

**Cost-effectiveness of ambulatory care management of primary spontaneous
pneumothorax: an open-label, randomised controlled trial**

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ABSTRACT

Background

Ambulatory management of primary spontaneous pneumothorax has been shown to reduce initial hospitalisation, but at the expense of increase adverse events. As a result, questions remain about the cost-effectiveness of this option.

Objectives

A within-trial economic evaluation alongside a randomised controlled trial was performed to assess the cost-effectiveness of ambulatory care when compared to standard guideline-based management.

Methods

Patients were randomly assigned to treatment with either an ambulatory device or standard guideline-based management (aspiration, standard chest tube insertion, or both). Follow-up was 12 months. Outcomes included healthcare resource use and costs, quality of life, quality-adjusted life-years (QALYs) and cost-effectiveness.

Results

236 patients were recruited and randomly assigned to ambulatory care (n=117) and standard care (n=119). After multiple imputation for missing data, patients in the ambulatory care group had significantly lower NHS healthcare costs (-£788, 95% CI difference: -1,527 to -50; p=0.037) than those in the standard care group. There were no differences in the number of QALYs gained (mean difference: -0.001, 95% CI difference: -0.032 to 0.030; p=0.95). When standard care was compared to ambulatory care, the incremental cost-effectiveness ratio was

£799,066 per QALY gained, well above current thresholds of cost-effectiveness. As a result, the probability of ambulatory care being cost-effective was 0.93.

Conclusion

Outpatient ambulatory management is highly likely to be a cost-effective option in the management of primary pneumothorax.

Trial registration number ISRCTN79151659.

Key messages

What is already known on this topic

- Ambulatory management of primary spontaneous pneumothorax (PSP) has been shown to reduce initial hospital stay over aspiration and/or drainage at the expense of increased adverse events. This raises concerns on whether the benefits of ambulatory care are offset by increases in healthcare use over the longer-term.

What this study adds

- This is the first randomised controlled trial that evaluates the cost-effectiveness of ambulatory care management when compared to standard guideline-treatment showing that ambulatory management is cost-effective.

How this study might affect research, practice or policy

- This data suggests that primary spontaneous pneumothorax can be cost-effectively managed for outpatients, using ambulatory devices in those who require intervention.

INTRODUCTION

Pneumothorax is a common clinical problem, occurring in approximately 3,000 patients per year in the UK.^{1,2} Most patients require an intervention to re-expand the lung, and more than half of patients subsequently requiring the insertion of a chest tube.³ This results in hospital stays of up to 8 days⁴ and so the cost of treating pneumothorax can be considerable.

Therefore, interventions that remove the need for long hospital admissions, such as ambulatory management, could provide a highly cost-effective alternative to hospital treatment and admission. The recent Randomised Ambulatory Management of Primary Pneumothorax (RAMPP) trial showed that ambulatory care resulted in a significant decrease in hospital stays (median 0 vs 4 days) when compared to standard guideline-based management (i.e. aspiration, drainage or both).⁵ However, this positive finding was at the expense of increased adverse events, some of which were serious, and required regular review of patients. This, coupled with the fact that pleural vent kits for use in ambulatory care are relatively costly (£212 each),⁶ raises concerns on whether ambulatory care represents a cost-effective intervention in the treatment of primary spontaneous pneumothorax (PSP).

Using the RAMPP trial data, a prospective, within-trial economic analysis was done to determine whether ambulatory management of patients with primary spontaneous pneumothorax was cost-effective when compared to standard care.

METHODS

Trial design

Details of the RAMPP trial have been reported in detail elsewhere.⁵ Briefly, RAMPP was a multicentre, open-label, randomised controlled trial comparing ambulatory management of primary pneumothorax with standard care based on national guidelines.⁷

Participants

Eligible patients had presented with a symptomatic spontaneous pneumothorax (confirmed by a chest radiograph or CT scan) and were aged 16–55 year. Patients requiring intervention could be enrolled and randomly assigned up to 24 h after presentation, provided that they remained hospitalised with an ongoing symptomatic pneumothorax despite initial intervention (e.g., patients treated initially with aspiration and observed overnight) requiring chest tube insertion.

Interventions

Patients were randomly assigned (1:1) to either insertion of an ambulatory device (Rocket Pleural Vent, Rocket Medical, Watford, UK) or standard care (aspiration, standard chest tube insertion, or both). All patients were followed up at 1 week after the completion of treatment, and 30 days, 6 months, and 12 months after randomisation. Hospital admissions and pneumothorax recurrence were measured at each follow-up point. Data were collected on further hospital admissions, wider healthcare resource use, pain and breathlessness visual analogue scale (VAS) scores, quality of life, days off work (if applicable) and smoking status. Patients who were not able to attend face-to-face follow-up appointments were contacted by telephone to check for complications or recurrence, and if this was not possible, data on recurrence was collected through hospital medical records.

Follow-up and outcomes

The primary outcome used in the trial was the total length of hospital stay up to 30 days after randomisation, including initial hospital stay and re-admissions.⁵

For this analysis, the perspective adopted in the economic evaluation was that of the National Health Service (NHS). We included the costs associated with the following healthcare resource use categories from randomisation to 12-month follow-up:

- Initial procedures for the treatment of spontaneous pneumothorax (including insertion of an ambulatory device, aspiration, standard chest tube insertion, or a combination of the latter two);
- Initial length of stay following spontaneous pneumothorax;
- Subsequent procedures for pneumothorax;
- Subsequent stays in hospital or day cases due to any reason;
- Accident and emergency (A&E) visits;
- Secondary outpatient care visits;
- Primary care visits, including visits to a general practitioner (GP) at home, doctor's office or via telephone; or to nurse; and
- Visits for physiotherapy.

Costs of performing the initial procedures to treat pneumothorax were obtained through a micro-costing study in which a number of interventions performed in RAMPP were observed. Staff time included the consultant physician, specialist registrar, nurse and health-care assistant and was valued using average salaries for that position.⁸ Unit costs of disposables were valued using prices obtained from the NHS Supply Chain.⁶ Costs of medications and sedation drugs were obtained from the British National Formulary

(<https://bnf.nice.org.uk/>). Finally, costs of investigations undertaken as part of the intervention, including chest x-rays, were obtained from NHS reference costs.⁹

All other follow-up resource use was collected using patient questionnaires administered at treatment completion, 1, 6 and 12 months. As an aide memoire, patients were also provided with a resource-use log designed for them to fill in every time they had a contact with the health-care system.

Unit costs for consultations with general practitioners and nurses were obtained from the Personal Social Services Research Unit's Unit Costs of Health and Social Care publications for 2019.⁸ For all other contacts, unit costs were derived from the NHS National Schedule of Reference Costs 2018 to 2019.⁸ Using the reasons for hospitalisation reported by patients in the resource-use questionnaires, we obtained diagnosis and procedure codes. These were then translated into a Healthcare Resource Group (HRG) using the HRG4+ 2018/19 Reference Costs Grouper (NHS Digital). Each HRG was then linked to a series of elective, non-elective and day-case reference costs obtained from the 2018/19 schedule of reference costs. All costs are reported in 2019 prices.

Although not relevant to the NHS perspective adopted, an additional analyses was performed including the amount of days off work (if applicable) that patients had to take during the 12-month follow-up. Days off work were valued using UK mean earnings.¹⁰

Generic health-related quality of life HRQoL was measured using the EuroQol-5 Dimensions-5 Levels (EQ-5D-5L) questionnaire and EQ-Visual Analogue Scale (VAS) at time of randomisation (i.e. baseline) and at each follow-up point.¹¹ EQ-5D-5L responses were

converted into utilities using the validated mapping function to derive utility values for the EQ-5D-5L from the existing EuroQol-5 Dimensions, three-level version.¹²

Statistical analysis

Utility and VAS scores at each follow-up point was presented as means (standard deviation, SD). A quality-adjusted survival curve was generated by plotting, against time, the product of the mean utility of patients living at time t and the probability of surviving to time t , in this case 1 as no deaths were observed during 12-month follow-up, in order to create three periods (i.e. randomisation to 1-month follow-up, 1- to 6-month follow-up and 6- to 12-month follow-up). The area under this quality-adjusted survival curve then gave the mean quality-adjusted survival in each treatment group, or Quality Adjusted Life Years (QALYs) gained over the 12-month follow-up. Utility was assumed to change linearly between each follow-up, rather than changing at the mid-point between follow-ups or being maintained from one follow-up to another.

For the base case, given we had missing data for follow-up resource use and EQ-5D responses, multiple imputation was used to impute missing cost and utility values (please see the Online Supplementary material for more details and **Table e1**).¹³⁻¹⁵ As per recommended best practice, imputation was implemented separately by randomised treatment allocation.¹⁶ Costs were imputed at the most disaggregated level at which the model would converge. As a result, we imputed values for general practice consultation costs (at practice, home and telephone); hospitalisation readmission costs; outpatient care costs (outpatient visits and transportation to visits); emergency care costs (visits to emergency departments and transport by ambulance); and other health-care costs (physiotherapy and nurse visits). There were no missing data for treatment and initial hospitalisation costs. Rather than imputing missing

responses for each of the five domains in the EQ-5D-5L, we imputed the overall EQ-5D-5L utility.¹⁷ The imputation of costs and utility was conducted using predictive mean matching (i.e. imputes data from similar patients with complete data). Imputation was conducted using age, sex, ethnicity, tobacco and marijuana use history, history of pneumothorax, and pneumothorax recurrence. We generated 40 replacement values for each missing case, generating 40 imputed data sets. Using the Stata 'mi estimate' command, we obtained mean estimates of cost and utility and SD. Differences across patients groups were obtained using ordinary least squares regression using the 'mi estimate: reg' command.

In a sensitivity analysis, we also performed an available-case analysis. For each treatment group, average resource use/costs were summed over the follow-up periods. Results are then presented as means together with 95% CIs, generated through 10,000 bootstrap estimates. Mean differences in QALYs, resource use and costs between the two treatment groups were also estimated, as well as the 95% CI of the difference using bootstrapping.

Cost-effectiveness was assessed through estimation of the incremental cost per QALY gained. This is based on the difference in mean total cost per patient between the intervention and control group (ambulatory and standard care, respectively), divided by the difference in mean QALYs in the two groups. The resulting incremental cost-effectiveness ratio (ICER) was compared with reference to what the NHS is willing to pay (WTP) for an additional QALY; this currently being \leq £20,000 per QALY gained.¹⁸ Results based on the 10,000 bootstrap replications of QALYs and total care costs at 12 months are displayed on a cost-effectiveness plane. The cost-effectiveness plane is used to visually represent the differences in costs and health outcomes between the two study groups in two dimensions. A cost-

effectiveness acceptability curve (CEAC) was drawn to represent the probability of cost-effectiveness for different values of WTP.¹⁹

Subgroup cost-effectiveness analysis was done for previous pneumothorax.¹

All analyses were performed using STATA MP 15 (64-Bit). Statistical significance was set at $p < 0.05$.

RESULTS

Study participants

We recruited patients between August 27, 2015, and March 12, 2019, reaching our target of 236 participants, of whom 117 were assigned to ambulatory care and 119 to standard care. For the primary outcome, we analysed 114 (97%) of 117 patients who received ambulatory care and 113 (95%) of 119 who received standard care, because data was not available for the remaining patients. These patients then formed the basis of the cost-effectiveness analysis (**Table 1**).

Quality of life

Responses to the EQ-5D-5L at baseline, treatment completion, 1 week, and 1, 6 and 12 months, as well as numbers responding, are reported in the Online Supplementary **Tables e2** and **e3**. We found that patients attending their 12-month follow-up were more likely to be female, and have no history of smoking tobacco or marijuana (Online Supplementary **Table e4**), but these did not differ by treatment group (Online Supplementary **Table e5**). EQ-5D responses were then converted into utilities (**Table 2**). There were no statistically significant differences in utilities or VAS scores at 1 week, 1, 6 and 12 months.

Given there were no observed deaths, follow-up duration (i.e. 12 months) was combined with EQ-5D-5L utilities to estimate QALYs at 12 months after randomisation. After imputing for missing EQ-5D data, patients receiving ambulatory care had a non-significant decrease of 0.001 (95% CI difference: -0.032 to 0.030) QALYs when compared to those receiving standard care. In the available case-analysis, ambulatory care patients also had a non-significant decrease of 0.005 (95% CI difference: -0.037 to 0.025).

Resource use and costs

For patients receiving ambulatory care, the initial mean hospital stay was of 1.33 (S.D. 3.24) days compared with 4.11 (S.D. 4.91) days in the standard care group, a statistically significant reduction of 2.78 (95% CI: -3.87 to -1.69; $p<0.0001$) days in hospital. There were no statistically significant differences between the two groups in hospital days due to readmissions up to the 1 month follow-up, with patients receiving ambulatory care having stays in hospital due to readmissions of 0.81 (S.D. 2.49) days vs. 1.06 (S.D. 3.04) days in the standard care group ($p=0.49$). Except for outpatient visits, where patients receiving ambulatory care had, on average, 0.98 (95% CI difference: 0.21 to 1.71; $p=0.013$) more visits than those receiving standard care over the course of 1 year, there were no other statistically significant differences in health care resource use (**Table 3**). Resource use by follow-up, as well the number of patients for whom we had data for, is reported in the Online Supplementary Material **Table e6**.

There was no missing data regarding the costs of initial hospital stays, trial treatments, and 1-month readmissions. Given the significant reduction in initial hospital stay, mean costs of the initial hospital stay were significantly lower in the ambulatory care group than the standard care group (-£1,036, 95% CI difference: -1,487 to -583 $p<0.0001$ – **Table 4**). However, costs of pneumothorax treatment were significantly higher for the ambulatory care group (£329) than the standard care group (£172; $p<0.0001$). There were no significant differences in 1-month readmissions or subsequent hospital admissions over the 1-year of follow-up.

For follow-up costs, results of the multiple imputation showed that, except for outpatient care costs, which were higher in the ambulatory care group (£188, 95%CI difference: 91 to 285, $p<0.001$), there were no other significant differences in cost categories (**Table 4**). Overall,

during the 1-year follow-up, patients in the ambulatory care group had significantly lower NHS healthcare costs than those in the standard care group (-£788, 95% CI difference: -1,527 to -50, $p=0.037$). **Figure e1** in the Online Supplement Material presents how mean QALY and cost differences between the two patient groups varied across the 40 imputed datasets used in the multiple imputation analysis.

Over the 12 months, mean number of days off work was 26 in patients receiving ambulatory care compared to 24 in those receiving standard care, a non-significant increase of 2 (95% CI difference: -14 to 25; $p=0.81$) days. This resulted in non-significantly higher productivity losses in the ambulatory care group (**Table 4**). Overall, when NHS and productivity losses were combined together, there were no overall significant differences across groups.

Cost-effectiveness

Cost-effectiveness was assessed using an NHS perspective. Given that standard care resulted in non-significantly higher QALYs and significantly higher NHS costs than ambulatory care, cost-effectiveness was assessed by comparing the additional costs of standard care vs. ambulatory care, divided by the additional QALY gains when standard care was compared to ambulatory care.

In the multiple imputation analysis, the incremental cost per QALY gained when standard care was compared to ambulatory care was £799,066, well above the current £20,000 cost-effectiveness threshold. At this cost-effectiveness threshold, the average, across the 40 imputed datasets, probability that ambulatory care was cost-effective over standard care was 0.93 (**Figure 1**). Across the 40 imputed datasets this probability ranged between 0.71 and 0.99 (online supplementary material **Figure e2**). Repeating the analysis, using a wider

perspective (i.e. including NHS costs and productivity losses), the ICER when standard care was compared to ambulatory care was £696,986 per QALY gained, again above current thresholds of cost-effectiveness. From an NHS perspective, results of the available case analysis showed that the ICER of standard care vs. ambulatory care was £151,438 (**Table 4**, online supplementary material **Table e7**, well above conventional thresholds of cost-effectiveness, with the probability that ambulatory care was cost-effective at a £20,000 per QALY threshold being 0.87 (**Figure 2**). From a wider perspective, the ICER was £89,904 per QALY gained when standard care was compared to ambulatory care.

When the multiple imputation analysis was restricted to patients with previous history of pneumothorax, patients receiving ambulatory care had significantly lower NHS costs than those receiving standard care (-£1,960, 95% CI difference: -3,267 to -654, and non-significantly lower QALYS (-0.010, 95% CI difference: -.070 to .051). In this subgroup, therefore, the incremental cost per QALY gained when standard care was compared to ambulatory care was £201,140.

DISCUSSION

This multicentre, open-label, randomised controlled trial assessed the cost-effectiveness of an ambulatory treatment strategy for PSP with standard care using evidence-based guidelines (aspiration, chest drain insertion, or both). The results show the cost-efficiency of the ambulatory strategy, resulting in significantly lower NHS costs during the one-year of follow-up, with no difference in health outcome.

Given that the difference in QALYs between the two study groups was very small and non-significant, our results of cost-effectiveness were driven by differences in cost. We found that the additional cost per QALY gained when standard care was compared to ambulatory care was £799,066 after imputing for missing data. This high ICER, which is well above current UK cost-effectiveness thresholds, was obtained by dividing the difference in costs (standard care generated significant additional costs per patient when compared to ambulatory care) by the very small difference in QALYs.

Serious adverse events, defined as those needing admission to hospital, occurred exclusively in the ambulatory care arm.¹ Serious adverse events related to treatment included enlargement of pneumothorax despite the ambulatory device being in place and device blockage and kinking, requiring chest tube insertion and hospitalisation. In the ambulatory care group, three patients had unrecognised haemopneumothoraces, which at review were not considered related to the intervention. Although this higher rate of serious adverse events is clearly important, it did not translate into higher costs of hospital readmissions in the ambulatory care group or negative health outcomes, as QALY gains were similar in both treatment groups.

Despite patients in the ambulatory care group spending significantly less time in hospital than those receiving standard care, we saw no differences, over the course of the year, in the number of days patients had to take off work. Although patients with primary pneumothorax being relatively young, and otherwise healthy, on average, over the course of the year following pneumothorax, patients lost approximately 25 days off work, considerably more than the average 4.68 days lost due to sickness per employee in the UK.²⁰

The burden of pneumothorax on patients was also observed in low levels of self-reported HRQoL in patients, particularly at time of pneumothorax and shortly after. At time of randomisation, patients reported utilities of 0.57 (out of a maximum of 1), with 59% reporting moderate to extreme pain. However, by end of follow-up mean EQ-5D utility was 0.92, with 62% of patients reporting perfect health. Our results also show that most of the care for pneumothorax at follow-up was in hospital. For example, irrespective of treatment group, patients made less than 1.5 visits to their general practitioner over the course of the year. In addition, virtually all (98%) the NHS costs incurred over 1-year follow-up were incurred in hospital (treatment, hospitalisations, outpatient specialist care, and emergency care).

Limitations

In addition to the trial limitations already reported,¹ this economic evaluation alongside RAMPP also had some shortcomings. Firstly, despite best efforts, we had considerable missing quality of life and resource use data at the latter follow-ups, especially at the one-year follow-up. Patients who suffer with PSP are usually young with minimal comorbidity, and after resolution of their pneumothorax, their quality of life quickly returns to pre-morbid levels (see high EQ-5D scores at follow-up). As such, we presume that they no longer feel the

need to attend follow-up, even as part of a clinical trial. This missing data can not only lead to loss of statistical power but also to bias.²¹ We, therefore, used multiple-imputation methods. Both after multiple imputation and when using available information only, we found that our conclusions that ambulatory care was cost-effective remained unaltered. If anything, the likelihood of ambulatory care being cost-effective was increased.

Quality of life was assessed at defined fixed time points over follow-up, rather than regularly (e.g. weekly), or when an adverse or subsequent event occurred. As a result, the true impact of the interventions on quality of life might not have been captured in full. For example, the benefits of shorter admissions might not have been captured. Equally, the impact of adverse events or subsequent pneumothoraces happening half-way through follow-up might not have been captured at the follow-up visit. Therefore, the impact of an adverse event, whose consequences could last for a number of days and result in a reduction in quality of life during that time, but had resolved at the time of the follow-up visit would not have been captured.

In a bid to avoid patient overburden, follow-up questionnaires were kept to a minimum. As a result we did not include questions on informal care, more in depth questions about return to work, and other NHS resource use.

There was a slight difference in proportion of patients with previous pneumothorax between the two groups. However, in this pragmatic study this information would not have impacted on the initial treatment options for the patients assessed by the primary outcome. In the longer term, the patients with recurrent episodes may have been more likely to be referred for

elective thoracic surgery (for recurrence prevention). However, the authors' feel that this would not have a significant impact on the HE analysis.

In conclusion, in patients with PSP, ambulatory management not only reduces initial hospital stay, but overall NHS costs over 12 months follow-up, with no decrease in health outcomes as measured by quality of life. Outpatient ambulatory management is highly likely to be a cost-effective option in the management of this condition.

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Footnotes

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Contributions

The study design was conceived by RJH and NMR. Trial management and oversight was done by RJH and NMR. Patient recruitment and data collection was done by RJH and NMR. Statistical analysis was done by RLF and FL. RLF did the literature search and initial manuscript preparation, and all authors reviewed and approved the final manuscript.

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Disclaimer

The sponsors and funders of the study had no involvement or any influence in study design; in the collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

Competing interests

NMR reports consultancy fees from Rocket Medical, during the conduct of the study, and consultancy fees from Lung Therapeutics and grants from BD Biosciences, outside the submitted work. All other authors declare no competing interests.

Patient consent for publication

Obtained

Ethics approval

Ethical approval was provided by the UK National Research Ethics Service Committee (15/SC/0240).

Data availability statement

All data requests should be submitted to the Chief Investigator (NMR) for consideration.

Access to anonymised data may be granted for non-commercial research at the discretion of the Chief Investigator (NMR).

Table 1. Baseline characteristics by treatment allocation

	Patients receiving standard care (n=113)	Patients receiving ambulatory care (n=114)
Female	21 (18%)	21 (19%)
Age, years (S.D.)	30 (9)	31 (8)
Ethnicity		
White	103 (91%)	102 (90%)
Ethnic minority	10 (9%)	11 (10%)
Previous pneumothorax	31 (27%)	24 (21%)
Tobacco smoking status*		
Never smoked	36 (32%)	35 (32%)
Ex-smoker	24 (21%)	18 (16%)
Current smoker	53 (47%)	57 (52%)
Marijuana smoking status**		
Never smoked	54 (49%)	57 (52%)
Ex-smoker	27 (25%)	19 (17%)
Current smoker	29 (26%)	33 (30%)

Data reported as responses/denominator (%), except age which was reported as mean (S.D.).

*Missing: ambulatory care n=4

**Missing: standard care n=3; ambulatory care n=5

Table 2. EQ-5D utility and EQ-VAS scores at follow-up by treatment allocation

	Patients receiving standard care	Patients receiving ambulatory care	Mean difference (95% CI)	p> z
EQ-5D utilities (S.D.)				
Baseline	0.57 (0.24) n=110	0.57 (0.26) n=109	-0.01 (-0.07 to 0.06)	0.86
Treatment completion	0.75 (0.19) n=60	0.76 (0.17) n=76	0.01 (-0.05 to 0.07)	0.65
1 week	0.83 (0.17) n=97	0.86 (0.12) n=90	0.03 (-0.01 to 0.07)	0.15
1 month	0.87 (0.16) n=88	0.89 (0.12) n=87	0.02 (-0.02 to 0.07)	0.29
6 months	0.91 (0.12) n=70	0.87 (0.23) n=73	-0.03 (-0.09 to 0.03)	0.30
12 months	0.92 (0.12) n=54	0.93 (0.10) n=55	0.01 (-0.03 to 0.05)	0.60
EQ-VAS scores (S.D.)				
Baseline	60 (23) n=110	56 (21) n=109	-3 (-9 to 2)	0.25
Treatment completion	78 (15) n=60	75 (19) n=76	-3 (-9 to 2)	0.26
1 week	84 (14) n=97	84 (13) n=90	0 (-4 to 4)	0.84
1 month	85 (17) n=88	88 (11) n=86	4 (-1 to 8)	0.10
6 months	89 (14) n=70	88 (11) n=73	-1 (-5 to 3)	0.65
12 months	94 (7) n=54	91 (9) n=55	-3 (-6 to 0)	0.06

Table 3. 12-month mean healthcare resource use (S.D.) by treatment allocation in the available case analysis

	Patients receiving standard care	Patients receiving ambulatory care	Mean difference (95% CI)	p> z
Initial length of stay, days	4.1 (4.9)	1.3 (3.2)	-2.8 (-3.8 to -1.7)	<0.0001
Hospital days due to readmissions at 1 month, days	1.1 (3.0)	0.8 (2.5)	-0.3 (-1.0 to 0.5)	0.49
Hospital days due to subsequent admissions, days	1.6 (4.7)	1.8 (8.7)	0.3 (-1.3 to 2.3)	0.77
Primary care visits				
General practice surgery	1.3 (2.6)	1.2 (2.3)	-0.1 (-0.8 to 0.5)	0.70
Home	0	0	0	n/a
Telephone	0.1 (0.4)	0.2 (0.7)	0.1 (-0.0 to 0.2)	0.24
Outpatient visits	1.7 (3.0)	2.6 (2.8)	1.0 (0.2 to 1.7)	0.012
Outpatient transport, rides	0	0.0 (0.3)	0.0 (0.0 to 0.1)	0.18
A&E visits	0.8 (1.4)	0.8 (1.1)	0 (-0.3 to 0.3)	0.98
Ambulance use, rides	0.1 (0.3)	0.1 (0.3)	-0.0 (-0.1 to 0.1)	0.75
Practice nurse visits	0.5 (2.1)	0.2 (0.8)	-0.3 (-0.8 to 0.1)	0.17
Physiotherapy visits	0.3 (1.7)	0.1 (0.7)	-0.2 (-0.6 to 0.1)	0.26

Table 4. One-year mean cost differences between patients randomised to standard care and ambulatory care

	Difference Mean (95% CI)	p> z
Base case: Multiple imputation		
Initial admission	-£1,035 (-1,490 to -578)	<0.001
Treatment	£158 (134 to 179)	<0.001
Re-admissions at 1 month	-£147 (-454 to 141)	0.34
Subsequent admissions	£61 (-444 to 567)	0.81
Primary care	£1 (-20 to 22)	0.94
Outpatient care	£188 (91 to 285)	<0.001
Emergency care	10 (-47 to 67)	0.74
Other health	-9 (-22 to 4)	0.18
TOTAL NHS	-£788 (-1,527 to -50)	0.037
Productivity losses	101 (-1,625 to 1,826)	0.91
TOTAL COSTS	-688 (-2,688 to 1,312)	0.50
Sensitivity analysis: Available case		
Initial admission	-£1,036 (-1,487 to -583)	<0.001
Treatment	£157 (135 to 179)	<0.001
Re-admissions at 1 month	-£143 (-456 to 162)	0.36
Subsequent admissions	£120 (-468 to 718)	0.70
Primary care	-£3 (-29 to 24)	0.86
Outpatient care	£140 (30 to 248)	0.012
Emergency care	-£4 (-70 to 58)	0.90
Other health	-£15 (-37 to 2)	0.14
TOTAL NHS	-£782 (-1,550 to -4)	0.049
Productivity losses	£325 (-1,857 to 3,272)	0.80
TOTAL COSTS	-£456 (-2,995 to 2,644)	0.76

Figure 1. Cost-effectiveness acceptability curve – probability that ambulatory care was cost-effective when compared standard care after multiple imputation analysis

Figure 2. Cost-effectiveness plane – cost-effectiveness of standard care when compared to ambulatory care in the available case analysis

y-axis: Incremental costs when standard care was compared to ambulatory care

x-axis: Incremental Quality-Adjusted Life-Years when standard care was compared to ambulatory care