Good practice recommendations for paediatric outpatient parenteral antibiotic therapy (p-OPAT) in the UK: a consensus statement

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There is compelling evidence to support the rationale for managing children on intravenous antimicrobial therapy at home whenever possible, including parent and patient satisfaction, psychological well-being, return to school/employment, reductions in healthcare-associated infection and cost savings. As a joint collaboration between the BSAC and the British Paediatric Allergy, Immunity and Infection Group, we have developed good practice recommendations to highlight good clinical practice and governance within paediatric outpatient parenteral antibiotic therapy (p-OPAT) services across the UK. These guidelines provide a practical approach for safely delivering a p-OPAT service in both secondary care and tertiary care settings, in terms of the roles and responsibilities of members of the p-OPAT team, the structure required to deliver the service, identifying patients and pathologies that are suitable for p-OPAT, ensuring appropriate vascular access, antimicrobial choice and delivery and the clinical governance aspects of delivering a p-OPAT service. The process of writing a business case to support the introduction of a p-OPAT service is also addressed.

Keywords: children, ambulatory, stewardship

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1. Introduction

Although the origins of outpatient parenteral antibiotic therapy (OPAT) lie firmly within paediatrics, with Rucker and Harrison introducing the concept of home intravenous (iv) antibiotics for children with cystic fibrosis (CF) in 1974, recent advances in OPAT have focused on adult practice. Within the UK, the development of adult OPAT services has been driven by the BSAC.

Children are currently ambulated on iv antibiotics from paediatric units across the country. Formal good practice recommendations for paediatric OPAT (p-OPAT), including robust clinical governance frameworks and prospective outcome monitoring, would potentially enhance the patient experience, enable significant cost savings and, above all, improve patient safety while reducing adverse events. As a joint collaboration between BSAC and the British Paediatric Allergy, Immunity and Infection Group...
(BPAIIG) and through a process of national consultation (a list of the organizations involved is available as Supplementary data at JAC Online), we propose to formalize clinical practice and governance of p-OPAT through these good practice recommendations.

There is compelling evidence to support the rationale for managing children on iv antimicrobial therapy at home whenever possible, including parent and patient satisfaction, psychological well-being, return to school/employment, reductions in healthcare-associated infection and cost savings. In addition, formalizing such services could help overcome some of the challenges currently facing the UK NHS, such as significant efficiency savings, reconfiguration of acute paediatric services, and addressing the deficiencies highlighted in the Francis report.

In its most basic form, OPAT simply refers to the administration of iv antimicrobials for at least two consecutive days without an intervening hospitalization. Within paediatrics, this covers a wide spectrum of children, from those with common infections being treated with relatively short courses of antimicrobials in secondary care settings to those with complex infections being managed with long courses of antibiotics in tertiary paediatric centres (see Figure 1). In some cases, hospitalization may be entirely avoided and in others the length of admission may be shortened.

The following criteria must be met before a patient can be considered for p-OPAT:

(i) The patient has currently no further predictable need for hospital-based care apart from the administration of antimicrobial therapy.
(ii) The infection and any associated comorbidity should have a stable or predictable course suitable for non-inpatient management.
(iii) There is no equally safe and effective oral antimicrobial that can be given. This component should be overseen as part of a formal antibiotic stewardship programme.

Despite a wealth of experience in paediatrics, there remains considerable anxiety about ambulating children with infection. The successful introduction of a p-OPAT service requires appropriate personnel, clear channels of communication and robust clinical governance structures, to ensure that children managed at home receive the same quality of care that they would receive in hospital. Specific consideration of the patient’s suitability for p-OPAT, the most appropriate route of iv access and choice of antibiotic is required before the child is discharged home. This is best achieved using a multidisciplinary approach involving medical, nursing and pharmacist input.

This document has been divided into eight key areas to provide practical guidance about developing and running p-OPAT services both in secondary and tertiary care settings (see Table 1). These good practice guidelines will not specifically address children with CF. Variation in practice between different respiratory centres meant that the working group felt unable to comment on the optimal strategy for administering iv therapy to this particular cohort of children. However, the principles discussed in these recommendations may be broadly applied to paediatric CF practice.

2. Methods

A working group set up under the joint auspices of BSAC and BPAIIG was established, consisting of individuals with experience in delivering p-OPAT, ambulatory paediatric care, paediatric infectious diseases, adult OPAT, microbiology and pharmacy. The development of these recommendations forms part of the BSAC national OPAT initiative and complements the adult BSAC/BIA 2012 OPAT recommendations.

A comprehensive literature review was undertaken. The following electronic databases were searched (all 1970 to June 2012): MEDLINE, EMBASE, Web of Science (Science Citation Index Expanded) and Cochrane Library (including CENTRAL Register of Controlled Trials). The search terms used were as follows: ‘outpatient parenteral antibiotic therapy’, ‘outpatient parenteral antimicrobial therapy’, ‘home infusion therapy’ AND ‘anti-bacterial agents’, ‘home intravenous antibiotic, outpatient parenteral therapy’ AND ‘antibiotic’ OR ‘antimicrobial’ OR ‘antifungal’ OR ‘anti-infective’, ‘OPAT’, ‘OHPAT’ AND ‘P-OPAT’. Within the initial search results, a separate search for paediatric studies was done using the terms ‘child’ OR ‘pediatric’ OR ‘paediatric’ OR ‘infant’.

The initial search resulted in 1256 references, of which 273 related to children. These were screened on the basis of the abstract and those lacking relevance were excluded. Sixty-two relevant papers were divided into key areas (see Table 1) and the full-text articles were obtained. These articles were reviewed by members of the working group and the information relevant to guide good practice recommendations extracted. Papers that covered more than one area were cross-referenced.

<table>
<thead>
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<th>Table 1. Key areas reflecting the different components of a p-OPAT service</th>
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<td>p-OPAT team—roles and responsibilities</td>
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Children with complex infections requiring long courses of antibiotics in tertiary centres (small numbers) – e.g. the child with endocarditis

Children with common infections requiring relatively short courses of antibiotics discharged from general paediatric wards (moderate numbers) – e.g. the stable child with pyelonephritis

Children with possible bacterial infection ambulated directly from short-stay units or paediatric emergency departments – e.g. the febrile but stable child with a petechial rash (large numbers)

Figure 1. Spectrum of patients to whom p-OPAT services can be delivered.
Members of the working group then met to review and combine the recommendations into a working draft. This draft underwent a consultation process involving relevant stakeholders and the draft was revised and amended in response to this. A list of the stakeholders involved in the consultation process is available in the Supplementary data.

3. p-OPAT team: roles and responsibilities

The key personnel within a p-OPAT service vary according to local resources. The majority of p-OPAT patients will be managed within a secondary care setting, where access to a paediatric infectious diseases specialist is not necessary.

In a secondary care setting, the medical role should be undertaken by a general paediatrician or paediatric accident and emergency (A+E) consultant (named ‘p-OPAT consultant’), with input from a clinical microbiologist where appropriate and community- or hospital-based nursing input. The team should have access to pharmacy support and ideally an iv preparation unit.

In a tertiary centre, the management of complex infections should be overseen by a paediatric infectious diseases consultant who should also take clinical responsibility for patient management and clinical governance of the p-OPAT service. The nursing role is vital in patient selection, logistical support and patient/carer education and clinical pharmacy support is vital to ensure the equivalent pharmaceutical care as would be expected for inpatients with infection and also to support the antimicrobial stewardship process. Ideally, a specialist iv preparation unit would be an integral part of the p-OPAT service.

A general framework for delivery of ambulatory and tertiary p-OPAT services can be based on current services within the UK (Figures 2 and 3). The roles and responsibilities of the various members of the p-OPAT team are outlined in Table 2. There may be scope to share resources with a colocated adult OPAT service.

4. Service structure

Various service models for p-OPAT are described below and their relative advantages and disadvantages are outlined in Table 3.19 They may be used independently or in combination within a single p-OPAT service.

4.1 Home administration by a carer or parent

Following training by a competent member of the p-OPAT team, iv antimicrobials are administered by the carer or patient at home.5,20 This model has been widely used in the USA. Specific patient groups who require regular courses of iv antibiotics and whose families/carers are trained in central line care/access may be managed using this model.

4.2 Home administration by a trained paediatric nurse

Antimicrobials are administered at home by an appropriately trained NHS nurse (hospital- or community-based nurse) or private healthcare provider with the relevant competencies.

4.3 Infusion centre administration

Children receive their antimicrobials at an infusion centre each day. The venue may be a paediatric emergency department, paediatric assessment unit, acute paediatric ward or within an outpatient department. Antimicrobials are administered by a hospital-based nurse with the relevant competencies.

5. Patient suitability for p-OPAT

Assessing the eligibility of a patient for p-OPAT should be formally conducted by both the p-OPAT clinician and p-OPAT nurse in terms of clinical, social and caregiver criteria (see Table 4). Failure to meet these criteria poses an increased risk of an adverse outcome.

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**Figure 2.** Tertiary hospital p-OPAT service structure. CIVAS, centralized intravenous additive service.
at home and extremely careful consideration should be taken before accepting the patient for p-OPAT.\textsuperscript{21}

Decision making about the need to continue iv antibiotics should be based on antibiotic stewardship principles.\textsuperscript{14}

6. Pathologies suitable for p-OPAT management including special considerations

Table 5 outlines the various pathologies that can be considered for p-OPAT management. Not only does p-OPAT offer the potential for early discharge from hospital, but in some cases will allow admission to be avoided.

Special considerations are listed below.

6.1 Febrile infants aged 1–3 months

In the post-conjugate vaccine era, the rate of serious bacterial infection in febrile infants aged 1–3 months in developed countries is reported as being <3\%.\textsuperscript{22} Factors supporting the ambulation of these infants on once-daily ceftriaxone include a normal CSF white cell count, haemodynamic stability, adequate feeding, cooperative parent and no other reason for admission to hospital.\textsuperscript{23}

6.2 Children being discharged directly from the paediatric emergency department/paediatric assessment unit (admission avoidance)

A number of clinical scenarios are suitable for p-OPAT direct from the emergency department or short-stay unit, provided the child is clinically stable, the carers are supportive of the decision and there is 24 h access back to the service for reassessment in the event of an unexpected change in the predicted clinical course. Suitable pathologies include pyelonephritis where the indications for iv antibiotic therapy are met,\textsuperscript{24–26} cellulitis,\textsuperscript{27,28} pre-septal cellulitis,\textsuperscript{29,30} acute lymphadenitis, the well child with petechiae and infants between 1 and 3 months of age with fever.\textsuperscript{23,31}

6.3 Endocarditis

Most patients with endocarditis can be managed within a p-OPAT service once stable after an initial period of hospitalization. However, patients with prosthetic valves, vegetations >10 mm in length, recurrent embolic events, persistently positive blood cultures, conduction abnormalities, \textit{Staphylococcus aureus} infection or heart failure are at increased risk of complications.\textsuperscript{3} Although none of these risk factors is an absolute contraindication to p-OPAT, the initial period of hospitalization may be longer.\textsuperscript{32,33}

6.4 Meningitis

Complications of meningitis occur most frequently by days 2–3 and are very rare after days 3–4. Fever lasts 5–9 days in 13\% of patients.\textsuperscript{34} Consider p-OPAT management if the patient is seizure-free and afebrile for >24 h. Be cautious about discharging a child with meningitis before day 5 and if abnormal neurology persists.\textsuperscript{35,36}

7. Vascular access

Due to the technological advancements of venous access devices, it is now considerably easier and safer to administer iv therapy in the outpatient setting over longer periods of time.\textsuperscript{37} Midlines, peripherally inserted central catheters (PICC), tunnelled central venous catheters (CVC) and implanted ports have all contributed to the safe and successful delivery of antimicrobial therapy for patients under p-OPAT.\textsuperscript{19,37} Peripheral cannulae may also be considered for short-course home therapy. Table 6 summarizes the
7.1 Device selection

Device selection criteria must reflect the individual needs of the patient; including clinical status, diagnosis, age, vein condition, current vascular access, antimicrobials prescribed, frequency of administration and the duration of therapy as well as the clinical expertise available to site the device. It is essential that secure venous access is in place prior to p-OPAT discharge.

The use of PICC has surpassed that of any other vascular access device and is now standard practice in p-OPAT. They are commonly used in patients requiring long-term therapies and can remain in place for extended periods of time (weeks or months) providing the device is appropriately managed. Compared with tunnelled CVC, PICC can be inserted either under local or general anaesthetic, are generally easier and cheaper to insert, are not associated with complications such as pneumothorax and can be easily removed if necessary. Insertion under ultrasound guidance is associated with improved rates of success, reduced numbers of attempts and can enable larger catheters to be placed in larger vessels. PICC have a relatively low incidence of complications and are well tolerated by patients, also reducing the number of venous punctures required in comparison to the use of peripheral catheters. Even though PICC are more expensive than peripheral cannulae and midlines, they require resiting less frequently and usually allow blood sampling.

7.2 Device care and complications

The UK Department of Health, the Royal College of Nursing and the Infusion Nurses Society have all published standards of practice addressing the maintenance of venous access devices and...
the administration of iv medications. In addition, the US CDC has also developed guidelines for the prevention of catheter-related infection. Practitioners should utilize information from such established national guidelines and local policies, safely adapting them to the unique needs of the patient under their p-OPAT service.

Catheter-associated complications include mechanical complications (dislodgement, occlusion, clotting, phlebitis, infiltration, embolism, thrombosis and catheter malfunction) and non-mechanical complications (local and systemic catheter infections). Peripheral cannulae have a higher incidence of mechanical complications in comparison to midlines, with PICC being more problematic than tunneled CVC. 

Infection rates are comparable between PICC and tunneled CVC. The risk of complications is greater with increased dwell time and therefore close monitoring and cessation of iv therapy is essential at the earliest possible timepoint. Prevention and early detection of complications in venous access devices is vital for the success of p-OPAT. This can be achieved through the promotion of safe and effective venous access device care and infection control practices.

Patients and caregivers must also be educated in the care of their venous access device prior to discharge home under p-OPAT and instructed on the early identification of any complications.

<table>
<thead>
<tr>
<th>Model</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
</table>
| Home infusion by carer or parent | • independence for families and cost savings for healthcare providers  
• enables the use of antimicrobial agents that require multiple daily dosing  
• allows more flexibility in terms of timing of drug administration | • there is evidence to suggest that the responsibility of administering antibiotics increases stress for families  
• such a model does not include an initial review of the home environment or daily patient review, which may result in delays in identifying deterioration or complications  
• adherence to treatment cannot be ensured  
• although experience is growing, there are currently no national guidelines in place to formally evaluate the competence of caregivers in administering iv antibiotics  
• the time taken for a hospital-based nurse to travel to patient’s houses may be excessive if the p-OPAT service covers a wide geographical area  
• existing community nursing teams may not have the capacity to take on the increased workload of p-OPAT patients  
• existing community nursing teams may not work 7 days per week  
• the cost of providing paediatric trained nurses through a private healthcare provider may be expensive  
• inconvenience for families having to return to hospital each day  
• logistics of providing a 7 day/week service | |
| Home administration by a paediatric trained nurse | • convenience of having antimicrobials administered at home  
• visiting nurse is able to review the patient and the home environment each day and inform the p-OPAT team if there are any concerns  
• adherence to treatment is ensured  
• using pre-existing community nursing teams may reduce staffing costs required to implement the service | |
| Infusion centre administration | • children can be reviewed each day by the medical team and immediate decisions can be made about stopping antimicrobials; this can be beneficial in certain pathologies such as cellulitis  
• if vascular access is lost (i.e. extravasation of cannula), this can be immediately addressed  
• cost benefits for healthcare providers in terms of using nursing staff already in place | |

8. Antimicrobial selection, drug delivery and patient monitoring

8.1 Principles of antimicrobial selection

It is paramount that the antimicrobial agent chosen reflects microbiological susceptibilities (if known) and that the tissue penetration is appropriate for the site of infection. Choice of agent should also comply with local antimicrobial stewardship guidance. In addition, the following factors may influence antibiotic choice:

(i) Dosing convenience—ideally once daily.
(ii) Side-effect profile.
(iii) Stability in pre-filled syringes/elastomeric devices.
(iv) Cost.
(v) Monitoring required.
(vi) Pharmacokinetics—relating to renal/hepatic metabolism/clearance and comorbidities as well as tissue penetration.
(vii) Pharmacodynamics—if time-dependent activity, consider a continuous infusion over 24 h instead of intermittent doses (i.e. piperacillin/tazobactam or fluclouxacillin).

The first dose of antibiotic should be administered in a supervised healthcare setting to ensure that the patient does not develop an
anaphylactic reaction. It is extremely unlikely for anaphylaxis to occur beyond the first dose. For this reason, the working group agreed with the adult good practice recommendations that it is not necessary for patients to be discharged home with adrenaline. The prolonged use of any antimicrobial agent may result in drug fever due to a type 1 hypersensitivity reaction.

8.2 Choice of antimicrobial agent

Table 7 lists various antimicrobial agents that can be used within a p-OPAT service. It is beyond the remit of these guidelines to provide detailed information about drug dosing and long-term stability data. For dosing recommendations, readers are encouraged to refer to the latest version of the British National Formulary for Children. The stability data provided in Table 7 are for guidance only and can vary between devices; for detailed stability information, readers should refer to manufacturer’s information, consult peer-reviewed online resources such as Stabilis (http://www.stabilis.org) and liaise with their local pharmacy department. The BSAC OPAT initiative has a workstream dedicated to drug stability and dosing (http://e-opat.com/workstreams/workstream-five-drug-stability-and-testing/).

8.3 Drug delivery

All prescriptions should be reviewed by a pharmacist, preferably with specialist knowledge in OPAT and/or antimicrobials. The rationale for this is to ensure proper pharmaceutical care including appropriate dosage of antimicrobials, to identify potential drug–drug interactions and contraindications for the antimicrobials chosen, and to assist with selection of diluents and administration regimens.

8.3.1 Compounding

The supply of antimicrobials for p-OPAT is generally arranged via the hospital pharmacy or supplied by a homecare company. According to the National Patient Safety Agency alert on the safer use of injectable medicines in the hospital setting, it is preferable to procure ready-to-use/ready-to-administer injectables to minimize the risk of dosing and dilution errors. Where an unlicensed product has to be prepared (e.g. elastomeric devices and syringes), this should take place in a hospital pharmacy aseptic production unit or NHS manufacturing unit or be obtained from a commercial specialists manufacturer. Where p-OPAT services are outsourced to a private contractor, drugs may be compounded and supplied directly by the contractor.

Reconstitution in the patient’s home may represent a higher risk of contamination and dosing error compared with reconstitution in a manufacturing unit and should be subject to strict risk assessment. If a drug is to be reconstituted other than in an aseptic manufacturing unit, strict aseptic non-touch technique should be used and the reconstituted drug used immediately. One should consider the use of worksheets and detailed standard operating procedures between pharmacy and the nursing team to reduce the risk of dosing errors. If parents or caregivers are reconstituting medication (see Table 8). Each technique varies in terms of cost,
convenience and reliability. Factors influencing the device chosen include:

(i) Patient factors—ability to tolerate being connected to a device for 24 h.
(ii) Resources available including access to compounding department and devices.
(iii) Drug being used, infusion time and stability.
(iv) Type of iv access in situ—24 h infusion is less suitable for peripheral cannulae.
(v) Competency of healthcare staff and/or caregivers to manage drug delivery via the chosen method.

8.3.3 Drug delivery and storage
Stability of an antimicrobial in an infusion device can vary from <24 h to >1 week, depending on the drug, diluent, concentration, device and storage temperature amongst other factors; for detailed information, discuss with the hospital pharmacy or compounding unit. However, the majority of compounded drugs and Table 6. Indications and complications associated with various iv devices

<table>
<thead>
<tr>
<th>Access device</th>
<th>Entry site</th>
<th>Usual recommended treatment period</th>
<th>Complications (rare complications are indicated)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral cannula</td>
<td>peripheral veins, i.e. hand, forearms, (foot)</td>
<td>&lt;7 days in children</td>
<td>pain, phlebitis, infiltration, dislodgement, clotting, occlusion, malfunction (rare), local infection (rare)</td>
<td>may require repeated reinsertion in hospital</td>
</tr>
<tr>
<td>Midline catheter</td>
<td>peripheral veins, i.e. forearm, (foot)</td>
<td>&lt;10 days in children</td>
<td>dislodgement, clotting, occlusion, phlebitis, pain (rare), infiltration (rare), malfunction (rare), local infection (rare)</td>
<td>lower rates of dislodgement and phlebitis than peripheral short catheters</td>
</tr>
<tr>
<td>Peripherally inserted central catheter (PICC)</td>
<td>peripheral veins, typically the basilic, cephalic or axillary veins</td>
<td>&lt;6 weeks (but can remain in situ for longer if necessary)</td>
<td>insertion phlebitis (usually settles within 24 h with heat therapy and non-steroidal anti-inflammatory drugs), dislodgement (rare), clotting (rare), occlusion (rare), malfunction (rare), local infection (rare)</td>
<td>complications more common in comparison to tunnelled CVC</td>
</tr>
<tr>
<td>Tunnelled CVC</td>
<td>implanted into the subclavian, internal jugular, (femoral vein)</td>
<td>&gt;6 weeks or in patients with great risk of dislodgement with PICC</td>
<td>pain at the site of insertion (short-term post-insertion), dislodgement (rare), occlusion (rare), malfunction (rare), local and systemic infection (rare), embolism (rare), thrombosis (rare)</td>
<td>not recommended as first-line device choice requires general anaesthesia to insert and remove requires technical expertise to insert</td>
</tr>
<tr>
<td>Implanted port</td>
<td>implanted into the subclavian or internal jugular vein</td>
<td>not recommended unless already in situ</td>
<td>pain at the site of insertion (short-term post-insertion), occlusion (rare), malfunction (rare), local and systemic infection (rare), embolism (rare), thrombosis (rare)</td>
<td>lowest risk of all access devices of catheter-related infections requires general anaesthesia to insert and remove requires technical expertise to insert</td>
</tr>
</tbody>
</table>
Table 7. Indications, mode of delivery, common side effects and monitoring of various antimicrobial agents suitable for p-OPAT (note: stability will vary depending on brands, diluents, delivery device/container and storage conditions. Every prescription should be screened by a pharmacist)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Common indications</th>
<th>Mode of administration/stability</th>
<th>Common side effects/monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibacterials</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ceftriaxone</td>
<td>febrile illness in young infants, cellulitis, lymphadenitis, pyelonephritis, osteoarticular infections, pneumonia and meningitis</td>
<td>short infusion via syringe; stable for 7 days if refrigerated (2 – 8°C) up to concentration of 50 mg/mL</td>
<td>side effects uncommon; potential neutropenia and deranged LFTs with prolonged courses</td>
</tr>
<tr>
<td>ceftazidime</td>
<td><em>Pseudomonas</em> infections in children with cystic fibrosis</td>
<td>intermittent infusions via syringe but frequency not ideal for p-OPAT administration; stable for 24 h at room temperature and for 7 days if refrigerated (2 – 8°C) when diluted to 5 – 60 mg/mL in 0.9% saline; consider 24 h infusion via elastomeric device</td>
<td>side effects uncommon; potential neutropenia and deranged LFTs with prolonged courses</td>
</tr>
<tr>
<td>daptomycin</td>
<td>resistant Gram-positive infections including skin/soft tissue infections, osteoarticular infections, infective endocarditis</td>
<td>bolus over 2 min or infusion over 30 min; unstable once reconstituted, not suitable for pre-compounding</td>
<td>check baseline CK and monitor CK to identify myopathy; eosinophilic pneumonitis in prolonged treatment; not licensed for children in the UK drug fever may occur with prolonged use</td>
</tr>
<tr>
<td>ertapenem</td>
<td>infections with resistant Gram-negative bacteria (not <em>Pseudomonas</em>) including intra-abdominal infections, urinary tract infections</td>
<td>once-daily short infusion via syringe for children ≥ 13 years; stable for 5 days if refrigerated (2 – 8°C) when diluted to 10 – 20 mg/mL</td>
<td>drug fever may occur with prolonged use</td>
</tr>
<tr>
<td>flucloxacillin</td>
<td>Osteoarticular infections, infective endocarditis</td>
<td>6 hourly dosing regimen makes it unsuitable for p-OPAT use unless administered as a 24 h infusion using an elastomeric device; stable for 24 h at room temperature and for 7 days if refrigerated (2 – 8°C)</td>
<td>side effects not common; potential neutropenia or drug fever with prolonged courses</td>
</tr>
<tr>
<td>gentamicin</td>
<td>urinary tract infections, cystic fibrosis and infective endocarditis</td>
<td>once-daily short infusion over 30 min via syringe; stable for 7 days if refrigerated (2 – 8°C)</td>
<td>nephrotoxicity, irreversible ototoxicity; monitor trough levels every 3rd dose until stable levels, then twice weekly drug fever may occur with prolonged use</td>
</tr>
<tr>
<td>meropenem</td>
<td>infections with resistant Gram-negative organisms including <em>Pseudomonas</em></td>
<td>8 hourly dosing and limited stability despite refrigeration (2 – 8°C) restricts its role within p-OPAT unless parental administration</td>
<td>drug fever may occur with prolonged use</td>
</tr>
<tr>
<td>piperacillin/ tazobactam</td>
<td>febrile neutropenia, complicated intra-abdominal infections, <em>Pseudomonas</em> infections</td>
<td>intermittent infusions via syringe but frequency not ideal for p-OPAT administration; stable for 24 h at room temperature and for 7 days if refrigerated (2 – 8°C); consider 24 h infusion via elastomeric device</td>
<td>side effects not common; potential neutropenia or drug fever with prolonged courses</td>
</tr>
<tr>
<td>teicoplanin</td>
<td>infections with Gram-positive organisms such as <em>Staphylococcus epidermidis</em> line infections and <em>Staphylococcus aureus</em> infections including MRSA</td>
<td>once-daily short infusion over 30 min via syringe; stable for 7 days if refrigerated (2 – 8°C) in a silicone-free syringe (degrades in standard syringe)</td>
<td>therapeutic drug monitoring is required for all indications apart from the treatment of central line infections; target trough levels of &gt;10 mg/L (HPLC method) for pneumonia, UTI and SSTI and 15 – 30 mg/L (HPLC method) for osteoarticular infections or endocarditis; watch for blood dyscrasias (especially neutropenia and thrombocytopenia) with prolonged use</td>
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Continued
devices require refrigeration and therefore maintenance of a ‘cold chain’ is required should infusion devices need to be stored in a patient’s home. Where a commercial supplier is involved, they may provide a dedicated drug refrigerator for the patient’s home, deliver the infusion devices via refrigerated transport and provide calibration, monitoring and maintenance of the refrigerator; this should all be specified in the service level agreement with the provider. In practice, NHS units rarely supply refrigerators. The adequacy of domestic fridges for this purpose is questionable; if used, daily recording of the temperature is recommended.

8.3.4 Patient monitoring

The monitoring of p-OPAT patients should be no different from the monitoring of inpatients, in terms of good antibiotic stewardship, pharmacy practice and medical review. Recommended monitoring for p-OPAT patients includes the following.

Clinical monitoring Daily review with monitoring of physiological parameters (temperature, heart rate and respiratory rate) and checking of the line site. This can be performed by the hospital-based nurse/doctor within an infusion centre model or by the visiting nurse if antibiotics are being administered at home. Daily clinical monitoring is difficult when parents/carers administer antibiotics and this delivery model should only be considered for patients who are clinically stable on prolonged courses of antibiotics.

Laboratory monitoring For children on long-term iv antibiotics, weekly laboratory tests should be performed (full blood count, renal function, liver function and C-reactive protein). In addition, creatine kinase should be monitored once weekly for children on daptomycin and therapeutic drug monitoring should be performed when indicated (see Table 7).

9. Clinical governance and outcome monitoring

The p-OPAT service must be first and foremost a safe service. A safe, effective service requires robust clinical governance structures in place. Mapping out the p-OPAT pathway within the organization is a useful process to identify risk inherent in the existing

<table>
<thead>
<tr>
<th>Drug</th>
<th>Common indications</th>
<th>Mode of administration/stability</th>
<th>Common side effects/monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>tobramycin</td>
<td>treatment of Pseudomonas infections in cystic fibrosis</td>
<td>once-daily short infusion over 30 min via syringe; stable for 7 days if refrigerated (2–8°C) at concentrations of 13.33–40 mg/mL in 0.9% saline</td>
<td>nephrotoxicity, irreversible ototoxicity; monitor trough levels every 3rd dose until stable levels, then twice weekly</td>
</tr>
<tr>
<td>vancomycin</td>
<td>infections with Gram-positive organisms such as S. epidermidis line infections and S. aureus infections including MRSA</td>
<td>intermittent infusions via syringe but frequency not ideal for p-OPAT administration; stable for 24 h at room temperature and for 7 days if refrigerated (2–8°C); consider 24 h infusion via elastomeric device</td>
<td>nephrotoxicity, irreversible ototoxicity; monitor trough levels every 3rd dose until stable levels, then twice weekly</td>
</tr>
<tr>
<td>Antifungals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>liposomal amphotericin B</td>
<td>invasive fungal disease including Candida or Aspergillus species</td>
<td>once-daily infusion via syringe (&gt;2 h) or via an elastomeric device; flush with 5% glucose, not compatible with 0.9% sodium chloride</td>
<td>disturbances in renal function including hypokalaemia</td>
</tr>
<tr>
<td>caspofungin</td>
<td>invasive fungal disease including Candida or Aspergillus species</td>
<td>once-daily infusion via syringe over 1 h or via an elastomeric device; stable for 48 h if refrigerated (2–8°C) at concentrations up to 0.5 mg/mL</td>
<td>side effects uncommon</td>
</tr>
<tr>
<td>Antivirals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aciclovir</td>
<td>HSV encephalitis, VZV infection in the immunocompromised host</td>
<td>intermittent infusions via syringe but frequency not ideal for p-OPAT administration; consider 24 h infusion via elastomeric device; stable for 7 days at room temperature at concentrations up to 10 mg/mL</td>
<td>side effects are not common; rarely reversible nephrotoxicity due to crystallization in renal tubules or neurotoxicity; extravasation can cause severe local inflammation and phlebitis</td>
</tr>
</tbody>
</table>

CK, creatine kinase; HSV, herpes simplex virus; LFTs, liver function tests; SSTI, skin and soft tissue infection; UTI, urinary tract infection; VZV, varicella-zoster virus.
Risks can be identified at every stage of the p-OPAT process and can be reduced with suitable safeguards and checks. Common themes emerge and the following actions help to ensure a safe service.

(i) Establish clinical responsibility

Overall clinical responsibility for the patient must be clearly defined before the patient leaves the hospital. Within a tertiary hospital, this may involve shared care between the p-OPAT team and the referring team. Failure to assign responsibility can result in patients being overlooked in the community, difficulties in the readmission process and ultimately suboptimal care.

(ii) Ensure effective communication

While this is essential in all clinical care, the multiple agencies involved in the p-OPAT process and the increased distance between healthcare provider and the patient make good communication vital. Examples of good communication include regular meetings between the community team and hospital staff including virtual ward rounds and notifying the patient’s GP that the patient has been discharged on p-OPAT. If applicable, the referring clinician needs to be kept informed of the patient’s progress on p-OPAT. There needs to be a system for providing contact points for both parents/carers and community staff. An out-of-hours service needs to be provided to cover acute clinical issues.

(iii) Develop and maintain good documentation

Good documentation either in electronic or written format is important. This needs to be readily available to community nursing staff and hospital staff who may need to readmit patients. Parent/carer-owned folders are one way to achieve this. Standard care pathway documentation is an effective way to capture and standardize clinical information. The development of standard operating procedures and policies based on good practice guidelines is encouraged. Patient and parent education information detailing contact details, service description, common problems and instructions on what to do in the event of adverse events aids compliance and understanding. Examples of documentation for parents/carers and trouble-shooting guides for doctors can be found on the e-OPAT web site (http://e-opat.com/workstreams/workstream-four/).

(iv) Establish a pathway for urgent review and readmission

Some patients will require readmission and a clear pathway for urgent review and readmission needs to be established to facilitate this process. All staff, including those providing out-of-hours care, must be aware of this pathway.

(v) Organizational governance

There should be an identified lead for p-OPAT. The p-OPAT service should come under the oversight of local paediatric clinical governance committees or, if the service is sufficiently large, could have a separate clinical governance committee. The committee should include all the partners involved in delivering the service. If the community service is provided by a third party, then a contract monitoring process should be in place with agreed key performance indicators.

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Table 8. Comparison of the devices available for delivering iv antibiotics

<table>
<thead>
<tr>
<th>Drug delivery method</th>
<th>Description</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolus or ‘push’†</td>
<td>slow administration of a drug (usually over 3–5 min) through an iv access device using a syringe only</td>
<td>simple technology most commonly used (hospital and community) least expensive (supply and administration costs)</td>
<td>not all antibiotic regimens can be delivered; some drugs require longer infusion times to avoid infusion related-toxicity or mitigate irritant properties</td>
</tr>
<tr>
<td>Non-electrical pump (elastomeric devices are the most commonly used)‡,16,21,37,63</td>
<td>controlled-rate, low-pressure, self-infusing devices flow rate relies upon mechanical restriction through a narrow-bore tube</td>
<td>disposable portable lightweight relatively inexpensive (costs dependent on medication regimen) closed, pre-filled system resulting in less handling of the drug fixed rates so programming errors are eliminated</td>
<td>device size and relative rates are fixed pharmacy input is required to fill each device antimicrobial selection is limited due to drug stability, e.g. a drug selected for a 24 h infusion must be stable at room temperature for 24 h</td>
</tr>
<tr>
<td>Electrical pump18,19,37</td>
<td>programmable, high-pressure electrical devices</td>
<td>controlled delivery flexible rates extending the range of drugs that can be used</td>
<td>comparatively expensive patient activity restricted due to battery life and transportability of the pump reliant on trained users to program the pumps device supply and maintenance can be an issue</td>
</tr>
</tbody>
</table>

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*Risks can be identified at every stage of the p-OPAT process and can be reduced with suitable safeguards and checks. Common themes emerge and the following actions help to ensure a safe service.*

**(i) Establish clinical responsibility**

Overall clinical responsibility for the patient must be clearly defined before the patient leaves the hospital. Within a tertiary hospital, this may involve shared care between the p-OPAT team and the referring team. Failure to assign responsibility can result in patients being overlooked in the community, difficulties in the readmission process and ultimately suboptimal care.

**(ii) Ensure effective communication**

While this is essential in all clinical care, the multiple agencies involved in the p-OPAT process and the increased distance between healthcare provider and the patient make good communication vital. Examples of good communication include regular meetings between the community team and hospital staff including virtual ward rounds and notifying the patient’s GP that the patient has been discharged on p-OPAT. If applicable, the referring clinician needs to be kept informed of the patient’s progress on p-OPAT. There needs to be a system for providing contact points for both parents/carers and community staff. An out-of-hours service needs to be provided to cover acute clinical issues.

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Good documentation either in electronic or written format is important. This needs to be readily available to community nursing staff and hospital staff who may need to readmit patients. Parent/carer-owned folders are one way to achieve this. Standard care pathway documentation is an effective way to capture and standardize clinical information. The development of standard operating procedures and policies based on good practice guidelines is encouraged. Patient and parent education information detailing contact details, service description, common problems and instructions on what to do in the event of adverse events aids compliance and understanding. Examples of documentation for parents/carers and trouble-shooting guides for doctors can be found on the e-OPAT web site (http://e-opat.com/workstreams/workstream-four/).
Activity data such as bed-days saved and patient numbers should be routinely collected to provide evidence regarding the benefits of p-OPAT to commissioners if required.

10. Developing a business case and obtaining funding to set up a p-OPAT service

Although additional funding may not be required to introduce a p-OPAT service in a secondary care setting, additional staff such as a p-OPAT nurse and an antibiotic pharmacist may be required to deliver a p-OPAT service within a tertiary setting. Obtaining such funding is likely to require the development of a business case.

The first step is to quantify the potential cost savings delivered by a p-OPAT service within one's own organization. Identifying the number of patients on iv antibiotics who could safely be managed at home allows the number of potential bed-days saved to be calculated. There is no standardized tariff for children being managed within a p-OPAT service, which means that, at present, individual organizations must determine how their p-OPAT service is funded, either in terms of revenue generation or cost savings. Although a detailed description of the development of a business case is beyond the scope of these guidelines, an interactive business case toolkit is available on the BSAC e-OPAT web site (http://e-opat.com/toolkit/) and information about funding options is available from http://e-opat.com/assets/zept/drrcase_debbieCumming.pptx.

11. Conclusions

There is compelling evidence to support the rationale for managing children on iv antimicrobial therapy at home whenever possible, including parent and patient satisfaction, psychological well-being, return to school/employment, reductions in healthcare-associated infection and cost savings. As a joint collaboration between BSAC and the BPAIIG, we have developed good practice recommendations to highlight good clinical practice and governance within p-OPAT services across the UK.

Although there are a number of differences between p-OPAT services delivered in secondary care settings as compared with those in tertiary care settings, especially in terms of the clinical team members available and treated conditions, the fundamental principles of p-OPAT remain identical. These principles are robust clinical governance systems, clear channels of communication and accurate outcome monitoring. To help support these principles in p-OPAT, BSAC has developed a paediatric PMS, which allows prospective data to be collected on all p-OPAT patients (http://e-opat.com/opat-pms/), and an OPAT registry, which allows benchmarking between centres (http://e-opat.com/outcomes-registry/).

The time has come for p-OPAT to reassert its early lead in OPAT and emerge from the shadow of its big brother!

Funding

This work was supported by the BSAC and the BPAIIG who provided travel expenses for the working group. The literature search was funded by BSAC.

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Table 9. Standardized BSAC outcome definitions

<table>
<thead>
<tr>
<th>Patient infection outcome on completing OPAT</th>
<th>p-OPAT outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>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)</td>
<td><strong>Success</strong>: completed p-OPAT therapy with no change in antibiotics, no adverse events, cure of infection and no readmission</td>
</tr>
<tr>
<td>Improved: (i) completed OPAT therapy + oral step down with partial resolution of infection but need for further follow-up; OR (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)</td>
<td><strong>Partial success</strong>: completed p-OPAT therapy with either change in antimicrobial agent or adverse event not requiring readmission</td>
</tr>
<tr>
<td>Failure: progression or non-response of infection despite OPAT, required admission, surgical intervention or died for any reason</td>
<td><strong>Failure</strong>: readmission due to worsening infection or adverse event; death due to any cause during p-OPAT</td>
</tr>
<tr>
<td>Indeterminate: readmission due to unrelated event</td>
<td></td>
</tr>
</tbody>
</table>

**(vi) Outcome measurements**

The measurement of outcomes in p-OPAT is an important part of good clinical governance. Recommendations for outcome measures have been made in the US IDSA OPAT guidelines as well as suggestions by the UK BSAC adult OPAT guidelines. Data required for benchmarking include clinical outcome, p-OPAT programme outcome, microbiological outcome, adverse drug events, adverse line events and antibiotics used (see Table 9). There should be a regular programme of audit against local and national standards and guidelines.

The BSAC OPAT initiative has developed a database tool for standardizing the collection of data (http://e-opat.com/opat-pms/). This patient management system (PMS) allows data on patients being actively managed within a p-OPAT service to be recorded within a virtual ward. It also has the potential to generate quarterly summary reports, which can be used to inform the local p-OPAT service as well as being uploaded to the national BSAC registry (http://e-opat.com/outcomes-registry/). This ability to share data will allow centres to benchmark themselves against other similar services in the UK and may provide data of how best to manage this cohort of patients in order to support further development of p-OPAT services across the country and to guide future research.

Patient/parent/carer satisfaction is an equally important part of a p-OPAT service. Units should routinely undertake patient/parent/carer surveys to ensure the service is providing what is required. Other outcomes such as the child's ability to return to education and parent's ability to return to work should also be captured. The parent information questionnaire on the BSAC PMS allows these data to be captured in a standardized format.
Transparency declarations
The authors have none to declare. These recommendations underwent a process of national consultation which replaced the usual JAC external peer review process. Organizations involved in the national consultation process are listed in the Supplementary data.

Supplementary data
A list of the organizations involved in the national consultation process is available as Supplementary data at JAC Online (http://jac.oxfordjournals.org/).

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