# An Outpatient Parenteral Antimicrobial Therapy Practice in United Kingdom Over 27 Months: A Single-Center Experience

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#### Abstract

**Background:** Outpatient parenteral antimicrobial therapy (OPAT) is used and accepted in many countries because of its safety, feasibility, and cost-effectiveness. Here, we report on the outcomes of OPAT services, in terms of types and duration of antimicrobials administered, and assess whether these services are in line with current good practice recommendations.

**Methods:** The electronic healthcare records of all stable patients with infectious disease, aged  $\geq 18$  years, which received OPAT services between January 2019 and March 2021 were analyzed. For statistical analysis, patients were divided into younger (< 65 years) and older ( $\geq 65$  years) adults and difference between them, in terms of healthcare resources utilization, was assessed.

**Results:** Over 27 months, 199 patients received OPAT services, resulting in saving of 7514 bed-days. Bone and joint infections (38.7%) were the predominant diagnosis. The median actual OPAT duration was significantly greater than the planned duration for total study population, younger adults, and older adults (all p-values<0.05). Of 28 patients with adverse events, 25 were related to antimicrobials, while remaining 3 were associated with catheter. There was no significant difference between younger and older adults in all the characteristics evaluated, except for greater median age and higher incidence of *Staphylococcus aureus* (p-value<0.0001) and *E. coli, Staphylococcal* spp., *Streptococcal* spp. and *Pseudomonas* spp. (p-value=0.003) in older adults.

**Conclusion:** The actual duration of OPAT services was significantly longer than planned and less adherence to the principles of antimicrobial stewardship. OPAT has been shown to be safe for both younger and older adults.

**Keywords:** Antimicrobial stewardship, Bones and joints infection, Outpatient parenteral antimicrobial therapy, Safety

#### Introduction

Parenteral outpatient antimicrobial therapy (OPAT) was first introduced in the United States and has been routinely used in many countries over the past 4 decades<sup>1,2</sup>. Its rapid acceptance is due to its proven benefit to both the healthcare system and patients. Compared to traditional inpatient care, OPAT has proven to be a safe, effective and more cost-effective approach to the treatment of various infectious conditions. The available literature refers to the gradual increase and development of experience with OPAT services. These bring benefits such as better-quality care, shortened hospital stays resulting in greater savings, shortening waiting lists, greater availability of hospital beds and greater patient comfort in maintaining daily activities, resulting in patient satisfaction<sup>3</sup>.

OPAT involves administering intravenous (IV) antimicrobials to patients with infectious diseases in outpatient care (hospital OPAT) or at home, by a nurse (homecare OPAT) or by themselves/relatives (self OPAT)<sup>4</sup>. These services are usually used in indications such as cystic fibrosis, infectious endocarditis, complicated urinary tract infections, bone and joint infections (BJI), and skin and soft tissue infections (SSTI)<sup>5</sup>. While initial OPAT services focused on timely dismissal of infection patients in stable, inpatient care requiring only extensive parenteral antimicrobial therapy, over the past two decades the services have made concerted efforts to avoid hospitalization of many acutely infected patients<sup>6-10</sup>.

Following the original Consensus Statement issued in 1998, the recommendations for OPAT in the UK were regularly updated and the most recent recommendations were published in 2019 to keep pace with the changing scenario<sup>11,12</sup>. Despite the late start and slower initial introduction, OPAT services have expanded significantly in UK<sup>13</sup>. Recently, the link between OPAT and antimicrobial stewardship (AMS) has been recognised. Thus, OPAT is diligently disseminated as part of the UK government's AMS programme<sup>14</sup>.

However, the expansion of these services has resulted in significant differences in OPAT practices, supply models and governance rules. In addition, compliance with the national OPAT practice recommendations is weak<sup>13</sup>. Therefore, this study was conducted to review the OPAT services provided by our hospital for the OPAT model and duration and to understand the demographic and clinical profile of patients receiving OPAT. We also assessed whether OPAT services are in line with the recommendations for current good practice in the treatment of infections and made recommendations to minimise gaps.

#### Methods

This was a retrospective study performed in a 550-bed tertiary hospital providing care in all major specialties. The electronic healthcare records of all the patients that received OPAT services between January 2019 and March 2021 were analysed. The stable patients with infectious diseases, belonging to either-sex, aged 18 years or more and receiving outpatient IV antimicrobials were included in the study. While, those receiving antimicrobials through oral or parenteral routes other than IV were excluded.

The UK OPAT good practice recommendations and their subsequent updates formed the basis of the organisational aspects of the OPAT team<sup>11,12</sup>. Our hospital used to outsource the OPAT services and inhouse OPAT services began from 1<sup>st</sup> October 2020. The multidisciplinary team comprised of clinical microbiologist, physician, clinical pharmacists and specialist nurses. The team catered to the patients with infectious diseases that were referred by the physicians from the inpatient hospital wards and outpatient clinics. A weekly multidisciplinary team meeting was held for review of symptoms, inspection and care of the catheters with discussion regarding the treatment. Follow-up laboratory and radiological investigations were performed, if required.

The patients received antimicrobials through peripheral catheters or peripherally inserted central catheters (PICC lines), the latter being inserted by the specialist radiologists. The choice of catheter was dependent on the duration of therapy (short vs long term) and the type of therapy (intermittent vs continuous administration). The PICC lines were used if the therapy was required for more than 7 days and continuous administration was advised by the treating physician. We used one of the two models of antimicrobial administration: clinic and homecare OPAT, where the nurses administered the therapy at the infusion site and home, respectively. The former model

was mainly used for mobile patients requiring short-term antimicrobials (less than 4 days), while the latter model was used for those with limited mobility.

## Data collection

Data related to demographics (age and sex), diagnosis, presence of comorbidities (diabetes mellitus (DM), rheumatoid arthritis and immunosuppression), status of microbiological examination (prior to and during OPAT), antimicrobials used, duration of therapy (planned and actually administered), antimicrobials changed after microbiological examination, radiological examination (computed tomography (CT) and magnetic resonance imaging (MRI)) and outcomes of infection were recorded. Moreover, adverse events (AEs) related to antibiotics requiring discontinuation of therapy, vascular access complications and death were also noted.

# Statistical analysis

The data was analysed with SPSS (IBM, Armonk, NY, USA) version 23.0 for Windows. Normality of the continuous variables was tested with Shapiro-Wilk's test and non-normality distributed data was represented as median [interquartile range (IQR)]. While, the categorical variables were represented as frequencies (percentages). For the purpose of analysis, the patients were distributed into two groups: younger adults (< 65 years) and older adults ( $\geq$ 65 years). Comparison between continuous and categorical variables was done with Mann-Whitney U and Chi-square test, respectively. A two-tailed p-value < 0.05 was considered as statistically significant.

# Results

Over 27 months, a total of 199 patients received OPAT services. The study population was predominantly male (60.8%), with the median age of 74 [IQR; 62, 84] years. Patients were most commonly referred from in-patient wards (63.3%), and received hospital OPAT (50.8%), through PICC lines (51.8%). DM (35.2%) was the most common co-morbidity. Among various indications requiring IV antimicrobial therapy, the most commonly observed were BJI (38.7%), pulmonary infection (12.1%), infected prosthesis (12.1%) and skin and soft tissue infection (10.1%), in the decreasing order. Microbiological and radiological examinations were performed in 94.5% and 50.8% patients, respectively. Among those in which microbiological examination was performed, 75.5% patients had it prior to initiation of antimicrobials. While, 18.6% and 4.3% patients underwent microbiological examination both prior to and after the initiation of antimicrobials (Table 1).

| Characteristics                       | N (199)     | %    |
|---------------------------------------|-------------|------|
| Age, year (median [IQR])              | 74 [62, 84] | -    |
| Male                                  | 121         | 60.8 |
| Comorbidities                         |             |      |
| Diabetes mellitus                     | 70          | 35.2 |
| Rheumatoid arthritis                  | 9           | 4.5  |
| Immuno-compromised host               | 62          | 31.2 |
| Catheter type                         |             |      |
| Peripheral catheter                   | 96          | 48.2 |
| PICC lines                            | 103         | 51.8 |
| Referred from                         |             |      |
| Inpatient wards                       | 126         | 63.3 |
| Outpatient clinics                    | 73          | 36.7 |
| Model of antimicrobial administration |             |      |
| Hospital OPAT                         | 101         | 50.8 |
| Home OPAT                             | 98          | 49.2 |
| Indications for OPAT                  |             |      |
| Osteomyelitis                         | 49          | 24.6 |
| Bones and joints infection            | 28          | 14.1 |
| Pulmonary infection                   | 24          | 12.1 |
| Infected prosthesis                   | 24          | 12.1 |

**Table 1:** Characteristics of patients receiving OPAT.

| Skin and soft tissue infection                         | 20      | 10.1 |
|--|---------|------|
| Sepsis   | 19      | 9.5  |
| Renal and urinary infections                           | 8       | 4.0  |
| Others   | 27      | 13.6 |
| Radiological examination performed                     | 101     | 50.8 |
| Microbiological examination                            | 188     | 94.5 |
| Timing of microbiological examination                  |         |      |
| Prior to initiation of antimicrobials                  | 142/188 | 75.5 |
| Within 2 weeks of antimicrobials initiation            | 35/188  | 18.6 |
| 2 weeks after antimicrobials initiation                | 8/188   | 4.3  |
| Both prior and 2 weeks after antimicrobials initiation | 3/188   | 1.6  |

IQR: Interquartile range; PICC lines: Peripherally inserted central catheters; OPAT: outpatient parenteral antimicrobial therapy.

Among patients who underwent microbiological examination, 30.9% had no growth of microorganisms. Those with growth of microorganisms, *Staphylococcus aureus* (20.2%) was most commonly isolated. Majority of the patients received single antimicrobial (73.9%) and flucloxacillin (24.6%), teicoplanin (16.1%) and piperacillin-tazobactam (9.5%) were the most common single antimicrobial agents to be used. Of all the antimicrobials administered, any flucloxacillin combination (33.7%) followed by any teicoplanin combination (24.6%) were most common. Though 94.5% patients underwent microbiological examination, only 16.5% antimicrobials were changed after receiving the culture reports. The planned and actual duration for which the antimicrobials were administered ranged from 3 to 90 days and from 3 to 187 days, respectively. Moreover, 67.8% patients received antimicrobials for more than the planned duration. While, those who received antimicrobials as per and less than the planned duration were 17.1% and 15.1%, respectively. Five patients (2.51%) received antimicrobials for 100 days or more, with 1 patient (0.5%) received antimicrobials for 187 days. A small proportion of patients required re-treatment (15.07%). Around 14% patients developed AEs, of which those involving gastrointestinal system (46.4%) were most frequent (Table 2).

Of 28 patients with AEs, 25 were antimicrobials-related, while remaining 3 were catheter-associated. Among patients with AEs to antimicrobials, 6 had diarrhoea, 3 had vomiting, 2 each had nausea and lethargy, and 1 each had acute kidney injury, anaemia, neutropenia, hyperkalemia, chest pain, raised alkaline phosphatase levels, insomnia, relapse of infection, septic infection, sepsis secondary to chest drains, septic emboli and death. Catheter-associated AEs were line blockage, swelling of skin adjacent to catheter, and thrombophlebitis, in 1 patient each. Finally, 2 patients died after 30 days of completing OPAT, while after 1 years, this number rose to 18. These deaths were related to relapse of pulmonary infection in 8 patients, malignancy in 5 patients, and sepsis in remaining 5 patients (Table 2).

| Table 2:  | Microbiological   | findings. | antimicrobials used  | . and com | plications of | of OPAT. |
|-----------|-------------------|-----------|----------------------|-----------|---------------|----------|
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| Characteristics  | N (199)     | %    |
|--|-------------|------|
| Microorganisms identified                                |             |      |
| No growth  | 58/188      | 30.9 |
| Staphylococcus aureus                                    | 38/188      | 20.2 |
| E. coli  | 18/188      | 9.6  |
| Staphylococcal spp.                                      | 6/188       | 3.2  |
| Streptococcal spp.                                       | 16/188      | 8.5  |
| Pseudomonas spp.   | 12/188      | 6.4  |
| Others   | 40/188      | 21.3 |
| Antimicrobials used                                      |             |      |
| Any Flucloxacillin combination                           | 67          | 33.7 |
| Any Teicoplanin combination                              | 49          | 24.6 |
| Any Amoxicillin combination                              | 18          | 9.1  |
| Any Ertapenem combination                                | 10          | 5.0  |
| Any Ceftriaxone combination                              | 9           | 4.5  |
| Piperacillin/tazobactam                                  | 19          | 9.5  |
| Others   | 27          | 13.6 |
| Antimicrobials changed after microbiological examination | 31/188      | 16.5 |
| Duration of antimicrobials prescribed                    |             |      |
| Planned (median [IQR])                                   | 42 [14, 42] | -    |
| Actual (median [IQR])                                    | 37 [15, 51] | -    |

| Duration of OPAT                   |     |      |
|------------------------------------|-----|------|
| More than planned                  | 135 | 67.8 |
| As planned                         | 34  | 17.1 |
| Less than planned                  | 30  | 15.1 |
| Complications                      | 28  | 14.1 |
| Gastrointestinal                   | 13  | 46.4 |
| Haematological                     | 4   | 14.3 |
| Others                             | 11  | 39.3 |
| Mortality after completion of OPAT |     |      |
| At 30 days                         | 2   | 1.0  |
| At 1 year                          | 18  | 9.0  |
|                                    |     |      |

*IQR: Interquartile range; OPAT: outpatient parenteral antimicrobial therapy.* 

Comparison of various characteristic between younger and older adults revealed statistically significant difference in age (p-value < 0.0001). However, there was no significant difference between them in other characteristics i.e. gender, comorbidities, catheter type, referral status, model of antimicrobial administration, indications of antimicrobial and radiological and microbiological investigations (all p-values > 0.05) (Table 3).

Table 3: Comparison of characteristics of patients receiving OPAT.

| Characteristics                         | Younger adults | ounger adults Older adults |                 |
|---|----------------|----------------------------|-----------------|
|   | (<65 yrs) N=54 | (≥65 yrs) N=145            |                 |
| Age, year (median [IQR])                | 55 [50, 60]    | 80 [72, 85]                | $< 0.0001^{\$}$ |
| Male                                    | 33 (61.1)      | 88 (60.7)                  | 0.957*          |
| Comorbidities                           |                |                            |                 |
| Diabetes mellitus                       | 22 (40.7)      | 48 (33.1)                  | 0.316*          |
| Rheumatoid arthritis                    | 4 (7.4)        | 5 (3.4)                    | 0.232*          |
| Immuno-compromised host                 | 12 (22.2)      | 50 (34.5)                  | 0.097*          |
| Catheter type                           |                |                            |                 |
| Peripheral catheter                     | 26 (48.1)      | 70 (48.3)                  | 0.987*          |
| PICC lines                              | 28 (51.9)      | 75 (51.7)                  |                 |
| Referred from                           |                |                            |                 |
| Inpatient wards                         | 36 (66.7)      | 90 (62.1)                  | 0.550*          |
| Outpatient clinics                      | 18 (33.3)      | 55 (37.9)                  |                 |
| Model of antimicrobial administration   |                |                            |                 |
| Hospital OPAT                           | 29 (53.7)      | 72 (49.7)                  | 0.611*          |
| Home OPAT                               | 25 (46.3)      | 73 (50.3)                  |                 |
| Indications for OPAT                    |                |                            |                 |
| Osteomyelitis                           | 14 (25.9)      | 35 (24.1)                  | 0.795*          |
| Bones and joints infection              | 7 (12.9)       | 21 (14.5)                  | 0.784*          |
| Pulmonary infection                     | 5 (9.3)        | 19 (13.1)                  | 0.259*          |
| Skin and soft tissue infection          | 4 (7.4)        | 16 (11.0)                  |                 |
| Infected prosthesis                     | 7 (12.9)       | 17 (11.7)                  | 0.811*          |
| Sepsis                                  | 4 (7.4)        | 15 (10.3)                  | 0.879*          |
| Renal and urinary infections            | 3 (5.6)        | 5 (3.4)                    |                 |
| Others                                  | 10 (18.5)      | 17 (11.7)                  | 0.213*          |
| Radiological examination performed      | 31 (57.4)      | 70 (48.3)                  | 0.252*          |
| Microbiological examination             | 51 (94.4)      | 137 (94.5)                 | 0.992*          |
| Timing of microbiological examination   |                |                            |                 |
| Prior to initiation of OPAT             | 41 (80.4)      | 101 (73.7)                 | 0.140*          |
| Within 2 weeks of OPAT initiation       | 9 (17.6)       | 26 (18.9)                  | 0.344*          |
| 2 weeks after antimicrobials initiation | 1 (1.9)        | 7 (5.1)                    |                 |
| Both prior and 2 weeks after OPAT       | 0 (0)          | 3 (2.2)                    |                 |
| initiation                              |                |                            |                 |

*IQR:* Interquartile range; PICC lines: Peripherally inserted central catheters; OPAT: outpatient parenteral antimicrobial therapy; \*: Chi-square test; \$: Mann-Whitney U; p-value < 0.05 was considered as statistically significant.

Comparison of microbiological findings, antimicrobials used and OPAT AEs revealed significantly greater number of older adults with infection due to *Staphylococcus aureus* (p-value < 0.0001), and *E. coli*,

*Staphylococcal* spp., *Streptococcal* spp. and *Pseudomonas* spp. (p-value = 0.003). However, there was no significant difference between younger and older adults in terms of other isolated microorganisms, antimicrobials used, duration of antimicrobials prescribed and OPAT AEs (all p-values > 0.05). Though greater number of older adults had mortality both after 30 days and 1 year, this did not reach statistically significant level (p-value = 0.069) (Table 4).

| Characteristics                       | Younger adults Older adults |                 | p-value   |
|---------------------------------------|-----------------------------|-----------------|-----------|
|                                       | (<65 yrs) N=54              | (≥65 yrs) N=145 |           |
| Microorganisms identified             |                             |                 |           |
| No growth                             | 14 (27.5)                   | 44 (32.1)       | 0.538*    |
| Staphylococcus aureus                 | 20 (39.2)                   | 18 (13.1)       | < 0.0001* |
| E. coli                               | 1 (1.9)                     | 17 (12.4)       | 0.003*    |
| Staphylococcal spp.                   | 1 (1.9)                     | 5 (3.6)         |           |
| Streptococcal spp.                    | 3 (5.9)                     | 13 (9.5)        | _         |
| Pseudomonas spp.                      | 1 (1.9)                     | 11 (8.0)        |           |
| Others                                | 11 (21.6)                   | 29 (21.2)       | 0.952*    |
| Antimicrobials used                   |                             |                 |           |
| Any Flucloxacillin combination        | 23 (42.6)                   | 44 (30.3)       | 0.104*    |
| Any Teicoplanin combination           | 10 (18.5)                   | 39 (26.9)       | 0.223*    |
| Any Amoxicillin combination           | 4 (7.4)                     | 14 (9.7)        | 0.987*    |
| Any Ertapenem combination             | 3 (5.6)                     | 7 (4.8)         |           |
| Any Ceftriaxone combination           | 3 (5.6)                     | 6 (4.1)         |           |
| Piperacillin/tazobactam               | 5 (9.3)                     | 14 (9.7)        | 0.933*    |
| Others                                | 6 (11.1)                    | 21 (14.5)       | 0.537*    |
| Antimicrobials changed after          | 7 (12.9)                    | 24 (16.6)       | 0.535*    |
| microbiological examination           |                             |                 |           |
| Duration of antimicrobials prescribed |                             |                 |           |
| Planned (median [IQR])                | 42 [14, 42]                 | 42 [14, 42]     | 0.771\$   |
| Actual (median [IQR])                 | 41 [15, 51]                 | 36 [14, 51]     | 0.569\$   |
| Antimicrobials for duration more than | 29 (53.7)                   | 77 (53.1)       | 0.940*    |
| planned                               |                             |                 |           |
| Complications                         |                             |                 |           |
| Gastrointestinal                      | 5 (9.3)                     | 8 (5.5)         | 0.342*    |
| Haematological                        | 1 (1.9)                     | 3 (2.1)         | 0.575*    |
| Others                                | 4 (7.4)                     | 7 (4.8)         |           |
| Mortality after completion of OPAT    |                             |                 |           |
| At 30 days                            | 0 (0)                       | 2 (1.4)         | 0.069*    |
| At 1 year                             | 2 (3.7)                     | 16 (11.0)       |           |

**Table 4:** Comparison of microbiological findings, antimicrobials used and complications of OPAT.

*IQR:* Interquartile range; OPAT: outpatient parenteral antimicrobial therapy; \*: Chi-square test; \$: Mann-Whitney U; p-value < 0.05 was considered as statistically significant.

The median actual OPAT duration was significantly greater than the median planned OPAT duration for total study population (p-value < 0.0001), younger adults (p-value = 0.031) and older adults (p-value = 0.002) (Fig. 1).



**Figure 1:** Association between planned and actual duration of OPAT in total study population, younger adults, and older adults. \*\*\* - statistically significant difference between the planned and actual duration of OPAT services (p-value < 0.05).

Analysis of association between death and various characteristics revealed no statistically significant association between death and gender, comorbidities (DM, rheumatoid arthritis, immunosuppression), microbiological examination prior to antimicrobials, administration of antimicrobials further than planned, AEs, PICC lines, referral from inpatient wards and hospital OPAT (all p-values > 0.05) (Table 5).

**Table 5:** Association between death and various characteristics.

| Characteristics                                   | De         | *p-         |       |
|---|------------|-------------|-------|
|   | Yes (N=18) | No (N=181)  | value |
| Male gender (N=121)                               | 11 (61.1%) | 110 (60.8%) | 0.978 |
| Diabetes mellitus (N=70)                          | 10 (55.6%) | 60 (33.1%)  | 0.058 |
| Rheumatoid arthritis (N=9)                        | 1 (5.6%)   | 8 (4.4%)    | 0.825 |
| Immunosuppression (N=62)                          | 9 (50%)    | 53 (29.3%)  | 0.070 |
| Microbiological examination prior to OPAT (N=142) | 12 (66.7%) | 130 (71.8%) | 0.266 |
| Antimicrobials further than planned (N=106)       | 8 (44.4%)  | 98 (54.1%)  | 0.432 |
| Adverse events (N=28)                             | 0 (0%)     | 28 (15.5%)  | NA    |
| PICC Lines (N=103)                                | 7 (38.9%)  | 96 (53%)    | 0.252 |
| <b>Referral from in-patient wards (N=126)</b>     | 9 (50%)    | 117 (64.6%) | 0.219 |
| Hospital OPAT (N=101)                             | 8 (44.4%)  | 93 (51.4%)  | 0.575 |

*PICC lines: Peripherally inserted central catheters; OPAT: outpatient parenteral antimicrobial therapy;* \* - *Chi-square test; p-value < 0.05 was considered as statistically significant.* 

#### Discussion

Antimicrobials agents are among the most frequently used drugs. They are indispensable in treating severe and potentially fatal infections<sup>15</sup>. They should be used only for the indicated conditions, as their injudiciously use can lead to AEs including hypersensitivity reaction. Some antimicrobials (aminoglycosides) used in combinations with other antimicrobials (amphotericin) or other class of drugs produce toxic AEs. Their frequently use can lead to increasing bacterial resistance. Use of broad-spectrum antimicrobials result in disruption of normal body flora, thereby permitting colonisation by and multiplication of resistant and opportunistic microorganisms. The growth of these opportunistic pathogens leads to secondary infection<sup>16</sup>. Thus, microbiological examination should be performed before initiating the antimicrobial therapy and duration of therapy should be adjusted according to the results of microbiological examination.

The OPAT is a common practice in Canada and the UK. It is also practiced in various forms in some countries in South America, Europe, and the Asia Pacific<sup>1,17-20</sup>. In Australia, OPAT services began around 20 years ago and has been successfully implemented by several health care centres across Australia and New Zealand<sup>21-24</sup>. In Asia, there is a huge unrecognized problem of unchecked OPAT with 57% (97/171) healthcare facilities across 17 countries<sup>25</sup>.

OPAT services are multidisciplinary and include at least one physician, an infectious disease specialist, a specialist nurse, and a clinical antimicrobial pharmacist. Initially, these services operate in infectious disease departments and less often in specialized units<sup>12</sup>. In our hospital, OPAT services are provided by a multidisciplinary group compiled in accordance with national recommendations. In this study, we report on the results of OPAT services provided by our hospital in Surrey, England, between January 2019 and March 2021.

Over the course of 27 months, 199 patients were treated with OPAT. This resulted in savings of 7514 beddays, so it met the needs of both patients and healthcare. The majority of these patients were referred from inpatient wards and this reflects the actual needs of inpatient centres. These results are consistent with those reported in other studies<sup>26,27</sup>. Therefore, the practice of extended OPAT services may lead to a reduction in hospital stays, which may be particularly beneficial for hospitals with high bed occupancy. In addition, it has been reported that these services result in high patient satisfaction, leading to a higher admission rate<sup>28,29</sup>.

BJI and infected prosthesis combined were the dominant indications that required antimicrobial therapy. Other studies have reported a high prevalence of these infections<sup>27,30</sup>. BJI and SSTI lead to a significant number of hospital admissions with longer hospital stays<sup>31</sup>. Although they do not occur frequently, prosthetic joint infections (PJI) have serious consequences and a 2-3 times higher risk of revision surgery. With a growing population of older people, the proportion of joint prosthesis is expected to increase exponentially and this is likely to lead to an increase in frequency of PJI<sup>32</sup>. Thus, the number of patients requiring OPAT services is expected to increase. This is supported by the findings of our study, where adults aged 65 and over were the dominant population.

Our OPAT team treated patients who were predominantly infected with *Staph. aureus* and *E. coli*. Among the other isolated microorganisms, one patient each had infection with *Clostridium difficle* and methicillin resistant *Staph. aureus*. The infection prone factors in the patient population were advanced age, the majority of patients were aged 65 or over as well as immunosuppression due to co-morbidities such as DM, steroid use, and malignant cancers. Antimicrobial resistance is a growing health problem in the UK, as in the whole world<sup>33,34</sup>. This leads to a further increase in demand for parenteral antimicrobials. Available OPAT services are increasingly needed to address difficult-to-treat infections and new scenarios arising from resistant Gram-negative bacterial infection.

We observed that flucloxacillin, teicoplanin and their combinations with other antimicrobials were most often used. Similar results have been reported by other studies<sup>35,36</sup>. Although hospital OPAT was the dominant model, we observed greater acceptance of home OPAT model in the last 1 year of services. However, none of the patients felt comfortable with the self-treating OPAT model. This was basically due to the relatively new OPAT set-up in our hospital, and as a confidence-building measure, the OPAT group actively supported the home model instead of the self-rationing model, which requires training and supervision.

In the case of infections with rapid clinical improvement, traditional long-acting IV antimicrobials are not necessarily necessary and an early transition from IV to oral treatment is possible. Longer durations of antimicrobials are associated with a higher risk of resistance<sup>37</sup>. Paradoxically, if they do not

receive AMS, OPAT services may result in excessively long durations of antimicrobial therapy, as observed in our study<sup>38,39</sup>. It has also been reported that patients treated partially or entirely at home receive longer therapy than those treated entirely in hospital<sup>38</sup>.

We observed that patients - both younger and older adults - were receiving antimicrobials for significantly longer than planned. Further observations showed that only three quarter of patients had a microbiological test before antimicrobials were administered. It is worth noting that only a fraction of patients had their antimicrobials changed after receiving the culture report. Although multidisciplinary team meetings were held weekly after the initiation of OPAT inpatient care to reviews patients' symptoms and treatment, retrospective analysis and internal discussion showed that only 29% patients were treated according to the recommended duration, appropriate testing and antibiotic selection. These findings were primarily attributed to temporary staffing and lack of adequate communication pathways between documentation and the OPAT multidisciplinary team. Other factor may include the outsourcing of OPAT services before October 2020 and the lack of monitoring of services. Thus, the quality of OPAT services could not be monitored. This may result in a lack of microbiological testing before and after the initiation antimicrobial therapy and a prolonged duration of OPAT. In addition, the contribution of the 2019 coronavirus outbreak to the functioning of OPAT team and attitudes of patients on prolonged antimicrobial therapy.

Few studies have compared the OPAT characteristics and results in younger and older adults. We did not notice any significant differences between them, except for the significantly greater median age and infection with Staph. aureus, E. coli, Staphylococcal spp., Streptococcal spp. and Pseudomonas spp. in older adults. Other studies reported similar results<sup>30,40</sup>. One study showed no difference between the younger and older patients in terms of AEs or access to health care within 30 days of OPAT cessation<sup>30</sup>. Another study reported that the rates and rehospitalization in of antibiotic treatment younger and older patients were the same due to poor control of underlying infection, however, older adults had a higher rate of re-hospitalization resulting from the exacerbation of the underlying diseases. In addition, AEs and catheter-related complications were identical across the age groups $^{40}$ .

Finally, no statistically significant association was found between mortality and the different parameters studied. Similar to our study, one study reported no significant association between mortality and various factors including age groups, gender, type of infection, OPAT model, type of catheter and microbiological test used to guide treatment. Mortality, however, was significantly associated with palliative care and post-enrolment physician visit<sup>41</sup>. Another study examined factors associated with increased mortality in nonagenarians receiving OPAT services and found a statistically significant association between mortality and age, as well as *Clostridioides difficile* infection, higher WBC count and lower platelet count at hospital admission<sup>42</sup>. These parameters were not part of our study, so we could not assess the association between these parameters and mortality.

Our study had many limitations. First, this was a retrospective study involving a review of electronic healthcare records, so it was not possible to randomize patients by age group. Second, we could not find accurate records of sensitivity reports, source data for various microbiological samples and decisions leading to extended OPAT. Third, no data were available on other comorbidities that might have influenced mortality or AEs. Similarly, the lack of data on immunomodulatory drugs meant that no drug-drug interactions leading to failure of antimicrobial therapy could be identified. Fourth, the retrospective nature of the study meant that we were unable to assess patient satisfaction and the lack of data on treatment costs did not allow us to perform cost analysis. Fifth, this was a single-centre audit and therefore the results cannot be generalised. Finally, no microorganisms were isolated from 30.9% patient samples. Thus, there is a high probability that infection was not the cause of the patients' presentation.

### **Recommendations**

The results of this study suggest that much more needs to be done to achieve the recommended level of OPAT functioning. Based on these findings, we make the following recommendations: First, the antibiotic registry should be easily accessible and available in the form of a single digital registry that includes antimicrobials prescribed in both inpatient and outpatient settings. These records should include patient details including diagnosis, comorbidities, specialties treating the patient, name of prescriber and administrator, antimicrobials prescribed with their rationale, dose, route, frequency and AEs, microbiological tests and their results, planned duration of treatment and actual duration of treatment (start and end dates). Second, active surveillance should be

carried out at regular intervals including microbiological, haematological and radiological examinations, notification of the examination results to the referring or responsible physician and the maintenance and followup of a digital record containing the physician's comments on the results of the examinations and the duration of any additional antimicrobial treatment required. Finally, an integrated outpatient system should be established. This system will alert all collaborating physicians when a patient arrives at the hospital, either in the emergency department or in the outpatient department, especially if the patient is receiving IV antimicrobials. Cooperation between physicians responsible for administering antimicrobials and physicians monitoring the patient for other conditions, the OPAT team and general practitioners should be enhanced.

## Conclusion

It can be concluded that OPAT services are needed, in addition to the gradually increasing acceptance of the home model. This study suggests that the actual duration of OPAT services was significantly longer than planned and that the AMS principles were less adhered to. In terms of different parameters, there was no significant difference between younger and older adults, except higher incidence of *Staph. aureus, E. coli, Staphylococcus spp., Streptococcus spp.* and *Pseudomonas spp.* infection in older adults. OPAT was found to be safe for both younger and older adults, with no significant association between mortality and different patient characteristics.

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# References

- 1. Rucker RW, Harrison GM. Outpatient intravenous medications in the management of cystic fibrosis. Paediatrics 1974;54:358-360.
- Esposito S, Noviello S, Leone S, Tice A, Seibold G, Nathwani D, Scaglione F; International OPAT Registry. Outpatient parenteral antibiotic therapy (OPAT) in different countries: a comparison. Int J Antimicrob Agents. 2004;24(5):473-478.
- Ravelingien T, Buyle F, Deryckere S, Sermijn E, Debrauwere M, Verplancke K, et al. Optimization of a model of out-of-hospital antibiotic therapy (OPAT) in a Belgian university hospital resulting in a proposal for national implementation. *Acta Clin Belg.* 2016;71(5):297-302.
- 4. Chapman ALN. Outpatient parenteral antimicrobial therapy. BMJ 2013;346:f1585.
- 5. Steffens E, Quintens C, Derdelinckx I, Peetermans WE, Van Eldere J, Spriet I, et al. Outpatient parenteral antimicrobial therapy and antibiotic stewardship: opponents or teammates? *Infection*. 2019;47(2):169-181.
- Kieran J, O'Reilly A, Parker J, et al. Self-administered outpatient parenteral antimicrobial therapy: a report of three years experience in the Irish healthcare setting. *Eur J Clin Microbiol Infect Dis.* 2009;28:1369–1374.
- Wai AO, Frighetto L, Marra CA, et al. Cost analysis of an adult outpatient parenteral antibiotic therapy (OPAT) programme. A Canadian teaching hospital and ministry of health perspective. *Pharmacoeconomics*. 2000;18:451–457.
- 8. Tice AD, Rehm SJ, Dalovisio JR, et al. Practice guidelines for outpatient parenteral antimicrobial therapy. IDSA guidelines. *Clin Infect Dis.* 2004;38:1651–1672.
- 9. Laupland KB, Gill MJ, Schenk L, et al. Outpatient parenteral antibiotic therapy: evolution of the Calgary adult home parenteral therapy program. *Clin Invest Med*. 2002;25:185–190.
- 10. Seaton RA, Sharp E, Bezlyak V, et al. Factors associated with outcome and duration of therapy in outpatient parenteral antibiotic therapy (OPAT) patients with skin and soft-tissue infections. *Int J Antimicrob Agents*. 2011;38:243–248.
- 11. Chapman AL, Seaton RA, Cooper MA, Hedderwick S, Goodall V, Reed C, et al.; BSAC/BIA OPAT Project Good Practice Recommendations Working Group. Good practice recommendations for outpatient parenteral antimicrobial therapy (OPAT) in adults in the UK: a consensus statement. *J Antimicrob Chemother*. 2012;67(5):1053-62.
- 12. Chapman ALN, Patel S, Horner C, Green H, Guleri A, Hedderwick S, et al. Updated good practice recommendations for outpatient parenteral antimicrobial therapy (OPAT) in adults and children in the UK. *JAC-Antimicrobial Resistance*. 2019;1(2):dlz026.
- 13. Durojaiye OC, Cartwright K, Ntziora F. Outpatient parenteral antimicrobial therapy (OPAT) in the UK: a cross-sectional survey of acute hospital trusts and health boards. *Diagn Microbiol Infect Dis.* 2019;93(1):58-62.

- 14. Ashiru-Oredope D, Sharland M, Charani E, et al. Improving the quality of antibiotic prescribing in the NHS by developing a new Antimicrobial Stewardship Programme: Start Smart–Then Focus. J Antimicrob Chemother 2012;67 Suppl 1:i51–63.
- Mohsen S, Dickinson JA, Somayaji R. Update on the adverse effects of antimicrobial therapies in community practice. Can Fam Physician. 2020;66(9):651-659.
- 16. Weledji EP, Weledji EK, Assob JC, Nsagha DS. Pros, cons and future of antibiotics. New Horiz Transl Med. 2017;4:9-14.
- 17. Upton A, Ellis-Pegler RB, Woodhouse A. Outpatient parenteral antimicrobial therapy (OPAT): a review of experience at Auckland Hospital. N Z Med J. 2004;117:U1020.
- Grayson ML, Silvers J, Turnidge J. Home intravenous antibiotic therapy: a safe and effective alternative to inpatient care. *Med J Aust*. 1995;162:249-53.
- 19. Fisher D, Kurup A, Lye D et al. Outpatient parenteral antibiotic therapy in Singapore. Int J Antimicrob Agents. 2006;28:545-50.
- Nathwani D, Zambrowski JJ. Advisory group on Home-based and Outpatient Care (AdHOC): an international consensus statement on noninpatient parenteral therapy. *Clin Microbiol Infect*. 2000;6:464-76.
- 21. Tran A, Taylor DM. Medical model for hospital in the home: effects on patient management. Aust Health Rev. 2009;33:494-501.
- Subedi S, Looke DFM, McDougall DA et al. Supervised self-administration of outpatient parenteral antibiotic therapy: a report from a large tertiary hospital in Australia. Int J Infect Dis. 2015;30:161-5.
- White H, Davis JS, Kittler P et al. Outpatient parenteral antimicrobial therapy-treated bone and joint infections in a tropical setting. *Intern* Med J. 2011;41:668-73.
- 24. Ingram PR, Cerbe L, Hassell M et al. Limited role for outpatient parenteral antibiotic therapy for community-acquired pneumonia. *Respirology*. 2008;13:893.
- 25. Fisher D, Michaels J, Hase R, Zhang J, Kataria S, Sim B, et al. Outpatient parenteral antibiotic therapy (OPAT) in Asia: missing an opportunity. *J Antimicrob Chemother*. 2017;72:1221-1226.
- Allison GM, Muldoon EG, Kent DM, et al. Prediction model for 30-day hospital readmissions among patients discharged receiving outpatient parenteral antibiotic therapy. *Clin Infect Dis.* 2014;58(6):812-819.
- 27. Hase R, Yokoyama Y, Suzuki H, Uno S, Mikawa T, Suzuki D, Muranaka K, Hosokawa N. Review of the first comprehensive outpatient parenteral antimicrobial therapy program in a tertiary care hospital in Japan. *Int J Infect Dis.* 2020;95:210-215.
- Durojaiye OC, Kritsotakis EI, Johnston P, Kenny T, Ntziora F, Cartwright K. Developing a risk prediction model for 30-day unplanned hospitalization in patients receiving outpatient parenteral antimicrobial therapy. *Clin Microbiol Infect*. 2019;25(7):905.e1-905.e7.
- 29. Saillen L, Arensdorff L, Moulin E, Voumard R, Cochet C, Boillat-Blanco N, Gardiol C, de Vallière S. Patient satisfaction in an outpatient parenteral antimicrobial therapy (OPAT) unit practising predominantly self-administration of antibiotics with elastomeric pumps. *Eur J Clin Microbiol Infect Dis.* 2017;36(8):1387-1392.
- 30. Brzozowski K, Datta R, Canterino J, Malinis M, Juthani-Mehta M. Adverse Events and Healthcare Utilization Associated With Outpatient Parenteral Antimicrobial Therapy Among Older Versus Younger Adults. *Open Forum Infect Dis.* 2020 Aug 26;7(10):ofaa358.
- Howell A, Parker S, Tsitskaris K, Oddy MJ. The burden of bone, native joint and soft tissue infections on orthopaedic emergency referrals in a city hospital. Ann R Coll Surg Engl 2016;98:34-39.
- 32. Ahmed SS, Haddad FS. Prosthetic joint infection. Bone Joint Res 2019;8:570-572.
- 33. Naylor NR, Pouwels KB, Hope R, Green N, Henderson KL, Knight GM, et al. The health and cost burden of antibiotic resistant and susceptible Escherichia coli bacteraemia in the English hospital setting: A national retrospective cohort study. PLoS ONE 2019;14(9):e0221944.
- 34. Hu XY, Logue M, Robinson N. Antimicrobial resistance is a global problem a UK perspective. Eur J Integr Med. 2020;36:101136.
- 35. Pensotti C, Nacinovich F, Vidiella G, Carbone E, Marin M, Di Stéfano C, Stamboulian D. Teicoplanin in the treatment of bone and joint infections due to methicillin resistant staphylococci. Experience in adult patients. *Medicina (B Aires)*. 2002;62 Suppl 2:40-7.
- 36. Mackintosh CL, White HA, Seaton RA. Outpatient parenteral antibiotic therapy (OPAT) for bone and joint infections: experience from a UK teaching hospital-based service. J Antimicrob Chemother. 2011 Feb;66(2):408-15.
- McMullan BJ, Andresen D, Blyth CC, Avent ML, Bowen AC, Britton PN, et al.; ANZPID-ASAP group. Antibiotic duration and timing of the switch from intravenous to oral route for bacterial infections in children: systematic review and guidelines. *Lancet Infect Dis.* 2016 Aug;16(8):e139-52.

- 38. Bryant PA, Katz NT. Inpatient versus outpatient parenteral antibiotic therapy at home for acute infections in children: a systematic review. Lancet Infect Dis. 2018;18(2):e45-e54.
- Mace AO, McLeod C, Yeoh DK et al. Dedicated paediatric outpatient parenteral antimicrobial therapy medical support: a pre-post observational study. Arch Dis Child 2018;103:165–9.
- 40. Mujal A, Sola J, Hernandez M, Villarino MA, Baylina M, Tajan J, Oristrell J. Safety and effectiveness of outpatient parenteral antimicrobial therapy in older people. *J Antimicrob Chemother*. 2016 May;71(5):1402-7.
- Salles TCG, Cerrato SG, Santana TF, Medeiros EA. Factors associated with successful completion of outpatient parenteral antibiotic therapy in an area with a high prevalence of multidrug-resistant bacteria: 30-day hospital admission and mortality rates. *PLoS ONE* 2020;15(11):e0241595.
- 42. Shrestha NK, Blaskewicz C, Gordon SM, Everett A, Rehm SJ. Safety of Outpatient Parenteral Antimicrobial Therapy in Nonagenarians. Open Forum Infect Dis. 2020;7(10):ofaa398.