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Safety and efficacy of an outpatient parenteral antimicrobial therapy program at a tertiary hospital in Belgium: a monocentric retrospective observational study

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ABSTRACT

Objectives: Outpatient parenteral antimicrobial therapy (OPAT) offers a safe, effective, and resource-sparing alternative to inpatient treatment for various infections. Despite its widespread adoption globally, the implementation of OPAT programs in Belgium has been limited until recently. This study evaluates the safety, efficacy and healthcare impact of an OPAT program at a university hospital in Liège, Belgium.

Methods: We conducted a retrospective observational study at a 1038-bed tertiary teaching hospital, including patients who received OPAT between January 2018 and December 2021. Electronic medical records were reviewed for demographics, diagnoses, treatment regimens, adverse events, and outcomes. Potential risk factors for adverse events and treatment failure were investigated.

Results: A total of 352 OPAT episodes in 327 patients were analyzed. The most frequent indications were bloodstream infections (29.8%) and urinary tract infections (27.8%). Continuous antibiotic administration was used in 60.6% of cases, with a median OPAT duration of 16 days. Clinical cure was achieved in 86.4% of patients. Unplanned readmission linked to OPAT, infection-related death, drug-related adverse events, and line-related complications occurred in 8.2%, 1.1%, 5.1%, and 4.2% of episodes, respectively. Risk factors for adverse outcomes were identified, including cirrhosis, hematological malignancies, osteoarticular infections, chronic renal failure, and the use of specific antibiotics. The program avoided a mean of 1692 hospitalization days per year, underscoring its significant healthcare impact.

Conclusion: This study highlights the favorable outcomes and safety profile of the OPAT program at our tertiary teaching hospital. Tailored interventions and careful antibiotic selection are warranted for specific patient groups.

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Outpatient parenteral antimicrobial therapy (OPAT); parenteral antibiotic; Belgium

Introduction

Outpatient parenteral antimicrobial therapy (OPAT) is a treatment approach that involves administering parenteral antimicrobial agents in an outpatient setting [1].

The concept of OPAT was first described in 1974 when it was successfully used to treat chronic bronchopulmonary infections in pediatric patients with cystic fibrosis [2]. Since then, numerous studies have found OPAT to be a safe and effective alternative to inpatient treatment for various infections in different populations and healthcare settings [3,4]. International guidelines have been published to support its implementation [1,5].

OPAT offers several advantages. It reduces the need for hospitalization, allowing patients to receive necessary antimicrobial therapy while remaining in their own homes or visiting specialized infusion centers [6–9]. This approach has been shown to be cost-effective by avoiding lengthy hospital stays and associated expenses [10,11]. Additionally, OPAT has the potential to prevent healthcare-associated conditions, as patients are not exposed to the same risks and pathogens commonly found in hospital settings [12].

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In Belgium, OPAT has only been eligible for reimbursement since July 2023, and few Belgian centers have reported their experience with such programs [9,13–16]. This study aims to assess the safety and efficacy of the OPAT program implemented at a university hospital in Liège, Belgium.

Materials and methods

This retrospective observational study was conducted at a 1038-bed tertiary teaching hospital in Liege, Belgium. The study focused on patients who received outpatient parenteral antibiotic therapy between January 2018 and December 2021. Electronic medical records were reviewed to gather data, and specific inclusion and exclusion criteria were outlined in Figure 1.

OPAT Program

The OPAT program at our institution employs a home-based model, wherein home-care nurses are responsible for the preparation and administration of parenteral antimicrobials in the patient's residence. The program is structured around a multidisciplinary framework involving the treating physician, infectious diseases (ID) specialist, microbiologist, clinical pharmacist, and home-care nurse, and is overseen by an ID physician who provides program coordination.

Antibiotics were administered at home either via intermittent infusion (once or twice daily, with each infusion lasting no more than 30 minutes) or continuously using an electronic pump. In the latter case, the infusion cartridge was replaced every 12 to 24 hours, depending on the stability of the antibiotic used.

Before initiating OPAT, patients typically underwent review by infectious disease (ID) experts, following the IDSA 2018 guidelines [1,17]. This allowed for discontinuation of unnecessary antibiotic treatments, switching from IV to oral medications when appropriate, and interventions such as dosage adjustments, treatment duration modifications, or changes in the choice of antimicrobials. However, an exception was

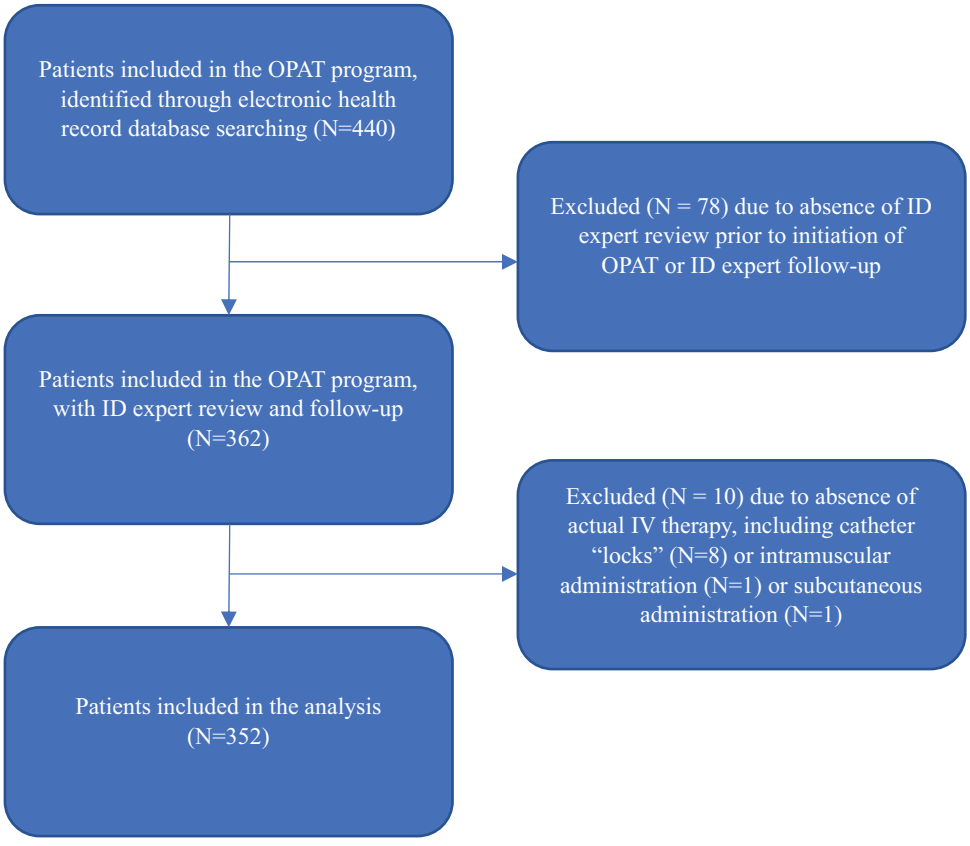

Figure 1. Inclusion and exclusion criteria flowchart.

made for patients with hematologic malignancies upon request from the hematology department. These patients were included in the program without ID review or follow-up, primarily for antiviral courses related to cytomegalovirus (CMV) viremia. Due to the lack of ID follow-up and associated data collection challenges, these 78 patients were excluded from our analysis.

Following discharge, patients were scheduled for weekly hospital visits with an ID physician to ensure ongoing monitoring, appropriate medical guidance, and provision of necessary resources throughout the outpatient period.

Data collection

Patient characteristics, including age, gender, and comorbidities, were collected from electronic medical records. The study evaluated the type of infection (including microbiological data), antimicrobial regimens used, type of IV administration (continuous versus intermittent), treatment duration, and type of vascular access device (VAD). Therapeutic drug monitoring was usually performed for selected beta-lactams (including cefazolin, temocillin, piperacillin/tazobactam, ceftazidim, cefepime, and meropenem) and vancomycin, except for short antibiotic courses (≤7 days).

Infections were categorized as blood stream infections (BSI, including spontaneous bacteremia without obvious source of infection, infective endocarditis and endovascular infections), skin and soft tissues infections (SSTI), respiratory tract infections (RTI), urinary tract infections (UTI), central nervous system infections (CNSI), bone and joint infections (BJI), complicated intra-abdominal infections (CIAI), febrile neutropenia and viraemia.

Outcomes

The measured outcomes included the clinical outcome of the infection (classified as 'cure','failure' or 'indeterminate'), the number of hospitalization days saved, unplanned emergency department or clinical ward readmissions (including reasons for readmission) during OPAT and within 30 days after its completion, and OPAT-related major adverse events (categorized as line-related or drug-related adverse events). For bone and joint infections, a 12-month follow-up was deemed necessary to ensure an adequate assessment of the clinical outcome [18].

'Treatment failure' was defined as relapse or recurrence with the same infecting microorganism, worsening of clinical symptoms present before initial treatment, unplanned infection-related readmission, or infection-related death within 30 days of treatment discontinuation. 'Cure' referred to the absence of these criteria. Cases were classified as 'indeterminate' if (i) death occurred during follow-up from an unequivocally unrelated cause, or (ii) the clinical outcome could not be assessed due to loss to follow-up [19,20].

If the OPAT was interrupted by planned hospitalization (e.g. in the context of two-stage surgical management protocols) or unplanned hospitalization, it was considered the same OPAT if the same intravenous treatment was resumed at discharge. However, if the antibiotic regimen had been changed at discharge, the OPAT was considered a new one.

Statistical methodology

Qualitative variables were summarized using frequency tables, accompanied by their respective percentages. For quantitative variables, median and interquartile range (IQR: Q1-Q3) were utilized. The normality of the distribution for quantitative variables was assessed through numerical and graphical methods, including the Shapiro-Wilks' normality test.

The impact of various factors, including the most common pathogens encountered and frequently used antibiotics, was assessed using univariate binary logistic regression. The results were reported as odds ratios (OR) along with their corresponding 95% confidence intervals (CI). Factors that showed statistical significance in the univariate analysis were further investigated using multivariate binary logistic regression to determine their independent association with the risk of antibiotic therapy failure.

The same methodology was applied to analyze the risk of other outcomes such as unplanned readmission, death, and adverse events related to both antibiotic therapy and the catheter. By examining the relationship between these factors and the respective outcomes, the study aimed to identify significant predictors and assess their impact on patient outcomes during the outpatient parenteral antibiotic therapy program. The analyses were based solely on observed data, and missing data were not replaced. Statistical significance was considered at the 95% confidence level ($p < 0.05$). The statistical analyses were performed using SAS version 9.4 and R version 4.2.

Ethics

This study was approved by the local ethics board (Le Comité d'Éthique Hospitalo-Facultaire Universitaire de Liège) on 17 December 2024. Patient consent was waived due to the retrospective design of the study and the use of anonymized data.

Results

During the period from 1 January 2018, to 31 December 2021, a total of 327 patients underwent 352 episodes of outpatient parenteral antibiotic therapy.

Patients' characteristics, as shown in Table 1, were assessed individually at the beginning of each OPAT episode. The median age was 64.5 years and 66.2% of patients were male ($N = 233$). Three pediatric (0.9%) patients were included in the study. The most prevalent comorbidities were high blood pressure ($N = 177$; 50.3%) and diabetes ($N = 93$; 26.4%). The median number of comorbidities per patient was 2.0 (IQR: 1.0–3.0).

Detailed information on the various types of infections encountered during the 352 OPAT episodes is provided in Figure 2. The most common types of infections were blood stream infections ($N = 105$; 29.8%), urinary tract infections ($N = 98$; 27.8%), and bone and joint infections ($N = 65$; 18.5%). Simultaneous infections were observed in 34 patients (9.7%): 25 (7.1%) had two sites of infection, 8 (2.3%) had three sites, and 1 (0.3%) had four sites. Additionally, 85 infections (24.1%) were associated with the presence of a medical device. The median duration of OPAT was 16 days, with a range of 1 to 82 days (IQR: 10–26 days).

The study identified the four most common pathogens as follows: *Escherichia coli* ($N = 73$; 20.74%), *Staphylococcus aureus* ($N = 57$; 16.2%), *Pseudomonas aeruginosa* ($N = 46$; 13.1%), and *Klebsiella pneumoniae*

Table 1. Patients' demographics and clinical characteristics at the initiation of each OPAT episode ($N = 352$).

Demographics and clinical characteristics		Number (%)
Gender	*Female*	119 (33.8%)
	Male	233 (66.2%)
Median (IQR) age in years		64.5 (52.1–72.7)
High blood pressure		177 (50.3)
Diabetes mellitus		93 (26.4)
Chronic renal failure		33 (9.4)
Chronic heart failure		43 (12.2)
Ischemic cardiomyopathy		56 (15.9)
Peripheral vascular disease		46 (13.1)
Chronic obstructive pulmonary disease		43 (12.2)
Cirrhosis		12 (3.4)
Solid tumor neoplasms		69 (19.6)
Hematological malignancies		35 (9.9)
Organ transplant	*Kidney*	28 (8.0)
	Liver	6 (1.7)
	Bone marrow	23 (6.5)
	Heart	2 (0.6)
	Pancreas	1 (0.3)
Stroke		24 (6.8)
Median (IQR) number of comorbidities		2.0 (1.0–3.0)
Number of comorbities	*0*	84 (23.9)
	1	75 (21.3)
	2	78 (22.2)
	3	54 (15.3)
	4+	61 (17.3)

IQR : interquartile range.

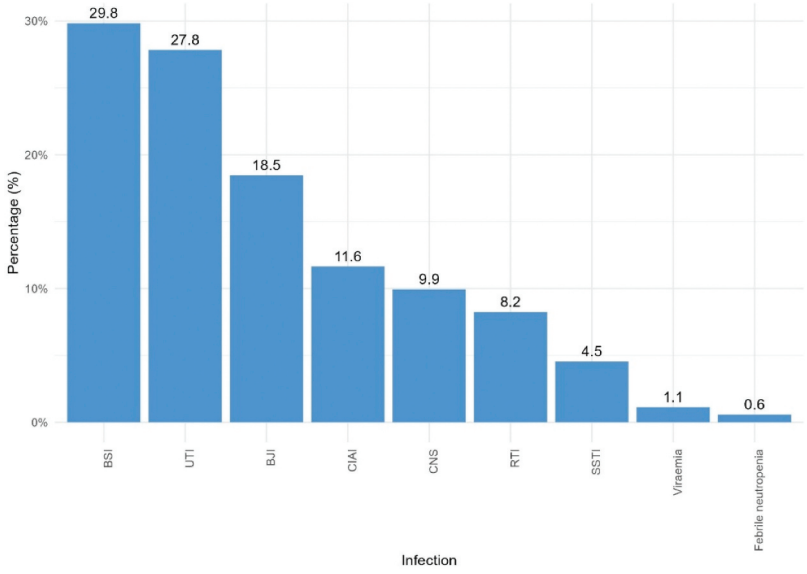

Figure 2. Types of infections found during the 352 OPAT episodes. BSI: blood stream infections (including bacteriemia, endocarditis and endovascular infections), UTI: urinary tract infections, BJI: bone and joint infections, CIAI: complicated intra-abdominal infections, CNSI: central nervous system infections, RTI: respiratory tract infections, SSTI: skin and soft tissues infections.

($N = 26$; 7.4%). Bacteremia was present in 36.1% of cases ($N = 127$). Central nervous system infections were primarily attributed to Lyme's disease and syphilis, accounting for 31.4% each ($N = 11$). Fungal infections were present in six episodes of outpatient parenteral antimicrobial therapy, amounting to 1.7% of cases. In 41 cases (11.6%), no causative pathogens were identified. In these culture-negative cases, empirical OPAT was initiated following specialist evaluation when infection was strongly suspected based on clinical, laboratory, and imaging findings. Several factors contributed to the absence of microbiological documentation, including prior antibiotic administration before sampling and, in some cases, the inability to obtain sterile samples due to the patient's clinical condition or procedural risk (e.g. complicated intra-abdominal infections where surgery or interventional drainage was not feasible). The complete list of identified pathogens is provided in a table in the appendix.

A total of twenty-two different parenteral antimicrobial agents were utilized (Table 2), with continuous infusion ($N = 223$; 60.6%), using electronic infusion devices (EIDs), being favored over intermittent administration ($N = 145$). The most frequently administered antibiotics, accounting for 76% of all treatments, were ceftriaxone, cefazolin, piperacillin-tazobactam, ceftazidime, benzylpenicillin, and cefepime. In three instances, the antimicrobial agent was replaced during OPAT, twice due to pharmacokinetic/pharmacodynamic considerations and once due to the presence of an ampCinducible gram-negative bacillus in culture. Additionally, 65 cases involved adjunctive oral antibiotics, with metronidazole ($N = 22$) and ciprofloxacin ($N = 15$) being the most commonly used. Therapeutic drug monitoring (TDM) was performed in 38.9% of all OPAT cases and in 82% of cases involving antibiotics for which TDM was available ($N = 137/167$). This resulted in antibiotic dose adjustments in 13.4% and 28.1% of cases, respectively ($N = 47$).

The most common vascular access device utilized in the study was the PICC-line, accounting for 89.2% of cases ($N = 314$). The port-a-cath was the second most frequently used device, with a prevalence of 6.8% ($N = 24$). The peripheral vascular catheter was employed in 2.8% of cases ($N = 10$), while the dialysis catheter was used in 1.1% of cases ($N = 4$).

The 352 OPAT episodes collectively resulted in the avoidance of 6767 hospital days, corresponding to a mean of 1692 days per year. The annual distribution of hospital days saved is presented in Table 3.

Out of the 352 OPAT episodes, 86.4% of patients ($N = 304$) achieved clinical cure. Treatment failure occurred in 37 cases (10.5%). Fourteen patients (4%) died during the follow-up period, of whom four (1.1%) deaths were directly related to their index infection. The remaining ten patients (2.8%) had previously

Table 2. Parenteral antimicrobials utilized in the OPAT program with a total of 352 episodes included in the analysis.

Parenteral antimicrobials	Number (% per OPAT episode)
Ceftriaxone	117 (33.24)
Cefazolin	39 (11.08)
Piperacillin/tazobactam	32 (9.09)
Ceftazidim	29 (8.24)
Benzylpenicillin	29 (8.24)
Cefepime	23 (6.53)
Temocillin	16 (4.55)
Flucloxacillin	15 (4.26)
Amoxicillin	14 (3.98)
Vancomycin	14 (3.98)
Meropenem	11 (3.13)
Cefotaxime	6 (1.70)
Tigecycline	6 (1.70)
Ganciclovir	5 (1.42)
Aztreonam	3 (0.85)
Ceftazidim/avibactam	3 (0.85)
Aciclovir	1 (0.28)
Ambisome	1 (0.28)
Amikacin	1 (0.28)
Caspofungin	1 (0.28)
Gentamicin	1 (0.28)
Moxifloxacin	1 (0.28)
Combination therapy	**Number (% per OPAT episode)**
ceftriaxone + amoxicillin	8 (2.27)
ceftriaxone + amikacin	1 (0.28)
ceftriaxone + benzylpenicillin	1 (0.28)
ceftriaxone + ganciclovir	1 (0.28)
ceftazidime + ganciclovir	1 (0.28)
cefepime + ganciclovir	1 (0.28)

Note: The numbers represent the count of episodes where the respective antimicrobial was used, and the percentages indicate the proportion of episodes in which the specific antimicrobial was administered. Antibiotics for which therapeutic drug monitoring (TDM) was available are highlighted in bold italics (piperacillin component for piperacillin-tazobactam; ceftazidime component for ceftazidime/avibactam).

Table 3. Distribution of hospitalization days saved per year.

Year	2018	2019	2020	2021
Number of OPAT episodes	81	80	88	103
Number of hospitalization days saved	1358	1585	1677	2147

shown signs of clinical improvement; their deaths were unequivocally attributed to unrelated medical conditions and were therefore classified as 'indeterminate' with respect to clinical outcome. The clinical characteristics of these patients are presented in the appendix. Additionally, the clinical outcome for one patient was unknown due to readmission to another hospital, and their electronic health record could not be retrieved; this case was also classified as indeterminate.

The study identified certain risk factors associated with clinical failure and death from any cause using multivariate binary logistic regression, as detailed in Tables 4 and 5.

Of the 65 patients with bone and joint infections, 15 (23.1%) did not achieve clinical cure, and seven (10.8%) had died at the one-year follow-up. The presence of a medical device was not found to be a predictor of treatment failure for these patients.

Table 4. Results of the multivariate binary logistic regression assessing the risk of treatment failure for significant variables identified using univariate binary logistic regression – N = 341.

Variable	OR (95%IC)	P-value
Cirrhosis	***5.223 (1.374–19.851)***	***0.015***
Hematological malignancies	***3.720 (1.404–3.861)***	***0.0082***
Bone and joints infections	***4.529 (2.109–9.723)***	***0.0001***

Significant risk factors are highlighted in bold italics (p-value < 0.05).

Table 5. Results of the multivariate binary logistic regression assessing the risk of death for significant variables identified using univariate binary logistic regression – N = 352.

Variable	OR (95%IC)	P-value
Age (year)	1.033 (0.984–1.084)	0.19
Chronic Kidney failure	***9.924 (2.222–44.331)***	***0.0027***
Ischemic cardiomyopathy	1.167 (0.295–4.624)	0.83
Peripheral vascular disease	3.514 (0.927–13.317)	0.065
Hematological malignancies	***10.531 (2.358–47.042)***	***0.0020***
Bone and joints infections	***6.952 (1.813–26.565)***	***0.0047***

Significant risk factors are highlighted in bold italics (p-value < 0.05).

A total of 107 patients (30.4%) required unplanned readmission to the hospital. However, only 29 (8.2%) were related to infection complications or worsening. The remaining 78 readmissions were due to various reasons such as acute coronary syndromes, gastrointestinal bleeding, graft-versus-host disease or pulmonary embolism.

Table 6 displays the variables associated with readmission, as identified using univariate binary logistic regression. Further investigation using multivariate binary logistic regression revealed that only two variables, flucloxacillin and vancomycin, were independently associated with the risk of readmission.

The study identified drug-related adverse events (DRAE) in 18 cases, accounting for 5.1% of the patients (cumulative risk: 2.6 events per 1000 OPAT patient-days). The most prevalent adverse event was rash, occurring in 10 patients. Other adverse events included acute renal failure ($N = 4$), *Clostridioides difficile* associated diarrhea (CDAD) ($N = 2$), neutropenia ($N = 1$), and hemolytic anemia ($N = 1$). The analysis revealed that only patients treated with vancomycin were at a higher risk of experiencing drug-related adverse events, with an OR of 5.873 (95%CI 1.481–23.287, p-value 0.012).

Regarding line-related adverse events (LRAE), there were fifteen cases (4.2%; cumulative risk: 2.2 events per 1000 OPAT patient-days), including nine catheter malfunctions, three central line-associated bloodstream infections, and three cases of venous thrombosis.

Four of 18 patients (22.2%) were readmitted due to DRAE, whereas 8 of 15 patients (53.3%) with LRAE required readmission.

No significant associations were found between the studied outcomes and factors such as bacteremia, presence of a medical device, continuous or intermittent infusion, therapeutic drug monitoring, OPAT duration, type of vascular access device, absence of pathogen documentation, age, or sex ($p > 0.05$). Tables detailing the univariate binary logistic regression analyses are provided in the appendix.

Discussion

The high clinical cure rates (86.4%) achieved in our OPAT program, as well as the low rates of DRAE (2.6 events per 1000 OPAT patient-days) and LRAE (2.2 events per 1000 OPAT patient-days), are consistent with findings reported in other OPAT programs [9,13,21,22].

Table 6. Results of the multivariate binary logistic regression assessing the risk of readmissions for significant variables identified using univariate binary logistic regression – N = 352.

Variable	OR (95%IC)	P-value
Age (years)	1.006 (0.990–1.023)	0.44
Diabetes mellitus	1.558 (0.885–2.744)	0.12
Ischemic cardiomyopathy	1.895 (0.980–3.662)	0.057
Cirrhosis	2.418 (0.692–8.449)	0.17
Hematological malignancies	1.308 (0.377–4.540)	0.67
Marrow transplant	2.853 (0.624–13.051)	0.18
Blood stream infections	0.940 (0.126–1.254)	0.86
Central nervous system infections	0.397 (0.126–1.254)	0.11
Medical device	1.626 (0.798–3.311)	0.18
Vancomycin	***5.907 (1.653–21.102)***	***0.0063***
Flucloxacillin	***4.941 (1.496–16.321)***	***0.0088***

Significant risk factors are highlighted in bold italics (p-value < 0.05).

Although only four deaths were infection-related (1.1%), the overall fatality rate in our study reached 4%, which is higher than in most OPAT observational studies, where over 90% reported rates below 2.5% [21]. Several factors may account for this difference. First, the extended follow-up period of one year, especially for bone and joint infections, which accounted for half of the deaths, increased the likelihood of capturing adverse outcomes, including all-cause mortality. Second, the complexity of infections treated in a tertiary hospital setting, particularly bloodstream infections (the most frequent at 29.8%) may also have contributed. Finally, our study population had a median age of 64.5 years and a median of two comorbidities, indicating substantial baseline medical complexity. The presence of specific comorbidities, including organ transplants (16.5%), solid tumors (19.6%), and hematological malignancies (9.9%), further increased the vulnerability of patients to adverse outcomes.

The rate of unplanned readmissions (30.4%) falls within the range reported in other studies [23,24]. It is important to note that the definition of readmission can vary among studies, which may impact the reported rates. In our study, all unplanned readmissions, regardless of whether they were infection-related, as well as emergency department visits, were included in the analysis. Notably, only 29 of 107 readmissions (27.1%) were associated with infection complications or worsening. This suggests that the OPAT program is successfully addressing the infectious aspect of patient care and that readmissions are primarily driven by other medical conditions or factors, including psycho-social factors not considered in this study.

The study identifies potential risk factors associated with clinical failure and death, including cirrhosis, hematological malignancies, bone and joint infections, and chronic renal failure. These findings highlight specific patient populations that may require closer monitoring and tailored interventions. The presence of such risk factors at the initial assessment by the infectious diseases specialist should prompt a cautious evaluation of OPAT eligibility, ensuring that patients are clinically stable and that intensified follow-up, such as more frequent clinical or laboratory reassessment beyond the standard weekly visit, is feasible. In situations where clinical stability cannot be guaranteed or enhanced monitoring is not achievable, continuation of inpatient therapy or deferral of OPAT initiation should be considered to optimize safety.

The significant association between bone and joint infections and treatment failure is a notable finding. The decision to extend the follow-up period to one year for these infections was driven by the understanding that osteoarticular infections are associated with late infection relapses. Another study that extended the follow-up period for bone and joint infections reported a similar failure rate (29.8%) at 24 months, with the majority (93.2%) of relapses occurring during the first year [25]. This approach provides a more comprehensive assessment of treatment outcomes for these specific types of infections and highlights the importance of long-term follow-up in assessing the success of OPAT in such cases.

The study findings also provide valuable insights into the utilization of continuous infusion using EIDs in the context of OPAT. Continuous infusion was favored over intermittent administration in 60.6% of antibiotic courses. Importantly, no association was found between continuous infusion and any adverse outcome, supporting its safety within the OPAT program. Some OPAT programs favor once-daily agents such as ceftriaxone, ertapenem, or teicoplanin for logistical reasons [22]. These agents offer simplified dosing regimens, reducing the frequency of intravenous administration and potentially improving patient convenience. However, reliance on broad-spectrum once-daily antibiotics, particularly third-generation cephalosporins or carbapenems, may increase the risk of healthcare-associated complications such as CDAD or the emergence of multidrug-resistant bacteria [26]. While OPAT-associated CDAD outbreaks remain rare [27,28], this does not eliminate the underlying risk. These findings suggest that continuous infusion using electronic infusion devices is a safe option, and once-daily agents should not be automatically favored over narrow-spectrum antibiotics if EIDs are readily accessible, particularly in the home-based model of OPAT.

In this study, narrow-spectrum antibiotics (cefazolin, benzylpenicillin, temocillin, flucloxacillin and amoxicillin) were used in 32.1% of cases (or in association in cases of infective endocarditis due to *Enterococcus faecalis*) which is an encouraging result in accordance with the policy of de-escalation and limitation of broad-spectrum agents. Of note, TDM was implemented in most cases where it was available, and it led to dose adjustments in a substantial proportion of patients, underlining its clinical relevance in the OPAT setting.

The study results shed light on the potential risks associated with the use of certain antibiotics in the outpatient parenteral antibiotic therapy program. Specifically, it highlighted vancomycin use as a potential risk factor for both readmissions and adverse drug events. Other studies also found vancomycin to be a risk

factor for adverse drug events or readmission [23,29,30]. This is consistent with the well-known toxicities associated with vancomycin, particularly renal toxicity and cytopenia. Nevertheless, vancomycin is frequently prescribed for complex infections, which themselves carry a higher risk of complications and readmission. In addition, flucloxacillin use was identified as a potential risk factor for readmission, although it was not associated with drug-related adverse events. All 15 patients receiving flucloxacillin had bloodstream infections (12 MSSA, 3 coagulase-negative Staphylococcus), eight of whom had infective endocarditis. It is therefore plausible that the observed associations for both vancomycin and flucloxacillin reflect the intrinsic severity and complexity of these deep-seated infections rather than drug-related toxicities per se. While our multivariate model adjusted for several clinical variables, residual confounding related to infection severity cannot be fully excluded. The small sample size of these subgroups further limits the strength of these observations, underscoring the need for careful monitoring and individualized management when these antibiotics are used in OPAT.

Ultimately, antibiotic selection and administration strategies in OPAT should be guided by a tailored approach that balances clinical efficacy, TDM, and potential risks.

We acknowledge several limitations that should be considered when interpreting the findings of this study. Firstly, the data collection relied on the reports provided by OPAT coordinators and infectious disease physicians, which introduces the possibility of underreporting certain adverse events. This could potentially lead to an underestimation of the rates of drug-related or line-related adverse events. The reliance on retrospective data also adds to this limitation, as retrospective studies are susceptible to recall bias and incomplete documentation. Secondly, it is important to note that the study was conducted at a single tertiary teaching hospital, which may limit the generalizability of the findings to other settings or patient populations. Lastly, despite the use of multivariate logistic regression to identify risk factors, there may still be unaccounted confounding factors, especially psycho-social parameters that could influence the study results. The complexity of patient conditions and the variability in clinical management among individuals could introduce additional factors that were not captured in the analysis. Therefore, caution should be exercised when extrapolating the results of this study to other OPAT programs or healthcare contexts. Further research involving larger multicenter studies with prospective designs is needed to validate these findings.

In summary, while our findings largely align with international OPAT literature, this study provides novel insights into the use of continuous infusion via electronic devices and the practical application of therapeutic drug monitoring in a large, real-world Belgian cohort, representing one of the largest national experiences to date.

Conclusion

This study highlights the effectiveness and safety of our OPAT program, demonstrating high clinical cure rates, low rates of adverse events, and readmissions primarily unrelated to infection. The program also proved to be resource-sparing, avoiding an average of 1692 hospital days per year.

Certain patient populations require closer monitoring, including those with cirrhosis, hematological malignancies, bone and joint infections, or chronic renal failure. Careful patient selection, close follow-up, and vigilant monitoring, notably when using vancomycin and flucloxacillin, are essential to minimize complications.

Our findings confirm the safety of continuous infusion via electronic infusion devices and suggest that once-daily broad-spectrum antibiotics should not be automatically favored when narrow-spectrum agents are feasible.

In conclusion, this study reinforces that OPAT is an effective, safe, and resource-efficient therapy, while emphasizing the importance of individualized patient selection and monitoring to optimize clinical outcomes.

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Author contributions

CRediT: **Vincent Infantino:** Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft; **Justine Monseur:** Formal analysis, Writing – review & editing; **Gilles Darcis:** Methodology, Writing – review & editing; **Catherine Orban:** Data curation, Writing – review & editing; **Frederic Frippiat:** Conceptualization, Methodology, Writing – review & editing; **Anne-Sophie Sauvage:** Conceptualization, Methodology, Supervision, Writing – review & editing.

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