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Cost-effectiveness of Outpatient Parenteral Antibiotic Therapy: A Simulation Modelling Approach

Short title: Cost-effectiveness of OPAT

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Abstract

Background

In the United Kingdom (UK) patients who require intravenous antimicrobial (IVA) treatment may receive this in the community through outpatient parenteral antimicrobial therapy (OPAT) services. Services include: IVA administration at hospital out-patient clinic (HO); at home by a general (GN) or specialist nurse (SN); or patient self-administered (SA) following training. There is uncertainty regarding which OPAT services represent value for money; this study aimed to estimate their cost-effectiveness.

Methods

A cost-effectiveness decision-analytic model was developed using a simulation technique utilising data from hospital records and a systematic review of the literature. The model estimates cost per quality-adjusted life year gained (QALY) from the National Health Service (NHS) perspective for short and long term treatment of infections and service combinations across these.

Results

In short term treatments, HO was estimated as the most effective (0.7239 QALYs) but at the highest cost (£973). SN, was the least costly (£710) producing 0.7228 QALYs. The combination between SN and HO was estimated to produce 0.7235 QALYs at a cost of £841. For long term treatments, SN was the most effective (0.6767 QALYs) costing £2,379 while SA was the least costly £1,883 producing 0.6660 QALYs. A combination of SA and SN was estimated to produce 0.6721 QALYs at a cost of costing £2,128.

Conclusion

SN and SA are cost-effective for short term and long term treatment of infections. While combining services may represent the second best alternative for OPAT in the UK.

Introduction

There is increased interest in the UK in offering patients who require intravenous antimicrobials (IVA), outpatient or community-based services rather than inpatient care.[1–3] Such outpatient parenteral antimicrobial therapy (OPAT) services are most often used to treat skin and soft tissue infections. However, facilitated by newer antibiotics with longer half-lives, a number of others disease: joint and bone infections, bacteraemia, osteomyelitis, diabetic foot and tuberculosis can be treated safely in an outpatient or home setting.[4]

Some authors have estimated that an OPAT service could reduce treatment costs by reducing bed days. A UK study by Chapman et al. (2009) found that OPAT reduced inpatient costs by 47%,[3] while another study in the UK reported that 7,394 bed days were saved over a period of 44 months; assuming a National Health Service (NHS) bed day costs of £208 (2015 prices) the associated potential savings would be over £1.5 million.[5,6]

In terms of safety, evidence has shown that OPAT has been associated with a low risk of adverse events including hospital re-admissions and line complications including infections and minor episodes of redness in the application site.[1,7–9] In addition, no difference in time to heal between OPAT and inpatient care has been observed, however, there are no randomised control trials (RCT) comparing the different OPAT services on offer.[1,10] A systematic review of the literature on cost-effectiveness analyses of OPAT services, found a number of cost-effectiveness studied but none that would meet the technology appraisal reference case criteria set out by the National Institute of Health and Care Excellence (NICE)[11] in the UK.

Despite the benefit of OPAT, service provision in the UK has been limited. It is possible that the evidence-gap on the models of care in the area has hindered investment from decision-makers and service commissioners. In the absence of RCT evidence and robust economic evaluations to commend one OPAT service over another, commissioning decision making in the area is fraught with uncertainty and barriers to the wider adoption of services remain. It is clear that further research is required to inform decision making. However, given that research

resources are scarce and RCTs often expensive and relatively slow to yield results, it is imperative that they are streamlined to answer the important questions and include the comparators most-likely to be cost-effective. This is especially true in OPAT services where a number of service configurations are possible.

There are a number of different OPAT service models currently in use in the UK but can be classified as follows: daily IVA delivery at hospital or clinic in an outpatient visit (HO); daily IVA delivery at home by nurse (general -GN- or specialist -SN-); and daily patient-administered IV antibiotics at home following receipt of training (SA).

The aim of the current study was to develop a decision-analytic model to estimate the cost-effectiveness of the four OPAT services offered in the UK (HO, GN, SN and SA) to provide evidence for decision-making.

Methods

A decision-analytic model employing a discrete event simulation (DES) approach was developed. Decision modelling is an analytical approach to performing an economic evaluation of at least two alternative courses of action and determines which offers best value for money. Such a model is created to reflect the healthcare process or pathway, capturing the events that occur to the patient or health system during care and estimating the expected costs and (dis)benefits of the treatment options.

Many modelling methods exist,[12] but with DES it is possible to follow individual patients through the duration of their treatment, explicitly accounting for time and treatment history. Within the context of IVA it allows to assess time-related risks and by recording their treatment history we were able to easily add events such as relapses which are difficult when using other types of methods. This allows for a better estimation of the overall impact of the services being evaluated. The DES model followed the methods outlined by J Caro et al. (2016)[13].

Two economic evaluations, for short and long term IVA treatments, were performed. The evaluations followed established methods, adhered to the NICE 'reference case'[11,14] and therefore adopt the NHS perspective (costs considered were those incurred by the NHS only). Patient pathways were modelled over a twelve month period.

To incorporate the impact of treatment on the health related quality of life of the patients and the length of time in a condition, the model uses quality-adjusted life years (QALYs) as an outcome measure. The QALY is a measure that encapsulates both quality and length life and is widely used in health economics.[15] By estimating the incremental costs (costs of intervention A minus costs of intervention B) and dividing them by the incremental outcomes (outcomes of intervention A minus outcomes of intervention B), we generate the incremental effectiveness ratio (ICER), which is used to assess cost-effectiveness.[16] In line with current UK guidelines, services with an ICER <£20,000 per QALY gained were considered cost-effective. To allow a linear comparison between interventions only in monetary terms and to aid in the determining cost-effectiveness, the Net Monetary Benefit (NMB) was also calculated (QALY*£20,000-Cost). A cost-effective strategy will have the highest NMB. Costs were not discounted as the evaluations period was of 12 months only. QALYs gained during treatment were not discounted, however QALYs lost due to premature death were discounted at a 3.5% rate. All prices are presented in pounds sterling 2015.

Population

We defined short term treatment as that required for skin and soft tissue (SSTI) or similar infections, usually taking between 4 and 7 days to heal (depending on the service) of IVA to heal or transition to oral antibiotics. We defined long term treatment as that required for bone infections infective exacerbations of cystic fibrosis and other infections for an average of more than seven days to heal.

Interventions

In the HO service, patients attend a hospital outpatient clinic to receive treatment on a daily basis, while in the GN and SN services, nurses administer the IVA at the patient's home every day. In contrast to GN, the SN team of nurses only deliver IVAs. Only HO, GN and SN were compared when analysing patients requiring short term treatments, as the SA model was unlikely to be offered to (or demanded by) this patient group. The evaluation for long term treatment compare the four service strategies (HO, GN, SN and SA).

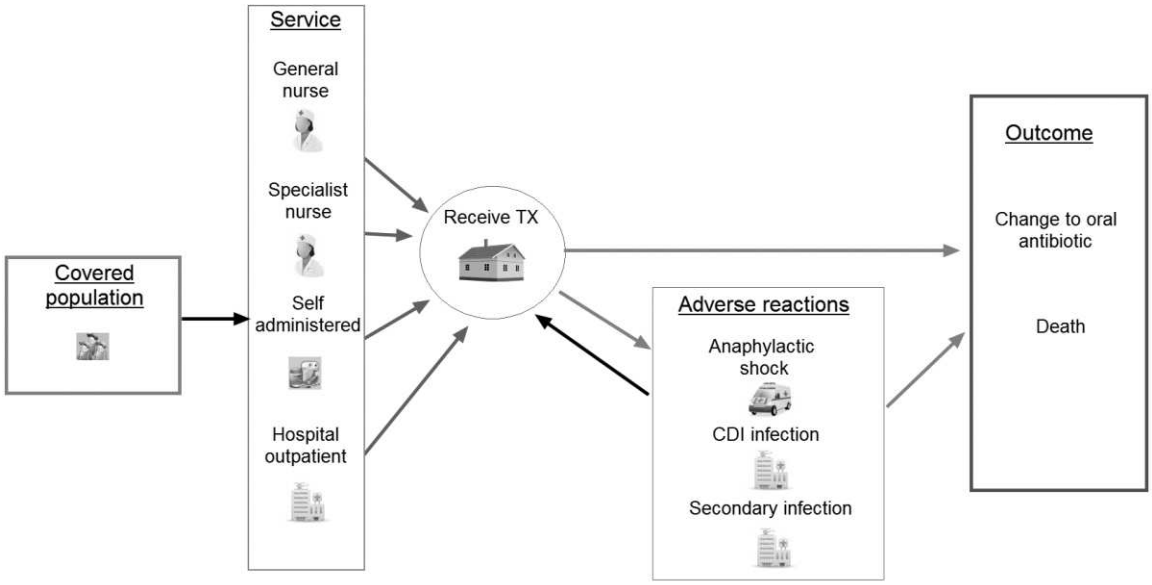
The HO service was considered the 'standard' OPAT care in the UK even though there is geographical variation in service provision. Interventions were initially compared against HO to evaluate its cost-effectiveness. If this analysis showed that it was not cost-effective, an incremental analysis (ordering interventions from the least costly) was carried out.

An additional analysis combining the most cost-effective service with a relevant second best strategy was carried out; these assume that 50% of the patients in a particular clinic would receive one service and 50% would receive the other. This combined setting was compared against the most cost-effective single service intervention.

Model structure

Model structure was informed by a rapid review of published decision models and through discussions with patients and clinicians. Patients enter the simulation after been referred to an OPAT service and they are followed from this point in time on a daily basis until they are healed (or switched to oral antibiotics) or die. Although patients can experience a variety of severe adverse events, we chose to include only three in the model, due to their use of medical resources: anaphylactic shock, clostridium difficile infection (CDI) and intravenous line infection. Patients that experience any of these were subject to a mortality risk. Patients were also exposed to a daily risk of a mild adverse event (rash, nausea, vomiting, dizziness, fever and line obstructions or leaking, phlebitis, redness, swelling, pain at the site of access or minor line events). These incurred additional costs but no quality of life decrement or increase in healing time, as they are both mild and transient in nature. Some patients were assumed to 'relapse' and begin IVA again (Figure 1).

Figure 1. Simulation model structure



*Model constructed using SIMUL8® [17]

Parameter Values - probabilities

The patient's transition through the treatment pathway depends on a series of probabilities. These, along with the costs and effects were taken from a number of sources including a systematic review[9,18–24], expert clinical opinion and hospital records of a group of patients (n=465) who had recently received OPAT (sample characteristics in supplementary Table S1). Patients were recruited from 6 centres in England (Bradford, Huddersfield, Hull, Leeds, Oxford and Sheffield) which between them provided all the models of service studied; some offered more than one model.

The measure of the service "effectiveness" was defined as the number of days of IVA treatment required. We derived these values from the hospital record data and applied adjusted 'time-to-heal' values for the base case analysis with sensitivity analyses exploring the same heal time across services. Not healed patients could travel to the CDI state according to a daily probability based on the time they spent in a hospital environment or in

contact with a GN or SN. It was assumed that HO patients had a greater chance of developing CDI compared to those treated at home. The smallest risk was for the SA service as they have less contact with a healthcare setting.

An anaphylactic shock was assumed to require one day of in-hospital treatment after which the patient resume treatment. The daily risk of such episode was assumed equal across services. Risks of secondary infection of intravenous lines were related to the duration of treatment irrespective of the type of service received.

A differential risk of mild adverse events was added for each service (from hospital record data). The base case analysis assumed that relapse rate was zero and equivalent between services. However, a sensitivity analysis was conducted where heal time was assumed equivalent but a differential relapse rate was adopted.

Mortality

Risk of death was only considered for those patients who had a severe adverse event. The daily mortality rate for patients with CDI was obtained from Wiegand et al. (2012) and was assumed the same for all services.[22] The associated mortality risk for patients who had an anaphylactic shock was obtained from Hopf et al. (2008).[19] This risk was assumed to be double for the home based services (SN, GN, SA) than for HO since patients experiencing a shock in hospital would receive more rapid access to intensive care. Lastly, the mortality risk for patients who had a secondary infection of intravenous lines was obtained from Thwaites et al. (2010) and was assumed the same for all services.[23]

Parameter values - costs

The costs of the services included: antimicrobials; additional expenses required for self-administration (training and equipment); nurse (including paperwork and travel) and hospital visit for IVA delivery and reviews; additional healthcare resources used by the patient (e.g. GP visits); and costs associated with mild and severe adverse events (e.g. hospitalisation following secondary infection). Unit costs were obtained from the NHS reference cost

resource. Personal Social Services Research Unit (PSSRU) report and drug and pharmaceutical electronic market information tool (eMit).[6,25,26]

The base case scenario assumes that one of the outpatient visits in the HO service will be led by an infection specialist, who will undertake an initial, review or discharge session. Patients in the GN, SN and SA, however, will have a discharge and a two-weekly review consultation with an infectious disease specialist (only for long term treatments). Only one infectious disease consultation was included for HO as it was assumed that they were being more closely monitored by attending the outpatient unit on a daily bases. To test the impact of these assumptions, a sensitivity analysis assuming that all services had an initial and discharge consultation with an infectious disease specialist was conducted.

Parameter values –utility/quality of life

Utility values were similar for short and long term treatments when healed but during the infection, the long term patients experienced a much larger utility drop.[27–30] Since the mortality risk linked to adverse events presents a risk of reduced length of life, a lifetime QALY loss value (16.6) was estimated. This represented the discounted (at 0.035% per annum) total QALYs lost for individuals who died during the model horizon using an average starting age of 50, survival estimates from life tables and 'healed' utility values. Given the rarity of mortality, it was not considered worthwhile including extensive survival analysis. The probability, cost and utility parameter values can be found in supplementary (Table S2).

Uncertainty

A number of deterministic one-way and scenario sensitivity analyses were conducted: same healing times for all services; increased number of IVAs per day; changes in risk, mortality rates and healing time from adverse events; changes to the per hour nurse visit rate; bed day costs and changes in the utility values for the heal/not heal state as well as for the utility losses due to adverse events. We also tested a scenario in which all patients irrespective of

the service model, received an initial and a discharge consultation led by an infection specialist.

Additionally, a probabilistic sensitivity analysis (PSA) was performed (2,000 Monte Carlo simulation runs) to allow for random changes in all parameter values at the same time based on pre-specified value distributions. Only 2,000 simulation runs were performed due to the computationally intensive nature of the simulation. To overcome the latter, Jackknife confidence intervals (CI) were estimated around the ICERs to determine if the number of iterations was sufficient to produce a robust answer. Jackknife is a tool to assess non-parametric estimates of bias.[31]

These simulated analyses results were plotted on a cost-effectiveness plane, where the vertical axis represents the simulated incremental costs, while the horizontal axis the incremental QALYs. The plane indicates the general spread of values and thus indicating the level of uncertainty in the results. The probability that services were cost-effective given a range of willingness to pay thresholds, however, was represented on a cost-effectiveness acceptability curve (CEAC).[32]

Results

Short term treatment

The deterministic base case analysis shows that HO (£973) is more expensive than GN (£788) and SN (£710). HO is also less effective than SN (-0.001 QALYs) but more effective than GN (0.005 QALYs). This results in HO being dominated by SN (as SN is less costly and more effective) and in an incremental cost-effectiveness ratio (ICER) close to £40,000 per QALY gained when compared against GN. Suggesting that both SN and GN are cost-effective when compared to HO individually (Table 1). The scatter plot comparing all interventions against HO confirms the results as most of the iterations from the PSA fall below the horizontal axis suggesting that SN and GN are generally cost-saving (Figure 2a).

An incremental analysis (ranking the interventions from the least to the most costly) based on the PSA was carried out. Given a £20,000 threshold, SN had the highest NMB, therefore was considered the most cost-effective strategy for short term treatments. The PSA estimated that in 79% of the iterations the NMB of SN was the highest of the three interventions (CEAC) (Figure 3a). A service providing both SN and HO result is more effective but more costly intervention than providing SN alone, but less costly and effective than providing HO alone (Table 1).

Table 1. Probabilistic cost-effectiveness analysis for short term infections

Intervention	Costs	QALYs	ICER*	Jackknife 95% CI**		Net monetary benefit	Result
				Lower bound	Upper bound		
SN	£710	0.7228				£13,745	Cost-effective
GN	£788	0.7193	n/a	n/a	n/a	£13,597	Dominated
SN 50%; HO 50%	£841	0.7235	£182,493	£157,046	£206,302	£13,628	Not cost-effective
HO	£973	0.7239	£233,034	£196,077	£267,269	£13,505	Not cost-effective

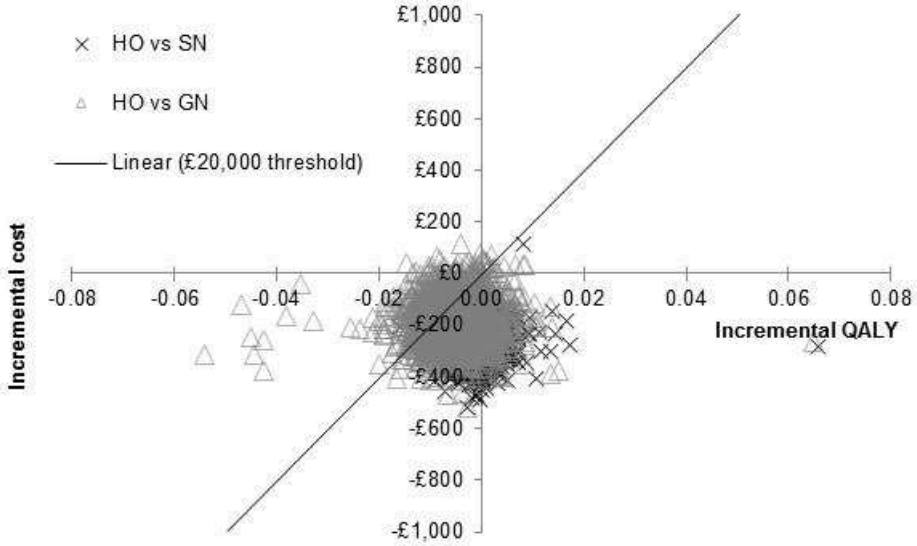
*ICER: Incremental analysis versus the next best strategy.
**Jackknifing was undertaken to assess the uncertainty in the mean value to determine if the number of iterations were sufficient for non-dominated strategies. The 95% CI shows that this was the case.[31]ICER or Jackknife CI was not estimated for dominated strategies

Long term treatment

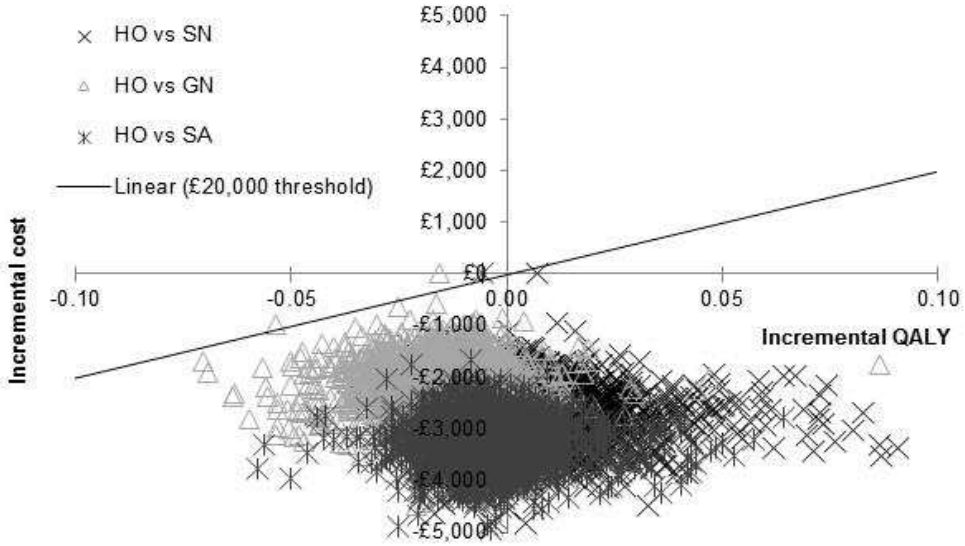
The deterministic analysis estimated that HO was the most costly (£5,135) strategy followed by GN (£2,957), SN (£2,379) while SA (£1,883) was the cheapest, suggesting that all strategies were cost saving compared to HO (Table 2). In terms of the effects, SN had the highest QALYs gained (0.678) followed by HO (0.667) and SA (0.666) while GN was had the lowest (0.655). The latter was confirmed in the scatter plot from the PSA since, comparing all interventions against HO show that all iterations fall below the horizontal axis (Figure 2b).

Figure 2. Scatterplot short and long term infections: all strategies versus HO

a) Short term treatment



b) Long term treatment



Please note different y-axis scales to account for the difference in the costs between short and long term treatment

The incremental analysis indicated HO and GN were more costly and less effective than (and consequently dominated by) SN. When SA (cheapest option) was compared to SN, the estimated ICER was higher than the £20,000 per QALY gained threshold. Furthermore, the estimated NMB for SA was the highest of the four interventions. These results suggest that SA is the most cost-effective strategy for long term treatments. The PSA estimated that in 70% of the iterations the NMB of SA were the highest of four interventions (Figure 3b).

Combining SA-SN services was cheaper, but less effective than SN alone. The ICER showed that SA remained the most cost-effective strategy. Several SA-SN combination strategies (55:45; 60:40; 40:60 ratio) were analysed but none were more cost-effective than SA alone (Table 2).

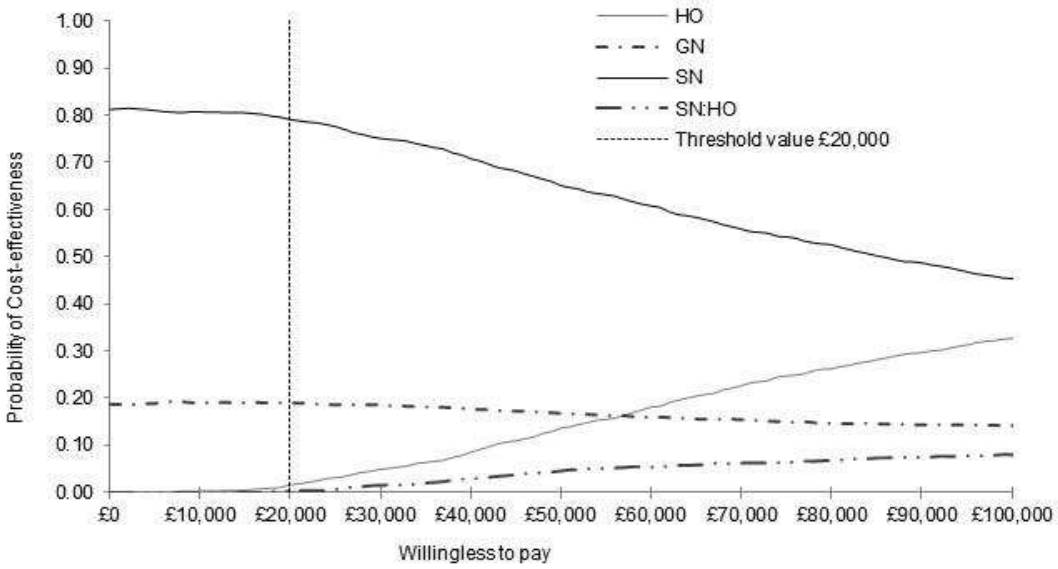
Table 2. Probabilistic cost-effective analysis for long term treatment

Intervention	Costs	QALYs	ICER*	Jackknife 95% CI**		Net monetary benefit	Result
				Lower bound	Upper bound		
SA	£1,883	0.6660				**£11,436**	Cost-effective
SA 50%;SN 50%	£2,128	0.6721	£39,819	£35,277	£44,136	£11,314	Not cost-effective
SN	£2,379	0.6767	£54,364	£46,059	£62,117	£11,155	Not cost-effective
GN	£2,957	0.6552	n/a	n/a	n/a	£10,147	Dominated
HO	£5,135	0.6698	n/a	n/a	n/a	£8,261	Dominated

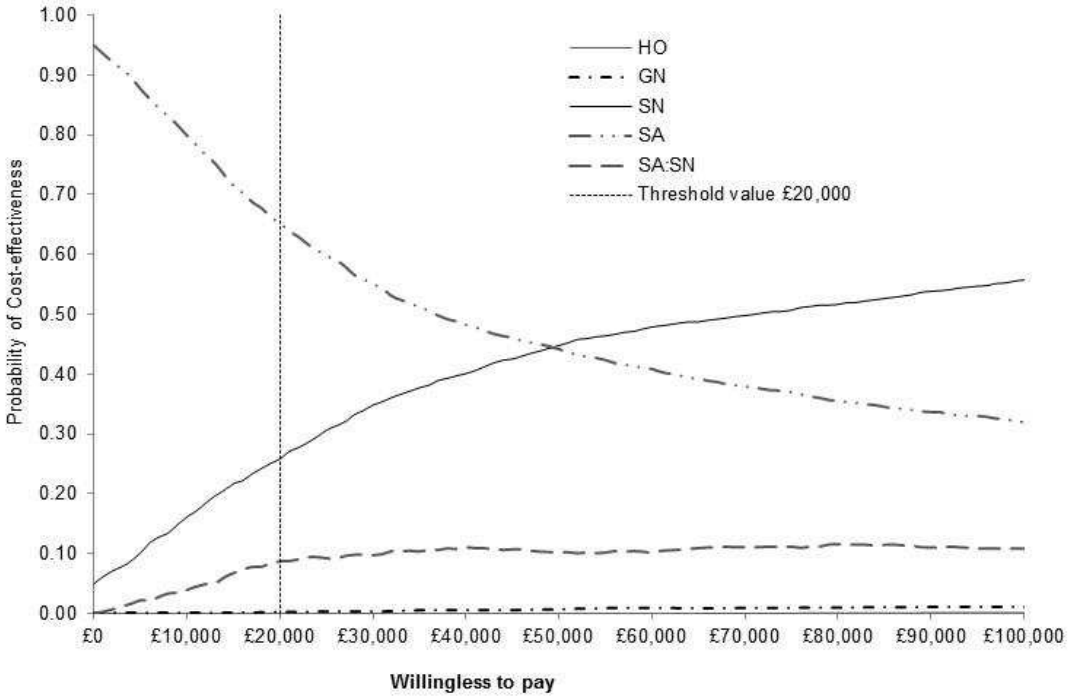
*ICER: Incremental analysis versus the next best strategy.
**Jackknifing was undertaken to assess the uncertainty in the mean value to determine if the number of iterations were sufficient for non-dominated strategies. The 95% CI shows that this was the case.[31]
ICER or Jackknife CI was not estimated for dominated strategies

Figure 3. Short and long term cost-effectiveness acceptability curve

a) Short term



b) Long term



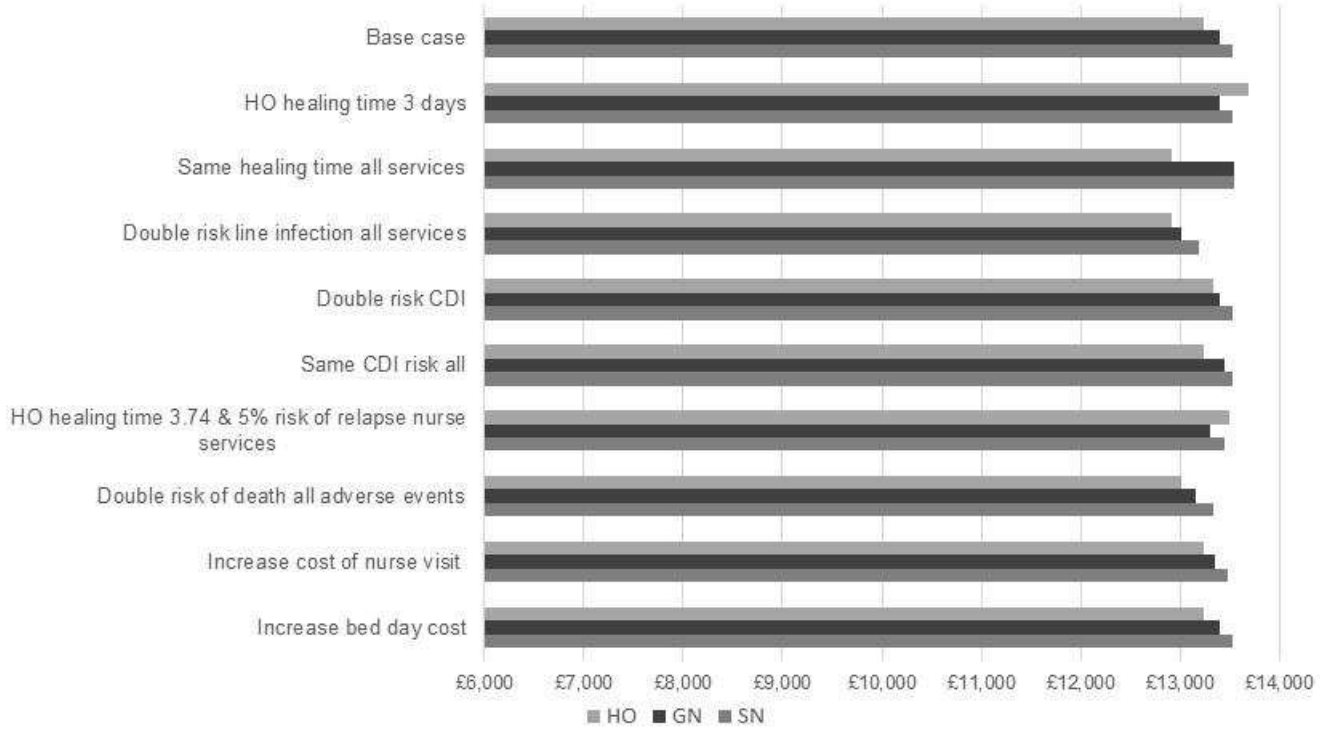
Sensitivity analysis

Several one-way sensitivity and scenario analyses were run. In both short and long term, the results remained the same: SN and SA had the highest NMB for short and long term treatments respectively.

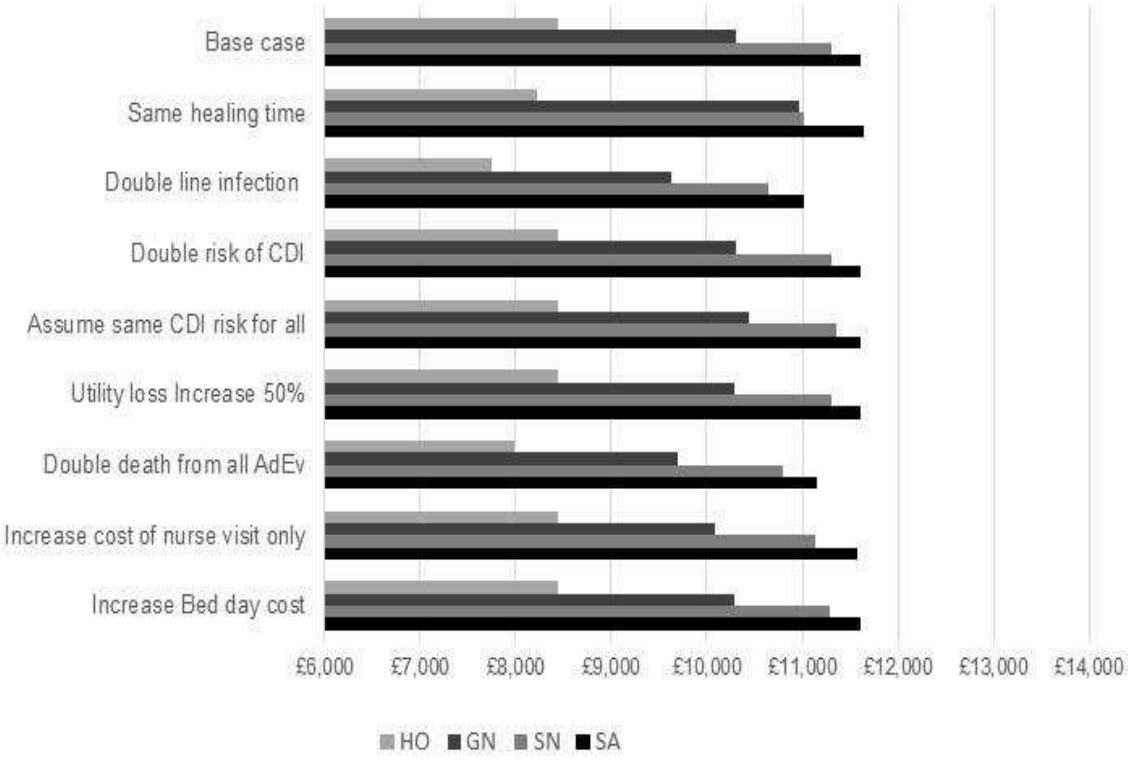
In the short treatment model, however, when healing time was assumed the same for all services, the NMB of GN and SN was almost identical. Furthermore, in one particular scenario where the healing time for HO was set to 3.74 days (reduced by 1 day from the base case) and a 5% risk of relapse introduced for the nurse-led services (0% in the base case), HO had the highest NMB and was therefore the most cost-effective strategy. When only the relapse rate was changed, the results remained unchanged. However, when the healing time was reduced further (from 4.74 to 3 days) HO became cost-effective. In the long treatment model, however, all one way and scenario analysis results suggested that SA was the most cost-effective strategy. Lastly, as expected, adding one initial and one discharge consultation with and infection specialist to all service models added the same net cost to all services, (£237.68), and so maintained the observed results (Figure 4).

Figure 4. Short and long term models: NMB estimation of the one way and scenario sensitivity analysis

a) Short term



b) Long term



Discussion

The aim of the study was to develop a decision-analytic model to estimate the cost-effectiveness of the four OPAT services offered in the UK for the infections requiring short or long term treatment.

The deterministic and PSA analysis in both models indicated that HO was not the optimal strategy. The incremental analysis results showed that SN and SA were the most cost-effective strategies for short and long term treatments respectively. The results were mainly driven by costs as the QALY difference observed was negligible (less than 0.01 QALY gained). The explanation for this is that the time horizon employed (12 months for both models) was relatively short and for many, the health event of interest is transient in nature with a very low risk of mortality. In contrast, there were significant cost differentials between the services which drove the cost-effectiveness results. The shorter healing time reported by HO and SN showed that these services can benefit from their ability to initiate IV to oral switch quicker than the GN or SA services. However, for HO in particular costs seem to outweigh this advantage. This is the case unless a significant reduction in healing time for short term treatments is observed (more than 30%). In general, results were robust to changes in the parameter values. Only a substantive reduction in average healing time or a particular combination of circumstances appear to change the decisions.

A combination of services for both short and long term treatment was tested to acknowledge that more than one service model will often be provided. However, none of the combinations was shown to be cost-effective. Despite the latter, this analysis found that they were second best in terms of NMB.

To our knowledge, this is the first study to compare the four analysed services following the NICE economic evaluation reference case. We found a study based in Canada, but it only compared home IVA against hospital inpatient based services[33]. Chapman et al. (2009)[3] did a complete cost-effectiveness analysis of OPAT for the UK, however, the study was based

on one health centre and it compared standard hospital inpatient care with daily attendances at a hospital facility.

The employed technique, DES allows us the possibility to simulate the operation of an OPAT service keeping track the progress and timing of the patients throughout their disease (i.e: account for side-effects or complications), therefore the measurement of costs and QALYs produced was more accurate than that provided by cohort models.

This work has some limitations. We were constrained to some extent by the available data. There was a paucity of useful comparative UK data on the effectiveness and safety of the OPAT services. We chose to use a hospital record dataset to derive our measure of 'effectiveness' (time to heal) as the systematic review could only identify effectiveness and risk values presented in observational studies. These were of limited value as the figures were likely to be biased; for example, some departments may only have considered certain patients (e.g. less severe or more independent) for particular OPAT services. The dataset, however, permitted adjustment for patient heterogeneity between services and did indicate differences in time to heal (or switch to oral antimicrobials).

Anti-microbial stewardship is currently a key concern but we chose not to model antimicrobial resistance. We believe the differential rate of resistance between the service models would have been negligible and did not warrant the additional layer of complexity in the models.

After discussing with clinicians it was apparent that dividing patients into those requiring short term and long term treatments was necessary as these two groups had distinct characteristics. For instance, it was not practical to train patients to self-administer antibiotics for short treatment courses while patients with long term treatments are more at risk of acquiring CDI or a secondary of intravenous lines infection. In terms of the adverse events considered, we focussed on those reported by the participants and which were expected to have a higher impact in terms of costs and quality of life. For example, we have not included deep venous thrombosis as none of the participants in the study suffered such event.

Future research on the cost-effectiveness of the OPAT service using a DES model could explore the need and use of resources (such as number of nurses needed) to provide information for commissioners on the requirements to establish an OPAT service in the UK. The findings of this paper as can also be used to inform future RCTs as they suggest that efforts should be focused on SN and HO for short and SA and SN for long term treatments.

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Transparency declarations

None to declare

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Supplementary material

Table S1 sample characteristics**.**

Parameter	Short term		Long term	
	n	**%**	**n**	**%**
	223		280	
Female	90	40.36	133	47.84
	Mean (SD)	**Range**	**Mean (SD)**	**Range**
Age	52.85 (16.36)	18-89	52.59 (18.25)	18-94
Ethnicity:				
White	195	87.44	257	91.79
Asian	20	8.97	16	5.71
Black	2	0.9	3	1.07
Mixed ethnicity	6	2.69	4	1.43
Type of service received:				
HO	154	69.37	63	22.58
GN	18	8.11	68	24.37
SN	36	16.22	34	12.19
SA	0	0	68	24.37
Combination	14	6.31	46	16.49
Type of infection:				
Cellulitis/SSTI	196	87.89	44	15.71
Cystic Fibrosis	0	0	44	15.71
Respiratory	8	3.59	37	13.21
Bone and Joint	0	0	73	26.07
Cardiovascular	1	0.45	11	3.93
Urinary tract	3	1.35	7	2.5
Intra-abdominal	2	0.9	7	2.5
Other	13	5.83	57	20.36
No. with infection in last 6 months	55	24.66	154	55.0
No. with complex infection	0	0	75	26.79
	Mean (SD)	**Range**	**Mean (SD)**	**Range**
C-reactive protein level	87.28 (93.01)		80.46 (99.52)	
White blood cell count	10.11 (3.55)		10.84 (5.12)	
Days to heal	5.77 (5.35)	1-55	28.54 (20.64)	4-119
Side effects	**N**	**%**	**N**	**%**
Rash	3	6.38	5	5.49
Nausea/vomiting	3	6.38	12	13.19
Dizziness	1	2.13	2	2.2
Fever	2	4.26	1	1.1
Diarrhoea	5	10.64	4	4.4
Infection of IV access device	1	2.13	2	2.2
Blocked IV device	9	19.15	13	14.29
Other	23	48.94	52	57.14

Table S2. Model parameter values – effectiveness, risks, quality of life and resource use

Parameter	Mean	SD	Distribution	Source
Short-term model effectiveness (days to heal)				
HO	4.73	0.24	Gamma	Adjusted hospital record data
GN	7.36	1.00	Gamma	Adjusted hospital record data
SN	6.33	0.65	Gamma	Adjusted hospital record data
Long-term model effectiveness (days to heal)				
HO	27.21	2.30	Gamma	Adjusted hospital record data
GN	31.16	2.65	Gamma	Adjusted hospital record data
SN	25.46	3.02	Gamma	Adjusted hospital record data
SA	28.20	2.52	Gamma	Adjusted hospital record data
Daily risk of an anaphylactic shock	0.00005	0.00099	Beta	(Matthews et al. 2007)
Anaphylactic shock mortality risk				
HO	0.067	0.04480	Beta	(Hopf et al. 2008)
GN	0.13	0.04480	Beta	Assumed double HO risk
SN	0.13	0.04480	Beta	Assumed double HO risk
SA	0.27	0.04480	Beta	Assumed double GN/SN risk
Risk of CDI				
HO	0.000105	0.000023	Gamma	Hourly risk x 4 (Ryan et al. 2007)
GN	0.0000087	0.000004	Gamma	Assumed third HO risk and 1 hour contact
SN	0.0000087	0.000004	Gamma	Assumed third HO risk and 1 hour contact
SA	0.00	N/A	Fixed	Assumed no risk
Time to heal from CDI (for all services; days to heal)	16	0.40	Log normal	(Forster et al. 2012)
Daily CDI mortality risk	0.00040	0.00004	Beta	(Wiegand et al. 2012)
Risk of a line infection that leads to a S. Aureus	0.00052	0.01580	Gamma	(Barr et al. 2012)
Time to heal from S. Aureus	17	0.32	Log normal	(Forster et al. 2012)
Daily S. Aureus mortality risk	0.0092	0.03346	Beta	(Thwaites & United Kingdom Clinical Infection Research 2010)
Short term model - mild adverse events				
HO	0.020	0.006	Gamma	Hospital record data
GN	0.046	0.032	Gamma	Hospital record data
SN	0.054	0.025	Gamma	Hospital record data
Long term model - mild adverse events				

HO	0.008	0.003	Gamma	Hospital record data
GN	0.007	0.003	Gamma	Hospital record data
SN	0.009	0.004	Gamma	Hospital record data
SA	0.033	0.009	Gamma	Hospital record data
Probability of infection relapse				
HO	0.0	N/A	Beta	Assumed 5% lower than SN
GN	0.0	N/A	Beta	Assumed same as SN
SN	0.0	N/A	Beta	(Lillie et al. 2010)
SA	0.0	N/A	Beta	Assumed same as SN
Quality of life				
Utility Short term				
Not healed	0.4360	0.342	Beta	(Mason et al. 2014)
Healed	0.7395	0.280	Beta	(Mason et al. 2014)
Utility Long term				
Not healed	0.0100	0.400	Normal	(Bernard et al. 2015)
Healed	0.7200	0.300	Beta	(Bernard et al. 2015)
Common parameters				
Hospital acquired CDI	-0.1150	Fixed	Beta	(Konijeti et al. 2014)
Utility loss per hospital stay due to line infection/anaphylaxis	-0.2400	0.0300	Beta	Assumed same as for asthma patients (Lloyd et al. 2007)
Death	-16.660	Fixed	Fixed	Life tables UK based on mean age of 50 and not healed utility value
Resource use				
HO				
One infectious disease specialist led-consultation (either at the start of treatment, as a review session or discharge)	£237.68		Fixed	NHS Ref costs 2013-14 - Consultant led infectious disease outpatient visit, first visit (Department of Health 2014)
Subsequent visit	£145.23		Fixed	NHS Ref costs 2013-14 - Non-Consultant led infectious disease outpatient follow-up visit (Curtis 2014; Department of Health 2014)
GN				
General nurse visit	£33.04		Fixed	PSSRU 2014 - Community nurse (Band 6). Band 5 equivalent estimated using mid-range salary (£24,063) Hourly cost. Each visit =1 hour except 1st which =1.5 hours. (Curtis 2014)
Discharge consultation by an infectious disease specialist	£237.68		Fixed	NHS Ref costs 2013-14 - Consultant led infectious disease outpatient visit, first visit (Department of Health 2014)
Two-weekly review session with an infectious disease specialist (only for the treatment of long term infections)	£237.68		Fixed	NHS Ref costs 2013-14 - Consultant led infectious disease outpatient visit, first visit (Department of Health 2014)
Paper work per visit	£7.30		Fixed	As above. Assume 10 minutes. (Curtis 2014)
SN				

Specialist nurse visit	£33.04	Fixed	PSSRU 2014 - Community nurse (Band 6). Band 5 equivalent estimated using mid-range salary (£24,063)*** Hourly cost. Each visit =1 hour except 1st which =1.5 hours (Curtis 2014)
Discharge consultation by an infectious disease specialist	£237.68	Fixed	NHS Ref costs 2013-14 - Consultant led infectious disease outpatient visit, first visit (Department of Health 2014)
Two-weekly review session with an infectious disease specialist (only for the treatment of long term infections)	£237.68	Fixed	NHS Ref costs 2013-14 - Consultant led infectious disease outpatient visit, first visit (Department of Health 2014)
Paper work per visit	£7.30	Fixed	As above. Assumes 10 minutes. (Curtis 2014)
SA			
Training session cost	£66.08	Fixed	£33.04*2. Assumes delivered by Band 5 Community nurse over 2 hours. (Curtis 2014)
Eclipse Balloon/Pump Device	£52.96	Fixed	Per-patient - based on expert opinion
Check-up nurse visit once a week (daily cost)	£4.72	Fixed	PSSRU 2014 (Community nurse Band 5) (Curtis 2014)
Two telephone calls per week (daily cost)	£0.94	Fixed	PSSRU (Community nurse Band 5) Assumes two phone calls lasting 6 minutes.(Curtis 2014) (Curtis 2014)
Discharge consultation by an infectious disease specialist	£237.68	Fixed	NHS Ref costs 2013-14 - Consultant led infectious disease outpatient visit, first visit (Department of Health 2014)
Two-weekly review session with an infectious disease specialist (only for the treatment of long term infections)	£237.68	Fixed	NHS Ref costs 2013-14 - Consultant led infectious disease outpatient visit, first visit (Department of Health 2014)
General costs			
Cost for use of healthcare services (per day)	£12.81	Fixed	Hospital record data
Antimicrobial treatment (per day)	£24.59	Fixed	Hospital record data, emit
GP surgery visit	£44.35	Fixed	PSSRU 2014 (Curtis 2014)
GP home visit	£113.45	Fixed	PSSRU 2014 (Curtis 2014)
Inpatient care cost	£208.33	Fixed	NHS Reference costs 2013-14 (Department of Health 2014)
Outpatient care costs	£146.45	Fixed	NHS Reference costs 2013-14 (Department of Health 2014)
A&E Cost	£117.58	Fixed	NHS Reference costs 2013-14 (Department of Health 2014)
Cost of adverse events			
Cost of severe line infection treatment	£236.66	Fixed	NHS Reference costs 2013-14 - Assumed equivalent to Kidney or Urinary Tract Infections, with Interventions excess bed day (LA04L). (Department of Health 2014)
Cost of CDI treatment	£289.62	Fixed	NHS Reference costs 2013-14 - Assumed equivalent to Kidney or Urinary Tract Infections, with Interventions excess bed day

			(LA04L) and isolation cost. (Department of Health 2014)
CDI isolation cost	£52.96	Fixed	Updated guidance of the diagnosis and reporting of CDI. Department of Health 2012 (Department of Health 2012)
Cost of treating anaphylaxis	£732.34	Fixed	NHS Reference costs 2013-14 - Shock or Anaphylaxis, with CC Score of 1 (WA16W) Total HRG (Department of Health 2014)
Patient visit costs			
Patient travel per day (miles)	6	Fixed	Assumption
Mileage costs (per mile)	£0.67	Fixed	NHS expense reimbursement rate
Car parking per visit	£6.30	Fixed	£4.20 per hour for 1.5 hours - assumption