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# Effectiveness and safety of a disposable elastomeric continuous infusion pump for outpatient parenteral antimicrobial therapy (OPAT) in a UK setting

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**Short Running Title:** Use of an elastomeric infusion pump for OPAT.

**ABSTRACT**

We evaluated the effectiveness and safety of continuous antimicrobial infusion using a disposable elastomeric device in an outpatient parenteral antimicrobial therapy (OPAT) setting. We conducted a retrospective analysis of all patients who received either flucloxacillin (*n*=131 episodes) or piperacillin/tazobactam (*n*=301 episodes) as continuous infusion via elastomeric devices over 5 years (January 2018-December 2022) at a tertiary referral hospital in Derbyshire, UK. Overall, 81 adverse events were recorded in 77 (18%; 77/432) patient-episodes. Most adverse events were vascular access-related (59%; 4.6 events per 1000 OPAT-days), including one line-related infection (0.2%; 0.1 events per 1000 OPAT-days). 165 (38%) patient-episodes experienced at least one incident of incomplete infusion. Successful outcome (cure or improvement) occurred in 364 (84%) episodes. Our findings suggest that elastomeric infusion pumps are safe and effective for administering selected antimicrobial agents in OPAT. However, close monitoring of patients and the device are essential to ensure optimal delivery of prescribed therapy.

**Keywords:** continuous infusion; elastomeric infusion pump; flucloxacillin; outpatient parenteral antimicrobial therapy; OPAT; piperacillin/tazobactam

## Introduction

Outpatient parenteral antimicrobial therapy (OPAT) has been recognised to be a safe and effective alternative to inpatient care for treating a wide range of infections [1-3]. However, patients receiving OPAT are at risk of adverse events that could result in unplanned hospital readmissions [4,5]. The choice of antimicrobial therapy in OPAT is often limited to agents that can be administered once daily or less frequently for convenience in dosing and due to staffing constraints. Infrequent dosing minimises handling of vascular access and hence reduces the risk of line-related complications such as thrombosis and infection. Furthermore, the use of relatively broad-spectrum once-daily agents such as ceftriaxone to facilitate OPAT for infections (e.g., cellulitis) that could be better treated with narrower spectrum agents with multiple daily doses (e.g., flucloxacillin) represents a major challenge to effective antimicrobial stewardship [6]. Portable continuous infusion pumps and elastomeric devices allow prolonged infusions of narrow-spectrum antimicrobial agents with time-dependent killing profiles and short half-lives such as penicillins, thereby avoiding multiple daily dosing [7]. Elastomeric pumps are increasingly used to deliver antimicrobials with documented success [8,9]. The lack of antimicrobial stability data, however, limits the use of continuous infusions of most antibiotic agents in the OPAT setting. Recently published data from the British Society for Antimicrobial Chemotherapy (BSAC) drug stability group suggest that flucloxacillin and piperacillin/tazobactam are suitable for continuous 24-hour infusion via an elastomeric device [10,11].

With the continued widespread utilisation of elastomeric devices in OPAT, it is essential to further review clinical outcomes across a range of clinical conditions, especially within the UK National Health Service [12,13]. In the current study, we examine the clinical characteristics, safety profile and outcomes of patients who were

treated with disposable elastomeric continuous infusion pumps at an OPAT service based in a large tertiary referral teaching hospital in Derbyshire, UK.

## Patients and methods

### *Study design and setting*

In this cohort study, we reviewed and followed up all patients who received antibiotics as continuous infusion via elastomeric pumps at the OPAT unit of University Hospitals of Derby and Burton (Derbyshire, England, UK) between 1 January 2018 and 31 December 2022. The number of eligible patients over the study period determined the study size and no a priori statistical calculation of sample size was performed. Patient outcomes were determined at the end of intravenous (IV) antimicrobial therapy.

The OPAT service was established in 2013 and has been previously described [14,15]. The service is managed by a multidisciplinary team of infection specialists, specialist nurses, clinical antimicrobial pharmacists, and community nurses. The service maintains electronic databases to prospectively record patient demographics, antimicrobial agents, indication and duration of antimicrobial therapy, model of delivery, clinical outcome, and complications.

Use of flucloxacillin and piperacillin/tazobactam in disposable elastomeric infusion pumps began in late 2017. The pre-filled elastomeric pump devices were sourced from an external healthcare company and required cold chain maintenance. The selection of patients for OPAT, antimicrobial regimens, and mode of OPAT delivery were the responsibility of the OPAT infection specialists. Antimicrobials were delivered through three distinct pathways: administration in the patient's home by a district/community nurse, daily attendance at the OPAT facility, and self or care administration in the patient's home (after appropriate training). The clinical responsibility for patients during

their OPAT course and follow-up was shared between the referring clinicians and the OPAT team, unless otherwise agreed upon. Patients receiving OPAT were regularly reviewed and their clinical progress was assessed during a weekly multidisciplinary meeting/virtual ward round. The residual volumes of antibiotic solution in the elastomeric devices were assessed daily with the aid of a pictorial 'infusion progress' chart, which was provided by the healthcare company that supplied the devices, to service as a guide.

### *Data Collection*

The OPAT databases and hospital electronic health records were reviewed. The following data were extracted: patient demographics, treatment indication, microbiological culture data, antimicrobial regimen, duration of OPAT course (bed-days saved), mode of OPAT delivery, type of vascular access device, OPAT outcome, complications, and hospital readmission. Age (in years) was determined at the time of commencing OPAT. Clinical records were anonymised at the time of data extraction. The study was approved by the local clinical audit/effectiveness team as part of ongoing commitment to clinical governance, service development, and evaluation.

### *Outcomes and definitions*

Clinical outcomes (cure, improvement or failure) were determined at the end of IV antimicrobial therapy using the definitions provided in the BSAC National Outcomes Registry System (NORS) [see Supplementary Table S1] [16]. Adverse events included adverse drug reactions (i.e., events possibly related to study medications, including diarrhoea, rash, blood dyscrasia, renal and hepatic dysfunction), vascular access-related complications (such as infection, line migration, occlusion, thrombosis, and allergy to dressing) and infusion device-related complications (such as leaking devices and device

malfunction). Major adverse events were defined as those that resulted in hospital readmissions, change in antimicrobial regimen(s), *Clostridium difficile* infection or death. Other adverse events that were not major were classified as minor. A 30-day unplanned hospitalisation was defined as unplanned inpatient admission to an acute care hospital for any reason during or within 30 days of OPAT discharge.

### *Statistical analysis*

Categorical data were presented as frequency counts and percentages. Numerical data were summarised as medians with interquartile ranges (IQR) or means with standard deviations (SD), depending on the degree of skewness in the distributions. Categorical outcome frequencies were compared using the Chi-square test (or Mid-P exact test where required). Confidence intervals for proportions were calculated using Wilson's score method. Analyses were performed using Prism version 9.5.1 (GraphPad Software, Boston, MA, USA). A two-tailed *p*-value of less than 0.05 was considered statistically significant.

### *Sensitivity analysis*

A sensitivity analysis of observed adverse event rates, restricted to the first OPAT encounter for each patient, was conducted to examine the potential for overestimating the apparent safety of the antibiotic regimens. This analysis was considered necessary since patients who tolerated their initial course of therapy might have a higher likelihood of tolerating subsequent courses of therapy.

## Results

### *Cohort characteristics*

Over the five-year study period, we recorded 1237 episodes of OPAT, of which 432 episodes (involving 340 individual patients) received antibiotics (flucloxacillin, 131 (30.3%) episodes; piperacillin/tazobactam, 301 (69.7%) episodes) administered as continuous infusion via elastomeric pumps. Respiratory infection, specifically recurrent exacerbation of bronchiectasis, was the main indication for repeated courses of OPAT. Table 1 presents the demographic, treatment characteristics, and clinical outcomes of the cohort. The median age of the patients was 71 (range, 17 - 98) years, and 45.4% (196/432) were female. The most frequent indications for flucloxacillin and piperacillin/tazobactam therapy were bone and joint infection (60.3%; 79/131) and respiratory infection (mostly infective exacerbation of bronchiectasis/chronic obstructive pulmonary disease (54.5%; 164/301) respectively. Antibiotic therapy was mainly administered in patient's home by visiting nurses (83.3%; 360/432). The median duration of OPAT for the cohort was 14 days (IQR, 7 - 33; range, 1 - 230 days). The longest antibiotic course was administered to control, rather than cure, chronic mandibular osteomyelitis in a patient with locally advanced oropharyngeal cancer (palliative OPAT) [14]. The median duration of piperacillin/tazobactam therapy was 14 days (IQR, 7 – 34; range, 1 - 230 days) while the mean duration of flucloxacillin therapy was 22.5 days (SD, 17; range, 2 – 93).

***Clinical outcomes***

364 (84.3%; 95% CI: 80.5 – 87.4%) episodes met the BSAC NORS definition of cure or clinical improvement [16]. Failures were recorded in 68 episodes (15.7%; 95% CI: 12.6 – 19.5%), mostly due to hospital readmission from non-OPAT related causes [Supplementary Table S2]. Non-OPAT related (new) events (e.g., falls, worsening heart failure, etc.) accounted for 42.2% (27/64) of readmissions. Two patients died. One of these patients had palliative OPAT for an incurable infection [14] while the other patient

died due to underlying comorbidities unrelated to OPAT. 30-day unplanned readmission was recorded in 117 episodes (27.1%; 95% CI: 23.1 – 31.5%). The reasons for the 30-day unplanned readmission are shown in Supplementary Table S3. The leading indication for 30-day hospitalisation was also due to non-OPAT related events (41.9%; 49/117). Compared with other models of delivery, self/carer administered OPAT was associated with a lower failure rate (6.3% vs 17.4%; $P = 0.02$) and a lower 30-day unplanned readmission rate (7.8% vs 30.4%; $P < 0.001$).

In all, 81 adverse events were recorded in 77 (17.8%; 77/432) infusions administered through elastomeric pumps [Table 1]. Most of the adverse events were vascular access-related (59.3%; 48/81; 4.6 events per 1000 OPAT-days) – mainly due to line migration (52.1%; 25/48). One line-related infection (0.2%, 95% confidence interval (CI): 0.04 – 1.29%; 0.1 events per 1000 OPAT-days) and two catheter-related thromboses (0.5%; 95% CI: 0.12 – 1.67%; 0.2 events per 1000 OPAT-days) were recorded. There were no complications related to the elastomeric device (e.g., leaking device, device malfunction). In all, major adverse events were observed in 29 (6.7%; 95% CI: 4.7 – 9.5%) episodes. Full details of the adverse events are shown in Supplementary Table S4.

The frequencies of adverse events (i.e., line-related complications and drug reactions) were similar between the flucloxacillin and piperacillin/tazobactam groups. These findings were robust in a sensitivity analysis restricting the observed adverse event rates to the first OPAT encounter for each patient (Supplementary Table S5).

There was also no significant relationship between line-related complications and type of vascular access device (PICC vs midline; 19/145 [13.1%] vs. 29/287 [10.1%] events; $P = 0.35$); and between adverse events and mode of OPAT delivery (self/carer administered vs other modes, 23.4% vs 16.9%; $P = 0.20$). There were no adverse complications recorded in the eight patient-episodes who attended the OPAT facility

daily for their antibiotic therapy. Overall, 165 (38.2%; 95% CI: 33.7 – 42.9%) patient-episodes experienced at least one incident of incomplete infusion (emptying) of elastomeric devices. There was no statistically significant difference in cure rates between patients with complete infusions and those who had at least one incomplete infusion (83.2% vs. 86.1%; $P = 0.42$). However, the number of incomplete infusions per patient-episode during the course of OPAT was not captured in our database.

## Discussion

Portable elastomeric pump devices are increasingly used in diverse healthcare environments to intermittently or continuously infuse therapeutic medications, including chemotherapy, analgesia, diuretics, and antimicrobial agents [17,18]. Elastomeric devices contain a stretchable balloon reservoir that contracts to deliver a continuous flow over a set time period without the need for needles, gravity, or electricity. They allow for the continuous infusion of antimicrobial agents with short half-lives that would otherwise require multiple daily dosing. Here, we report our experience with the continuous infusion of flucloxacillin and piperacillin/tazobactam via elastomeric devices in an OPAT setting in the UK. Similar to other OPAT-related studies [8,9,12,13,19-24], we found a high rate of therapeutic success, low complication rates, and low OPAT-related readmission rates among our cohort.

Although 15% of antibiotic therapies were administered by patients (or their carers) in our cohort, we observed that self/carer administration of continuous infusion via elastomeric device was associated with equivalent adverse events but a lower risk of poor outcomes and readmission within 30 days when compared to other mode of delivery. While this may add to the growing evidence that self-administered OPAT is safe and effective [25-27], we cannot rule out the possibility that these findings were confounded

by differences in underlying comorbidities between the groups. In selected patients who self-administered their antibiotics using elastomeric pumps, telemedicine could be used for remote monitoring to allow timely identification and appropriate management of complications and concerns as soon as they arise [28].

As regards time-dependent antibiotics like flucloxacillin and piperacillin/tazobactam, continuous infusion helps optimise the pharmacokinetic/pharmacodynamic ratio (percentage of the time between two injections during which the antibiotic is superior to the minimum inhibitory concentration) and reduces the risk of treatment failure and emergence of resistance [7]. As the infusion pumps are changed less frequently, either by a healthcare professional or by the patient (or their carer), they allow for patient-centred care, greater patient autonomy, and reduce the burden on the healthcare system and daily nurse visits [8]. The frequency of accessing lines is also reduced, thereby lowering the risk of vascular access-related complications such as infection and thromboembolic events.

Use of elastomeric pumps in the OPAT settings has also been associated with improved quality of life [7], high levels of patient satisfaction and acceptance [29], positive nurse evaluation [12], and cost savings when compared to inpatient care [9]. However, 'elastomeric' OPAT is more costly compared to 'traditional' OPAT antimicrobial therapies due to significant cost relating to the devices and consumables. For example, in our hospital the elastomeric pumps pre-filled with flucloxacillin 8g (sourced from a healthcare company) cost £99.36 per device compared to a daily drug cost of £5.09 for intermittent bolus infusion of flucloxacillin 2g every 6 hours (excluding consumables). Cost, wastage, and procurement challenges (e.g., cold chain, procurement delays which may cause delayed hospital discharge, etc.) could be minimised by in-house preparation of the elastomeric device or use of 'fresh-fill' approach without refrigerated

storage (allowing for drug stability) subject to appropriate safeguards and risk assessments [12,30]. We suggest future analyses should assess the cost-effectiveness of elastomeric pumps compared to 'traditional' antimicrobial treatment in the OPAT setting.

The maximum infusion duration of an antimicrobial agent, as well as the minimum frequency of device change, depends on its stability in an infusion device [7]. However, not all antimicrobial agents are suitable for continuous infusion via an elastomeric device due to variable stability over the infusion period, resulting in lower effectiveness and the risk of producing potentially toxic degradation products. For example, the degradation of ceftazidime via hydrolysis results in the production of pyridine, which can cause neurological, liver, kidney and gastrointestinal disorders [31]. A literature review of 121 studies published between 1975 and 2015, carried out by the UK BSAC Drug Stability Working Group, found no published studies that comply with UK national standards for stability [32]. However, an updated literature review published in 2021 identified the acceptable stability of flucloxacillin and piperacillin/tazobactam for continuous infusion over 24 hours, ceftolozane-tazobactam for infusion over 12 hours, and the potential for acceptable stability of cefazolin, subject to adequately performed stability testing [33]. Subsequent works by the group showed that flucloxacillin [10], piperacillin/tazobactam [11], and temocillin [34] are suitable for continuous infusion via an elastomeric device, while meropenem is not [35]. Continuous infusion of other antimicrobial agents via an elastomeric device within an OPAT setting would only be appropriate if supported by robust antimicrobial stability data.

The rate of adverse events in our cohort was comparable to other similar OPAT studies [8,19]. We did not observe any cases of *C. difficile* infection or adverse events related to the elastomeric device (e.g., leaky devices). However, we recorded a high number of patients experiencing at least one episode of incomplete infusion (failure of

flow event) of the elastomeric device. The number of incomplete infusions per patient and the proportion of antibiotic dose infused/residual volume were not captured in our database. Therefore, we could not fully assess the effect of incomplete infusion on clinical outcomes. However, we did not detect any difference in cure rate between patients with and without incomplete infusion. Incomplete infusion of elastomeric devices is very common and could be due to suboptimal use of the device (e.g., temperature, position, storage), faulty device or vascular access-related issues [12,19,36,37]. Depending on the residual volume, top-up doses of antibiotics may be required to optimise antimicrobial dosing. In our OPAT centre, we often administer extra doses of antibiotics when the residual volume in the elastomeric device is more than two-thirds to three-quarters. Ultimately, the decision of whether or not to administer an extra dose of antibiotic should be made on a case-by-case basis, taking into account the individual patient's needs and the characteristics of the antibiotic being administered. The risks associated with elastomeric device use, thus, reinforce the need for close monitoring and escalation plans for patients receiving OPAT.

Our study is limited by a number of factors, including its retrospective design and restriction to single centre experience. We did not assess antibiotic plasma concentration and its effect on clinical outcome or adverse events since it was outside the scope of the study. Due to incomplete data, we were not able to assess fully the effect of incomplete infusion on clinical outcome. Nevertheless, despite a high number of patients experiencing incomplete infusion, the overall clinical failure rate was relatively low. A further limitation is that patient outcomes were only determined at the end of OPAT care. Hence, the true rate of clinical failure may have been underestimated since infection relapse can occur several weeks after completion of OPAT. Nonetheless, we documented the reasons for the 30-day unplanned readmission. Lastly, we could not be entirely certain

that the observed adverse events are all related to flucloxacillin and piperacillin/tazobactam because some patients received additional antimicrobial agents prior to or during their OPAT care.

In conclusion, our study adds to the growing body of evidence that elastomeric infusion pumps are a safe and effective option for administering certain antimicrobial agents via continuous infusion in the OPAT setting. However, it is worth noting that adverse events and incomplete infusions are not uncommon. Therefore, careful patient selection, close monitoring, and regular review of the device are essential to ensure optimal delivery of prescribed therapy and achieve favourable clinical outcomes.

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**Disclosure statement**

The authors report there are no competing interests to declare.

**Author Contributions**

Conceptualization, O.C.D.; methodology, O.C.D.; software, O.C.D.; validation, E.I.K. and J.C.; formal analysis, E.I.K. and O.C.D.; investigation, O.C.D.; data curation, O.C.D.; writing—original draft preparation, O.C.D.; writing—review and editing, E.I.K. and J.C.; visualization, O.C.D. All authors have read and agreed to the final version of the manuscript.

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**Table 1.** Characteristics of patients, treatment, and outcomes

| Characteristic | Flucloxacillin (*n* = 131) | Piperacillin/tazobactam (*n* = 301) | Total (*n* = 432) |
|---|---|---|---|
| Demographics | | | |
| Age (years), median [(IQR)] | 67 [58 – 75] | 72 [66 – 78] | 71 [63 - 77] |
| Sex (Male: Female) | 1.6:1 | 1.1:1 | 1.2:1 |
| Indication for OPAT | | | |
| Respiratory infection[a] | - | 164 (54.5) | 164 (38.0) |
| Bone and joint infection[b] | 79 (60.3) | 70 (23.3) | 149 (34.5) |
| Necrotising otitis externa | - | 50 (16.6) | 50 (11.6) |
| Spinal infection[c] | 31 (23.7) | 5 (1.7) | 36 (8.3) |
| Endovascular infection[d] | 14 (10.7) | 3 (1.0) | 17 (3.9) |
| Intra-abdominal infection[e] | 2 (1.5) | 5 (1.7) | 7 (1.6) |
| Urinary tract infection[f] | 2 (1.5) | 4 (1.3) | 6 (1.4) |
| Bacteraemia | 3 (2.3) | - | 3 (0.7) |
| Main pathogen identified | | | |
| No organism identified | 10 (7.6) | 38 (12.6) | 48 (11.1) |
| MSSA | 116 (88.6) | - | 116 (26.9) |
| *Pseudomonas spp.* | - | 214 (71.1) | 214 (49.5) |
| MSSA + *Pseudomonas spp.* | - | 5 (1.7) | 5 (1.2) |
| MSSA + other organisms | - | 9 (3.0) | 9 (2.1) |
| *Pseudomonas spp.* + other organisms | - | 18 (6.0) | 18 (4.2) |
| Other organisms[g] | 5 (3.8) | 17 (5.6) | 22 (5.1) |
| Duration of OPAT (days), median [(IQR)] | 18 [9 – 32] | 14 [7 – 34] | 14 [7 – 33] |
| Mode of antimicrobial (OPAT) delivery | | | |
| Visiting nurse | 101 (77.1) | 259 (86.1) | 360 (83.3) |
| Self/carer administration | 26 (19.8) | 38 (12.6) | 64 (14.8) |
| Daily attendance | 4 (3.1) | 4 (1.3) | 8 (1.9) |
| Type of vascular access device | | | |
| Midline | 61 (46.6) | 226 (75.1) | 287 (66.4) |
| PICC | 70 (53.4) | 75 (24.9) | 145 (33.6) |
| Concomitant IV antimicrobial therapy | 2 (1.5) | 10 (3.3) | 12 (2.8) |
| Concomitant oral antimicrobial therapy | 38 (29.0) | 22 (7.3) | 60 (13.9) |
| Incomplete infusion[h] | 46 (35.1) | 119 (39.5) | 165 (38.2) |
| OPAT-related adverse event | 23 (17.6) | 54 (17.9) | 77 (17.8) |
| Type of adverse event[i] | | | |
| Major adverse event, *n* (%); events per 1000 OPAT-days | 8 (6.1); 2.7/1000 days | 21 (7.0); 2.8/1000 days | 29 (6.7); 2.8/1000 days |
| Medication related, *n* (%); events per 1000 OPAT-days | 8 (6.1); 2.7/1000 days | 25 (8.3); 3.4/1000 days | 33 (7.6); 3.2/1000 days |
| Vascular access related, *n* (%); events per 1000 OPAT-days | 16 (12.2); 5.4/1000 days | 32 (10.6); 4.3/1000 days | 48 (11.1); 4.6/1000 days |
| Infection outcome | | | |
| Cured or improved | 104 (79.4) | 260 (86.4) | 364 (84.3) |
| Failure | 27 (20.6) | 41 (13.6) | 68 (15.7) |
| 30-day unplanned hospitalisation[j] | 31 (23.7) | 86 (28.6) | 117 (27.1) |

Data are presented as *n* (%) unless otherwise indicated.

IQR, interquartile range; IV; intravenous; MSSA, methicillin-sensitive *Staphylococcus aureus*; OPAT, outpatient parenteral antimicrobial therapy; PICC, peripherally inserted central catheter; SD, standard deviation.

[a] Respiratory infection – mainly infective exacerbation of bronchiectasis/chronic obstructive pulmonary disease.

[b] Bone and joint infection – excluded spinal infection but included septic arthritis, prosthetic joint infection, non-diabetic osteomyelitis, and diabetic foot osteomyelitis.

[c] Spinal infection included discitis, vertebral osteomyelitis, and epidural abscess.

[d] Endovascular infection included infective endocarditis and vascular graft infection.

[e] Intra-abdominal infection included hepatic abscess and intrabdominal collection.

[f] Mainly complex urinary tract infection.

[g] Other organisms - *S. epidermidis* (*n* = 1), *Proteus mirabilis* (*n* = 1), *Serratia marcescens* (*n* = 1), *S. lugdunensis* (*n* = 2), *Streptococcus spp* (*n* = 2), *Klebsiella oxytoca* (*n* = 2), *Escherichia coli* (*n* = 3), and mixed culture (*n* = 10).

[h] Patient-episode who experienced at least one incident of incomplete infusion (emptying) of elastomeric device during course of OPAT.

[i] Some patient-episodes had more than one adverse event.

[j] Defined as unplanned inpatient admission for any reason during or within 30 days of OPAT discharge.

# APPENDIX

# Effectiveness and safety of a disposable elastomeric continuous infusion pump for outpatient parenteral antimicrobial therapy (OPAT) in a UK setting

## SUPPLEMENTARY DATA

**Supplementary Table S1.** BSAC NORS Definitions of OPAT Outcomes.[16]

| | |
|---|---|
| **Infection outcomes** | |
| Cure | Completed OPAT therapy +/- oral step down for defined duration with resolution of infection and no requirement for long term antibiotic therapy (usually relates to less severe infections e.g., SSTI, UTI unless prosthetic material removed). |
| Improved | i. Completed OPAT therapy +/- oral step down with partial resolution of infection but need for further follow up OR<br>ii. Completed OPAT therapy but required escalation of antimicrobial therapy during OPAT (without admission) +/- oral step down with ultimate cure or partial improvement (as above) e.g., osteomyelitis, any infections where prosthetic material has not been removed. |
| Failure | Progression or non-response of infection despite OPAT, required admission, surgical intervention or died for any reason. |
| **OPAT outcomes** | |
| Success | Completed therapy in OPAT with no change in antimicrobial agent, no adverse events, cure or improvement of infection and no readmission |
| Partial Success | Completed therapy in OPAT with either change in antimicrobial agent or adverse event not requiring admission |
| Failure of OPAT | Readmitted due to infection worsening or due to adverse event. Death due to any cause during OPAT |
| Indeterminate | Readmission due to unrelated event e.g., chest pain |

BSAC, British Society for Antimicrobial Chemotherapy; NORS; national outcomes registry system; OPAT, outpatient parenteral antimicrobial therapy; SSTI, skin and soft tissue infection; UTI, urinary tract infection.

**Supplementary Table S2.** Description of patient outcomes

| Patient Outcome | Flucloxacillin (*n* = 131) | Piperacillin/tazobactam (*n* = 301) | Total (*n* = 432) |
|---|---|---|---|
| Cure | 5 (3.8) | 27 (9.0) | 32 (7.4) |
| Improved | 99 (75.6) | 233 (77.4) | 332 (76.9) |
| Failure | 27 (20.6) | 41 (13.6) | 68 (15.7) |
| Progression or non-response of infection[a] | 1 (0.8) | 1 (0.3) | 2 (0.5) |
| Death | - | 2 (0.7) | 2 (0.5) |
| Readmission[b] | 26 (19.8) | 38 (12.6) | 64 (14.8) |
| Non-OPAT related | 8 (30.8)* | 19 (50.0)* | 27 (42.2)* |
| Worsening of infection/no improvement | 8 (30.8)* | 8 (21.1)* | 16 (25.0)* |
| New infection[c] | 6 (23.1)* | 4 (10.5)* | 10 (15.6)* |
| Vascular access related complications | 2 (7.7)* | 4 (10.5)* | 6 (9.4)* |
| Adverse drug reaction | 2 (7.7)* | 3 (7.9)* | 5 (7.8)* |

Data are presented as *n* (%).
OPAT, outpatient parenteral antimicrobial therapy.
* As a percentage of number of readmissions.
[a] Not requiring hospital readmission.
[b] Readmission resulting in early termination of OPAT therapy.
[c] New infection included bacteria pneumonia (*n* = 5), COVID-19 infection (*n* = 4) and urinary tract infection (*n* = 1).

**Supplementary Table S3.** Reasons for 30-day unplanned readmission[a] (*n* = 117)

| Reason for readmission | Flucloxacillin (*n* = 31) | Piperacillin/tazobactam (*n* = 86) | Total (*n* = 117) |
|---|---|---|---|
| Non-OPAT related | 12 (38.7) | 37 (43.0) | 49 (41.9) |
| Worsening of existing infection/no improvement[b] | 8 (25.8) | 34 (39.5) | 42 (35.9) |
| New infection | 8 (25.8) | 7 (8.1) | 15 (12.8) |
| Vascular access-related complications | 2 (6.5) | 4 (4.7) | 6 (5.1) |
| Adverse drug reaction | 1 (3.2) | 4 (4.7) | 5 (4.3) |

Data are presented as *n* (%).
OPAT, outpatient parenteral antimicrobial therapy.
[a] Defined as unplanned inpatient admission for any reason during or within 30 days of OPAT discharge.
[b] Worsening infection by diagnosis: endocarditis (*n* = 1), discitis (*n* = 2), necrotising otitis externa (*n* = 3), prosthetic joint infection (*n* = 4), diabetic foot osteomyelitis (*n* = 6), and recurrent infective exacerbation of bronchiectasis/chronic obstructive pulmonary disease (*n* = 26).

**Supplementary Table S4.** Frequency of adverse events

| Type of adverse event[a] | Flucloxacillin | Piperacillin/tazobactam | Total |
|---|---|---|---|
| Major adverse event | 8 | 21 | 29 |
| Hospitalisation | 4 (50.0)[b] | 11 (52.4)[b] | 15 (51.7)[b] |
| Change in antimicrobial regimen(s) | 4 (50.0)[b] | 10 (47.6)[b] | 14 (48.3)[b] |
| Drug-related adverse event | 8 | 25 | 33 |
| Drug Rash | 2 (25.0)[c] | 11 (44.0)[c] | 13 (39.4)[c] |
| Antibiotic induced diarrhoea | 2 (25.0)[c] | 8 (32.0)[c] | 10 (30.3)[c] |
| Blood dyscrasia | 2 (25.0)[c] | 3 (12.0)[c] | 5 (15.2)[c] |
| Hypokalaemia | - | 2 (8.0)[c] | 2 (6.1)[c] |
| Deranged liver function | 1 (12.5)[c] | 1 (4.0)[c] | 2 (6.1)[c] |
| Gastrointestinal disturbance | 1 (12.5)[c] | - | 1 (3.0)[c] |
| Vascular access-related adverse event | 16 | 32 | 48 |
| Line migration | 8 (50.0)[d] | 17 (53.1)[d] | 25 (52.1)[d] |
| Line occlusion | 6 (37.5)[d] | 11 (34.4)[d] | 17 (35.4)[d] |
| Allergy to dressing | - | 2 (6.3)[d] | 2 (4.2)[d] |
| Thrombus | 1 (6.3)[d] | 1 (3.1)[d] | 2 (4.2)[d] |
| Line infection | - | 1 (3.1)[d] | 1 (2.1)[d] |
| Damaged line | 1 (6.3)[d] | - | 1 (2.1)[d] |

Data are presented as *n* (%).

[a] Some patient-episodes had more than one adverse event.

[b] As a percentage of number of major adverse events

[c] As a percentage of number of drug-related adverse events

[d] As a percentage of number of vascular access related adverse events

**Supplementary Table S5.** Sensitivity analysis restricting the observed adverse event rates to the first OPAT encounter for each patient.

| Characteristic | Flucloxacillin (*n* = 121) | Piperacillin/tazobactam (*n* = 219) | Total (*n* = 340) |
|---|---|---|---|
| Incomplete infusion[a] | 42 (34.7) | 88 (40.2) | 130 (38.2) |
| OPAT-related adverse event | 22 (18.1) | 40 (18.3) | 62 (18.2) |
| Type of adverse event[b] | | | |
| Major adverse event, *n* (%); events per 1000 OPAT-days | 8 (6.6); 3.1/1000 days | 18 (8.2); 3.1/1000 days | 26 (7.6); 3.1/1000 days |
| Medication related, *n* (%); events per 1000 OPAT-days | 8 (6.6); 3.1/1000 days | 20 (9.1); 3.5/1000 days | 28 (8.2); 3.4/1000 days |
| Vascular access related, *n* (%); events per 1000 OPAT-days | 15 (12.4); 5.8/1000 days | 24 (11.0); 4.2/1000 days | 39 (11.5); 4.7/1000 days |
| Infection outcome | | | |
| Cure and improved | 97 (80.2) | 186 (84.9) | 283 (83.2) |
| Failure | 24 (19.8) | 33 (15.1) | 57 (16.8) |
| 30-day unplanned hospitalisation[c] | 28 (23.1) | 64 (29.2) | 92 (27.1) |

Data are presented as *n* (%).
OPAT, outpatient parenteral antimicrobial therapy.
[a] Patient-episode who experienced at least one incident of incomplete infusion (emptying) of elastomeric device during course of OPAT.
[b] Some patient-episodes had more than one adverse event.
[c] Defined as unplanned inpatient admission for any reason during or within 30 days of OPAT discharge.

**STROBE Statement—checklist of items that should be included in reports of observational studies**

| | Item No. | Recommendation | Manuscript section |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | Synopsis |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | Synopsis |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | Introduction |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | Introduction |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | Study design and setting |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Study design and setting, Data Collection |
| Participants | 6 | *(a) Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | Study design and setting |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | Outcomes and definitions, Supplementary Table S1 |
| Data sources/ measurement | 8 | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | Data Collection, Outcomes and definitions |
| Bias | 9 | Describe any efforts to address potential sources of bias | Outcomes and definitions |
| Study size | 10 | Explain how the study size was arrived at | Study design and setting |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | Statistical analysis |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | Statistical analysis |
| | | (*b*) Describe any methods used to examine subgroups and interactions | N/A |
| | | (*c*) Explain how missing data were addressed | N/A (no missing data) |
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed | N/A (no loss to follow-up) |
| | | (*e*) Describe any sensitivity analyses | Statistical analysis |
| **Results** | | | |
| Participants | 13 | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, | Cohort characteristics |

| | | | |
|---|---|---|---|
| | | examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | |
| | | (b) Give reasons for non-participation at each stage | N/A |
| | | (c) Consider use of a flow diagram | N/A |
| Descriptive data | 14 | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | Cohort characteristics, Table 1 |
| | | (b) Indicate number of participants with missing data for each variable of interest | N/A |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) | Cohort characteristics, Table 1 |
| Outcome data | 15 | *Cohort study*—Report numbers of outcome events or summary measures over time | Table 1, Supplementary Tables S2-S4 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | Clinical outcomes |
| | | (*b*) Report category boundaries when continuous variables were categorized | N/A (no such categorization done) |
| | | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A – not relevant |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | Supplementary Table S5 |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | Discussion, first 6 paragraphs |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | Disscussion, 7th paragraph |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | Discussion, last paragraph |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | Disscussion, 7th and last paragraphs |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | Funding, Transparency declarations |

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.