	0,9%	BETA	316,93	1.493,11
Gram-negative	9%	8,1%	9,9%	0,5%	BETA	349,59	3.533,70
Gram-positive	56%	50,4%	61,6%	2,9%	BETA	169,03	131,81
Purulent patient – Sort of origin							
Surgical	95,0%	85,5%	100,0%	2,6%	BETA	69,34	2,65
Non surgical	5,0%	4,5%	5,5%	0,3%	BETA	364,95	6.933,09
Surgical eligible to ED	30,0%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Surgical No eligible to ED	70,0%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Discharge distribution with dalbavancin	Mean	Min	Max				
Nonpurulent patient: Indeterminate or polymicrobial	**100%**						
Discharge(4 day)	60,0%	54,0%	66,0%	3,1%	BETA	153,66	101,44
Observation(4 day)	40,0%	36,0%	44,0%	2,0%	BETA	230,50	344,74
Discharge(8 day)	70,0%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Observation up to clinical evaluation	30,0%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Nonpurulent patient: Gram-positive							

(*Continued*)

Table A2. (Continued).

Number of patients with ABSSSI	Base case	Min	Max	SD	DISTRIBUTION	ALPHA	BETA
Discharge(4 day)	70,0%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Observation(4 day)	30,0%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Discharge(8 day)	90,0%	81,0%	99,0%	4,6%	BETA	38,42	3,27
Observation up to clinical evaluation	10,0%	9,0%	11,0%	0,5%	BETA	345,74	3.110,70
Purulent patient: surgical							
Discharge(4 day)	70%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Observation(4 day)	30%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Discharge(8 day)	80%	72,0%	88,0%	4,1%	BETA	76,83	18,21
Observation up to clinical evaluation	20%	18,0%	22,0%	1,0%	BETA	307,33	1.228,31
Purulent patient: nonsurgical							
Discharge(4 day)	65%	58,5%	71,5%	3,3%	BETA	134,46	71,40
Observation(4 day)	35%	31,5%	38,5%	1,8%	BETA	249,70	462,74
Discharge(8 day)	80%	72,0%	88,0%	4,1%	BETA	76,83	18,21
Observation up to clinical evaluation	20%	18,0%	22,0%	1,0%	BETA	307,33	1.228,31
Discharge distribution with standard therapy	Model value	Min	Max				
Nonpurulent patient: Indeterminate or polymicrobial							
Discharge(4 day)	10%	9%	11%	0,01	BETA	345,74	3.110,70
Observation(4 day)	90%	81%	99%	0,05	BETA	38,42	3,27
Discharge (8 day)	35%	32%	39%	0,02	BETA	249,70	462,74
Observation up to clinical evaluation	65%	59%	72%	0,03	BETA	134,46	71,40
Nonpurulent patient: Gram-positive							
Discharge(4 day)	31%	28%	34%	1,6%	BETA	265,07	589,00
Observation(4 day)	69%	62%	76%	3,5%	BETA	119,09	52,50
Discharge (8 day)	55%	50%	61%	2,8%	BETA	172,87	140,44
Observation up to clinical evaluation	45%	41%	50%	2,3%	BETA	211,29	257,24
Purulent patient: surgical							
Discharge(4 day)	55%	50%	61%	2,8%	BETA	172,87	140,44
Observation(4 day)	45%	41%	50%	2,3%	BETA	211,29	257,24
Discharge(8 day)	65%	59%	72%	3,3%	BETA	134,46	71,40
Observation up to clinical evaluation	35%	32%	39%	1,8%	BETA	249,70	462,74
Purulent patient: nonsurgical							
Discharge(4 day)	33%	30%	36%	1,7%	BETA	257,39	521,57
Observation(4 day)	67%	60%	74%	3,4%	BETA	126,77	61,44
Discharge(8 day)	67%	60%	74%	3,4%	BETA	126,77	61,44
Observation up to clinical evaluation	33%	30%	36%	1,7%	BETA	257,39	521,57
Risks of nosocomial infections	Model value	Min	Max				
PICC related							
Risk thrombophlebitis (per day)	0,8%	0,7%	0,9%	0,0%	BETA	381,16	48.353,04
Risk infection (per day)	0,2%	0,2%	0,2%	0,0%	BETA	383,30	170.089,84
Risk malposition(per day)	9,3%	8,3%	10,2%	0,5%	BETA	348,59	3.415,18
Risk malfunction (per day)	0,8%	0,7%	0,9%	0,0%	BETA	381,16	48.468,38
Costs parameter							
Drug therapy	Model value	Min	Max				
Dalbavancin (1 + 1 dose)	€ 660	€ 594	€ 726	€ 34	GAMMA	€ 384,16	€ 1,72
Dalbavancin (3 dose)	€ 330	€ 297	€ 363	€ 17	GAMMA	€ 384,16	€ 0,86
Vancomycin (cost per day of administration)	€ 23	€ 21	€ 25	€ 1	GAMMA	€ 384,16	€ 0,06
Teicoplanin (cost per day of administration)	€ 24	€ 22	€ 26	€ 1	GAMMA	€ 384,16	€ 0,06
Linezolid	€ 50	€ 45	€ 55	€ 3	GAMMA	€ 384,16	€ 0,13
% use vancomycin	59%	53%	65%	3,0%	BETA	157,51	108,45
% use teicoplanin	11%	10%	12%	0,6%	BETA	341,90	2.765,30
% use linezolid	30%	27%	33%	1,5%	BETA	268,91	626,46
Gram-positive therapy (per day of administration)	€ 31	€ 28	€ 34	€ 2	GAMMA	€ 384,16	€ 0,08
Piperacillin tazobactam	€ 26	€ 23	€ 29	€ 1	GAMMA	€ 384,16	€ 0,07
Oral therapy (Amoxicillin Clavulanate)	€ 3	€ 3	€ 3	€ 0	GAMMA	€ 384,16	€ 0,01
Hospitalization							
Hospitalization purulent patient	€ 310	€ 279	€ 341	€ 16	GAMMA	€ 384,16	€ 0,81
Hospitalization nonpurulent patient	€ 654	€ 589	€ 720	€ 33	GAMMA	€ 384,16	€ 1,70
Cost per day of hospitalization	€ 100	€ 90	€ 110	€ 5	GAMMA	€ 384,16	€ 0,26
Diagnostic tests							
Swab	€ 3	€ 3,05	€ 20	€ 0,2	GAMMA	€ 384,16	€ 0,01
Ultrasound	€ 6	€ 5	€ 6	€ 0	GAMMA	€ 384,16	€ 0,01
CAT	€ 40	€ 36	€ 44	€ 2	GAMMA	€ 384,16	€ 0,10
MRI	€ 156	€ 140	€ 180	€ 12	GAMMA	€ 155,49	€ 1,00
Specialist service							
Examination	€ 5	€ 4	€ 5	€ 0	GAMMA	€ 384,16	€ 0,01
Installation PICC and other related costs							

(*Continued*)

Table A2. (Continued).

Number of patients with ABSSSI	Base case	Min	Max	SD	DISTRIBUTION	ALPHA	BETA
Installation of Peripherally Inserted Central Catheter (PICC)	€ 267	€ 240	€ 294	€ 14	GAMMA	€ 384,16	€ 0,70
Thrombophlebitis	€ 960	€ 864	€ 1.056	€ 49	GAMMA	€ 384,16	€ 2,50
Infection PICC related	€ 1.038	€ 935	€ 1.142	€ 53	GAMMA	€ 384,16	€ 2,70
Malposition	€ 134	€ 120	€ 147	€ 7	GAMMA	€ 384,16	€ 0,35
Malfunction	€ 267	€ 240	€ 294	€ 14	GAMMA	€ 384,16	€ 0,70
PICC dressing patch costs (to be changed every 7 days)	€ 10	€ 9	€ 11	€ 1	GAMMA	€ 384,16	€ 0,03
Additional costs due to Vancomycin							
EA Dialysis (CVC device for dialysis + Hemofiltration)	€ 19	€ 17	€ 20	€ 1	GAMMA	€ 384,16	€ 0,05
EA Nephrotoxicity	€ 3	€ 2	€ 3	€ 0	GAMMA	€ 384,16	€ 0,01
Monitoring Vancomycin (twice daily for 3 days)	€ 46	€ 41	€ 51	€ 2	GAMMA	€ 384,16	€ 0,12
Lenght of hospital stay							
Average length of hospital stay purulent	8,0	7,2	8,8	0,41	GAMMA	€ 384,16	€ 0,02
Average length of hospital stay nonpurulent	9,4	8,5	10,3	0,48	GAMMA	€ 384,16	€ 0,02
Average length of hospital stay purulent >11,7	14,8	13,3	16,2	0,75	GAMMA	€ 384,16	€ 0,04
Average length of hospital stay nonpurulent >11,2	14,6	13,1	16,0	0,74	GAMMA	€ 384,16	€ 0,04
Additional day per purulent >11,7	5,8	5,2	6,3	0,29	GAMMA	€ 384,16	€ 0,02
Additional day per nonpurulent >11,2	5,6	5,0	6,1	0,29	GAMMA	€ 384,16	€ 0,01
Spanish parameters and distribution							
Number of patients eligible to early discharge	13.499						
Purulent > 3 day	6.214						
Nonpurulent > 3 day	7.248						
Sort of infection (> 3 day)	Model value	Min	Max				
Purulent ABSSSI	46%	41,4%	50,6%	2,3%	BETA	207,29	241,95
Nonpurulent ABSSSI	54%	48,6%	59,4%	2,8%	BETA	176,87	149,91
Nonpurulent patient – Sort of bacteria	Model value	Min	Max				
Indeterminate	70%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Polymicrobial	10%	9,0%	11,0%	0,5%	BETA	345,74	3.110,70
Gram-negative	7%	6,3%	7,7%	0,4%	BETA	357,27	4.745,57
Gram-positive	13%	11,7%	14,3%	0,7%	BETA	334,22	2.235,70
Purulent patient – Sort of origin							
Surgical	70%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Non surgical	30%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Surgical eligible to ED	50%	45,0%	55,0%	2,6%	BETA	192,08	191,08
Surgical No eligible to ED	50%	45,0%	55,0%	2,6%	BETA	192,08	191,08
Discharge distribution with dalbavancin	Mean	Min	Max				
Nonpurulent patient: Indeterminate or polymicrobial	**100%**						
Discharge(4 day)	60%	54,0%	66,0%	3,1%	BETA	153,66	101,44
Observation(4 day)	40%	36,0%	44,0%	2,0%	BETA	230,50	344,74
Discharge(8 day)	70%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Observation up to clinical evaluation	30%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Nonpurulent patient: Gram-positive							
Discharge(4 day)	70%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Observation(4 day)	30%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Discharge(8 day)	90%	81,0%	99,0%	4,6%	BETA	38,42	3,27
Observation up to clinical evaluation	10%	9,0%	11,0%	0,5%	BETA	345,74	3.110,70
Purulent patient: surgical							
Discharge(4 day)	50%	45,0%	55,0%	2,6%	BETA	192,08	191,08
Observation(4 day)	50%	45,0%	55,0%	2,6%	BETA	192,08	191,08
Discharge(8 day)	70%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Observation up to clinical evaluation	30%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Purulent patient: nonsurgical							
Discharge(4 day)	40%	36,0%	44,0%	2,0%	BETA	230,50	344,74
Observation(4 day)	60%	54,0%	66,0%	3,1%	BETA	153,66	101,44
Discharge(8 day)	70%	63,0%	77,0%	3,6%	BETA	115,25	48,39
Observation up to clinical evaluation	30%	27,0%	33,0%	1,5%	BETA	268,91	626,46
Discharge distribution with standard therapy	Model value	Min	Max				
Nonpurulent patient: Indeterminate or polymicrobial							
Discharge(4 day)	11%	9,8%	11,9%	0,6%	BETA	342,51	2.815,61
Observation(4 day)	89%	80,2%	98,1%	4,5%	BETA	41,65	4,06
Discharge (8 day)	58%	52,6%	64,2%	3,0%	BETA	159,82	112,85
Observation up to clinical evaluation	42%	37,4%	45,8%	2,1%	BETA	224,34	313,92
Nonpurulent patient: Gram-positive							
Discharge(4 day)	11%	9,8%	11,9%	0,6%	BETA	342,51	2.815,61
Observation(4 day)	89%	80,2%	98,1%	4,5%	BETA	41,65	4,06
Discharge (8 day)	58%	52,6%	64,2%	3,0%	BETA	159,82	112,85
Observation up to clinical evaluation	42%	37,4%	45,8%	2,1%	BETA	224,34	313,92

(*Continued*)

Table A2. (Continued).

Number of patients with ABSSSI	Base case	Min	Max	SD	DISTRIBUTION	ALPHA	BETA
Purulent patient: surgical							
Discharge(4 day)	11%	10,1%	12,4%	0,6%	BETA	340,92	2.686,75
Observation(4 day)	89%	79,9%	97,6%	4,5%	BETA	43,24	4,48
Discharge(8 day)	50%	45,1%	55,1%	2,6%	BETA	191,70	189,93
Observation up to clinical evaluation	50%	44,9%	54,9%	2,5%	BETA	192,46	192,23
Purulent patient: nonsurgical							
Discharge(4 day)	12%	10,9%	13,3%	0,6%	BETA	337,77	2.458,47
Observation(4 day)	88%	79,1%	96,7%	4,5%	BETA	46,39	5,37
Discharge(8 day)	57%	51,3%	62,6%	2,9%	BETA	165,38	124,01
Observation up to clinical evaluation	43%	38,7%	47,4%	2,2%	BETA	218,78	288,42
Risks of nosocomial infections	Model value	Min	Max				
PICC related							
Risk thrombophlebitis (per day)	0,8%	0,7%	0,9%	0,0%	BETA	381,16	48.353,04
Risk infection (per day)	0,2%	0,2%	0,2%	0,0%	BETA	383,30	170.089,84
Risk malposition(per day)	9,3%	8,3%	10,2%	0,5%	BETA	348,59	3.415,18
Risk malfunction (per day)	0,8%	0,7%	0,9%	0,0%	BETA	381,16	48.468,38
Costs parameter							
Drug therapy	Model value	Min	Max				
Dalbavancin (1 + 1 dose)	€ 844	€ 760	€ 928	€ 43	GAMMA	€ 384,16	€ 2,20
Dalbavancin (3 dose)	€ 422	€ 380	€ 464	€ 22	GAMMA	€ 384,16	€ 1,10
Vancomycin (cost per day of administration)	€ 14	€ 12	€ 15	€ 1	GAMMA	€ 384,16	€ 0,04
Teicoplanin (cost per day of administration)	€ 22	€ 19	€ 24	€ 1	GAMMA	€ 384,16	€ 0,06
Linezolid	€ 72	€ 64	€ 79	€ 4	GAMMA	€ 384,16	€ 0,19
% use vancomycin	*54%*	49%	59%	2,8%	BETA	176,71	149,53
% use teicoplanin	*7%*	6%	8%	0,4%	BETA	357,27	4.745,57
% use linezolid	*39%*	35%	43%	2,0%	BETA	234,34	365,53
Gram-positive therapy (per day of administration)	€ 36,86	€ 33	€ 41	€ 2	GAMMA	€ 384,16	€ 0,10
Piperacillin tazobactam	€ 5	€ 5	€ 6	€ 0	GAMMA	€ 384,16	€ 0,01
Oral therapy (Amoxicillin Clavulanate)	€ 3	€ 3	€ 3	€ 0	GAMMA	€ 384,16	€ 0,01
Hospitalization							
Hospitalization purulent patient	€ 884,4	€ 796	€ 973	€ 45	GAMMA	€ 384,16	€ 2,30
Hospitalization nonpurulent patient	€ 870,0	€ 783	€ 957	€ 44	GAMMA	€ 384,16	€ 2,26
Cost per day of hospitalization	€ 601,0	€ 541	€ 661	€ 31	GAMMA	€ 384,16	€ 1,56
Diagnostic tests							
Swab	€ 7	€ 6,51	€ 20	€ 0,4	GAMMA	€ 384,16	€ 0,02
Ultrasound	€ 20	€ 18	€ 22	€ 1	GAMMA	€ 384,16	€ 0,05
CAT	€ 86	€ 77	€ 95	€ 4	GAMMA	€ 384,16	€ 0,22
MRI	€ 126	€ 113	€ 180	€ 28	GAMMA	€ 20,92	€ 6,02
Specialist service							
Examination	€ 37	€ 33	€ 41	€ 2	GAMMA	€ 384,16	€ 0,10
Installation PICC and other related costs							
Installation of Peripherally Inserted Central Catheter (PICC)	€ 495	€ 446	€ 545	€ 25	GAMMA	€ 384,16	€ 1,29
Thrombophlebitis	€ 498	€ 448	€ 548	€ 25	GAMMA	€ 384,16	€ 1,30
Infection PICC related	€ 945	€ 851	€ 1.040	€ 48	GAMMA	€ 384,16	€ 2,46
Malposition	€ 248	€ 223	€ 272	€ 13	GAMMA	€ 384,16	€ 0,64
Malfunction	€ 495	€ 446	€ 545	€ 25	GAMMA	€ 384,16	€ 1,29
PICC dressing patch costs (to be changed every 7 days)	€ 7	€ 6	€ 8	€ 0	GAMMA	€ 384,16	€ 0,02
Additional costs due to Vancomycin							
EA Dialysis (CVC device for dialysis + Hemofiltration)	€ 13	€ 11	€ 14	€ 1	GAMMA	€ 384,16	€ 0,03
EA Nephrotoxicity	€ 2	€ 2	€ 3	€ 0	GAMMA	€ 384,16	€ 0,01
Monitoring Vancomycin (twice daily for 3 days)	€ 62	€ 56	€ 68	€ 3	GAMMA	€ 384,16	€ 0,16
Length of hospital stay							
Average length of hospital stay purulent	11,6	10,4	12,8	0,59	GAMMA	€ 384,16	€ 0,03
Average length of hospital stay nonpurulent	11,1	10,0	12,2	0,57	GAMMA	€ 384,16	€ 0,03
Average length of hospital stay purulent >11,7	17,2	15,5	18,9	0,88	GAMMA	€ 384,16	€ 0,04
Average length of hospital stay nonpurulent >11,2	16,7	15,0	18,4	0,85	GAMMA	€ 384,16	€ 0,04
Additional day per purulent >11,7	8,2	7,4	9,0	0,42	GAMMA	€ 384,16	€ 0,02
Additional day per nonpurulent >11,2	7,7	6,9	8,5	0,39	GAMMA	€ 384,16	€ 0,02
Romanian parameters and distribution	5,6	5,0	6,1	€ 0	GAMMA	€ 384,16	€ 0,01