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Factors associated with successful completion of outpatient parenteral antibiotic therapy (OPAT): A 10-year review from a large West London service

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ABSTRACT

Outpatient parenteral antibiotic therapy (OPAT) is an established antimicrobial delivery method in the UK. OPAT services differ nationwide, with a paucity of high-quality outcome data to enable benchmarking. A retrospective review of clinical outcomes and adverse events (AEs) of all patients treated during 2008–2017 was performed to identify factors associated with success and failure. Regression models were used to identify factors associated with OPAT success, and AEs were described for the study population using definitions recommended by BSAC. In the 10-year period, 2870 patient episodes resulted in 69 610 days of treatment, with a 91.7% rate of successful therapy completion and 92.0% of infections cured or improved. We encountered 196 AEs, including 1 case of *Clostridium difficile*-associated diarrhoea. AEs occurred in 10.9% of patient episodes. Adverse drug and line events occurred at a rate of 3.3 and 1.78 per 1000 treatment days, respectively. Rashes, blood dyscrasias and hepatitis were the most common drug AEs. The odds of OPAT success was greater for patients who spent more time (>14 days) on OPAT therapy (OR = 2.32; $P < 0.01$), utilised a peripheral line (OR = 1.83; $P < 0.01$), were treated in the clinic compared with self-administration (OR = 2.1; $P < 0.02$) and did not experience an AE (OR = 0.23; $P < 0.01$). In our setting, the odds of a successful OPAT episode were associated with longer treatment course, OPAT delivered via a peripheral line, administration in an OPAT clinic setting, and no adverse line or drug events.
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1. Introduction

Outpatient parenteral antibiotic therapy (OPAT) is now an established clinical care model in the UK. Within the UK, Public Health England (PHE) recommends OPAT as an integral pathway for antimicrobial stewardship within the 'Start Smart – Then Focus' guidance published in 2015 [1]. The ability to deliver intravenous (i.v.) antibiotic therapy on an outpatient basis empowers patients to be actively involved in their treatment, improves their experience, whilst also reducing costs by reducing inpatient length of stay or avoiding hospital admission.

Delivering i.v. antibiotic therapy in a patient's home environment is complex. This inherent complexity means that it is difficult to predict whether an individual patient may fail to complete therapy. Adverse drug events often occur within the first few weeks of therapy, and re-admission can occur in up to 27% of patients [2,3]. In inpatient settings, every 10 days of additional therapy confers a 3% increased risk of an adverse drug event [4]. Drug selection is crucial, and narrow-spectrum targeted antibiotics are recommended to help combat antimicrobial resistance. Ceftriaxone and ertapenem are the mainstay of many OPAT services owing to their convenient once-daily administration, but are both broad-spectrum antibiotics. This contradiction to the stewardship agenda needs to be weighed against the numerous benefits as well as a clear demonstration both of safety and efficacy [5].

Expansion of OPAT has driven a need for clear governance structures, standardisation of clinical definitions and protocols, effective antimicrobial stewardship, and outcome monitoring. There are now standards for OPAT care published by professional societies in the USA, Europe and the UK [6–8]. All recommend prospective audit but as yet there is a paucity of data for units to use to benchmark their outcomes and to evaluate their practice.

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The British Society for Antimicrobial Chemotherapy (BSAC) developed an OPAT initiative to support the development of OPAT services in the UK. In June 2015, BSAC launched the OPAT National Outcomes Registry System (NORS) allowing data from local patient management systems to contribute to a national registry [9]. This allows both regional and national comparison of OPAT services giving a greater in-depth analysis of outcomes and adverse events (AEs). This report describes a large OPAT service over 10 years focusing on factors associated with OPAT success or failure.

2. Patients and methods

2.1. Setting and population

Imperial College Healthcare NHS Trust is a large acute Trust in West London (UK) consisting of five hospitals (Charing Cross, Hammersmith, Queen Charlotte's and Chelsea, St Mary's and Western Eye Hospitals). Two distinct OPAT services existed prior to the Trusts merging in October 2007. The first was set up in 2004 at St Mary's Hospital and the second in 2007 at Charing Cross Hospital. Both services have dedicated weekly clinics and multidisciplinary team meetings to discuss ongoing patient management.

2.2. Data collection

Prospective data are routinely collected for both OPAT services and are stored in local databases. Data captured include age, primary infective diagnoses, OPAT treatment days, antimicrobial regimen, route of administration, referring specialty and method of OPAT delivery. AEs and outcomes were not recorded on the St Mary's Hospital OPAT service during the years 2008–2015 and are therefore not included in the outcome analysis. Two authors (JH and MG) interrogated these databases and missing data were added retrospectively from clinic notes. Data were then mapped to the BSAC adult good practice recommendations (GPR) [7].

2.3. Definitions

Outcome measures used were those recommended by BSAC adult GPR and those used for the National Registry, as follows.

Infection outcome was defined as: (i) cure (completed OPAT therapy ± oral stepdown for defined duration with resolution of infection and no requirement for long-term antibiotic therapy); (ii) improved (completed OPAT therapy ± oral stepdown with partial resolution of infection but need for further follow-up, or completed OPAT therapy but required escalation of antimicrobial therapy during OPAT ± oral stepdown); and (iii) failure (progression or non-response of infection, required admission, surgical intervention or died for any reason). In this study, the infection outcomes cure and improved were combined to a single infection outcome of 'success'.

OPAT outcome was defined as: (i) success (completed therapy in OPAT with no change in antimicrobial agent, no AEs, cure or improvement of infection and no re-admission); (ii) partial success (completed therapy in OPAT with either change in antimicrobial agent or AE not requiring admission); (iii) indeterminate outcome (re-admission due to unrelated event); and (iv) failure (re-admitted due to infection worsening or due to an AE, or death by any cause during OPAT). In this study, the OPAT outcomes success and partial success were combined to a single infection outcome of 'success'. Indeterminate outcomes were removed from the final analysis.

Venous access was divided into either central, midline or peripheral. Central venous access refers to any vascular device that accessed the central venous system, which includes Hickmann® and peripherally inserted central catheters (PICCs). Peripheral venous access includes peripheral cannulae and Leaderflex cannulae.

Duration of therapy was divided into short- and long-term duration. Any duration of therapy $\leq$14 days was defined as short-term, and any therapy $>$14 days was defined as long-term.

Type of antibiotic was divided into either β-lactam or non-β-lactam therapy.

The severity of AEs was classed as either minor or severe. Severe AEs were those that led to re-admission and failure of OPAT therapy, or any condition that would be considered a significant AE such as *Clostridium difficile* infection, anaphylaxis or line-related bacteraemia. All other AEs were classed as minor.

Method of delivery relates to the setting in which OPAT was administered. These are defined by the clinical setting where the predominance of administrations occurred, i.e. community district nursing teams, hospital-based OPAT clinic or patient self-administration.

A full list of definitions is available in the supplementary material, including a breakdown of the specific infection diagnoses that were combined into the infection diagnoses used in this study and the rationale for definition for duration of therapy and distribution of conditions using the 14-day cut off (Appendix 1).

2.4. Statistical analysis

Patient characteristics were described for the total study population, and χ^2 test was used to explore differences in proportions across categories. Unpaired *t*-test was used to explore differences between continuous variables. Histograms were used to examine the frequency distribution for individual variables, and transformed variables were used where appropriate. Univariate logistic regression was used to examine associations between individual variables and OPAT outcome. A multivariable logistic regression model was used to examine factors associated with OPAT outcome adjusted for covariates. A *P*-value of $<$0.05 was considered statistically significant.

3. Results

3.1. Service overview

During the 10-year period between 1 January 2008 and 31 December 2017, the combined OPAT services delivered 2870 patient episodes to 2440 unique patients resulting in 69 610 days of treatment (DoT) (Table 1).

The mean patient age was 57 years and the median duration of therapy was 17 days. The majority of patients had a single OPAT episode, however 308 patients had multiple episodes, including 2 patients completing eight separate episodes. There were 64 individual infection diagnoses managed from over 30 referring hospital specialties. It was not possible to ascertain details on three patient episodes for antimicrobial therapy and on one patient for length of therapy owing to incomplete notes. β-Lactam antibiotics were the most common antimicrobial agents administered (ceftriaxone 30 677, ertapenem 11 055, meropenem 5142 and ceftazidime 4929 DoT, respectively), followed by glycopeptides (teicoplanin 8693 DoT) (Appendix 3, Figs S1 and S2). The single longest patient episode was a patient receiving meropenem for 585 days for malignant otitis externa. The busiest year of service was 2017 delivering 8117 DoT (Fig. 1).

Surgical specialties made up six of the top ten referral specialties, with orthopaedic infections leading to 14 635 DoT (Appendix 3, Fig. S5). The most common orthopaedic infections treated on OPAT were osteomyelitis and prosthetic knee/hip joint infections. Cellulitis was the most common single condition resulting in 345 patient episodes, followed by urinary tract infection with 271 patient episodes (Appendix 3, Table S6).

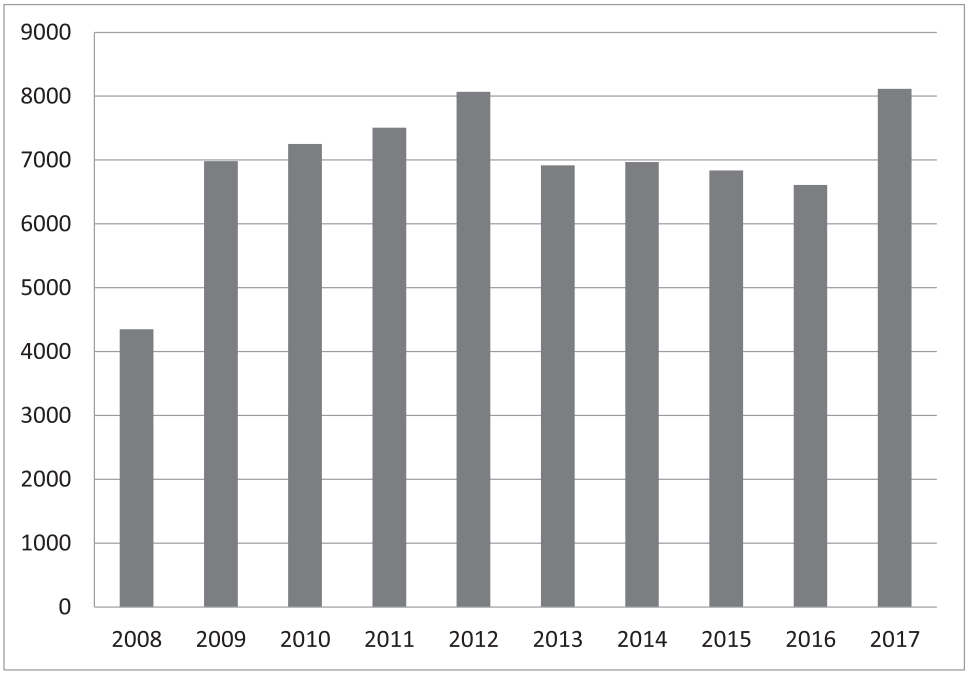

Fig. 1. Total days of treatment over the 10-year period by year.

Table 1
Conditions, antibiotics and specialties, with corresponding patient episodes and days of therapy (DoT).

Variable	Patient episodes ($n = 2870$)	DoT ($n = 69\ 610$)
Condition (%)		
Bloodstream infection (other)	35 (1.2)	496 (0.7)
Bloodstream infection (line-related)	48 (1.7)	847 (1.2)
Cardiac infection	147 (5.1)	3869 (5.6)
CNS infection	180 (6.3)	4294 (6.2)
CNS infection (device-related)	15 (0.5)	508 (0.7)
ENT infection	49 (1.7)	2933 (4.2)
Intra-abdominal infection	204 (7.1)	5414 (7.8)
Joint infection	118 (4.1)	2821 (4.1)
Joint infection (device-related)	216 (7.5)	6424 (9.2)
(Bloodstream infection) MSSA	46 (1.6)	717 (1.0)
Mycobacteria	50 (1.7)	4424 (6.4)
Osteomyelitis	282 (9.8)	9964 (14.3)
Osteomyelitis (device-related)	175 (6.1)	5785 (8.3)
Respiratory tract infection	260 (9.1)	4016 (5.8)
Skin and soft-tissue infection	581 (20.2)	7739 (11.1)
Urinary tract infection	309 (10.8)	3882 (5.6)
Vascular infection	7 (0.2)	148 (0.2)
Vascular infection (device-related)	118 (4.1)	4535 (6.5)
Other	30 (1.0)	794 (1.1)
Top five antibiotics (%)		
Ceftriaxone	1454 (50.7)	30 667 (44.1)
Ertapenem	485 (16.9)	11 055 (15.9)
Teicoplanin	324 (11.3)	8693 (12.5)
Ceftazidime	196 (6.8)	5142 (7.4)
Meropenem	133 (4.6)	4929 (7.1)
Top six specialties (%)		
Orthopaedics and trauma	484 (16.9)	14 635 (21.0)
Infectious diseases	296 (10.3)	6513 (9.4)
Respiratory medicine	256 (8.9)	5370 (7.7)
General and acute medicine	252 (8.8)	3153 (4.5)
Neurosurgery	177 (6.2)	4814 (6.9)
Vascular surgery	160 (5.6)	5976 (8.6)

CNS, central nervous system; ENT, ear, nose and throat; MSSA, methicillin-susceptible *Staphylococcus aureus*.

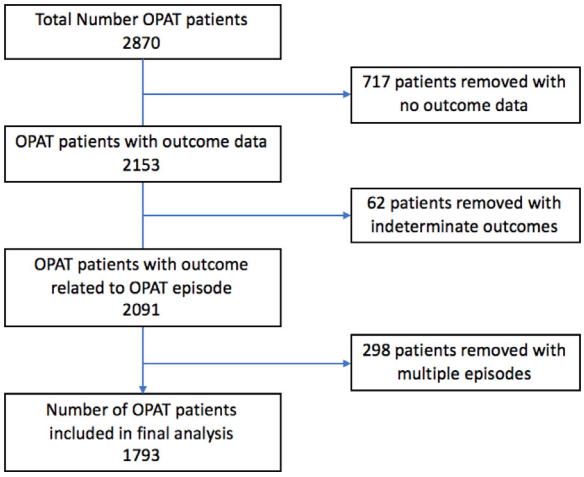

Fig. 2. Breakdown of number of patients included for the final outpatient parenteral antibiotic therapy (OPAT) outcome analysis.

3.2. OPAT and infection outcomes

OPAT outcome data were available for 1793 patients after removal of patients with no outcome data, indeterminate outcomes or multiple episodes (Fig. 2).

Table 2 details the patient characteristics for 1793 patient episodes and shows 91.7% (1645 patient episodes) successfully completed therapy on OPAT, and 92.0% (1649 patient episodes) were recorded as 'cure' or 'improved' for their infection. The mean age of the study population was 56.4 years with no significant difference between the OPAT success of failure groups (56.4 years vs. 56.9 years, respectively; $P = 0.72$). The 1793 patient episodes led to a total of 38 289 DoT. The most common condition treated was skin and soft-tissue infection (SSTI). The distribution of conditions differed across OPAT success and failure categories. The most

Table 2
Characteristics of 1793 patient episodes for patients on outpatient parenteral antibiotic therapy (OPAT).

Variable	Total patients with outcome data ($N = 1793$)	OPAT success ($n = 1645$; 91.7%)	OPAT failure ($n = 148$; 8.3%)	*P*-value
Age (years) (mean ± S.D.)	56.4 ± 17.8	56.4 ± 17.9	56.9 ± 17.4	0.72
Duration of treatment (days) [median (range)]	15 (1–550)	17 (1–550)	10 (1–166)	<0.001
Condition (%)				
Bloodstream infection (other)	20 (1.1)	19 (1.2)	1 (0.7)	0.016
Bloodstream infection (line-related)	40 (2.2)	38 (2.3)	2 (1.4)	
Cardiac infection	115 (6.4)	101 (6.1)	14 (9.5)	
CNS infection	151 (8.4)	136 (8.3)	15 (10.1)	
CNS infection (device-related)	12 (0.7)	9 (0.5)	3 (2.0)	
ENT infection	35 (2.0)	32 (1.9)	3 (2.0)	
Intra-abdominal infection	127 (7.1)	112 (6.8)	15 (10.1)	
Joint infection	63 (3.5)	57 (3.5)	6 (4.1)	
Joint infection (device-related)	121 (6.7)	109 (6.6)	12 (8.1)	
(Bloodstream infection) MSSA	32 (1.8)	30 (1.8)	2 (1.4)	
Mycobacteria	21 (1.2)	18 (1.1)	3 (2.0)	
Osteomyelitis	160 (8.9)	140 (8.5)	20 (13.5)	
Osteomyelitis (device-related)	118 (6.6)	112 (6.8)	6 (4.1)	
Respiratory tract infection	130 (7.3)	121 (7.4)	9 (6.1)	
Skin and soft-tissue infection	405 (22.6)	379 (23.0)	26 (17.6)	
Urinary tract infection	193 (10.8)	189 (11.5)	4 (2.7)	
Vascular infection	5 (0.3)	4 (0.2)	1 (0.7)	
Vascular infection (device-related)	27 (1.5)	24 (1.5)	3 (2.0)	
Other	18 (1.0)	15 (0.9)	3 (2.0)	
Duration of treatment				
Short-term	892 (49.7)	791 (48.1)	101 (68.2)	<0.001
Long-term	901 (50.3)	854 (51.9)	47 (31.8)	
OPAT delivery method [*n* (%)]				
Self-administration	252 (14.1)	233 (14.2)	19 (12.8)	0.001
Community nurse-led	1165 (65.0)	1050 (63.8)	115 (77.7)	
OPAT clinic	376 (21.1)	362 (22.0)	14 (9.5)	
Infection outcome [*n* (%)]				
Success	1649 (92.0)	1628 (99.0)	21 (14.2)	
Failure	144 (8.0)	17 (1.0)	127 (85.8)	<0.001
Venous access				
Central	949 (52.9)	836 (50.8)	113 (76.4)	
Midline	214 (11.9)	214 (13.0)	0 (0.0)	<0.001
Peripheral	630 (35.1)	595 (36.2)	35 (23.6)	
Antibiotic use [*n* (%)]				
β-Lactam	1505 (83.9)	1385 (84.2)	120 (81.1)	0.323
Non-β-lactam	288 (16.1)	260 (15.8)	28 (18.9)	

S.D., standard deviation; CNS, central nervous system; ENT, ear, nose and throat; MSSA, methicillin-susceptible *Staphylococcus aureus*.

common method of OPAT delivery was community nurse-led and via a central line. The majority of patients were treated with a β-lactam antibiotic. There were differences in the method of delivery and line of delivery across OPAT success and failure categories. Overall OPAT outcomes showed 8.3% (148 patient episodes) who failed to complete their OPAT episode. Patients classed as indeterminate were re-admitted for reasons unrelated to their OPAT episode and were removed from the outcome analysis (Appendix 2, Table S4).

Differences existed between patients who had a successful OPAT outcome and those who did not in terms of all clinical condition variables except age (P =0.72) and β-lactam therapy ($P = 0.323$). Univariate analysis indicated that patients who had successful OPAT outcomes had a longer course of treatment (17 days vs. 10 days; $P < 0.001$), experienced clinic- or nurse-led OPAT ($P = 0.001$) and had therapy administered via a peripheral line ($P < 0.01$).

To quantify the magnitude of differences adjusted for covariates, a multivariable logistic regression model was produced (Table 3). Factors showing an association with outcome in the univariate analysis, as well as a priori-defined clinically important factors, were included in this model. After adjusting for covariates, the odds of OPAT success were greater for those patients who did not experience an AE [odds ratio (OR) = 0.23; $P < 0.01$], who spent more time (>14 days) on OPAT therapy (OR = 2.32; $P < 0.01$) and who utilised a peripheral line (OR = 1.83; $P < 0.01$). In the multivariable analysis, clinic-led therapy was associated with an increased odds of OPAT success compared with self-administered OPAT [OR = 2.1, 95% confidence interval (CI) 1.03–2.28; $P = 0.02$]. There was no difference between self-administered OPAT and community nurse-led OPAT (OR = 0.75, 95% CI 0.45–1.23; $P = 0.2$).

Table 3
Multivariable analysis of factors associated with outpatient parenteral antibiotic therapy (OPAT) success.

Factor	OR (95% CI)	*P*-value
Age	0.99 (0.98–1.00)	0.72
Venous access		
Central venous access	Ref.	
Peripheral venous access	1.83 (1.24–2.71)	<0.01
Delivery method		
Self-administration	Ref.	
Community nurse-led	0.75 (0.45–1.23)	0.2
OPAT clinic	2.1 (1.03–2.28)	0.02
Duration of treatment (short-term vs. long-term)	2.32 (1.62–3.32)	<0.01
Adverse event	0.23 (0.15–0.34)	<0.01
β-Lactam	1.57 (0.70–3.52)	0.272

OR, odds ratio; CI, confidence interval.

Midline venous access was reported as a separate category, but as all patients ($n = 214$) had a successful OPAT outcome this could not be included in the regression model. Midline was therefore considered in two ways: first as included in 'central venous access' and second as included in 'peripheral venous access' in univariate models. When midlines were categorised as central

Table 4
Descriptive and comparative investigation of outpatient parenteral antibiotic therapy (OPAT)-related adverse events (AEs).

	Total patient episodes ($n = 1793$)	OPAT success ($n = 1645$)	OPAT failure ($n = 148$)
AE [*n* (%)]			
Yes	196 (10.9)	151 (9.2)	45 (30.4)
No	1597 (89.1)	1494 (90.8)	103 (69.6)
Cause of AE			
Drug	128	101	27
Line	68	50	18
Days to AE day [median (range)][a]			
Drug	14 (1–95)	16 (1–95)	9 (1–90)
Line	17 (1–75)	17 (1–75)	12 (3–56)
Detail of AE			
Direct line issue	45	37	8
Rash	32	27	5
Blood dyscrasia	32	25	7
Hepatitis	19	19	0
Gastrointestinal	17	15	2
Bacteraemia	12	2	10
Nephrotoxicity	9	5	4
Line allergy/inflammation	8	8	0
Anaphylaxis	4	2	2
Ototoxicity	4	3	1
CDAD	1	0	1
Drug-induced fever	1	1	0
Other[b]	12	7	5
Severity of AE			
Minor	153	143	10
Severe	43	8	35
Line-only AEs ($n = 68$)			
Venous access			
Central	44	27	17
Midline	16	16	0
Peripheral	8	7	1
Method of delivery			
Clinic-led	7	6	1
Nurse-led	45	31	14
Self-led	16	13	3

CDAD, *Clostridium difficile*-associated diarrhoea.
[a] Unable to ascertain timing of the AE for 13 patients, all in the line-related AE category.
[b] Refer to Appendix 5 (Table S9) for a full description of the 'Other' category.

venous access there was an increased odds of success with peripheral venous access (OR = 1.82, 95% CI 1.24–2.71; $P = 0.003$). When midlines were categorised as peripheral venous access there was also an increased odds of OPAT success with peripheral venous access (OR = 3.12, 95% CI 2.11–4.62; $P < 0.001$). Overall the results confirmed that regardless of inclusion or exclusion of midline catheter patients, peripheral venous access was associated with an increased odds of OPAT success compared with central venous access.

3.3. Adverse events

There were 196 AEs for 1793 patient episodes and 38 289 DoT. A total of 128 antimicrobial drug-related AEs and 68 line-related AEs occurred (Table 4). The median time to AEs related to drug or line was 14 days (range 1–95 days) and 17 days (range 1–75 days), respectively.

Although all patients who had midline venous access experienced successful OPAT outcome, there was a higher rate of midline-associated AEs compared with other lines. AEs occurred in 7.5% (16/214 episodes) of patients with midline venous access compared with 4.6% (44/949 episodes) of patients with central venous access and 1.3% (8/630 episodes) of patients with peripheral venous access.

There were 43 severe AEs. Any AE occurred at a rate of 5 per 1000 DoT. Drug- and line-related AEs occurred at rates of 71.4 and 37.9 per 1000 patient episodes and 3.34 and 1.78 per 1000 DoT, respectively (Table 5). The three most common AEs were events directly related to lines, rashes and blood dyscrasias. One episode of *C. difficile*-associated diarrhoea (CDAD) occurred that resulted in re-admission and failure of OPAT therapy. Four documented episodes of anaphylaxis occurred, of which three were related to ceftriaxone and one to teicoplanin. One of these episodes occurred at Week 4 into treatment, raising the possibility that this was

Table 5
Number and rate of adverse events (AEs).

	Total AEs ($n = 196$) [*n* (%)]	Rate of AE/1000 patient episodes ($n = 1793$)	Rate of AE/1000 DoT ($n = 38\ 289$)
Drug-related AEs ($n = 128$)		71.4	3.34
Rash	32 (16.3)	17.8	0.84
Blood dyscrasia	32 (16.3)	17.8	0.84
Hepatitis	19 (9.7)	10.6	0.50
Gastrointestinal	17 (8.7)	9.5	0.44
Nephrotoxicity	9 (4.6)	5.0	0.24
Anaphylaxis	4 (2.0)	2.2	0.10
Ototoxicity	4 (2.0)	2.2	0.10
CDAD	1 (0.5)	0.6	0.03
Drug-induced fever	1 (0.5)	0.6	0.03
Other[a]	9 (4.6)	5.0	0.24
Line-related AEs ($n = 68$)		37.9	1.78
Direct line issue	45 (23.0)	25.1	1.18
Infection, bacteraemia	12 (6.1)	6.7	0.31
Line allergy/inflammation	8 (4.1)	4.5	0.21
Other[a]	3 (1.5)	1.7	0.08

DoT, days of treatment; CDAD, *Clostridium difficile*-associated diarrhoea.
[a] Refer to Appendix 5 (Table S9) for a full description of the 'Other' category.

independent of the ceftriaxone administration or that a delayed hypersensitivity reaction was falsely documented as anaphylaxis.

Ertapenem caused four AEs relating to central nervous system (CNS) toxicity (categorised as 'Other'), of which all were classed as severe (Appendix 5, Table S9). These included hallucinations, seizures and tremor likely related to accumulation of ertapenem and reduced renal excretion.

4. Discussion

OPAT is an attractive service delivery option to healthcare institutions owing to high patient satisfaction and potential cost savings. The data reported here add to the growing body of evidence that a well-structured OPAT service delivers safe and effective treatment in the outpatient environment. We report a 92.0% cure or improvement rate in primary infection diagnoses. This is similar to previously reported rates of 92.4% and 88% from large UK OPAT cohorts in Glasgow and Sheffield, respectively [10,11]. Higher rates of success have been reported in Dundee (97% cured or improved in 2012–2013) and a decade ago from the US OPAT outcomes registry (96.6% clinical improvement in 7892 patients) [12,13]. It is impossible to know whether the differences reflect the type of patients accepted onto the service, the quality of their care or differences in outcome definitions.

This study focused on factors that are associated with success or failure of an OPAT service. No difference between outcomes relating to age was found. Patients were grouped into short-term and long-term therapy with a 14-day cut-off and it was found that longer therapy was associated with an increased odd of success. The majority of patients in the short-term group were treated for SSTI (37.0%), urinary tract infection (17.3%) or respiratory tract infection (10.0%). The most common conditions treated in the long-term patients were osteomyelitis (14.4%), device-related osteomyelitis (11.0%) and device-related joint infections (11.0%) (Appendix 1, Table S3). The higher odds of success relating to longer therapy may related to the clinical stability of the patient and the relationship built between the OPAT team and the patient. In a well-structured OPAT service with regular (weekly in our service) clinical review by medical, nursing and pharmacy teams, patients who become established on service are more likely to have a successful outcome. The early phase of infection and trial of medical therapy, often in the setting of incomplete source control (such as an underlying abscess), is the riskiest period. Most long-term patients with conditions such as osteomyelitis or prosthetic joint infection will have had a hospital stray prior to discharge and will be more likely to be clinically stable on therapy prior to discharge. In a recent paper from the USA, the authors also used 2 weeks as a comparator duration and showed that there was a stepwise decrease in re-admission associated with increasing weeks of therapy [14].

It was shown that peripheral lines are associated with an increased odds of successful OPAT outcome when adjusted for other variables and also if midlines were either included or excluded within the peripheral line data set. We chose to include midlines as a separate category even though they are classed as peripheral catheters owing to similar placement methodology and reports of higher AEs. A recent study showed that i.v. lines were associated with a higher rate of AEs compared with drug-related AEs; in particular, the authors found a high complication rate with non-radiologically-guided midlines [15]. Peripheral lines are usually placed for shorter-term therapy, therefore we expected to find a similar association in relation duration in therapy; however, this study showed an increased odds of success with longer therapy. Our service moved to utilising Leaderflex peripheral catheters during the last few years of the study, which can dwell for longer periods of time (up to 28 days). This finding requires further investigation that was beyond the scope of this study. The numbers in this study would be too small to break down reliably by condition, but a larger combined national data set might be able to explore reasons behind this finding.

An overall OPAT success rate of 91.7% was observed, therefore 8.3% (148 patient episodes) failed to complete their OPAT episode. A total of 62 patients were classed as indeterminate outcomes and were re-admitted due to other reasons not directly related to their OPAT treatment episode. Literature commonly reports completion of OPAT with monitoring of re-admission rates (between 6% and 12%) rather than success rates [13,16,17].

In this study, 10.9% of patients experienced an AE (196 AEs in 1793 patient episodes). The line complication rate was 1.78 per 1000 line-days. This is lower than other published studies (3.2–5.7 per 1000 line-days) and may reflect our high use of PICCs rather than longer-term indwelling catheters [12,15]. Although no patients with midline venous access failed OPAT, they did experience a higher rate of occurrence of AEs (7.5%), although this is lower than a recent study reporting a 19.5% AE occurrence [15]. Adverse drug events occurred at a rate of 3.3 per 1000 treatment days. It is difficult to benchmark adverse drug events as the literature ranges from lower rates of 0.5%, 1.6% and 6.7% in Sheffield, London and Dublin cohorts, respectively, to higher rates of 9.8% in Glasgow [10,12].

There is a paucity of data comparing adverse drug reactions in the outpatient environment with an inpatient setting, however there continues to be a reluctance to administer antimicrobials that might drive antimicrobial resistance or an increase in CDAD. It appears that CDAD is much lower in the OPAT setting and antimicrobial resistance is not consistently reported [18]. Antimicrobial stewardship strategies recommend narrow-spectrum antibiotic treatment, but OPAT services rely on single daily dosing regimens, which lead to administration of broad-spectrum antibiotic therapy. Third-generation cephalosporins have been associated with a higher risk of CDAD but this association is not robust regarding outpatient therapy [19]. We reported only one confirmed case of CDAD despite 30 677 days of ceftriaxone therapy. Patients were not followed-up specifically for diarrhoea, although a previous report from a similar London cohort showed no cases of CDAD at 28 days follow-up [20]. OPAT services must acknowledge this antimicrobial stewardship dilemma as a potential risk, but robust prospective follow-up data would allow further clarification [5].

The most commonly used antibiotic was ceftriaxone, followed by ertapenem. We did not show a significant association with β-lactam use and successful OPAT outcome, unlike a similar study from a large cohort in the USA [21]. In this study the authors also reported four cases of neurotoxicity with ertapenem (two cases of seizure and two cases of mental status change). Here we reported four cases of CNS toxicity with ertapenem and this needs to be considered in patients who might be at higher risk, such as those with poor renal clearance or older age.

The majority of patients received antimicrobial therapy via community nurses, with a smaller number of patients ($n = 252$) undergoing self-administration. The opportunity for self-administration allows true patient-centred care but requires careful patient selection. A study of a large Asian cohort showed a significant clinical deterioration of homecare patients compared with hospital or self-administration [11]. The authors concluded that this was most likely due to homecare patients having significant co-morbidities and poorer functional status rather than relating to OPAT specifically. In our cohort, we found an association with OPAT failure and self-administration compared with clinic-led administration but not community nurse-led administration on multivariable analysis. A cohort of 2059 OPAT episodes over 13 years comparing self to home OPAT showed that this method

of administration in selected patients was safe with comparable outcomes [16].

A greater success rate was observed with patients who were on longer courses of therapy, delivered in the clinic or by district nurses, and administered via peripheral lines. This may reflect the importance of strong governance structures as these are areas in which we have greater clinical experience. Longer courses allow OPAT services to monitor patients closely, and clinic- or district nurse-led administration allow OPAT services to respond rapidly to any complications or changes in therapy.

Surveys have shown that there is a wide variation in OPAT practice and have led people to believe a 'care bundle' approach to OPAT may be beneficial [22–24]. Comparing national data and benchmarking practice allows the opportunity to improve local OPAT services by joining a national network of similar programmes. Rollout of the National Outcomes Registry System (NORS) provides an opportunity to gain further clarity as to optimum management for the complex array of potential conditions referred for OPAT. Increasing experience at a national level, filtering down to local services, may give the opportunity to stratify patients and conditions enabling services to predict the likely outcomes and potential AEs. This study helps to identify the patient cohorts that might be associated with failure and therefore allow careful planning prior to acceptance onto service.

4.1. Limitations and strengths

Although the data within this cohort were documented prospectively, a retrospective process was undertaken to map the national outcome measures to the patient episodes. We attempted to mitigate any potential bias by triangulating reference sources for raw data by comparing the OPAT database with patient notes and electronic records. We did not follow-up patients beyond the OPAT episode and therefore any adverse outcome or event that may have been attributable to OPAT may have been missed, especially related to CDAD. In order to undertake statistical analysis with patient numbers to make reliable associations, we had to group individual infection diagnoses. This has inherent assumptions that conditions have enough similarity to be treated equally. This lack of granularity could be mitigated in the future by larger national data sets to map outcomes to specific diagnoses.

We were unable to obtain the antibiotic history prior to commencing the OPAT episode. This may have influenced variables in the duration of treatment category as some chronic, long-term patients may have completed their therapy in the short-term group, which could skew the data. Comparing the distribution of conditions within the duration categories there are some conditions, such as osteomyelitis or cardiac infection, that fall into the short-term group implying that these patients were completing the tail end of therapy. Our results show that the long-term group had a greater odds of success and therefore if some of these patients were categorised within the short-term group then the most likely outcome would have been to increase the odds of success in the long-term group. This would not have changed the overall conclusions.

We were not able to ascertain the timing of 13 episodes of line-related AEs owing to lack of documentation. This could be a reflection of poor documentation of line-related AEs leading to an inaccurate description of line rate complications. This risk was mitigated by thorough patient note review on all patients flagged with an AE.

A strength of this study is the real-world nature of an OPAT service reflecting the complexity of management from a large cohort of patients. It shows a benchmark of a large cohort of patients and allows further work to identify factors related to the findings.

5. Conclusion

OPAT remains a safe and effective care model with low AE rates. Patients who had successful OPAT outcome had a longer course of treatment (>14 days), experienced OPAT delivered via a peripheral line, and administered OPAT in the clinic rather than self-administration. This study shows the benefit of a well-structured, experienced OPAT service with robust governance structures leading to low rates of AEs and good outcomes. We recognise the need for further data on a national level to explore some of the study's findings and to benchmark outcome measures between OPAT services.

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Competing interests

MG and FS serve on the BSAC UK OPAT Initiative Steering Group receiving reimbursement of travel expenses only from the British Society for Antimicrobial Chemotherapy (BSAC) for attending and speaking at OPAT-related events; MG reports attending advisory board and consultancy for Merck and Pfizer; JH reports receiving educational travel and speaker grants from Astellas Pharmaceuticals. All other authors declare no competing interests.

Ethical approval

Not required.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijantimicag.2019.04.008.

References

[1] Public Health England Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infections (ARHAI). Start Smart – Then Focus. Antimicrobial stewardship toolkit for English hospitals March 2015. Updated https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/417032/Start_Smart_Then_Focus_FINAL.pdf [accessed 11 March 2016].

[2] Keller SC, Willliams D, Gavgani M, Hirsch D, Adamovich J, Hohl D, et al. Rates of and risk factors for adverse drug events in outpatient parenteral antimicrobial therapy. Clin Infect Dis 2018;66:11–19. doi:10.1093/cid/cix733.

[3] Means L, Bleasdale S, Sikka M, Gross AE. Predictors of hospital readmission in patients receiving outpatient parenteral antimicrobial therapy. Pharmacotherapy 2016;36:934–9.
[4] Tamma P, Avdic E, Li DX, Dzintars K, Cosgrove SE. Association of adverse events with antibiotic use in hospitalized patients. JAMA Intern Med 2017; 177:1308–15.
[5] Gilchrist M, Seaton RA. Outpatient parenteral antimicrobial therapy and antimicrobial stewardship: challenges and checklists. J Antimicrob Chemother 2015;70:965–70.
[6] Norris AH, Shrestha NK, Allison GM, Keller SC, Bhavan KP, Zurlo JJ, et al. 2018 Infectious Diseases Society of America clinical practice guideline for the management of outpatient parenteral antimicrobial therapy. Clin Infect Dis 2019;68:e1–35.
[7] Chapman AL, Seaton RA, Cooper MA, Hedderwick S, Goodall V, Reed C, et al. Good practice recommendations for outpatient parenteral antimicrobial therapy (OPAT) in adults in the UK: a consensus statement. J Antimicrob Chemother 2012;67:1053–62.
[8] Patel S, Abrahamson E, Goldring S, Green H, Wickens H, Laundy M. Good practice recommendations for paediatric outpatient parenteral antibiotic therapy (p-OPAT) in the UK: a consensus statement. J Antimicrob Chemother 2015;70:360–73.
[9] British Society for Antimicrobial Chemotherapy. *The OPAT National Outcomes Registry System (NORS)*. http://opatregistry.com [accessed September 2018].
[10] Barr DA, Semple L, Seaton RA. Outpatient parenteral antimicrobial therapy (OPAT) in a teaching hospital-based practice: a retrospective cohort study describing experience and evolution over 10 years. Int J Antimicrob Agents 2012;39:407–13.
[11] Durojaiye OC, Bell H, Andrews D, Ntziora F, Cartwright K. Clinical efficacy, cost analysis and patient acceptability of outpatient parenteral antibiotic therapy (OPAT): a decade of Sheffield (UK) OPAT service. Int J Antimicrob Agents 2018;51:26–32.
[12] Mackenzie M, Rae N, Nathwani D. Outcomes from global adult outpatient parenteral antimicrobial therapy programmes: a review of the last decade. Int J Antimicrob Agents 2014;43:7–16.
[13] Paladino JA, Portez D. Outpatient parenteral antimicrobial therapy today. Clin Infect Dis 2010;51(Suppl 2):S198–208.
[14] Palms DL, Jacob JT. Close patient follow-up among patients receiving outpatient parenteral antimicrobial therapy. Clin Infect Dis 2019 Feb 27 [Epub ahead of print]. doi:10.1093/cid/ciz150.
[15] Underwood J, Marks M, Collins S, Logan S, Pollara G. Intravenous catheter-related adverse events exceed drug-related adverse events in outpatient parenteral antimicrobial therapy. J Antimicrob Chemother 2019;74:787–90.
[16] Matthews PC, Conlon CP, Berendt AR, Kayley J, Jefferies L, Atkins BL, et al. Outpatient parenteral antimicrobial therapy (OPAT): is it safe for selected patients to self-administer at home? A retrospective analysis of a large cohort over 13 years. J Antimicrob Chemother 2007;60:356–62.
[17] Chapman AL, Dixon S, Andrews D, Lillie PJ, Bazaz R, Patchett JD. Clinical efficacy and cost-effectiveness of outpatient parenteral antibiotic therapy (OPAT): a UK perspective. J Antimicrob Chemother 2009;64:1316–24.
[18] Duncan CJ, Barr DA, Seaton RA. Outpatient parenteral antimicrobial therapy with ceftriaxone, a review. Int J Clin Pharm 2012;34:410–17.
[19] Slimings C, Riley TV. Antibiotics and hospital-acquired *Clostridium difficile* infection: update of systematic review and meta-analysis. J Antimicrob Chemother 2014;69:881–91.
[20] Hitchcock J, Jepson AP, Main J, Wickens HJ. Establishment of an outpatient and home parenteral antimicrobial therapy service at a London teaching hospital: a case series. J Antimicrob Chemother 2009;64:630–4.
[21] Lee B, Tam I, Weigel B 4th, Breeze JL, Paulus JK, Nelson J, et al. Comparative outcomes of β-lactam antibiotics in outpatient parenteral antibiotic therapy: treatment success, readmissions and antibiotic switches. J Antimicrob Chemother 2015;70:2389–96.
[22] Muldoon EG, Switkowski K, Tice A, Snydman DR, Allison GM. A national survey of infectious disease practitioners on their use of outpatient parenteral antimicrobial therapy (OPAT). Infect Dis (Lond) 2015;47:39–45.
[23] Muldoon EG, Snydman DR, Penland EC, Allison GM. Are we ready for an outpatient parenteral antimicrobial therapy bundle? A critical appraisal of the evidence. Clin Infect Dis 2013;57:419–24.
[24] Conant MM, Erdman SM, Osterholzer D. Mandatory infectious diseases approval of outpatient parenteral antimicrobial therapy (OPAT): clinical and economic outcomes of averted cases. J Antimicrob Chemother 2014;69:1695–1700.