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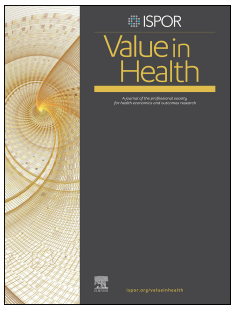

Cost-effectiveness of two models of pessary care for pelvic organ prolapse: Findings from the TOPSY randomised controlled trial.

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Title:

Cost-effectiveness of two models of pessary care for pelvic organ prolapse: Findings from the TOPSY randomised controlled trial.

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Precis:

Pelvic organ prolapse affects a substantial proportion of women with negative symptoms.

Pessary self-management is a cost-effective conservative treatment option for women in the UK.

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Highlights

- Women who experience pelvic organ prolapse report discomfort and associated urinary, bowel and sexual problems with considerable costs and negative impact on quality of life. Pessary self-management may offer benefits to women and to the health service without increased risk when compared to clinic-based care.
- With pessary self-management women receive training to be able to remove and reinsert the pessary themselves at home, thus by design offering more personal control and less physical contact with healthcare staff. The aim of the economic evaluation in this study was to investigate health service resources required and cost-effectiveness of pessary self-management (SM) when compared to clinic-based care (CBC) at 18 months, from a health sector perspective.
- Pessary self-management for prolapse is cost-effective when compared to clinic-based care. Decision analytic modelling showed self-management remained a cost-effective option for durations longer than the 18 month trial. Self-management is an approach that can be used for non-surgical management of prolapse without negatively impacting women's QoL, which can release scarce resources in a health system under pressure.

Abstract

Objectives: Pelvic organ prolapse is the descent of one or more reproductive organs from their normal position, causing associated negative symptoms. One conservative treatment option is pessary management. The aim of this study was to investigate the cost-effectiveness of pessary self-management (SM) when compared to clinic-based care (CBC). A decision-analytic model was developed to extend the economic evaluation.

Methods: A randomised controlled trial with health economic evaluation. The SM group received: 30-minute self-management teaching session; information leaflet; 2-week follow-up call; and a local helpline number. The CBC group received routine outpatient pessary appointments, determined by usual practice. The primary outcome for the cost-effectiveness analysis was incremental cost per QALY, 18 months post-randomisation. Uncertainty was handled using nonparametric bootstrap analysis. In addition, a simple decision analytic model was developed using the trial data to extend the analysis over a 5-year period.

Results: There was no significant difference in the mean number of QALYs gained between SM and CBC (1.241 vs 1.221) but mean cost was lower for SM (£578 vs £728). The incremental net benefit estimated at a willingness to pay of £20,000 per QALY gained was £564, with an 80.8% probability of cost-effectiveness. The modelling results were consistent with the trial analysis: the incremental net benefit was estimated as £4,221 and the probability of SM being cost-effective at 5 years was 69.7%.

Conclusions: Results suggest that pessary self-management is likely to be cost-effective. The decision analytic model suggests this result is likely to persist over longer durations.

Key words

Pelvic organ prolapse

Pessary

Self-management

Cost-effectiveness analysis

Introduction

Pelvic organ prolapse is the descent of one or more of the anterior vaginal wall, posterior vaginal wall, uterus or vaginal vault, from their normal position, causing associated negative symptoms[1]. Prolapse is a common problem, with studies suggesting that up to 50% of women have prolapse on examination in the UK: some cases have minimal symptoms but the overall lifetime risk of prolapse surgery is high at 9.5%[2, 3]. Pelvic organ prolapse can be uncomfortable, distressing and embarrassing; women who experience prolapse report discomfort and associated urinary, bowel and sexual problems with considerable costs in terms of productivity[4]. Prolapse often causes embarrassment which may be the reason behind under-reporting[2] and has been shown to negatively affect women's quality of life and body image[5, 6].

Prolapse can be treated conservatively or surgically, the latter being associated with increased health service and societal costs[7, 8]. Due to publicised surgical management risks women are more likely to prefer conservative treatment options prior to surgery, which is also the UK guideline-recommended course of action[9, 10]. It is important to improve our understanding of conservative options as these have fewer side-effects, are more suitable for some groups of women and are less costly than surgery[2, 11]. One conservative treatment option is insertion of a vaginal pessary which is an inexpensive device designed to support the pelvic organs[12, 13]. Pessaries have been shown to be cost-effective when compared to expectant management, some surgical options and pelvic floor muscle training[14, 15]. However, there are no studies that offer a cost-effectiveness comparison between different care pathways for women who use a pessary for prolapse. This study seeks to address this.

Current UK care guideline for women who use a pessary as treatment for prolapse suggest that the pessary is usually fitted and monitored in a healthcare setting every 3 to 6 months[16].

An alternative to clinic-based care is pessary self-management where a woman receives training to be able to remove and reinsert the pessary herself at home, thus by design offering more personal control and less physical contact with healthcare staff[17]. Pessary self-management may offer benefits to some women and economic benefits to the health service without increased risk when compared to clinic-based care[17, 18]. However, the impact of self-management on patient outcomes or the extent of cost-savings, given the reduced contact with the health service when compared to clinic-based care, is unknown. It is also uncertain if potential benefits can be sustained over the medium to long term.

The TOPSY study was a randomised controlled trial which aimed to determine the clinical and cost-effectiveness of self-management of vaginal pessaries[19]. The aim of the economic evaluation in this study was to investigate health service resources required and cost-effectiveness of pessary self-management (SM) when compared to clinic-based care (CBC) at 18 months, from a health sector perspective. This study also employed a simple decision analytic model to extend the primary economic evaluation to 5 years. This research is important because the impact of pessary SM on women's health related quality of life (HR-QoL) and the cost implications of SM when compared with CBC over different time periods are unclear. There are also wider implications around SM as an approach which has been used successfully to treat other conditions[20, 21] and has the potential to reduce pressures during times of high demand for the UK health service[22].

Methods

The TOPSY study design was a parallel-group, superiority randomised controlled trial with a within-trial health economic evaluation that was extended with decision analytic modelling. The intervention was developed utilising the findings from a prior service development project, self-efficacy theory, relevant literature, clinician experience and feedback from

pessary-using women[23]. Details of the trial methods have been published previously[19]. The superiority hypothesis applied to the primary outcome which was measured with the Pelvic Floor Impact Questionnaire (PFIQ-7), a pelvic floor specific quality of life instrument. Analysis methods for the trial, the process evaluation and economic evaluation were pre-specified in separate analysis plans and are publicly available[24]. A total sample size of 330 women was required to provide 90% power to detect a difference of 20 points in the PFIQ−7 score at 18 months after randomisation[19]. The study population consisted of women aged 18 or older with prolapse who were new and existing users of a vaginal pessary. 340 women were recruited and randomised (169 SM, 171 CBC) at outpatient clinics in the UK National Health Service between May 2018 and February 2020. Participants were followed for 18 months with follow-up completed in September 2021.

Comparators

The trial compared pessary SM with standard CBC, detail of the interventions is described elsewhere[19, 23]. SM included an initial self-management teaching appointment, information leaflet, a 2-week follow-up telephone call, and telephone access to their local clinical site for extra support if required. Participants in the SM group were taught to remove and reinsert the pessary themselves. CBC involved routine outpatient appointments with a healthcare professional to remove, clean and re-insert (or replace) the pessary and inspect surrounding vaginal tissue. Participants in CBC returned every three to six months for follow-up with exact timing of appointments following local protocols. In both trial groups, additional review appointments in clinic were arranged if necessary, for example, if pessary complications occurred.

Economic evaluation

For this economic evaluation a within-trial cost-utility analysis (CUA) was conducted where costs were attached to resource use for the delivery of the intervention and comparator

treatments, as well as all healthcare-related resource use for each participant during the follow-up period. A health sector payer (NHS) perspective was taken for the CUA. The analysis of all outcomes was by intention-to-treat and all participants were analysed as randomised. Group comparisons were performed using non-parametric Mann–Whitney tests. All study analyses were conducted using Stata version 16[25].

The primary economic analysis compared the costs and benefits of each trial group over the 18 months after randomisation. The incremental net monetary benefit (INB) was calculated for the treatment (self-management) versus the comparator group (clinic-based care). The INB has been proposed[26] as a more informative alternative to the incremental cost effectiveness ratio (ICER), especially in situations where incremental cost-effectiveness is negative. The INB is calculated by multiplying incremental effectiveness by the policymaker cost-effectiveness threshold and then subtracting the incremental cost of the treatment. In the UK the National Institute for Health and Care Excellence (NICE) recommends interventions are adopted with an ICER below a threshold of £20,000 or £30,000 willingness-to-pay (WTP) per quality adjusted life year (QALY) gained[27, 28]. This study adopted a threshold of £20,000 per QALY as a conservative approach therefore all INBs were calculated using the lower threshold[29]. Positive INBs imply that SM is the cost-effective option whereas a negative INB suggests the opposite, implying that CBC should be the preferred option.

A secondary analysis over a 5-year time horizon was performed using modelling beyond the 18-month trial data collection period. A discount rate of 3.5% was applied to all costs and outcomes over 1 year as recommended by NICE[27]. Health outcomes in all analyses were measured in terms of QALYs. Euroqol's EQ-5D-5L[30] was used to measure participants' general HR-QoL. Data were collected at each time-point to give a complete profile of QALYs across the trial. QALYs were calculated using an area under the curve method using

a cross-walk from the UK EQ-5D-3L tariff[30]. Subgroup analysis was performed using baseline demographic and clinical characteristics.

Healthcare resource use was collected from the clinic visit and the telephone support case report forms (CRF) and from a participant completed Resource Use Questionnaire (RUQ) designed for this study (see appendix 1). The RUQ was completed by participants at the 6, 12 and 18 month follow-up time-points and they were asked to report all resource use over the period since the last questionnaire. Given the long time period between follow up questionnaires, an aide memoire was given to the participants so that they could note down any appointments attended or medication used during the intervening period. The RUQ consisted of 6 questions related to the use of primary care services, secondary care services, medications (prolapse-related treatments) and for any personal out of pocket expenses resulting from experiencing prolapse or having a pessary. For primary care services, participants were asked to record: the number of GP appointments in person and home visits, nurse appointments in person and home visits, district nurse home visits, community physiotherapy appointments and community dietician appointments. For secondary care services, participants were asked to record: the number of outpatient appointments with a doctor, outpatient appointments with a nurse, attendances at A&E, inpatient stays including the number of nights.

For the purposes of this economic evaluation the SM intervention was defined as the additional training in SM a woman received at her first clinic appointment, plus an 18-month follow-up clinic appointment. These were costed as a 30-minute extra appointment (not received in CBC group) with a specialist nurse, physiotherapist or consultant. COVID-19 may have impacted on some appointments. Our approach involved costing telephone appointments as clinic-visits when it was known from CRFs that these would have been in person without pandemic restrictions. However, aside from this modification the observed

results were maintained without further alterations. The unit costs attached to each item of resource use are presented in Table 1. The statistical analysis accounted for the uncertainty in the unit costs by drawing Monte Carlo samples from normal distributions. Unit costs were identified using Unit Costs of Health and Social Care for staff and British National Formulary for prescribed medication[31, 32]. All costs are reported in British Pounds (GBP£) in 2019/2020 prices.

To calculate an accident and emergency unit cost we used the weighted average of all acute outpatient appointments as published by the Personal Social Services Research Unit (PSSRU, p. 87)[31]. For hospital episodes we used the average cost per non-elective inpatient stay (short stays) which is based on national data and reported by the PSSRU (p. 87)[31]. The costing of the initial training appointment was based on patient level data from the trial, costed using the PSSRU figures, depending on the grade of the healthcare professional who provided the training. Detailed description of other costings is shown in appendix 1. Unit costs were attached to each item of resource use to calculate the total cost per participant, and the mean cost per participant was estimated for each group. This was done with methods that account for the uncertainty around the mean estimates of both costs and QALYs while incorporating uncertainty in unit costs. Non-parametric bootstrap methods were employed to produce unbiased standard errors given the distribution of cost and effects. The economic analysis also reported the probability of cost-effectiveness for WTP at £20,000 per QALY gained.

Primary analysis excluded patients with missing outcome data. In sensitivity analysis missing data were handled using multiple imputation (MI) with predictive mean matching[33]. This was combined with rule-based imputation to maximise usable data in the economic evaluation, for more detail see appendix 2. Resource use data in this evaluation were generally very well completed, when excluding non-response participants, with less than 2% missing values. The imputation was run 100 times, resulting in 100 different data sets to be used in the cost-

effectiveness analysis. The imputation was implemented separately for the intervention and control groups to account for differences in the missing values between the two groups. The SM group had 10% less full completion than the CBC group (among participants who completed the study approximately 85% of SM group had full completion versus 95% in CBC group) therefore we took a missing not completely at random approach. The MI model used baseline covariates and QALYs at each follow-up to impute unobserved QALYs, so that, for example, missing QALYs at 12 months were imputed using data on baseline covariates, utility at baseline and 6 months (if available) and QALYs between baseline and 6 months (if available). MI results are available in appendix 2.

Decision analytic model

Decision analytic modelling was undertaken to extrapolate costs and outcomes beyond the 18 month follow-up period of the trial to investigate potential for cost-effectiveness to deviate from base case results under a 5-year horizon. A 5-year horizon was chosen as it was assumed that conditions and characteristics of participants would be broadly the same across this period while still being relevant to NHS funding cycles. The model simulated progression over time given the baseline analysis. The observed data in the first 18 months were extended in time with uncertainty allowed. A Markov decision model with a monthly cycle was employed to evaluate effects of the intervention on costs, QALYs and cost-effectiveness over the 5-year horizon[34, 35].

The model was run both as a cohort and a Monte Carlo simulation. The decision model was run twice, once for each group of participants reflecting the interventions in the trial (SM and CBC). Each model run was structured as a Markov model built around health states to which healthcare cost and QALY data collected as part of the trial are linked. The model structure is shown in appendix 3. The health states (poor, moderate, good) simulated the type of

participant that was encountered in the trial, focusing on light or heavy resource use trial data distributions and associated quality of life with uncertainty allowed. Participants could remain in the same health state throughout the 5-year period or move between states. Participants could change states at the beginning of each month depending on model parameters, see appendix 3. Participants start in the moderate state in both groups assuming an equal distribution in baseline health states between randomised groups. Assuming all participants to be in the moderate state at outset isolated the impact of randomisation and minimised between-subject variance.

The model parameters were derived from the trial data. 1) Transition probabilities between states 2) Treatment effects of the intervention 3) Quality of life 4) Healthcare costs. Key transition probability parameters were manually varied to examine the impact on cost-effectiveness shown using an INB tornado diagram which reports the range of INBs generated for each parameter's uncertainty range. Probabilistic sensitivity analysis was employed to account for uncertainty across all model parameters which includes 10,000 Monte Carlo draws of values from cost and participant utility distributions[34] , see appendix 3.

Results

A total of 340 participants were randomised (see appendix 1 for demographics), 333 participants completed the EQ-5D-5L at baseline and 293 at 18 months. Six month resource use assessment was available for 310 participants, 12 month follow-up for 298 participants, and 18 month followup for 297 participants. The final sample excluded participants who dropped out at baseline or had complete missing data in either EQ-5D-5L or resource questions at any timepoint. The analysis sample with full completion included 264 (125 SM, 139 CBC) participants with utility scores calculated for both groups at each follow-up (appendix 1). No significant difference was found in participants' utility scores over time, or

between treatment and control groups at each time point. This was tested at each time point separately and it was not possible to reject the null hypothesis that there was no difference between the groups at any time point for both EQ-5D index scores (utility) and VAS (appendix 1). Analyses by subgroup did not reveal statistically significant differences by subgroup based on age, BMI, number of previous births and a selection of participant clinical characteristics at baseline (not shown).

Raw data on resource use suggested that CBC participants had more contacts with healthcare services over the 18 month period across most categories. (see appendix 1 for details). Given unit costs and raw data utilisation the most important NHS resource use was in GP surgery settings, physiotherapy and outpatient appointments (appendix 1). Total healthcare resource use in monetary terms by category and trial group is shown in Table 2.

The incremental cost and incremental effectiveness (QALYs) of self-management compared to clinic-based care are presented in Table 3 along with the ICER and INB. CBC was dominated by SM which means that SM was less costly than CBC and was not less effective in terms of the number of QALYs gained from treatment. The INB (INB=£564.32) is positive thus the intervention is cost-effective when compared to the alternative, meaning the cost to derive the benefit from SM is less than the maximum amount that the decision-maker would be willing to pay for this benefit. The probability of cost-effectiveness can be described as the probability that a random individual will have a positive individual INB. This is shown in Table 4 where the probability of cost-effectiveness of SM is 80.81% at a WTP threshold of £20,000 per QALY gained. The results reveal a notable concentration of data points within the south-eastern quadrant of the incremental cost-effectiveness scatterplot, indicating favourable cost-effectiveness outcomes for the intervention. This implies that in the majority of bootstrapped cases there were lower costs and better health outcomes, see Figure 1.

These results are complemented with the fully maximised sample results based on imputation that are also shown in the appendix. Both methodologies presented (multiple imputation and non-parametric bootstrapping) arrive at a 71% probability of cost-effectiveness that conveys a similar message to the primary analysis results (appendix 2).

The decision analytic model suggests SM remains a cost-effective intervention when compared to CBC 5-years after the initial trial period. The modelling results are consistent with the main analysis. The results of the base case analysis are shown in Table 5. The cost-effectiveness acceptability curve and cost-effectiveness scatterplot are presented in the appendix. At £20,000 WTP the probability of SM being a cost-effective intervention is 69.74% reflecting the probability of SM remaining cost-effective for 5-years. The modelling cost-effectiveness scatterplot (appendix) shows a similar picture to the economic evaluation scatterplot (Figure 1). Deterministic sensitivity analysis is shown in appendix 3. The tornado diagram suggests that varying these parameters had a moderate impact on the sign of the INBs which remained positive for most values in the uncertainty ranges. These deterministic sensitivity results suggest the ability of SM to prevent patients from transitioning into the poor health state, when compared to CBC, was a key parameter in determining cost-effectiveness in the model.

Discussion

The evidence presented indicates SM is a cost-effective option when compared to CBC at 18 months for women who use a pessary for prolapse. Decision analytic modelling suggests cost-effectiveness is likely to persist for longer than the duration of the trial. This study contributes to the existing body of literature on SM in a range of clinical areas, building upon previous evidence that underscores this approach can enhance current treatment pathways[20,

[21]. The results presented in this study are consistent with the primary outcome trial analysis which found that there was no statistically significant difference between groups at 18 months. The cost-effectiveness results add to prior evidence regarding pessary SM reinforcing that this can be a successful conservative treatment of pelvic organ prolapse[17, 18, 36, 37]. The UK National Health Service, like many publicly funded health systems, is operating at near full capacity with long waiting lists so it is important to explore and adopt treatment pathways that have the potential to create capacity within the system while not increasing risk or reducing clinical effectiveness for the patient [22]. Pessary SM has been shown to both reduce resource use and produce similar outcomes to CBC.

The results are driven by differences in resource use between the two groups with participants in the SM group reporting reduced contact with primary and secondary healthcare services, less need for clinic-based or telephone support and a decreased consumption of medications. That was the case across most categories and applied to either healthcare utilisation due to prolapse or for any other health reason. On the other hand, HR-QoL measured in QALYs was estimated to be similar between the two groups suggesting SM is not inferior to CBC in this respect. This similarity in HR-QoL is perhaps not surprising as both groups were receiving active care for their prolapse (pessary) with the difference between the two trial groups being the management of the pessary. It may be possible that the general measure of HR-QoL (EQ-5D) was not sensitive enough to capture differences in quality of life given both groups of women used a pessary which is likely to have improved symptoms and quality of life, irrespective of the delivery model (SM vs CBC).

There is a degree of uncertainty in the results stemming from parameter, variability, sampling and assumption uncertainty. The methods used in this economic evaluation, particularly with the probabilities of cost-effectiveness and cost-effectiveness scatterplots, addressed these issues by quantifying and communicating the impact of uncertainty on cost-effectiveness

outcomes based on the observed trial data. The results offer insights for decision-makers into the probability that SM is economically favourable under varying conditions. The probabilities of cost-effectiveness in this study suggest that SM is more likely than not to be a cost-effective alternative to CBC. One interpretation is that most individual randomly selected patients out of a pool of all pessary users will have a positive individual INB if they receive SM when compared to CBC. The probability of cost-effectiveness can also be seen as the likelihood an individual patient in this population will have a positive individual INB when in SM rather than CBC.

The reduction in resource utilisation within the SM group was intentional, as the design of the intervention involved educating women to self-manage their pessaries. This approach primarily aimed to enhance patient experience while concurrently minimising the need for outpatient and other clinic attendances thus releasing health service capacity for other uses[17]. However, participants in the SM group exhibited decreased resource utilisation patterns across most categories of resource use, not necessarily related to the design of the intervention, highlighting the unexpected impact of SM on women's health seeking behaviour. It is known that pelvic organ prolapse can affect treatment seeking behaviour for some women[5] and it can be argued that SM had an impact on this mechanism. Participants in the SM group may have felt more confident to deal with their medical issues on their own or were empowered to take charge of their lives and depend on others less, therefore perhaps reducing healthcare contacts, something that is expected by self-management interventions[20, 21, 23, 38]. Fewer adverse events were reported in the SM group which may have resulted in less healthcare contact[17, 23, 39]. The costs of all complications were accounted for in the resource use quationnaires completed by women in this study. In general very few serious events were reported, not necessarily related to pessary use, with only four of these requiring surgical

interventions, the costs of these were captured in the hospital episodes and were similar between the two groups.

When designing self-management interventions it is important to take into account patient acceptability of self-management and the likelihood of pessary SM being a successful intervention for the patient's symptoms[11, 40]. SM has potential to reduce adverse effects in this population if presented to patients appropriately[38, 39, 41]. Results across all methodologies presented suggest that SM was successful in reducing contacts with the health service without compromising patient safety or quality of life. This was the case for both pessary-specific clinic visits and overall contact with primary and secondary care services. The cost-effectiveness scatterplots suggest there was a substantial number of self-managing participants who experienced gains in quality of life and at the same time had less demand for health services when compared to those receiving CBC. The recent COVID-19 pandemic impacted on participants' access to appointments with healthcare professionals. It is possible that this study has underestimated the overall costs associated with pessary management due to participants being unable to have some appointments. We believe that COVID-19 restrictions would have affected access for CBC more than SM participants, given the nature of CBC versus SM, which would make the results of this study conservative.

Given the available data it was not possible to say more on the characteristics of patients who would benefit more by pessary SM. This study employed methods with a heavy reliance on data from a single trial which has known limitations. Even though the methods accounted for a wide range of uncertainty there is always the possibility of unaccounted sources of uncertainty beyond the scope of this study. Moreover, decision analytic modelling employed a highly simplified representation of real-life conditions and the results should be interpreted with this context in mind. Further research is needed to establish the mechanism that SM reduces demand for health services and the type of patient who will gain the most from SM.

Research is also needed to establish how to best design and offer SM locally, nationally and internationally taking into account local conditions and in different scenarios so that it can have maximum impact for patients. In the meantime, however, we can be relatively confident that SM is a cost-effective option for the majority of patients receiving pessary treatment for pelvic organ prolapse in the UK.

Conclusions

Results suggest that pessary self-management for prolapse is cost-effective at a WTP of £20,000 per QALY gained when compared to clinic-based care. Decision analytic modelling supports this result and suggests that the self-management remains a cost-effective option for the health service for durations longer than the 18 month trial follow-up. Self-management is an approach that can be used for non-surgical management of prolapse without negatively impacting women's QoL, which can release scarce resources in a health system under excess demand conditions.

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Tables:

Service	Mean (£)	SD*
Accident and emergency	154	30.8
Hospital episode	602	102
Outpatient doctor	135	27
Outpatient nurse	60	12
Outpatient physio	50	10
GP	33	6.6
Community nurse	9.5	1.9
GP @ Home	223	44.6
Nurse @ home	120	24
District nurse @ home	89	17.8
Physio local clinic	58	11.6
Dietician	60	12
Initial training appointment	29.90	12
Clinic visits	37	7.4
Telephone support	8.3	1.7

*Monte Carlo samples were drawn from normal distributions with mean and standard deviation parameters as shown in this table.

Table 1 Unit Costs in GBP£ 2019/2020 prices; source PSSRU[31]

	Self-management					Clinic-based Care				
	Obs	Mean* (GBP£, 2019 prices)	SD	Min	Max	Obs	Mean* (GBP£, 2019 prices)	SD	Min	Max
Initial appointment**	125	31.77	9.98	20	56.88	139	0	0	-	-
Clinic visits***		16.81	39.54	0	324.59		77.45	42.37	0	338.41
Telephone support***		1.45	3.51	0	17.09		1.76	4.07	0	18.85
NHS costs		528.27	588.34	0	3,743.29		649.63	654.02	0	3,542.48
Medications		15.52	45.57	0	348.00		24.90	79.88	0	667.88

*Mean calculations include zero reported resource use.

**Training appointment that applies only to self-management.

***From CRF data; some telephone appointments were costed as clinic visits if these were supposed to take place in person but were not due to COVID-19.

Table 2 Healthcare resource use by trial group over the 18 month trial period.

	Total Cost (£GBP)	Total QALYs	Incremental cost	Incremental QALYs	ICER	INB (SE)
Self-management	£578.30	1.241	-150.53	0.021	Dominated	£564.32 (£581.50)
Clinic-based care	£728.84	1.221				

Table 3 Cost-effectiveness results over 18 month period.

Self-management compared to Clinic-based care	**Observed coefficient**	**Bootstrapped SE***
Incremental Cost (£)	-150.53	77.22
Incremental benefit (QALYs)	0.021	0.031
Incremental net benefit (£)	564.32	648.37
Probability of cost-effectiveness at £20,000 WTP		80.81%
* Standard error based on 10,000 bootstrap resamples of incremental cost and effects		

Table 4 Distribution of incremental costs and effects associated with self-management compared to clinic-based care.

	Total Cost (GBP)	Total QALYs	Incremental cost (£)	Incremental QALYs	ICER	Incremental Net Benefit
Self-management	£2,044	4.92	-494	0.19	Dominated	£4,221
Clinic-based care	£2,538	4.73				

Table 5 Decision analytic modelling cost-effectiveness results over a 5 year horizon.

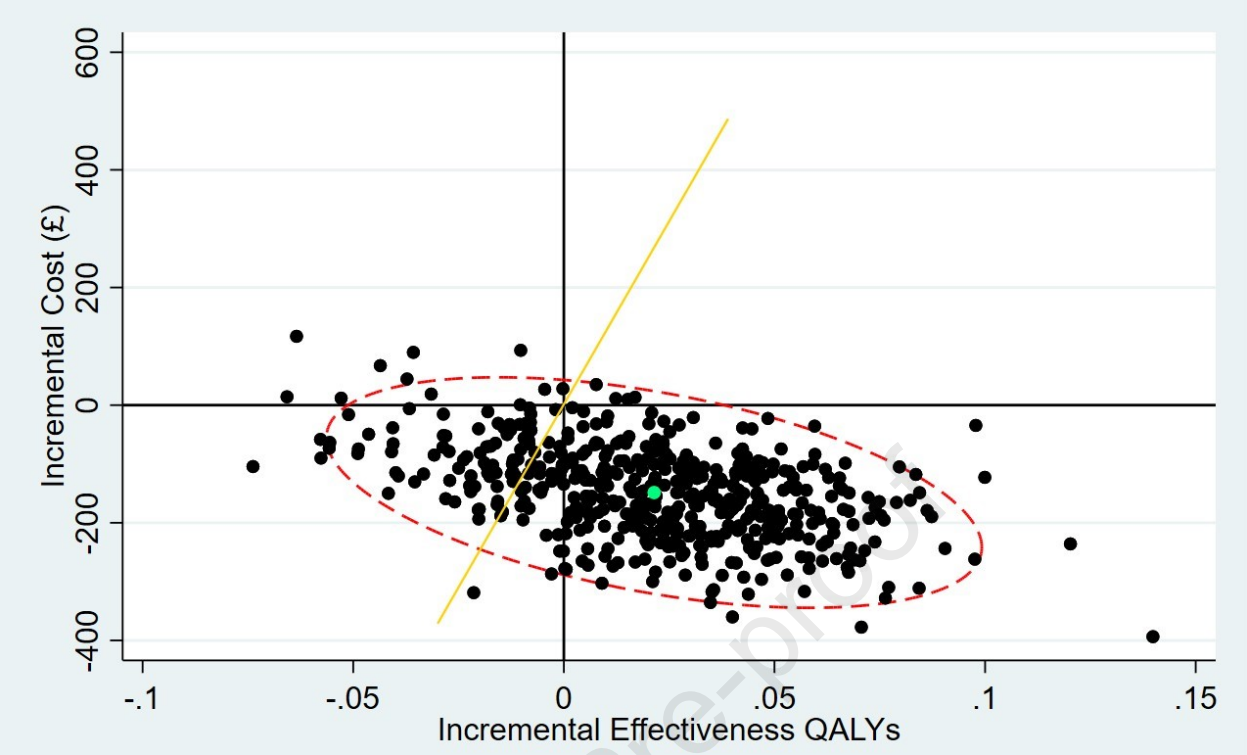

Figure Title

Figure 1 Incremental cost-effectiveness scatterplot of self-management compared to clinic-based care for 10,000 sampled individuals (5% of values shown).

Figure Caption

--------- 95% CI

· Mean

——— WTP = £20,000 Threshold