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Outpatient parenteral antimicrobial therapy (OPAT) versus inpatient care in the UK: a health economic assessment for six key diagnoses

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Abstract:

Objectives To compare costs associated with different models of outpatient parenteral antimicrobial therapy (OPAT) delivery with costs of inpatient care across six key infection groups typically managed via OPAT in the UK.

Design The analysis used a cost-minimisation design due to evidence of similarities in patient and treatment outcomes between OPAT and inpatient care. A bottom-up approach was undertaken for the evaluation of costs associated with OPAT. The British Society of Antimicrobial Chemotherapy (BSAC) National Outcomes Registry System (NORS) was used to determine the key infection diagnoses, mean duration of treatment episodes and (with expert consensus) most frequent antibiotics used.

Setting Several OPAT delivery settings were considered in the costing analysis including outpatient clinic and care at the home and were compared with inpatient care.

Interventions The OPAT models considered in the analysis were outpatient clinic model, nurse home visits, self (or carer)-administration by a bolus IV, self-administration by a commercially pre-filled elastomeric device, continuous intravenous infusion (CIVI) of piperacillin with tazobactam or flucloxacillin with elastomeric device as outpatient once daily and, specifically for bone and joint and diabetic foot infections, complex outpatient oral antibiotic therapies.

Results Base case and a range of scenario results from the analysis showed all evaluated OPAT service delivery models to be consistently less costly than inpatient stay of equivalent duration across a range of key infections in the UK. Main costs of OPAT were associated with staff time and antimicrobial medications. The extent of savings associated with OPAT varies with selected models of healthcare delivery.

Conclusions OPAT is a cost-effective use of National Health Service (NHS) resources for the treatment of a range of infections in the UK in patients who can be safely managed in a non-inpatient setting.

Strengths and limitations of this study

- First study to use a bottom-up costing approach applied across a range of infections and healthcare delivery models in OPAT using UK-specific registry data
- First study to compare the cost of various models of care in OPAT with inpatient stay
- Base case results were consistent across a range of scenario analyses
- Assumed equivalence in OPAT and inpatient outcomes and between different OPAT models of care is associated with some uncertainty
- There are uncertainties in the quantification of some indirect OPAT costs (and their contribution to each OPAT model) and with inpatient bed day costs stay

INTRODUCTION

Outpatient parenteral antimicrobial therapy (OPAT) is a well-established and safe method of delivering intravenous antimicrobial therapy to carefully selected patients in whom other aspects of care can be addressed without hospitalisation.[1] [2] The British Society of Antimicrobial Chemotherapy (BSAC) have developed good practice recommendations for safe adult and paediatric OPAT practice and clinical governance including promotion of antimicrobial stewardship.[2] The recommendations acknowledged that a variety of OPAT delivery models were available and widely practised in the UK including home or clinic administration, administration by nurse or self/carer and administration via bolus or infusion. In 2015 BSAC launched the National Outcomes Registry System (NORS) for UK OPAT services in order to describe the OPAT landscape (including infections treated and antimicrobials used) and to enable participating centres to benchmark practice and outcomes.[3] Despite popularity and growth in OPAT practice in the UK, funding/reimbursement of OPAT has been inconsistent and as a result OPAT has not been uniformly established. A previous publication attempted to describe cost-effectiveness of OPAT in a tariff based UK health model for a single condition (cellulitis).[4] Herein we estimate OPAT related costs for a number of key indicator conditions utilising different established OPAT delivery models and compare with reference inpatient costs. The analysis also set out to take into account evolution of practice with greater use of supervised complex oral antibiotic therapies within the OPAT setting.[5]

METHODS

The costs of six OPAT healthcare delivery models were estimated and compared against the cost of equivalent duration of inpatient stay for six key infection categories typically managed via OPAT in the UK. Based on available clinical evidence and clinical expert opinion, equivalence in patient outcomes was assumed for OPAT and inpatient stay as well as for the different models of healthcare delivery in OPAT.[6-8] A cost-minimisation analysis was therefore

deemed appropriate. A list of detailed costing model assumptions primarily based on the BSAC updated good practice recommendations[2] and clinical expert opinion is available in the supplementary materials (Table S1).

NORS data

The cost-minimisation analysis used five years of retrospective data relating to 21,632 adult treatment episodes collected from 57 OPAT centres (44 in England, 5 in Scotland, 4 in Wales and 4 in Northern Ireland), that all reported to NORS[3] (Table 1). In the cost-minimisation model, patients were treated in OPAT for one of six broadly defined infection categories, representing approximately 82% of primary OPAT diagnoses recorded in NORS. These were infections requiring short-term (up to 7 days) antimicrobial treatment such as skin and soft tissue infections including cellulitis (SSTI) and complex urinary tract infections (UTI) (including drug resistant lower UTI and pyelonephritis) or longer-term antimicrobial treatment such as bone and joint (including spinal, native osteomyelitis and orthopaedic metal work associated infections), diabetic foot infections (both osteomyelitis and complex soft tissue infections), bronchiectasis, and intra-abdominal infections (including liver abscess and other abdominal and pelvic infections)(Table S2).

Table 1 Average duration and total number of treatment episodes in OPAT for six categories of infection

Condition	Average duration (days)	Total number	Source
SSTI	6.4	7,371	NORS 2015-19 (UK)[3]
Complex UTI	7.0	1,896	
Bone-Joint	27.8	5,355	
Diabetic foot	28.3	1,797	
Bronchiectasis	11.0	4,096	
Intra-abdominal	22.2	1,117	

SSTI, skin and soft tissue infections; UTI, urinary tract infections; NORS, National Outcomes Registry System

OPAT healthcare delivery models

The OPAT models considered were based on those currently practiced in the UK: outpatient clinic model, nurse home visits, self (or carer)-administration by a bolus IV, self-administration via an elastomeric device including continuous intravenous infusion (CIVI) of piperacillin with tazobactam or flucloxacillin and (for bone and joint or diabetic foot infections) complex outpatient antibiotic therapy (COpAT). Only suitable healthcare models were considered for the treatment of each of the six conditions in OPAT.

The care pathway for the outpatient clinic model requires a patient to travel daily to the OPAT unit following an initial assessment in hospital. At the clinic, an OPAT nurse prepares and administers antimicrobial medication intravenously by bolus IV. The nurse home visit model entails a specialist nurse (or a community based nurse) travelling to the patient's home instead.

The self-administration model of OPAT care requires the patient (or carer) to administer the antimicrobials at home, without the need to travel to hospital or for a nurse to visit on a daily basis. It is assumed that prior to commencing antimicrobial self-administration, patients (or their carers) receive on average three training sessions (60 minutes each with a nurse) on how to safely prepare and administer their medication through a peripherally inserted central catheter (PICC) line using a bolus IV. It is further assumed that only one training session is required for patient/carer administration of pre-prepared medication via an elastomeric home infusion device which only needs to be connected to and disconnected from the PICC line correctly. The patient is discharged with the necessary consumables (e.g. a leaflet of instructions, syringes, needles, 70% alcohol wipes, 0.9% sodium chloride ampoules, sharps bin, vials with medication powder for infusion, etc.) and is given a contact number related to the OPAT service for use if any problems occur out of hours. On the occasion where an elastomeric pump is used for self-administration, these are commercially pre-filled devices due to safety issues regarding the process of reconstituting drugs into elastomeric devices outside of an aseptic unit and the associated reduction in shelf life (approximately 24 hours). A continuous intravenous infusion (CIVI) model of service delivery in OPAT involves reconstitution of drugs into elastomeric devices by hospital staff with piperacillin with tazobactam or flucloxacillin on the same day of administration with the patient visiting clinic once daily.[9 10]

Patients referred to OPAT with bone and joint infections (e.g. diabetic foot and orthopaedic infections) are increasingly considered for suitability for discharge on supervised complex oral therapies as an alternative to "traditional" OPAT IV therapy. Suitable patients may be commenced directly onto supervised oral antimicrobial treatment which frequently requires enhanced monitoring due to potentially serious adverse events (e.g. linezolid or combination oral antibiotic regimens).[5]

In all OPAT models where treatment is required for > 1 week patients will also attend the OPAT clinic once weekly as a minimum and management/progress will be reviewed via a weekly virtual multi-disciplinary meeting.[2]

Antimicrobials

Antimicrobial medications with a lower frequency of administration compared with inpatient care are primarily selected for use in OPAT. In the analysis, the type and distribution of antimicrobial medicines are based on clinical expert opinion and the most prevalent agents used within the NORS database (Table S3).

Antimicrobial medicines which require more than once daily administration (e.g. piperacillin with tazobactam, flucloxacillin, temocillin, ceftazidime and meropenem) would be primarily administered by the patient or carer. However, if an antibiotic is stable to degradation in the outpatient setting (piperacillin with tazobactam and flucloxacillin), patients may receive the antibiotic via a 24-hour continuous infusion (CIVI) via an elastomeric device as an outpatient requiring once daily attendance. All other antimicrobial medicines where data on stability are either not available or are not compatible with 24-hour infusion may be administered with bolus IV or 30 minute IV infusion.

Re-hospitalization

The cost-minimisation model assumed hospital re-admission to occur in 6.4% of treatment episodes in OPAT.[7] Re-hospitalised patients were assumed to only spend 50% of the duration of their treatment episode in OPAT.

Costs

Costs considered in the analysis included specialist staff time (specialist nurses, infectious diseases consultant, and specialist antimicrobial/ clinical pharmacist), antimicrobial medications, elastomeric infusion devices (empty or commercially pre-filled), consumables, laboratory tests and the cost of travel to and from the OPAT clinic where necessary (Tables S4-6). Additionally, costs of re-hospitalisation for patients in OPAT have been included. A daily "overhead" cost per patient to account for administration and support costs of using a healthcare service consistent with published literature has also been assumed in the analysis.[8]

Costs were obtained from various sources. These included the Personal and Social Services Research Unit (PSSRU)[11], British National Formulary (BNF)[12], drugs and pharmaceutical electronic market information tool (eMIT)[13], National Procurement Scotland, Information Services Division (ISD) Scotland cost book[14] and NHS England reference costs[15].

An appropriate healthcare resource group (HRG) code[15] was identified for each diagnosis to account for costs of inpatient care (Table S7). Costs were based on a weighted average of excess bed day costs as elective and non-elective inpatient stay across various severity levels. No potential additional hospital costs were included.

RESULTS

Base case results from the cost-minimisation analysis are presented as estimated average cost per treatment episode in inpatient care and models of OPAT healthcare delivery, as well as cost of OPAT as a percentage of the estimated cost of inpatient stay (Tables 2 and 3)

Infections requiring short-term treatment

Skin and soft tissue infections (SSTI)

In the cost-minimisation analysis, patients attending once daily for the duration of antimicrobial treatment, were primarily treated with IV ceftriaxone, but also with teicoplanin and daptomycin (for betalactam allergy). Treatment with the same medicines was assumed in the specialist nurse visit model. A small number of patients could also be treated with dalbavancin 1g as a one-off dose, consistent with clinical practice for patients

unable to attend for daily treatment. Patients who were offered an elastomeric home infusion device were primarily treated with ceftriaxone once daily and less often with flucloxacillin as 24h (CIVI). Dependant on the OPAT service delivery model, the cost of treating patients with SSTI was estimated in the range of 25%-51% of the cost of inpatient stay for the equivalent duration of treatment.

Complex urinary tract infections (UTI)

In the analysis, patients were primarily treated with ertapenem (90%) and a minority of patients were treated with temocillin. It was assumed that patients attending daily or treated by a nurse at home were only given ertapenem due to twice daily dosing of temocillin. Both antibiotics can be self-administered using either short infusion or IV bolus respectively. No patients were assumed to be treated using home infusion elastomeric devices. Dependant on the OPAT service delivery model, the cost of treating patients with complex UTI was estimated in the range of 34%-46% of the cost of inpatient stay for the equivalent duration of treatment.

Infections requiring longer-term treatment

Orthopaedic infections

Patients with orthopaedic infections were assumed to be treated once daily with ceftriaxone, teicoplanin or ertapenem in the outpatient visit, nurse home visit and self-administration () OPAT service delivery models. Ceftriaxone was the only antimicrobial used for self-administration via commercially pre-filled elastomeric device. An analysis is also presented where patients were treated with oral therapies only or assuming IV to oral switch at different time points during supervised outpatient therapy. Dependant on the OPAT service delivery model (excluding oral therapies), the cost of treating patients with orthopaedic infections was estimated in the range of 22%-41% of the cost of inpatient stay for the equivalent duration of treatment. Additionally, a movement in treatment practice from IV to oral antibiotics could results in treatment cost of 13% to 24% of the cost of inpatient stay, dependent on how early a patient is switched to oral therapy.

Diabetic foot infections

Similarly to orthopaedic infections, patients with diabetic foot infections were assumed to be treated with ceftriaxone, ertapenem and teicoplanin, although the proportion of patients treated with each agent varied. All antimicrobial medicines are suitable for once daily administrations. The cost of treatment in OPAT was estimated in the range of 22%-42% of the cost of inpatient stay for the equivalent duration of treatment. Additionally, a movement in treatment practice from IV to oral antibiotics could results in treatment cost of 13% to 26% of the cost of inpatient stay, dependent on how early a patient is switched to oral therapy.

Bronchiectasis

In the analysis, patients were assumed to be treated with either ceftazidime, meropenem or piperacillin with tazobactam. All medications are suitable for IV self-administration with either a bolus or 30 minute infusion. Only piperacillin with tazobactam was assumed to be administered with an elastomeric device via 24 hour continuous infusion in an outpatient setting (CIVI). The per-episode estimated cost for the same treatment plan with a visiting nurse is also presented. Since all of these medications require more than once daily administration or continuous daily administration, the general outpatient daily visits and nurse home visits OPAT service models are highly unlikely to be used in clinical practice so the results from CIVI models are presented instead. The estimated per treatment episode cost is in the range of 40%-56% of the cost of inpatient stay and varies with selected OPAT model of care.

Intra-abdominal infections

In the cost-minimisation analysis, patients were primarily treated with ertapenem or piperacillin with tazobactam. The latter was assumed to be used only in patients who were suitable for self-administration or attend daily for change of elastomeric device (CIVI). Patients who visit daily for IV infusions or receive nurse visits were assumed to only be treated with ertapenem. The estimated per treatment episode cost is in the range of 25%-42% of the cost of inpatient stay and varies with selected OPAT model of care.

Table 2 Base case results – intravenous infusions

	Cost per treatment episode											
Condition	**SSTI**		**Complex UTI**		**Orthopaedic -Bone and joint**		**Diabetic foot**		**Bronchiectasis**		**Intra-abdominal**	
Model of care												
Inpatient stay	£2,476	-	£2,104	-	£8,279	-	£8,428	-	£3,269	-	£7,124	-
OPAT - once daily visits	£631	25%	£758	36%	£2,506	30%	£2,671	32%	-	-	£2,312	32%
OPAT - specialist nurse daily home visit	£831	34%	£977	46%	£3,375	41%	£3,556	42%	£1,839	56%	£3,006	42%
OPAT - self-administration - IV bolus	£566	23%	£720	34%	£1,855	22%	£2,006	24%	£1,301	40%	£1,811	25%
OPAT - self-administration - elastomeric device	£611	25%	-	-	£2,394	29%	£2,433	29%	£1,588	49%	£2,952	41%
OPAT - elastomeric device (CIVI; outpatient)	£802	32%	-	-	-	-	-	-	£1,495	46%	£2,807	39%
OPAT - once-off dalbavancin (1g)	£1,266	51%	-	-	-	-	-	-	-	-	-	-

SSTI, skin and soft tissue infections, UTI, urinary tract infections; OPAT, outpatient parenteral antimicrobial therapy; IV, intravenous; CIVI, continuous intravenous infusion;

Table 3 Base case results – oral antimicrobials for orthopaedic and diabetic foot infections

Condition	**Orthopaedic/ Bone and joint**		**Diabetic foot**	
Model of care				
Inpatient stay	£8,279		£8,428	
OPAT - Oral 100%	£1,114	13%	£1,089	13%
OPAT - Oral 25%; 75% IV	£2,009	24%	£2,161	26%
OPAT - Oral 50%; 50% IV	£1,710	21%	£1,816	22%
OPAT - Oral 75%; 25% IV	£1,410	17%	£1,470	17%

OPAT, outpatient parenteral antimicrobial therapies; IV, intravenous;

Scenario analyses

In scenario analyses described in table 4, certain modelling assumptions were challenged to assess impact on results in the outpatient setting model. Detailed scenario analysis results are provided in supplementary table 8.

Table 4 Scenarios: OPAT outpatient vs inpatient stay

	Scenario	Base case
0	Base case (outpatient)	
1	Using cost of inpatient care in infectious disease unit (ISD Scotland)[14]	Using condition-specific healthcare resource group (HRG) costs [15]
2	Using ISD Scotland[14] cost for outpatient appointments and inpatient stay (IDU)	Using micro-costing of nurse and consultant outpatient appointments
3	Assuming overheads are 44.8% of total costs consistent with a published source[16]	Assuming per day cost of using healthcare services consistent with a published source[8]
4	Using BNF[12] as a source for the cost of linezolid (orthopaedic and diabetic foot infections)	Using eMIT[13] as a source for the cost of linezolid (orthopaedic and diabetic foot infections)
Skin and soft tissue infections only		
5	Including the cost of consultant time	Nurse-led condition; no consultant time
6	Using the licensed dose of dalbavancin (1.5g) once off	Using dalbavancin 1g as a once-off treatment consistent with clinical practice
7	Using the licensed dose of dalbavancin 1g followed by 0.5g	Using dalbavancin 1g as a once-off treatment consistent with clinical practice

ISD, information services division; IDU, infectious disease unit; BNF, British National Formulary; eMIT, electronic market information tool;

Results from scenarios 1 and 2 (costs ranging between 21% and 34% of inpatient costs) are consistent, although lower than base case (25%-44%) across all infection categories due to the higher cost per bed day generally associated with an infectious disease unit.

Given the modelling approach, one of the uncertainties comes from the extent of model-specific per-patient overhead costs (scenario 3). The uncertainty is especially relevant to the outpatient clinic model. One study[16] reported overall overhead and support costs in the outpatient department of their infectious disease unit (IDU) to be 44.8% of total costs excluding re-hospitalization. When the equivalent assumption was made in the outpatient clinic model, the cost of treatment episode in OPAT did not increase over 52% of the cost of

inpatient stay, except for bronchiectasis (77%) which is treated with continuous intravenous infusion with elastomeric device as an outpatient visit once daily in the analysis which is generally associated with higher cost.

There are uncertainties around the source of cost for linezolid for the oral treatment of orthopaedic and diabetic foot infections (scenario 4). The cost reported in the British National Formulary[12] is substantially higher than what clinicians have advised and also reported in the electronic market information tool (eMIT)[13] which has been used in the base case analysis. Using the higher cost of linezolid results in the cost of oral therapies increasing from 13% to 21% of the cost of inpatient stay.

Additionally, variations in the treatment protocol with dalbavancin seems to have the highest impact on costs of treatment of skin and soft tissue infections in OPAT due to the high medicine acquisition cost (scenarios 6 and 7). Treatment with dalbavancin can be as costly as 74-76% of the cost of inpatient stay.

DISCUSSION

Although OPAT has been developing in the UK over the last 25 years, and despite the clinical benefits of avoiding hospitalisation and keeping care closer to home, there remains wide variation in OPAT availability and inconsistency in funding/commissioning of services in the UK. It is possible that OPAT may be perceived as an additional healthcare cost and this could be a significant barrier to more systematic support for service development. This study therefore set out to systematically detail OPAT costs and compare with inpatient costs for key OPAT-treated conditions. To our knowledge, a detailed costing of various OPAT healthcare delivery models in a UK setting has not been published before. Nevertheless, results are consistent with previous studies where overall cost of OPAT have been reported and/or compared with the cost of inpatient care.[6 16-18] Key findings are that the self (or care)-administration model of care was associated with the lowest cost and nurse home visits generally had the highest estimated cost per treatment episode across all conditions evaluated. From all available OPAT models for patients with skin and soft tissue infections, treatment with a single dose of dalbavancin was estimated to have the highest cost.

However, only a small proportion of patients (an estimated 5%) are expected to be treated with dalbavancin in clinical practice. As expected, oral therapies were the lowest cost treatment option for patients with orthopaedic (bone and joint) or diabetic foot infection. If patients are switched from IV as outpatient to oral therapies at least half way through their treatment duration, the results show the cost of treatment episode to be lower than the cost of self-administering IV antimicrobials for the whole treatment duration.

The cost-minimisation analysis found all OPAT service delivery models to be consistently associated with lower cost than inpatient stay of equivalent duration across a range of conditions in the UK NHS. The analysis shows the potential of OPAT to provide quality health care for suitable patients in an outpatient setting at a fraction of the cost of inpatient care. When the 4 most frequently used OPAT models of care (outpatient clinic, nurse home visit self (carer)-administration (bolus IV or elastomeric device) are considered individually, using NORS UK data[3], the 5-year estimated savings to the UK National Health Service (NHS) associated with treatment in OPAT was found to be in the range of £60-77 million (Table S9). It should be noted that these data only relate to 57 OPAT services and many have not contributed data consistently for all 5 years (data not shown). The estimated cost savings to the NHS through systematic roll out of OPAT therefore is likely to be considerably higher.

Strengths of the presented analysis include a bottom-up costing approach applied across a range of infections, and healthcare delivery models in OPAT using UK-specific registry data. Furthermore, each of these estimated costs were compared against the cost of inpatient care in a UK setting and a comprehensive list of scenario analyses showed consistency with base case findings. However, the study also had some limitations. The assumption of equivalence in patient and treatment outcomes for OPAT and inpatient care as well as among various models of care in OPAT is based on published systematic reviews [6-8] but direct comparative evidence is lacking. Furthermore, there was one study [8] to suggest that a specialist nurse visit model is generally associated with better outcomes compared with other healthcare delivery models in OPAT. A published source was used for the cost of inpatient stay which is inconsistent with the bottom-up costing approach undertaken for the cost of OPAT.[15] The assumption of cost of bed day in the analysis to be equivalent to the cost of excess bed days, as reported in NHS England Reference costs[15], is also associated with uncertainties due to the structure of the reimbursement system in NHS England (e.g.

the presence of trim points). Nevertheless, this is considered to be the most suitable published source of costs of inpatient stay as it provides cost estimates for each of the six infection categories in the analysis. Lastly, the estimated average costs per treatment episode in OPAT aim to reflect existing OPAT services and thus set-up and implementation costs have not been included.

It is important to note that most OPAT services will not rely on one particular delivery model and that individual patient factors such as, ability to self-administer or to attend the OPAT clinic, and choice of antimicrobial, will be the major determinants of the delivery model used. The data presented necessarily incorporate multiple variables to allow for variation based on patient need.

OPAT is primarily about delivering high quality patient centered care closer to home whilst avoiding inherent risks associated with hospitalisation. These positive health economic findings should be utilised by OPAT clinician/practitioners, healthcare managers and policy makers alongside the already powerful clinical effectiveness and patient safety data to drive further OPAT development in the UK.

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REFERENCES

1. Chapman ALN. Outpatient parenteral antimicrobial therapy. *BMJ* 2013;346:f1585.
2. Chapman ALN, Patel S, Horner C, 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)
3. British Society for Antimicrobial Chemotherapy. National Outcomes Registry System (NORS) c2019 [2020 Oct 26]. Available from: https://www.e-opat.com/opat-registry/.
4. Jones GR, Cumming DV, Honeywell G, et al. How is income generated by outpatient parenteral antibiotic treatment (OPAT) in the UK? Analysis of payment tariffs for cellulitis. *Journal of Antimicrobial Chemotherapy* 2015;70(4):1236-40.
5. Seaton RA, Ritchie ND, Robb F, et al. From 'OPAT' to 'COpAT': implications of the OVIVA study for ambulatory management of bone and joint infection. *J Antimicrob Chemother* 2019;74:2119-21.
6. Mitchell ED, Czoski Murray C, Meads D, et al. Clinical and cost-effectiveness, safety and acceptability of community intravenous antibiotic service models: CIVAS systematic review. *BMJ Open* 2017;7(4):e013560. doi: 10.1136/bmjopen-2016-013560 [published Online First: 2017/04/22]
7. Sriskandarajah S, Hobbs J, Roughead E, et al. Safety and effectiveness of 'hospital in the home' and 'outpatient parenteral antimicrobial therapy' in different age groups: A systematic review of observational studies. *Int J Clin Pract* 2018:e13216. doi: 10.1111/ijcp.13216 [published Online First: 2018/06/20]
8. Minton J, Murray CC, Meads D, et al. The Community IntraVenous Antibiotic Study (CIVAS): a mixed-methods evaluation of patient preferences for and cost-effectiveness of different service models for delivering outpatient parenteral antimicrobial therapy. *NIHR Journals Library Health Services and Delivery Research* 2017;02:02.
9. Allwood MC, Stonkute D, Wallace A, et al. Assessment of the stability of citrate-buffered flucloxacillin for injection when stored in two commercially available ambulatory elastomeric devices: INfusor LV (Baxter) and Accufuser (Woo Young Medical): a study compliant with the NHS Yellow Cover Document (YCD) requirements. *Eur J Hosp Pharm* 2018;27(2):90-4.
10. Jamieson C, Ozolina L, Seaton RA, et al. Assessment of the stability of citrate-buffered piperacillin/tazobactam for continuous infusion when stored in two commercially available

elastomeric devices for outpatient parenteral antimicrobial chemotherapy: a study compliant with the NHS Yellow Cover Document requirements. *Eur J Hosp Pharm* 2020
11. PSSRU. Unit costs of health and social care 2020 [2020 October 28]. Available from: https://www.pssru.ac.uk/project-pages/unit-costs/.
12. BNF: British national formulary 2020 [2020 October 28]. Available from: https://bnf.nice.org.uk.
13. Department of Health. Drugs and pharmaceutical electronic market information tool (eMIT) 2020 [2020 October 28]. Available from: https://www.gov.uk/government/publications/drugs-and-pharmaceutical-electronic-market-information-emit#:~:text=National%20Health%20Service-,Drugs%20and%20pharmaceutical%20electronic%20market%20information%20tool%20(eMIT),generic%20drugs%20and%20pharmaceutical%20products.
14. Public Health Scotland. Cost books 2018/19 2019 [2020 October 28]. Available from: https://www.isdscotland.org/Health-Topics/Finance/Costs/Detailed-Tables/.
15. NHS Digital. Reference costs: 2019-20 reference costs collection 2020 [2020 October 28]. Available from: https://digital.nhs.uk/data-and-information/data-collections-and-data-sets/data-collections/reference-costs.
16. Chapman ALN, Dixon S, Andrews D, et al. Clinical efficacy and cost-effectiveness of outpatient parenteral antibiotic therapy (OPAT): a UK perspective. *J Antimicrob Chemother* 2009;64:1316-24.
17. Durojaiye OC, Bell H, Andrews D, et al. Clinical efficacy, cost analysis and patient acceptability of outpatient parenteral antibiotic therapy (OPAT): a decade of Sheffield (UK) OPAT service. *International Journal of Antimicrobial Agents* 2018;51(1):26-32.
18. Seaton RA, Johal S, Coia JE, et al. Economic evaluation of treatment for MRSA complicated skin and soft tissue infections in Glasgow hospitals. *European Journal of Clinical Microbiology & Infectious Diseases* 2014;33(3):305-11.

Supplementary materials:

Table S1 Costing model assumptions

No	Assumption	Source/Justification
1	All patients with long term infections are assessed on admission and upon discharge by a specialist consultant. Patients spend 30 minutes with a specialist consultant and 1h with a nurse at initial and final assessment.	BSAC good practice recommendations (3.1-3.15); communication with clinical experts in OPAT.
2	Skin and soft tissue infections are a nurse-led condition unless patient is treated with dalbavancin.	BSAC good practice recommendations (3.1-3.15); communication with clinical experts in OPAT.
3	All patients with complex UTI are assessed by a consultant once.	BSAC good practice recommendations (3.1-3.15); communication with clinical experts in OPAT.
4	All patient are allocated 15 minutes of pharmacist time per treatment episode.	BSAC good practice recommendations (3.1-3.15); communication with clinical experts in OPAT.
5	Laboratory tests including UE, LFT, FBC, C-reactive protein are done at initial and final assessment and once weekly for longer-term infections. Patients treated with teicoplanin receive weekly teicoplanin levels blood tests.	BSAC good practice recommendations (4.4); personal communication with clinical experts in OPAT. Type of tests might vary with the choice of antimicrobial
6	All patients requiring longer term treatment (more than 7 days), are assessed weekly at a MDT meeting. This is approx. 5 minutes of consultant, pharmacist and specialist nurse time per patient.	BSAC good practice recommendations (4.2); personal communication with clinical experts in OPAT
7	Each daily visit to outpatient clinic lasts 40 minutes during which a band 6 nurse examines the patient, prepares and administers medication. A nurse visiting patient's home would spend the equivalent amount of time.	Personal communication with clinical experts in OPAT This might be a conservative approach given that some antimicrobials are administered in 2-3 minutes.
8	Patients with infections requiring longer-term treatment who self-administer, visit the clinic once weekly for a check-up with a nurse and to have blood work done.	BSAC good practice recommendations (4.3); assumption
9	Patients who self-administer with bolus IV receive 3 training sessions with a nurse (50:50 split band 5/band 6), each lasting 1 h. Patients who self-administer with elastomeric device receive 1 training session.	Personal communication with clinical experts in OPAT. Assumption BSAC good practice recommendations (3.13);

10	Single-use elastomeric devices administered in an outpatient setting (CIVI) are filled up by hospital staff (approximately 15 minutes of nurse's time).	Assumption; Expert opinion;
11	Single-use elastomeric devices used for self-administration are commercially pre-filled.	Assumption; Expert opinion;
12	Consumables: each patient receives 1 PICC line; per administration: 1 apron, 1 pair of gloves, 4 needles, 4 syringes, 1 pre-injection swab, 3 0.9% sodium chloride ampoules;	Personal communication with clinical experts in OPAT. Assumption Varies with method of administration
13	A nurse travelling to patients home would spend 33 minutes (non-patient contact time) per journey travelling with an ambulance car (£10.63 per journey). This is approximately 11 miles per journey.	ISD Cost book for Scotland. This is an approximation due to lack of available data for distances travelled in OPAT. Distance travelled varies with geographic location. Longer distances might be travelled in the Highlands and islands in Scotland. It was assumed that this estimate for Scotland is relevant to UK.
14	Type and distribution of medicines for each condition in the analysis are based on clinical expert opinion	NORS data do not link conditions to antimicrobials.
15	Cost of linezolid comes from eMIT; all other costs of antimicrobials come from the BNF (cheapest tariff)	A generic version of linezolid is used in OPAT but this is not reflected in the BNF. The BNF cost is substantially higher.
16	Antimicrobials requiring more than once daily administration (temocillin, ceftazidime, meropenem and piperacillin with tazobactam) are assumed to be self-administered (bolus IV) only.	More than once daily visit (hospital or nurse home visit) in OPAT are not primarily available options in clinical practice.
17	Piperacillin with tazobactam, flucloxacillin and ceftriaxone are administered with commercially pre-filled elastomeric device in the six conditions included in the analysis. Only piperacillin with tazobactam and flucloxacillin can be administered with elastomeric device filled up by hospital staff.	BSAC good practice recommendations (3.12); Clinical expert opinion;
18	For bronchiectasis: patients can travel daily to outpatient clinic for piperacillin with tazobactam (with buffered saline) to be administered as continuous IV with elastomeric device; Although the same model of care with piperacillin with tazobactam is available for the treatment of intra-abdominal infections, for simplicity only ertapenem was assumed to be used if patients attend clinic daily in the outpatient service delivery model. A CIVI as outpatient model is shown separately.	An assumption was made that if a patient attends the OPAT clinic daily or is visited by a nurse, the cheapest treatment option will be used in clinical practice. In the case of treating intra-abdominal infections, ertapenem once daily is cheaper than continuous piperacillin with tazobactam with elastomeric device. In patients with bronchiectasis, continuous piperacillin with tazobactam with elastomeric device is the only treatment option in the hospital or nurse daily visits OPAT service delivery models.

19	The cost of empty elastomeric devices is based on the average cost of 2 commercially available devices assuming equal market share	BSAC good practice recommendations (3.12); Clinical expert opinion;
20	A patient would spend the equivalent amount of time in hospital care in absence of OPAT	Clinical expert opinion
21	A patient has a small probability (0.064) to be re-admitted to hospital half-way during their treatment in OPAT	Clinical effectiveness data; Clinical expert opinion
22	Condition-specific HRG cost per excess bed day in hospital to estimate the cost of inpatient stay	The true cost per day of inpatient stay of patients who are eligible for OPAT is unknown. NHS England reference costs are considered a standard source of cost estimates associated with certain diagnoses or interventions. However, costs are presented as per episode of average treatment duration and cost of excess bed days if treatment goes beyond the expected treatment duration (trim point). Due to lack of better evidence, excess bed day costs were considered the best source of costs of inpatient stay for the purposes of this analysis. Condition-specific costs were selected to allow for granularity. However, costs were similar so assuming the same cost for each condition is also a reasonable assumption.

BSAC, British Society for Antimicrobial Chemotherapy; OPAT, Outpatient Parenteral Antimicrobial Therapy ; UTI, urinary tract infections ; UE, urea and electrolytes; LFT, liver function test; FBC, full blood count; MDT, multi-disciplinary team; IV, intravenous ;CIVI, continuous intravenous infusion; ISD, information services division; PICC, peripherally inserted central catheter ; HRG, health resource group ;eMIT, electronic market information tool ; BNF, British National Formulary ;

Table S2 Breakdown of infection categories

Infection category	Infection included in this category
Skin and soft tissue infections	Cellulitis
	Other skin and soft tissue infections
Orthopaedic infections (bone and joint)	Prosthetic joint infection (knee)
	Osteomyelitis – native
	Prosthetic joint infection (hip)
	Osteomyelitis - surgically related
	Discitis/vertebral osteomyelitis
	Prosthetic joint infection (other)
	Discitis/vertebral osteomyelitis - device related
	Osteomyelitis (other)
Diabetic foot infections	Osteomyelitis - diabetic foot
	Diabetic foot infection - no osteomyelitis

Complex urinary tract infections	Drug resistant lower urinary tract infections and pyelonephritis
Bronchiectasis	Bronchiectasis
	Other complex respiratory tract infection
Intra-abdominal infections	Gastro-intestinal infection
	Hepatic abscess
	Pelvic abscess

Table S3 Condition-specific antimicrobials in OPAT

Condition	Medication	Distribution
Skin and soft tissue infections (IV)	Ceftriaxone	75%
	Teicoplanin	10%
	Daptomycin	5%
	Flucloxacillin	5%
	Dalbavancin	5%
Orthopaedic; Bone-Joint (IV)	Ceftriaxone	60%
	Teicoplanin	30%
	Ertapenem	10%
Orthopaedic; Bone-Joint (oral)	Ciprofloxacin/Rifampicin	25%
	Levofloxacin/Rifampicin	12.50%
	Co-trimoxazole/Rifampicin	12.50%
	Clindamycin/Rifampicin	12.50%
	Linezolid/ciprofloxacin	12.50%
	Linezolid	25%
Diabetic foot (IV)	Ceftriaxone	45%
	Teicoplanin	10%
	Ertapenem	45%
Diabetic foot (oral)	Clindamycin/Doxycycline	25%
	Clindamycin/Co-trimoxazole	12.50%
	Clindamycin/Ciprofloxacin	12.50%
	Linezolid/ciprofloxacin	12.50%
	Ciprofloxacin/Doxycycline	25.00%
	Levofloxacin/Doxycycline	12.50%
Complex urinary tract infections (IV)	Ertapenem	90%
	Temocillin	10%
Bronchiectasis (IV)	Ceftazidime	70%
	Piperacillin with tazobactam	15%
	Meropenem	15%
Intra-abdominal (IV)	Ertapenem	75%
	Piperacillin with tazobactam	25%

IV, intravenous;

Table S4 Unit costs of resources used in OPAT services

Item	Unit cost	Notes	Source
Medical consultant	£109	Per working hour	PSSRU,2019
Pharmacist band 8a	£67	Per working hour	PSSRU,2019
Nurse band 6	£47	Per working hour	PSSRU,2019
Nurse band 5	£38	Per working hour	PSSRU,2019
Antimicrobial medicine (IV)	Variable*	Condition-specific	BNF,2020, eMIT, 2020
Antimicrobial medicine (oral)	Variable*	Condition-specific	BNF,2020, eMIT, 2020
Laboratory tests	£8	UE,LFT,CRP and FBC	ISD Cost book,2020
Laboratory tests (specialist)	£47	Teicoplanin levels	Expert
Consumables - PICC line	£36	Per patient	National Procurement
Consumables - Butterfly needle	£1	Per administration	National Procurement
Consumables (other)	£1.65	Single use; apron, needles, syringe, pre-injection swab	National Procurement
Elastomeric device; empty	£31	Based on equal market share of two devices (single use)	National Procurement
Elastomeric device; commercially pre-filled (piperacillin with tazobactam; flucloxacillin)	£90	Per administration	Expert
Elastomeric device; commercially pre-filled (ceftriaxone)	£45	Per administration	Expert
Buffered saline	£2	Per administration	Expert
Nurse travel	£11	Per journey - based on average travel of 11 miles	ISD Cost book,2020
Patient transport service	£42	Per journey - based on average travel of 11 miles	ISD Cost book,2020
General cost of using healthcare services (inflated)	£13	Per patient; per day (inflated to 2019 prices using the NHS cost inflation index)	Minton, 2017[3]

*See tables S5 and S6 for costs of antimicrobials in OPAT

UE, urea and electrolytes; LFT, liver function test; CRP, c-reactive protein test; FBC, full blood count; PSSRU, Personal Social Services Research Unit; BNF, British National Formulary; eMIT, electronic market information tool; ISD, Information Services Division

Table S5 Intravenously administered antimicrobials in OPAT

Medicines (IV) - BNF	Dose in OPAT	Frequency of administration	Cost per pack	Source
Ceftriaxone	2g	Once daily	£19.18	BNF, 2020

Teicoplanin	600mg	Once daily or 1200mg; 3 times per week	£3.93	BNF, 2020
Daptomycin	700mg	Once daily	£60.00	BNF, 2020
Flucloxacillin	8g	24h infusion	£6.00	BNF, 2020
Dalbavancin	1000 mg	One-off	£558.70	BNF, 2020
Ertapenem	1g	Once daily	£31.65	BNF, 2020
Temocillin	2g	every 12 h	£25.45	BNF, 2020
Ceftazidime	2g	3 times a day	£17.59	BNF, 2020
Piperacillin with tazobactam	4.5g/18g	4 times per day/24h infusion	£76.50	BNF, 2020
Meropenem	1g	0.5-1g every 8 hours	£186.70	BNF, 2020

IV, intravenous; BNF, British National Formulary

Table S6 Oral antimicrobials for the treatment of orthopaedic and diabetic foot infections in OPAT

Medicines (oral)	Dose in OPAT	Frequency of administration	Cost per pack	Source
Ciprofloxacin	750mg	every 12h	£8.00	BNF,2020
Levofloxacin	500mg	every 12h	£24.50	BNF,2020
Co-trimoxazole	960mg	every 12h	£23.48	BNF,2020
Clindamycin	600mg	every 8h	£38.23	BNF,2020
Linezolid	600mg	every 12h	£7.48	eMIT,2020
Linezolid	600 mg	every 12h	£327.24	BNF, 2020
Doxycycline	100mg	every 12h	£1.64	BNF,2020
Rifampicin	400mg	every 12h	£123.60	BNF,2020
Rifampicin	50mg	every 12h	£54.69	BNF,2020

BNF, British National Formulary

Table S7 Condition-specific healthcare resource group (HRG) and bed-day cost of inpatient stay

Condition	HRG code	Description	Cost	Source
SSTI	HD21 D-H	Soft Tissue Disorders with CC Score 0-12+	£387	NHS England Reference costs,2019
Complex UTI	LA04 N-S	Kidney or Urinary Tract Infections, without Interventions, with CC Score 0-13+	£301	
Orthopaedic /Diabetic foot infections	HD25 D-H	Infections of Bones or Joints, with CC Score 13+	£298	
	HE81 A-C	Infection or Inflammatory Reaction, due to, Internal Orthopaedic Prosthetic Devices, Implants or Grafts, with CC Score 0-13+		
Bronchiectasis	DZ23 M-N	Bronchopneumonia without Interventions, with CC Score 0-10	£297	
Intra-abdominal	FD01 F-J	Gastrointestinal Infections without Interventions, with CC Score 8+	£321	

SSTI, skin and soft tissue infections; UTI, urinary tract infections; NHS, National Health Service;

Table S8 Scenario Analyses: Results

Scenario	SSTI	Complex UTI	Orthopaedic	Diabetic foot	Bronchiectasis	Intra-abdominal

0	25%	36%	30%	32%	44%	32%
1	21%	25%	22%	22%	34%	24%
2	20%	28%	24%	24%	31%	25%
3	33%	52%	40%	44%	77%	46%
4	-	-	21%	21%	-	-
5	28%	-	-	-	-	-
6	74%	-	-	-	-	-
7	76%	-	-	-	-	-

SSTI, skin and soft tissue infections; UTI, urinary tract infections

Table S9 Total costs of models of care and savings associated with OPAT across all conditions included within the NORS data set

Model of care	Total costs	Total savings (OPAT)
Inpatient stay	£103,070,256	
OPAT - once daily visits[1]	£33,014,148	£70,056,108
OPAT - nurse home visits	£43,333,446	£59,736,809
OPAT - self-administration (bolus IV)	£26,421,799	£76,648,457
OPAT - self-administration (device)[2]	£31,502,516	£67,578,565

[1]bronchectasis excluded; [2]complex urinary tract infections excluded;
OPAT, outpatient parenteral antimicrobial therapy, IV, intravenous;

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Outpatient parenteral antimicrobial therapy (OPAT) versus inpatient care in the UK: a health economic assessment for six key diagnoses

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Abstract:

Objectives To compare costs associated with different models of outpatient parenteral antimicrobial therapy (OPAT) delivery with costs of inpatient (IP) care across key infection groups managed via OPAT in the UK.

Design A cost-minimisation design was used due to evidence of similarities in patient and treatment outcomes between OPAT and IP care. A bottom-up approach was undertaken for the evaluation of OPAT associated costs. The British Society of Antimicrobial Chemotherapy (BSAC) National Outcomes Registry System was used to determine key infection diagnoses, mean duration of treatment and most frequent antibiotics used.

Setting Several OPAT delivery settings were considered and compared with IP care.

Interventions OPAT models considered were OP clinic model, nurse home visits, self (or carer)-administration by a bolus IV, self-administration by a commercially pre-filled elastomeric device, continuous intravenous infusion of piperacillin with tazobactam or flucloxacillin with elastomeric device as OP once daily and, specifically for bone and joint and diabetic foot infections, complex outpatient oral antibiotic therapies.

Results Base case and a range of scenario results showed all evaluated OPAT service delivery models to be less costly than IP stay of equivalent duration. The extent of savings varied by OPAT healthcare delivery models. Estimated OPAT costs as a proportion of IP costs were estimated at 0.23-0.53 (skin and soft tissue infections), 0.34-0.46 (complex urinary tract infections), 0.22-0.41 (orthopaedic infections), 0.24-0.42 (diabetic foot infections) 0.40-0.56 (exacerbations of bronchiectasis) and 0.25-0.42 (intra-abdominal infections). Partial or full complex oral antibiotic therapies in orthopaedic or diabetic foot infections costs were estimated to be 0.13-0.26 of IP costs. Main OPAT costs were associated with staff time and antimicrobial medications.

Conclusions OPAT is a cost-effective use of National Health Service (NHS) resources for the treatment of a range of infections in the UK in patients who can be safely managed in a non-inpatient setting.

Strengths and limitations of this study

- First study to use a bottom-up costing approach applied across a range of infections and healthcare delivery models in OPAT using UK-specific registry data
- First study to compare the cost of various models of care in OPAT with inpatient stay
- Base case results were consistent across a range of scenario analyses
- Assumed equivalence in OPAT and inpatient outcomes and between different OPAT models of care is associated with some uncertainty
- There are uncertainties in the quantification of some indirect OPAT costs (and their contribution to each OPAT model) and with inpatient bed day costs stay

INTRODUCTION

Outpatient parenteral antimicrobial therapy (OPAT) is a well-established and safe method of delivering intravenous antimicrobial therapy to carefully selected patients in whom other aspects of care can be addressed without hospitalisation.[1] [2] The British Society of Antimicrobial Chemotherapy (BSAC) have developed good practice recommendations for safe adult and paediatric OPAT practice and clinical governance including promotion of antimicrobial stewardship.[2] The recommendations acknowledged that a variety of OPAT delivery models were available and widely practised in the UK including home or clinic administration, administration by nurse or self/carer and administration via bolus or infusion. In 2015 BSAC launched the National Outcomes Registry System (NORS) for UK OPAT services in order to describe the OPAT landscape (including infections treated and antimicrobials used) and to enable participating centres to benchmark practice and outcomes.[3] Despite popularity and growth in OPAT practice in the UK, funding/reimbursement of OPAT has been inconsistent and as a result OPAT has not been uniformly established. A previous publication attempted to describe cost-effectiveness of OPAT in a tariff based UK health model for a single condition (cellulitis).[4] Herein we estimate OPAT related costs for a number of key indicator conditions utilising different established OPAT delivery models and compare with reference inpatient costs. The analysis also set out to take into account evolution of practice with greater use of supervised complex oral antibiotic therapies within the OPAT setting.[5]

METHODS

The costs of six OPAT healthcare delivery models were estimated and compared against the cost of equivalent duration of inpatient stay for six key infection categories typically managed via OPAT in the UK. Based on available clinical evidence and clinical expert opinion, equivalence in patient outcomes was assumed for OPAT and inpatient stay as well as for the different models of healthcare delivery in OPAT.[6-8] A cost-minimisation analysis was therefore

deemed appropriate. A list of detailed costing model assumptions primarily based on the BSAC updated good practice recommendations[2] and clinical expert opinion is available in the supplementary materials (supplementary table 1).

NORS data

The cost-minimisation analysis used five years of retrospective data relating to 21,632 adult treatment episodes collected from 57 OPAT centres (44 in England, 5 in Scotland, 4 in Wales and 4 in Northern Ireland), that all reported to NORS[3] (Table 1). In the cost-minimisation model, patients were treated in OPAT for one of six broadly defined infection categories, representing approximately 82% of primary OPAT diagnoses recorded in NORS. These were infections requiring short-term (up to 7 days) antimicrobial treatment such as skin and soft tissue infections including cellulitis (SSTI) and complex urinary tract infections (UTI) (including drug resistant lower UTI and pyelonephritis) or longer-term antimicrobial treatment such as bone and joint (including spinal, native osteomyelitis and orthopaedic metal work associated infections), diabetic foot infections (both osteomyelitis and complex soft tissue infections), bronchiectasis, and intra-abdominal infections (including liver abscess and other abdominal and pelvic infections)(supplementary table 2).

Table 1 Average duration and total number of treatment episodes in OPAT for six categories of infection

Condition	Average duration (days)	Total number	Source
SSTI	6.4	7,371	NORS 2015-19 (UK)[3]
Complex UTI	7.0	1,896	
Bone-Joint	27.8	5,355	
Diabetic foot	28.3	1,797	
Bronchiectasis	11.0	4,096	
Intra-abdominal	22.2	1,117	

SSTI, skin and soft tissue infections; UTI, urinary tract infections; NORS, National Outcomes Registry System

OPAT healthcare delivery models

The OPAT models considered were based on those currently practiced in the UK: outpatient clinic model, nurse home visits, self (or carer)-administration by a bolus IV, self-administration via an elastomeric device including continuous intravenous infusion (CIVI) of piperacillin with tazobactam or flucloxacillin and (for bone and joint or diabetic foot infections) complex outpatient antibiotic therapy (COpAT). Only suitable healthcare models were considered for the treatment of each of the six conditions in OPAT.

The care pathway for the outpatient clinic model requires a patient to travel daily to the OPAT unit following an initial assessment in hospital. At the clinic, an OPAT nurse prepares and administers antimicrobial medication intravenously by bolus IV. The nurse home visit model entails a specialist nurse (or a community based nurse) travelling to the patient's home instead.

The self-administration model of OPAT care requires the patient (or carer) to administer the antimicrobials at home, without the need to travel to hospital or for a nurse to visit on a daily basis. It is assumed that prior to commencing antimicrobial self-administration, patients (or their carers) receive on average three training sessions (60 minutes each with a nurse) on how to safely prepare and administer their medication through a peripherally inserted central catheter (PICC) line using a bolus IV. It is further assumed that only one training session is required for patient/carer administration of pre-prepared medication via an elastomeric home infusion device which only needs to be connected to and disconnected from the PICC line correctly. The patient is discharged with the necessary consumables (e.g. a leaflet of instructions, syringes, needles, 70% alcohol wipes, 0.9% sodium chloride ampoules, sharps bin, vials with medication powder for infusion, etc.) and is given a contact number related to the OPAT service for use if any problems occur out of hours. On the occasion where an elastomeric pump is used for self-administration, these are commercially pre-filled devices due to safety issues regarding the process of reconstituting drugs into elastomeric devices outside of an aseptic unit and the associated reduction in shelf life (approximately 24 hours). A continuous intravenous infusion (CIVI) model of service delivery in OPAT involves reconstitution of drugs into elastomeric devices by hospital staff with piperacillin with tazobactam or flucloxacillin on the same day of administration with the patient visiting clinic once daily.[9 10]

Patients referred to OPAT with bone and joint infections (e.g. diabetic foot and orthopaedic infections) are increasingly considered for suitability for discharge on supervised complex oral therapies as an alternative to "traditional" OPAT IV therapy. Suitable patients may be commenced directly onto supervised oral antimicrobial treatment which frequently requires enhanced monitoring due to potentially serious adverse events (e.g. linezolid or combination oral antibiotic regimens).[5]

In all OPAT models where treatment is required for > 1 week patients will also attend the OPAT clinic once weekly as a minimum and management/progress will be reviewed via a weekly virtual multi-disciplinary meeting.[2]

Antimicrobials

Antimicrobial medications with a lower frequency of administration compared with inpatient care are primarily selected for use in OPAT. In the analysis, the type and distribution of antimicrobial medicines are based on clinical expert opinion and the most prevalent agents used within the NORS database (supplementary table 3).

Antimicrobial medicines which require more than once daily administration (e.g. piperacillin with tazobactam, flucloxacillin, temocillin, ceftazidime and meropenem) would be primarily administered by the patient or carer. However, if an antibiotic is stable to degradation in the outpatient setting (piperacillin with tazobactam and flucloxacillin), patients may receive the antibiotic via a 24-hour continuous infusion (CIVI) via an elastomeric device as an outpatient requiring once daily attendance. All other antimicrobial medicines where data on stability are either not available or are not compatible with 24-hour infusion may be administered with bolus IV or 30 minute IV infusion.

Re-hospitalization

The cost-minimisation model assumed hospital re-admission to occur in 6.4% of treatment episodes in OPAT.[7] Re-hospitalised patients were assumed to only spend 50% of the duration of their treatment episode in OPAT.

Costs

Costs considered in the analysis included specialist staff time (specialist nurses, infectious diseases consultant, and specialist antimicrobial/ clinical pharmacist), antimicrobial medications, elastomeric infusion devices (empty or commercially pre-filled), consumables, laboratory tests and the cost of travel to and from the OPAT clinic where necessary (supplementary tables 4 to 6). Additionally, costs of re-hospitalisation for patients in OPAT have been included. A daily "overhead" cost per patient to account for administration and support costs of using a healthcare service consistent with published literature has also been assumed in the analysis.[8]

Costs were obtained from various sources. These included the Personal and Social Services Research Unit (PSSRU)[11], British National Formulary (BNF)[12], drugs and pharmaceutical electronic market information tool (eMIT)[13], National Procurement Scotland, Information Services Division (ISD) Scotland cost book[14] and NHS England reference costs[15].

An appropriate healthcare resource group (HRG) code[15] was identified for each diagnosis to account for costs of inpatient care (supplementary table 7). Costs were based on a weighted average of excess bed day costs as elective and non-elective inpatient stay across various severity levels. No potential additional hospital costs were included.

Patient and public involvement

No patient involved.

RESULTS

Base case results from the cost-minimisation analysis are presented as estimated average cost per treatment episode in inpatient care and models of OPAT healthcare delivery, as well as cost of OPAT as a percentage of the estimated cost of inpatient stay (Tables 2 and 3). Total costs of models of care and savings associated with OPAT across all conditions included within the NORS data set are shown in supplementary table 8.

Infections requiring short-term treatment

Skin and soft tissue infections (SSTI)

In the cost-minimisation analysis, patients attending once daily for the duration of antimicrobial treatment, were primarily treated with IV ceftriaxone, but also with teicoplanin and daptomycin (for betalactam allergy). Treatment with the same medicines was assumed in the specialist nurse visit model. A small number of patients could also be treated with dalbavancin 1g as a one-off dose, consistent with clinical practice for patients unable to attend for daily treatment. Patients who were offered an elastomeric home infusion device were primarily treated with ceftriaxone once daily and less often with flucloxacillin as 24h (CIVI). Dependant on the OPAT service delivery model, the cost of treating patients with SSTI was estimated in the range of 25%-51% of the cost of inpatient stay for the equivalent duration of treatment.

Complex urinary tract infections (UTI)

In the analysis, patients were primarily treated with ertapenem (90%) and a minority of patients were treated with temocillin. It was assumed that patients attending daily or treated by a nurse at home were only given ertapenem due to twice daily dosing of temocillin. Both antibiotics can be self-administered using either short infusion or IV bolus respectively. No patients were assumed to be treated using home infusion elastomeric devices. Dependant on the OPAT service delivery model, the cost of treating patients with complex UTI was estimated in the range of 34%-46% of the cost of inpatient stay for the equivalent duration of treatment.

Infections requiring longer-term treatment

Orthopaedic infections

Patients with orthopaedic infections were assumed to be treated once daily with ceftriaxone, teicoplanin or ertapenem in the outpatient visit, nurse home visit and self-administration OPAT service delivery models. Ceftriaxone was the only antimicrobial used for self-administration via commercially pre-filled elastomeric device. An analysis is also presented where patients were treated with oral therapies only or assuming IV to oral switch at different time points during supervised outpatient therapy. Dependant on the OPAT service delivery model (excluding oral therapies), the cost of treating patients with orthopaedic infections was estimated in the range of 22%-41% of the cost of inpatient stay

for the equivalent duration of treatment. Additionally, a movement in treatment practice from IV to oral antibiotics could results in treatment cost of 13% to 24% of the cost of inpatient stay, dependent on how early a patient is switched to oral therapy.

Diabetic foot infections

Similarly to orthopaedic infections, patients with diabetic foot infections were assumed to be treated with ceftriaxone, ertapenem and teicoplanin, although the proportion of patients treated with each agent varied. All antimicrobial medicines are suitable for once daily administrations. The cost of treatment in OPAT was estimated in the range of 22%-42% of the cost of inpatient stay for the equivalent duration of treatment. Additionally, a movement in treatment practice from IV to oral antibiotics could results in treatment cost of 13% to 26% of the cost of inpatient stay, dependent on how early a patient is switched to oral therapy.

Bronchiectasis

In the analysis, patients were assumed to be treated with either ceftazidime, meropenem or piperacillin with tazobactam. All medications are suitable for IV self-administration with either a bolus or 30 minute infusion. Only piperacillin with tazobactam was assumed to be administered with an elastomeric device via 24 hour continuous infusion in an outpatient setting (CIVI). The per-episode estimated cost for the same treatment plan with a visiting nurse is also presented. Since all of these medications require more than once daily administration or continuous daily administration, the general outpatient daily visits and nurse home visits OPAT service models are highly unlikely to be used in clinical practice so the results from CIVI models are presented instead. The estimated per treatment episode cost is in the range of 40%-56% of the cost of inpatient stay and varies with selected OPAT model of care.

Intra-abdominal infections

In the cost-minimisation analysis, patients were primarily treated with ertapenem or piperacillin with tazobactam. The latter was assumed to be used only in patients who were suitable for self-administration or attend daily for change of elastomeric device (CIVI). Patients who visit daily for IV infusions or receive nurse visits were assumed to only be

treated with ertapenem. The estimated per treatment episode cost is in the range of 25%-42% of the cost of inpatient stay and varies with selected OPAT model of care.

Table 2 Base case results – intravenous infusions

	Cost per treatment episode											
Condition	**SSTI**		**Complex UTI**		**Orthopaedic -Bone and joint**		**Diabetic foot**		**Bronchiectasis**		**Intra-abdominal**	
Model of care												
Inpatient stay	£2,476	-	£2,104	-	£8,279	-	£8,428	-	£3,269	-	£7,124	-
OPAT - once daily visits	£631	25%	£758	36%	£2,506	30%	£2,671	32%	-	-	£2,312	32%
OPAT - specialist nurse daily home visit	£831	34%	£977	46%	£3,375	41%	£3,556	42%	£1,839	56%	£3,006	42%
OPAT - self-administration - IV bolus	£566	23%	£720	34%	£1,855	22%	£2,006	24%	£1,301	40%	£1,811	25%
OPAT - self-administration - elastomeric device	£611	25%	-	-	£2,394	29%	£2,433	29%	£1,588	49%	£2,952	41%
OPAT - elastomeric device (CIVI; outpatient)	£802	32%	-	-	-	-	-	-	£1,495	46%	£2,807	39%
OPAT - once-off dalbavancin (1g)	£1,266	51%	-	-	-	-	-	-	-	-	-	-

SSTI, skin and soft tissue infections, UTI, urinary tract infections; OPAT, outpatient parenteral antimicrobial therapy; IV, intravenous; CIVI, continuous intravenous infusion;

Table 3 Base case results – oral antimicrobials for orthopaedic and diabetic foot infections

Condition	**Orthopaedic/ Bone and joint**		**Diabetic foot**	
Model of care				
Inpatient stay	£8,279		£8,428	
OPAT - Oral 100%	£1,114	13%	£1,089	13%
OPAT - Oral 25%; 75% IV	£2,009	24%	£2,161	26%
OPAT - Oral 50%; 50% IV	£1,710	21%	£1,816	22%
OPAT - Oral 75%; 25% IV	£1,410	17%	£1,470	17%

OPAT, outpatient parenteral antimicrobial therapies; IV, intravenous;

Scenario analyses

In scenario analyses described in table 4, certain modelling assumptions were challenged to assess impact on results in the outpatient setting model. Detailed scenario analysis results are provided in supplementary table 9.

Table 4 Scenarios: OPAT outpatient vs inpatient stay

	Scenario	Base case
0	Base case (outpatient)	
1	Using cost of inpatient care in infectious disease unit (ISD Scotland)[14]	Using condition-specific healthcare resource group (HRG) costs [15]
2	Using ISD Scotland[14] cost for outpatient appointments and inpatient stay (IDU)	Using micro-costing of nurse and consultant outpatient appointments
3	Assuming overheads are 44.8% of total costs consistent with a published source[16]	Assuming per day cost of using healthcare services consistent with a published source[8]
4	Using BNF[12] as a source for the cost of linezolid (orthopaedic and diabetic foot infections)	Using eMIT[13] as a source for the cost of linezolid (orthopaedic and diabetic foot infections)
Skin and soft tissue infections only		
5	Including the cost of consultant time	Nurse-led condition; no consultant time
6	Using the licensed dose of dalbavancin (1.5g) once off	Using dalbavancin 1g as a once-off treatment consistent with clinical practice
7	Using the licensed dose of dalbavancin 1g followed by 0.5g	Using dalbavancin 1g as a once-off treatment consistent with clinical practice

ISD, information services division; IDU, infectious disease unit; BNF, British National Formulary; eMIT, electronic market information tool;

Results from scenarios 1 and 2 (costs ranging between 21% and 34% of inpatient costs) are consistent, although lower than base case (25%-44%) across all infection categories due to the higher cost per bed day generally associated with an infectious disease unit.

Given the modelling approach, one of the uncertainties comes from the extent of model-specific per-patient overhead costs (scenario 3). The uncertainty is especially relevant to the outpatient clinic model. One study[16] reported overall overhead and support costs in the outpatient department of their infectious disease unit (IDU) to be 44.8% of total costs excluding re-hospitalization. When the equivalent assumption was made in the outpatient clinic model, the cost of treatment episode in OPAT did not increase over 52% of the cost of

inpatient stay, except for bronchiectasis (77%) which is treated with continuous intravenous infusion with elastomeric device as an outpatient visit once daily in the analysis which is generally associated with higher cost.

There are uncertainties around the source of cost for linezolid for the oral treatment of orthopaedic and diabetic foot infections (scenario 4). The cost reported in the British National Formulary[12] is substantially higher than what clinicians have advised and also reported in the electronic market information tool (eMIT)[13] which has been used in the base case analysis. Using the higher cost of linezolid results in the cost of oral therapies increasing from 13% to 21% of the cost of inpatient stay.

Additionally, variations in the treatment protocol with dalbavancin seems to have the highest impact on costs of treatment of skin and soft tissue infections in OPAT due to the high medicine acquisition cost (scenarios 6 and 7). Treatment with dalbavancin can be as costly as 74-76% of the cost of inpatient stay.

DISCUSSION

Although OPAT has been developing in the UK over the last 25 years, and despite the clinical benefits of avoiding hospitalisation and keeping care closer to home, there remains wide variation in OPAT availability and inconsistency in funding/commissioning of services in the UK. It is possible that OPAT may be perceived as an additional healthcare cost and this could be a significant barrier to more systematic support for service development. This study therefore set out to systematically detail OPAT costs and compare with inpatient costs for key OPAT-treated conditions. To our knowledge, a detailed costing of various OPAT healthcare delivery models in a UK setting has not been published before. Nevertheless, results are consistent with previous studies where overall cost of OPAT have been reported and/or compared with the cost of inpatient care.[6 16-18] Key findings are that the self (or care)-administration model of care was associated with the lowest cost and nurse home visits generally had the highest estimated cost per treatment episode across all conditions evaluated. From all available OPAT models for patients with skin and soft tissue infections, treatment with a single dose of dalbavancin was estimated to have the highest cost.

However, only a small proportion of patients (an estimated 5%) are expected to be treated with dalbavancin in clinical practice. As expected, oral therapies were the lowest cost treatment option for patients with orthopaedic (bone and joint) or diabetic foot infection. If patients are switched from IV as outpatient to oral therapies at least half way through their treatment duration, the results show the cost of treatment episode to be lower than the cost of self-administering IV antimicrobials for the whole treatment duration.

The cost-minimisation analysis found all OPAT service delivery models to be consistently associated with lower cost than inpatient stay of equivalent duration across a range of conditions in the UK NHS. The analysis shows the potential of OPAT to provide quality health care for suitable patients in an outpatient setting at a fraction of the cost of inpatient care. When the 4 most frequently used OPAT models of care (outpatient clinic, nurse home visit self (carer)-administration (bolus IV or elastomeric device) are considered individually, using NORS UK data[3], the 5-year estimated savings to the UK National Health Service (NHS) associated with treatment in OPAT was found to be in the range of £60-77 million (Table S9). It should be noted that these data only relate to 57 OPAT services and many have not contributed data consistently for all 5 years (data not shown). The estimated cost savings to the NHS through systematic roll out of OPAT therefore is likely to be considerably higher.

Strengths of the presented analysis include a bottom-up costing approach applied across a range of infections, and healthcare delivery models in OPAT using UK-specific registry data. Furthermore, each of these estimated costs were compared against the cost of inpatient care in a UK setting and a comprehensive list of scenario analyses showed consistency with base case findings. However, the study also had some limitations. The assumption of equivalence in patient and treatment outcomes for OPAT and inpatient care as well as among various models of care in OPAT is based on published systematic reviews [6-8] but direct comparative evidence is lacking. Furthermore, there was one study [8] to suggest that a specialist nurse visit model is generally associated with better outcomes compared with other healthcare delivery models in OPAT. A published source was used for the cost of inpatient stay which is inconsistent with the bottom-up costing approach undertaken for the cost of OPAT.[15] The assumption of cost of bed day in the analysis to be equivalent to the cost of excess bed days, as reported in NHS England Reference costs[15], is also associated with uncertainties due to the structure of the reimbursement system in NHS England (e.g.

the presence of trim points). Nevertheless, this is considered to be the most suitable published source of costs of inpatient stay as it provides cost estimates for each of the six infection categories in the analysis. Lastly, the estimated average costs per treatment episode in OPAT aim to reflect existing OPAT services and thus set-up and implementation costs have not been included.

It is important to note that most OPAT services will not rely on one particular delivery model and that individual patient factors such as, ability to self-administer or to attend the OPAT clinic, and choice of antimicrobial, will be the major determinants of the delivery model used. The data presented necessarily incorporate multiple variables to allow for variation based on patient need.

OPAT is primarily about delivering high quality patient centered care closer to home whilst avoiding inherent risks associated with hospitalisation. These positive health economic findings should be utilised by OPAT clinician/practitioners, healthcare managers and policy makers alongside the already powerful clinical effectiveness and patient safety data to drive further OPAT development in the UK.

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REFERENCES

1. Chapman ALN. Outpatient parenteral antimicrobial therapy. *BMJ* 2013;346:f1585.
2. Chapman ALN, Patel S, Horner C, 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)
3. British Society for Antimicrobial Chemotherapy. National Outcomes Registry System (NORS) c2019 [2020 Oct 26]. Available from: https://www.e-opat.com/opat-registry/.
4. Jones GR, Cumming DV, Honeywell G, et al. How is income generated by outpatient parenteral antibiotic treatment (OPAT) in the UK? Analysis of payment tariffs for cellulitis. *Journal of Antimicrobial Chemotherapy* 2015;70(4):1236-40.
5. Seaton RA, Ritchie ND, Robb F, et al. From 'OPAT' to 'COpAT': implications of the OVIVA study for ambulatory management of bone and joint infection. *J Antimicrob Chemother* 2019;74:2119-21.
6. Mitchell ED, Czoski Murray C, Meads D, et al. Clinical and cost-effectiveness, safety and acceptability of community intravenous antibiotic service models: CIVAS systematic review. *BMJ Open* 2017;7(4):e013560. doi: 10.1136/bmjopen-2016-013560 [published Online First: 2017/04/22]
7. Sriskandarajah S, Hobbs J, Roughead E, et al. Safety and effectiveness of 'hospital in the home' and 'outpatient parenteral antimicrobial therapy' in different age groups: A systematic review of observational studies. *Int J Clin Pract* 2018:e13216. doi: 10.1111/ijcp.13216 [published Online First: 2018/06/20]
8. Minton J, Murray CC, Meads D, et al. The Community IntraVenous Antibiotic Study (CIVAS): a mixed-methods evaluation of patient preferences for and cost-effectiveness of different service models for delivering outpatient parenteral antimicrobial therapy. *NIHR Journals Library Health Services and Delivery Research* 2017;02:02.
9. Allwood MC, Stonkute D, Wallace A, et al. Assessment of the stability of citrate-buffered flucloxacillin for injection when stored in two commercially available ambulatory elastomeric devices: INfusor LV (Baxter) and Accufuser (Woo Young Medical): a study compliant with the NHS Yellow Cover Document (YCD) requirements. *Eur J Hosp Pharm* 2018;27(2):90-4.
10. Jamieson C, Ozolina L, Seaton RA, et al. Assessment of the stability of citrate-buffered piperacillin/tazobactam for continuous infusion when stored in two commercially available

elastomeric devices for outpatient parenteral antimicrobial chemotherapy: a study compliant with the NHS Yellow Cover Document requirements. *Eur J Hosp Pharm* 2020
11. PSSRU. Unit costs of health and social care 2020 [2020 October 28]. Available from: https://www.pssru.ac.uk/project-pages/unit-costs/.
12. BNF: British national formulary 2020 [2020 October 28]. Available from: https://bnf.nice.org.uk.
13. Department of Health. Drugs and pharmaceutical electronic market information tool (eMIT) 2020 [2020 October 28]. Available from: https://www.gov.uk/government/publications/drugs-and-pharmaceutical-electronic-market-information-emit#:~:text=National%20Health%20Service-,Drugs%20and%20pharmaceutical%20electronic%20market%20information%20tool%20(eMIT),generic%20drugs%20and%20pharmaceutical%20products.
14. Public Health Scotland. Cost books 2018/19 2019 [2020 October 28]. Available from: https://www.isdscotland.org/Health-Topics/Finance/Costs/Detailed-Tables/.
15. NHS Digital. Reference costs: 2019-20 reference costs collection 2020 [2020 October 28]. Available from: https://digital.nhs.uk/data-and-information/data-collections-and-data-sets/data-collections/reference-costs.
16. Chapman ALN, Dixon S, Andrews D, et al. Clinical efficacy and cost-effectiveness of outpatient parenteral antibiotic therapy (OPAT): a UK perspective. *J Antimicrob Chemother* 2009;64:1316-24.
17. Durojaiye OC, Bell H, Andrews D, et al. Clinical efficacy, cost analysis and patient acceptability of outpatient parenteral antibiotic therapy (OPAT): a decade of Sheffield (UK) OPAT service. *International Journal of Antimicrobial Agents* 2018;51(1):26-32.
18. Seaton RA, Johal S, Coia JE, et al. Economic evaluation of treatment for MRSA complicated skin and soft tissue infections in Glasgow hospitals. *European Journal of Clinical Microbiology & Infectious Diseases* 2014;33(3):305-11.

Supplementary tables:

Supplementary table 1 Costing model assumptions

No	Assumption	Source/Justification
1	All patients with long term infections are assessed on admission and upon discharge by a specialist consultant. Patients spend 30 minutes with a specialist consultant and 1h with a nurse at initial and final assessment.	BSAC good practice recommendations (3.1-3.15); communication with clinical experts in OPAT.
2	Skin and soft tissue infections are a nurse-led condition unless patient is treated with dalbavancin.	BSAC good practice recommendations (3.1-3.15); communication with clinical experts in OPAT.
3	All patients with complex UTI are assessed by a consultant once.	BSAC good practice recommendations (3.1-3.15); communication with clinical experts in OPAT.
4	All patient are allocated 15 minutes of pharmacist time per treatment episode.	BSAC good practice recommendations (3.1-3.15); communication with clinical experts in OPAT.
5	Laboratory tests including UE, LFT, FBC, C-reactive protein are done at initial and final assessment and once weekly for longer-term infections. Patients treated with teicoplanin receive weekly teicoplanin levels blood tests.	BSAC good practice recommendations (4.4); personal communication with clinical experts in OPAT. Type of tests might vary with the choice of antimicrobial
6	All patients requiring longer term treatment (more than 7 days), are assessed weekly at a MDT meeting. This is approx. 5 minutes of consultant, pharmacist and specialist nurse time per patient.	BSAC good practice recommendations (4.2); personal communication with clinical experts in OPAT
7	Each daily visit to outpatient clinic lasts 40 minutes during which a band 6 nurse examines the patient, prepares and administers medication. A nurse visiting patient's home would spend the equivalent amount of time.	Personal communication with clinical experts in OPAT This might be a conservative approach given that some antimicrobials are administered in 2-3 minutes.
8	Patients with infections requiring longer-term treatment who self-administer, visit the clinic once weekly for a check-up with a nurse and to have blood work done.	BSAC good practice recommendations (4.3); assumption
9	Patients who self-administer with bolus IV receive 3 training sessions with a nurse (50:50 split band 5/band 6), each lasting 1 h. Patients who self-administer with elastomeric device receive 1 training session.	Personal communication with clinical experts in OPAT. Assumption BSAC good practice recommendations (3.13);

10	Single-use elastomeric devices administered in an outpatient setting (CIVI) are filled up by hospital staff (approximately 15 minutes of nurse's time).	Assumption; Expert opinion;
11	Single-use elastomeric devices used for self-administration are commercially pre-filled.	Assumption; Expert opinion;
12	Consumables: each patient receives 1 PICC line; per administration: 1 apron, 1 pair of gloves, 4 needles, 4 syringes, 1 pre-injection swab, 3 0.9% sodium chloride ampoules;	Personal communication with clinical experts in OPAT. Assumption Varies with method of administration
13	A nurse travelling to patients home would spend 33 minutes (non-patient contact time) per journey travelling with an ambulance car (£10.63 per journey). This is approximately 11 miles per journey.	ISD Cost book for Scotland. This is an approximation due to lack of available data for distances travelled in OPAT. Distance travelled varies with geographic location. Longer distances might be travelled in the Highlands and islands in Scotland. It was assumed that this estimate for Scotland is relevant to UK.
14	Type and distribution of medicines for each condition in the analysis are based on clinical expert opinion	NORS data do not link conditions to antimicrobials.
15	Cost of linezolid comes from eMIT; all other costs of antimicrobials come from the BNF (cheapest tariff)	A generic version of linezolid is used in OPAT but this is not reflected in the BNF. The BNF cost is substantially higher.
16	Antimicrobials requiring more than once daily administration (temocillin, ceftazidime, meropenem and piperacillin with tazobactam) are assumed to be self-administered (bolus IV) only.	More than once daily visit (hospital or nurse home visit) in OPAT are not primarily available options in clinical practice.
17	Piperacillin with tazobactam, flucloxacillin and ceftriaxone are administered with commercially pre-filled elastomeric device in the six conditions included in the analysis. Only piperacillin with tazobactam and flucloxacillin can be administered with elastomeric device filled up by hospital staff.	BSAC good practice recommendations (3.12); Clinical expert opinion;
18	For bronchiectasis: patients can travel daily to outpatient clinic for piperacillin with tazobactam (with buffered saline) to be administered as continuous IV with elastomeric device; Although the same model of care with piperacillin with tazobactam is available for the treatment of intra-abdominal infections, for simplicity only ertapenem was assumed to be used if patients attend clinic daily in the outpatient service delivery model. A CIVI as outpatient model is shown separately.	An assumption was made that if a patient attends the OPAT clinic daily or is visited by a nurse, the cheapest treatment option will be used in clinical practice. In the case of treating intra-abdominal infections, ertapenem once daily is cheaper than continuous piperacillin with tazobactam with elastomeric device. In patients with bronchiectasis, continuous piperacillin with tazobactam with elastomeric device is the only treatment option in the hospital or nurse daily visits OPAT service delivery models.

19	The cost of empty elastomeric devices is based on the average cost of 2 commercially available devices assuming equal market share	BSAC good practice recommendations (3.12); Clinical expert opinion;
20	A patient would spend the equivalent amount of time in hospital care in absence of OPAT	Clinical expert opinion
21	A patient has a small probability (0.064) to be re-admitted to hospital half-way during their treatment in OPAT	Clinical effectiveness data; Clinical expert opinion
22	Condition-specific HRG cost per excess bed day in hospital to estimate the cost of inpatient stay	The true cost per day of inpatient stay of patients who are eligible for OPAT is unknown. NHS England reference costs are considered a standard source of cost estimates associated with certain diagnoses or interventions. However, costs are presented as per episode of average treatment duration and cost of excess bed days if treatment goes beyond the expected treatment duration (trim point). Due to lack of better evidence, excess bed day costs were considered the best source of costs of inpatient stay for the purposes of this analysis. Condition-specific costs were selected to allow for granularity. However, costs were similar so assuming the same cost for each condition is also a reasonable assumption.

BSAC, British Society for Antimicrobial Chemotherapy; OPAT, Outpatient Parenteral Antimicrobial Therapy ; UTI, urinary tract infections ; UE, urea and electrolytes; LFT, liver function test; FBC, full blood count; MDT, multi-disciplinary team; IV, intravenous ;CIVI, continuous intravenous infusion; ISD, information services division; PICC, peripherally inserted central catheter ; HRG, health resource group ;eMIT, electronic market information tool ; BNF, British National Formulary ;

Supplementary table 2 Breakdown of infection categories

Infection category	Infection included in this category
Skin and soft tissue infections	Cellulitis
	Other skin and soft tissue infections
Orthopaedic infections (bone and joint)	Prosthetic joint infection (knee)
	Osteomyelitis – native
	Prosthetic joint infection (hip)
	Osteomyelitis - surgically related
	Discitis/vertebral osteomyelitis
	Prosthetic joint infection (other)
	Discitis/vertebral osteomyelitis - device related
	Osteomyelitis (other)
Diabetic foot infections	Osteomyelitis - diabetic foot
	Diabetic foot infection - no osteomyelitis

Complex urinary tract infections	Drug resistant lower urinary tract infections and pyelonephritis
Bronchiectasis	Bronchiectasis
	Other complex respiratory tract infection
Intra-abdominal infections	Gastro-intestinal infection
	Hepatic abscess
	Pelvic abscess

Supplementary table 3 Condition-specific antimicrobials in OPAT

Condition	Medication	Distribution
Skin and soft tissue infections (IV)	Ceftriaxone	75%
	Teicoplanin	10%
	Daptomycin	5%
	Flucloxacillin	5%
	Dalbavancin	5%
Orthopaedic; Bone-Joint (IV)	Ceftriaxone	60%
	Teicoplanin	30%
	Ertapenem	10%
Orthopaedic; Bone-Joint (oral)	Ciprofloxacin/Rifampicin	25%
	Levofloxacin/Rifampicin	12.50%
	Co-trimoxazole/Rifampicin	12.50%
	Clindamycin/Rifampicin	12.50%
	Linezolid/ciprofloxacin	12.50%
	Linezolid	25%
Diabetic foot (IV)	Ceftriaxone	45%
	Teicoplanin	10%
	Ertapenem	45%
Diabetic foot (oral)	Clindamycin/Doxycycline	25%
	Clindamycin/Co-trimoxazole	12.50%
	Clindamycin/Ciprofloxacin	12.50%
	Linezolid/ciprofloxacin	12.50%
	Ciprofloxacin/Doxycycline	25.00%
	Levofloxacin/Doxycycline	12.50%
Complex urinary tract infections (IV)	Ertapenem	90%
	Temocillin	10%
Bronchiectasis (IV)	Ceftazidime	70%
	Piperacillin with tazobactam	15%
	Meropenem	15%
Intra-abdominal (IV)	Ertapenem	75%
	Piperacillin with tazobactam	25%

IV, intravenous;

Supplementary table 4 Unit costs of resources used in OPAT services

Item	Unit cost	Notes	Source
Medical consultant	£109	Per working hour	PSSRU,2019
Pharmacist band 8a	£67	Per working hour	PSSRU,2019
Nurse band 6	£47	Per working hour	PSSRU,2019
Nurse band 5	£38	Per working hour	PSSRU,2019
Antimicrobial medicine (IV)	Variable*	Condition-specific	BNF,2020, eMIT, 2020
Antimicrobial medicine (oral)	Variable*	Condition-specific	BNF,2020, eMIT, 2020
Laboratory tests	£8	UE,LFT,CRP and FBC	ISD Cost book,2020
Laboratory tests (specialist)	£47	Teicoplanin levels	Expert
Consumables - PICC line	£36	Per patient	National Procurement
Consumables - Butterfly needle	£1	Per administration	National Procurement
Consumables (other)	£1.65	Single use; apron, needles, syringe, pre-injection swab	National Procurement
Elastomeric device; empty	£31	Based on equal market share of two devices (single use)	National Procurement
Elastomeric device; commercially pre-filled (piperacillin with tazobactam; flucloxacillin)	£90	Per administration	Expert
Elastomeric device; commercially pre-filled (ceftriaxone)	£45	Per administration	Expert
Buffered saline	£2	Per administration	Expert
Nurse travel	£11	Per journey - based on average travel of 11 miles	ISD Cost book,2020
Patient transport service	£42	Per journey - based on average travel of 11 miles	ISD Cost book,2020
General cost of using healthcare services (inflated)	£13	Per patient; per day (inflated to 2019 prices using the NHS cost inflation index)	Minton, 2017[3]

*See tables S5 and S6 for costs of antimicrobials in OPAT

UE, urea and electrolytes; LFT, liver function test; CRP, c-reactive protein test; FBC, full blood count; PSSRU, Personal Social Services Research Unit; BNF, British National Formulary; eMIT, electronic market information tool; ISD, Information Services Division

Supplementary table 5 Intravenously administered antimicrobials in OPAT

Medicines (IV) - BNF	Dose in OPAT	Frequency of administration	Cost per pack	Source
Ceftriaxone	2g	Once daily	£19.18	BNF, 2020

Teicoplanin	600mg	Once daily or 1200mg; 3 times per week	£3.93	BNF, 2020
Daptomycin	700mg	Once daily	£60.00	BNF, 2020
Flucloxacillin	8g	24h infusion	£6.00	BNF, 2020
Dalbavancin	1000 mg	One-off	£558.70	BNF, 2020
Ertapenem	1g	Once daily	£31.65	BNF, 2020
Temocillin	2g	every 12 h	£25.45	BNF, 2020
Ceftazidime	2g	3 times a day	£17.59	BNF, 2020
Piperacillin with tazobactam	4.5g/18g	4 times per day/24h infusion	£76.50	BNF, 2020
Meropenem	1g	0.5-1g every 8 hours	£186.70	BNF, 2020

IV, intravenous; BNF, British National Formulary

Supplementary table 6 Oral antimicrobials for the treatment of orthopaedic and diabetic foot infections in OPAT

Medicines (oral)	Dose in OPAT	Frequency of administration	Cost per pack	Source
Ciprofloxacin	750mg	every 12h	£8.00	BNF,2020
Levofloxacin	500mg	every 12h	£24.50	BNF,2020
Co-trimoxazole	960mg	every 12h	£23.48	BNF,2020
Clindamycin	600mg	every 8h	£38.23	BNF,2020
Linezolid	600mg	every 12h	£7.48	eMIT,2020
Linezolid	600 mg	every 12h	£327.24	BNF, 2020
Doxycycline	100mg	every 12h	£1.64	BNF,2020
Rifampicin	400mg	every 12h	£123.60	BNF,2020
Rifampicin	50mg	every 12h	£54.69	BNF,2020

BNF, British National Formulary

Supplementary table 7 Condition-specific healthcare resource group (HRG) and bed-day cost of inpatient stay

Condition	HRG code	Description	Cost	Source
SSTI	HD21 D-H	Soft Tissue Disorders with CC Score 0-12+	£387	NHS England Reference costs,2019
Complex UTI	LA04 N-S	Kidney or Urinary Tract Infections, without Interventions, with CC Score 0-13+	£301	
Orthopaedic /Diabetic foot infections	HD25 D-H	Infections of Bones or Joints, with CC Score 13+	£298	
	HE81 A-C	Infection or Inflammatory Reaction, due to, Internal Orthopaedic Prosthetic Devices, Implants or Grafts, with CC Score 0-13+		
Bronchiectasis	DZ23 M-N	Bronchopneumonia without Interventions, with CC Score 0-10	£297	
Intra-abdominal	FD01 F-J	Gastrointestinal Infections without Interventions, with CC Score 8+	£321	

SSTI, skin and soft tissue infections; UTI, urinary tract infections; NHS, National Health Service;

Supplementary table 8 Total costs of models of care and savings associated with OPAT across all conditions included within the NORS data set

Model of care	Total costs	Total savings (OPAT)
Inpatient stay	£103,070,256	
OPAT - once daily visits[1]	£33,014,148	£70,056,108
OPAT - nurse home visits	£43,333,446	£59,736,809
OPAT - self-administration (bolus IV)	£26,421,799	£76,648,457
OPAT - self-administration (device)[2]	£31,502,516	£67,578,565

[1]bronchectasis excluded; [2]complex urinary tract infections excluded;
OPAT, outpatient parenteral antimicrobial therapy, IV, intravenous;

Supplementary table 9 Scenario Analyses: Results

Scenario	SSTI	Complex UTI	Orthopaedic	Diabetic foot	Bronchiectasis	Intra-abdominal
0	25%	36%	30%	32%	44%	32%
1	21%	25%	22%	22%	34%	24%
2	20%	28%	24%	24%	31%	25%
3	33%	52%	40%	44%	77%	46%
4	-	-	21%	21%	-	-
5	28%	-	-	-	-	-
6	74%	-	-	-	-	-
7	76%	-	-	-	-	-

SSTI, skin and soft tissue infections; UTI, urinary tract infections