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TITLE PAGE

Article Title:

Clinical predictors of outcome in patients with infective endocarditis receiving outpatient parenteral antibiotic therapy (OPAT)

Running Title:

Predictors of outcome for endocarditis in OPAT

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Abstract

Objectives

Outpatient parenteral antimicrobial therapy (OPAT) is increasingly used to treat infective endocarditis (IE) with documented success. This study aims to identify risk factors for treatment failure and poor outcomes in patients with IE treated through OPAT.

Methods

We conducted a retrospective analysis of all episodes of IE treated over 13 years (September 2006 - September 2019) at a large teaching hospital in Sheffield, UK. We defined OPAT failure as unplanned readmission or death within 30 days of discharge from the OPAT service. Major adverse cardiac events (MACE) were defined as a composite of IE-related death, cardiac surgery, and recurrence of IE within the first year of completion of OPAT.

Results

Overall, 168 episodes of IE were reviewed. OPAT failure and MACE occurred in 44 episodes (26.2%) and 29 episodes (17.3%) respectively. On multivariable analysis, pre-existing renal failure (adjusted odds ratio [aOR], 3.00; 95% confidence interval [CI], 1.08-8.30; *P* = 0.034) and Charlson comorbidity score (aOR, 1.29 per unit increase; 95% CI, 1.06-1.57; *P* = 0.011) were associated with increased risk of failure. Previous endocarditis (aOR, 3.60; 95% CI, 1.49-8.70; *P* = 0.004) and cardiac complications (aOR, 3.85; 95% CI, 1.49-9.93; *P* = 0.005) were risk factors for MACE, whereas cardiac surgery during the initial hospitalisation for IE (aOR, 0.34; 95% CI, 0.12-0.22; P <0.001) was a protective factor.

Conclusions

Our findings suggest that OPAT is safe and effective for completing antibiotic treatment for IE, including cases deemed to be at increased risk of complications. However, careful patient selection, monitoring and timely follow-up (especially in patients with significant comorbidities) are paramount to optimise clinical outcomes.

Keywords

Infective endocarditis; Outcomes; Outpatient parenteral antimicrobial therapy; Risk factors; Treatment failure.

Introduction

Infective endocarditis (IE) is a serious and potentially fatal infection that often requires prolonged parenteral antimicrobial therapy. The efficacy and safety of outpatient parenteral antimicrobial therapy (OPAT) in the management of IE have been demonstrated in several observational studies.[1-7] OPAT is often used to consolidate antimicrobial therapy after initial inpatient treatment. Despite its benefits, OPAT is potentially associated with increased clinical risk due to reduced clinical supervision and monitoring. Even with careful patient selection and multidisciplinary team-driven therapeutic plans, the use of potentially toxic antimicrobial agents and duration of treatment imply complications including treatment failure, and readmission for some patients managed through OPAT are inevitable. Predicting and preventing treatment failure could improve patient outcomes and reduce healthcare costs. Nevertheless, the predictors of failure and poor outcomes in patients with IE treated with OPAT are not totally clear.[7,8]

This study aimed to identify factors that might be associated with increased risk of treatment failure and poor outcomes in patients with IE treated at an OPAT service based in a large tertiary referral teaching hospital in Sheffield, UK.

Methods

Patient population and setting

We conducted a retrospective cohort study of all episodes of presumed or definite IE treated with OPAT between September 2006 and September 2019 at Sheffield Teaching Hospitals, South Yorkshire, England, UK. Cases of IE were defined according to the modified Duke criteria.[9] Patients with an implantable cardiac electronic device (ICED) infection but without evidence of endocarditis were excluded. The Sheffield OPAT service, established in January 2006, is one of the largest in the United Kingdom. The OPAT service, patient selection criteria and a prospectively maintained database have been previously described.[10] Patient selection, antimicrobial regimen and mode of OPAT delivery were the responsibility of the OPAT physicians. Patients with IE were offered OPAT when deemed clinically stable on careful assessment by cardiology and infectious diseases physicians. They were required to have at least a 2-week period of inpatient care prior to starting OPAT, since the risk of complications is greatest during this period. Patients were reviewed in person at least once a week during their OPAT treatment and regularly by their cardiology team. Individual patient's progress was discussed at a weekly multidisciplinary meeting.

Data collection

The OPAT databases, hospital electronic clinical and laboratory databases were reviewed. Data extracted included patient demographics, comorbidities, risk factors for IE, microbiology culture results, echocardiographic findings, associated ICED infection, inpatient cardiac surgery, complications of IE, antimicrobial regimen, duration of inpatient and OPAT therapy, mode of OPAT delivery, type of vascular access, OPAT outcome, hospital readmission, and reason for and length of hospitalisation. Age (years) was determined at the time of commencing OPAT. Weighted Charlson comorbidity score was calculated for each patient and was determined at the time OPAT was commenced.[11] Chronic kidney disease was based upon an estimated glomerular filtration rate of <60 ml/min/1.73 m^2.[12] Drug-resistant organisms included methicillin-resistant *Staphylococcus aureus* and penicillin-resistant streptococci. The study was approved by the Trust's clinical effectiveness unit.

Outcomes and Definitions

The outcomes were OPAT failure at 30 days and one-year major adverse cardiac events (MACE). 30-day OPAT failure was defined as unplanned cardiac surgery during OPAT, unplanned readmission to an acute care hospital for any reason or death within 30 days of discharge from the OPAT service. MACE were defined as a composite of IE-related death, cardiac surgery and recurrence of IE within the first year of completion of OPAT. IE-related death included cardiac death and death caused by complications of endocarditis. Deaths unrelated to IE (e.g. death from malignant disease) were excluded. A recurrence (relapse or reinfection) was defined as a new episode of IE caused by the same or a different microorganism occurring within one year after completion of OPAT.

Statistical analysis

Categorical data were presented as counts and percentages. Numerical data were summarised as mean with standard deviation or median with interquartile range (IQR) depending on the degree of skewness in the distributions. Logistic regression was used for the analysis of risk factors of 30-day OPAT failure and one-year MACE. A set of 20 potential risk factors were examined, including patient-related, infection-related and treatment-related variables selected by clinical judgment and literature review. None of the candidate risk factors had missing values. An initial multivariable logistic regression model for each outcome was constructed with forward stepwise selection of variables with $P < 0.30$ on univariate analysis. Variables that were identified as risk factors in other studies but did not enter the initial model were forced one-by-one into the initial model to examine the possibility of negative confounding. The final model retained variables with a two-sided $P < 0.05$. The ratio of cases to variables was maintained to at least 10:1 during the model building process. Multicollinearity among model predictors was ruled out by examining Spearman correlations and variance inflation factors. Linearity in the log (odds) for continuous variables (age and Charlson score) was assessed using

restricted cubic splines. Potential within-patient correlation caused by having different OPAT episodes in the same patient was taken into account by performing cluster-robust variance estimation relaxing the assumption of independent observations. Analyses were performed using STATA v.14 (StataCorp, College Station, TX, USA).

Results

Cohort characteristics

Over the 13-year study period, we recorded 168 episodes of IE in 146 individual patients. Table 1 shows the demographic and clinical characteristics of the cohort. The mean age of the patients was 60 (range, 16-91) years; 78% (131/168) were male and 68% (115/168) had native valve endocarditis. 109 (65%) episodes were classified as definite IE by modified Duke criteria. The most common causative pathogens isolated were viridans group streptococci (26%; 43/168), *S. aureus* (21%; 36/168), and coagulase-negative staphylococci (14%; 23/168). The median duration of inpatient antimicrobial therapy was 21 days (IQR, 16-30; range, 7-65 days). Patients with complications of IE such as cardiac or embolic events received longer inpatient treatment. The median length of OPAT therapy was 23 days (IQR, 17-31; range, 1-61 days).

Clinical outcomes

OPAT failure was recorded in 44 (26%) episodes – mostly due to unplanned readmission (93%; 41/44). The reasons for unplanned readmission are shown in Supplementary Table 1. MACE occurred in 29 (17%) episodes. Heart valve surgery was the main cause of MACE (59%; 17/29). One-year mortality was 2% (4/168). Four episodes of recurrence occurred within 6 months of completing OPAT (relapse). All recurrences were caused by microorganisms of same species that caused the initial episode.

Risk factor analysis

The results of the logistic regression analyses of predictors of OPAT failure and MACE are shown in Table 3. Chronic kidney disease (adjusted odds ratio [aOR], 3.00; 95% confidence interval [CI], 1.08-8.30; *P* = 0.034) and Charlson comorbidity score (aOR, 1.29; 95% CI, 1.06-1.57; *P* = 0.011) were independently associated with increased risk of 30-day OPAT failure. Previous IE (aOR, 3.60; 95% CI, 1.49-8.70; *P* = 0.004), cardiac complications (aOR, 3.85; 95% CI, 1.49-9.93; *P* = 0.005) and cardiac surgery during the initial hospitalisation for IE (aOR, 0.34; 95% CI, 0.12-0.22; P <0.001) were independent predictors of one-year MACE.

Discussion

Our study highlights the fact that patients with IE treated with OPAT are at risk of treatment failure and poor outcomes. We have previously found that patients with endovascular infection (including IE) treated with OPAT are at increased risk of unplanned readmission.[13] In this study, we explore factors associated with 30-day OPAT failure and one-year poor outcomes. Our definitions of OPAT failure and MACE are supported by previous studies.[14-16] We found two factors, which are readily available at the time of commencing OPAT, to be important predictors of OPAT failure: pre-existing renal failure and Charlson comorbidity index score. In addition, patients with a history of previous IE and those who developed cardiac complications, such as severe valvular insufficiency, perivalvular abscess or intracardiac fistula, were more likely to have worse long-term outcomes. However, patients who had cardiac surgery prior to OPAT were found to have favourable long-term outcomes.

The rates of unplanned readmission (24%) and one-year mortality (2%) in our cohort were comparable to other OPAT studies.[3,4,7,14,17-19] Renal failure and multimorbidity have been shown to be associated with OPAT failure in patients with IE.[14,15] Patients with multimorbidity were likely to be readmitted due to the underlying comorbidities and related complications.[20] For some patients, the risk of OPAT failure may be a direct consequence of their non-cardiac comorbidities rather than cardiac pathology. In non-OPAT related studies, recurrent endocarditis and cardiac complications have been associated with long-term adverse cardiac outcomes.[21-25] Hence, these risk factors observed in our study may not be directly related to the OPAT therapy. In our cohort, antibiotic dosing was appropriately adjusted according to renal function based on established guidelines. Although we did not explore the effects of antimicrobial concentration on clinical outcomes in patients with impaired renal function, serum drug levels were closely monitored to ensure therapeutic levels were achieved were required (i.e. aminoglycoside and glycopeptide therapy). We did not find any association between an antimicrobial agent and OPAT failure.

Similar to Pericàs et al., we found that cardiac surgery during the initial hospitalisation for IE is independently associated with favourable long-term outcomes.[1] Although we did not assess the timing of cardiac surgery, a number of non-OPAT related studies have shown that early valve surgery improves the prognosis of IE in certain groups of patients.[16,22,25] In our study, four patients were readmitted during their OPAT treatment for cardiac surgery. Two of the cardiac surgeries were pre-planned and were not considered as OPAT failure. The optimal timing of surgery in IE is not fully understood.[26] Studies are required to optimise the use of surgery, especially in higher risk patients.

OPAT has been shown to be safe and effective for intravenous drug users (IVDUs).[27,28] However, the number of IVDUs in our study is too small to draw meaningful conclusions. Active IVDUs are often

excluded from our OPAT service due to a number of challenges including vascular access and social issues. Nevertheless, carefully selected and closely monitored IVDUs with IE may be safely treated with OPAT. Long-active antimicrobial agents, such as dalbavancin and oritavancin, which could be administered once a week, may offer a novel outpatient treatment option for IE in IVDUs and other hard-to-reach groups.[29,30] In our study, one patient was successfully treated (sequential treatment) for *Streptococcus* IE with dalbavancin.

There has been increasing interest in oral therapy for infections traditionally treated with prolonged courses of parenteral antibiotics.[31] Sequential oral antimicrobial therapy may be a suitable alternative to OPAT in carefully selected patients with uncomplicated left-sided IE caused by staphylococci, streptococci and enterococci (POET study).[32] Whilst further works are required before recommending routine use of oral antimicrobials for IE, OPAT remains a safe and effective alternative to inpatient treatment, especially when oral therapy is not appropriate due to drug interactions, intolerance, poor adherence, antibiotic resistance or poor oral absorption. In addition, patients with complications of IE such as embolic or cardiac abscess may require prolonged parenteral therapy. It is possible that oral antibiotic therapy for IE could be administered within an OPAT setting to allow close monitoring and timely follow-up.[33]

OPAT failure and poor long-term outcomes have been associated with *S. aureus* IE and glycopeptide therapy.[3,14,15,34] However, we did not identify these risk factors as significant. In our study, poor outcomes were also not associated with most of the factors (e.g. aortic valve disease, prosthetic value disease and IE caused by virulent organisms) deemed to be associated with increased risk of complications and preclude use of OPAT by Andrews and von Reyn.[35] As a general rule, it seems logical to consider OPAT for all medically stable patients without major IE complications after an initial period of inpatient therapy. During OPAT therapy, patients should be carefully monitored for early detection of complications, treatment failure, or clinical deterioration, which may necessitate further interventions including readmission.

This study has limitations that should be acknowledged. This was a single-centre, retrospective analysis with no hospitalised comparators. The data were originally collected prospectively, which reduces the risk of measurement bias or poor accuracy of data records. Despite extensive analysis of factors previously reported to be associated with OPAT failure in IE, we cannot be certain that we have not missed other important risk factors or the influence of unrecorded confounders on our findings. Although our epidemiologic data are comparable to other cohort studies, the relatively low incidence of IE suggests that large multicentre studies are needed to confirm our findings and comprehensively explore risk factors for poor outcomes in IE treated with OPAT.

Conclusions

Our study adds to the growing evidence that OPAT for IE is a safe and effective alternative to inpatient treatment. It also demonstrates that patients deemed to be at higher risk of complications, such as prosthetic valve IE or *S. aureus* IE, may be successfully treated in outpatient settings. However, careful patient selection and monitoring of patients with pre-existing comorbidities and cardiac complications are recommended to optimise clinical outcomes.

Author contributions

OCD conceived the study, collected data, and wrote the manuscript. RM collected data and revised the manuscript; NC collected data and revised the manuscript. EIK analysed data and revised the manuscript.

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Declarations of Competing Interest

The authors declare that there is no conflict of interest.

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TABLES

Table 1. Baseline characteristics of patients and episodes of infective endocarditis (*N* = 168).

Characteristic	**n (%)**
Age (years), mean ± SD (range)	60 ± 17.6 (16-91)
Male sex	131 (78.0)
Comorbidities	
Pre-existing renal failure[a]	32 (19.0)
Heart failure	35 (20.8)
Charlson comorbidity score, median (IQR)	1 (0-2)
Predisposing factors	
Any predisposing factor	95 (56.5)
Congenital cardiac abnormality	42 (25.0)
Previous endocarditis	31 (18.5)
Rheumatic heart disease	4 (2.4)
Intravenous drug use	3 (1.8)
Diagnostic criteria (modified Duke criteria)	
Possible	59 (35.1)
Definite	109 (64.9)
Cardiac structure involved	
Aortic valve	71 (42.3)
Mitral valve	58 (34.5)
Tricuspid valve	20 (11.9)
Pulmonary valve	4 (2.4)
Multivalvular	9 (5.4)
Other cardiac structures[b]	6 (3.6)
Type of endocarditis	
Native	115 (68.5)
Prosthetic	53 (31.5)
Size of vegetation	
<10 mm	81 (48.2)
≥10 mm	30 (17.9)
Affected side	
Left-sided	140 (83.3)
Right-sided	26 (15.5)
Double-sided	1 (0.6)
Etiology	
Streptococci	62 (36.9)
Viridans group streptococci	43 (25.6)
Beta-haemolytic *streptococci*	10 (6.0)
S. gallolyticus	4 (2.4)

Nutritionally variant *streptococci*	2 (1.2)
Other streptococci	3 (1.8)
Staphylococci	59 (35.1)
Staphylococcus aureus	36 (21.4)
Meticillin-sensitive *S. aureus*	35 (20.8)
Meticillin-resistant *S. aureus*	1 (0.6)
Coagulase-negative staphylococci	23 (13.7)
Enterococci	17 (10.1)
Culture negative	14 (8.3)
Gram-negative bacilli	10 (6.0)
HACEK organisms	7 (4.2)
Non-HACEK	3 (1.8)
Fungi	1 (0.6)
Other organisms[c]	5 (3.0)
Multidrug resistant organism	3 (1.8)
Associated ICED infection	22 (13.1)
Embolic complications	47 (28.0)
Cardiac complications	72 (42.9)

Data are presented as n (%) unless otherwise indicated.
HACEK, Haemophilus, Aggregatibacter, Cardiobacterium, Eikenella and Kingella species.
ICED, implantable cardiac electronic device; IQR, interquartile range; SD, standard deviation
[a] Estimated glomerular filtration rate <60 ml/min/1.73 m^2.
[b] Other cardiac structures included: atrial septal defect *(*n = 1), mural endocardium (n = 3), ventricular septal defect (n = 1) and Waterston shunt (n = 1)*.*
[c] Other organisms included: *Actinomyces, Lactococcus*, *Propionibacterium*, *Tropheryma* species and mixed culture (1 each).

Table 2. Treatment characteristics and outcomes (*N* = 168).

Characteristic	n (%)
Pre-OPAT (inpatient) cardiac surgery	46 (27.4)
Duration of pre-OPAT (inpatient) antimicrobial therapy (days), median (IQR)	21 (16-30)
Duration of OPAT (days), median (IQR)	23 (17-31)
Mode of antimicrobial (OPAT) delivery	
Self/carer administration	79 (47.0)
Visiting nurse	56 (33.3)
Daily attendance	33 (19.6)
Class of antimicrobial (OPAT) agent[a]	
Cephalosporin	76 (40.4)
Penicillin	44 (23.4)
Glycopeptide	33 (19.6)
Cyclic lipopeptide	22 (11.7)
Aminoglycoside	9 (4.8)
Other agents[b]	4 (2.4)
Concurrent IV antimicrobial therapy	19 (11.3)
Use of central venous access	160 (95.2)
Outcomes	
30-day OPAT failure	44 (26.2)
Unplanned readmission	41 (24.4)
Cardiac surgery	2 (1.2)
Death	1 (0.6)
One-year MACE	29 (17.3)
Cardiac surgery	17 (10.1)
IE-related death	4 (2.4)
Recurrence	8 (4.8)

Data are presented as n (%) unless otherwise indicated.
IE, infective endocarditis; IQR, interquartile range; IV, intravenous; MACE; major adverse cardiac events; OPAT, outpatient parenteral antimicrobial therapy
[a] Some patients received more than one parenteral antimicrobial agent. Thus, total number of antimicrobial agents is greater than total number of patient episodes.
[b] Other agents included: antifungal (n = 1) and carbapenem (n = 3)

Table 3. Risk factors for 30-day outpatient parenteral antimicrobial therapy failure and one-year major adverse cardiac events (*N* = 168)

	30-day OPAT failure				1-year MACE			
	Univariate		Multivariable		Univariate		Multivariable	
Variable	OR (95% CI)	*P*	aOR (95% CI)	*P*	OR (95% CI)	*P*	aOR (95% CI)	*P*
Age, per 10 years	1.14 (0.9 – 1.37)	0.172	-	-	0.98 (0.72 – 1.33)	0.883	-	-
Age, restricted cubic splines[a]								
Spline 1, per 10 years	1.25 (0.85 – 1.84)	0.251	-	-	0.76 (0.52 – 1.10)	0.147	-	-
Spline 2, per 10 years	0.88 (0.59 – 1.30)	0.516	-	-	1.46 (0.78 – 2.74)	0.239	-	-
Male sex	0.80 (0.37 – 1.69)	0.553	-	-	2.81 (0.79 – 9.93)	0.109	-	-
Comorbidities								
Pre-existing renal failure	6.49 (2.84 – 14.81)	<0.001	3.00 (1.08 – 8.30)	0.034	0.44 (0.10 – 2.01)	0.288	-	-
Heart failure	1.65 (0.78 – 3.48)	0.191	-	-	1.58 (0.51 – 4.92)	0.429	-	-
Charlson comorbidity score, per unit	1.50 (1.26 – 1.78)	<0.001	1.29 (1.06 – 1.57)	0.011	0.74 (0.49 – 1.12)	0.157	-	-
Predisposing factors								
Congenital cardiac abnormality	0.59 (0.25 – 1.40)	0.231	-	-	3.70 (1.47 – 9.30)	0.005	-	-
Previous endocarditis	1.19 (0.51 – 2.79)	0.685	-	-	3.64 (1.51 – 8.76)	0.004	3.60 (1.49 – 8.70)	0.004
Cardiac structure involved								
Aortic valve	0.93 (0.47 – 1.83)	0.828	-	-	1.34 (0.53 – 3.43)	0.537	-	-
Mitral valve	0.97 (0.48 – 1.98)	0.943	-	-	1.00 (0.37 – 2.68)	0.997	-	-
Tricuspid valve	0.46 (0.13 – 1.67)	0.238	-	-	0.23 (0.03 – 1.80)	0.160	-	-
Prosthetic valve endocarditis	1.34 (0.68 – 2.67)	0.398	-	-	1.41 (0.52 – 3.79)	0.495	-	-
Left-sided IE vs. right-sided IE	0.74 (0.30 – 1.81)	0.513	-	-	0.54 (0.16 – 1.82)	0.322	-	-
Etiology								
Streptococcus species	0.64 (0.32 – 1.29)	0.216	-	-	0.88 (0.35 – 2.20)	0.785	-	-
Staphylococcus aureus	1.84 (0.82 – 4.13)	0.138	-	-	0.95 (0.33 – 2.76)	0.922	-	-
Enterococcus species	0.85 (0.30 – 2.40)	0.764	-	-	3.04 (0.70 – 13.11)	0.137	-	-
Associated ICED infection	1.07 (0.35 – 3.21)	0.910	-	-	-[b]	-	-	-
Embolic complications	1.29 (0.63 – 2.65)	0.493	-	-	0.98 (0.31 – 3.12)	0.968	-	-
Cardiac complications	1.02 (0.52 – 2.00)	0.959	-	-	3.08 (1.14 – 8.31)	0.026	3.85 (1.49 – 9.93)	0.005
Other sites of infection	1.37 (0.66 – 2.82)	0.393	-	-	0.91 (0.29 – 2.90)	0.874	-	-
Pre-OPAT (inpatient) cardiac surgery	0.60 (0.27 – 1.37)	0.228	-	-	0.50 (0.18 – 1.41)	0.189	0.34 (0.12 – 0.22)	<0.001
Mode of antimicrobial (OPAT) delivery								
Self/carer administration	1.00	-	-	-	1.00	-	-	-
Visiting nurse	0.83 (0.38 – 1.85)	0.658	-	-	0.89 (0.30 – 2.61)	0.831	-	-
Daily attendance	1.20 (0.53 – 2.72)	0.661	-	-	1.03 (0.28 – 3.76)	0.962	-	-
Class of antimicrobial (OPAT) agent								
Cephalosporin	0.79 (0.40 – 1.53)	0.483	-	-	0.58 (0.23 – 1.44)	0.243	-	-
Penicillin	1.26 (0.59 – 2.67)	0.549	-	-	1.09 (0.39 – 3.08)	0.871	-	-
Glycopeptide	1.07 (0.46 – 2.48)	0.872	-	-	0.83 (0.22 – 3.12)	0.778	-	-
Concurrent IV antimicrobial therapy	1.35 (0.47 – 3.88)	0.579	-	-	0.53 (0.12 – 2.43)	0.416	-	-

aOR, adjusted odd ratios; CI; confidence interval; IECD, implantable cardiac electronic device; IV, intravenous; MACE; major adverse cardiac events; OPAT, outpatient parenteral antimicrobial therapy; OR, odds ratio

[a] Age was modelled using restricted cubic splines with slopes defined at quartiles (47, 62 and 73 years).

[b] None of the patients with associated ICED infection experienced a 1-year MACE.

Supplementary Table 1. Reasons for 30-day unplanned readmission (*n* = 41).

Reason for readmission	***n* (%)**
IE-related	21 (51.2)
Heart failure	4 (9.8)
Embolic complications	7 (17.1)
Cardiac surgery related	1 (2.4)
Worsening of existing infection/no improvement	9 (22.0)
Non-OPAT related[a]	8 (19.5)
Intravenous line-related complications	5 (12.2)
Adverse drug reaction	3 (7.3)
Clostridium difficile–associated diarrhoea	2 (4.9)
Respiratory infection	1 (2.4)
Not specified	1 (2.4)

OPAT, outpatient parenteral antimicrobial therapy
[a] Non-OPAT related included: fall (*n* = 1), constipation (*n* = 1), social admission (*n* = 1), musculoskeletal pain (*n* = 2), neoplasm related (*n* = 3).

Supplementary Table 2. Duration of pre-OPAT (inpatient) antimicrobial therapy (N = 168).

Duration of therapy (days)	***n* (%)**
1-2 weeks	13 (7.7)
2-3 weeks	67 (39.9)
3-4 weeks	39 (23.2)
>4 weeks	49 (29.2)

OPAT, outpatient parenteral antimicrobial therapy

Supplementary Table 3. Other sites of infections (*n* = 49).

Site	***n* (%)**
Multiple sites	13 (26.5)
Spinal infection	11 (22.4)
CNS infection	9 (18.4)
Other bone & joint infections	5 (10.2)
Lung infection	3 (6.1)
Splenic abscess	2 (4.1)
Renal abscess	2 (4.1)
Other sites[a]	4 (8.2)

[a] Other sites included: breast implant, dental abscess, endophthalmitis and cellulitis (one each)

Supplementary Table 4. Antimicrobial agents (*n* = 188)[a]

Antimicrobial agent	*n* (%)
Cephalosporin	**76 (40.4)**
Ceftriaxone	76 (40.4)
Penicillin	**44 (23.4)**
Flucloxacillin	38 (20.2)
Amoxicillin	6 (3.2)
Glycopeptide	**33 (17.6)**
Teicoplanin	20 (10.6)
Vancomycin	12 (6.4)
Dalbavancin	1 (0.5)
Cyclic lipopeptide	**22 (11.7)**
Daptomycin	22 (11.7)
Aminoglycoside	**9 (4.8)**
Gentamicin	9 (4.8)
Others	**4 (2.1)**
Meropenem	2 (1.1)
Ertapenem	1 (0.5)
Amphotericin B	1 (0.5)

[a] Some patients received more than one parenteral antimicrobial agent. Thus, total number of antimicrobial agents is greater than total number of patient episodes.