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An economic evaluation of outpatient versus inpatient polyp treatment for abnormal uterine bleeding

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Running title:

OPT economic analysis

Abstract:

Objectives – To undertake a cost-effectiveness analysis of outpatient uterine polypectomy compared with standard inpatient treatment under general anaesthesia.

Design – Economic evaluation carried out alongside the multi-centre, pragmatic, non-inferiority, randomised controlled Outpatient Polyp Treatment (OPT) trial. The UK National Health Service (NHS) perspective was used in the estimation of costs and the interpretation of results.

Setting – 31 secondary care UK NHS hospitals between April 2008 and July 2011

Participants - 507 women with abnormal uterine bleeding and hysteroscopically diagnosed endometrial polyps.

Interventions – Outpatient uterine polypectomy versus standard inpatient treatment. Clinicians were free to choose the technique for polypectomy within the allocated setting.

Main outcome measures - Patient reported effectiveness of the procedure determined by the women's self-assessment of bleeding at six months, and QALY gains at six and 12 months.

Results – Inpatient treatment was slightly more effective but more expensive than outpatient treatment, resulting in relatively high incremental cost effectiveness ratios. Intention to treat analysis of the base case at six months revealed that it cost an additional £ 9,421 per successfully treated patient in the inpatient group and £ 1,099,167 per additional QALY gained, when compared to outpatient treatment. At 12 months, these costs were £ 22,293 per additional effectively treated patient and £ 445,867 per additional QALY gained respectively.

Conclusions –Outpatient treatment of uterine polyps associated with abnormal uterine bleeding appears to be more cost-effective than inpatient treatment at willingness to pay thresholds acceptable to the NHS.

Trial registration – ISRCTN: 65868569

Tweetable abstract: HTA funded OPT trial concluded that outpatient uterine polypectomy is cost effective compared with inpatient.

Introduction

Abnormal uterine bleeding (AUB) is one of the four most common reasons for consulting a general practitioner and accounts for 70% of all referrals to hospital gynaecology clinics[1], making this complaint one of the commonest problems in gynaecology. A large proportion of health care resources in both primary care and hospital settings are used up in managing this condition[1]. Uterine polyps are one of the most prevalent pathologies underlying AUB being diagnosed in 20 to 30%[2-4] of women with this presenting complaint. Until recently, conventional practice has been to undertake this simple procedure under general anaesthesia as an inpatient in hospital usually by blind uterine curettage ('D&C'). Due to the need for inpatient hospital admission and general anaesthesia, this approach is associated with relatively heavy use of health care resources, with over 25,000 inpatient procedures being performed during 2011/12 in the United Kingdom[5]. Recent advances in endoscopic technology have now made it now possible to perform uterine polypectomy in a convenient outpatient setting without the need for hospital admission and anaesthesia. Furthermore, treatment can be carried out at the same time as diagnosis; the "see & treat" approach. However, the limitations of operating within the genital tract of a conscious patient may offset any apparent benefits over traditional practice.

This economic evaluation was carried out alongside the Outpatient Polyp Treatment (OPT) trial which was a pragmatic multicenter randomized controlled non-inferiority study, comparing outpatient uterine polypectomy to inpatient treatment. The clinical findings of the trial are reported elsewhere [2]. The primary objective of the study was to determine whether outpatient removal of uterine polyps was non-inferior to inpatient polypectomy, the standard treatment offered by the National Health Service (NHS) in the UK. The primary end point was patient reported improvement in bleeding symptoms at six and

twelve months. The aim of the economic evaluation was to determine the cost-effectiveness of outpatient polyp treatment compared with standard inpatient treatment.

Methods

Women who attended outpatient hysteroscopy clinics complaining of abnormal uterine bleeding and were found to have a uterine polyp were eligible to take part in the OPT trial. If they gave consent, they were randomised to either outpatient or inpatient polypectomy.

The base case economic evaluation adopted the perspective of the NHS and took the form of cost-effectiveness and cost utility analyses.. The outcomes of interest were patient self-assessment of treatment success at six and twelve months for the cost effectiveness analysis, and quality adjusted life years (QALYs) gained at one year for the cost-utility analysis. The costs and outcome measures used for this economic analysis were collected prospectively during the OPT trial. In addition, in order to explore societal perspective on costs, the out of pocket expenses incurred by the patients when attending for appointments and private time costs (including loss of time from work) were also collected using a separate questionnaire which was administered to the patients at randomisation and again on the day of procedure, if this was performed at a later date.

All analyses were carried out using SAS 9.2®, Stata 12® and Microsoft Excel 2007®. The reporting of this analysis follows the Consolidated Health Economic Evaluation Reporting Standards (CHEERS)[6].

Costs:

All costs in the analysis are in UK pounds (£), based on 2011/12 values. An *a priori* decision was made to use two separate methods to estimate the costs in this analysis: The first method was to use the published standard sources of costs for NHS procedures (NHS Reference costs 2011-12[7] and Personal Social Services Resource Unit (PSSRU)[8] Costs 2012) which was preferred for the base case analysis as it

ensured that the results would be generalisable to all centres in the UK. The second method was to estimate the costs of inpatient and outpatient polypectomy by estimating the costs of the individual components of these procedures (bottom-up costing). Health and Community Health Services (HCHS) pay and price indices were used to inflate costs, where appropriate[8].

Unit costs were attached to the cumulative resource use in each treatment group in order to calculate costs in both arms of the trial. Outpatient and inpatient polypectomy costs were estimated as per the NHS Reference costs (Table1). All patients recruited into the trial were assessed in an outpatient clinic and underwent an outpatient hysteroscopy where the uterine polyps were diagnosed. Whilst most of the patients randomised to an outpatient procedure were treated on their initial visit, 28% were scheduled to attend for their treatment at a later clinic appointment. All patients randomised to inpatient were assumed to have undergone pre-assessment in a nurse led clinic to ensure that they were suitable to receive general anaesthesia before being scheduled for their day-case inpatient procedure.

Outcomes:

Outcome data of interest within the trial were patient reported effectiveness of the procedure and also QALY gains at 6 and 12 months respectively. Within the OPT trial, the woman's own assessment of bleeding symptoms was used to establish if the treatment had been successful. Those patients whose predominant complaint before the procedure was postmenopausal bleeding or intermenstrual bleeding were determined to have had a successful treatment if their abnormal bleeding had stopped. In women with heavy menstrual bleeding, treatment was successful if the patient reported that their bleeding had returned to an acceptable level following the procedure.

All the patients in the trial were asked to complete EQ-5D (3L) questionnaires at baseline, 6 and 12 months and the responses obtained were used as the basis for the cost utility analysis.

Assumptions:

It was necessary to make the following pragmatic assumptions before the analysis could be carried out.

- All the centres involved in the trial were assumed to have the same expertise and to have followed similar protocols in the management of these patients.

- Only the related events (REs) that occurred within 1 year of the procedure and were deemed relevant to the polypectomy were included in the analysis. Related events included immediate complications of the procedure, all hysterectomies (irrespective of the indication), endometrial ablations and hysteroscopic procedures (excluding polypectomies) . Costs relating to further polyp related procedures, if any, were also estimated and stated separately to the REs.

- The costs of procurement of the different endoscope camera systems used by participating centres in this study (Versascope™, Olympus™, Storz®) were assumed to be the same (at £50,500- see Table 2). The costs obtained by contacting the individual manufacturers of this equipment only varied from each other by around £1,000.

Analysis:

The base case analysis estimated costs and outcomes as per intention to treat.

Cost effectiveness analysis (CEA) was carried out at 6 and 12 months based on the outcomes expressed in natural units which were estimated using responses obtained from patients to the question regarding effectiveness of the procedure. The results are expressed in terms of cost per additional patient successfully treated (based on alleviation of symptoms) at 6 months and 12 months.

A cost utility analysis (CUA) was also carried out at 6 and 12 months and the results are expressed as additional cost incurred per QALY gained. Quality of life estimates were derived from the EQ5D responses provided by patients at baseline, 6 and 12 months by applying the standard UK tariff values. These estimates were then used to calculate total QALYs over 6 and 12 months for every individual in the study, using standard methods [9].

. The results of the CUA are presented using cost-effectiveness acceptability curves (CEAC) to reflect sampling variation and uncertainties in the appropriate threshold cost-effectiveness value.

Since the time frame of this economic evaluation was only one year, discounting was not necessary. Also, given that there was no significant difference in the baseline EQ5D scores (Table 3), a baseline adjustment was not performed during the analysis.

All missing data were treated as missing at random and imputed using the Markov Chain Monte Carlo multiple imputation method. Bootstrapping was carried out to compare arithmetic means of the skewed cost and outcome data without making any assumptions regarding the sampling distributions (Table 3) [11]

A range of one-way sensitivity analyses were carried out to explore the robustness of the base case results to plausible variations during the uptake of these procedures in routine NHS use. A deterministic sensitivity analysis (DSA) was carried out to assess the uncertainty associated with input parameters for the base case and to widen the perspective. This technique estimates the effect of changing a single parameter (i.e., either cost or effectiveness) on the overall ICER obtained. The point estimates used for all the other parameters remain unchanged. In summary the following four options were considered.

1. Using bottom-up costs for outpatient and inpatient polypectomy (DSA1): In the initial analyses, we only considered costs that were stipulated in the NHS reference costs. Whilst these costs are representative of the expenses incurred in the UK, in order to make the results more

generalisable we calculated the costs of the procedures by breaking them down to the individual components involved and then adding up all the costs to obtain an overall cost (i.e. bottom up costing) and repeated the analyses. The estimated 'bottom-up' costs for the outpatient and inpatient procedures are outlined in Tables 4 and 5 respectively.

2. <u>Considering the out-of-pocket costs incurred by patients for the treatment (Societal perspective) (DSA2):</u> Since polypectomy is a quick procedure that is not expected to result in long standing illness or absence from work, the human capital approach method was used to estimate the societal costs of inpatient versus outpatient polypectomy. For those patients (and companions) who were in paid employment, the average hourly wage was calculated using the Office for National Statistics (ONS) estimates for the whole UK economy[12] and an estimated 38.5 hours of work per week. Estimates used for leisure activities and house hold work were 42% and 57% of the net wage rate. These were derived from published literature [13]. The cost of looking after relatives was assumed to be the same as that of household work (57% of net hourly wage). Where patients had taken paid time off work, these costs would have been incurred by the employers and were therefore included in the analysis. Those who were not involved in housework and were not in active employment (e.g. university students, retired persons) were assumed to incur the same costs as that for leisure activities.

Private travel costs were derived from the automobile association (2012)[14]. These costs include total standing and running costs (fuel, parking, tolls, depreciation, wear and tear, tyre replacement, servicing etc.) and depend upon the annual mileage and type of car[14]. The cost of using public transport and car parking fees (where relevant) were directly obtained from the patients. Where time and mileage data were missing, these were assumed to be the same as the average for the entire group.

3. Effect of 'See and treat' clinics (DSA3a and DSA3b): We re-analysed the data assuming that all patients (100%) and no patients (0%) were treated on the day of randomization (DSA3a and DSA3b respectively)

4. Using new tariffs for outpatient polypectomy (DSA4): Previously there was a lack of incentive for 'see and treat' outpatient clinics given that the remuneration was low. During the course of the study, the tariff for outpatient hysteroscopic procedure was increased and thus we used a higher cost (£ 1000) in a sensitivity analysis to predict the effect of this change.

In addition, a probabilistic sensitivity analysis (PSA) of the base case was carried out to enable the simultaneous exploration of the uncertainties in the cost and outcome data. ,000 simulations were carried out using the Monte Carlo principle and the results were used to generate cost-effectiveness acceptability curves (CEACs), to demonstrates the probability of either intervention being cost effective at various willingness-to-pay thresholds. The results of these analyses are presented in terms of incremental cost effectiveness ratios (ICER) which reflect the additional cost per additional outcome of interest of outpatient versus inpatient treatment. 5

Results

The results for the base case analysis are presented in Table 6. The point estimates of the mean costs incurred at 6 months on the outpatient and inpatient arm were £ 822 and £ 1482 respectively, a cost difference of approximately £ 660 (95% CI: 516.2-780.7). At the end of 12 months, the costs increased slightly to £ 938 and £ 1606 respectively, a cost difference of approximately £ 669 (95% CI: 517.0-833.1). The point estimates for difference in QALY were 0.0006 and 0.001 at 6 and 12 months respectively. The proportion of patients who reported improvement in symptoms following polypectomy was 0.74 and 0.81 at 6 months and 0.82 and 0.85 at 12 months in the outpatient and inpatient arms respectively.

Thus, the difference in effectiveness at 6 and 12 months was 0.07 (95% CI: -0.15- -0.01) and 0.03 (95% CI: -0.09-0.04)

The incremental cost effectiveness ratio (ICER) for the inpatient arm compared to outpatient arm at 6 months was £ 1,099,167 per QALY, meaning that each additional QALY gained in the inpatient cost an additional £ 1,099,167. At 12 months the ICER was £ 445,867 per QALY. In the inpatient arm for each patient that had their symptoms successfully resolved, it cost an extra £9,421 compared to the outpatient arm. By twelve months post treatment this cost increased to £ 22,293. (Table 6).

Deterministic Sensitivity analysis:

Holding the outcome data constant, one-way deterministic sensitivity analyses were carried out by changing the cost data. As shown in Table 7, inpatient polypectomy remained more expensive than outpatient treatment in all of the scenarios considered.

Probabilistic Sensitivity Analysis (PSA):

Probabilistic sensitivity analysis showed that the likelihood of outpatient polypectomy being effective (when EQ5D estimates are used as outcome of interest) is similar to that of inpatient treatment. Figures 1 and 2 clearly demonstrate that whilst inpatient treatment is definitely more expensive than the outpatient treatment, the difference in effectiveness is more uncertain. The mean cost differences between the groups as per the PSA were £ 661 and £ 658 at 6 and 12 months respectively (the inpatient costs are higher). The corresponding values for QALY difference were 0.0002 and 0.0005 respectively at 6 and 12 months (the inpatient QALY gain is higher). This suggests that the effects of the treatment on costs and QALYs beyond 6 months, as expected, are minimal.

The CEACs shown in Figure 3 demonstrate that since both treatments are equally effective, the cheaper treatment will be the preferred procedure at lower willingness to pay (WTP) thresholds. Indeed,

inpatient and outpatient therapy only start to become equally cost effective at a WTP threshold of £ 90,000.

Discussion

Main findings:

We found that inpatient polypectomy was more expensive than outpatient treatment and marginally more effective, resulting in slightly higher point estimates of self-reported effectiveness and QALY values at six and 12 months. The differences in costs and outcomes between these procedures were fairly constant at these time points reflecting that the treatment has very little long term (i.e. beyond six months) implications for health and resource use. The ICERs obtained by cost-effectiveness and cost-utility analyses were very high, reflecting the equivalence in effectiveness between these procedures.

Whilst the mean estimates of outcomes appear to favour inpatient treatment, it is important to note that there was considerable uncertainty around these point estimates. This was explored further using probabilistic sensitivity analysis, clearly demonstrating that whilst outpatient therapy is definitely cheaper than inpatient treatment, the effectiveness estimates are uncertain with the likelihood of effectiveness being roughly equal in both groups at 6 and 12 months (Fig. 1 and 2).

A range of cost variations which were considered plausible during the implementation of these treatment pathways within the NHS were considered. However, these did not make a difference to the conclusions from the base case analysis. It is notable that the bottom-up costs estimated for outpatient and inpatient procedure during this analysis were quite close to the tariffs from the NHS reference costs (Tables 4 and 5).

Although this was a non-inferiority trial and there was equivalence in effectiveness whilst costs were different between the groups (the so called 'weak dominance' situation as postulated by Drummond et

al[15]), a cost minimization analysis was not considered appropriate since this would not provide adequate information regarding the uncertainty in the estimates. This was better estimated by carrying out a full cost effectiveness and probabilistic sensitivity analyses [16].

Strengths and limitations:

The OPT trial is the first, large randomised prospective study to estimate the costs and effectiveness of inpatient versus outpatient treatment for uterine polyps in women with abnormal uterine bleeding. Economic data in this study were collected prospectively alongside clinical outcome data enabling accurate estimation of the costs and outcomes. In addition, robust techniques were used to account for data uncertainty, missing data and the skewness of data. Although the base case analysis is mainly relevant to the UK, the sensitivity analyses enhance the generalisability of the findings of the study.

It was assumed for the purposes of this analysis that all the participating UK centres had similar expertise with regards to inpatient and outpatient treatments, but it is possible that centres where outpatient therapy has been offered on the NHS for many years perform the procedure better when compared to those with relatively inexperienced clinicians. It was not considered appropriate to explore in detail the heterogeneity across centres using approaches such as a random effects model. Such an approach is unlikely to be illuminating because of the additional limitations associated with trying to incorporate a large number of centres who recruited a small number of patients into a model as this would lead to model convergence problems. In addition, in the interests of simplicity and clarity, the economic analysis did not explore the differences in costs and outcomes in subgroups of patients considered within the trial (e.g. pre vs. post-menopausal; different age groups etc.). The clinical effectiveness results for these groups were roughly similar[2] and it was, therefore, felt that no further value could be added by extending the analysis.

Training costs were not included in this analysis. However, hysteroscopy is now routinely performed in the outpatient setting by most gynaecologists and performing an outpatient polypectomy will need relatively little further training for those already proficient with the diagnostic procedure. In addition, it is envisaged that all current clinical trainees (and future consultants) will have acquired the skills necessary for this procedure during their training.

Interpretation (in light of other evidence)

To our knowledge, this is the only study to prospectively estimate and compare the costs and outcomes of inpatient versus outpatient treatment for this common condition[17]. An earlier economic analysis, conducted alongside a single centre, retrospective audit of 60 patients had identified the potential cost-effectiveness of polyp treatment in an outpatient setting [18].

Conclusion

In conclusion, outpatient polypectomy appears to be more cost-effective than the inpatient approach to uterine polypectomy at currently acceptable willingness to pay thresholds for the NHS. Thus, for the many women presenting with abnormal uterine bleeding due to uterine polyps, the outpatient hospital or community treatment setting should be recommended as the best use of limited NHS resources.

We also acknowledge the vital role played by the trial steering committee and the data monitoring committee during this trial.

Contributions to authorship:

LD carried out the economic analysis for this study under the supervision of TER and SJ. SJ was involved with the planning and supervision of the economic analysis,; NAMC was involved in the recruitment of patients into the trial, analysis and presentation of the results; LJM was the statistician for the OPT trial and was involved with study planning, data analysis and presentation; PS was involved with patient recruitment and data collection; JD was involved with the initial planning of the trial. TJC was the chief investigator for the OPT trial and was involved with the planning, analysis and oversight if the trial; TER planned and supervised the health economic evaluation and is the guarantor for this work.

All the authors have reviewed and approved the manuscript.

Ethical approval:

Ethical approval was obtained from the South West Research Ethics Committee on 15th February 2008. Reference number: 08/H0206/6.

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Table 1: Costs allocated to outpatient and inpatient polypectomy

Resource	Details[1]	Cost (£)
Outpatient Costs		
Initial outpatient clinic	Consultant gynaecologist led face to face clinic; non-admitted	146

Hysteroscopy	Initial outpatient hysteroscopy for diagnosis of polyps; MA21Z	197
Follow-up outpatient clinic	Gynaecology: Follow-up appointment consultant led; face to face; no admission	112
Outpatient polypectomy procedure	Outpatient procedure; MA12Z	188
	Total cost	**643**

Inpatient costs

Initial outpatient clinic	Consultant gynaecologist led face to face clinic; non-admitted	146
Hysteroscopy	Initial outpatient hysteroscopy for diagnosis of polyps; MA21Z	197
Pre-op assessment clinic	Gynaecology: First appointment non-consultant led; face to face; no admission	118
Daycase polypectomy procedure	Daycase procedure; MA12Z	995
	Total cost	**1456**

[1] All costs are derived from the NHS reference costs 2011/12

Costs are for patients who had diagnostic polypectomy at their first appointment and treatment at a second appointment. Where patients are seen and treated in the same clinic, the costs will be £531 (i.e excluding follow up clinic costs.

Table 2: Equipment procurement costs

Equipment	Procurement Cost (£)*	equipment lifespan in years	Annutisation factor^	Annuitised costs (£)^^	times re-used per week	Sterilisation/ maintenance per patient(£)	Cost per patient (£)
Cervical Speculum	2	0 (disposable)	0	2	0	0	2
Grasping Forceps**	662.5	5	0.842	773.7	5	0.2	0.8
Hysteroscope	5,400	10	0.71	6,493	5	1.5	4
Electrode	212**	0 (disposable)	0	0	0	0	212
Hysteroscope camera system (Olympus / Versascope / Storz)	50,500	5	0.71	59,268	20	14.1	25.5
Total cost for equipment	**56,776.5**						**237.5**

Grasping forceps (reusable 3 prong forceps for large polyp and foreign body retrieval length 1650mm opening diameter 20mm)- procurement cost per year = 662.5; Annuitised cost = 773.7; Cost per year = 773.7/5=154.7; cost per patient = 154.7/260 = 0.6; Including sterilisation costs = 0.6+0.2 = 0.8

** costs inflated from 2000 prices [129] to 2011 using the PSSRU inflation indices ^ at 3.5% discount rate over the lifespan of the equipment ;

^annuitisation costs (E) calculated as per [147] : $E=[K-(S/(1+r)n)]/A(n,r)$; where K is the procurement cost, S is the re-sale value, r is the discount factor (3.5%) and n is the estimated lifespan of the equipment. A is the annuitisation factor that is estimated from the values of n and r (adapted from Drummond, M.F. et al, Methods for the Economic Evaluation of Health Care Programmes. Third ed. 2005, Oxford: Oxford University Press)

Table 3: Outcome data at baseline, 6 and 12 months

	Outpatient	Inpatient
Base case analysis (ITT):	N=254	N=253
Effectiveness 6 months	0.73; 0.45 (10.2%)*	0.80; 0.40 (16.6%)*
Effectiveness 12 months	0.81; 0.39 (11.4%)	0.83; 0.38 (15.4%)
EQ5D baseline	0.78; 0.25 (4.7%)	0.79; 0.27 (8.3%)
EQ5D 6 months	0.87; 0.22 (9.5%)	0.87; 0.2 (16.6%)
EQ5D 12 months	0.86; 0.25 (10.6%)	0.86; 0.24 (13.4%)

*results shown as mean; standard deviation
*numbers in brackets signify percentage of data missing/ unavailable for analysis

Table 4: Bottom up costs for outpatient polypectomy

Resource	Cost per patient (£)	Source	Details
Initial clinic	86	PSSRU	30 min of gynaecological consultant time including training cost
Hysteroscopy	239.6	Critchley et al	Inflated to 2011/12 rates from 2004 costs^
Nurse (Band 6)	21.50	PSSRU	30 min
Consultant	73.5	PSSRU	30 min of gynaecological consultant time
Procedure costs	237.5	Estimated	See table 3
Local Anaesthetic costs	0.35	Estimated	Derived based on usage data from the trial
Total cost	**658.45**		

*A further cost of £ 86 was added for patients who did not have treatment on the day of initial assessment.

^Inflated using PSSRU hospital and community health services (HCHS) index.

Table 5: Bottom up costs for inpatient polypectomy

Resource	Cost per patient (£)	Source	Details
Initial assessment:			
Initial clinic	86	PSSRU	30 mins of consultant time incl training costs
Hysteroscopy	239.6	Critchley et al	Inflated to 2011/12 rates from 2004 costs*
Pre-assessment clinic	78.8	PSSRU	45 min of Band 6 nurse time – with patient contact
ECG	61	NHS ref	Monitoring Electrocardiogram EA47Z
Blood tests	5	Local NHS laboratory	Full blood count (£ 2) and urea and electrolytes (£ 3)
Procedure costs:			
Day case admission cost	673	NHS ref	Unit price; Day case admission
Nurse assessment (Band 6)	10.75	PSSRU	Assessment for admission; 15 min
Anaesthetist	24.5	PSSRU	Consultant; 10 min pre-op assessment
Porter costs	5.25	PSSRU	Transfer to operating theatre 30 min
Nurse cost (Band 5)	17.5	PSSRU	Transfer to operating theatre 30 min
Equipment cost	237.5	Derived	See Table 3
GA drugs	17.5	Estimated	Derived based on usage data from the trial
GA equipment	116.8	Estimated	Derived based on usage data from the trial
Post- operative			
Recovery ward	52.5	PSSRU	30 mins nurse time (Band 6); patient contact
Porter costs	5.25	PSSRU	Transfer to ward; 15 min
Nurse cost	17.5	PSSRU	Transfer to ward; 30 min
Discharge	14.75	PSSRU	Trainee doctor 5 min; Staff nurse 15 min (Band 5)

Overall cost	1,663.2

*Inflated using PSSRU hospital and community health services (HCHS) index.

Table 6: Results of the base case analysis:

	Outpatient^ n=254	Inpatient^ n=253	difference*
ITT analysis: (6 months)			
Overall cost	822.1 (832.3)	1481.6 (680.5)	-659.5 [65.7]
Overall QALY	0.41 (0.09)	0.41 (0.09)	-0.0006 [0.01]
Patient reported Effectiveness	0.74 (0.44)	0.81 (0.39)	-.07 [.04]
ICER (Δ cost / Δ effectiveness)	£9,421 per extra patient who feels better with inpatient treatment		
ICER (Δ cost/Δ QALY)	£1,099,167 per QALY gained on the inpatient arm		
ITT analysis: (12 months)			
Overall cost	937.6 (971.4)	1606.3 (861.5)	-668.8 [82.9]
Overall QALY	0.83 (0.19)	0.84 (0.18)	-0.001 [0.02]
Patient reported Effectiveness	0.82 (0.39)	0.85 (0.36)	-.03 [0.31]
ICER (Δ cost / Δ effectiveness)	£22,293 per additional patient who feels better with inpatient treatment		
ICER (Δ cost/Δ QALY)	£668,800 per additional QALY gained on the inpatient arm		

Table 7: Results of the Deterministic Sensitivity Analyses (DSA)

ITT analysis:	DSA1 (Bottom up costs)		DSA-2 (Out of pocket costs)		DSA-3a (see and treat at same appt for all OP)		DSA-3b (see then treat for all OP)		DSA-4 (New OP tariffs)	
	6 months	12 months	6 months	12 months	6 months	12 months	6 months	12 months	6 months	12 months
Cost difference^	-719.8 [68.8]	-664.2 [83.2]	-671.7 [66.2]	-618.6 [84.3]	-673.5 [66.8]	-620.4 [80.0]	-584.5 [65.7]	-531.4 [79.0]	-294.1 [63.0]	-241.0 [76.2]
ICER*	10,282.9	22,140	9,595.7	20,620	9,621.4	20,680	8,350	17,713.3	4,201.4	8,033.3
Cost/ QALY	1,199,666.7	664,200	1,119,500	618,600	1,122,500	620,400	974,166.7	531,400	490,166.7	241,000

^The negative values of cost difference imply that the cost of inpatient therapy is higher than that of outpatient treatment.

^Differences have been estimated using bootstrapping techniques so that the uncertainty around the mean cost estimates can be accounted for. The results are shown as mean difference [standard error of the difference]

*ICER here refers to cost difference/ difference in self-reported effectiveness at 6 and 12 months respectively. Effectiveness and QALY difference are assumed constant for DSA1 through to DSA4.

Figure 1: Probabilistic Sensitivity Analysis (PSA) for Outpatient vs Inpatient treatment (6 months)
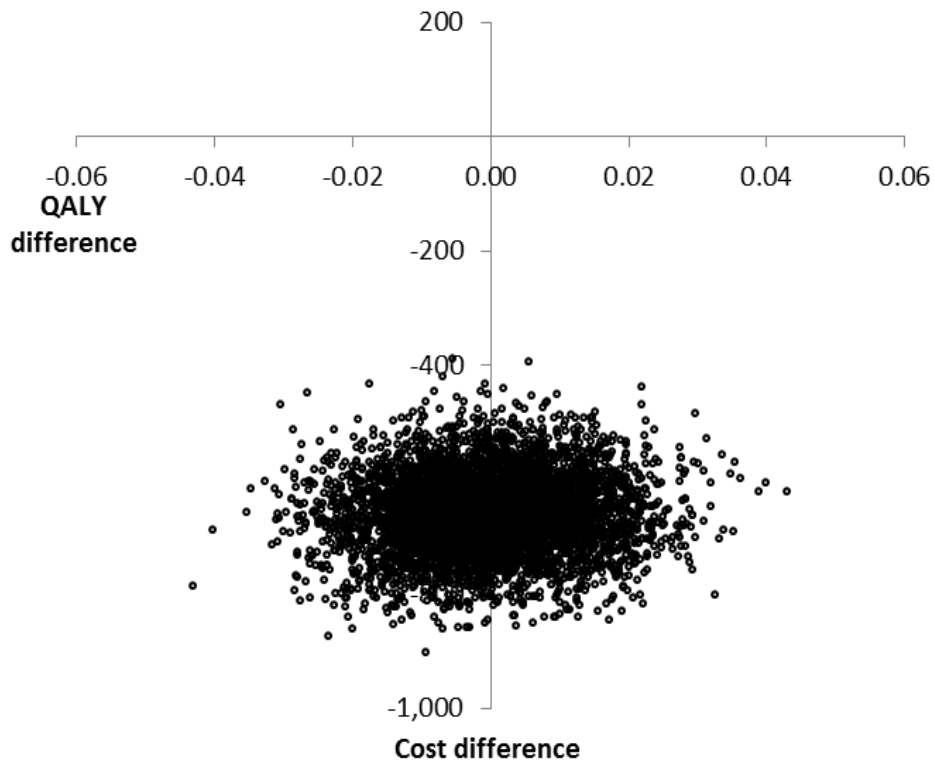

Figure 2: Probabilistic Sensitivity Analysis (PSA) Outpatient vs Inpatient treatment (12 months)
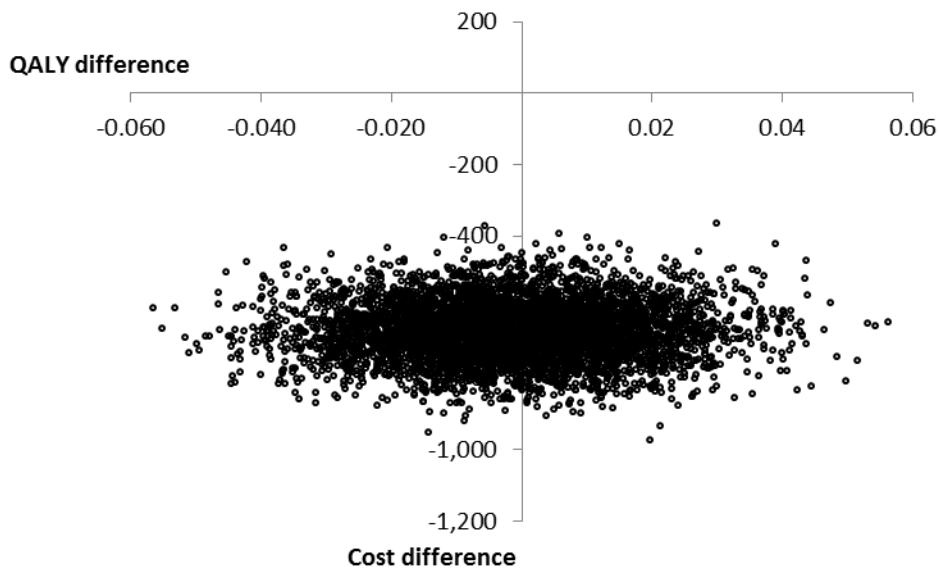

Figure 1 and 2: PSA analysis which simultaneously represents uncertainty in cost and QALY values at 6 and 12 months. The x and y axes represent the incremental effectiveness and cost of OP treatment compared with IP

treatment respectively. Most of the values fall in the lower right and left quadrants demonstrating that inpatient therapy is more expensive than outpatient treatment. The equal distribution between the left and right quadrants suggests that there is considerable uncertainty regarding the effectiveness of one treatment over the other (based on QALY values). In other words, the effectiveness of both treatments is similar.

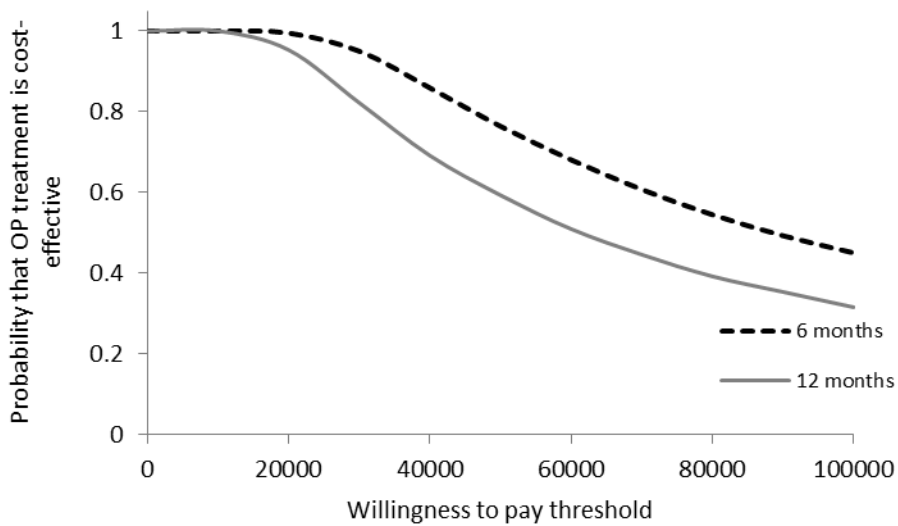**Figure 3: Cost effectiveness acceptability curve (CEAC) Outpatient vs Inpatient treatment**

Figure 3: A CEAC illustrates the uncertainty around the cost effectiveness estimates by demonstrating the likelihood of an intervention being cost effective at a given cost threshold compared to the proposed alternative. In this case, given that the likelihood of effectiveness of both treatments is roughly the same, the cheaper treatment is considered most cost-effective at baseline.