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RESEARCH ARTICLE

The cost effectiveness of a telephone-based pharmacy advisory service to improve adherence to newly prescribed medicines

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Abstract *Objective* This ''proof of concept'' study aimed to assess the cost effectiveness of pharmacists giving advice via telephone, to patients receiving a new medicine for a chronic condition, in England. *Methods* The self-regulatory model (SRM) theory was used to guide development of our intervention and used in training pharmacists to adopt a patient-centred approach. Non-adherence to new medicines for chronic conditions develops rapidly so we developed a study intervention in which a pharmacist telephoned patients two weeks after they had started a new medicine for a chronic condition. Patients were included if they were 75 or older, or were suffering from stroke, cardiovascular disease, asthma, diabetes or rheumatoid arthritis, and were randomized into treatment or control arms. Main outcome measures were non-adherence and cost to the UK NHS, obtained via a questionnaire sent two months after starting therapy. Cost of the intervention was also included. Incremental cost effectiveness ratios (ICERs) were generated. *Results* Five hundred patients were recruited. At 4-week follow-up, non-adherence was significantly lower in the intervention group (9% vs 16%, $p = 0.032$). The number of patients reporting medicine-related problems was significantly lower in the intervention group compared to the control, (23% vs 34% $p = 0.021$). Mean total patient costs at 2-month follow-up (median, range) were intervention: £187.7 (40.6, 4.2–2484.3); control: £282.8 (42, 0–3804) ($p < 0.0001$). The intervention was dominant (less costly and more effective). If the decision maker is not willing to pay anything for one extra adherent patient, there is still a 90% probability that the intervention is cost effective. *Conclusions* These findings suggest that pharmacists can meet patients' needs for information and advice on medicines, soon after starting treatment. While a larger trial is needed to confirm that the effect is real and sustained, these initial findings suggest the study intervention may be effective, at least in the short term, with a reduced overall cost to the health provider.

Keywords Patient adherence · Economic evaluation · Randomised controlled trial · Pharmacist · England · Telephone service

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Impact of findings on practice

- A telephone based pharmacy advisory service seems to reduce non-adherence in elderly medicine users.
- The sustainability of the impact of such a service needs to be studied in a large trial.

Introduction

Harm caused by non-adherence to appropriately prescribed medicines is an important public health issue in most chronic illnesses [1–5]. Potential consequences of non-adherence are health benefits forgone[6] and personal and

social economic burden. The economic wider societal burden of non-adherence, if it exists, arises from morbidity associated with sub-optimal medicine use, and includes cost to the patient, cost to the health care provider and cost to society. Cost of illness in the US due to non-adherence was estimated at $100 bn per annum in 1997[7] and is referred to as the nation's 'other drug problem' [8]. In Canada, cost of illness due to non-adherence was estimated at $8 billion in 1998 [9]. Non-adherence causes unscheduled hospital admissions [10]. In the UK, 6.5% of adult hospital admissions may be medicine-related, 30% of these due to non-adherence to medicines for chronic illness [11].

However, interventions to improve adherence are often complex, costly and not very effective [12]. A Cochrane review discovered only 58 satisfactorily designed studies of interventions, of which 26 improved adherence; these were complex and multifaceted [13]. A recent review of 45 studies on efficiency of adherence-enhancing interventions suggested that studies were limited by the validity of the adherence-enhancing interventions, quality of interventional study design, and quality of economic evaluation [12]. Cost data were particularly badly prepared and analysed. Many interventions were very resource-intensive and, if implemented widely, would divert large amounts of resources from other aspects of health care. From these reviews, and others, it is clear that future interventions to improve adherence must be developed systematically, with staged studies accumulating evidence for effective, efficient and deliverable solutions. The recently developed MRC framework for complex interventions supports this systematic approach [14]. A recent university-hospital based intervention carried out by pharmacists improved both adherence and outcome, showing that well-designed studies can demonstrate the value of pharmacist-led services [15]. However, carrying out adherence-enhancing interventions in the community carries different challenges.

Previous research suggests that non-adherence to new medications for chronic conditions develops rapidly, 30% of patients were non-adherent 10 days after starting therapy [16]. Therefore, we developed a study intervention in which a pharmacist telephoned patients two weeks after they had started a new medicine for a chronic condition. We followed the Medical Research Council (MRC) framework, using theory-based intervention components in an exploratory trial to explore the feasibility of that intervention [14]. Details of the process of the intervention, and the safety, utility and patient acceptability of the intervention have been reported elsewhere [16]. In this study we assess the cost effectiveness of the study intervention, compared with current counselling or medicine provision service in community pharmacy, from the perspective of the health provider (the UK National Health Service (NHS).

Methods

Design

A randomised controlled trial was carried out to assess the effect of the study intervention on adherence and associated costs of the study intervention. The study was approved by the London Multi-Centre Research Ethics Committee.

Selection criteria and randomisation

Patients were recruited from a convenience sample of 40 Moss (now Alliance) community pharmacies across England. Patients were identified if they were receiving the first prescription for a new medicine for a chronic condition. Patients within this group were eligible if they were 75 or older, or suffering from stroke, cardiovascular disease, asthma, diabetes, or rheumatoid arthritis. Exclusion criteria were an inability to understand written or spoken English or not having a telephone. Patients were recruited opportunistically when they presented a prescription in one of the pharmacies, and gave consent before entering the study. Randomisation was by the pharmacist giving a sealed envelope to the patients, this contained their treatment group; the pharmacist was blind to the contents. The pharmacist recorded the name and address of the patient and referred this to the intervention pharmacists.

Intervention

The intervention group received a telephone call from one of two community pharmacists at the head office of the Moss group of pharmacies, two weeks after the patient was recruited. The intervention phone call was based on a semi structured interview schedule developed previously [16]. The self-regulatory model (SRM) theory and the necessity-concerns framework were used to guide development of the intervention as they recognise that adherence can be influenced by patients' beliefs about their illness and treatment [17;18]. This theory was used in training pharmacists to adopt a patient-centred approach. The pharmacist listened to the patient's problems and gave advice if needed. The pharmacist asked patients 'How are you getting on with your medicines?', enquired about any medicine-related problems, adherence to the new medicine and whether they required any further information. The

pharmacist followed the flow of the patient's conversation, using the interview schedule as a checklist if the patient spoke of issues in a different order. The pharmacist gave information, advice or reassurance in response to the patients' expressed needs.

Collection of data

Four weeks after recruitment a researcher phoned the patient and interviewed them about their medicines and the intervention (if they received it). The researcher recorded self reported non-adherence. In our study, based on recommendations from the literature, non-adherence was defined as a self report of at least one dose of the new medicine having been missed in the last seven days [19].

The perspective of the economic evaluation was the NHS, so data were required on the use of primary care and secondary care resources. The data were collected for the two month period after the initiation of the new medicine. To obtain these data, a second questionnaire was sent to the patients two months after starting therapy.

Sample size

Sample size was calculated from the primary outcome measure, using a clinically useful reduction in self reported non-adherence from 22% to 12%, based on an alpha of 0.05 (two sided) and a power of 80%. Assuming 10% of patients dropped out 490 patients were needed.

Analysis

The perspective of the study was that of the NHS in terms of the direct costs of providing a pharmacist based intervention to improve patients' adherence and related follow up care. It was not possible to calculate sample size on the basis of cost due to lack of prior work in this area. NHS resource use data (NHS contact, pharmacist training and time) were collected prospectively for each patient six weeks after the intervention and combined with unit costs for 2004/5. The total cost was calculated for each of the patients enrolled in the trial who completed follow-up. The data were not normally distributed, so non-parametric bootstrapping was used to compare arithmetic means of cost data [20).

A decision analytic model was developed to generate incremental cost effectiveness ratios (ICERs), expressed as cost per extra adherent patient. Data were applied to the model as outlined in Fig. 1. The ICER was generated from the following expression:(Cost intervention – Cost control)/(Outcome intervention - Outcome control).

The 2.5% and 97.5% percentiles of the ICER distribution were obtained by generation of a bootstrap estimate of the ICER sampling distribution. Non-parametric bootstrapping with replacement was employed, utilising MS Excel®, using 1000 iterations.

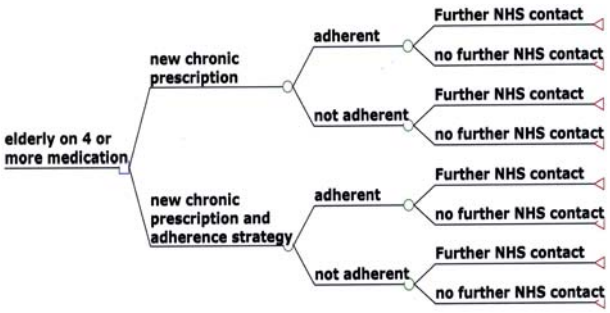

Fig. 1 Decision analytic model for the pharmacy-based intervention compared with control ''further NHS contact'': GP, accident and emergency, and outpatient visits, and hospitalizations

Uncertainty in cost effectiveness analysis exists on two levels: uncertainty in the estimated values of cost effectiveness and uncertainty around the maximum (or ceiling) cost effectiveness ratio that a decision-maker would consider acceptable [21]. We constructed a cost effectiveness acceptability curve to reflect uncertainty in costs, effects and the maximum willingness to pay.

Results

Five hundred patients were recruited and consented from 40 Moss community pharmacies in eight areas of England, from Cornwall to Yorkshire. Eight patients were ineligible, leaving 255 patients in the intervention group and 237 in the control group. Drop-out occurred when the patient had been taken off the new medicine by their doctor, happening to 48 (19%) of the intervention group and 29 (12%) of the control group. The response rates to the questionnaires were 72% (intervention) and 66% (control). The section on use of resources was responded to by 87 in the intervention group and 118 in the control group. This substantial loss to follow-up could affect internal validity, and reduced power to detect statistically significant differences in cost. Those patients who were lost to follow up did not have significantly different demographics (age, sex, comorbidities, work status, prescription payment status) or 4-week adherence from those patients included in the economic analysis.

Adherence

In the 205 patients used in this analysis, non-adherence was significantly lower in the intervention group (10/87, 11%) when compared to the control group (23/118, 19%), $p < 0.05$. Adherence at 4 weeks was assumed to remain unchanged at 2 months, when the cost data were collected.

Costs

The intervention pharmacists made a median of one (1st, 3rd quartiles: 1,2) call per patient and spent a median of 12 [8,18] min on each call. Associated administration took a further median of 6 [4,10] min per patient.

Frequency of patient contact with the NHS was not significantly different between the control and intervention (Table 1). However, once these data were combined with unit costs listed in Table 2, the difference in costs was highly significant, suggesting that the intervention group had a significantly lower cost to the NHS (Table 2).

Incremental economic analysis

ICERs were generated for the primary outcome measure against total cost in the sample of patients with both cost and outcome data (n = 205). The mean ICER was -£2168 per extra adherent patient (median -£1116, 2.5th percentile: -£12925, 97.5th percentile: £7227). The intervention was more effective and less costly, suggesting that the intervention was dominant. Figure 2 shows the distribution of the bootstrapped ICERs on the cost effectiveness plane. It can be seen that most of the ICER point estimates are in the south east quadrant, suggesting a high probability that the intervention is dominant (more effective and less expensive than normal treatment).

A cost effectiveness acceptability curve (CEAC) provides a measure of the probability that an ICER will be less than the decision-maker's ceiling willingness to pay. Generating a CEAC shows there is an 90% probability that this intervention is cost effective for the English National Health Service even if the decision-maker is not willing to pay anything for one extra adherent patient.(see Fig. 3)

Table 1 Summary of patient demographics and contact with the NHS

Proportion of patients (%)	Control (n = 118)	Intervention (n = 87)
Sex (% male)	51	44
Mean age (range)	67 (34–85)	67 (28–88)
Condition (% reporting)		
Angina	4	2
Arthritis	7	10
Asthma	4	6
High blood pressure/heart	52	47
High cholesterol	8	8
Diabetes	11	8
Stroke	0	2
Other	1	14
Don't know	1	3
Employment status		
Working	19	20
Retired	73	71
Not in paid employment	8	9
Pay for own prescription	96	95
One or more GP visits (mean number of visits per patient)	80.0 (1.53)	81.4 (1.34)[a]
One or more Accident and Emergency visits (mean number of visits per patient)	9.0 (0.14)	2.6(0.03)[b]
One or more outpatient visits (mean number of visits per patient)	32.0 (0.51)	36.3 (0.46)[c]
One or more hospitalisations (mean number per patient)	8.9 (0.18)	3.9 (0.06)[d]

[a] χ^2: 0.005, p = 0.946; [b] χ^2: 2.06, p = 0.151; [c] χ^2: 0.193, p = 0.660; [d] χ^2: 1.04, p = 0.308

Discussion

Adherence-enhancing interventions, policies or initiatives use scarce resources, so should be informed by theory, based on causes for non-adherence and targeted at key patient groups. A cost-effective intervention to enhance adherence is one that is effective in reducing the burden of illness associated with non-adherence, at an optimal level of resource use.

These findings provide evidence that a telephone call from a pharmacist, with the aim of solving patients' problems with a new medicine, can significantly reduce non-adherence and is less costly than usual care. These findings are tentative as the study was a feasibility study and was not powered for an economic evaluation. We developed an intervention based on theories of non-adherence in an exploratory trial to explore the feasibility of that intervention using the MRC framework [14]. Our intervention is novel in that it is relatively simple and cost-effective. This contrasts with the findings from the Cochrane review which found most effective interventions to be complex, difficult to implement in practice and resource intensive [24]. This intervention may have general applicability across a wide range of patients and, in the way we have applied it, across a wide geographical area. Recent developments in remuneration for professional community pharmacy services in the UK mean that this service is now also likely to be deliverable in practice [25].

The next stage is to test this hypothesis and to carry out a definitive RCT with appropriate statistical power [14]. Limitations of this study are the methods used to recruit pharmacies, measure adherence, health provider resource use and length of follow-up, and loss to follow-up. The use of a convenience sample of pharmacies may have introduced some bias. There is no standard measurement of adherence. The most commonly used methods are self-report, using health care providers' judgement, prescription

Table 2 Principal patient-based resource use and costs

Cost parameter	Cost per unit resource use (£)[22, 23]	Control (n = 118) (£)	Intervention (£) (n = 87)
Mean GP costs (median, range)	21	26.3 (21.0, 0–63.0)	23.2 (21.0, 0–63.0)
Mean Accident and Emergency costs (median, range)	100	10.1 (0, 0–300)	2.3 (0, 0–100)
Mean outpatient costs (median, range)	251	97.8 (0, 0–753)	98.1 (0, 0–502)
Mean hospitalization costs (median, range)	1168	148.5 (0, 0–3504)	53.7 (0, 0–2336)
Mean NHS costs (median, range)	(GP + A&E + outpatient + inpatient)	282.8 (42.0, 0–3804)	177.3 (21.0, 0–2478)
Mean intervention costs (median, range)	£30 per hour (Moss Pharmacist) + call tariff	0	10.9 (9.2, 2.1–40.8)
Mean total patient costs (median, range)	NHS costs + intervention costs	282.8[a] (42.0, 0–3804)	187.7[a] (40.6, 4.2–2484.3)

[a] Bootstrapped t-test (assuming unequal variance): t: 45.39, $p < 0.00001$

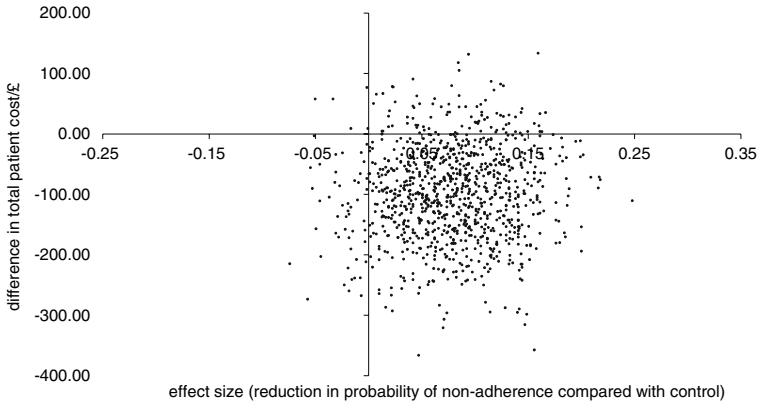

Fig. 2 Cost effectiveness plane for cost versus adherence for the pharmacy-based intervention compared with control

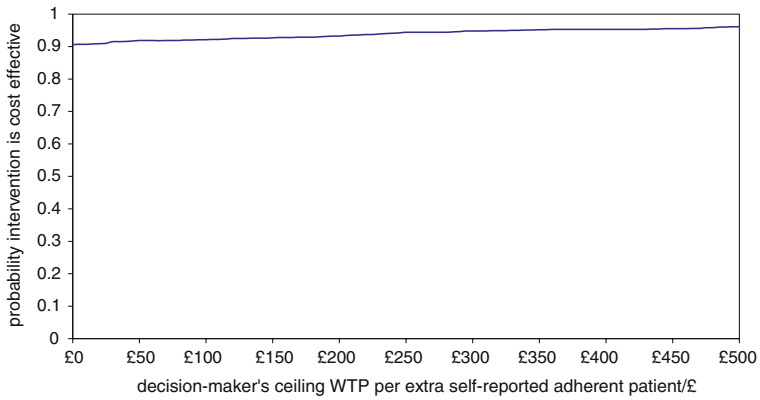

Fig. 3 Cost effectiveness acceptability curve for the pharmacy-based intervention compared with control, demonstrating decision-maker's ceiling willingness-to-pay

filling, electronic measurement devices, tablet counts, canister weights, clinical outcome measures and measurement of blood or urine levels of the medicine [26]. Self-report has been shown to provide increased rates of adherence to asthma medications over other methods [27–29]. Respondents commonly cannot accurately recall their adherence or may intentionally exaggerate their adherence to avoid being perceived negatively. [30] Self-report of non-adherence is generally accurate, because if a person reports that they are non-adherent, it is likely that they are truly non-adherent [31]. This suggests that the difference in adherence demonstrated in this study is informative, even if the baseline overestimates overall adherence levels. Health provider resource use was reported by patients, not obtained from medical records, so the quality of these data were reliant on patient recall, and may over or underestimate actual resource use. In future, more reliable methods need to be investigated to obtain sources of health care

contact information, as many patients were lost to follow-up, reducing the internal validity of the data. Also, it is likely that the two month follow-up period of this study was not long enough to detect health-related resource use triggered by non-adherence. The resource-related consequences of morbidity caused by non-adherence can take many years to present. For example, tight blood pressure control (ACE inhibitor or beta-blocker) reduces risk of diabetic retinopathy, but the improvement is only significant after 4.5 years of treatment [32]. The follow-up period is also not long enough to assess the long-term impact of the intervention. A future study should also include assessment at a later time, at least six to twelve months after the intervention, to determine whether the effect is sustained, and should ideally show an improved clinical outcome, although this is difficult in interventions like this that cover many disease states. The sample size here was too small to allow disease-specific analysis, but future studies need to focus on specific disease states to assess their different impact. One of the study limitations is the opportunistic recruitment of patients in the community pharmacy affecting the generalisability of the sample. This has been reported as a limitation in other studies of the same design [33]. It may be attributed to pharmacists' inexperience and initial hesitation with informed consent and enrollment procedures. Simpson et al (2001) reported that patients were sometimes surprised when approached by their pharmacist for participation in a ''research study'' [33].

Other studies have shown that pharmacists working with patients and their medicines can improve adherence, and also, clinical outcomes such as the control of blood pressure[15;34] and heart failure [35]. Current health policy in the UK is expanding the role of the pharmacist and other health professionals into a greater involvement in medicines management and both supplementary and independent prescribing [36–38]. These developments allow the funding of new professional services, including payment for community pharmacists for medication use reviews. Importantly, the benefits of adherence to effective medication can only be realised if appropriate prescribing takes place so these interventions need to be carried out alongside evidence-based prescribing. National Service Frameworks (NSFs) outline optimal prescribing in key areas such as diabetes, cardiovascular disease and the elderly [39–41].

Conclusions

In summary, clinical practitioners need support in their management of people with chronic illness in both prescribing and supporting adherence. Management of most chronic illness is based on a complex set of strategies, many promoting the use of regular medication when the patient is symptom-free. It is perhaps, not surprising that adherence to some medication is low [42]. It is clear that trying to coerce patients into using medicines that they are unwilling or unable to use, will result in failure.

Interventions to improve adherence must be effective, patient-centred and provide value for money for the health care provider. Our proof of concept study suggests that a relatively simple intervention by a pharmacist in the early stages of a new medication can improve adherence at overall reduced cost to the health care provider and is acceptable to patients. Further work is required, namely a larger study is needed to see if the effect is sustainable, and also to examine how this intervention could be carried out on a larger scale within current models of service delivery.

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Conflicts of interest The author have not reported any conflicts of interest.

References

1. Dartnell JGA, Anderson RP, Chohan V, Galbraith KJ, Lyon MEH, Nestor PJ et al. Hospitalisation for adverse events related to drug therapy: incidence, avoidability and costs. Med J Aust 1996;164:659–62.
2. Psaty BM, Koepsell TD, Wagner EH, lo Gerfo JP, Inui TS. The relative risk of incident coronary heart disease associated with recently stopping the use of B-Blockers. J Am Med Assoc 1990;263(12):1653–7.
3. Weiden PJ, Olfson M. Cost of relapse in schizophrenia. Schizophr Bull 1995;21(3):419–29.
4. Lau DT, Nau DP. Oral antihypoglycaemic medication nonadherence and subsequent hospitalization among individuals with Type 2 diabetes. Diabetes Care 2004;27:2149–53.
5. Balkrishnan R, Rajagopalan R, Camacho FT, Huston SA, Murray FT, Anderson RT. Predictors of Medication Adherence and Associated Health Care Costs in an Older Population with Type 2 Diabetes Mellitus: A Longitudinal Cohort Study. Clinical Therapeutics 2003;(11):2958–71.
6. Simpson SH, Eurich DT, Majumdar SR, Padwal RS, Tsuyuki RT, Varney J et al. A meta-analysis of the association between adherence to drug therapy and mortality. Br Med J 2006;333 (7557):15–21.
7. Lewis A. Noncompliance: A $100 billion problem. Remington Rep 1997;5:14–5.
8. Zuger A. The 'other' drug problem: forgetting to take them. The New York Times 1998 Jun 2.
9. Coambs RB, Jarry JL, Jensen P, Her MH, Porter J, Ferguson BS et al. Prescription non-compliance and inappropriate prescribing in Canada: causes, consequences and costs. Toronto, Canada: Health Canada Publications; 1998.

10. Cerveri I, Locatelli F, Zoia MC, Corsico A, Accordini S, Marco R. International variations in asthma treatment compliance. Eur Respir J 1999;14:288–94.
11. Howard RL, Avery AJ, Howard PD, Partridge M. Investigation into the reasons for preventable drug related admissions to a medical admissions unit: observational study. Qual Saf Health Care 2003;12:280–5.
12. Elliott RA, Barber N, Horne R. Cost-effectiveness of adherence-enhancing interventions: a quality assessment of the evidence. Ann Pharmacother 2005;39:508–15.
13. Haynes RB, McKibbon KA, Kanani R. Systematic review of randomised trials of interventions to assist patients to follow prescriptions for medications. J Lancet 1996;348:383–6.
14. Campbell M, Fitzpatrick R, Haines A, Kinmonth A-L, Sandercock P, Spiegelhalter DJ. Framework for design and evaluation of complex interventions to improve health. Br Med J 2000; 321:694–6.
15. Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density lipoprotein cholesterol: A randomized controlled trial. JAMA 2006;296(21):2563–71.
16. Barber N, Parsons J, Clifford S, Darracott R, Horne R. Patients' problems with new medication for chronic conditions. Qual Saf Health Care 2004;13:172–5.
17. Horne R. Treatment perceptions and self regulation. In: Cameron D, Leventhal H eds., The self-regulation of health and illness behaviour.London: Routledge; 2003. p. 138–53, ISBN 0415297001.
18. Leventhal H, Cameron LD. Behavioral theories and the problem of compliance. Patient Educ Couns 1987;10:117–38.
19. Haynes RB, McDonald H, Garg AX, Montague P. Interventions for helping patients to follow prescriptions for medications. The Cochrane Database of Systematic Reviews 2002;(Issue 2).
20. Briggs A, Gray A. The distribution of health care costs and their statistical analysis for economic evaluation. J Health Serv Res Policy 1998;3(4):233–45.
21. Fenwick E, Claxton K, Sculpher MJ. Representing uncertainty: the role of cost effectiveness acceptability curves. Health Econ 2001;10:779–87.
22. National Health Service Executive. NHS Reference Costs 2004. http://www dh gov uk/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/PublicationsPolicyAndGuidanceArticle/fs/en?CONTENT_ID=4069646&chk=vzKK5z 2005 [cited 2003 Jul 10];.
23. Netten A, Dennett J. Unit costs of community care. Kent: Personal Social Services Research Unit; 2005. Report No.: ISBN 1092671406.
24. Haynes RB, Yao X, Degani A, Kripalani S, Garg A, MacDonald HG. Interventions for enhancing medication adherence. The Cochrane Database of Systematic Reviews 20054(Art. No.: CD000011.pub2.).
25. NHS Business Services Authority Prescription Pricing Division. New Contractual Framework for Community Pharmacy: Payment for Advanced Services; Medication Use Reviews. http://www ppa org uk/ppa/contract_framework_for_community_pharmacy htm#medsusereview 2007 [cited 2007 Jan 12];.
26. Myers LB, Midence K. Methodological and conceptual issues in adherence. In: Myers LB, Midence K, (eds.), Adherence to treatment in medical conditions. Amsterdam: Harwood Academic Publishers; 1998. ISBN 9057022648.
27. Milgrom H, Bender BG, Ackerson LM, Bowry P, Smith B, Rand C. Noncompliance and treatment failure in children with asthma. J Allergy Clin Immunol 1996;98:1051–7.
28. Bender BG, Milgrom H, Rand C, Ackerson LM. Psychological factors associated with medication non-adherence in asthmatic children. J Asthma 1998;35:347–53.
29. Bender BG, Wamboldt FS, O'Connor SL, Rand C, Szefler S, Milgrom H et al. Measurement of children's asthma medication adherence by self-report, mother report, canister weight, and Doser CT. Ann Allergy Asthma Immunol 2000;85:416–21.
30. Nichol MB, Venturini F, Sung JCY. A critical evaluation of the methodology of the literature on medication compliance. Ann Pharmacother 1999;33:531–40.
31. Choo PW, Rand CS, Inui TS, Lee M, Cain E, Cordeiro-Breault M et al. Validation of patient reports, automated pharmacy records, and pill counts with electronic monitoring of adherence to antihypertensive therapy. Med Care 1999;37:846–57.
32. Matthews DR, Stratton IM, Aldington SJ, Homan RR, Kohner EM. UKPDS 69 Risks of progression of retinopathy and vision loss related to tight blood pressure control in type 2 diabetes mellitus. Arch Ophthal 2004;122:1631–40.
33. Simpson SH, Johnson JA, Biggs C, Biggs RS, Kuntz A, Semchuk W et al. Practice-based research: Lessons from community pharmacist participants. Pharmacotherapy 2001;21(6):731–9.
34. Blenkinsopp A, Phelan M, Bourne J, Dakhil N. Extended adherence support by community pharmacists for patients with hypertension: a randomised controlled trial. Int J Pharm Pract 2000;8:165–75.
35. Goodyer LI, Miskelly F, Milligan P. Does encouraging good compliance improve patients' clinical condition in heart failure? Br J Clin Pharmacol 1995;49:173–6.
36. Department of Health. NHS R & D Strategic Review Primary Care Working Group: Report of the Pharmacy subgroup. https://www dh gov uk/assetRoot/04/02/09/41/04020941 pdf 1999 [cited 2006 Jul 10].
37. Department of Health. Pharmacy in the future: Implementing the NHS Plan. http://195 33 102 76/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/PublicationsPolicyAndGuidanceArticle/fs/en?CONTENT_ID=4005917&chk=/4q1tW 2000 [cited 2006 Jul 10].
38. Department of Health. A vision for pharmacy in the new NHS. http://www dh gov uk/Consultations/ClosedConsultations/ClosedConsultationsArticle/fs/en?CONTENT_ID=4068353&chk=Y2fMuy 2003 July [cited 2006 Jul 10].
39. Department of Health. National Service Framework for Coronary Heart Disease. www dh gov uk/PolicyAndGuidance/HealthAndSocialCareTopics/CoronaryHeartDisease/fs/en 2000 [cited 2006 Jul 10].
40. Department of Health. National Service Framework for Older People. www dh gov uk/PolicyAndGuidance/HealthAndSocialCareTopics/olderpeople/fs/en 2001 [cited 2006 Jul 10].
41. Department of Health. National Service Framework for Diabetes. www dh gov uk/PolicyAndGuidance/HealthAndSocialCareTopics/diabetes/fs/en 2003 [cited 2006 Jul 10].
42. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. J Psychosom Res 1999;47(6):555–67.