



Contents lists available at ScienceDirect

Research in Social and Administrative Pharmacy

journal homepage: www.elsevier.com/locate/rsap

The pharmacy care plan service: Service evaluation and estimate of cost-effectiveness

Michael J. Twigg^{a,*}, David Wright^a, Garry Barton^b, Charlotte L. Kirkdale^c, Tracey Thornley^{c,d}

^a School of Pharmacy, University of East Anglia, Norwich Research Park, Norwich, UK

^b Norwich Medical School, University of East Anglia, Norwich Research Park, Norwich, UK

^c Boots UK, D90 EF06, Thane Road, Beeston, Nottingham, UK

^d School of Pharmacy, University of Nottingham, Nottingham, UK

ARTICLE INFO

Keywords:

Community pharmacy
Patient activation
United Kingdom
Cost-effectiveness
Goal setting
Long-term conditions

ABSTRACT

Background: The UK Community Pharmacy Future group developed the Pharmacy Care Plan (PCP) service with a focus on patient activation, goal setting and therapy management.

Objective: To estimate the effectiveness and cost-effectiveness of the PCP service from a health services perspective.

Methods: Patients over 50 years of age prescribed one or more medicines including at least one for cardiovascular disease or diabetes were eligible. Medication review and person-centred consultation resulted in agreed health goals and actions towards achieving them. Clinical, process and cost-effectiveness data were collected at baseline and 12-months between February 2015 and June 2016. Mean differences are reported for clinical and process measures. Costs (NHS) and quality-adjusted life year scores were estimated and compared for 12 months pre- and post-baseline.

Results: Seven hundred patients attended the initial consultation and 54% had a complete set of data obtained. There was a significant improvement in patient activation score (mean difference 5.39; 95% CI 3.9–6.9; $p < 0.001$), systolic (mean difference -2.90 mmHg; 95% CI -4.7 to -1 ; $p = 0.002$) and diastolic blood pressure (mean difference -1.81 mmHg; 95% CI -2.8 to -0.8 ; $p < 0.001$), adherence (mean difference 0.26; 95% CI 0.1–0.4; $p < 0.001$) and quality of life (mean difference 0.029; 95% CI 0.015–0.044; $p < 0.001$). HDL cholesterol reduced significantly and QRisk2 scores increased significantly over the course of the 12 months.

The mean incremental cost associated with the intervention was estimated to be £202.91 (95% CI 58.26 to £346.41) and the incremental QALY gain was 0.024 (95% CI 0.014 to 0.034), giving an incremental cost per QALY of £8495.

Conclusions: Enrolment in the PCP service was generally associated with an improvement over 12 months in key clinical and process metrics. Results also suggest that the service would be cost-effective to the health system even when using worst case assumptions.

1. Introduction

The increasing age of the population and increased life expectancy¹ has led to general practice in England managing increasing numbers of complex patients with more conditions and multiple medicines and treatments, which require greater input from the healthcare system.^{2–4} With the current workload and resourcing issues in primary care not

likely to improve significantly in the coming years, it has become apparent that new models of care are needed to support professionals and patients, particularly those with long-term conditions, to ensure that high quality care is maintained.² The Community Pharmacy Future (CPF) team is a partnership of four UK multiple pharmacy companies (Boots UK, Lloyds Pharmacy, Rowlands Pharmacy and Well) that collaborated to develop, implement and evaluate new models of care in

List of abbreviations: CEAC, Cost-effectiveness acceptability curve; CPF, Community Pharmacy Future; GP, General Practitioner; HCA, Healthcare assistant; HDL, High density lipoprotein; ICER, Incremental cost-effectiveness ratio; MMAS-8, Morisky Measure of Adherence Scale – 8; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; PAM*, Patient Activation Measure; PCP, Pharmacy Care Plan; QALY, Quality-adjusted life year; SMART, Specific, measurable, achievable, realistic, timely; UEA, University of East Anglia; UK, United Kingdom

* Corresponding author.

E-mail addresses: m.twigg@uea.ac.uk (M.J. Twigg), d.j.wright@uea.ac.uk (D. Wright), g.barton@uea.ac.uk (G. Barton), charlotte.kirkdale@boots.co.uk (C.L. Kirkdale), tracey.thornley@boots.co.uk (T. Thornley).

<https://doi.org/10.1016/j.sapharm.2018.03.062>

1551-7411/ © 2018 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

community pharmacy to support the primary care team in managing patients with long-term conditions. Previous CPF services have focused on chronic obstructive pulmonary disease and patients taking four or more medicines, and have demonstrated significant improvements in medicines adherence and quality of life.^{5,6} The aim of this project was to extend this work to provide more patient-centred care across a wider patient group with multi-morbidities, and over a longer period of time.

In response to the increasing prevalence of long term conditions in developed countries and concerns regarding the sustainability of current models of care, there is a transition from a “healthcare professional knows best” viewpoint to a more patient centred approach which empowers patients to manage their own condition.^{7–10} Patient activation is increasingly seen as an important concept in relation to person-centred care and central to encouraging self-care behaviours. Patient activation was first conceptualised and used as a tool for healthcare conversations in 2004 by Hibbard et al.^{11,12} ‘Patient activation’ describes the knowledge, skills and confidence a person has in managing their own health and healthcare. With an increased activation level, patients are more likely to have clinical indicators in the normal range and have a positive experience of care.¹³ Increased activation has also been shown to be related to reduced healthcare costs particularly with respect to fewer secondary care admissions^{14–16} and re-admissions.¹⁷ Examples of interventions aimed at increasing patient activation include tailored coaching, peer support and self-management guidance.¹³ A central component is the breaking down of large healthcare targets into small, manageable goals that can be addressed more easily by the patient. These can then be monitored and allow the patient to build confidence in managing their own health as changes are more readily observed. Conversely, for patients with a high, or increasing, level of activation, more stretching and challenging goals and actions can be agreed.

With the growing evidence for the impact of patient activation in healthcare, the CPF team developed the Pharmacy Care Plan (PCP) service with a focus on patient activation, goal setting and therapy management. The aim of this paper is to evaluate the PCP service and assess its cost-effectiveness from a UK National Health Service (NHS) perspective.

2. Methods

Approval for this service evaluation was provided by the Faculty of Medicines and Health Sciences Ethics Committee at the University of East Anglia (UEA) before commencement.

The pharmacist training and intervention have been described in detail in a previous publication.¹⁸ Briefly, 38 pharmacies in Northern England, including independent pharmacies, provided the PCP service to patients over 50 years old and prescribed one or more medicines (including at least one for cardiovascular disease or diabetes type 1 or type 2). Patients were excluded if they had experienced a myocardial infarction, transient ischaemic attacks, angina or stroke. Identification was via the pharmacy medication record or referral from the general practitioner (GP), and patients were consented to participate. The initial screen of suitability was performed by the pharmacist with access to the patient medication record. The initial approach was made by either the pharmacist or a technician who had received the training. The service was operational between February 2015 and June 2016.

Patients were offered multiple consultations with the pharmacist over the course of 12 months. The patient was asked to commit to meeting with their pharmacist at baseline, six and 12 months to allow for follow-up and data collection. However, there were no restrictions on how many times the patient could meet the pharmacist outside of these ‘core’ consultations. This was decided between the patient and pharmacist according to need and suggested to coincide with monthly prescription collection.

The initial consultation consisted of several elements:

- Medication review using relevant National Institute of Health and

Care Excellence (NICE) guidance^{19–21} and a modified STOPP/START tool²² previously used in a community pharmacy setting.⁵

- Obtaining data to calculate the patient’s cardiovascular risk using the QRISK2 (2016) instrument²³ e.g. blood pressure, lipid profile.
- Provision of adherence advice including inhaler technique (where necessary).
- Development of a jointly-produced personalised care plan that included agreed goals for their condition and treatment.
- Referral to the GP where necessary.
- Referral to other services e.g. smoking cessation, weight loss, where necessary.

At subsequent consultations, the patient and pharmacist discussed progress with the goals agreed at the initial session and made further recommendations. Clinical measures were obtained and reviewed with the patient and, if appropriate, new goals and/or actions were agreed.

3. Data collection

The following data were requested from patients at baseline, six and 12 months via questionnaire and were used to inform the consultation at each stage:

- Patient reported medication adherence (Morisky MMAS-8)^{24–26}
- Quality of life measure (EuroQol EQ-5D-5L)²⁷
- Patient Activation Measure® (PAM®, 10 item version), designed to measure patient knowledge, skills and confidence in managing their health¹²

Additional data collected by the healthcare assistant (HCA), to enable the calculation of QRisk2 score, included:

- Blood pressure (lowest of two measurements used)
- Non-fasting lipid profile (total cholesterol, HDL cholesterol)
- Weight and height
- Smoking status (options aligned with QRisk2)
- Condition status

Blood pressure measurements were obtained using machines routinely available in each pharmacy. Point of care testing, using the CardioChek®, Polymer Technology Systems Inc. was used to obtain the cholesterol results.

4. Clinical and process data analysis

All data were entered by pharmacists providing the service to an online database used routinely in the UK for the provision and evaluation of community pharmacy services. Anonymised data were first assessed for accuracy via visual, range and logic checks by the CPF team responsible for implementing the service. This involved selecting a sample of entries and contacting pharmacists to confirm values entered to the database, to ensure the information received by the evaluation team was accurate. Anonymised data were then transferred to the UEA for analysis.

The MMAS-8 measure of adherence was scored according to instructions provided by Morisky and colleagues, with a final score of 8 = high adherence, 6- < 8 = medium adherence and < 6 = low adherence.^{24–26} The PAM® score was derived from the ten questions of the instrument resulting in a score of 0–100 (where a higher score denotes greater activation).¹² Depending on the score, patients were then assigned a PAM level from one (low activation) to four (high activation) using algorithms supplied by Insignia Health LLC. QRisk2 data was collected by pharmacists and calculated by the CPF team using the 2016 risk calculator at the end of the study.²⁸

Descriptive statistics were reported for quantitative data: mean and standard deviation for interval data, median and interquartile ranges

for ordinal or skewed interval data, and number and percent for nominal data. To compare the baseline characteristics of those who completed the service evaluation and those who did not, independent samples *t*-tests or Mann-Whitney *U* tests were performed, depending on the nature of the data. Paired-samples *t*-test was used to compare before and after interval data. Mean differences (95% CI) were presented alongside the associated *p*-values. The level of significance was set at 0.05.

5. Cost-effectiveness

5.1. Intervention costs

Average times (total patient contact and non-contact) for both the pharmacist and health care assistant (HCA) were estimated for each of the consultations (baseline, six and 12-months, plus any interim consultations). Unit costs (cost per hour of employment²⁹) were then assigned to these times in order to enable the mean cost of each consultation to be estimated. These and all subsequent costs are reported from an NHS perspective in £GBP for the 2014-15 financial year (no discounting has been undertaken as the follow up period is 12 months). Per participant attendance rates (recorded by the pharmacist and HCA staff who delivered the intervention) were then combined with the estimated cost per consultation, enabling the total cost of all consultations to be estimated for each participant.

Pharmacist and HCA staff were provided with training in order to deliver the intervention and certain equipment was required for each of the pharmacies that participated.¹⁸ These items were documented along with associated costs (pharmacist and HCA times were costed as above). This enabled the cost of equipment, associated consumables for cholesterol testing, and training to be estimated. These costs were subsequently equally apportioned across all participants who received the intervention, and then added to the aforementioned per patient total consultation cost in order to estimate the total intervention cost for each participant.

5.2. Other (non intervention) NHS costs

Participants were asked to report the total number of:

- Days in hospital
- GP visits
- Practice nurse visits
- Hospital doctor visits.

At the initial consultation (baseline), the period over which patients were asked to report such visits was the previous 12 months. At each subsequent consultation, participants were also asked to report the number of such visits since their last consultation. For those that reported such information at the 12-month review, and any previous consultations, it was thereby possible to estimate the total number of the above four types of visits for the 12 months since their initial consultation. Unit costs^{29,30} were subsequently assigned to these visits, and they were summed together in order to provide an estimate of total other (non-intervention) NHS costs. For the 12 months prior to the initial consultation, this provided an estimate of the total NHS costs, as there were no intervention costs prior to the baseline consultation. For the 12 months after the baseline consultation, total other (non intervention) NHS costs were added to the aforementioned total intervention costs in order to estimate the total NHS costs. The difference between the total NHS costs before the initial consultation, compared to the total NHS costs in the subsequent 12 months, provided an estimate of the incremental cost associated with the intervention. This constituted a before and after analysis, where it is assumed that any change was due to the intervention.

5.3. Outcomes

In line with the NICE methods guide,³¹ quality of life was measured using the EQ-5D-5L.²⁷ Participants were asked to complete this at the baseline consultation and again at the six and 12-month follow-up. Responses were converted into utility scores (a scale where zero is equal to death and one is full health)³² using an EQ-5D-5L value set for England.³³ Quality Adjusted Life Year (QALY) scores were subsequently calculated for the 12 months after the baseline consultation using the area under the curve approach,³⁴ where baseline adjustment was undertaken in order to estimate the QALY gain over the 12 months since the initial consultation. The QALY gain could thereby be estimated for all participants who at least completed the EQ-5D-5L at the baseline consultation and the 12-month review.

5.4. Analyses

In the base-case analysis, a complete case approach³⁵ was undertaken, whereby participants were only included if the incremental cost and incremental QALY gain could be calculated. This required a response to, at least, the aforementioned questions relating to the EQ-5D-5L and four visit types at both the baseline consultation and the 12-month review, as well as information relating to the number of intervention consultations attended.

The mean per participant incremental cost and QALY gain was estimated and subsequently used to estimate the incremental cost-effectiveness ratio (ICER) (mean incremental cost/mean incremental QALY gain).³² In the UK, NICE refers to a cost-effectiveness threshold (λ) value of £20,000–30,000 per QALY,³¹ and we considered that an estimated ICER below £20,000 would indicate that the intervention constituted value for money.

In order to estimate the level of uncertainty associated with the decision regarding cost-effectiveness, the cost effectiveness acceptability curve (CEAC)³⁶ was estimated. The CEAC estimates the probability of the intervention being cost-effective, and this probability was specifically estimated at a λ (threshold) value of £20,000 per QALY. Additionally, bootstrapping³⁷ (5000 replications were resampled with replacement) was performed to estimate the 95% confidence interval (CI) (based on the percentile method³⁸) associated with the incremental cost, incremental QALY gain and the ICER. For the ICER these were presented in the net benefit format as there is the potential for negative ICERs to be misinterpreted.³⁹ Net benefits were calculated using a λ value of £20,000 per QALY, where a positive value would indicate that the intervention was estimated to be cost-effective at that threshold.³⁹

5.5. Sensitivity analyses

We undertook a number of sensitivity analyses³² to assess the robustness of conclusions to changes in key assumptions that were included in the above described base-case³² analysis. Within the first sensitivity analysis (best case), we excluded the intervention costs relating to training and equipment, on the assumption that these costs would not need to be incurred again if the intervention continued to be provided in current sites (we acknowledge that the results would not be applicable to new sites as they would likely require training/additional equipment). In the second sensitivity analysis (worst case) all participants were included and where data was missing it was assumed that the intervention had had no effect (a QALY gain of zero), but a cost for the intervention and other (non intervention) NHS costs was included. When considering these sensitivity analyses, in line with the recommendation when using ‘extreme but plausible’ upper and lower bounds,³² we particularly focus upon whether the decision about whether the intervention is estimated to constitute value for money would change from that in the base-case, where it has been argued⁴⁰ that decisions regarding cost-effectiveness should be made on the basis of mean values, rather than associated levels of uncertainty.

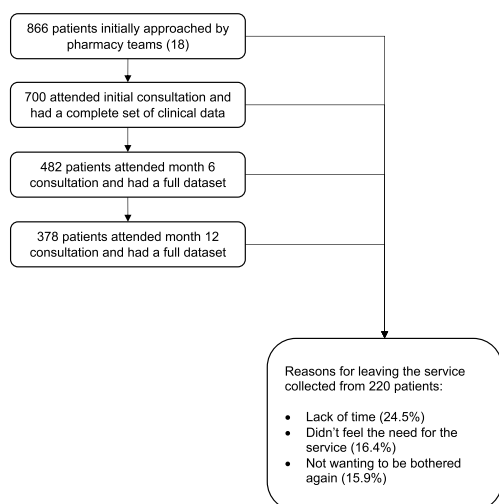


Fig. 1. CONSORT diagram.

6. Results

A total of 700 patients attended the initial consultation and had a complete set of clinical and process data obtained. At month 12, 378 (54%) patients (spread across 38 pharmacies) remained in the service and had a complete set of clinical data. A CONSORT diagram is provided in Fig. 1. The patients that completed the service received an average of 2.93 (range 1–7) consultations, mean (SD) age was 68 (8.1) years, with 212 (56.1%) female patients and 371 (98.1%) classifying themselves as white. Patients who left the service before the 12-month consultation were similar for most clinical and process measures, with the exception that they had a significantly higher BMI, lower patient activation (PAM[®] score), lower adherence to medicines, lower quality of life and more GP visits (see Table 1). Reasons for drop-out were collected from 220 (31.4%) patients, with the main reasons stated as a lack

of time (24.5%), patient did not feel the need for the service (16.4%) and patient did not want to be bothered again (15.9%).

6.1. Clinical and process data

Table 2 shows the changes in all outcome measures from baseline (all patients and those completing the service) to 12-months. It shows a significant improvement in systolic and diastolic blood pressure, PAM[®] score, adherence and quality of life. HDL cholesterol reduced significantly and QRisk2 scores increased significantly over the course of the 12 months. Further analysis showed that the increase in mean QRisk2 over this time period was largely due to patients' (recorded) condition status changing. Controlling for changes in condition status, the mean difference became non-significant (0.48 (−0.2–1.1)). Smoking status did not change appreciably over the course of 12 months. The number of patients with a high blood pressure (> 140/90 mmHg) reduced over the course of the study. The percentage of patients achieving the two higher patient activation level and adherence levels also increased over the 12 months, while the percentage of patients in the lower levels of activation and adherence showed a corresponding decrease.

In terms of goals agreed between the patient and pharmacist, 669 patients (93.2% of 718 who had any baseline interaction) set one or more goals. Overall, 1181 goals were set, ranging from one to six per patient, with an average of 1.8 goals per patient. Of these, 410 (61.3%) patients reviewed 608 goals, of which 263 patients (61.4%) achieved 359 goals (59.0%). The majority of goals set related to weight (377 patients setting 380 goals in this area, representing 32.2%) and condition control (265 patient set 322 goals, representing 27.3%; Table 3). The largest number of goals that patients indicated had been achieved were primarily concerned with weight and condition control (Table 3).

6.2. Cost-effectiveness

In total, 378 completed the EQ-5D-5L at both the baseline and 12-month follow-up point (enabling the incremental QALY gain to be

Table 1
Baseline and drop-out data comparison.

Measure		N	Baseline result, completed 12 months	N	Drop outs, between baseline and FU	p-value
Weight (Kg)	Mean (SD)	378	83.4 (17.8)	322	85.5 (19.4)	0.114 ^a
BMI (Kg/m ²)	Mean (SD)	378	30.2 (5.8)	322	31.4 (6.3)	0.011 ^a
Systolic BP (mmHg)	Mean (SD)	378	139.5 (18.1)	322	141.7 (18.6)	0.126 ^a
Diastolic BP (mmHg)	Mean (SD)	378	78.4 (10.1)	322	79.4 (11.3)	0.186 ^a
High BP (≥140/90 mmHg)	N (%)	378	196 (51.9)	322	183 (56.9)	
Total cholesterol (mmol/L)	Median (IQ)	378	3.9 (3.2–4.8)	322	3.8 (3.1–4.8)	0.643 ^b
HDL cholesterol (mmol/L)	Median (IQ)	378	1.2 (0.9–1.6)	322	1.2 (0.9–1.5)	0.250 ^b
Cholesterol/HDL ratio	Median (IQ)	378	3.0 (2.4–4.2)	322	3.1 (2.4–4.4)	0.616 ^b
QRisk score	Median (IQ)	370	24.2 (14.8–34.8)	306	25.5 (17.3–37.2)	0.073 ^b
High QRisk score	N (%)	370	230 (62.2)	306	208 (68.0)	
PAM Score	Mean (SD)	378	60.3 (14.2)	322	57.8 (14.3)	0.022 ^a
Level 1	N (%)	378	46 (12.7)	322	50 (15.5)	
Level 2	N (%)		92 (24.3)		90 (28.0)	
Level 3	N (%)		181 (47.9)		140 (43.5)	
Level 4	N (%)		57 (15.1)		42 (13.0)	
MMAS-8	Median (IQ)	378	8.0 (6.2–8.0)	322	7.0 (6.0–8.0)	0.028 ^b
Low	N (%)	378	75 (19.8)	322	71 (22.0)	
Medium	N (%)		113 (29.9)		115 (35.7)	
High	N (%)		190 (50.3)		136 (42.2)	
EQ-5D-5L score	Mean (SD)	378	0.799 (0.203)	322	0.752 (0.243)	0.005 ^a
EuroQol VAS	Mean (SD)	378	74.30 (20.02)	322	70.52 (20.27)	0.013 ^a
Total cost	Mean (SD)	249	592.08 (1051.92)	436	673.51 (1528.30)	0.411 ^a
Days in hospital	Mean (SD)	249	0.76 (2.86)	436	1.02 (4.37)	0.398 ^a
GP visits	Mean (SD)	249	3.41 (3.00)	436	4.18 (4.66)	0.019 ^a
Practice nurse visits	Mean (SD)	249	2.24 (2.40)	436	2.41 (2.96)	0.442 ^a
Hospital doctor visits	Mean (SD)	249	1.82 (2.86)	436	1.58 (2.82)	0.272 ^a

^a ISTT.

^b MWU.

Table 2
Clinical data for patients in receipt of the PCP service.

Clinical measure	Measure	N	All participants at baseline	N	Baseline result for those who completed FU	Follow-up result at 12 months	Mean difference (95% CI)	P-value*
Weight (Kg)	Mean (SD)	700	84.4 (18.6)	378	83.4 (17.8)	82.8 (17.5)	−0.53 (−1.1–0.0)	0.067
BMI (Kg/m ²)	Mean (SD)	700	30.8 (6.1)	378	30.2 (5.8)	30.1 (5.4)	−0.19 (−0.4–0.0)	0.112
Systolic BP (mmHg)	Mean (SD)	700	140.5 (18.3)	378	139.5 (18.1)	136.6 (18.8)	−2.90 (−4.7 to −1.)	0.002
Diastolic BP (mmHg)	Mean (SD)	700	78.9 (10.7)	378	78.4 (10.1)	76.6 (10.8)	−1.81 (−2.8–−0.8)	< 0.001
High BP (≥140/ 90 mmHg)	N (%)	700	379 (54.1)	378	196 (51.9)	172 (45.5)		
Total cholesterol (mmol/ L)	Median (IQ)	700	3.8 (3.1–4.8)	378	3.9 (3.2–4.8)	3.9 (3.1–4.5)	−0.07 (−0.2–0.0)	0.225
HDL cholesterol (mmol/ L)	Median (IQ)	700	1.2 (0.9–1.6)	378	1.2 (0.9–1.6)	1.2 (0.9–1.5)	−0.10 (−0.2–0.0)	0.001
Total/HDL Cholesterol ratio	Median (IQ)	700	3.1 (2.4–4.3)	378	3.0 (2.4–4.2)	3.1 (2.5–4.4)	0.16 (−0.0–0.4)	0.119
QRisk score	Median (IQ)	676	25.3 (16.0–36.0)	370	24.2 (14.8–34.8)	26.0 (16.5–37.0)	2.22 (1.4–3.1)	< 0.001
High QRisk score	N (%)	676	438 (64.8)	370	230 (62.2)	250 (67.6)		
PAM [®] Score	Mean (SD)	700	59.1 (14.3)	378	60.3 (14.3)	65.7 (15.4)	5.39 (3.9–6.9)	< 0.001
Level 1	N (%)	700	98 (14.0)	378	48 (12.7)	14 (3.7)		
Level 2	N (%)		182 (26.0)		92 (24.3)	60 (15.9)		
Level 3	N (%)		321 (45.9)		181 (47.9)	204 (54.0)		
Level 4	N (%)		99 (14.1)		57 (15.1)	100 (26.5)		
MMAS-8	Median (IQ)	700	7.0 (6.0–8.0)	378	8.0 (6.2–8.0)	8.0 (7.0–8.0)	0.26 (0.1–0.4)	< 0.001
Low	N (%)	700	146 (20.9)	378	75 (19.8)	40 (10.6)		
Medium	N (%)		228 (32.6)		113 (29.9)	135 (35.7)		
High	N (%)		326 (46.6)		190 (50.3)	203 (53.7)		
EQ-5D-5L score	Mean (SD)	700	0.778 (0.223)	378	0.799 (0.203)	0.829 (0.199)	0.029 (0.015–0.044)	< 0.001
EuroQol VAS	Mean (SD)	700	72.56 (20.21)	378	74.30 (20.02)	77.46 (20.70)	3.15 (1.15–5.15)	0.002

Table 3
Goals set and achieved by patients enrolled in the PCP service.

Goal Category	Number (%) patients who set goals	Number (%) of total goals set	Range per patient	Number patients who achieved goals (%) patients who achieved goals
Weight	377 (52.5)	380 (32.2)	1–2	104 (27.6%)
Condition control	265 (36.9)	322 (27.3)	1–4	92 (31.7%)
Exercise/activity	155 (21.6)	158 (13.4)	1–2	45 (29.7%)
Diet	77 (10.7)	77 (6.5)	1	24 (31.2%)
Adherence	71 (9.9)	73 (6.2)	1–2	27 (38.4%)
Smoking	48 (6.7)	48 (4.1)	1	13 (27.1%)
Knowledge	44 (6.1)	45 (3.8)	1–2	22 (48.9%)
Mental health	43 (6.0)	43 (3.6)	1	8 (8.6%)
Alcohol	12 (1.7)	12 (1.0)	1	6 (50.0%)
Other	23 (3.2)	23 (1.9)	3	4 (17.4%)
Total	669 (93.2)	1181	1–6	

estimated), 249 provided data on the four visit types at both these time points (enabling the incremental cost to be estimated) and 246 provided data that enabled both the incremental cost and incremental QALY gain to be estimated and were thereby included in the subsequently reported base-case analysis.

6.2.1. Costs

Estimated unit costs (cost per hour of employment) for the pharmacist and HCAs are reported in Table 4. The total intervention cost was estimated to be £160.67 (see Table 5, where the costs relating to the component parts of training, equipment and intervention contacts are reported). For the 249 that provided resource use data on the four visit types at both baseline and 12-month follow-up (enabling the incremental cost to be estimated, see Table 6), it can be seen that there was no significant difference between the previous 12-month levels of resource use at both these time points. As such, the total other (non intervention) NHS costs, in the previous 12 months, were not significantly different between baseline and 12 months (see Table 6). However, total NHS costs were higher in the 12-month follow-up period

Table 4
Unit costs attached to different items of resource use, with associated source.

Item	Estimated unit cost
Pharmacist (Band 6, cost per hour of employment, including overheads) ^a	£42.08
Health care assistant (cost per hour of employment, including overheads) ^a	£22.61
GP visit ^a	£37.00
Hospital admission (cost per bed day) ^b	£302.97
Hospital out-patient visit ^b	£139.00
Practice nurse visit ^a	£12.09

^a Based on Curtis.²⁹

^b Based on the National Schedule of Reference Costs.³⁰

(see Table 6), largely due to the intervention cost, and in the base-case analysis the mean incremental cost associated with the intervention was estimated to be £202.91 (95% CI 58.26 to £346.41) (see Table 6).

6.2.2. Outcomes

For the 378 with complete EQ-5D-5L data, the mean improvement in quality of life was estimated to be 0.029 (95% CI 0.015–0.044) (see Table 2). For those who also had incremental cost data, and were thereby included in the base-case analysis, the mean incremental QALY gain was estimated to be 0.024 (95% CI 0.014 to 0.034) (see Table 7).

6.2.3. Cost-effectiveness

Based on the aforementioned incremental cost and incremental QALY gain, in the base-case analysis, the ICER was estimated to be £8495 per QALY, where the 95% CI for the incremental net benefit was estimated to be below the £20,000 per QALY threshold value (see Table 7). Additionally, according to the CEAC, there was a 97% probability that the intervention was cost-effective at the £20,000 per QALY threshold value (see Table 7 and Fig. 2).

6.2.4. Sensitivity analyses

The ICER, associated 95% CI and CEAC value were estimated to be more favourable in the 'best case' sensitivity analysis when training and equipment costs were excluded from the intervention costs (see Table 7

Table 5
Intervention costs.

Component part	Resources costed & participant attendance/assumptions	Mean cost (£ per participant)
Training	A pharmacist and health care assistant (HCA) from each of the 52 sites received a delegate pack (£30 per pack) and attended a 1 day training event. Four such events were held, with two trainers (@£500 per day each), medical actors (@£590 per day in total) and associated facilities (@£300 per day). Apportioned across all N = 718 attendees.	50.01
Initial consultation	15 min patient contact time with a HCA, 30 min patient contact time with pharmacist, 15 min non-patient contact time by the pharmacist for paperwork, etc. N = 718 attended.	33.70
Interim review(s)	10 min patient contact time and 5 min non-patient contact time with/by the pharmacist. A total of N = 513 took place.	7.52
6 monthly review	15 min patient contact time with a HCA, 15 min patient contact time with pharmacist, 10 min non-patient contact time by the pharmacist for paperwork, etc. N = 486 attended.	15.69
12 monthly review	15 min patient contact time with a HCA, 15 min patient contact time with pharmacist, 10 min non-patient contact time by the pharmacist for paperwork, etc.. N = 386 attended.	12.46
Equipment	Cholesterol testing kit (£470 per site) and equipment to measure blood pressure (£40 per site), weight (£40 per site) and height (£20 per site). Apportioned across all N = 718 attendees.	41.28
Total		160.67

See Table 4 for pharmacist HCA unit costs. NB N = 718 as resource use data was available for more patients than data for clinical measures. Ten patients had baseline resource data but no baseline clinical data were recorded, demonstrating that they did attend a baseline consultation. An additional 8 patients had data collected at later time points, but no resource use or clinical data recorded for the baseline consultation, it was assumed that these 8 patients did have a first consultation. These 18 patients were therefore excluded from the clinical analysis, but included for goals analysis and this analysis as they were shown or assumed to have also had a baseline consultation.

and Fig. 1). This reflects the fact that together the training and equipment costs are estimated to constitute the majority of the intervention costs (see Table 5), and if, for example, not all of these costs had been loaded on trial participants, then more favourable results might have been seen in the base-case. In the second (worst case) sensitivity analysis, for those participants who had missing data in relation to other (non intervention) NHS costs, a cost of £39.76 was assigned to this variable (this is the mean value for those who had complete data on this variable, see Table 6). Even in this worst-case (where, when data was missing, it has been assumed that there was no change in quality of life and a cost for other (non intervention) NHS services has been included, as participants may have still been referred to the GP/other services) the ICER was still estimated to be below the £20,000 per QALY value (see Table 7). There was however an increased level of uncertainty, as reflected in the 95% CI associated with the ICER (see Table 7) and the CEAC (see Fig. 1).

7. Discussion

For most patients, enrollment on the pharmacy care plan (PCP) service was associated with an improvement over 12 months in key clinical, process and humanistic data. Improvements were observed in patients for systolic and diastolic blood pressure, patient activation, adherence and quality of life. The service was also estimated to be cost-

effective from the perspective of the NHS. The mean estimate was < £20,000/QALY even in what might be considered a worst case scenario.

There were several strengths and limitations associated with this evaluation. This was a before-and-after study and as such, any changes in outcome measures cannot automatically be attributed directly to the intervention as no control group was used. However, this represents a pragmatic design in a setting where it may be difficult to recruit patients to a control group. In order to estimate cost-effectiveness, data was collected from patients on their resource use in the 12 months prior to commencing the service. This resource use data, along with adherence, patient activation and quality of life are all patient self-reported measures, which are subject to recognised limitations.^{41,42} To address concerns over the nature of the study design, a worst case cost-utility analysis was performed and this still produced positive results. A limited NHS perspective was taken and certain items e.g. medication usage were not requested as, in line with recommendations,⁴³ we focused on what were expected to be the main cost drivers.

Almost 50% of the patients who started the service did not remain until the end. Stated reasons for dropping-out included a lack of time and feeling no need for the ongoing service. Indications from the outcome data point to patients dropping out who were less activated, less likely to take their medicines, had a lower quality of life and visited their GP more. This will impact on the generalizability of the results and

Table 6
Mean (SD) levels of resource use data for particular health care services, with associated costs (£).

Measure	N	All participants at baseline	N	Baseline result for those who completed FU	Follow-up result at 12 months	Mean difference (95% CI)	P-value*
Days in hospital	685	0.93 (3.89)	249	0.76 (2.86)	0.96 (3.51)	0.20 (-0.29 to 0.70)	0.424
Cost		280.41 (1178.47)		229.96 (864.98)	290.80 (1064.84)	60.84 (-88.93 to 210.60)	0.424
GP visit	685	3.90 (4.15)	249	3.41 (3.00)	3.89 (3.67)	0.48 (-0.02 to 0.98)	0.062
Cost		144.43 (153.40)		126.31 (111.01)	143.99 (135.83)	17.68 (-0.89 to 36.25)	0.062
Practice nurse visits	685	2.34 (2.77)	249	2.24 (2.40)	1.88 (2.07)	-0.35 (-0.67 to -0.04)	0.029
Cost		28.35 (33.45)		27.04 (29.04)	22.77 (24.99)	-4.27 (-8.11 to -0.44)	0.029
Hospital doctor visits	685	1.67 (2.84)	249	1.82 (2.86)	1.52 (3.02)	-0.30 (-0.29 to 0.70)	0.156
Cost		190.72 (324.87)		208.77 (327.44)	174.28 (346.27)	-34.49 (-82.25 to 13.28)	0.156
Total other (non intervention) NHS costs	685	643.91 (1374.10)	249	592.08 (1051.92)	631.84 (1317.61)	39.76 (-133.94 to 213.46)	0.653
Total NHS costs	685	643.91 (1374.10)	249	592.08 (1051.92)	814.96 (202,925.99)	222.89 (49.24-396.54)	0.012

At the initial consultation (baseline) participants were asked to report the total number of each item of resource use in the last 12 months. At each subsequent review participants were asked to report the total number of each item of resource use, since their previous consultation/review where they reported such values. For those who attended the 12 month review, the reported values over the 12 month follow up period have been summed. *Paired samples t-test.

Table 7
Base-case and sensitivity Analysis.

	N	Mean incremental cost (95% CI)	Mean QALY gain (95% CI)	Mean ICER (95% CI incremental net benefit)	CEAC probability of cost-effectiveness ^c
Base case	246	202.91 (63.05–348.87)	0.024 (0.014–0.034)	8495.29 (34.31–514.35)	97.0%
Best case ^a	246	111.62 (–30.36 to 252.12)	0.024 (0.014–0.034)	4673.10 (124.63–607.62)	99.2%
Worst case ^b	718	200.43 (152.95–251.69)	0.010 (0.006–0.014)	19,392.12 (–90.66 to 100.56)	54.2%

^a As in base case but with the exclusion of training and equipment costs.

^b Where data was missing a value of 0 was used for QALY data and £39.76 for other (non intervention) NHS costs. A cost for the intervention is also included for all participants.

^c CEAC = Cost-effectiveness acceptability curve, where the associated probability of the intervention being cost-effective is estimated for a threshold of £20,000 per QALY.

more work needs to be undertaken to understand reasons for not remaining in the service. To address the high attrition rate in future, the service could be offered to those most likely to keep attending, or the pharmacist could explain to patients the importance of the service to encourage their continued participation. A further factor that will influence the generalizability of the results is the targeted recruitment of patients with cardiovascular disease for the service in order to capture a clinical outcome that was appropriate across all patients.

A further limitation of this study is the self-report nature of the questionnaires measuring activation, adherence, resource use and quality of life where patients were unblinded to the intervention. However, these were used at baseline and follow-up and analysis focused on changes rather than absolute values. Despite this, patients may have underestimated their resource use at baseline due to the 12 months period over which they were asked to recall visits (post baseline patients were asked to report resource use since their last visit). That said, other studies have used such a time period and there is no consensus on aspects such as the optimal time period within patient resource use questionnaires.⁴⁴

Finally, a strength of this study was the long follow-up of patients. In previous services by the same team follow-up has been limited to six months.^{5,6} However, in this service patients were enrolled for a total of 12 months. This indicates that changes observed over this time are more likely to be maintained.

With the exception of QRisk2 and HDL cholesterol, clinical indicators improved in patients enrolled in the PCP service. The increase in QRisk2 was observed as being largely due to changes in condition status, something that cannot necessarily be attributed to the pharmacist providing the service. Indeed, it may be that more conditions were recorded as more consultations took place, simply because the patient divulged more information to the HCA/pharmacist. No data was

collected to determine whether the pharmacist was responsible for identifying any of these additional diagnoses. In addition, the reduction in HDL cholesterol over the 12 month service is surprising and requires further work to understand whether this was as a result of the diet and lifestyle goals agreed between the patient and pharmacist or whether something else was responsible. Without a control group, it is difficult to determine this information with any certainty.

Although the aforementioned differences were small, it indicates movement in the right direction. This improvement may be linked to goals agreed between the patient and pharmacist with the majority focusing on weight and control of their conditions. The use of goal setting to target key behaviours such as weight loss, diet and exercise is one that has been explored repeatedly in the literature.^{45,46} When looking at the goals achieved by patients, those relating to knowledge and adherence were among the highest achieved categories, whereas only about 1 in 3 patients who set weight goals indicated that they had achieved them. These results seem to correlate with the clinical outcomes, as weight did not change significantly, but adherence and patient activation (which includes understanding) did. Further research should be undertaken on the types of goals set as some of these set in this service were achievable and measurable and some were not. This may imply that more training of the pharmacist is required to help patients set SMART goals as part of the service.

In terms of activation and adherence, patients demonstrated a significant increase in both over the course of 12 months. Improvements in adherence scores have previously been linked to improved clinical outcomes in diabetes,⁴⁷ hypertension⁴⁸ and asthma and COPD^{49,50} which may be responsible for some clinical improvements observed in this evaluation. Patient activation is also important in this group of patients as condition management will involve changes to diet, lifestyle and exercise habits for which the patient will need to be motivated to

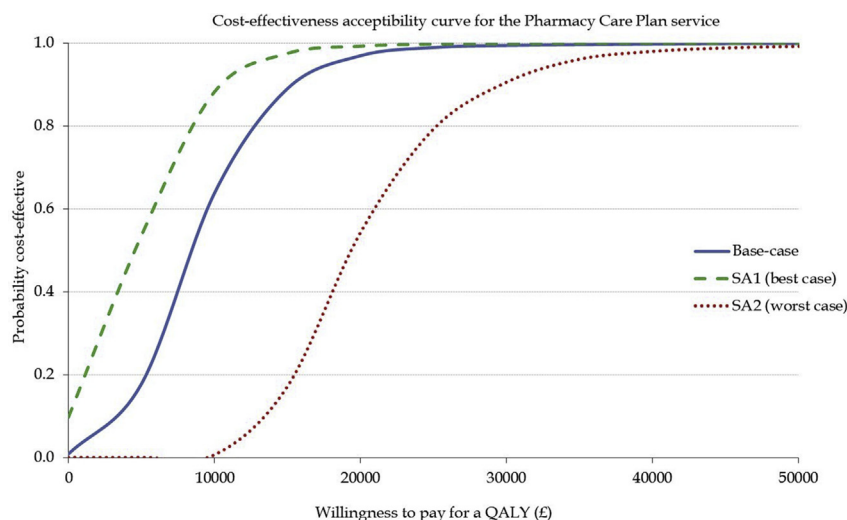


Fig. 2. Cost-effectiveness acceptability curve for the Pharmacy Care Plan service.

achieve.

The increase in PAM[®] score is positive for community pharmacy as it demonstrates pharmacists' ability to motivate and empower patients with long-term conditions. To our knowledge, this is the first community pharmacy evaluation to use this approach and as a result these findings warrant further exploration in this settings. However, this is a positive start to the use of this tool in this setting. With the link between patient activation and improved health outcomes, patient experience and reduced costs^{13–17} becoming more firmly established it is clear that this approach is one that requires further investigation in the context of primary care in the UK. By moving from the lowest activation level to the highest estimates suggest that healthcare costs can be reduced by up to 21%.¹⁵

Even when using worst case estimates this service is estimated to be cost-effective in relation to NICE thresholds.³¹ Despite the intensive nature of the service, with multiple consultations over an extended period of time, costs were kept low by making use of the whole pharmacy team including HCAs obtaining clinical measurements instead of the pharmacist. This is something that has been explored with other pharmacy services, for example, as part of health living pharmacies⁵¹ and NHS Health Checks.⁵²

In a previous publication, pharmacists reported a willingness to deliver this service but also concerns regarding time commitment and support.¹⁸ Despite this, the service managed to demonstrate an improvement to patient care and outcomes. This service was delivered by a small number of well-motivated pharmacists and pharmacy staff and in order to be successfully implemented on a larger scale and achieve similar outcomes, appropriate remuneration and support needs to be provided.

Although there are few other examples of complex interventions of this nature being provided and evaluated within the community pharmacist setting, the previous work carried out by the CPF team to evaluate other services focused on long-term conditions also demonstrated favourable clinical and cost-effectiveness results.^{5,6} Taken together, this suggests that community pharmacies are likely to represent a cost-effective use of NHS resources.

8. Conclusion

Enrollment on the PCP service was generally associated with an improvement over 12 months in key clinical and process metrics, including statistically significant improvements in patient activation, adherence, blood pressure and quality of life. Results also suggest that the service would be cost-effective to the health service (below the £20,000 per QALY threshold value) even when using worst case assumptions. The vast majority of patients set goals as part of the PCP service, suggesting that pharmacists were able to engage with patient's understanding of what health outcomes were important to them, and in many cases, help patient's to achieve them. Further research needs to be conducted to determine the effect of goal setting on patient activation together with qualitative work to understand how professionals and patients responded to the use of the PAM[®] measure in practice.

Ethics approval

Approval for this service evaluation was provided by the Faculty of Medicines and Health Sciences Ethics Committee at the University of East Anglia (UEA) (Reference: 20142015/39/SE) before commencement. Patients provided written consent to participate in the service.

Funding

The study design and implementation was funded by the Community Pharmacy Future (CPF) group. The CPF group also paid a consultancy fee to the team at UEA (MT, DW) to provide advice on service design, to support training and to undertake the evaluation for

this service. The CPF research team (CLK and TT) are both employees receiving salaries from Boots UK. The specific roles of these authors are articulated in the 'author contributions' section.

Funding sources

The design and implementation of this project was funded by the CPF group, with support from an educational grant from Pfizer.

Authors' contributions

All authors contributed to conceptualisation of the project and development of the methodology. CK and TT contributed to study management, data collection and paper editing and review. MT performed formal analysis and original manuscript preparation. DW and GB performed formal analysis and contributed to review and editing of the manuscript. DW was responsible for the academic supervision of the project.

Competing interests

We have the following interests. The team at UEA (MT, DW, GB) were paid a consultancy fee to provide advice, training and evaluation for this service by the Community Pharmacy Future (CPF) group. The CPF group (the funders) designed and implemented the service and had sight and approved the submission to the journal. CLK and TT are employees of Boots UK (and part of CPF group) and were part of the evaluation team who were involved in the study design, data collection and analysis, decision to publish, and preparation of the manuscript. There are no patents, products in development or marketed products to declare.

Declaration of interest

CK and TT are employees of Boots UK Ltd. MT, DW and GB are employees of UEA. UEA was remunerated by the CPF team to manage the academic evaluation of the CPF services.

Acknowledgements

The CPF team would like to thank contributors and advisors to the project together with the pharmacists and patients who provided and participated in the service. In particular, the team acknowledges the contribution made by Pfizer. and the Pharmaceutical Services Negotiating Committee (PSNC) in training of the pharmacy teams. License agreements for use of the ©MMAS and the PAM[®] were obtained prior to conducting this project. Use of the ©MMAS is protected by US copyright laws. Permission for use is required. A license agreement is available from: Donald E. Morisky, ScD, ScM, MSPH, Professor, Department of Community Health Sciences, UCLA Fielding School of Public Health, 650 Charles E. Young Drive South, Los Angeles, CA 90095-1772, dmorisky@ucla.edu.

References

- Office for National Statistics. *National Life Tables, UK: 2013–2015*. 2016; 2016 <http://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/lifexpectancies/bulletins/nationallifetablesunitedkingdom/20132015>, Accessed date: 29 November 2016.
- NHS England. *Five Year Forward View*. 2014; 2014 <https://www.england.nhs.uk/wp-content/uploads/2014/10/5yfv-web.pdf>, Accessed date: 29 November 2016.
- NHS England. *General Practice Forward View*. 2016; 2016 <https://www.england.nhs.uk/wp-content/uploads/2016/04/gp-fv.pdf>, Accessed date: 29 November 2016.
- The King's Fund. *Understanding Pressures in General Practice*. 2016; 2016 https://www.kingsfund.org.uk/sites/files/kt/field/field_publication_file/Understanding-GP-pressures-Kings-Fund-May-2016.pdf, Accessed date: 29 November 2016.
- Twigg MJ, Wright D, Barton GR, Thornley T, Kerr C. The four or more medicines (FOMM) support service: results from an evaluation of a new community pharmacy service aimed at over-65s. *Int J Pharm Pract*. 2015;23(6):407–414.

6. Wright D, Twigg M, Barton G, Thornley T, Kerr C. An evaluation of a multi-site community pharmacy-based chronic obstructive pulmonary disease support service. *Int J Pharm Pract.* 2015;23(1):36–43.
7. Department of Health. *Equity and Excellence: Liberating the NHS.* London: The Stationery Office; 2010.
8. The Health Foundation. *Person Centred Care Made Simple: What Everyone Should Know about Person Centred Care.* London: The Health Foundation; 2014.
9. The King's Fund. *From Vision to Action: Making Patient-centred Care a Reality.* London: The King's Fund; 2012.
10. Royal Pharmaceutical Society. *Improving Care for People with Long Term Conditions.* 2016; <http://www.rpharms.com/policy-pdfs/32.-long-term-conditions-report.pdf>, Accessed date: 8 November 2016.
11. Hibbard JH, Stockard J, Mahoney ER, Tusler M. Development of the Patient Activation Measure (PAM): conceptualizing and measuring activation in patients and consumers. *Health Serv Res.* 2004;39(4p1):1005–1026.
12. Hibbard JH, Mahoney ER, Stockard J, Tusler M. Development and testing of a short form of the patient activation measure. *Health Serv Res.* 2005;40(6p1):1918–1930.
13. Hibbard J, Gilbert H. *Supporting People to Manage Their Health: an Introduction to Patient Activation.* London: The King's Fund; 2014.
14. Greene J, Hibbard JH. Why does patient activation matter? An examination of the relationships between patient activation and health-related outcomes. *J Gen Intern Med.* 2013;32(2):216–222.
15. Hibbard JH, Greene J, Overton V. Patients with lower activation associated with higher costs; delivery systems should know their patients' scores'. *Health Aff.* 2013;32(2):216–222.
16. Remmers C, Hibbard J, Mosen DM, Wagenfield M, Hoye RE, Jones C. Is patient activation associated with future health outcomes and healthcare utilization among patients with diabetes? *J Ambul Care Manag.* 2009;32(4):320–327.
17. Mitchell SE, Gardiner PM, Sadikova E, et al. Patient activation and 30-day post-discharge hospital utilization. *J Gen Intern Med.* 2014;29(2):349–355.
18. Twigg MJ, Wright D, Kirkdale CL, Desborough JA, Thornley T. The UK Pharmacy Care Plan service: description, recruitment and initial views on a new community pharmacy intervention. *PLoS One.* 2017;12(4) e0174500.
19. National Institute for Health and Care Excellence. Hypertension: clinical management of primary hypertension in adults. *Clinical guideline.* 2011;127.
20. National Institute for Health and Care Excellence (NICE). *Lipid Modification: cardiovascular Risk Assessment and the Modification of Blood Lipids for the Primary and Secondary Prevention of Cardiovascular Disease CG181.* 2014; 2014; <http://www.nice.org.uk/guidance/cg181>, Accessed date: 12 August 2014.
21. NICE. Type 2 diabetes. *The Management of Type 2 Diabetes (CG87).* London: National Institute of Health and Clinical Excellence; 2009.
22. O'Mahony D, Gallagher P, Ryan C, et al. STOPP & START criteria: a new approach to detecting potentially inappropriate prescribing in old age. *Eur Geriatric Med.* 2010;1(1):45–51.
23. Collins GS, Altman DG. Predicting the 10 year risk of cardiovascular disease in the United Kingdom: independent and external validation of an updated version of QRISK2. *BMJ.* 2012;344.
24. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. *J Clin Hypertens.* 2008;10(5):348–354.
25. Krousel-Wood M, Islam T, Webber LS, Re RN, Morisky DE, Muntner P. New medication adherence scale versus pharmacy fill rates in seniors with hypertension. *Am J Manag Care.* 2009;15(1):59–66.
26. Morisky D, DiMatteo M. Improving the measurement of self-reported medication nonadherence: final response. *J Clin Epidemiol.* 2011;64:258–263.
27. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res.* 2011;20:1727–1736.
28. ClinRisk Ltd. *QRisk2(R) scoring webpage.* 2016; 2016; <https://qrisk.org/2016/>.
29. Curtis L, Burns A. *Unit Costs of Health and Social Care 2015.* University of Kent; 2015.
30. Department of Health. *National Schedule of Reference Costs 2014-15.* 2015; <https://www.gov.uk/government/publications/nhs-reference-costs-2014-to-2015>.
31. NICE. *Guide to the Methods of Technology Appraisal 2013.* National Institute of Health and Clinical Excellence (NICE) publications; 2013.
32. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. *Methods for the Economic Evaluation of Health Care Programmes.* fourth ed. New York: Oxford University Press; 2015.
33. Devlin N, Shah K, Feng Y, Mulhern B, van Hout B. *Valuing Health-related Quality of Life: an EQ-5D-5L Value Set for England.* School of Health and Related Research (University of Sheffield): Health Economics & Decision Science (HEDS); 2016 Discussion Paper Series.
34. Manca A, Hawkins N, Sculpher MJ. Estimating mean QALYs in trial-based cost-effectiveness analysis: the importance of controlling for baseline utility. *Health Econ.* 2005;14:487–496.
35. Briggs AH, Ades AE, Price MJ. Probabilistic sensitivity analysis for decision trees with multiple branches: use of the Dirichlet distribution in a Bayesian framework. *Med Decis Making.* 2003;23:341–350.
36. Fenwick E, O'Brien BJ, Briggs AH. Cost-effectiveness acceptability curves-falacies and frequently asked questions. *Health Econ.* 2004;13:405–415.
37. Efron B, Tibshirani R. *An Introduction to the Bootstrap.* New York: Chapman and Hall; 1993.
38. Heyse JF, Cook JR, Carides GW. Statistical considerations in analysing health care resource utilization and cost data. In: Drummond M, McGuire A, eds. *Economic Evaluation in Health Care.* Oxford: Oxford University; 2001.
39. Stinnett AA, Mullahy J. Net health benefits: a new framework for the analysis of uncertainty in cost-effectiveness analysis. *Med Decis Making.* 1998;18:S68–S80.
40. Claxton K. The irrelevance of inference: a decision-making approach to the stochastic evaluation of health care technologies. *J Health Econ.* 1999;18(3):341–364.
41. Matsuyama JR, Mason BJ, Jue SG. Pharmacists' interventions using an electronic medication-event monitoring device's adherence data versus pill counts. *Ann Pharmacother.* 1993;27(7–8):851–855.
42. Atkinson M, Zibin S, Chuang H. Characterizing quality of life among patients with chronic mental illness: a critical examination of the self-report methodology. *Am J Psychiatr.* 1997;154(1):99–105.
43. Ramsey S, Willke RJ, Glick H, et al. Cost-effectiveness analysis alongside clinical trials II-An ISPOR good research practices task force report. *Value Health.* 2015;18:161–172.
44. Thorn JC, Coast J, Cohen D, et al. Resource-use measurement based on patient recall: issues and challenges for economic evaluation. *Appl Health Econ Health Pol.* 2013;10:1–7.
45. Shilts MK, Horowitz M, Townsend MS. Goal setting as a strategy for dietary and physical activity behavior change: a review of the literature. *Am J Health Promot.* 2004;19(2):81–93.
46. Bodenheimer T, Handley MA. Goal-setting for behavior change in primary care: an exploration and status report. *Patient Educ Counsel.* 2009;76(2):174–180.
47. Schectman JM, Nadkarni MM, Voss JD. The association between diabetes metabolic control and drug adherence in an indigent population. *Diabetes Care.* 2002;25(6):1015–1021.
48. Krousel-Wood M, Thomas S, Muntner P, Morisky D. Medication adherence: a key factor in achieving blood pressure control and good clinical outcomes in hypertensive patients. *Curr Op Cardiol.* 2004;19(4):357–362.
49. Vestbo J, Anderson JA, Calverley PMA, et al. Adherence to inhaled therapy, mortality and hospital admission in COPD. *Thorax.* 2009;64(11):939–943.
50. Mäkelä MJ, Backer V, Hedegaard M, Larsson K. Adherence to inhaled therapies, health outcomes and costs in patients with asthma and COPD. *Respir Med.* 2013;107(10):1481–1490.
51. Brown D, Portlock J, Rutter P, Nazar Z. From community pharmacy to healthy living pharmacy: positive early experiences from Portsmouth, England. *Res Soc Adm Pharm.* 2014;10(1):72–87.
52. McNaughton RJ, Oswald NT, Shucksmith JS, Heywood PJ, Watson PS. Making a success of providing NHS Health Checks in community pharmacies across the Tees Valley: a qualitative study. *BMC Health Serv Res.* 2011;11(1):222.