Are We Ready for an Outpatient Parenteral Antimicrobial Therapy Bundle? A Critical Appraisal of the Evidence

Eavan G. Muldoon, David R. Snydman, Elizabeth C. Penland, and Geneve M. Allison
Division of Geographic Medicine and Infectious Diseases, Tufts Medical Center, Boston, Massachusetts

Healthcare “bundles” have been developed to help providers improve the reliability and delivery of essential healthcare processes. Bundles have been shown to be effective in reducing healthcare-associated infection rates and are increasingly used to ensure the quality of patient care. Outpatient parenteral antimicrobial therapy (OPAT) is now standard medical practice in the treatment of a wide variety of infections. We review 6 components that we believe comprise an OPAT bundle and the evidence supporting each: patient selection, infectious disease consultation, patient/caregiver education, discharge planning, outpatient monitoring/tracking, and OPAT program review. To ensure that patients are receiving optimal care, further program development and outcomes research should target these bundle components to bring the evidence base up to date with current medical practices.

**Keywords.** OPAT (outpatient parenteral antimicrobial therapy); bundle; quality improvement; patient safety; hospital readmissions.

Healthcare “bundles” have been developed to help providers improve the reliability and delivery of essential healthcare processes. A care bundle is a set of practices that together should improve patient outcomes [1]. Bundles are increasingly used to ensure the quality of patient care; they should be evidence based and consist of 3–6 elements that are not being delivered consistently [1]. Outpatient parenteral antimicrobial therapy (OPAT) has become widely used since it was first described in 1974, serving 250,000 patients per year in the United States alone. The Infectious Diseases Society of America (IDSA) OPAT guidelines acknowledge the need for OPAT centers to “have an active performance improvement program,” but further details on what such a program should involve are not specified. To this end we propose an “OPAT bundle.” This bundle would have 6 distinct components as outlined in Table 1. The aim in proposing this bundle is to review the current literature and to encourage research where a paucity of data is identified. A strengthened evidence base would ultimately allow implementation of the bundle to optimize and standardize OPAT care.

**METHODS**

Peer-reviewed published articles were searched through PubMed. Search terms utilized were OPAT, outpatient parenteral antibiotics, hospital in the home, home intravenous antibiotics, and home antibiotics. Articles from all years of publication, representing all medical disciplines, and written in English were considered. OPAT practice guidelines from the United States (published by IDSA) [2] and the United Kingdom (published by the British Society for Antimicrobial Chemotherapy and British Infection Association) [3] were used as reference.

**Patient Selection**

International guidelines are in agreement that careful patient selection should occur prior to OPAT [2, 3].
Patient selection encompasses where to discharge the patient (eg, home vs rehabilitation center); this will be influenced by the models of OPAT care available in any given center. Patient selection encompasses patient factors (likelihood of adherence, willingness to learn OPAT techniques, social supports, insurance coverage) and medical factors (control of infection, suitability of intravenous antibiotic treatment at home, readiness for discharge) [2]. Given the heterogeneity of healthcare funding, financial factors affecting the provision of OPAT are outside the purview of this article. Reimbursement and conflict of interest issues for OPAT are reviewed elsewhere [5].

The IDSA guidelines state that OPAT is inappropriate if the patient’s needs would be better met as an inpatient [2], and recommend that physicians with training in infectious diseases or knowledge of OPAT be involved in the evaluation of candidates for discharge with OPAT. In the UK Good Practice Guidelines, patient selection has 5 key components:

1. An infection specialist should determine inclusion and exclusion criteria for specific infections.
2. Standardized and documented patient suitability criteria should incorporate physical, social, and logistic elements.
3. A member of the OPAT team should provide an initial assessment of patient suitability.
4. Patients and caregivers should be fully informed of the risks and benefits of OPAT and have the opportunity to decline OPAT.
5. If the patient is at risk of deep venous thrombosis, ongoing prophylaxis should be considered [3].

In a recent national survey of infectious disease (ID) practitioners, 70% had experienced situations in which patients were discharged with intravenous antibiotics and without prior input of an ID or OPAT team [6]; such practice is not in accordance with published guidelines and is strongly discouraged.

Although both guidelines agree that patients should be carefully selected for OPAT, more specific details on patient selection criteria are unavailable. Analysis of the available literature demonstrates that specific infections have been predominantly studied in the field of patient selection for OPAT: infective endocarditis (IE), pneumonia, and skin and soft tissue infection (SSTI) [7–11].

Case series documenting the successful treatment of IE with OPAT feature carefully selected patients, who were hemodynamically stable, with no complications and an appropriate home environment [9]. Despite successes in treating IE, there are also documented failures, resulting in mortality [10]. A more selective approach in considering patients with IE for OPAT has been proposed, including the duration of time the infection has been treated and consideration of the causative organism [10]. In the selection of patients with pneumonia, after applying criteria based on the severity of the illness and patient characteristics, only 30% were eligible for OPAT [11]. Similarly, selecting patients without signs of sepsis or severe laboratory alterations, who can give informed consent, have a telephone, and have a caregiver nearby, has been shown to be

### Table 1. Proposed Outpatient Parenteral Antimicrobial Therapy Bundle

<table>
<thead>
<tr>
<th>Key Aspects of Component</th>
<th>Main Bundle Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fully aware of risks/benefits</td>
<td>Patient identification/selection</td>
</tr>
<tr>
<td>Appropriate home environment/adequate support</td>
<td></td>
</tr>
<tr>
<td>No clinical contraindications to discharge from hospital</td>
<td></td>
</tr>
<tr>
<td>Willingness to comply with follow-up plan</td>
<td></td>
</tr>
<tr>
<td>Insurance/copayment issues resolved</td>
<td></td>
</tr>
<tr>
<td>Prior to intravenous access</td>
<td>ID consultation</td>
</tr>
<tr>
<td>Prior to discharge home</td>
<td></td>
</tr>
<tr>
<td>Vascular access education/sterile technique/teach-back method</td>
<td>Patient/family education</td>
</tr>
<tr>
<td>Emergency contact numbers for patients</td>
<td></td>
</tr>
<tr>
<td>Physician responsible until patient seen in clinic</td>
<td></td>
</tr>
<tr>
<td>Side effects of medication</td>
<td></td>
</tr>
<tr>
<td>Potential complications</td>
<td></td>
</tr>
<tr>
<td>ID appointment handed to patient prior to discharge</td>
<td>Care transition</td>
</tr>
<tr>
<td>Clear communication between inpatient and outpatient services</td>
<td></td>
</tr>
<tr>
<td>ID/OPAT plan documented in discharge summary</td>
<td></td>
</tr>
<tr>
<td>Safety labs ordered as part of discharge plan</td>
<td></td>
</tr>
<tr>
<td>Safety labs: identifying missing labs, addressing lab abnormalities, adjust medications as needed (dose, duration, medication change)</td>
<td>Outpatient monitoring</td>
</tr>
<tr>
<td>PICC line care and removal at end of therapy</td>
<td></td>
</tr>
<tr>
<td>Change in management: communication between ID and infusion company/rehabilitation facility</td>
<td></td>
</tr>
<tr>
<td>Monitoring of microbiological cure, laboratory cure</td>
<td></td>
</tr>
<tr>
<td>Patient satisfaction</td>
<td>OPAT program measures</td>
</tr>
<tr>
<td>Readmission rates</td>
<td></td>
</tr>
<tr>
<td>Program improvements, audit</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ID, infectious disease; OPAT, outpatient parenteral antimicrobial therapy; PICC, peripherally inserted central catheter.

Given that there are a number of models of OPAT care [4], patient selection criteria will vary depending on the model(s) used by any individual center. In many instances the ultimate decision is not whether to discharge a patient with OPAT, but where to discharge the patient (eg, home vs rehabilitation center); this will be influenced by the models of OPAT care available in any given center. Patient selection encompasses patient factors (likelihood of adherence, willingness to learn...
successful in the treatment of SSTI through OPAT programs [8]. Although osteomyelitis is commonly treated with OPAT, there are no published studies on patient selection specifically related to bone infection. A recent retrospective study demonstrated that methicillin-resistant Staphylococcus aureus, older age, and osteomyelitis related to diabetic foot infection were all associated with poorer outcomes [7].

As the population ages, the number of older adults who may require OPAT will increase. Traditionally, older patients were less likely to be considered for OPAT [12]. However, in a study of patients aged >60 years treated through a Veterans Administration hospital, there was no difference in cure rates compared to patients aged <60 years [13]. Nephrotoxicity was more common in the older age group (P = .02). Older patients were more likely to have urgent care visits or have a problem or question related to their therapy. Similarly, Perez-Lopez et al have shown success in patients aged >70 years, with adverse events developing in 12% of patients [14]. Studies such as these indicate that older adults can be treated with OPAT but that systems need to adapt and recognize the specific needs of older patients.

Intravenous drug users represent another population often considered inappropriate for OPAT. However, Ho et al have reported on the successful treatment of 29 intravenous drug users, using predefined criteria and a tamper-proof security seal over the vascular access [15]. All but 1 patient completed OPAT and the readmission rate was 21%, which is comparable to other series [16]. This work demonstrates how rigorous patient selection and follow-up can help overcome one traditional barrier to OPAT.

**ID Consultation**

Both US and UK OPAT guidelines recommend that an individual with ID or OPAT experience should be involved in the patient selection prior to OPAT [2, 3]. Involvement of ID specialists in the care of patients with serious infections such as S. aureus bacteremia has been shown to increase adherence to standards of care, decrease the use of inappropriate therapy [17], and improve patient outcomes [18]. This phenomenon is not limited to S. aureus or the United States; in a study of IE in Japan, involvement of an ID physician also significantly lowered the relapse rate among patients diagnosed with IE [19]. An added benefit of involving ID physicians is to decrease the number of inappropriate antibiotic prescriptions. ID review resulted in intravenous to oral antibiotic switch in 27%–40% of cases, saving an estimated €662 sterling per patient assessed [20–23]. One of these studies also showed that ID consultation did not delay hospital discharge [21]. A small study has suggested that ID consultation should occur prior to peripherally inserted central catheter (PICC) insertion [24]; however, to date there is little in the published literature on this specific question. Given the recognized complications of PICC lines, avoidance of PICC line placement when not absolutely necessary is to be encouraged.

**Patient and Family Education**

It stands to reason that discharging any patient with therapy that would otherwise be administered in a hospital should be preceded by patient and caregiver education. However searches for OPAT patient education, hospital in the home patient education, and home antibiotics patient education, as well as similar searches with only the term education, yielded surprisingly few results. Much of the available literature focuses on improving staff knowledge, and little is published on patient or caregiver education. In other medical disciplines, patient education has been studied. For example, poor patient education in patients undergoing pancreaticoduodenectomy has been associated with higher readmission rates [25]. Similarly, implementation of a teaching program for patients being anticoagulated decreased 60-day readmissions from 51% to 38% (P = .014), with the majority of the decrease being accounted for by a decrease in anticoagulation-related readmissions [26]. The use of simple cartoon-based educational materials has been shown to improve bowel preparation in patients undergoing colonoscopy [27]. Novel approaches to patient education, such as the use of mobile phone applications [28], have been suggested but have not yet been evaluated. Further studies to assess the impact of patient education on OPAT patient outcomes are urgently needed.

**Care Transition**

Thirty-day readmission rates are being targeted to reduce healthcare costs and are becoming a quality-of-care metric. However, data are limited on care transitions of OPAT patients. The reported readmission rates for patients discharged with OPAT are between 6% and 20% [15, 16, 29–31]. Successful care transition from hospital to home or alternative healthcare facility is important for patients’ well-being, as well as to limit the financial impact of readmission. Aside from readmission rates in published series of OPAT patients, there are no other available studies on care transition in OPAT patients.

Communication is a key element in the successful hospital discharge of patients. The follow-up care of patients has been shown to be compromised in up to 25% of patients following hospital discharge due to the lack of availability of a discharge summary [32]. Although this study specifically looked at primary care physicians, a similar situation could arise where inpatient and outpatient ID care is not performed by the same physician. Weekend discharges, lack of a primary care provider, discharge diagnosis, poor social support, and lack of ancillary services may all contribute to failed discharges [32–34]. Patients being discharged to other care facilities could also benefit with
OPAT, this area is ripe for future study. An intervention, studied in an elderly population, that included specific actions to empower and educate patients, coordinate data flow, and facilitate follow-up within 7 days reduced readmissions, and improved patient knowledge and understanding of their diagnoses and medications [36]. Jack et al reported on a similar intervention to reduce readmissions in general medical patients involving both an in-hospital component using a “discharge advocate” and an aftercare plan, and showed a lower rate of subsequent hospital utilization in the intervention group [37]. More recently, data on the relationship between admission rates and rehospitalizations would suggest that efforts also need to be directed at reducing hospital utilization as a means to decreasing readmissions [38]. However, in a systematic review of 386 articles regarding interventions to reduce readmission, no discrete intervention, or bundle of interventions, was shown to reduce readmissions [39]. To date, there are no studies investigating interventions specifically targeting OPAT recipients.

In the discharge of patients with OPAT, the responsibility for some or all of the patients’ care commonly falls to family members or caregivers [30]. Becoming a caregiver for one’s relative can bring its own stresses, which are not yet well documented or quantified.

Awareness of predictors for readmission will be important in developing appropriate treatment and monitoring plans for patients. Given the lack of published data on care transitions in OPAT, this area is ripe for future study.

**Outpatient Monitoring**

Patients discharged with OPAT receive potentially toxic treatment, thus necessitating close patient monitoring. However, relatively little is available on the best practice of outpatient monitoring. This is likely because the frequency of monitoring will be determined not only by the infection treated, but also by patient characteristics and the pharmacodynamics and pharmacokinetics of the selected antibiotic(s) [40]. In a 2004 survey of ID practitioners regarding OPAT, there was considerable variation in reported patient monitoring [4]. While 92% of respondents monitored laboratory parameters weekly, only 29% saw their patients weekly. The majority stated that an ID physician could be contacted nights or weekends if complications arose; however, 14% said this was not possible. The IDSA OPAT guidelines recommend that the frequency of patient follow-up be determined at the beginning of therapy and that in most circumstances patients see their physician “once or twice a week,” whereas less frequent visits may be appropriate for patients with chronic conditions, few comorbidities, and good social supports [2]. Guidelines are also provided for the frequency of laboratory monitoring depending on the class of antibiotic administered [2]. Patients should be informed of potential toxicities, and consideration should be given to obtaining written consent, particularly for aminoglycoside therapy. Likewise, the Good Practice Recommendations for OPAT in the United Kingdom recommend at least weekly laboratory monitoring and that there should be a well-defined system in place for patients who need urgent review and readmission [3]. In addition to regular physician review, a weekly multidisciplinary virtual ward round is recommended to discuss the progress of patients on OPAT [3]. While regular communication with the patient’s other physicians is vital, both guidelines emphasize the responsibility of the ID specialist for monitoring and responding to laboratory studies.

The most commonly reported adverse events among OPAT patients are antibiotic reactions, hematological complications, diarrhea, readmission, and line complications [4, 8, 9, 13, 15, 16]. Complications directly associated with OPAT occur in 24% of patients [30]. Although care bundles are used in hospitalized patients with central vascular access to minimize catheter-associated bloodstream infection [41], prospective data are lacking on line complication rates in patients discharged from hospital. One retrospective study reported a rate of 0.79 infections per 1000 line days, with other line events being reported as 4.9 per 1000 line days [42].

Systematic procedures should be in place to ensure the appropriate and safe follow-up and monitoring of patients discharged with OPAT. We would suggest investigation of a system that monitors the following components as well as further research into which components are associated with improved patient outcomes: (1) safety laboratory result monitoring, which would include methods of identifying missing laboratory results, addressing abnormal results, and adjusting medications as needed; (2) PICC care and documented removal of the line at end of therapy; (3) the communication systems for changing patient management, including methods and speed of communication between managing physician, visiting nurse, infusion pharmacist, patient, and care providers as appropriate; and (5) documentation of microbiological and/or clinical cure as appropriate.

**Outcome Measures**

In the development of any service, systems should be put in place for review and quality improvement. Such an audit cycle ensures quality care and ongoing program development. Development of OPAT registries are critical to providing large-scale numbers and experience from which good data can be generated to review outcomes and procedures [43]. Mapping the processes involved in OPAT can be helpful in both setting up an OPAT service and in its ongoing monitoring. Gilchrist et al [44]
report on using a healthcare failure mode effect analysis tool [45]. Using such processes allows for identification of areas where potential harm and errors could occur to affect patient care. It also provides a framework for ongoing quality improvement. The recording and evaluation of readmission rates among OPAT patients should be an integral part of any program quality improvement measures. Given that OPAT is a method of hospital cost saving [23], it would be counterproductive if early discharge with OPAT had high readmission rates. Studies of patient satisfaction have shown that patients who receive OPAT are highly satisfied (up to 98%) and report they are likely to choose it again if needed [16]. One dedicated study done in Canada confirms the preference of patients to receive intravenous antibiotics at home as opposed to in a rehabilitation or other medical facility, using patients’ potential willingness to pay to quantify patient preference [46]. Ideally, patient satisfaction measures would be a part of OPAT program outcome measures for ongoing improvement [16].

CONCLUSIONS

In conclusion, OPAT is a mainstay of current medical therapy, and there is an anticipated rise in OPAT usage given changing patient demographics and the economic pressures faced by most healthcare systems. Enthusiasm for OPAT must be tempered by the understanding that the administration is complex, potentially toxic, and involves many members of the healthcare team. We have reviewed 6 components that we believe comprise an OPAT “bundle,” and the evidence supporting each: patient selection, ID consultation, patient/caregiver education, discharge planning, outpatient monitoring/tracking, and OPAT program review. Given the lack of evidence base in a number of key areas, we cannot yet recommend implementation of an OPAT bundle as an evidence-based intervention. While the evidence base is poor in each of the 6 identified components, knowledge is particularly lacking in the areas of patient education and care transition. However, in the interim, it is reasonable to consider the use and assessment of a checklist based on the proposed bundle as has been utilized successfully in other medical disciplines [47, 48]. Additional outcomes research should target each of the OPAT bundle components to find the evidence-based interventions that are associated with the best patient outcomes.

Notes

Acknowledgments. We thank Dr Shira Doron for her time in reviewing the article.

Financial support. E. G. M. is the inaugural recipient of the Francis P. Tally endowed fellowship in infectious diseases, Tufts Medical Center. G. M. A. was supported by the National Center for Research Resources (grant number UL1RR025752), now the National Center for Advancing Translational Sciences; the National Institutes of Health (grant number UL1 TR000073); and the National Cancer Institute (grant number K12 CA156726).

Disclaimer. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Author contributions. E. G. M. contributed to bundle development, performed the literature review, and wrote the paper. D. R. S. performed document review and editing. E. C. P. conceived the OPAT bundle. G. M. A. contributed to bundle development, document review, and editing.

Potential conflicts of interest. G. M. A. is a consultant for Coram Healthcare, a Home Infusion Company; has received payment for providing hepatitis B continuing medical education talks supported by Gilead; and has received grant support from Merck and Tufts University. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References


