Evidence Extractions

Question: Do interventions to increase patient involvement increase length of the consultation?

Grading: 1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

Kinnersley P;Edwards A;Hood K;Cadbury N;Ryan R;Prout H;Owen D;Macbeth F;Butow P;Butler C;

Interventions before consultations for helping patients address their information needs

Ref ID 27 2007

Study Type Systematic Review **Funding** Cochrane Collaboration

Number of participant	RCTs only (see above)
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	This answers the question very well of as many of the studies included consultation length and this study looked at the interventions before consultations to help patients address their information needs - which included interventions before consultations to encourage question asking and information gathering by the patient, which can lead to increased patient participation. The main conclusion of the review: Often the outcomes included question asking, patient participation, patient anxiety, knowledge, satisfaction and consultation length. Interventions before consultations led to a small and statistically significant increase in consultation length, whereas those implemented some time before the consultation had no effect. This study is a very strong systematic review for guideline evidence, however not all the studies were within the remit of the guideline as they included patient participation within other areas than medicine taking. This should be noted.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	

Lewin SA;Skea ZC;Entwistle V;Zwarenstein M;Dick J;

Interventions for providers to promote a patient-centred approach in clinical consultations

Ref ID 8713 2001

Study Type	Systematic Review	**Funding**	Health in Partnership initiative, DOH (UK); Dept for International Development (UK); Nuffield Commonwealth Programme (UK); Chief Scientist Office of the Scottish Executive Health Department (UK); Medical Research Council (South Africa).

Number of participant RCTs; Controlled clinical trials; Controlled before and after studies; Interrupted time series studies.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

The main conclusion is that there is 'fairly strong evidence to suggest that some interventions to promote patient-centred care in clinical consultations may lead to significant increases in the patient centredness of consultation processes'. However the evidence on patient-centred care in consultations is limited and the effects are mixed for behaviours and health status. Further research is required.

17 studies were included all of which included an element of training for HCPs. Seven studies involved multi-faceted interventions. 12/14 studies which assessed consultation processes found some improvement. 6/11 studies which looked at patient satisfaction found significant differences on one or more measures for the intervention group.

It may not be completely relevant to the question as it is about improving patient-centeredness care and may not involve increasing patient involvement.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

McKinstry B;Ashcroft RE;Car J;Freeman GK;Sheikh A;

Interventions for improving patients' trust in doctors and groups of doctors

Ref ID 672 2006

Study Type Systematic Review **Funding** Cochrane Review

Number of participant RCT

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? These studies assessed patient trust rather than patient involvement in decision making. Consultation style was not considered in two of the three included studies. One study was a trial of training interventions for doctors. One explored the impact on trust of disclosing physician incentives to patients in an HMO and another investigated the effect of induction visits on new HMO members. Only the latter study relates to consultation style but the HMO model is not applicable in the UK NHS in this instance.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

O'Connor AM;Stacey D;Entwistle V;Llewellyn-Thomas H;Rovner D;Holmes-Rovner M;Tait V;Tetroe J;Fiset V;Barry M;Jones J;

Decision aids for people facing health treatment or screening decisions

Ref ID 8717 2003

Study Type Systematic Review

Funding Canadian Institute of Health Research (Canada); Nuffield Trust of University of Oxford (UK); Ontario Ministry of Health Career Scientist funding for AO'C (Canada); Leverhulme Trust Research Fellowship funding for VE (UK); Canada Res. Chair Program.

Number of participant RCTs.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? 35 RCT studies were included in the systematic review. 221 decision aids were identified but very few had been evaluated, with only 31 assessed in the RCTs. It was difficult to make conclusions because of the variability of decision contexts, decision aid designs, type of comparison interventions, targeted outcomes and how they were measured. This withstanding the RCTs showed that decision aids do a better job than usual care interventions in improving people's knowledge regarding options, enhancing realistic expectations about the benefits/harms of options, reducing decisional conflict, decreasing the amount of people remaining undecided, and stimulating a more active role in decision making.

Therefore this is a high quality systematic review which has shown that there are decision aids which can support the patient to reach an informed decision.

It should be noted that many of the decisions involved populations which were not included in our search. However there were trials which included HRT.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Wetzels R;Harmsen M;van WC;Grol R;Wensing M;

Interventions for improving older patients' involvement in primary care episodes

Ref ID 5434 2007

Study Type Systematic Review **Funding** Cochrane Collaboration.

Number of participant RCT and quasi experimental

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

It helps only a little as it is interventions for improving older patients' involvement. Therefore this is partially the population we are looking at - would be better if whole population.

Also two of the studies were not relevant as they were not relating to consultation length.

They found some positive effects of specific methods to improve the involvement of older people in health care episodes. However there is not enough studies to conclude and recommend the use of any intervention in practice. The field of older patients is sparse.

One study is therefore relevant to us (Cegala 2001) which had a partly open method of allocation; double blinding; 45 participants (22 intervention and 23 control) which is small; They gave a brief pre-interview questionnaire for baseline measurement.

It is strong because it is well-conducted but it did not find enough strong studies to be of a good source of evidence for a guideline.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

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It is strong because it is well-conducted but it did not find enough strong studies to be of a good source of evidence for a guideline.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Brook OH;van H;Stalman W;Nieuwenhuyse H;Bakker B;Heerdink E;de H;

A pharmacy-based coaching program to improve adherence to antidepressant treatment among primary care patients

Ref ID 1286 2005

Study Type Randomised Controlled Trial **Funding** No details given.

Number of participant	135 patients. Intervention group: 64, control group: 71.
Inclusion/Exclusion Criteria	Inclusion/Exclusion: patients of general practitioners who were 18 years or older, who had a new prescription for a nontricyclic antidepressant, and who were able to fill out questionnaires in Dutch.
Patient Characteristics	Characteristics not given per group: No significant differences between the groups on demographic or health-related variables were noted at baseline. The patients' mean ± SD age was 43 ± 13 years. A total of 95 patients (70 percent) were women.
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	Intervention group: three coaching contacts, which lasted between ten and 20 minutes. Delivered by pharmacists who were asked to use a list of important themes to discuss with the patients (themes not given in study). In addition, the patients in the intervention group received a 25-minute take-home video addressing the importance of adherence.
Comparisons	
Length of Study/ Follow-up	6 months.
Outcome measures studied	Adherence was measured with an electronic pill container (EDEM) and was also derived from computerised pharmacy medication records (both over 6 months).
Results	NOTE BEFORE: The comparison with the eDEM recordings showed an overestimation of adherence of 5 percent in the pharmacy records. For the 28 patients for whom only the pharmacy registration was available, we subsequently reduced estimated adherence by 5 percent. Adherence: Intention-to-treat analyses showed no intervention effect on adherence (Intervention group: 76 percent mean, s.d: 29, compared with control group: 73 percent mean, s.d. 31, 95% CI: –7.3 to 13.3), whereas analyses of patients who received the intervention (per protocol) showed improved adherence (Intervention group: 90 percent mean, s.d: 14 compared with control group: 73 percent mean, s.d. 31, 95% CI: 5.1 to 28.9). Other outcomes: Neither intention to treat analysis or protocol analysis showed effects on depressive symptoms.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention did significantly improve adherence according to the protocol but not intention to treat analysis.
Effect due to factor in study?	Fairly, some potential problems with internal validity (see above).

Consistency of results with other studies?

Directly applicable to guideline population? Yes.

Internal Validity

Cohen D;Longo MF;Hood K;Edwards A;Elwyn G;

Resource effects of training general practitioners in risk communication skills and shared decision making competences

Ref ID 7456 2004

Study Type Randomised Controlled Trial **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Edwards A;Elwyn G;Hood K;Atwell C;Robling M;Houston H;Kinnersley P;Russell I;Study Steering Group;

Patient-based outcome results from a cluster randomized trial of shared decision making skill development and use of risk communication aids in general practice

Ref ID 236 2004

Study Type Randomised Controlled Trial **Funding** DOH

Number of participant	20 GPs participated and 747 patients attended. 715 patients completed the exit questionnaire; 655 completed the 1 month questionnaire and 618 completed the 6 month questionnaire.
Inclusion/Exclusion Criteria	Physicians: In practice between 1-10 years; to have sufficient practice computerization for identification of relevant patients and to be audio taped in routine surgery consultations before the stud. Patients were identified from practice registers with one of four conditions: Non-valvular atrial fib; prostatism; menorrhagia; and menopause related problems.
Patient Characteristics	Physicians: 12 men and 8 women with an average of 38 years. Among patients the mean age in each condition category was as follows: prostatic symptoms 63 years, atrial fib 65 years, menorrhagia 45 years and hormone replacement therapy 56 years. There were no statistically significant differences between groups in mean ages, gender or response rates.
Recruitment	Physicians who met inclusion criteria were recruited from practices in Gwent, South Wales. Patients were identified from practice registers
Setting	Research clinic and GP surgery
Interventions/ Test/ Factor being investigated	The use of shared decision making skills or the use of simple rick communication aids on patient confidence in the decision, anxiety, enablement, health status, satisfaction, intention to adhere to chosen treatment and perceived support in decision.
Comparisons	The comparison is between shared decision making or risk communication
Length of Study/ Follow-up	6 months
Outcome measures studied	The primary outcome measure was patient confidence in the decision as measured by the COMRADE instrument , anxiety, enablement, health status, satisfaction, intention to adhere to chosen treatment and perceived support in decision.
Results	No statistically significant effects of the risk communication or shared decision intervention were seen on the whole range of patient based outcomes. Patient confidence in the decision (2.1 increase, 95% CI (0.7--3.5). P<0.01) and expectation to adhere to chosen treatments (0.7 increase, 95% CI 0.04-1.36, p<0.05) were significantly greater among patients seen in the research clinics when more time was available compared with usual surgery time.
Safety and adverse effects	None
Does the study answer the question?	As no statistically significant effects of the risk communication or shared decision intervention were seen on the whole range of patient based outcomes this study can only conclude that there was no improvement or deterioration in patient based outcomes following skills based interventions to UK GPs regarding shared decision making and risk communication. ** Note: A further report on this study by Cohen et al provided data on the resource effects of training GPs in risk communication skills and shared decision making competences and concluded that the training cost £1218 per practitioner which increased the cost of a consultation by £2.89.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	

Internal Validity No control group for physicians or for patients

Fraenkel L;Rabidou N;Wittink D;Fried T;

Improving informed decision-making for patients with knee pain

Ref ID 3718 2007

Study Type Randomised Controlled Trial

Funding From the Veterans Affairs Connecticut Healthcare system and the Yale University School of Medicine. In part by a grant by the Claude D. Pepper Older Americans Independence Center at Yale University School of Medicine

Number of participant	87 patients. Data available for 40 in the pamphlet group and 43 in the ACA Task group.
Inclusion/Exclusion Criteria	Over the age of 60 years; self-report of pain involving one or both knees on most days of the month; the ability to read and understand English; ability to perform a choice on this task; Excluded if judged to be too ill to participate; were scheduled for an urgent visit; had a disease other than osteoarthritis that causes knee pain; had relative or absolute contraindications to one or more of the proposed treatment options. These were ascertained by self-report.
Patient Characteristics	Mean age was 74 years, Most were Caucasian 65% control and 72% intervention group;
Recruitment	A research assistant recruited participants by approaching patients waiting in the primary care waiting room area.
Setting	Veteran Affairs Connecticut Healthcare System.
Interventions/ Test/ Factor being investigated	Performed an Adaptive Conjoint Analysis (ACA). This is an interactive computer tool which could generate immediate feedback to the participant and help them construct treatment preferences by means of tradeoffs by rating tasks.
Comparisons	The intervention vs. the control group who received an Arthritis Foundation information pamphlet.
Length of Study/ Follow-up	Immediately and at 3 months.
Outcome measures studied	Primary outcome measure was decision conflict scale immediately after the consultation. Questionnaire. Secondary outcomes were anxiety, knowledge, and decision-making preferences.
Results	The computerised decision aid group had lower decision conflict immediately after the clinic (mean 0.18, 95%CI -0.34 to -0.01) and mean -0.15 (-0.37 to 0.06) at three month follow-up. Both groups had less decision conflict after the consultation but the difference between groups was significant at 5% level. Subscales suggest this was due to feeling better informed and clearer of their personal values for the risks and benefits of alternative options. The reduction in anxiety fell significantly but was not different between groups. Knowledge scores improved slightly after the consultation but at three months were back at baseline level. Participants in the decision aid group were less likely to start warfarin than those in the guideline arm (39/53, 73.6%) compared to guidelines (50/56, 81.7%), RR0.82, 95% CI 0.68 to 0.99, this was however almost completely due to participants not already on warfarin, here the difference was 4/6, 25% compared to guidelines 15/16, 93.8%, RR 0.27, 95%CI 0.11 to 0.63. There was no difference in health outcomes 3 months after the clinic.

Safety and adverse effects	None
Does the study answer the question?	Participants using this computer tool designed to increase patient awareness of choice and evaluate the tradeoffs related to available treatment options were more confident in their ability to obtain information about available treatment options, were better prepared to participate in their visit and had better arthritis related self efficacy compared to patients receiving an information pamphlet.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	Subjective outcome measure

Hamilton W;Russell D;Stabb C;Seamark D;Campion-Smith C;Britten N;

The effect of patient self-completion agenda forms on prescribing and adherence in general practice: a randomized controlled trial

Ref ID 13907 2007

Study Type	Randomised Controlled Trial	**Funding**	Grants from the Medicines Partnership, East Devon and Exeter Primary Care Trusts. Also funding from a NHS Researcher Development Award.

Number of participant	1610 completed all details initially (all prescribing outcomes known) 811 were in the intervention group and 799 were in the control group.
Inclusion/Exclusion Criteria	No exclusion criteria - stated that all patients attending during normal working hours of the g.p practice were eligible.
Patient Characteristics	For those with prescribing outcomes known the median age was 56 (IQR=38,70) and the no. of males was 623(38%).
Recruitment	When arriving at g.p surgery offered an envelope with a brief description of the study. If wished to proceed they opened the envelope. This was a covering letter, short form to write down contact details, pen and in half was a SCAF (see intervention).
Setting	Ten g.p practices in Devon (9) and Dorset (1).
Interventions/ Test/ Factor being investigated	The intervention group received a SCAF, which was (previously piloted) a one-sided sheet with 5 questions: 1. What made you decide to come to see the doctor? Please describe the problem you have e.g. symptoms or current illness. 2. Your ideas about your illness: What do you think is wrong with you? 3. Your concerns: Have you any particular worries about your illness? 4. Your expectations: How do you think your problem should be treated? What do you hope the doctor will do? 5. Medication: Do you think you should receive a prescription for your problem? The participants (or their carers) were asked to complete this while waiting for their appointment and to give it to the doctor when they went in. The g.p was allowed to use the SCAF in any way they deemed appropriate for that consultation. The SCAFS were not retained or returned to the study team. A letter was sent out to the patient within 24 hours of their consultation with 2 questionnaires: the Medical Interview Satisfaction Scale and the Satisfaction with Decision Questionnaire. They also requested consent for the researchers to look at

	their GP records for prescriptions issued in the consultation. Prescripiton details and re-attendances were identified from the practices' computer systems. Adherence was measured by structured telphone interviews by a researcher blinded to the intervention status at 2 weeks and 12 weeks. Up to 5 telephone calls were made. The GPs participating were offered a semi-structured telephone interview after participation with a researcher in Medicines Partnership (one of the funders) to allow criticisms to be aired. The interview focused on whether g.ps believed the SCAF affected the consultation and their prescribing. Also to see if change in consultation style also occurred for the control patients.
Comparisons	Intervention and usual care.
Length of Study/ Follow-up	Up to 12 weeks follow-up.
Outcome measures studied	Prescribing, reattendance and adherence data.
Results	56% of the intervention and 53% of the control group were given a prescription, p=0.10. Mean no. of items on prescription: 1.78 (SD=1.37) for intervention and 1.87 (SD=1.34) for control (p=0.32). Median cost of prescription: £5.60 (SD=£2.12, £16.05) vs £5.94 (£2.46, £18.89), p=0.30). 9.9% of the intervention and 10.4% of the control group re-attended (p=0.79). Mean satisfaction was 5.37 for intervention group and 5.40 for control gorup (p=0.64). The overall mean adherence for short-term medication: intervention group 89% and control 85%; for long-term medication at 2 weeks: intervention 93% and control 95%; No significant differences found between the groups. Only 29 out of the 53 doctors completed the telephone interview. 28% considered that the SCAF had affected their prescribing on at least one patient and 31% believed it had an effect on their consultation style, although any effect was considered 'slight' and only related to patients who had actually received a SCAF.
Safety and adverse effects	No safety issues reported. Ethical approval from North & East Devon Research Ethics Committee.
Does the study answer the question?	Yes the SCAF may be an instrument to be used to elicit patients' beliefs and concerns about their medication. The results did not support the hypothesis tested, none of the outcome measures produced any differences between the groups.
Effect due to factor in study?	Most considerations were taken into account in the methodology. However the control group may be confounded by the intervention as the same doctor is used. They used a telephone interview to see if this had occurred and 28% of the doctors said it had. However only 29 out of 53 doctors took the interview and none of them reported anything about the control group.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	Intervention may confound control group-see below

Harrington-Jane NL;

Improving patients' communication with doctors: A systematic review of intervention studies

Ref ID 8780 2004

Study Type Systematic Review **Funding** NHS London Regional

Number of participant	RCT and Quasi-experimental.
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Out of 16 studies, 10 reported a significant increase and five reported a non-significant increase in patient participation. This participation was measured by patient question asking, patient clarification, consultation length, expressed affect, doctor encouraging patient participation. Equal numbers of studies reported significant and non-significant trends in question-asking behaviour. Four out of five studies showed significant increase in patient clarification. Only 2 studies showed significant increases in patient satisfaction due to the interventions. However overall high levels of satisfaction were reported. Overall, half of the interventions resulted in increased patient participation. With more significant results for bids for clarification than question asking. This study aimed to examine the intervention studies which were designed to increase patients' participation in medical consultations and so answers the question of what tools are available to help practitioners elicit patients beliefs about medicines and information needs. Those interventions which encourage patients to gain clarification may increase patient participation and satisfaction. The review noted any weaknesses within the review of the studies. There was a problem in that the use of different systems of reporting - audiotaped, video, made it hard to be comparable. Most of the studies were not blind to group allocation which could cause bias. There was little consistency in the measures used - the most frequent used was question-asking.
Effect due to factor in study?	
Consistency of results with other studies?	

Directly applicable to guideline population?

Internal Validity

Harrington-Jane NL;

Improving patients' communication with doctors: A systematic review of intervention studies

Ref ID 8780 2004

Study Type Systematic Review **Funding** NHS London Regional Office, Research and Development Programme.

Number of participant RCT and Quasi-experimental.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Out of 16 studies, 10 reported a significant increase and five reported a non-significant increase in patient participation. This participation was measured by patient question asking, patient clarification, consultation length, expressed affect, doctor encouraging patient participation.

Equal numbers of studies reported significant and non-significant trends in question-asking behaviour. Four out of five studies showed significant increase in patient clarification.

Only 2 studies showed significant increases in patient satisfaction due to the interventions. However overall high levels of satisfaction were reported.

Overall, half of the interventions resulted in increased patient participation. With more significant results for bids for clarification than question asking.

This study aimed to examine the intervention studies which were designed to increase patients' participation in medical consultations and so answers the question of what tools are available to help practitioners elicit patients beliefs about medicines and information needs. Those interventions which encourage patients to gain clarification may increase patient participation and satisfaction.

	The review noted any weaknesses within the review of the studies. There was a problem in that the use of different systems of reporting - audiotaped, video, made it hard to be comparable. Most of the studies were not blind to group allocation which could cause bias. There was little consistency in the measures used - the most frequent used was question-asking.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Little P;Dorward M;Warner G;Moore M;Stephens K;Senior J;Kendrick T;

Randomised controlled trial of effect of leaflets to empower patients in consultations in primary care

Ref ID 8864 2004

Study Type Randomised Controlled Trial **Funding** Southampton University

Number of participant	N=636 total General leaflet - 317 No general leaflet - 319 Depression leaflet - 318 No depression leaflet - 319
Inclusion/Exclusion Criteria	Aged 16-80 years, consulting at one of five general practices in the UK. Patients were excluded if they were receiving specialist psychiatric treatment, had dementia, were too unwell to consent, were receiving treatment for depression or were only collecting a prescription.
Patient Characteristics	42.5% male; 70% married and 53% in paid work
Recruitment	Patients were consulting at one of five general practices in the UK.
Setting	GP practice in the UK
Interventions/ Test/ Factor being investigated	Participants were randomised to four conditions: receipt of a general leaflet, depression leaflet, both leaflets and no leaflets (control group). The general leaflet which asked patients to list issues they wanted to raise and explained that the doctor wanted them to ask questions, talk and discuss any problems of concern to them. The depression leaflet listed symptoms of depression (without labelling as such) and asking if had them and that the doctor would like to discuss them. The outcomes measured were patient satisfaction (the scores reflected aspects of doctor patient communication), consultation time, prescribing, referral and investigation.
Comparisons	Comparisons are made between receiving a general leaflet, a depression leaflet, both or neither
Length of Study/ Follow-up	Before and after consultation
Outcome measures studied	Self measured satisfaction and enablement scale
Results	The only significant interaction was the increase in satisfaction for those who received the general leaflet, the mean difference was 0.17 (95% CI 0.01 to 0.32, p=0.04). The general leaflet was significantly more effective when consultations were shorter (leaflet 0.64, 95% CI 0.19 to 1.08; time 0.31, 0.0 to 0.06; interaction between both showed that consultations of 5, 8, and 10 mins increased satisfaction by 14%, 10% and 7%). The leaflet overall caused a small non-significant increase in consultation time. This was also shown for subscales of satisfaction – comfort from

	communication 1.02 (0.36 to 1.68), relief of distress 0.74 (0.0 to 1.49), intention to comply with management decisions 0.65 (0.06 to 1.23) and rapport 0.81 (0.16 to 1.45). The general leaflet increased the number of investigations by the doctor (OR 1.43, 1.00 to 2.05), which was unlikely to be due to chance or confounders after controlling.
Safety and adverse effects	None
Does the study answer the question?	The results show an increased number of consultations and general leaflets may help to empower patients in the context of a GP consultation
Effect due to factor in study?	This is a self measured outcome and is subject to bias
Consistency of results with other studies?	Unknown
Directly applicable to guideline population?	Yes
Internal Validity	Self report

Little P;Dorward M;Warner G;Moore M;Stephens K;Senior J;Kendrick T;

Randomised controlled trial of effect of leaflets to empower patients in consultations in primary care

Ref ID 8864 2004

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Patient Characteristics	42.5% male; 70% married and 53% in paid work
Recruitment	Patients were consulting at one of five general practices in the UK.
Setting	GP practice in the UK
Interventions/ Test/ Factor being investigated	Participants were randomised to four conditions: receipt of a general leaflet, depression leaflet, both leaflets and no leaflets (control group). The general leaflet which asked patients to list issues they wanted to raise and explained that the doctor wanted them to ask questions, talk and discuss any problems of concern to them. The depression leaflet listed symptoms of depression (without labelling as such) and asking if had them and that the doctor would like to discuss them. The outcomes measured were patient satisfaction (the scores reflected aspects of doctor patient communication), consultation time, prescribing, referral and investigation.
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Length of Study/ Follow-up	Before and after consultation
Outcome measures studied	Self measured satisfaction and enablement scale

Results	The only significant interaction was the increase in satisfaction for those who received the general leaflet, the mean difference was 0.17 (95% CI 0.01 to 0.32, p=0.04). The general leaflet was significantly more effective when consultations were shorter (leaflet 0.64, 95% CI 0.19 to 1.08; time 0.31, 0.0 to 0.06; interaction between both showed that consultations of 5, 8, and 10 mins increased satisfaction by 14%, 10% and 7%). The leaflet overall caused a small non-significant increase in consultation time. This was also shown for subscales of satisfaction – comfort from communication 1.02 (0.36 to 1.68), relief of distress 0.74 (0.0 to 1.49), intention to comply with management decisions 0.65 (0.06 to 1.23) and rapport 0.81 (0.16 to 1.45). The general leaflet increased the number of investigations by the doctor (OR 1.43, 1.00 to 2.05), which was unlikely to be due to chance or confounders after controlling.
Safety and adverse effects	None
Does the study answer the question?	The results show an increased number of consultations and general leaflets may help to empower patients in the context of a GP consultation
Effect due to factor in study?	This is a self measured outcome and is subject to bias
Consistency of results with other studies?	Unknown
Directly applicable to guideline population?	Yes
Internal Validity	Self report

Longo MF;Cohen DR;Hood K;Edwards A;Robling M;Elwyn G;Russell IT;

Involving patients in primary care consultations: assessing preferences using discrete choice experiments.[see comment]

Ref ID 7453 2006

Study Type Randomised Controlled Trial **Funding**

Number of participant	584/747 questionnaires were returned (78% returned)
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	Does the doctor listen, B=2.63, SE 0.22, p<0.001 How easy is the information to understand? B=2.30, SE 0.17, p<0.01 Who chooses your treatment? B Doctor 0, You 0.10, Ref 0.13, p=0.001.

	Length of consultation B=1.05, SE 0.10, p<0.001 Type of training - risk communication B 0.56,SE 0.32, p=0.08, SDM B -0.609, SE 0.33, p=0.063.
Safety and adverse effects	
Does the study answer the question?	The discrete choice experiment explores the different attributes of a consultation and which are most important to the patient. It showed that all attributes were significant, having a doctor who listens and who gives information which is easy to understand is more important than other attributes. Shows SDM and consultation length are of lesser priority than other consultation attributes. But that SDM may have greater value once the patient has experienced it.
Effect due to factor in study?	Yes
Consistency of results with other studies?	
Directly applicable to guideline population?	Is a discrete choice experiment derived from Edwards (2004) RCT. Therefore it is of interest alongside this study rather than standing alone. It looks at patient preferences rather than the change in time of consultation due to SDM intervention.
Internal Validity	

Middleton JF;McKinley RK;Gillies CL;

Effect of patient completed agenda forms and doctors' education about the agenda on the outcome of consultations: randomised controlled trial

Ref ID 8884 2006

Study Type	Randomised Controlled Trial	**Funding**	Scientific Foundation Board of the Royal College of General Practitioners.

Number of participant	976 in total sample size. 480 were allocated to the no education arm. 496 were allocated to the education arm. 237 were allocated to the agenda form no education arm. 242 were allocated to the no agenda form no education arm. 236 were allocated to the agenda form education arm. 240 were allocated to the no agenda form education arm.
Inclusion/Exclusion Criteria	Inclusion criteria: accepted an appointment in a study consultation with their g.p. Exclusion criteria: none.
Patient Characteristics	No data given.
Recruitment	If requested an appointment at the participating practitioners. Told about the study by the receptionist and given choice to be included or not.
Setting	Leicestershire and Nottinghamshire.
Interventions/ Test/ Factor being investigated	Educational workshop attended by the doctors to increase their awareness of the patient agenda model of the consultation.
Comparisons	Comparison is between intervention and no intervention. Within each arm there is another intervention and no intervention.
Length of Study/ Follow-up	No follow-up.

Outcome measures studied	Number of problems identified. Time required to manage each problem. Duration of consultations. Number of problems raised. Patient satisfaction.
Results	Duration of consultation: No education plus no agenda form: mean 7.1 (95% CI 6.5 to 7.7) Change in means (Reference group-intervention group): No education plus agenda form:0.9 (95% CI 0.3 to 1.5) Education plus no agenda form: 0.7 (95% -0.18 to 1.6) Education plus agenda form: 1.9 (95% CI 1.0 to 2.8) No. of problems identified: (each group as above) Mean 1.7 (95% CI 1.5 to 1.8) 0.2 (95% CI 0.1 to 0.4) 0.3 (95% CI 0.1 to 0.6) 0.5 (95% CI 0.3 to 0.7) Time per problem (seconds) 305.7 (276.8 to 334.5) -10.8 (-39.1 to 17.5) -26.4 (-67 to 14.1) -14.7 (-55.2 to 25.7) General satisfaction 83.6 (81.5 to 85.8) 1.4 (-1.1 to 3.8) -0.3 (-3.2 to 2.7) 0.1 (-2.9 to 8.0) Professional care 83.7 (81.8 to 85.6) 1.0 (-1.0 to 8.0) 1.16 (-1.4 to 3.7) 1.2 (-1.3 to 3.7) Perceived time 80.0 (72.4 to 77.6) 1.7 (-1.4 to 4.7) -0.1 (-3.7 to 3.4) 2.5 (-1.0 to 6.p) Depth of doctor-patient relationship 74.2 (71.7 to 76.7) 3.0 (0.5 to 5.6) 1.7 (-1.7 to 5.0) 2.5 (-0.8 to 5.8) By the way presentations 1.00 0.7 (0.4 to 1.0) 1.2 (0.7 to 2.1) 0.9 (0.5 to 1.5)
Safety and adverse effects	Study approved by Leicestershire local research ethics committee.
Does the study answer the question?	Yes. An agenda form completed by the patient before the consultation or general practioner education about the agenda from or both helped identify more problems in the consultation even though consultations were longer.
Effect due to factor in study?	The methodology is generally sound and the power of the study was 5% significance level and 80% power used.
Consistency of results with other studies?	Varied.

Directly applicable to guideline population?	Population - includes anyone attending g.p. therefore any patient will be included, not specific to medication-taking population, however will include a lot of patients on medication Intervention directly comparable to that of interest for guideline.
Internal Validity	Blinding; groups differ?

Montgomery AA;Fahey T;Peters TJ;

A factorial randomised controlled trial of decision analysis and an information video plus leaflet for newly diagnosed hypertensive patients

Ref ID 257 2003

Study Type Randomised Controlled Trial **Funding** Unknown

Number of participant	Patients were allocated to decision analysis only (n=52)video/leaflet only (n=55); video/leaflet and decision analysis (n=51) or usual care (n=59)
Inclusion/Exclusion Criteria	Patients aged 32 to 80 years (mean age 59 years) newly diagnosed with hypertension.
Patient Characteristics	Mean age 58.5 years; 48% female
Recruitment	Patients were recruited in the Avon Health Authority, UK
Setting	South west England
Interventions/ Test/ Factor being investigated	The value of tools designed to aid decision making in patients with newly diagnosed hypertension is assessed in this study. Two tools are considered: a decision analysis and video/leaflet
Comparisons	Comparisons are made between treatments, treatment combination and no treatment
Length of Study/ Follow-up	3 months
Outcome measures studied	Decisional Conflict Scale and subscales , state anxiety , knowledge about hypertension and actual treatment decision
Results	Both interventions successfully reduced patients' total decisional conflict at follow-up. Decision analysis decreased the decisional conflict more than the video/leaflet. Total decisional conflict mean for decision analysis was 27.6 (SD=12.1), no decision analysis 38.9(18.3) adjusted difference 95%CI -9.4 (-13.0 to -5.8) p<0.001; video/leaflet 30.3 (13.4) and no video/leaflet was 36.8(18.8), 95% CI -4.2(-7.8 to -0.6), p=0.021. The Decisional conflict subscales showed a clear reduction in three of the five subscales - uninformed 23.7 (11.8) compared to no decision analysis 40.7 (23.1) adjusted difference 95% CI -15.7 (-20.2 to -11.2), unclear values 28.4 (14.7) vs. 43.8 (24.3) adjusted difference -13.1 (-18.0 to -8.1) and unsupported 24.4 (13.4 vs. 34.8 (18.3) adjusted difference -8.7 (-12.8 to -4.7) and some evidence for reduction in uncertainty and no evidence for decision quality. The video/leaflet intervention showed no evidence in these last two subscales and there was only clear evidence on the uninformed subscale. For the intention to start treatment when followed up the adjusted risk ration (95% CI): Yes versus unsure 1.19 (0.59 to 2.40) for decision analysis and 1.80 (0.89 to 3.63) for the video/leaflet. No versus unsure 3.15 (0.91 to 10.98) and 0.52 (0.15 to 1.77) respectively. The overall p values were 0.09 and 0.17 respectively. Actual prescription of medication was not different for either intervention or controls. There was a suggestion (p=0.055) that anxiety may be reduced by decision analysis although the evidence there was weak and no evidence of this for the video/leaflet intervention. Both interventions significantly increased knowledge of hypertension. Those who received both interventions had the lowest decisional conflict (27.1 compared with 28.2 and 33.3 and 44.2 for decision analysis only, video/leaflet and control). They had a high knowledge score – the same as video/leaflet. Within the regression models there was a significant (antagonistic) interaction between decision analysis and video/leaflet, so the effect of each was reduced by the presence of the other (interaction coefficient 12.5, 95% CI 5.4 to 19.5, p=0.001 for decisional conflict and -9.1, 95% CI-16.3 to -1.9, p=0.013 for knowledge.

	This study was followed up in 2005 by Emmett et al, who found that there was no evidence of any difference in blood pressure, cardiovascular disease risk for either intervention or between them. There were also no effects on medication prescribing, self-reported adherence, consulting behaviour or management changes.
Safety and adverse effects	None
Does the study answer the question?	Both interventions were successful in reducing patients' total decisional conflict with decision analysis resulting in a greater decrease than video/leaflet however the decision analysis took 45 minutes to an hour to complete.
Effect due to factor in study?	Yes
Consistency of results with other studies?	Yes
Directly applicable to guideline population?	Yes
Internal Validity	Multiple sites

Oakley S;Walley T;

A pilot study assessing the effectiveness of a decision aid on patient adherence with oral bisphosphonate medication

Ref ID 3611 2006

Study Type Randomised Controlled Trial **Funding** Eli Lilly and Merck Sharp & Dohme.

Number of participant	33 women - 16 in intervention group and 17 in control group
Inclusion/Exclusion Criteria	Post menopausal women prescribed oral bisphosphonates with a diagnosis of osteoporosis or aged over 65 and had radiological evidence of fragility fracture. Patients prescribed oral bisphosphonates because of long term steroid use were excluded.
Patient Characteristics	Average age 77 years with 'no differences between groups.'
Recruitment	The women were patients in one practice in Dorset.
Setting	GP practice in Dorset
Interventions/ Test/ Factor being investigated	This study was done to assess the acceptability of a decision aid and its potential impact on patient adherence with oral bisphosphonate. The aid comprised of an information booklet, an audiocassette and worksheet to be used at home by the patient before an appointment with a doctor.
Comparisons	The intervention group was compared to a control group receiving normal care.
Length of Study/ Follow-up	Patients were followed up for 4 months.
Outcome measures studied	Adherence was measured by monitoring repeat prescriptions. Patients views were assessed by open questions. Patient satisfaction was assessed using the Satisfaction with Information about Medicines Scale (SIMS) & Beliefs about Medicines Questionnaire.
Results	There were no statistically significant changes in adherence & satisfaction over the course of the study (p=0.47) and changes in adherence did not differ between the 2 groups (p=0.80). Patients using the decision aide valued the opportunity to discuss their treatment with the GP in a dedicated consultation.
Safety and adverse effects	None

Does the study answer the question?	Although the decision aid was appreciated for the ability to discuss their medication with the GP it did not appear to affect patient adherence to medication.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	Possible differences between groups

Rao JK;

Communication interventions make a difference in conversations between physicians and patients: A systematic review of the evidence

Ref ID 8777 2007

Study Type	Systematic Review	**Funding**	National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, and ORC Macro Inc.

Number of participant	RCT
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	2193+ citations found, 344 articles pulled for detailed review, 69 of which described trials of communication interventions that targeted physicians or patients and reported an objective measure of verbal communicative behaviour. Of these 30 were nonrandomised controlled trials and excluded. 36 RCTs eligible for review and abstraction. 18 were interventions for practicing physicians or residents, 15 interventions on patients and 3 intervened on both. They rated the interventions low to high intensity. Most of the studies were

moderately or highly intense.

The 21 studies which included physicians most found that there was significant improvement in communication behaviours of physicians/residents. Especially high intensity interventions leading to more open-ended questions (4 studies) and fewer biomedically focused questions (2 studies) than compared to the comparison physicians. Compared to controls studies found that intervention physicians were more likely to elicit patients' previsit concerns (3 studies) and show an overall patient-centred communication style (6 studies).

Intervention physicians gave more information on specific issues (6 studies), received higher ratings for their skills (3 studies) than comparison physicians. Some findings showed no effect on communication style (2 studies).

18 studies of interventions focusing on patients, were mixed new, continuing or both types of patients. Information was the most common type of intervention, often through written instructions. Some studies included models of desirable communication behaviours such as examples of questions to ask physicians (7 studies).

Of the 18 studies 3 assessed the effects on patients information providing behaviours - results were mixed. 17 studies assessed patient involvement using different measures - the findings were mixed even the moderately intense interventions. The 7 studies that assessed the degree that patients spoke during the visit 5 of these showed significant changes in their communication patterns. All of these included skills practice as part of the intervention, they demonstrated a greater ability to direct, or initiate conversation and obtained more information than controls. 2 studies that were of low-intensity did not have significant changes in patient involvement.

Authors Conclusions: They found that generally the interventions enhanced communication behaviours among physicians. Similar modest effects were found for the patient interventions. Intervention intensity was important in physicians' behaviours but was less pronounced with patients. Few studies assessed the effect of the interventions on information verifying behaviours (e.g checking understanding, summarising information). Many of the interventions cannot be implemented into everyday practice and so more practical interventions need to be designed.

Strengths: Low in bias as only RCTs included and quality assessed. Noted the intensity of the intervention studies. Methodology annotated well. Weaknesses: different populations and settings make comparability difficult.

Relationship to question: there are interventions available, for physicians which can improve their communication to the individuals and elicit more patient-centred dialogue. There are also interventions which can improve patients communication when visiting their physician thus gaining more information. These can both lead to more elicitation of patients beliefs about medicines and information needs.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Ross SE;Moore LA;Earnest MA;Wittevrongel L;Lin CT;

Providing a web-based online medical record with electronic communication capabilities to patients with congestive heart failure: randomized trial.[see comment]

Ref ID 1819 2004

Study Type Randomised Controlled Trial **Funding** Commonwealth Fund.

Number of participant	Total sample: 107. intervention group: 54, control group: 53.
Inclusion/Exclusion Criteria	Inclusion: Patients were eligible for the study if they were followed in the practice, spoke English, and were 18 years of age or older. They needed to have used a Web browser before, although they did not need to have access to the Internet at home. Exclusion: Physicians, nurses, physician assistants, and nurse practitioners.
Patient Characteristics	Mean age (years): Intervention group: 57, Control group: 55. Gender: Male: intervention group: 80%, control group: 74%. White, non-Hispanic: Intervention group: 92%, control group: 88%. No significant differences reported between treatment and control groups. External validity: participants enrolled in study had significant baseline differences in baseline characteristics from those who refused to enrol in the study but who were offered the opportunity to do so.
Recruitment	Patients were approached in waiting room on hospital and asked if they wished to participate.
Setting	
Interventions/ Test/ Factor being investigated	The SPPARO (System Providing Access to Records Online) software consisted of a web-based electronic medical record, an educational guide, and a messaging system enabling electronic communication between the patient and staff. The medical record consists of clinical notes, laboratory reports, and test results (including reports of radiographs and echocardiograms). The educational guide is an online version of the printed materials that all patients in the heart failure practice receive at their first visit. The messaging system allowed patients to exchange secure messages with the nursing staff in the practice. Staff regularly contacted participants to encourage them to use the system.
Comparisons	System Providing Access to Records Online (SPPARO) intervention v standard care. Intervention v control.
Length of Study/ Follow-up	1 year.
Outcome measures studied	Surveys assessing doctor-patient communication, adherence, and health status were conducted at baseline, 6 months, and 1 year (1 year results given below). Adherence assessed by two mailed self-report questionnaires.
Results	Adherence: General adherence to medical advice showed significant improvement in the intervention group compared with the control group (intervention group: 85, Control group: 78. Difference (CI) +6.4 (1.8, 10.9), p = 0.01). Adherence to medications showed a similar trend but did not reach statistical significance (intervention group: 3.6, Control group: 3.4, Difference (CI) +0.2 (-0.1, 0.6), p = 0.15). Other outcomes: At 12 months, the intervention group was not found to be superior in self-efficacy or for other measures of health status. Patient satisfaction with doctor patient-communication demonstrated a trend towards improvement in two areas: how well patients felt their problems were understood, and how well doctors explained information. While significant results were found for these two items individually, the findings did not reach statistical significance when adjusted for multiple comparisons. There was no significant improvement in the other patient satisfaction domains. The intervention group had more emergency department visits (20 vs. 8, p = 0.03), but these visits were not temporally related to use of the online medical record. There were no differences between the two groups in terms of the number of deaths, number of patients hospitalized, number of hospitalizations, number of patients taken to emergency rooms, number of visits to emergency rooms, number of patients in heart failure practice or Number of visits to heart failure practice.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention was to improve patient education, engagement and empowerment. An internet-accessible medial record can offer modest benefits, with improvements in adherence, patient satisfaction with doctor-patient communication.
Effect due to factor in study?	Yes.

Consistency of results with other studies?	
Directly applicable to guideline population?	Sort of relevant outcomes relating to SDM (self-efficacy, adherence and satisfaction).

Internal Validity

Shields CG;Epstein RM;Fiscella K;Franks P;McCann R;McCormick K;Mallinger JB;

Influence of accompanied encounters on patient-centeredness with older patients

Ref ID 8827 2005

Study Type Randomised Controlled Trial **Funding** National Institute on Aging

Number of participant	30 - 13 accompanied and 17 unaccompanied
Inclusion/Exclusion Criteria	Patients were at least 65 years and not cognitively impaired and had a companion who could accompany them
Patient Characteristics	There were no significant differences in demographic data between groups. Age in two groups 66.1-68.5; years of education 13.6 - 14.1; general health on SF-36 61.3 - 62.5.
Recruitment	Patients were recruited through a large residency-based family medicine practice and a small hospital based geriatric practice.
Setting	Rochester, New York
Interventions/ Test/ Factor being investigated	The influence of accompanied visits on physician patient communication
Comparisons	Accompanied versus unaccompanied
Length of Study/ Follow-up	One GP visit only
Outcome measures studied	Communication measures including numbers of words used and MPCC which measures 3 aspects of PCC (patient centred communication)
Results	Companions were not assigned a specific role during the session and physicians were not asked to conduct the sessions in any particular way. There were no statistically significant differences between accompanied and unaccompanied visits on the number of issues that patients raised, however patients did raise more issues in unaccompanied visits. No statistically significant differences were observed for levels of patient-centeredness, or satisfaction, even if patients who were accompanied reported being slightly more satisfied. Physicians were more likely to promote collaboration in treatment decision making with patients than with companions ($p<0.0001$). Physicians were also more responsive to issues regarding exploring the disease and illness when the issues were raised by the patient compared with the companion ($p<0.03$).
Safety and adverse effects	None
Does the study answer the question?	Being accompanied does not appear to make a difference in physician patient interaction in this small pilot study.
Effect due to factor in study?	No - this study is a small pilot and needs to be repeated with a larger sample.
Consistency of results with other studies?	No

Directly applicable to guideline population?	Yes
Internal Validity	Possible Hawthorne effect

Trevena LJ;Davey HM;Barratt A;Butow P;Caldwell P;

A systematic review on communicating with patients about evidence

Ref ID 2400 2006

Study Type	Systematic Review	**Funding**	Not mentioned.

Number of participant	RCTs and Systematic Reviews.
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	The review concluded that communicating with patients about evidence does increase their understanding regardless of the tools used. The authors also found that there was a greater effect if information was structured (either written, verbal or video) or interactive (computer, touch screen, question prompts) and particularly if the information was tailored to the individual. Probabilitistic information was found to be best represented as even rates in relevant groups of people, rather than words, probabilities or summarized as effect measures such as relative risk reduction. Written information was reported to be more effective if illustrations and graphs were used. This helps answer the question by showing which types of information, through which medium and which format information is best provided as shown by a range of systematic reviews and RCTs.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

van-Dam HA;

Provider-patient interaction in diabetes care: Effects on patient self-care and outcomes A systematic review

Ref ID 5988 2003

Study Type Systematic Review **Funding** Unknown

Number of participant RCT

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? Eight studies were included after a rigorous methodological quality assessment, and these showed different interventions on different levels of the provider-patient interaction in diabetes care. Four studies focused on provided consulting behaviour modifications (studies 1-4), and four studies focused directly on patient behaviour change (studies 5-8).
All studies were conducted in practical diabetes care, three in hospital outpatient clinics and five in general practices.
The main findings suggest that the most effective interventions are those with a direct approach to support patient participation (i.e. by assistant-guided patient preparation for visits to doctors, empowering group education, group consultations, or automated telephone management) in diabetes care and self-care behaviour, while interventions which focus on change of provider behaviour were less effective. Thus, the authors advocate a shift from the traditional medical model to a more patient centred, patient participation and empowerment paradigm of delivery of diabetes care.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Wetzels R;Wensing M;van WC;Grol R;

A consultation leaflet to improve an older patient's involvement in general practice care: A randomized trial

Ref ID 4945 2005

Study Type	Randomised Controlled Trial	**Funding**	EU (Quality of life and management of living resources programme 1998-2002); The ageing population and disabilities; Netherlands Organisation for Health Research and Development.

Number of participant	315 pre-intervention and 263 post-intervention.
Inclusion/Exclusion Criteria	G.P patients aged 70 years or older who had consulted them recently during the period June to November 2002. Exclusion criteria: visually impaired or if GP thought not suitable for participating.
Patient Characteristics	Mean age 75 years. Mainly male.
Recruitment	Letter sent by g.p.
Setting	G.P practice. Netherlands.
Interventions/ Test/ Factor being investigated	The intervention practices received a consultation leaflet by mail. This leaflet included a short motivating text on patient involvement and a mixture of open and pre-structured questions to help patients prepare for the next consultation and prioritize which problems they wanted to discuss with their g.p. The questions were chosen as they would help to explore patient's ideas, fears and expectations and encourage them to address important issues. GPs received a 30 minute practice visit to motivate them to involve patients and instruct them on use of the consultation leaflet.
Comparisons	Leaflet by mail compared to usual care.
Length of Study/ Follow-up	Questionnaire sent after consultation.
Outcome measures studied	Perceived involvement in primary care was the primary outcome after use of the leaflet. Secondary outcomes were consultation length, demographic characteristics, and whether discussed one of eight underreported health problems.
Results	Subjects were satisfied with their involvements and the GPs behaviour during the consultation, however no difference in effect as a result of the leaflet on involvement, enablement or satisfaction were found between the intervention and control groups. Estimated effect size difference of PEI -0.226 (-0.475 to 0.022, p=0.075); COMRADE 0.091 (-0.129 to 0.311, p=0.42); EUROPEP -0.171 (-0.472 to 0.131), p=0.267) and consultation length 0.411 (-2.043 to 2.866, p=0.74) when adjusted for clustering and leaflet used correctly. Intervention group leaflet users reported more psychological symptoms to their GP compared with non-users of the leaflet (p=0.034).
Safety and adverse effects	Ethical committee of the University Medical Centre Nijmegen assessed the study and gave approval.
Does the study answer the question?	Overall the main findings do not support the use of the implementation programme on improving involvement, enablement or satisfaction of older patients in their care. This relates to the question as it is tools to elicit beliefs about patient beliefs.
Effect due to factor in study?	Power of study – the needed 30 patients per gp was not always possible to gather. To detect a medium effect (effect size 0.50 between groups required 24 GPs and 10 patients per GP (power=0.80), alpha =0.05. As pre-intervention response rates were low post-intervention GPs were asked to send questionnaires to the last 30 patients who visited them.
Consistency of results with other studies?	

Directly applicable to guideline population?	The population of gp patients is the population of interest, some of the patients will not be. The intervention is of interest to this guideline.
Internal Validity	Sig more females in the intervention group.

Weymiller AJ;Montori VM;Jones LA;Gafni A;Guyatt GH;Bryant SC;Christianson TJ;Mullan RJ;Smith SA;

Helping patients with type 2 diabetes mellitus make treatment decisions: statin choice randomized trial

Ref ID 707 2007

Study Type Randomised Controlled Trial **Funding** Mayo Clinic and American Diabetes Association

Number of participant	52 patients received the Decision Aid and 46 received usual care
Inclusion/Exclusion Criteria	Eligible patients had type 2 diabetes, no contraindications to statins, no major visual, hearing or cognitive impairment and were willing to provide informed consent.
Patient Characteristics	Mean age in treatment group was 64 (SD 12) and in the control group was 66 (SD 8). There were only 16 women in the treatment group and 26 women in the control group. Six people in the treatment group had a CV risk less than 15%; there were 15 control patients in this category. 15-30% risk was assigned to 16 of the treatment group and 7 of the control group. Greater than 30% group was found in 30 treatment patients and 24 control patients.
Recruitment	Patients were referred to the metabolic clinic for a one off consultation Faculty and fellows at the clinic were randomized.
Setting	Mayo Clinic Rochester Minn.
Interventions/ Test/ Factor being investigated	Use of a Decision Aid about statin drugs versus control pamphlet and its effect on treatment decision making
Comparisons	Comparisons are made between groups in knowledge level, decisional conflict, acceptability and adherence
Length of Study/ Follow-up	3 months
Outcome measures studied	Self reported adherence and a likert scale for acceptability. Knowledge testing was not described
Results	Amount of information was significantly higher in treatment group (OR3.4 [1.7-6.7]). Helpfulness of the information and overall acceptability were also significantly higher in the treatment group (or 2.3 [1.4-3.8] respectively and 2.8 [1.2-6.9] respectively). The treatment group had less decisional conflict (difference, -10.6; 95% CI -15.4--5.9 on a 100 point scale) than the control group. At three months there was no significant difference in adherence to patient choice (analysis adjusted by sex, cardiovascular risk, and number of medications; OR1.9; 95% CI 0.4-9.8).
Safety and adverse effects	None
Does the study answer the question?	A decision aid may reduce decisional conflict but is does not appear to affect long term adherence. Further research is recommended.
Effect due to factor in study?	Small trial but good consistency with other studies
Consistency of results with other studies?	Yes
Directly applicable to guideline population?	Yes

Internal Validity The outcome measurement is by self report

Wills CE;Holmes RM;

Patient comprehension of information for shared treatment decision making: State of the art and future directions

Ref ID 232 2003

Study Type Systematic Review **Funding** Not mentioned.

Number of participant Not reported. Assume that it is other types of study.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? They found two studies where participants preferred presentation of medication in terms of relative risk rather than absolute risk format. They found that people simplify relative risk information into a simplified format of small or large risks and there is a tendency to seriously under or overestimate their personal risks for health outcomes. There is a need to tailor the format of risk communication to the individual's level of numeracy. In routine clinical encounters information should be presented balanced, in both positive and negative frames. Graphics can improve the understanding of numerical probability information. However some people may dislike some types of displays or misunderstand them. Consistent finding of individual differences in preferences for probability information in words, numbers of both formats implies a need for routine individualized assessments of patient preferences for format.

The review concluded that the impact of information presentation in different formats on patients' understanding and preferences was variable. Most of the studies were not clinical patients and so may not be able to generalise to a clinical setting. The goal is to give balanced, complete and parsimonious information, and take into account individual needs and preferences.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Hamann J;Cohen R;Leucht S;Busch R;Kissling W;

Shared decision making and long-term outcome in schizophrenia treatment

Ref ID 3748 2007

Study Type	Randomised Controlled Trial	**Funding**	By the German Ministry of Health and Social Security within a funding project.

Number of participant	107 patients were included in the original study and agreed to be followed up.
Inclusion/Exclusion Criteria	Inclusion: All men and women aged 18-65 years who had an ICD-10 diagnosis of schizophrenia or schizophreniform disorder. Exclusion: Severe mental retardation, lack of fluency in German, refusal to give written informed consent.
Patient Characteristics	Intervention vs control group: Mean age: 38 years old (SD=11.4) Gender: 48% female Mean duration of illness: 9.2 years (SD=8.5) Mean number of hospitalisations due to schizophrenia: 5.6 (SD=5.7)
Recruitment	Follow-up of patients from original study (Hamann, 2006) who agreed to be included. Originally recruited in the wards.
Setting	12 acute psychiatric wards of 2 German hospitals.
Interventions/ Test/ Factor being investigated	Intervention was an experimental SDM intervention. The intervention was to inform of treatment options and prepare them for a 'planning talk' with their physicians. A printed decision aid was given - a 16 page booklet covering the pros and cons of oral vs depot formulation, first vs second generation antipsychotics, psycho education, and type of socio-therapeutic intervention. Nurses were trained in assisting patients to work through the booklet. Within the booklet patients were to write down their experiences with previous antipsychotic medication and to indicate their preferences regarding the different options on each topic. The planning talk with the psychiatrist regarded further treatment according to their preferences indicated by the patient.
Comparisons	Intervention versus treatment as usual, with no further instructions for physicians and nursing staff.
Length of Study/ Follow-up	Long-term follow up of patients for 18 months after discharge.
Outcome measures studied	Outcomes (patients view): Perceived involvement in medical decisions; knowledge about disease and treatment at time of discharge; satisfaction with treatment. Outcomes (psychiatrist's view): Psychopathology scores: time spent in individual contacts;
Results	Univariate analysis found no significant differences between groups. When multivariate analysis was conducted to control for the re-hospitalisation rate it showed that there was a positive trend for the decision aid and planned talk in reducing rehospitalisation. Higher participation preferences (OR= 1.06, p=0.03) and better knowledge (OR =1.23, p=0.03) rates significantly predicted rehospitalisation. No other effects were shown. Patients showing good compliance at 6 months were 41% in the intervention and 55% in the control, p>0.05. Patients showing good compliance at 18 months was 60% vs 58%, p>0.05.
Safety and adverse effects	None mentioned but was approved by an ethics committee of the Technische Universitat, Munchen.

Does the study answer the question?	Yes the intervention is a decision aid booklet. SDM with acutely ill in-patients with schizophrenia is possible and feasible and improves important treatment patterns - increases patients perceived involvement, knowledge about disease and attitudes to treatment. The structured intervention increased participation in psycho education and socio-therapeutic interventions.
Effect due to factor in study?	There were differences in the study groups - the patients in the intervention group were hospitalised a week longer than patients in the control group (statistically significant) and the knowledge of treatment was higher in the intervention group (statistically significant). Power calculation was not used. Therefore the overall effect may not be due to the intervention.
Consistency of results with other studies?	Consultation time with the psychiatrist was increased in the intervention group 4min/week, however this was not statistically significant p>0.05.This is similar to some other studies as most do not have statistical significance and time is longer/shorter.
Directly applicable to guideline population?	This is comparable as it is a decision aid intervention to increase SDM, yet unlike the other studies is with acute psychiatric patients, which is included in our remit. Therefore it is of relevance to the guideline.
Internal Validity	Allocation concealment;

Hamann J;Langer B;Winkler V;Busch R;Cohen R;Leucht S;Kissling W;

Shared decision making for in-patients with schizophrenia

Ref ID 3119 2006

Study Type	Randomised Controlled Trial	**Funding**	By the German Ministry of Health and Social Security thorough the funding of a project.

Number of participant	107 patients. 49 in the intervention group and 58 in the control group.
Inclusion/Exclusion Criteria	Inclusion: All men and women aged 18-65 years who had an ICD-10 diagnosis of schizophrenia or schizophreniform disorder. Exclusion: Severe mental retardation, lack of fluency in German, refusal to give written informed consent.
Patient Characteristics	Intervention vs control group: Age 35.5 (SD 11.9) vs 29.6 (SD 10.8), p=0.06 Gender 20 (41%) vs 31 (53%), p=0.24 Education 10 or more years 21 (43%) vs 22 (38%), p=0.43 Duration of illness 8.8 (SD 8.6) vs 9.5 (SD 8.5), p=0.70 Number of hospitalisations 5.4 (SD 5.0) vs 5.8 (SD 6.6), p=0.78 PANSS total score 82.8 (SD 22.7)p=0.07 Knowledge 12.5 (SD 4.8) vs 10.4 (SD 4.9), p=0.04 No. of days from admission to inclusion in the study 19.5 (SD 19.8) vs 11.2 (SD 12.1), p=0.01
Recruitment	Consecutively recruited in the wards.
Setting	12 acute psychiatric wards of 2 German hospitals.
Interventions/ Test/ Factor being investigated	Intervention was an experimental SDM intervention. The intervention was to inform of treatment options and prepare them for a 'planning talk' with their physicians. A printed decision aid was given - a 16 page booklet covering the pros and cons of oral vs depot formulation, first vs second generation antipsychotics, psycho education, and type of socio-therapeutic intervention. Nurses were trained in assisting patients to work through the booklet. Within the booklet patients were to write down their experiences with previous antipsychotic medication and to indicate their preferences regarding the different options on each topic. The planning talk with the psychiatrist regarded further treatment according to their preferences indicated by the patient.

Comparisons	Intervention versus treatment as usual, with no further instructions for physicians and nursing staff.
Length of Study/ Follow-up	Long-term follow up of patients for 18 months after discharge.
Outcome measures studied	Outcomes (patients view): Perceived involvement in medical decisions; knowledge about disease and treatment at time of discharge; satisfaction with treatment. Outcomes (psychiatrist's view): Psychopathology scores: time spent in individual contacts;
Results	Outcome the patients view: - Perceived involvement COMRADE* 79.5 (SD 18.6) after the intervention vs 69.7 (SD 20) at study entry, f=4.94, p=0.03. - COMRADE before discharge 76.8 (SD 20.9) vs 73.5 (SD 19.3), f=1.88, p=0.18. - Knowledge before discharge 15.0 (SD 4.4) vs 10.9 (SD 5.4), f=6.65, p=0.01. - Drug Attitude Inventory (DAI) before discharge 6.9 (SD 2.8) vs 5.5 (SD 2.9), f=3.60, p=0.06. - ZUF8 (patients satisfaction) 16.3 (SD 3.7) vs 16.4 (SD 3.2), f=0.66, p=0.42. Outcome the psychiatrists view: - Psychopathology (PANSSS score) means 58.0 vs 59.3, p>0.05. - Co-operation means 60.6 vs 60.9, p>0.05. - Time spent in individual contacts: means 64 vs 60 min/weeks, p>0.05. - Estimated (by Doctor) compliance: means 1.7 vs 2.0, p>0.05. - Psychiatrist in the intervention group were more satisfied with what had been achieved during hospitalisation means in 5 point scale overall satisfaction 3.8 vs 3.5, p=0.02. * COMRADE: Combined Outcome Measure for Risk Communication and Treatment Decision Making Effectiveness.
Safety and adverse effects	None mentioned but was approved by an ethics committee of the Technische Universitat, Munchen.
Does the study answer the question?	Yes it shows values for the amount of time patients spent with the psychiatrists - for those in the intervention and those not. SDM with acutely ill in-patients with schizophrenia is possible and feasible and improves important treatment patterns - increases patients perceived involvement, knowledge about disease and attitudes to treatment. The structured intervention increased participation in psycho education and socio-therapeutic interventions.
Effect due to factor in study?	There were differences in the study groups - the patients in the intervention group were hospitalised a week longer than patients in the control group (statistically significant) and the knowledge of treatment was higher in the intervention group (statistically significant). Power calculation was not used. Therefore the overall effect may not be due to the intervention.
Consistency of results with other studies?	Consultation time with the psychiatrist was increased in the intervention group 4min/week, however this was not statistically significant p>0.05.This is similar to some other studies as most do not have statistical significance and time is longer/shorter.
Directly applicable to guideline population?	This is comparable as it is an intervention to increase SDM, yet unlike the other studies is with acute psychiatric patients, which is included in our remit. Therefore it is of relevance to the guideline.
Internal Validity	Allocation concealment;

Loh A;Simon D;Wills CE;Kriston L;Niebling W;Hõrter M;

The effects of a shared decision-making intervention in primary care of depression: a cluster-randomized controlled trial

Ref ID 3740 2007

Study Type Randomised Controlled Trial **Funding** German Ministry of Health

Number of participant	Primary care physicians were the unit of randomisation. The sampling frame (n=148) were sent a letter, 30 accepted the invitation to take part, 20 were randomly assigned to the intervention group and 10 to the control group, after drop out 15 and 8 were left respectively. The physicians had to recruit newly diagnosed depressive patients. The intervention physicians enrolled 263 patients and the control group 142.
Inclusion/Exclusion Criteria	Age 18 and above, with new diagnosis of depression and functional language and literacy ability
Patient Characteristics	Mean age of patients ranged from 40.8-50.4; the proportion of female patients ranged from 65.3% to 77.8%.
Recruitment	Patients were recruited through their primary care physicians.
Setting	Primary care in Germany
Interventions/ Test/ Factor being investigated	The effects of a shared decision-making intervention in primary care of depression were compared to usual care on adherence, satisfaction and clinical outcomes.
Comparisons	The intervention was a multifaceted program including physician training, a decision board for use during the consultation and afterwards by the patient, and printed patient interpenetration vs. no intervention
Length of Study/ Follow-up	16 weeks total
Outcome measures studied	Patient participation, treatment adherence, patient satisfaction, consultation time and clinical outcomes.
Results	There was no difference for the control group in patient participation before and after, whereas the intervention group had significantly higher patient participation from pre to post intervention for the doctor facilitation scale (p=0.001) and there was an increase in the patient participation scale (p=0.010). There were no significant differences in treatment adherence. Patient satisfaction was significantly higher in the intervention 29.8 (2.7) than the control group 27.0 (3.6), p=0.14. There were no values taken for satisfaction before the intervention. There was no difference between groups for length of consultation. Neither group had a statistically significant reduction in depression severity from baseline to post-intervention.
Safety and adverse effects	No
Does the study answer the question?	Shared decision making appears to increase satisfaction but not adherence.
Effect due to factor in study?	No - validity of outcome measures should be described
Consistency of results with other studies?	Unknown
Directly applicable to guideline population?	Yes
Internal Validity	Self reported outcomes

Loh A;Simon D;Wills CE;Kriston L;Niebling W;Hõrter M;

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Length of Study/ Follow-up	16 weeks total
Outcome measures studied	Patient participation, treatment adherence, patient satisfaction, consultation time and clinical outcomes.
Results	There was no difference for the control group in patient participation before and after, whereas the intervention group had significantly higher patient participation from pre to post intervention for the doctor facilitation scale (p=0.001) and there was an increase in the patient participation scale (p=0.010). There were no significant differences in treatment adherence. Patient satisfaction was significantly higher in the intervention 29.8 (2.7) than the control group 27.0 (3.6), p=0.14. There were no values taken for satisfaction before the intervention. There was no difference between groups for length of consultation 29.2 (SD 10.7) vs 26.7 (SD 12.5), p=0.14. Neither group had a statistically significant reduction in depression severity from baseline to post-intervention.
Safety and adverse effects	No
Does the study answer the question?	Shared decision making appears to increase satisfaction but not adherence.
Effect due to factor in study?	No - validity of outcome measures should be described
Consistency of results with other studies?	Unknown
Directly applicable to guideline population?	Yes
Internal Validity	Self reported outcomes

McLean M;Armstrong D;

Eliciting patients' concerns: a randomised controlled trial of different approaches by the doctor

Ref ID 723 2004

Study Type	Randomised Controlled Trial	**Funding**	Study derived from an MSc at Guys Kings and St Thomas' School of Medicine. No funding

mentioned.

Number of participant	56 in the intervention group and 54 in the control group.
Inclusion/Exclusion Criteria	Inclusion: Self-limiting illness. Exclusion: If were to be referred to hospital or given a prescription other than for symptom control or if spontaneously expressed a clear concern about their illness.
Patient Characteristics	No details mentioned apart from disease status: Musculoskeletal 23%, cough 20%, upper respiratory tract infection 18%, Virus 17%, Ear infection 6%, other 16%.
Recruitment	They were recruited by asking them when they presented in the surgery if they wished to be part of a study.
Setting	Four training general practices in SE of UK
Interventions/ Test/ Factor being investigated	The intervention is a written prompt to elicit patients concerns: -May I ask if you have any concerns about this…(illness/pain) you have come about today? Followed by - Anything in particular about the…? And, if still unforthcoming - What is it about the… that concerns you?
Comparisons	Comparison between the above written prompt and no written prompt (usual care). - This could be difficult to separate as both spoken by same doctor.
Length of Study/ Follow-up	Questionnaire given after consultation while still in the surgery. No further follow-up.
Outcome measures studied	'Professional care' score General satisfaction Depth of relationship Perceived time Enablement Anxiety
Results	Length of consultations: 11 minutes vs 10 minutes - not statistically significant When entered into a multiple regression to assess their ability to predict satisfaction with professional care - consultation length coefficient=0.21, $p<0.05$) contributed less than the intervention status (0.29, $p<0.005$) but was still a major predictive factor. CSQ scores: Professional care: intervention group 80.9 (SD 16.1) control group 88.2 (SD 11.8), Mean diff 7.2 (95% CI 2.0 to 12.6). General satisfaction: 81.2 (19.9) vs 80.3 (19.5), -0.9 (-8.4 to 6.5) Depth of relationship: 61.3 (21.4) vs 66.1 (19.1), 4.8 (-2.8 to 12.5) Perceived time 71.9 (27.1) vs 72.8 (26.5), 0.9 (-9.2 to 11.1) Enablement 37.0 (24.7) vs 39.0 (30.9), 2.0 (-8.6 to 12.6) Anxiety 35.4 (9.9) vs 32.9 (10.8), -2.5 (-6.4 to 1.5)
Safety and adverse effects	None mentioned. Ethical approval obtained from 3 relevant local research ethics committees.
Does the study answer the question?	It helps in answering the question as it is an intervention aimed to increase patient participation and it looks at consultation length. They found a small but significant increase in the professional care score of the consultation satisfaction questionnaire but no other benefits detected. Patients with acute self-limiting illness are more satisfied when GPs are prompted to ask them about their concerns. There was only a 10% increase in consultation time (which itself seemed responsible for some of the benefit). The benefit is meagre, a larger study might change these measures.
Effect due to factor in study?	The power was flawed, as mentioned in the limitations of the study (from erroneous published data) so the study did not have the power to detect smaller differences, and therefore a larger sample size would be needed. There could have been bias from the randomisation and the allocation concealment and the two groups may not have got a different treatment due to the methodology.

Consistency of results with other studies?	The result that consultation length was increased but not significant is consistent with the majority of other studies in the field.
Directly applicable to guideline population?	This is directly comparable to the population and one of the interventions relevant to this guideline.
Internal Validity	Allocation concealment,randomisation.

Savage R;Armstrong D;

Effect of a general practitioner's consulting style on patients' satisfaction: a controlled study

Ref ID 1752 1990

Study Type Randomised Controlled Trial **Funding** RCGP Schering scholarship

Number of participant	350 were invited to participate. 200 completed both assessments
Inclusion/Exclusion Criteria	Ages 16-75 with any presenting symptom; excluded if they had a life threatening condition
Patient Characteristics	There were not significant differences in terms of age, sex, ethnic origin, presenting problem.
Recruitment	Patients in a deprived inner city area were invited to participate
Setting	GP surgery, London
Interventions/ Test/ Factor being investigated	Patients were randomised to receive a directing or sharing style in the part of the consultation regarding treatment, advice and prognosis.
Comparisons	The styles were compared on measures of satisfaction with the gp's perceived understanding of their problem and the explanation they received and whether they felt that they had been helped immediately after the consultation and one week later.
Length of Study/ Follow-up	1 week
Outcome measures studied	Patient questionnaires were analysed which measured 3 areas of satisfaction
Results	There were no significant differences in the mean length of consultations between the two experimental groups. Patients who had the directing style of consultation reported significantly higher levels of satisfaction on almost all the outcome measures, and was particularly strong for patients with physical problems (excellent explanation $p<0.02$; excellent understanding $p=0.04$). There was no significant difference in the responses to the directing and sharing styles in longer consultations, where the main treatment was advice and among patients with psychological or chronic problems. Statistical significance values were not reported.
Safety and adverse effects	None
Does the study answer the question?	Direct consultation appeared to be more satisfactory particularly for patients with physical problems and for patients who received a prescription.
Effect due to factor in study?	No - outcome measures not validated and high dropout rate
Consistency of results with other studies?	Unknown
Directly applicable to guideline population?	Yes

Internal Validity Self report; Hawthorne effect

Schneider PJ;Murphy JE;Pedersen CA;

Impact of medication packaging on adherence and treatment outcomes in older ambulatory patients

Ref ID 17942 2008

Study Type Randomised Controlled Trial

Funding Centers for Medicare and Medicaid Services. Medications provided by Merck (Whitehouse Station, N.J) Packaging by PCI services, Philadelphia.

Number of participant	85 participants. 47 in the intervention group and 38 in the control group.
Inclusion/Exclusion Criteria	Inclusion: Patients taking or just starting lisinopril for hypertension. 65 years or over. Exclusion: If assessed by physician as having cognitive impairment e.g psychoses or Alzeimers disease, visual impairment or severe asthma.
Patient Characteristics	Mean age 72 years Mean no medications 5 26 men in the intervention group and 16 ment in the control group
Recruitment	Not reported.
Setting	3 health centres/hospital clinics, USA.
Interventions/ Test/ Factor being investigated	Randomised to receive daily-dose blister packaged medication (pill calendar) as the intervention compared to traditional bottles of loose tablets as the control group. Patients returned for refills every 28 days during a 12 month period where the pharmacist would record the time between prescription refills for the medication and any study-related problems. At 6 and 12 months after enrolling the patients visited the physician to find out blood pressure management; the occurrence of morbidity in the past 6 months e.g. angina, myocardial infarction and stroke; and any medical services they had required in the past 6 months e.g. hospitalisations or emergency department visits. Medical charts were reviewed by two pharmacists to gather this information.
Comparisons	The intervention group compared to usual care.
Length of Study/ Follow-up	12 months.
Outcome measures studied	% of prescriptions refilled on time. Medication possession ration (MPR -the sum of the day's supply for all prescriptions received during the study divided by the number of days between the first and last prescription dispensed. Blood pressure.
Results	The percentage of times prescriptions were refilled on time (within 5 days before or after due date) were significantly higher 80.4% (SD=21.2) for the intervention group than the control group, 66.1% (SD=28), p=0.012. The Medication possession rate was also significantly higher for the intervention group, 0.93 (SD=11.4) and 0.87 (SD 14.2) for the control group, p=0.039. No differences were found between the groups for systolic blood pressure and diastolic blood pressure measures at 6 and 12 months.
Safety and adverse effects	None reported. Approval for study obtained from the human subjects committee at each centre and written informed consent obtained before enrollment from each participant.

Does the study answer the question?	2 different ways of packaging medication, one which shows the day each dose is intended to be taken and provides information on how to take properly can improve the treatment regimen adherence and treatment outcomes in elderly patients.
Effect due to factor in study?	Possibly.
Consistency of results with other studies?	Yes as the intervention is simpler than most of the other interventions in the area which are multi-component.
Directly applicable to guideline population?	The population is relevant as they are taking medications.
Internal Validity	Selection bias.

Thomson RG;Eccles MP;Steen IN;Greenaway J;Stobbart L;Murtagh MJ;May CR;

A patient decision aid to support shared decision-making on anti-thrombotic treatment of patients with atrial fibrillation: randomised controlled trial

Ref ID 8831 2007

Study Type Randomised Controlled Trial **Funding** Welcome Trust

Number of participant	145 patients randomised - 69 to implicit tool and 67 to guidelines
Inclusion/Exclusion Criteria	Aged 60 and had either chronic non-valvular atrial fibrillation or paroxysmal atrial fibrillation. Exclusion criteria: acute onset of AF including cardioversion; previous stroke or TIA; dementia or contraindication to warfarin
Patient Characteristics	Mean age of 73 years and 44% female. 71.4% of guideline group and 69.8% of decision aid group were already taking warfarin. There were no significant differences between the groups.
Recruitment	Recruited from 40 GP practices in northwest England.
Setting	Research clinic
Interventions/ Test/ Factor being investigated	This study compares an implicit computerised decision aid with evidenced based paper guidelines
Comparisons	The primary outcome measure was the decision conflict scale measured after the clinic visit
Length of Study/ Follow-up	3 months
Outcome measures studied	Decision Conflict Scale (DCS) was the primary outcome. Secondary outcome measures were the State Trait Anxiety Inventory, a knowledge scale and Degner's decision making preference scale (these were not described)
Results	Post clinic participants in the decision aid arm were significantly more likely to judge that they were more important in making the decision (p=0.018) consistent with the anticipated impact of the delivery mode. Decision conflict fell in both groups post clinic compared to preclinic, the difference between groups post clinic was significant at the 5% level (p=0.036). There were no differences between groups in the DCS at three months. There was not significant difference between groups in anxiety or knowledge scores. Those not on warfarin already were significantly less likely to start warfarin than those in the paper guidelines arm: here the difference was 4/16, 25% compared to guidelines 15/16, 93.8%, RR 0.27 (95%CI 0.11-0.63).
Safety and adverse effects	Although this approach has a positive impact on decision conflict comparable to other studies of decision aids, it also reduced the uptake of a clinically effective treatment to prevent stroke that may have important implications for health outcomes.
Does the study answer the question?	Yes, this study raises an important point about shared decision making and potentially about the unbiased development of decision making tools.

Effect due to factor in study?	The outcome measure validation was not described
Consistency of results with other studies?	Unknown
Directly applicable to guideline population?	Yes
Internal Validity	Outcome measures subjective

Wilkinson CR;Williams M;

Strengthening patient-provider relationships

Ref ID 8834 2002

Study Type Randomised Controlled Trial **Funding** Not mentioned.

Number of participant	278, 136 in the control arm and 141 in the intervention arm.
Inclusion/Exclusion Criteria	Not mentioned.
Patient Characteristics	Mean age approximately 60 years; 12% female; Main diagnoses: diabetes mellitus, alcohol dependency, hypertension, prolonged PTS, cardiovascular problems; chronic renal failure.
Recruitment	Questionnaires were sent from the g.p.
Setting	G.P practice.
Interventions/ Test/ Factor being investigated	Participants for both groups were randomly selected and a letter asked if they would like to participate. The intervention group were mailed an appointment guidebook with instructions before their scheduled routine visits with gp. After the visit both groups were sent a short questionnaire to be posted back. The guidebook was 10 pages and title 'How to be prepared', with appointment lists, suggestions for getting ready, including writing down questions and concerns to discuss. Instructions for the day, sample phrases, suggestions for follow-up issues and health promotion, notes page. The questionnaire assessed patient perceptions relating to preparedness, self-effectiveness, and visit effectiveness. The intervention group received a questionnaire with six more questions relating to the guidebook itself, on its usefulness and that they did receive the book (questionnaire on page 92).
Comparisons	Intervention group versus usual care (a standard letter reminding of visit).
Length of Study/ Follow-up	The questionnaire was sent after their visit to the g.p by post.
Outcome measures studied	Perceptions of preparedness, self-effectiveness, visit effectiveness and usefulness of guidebook. By questionnaire.
Results	There were no significant differences between the two groups who agreed or strongly agreed on the five questions of the questionnaire. Proportion of patients indicating agree or strongly agree for intervention and control respectively: Prepared for appointment – 0.87 vs 0.86, difference +0.26, not significant (sig. alpha 0.10); questions answered +1.52, ns; did not leave with unresolved issues +0.72, ns; listened to what I had to say +1.09, ns; involved in making decisions +0.17 ns; better than usual in meeting needs +0.96, ns. Feedback on service provision: 82% of the comments from the control group were positive. Comments from intervention group were mainly on how to improve/or the

	usefulness of the guidebook. 100% read it.
Safety and adverse effects	Safety: data collection completed following human subject guidelines and study approval. Informed responses would be part of a research project and would remain confidential. They had the right to participate or to not. Giving back the questionnaire was giving consent to participate.
Does the study answer the question?	There was no significant differences in the consultation between the two groups therefore there was no effect of the guidebook on the outcomes of interest. This suggests that this tool (guidebook) did not improve the patient outcomes of preparedness, self-effectiveness significantly. This relates to the question as this tool would not be able to improve the patient participation and to help elicit beliefs and information needs any more than without this guidebook.
Effect due to factor in study?	There was no power calculation. There is no reference as to whether the drop-our rate difference between the control and intervention group was significant. The blinding and allocation concealment was not clear so can not be certain that the overall effect is due to the study intervention.
Consistency of results with other studies?	Consistent.
Directly applicable to guideline population?	Some of the population were relevant while some had not been e.g those with alcohol dependency. It does look at whether a guidebook improves shared decision-making between providers and patients.
Internal Validity	Allocation concealment, blinding.

Question: Effect of reminders - do reminders (and what types of reminders help increase adherence? Are these more important before or after a review?

Grading: 1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

Beaucage K;Lachance-Demers H;Ngo TT;Vachon C;Lamarre D;Guevin JF;Martineau A;Desroches D;Brassard J;Lalonde L;

Telephone follow-up of patients receiving antibiotic prescriptions from community pharmacies

Ref ID 582 2006

Study Type Randomised Controlled Trial **Funding** Pro Coc Ltee.

Number of participant	Total sample: 255. Intervention group: 126, Control group: 129.
Inclusion/Exclusion Criteria	Inclusion: 1. have an expected duration of antibiotic treatment, 2. speak English or French, 3. be able to converse over the telephone, 4. be available for a telephone call during and at the expected end of antibiotic treatment and for up to 48 hours after. Exclusion: 1/ were initiating prophylactic antibiotic treatment 2/ did not self-manage their medication 3/ were already participating in another clinical trial 4/ in the opinion of the pharmacist, required intense clinical follow up or 5/ would benefit from more intense clinical follow up in a special medical hospital clinic.
Patient Characteristics	Age (m, SD): Intervention group: 47, +/- 20 , control group: 49 +/- 20. Sex: women: Intervention group: 55% , control group: 60%.
Recruitment	
Setting	Six community pharmacies.
Interventions/ Test/ Factor being investigated	Pharmacist telephone follow up intervention (PTFI): A telephone call was made to patients in the intervention group by a pharmacist 3 days into treatment. The pharmacist asked about the patient's general condition, on the presence of adverse effects, the participants understanding of dosing. The pharmacist emphasized the importance of adherence and offered motivation for the patient. The patients were offered an opportunity to ask questions and were given the pharmacists contact details in case they wanted to make contacted there pharmacist at a later time. Usual pharmacist intervention (UPI): Given pharmacists contact details. No follow up calls.
Comparisons	Pharmacist telephone follow up intervention (PTFI) vs usual pharmacist intervention (UPI). Intervention vs control.
Length of Study/ Follow-up	Length of antibiotic treatment.
Outcome measures studied	Adherence: measured on the expected last day of antibiotic treatment. Patients reported the number of tablets they had left.
Results	Note: adherence defined as the percentage of tablets consumed of total number tablets provided. Adherence: Mean +/- S.D adherence to treatment was 94% +/- 9% and 94% +/- 12% in the intervention and control groups respectively (p = .803). The proportion of patients with less than 80% adherence was similar in the two groups (Intervention group: 8%, control group: 9%). Number of infectious symptoms and infection severity: There were no significant differences between the groups on these two variables. Other outcomes: drug related problems were identified in 53% of intervention group patients and 8% of control patients (p < 0.001). Oral recommendations were made more often for intervention group patients (52%) than control patients (6%) (p < 0.001). Recognized pharmaceutical advise was given to 10% of intervention patients and 2% of control patients (p = 0.015). Study-specific advise was given to 5% of intervention patients and 1% of control patients (p = 0.064, NS).

Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention had no effect on participants' adherence.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	

Lam DH;Watkins ER;Hayward P;Bright J;Wright K;Kerr N;Parr-Davis G;Sham P;

A randomized controlled study of cognitive therapy for relapse prevention for bipolar affective disorder: outcome of the first year

Ref ID 23 2003

Study Type	Randomised Controlled Trial	**Funding**	No information given regarding funding.

Number of participant	103 in total sample. CT group: 59; Control group: 60.
Inclusion/Exclusion Criteria	Inclusion criteria: (1) bipolar 1 disorder according to the DSM-IV18; (2) prescribed prophylactic medication at an adequate dose according to the British National Formulary 19; (3) aged 18 to 70 years; (4) at least 2 episodes in the last 2 years or 3 episodes in the last 5 years (to identify a subgroup vulnerable to relapses); (5) currently not fulfilling criteria for a bipolar episode; (6) Beck Depression Inventory 20 (BDI) score lower than 30; and (7) Bech-Rafaelsen Mania Rating Scale21 (MRS) score lower than 9. Patients in an acute episode or with high residual symptoms were excluded because the focus of this study was relapse prevention and we did not want to use most therapy sessions for the treatment of an acute episode. Exclusion criteria: being actively suicidal (BDI suicide item score of 3) and currently fulfilling the criteria for substance use disorders.
Patient Characteristics	Age y: CT group 46.4 ± 12.1, control group 41.5 ± 10.8. Female sex (No. of patients): CT group: 28, control group 30. Age at onset, y: CT group 28.2 ± 11.4, control group: 26.2 ± 9.5. No significant baseline differences between groups.
Recruitment	Participants were either referred by their psychiatrists or contacted directly via a list of patients who had had blood drawn in the last 12 months to evaluate the serum level with mood stabilizers.
Setting	Not given.
Interventions/ Test/ Factor being investigated	Traditional cognitive therapy for depression with new elements highlighting the need for combined psychological and drug treatment, to help monitor mood and prevent relapse and to highlight the importance of sleep and routine and the therapy also addressed illness beliefs. Delivered by clinical psychologists. Consisted of 12 to 18 individual sessions within the first 6 months and 2 booster sessions in the second 6 months.
Comparisons	Cognitive therapy and minimal psychiatric care v minimal psychiatric care alone. So, intervention + usual care v usual care alone.
Length of Study/ Follow-up	12 months.

Outcome measures studied	Adherence: Monthly questionnaires returned by the patients (and every 6 months by key workers) to the psychiatric service who had the most contact with the patient. Broad scales were used to report if the patient had been fully adherent to non adherent.
Results	Adherence: 93.1% (27/29) of patients with available serum levels (after 6 months) in the CT group compared with 78.3% (18/23) of the control group had adequate serum levels (p = .06). There was significant agreement between patients' own compliance reports and serum levels: at month 6, a significantly greater proportion of patients in the CT group (88.4% [38/43]) than in the control group (66.7% [26/39]) reported good compliance (i.e. missing their medication <3 times in a month). After co varying for the compliance rating at baseline, this remained significant (p = .02). There was a significant correlation between key workers' and patients' reports (r = 0.75; n = 64; p = <.001). Other outcomes: The hazard ratio for relapse in the CT group relative to the controls was 0.40 (95% confidence interval, 0.21-0.74; p = .004) after medication compliance was controlled for. When both medication compliance and the previous number of episodes were controlled for, significantly fewer patients in the CT group experienced a bipolar episode during the 12 months than in the control group (P=.008). After medication compliance and the number of previous episodes were controlled for, patients in the CT group still had significantly fewer days in bipolar episodes than the control group (p = .008). The CT group had significantly fewer days in the hospital for bipolar episodes as a whole and significantly fewer hospital days for depression. Over the 12 months, the CT group showed significantly higher social functioning, less mood symptoms on the monthly mood questionnaires and significantly less fluctuation in manic symptoms compared to control group. The CT group also coped better with manic prodromes at 12 months. There were no differences between the groups in number of psychiatric appointments or prescriptions changes.
Safety and adverse effects	None
Does the study answer the question?	Yes
Effect due to factor in study?	Fairly certain.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	Measurement of adherence.

Miklowitz DJ;George EL;Richards JA;Simoneau TL;Suddath RL;

A randomized study of family-focused psychoeducation and pharmacotherapy in the outpatient management of bipolar disorder

Ref ID 2474 2003

Study Type	Randomised Controlled Trial	**Funding**	Grants: National Institute of Mental Health; a Distinguished Investigator Award; grant from the John D. and Catherine T. MacAuthor Foundation Network on the Psychobiology of Depression.

Number of participant	Total sample: 101 participants. Intervention group: 31, control group: 70.
Inclusion/Exclusion Criteria	Inclusion: DSM-3-R criteria for bipolar disorder (manic, mixed, or depressed episode0 within the past 3 months, aged 18 to 65 years, No evidence of developmental disability or neurological disorder, no alcohol other substance use disorders in previous 6 months, living with or in regular contact (at least 4 hours a week) with a care giving family member, English speaking, willingness to take mood stabilizing medications or antipsychotic agents, willingness and ability of all relatives and patients to give written informed consent to participate
Patient Characteristics	Age: intervention group: 35.7 +/- 9.2 control group: 35.6 +/- 10.6. Sex: female: intervention group: 58%, control group: 66%. Ethnic minority: intervention group: 10% control group: 14%. No significant baseline differences between groups.
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	Family focused therapy (intervention) (9 month length): Early sessions assessed patient and the families coping styles. Following sessions in three modules 1/ psycho education (7 sessions): teaching about the disorder, its aetiology, signs, symptoms, how to prevent relapse 2/ Communication training (7-10 sessions): participants through role play etc skills of listening, offering feedback, and requesting changes in behaviour 3/ problem solving skills (4-5 sessions): participants identify potential problems, come up with and evaluate various solutions. Involved 21 one hour sessions. All of family involved. Conducted at patient or parents home. Crisis management (9 month length): Early sessions assessed patient and the families coping styles. 2 one hour psycho education sessions (for content see above). Then crisis intervention sessions offered as needed for 9 months. Conducted at patient or parents home. Pharmacotherapy (2 year length): study physician could adjust the frequency of a patient's clinical visits, drugs and dosage as required.
Comparisons	Family focused therapy and pharmacotherapy (intervention) vs crisis management and amd pharmacotherapy (serves as control). Intervention vs control.
Length of Study/ Follow-up	2 years.
Outcome measures studied	Adherence: patient self-report validated by physician and family ratings.
Results	Adherence: Patients in the intervention group had higher mean drug adherence scores (1-3 scale) during follow up (2.77 +/- 0.43) than patients in the control group (2.56 +/- 0.48, p = 0.04). Pharmacotherapy regimens: The 2 groups could not be distinguished on drug treatment intensity scores at any point during follow-up. The groups were also equivalent at all points in time on frequency of psychiatric visits, the use of lithium carbonate vs anticonvulsants, or the use of adjunctive anti depressants or antipsychotics. Relapse and survival time: Of the 70 intervention patients, 54% experienced disease relapse during the two year follow-up, 17% survived without disease relapse, 6% were unchanged, and 23% terminated prematurely. Of the 31 control patients, 35% experienced disease relapse during the two year follow-up, 52% survived without disease relapse, 3% were unchanged, a 10% terminated prematurely. The group differences in relapse and non-relapse rates were significant (p < .005). Patients in the intervention group remained remitted or partially remitted for longer periods than control patients (p = .003, hazard ratio, 0.38, 95% CI, 0.20-0.75). On average intervention group patients survived 73.5 +/- 28.8 weeks whereas control patients survived 53.2 =/- 39.6 weeks. Symptom type and severity: intervention group patients had a similar affective symptom scores to control patients for the first 6 months of follow up but then stabilized at the lower levels of symptom severity (p =.007).

Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention significantly improved adherence.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	

Orton L;Barnish G;

Unit-dose packaged drugs for treating malaria. [Review] [40 refs]

Ref ID 1251 2005

Study Type Systematic Review **Funding** Cochrane review

Number of participant	3 quasi RCTs and one cluster RCT
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	A meta analysis of two trials (596 participants) showed that participant reported treatment adherence was higher with blister packed tablets compared with tablets in paper envelopes (RR 1.18, 1.12 to 1.25). Two trials using tablets in sectioned polythene bags as the intervention also noted an increase in participant reported treatment adherence. The cluster RCT (6 clusters) compared it with tablets in paper envelopes and the other trial compared it with syrup in bottles (RR2.15, 1.76 to 2.61; 299 participants). The authors stated that there was insufficient evidence to determine the effect of unit dose packaged antimalarial drugs on treatment failure. Unit dose packaging supported by prescriber training and patient information appears to improve participant reported treatment adherence, but these data come from trials with

methodological limitations.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Raynor DK;Blenkinsopp A;Knapp P;Grime J;Nicolson DJ;Pollock K;Dorer G;Gilbody S;Dickinsn D;Maule AJ;Spoor P;

A system review of quantitative and qualitative research on the role and effectiveness of written information available to patients about individual medicines

Ref ID 8723 2007

Study Type Systematic Review **Funding** HTA study.

Number of participant RCTs; controlled clinical trials; controlled before and after studies; interrupted time series; before and after cohort studies; other uncontrolled designs.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? Key findings of the report show that
•the majority of people do not value the written information they receive, and
•no robust evidence was found that the information had any effect on patient satisfaction or compliance.
The review showed that patients did not value the PILS supplied due to deficiencies in the content (e.g. complexity of language) and layout (e.g. print size). However, it did show that patients valued written information that contained condition-based details along with the medicines information, in addition to alternative treatments for the condition.
Most patients did not value the current package insert patient information leaflets (PILS) and did not consider information written by medicine manufacturers to be sufficiently independent.
In addition, the qualitative evidence included in the report did not show that patients

perceive improvement of compliance as a function of PILs. This can be explained by how an informed decision not to take medication is a legitimate and acceptable outcome. In contrast, some health care professionals viewed that the increase of compliance was one of the main PIL uses.
The key points for improvement of written medicines information outlined by the review were:
•The need to involve patients in all stages of the process, as to reflect better their needs.
•To incorporate the findings from the review to improve future information design and content
•To present risk information numerically instead of verbal descriptions.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Raynor DK;Blenkinsopp A;Knapp P;Grime J;Nicolson DJ;Pollock K;Dorer G;Gilbody S;Dickinsn D;Maule AJ;Spoor P;

A system review of quantitative and qualitative research on the role and effectiveness of written information available to patients about individual medicines

Ref ID 8723 2007

Study Type Systematic Review **Funding**

Number of participant

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

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Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Grading: 1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

Adler DA;Bungay KM;Wilson IB;Pei Y;Supran S;Peckham E;Cynn DJ;Rogers WH;

The impact of a pharmacist intervention on 6-month outcomes in depressed primary care patients

Ref ID 1974 2004

Study Type	Randomised Controlled Trial	**Funding**	Grant from the National Institute of Mental Health.

Number of participant	N= 258 intervention, and n= 249 control.
Inclusion/Exclusion Criteria	Inclusion criteria: 1) received care from a PCP in any site; 2) met DSM-IV criteria for major depressive disorder (MDD) and/or dysthymia; 3) were 18 years of age or older; 4) could read and understand English; 5) had no acute life threatening condition with a terminal prognosis of <6 months; 6) were not pregnant (or had not given birth within the last 6 months). Exclusion criteria: patients with current alcoholism (defined as more than one positive response on the CAGE, plus one item assessing current usage), bipolar disorder, and/or psychotic disorders. Patients with life-time alcoholism, long-term/chronic depression (those with > = 4 MDD episodes in their lifetime plus their first diagnosis > 10 years ago), anxiety disorders, likely personality disorders (as indicated by NEO scores > = 17), or comorbid medical conditions were not excluded.
Patient Characteristics	The sociodemographic characteristics of the patients were: 42.3 years, mean age; 71.8% female; 72.4% White; 29.7% married; 60.9% employed 20 or more hours per week; and 17.6% mean household income <10 K. Overall, 37.1% of patients had seen a psychiatrist or mental health provider in the last 3 months. There were 40% who met the criteria for MDD, 24% for dysthymia, and 36% for DD. There were no differences in these characteristics in any of the intent to treat analyses.
Recruitment	Recruited from 9 primary care practices (PCP) in metropolitan Boston.
Setting	Primary Care Practices (PCP). USA.
Interventions/ Test/ Factor being investigated	The intervention was based on the use of a protocol based on clinical pharmacy principles and AHCPR guidelines, and did not involve prescribing a specific AD medication. The protocol emphasized: 1) obtaining a thorough medication history,, 2) assessing a patient's medication regimen for drug-related problems (such as side effects or drug interactions), 3) monitoring drug efficacy and toxicity, especially for the symptoms of depression, 4) educating patients about depression and antidepressants, 5) encouraging patients to start and maintain AD therapy, and 6) facilitating communication with a patient's PCP. Pharmacists contacted the patients initially by telephone to set up an appointment. After the initial appointment they informed the patient's PCP and provided the PCP with a thorough medication history (including adherence to prescribed medications and drug-related problems) and whatever recommendations the pharmacist may have suggested to improve the regimen. In addition to the pharmacist activities, pharmacists fulfilled some basic patient needs, such as that of general social support and overcoming system inadequacies. Control group: The PCPs who saw the control patients received the results of the depression screener indicating a DSM-IV diagnosis of major depressive disorder (MDD) and/or dysthymia. Other than that, control patients received usual care.
Comparisons	Between Treatments.
Length of Study/ Follow-up	Up to 6 months.
Outcome measures studied	Anti-Depressant (AD) use rates at 6 months and changes in severity of depression as assessed by a modification of the Beck Depression Inventory (BDI).
Results	The intervention group had more patients on ADs at 3 and 6 months than the control group (3 months, 60.6% vs.48.9%, p = 0.024; 6 months, 57.5% vs. 46.2% adjusted, p = 0.025).

Outcomes (mBDI scores) at 6 months favoured the intervention group, but the trend did not reach statistical significance (17.7 for intervention vs. 19.4 for control, adjusted, P = .16, based on 384 patients who completed both initial and 6 month questionnaire.. Results at 3 months were similar. Adjusted results at 6 months for the MHI were similar in direction (51.9 vs. 49.0, p= 0.15) and MCS (40.4 vs. 38.6, p = 0.19), but were not statistically significant. Furthermore, there were no differences in 6-month outcomes for PCS (42.9 in both groups).

For patients not on ADs at study entry (n = 234), rates of AD use were higher in the intervention group at both 3 months (29.2% vs. 11.0%, p = 0 .005) and 6 months (32.3% vs. 10.9% adjusted P = .001). For patients using ADs at study entry (n = 227), there were no significant differences in AD use between intervention and control groups either at 3 (90.7% vs. 87.2, p = 0.50) or 6 months (83.4% vs. 78.4%, P = 0.33).

For patients not on ADs at enrolment, mental health outcomes for the intervention patients were no different than control patients, including mBDI (18.1 vs. 19.9, p= 0.32).

Rates of AD use at 6 months were higher in intervention than control patients who had chronic depression (42.7% vs. 13.9%, p = 0.05), dysthymia (47.8% vs. 15.6%, p = 0.06), and potential personality disorder (37.1% vs. 13.4%, p =0 .01).

Safety and adverse effects None reported.

Does the study answer the question? Pharmacists significantly improved rates of AD use in PC patients, especially for those not on ADs at enrolment, but outcome differences were too small to be statistically significant. Difficult-to-treat subgroups may benefit from pharmacists' care.

Effect due to factor in study? Yes.

Consistency of results with other studies?

Directly applicable to guideline population? Relevant study.

Internal Validity Not blinded study. Self-reported outcomes.

Atherton-Naji A;Hamilton R;Riddle W;Naji S;

Improving adherence to antidepressant drug treatment in primary care: A feasibility study for a randomized controlled trial of education intervention.

Ref ID 2507 2001

Study Type Randomised Controlled Trial **Funding** Grampian Primary Care Trust.

Number of participant Total sample 45. Intervention group: 23, control group: 21.

Inclusion/Exclusion Criteria Inclusion/exclusion: 1. Patients aged over 16 years. 2. Clinically depressed patients. 3. First consultation of a patient for depression or new episode of depression. 4. Antidepressant prescribed for patients' depression (i.e. not for other conditions). 5. Patients not suffering from dementia.

Patient Characteristics No separate break down by group. Total sample: 88.9% were female. Age: 84.4%: 21- 60 years, 6.7%) < 21 years, 8.9% > 60 years.

Recruitment

Setting Five large general practices.

Interventions/ Test/ Factor being investigated	Intervention: Patients in the intervention groups received simple tailored information (mailed leaflets with written and pictorial information) 1, 6 and 16 weeks after the initial prescription (in order to reflect acknowledged 'critical periods' for non-compliance during a course of antidepressant treatment) which was personalized for each patient and specific drug and generated by a specially constructed computer programme. Leaflets contained basic information about condition, treatment and general problems people may have with adherence.
Comparisons	Intervention v usual care. Intervention vs control.
Length of Study/ Follow-up	6 months.
Outcome measures studied	Adherence: Data assessed by collection of prescriptions over 6 months. Other measurements also taken.
Results	Adherence: only 16 (35.6%) participants collected prescriptions in all 6 months, with no significant difference between the intervention and control groups (37.5 versus 33.3%) (p = 0.085 and 95% confidence interval (CI) –23.9 to 32.1). Overall, prescription collection declined from 97.7% in month 1 to 55.6% in month 6. Other outcomes: There were no significant differences in the numbers of consultations, referrals and admissions between the two groups. The participants in the intervention group had significantly lower Hospital Anxiety and Depression Scale (HADS) score on subscale and total scores than the participants in the control group. The intervention group experienced significantly less depression (median (interquartile range): Intervention group: 4.0 (1–7), control group: 8.0 (4–10). CI: –7 to 0, p = 0.034), anxiety (Anxiety – median (interquartile range): intervention group: 7.0 (4–11), control group: 11.0 (8–14), CI: –7 to –1, p = 0.022) and total scores (Total – median (interquartile range): intervention group: 11.0 (6–20), control group: 18.0 (15–24), CI –13 to –1, p = 0.021) than the control group. There was no significant difference between the groups in total treatment satisfaction scores.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention did not increase adherence.
Effect due to factor in study?	Fairly.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	

Bechdolf A;K÷hn D;Knost B;Pukrop R;Klosterk÷tter J;

A randomized comparison of group cognitive-behavioural therapy and group psychoeducation in acute patients with schizophrenia: Outcome at 24 months

Ref ID 4504 2005

Study Type	Randomised Controlled Trial	**Funding**	This work was supported by grant from the Koln Fortune Program, Faculty of Medicine, University of Cologne, Germany.
Number of participant	88 total sample. CBT group: 40, PE group: 48.		

Inclusion/Exclusion Criteria	Inclusion: Participants were aged 18–64 years and met criteria for an episode of a schizophrenic or related disorder (ICD-10: F 20, F 23, F 25). Exclusion: Participants with a primary diagnosis of drug or alcohol dependence, organic brain disease, learning disability or hearing impairment was excluded from the study. Non-speakers of German were also excluded.
Patient Characteristics	At baseline: Age, years [mean (SD)]: CBT group: 32.2 (9.9), PE group: 31.4 (10.6). Gender [n (%)] Female: CBT group: 22 (55.0), PE group: 26 (54.2). Time since diagnosis, months [mean (SD)]: CBT group: 56.7 (65.4), PE group: 50.0 (58.7). Number of admissions [mean (SD)]: CBT group: 2.6 (3.8), PE group: 2.4 (3.2). No significant differences between groups. At 24 months follow-up: Age, years [mean (SD)]: CBT group: 35.35 (10.54), PE group: 33.15 (10.76); Gender [n (%)] Female: CBT group: 8 (50.0), PE group: 15 (55.6). Time since diagnosis, months [mean (SD)]: CBT group: 70.63 (84.4), PE group: 52.00 (60.41). No. of admissions [mean (SD)]: CBT group: 4.00 (4.8), PE group: 2.59 (3.8). No significant differences between groups.
Recruitment	Participants recruited from consecutive acute admissions to the in-patient unit of the Department of Psychiatry and Psychotherapy at the University of Cologne.
Setting	
Interventions/ Test/ Factor being investigated	Group CBT: 16 sessions in 8 weeks by psychiatrist or clinical psychologist focused on assessment and engagement (sharing information about voices and delusions, models of psychosis), improving self-esteem, formulation of key-problems, interventions directed at reducing the severity and the occurrence of key problems, relapse prevention/keeping well and enhancing medication compliance. A specific focus on the component "improving self-esteem" to foster feelings of hope and engagement with therapy. Group PE: used as comparison and involved 8 sessions in eight weeks delivered by psychiatrist or clinical psychologist and focused on symptoms of psychosis, models of psychosis, effects and side-effects of medication, maintenance medication, early symptoms of relapse, relapse prevention.
Comparisons	Group Cognitive Behavioral Therapy (CBT) vs group psycho-education (PE). Intervention vs Intervention.
Length of Study/ Follow-up	24 months.
Outcome measures studied	Compliance was measured by a 4-point rating scale based on corroboration from as many sources as possible including patient, relatives, psychiatric nurse and psychiatrist-in-charge (m *2 sources).
Results	Adherence: Compliance with medication was high in both groups at intake (CBT: 3.9 (0.3), PE: 3.8 (0.5)). This high compliance level was maintained during the intervention period and declined during follow-up. On a descriptive level, the CBT group showed higher compliance ratings at post-treatment (CBT: 3.9 (0.3), PE 3.7 (0.7)) and at 24 month follow-up (CBT: 3.4 (0.7), PE: 2.9 (1.1)). However, there were no significant differences between the two interventions at any assessment point (post treatment: p = 0.10,24 month follow up, p = 0.26). Other outcomes: There was not a significant difference between the groups in terms of re-hospitalization rates or the overall length of hospital stays (part time and full time). When scores at 24-month follow-up were controlled for pre-treatment scores by ANCOVA no significant differences emerged between CBT and PE in any psychopathological syndrome at 24-month follow-up. No significant differences between treatment groups were observed when calculating individuals with clinical significant change. No significant differences emerged between treatment groups at pre-, post-treatment or 24-month follow-up.
Safety and adverse effects	None.
Does the study answer the question?	Yes. CBT does not significantly improve medication compliance compared to PE.

Effect due to factor in study?	Probably. Problem that 16 sessions of CBT were given compared to only 8 PE sessions.
Consistency of results with other studies?	
Directly applicable to guideline population?	Direct.
Internal Validity	

Begley S;Livingstone C;Hodges N;Williamson V;

Impact of domiciliary pharmacy visits on medication management in an elderly population

Ref ID 7555 1997

Study Type Randomised Controlled Trial **Funding** Not reported.

Number of participant	Intervention group n=61; control group (V) n=63; and control group (NV) n=66.
Inclusion/Exclusion Criteria	Inclusions criteria: to be aged 75 years or older; prescribed three or more different drugs; at least a twice daily dosage for one or more of the drugs; under the care of a participating consultant; consented to participate in the study; and was returning to their home (not further institutional care).
Patient Characteristics	Majority of the patients were female (61% in the intervention group; 65% in the V group and 56% in the NV group). The median ages were 84 years (range 75 to 94) for the intervention group, 81 years (range 75 to 96) for the V group, and 82 years (range 76 to 92) for the NV group.
Recruitment	Through discharge prescriptions were presented in the hospital pharmacy (provided they met the inclusion criteria). These were three hospitals from the Crawley and Worthing district health authorities.
Setting	hospital pharmacies
Interventions/ Test/ Factor being investigated	group A receiving home visits and counselling, group B which was the control and received visits only (called V group), and group C was the control group that received traditional pharmaceutical services with no visits except for the beginning and the end of the study (NV group). Structured patient interviews were conducted during the domiciliary visits and consisted of six sections: Patient information; drug knowledge; Patient dexterity; abbreviated mental test; medication management; and compliance with medication regimen. Patients were seen during 12 months. Other strategies were employed for improving patient compliance: emphasising the importance of compliance; giving clear instruction on the exact treatment regimen, in writing if necessary; arranging dosing times to fit into the patients daily routine; recognising the patients effort to comply at each visit; and simplification of the regimen if necessary.
Comparisons	between treatments.
Length of Study/ Follow-up	Up to 12 months.
Outcome measures studied	
Results	At each visit there were significant differences between the groups in terms of distribution of patients at the various levels of compliance ($p<0.001$).Compliance was higher at 3 months and 12 months for the intervention group compared to the other control groups ($p<0.001$), despite the low compliance value for the intervention group at the 12 month visit. Patients in the intervention group who increased their compliance rates between visits also increased their drug knowledge scores ($p<0.005$).

Mean scores for drug knowledge did not differ significantly between the groups at any of the visits, although the mean score for the intervention group increased significantly between the initial and the two weeks visits (p=0.001). There were no changes for patient dexterity scores between groups at any point of the study.
The intervention group did not report any significant changes in abbreviated mental test score, but control V group showed a 0.2 fall and control group NV a 0.4 rise in score, both statistically significant at p=0.05.
Contacts with GP and health workers was lower for the intervention group than for the control (V) in each of the four time periods (p<0.01).

There was a significant decrease in in the number of patients in the intervention group storing their drugs inappropriately (p<0.01); no statistically significant decrease was seen in any of the control groups.

The proportion of patients in the intervention group hoarding drugs significantly decreased from 61% to) at the two weeks and one month visits (p<0.001).

Safety and adverse effects

None reported.

Does the study answer the question?

Patients in the intervention group had better compliance, better drug storage practices and a reduced tendency to hoard drugs, and required fewer GP consultations than patients in the control groups.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Bernsten C;Bjorkman I;Caramona M;Crealey G;Frokjaer B;Grundberger E;Gustafsson T;Henman M;Herborg H;Hughes C;McElnay J;Magner M;van Mil F;Schaeffer M;Silva S;Sondegaard B;Sturgess I;Tromp D;Vivero L;Winterstein A;

Improving the well-being of elderly patients via community pharmacy-based provision of pharmaceutical care

Ref ID 17983 2008

Study Type Randomised Controlled Trial **Funding** European Commission funding.

Number of participant

A total of 1290 intervention patients and 1164 control patients were recruited.

Inclusion/Exclusion Criteria

Patients were 65 years or older, taking 4 or more prescribed medications and oriented with respect to self, time and place. They were community dwelling and regular visitors to a recruited community pharmacy.
Patients were excluded if they were housebound or resident in a nursing/residential home. Identification of patients was performed via a personal approach by the pharmacy.

Patient Characteristics

Median age was 74±8 for the intervention and control group. 42.1% was male and 57.9% was female in the intervention group. 42.7% was male and 57.3% was female for the control group.

Recruitment

Study sites were selected using the responses of community pharmacists who expressed interest in participating in the research, following publicity via mailshots, advertisments in pharmaceutical publications and at professional meetings.

Setting

community pharmacies

Interventions/ Test/ Factor being investigated	Pharmaceutical care program by trained pharmacists compared to usual care which was normal services provided to the recruited patients. Pharmacy interventions included: 1) educating the patient about their drug regimen and their condition; 2) implementing compliance-improving interventions such as drug reminder charts; 3) rationalising and simplifying drug regimens in collaboration with the patients GP. This was a continuos process throughout the 18 months of the study.
Comparisons	Between treatments.
Length of Study/ Follow-up	Up to 18 months
Outcome measures studied	Hospitalisations, quality of life, satisfaction with service provided, clinical signs and symptom control, knowledge of medicines, contact with GPs, prescription and nonprescription drug use.
Results	Seven countries were involved: Denmark, Germany, The Netherlands, Northern Ireland, Portugal, Republic of Ireland, and Sweden. Drop-outs were higher in some countries that others, however most withdrew in the first 6 months. Those who withdrew from the study were significantly older ($p<0.05$) and reported poorer quality of life at baseline ($p<0.05$). Generally, the programme had some positive effects on humanistic health outcomes such as satisfaction with treatment, and sign and symptom control, and on economic outcomes, but had less impact than anticipated on drug therapy, drug knowledge and compliance with medication. An analysis of changes in compliance during the study indicated that at 18 months a significantly higher proportion of the intervention patients changed from being noncompliant to compliant compared with the control groups ($p=0.028$). Intervention patients rated the services provided higher that the control at 6 and 18 months ($p<0.05$). There was a small statistically significant increase in satisfaction in the intervention group over time (baseline vs 12 months $p=0.039$).
Safety and adverse effects	None.
Does the study answer the question?	It is a large-scale multicentre study that assessed the effects of a pharmaceutical care programme by community pharmacists to elderly. Intervention patients reported better control of their conditions. The new service was well accepted by the intervention patients and patient satisfaction with the services improved during the study.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Collier AC;Ribaudo H;Mukherjee AL;Feinberg J;Fischl MA;Chesney M;Adult AIDS;

A randomized study of serial telephone call support to increase adherence and thereby improve virologic outcome in persons initiating antiretroviral therapy

Ref ID 966 2005

Study Type	Randomised Controlled Trial	**Funding**	National Institute of Allergy and Infectious Disease, National Institutes of Health; National HIV/AIDS Research Programme.

Number of participant	Total sample: 282. Intervention group: 142, control group: 140.
Inclusion/Exclusion Criteria	Inclusion/exclusion: All participants had < 200 CD4 T cells/mm3 or >80000 HIVE RNA copies/ML of plasma at screening, no or limited previous antiretroviral therapy (no previous use of lamivudine, nonnucleoside reverse transcriptase inhibitors, or protase inhibitors), hemoglobin > 9.1 g/DL (for men) or > 8.9 g/dL (for women) > 850 neutrophils/mm3, > 65000 platelets/mm3, hepatic aminotranferase levels <5 times the upper limit of reference values and amylase <1.5 times the upper limit of reference values and they could not be pregnant or breast feeding.
Patient Characteristics	Sex: male: control group: 84%, intervention group: 76%. Age (mean, sd): control group: 38.2 +/- 8.7, intervention group: 39.8 +/- 9.7. Race: white: control group: 44, intervention group: 51. Black: control group: 34, intervention group: 23, Hispanic: control group: 18, intervention group: 21.
Recruitment	
Setting	30 centres.
Interventions/ Test/ Factor being investigated	Intervention: Scripted phone calls (16 over 96 weeks) + usual care: The calls focused on the participants medication related behaviour and barriers to adherence were identified and discussed. Targets/strategies to improving adherence were developed and calls also offered social support and advice around side effects.
Comparisons	Scripted phone calls + usual care v usual care. Intervention v control.
Length of Study/ Follow-up	96 weeks.
Outcome measures studied	Self report questionnaire. Subjects who reported having missed <1 dose during the previous 4 days were considered >95% adherent. Given in weeks 8, 16, 24, 48, 72, 96.
Results	Adherence: Self reported adherence was high in both groups, with 72% of participants in each group reporting >95% adherence (OR, 0.86, 95% CI, 0.57-1.29; p = .46) (data for means across time points given in graph, impossible to figure out exact means from this). Virologic failure: The two groups did not differ significantly in time to virologic failure.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention did not increase adherence relative to usual care.
Effect due to factor in study?	Fairly. Possible confounding factors (see above).
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	

Connor J;Rafter N;Rodgers A;

Do fixed-dose combination pills or unit-of-use packaging improve adherence? A systematic review. [Review] [26 refs]

Ref ID 1501 2004

Study Type	Systematic Review	**Funding**	Unknown

Number of participant	Randomized or quasi-randomized controlled trials

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

15 trials met inclusion criteria: fixed dose combination pills were investigated in three of these while unit-of-use packaging was studied in 12 trials. The results of the trials suggested that there were trends towards improved adherence which reached statistical significance in seven out of thirteen trials reporting medication adherence. Measures of adherence were however heterogeneous and interpretation was further limited by methodological issues, particularly small sample size, short duration and loss to follow up. Uncertainty remains about the size of the benefits of drug formulation and packaging.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

De Geest; Schafer-Keller P;Denhaerynck K;Thannberger N;Kofer S;Bock A;Surber C;Steiger J;

Supporting medication adherence in renal transplantation (SMART): a pilot RCT to improve adherence to immunosuppressive regimens

Ref ID 354 2003

Study Type Randomised Controlled Trial **Funding** No details given.

Number of participant Total sample: 18. Intervention group: 6, control group: 12.

Inclusion/Exclusion Criteria

Inclusion: the patient had to be non-adherent to their immunosuppressive regimen (defined as <98% taking adherence and/or one or more drug holidays: No medication intake >36 h for a twice daily dosing regimen or >60 h for a once daily dosing regimen), at least 18 yr old; to be in follow-up at the University Hospital Basel, Switzerland, or at the Cantonal Hospital, Aarau, Switzerland; to speak German or French; to be literate; to have undergone kidney transplant surgery at least one year prior to the study; to be able to self-administer immunosuppressive drugs; to reside within a 180 km radius of Basel; and to provide written informed consent to

	participate in the RCT. Exclusion: Patients were excluded if they lacked mental clarity based on clinician's appraisal, could not read forms or EM printouts with at least corrective lens, or had no telephone service at home.
Patient Characteristics	Total sample: age: 45.6±1.2 yr; 78.6% male. Baseline characteristics not given in detail (may be reported in a different study).
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	Intervention group (IG): The IG received one home visit and three telephone interviews, one at the end of the month for three consecutive months (from) a nurse. The intervention was aimed at increasing patients' self-efficacy in taking their medication. During the home visit EM printouts were discussed with patient for problem detection, and adherences goals were made. All patients received self-efficacy interventions consisting of four elements: developing mastery experiences in taking medications correctly (2) participating in role modelling (3) verbally persuading by the intervention nurse and (4) addressing negative effects of physiological arousal. Nurses also implemented additional educational (refreshment course on adherence), behavioral (e.g. the use of reminders) and/or social support interventions (e.g. asking family members to fill in prescriptions) if they felt this would help the patient. Telephone calls served to discuss adherence in previous month (using EM data, checking on health status, and discussing (and changing if appropriate) adherence interventions.
Comparisons	Intervention and usual care vs usual care. Intervention vs control.
Length of Study/ Follow-up	9 months.
Outcome measures studied	Adherence: assessed through electronic monitoring (EM) of medication intake during a nine-month period (three months intervention, six months follow-up). Time and date of each bottle opening was recorded.
Results	Adherence: Non-adherence declined remarkably in both groups during the first three months of the study (Intervention group: $p = 0.04$; Control group: $p = 0.06$). Although the intervention group patients' chance of being non-adherent during the first three months decreased more than the control groups patients' chance this group difference did not reach statistical significance ($p = 0.31$). This was also the case at nine months ($p = 0.58$). Note of interest: Authors suggest results indicate an inclusion effect (inclusion in the study results in more adherence). They also note that although the intervention appeared to add further benefit in medication compliance, a lack of statistical power may have prevented a strong statistical statement.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention did not significantly improve adherence relative to the improvement in the control group.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Direct.
Internal Validity	

Gray R;Leese M;Bindman J;Becker T;Burti L;David A;Gournay K;Kikkert M;Koeter M;Puschner B;Schene A;Thornicroft G;Tansella M;

Adherence therapy for people with schizophrenia: European multicentre randomised controlled trial

Study Type	Randomised Controlled Trial	**Funding**	Quality of Life and Management of Living Resources of the European Union.

Number of participant	Total Sample: 409, AT Group: 204, HE Group: 205.
Inclusion/Exclusion Criteria	Inclusion: A clinical diagnosis of schizophrenia using ICD-10 criteria, patients should need continuing antipsychotic medication for a year after baseline assessment in the judgement of a senior psychiatrist, there needed to be evidence of clinical instability in the year before baseline, defined by one or more of the following: at least one admission to a hospital on mental health grounds, a change in type or dose of antipsychotic medication, planned or actual increased frequency of contact with mental health services, and indications of clinical instability reported by friends, carers or clinical team. Exclusion: presence of moderate or severe mental handicap (learning disability), organic brain disorders, current treatment by forensic psychiatric services, alcohol or drug dependence, inability to speak the language of the host country to a sufficient standard to receive the intervention, or assessment by the treating clinician as lacking capacity to give valid consent to participate.
Patient Characteristics	Age: AT group: 40.9 (11.7), HE Group: 42.1 (11.4). Male: AT group: 122 (60%), HE Group: 123 (60%). White European: AT group: 151 (74%), HE Group: 159 (78%). No significant differences at baseline between groups.
Recruitment	
Setting	Regular psychiatric care services. 4 study sites.
Interventions/ Test/ Factor being investigated	Experimental intervention: Adherence therapy: a brief, individual CBT approach. A collaborative, patient centred phased approach to promoting treatment adherence. There are 6 elements that form the core of therapy: assessment, medication problem solving, a medication time line, exploring ambivalence, discussing beliefs and concerns about medication and using medication in the future. Key therapy skills that the therapists use include exchanging information, developing discrepancies between participants thoughts and behaviours about medications and working with resistance to discussing psychiatric medication and treatment. The overall aim of process is to achieve a joint decision about the medication. Control intervention: Health education: Didactic health education package focused on the presentation of health related topics such as diet and healthy lifestyle. Delivery of both interventions: Both delivered in addition to standard care: Participants offered a maximum of 8 sessions lasting 30-50 minutes over a 5 month period. Delivered by 9 therapists (four psychologists, three psychiatrists and 2 mental health nurses).
Comparisons	Adherence therapy (AT) vs Health education (HE). Intervention (experimental) vs Intervention (control).
Length of Study/ Follow-up	52 weeks.
Outcome measures studied	Adherence: All measures after 12 months: Two measures; a key worker rating of adherence (SAIC) and a self report questionnaire MAQ. Also measured: Q of L and assessment of psychopathology.
Results	Adherence: There were no significant differences between the groups in terms of adherence at follow up using either the MAQ measure (AT group: 3.20 (1.07), HE group: 3.33 (1.02)) or SACI-C measure (At group: 5.22 (1.57), HE group: 5.03 (1.55)) at 12 month follow up. Q of L: There were no significant differences between the two groups in terms of Q of L.. Psychopathology: there were no significant differences between the groups in terms

	of psychopathology.
Safety and adverse effects	
Does the study answer the question?	Yes. There was no difference between the adherence therapy group and health education group in terms of adherence.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	

Hamet P;Campbell N;Curnew G;Eastwood C;Pradhan A;

Avapromise: a randomized clinical trial for increasing adherence through behavioural modification in essential hypertension.

Ref ID 2526 2003

Study Type Randomised Controlled Trial **Funding** Not reported.

Number of participant	N= 2402 to the intervention group; n= 2462 to the control group.
Inclusion/Exclusion Criteria	Inclusion criteria: History of diastolic blood pressure higher than 90mmHg and/or systolic blood pressure higher than 140 mmHg; and untreated or current hypertension treatment requiring alteration in the opinion of the physician aged 18 to 79 years and if female; unable to become pregnant and willingness to give informed consent. Exclusion criteria: pregnant; breastfeeding or women with childbearing potential; taking any investigational drug given within 30 days of initiation of therapy, and participation in other clinical studies while enrolled in the protocol; undergoing peritoneal dialysis; presence of certain cardiovascular disorders and allergies/hypersensitivities; requiring active treatment for substance abuse within the past two years; mentally or legally incapacitated; any other condition that might pose a risk to the patient of interfere with the study objectives.
Patient Characteristics	The mean age of patients was 58 years (range 16 to 89 years), 51% of those enrolled were female. Eighty-four percent of patients had chronic hypertension. The mean baseline systolic blood pressure was 160 mmHg and the mean diastolic blood pressure was 95mmHg.
Recruitment	From the GP practices.
Setting	GP practice. Canada.
Interventions/ Test/ Factor being investigated	Patients were assigned to receive a once daily dose of irbesartan 150mg that could be increased to 300mg, with our without the intervention avapromise. The avapromise intervention was created to modify behaviour by medication adherence through reinforcement and lifestyle modification. It is made up of two elements that are delivered in unison. The first element attempts to reinforce medication behaviours by using medication reminder letters, blood pressure diaries and telephone nurse counselling sessions. The second element addresses lifestyle management through educational brochures dealing with topics such as healthy living, nutrition, physical fitness and stress management. Patients assigned to the intervention group were mailed the material at one, two, three, four, six and 12 months. Patients in the control group received usual care educational materials in their physician's offices.
Comparisons	Between treatments.

Length of Study/ Follow-up	Up to 12 months.
Outcome measures studied	Patient's discontinuation with their irbesartan treatment regimens. Patient compliance was assessed by comparing the rate and time to discontinuation between the 2 groups.
Results	A total of 25% of patients discontinued their treatment from the intervention group and 25.5% form the control group (p= 0.94). There was no statistically significant difference in the duration of irbesartan compliance between the treatment groups. Overall the average duration of irbesartan compliance 267 days (SD=127) and was similar between treatment groups (267 days for the intervention group and 269 days for the control group).
Safety and adverse effects	Nineteen percent of the patients prematurely terminated the study due to serious adverse drug reactions. Five deaths were reported. Fifty-four per cent of patients who discontinued reported side effects.
Does the study answer the question?	The intervention did not yield an increase in the rates of adherence in patients with essential hypertension.
Effect due to factor in study?	Relative certainty.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant study.
Internal Validity	

Hanlon JT;Weinberger M;Samsa GP;Schmader KE;Uttech KM;Lewis IK;Cowper PA;Landsman PB;Cohen HJ;Feussner JR;

A randomized, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy

Ref ID 5012 1996

Study Type	Randomised Controlled Trial	**Funding**	Grant from the National Institute on Aging; An Academic Award from the National Institute on Aging; The Claude D. Pepper Older Americans Independence Center.

Number of participant	208 in total were randomised, 105 to the intervention group and 103 in the control group.
Inclusion/Exclusion Criteria	Inclusion: 65 years or over, evidence of polypharmacy (5+ medicines prescribed), received primary care in the GMC. Exclusion: Residents of a nursing home, cognitively impaired (mental status questionnaire) were excluded unless a caregiver was available for involvement in intervention.
Patient Characteristics	Mean values: Mostly male 99%, white 77%, 70 years old, married (65.7% intervention, 85.4% control), compliance rates of 73.5%, medication knowledge 80.5%, 10 years of education, 9 chronic medical conditions, 8 prescribed medications, 3 medications recommended.
Recruitment	Those with regular scheduled medications by a Veterans Affairs physician receiving primary care in a General Medicine Clinic; computerized and manual chart audits identified participants.
Setting	The Durham Veterans Affairs Medical Centre GMC.

Interventions/ Test/ Factor being investigated	Usual care plus pharmacist intervention - Before the patients visit to the GMC the clinical pharmacist monitored their drug therapy outcomes by reviewing their medical records and medication lists and ascertaining their current medication use, drug - related problems and evaluating their needs by applying the Medication Appropriateness Index. This was then reported to the physician. After the visit to the physician the pharmacist educated the patient on the drug-related problems and encouraged compliance with strategies such as medication reminder packages or calendars and written patient materials. Reviewed principles of safe medicine use and the importance of discussing medications with their physicians.
Comparisons	Pharmacist intervention versus usual care (which included a clinical nurse reviewing patients current medications before their visit, the physician visit and then the nurse reviewing andy medication modifications).
Length of Study/ Follow-up	Followed up for one year (Last telephone interview between 11.5 to 13 months after randomisation).
Outcome measures studied	Prescribing appropriateness; Health-related quality of life; Potential adverse drug events that had occurred during the past year; Patient compliance and knowledge; Patient satisfaction at end of year.
Results	Compliance was assessed by patient self-report. There were no significant differences between the groups at the end of the follow-up period with regard to medication compliance (77.4% of intervention group and 76.1% of control group complied, p=0.88) knowledge, number of medications or patient health care satisfaction. More control patients experienced adverse drug events than the intervention group (40% vs 30.2%, p=0.19). Written recommendations were enacted more (by physicians) in the intervention group than the control group (55.1% vs 19.8%, p<0.001).
Safety and adverse effects	None reported.
Does the study answer the question?	It does partially, however it should be noted that the pharmacist intervention involves not only medication review but medication education and compliance strategies. The study did not find that these increased compliance to medication, therefore this suggests that an intervention which included pharmacist medication review did not have an effect on compliance to medication.
Effect due to factor in study?	Yes
Consistency of results with other studies?	
Directly applicable to guideline population?	Patient population is of interest for this guideline the intervention is partially comparable to the intervention of interest.
Internal Validity	Subjects not blinded to treatment.

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.[see comment]

Ref ID 190 2006

Study Type	Randomised Controlled Trial	**Funding**	This study was partially funded by a competitive junior investigator grant award from the American Society of Health-System Pharmacists Research and Education Foundation, managed under the

auspices of the TRUE Research Foundation.

Number of participant	200. 159 after randomization for 2nd stage of study: 83 in follow up group, 76 in return to usual care group.
Inclusion/Exclusion Criteria	Inclusion: aged 65 years or over, taking 4 or more chronic medications daily. Exclusion: Patients were excluded if they did not live independently (assisted living or nursing home residents were excluded) or in the presence of any serious medical condition for which 1-year survival was expected to be unlikely.
Patient Characteristics	Age, mean (SD), y: Usual Care (UC) Group: 78 (6.2); Intervention group: 77 (10.5). Men: UC group: 56 (73.7), Intervention group: 62 (74.7). Race: White: Intervention group: 51 (61.4) , UC group: 43 (56.6); Black: Intervention group: 29 (34.9), UC group: 29 (34.9). No. of chronic medications, mean (SD): intervention group: 9.1 (3.2), UC group: 8.3 (2.8). Significant differences between groups prior to randomization in antidepressant usage, using medication or chart listing and the number of participants taking ACE inhibitors and niacin. These differences are addressed by using multi-variable analysis.
Recruitment	
Setting	Walter Reed Army Medical Center.
Interventions/ Test/ Factor being investigated	Months 3-8 received by all patients: The comprehensive pharmacy care program consisted of 3 elements, including individualized medication education (using standardized scripts), medications dispensed using an adherence aid (blister packs) and regular follow-up with clinical pharmacists every 2 months. Individualized educational interventions were performed to teach participants their drug names, indications, strengths, adverse effects, and usage instructions during each visit. Patients in intervention group continued to receive intervention for study months 9-14. Patients in control group returned to usual care for this period.
Comparisons	Intervention for months 3-8 vs intervention for months 3-14.
Length of Study/ Follow-up	14 months.
Outcome measures studied	Adherence was assessed at baseline via pill counts and expressed as amount of medication taken compared to what should have been taken. Measured again at 1, 2, 4, 6, 8, 10, 12 and 14 months. Also measured: changes in blood pressure and LDL-C.
Results	Adherence: 1-8 months: Mean (SD) baseline medication adherence at completion of run-in phase was 61.2% (13.5%). After initiation of the 6-month pharmacy care program, there was improvement in medication adherence noted at the 4-month pharmacy visit. At 4, 6, and 8 months, medication adherence was 96% or higher. At the conclusion of phase 1 (8 months), the primary end point was met with a mean (SD) medication adherence of 96.9% (5.2%), representing an absolute change in adherence of 35.5% (95% confidence interval [CI], 31.2%-38.5%; p<.001). Adherence 8-14 months: For the primary end point of the randomized clinical trial, the continued pharmacy care group showed sustained mean (SD) medication adherence (95.5% [7.7%]), whereas medication adherence declined in the usual care group (69.1% [16.4%]; p <.001). However, medication adherence at the conclusion of phase 2 for the usual care group was modestly higher than at study entry (run-in phase, 66.5% [14.0%] vs 61.1% [14.1%]; p = .02). At the end of the study, those elderly patients assigned to usual care had a similar frequency (compared with their baseline method of medication administration) of receiving help with their medications (11.6% vs 15.9%; p=.58) and using a pillbox (62.3% vs 49.3%; p=.09), but were more likely to use a medication chart (65.2% vs 13.0%; p<.001). Multiple linear regression analysis controlling for baseline differences (p<.20) in the study groups showed that the assignment to usual care (B=.81; p<.001) and taking medications for psychiatric or memory problems (B=.15; p=.007) were independently related to the change in medication adherence during phase 2 Other outcomes: 1-8 months: Improved adherence was associated with improvements in both secondary end points (BP and LDL-C). Among patients with drug-treated hypertension (n=184), mean (SD) systolic BP was reduced from 133.2 (14.9) mm Hg to 129.9 (16.0) mm Hg (p=.02). Diastolic BP was not significantly reduced. There was no change in the number of antihypertensive agents taken from baseline to the end of phase 1. Among patients with drug-treated hyperlipidemia (n =

	162), mean (SD) LDL-C decreased from 91.7 (26.1) mg/dL (2.38 [0.68] mmol/L) to 86.8 (23.4) mg/dL (2.25 [0.61] mmol/L) (p =.001). Other outcomes months 8-14: A pre-specified analysis of the associated changes in BP and lipid levels in the continued pharmacy care group showed significant reductions in systolic BP (?6.9mmHg; 95% CI, ?10.7 to ?3.1mmHg; P=.04 vs usual care) and diastolic BP (?2.5mmHg; 95% CI, ?4.9 to ?0.2 mm Hg; P=.39 vs usual care). The mean number of antihypertensive agents used was similar between treatment groups. The LDL-C was not further reduced from 9 to 14 months in the continued pharmacy care group and was not different between study groups.
Safety and adverse effects	None.
Does the study answer the question?	Yes. Continued care in intervention group led to them keeping there improved adherence compared to control group.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Direct.
Internal Validity	

Mannheimer SB;Morse E;Matts JP;Andrews L;Child C;Schmetter B;Friedland GH;

Sustained benefit from a long-term antiretroviral adherence intervention: Results of a large randomized clinical trial

Ref ID 2766 2006

Study Type Randomised Controlled Trial **Funding** Not reported.

Number of participant	A total of 928 FIRST study participants (98% of target) were eligible for enrollment into the CPCRA Adherence Study, and data from these participants were used in the main ITT analyses. Participants were distributed into study groups by cluster randomization as follows: 10 clusters (256 patients) in the MM arm, 10 clusters (254 patients) in the ALR arm, 9 clusters (196 patients) in the MM + ALR arm, and 9 clusters (222 patients) in the control (usual care) arm.
Inclusion/Exclusion Criteria	Not reported.
Patient Characteristics	Age (y), mean 38 ± 10; Gende: Female 22%, Male 78%
Recruitment	Not reported.
Setting	Clinical research centres, Canada.
Interventions/ Test/ Factor being investigated	Medication manager (MM), A little reminder (ALR), MM + ALR, or neither (control). MM participants received individualized, structured, long-term adherence support from trained MMs. ALR participants received individually programmed ALR alarms for use throughout the study. The medication manager (MM) intervention involved a trained research staff member who worked individually with study participants to provide tailored adherence support over time in a standardized protocol-guided manner, identifying and addressing each participant's information, motivation, and skills for ARV adherence using detailed questionnaires. This multifaceted intervention was based on health behavioral theory, including the information, motivation, and behavioral skills model of behavior change. The second intervention was the electronic medication reminder system. The study used a small portable alarm (A Little Reminder [ALR]; individually programmed to sound and flash at times of all ARV doses. The ALR addressed

	the most common reason for missed ARV doses reported at the time the study was developed, forgetfulness.
Comparisons	Between treatments.
Length of Study/ Follow-up	A median of 30 months.
Outcome measures studied	Virologic failure was the primary outcome. Secondary outcomes were: plasma HIV RNA level, CD4 cell count, adherence, ARV regimen changes, ARV resistance, grade 4 adverse events, and quality of life.
Results	The 928 participants, followed a median of 30 months, included 22% women and 75% nonwhites; the median baseline CD4 count was 155 cells/mm. First virologic failure was 13% lower in all MM versus no-MM groups (P = 0.13) and 28% lower in MM versus no-MM subgroups randomized to 2-class ARV arms in the parent ARV study (P = 0.01). MM (vs. no-MM) participants had significantly better CD4 cells count (P = 0.01) and adherence (P < 0.001) outcomes. Participants randomized to the MM intervention had a higher rate of reporting 100% adherence over time compared with participants randomized to a no-MM intervention (OR = 1.42; p<0.001). No significant differences were seen between the ALR and no-ALR groups for any long-term secondary endpoint, including proportion over time with an HIV RNA level ,50 copies/mL, log HIV RNA level over time, CD4 change over time, adherence, changes in ARV drugs, grade 4 adverse events, and quality of life.
Safety and adverse effects	None reported.
Does the study answer the question?	This large randomized clinical trial demonstrated that interpersonal structured adherence support was associated with improved long-term medication adherence and virologic and immunologic HIV outcomes.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Mills EJ;Nachega JB;Bangsberg DR;Singh S;Rachlis B;Wu P;Wilson K;Buchan I;Gill CJ;Cooper C;

Adherence to HAART: a systematic review of developed and developing nation patient-reported barriers and facilitators

Ref ID 8844 2006

Study Type Systematic Review **Funding** Ontario HIV treatment network

Number of participant	This analysis includes 37 qualitative studies and 47 surveys using structured questionnaires or structured interviews.
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	

Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Barriers identified in both economic settings (developed and developing world) included: fear of disclosure, concomitant substance abuse, forgetfulness, suspicions of treatment, regimens that are too complicated, number of pills required, decreased quality of life, work and family responsibilities, falling asleep and access to medication. Important facilitators reported by patients in developed nation settings included having a sense of self work, seeing positive effects of antiretrovirals, accepting their seropositivity, understanding the need for strict adherence, making use of reminder tools, and having a simple regimen.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Molina JM;Podsadecki TJ;Johnson MA;Wilkin A;Domingo P;Myers R;Hairrell JM;Rode RA;King MS;Hanna GJ;

A lopinavir/ritonavir-based once-daily regimen results in better compliance and is non-inferior to a twice-daily regimen through 96 weeks

Ref ID 17958 2007

Study Type	Randomised Controlled Trial	**Funding**	Supported by Abbott Laboratories.

Number of participant	196 patients met the eligibility criteria. Subjects were randomized (3:2) to LPV/r soft gelatin capsules 800/200 mg QD (n = 115) or 400/100 mg BID (n = 75). Subjects received TDF 300 mg and FTC 200 mg QD.
Inclusion/Exclusion Criteria	
Patient Characteristics	for theQD group 81% were male, whilst in the BID group there were 75%. Mean agewas 39.2 (11.1) for the QG group and 37.7 (9.0) in the BID group.
Recruitment	Not reported.
Setting	French Clinics.
Interventions/ Test/ Factor being investigated	LLPV/r soft gelatin capsules 800/200 mg QD (once-daily regimen) (n = 115) or 400/100 mg BID (twice daily regimen) (n = 75). All Subjects received TDF 300 mg and FTC 200 mg QD.
Comparisons	Between treatments.

Length of Study/ Follow-up	Up to 96 weeks.
Outcome measures studied	Adherence, antiviral, immunologic changes, viral drug resistance.
Results	A total of 190 antiretroviral-naive subjects with plasma HIV-1 RNA above 1000 copies/ml and any CD4(+) T cell count were enrolled. Adherence to LPV/r through 96 weeks was measured using MEMS((R)) monitors. Median baseline VL and CD4(+) T cell count were 4.8 log(10) copies/ml and 216 cells/mm(3), respectively. Prior to week 96, 37% (QD) and 39% (BID) of subjects discontinued, primarily due either to adverse events (17% QD, 9% BID) or to loss to follow-up or nonadherence (12% QD, 17% BID). The proportion of subjects with VL <50 copies/ml (57% QD, 53% BID; p = 0.582 (ITT NC = F)), change in CD4 count (244 cells/mm(3) QD, 264 cells/mm(3) BID; p = 0.513), and evolution of resistance did not differ between groups through 96 weeks. Diarrhea (17% QD, 5% BID, p = 0.014) was the most common moderate or severe, study drug-related adverse event.
Safety and adverse effects	11% of the QD patients discontinued and 3% in the BID due to gastrointestinal adverse events.
Does the study answer the question?	Adherence to LPV/r was higher for the QD group than the BID group and declined over time in both groups. Time to loss of virologic response was significantly associated with adherence to LPV /r in both groups. LPV/r QD resulted in virologic response similar to LPV/r BID through 96 weeks in antiretroviral-naive subjects. Adherence was significantly higher in the QD group
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Munro SA;Lewin SA;Smith HJ;Engel ME;Fretheim A;Volmink J;

Patient adherence to tuberculosis treatment: a systematic review of qualitative research

Ref ID 8845 2007

Study Type Systematic Review **Funding** Unknown

Number of participant	Qualitative
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	

Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Eight primary themes arose. 1. Organisation of treatment and care including access to care, treatment requirements and relationship with the provider 2. Interpretation of illness and wellness 3. Financial burden including impact on work, cost of treatment, general poverty 4. Knowledge attitudes and beliefs about treatment 5. Law and immigration 6. Personal characteristics and adherence behaviour including substance abuse, gender ,religion, motivation 7. Side effects 8. Family, community and household influence. The majority of the studies in this review were conducted in developing countries but the conclusions are similar in many ways to the Pound study.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Nazareth I;Burton A;Shulman S;Smith P;Haines A;Timberal H;

A pharmacy discharge plan for hospitalized elderly patients--a randomized controlled trial

Ref ID 7484 2001

Study Type	Randomised Controlled Trial	**Funding**	The National Health Service research and development programme.

Number of participant	362 patients, 181 to the intervention and control group.
Inclusion/Exclusion Criteria	Inclusion: over 75 years and taking four or more medicines at discharge and living in the hospitals catchment area. Exclusion: not speaking English or too ill.
Patient Characteristics	Mean age of participants 84 years in both intervention and control group (SD 5.2 and 5.4 respectively). 62% of intervention and 66% of control group were women. 97% were white. Each patient had a mean of three chronic medical conditions and on mean 6 drugs (SD=2).
Recruitment	Patients discharged from three acute general and one long-stay hospital in a health authority in central London.
Setting	Community pharmacists visited at home.
Interventions/ Test/ Factor being investigated	Pharmacist check for discrepancies with the medicine taken and those prescribed. Assessing understanding and adherence to the medication regimen and intervened when appropriate. Counselling patients/carers on correct dosage, disposing of excess medicines and liaising with gps.
Comparisons	Intervention vs control group - who were discharged with standard procedures - a discharge letter to the gp indicating the diagnosis, investigations and current medications, no pharmacist review of medication or follow-up.
Length of Study/ Follow-up	At 3 and 6 months.

Outcome measures studied	Primary outcomes: re-admission to hospital in follow-up period. Secondary outcomes: number of deaths, attendances at hospital outpatient clinics and gps. well-being, satisfaction with service, adherence to and knowledge of medication, hoarding of meds.
Results	There was no significant differences in any of the outcome scores except patient knowledge. There was no significant difference in the mean adherence scores of those re-admitted to hospital and the rest of the subjects at 3 and 6 months.
Safety and adverse effects	None
Does the study answer the question?	Yes. Adherence to medication did not increase from a pharmacy discharge intervention with elderly patients.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	Blinding

Portsmouth SD;Osorio J;McCormick K;Gazzard BG;Moyle GJ;

Better maintained adherence on switching from twice-daily to once-daily therapy for HIV: a 24-week randomized trial of treatment simplification using stavudine prolonged-release capsules

Ref ID 1216 2005

Study Type	Randomised Controlled Trial	**Funding**	The study was sponsored by Bristol-Myers Squibb (USA).

Number of participant	43 patients, 22 once daily (intervention) group, 21 in twice daily (control) group.
Inclusion/Exclusion Criteria	Inclusion: Participants were were included in the study if they were over 18 years of age and weighed over 40 kg. In women of childbearing potential, pregnancy was excluded and consent was obtained to ensure that they were willing to use two effective forms of contraception (including barrier contraception). Exclusion: Subjects were excluded if they had proven or suspected hepatitis, an active AIDS-defining disease, a history of bilateral peripheral neuropathy or signs of bilateral peripheral neuropathy of grade 2 or higher.
Patient Characteristics	Twice daily (control group): Male:18, female:, 3, Median age (years) (range): 45 (31–62), Number on d4T: 19, Number on Combivir: 2, Time on current regimen at baseline (months) (range): 24 (4–55), Baseline median CD4 count (cells/mL) (range): 457 (94–983), Viral load at screening (HIV-1 RNA copies/mL): All undetectable (< 50). Once daily (intervention group): Male: 21, female: 1, Median age (years) (range): 40 (23–56), Number on d4T: 18, Number on Combivir: 4, Time on current regimen at baseline (months) (range): 17 (5–53), Baseline median CD4 count (cells/mL) (range): 403 (111–1083), Viral load at screening (HIV-1 RNA copies/mL): All undetectable (<50). All participants had a viral load currently suppressed below the level of assay detection (o50 HIV-1 RNAcopies/mL; bDNA Chiron; Chiron Corporation, Emeryville, CA, USA). All participants had been receiving one of the following regimens for a minimum of 16 weeks: d4T IR bid13TC 150 mg bid1EFV 600 mg qd or ZDV 300 mg bid13TC (as Combivirs; Glaxo, Uxbridge, UK) 150 mg bid1EFV 600 mg qd.

Recruitment	Participants were recruited from a large central London clinic cohort.
Setting	Single center study.
Interventions/ Test/ Factor being investigated	Once daily group (intervention): the prolonged release capsule group (PRC) were assigned to take d4T PRC/3TC/EFV all once-daily (24 h apart). Twice daily (control group): participants in the control group were assigned to continue either d4T IR/3TC/EFV or Combivirs/EFV as per their screening regimen. Note: participant weighing less than 60 kg were prescribed either 30 mg of d4T IR or 75 mg of d4T PRC.
Comparisons	Intervention treatment v Control treatment.
Length of Study/ Follow-up	28 weeks (screened 4 weeks prior to randomization).
Outcome measures studied	Adherence: Measured via MEMS Cap. Information from MEMSs was downloaded at baseline, week 12 and week 24 visits. Quality of Life (measured at baseline, week 12, 24). Also measured: general clinical examination, viral load, full blood counts, SR.
Results	ADHERENCE: At baseline, adherence observed in the study population was high at 98.5% (range 96.3–100%). After randomization, patients allocated to the PRC (intervention) maintained this high adherence, while those allocated to IR (control) showed a significantly reduced adherence in 'taking compliance' (P=0.0237) (percentage of prescribed number of doses taken), 'correct dosing compliance' (P=0.0104) (percentage of days with correct number of doses taken) and 'timing compliance' (P=0.028) (percentage of doses taken within 3 hours of the prescribed dosing intervals) at both weeks 12 and 24. QOL: No significant differences between groups from basdeline to week 24. Both groups showed improvement in cognitive function at week 12 and 24 (P<0.001). In the intevention group at week 24, 90.4% of patients had viral loads of <50 copies compared with 86.4% of those in the control group; 100% in both groups has viral loads of <50 copies on the observed analysis. No patients on the intervention virological rebound during the course of follow-up. There were no significant changes in CD4 counts (cells/mL) during 24 weeks of follow-up. There were no significant differences in total cholesterol, LDL, amylase, g-GT or serum lactate measurements during the study. No patients had signs or symptoms of peripheral neuropathy at baseline and no patient developed neuropathy over 24 weeks of follow-up.
Safety and adverse effects	One patient in the control group opted to switch to an alternative NRTI because of a loss of subcutaneous fat. One patient in the control group left the study to switch therapy, and one patient experienced dizziness on switching to d4T PRC (intervention treatment) and opted to switch back to d4T IR (control treatment). There were no significant changes in CD4 counts (cells/mL) during 24 weeks of follow-up. There were no significant differences in total cholesterol, LDL, amylase, g-GT or serum lactate measurements during the study. No patients had signs or symptoms of peripheral neuropathy at baseline and no patient developed neuropathy over 24 weeks of follow-up.
Does the study answer the question?	Yes. Subjects switching from twice-daily therapy to once-daily therapy demonstrate less of a decline in adherence over 24 weeks. The once-daily regimen is as effective and tolerable as a regimen containing the twice-daily formulation.
Effect due to factor in study?	Fairly confident, however, as concealment and blinding issues are not mentioned in study these may have potentially been a source of bias.
Consistency of results with other studies?	
Directly applicable to guideline population?	Direct relevance.

Internal Validity Concealment and blinding are not addressed.

Rathbun RC;Farmer KC;Stephens JR;Lockhart SM;

Impact of an adherence clinic on behavioral outcomes and virologic response in treatment of HIV infection: a prospective, randomized, controlled pilot study

Ref ID 1289 2005

Study Type Randomised Controlled Trial

Funding The study was funded by a research grant from the Society of Infectious Diseases Pharmacists.

Number of participant 43 total sample. Intervention group: 22, standard care: 21.

Inclusion/Exclusion Criteria Inclusion/exclusion criteria: Patients with or without prior antiretroviral therapy exposure were eligible to participate. Antiretroviral therapy selection was made by the patient's primary care provider and consisted of >3 antiretroviral agents. Medication recycling of 1 to 2 nucleoside reverse-transcriptase inhibitors (NRTIs) in the new regimen was allowed, provided no evidence of resistance was present by genotypic or phenotypic testing or suspected based on treatment history. Patients receiving a QD drug regimen, a medication regimen containing 3 NRTIs, or a salvage regimen (defined as presence of resistance to >2 agents in the regimen), or who were currently participating in a pharmaceutical company-sponsored clinical trial, were excluded. Patients actively being followed in the adherence clinic were also not eligible.

Patient Characteristics Age, median, y: Intervention group: 38.0, Control group: 38.0. Sex, no. (%): female: Intervention group: 4 (25), Control group: 1 (6). Race, no. (%): White: Intervention group: 12 (75), Control group: 11 (65), Black: Intervention group: 2 (13), Control group: 5 (29). Hispanic: Intervention group: 2 (13), Control group: 1 (6). Patients assigned to the adherence clinic group had higher CD4 counts (median [SD], 296 [278] vs 104 [103] cells4~L in the standard care group; p = 0.008). No other significant differences between groups reported.

Recruitment

Setting An early intervention service HIV clinic.

Interventions/ Test/ Factor being investigated Provided by a clinical pharmacist. The adherence intervention for the adherence clinic group consisted of education about appropriate HAART administration, food restrictions, and adverse-event management strategies, and also included monitoring of patient progress after therapy initiation. Information provided to patients was tailored to the individual. Visual aids developed by the pharmaceutical industry and reminder devices were used to reinforce optimal administration timing. Patients were seen for a 1.0- to 1.5-hour visit at the initiation of HAART and a 30-minute follow-up visit after 2 weeks to assess adverse events and medication scheduling. Phone follow-up was typically conducted within 1 week of the baseline visit to identify early problems. Additional visits and phone follow-up were conducted through week 12 for patients who required more assistance. The adherence intervention in the standard care group consisted of education provided during the patients' office visits with their primary care providers.

Comparisons Adherence clinic group v standard care group. Intervention v control.

Length of Study/ Follow-up 28 weeks.

Outcome measures studied Adherence: Assessed via 2 means: Electronic monitoring with the eDEM Monitor in System was used to measure adherence to one antiretroviral agent in the regimen and a self report measure given at weeks 4, 16, 28.

Results Adherence: Mean (SD) adherence at weeks 4, 16, and 28 was 86% (27%), 77% (28%), and 74% (31%) in the adherence clinic group versus 73% (32%), 56% (39%), and 51% (41%) in the standard care group (week-16 difference, 21% [90% CI, 1%-42%]; week-28 difference, 23% [90% CI, 1%-44%]). The proportions of patients with adherence >90% and >95% at week 4 were 81% and 62% in the adherence clinic group and 47% and 41%, respectively, in the standard care group, but the

	differences did not reach statistical significance. The mean decline in adherence between weeks 4 and 28 for the adherence clinic group was 12% (p = 0.15), whereas the mean decline in the standard care group was 22% (p = 0.002). Sixty-nine percent of patients in the adherence clinic group took their medication on schedule versus 42% in the standard care group (p = 0.025); mean decline in adherence from weeks 4 to 28 was 12% in the adherence clinic group (p = 0.15) versus 22% in the standard care group (p = 0.002). This difference was also observed after 28 weeks, when the mean dose precision was 53% versus 31% in the adherence clinic and standard care groups, respectively (P = 0.046). SELF REPORT: Patients overestimated their adherence when compared with electronic monitoring results (91% by self-report vs 76% by electronic monitoring). No difference in the rate of adherence between the 2 groups was observed (94% vs 89% for the adherence clinic and standard care groups, respectively; P = 0.51). OTHER OUTCOMES: HIV-1 RNA levels were <400 copies/mL at weeks 4, 16, and 28 in 63%, 100%, and 94% of the adherence clinic group and 29% (p = NS), 71% (p = 0.04), and 65% (p = NS) of the standard care group. The proportion of patients with HIV-1 RNA <50 copies/mL was not significantly different between the two groups. The change in CD4 count was similar in both groups
Safety and adverse effects	None.
Does the study answer the question?	Yes. Participants in the intervention group were more adherent than those in control group, although this difference was not significant (but see small sample size).
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	

Rickles NM;Svarstad BL;Statz-Paynter JL;Taylor LV;Kobak KA;

Pharmacist telemonitoring of antidepressant use: effects on pharmacist-patient collaboration

Ref ID 1097 2005

Study Type	Randomised Controlled Trial	**Funding**	Sonderegger Research Center. National Service Research Service Award from Nation Institute of Mental Health.

Number of participant	Total sample: 63 patients. Intervention group: 31, Control group: 32.
Inclusion/Exclusion Criteria	Inclusion: patients were eligible if they had no antidepressant use in the past 4 months, were 18 or over, were willing to pick up their antidepressant from a study pharmacy during the next 4 months, had no hearing impairment and planned to be in the local area for the next 4 months. Exclusion: patients were excluded if they had a score below 16 on Beck Depression Inventory 2, required a translator, were pregnant or nursing, were receiving medication for psychotic or bi-polar disorder, and/or had physical conditions requiring additional caution with their anti-depressant.
Patient Characteristics	Gender: Male: Intervention group: 19.4% , Control group: 12.5%. Age (m, SD): Intervention group: 37.8 +/-10.7 , Control group: 37.5 +/- 13.4. Race: white: Intervention group: 87.1% Control group: 96.9%. other: Intervention group: 12.9% , Control group: 3.1%. Intervention group were more likely at baseline to have a history of psychotropic medication (p < 0.05.)
Recruitment	Patients presenting new antidepressant prescriptions in their community pharmacies

	were approached.
Setting	8 community pharmacies.
Interventions/ Test/ Factor being investigated	Intervention (PGEM) group. Received 3 monthly calls from the study pharmacist. 1st call: patients knowledge of medication and beliefs, adverse events, concerns, treatment goals were assessed as well as how patients had been using the medication up to the call. Pharmacists made recommendations about adverse events, ways to decrease non-adherence etc. Follow-up calls: adherence issues, adverse events and concerns addressed as well if patient felt they had been progressing towards treatment goals. New recommendations were made
Comparisons	Pharmacist guided education and monitoring (PGEM) (intervention) vs usual care. Intervention vs control.
Length of Study/ Follow-up	6 months.
Outcome measures studied	Adherence: Pharmacy records assessed at 3 and 6 months. Validated by comparing to patients prescription insurance claims and self-reported adherence (high correlations so only pharmacy refill data given).
Results	Adherence: There was not a significant difference between the study groups in terms of missed doses over the first three months of the study (intervention group: 18.1%, SD 23.5, control group: 18.7%, SD 22.1, p = NS). There was, however, a significant difference at six months with the rate of missed doses significantly lower in the intervention group (30.3%, SD 36.4 vs 48.6%, SD 39.2, p = < 0.05). Patient feedback to pharmacist (FPFP) scale: the mean total was significantly higher on this scale for the intervention group (22.7, SD 4.83) than the control group (10.9, SD 4.32) (p < .001). Cognitive outcomes: The intervention group scored higher on three cognitive outcomes: antidepressant knowledge (mean: 2.54, SD 0.74 vs 2.06, SD 0.93, p < 0.05), antidepressant belief scale (15.7, SD 2.84 vs 14, SD 2.32, p < 0.001) and orientation towards treatment progress (12.4, SD 2.50 vs 9.37, SD 3.22, p < 0.001). Clinical outcomes: The two groups did not differ significantly in terms of depressive symptoms. Both groups showed improvements over the first three month period (p < 0.001).
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention group were not significantly more adherent at three months but were at six months.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	

Ruskin PE;Silver-Aylaian M;Kling MA;Reed SA;Bradham DD;Hebel JR;Barrett D;Knowles F;Hauser P;

Treatment outcomes in depression: comparison of remote treatment through telepsychiatry to in-person treatment

Ref ID 1778 2004

Study Type	Randomised Controlled Trial	**Funding**	Not reported.
Number of participant	N=59 in the remote group, and n=60 in the in-person group.		

Inclusion/Exclusion Criteria	Inclusion criteria: if patients scored 16 or higher on the Hamilton depression scale and met the DSM-IV (SCID) criteria for one of the following five diagnoses: major depressive disorder, dysthymic disorder, adjustment disorder with depressed mood, mood disorder due to a general medical condition, or depressive disorder not otherwise specified. Exclusion criteria: if patients met the criteria for bipolar disorder or schizophrenia at any point in their lifetime or met the criteria for substance abuse or dependence within the past year. They were also excluded if they required hospitalization or if they had been receiving pharmacological treatment for depression for more than a month immediately before the initial visit.
Patient Characteristics	The mean age of the participants was 49.7 years (SD=12.8). Thirty-six percent were African American, 61% were Caucasian, and 3% were Hispanic or Asian. Fifty percent had more than 12 years of education, 33% were high school graduates, and 17% had less than 12 years of education. Thirty-nine percent were employed full-time, 19% were employed part-time, 13% were unemployed, and 30% were retired or receiving disability.
Recruitment	By being referred to any of three mental health clinics within the Department of Veteran Affairs.
Setting	Mental Health Clinic. USA.
Interventions/ Test/ Factor being investigated	To compare patients being seen by a psychiatrist either in person or by means of telepsychiatry ("remote treatment"). Treatment consisted of eight sessions with a psychiatrist over a 6-month period. The first session occurred immediately after the initial assessment by the research assistant. At this session, the psychiatrist conducted his or her own clinical evaluation. Treatment sessions lasted approximately 20 minutes and consisted of antidepressant medication management, psycho-education, and brief supportive counselling. At each visit, the patient also had a separate meeting with a research assistant during which the patient participated in an interview and completed the self-report measures described in the next section. Subjects were paid $5 per visit for their participation
Comparisons	Between treatments.
Length of Study/ Follow-up	Up to 6 months
Outcome measures studied	Treatment response, treatment adherence, patient satisfaction, psychiatrist satisfaction, and resource consumption or "cost effects."
Results	Medication adherence data were available for 73 subjects. Patients were excluded from this analysis if they had fewer than three visits with complete medication counts. Patients who took at least 70% of the pills they were expected to take were considered adherent, and the others were considered non-adherent. There was no difference in the percentage of adherent patients between the two treatment groups (n.s.). There was no difference in patient satisfaction between the remote and in-person groups at visit 4 (n.s.), visit 6 (n.s.), or visit 8 (n.s.). Patients' depressive symptoms, as measured by the 24-item Hamilton depression scale, significantly improved over the treatment period ($p<0.001$), and improvement did not differ by treatment group (ns.).
Safety and adverse effects	None reported.
Does the study answer the question?	Remote treatment of depression by means of telepsychiatry and in-person treatment of depression have comparable outcomes and equivalent levels of patient adherence, patient satisfaction, and health care cost.
Effect due to factor in study?	Relative certainty.
Consistency of results with other studies?	Unknown.

Directly applicable to guideline population?	Relevant study
Internal Validity	Not blinded study.

Schroeder K;Fahey T;Ebrahim S;

How Can We Improve Adherence to Blood Pressure-Lowering Medication in Ambulatory Care? Systematic Review of Randomized Controlled Trials

Ref ID 1479 2004

Study Type Systematic Review **Funding** NHS R&D fund, Bristol

Number of participant	RCT
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Simplifying dosing regimens improved adherence in 7 of 9 studies with relative improvement in adherence increasing by 8% to 19.6%. All of the studies that used objective outcome measurement (Medication Event Monitoring System) showed an improvement in adherence through the use of once daily instead of twice daily dosing regimens, although 4 of these compared 2 different drugs. Only 1 study showed an increase in adherence (905 vs 82%;p<.01) together with a reduction in systolic blood pressure o 6 mm Hg (p<.01). Methodological quality of the studies reviewed was problematic in this review.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Segador J;Gil-Guillen VF;Orozco D;Quirce F;Carratala MC;Fernandez-Parker A;Merino J;

The effect of written information on adherence to antibiotic treatment in acute sore throat

Ref ID 1104 2005

Study Type Randomised Controlled Trial **Funding** None reported.

Number of participant	Intervention group n=79; control group n=79.
Inclusion/Exclusion Criteria	Inclusion criteria: over 18 years of age; presenting to the GP because of sore throat for less than 7 days and at least three of the four centre criteria (history of fever, absence of cough, swollen tender anterior cervical nodes and tonsillar exudates); ability to read and write correctly; ability to understand the verbal instructions given; and on the panel of a GP taking part in the research. Exclusion criteria: refusal of treatment; mental or social problems that could prevent the patient from complying with treatment; illiteracy or cognitive deficiency; allergy to the drugs prescribed in the protocol; refusal to take part in the research; pregnancy, breastfeeding or any illness that ay affect short-term prognosis; and not fulfilling any of the inclusion criteria.
Patient Characteristics	Both groups were similar in age, sex (39.3% male in the intervention group vs. 49.3% in the control group, p= 0.2) and antibiotic treatment, penicillin or erythromycin (p= 1).
Recruitment	From GP practice.
Setting	GP practice. Spain.
Interventions/ Test/ Factor being investigated	To give written information at the time of the first visit. The written information emphasised the importance of completing the antibiotic treatment, of respecting intervals between doses and the drawbacks of an early drop-out, and was given only at the time of initial consultation. The control group was given verbal information only.
Comparisons	Between treatments.
Length of Study/ Follow-up	9-12 days after first GP visit.
Outcome measures studied	Adherence.
Results	The pill count average was 87.4+/-25.2% and it was higher in the intervention group (93.7+/-24.5%) than in the control group (81.1+/-24.5%) (P < 0.05). Absolute risk reduction was 14% (95% confidence interval (CI), -3.77 to 26.56); relative risk reduction was 24.9% (95% CI, -11.04 to 58.28). Drop out rate was higher in the control group (p= 0.0001) due to improvements or resolution of symptoms.
Safety and adverse effects	None reported.
Does the study answer the question?	Written instructions, in addition to verbal ones, significantly improve compliance with antibiotic treatment in tonsillitis of acute sore throat in comparison with verbal instructions only.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant study.
Internal Validity	Not blinded study.

Shi, L., Hudges, M., Yurgin, N., Boye, K.S.

Impact of dose frequency on compliance and health outcomes: a literature review (1966-2006)

Ref ID 8865 2007

Study Type	Systematic Review	**Funding**	Eli Lilly and Company.

Number of participant	RCT and prospective observational studies.
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Looked at the impact of dose frequency on compliance and health outcomes, particularly for injectables. Of the 21 studies that measured compliance, 17 reported a positive impact of reducing dose frequency on compliance, whilst inconclusive results were seen in four. Details of the dose frequency reductions contained in the studies were not provided by the review. Articles not measuring compliance as the main outcome looked at efficacy and other outcomes of extended-release medications in comparison to the immediate-release forms. The studies also supported the general benefits of reducing dosing frequency on improved quality of life or patients satisfaction (6 studies), greater control over side effects (5 studies) and improved economic outcomes using extended-release formulation (2 studies).
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Sturgess IK;McElnay JC;Hughes CM;Crealey G;

Community pharmacy based provision of pharmaceutical care to older patients

Ref ID 2488 2003

Study Type	Randomised Controlled Trial	**Funding**	Supported by (no details of type of support given) Northern Pharmacies Trust, Northern Ireland and

	European Commission under the BIOMED 2 programme.
Number of participant	Total sample: 191 patients. Intervention group: 110, Control group: 81.
Inclusion/Exclusion Criteria	Inclusion: elderly patients (? 65 years) who were community dwelling, taking four or more prescribed medications, regular visitors to the participating community pharmacy and orientated to self, time and place were eligible. Exclusion: Patients were excluded if they were housebound or living in a nursing/residential home.
Patient Characteristics	Age (years): intervention group: 73.1 ± 5.0, control group: 74.2 ± 6.3. Gender (% male/% females): intervention group: 36.4/63.6, control group: 39.0/61.0. There were some differences between the two groups at baseline in mean number of prescribed medications (higher in control group, p = 0.05) and SF-36 domains of mental health (intervention group higher score, p = 0.05), physical functioning (intervention group higher score, p = 0.05) and vitality (intervention group higher score, p = 0.05).
Recruitment	
Setting	10 pharmacies in Northern Ireland.
Interventions/ Test/ Factor being investigated	Note: Only half of the sites saw the project through to completion (3 intervention (from five randomised to deliver intervention) and 2 control (also form 5 original)). Delivered by community pharmacists. Intervention pharmacists assessed patients to identify drug-related problems. A number of information sources were used by intervention pharmacists during this assessment procedure including: the patient (via informal questioning), the patient's GP, study questionnaires and computerised medication records. During the assessment, pharmacists were asked to document any identified drug-related problems and to form with the patient an intervention and monitoring plan e.g. education, implementation of adherence improving strategies. Pharmacists visited patients at home to assess storage of medi0cines where problems were identified.
Comparisons	Pharmaceutical care programme (PCP) (intervention) v usual care. Intervention vs Control.
Length of Study/ Follow-up	18 months.
Outcome measures studied	Precise Items used to measure adherence not given (given in a separate publication) although self report scale and refill compliance rates are reported in the analysis. All measurements taken at 6, 12 and 18 months.
Results	Adherence: Self reported compliance: between-group analysis at each assessment point indicated that a significantly higher proportion of intervention patients were compliant with their medicine at 12 (intervention group: 40.4% , control group: 24.4%) and 18 (intervention group: 47.3%, control group: 14.7%) months compared to control patients (p < 0.05) (6 months: intervention group: 34.5%, control group: 29.4%). Analysis of change in compliance during the study (change in compliance status compared to that reported at baseline) showed that a significantly higher proportion of intervention patients changed from non-compliant to compliant compared to control patients (intervention 13.4% vs control 9.1%) and a significantly higher proportion of control patients changed from compliant to non-compliant compared to intervention patients at 18 months (control 36.4% vs intervention 4.5%). Refill compliance results: between-group analysis at each assessment point indicated that a significantly higher proportion of intervention patients were compliant with their medicines at six months (intervention group: 46.2%, control group: 19.1%) compared to control patients (p = 0.02) (results 12 months: intervention group: 40.4%, control group: 25.0%. 18 months: intervention group: 40.0%, control group: 40.6%). Analysis of change in compliance during the study (change in compliance status compared to that reported at baseline) showed no differences between control and intervention patients. Other outcomes: Health related quality of life: During the study there was a trend for intervention patients' quality of life to decline over the 18 months whilst that of control patients appeared to significantly improve in some of the SF-36 dimensions (physical

	functioning: intervention group change: ?6.83, control group: +7.14 and vitality, intervention group change: ?2.26, control group: +7.24, $p < 0.05$), however, these findings were largely driven by patients attending one control site pharmacy who showed marked improvements in SF-36 scores over time. There was no significant difference between the two groups in terms of the number of hospitalizations, the extent of prescription drug use (after baseline) and knowledge about medications. Longitudinal analysis indicated that intervention patients were taking significantly more prescribed medicines at 6 (6.13, +/- 2.32), 12 (6.63, =/- 2.72) and 18 months (6.20, +/-2.32) compared to baseline (5.87, =/-1.86; $P < 0.05$), whilst that of control patients remained constant. Problems with medications: There were no significant differences between control and intervention patients during the first 12 months of the study, however, during the last 6 months, intervention patients (0.90, =/- 1.27) reported significantly fewer problems with their medicines compared to control patients (2.09, =/-2.38) ($p < 0.05$). There were no differences between the two groups in their reported contact with nurses, however, there were differences in GP contacts and contact with a specialist during the study. Intervention patients reported higher numbers of contacts with their GP during the first (0–6) (2.89, ±4.44) and second (7–12) (2.97, ±2.56) six month periods than control patients (0-6: 1.88, ±2.55. 6-12: 1.97, ±4.25) ($p < 0.05$). In addition, intervention patients reported more contact with a specialist during the second (7–12) (0.89, ±1.25) and third (13–18) (0.87, ±2.60) six-monthly periods compared to control patients (7-12: 0.16, 0.50. 13-18: 0.10, ±0.31) ($p < 0.05$).
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention helped to increase adherence according to the majority of analysis undertaken.
Effect due to factor in study?	Fairly. Baseline differences between groups a potential confounding factor.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	

Urien AM;Guillen VF;Beltran DO;Pinzotas CL;Perez ER;Arocena MO;Sanchez JM;

Telephonic back-up improves antibiotic compliance in acute tonsillitis/pharyngitis

Ref ID 2084 2004

Study Type Randomised Controlled Trial **Funding** Not stated.

Number of participant	64 patients in each group (intervention and control).
Inclusion/Exclusion Criteria	To be over 18 years, diagnosed as having tonsilitis/pharyngitis of possible bacterial aetiology, antibiotic treatment required according to medical criteria, to be on the phone and to have patient's oral agreement. Exclusion criteria: to have mental illness, to have started antibiotic treatment before consulting a doctor, refusal of treatment, pregnancy or breast feeding, allergy to the antibiotic chosen for the protocol, living with patients who had already taken part in the study and belonging to any group that according to the doctors opinion would make monitoring difficult.
Patient Characteristics	No significant differences for any variable.
Recruitment	By consecutive sampling via on-demand visits to the Health Centre.
Setting	Health Care Centre. Spain.

Interventions/ Test/ Factor being investigated	Intervention group was given mixed strategy and the control group only had thorough educational advice by detailed and appropriate verbal instructions to make diagnosis and prognosis understood. The control group was taught how to comply with treatment: duration, and frequency and time of dosage to avoid the risk of relapse, complications or bacterial resistance. The telephone call was undertaken on the 4th day after the start of treatment, when the first box of antibiotic should be finished. The patient was advised to continue the treatment according to the dosage and number of days that had been prescribed. The patient was also reminded that although he or she may feel better or even cured, the treatment was to be continued for 10 days. The criterion for evaluating the compliance was to count the tablets in a spot check at the patient's house. A tablet count of 80–110% defined good compliance.
Comparisons	Between treatments.
Length of Study/ Follow-up	Not clear but seems to be up to 10 days after beginning treatment.
Outcome measures studied	Adherence, clinical improvement.
Results	A good compliance percentage was 66.1% (57.7–74.5%) and was significantly higher in the intervention group (78.3%) than in the control group (54.1%) (P=0.005). Most frequent reasons for discontinuation alleged were clinical improvement (33.3%), oversight (24.2%) and side effects (18.2). Patients from both groups gave similar reactions (p= 0.304). Seventeen non-compliant patients who did not recognise any reason for their non-compliance were found. There were no differences between the two groups in terms of clinical improvement (p= 0.567).
Safety and adverse effects	None reported.
Does the study answer the question?	In conclusion telephonic back-up significantly improved the compliance obtained by educational strategy only. It should be used in clinical practice.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	Consistent.
Directly applicable to guideline population?	Relevant study.
Internal Validity	Single-blinded study.

Weber R;Christen L;Christen S;Tschopp S;Znoj H;Schneider C;Schmitt J;Opravil M;Gunthard HF;Ledergerber B;Swiss HIVC;

Effect of individual cognitive behaviour intervention on adherence to antiretroviral therapy: prospective randomized trial

Ref ID 2064 2004

Study Type	Randomised Controlled Trial	**Funding**	Swiss National Science Foundation. Equipment usage supported by a grant from GlaxoSmithKline, Switzerland.

Number of participant	60 patients total. CBT group = 32, 28 = control group.

Inclusion/Exclusion Criteria	Inclusion: therapy containing a combination of at least three antiviral drugs of at least two different drug classes, viral load below 50 copies/ml documented within the previous 3 months at a screening visit, participation in the Swiss HIV cohort study, no intravenous drug use or on stable methadone maintenance in the case of drug addiction.
Patient Characteristics	Number of female: CBT group: 25%, Control 7.1%. Median age: CBT group: 41.5 (24-71), Control group: 40.2 (25-65). No significant differences between groups on any demographic, disease status, treatment or psychosocial measurements.
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	Individual CBT: Delivered by 10 different licensed psychotherapists in private practice trained in CBT and who had attended a lecture on antiretroviral therapy. No fixed number of sessions but a minimum of 3 and max of 25 over a 1 year period. Individuals were told the focus of sessions would be focused on adherence rather than on any psychological problems. Psychotherapists where told to define with the client at least two goals for future interventions, at least one of which had to address medication adherence, although the therapists/participants could also define other goals (details of intervention poorly defined).
Comparisons	Individual cognitive behavioral therapy (CBT) and standard care v standard care alone. Intervention v control.
Length of Study/ Follow-up	1 year.
Outcome measures studied	Adherence: Assessed using the electronic medication exposure monitoring system. Measurements of 1st month used as baseline values. Adherence also assessed through a 10 point self report measure. Clinical, psychosocial assessments also taken.
Results	Adherence: (Note S.D's not given). Adherence at baseline (1 month) was not different between the study arms using either MEM's or self report. During the trial mean medication adherence as assessed by MEMs remained stable in the CBT group (month 1, 94.3% v month 10-12, 92.8%, with average individual slopes of -3% per year (p = 0.14). During the trial mean medication adherence as assessed by MEMs remained decreased in the control group (month 1, 94.3% v month 10-12, 88.9%, with average individual slopes of -8.7% per year (p = 0.006). There was no significant difference between the slopes of the two groups however (p = 0.15). The difference between the proportion of patients with -/+ 95% adherence at month 10-12 was 70.8% for CBT group and 50 % in control group (p =0.014). For self reported adherence the intervention arm were significantly more adherent than the control arm at follow-up (9.93 v 9.80, p = 0.012). Other outcomes: Psychosocial measures: The coping with disease scale, the health locus of control scale and the self-reported symptom inventory showed no differences between groups at any period in the study. There were significant differences between groups in participants perceptions of their mental state and behaviour with the CBT group showing more prominent perceptions. VIROLOGICAL AND IMMUNOLOGICAL OUTCOMES: Only 3 patients had a viral load of 50 copies ml at month 12, one in CBT group 2 in control group. In both groups nine patients had intermittently a viral load of 50 copies/ml, which mostly returned to normal levels at the next measurement. The probability of developing a viral rebound after the trial was similar in both groups.
Safety and adverse effects	
Does the study answer the question?	Yes. CBT helps t increase adherence compared to usual treatment in patients with HIV when adherence is defined as above or equal to 95% adherence (the level of adherence estimated if antiretroviral medication is to be effacious).
Effect due to factor in study?	Fairly. No mention of blinding, no intention to teat analysis performed.
Consistency of results with other studies?	

Directly applicable to guideline population? Relevant.

Internal Validity

Wyatt GE;Longshore D;Chin D;Carmona JV;Loeb TB;Myers HF;Warda U;Liu H;Rivkin I;

The efficacy of an integrated risk reduction intervention for HIV-positive women with child sexual abuse histories

Ref ID 1486 2004

Study Type Randomised Controlled Trial **Funding** National Institute of Mental Health, Office on AIDS.

Number of participant	147. 80 to the attention control condition and 67 to the enhanced sexual health intervention (ESHI).
Inclusion/Exclusion Criteria	Inclusion: female, 18 or older, HIV+, sexually active in the past year, history of childhood sexual abuse, self-identified as African American, Latina, or European American.
Patient Characteristics	Average age 41*, all female, 79 African American, 9 European American and 59 Latinas. On average had been living with HIV for 7 years, and 13% were diagnosed with AIDS. Community and hospital based. Discrepancy reported for mean age 39/41?.
Recruitment	From county and community-based clinics, county hospitals, ethnic and AIDS-specific organisations and drug rehabilitation centers.
Setting	Los Angeles.
Interventions/ Test/ Factor being investigated	The Enhanced Sexual Health Intervention, a cognitive-behavioural approach to risk reduction with cultural and gender specific concepts.
Comparisons	Comparison between ESHI intervention and the attention control condition, which was a one-time group meeting where they received HIV prevention and child sexual abuse information and pamphlets.
Length of Study/ Follow-up	They were post tested at the end of the 11-week intervention and followed up at 3 and 6 months. End of follow-up with death or drop-out.
Outcome measures studied	Primary outcome was sexual risk reduction. Secondary outcome was HIV treatment adherence.
Results	Sexual risk reduction: Higher in the ESHI group (63.6%) than in the attention control group (56.8%), ESHI: OR=2.96, p=0.039, one-tailed. When adjusted for covariates ESHI group risk reduction was 74.5% compared to 50.4% in attention control group. Medication adherence: Adherence was roughly equal between the groups (75.6% in intervention and 73.3% of controls). No evidence of effect of ESHI: OR=1.13, p=0.41, one-tailed. There was a significant effect for adherence for those who were high attendees in the ESHI group: OR=4.09, p=0.044, one-tailed. Medication adherence was higher in those who attended at least eight sessions (91.3%) compared to seven or fewer (49.7%). High attendees in the ESHI group 74.7% compared to the control group 91.3%.
Safety and adverse effects	Wait list for control subjects to receive the intervention at after the trial for ethical considerations for those with mental health, HIV and trauma-related symptoms.
Does the study answer the question?	Yes the study does assess whether this intervention had an impact on adherence rates, which it did not unless they were high attendees of the intervention. So possible dose-effect relationship.

Effect due to factor in study?	Yes. But is suggested that study should be increased in sample size and for diversity of ethnicity.
Consistency of results with other studies?	
Directly applicable to guideline population?	Intervention very specific - enhanced sexual health intervention, but is based on the cognitive-behavioural approach. Population women only.
Internal Validity	Self-reporting; concealment; blinding;

Zermansky AG;Petty DR;Raynor DK;Lowe CJ;Freemantle N;Vail A;

Clinical medication review by a pharmacist of patients on repeat prescriptions in general practice: A randomised controlled trial

Ref ID 7544 2002

Study Type Randomised Controlled Trial **Funding** Health Technology Assessment Programme.

Number of participant	1188 in total. 608 in the intervention group, 590 in the control group.
Inclusion/Exclusion Criteria	Inclusion: 65 years or older on repeat medication. Exclusion: in a clinical trial, a residential or nursing home or having a terminal illness.
Patient Characteristics	Data not found for ethnicity but the study was mainly a Caucasian population born in the UK.
Recruitment	A note was attached to their last prescription before their due date. This said to book an appointment with the practice receptionist.
Setting	Leeds g.p practices with 4 or more partners.
Interventions/ Test/ Factor being investigated	Pharmacist medication review to make recommendations on medication changes.
Comparisons	Between intervention and control group.
Length of Study/ Follow-up	12 months.
Outcome measures studied	Primary outcome - number of repeat medication changes for each patient. Secondary outcomes - effect on the medication costs; whether medication review taken place (Intervention group vs control group).
Results	The mean number of individual medication changes per patient were 2.2 intervention group vs 1.9 in control group (0.31, 95% CI, 0.06 to 0.57, p=0.02. The number of repeat items rose in both groups but was significantly less for intervention group (0.2 mean, SD 1.55), control (0.4, SD 1.53, difference -0.2, 95% CI, -0.4 to -0.1). Medication costs rose in both groups but the rise was significantly less in the intervention group £1.80 mean compared to £6.53 mean for control group, difference was £4.75 per 28-day month. Saving of £61.75 per patient per year. 97% of intervention group had medication reviews compared with 44% of the control group. The most common recommendations was to stop the medicine or removal of a redundant item from a list.
Safety and adverse effects	None.

Does the study answer the question?	It helps answer about the effectiveness of medication review but adherence is not a main outcome measured. Therefore it will be included in the introduction for medication review but not as an evidence narrative on medication review increasing adherence.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Intervention very relevant for guideline.
Internal Validity	

Grading: 1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*

Bangalore S;Kamalakkannan G;Parkar S;Messerli FH;

Fixed-dose combinations improve medication compliance: a meta- analysis

Ref ID 1682 2007

Study Type Metaananalysis **Funding** Unknown

Number of participant RCTs and retrospective reviews of data bases

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question? A total of 11,925 patients on fixed dose combination were compared against 8317 patients on free drug component regimen. Fixed dose combination resulted in a 26% decrease in the risk of non compliance compared with free drug component regimen (pooled RR 0.74 [CI 0.69-0.80]; p<0.0001). There was no evidence of heterogeneity in this analysis (p=.07). A subgroup analysis of the four studies on hypertension showed that fixed dose combination (pooled RR 0.76 [CI 0.71-0.81]; p<0.0001).decreased the risk of medication non-compliance by 24% compared with free drug combination regimens.

The results of this study should be viewed with caution due to methodological issues noted above.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Chisholm MA;Mulloy LL;Jagadeesan M;DiPiro JT;

Ref ID 61 2001

Study Type	Randomised Controlled Trial	**Funding**	Supported by a grant from the Carlos and Marguerite Mason Trust Fund.

Number of participant	24 total sample. Intervention group: 12, control group: 12.
Inclusion/Exclusion Criteria	Inclusion: patients must have been between the ages of 18 and 60 yr, received only one kidney transplant, received follow-up care at MCG for at least 1 yr post-transplantation, prescribed the same immunosuppressant medication for at least 1 yr post-transplantation, and received their immunosuppressant medications from the MCG Outpatient Pharmacy for the entire first year post-transplantation.
Patient Characteristics	Separate group analysis not given. The mean age in years of the patients was 49.2 +/- 10.2. The patient population consisted of 18 males (75%), 6 females (25%), 14 Caucasians (58.3%), 9 African–Americans (37.5%), and 1 Hispanic (4.2%).
Recruitment	
Setting	A tertiary care teaching facility.
Interventions/ Test/ Factor being investigated	Clinical pharmacy services (CPS) Intervention: Delivered by clinical pharmacists. Included the pharmacist taking medication histories and reviewing (at least once monthly) patients' medications with an emphasis on optimizing medication therapy to achieve compliance outcomes while minimizing adverse events related to medication. The clinical pharmacist also provided recommendations to the nephrologists with the goal of achieving desired outcomes. Counselling involved discussions of patients concerns around their medication therapy and instructing them how to properly take their medications. Counselling was both verbal and/or in writing emphasizing the importance of compliance, when and how to take medications, and the correct dose/number of tablets. Participants could contact the pharmacist via phone if necessary.
Comparisons	Clinical Pharmacy Services (CPS) + routine care vs routine care. Intervention v control.
Length of Study/ Follow-up	12 months.
Outcome measures studied	Compliance was estimated by comparing patients' monthly pharmacy refill records to the prescribed regimen documented in the patients' medical records. Immunosuppressive serum concentrations were measured to confirm compliance.
Results	A Compliance rate (CR) of 80% was used as a minimum threshold for a patient to be classed as compliant. Adherence: At the end of 1 yr post-transplant, the mean CR of 96.1 +/- 4.7% for patients who had clinical pharmacist intervention was statistically higher than the mean CR of 81.6 +/-11.5% for patients who did not have clinical pharmacist involvement ($p = 0.001$). For 6 of the 12 months post-transplant (months 6–8 and 10–12 post-transplant) there were differences between CRs between the intervention and control groups, with higher rates in the intervention group ($p = 0.05$). There was a significant difference in the duration of compliance between the groups ($p < 0.05$). At 12 months post transplant, 75% of the intervention patients remained complaint each month since transplant, whereas 33.3% (n=4) of the control patients remained compliant. The mean time to the first non-compliant month was 11 months for the intervention group, with a 95% confidence interval (CI) of 10–12 months. The mean time to the first non-compliant month was 9 months for the control group, with a 95% CI of 7–11 months. Other outcomes: Intervention patients (64% of levels classed as being in 'target' range) had a greater achievement of 'target' serum concentrations than control patients (48%) ($p = 0.05$).
Safety and adverse effects	None.

Does the study answer the question?	Yes. The Clinical pharmacy services (CPS) Intervention significantly improved adherence.
Effect due to factor in study?	Study has potential problems with internal validity which may have effected outcome (see above).
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.

Internal Validity

Chisholm MA;Mulloy LL;Jagadeesan M;DiPiro JT;

Impact of clinical pharmacy services on renal transplant patients' compliance with immunosuppressive medications

Ref ID 61 2001

Study Type	Randomised Controlled Trial	**Funding**	Grant from the Carlose and Marguerite Mason Trust Fund.

Number of participant	24 in total. 12 in the intervention group and 12 in the control group.
Inclusion/Exclusion Criteria	Inclusion criteria: Aged 18 to 60 years; had only one kidney transplant; received follow-up care at MCG for at least one year after transplant; prescribed same immunosuppressant for at least one years since transplant; received immunosuppressant from MCG Outpatient Pharmacy for whole year.
Patient Characteristics	75% were male, and 58.3% Caucasian, 37.5% African-American and 1 Hispanic. 33% had living-related donor kidneys, 67% had cadaveric kidneys. The mean age was 49 (SD 10.2). Twenty one of patients prescribed cyclosporine and the other 3 had tacrolimus.
Recruitment	All patients who had a renal transplant at MCG from February 1997 to January 1999.
Setting	Medical College of Georgia Hospital and Clinics
Interventions/ Test/ Factor being investigated	In addition to usual care, patients received direct patient care clinical services from a clinical pharmacist. They obtained medication histories and reviewed medications with emphasis on optimising medication therapy to achieve desired outcomes and to minimse adverse events. They also made recommendations to the nephrologists to get the desired outcomes. The pharmacists counselled patients on ther medication and instructed how to take correctly (verbally and/or in writing). The patients were encouraged to call the pharmacist with any questions or concerns. The patients understanding of their medication was assessed. The medication reviews and histories were conducted monthly for the intervention group. Compliance enhancement principles were used at visits or by phone.
Comparisons	Between the intervention group and the control group who received usual care but had no clinical pharmacist interaction.
Length of Study/ Follow-up	12 months.
Outcome measures studied	Compliance rate, directly observed by immunosuppressive serum concentrations.
Results	At end of 12 months the mean compliance rate was 96.1% (+/- 4.7%) for the intervention group and 81.6% (+/-11.5%) for control group, p<0.001 statistically significant. For 6 of the 12 months 6-8 and 10-12) there were differences in compliance rates (64-100% for control group and 89 to 100% for intervention group) always with the intervention group higher rates (p<0.05). Duration of compliance differed also, with the intervention group remaining 75%

compliant each month whereas only 33.3% of the control group remained compliant ($p<0.05$).

Intervention patients had a greater achievement of 'target' serum concentrations than control patients ($p<0.05$).

Safety and adverse effects Not mentioned.

Does the study answer the question? Yes. Patients who received clinical pharmacy services along with routine traditional patient care services had better immunosuppressive compliance than patients who only received traditional patient care services. The mean compliance rate for intervention was higher than the mean for the control group. Those in the intervention achieved higher achievement of the target immunosuppressive serum concentrations than the control group.

The pharmacist intervention is beneficial for enhancing medication compliance in post-transplant patients.

Effect due to factor in study? The study was very small, with only 24 participants and the methodology was not very strong so it can not be certain that the effect is due to the study intervention. Although all measurements were consistently higher for the intervention than the control group.

Consistency of results with other studies?

Directly applicable to guideline population? Not only medication review but includes a counselling, compliance-enhancing techniques. Not generic medication review.

Internal Validity Selection bias; performance bias; small sample;

Claxton AJ;Cramer J;Pierce C;

A systematic review of the associations between dose regimens and medication compliance

Ref ID 1542 2001

Study Type Systematic Review **Funding** Eli Lilly

Number of participant Study types were not described

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

This review of 76 studies that used gold-standard electronic monitoring devices demonstrated that patients take about 51% to 79% of doses daily as prescribed across a wide range of therapeutic areas. Compliance was inversely related to the number of doses per day. Mean dose taking compliance was 71% (34%-97% range), and declined as the number of daily doses increased: 1 dose = 79% +/- 14%, 2 doses=69% +/-, 3 doses = 65% +/- 16%, 4 doses = 51% +/- 20%. Compliance was significantly higher for once-daily versus 3 times daily (p=0.008), once daily versus 4 times daily (p=0.001) and twice daily versus 4 times daily regimens (p=0.001). However there were no significant differences in compliance between once daily and twice daily regimens or between twice daily and three times daily regimens. In the subset of 14 studies that reported dose timing results, mean dose timing compliance was 59% +/- 24%; more frequent dosing was associated with lower compliance rates.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Finley PR;Rens HR;Pont JT;Gess SL;Louie C;Bull SA;Lee JY;Bero LA

Impact of a collaborative care model on depression in a primary care setting: a randomized controlled trial

Ref ID 2521 2003

Study Type Randomised Controlled Trial **Funding** Not reported.

Number of participant N= 75 patients, intervention group and usual care group n= 50 patients. Mean age in control group: 54.1 ± 17.3 (SD) and in intervention group: 54.4 ± 14.1 (SD).

Inclusion/Exclusion Criteria All patients were members of the health maintenance organization (HMO) who were receiving primary care services and who had started antidepressant therapy. Exclusion criteria: evidence that subjects had received an antidepressant during the preceding 6 months; concurrent psychiatric or psychological treatment; current symptoms of mania or bipolar disorder; psychotic symptoms; eminent suicidal tendencies; and active substance abuse or dependence.

Patient Characteristics Mainly female patients (85% intervention, 84% control groups)

Recruitment Through the HMO.

Setting Primary care setting. USA.

Interventions/ Test/ Factor being investigated Subjects who returned study surveys were mailed a $20 cheque as reimbursement for participation.
Intervention group: An intake interview that lasted 30 minutes was conducted after randomization, in which care managers assessed the severity of psychopathology, identified potential stressors and other predisposing factors. Medical, psychiatric and drug histories were recorded. Symptoms, aetiology, and prognosis of depression were discussed, and a detailed explanation of the role of antidepressants was presented (including potential therapeutic effects and adverse effects). Patients were also advised of other treatment options and resources available at the centre. Care managers were permitted to titrate antidepressant drugs in a fashion consistent with the HMO-s clinical guidelines and current recommended practices. After the initial interview, the intervention group were scheduled for frequent follow-up phone calls and clinic appointments. Phone calls lasted 5-10 minutes and during these calls, pharmacists followed a standardized set of questions that assessed drugs

	adherence, therapeutic effects, adverse effects, and other social or medical factors. Documentation of all patient contacts was entered into the official medical record in the form of a detailed progress note. Adherence was determined from the HMO's computerized prescription refill records. Measurement of drug adherence was expressed as a medication possession ratio (MPR). The MPR was defined as the number of day's supply of drug that the patient received during the 6 month study period, including the quantity and strength of drug as well as prescribing directions. Usual care: subjects received brief counselling on the prescribed drug, therapeutic end points, and side effects in a manner consistent with patient education routinely delivered to members receiving prescriptions form the HMO's outpatient pharmacy.
Comparisons	Between treatments.
Length of Study/ Follow-up	Up to 6 months.
Outcome measures studied	Adherence; severity of symptoms; patient satisfaction; resource utilization.
Results	From the intervention group, 79% returned the mailed surveys, compared to 50% from the control group. After 6 months, the intervention group demonstrated a significantly higher drug adherence rate than that of the control group (67% vs 48%, p=0.038). The MPR was higher for the intervention group than for the control group at both 3 and 6 months, but the difference was not significant. Patient satisfaction was significantly greater among members randomly assigned to pharmacists' services than among controls ($p < 0.05$), and provider satisfaction surveys revealed high approval rates as well. Changes in resource utilization were favourable for the intervention group, but differences from the control group did not achieve statistical significance. Clinical improvement was noted in both groups, but the difference was not significant.
Safety and adverse effects	None reported.
Does the study answer the question?	Clinical pharmacists had a favourable effect on multiple aspects of patient care. Future studies of this model in other health care settings appear warranted.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	Consistent.
Directly applicable to guideline population?	Relevant study.
Internal Validity	Patients not blinded to study.

Grymonpre RE;Williamson DA;Montgomery PR;

Impact of a pharmaceutical care model for non-institutionalised elderly: Results of a randomised, controlled trial

Ref ID 2175 2001

Study Type	Randomised Controlled Trial	**Funding**	Not mentioned. Authors are from a University and one was a pharmacy consultant.

Number of participant	135 in total, 69 in the intervention group and 66 in the control group.
Inclusion/Exclusion Criteria	Inclusion criteria: 65 years or over, non-institutionalised, taking two or more prescribed or non-prescribed medications, and providing signed consent form.

Patient Characteristics	Mostly female (75% intervention vs 83% control, p=0.254); aged 76.9 (SD 8.4) and 77.2 (SD 8.8), p=0.786. All were Caucasian, Most lived alone 61% vs 77%, p=0.018)
Recruitment	Clients who presented at a clinic or were referred by Home Care programme.
Setting	A community-based health clinic.
Interventions/ Test/ Factor being investigated	Volunteers and staff were trained to conduct a comprehensive medication review and this is given to the pharmacist to identify and document potential and actual drug-related issues and to address the issues with the patient and they physician. This included their use of prescribed and non-prescribed medicines, social drugs, home remedies, their regime, their adherence and their communication with g.ps, any problems or side effects with drugs. The recommendations were given in a letter to physicians and were reviewed for appropriateness by a consultant geriatrician before given to the physician. The clients were followed up by the pharmacist when required to monitor therapeutic endpoints and sort out any problems that had arisen. The issues identified by the pharmacist were tested individually by a pharmacist and nurse to see if resolved. Physicians gave their opinion of the pharmacist's letter through a survey.
Comparisons	Between intervention group and control group. The control group received a detailed home medication history but were reviewed by a different pharmacist who referred clients to their usual pharmacist and answered any queries.
Length of Study/ Follow-up	No data given.
Outcome measures studied	Number of drugs taken, drug knowledge, adherence to drug therapy, cost of prescribed medicines, number of symptoms reported from home medication history, response of physicians' survey.
Results	The mean number of mediations adhered to at follow-up was 87 (+/-46) for the intervention and 85 (+/-41) for the control group, p=0.895, showing no significant difference in adherence.
Safety and adverse effects	If the pharmacist thought the clients were at risk of 'life-threatening' drug-related problems in the control group they were withdrawn from the study.
Does the study answer the question?	Yes. A medication review and recommendations given by the pharmacist to physicians did not change adherence or drug knowledge between the intervention and control group.
Effect due to factor in study?	The methodology is lacking in that the two groups may have been treated similarly and so a difference between the two groups would not be evident.
Consistency of results with other studies?	
Directly applicable to guideline population?	The intervention is comparable to the intervention and population of interest as it is medication review and measures adherence. However the medication history collection is conducted by a lay person rather than the pharmacist (who conducts the review).
Internal Validity	Attrition bias; Not blinded; group contamination.

Guthrie RM;

The effects of postal and telephone reminders on compliance with pravastatin therapy in a national registry: results of the first myocardial infarction risk reduction program

Ref ID 76 2001

Study Type	Randomised Controlled Trial	**Funding**	Bristol Myers Squibb Co. Princeton, New Jersey.
Number of participant	13,100 in total. Intervention group n=10,335; Control group n=2765.		

Inclusion/Exclusion Criteria	Inclusions: High risk for MI (determined by the First Heart Attack Risk Test). Those with risk scores of 4 or over on a scale of -1 to +16 for men and -1 and +17 for women were considered at increased risk for a first MI and suitable for enrolment. Exclusions: previous MI, current therapy with a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (statin); Membership in a federally funded health care program (except Medicare or plans for federal employees); Women of childbearing potential.
Patient Characteristics	Mean age 58 years. Sex 51% Female; 49% Male. Ethnicity 80% White; 9% Black; 6% Hispanic; 3% Asian, 2% other. Primary-care patients at increased risk of a first Myocardial Infarction (MI). Elevated total cholesterol level; Community-based.
Recruitment	By physicians who were enrolled in the study.
Setting	Community-based g.ps, USA.
Interventions/ Test/ Factor being investigated	Postal and telephone reminders given to the intervention group to comply with Pravastatin Therapy. Patients at enrolment are given a 2-week supply of pravastatin at no charge. They also received prescriptions from their physicians for additional prevastatin treatment and were given recommendations about modifying lifestyle and complying with medication regimens to limit the risk for a first MI. The intervention group received telephone reminders at weeks 2 and 8, as well as reminder postcards at week 4. These communications stressed the importance of following the physician's instructions and to take medications as prescribed. Reminder postcards were sent to both groups at 4 and 5 months after enrolment. Physicians completed follow-up evaluation forms after patient visits scheduled according to their normal practices.
Comparisons	The intervention group versus usual care.
Length of Study/ Follow-up	At 3 months then at 6 months (or study discontinuation).
Outcome measures studied	Compliance;
Results	No significant effect in compliance between the groups: 80% in the intervention group reported they were taking pravastatin as prescribed, compared to 77% in the usual care group. 64% in the intervention and 62% of the usual care group reported they missed no doses in the previous 7 days. Reported medication adherence was significantly ($p<0.05$) associated with the adoption of other coronary risk-reducing behaviours according. Of those reporting to take pravastatin 97% reported visiting their physicians as scheduled compared to 82% of those who were not compliant with pravastatin regimens ($p<0.01$). 62% of the compliant group modified eating habits compared to 51% in the noncompliant group ($p<0.01$); 39% reported losing weight compared to 35% in the noncompliant group ($p<0.01$) and 41% increased physical activity compared to 31% of those reporting non-compliance at 6 months ($p<0.01$).
Safety and adverse effects	Not reported.
Does the study answer the question?	Yes There was no significant results for the use of telephone and postcard reminders (or baseline characteristics) on compliance or with recommended coronary risk-reducing behaviours. Therefore this relates to the question that it does not support reminders increasing adherence to medications.
Effect due to factor in study?	No power calculation, but a large sample was included. And the effect was non-significant.
Consistency of results with other studies?	

Directly applicable to guideline population?	Relevant.
Internal Validity	No allocation concealment or blinding- selection

Iskedjian M;Einarson TR;MacKeigan LD;Shear N;Addis A;Mittmann- N;Ilersich AL;

Relationship between daily dose frequency and adherence to antihypertensive pharmacotherapy: Evidence from a meta-analysis

Ref ID 1530 2002

Study Type Systematic Review **Funding** No external funding

Number of participant	Prospective trials (RCTs and cohort studies), retrospective chart reviews and database analyses.
Inclusion/Exclusion Criteria	
Patient Characteristics	
Recruitment	
Setting	
Interventions/ Test/ Factor being investigated	
Comparisons	
Length of Study/ Follow-up	
Outcome measures studied	
Results	
Safety and adverse effects	
Does the study answer the question?	Eight studies involving a total of 11,465 observations were included (1830 for daily [QD] dosing, 4405 for twice a day dosing [BID] and 4147 for dosing >2 times daily [>BID] and 9655 for multiple daily dose [MDD]). The primary objective was to assess adherence. The average adherence rate for QD dosing (91.4%, SD=2.2%) was significantly higher than for MDD (83.2%, SD=3.5%; p<0.001). This rate was also significantly higher than for BID dosing (p=0.026); 92.7% [SD=2.3%] vs 87.1% [Sd=2.9%]). The difference in adherence rates between BID dosing (90.8%, SD 4.7%) and >BID dosing (86.3%, SD=6.7%) was not significant (p=0.069). All these figures must be reviewed with caution due to flaws in the methodology of the meta analysis.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Katon W;Russo J;Von KM;Lin E;Simon G;Bush T;Ludman E;Walker E;

Long-term effects of a collaborative care intervention in persistently depressed primary care patients

Ref ID 33 2002

Study Type	Randomised Controlled Trial	**Funding**	Supported with grants from the National Institute of Mental Health Services.

Number of participant	N= 114 for both intervention and control groups.
Inclusion/Exclusion Criteria	Inclusion criteria: Patients between the ages of 18 and 80 from 1 of the 4 primary care clinics who received a new antidepressant prescription (no prescriptions within the last 120 days) from a primary care physician for the diagnosis of depression or anxiety. Exclusion criteria: if patients had a screening score of 2 or more on the CAGE alcohol screening questionnaire, 13 were pregnant or currently nursing, planned to disenroll from the Group Health insurance plan within the next 12 months, were currently seeing a psychiatrist, had limited command of English, or had recently used lithium or antipsychotic medication.
Patient Characteristics	There were no significant differences between the 114 intervention and 114 usual-care patients on the following demographic variables, including age (I, 47.2 ± 14.0 years vs UC, 46.7 ± 13.4 years), percent employed full- or part-time (I, 72.6% vs UC, 64.9%), and percent Caucasian (I, 79.8% vs UC, 80.7%). There was a significant difference between intervention and control patients in the percent of female subjects (p = .02).
Recruitment	Using GHC automated registration, pharmacy, and visit data.
Setting	4 Large primary care clinics. USA.
Interventions/ Test/ Factor being investigated	Usual care group: provided by GHC family physicians and involved prescription of an antidepressant medication, 2 or 3 visits over the first 6 months of treatment, and an option to refer to GHC mental health services. Both intervention and usual-care patients could also self-refer to a GHC mental health provider. GHC usually scores at about the seventy-fifth percentile on National Committee for Quality Assurance/Health Plan Employer Data and Information Set measures of quality of depression care. Intervention group: a multifaceted intervention was developed that targeted patients, physicians, and process of care. Each patient received a book and companion videotape developed by the study team, which reviewed the biopsychosocial model of depression, how medications and psychotherapy help depression, and how to become involved as an active partner with their physician in the care of their depressive illness. After the baseline interview and randomization, the research assistant scheduled 2 sessions for intervention patients with a psychiatrist (one 50-minute initial session and one 25-minute follow-up session) in the primary care clinic. Visits were usually spaced 2 weeks apart, with a brief telephone call to review progress between the first and second visits and, if necessary, between the third and fourth visits. The psychiatrist reviewed the course of the current depressive episode and the patient's biopsychosocial history. When severe side effects or inadequate response to treatment occurred, the psychiatrist helped the patient and primary care physician alter the dosage or choose an alternative medication.
Comparisons	Between treatments.
Length of Study/ Follow-up	Up to 28 months.
Outcome measures studied	Adherence to antidepressant medication, severity of depressive symptoms, and functional impairment.
Results	In the high strata during the first 6 months, 72% (n = 24) of the intervention patients and 40% (n = 14) of the controls were adherent to an adequate dosage of medication (p < 0.01). This trend was also seen in the second 6-month period: 70% (n = 23) of the intervention patients and 37% (n = 13) of the controls were adherent to an adequate dosage of medication (p< 0 .05). For the moderate-severity strata, intervention patients were only more likely to adhere to 90 days or more of adequate

	dosage of antidepressants during the first 6-month block of time (76% of the intervention patients versus 46% of the controls, p< 0 .05) Similar, but non-significant, trends were observed for the second 6-month block. For the other three 6-month periods, the percentages were very similar for the treatment groups in both strata. The intervention group was associated with continued improvement in depressive symptoms at 28 months in patients in the moderate-severity group (p = 0 .004), but not in patients in the high-severity group (p = 0 .88). There were no significant differences in total ambulatory costs between intervention and control patients over the 28-month period (p = 0.40).
Safety and adverse effects	None reported.
Does the study answer the question?	The intervention group showed improvement in depressive outcomes without additional health care costs in approximately two thirds of primary care patients with persistent depressive symptoms.
Effect due to factor in study?	Some methodological limitations.
Consistency of results with other studies?	Consistent.
Directly applicable to guideline population?	Relevant study.
Internal Validity	Not blinded study.

Lipton HL;Bird JA;

The impact of clinical pharmacists' consultations on geriatric patients' compliance and medical care use: a randomized controlled trial

Ref ID 1627 1994

Study Type	Randomised Controlled Trial	**Funding**	John A Hartford Foundation in New York City.

Number of participant	1,383 eligible patients approached, 10% refused, 37% discharged before deciding whether or not to enrol. 52% of patients who were eligible and approachable were enrolled. After attrition (6.5%) 706 patients remained in the trial.
Inclusion/Exclusion Criteria	Inclusion: aged 65 years or over; covered by Medicare; admitted to a non-psychiatric ward; resided within 35 miles; English speaking (or proxy); mental competent (or proxy); access to telephone; 3/4 medications prescribed for a chronic condition; Exclusion: those discharged to a nursing home or hospice;
Patient Characteristics	Intervention vs control groups: Mean age: 74 both groups MediCal recipients: 9% both groups More than 12 years education: 52% vs 44% (p=0.03) All patients were discharged from hospitals. No mention of sex, ethnicity, comorbidity, disease status given.
Recruitment	Daily hospital records were looked at for eligible patients. At least one attempt was made to approach every patient meeting the eligibility criteria.
Setting	Community hospital in San Francisco Bay, USA.
Interventions/ Test/ Factor being investigated	Two clinical pharmacists' provided a drug consultation service for geriatric patients and their physicians. Intervention: Pharmacists' reviews of the hospital records and drug regimens of the experimental, and consultations with the patients and their physicians. Both control group and experimental group patients were given booklets when discharging from hospital, to record medication information eg drug purpose, dosage

	and schedule. After review of the records to determine the patient's (in intervention group) clinical condition and to assess appropriateness of prescribing, the pharmacist conducted a face-to-face consultation with the intervention patients to discuss the purpose and use of their medications and any potential drug-related problems. Follow-up was about 15 minutes in duration. 85% of the postdischarge meetings were by telephone and the rest were in the pharmacists' office or patient's home. If significant problems were detected the patients were provided with a consultation with their physician. The pharmacists promoted the use of fewer medications and simplified regimens where appropriate – by telephoning physician to recommend discontinuation of a prescribed product or by recommending directly to the patient discontinuation of a non-prescribed product. Patient compliance was assessed by structured telephone interviews with a subsample of experimental and control patients at 6-8 weeks postdischarge and again at 12-14 weeks postdischarge.
Comparisons	Intervention vs usual care.
Length of Study/ Follow-up	Follow-up consultations were given at 1 week, 2-4 weeks, 2 months and 3 months after discharge from hospital. 6 months.
Outcome measures studied	Medical care utilisation; Patient compliance; Knowledge, regularity, frequency, dosage, missed doses; polypharmacy.
Results	T-test results showed that the intervention did not have an impact on subsequent medical care utilisation and expenditures. No significant differences found for the mean number of drugs taken and the complexity of the regime at 6-8 weeks but there was a significant change at 12-14 weeks. Intervention group were taking significantly fewer medications than controls (5.16 vs 6.75, $p<0.001$). The intervention also had an impact on the second measure of regimen complexity, average daily doses per drug ($p=0.02$). Compliance results: 274 patients were selected for this sub-study. No significant demographic differences between this sample and the overall sample were found. 233 (124 intervention and 109 control) were interviewed for the first assessment and 206 (108; 98) for the second assessment. During the first assessment (6-8 weeks) intervention group had significantly higher mean compliance 94.4 (SD=9.4) vs 91.4 (SD=11.6) ($p=0.035$). This became non-significant ($p=0.334$) when knowledge was removed from the analysis. At 2nd assessment the interventions impact on knowledge was stronger ($p=0.001$). By this time the intervention had an effect on patients' drug use 96.3 (SD=10.2) vs 91.2 (SD=9.6) ($p<0.001$). With 92% of intervention vs 77% of control patients not missed any dose of their medications ($p<0.001$). This was still significant whether or not knowledge of the purpose of the medication was included.
Safety and adverse effects	None reported.
Does the study answer the question?	Clinical pharmacist's consultations can improve geriatric patients' drug regimens and compliance. The need for replication among large cohorts of patients at high risk. Shows the value of sustaining the clinical pharmacist intervention for some time.
Effect due to factor in study?	Not sure.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes
Internal Validity	Allocation concealment. Difference in the group.

Lowe CJ;Raynor DK;Purvis J;Farrin A;Hudson J;

Effects of a medicine review and education programme for older people in general practice

Ref ID 7537 2000

Study Type	Randomised Controlled Trial	**Funding**	Grant from the Department of Health under the Pharmacy Practice Research Enterprise Scheme.

Number of participant	161 patients in total: 77 in the intervention group and 84 in the control group.
Inclusion/Exclusion Criteria	Inclusion criteria: 65 years or older; taking 3 or more drugs. Exclusion criteria: lived in nursing or residential care; dependent on another to administer medicine; terminal illness with life expectancy less than one year.
Patient Characteristics	Intervention group: mean age 77.5 (65-96), mainly female 67%, living with spouse or relative 55% and 4 mean medicines scheduled (2-8). Control group: mean age 75 (65-88), 67% female, 57% living with spouse or relative, 4% mean (1-10) medicines scheduled.
Recruitment	They were recruited sequentially from a list of patients in the practice 65 or over.
Setting	General practice in suburbs of Leeds.
Interventions/ Test/ Factor being investigated	An investigator visited intervention and control participants and filled in a structured questionnaire regarding their medicines, medicines taken and understanding of their purpose. The investigator assessed the intervention group participants' ability to take their medications, then reported the findings to doctors where there was need to reduce dosage and discontinue medication. They also liaised with pharmacist for modifications to medicine containers. At the second visit they gave 1 months supply of medication and removed any other prescribed medications. They discussed the regimen and explained the right way to take medications and purpose and made a reminder chart. At 3 weeks follow-up another months supply was given and asked the patients to describe the medicines they took and their purpose, and counted the medications left over from the last visit.
Comparisons	Comparison made between intervention group and control group - who did not receive the intervention of medication review, education and discussing medication and problems.
Length of Study/ Follow-up	Followed up after one month, then after 3 weeks.
Outcome measures studied	Knowledge of medicines, compliance with medicines - through a structured questionnaire and tablet count and patient report.
Results	The mean compliance score was 91.3% for intervention group (95% CI, 89%-94%) and 79.5% for the control group (75%-84%), p<0.0001. At first visit 58% of intervention group correctly described the purpose of medication, compared to 67% of control these numbers were 88% of intervention and 70% of control group by the third visit, between groups the difference was significant (p=0.0001). 47% of patients had a fall in the mean number of medicines to take from 4.1 (95% CI 3.8-4.5) to 3.9 (3.5-4.2) the mean difference was -0.26 (o5% CI, p=0.003)
Safety and adverse effects	Approval given by Local Research Ethics Committee and informed consent from patients.
Does the study answer the question?	Yes this does answer the key question. The use of a medicine review and education increased compliance for the intervention group compared to the control group.
Effect due to factor in study?	Uncertain as to whether there may have been bias introduced into the study. The statistical power of the study was high. The overall effect is possibly due to the study intervention.

Consistency of results with other studies?

Directly applicable to guideline population? Intervention is under 6 months so is not exactly the requirement for the guideline but the intervention involves medication review as the intervention and compliance as an outcome so this is of direct interest to guideline.

Internal Validity Selection bias, performance bias

Makoul G;Clayman ML;

An integrative model of shared decision making in medical encounters

Ref ID 2371 2006

Study Type Systematic Review

Funding Program in Communication and Medicine and North-western University Feinberg School of Medicine.

Number of participant Articles published in medically oriented journals. Does not specify types of studies.

Inclusion/Exclusion Criteria

Patient Characteristics

Recruitment

Setting

Interventions/ Test/ Factor being investigated

Comparisons

Length of Study/ Follow-up

Outcome measures studied

Results

Safety and adverse effects

Does the study answer the question?

Essential elements of SDM are:
- define/explain problem
Present options
Discuss pros/cons (benefits/risks/costs)
Patient values/preferences
Discuss patient ability/self-efficacy
Doctor knowledge/recommendations
Check/clarify understanding
Make or explicitly defer decision
Arrange follow-up

Ideal elements are:
Unbiased information
Define roles
Present evidence
Mutual agreement

General qualities:
Deliberation/negotiation
Flexibility/individualised approach
Information exchange
Involves at least two people
Middle ground
Mutual respect
Partnership
Patient education
Patient participation
Process/stages

It helps answer the question of what to we mean/understand by patient involvement in decisions about medicines as it answers what the components of shared decision making are.

The review places these concepts into essential/ideal and general according to most cited authors. However if we look at a table they have of concepts of SDM most evident in the literature:

67.1% Patient values/preferences
50.9% Options
46.0% Partnership
37.3% Patient participation
36.6% Patient education
35.4% Benefits/risks (pros/cons)
31.7% Deliberation/negotiation
30.4% Doctor knowledge/recommendations
29.2% Mutual agreement
26.7% Process/stages
23.6% Middle ground
23.0% Information exchange
18.0% Make or explicitly defer decision
16.8% Present evidence
13.0% Define/explain problem
13.0% Define roles (desire for involvement)
11.8% Unbiased information
11.8% Check/clarify understanding
11.2% Flexibility/individualised approach
10.6% Mutual respect

There is no quality assessment of papers and there is no limitation on the type of study used and is limited in the search database. However it is useful to see the array of concepts most used by studies to conceptualise SDM.

Effect due to factor in study?

Consistency of results with other studies?

Directly applicable to guideline population?

Internal Validity

Parienti JJ;Massari V;Reliquet V;Chaillot F;Le MG;Arvieux C;Vabret A;Verdon R;

Effect of twice-daily nevirapine on adherence in HIV-1-infected patients: a randomized controlled study

Ref ID 378 2007

Study Type Randomised Controlled Trial **Funding** Academic grant.

Number of participant Nevirapine 400 mg once-daily (n = 31) or continue nevirapine 200 mg twice-a-day (n = 31)

Inclusion/Exclusion Criteria	Patients with chronically HIV-1 infection, receiving nevirapine-based antiretroviral therapy with RNA-HIV levels less than 400 copies/ml for more than 6 months and without liver enzyme abnormality.
Patient Characteristics	Patients with chronically HIV-1 infection, receiving nevirapine-based antiretroviral therapy with RNA-HIV levels less than 400 copies/ml for more than 6 months and without liver enzyme abnormality. Patients were aged 24-76 years (mean 48.1)
Recruitment	Sixty-two patients were recruited.
Setting	Four french academic medical centres
Interventions/ Test/ Factor being investigated	Adherence was measured using electronic monitoring devices and validated by sequential plasma drug levels. Participants were randomly assigned to switch to nevirapine 400 mg once-daily (n = 31) or continue nevirapine 200 mg twice-a-day (n = 31). After the randomized phase, participants had an opportunity to choose their antiretroviral dosage. Primary outcome was the mean percentage of adherence
Comparisons	Between treatments.
Length of Study/ Follow-up	follow-up period of 12 months. A first 3 month observational, 4 month randomized, 5 month interventional.
Outcome measures studied	Adherence and viral supression.
Results	Fifty-two patients qualified for electronic data analysis. During the randomized phase, the mean adherence rate was non-significantly superior by 0.5% in once-daily versus twice-a-day dosing (P = 0.68), adjusting for previous twice-a-day adherence rate (P < 0.0001). Once-daily group increased days without dose (odds ratio (OR) 1.7; 95% confidence interval (CI) 1.0, 2.8; P = 0.04), adjusting for previous drug interruptions (P < 0.0001). In the longitudinal analysis, once-daily dosing was significantly associated with at least two consecutive days without dose (OR 4.4; 95% CI 1.9, 10.3; P < 0.001).
Safety and adverse effects	ten serious adverse events including one death were reported in seven patients. None were drug related.
Does the study answer the question?	Changing from twice daily to once daily nevirapine does not improve adherence.
Effect due to factor in study?	
Consistency of results with other studies?	
Directly applicable to guideline population?	
Internal Validity	

Peterson GM;Fitzmaurice KD;Naunton M;Vial JH;Stewart K;Krum H;

Impact of pharmacist-conducted home visits on the outcomes of lipid-lowering drug therapy

Ref ID 2144 2004

Study Type	Randomised Controlled Trial	**Funding**	Community Pharmacy Practice Research Grant, through the Guild/Government (Community Pharmacy) Agreement and administered by the Commonwealth Department of Health and Aged Care. Equitment provided by

Number of participant	The participants were 94 adults, intervention group = 46; control group = 48.
Inclusion/Exclusion Criteria	Inclusion: Patients with established cardiovascular disease and an acute cardiovascular/cerebrovascular-related admission, discharged from the hospital between April andOctober 2001 on statin therapy. Exclusion: Patients were excluded if they had dementia, lived in a domiciliary care facility or lived beyond the greater Hobart area.
Patient Characteristics	Age (years) Mean ± SD: Intervention group: 63.5 ± 12.1, Control Group: 65.5 ± 11.0. Gender: Female: Intervention group: 13 (31%), control group: 17 (44%). No significant differences reported at baseline (although p values not given).
Recruitment	
Setting	Patients homes.
Interventions/ Test/ Factor being investigated	Intervention: All patients were visited 6 weeks after discharge and given a total blood cholesterol test and had there medication recorded. For intervention participants only, during visits were educated on the goals and proven benefits of lipid-lowering drug therapy, and appropriate lifestyle modifications. Dietary and lifestyle recommendations were obtained from various sources, (e.g. National Heart Foundation of Australia). Intervention group patients also assessed for any drug-related problems. For all patients, copies of blood cholesterol results and clinical recommendations were sent to their GP. For the intervention group the pharmacist conducted these home visits every month for a period of 6 months. For the control group, no further contact was made until 6 months (when data were collected).
Comparisons	Pharmacist conducted home visits vs usual care. Intervention vs control.
Length of Study/ Follow-up	6 months.
Outcome measures studied	Adherence: Self report measure: participants simply "asked how often would you say you forget to take your medication"? Classed on basis of answer as compliant or non-compliant.
Results	Adherence: Self-reported patient compliance with medication did not change over the course of the study, and total cholesterol levels were not significantly related to self-reported patient compliance either at the baseline ($p > .50$) or at follow-up ($p > .30$). Other outcomes: Although the total cholesterol levels tended to be lower in the intervention group patients at follow-up, the difference between the two groups was not statistically significant. However, the improvement over the course of the study in cholesterol levels within the intervention group was statistically significant (Baseline: m (sd): 4.8 +/- 0.7, Follow-up 4.4 +/- 0.6, $p < 0.005$), whereas it was not within the control group. At follow-up, 44% of the intervention group patients and 24%of the control group patients had cholesterol levels below 4.0 mmol/L ($p=.06$). The reduction in total cholesterol in the intervention group should translate to an expected 21% reduction in cardiovascular mortality risk and a 16% reduction in total mortality risk – more than twice the risk reduction achieved in the control group. In addition, the programme was very well received by the patients and their general practitioners, by satisfaction questionnaire.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention did not help to increase adherence.
Effect due to factor in study?	Unsure.
Consistency of results with other studies?	

Directly applicable to guideline population? Relevance.

Internal Validity

Sadik A;Yousif M;McElnay JC;

Pharmaceutical care of patients with heart failure

Ref ID 1052 2005

Study Type Randomised Controlled Trial **Funding** Not reported.

Number of participant	Total of 221 HF patients (109 intervention; 112 control) were recruited into the study
Inclusion/Exclusion Criteria	Inclusion criteria: confirmed diagnosis of HF (by a hospital consultant), cognitive status [score > 6 as assessed by the Clifton Assessments Procedures for the Elderly (CAPE) survey] and hospital consultant consent to patient entering trial. Exclusion criteria: significant airways disease, e.g. chronic obstructive airways disease and severe mobility problems due to other causes, e.g. osteoarthritis [since both these parameters would influence forced vital capacity (FVC) and walk tests used as outcome measures in the study].
Patient Characteristics	Baseline details not given - only how measurements and assessments were performed. Nonetheless, authors state that an attempt was made to match groups as closely possible, specially for severity of HF, renal function or other concomitant illness and cognitive status.
Recruitment	Patients were recruited from the general medical wards and from cardiology and medical outpatient clinics.
Setting	Hospital. United Arab Emirates.
Interventions/ Test/ Factor being investigated	Medication knowledge was scored as a percentage value relating to the number of correct answers given to questions on name of prescribed medications, daily dosage, strength, purpose of each medication and significant side effects. A score of < 50% was considered poor knowledge. In relation to compliance with prescribed medications, patient self-report on missing doses or taking extra doses of their medication, without medical advice to do so, was considered non-compliance. Intervention group: the research pharmacist discussed with their physicians if rationalization of drug therapy or simplification of dosage regimens were considered appropriate. Intervention patients were also educated (in a structured fashion) on HF, their prescribed medication and the management of HF symptoms by the research pharmacist. A printed booklet developed for this type of education programme was used and each patient was given a copy to take home. The booklet contained information on HF, its symptoms, the aims of treatment, the types of medication used and their possible side-effects, diet and lifestyle changes, advice to stick to one brand of digoxin (it having a narrow therapeutic index) and information on the action to take if doses of medication were missed. Intervention group patients were also instructed on a self-monitoring programme (signs and symptoms of HF; compliance with prescribed medication) in which they were asked to become involved; a monitoring diary card (covering 1 month) was used. Patients were asked to complete their monitoring diary cards at home and to show them to their physicians when attending an appointment. The patients were asked to return their completed diary cards to the research pharmacist for review when they visited the hospital to receive medication refills. Reinforcement of the educational message was carried out by the pharmacist as deemed necessary. Control group: patients received traditional management, i.e. excluding counselling and education by the research pharmacist, self-monitoring, pharmacist liaison with physicians, etc. Both groups of patients were asked to return to a hospital outpatient clinic at their scheduled appointment intervals followed by the hospital (3-month intervals).
Comparisons	Between treatments.
Length of Study/ Follow-up	Up to 12 months.

Outcome measures studied	Two minute walk test, forced vital capacity, blood pressure and pulse, quality of life questionnaires, HF symptoms, questionnaire outcome measures on medication knowledge and self-reported compliance with medications and lifestyle advice.
Results	The number of intervention group patients vs. control patients who exhibited self-reported compliance with the prescribed medicines (85 vs. 35) and lifestyle adjustment (75 vs. 29) was higher than in control group patients at 12 months ($p < 0.05$). The baseline scores for these parameters were 33 vs. 32 and 22 vs. 23 respectively ($p > 0.05$). At baseline the number of patients in the intervention group and the control group, respectively, whose medication knowledge was deemed poor was approximately the same (80 vs. 82); it was not statistically different ($p > 0.05$). There was a significant improvement in the intervention group patients after 12 months (20 vs. 84; $P < 0.05$).Over the study period, intervention patients showed significant ($P < 0.05$) improvements in a range of summary outcome measures [AUC (95% confidence limits)] including exercise tolerance [2-min walk test: 1607.2 (1474.9, 1739.5) 1 month in intervention patients vs. 1403.3 (1256.5, 1549.8) in control patients], forced vital capacity [31.6 (30.8, 32.4) l month in the intervention patients vs. 27.8 (26.8, 28.9) in control patients], health-related quality of life, as measured by the Minnesota living with heart failure questionnaire [463.5 (433.2, 493.9) unit month in intervention patients vs. 637.5 (597.2, 677.7) in control patients; a lower score in this measure indicates better health-related quality of life].
Safety and adverse effects	None reported.
Does the study answer the question?	The research provides clear evidence that the delivery of pharmaceutical care to patients with HF can lead to significant clinical and humanistic benefits.
Effect due to factor in study?	Yes.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant study.
Internal Validity	Participants not blinded. No ITT performed.

Sookaneknun P;Richards RM;Sanguansermsri J;Teerasut C;

Pharmacist involvement in primary care improves hypertensive patient clinical outcomes

Ref ID 1592 2004

Study Type Randomised Controlled Trial **Funding** Research grand from Chiang Mai University, Thailand.

Number of participant	235 total patients 118 in treatment group 117 in control group
Inclusion/Exclusion Criteria	Inclusion: Over 18 years Newly diagnosed during the pre-test period with hypertension Average DBP over or equal to 90 mm Hg or average SBP over or equal to 140 mm Hg Exclusion: secondary causes of hypertension Unable/unwilling to return for appointments Planned to move/family member in study SBP over 210 mmHG or DBP over 115mg Hg Severe complicating disease
Patient Characteristics	76 women and 42 men in the treatment group 84 women and 33 men in the control group p value 0.224 Aged 63 (SD 9), p=0.982 Hypertension 57 vs 54

	Hypertension with diabetes 39 vs 45 Hypertension with target organ damage 13 vs 7 Hypertension with diabetes and target organ damage 9 vs 11 p value 0.474
Recruitment	Databases from hospital and 2 PCUs screened for patients diagnosed as hypertensive. Or from medical records.
Setting	Mahasarakham Uni community pharmacy, Thailand
Interventions/ Test/ Factor being investigated	Pharmaceutical intervention: 30-50 minute face to face interview - assessed understanding of medications, counselled on use of medications, assessed adherence and lifestyle habits, reviewed for adverse events due to DRPs. Identified, resolved and prevented DRPs. Pharmacist recommendations for regimen changes made to physicians and on medical record Also looked at lifestyle eg exercise Education leaflets and diary to record lifestyle presented.
Comparisons	Pharmacist intervention versus usual care (no pharmacist involvement).
Length of Study/ Follow-up	6 months
Outcome measures studied	Primary outcomes: Blood pressure control, blood pressure difference. Secondary outcomes: adherence
Results	Primary outcomes: significant reduction in both systolic and diastolic BP compared with the control group (p=0.037, 0.027, respectively). Proportion of patients whose BP stabilised was higher in the treatment group (p=0.017). Secondary outcome: the treatment group showed significantly better adherence 70% with good adherence in the treatment group compared to 60% of the control group and 40% showing poor adherence in intervention compared to 48% of control group (p=0.014) at the end of the study.
Safety and adverse effects	None mentioned
Does the study answer the question?	Yes. Adherence was increased with the pharmacists involvement.
Effect due to factor in study?	The study power was 90%, the target size of the study sample was 95 patients, with 30% added to allow for drop-outs. Yes the effect is likely to be due to the study intervention.
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant as secondary outcome was change in adherence, from pharmacist involvement, which included medication review.
Internal Validity	Randomisation, concealment allocation.

Stewart A;Noakes T;Eales C;Shepard K;Becker P;Veriawa Y;

Adherence to cardiovascular risk factor modification in patients with hypertension

Ref ID 1176 2005

Study Type	Randomised Controlled Trial	**Funding**	Information not given.

Number of participant Total sample: 83 patients. Intervention group: 41, control group: 42 patients.

Inclusion/Exclusion Criteria	Inclusion: Attendance of a hypertension clinic in one geographical area and providing informed consent.
Patient Characteristics	Stated that groups did not differ significantly at baseline. Age, sex and ethnicity of sample not stated.
Recruitment	
Setting	Hypertension clinics in one geographical area.
Interventions/ Test/ Factor being investigated	5 (pairs) of telephone calls (to patient and family member) made once monthly over 24 weeks. Delivered by a physiotherapist. During calls patients (or family member) were asked about there exercise program and reminded about there diet and medication.
Comparisons	Four once monthly educational sessions, the prescription of a home based walking program + once monthly phone calls (intervention) vs Four once monthly educational sessions the prescription of a home based walking program (serving as control group).
Length of Study/ Follow-up	36 weeks.
Outcome measures studied	Self-report measurement of adherence (not adequately described). Participants presumably simply asked if they were taking medication correctly.
Results	Adherence: At week 24 significantly more patients in the intervention group (65%) were taking there medications as prescribed than in the control group (44.7%, p = 0.05), however, there was no difference between the groups at week 36 (82.4% vs 86.7%). Other outcomes: The adherence of 62.8% (SD 34.5) of the intervention group to the given health behaviour modification program was significantly higher than the 39.3% (SD 42.8%) of the control group (p = 0.007). There were no significant changes between the two groups in any blood pressure measurements. The intervention groups improvement in knowledge score from baseline to week 24 (48%, SD 14 to 72% SD 20) was significantly greater than that in the control group (47% SD 15 to 62% SD 21, p = 0.04) although there was not a significant difference between the groups from week 24 to 36. There were no significant differences in the distance walked between the two groups at anytime point. The weight lose in the intervention group at week 24 (1 kg, SD 4) was significantly greater than that in the control group (0 kg, SD 4, p = 0.03) although there was not a significant difference between the groups from week 24 to 36. There was a significant difference between the two groups at weeks 24 in terms of the number of patients reporting feeling tired (p = 0.05, mean and SD not given for groups) but not week 36. At week 24 significantly more patients in the intervention group (65%) were controlling their salt intake than in the control group (39.5%, p = 0.02), however, there was no difference between the groups at week 36. At week 24 significantly more patients in the intervention group (67.5%) reported being able to control their stress than patients in the control group (47.4%, p = 0.05) a difference that remained significant at week 36 (76.5% vs 38.5% p = 0.04). There was no difference between the groups at week 24 or 36 in self reported smoking and alcoholic intake.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention appeared to increase adherence at week 24 but not at week 36.
Effect due to factor in study?	Potential confounding factors (see above).
Consistency of results with other studies?	
Directly applicable to guideline population?	Relevant.
Internal Validity	

Taylor CT;Byrd DC;Krueger K;

Improving primary care in rural Alabama with a pharmacy initiative

Ref ID 46 2003

Study Type	Randomised Controlled Trial	**Funding**	Supported by the ASHP Research and Education Foundation.

Number of participant	69 in total, 33 in the intervention arm and 36 in the control arm.
Inclusion/Exclusion Criteria	Adults (over 18s) receiving care within the clinics. Those who were at high risk of medication-related adverse events (five or more medications prescribed, 12 or more doses per day, four or more medication changes in the last year, three or more concurrent diseases, previous medication compliance, drugs that require therapeutic monitoring). Exclusion criteria: significant cognitive impairment, history of missing office visits, scheduling conflicts or life expectancy under a year.
Patient Characteristics	Most patients were female 63.6% in the intervention group and 72.2% in the control group (p=0.445), Most were white 60.6% vs 61.1% (p=.966), and mean age was 64.4 and 66.7 years respectively (p=0.467) and the majority were married 75.8%vs 72.2 (p=0.935) with 12 years mean education in both groups. They were attending Community-based practices. Taking on average six medications each.
Recruitment	Identified by pharmacist evaluation of clinic medical records (manual and computer) from physician's offices, of the three community-based family medicine clinics.
Setting	GP offices, Alabama, USA.
Interventions/ Test/ Factor being investigated	Four pharmacists joined the clinics to give medication reviews. The intervention group received usual medical care, as did the control group but additionally received pharmaco-therapeutic interventions from a pharmacist during office visits. The pharmacists purpose was to prevent or identify and resolve problems with drug therapy. They evaluated a drug therapy's indication, effectiveness, and dosage as well as the correctness and practicality of directions, drug-drug interactions, drug-disease interactions, therapeutic duplication, the duration of treatment, untreated indications, and expense. They reviewed medial records for medication-related problems, documented problems accurately and examined medication history to determine compliance and complications with medication and gave individualised patient education reviewing the disease, lifestyle modifications and basic drug information. Therapeutic recommendations were made to the physicians and they made follow-up visits and gave more information or answered questions. Monitoring patients' responses to drugs and consolidating medication regimens, reducing dosage frequency, devising medication reminders and teaching techniques for using certain devices eg inhalers.
Comparisons	Between intervention and no intervention.
Length of Study/ Follow-up	12 months follow-up.
Outcome measures studied	Clinical outcomes: Hospitalisations and emergency department visits, hypertension, diabetes mellitus, dysipidemia, anticoagulation, quality of life. Prescribing appropriateness and medication misadventures: Medication compliance and medication knowledge.
Results	The intervention group's percentage of patients with medication compliance scores of 80-100% increased by 15%, but there was no change for the control group. However there was no significant difference at 12 months between the groups (100% of patients in the intervention group versus 88.9 (SD 6.3) of the control group had compliance scores of 80-100% at 12 months, p=0.115). At baseline this was 84.9% (SD=6.7) and 88.9 (s.D. 5.8) p=0.728 respectively. The most frequently sited reasons were forgetting to take the medications (n=10), having too many to take (n=9), found it hard to read or understand the directions (n=4) and too much trouble (n=4).

	Hospitalisations and Emergency Department visits decreased for the intervention group by 92% and 78% respectively, whereas the control group stayed constant. NB there was a much higher number of hospitalisations and ED visits in the intervention group than the control group at baseline 11 versus 24 hospitalisations and 6 versus 18 ED visits.
Safety and adverse effects	Not mentioned.
Does the study answer the question?	Yes There was increased compliance in the group who received the pharmacists' review of medications compared to the control group who received usual care. However this was not a significant difference in compliance at 12 months.
Effect due to factor in study?	It is unclear as there is no time period or statistical power given for the result that there was increased compliance in the intervention group, but there is for twelve months, which was non-significant. There was no concealment allocation so there may have been selection bias for the intervention group, although baseline scores were similar except for hospitalisation and ED admission which was higher in the intervention group, but then decreased significantly while the control group was constant.
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes this intervention and population is directly comparable to those of interest for the guideline.
Internal Validity	Selection bias; self-reporting bias;

van Servellen ;Nyamathi A;Carpio F;Pearce D;Garcia-Teague L;Herrera G;Lombardi E;

Effects of a treatment adherence enhancement program on health literacy, patient-provider relationships, and adherence to HAART among low-income HIV-positive Spanish-speaking Latinos

Ref ID 838 2005

Study Type	Randomised Controlled Trial	**Funding**	University wide Aids research programme. State Office of Aids.

Number of participant	Total sample: 85 participants, 42 in intervention group, 43 in control group.
Inclusion/Exclusion Criteria	Inclusion: (HIV infected patients) 18 year or older and had problems with medication adherence as noted in the patients medical records, Spanish speaking, detectable viral load and taking antiretroviral medications for at least 3 months.
Patient Characteristics	Age: control group: 39.5 (SD: 9.3), intervention group: 41.8 (SD: 8.3). Gender: male: control group: 92.9% , intervention group: 88.4%. Those in the comparison group were diagnosed more recently 4.8 years versus 7.6 years ($p = 0.01$) and to have spent less time on antiretroviral therapy, 44.7 versus 61.4 months ($p = 0.04$) at baseline. 45% of participants in the control group had viral loads less than 400 copies per millilitre versus 67% of those in the intervention group ($p = 0.04$) at baseline. Using CD4 count, there were statistically significant differences between the groups on absolute CD4 count (control group: 377 and intervention group: 212, $p = 0.01$) at baseline.
Recruitment	
Setting	2 clinics.
Interventions/ Test/ Factor being investigated	Enhanced adherence intervention: Consisted of two parts. 1/ modular instruction: aimed at increasing patients HIV knowledge and ability to communicate with medical staff. Delivered over 5 sessions (over 6 weeks from baseline data collection)) by health educators and nurse practitioners and followed up with 2/ face to face and phone call case management sessions (over 6 months from baseline data collection)

	by a nurse. These case management sessions concentrated on addressing patient' potential or actual risks for non adherence using motivational interviewing techniques. Content involved going over things misunderstood in stage 1, identifying barriers to adherence and finding strategies to challenge these and helping to find community, treatment and social support/referrals to help address adherence barriers.
Comparisons	Enhanced adherence intervention vs standard clinical care. Intervention vs control.
Length of Study/ Follow-up	6 months.
Outcome measures studied	Adherence: Collected at baseline, 6 weeks, 6 months via self report (collected via interview).
Results	Note adherence was calculated 3 ways: 1/ as a percentage of those missing 2 or more doses in the last 24 hours and the last 4 days, 2/ on the basis the average proportion of doses missed per day 3/ participants who had missed more then 5% and more than 10% of their doses over the last four days. Adherence: There where no significant differences between the group at 6 months in: Self efficacy of adherence management (control group, -0.06, SD 0.59 intervention group, 0.12, SD 0.95) 2+ doses missed in last 4 days (control group, 6.79% intervention group, -5.69%); 2+ doses missed pasted 24 hours (control group, 18.21% intervention group, -32%); average doses missed in last 4 days (control group, 0.04, SD 0.13 intervention group, 0.02, SD, 0.14); proportion > 95% adherent in last four days (control group, -4.85% intervention group, 1.71%); proportion > 90% adherent in last four days (control group, -11.47% intervention group, -0.49%); follow medication special instructions for 4 days (control group, 0.06, SD 0.34, intervention group, -0.07, SD 0.36) and following medication schedule (control group, -0.09, SD 1.60 intervention group, 0.33, SD 1.58). These findings are reflected in the results at 6 weeks. Health literacy: There were no significant differences between the groups in: global HIV disease treatment knowledge or HIV treatment related knowledge or knowledge risk of getting sicker. There were significant difference between the groups in recognition of HIV terms at 6 weeks (control group: 1.13, SD 4.24; intervention group: 4.23, SD 5.02, $p < .001$) and six months (control group: 1.34, SD 3.76 intervention group: 4.66, SD 4.80, $p < .001$). There were significant difference between the groups in understanding HIV terms at 6 weeks (control group: 1.30, SD 4.94, intervention group: 5,49, SD 5.63, $p < .001$) and six months (control group: 1.91, SD 3.60, intervention group: 6.16, 7.97, $p < .001$). Relationship/communications: there were significant differences between the groups in relationship/communications with HIV physician at 6 week (Control group, 0.58, SD 6.70, intervention group: 3.59, 6.32, $p < 0.05$) and 6 months (control group -1.17, SD 6.85 vs intervention group: 7.09, SD 8.04, $p < .001$) and in relationship/communications with medical staff at 6 months (control group: 1.11, SD 5.97, 5.28, SD 5.28, $p < .001$). Health Outcomes: There were significantly more individuals in the intervention group who had a drop in viral log load greater or equal to one with viral loads at 6 months (control group: 11.43%, intervention group 37.14%, $p < 0.01$). No other significant differences reported between the groups in terms of viral load, CD4 counts or general health status.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention did not improve adherence.
Effect due to factor in study?	I am unsure (see problems above).
Consistency of results with other studies?	

Directly applicable to guideline population? Yes.

Internal Validity

Vivian EM;

Improving blood pressure control in a pharmacist-managed hypertension clinic

Ref ID 2538 2002

Study Type Randomised Controlled Trial **Funding** Supported by the Christian R and Mary F Lindback Foundation.

Number of participant Total sample: 56. Intervention group: 27, control group: 29.

Inclusion/Exclusion Criteria Inclusion: age older than 18 years, confirmed diagnosis of hypertension (defined as systolic blood pressure > 140 mm Hg or diastolic > 90mm Hg), receiving antihypertensive drug therapy (and blood pressure >140/90mm Hg), receiving all drugs from the pharmacy participating in study, and not receiving care at the pharmacist managed clinic (until the study began).

Exclusion: a secondary cause of hypertension, such as chronic renal disease, renovascular disease, pheochromocytoma, Cushing's syndrome, and primary aldosteronism; had missed more than three appointments in the last year; or were in hypertensive crisis (defined as systolic blood pressure > 210 mm Hg or diastolic > 110 mm Hg). Patients were also excluded if they had a diagnosis of New York heart Association class 3 or 4 chronic heart failure, end stage renal disease, a psychiatric disorder, severe hepatic dysfunction defined as transaminase levels greater than 3 times the upper normal limit, or terminal cancer or other condition that limited life expectancy to less than one year.

Patient Characteristics All participants in study were male. Race no. Afro-American: intervention group: 22 , control group: 19, Caucasian: intervention group: 3, control group: 7. other: intervention group: 1, control group: 1. Age (mean, sd): intervention group: 64 +/- 10.9 , control group: 65.5 +/- 7.8. Significant difference in diastolic blood pressure between groups at baseline.

Recruitment

Setting A medical center.

Interventions/ Test/ Factor being investigated Pharmacist-managed hypertension clinic care (intervention): Patients in intervention group saw a clinical pharmacist once/month at a pharmacist-managed hypertension clinic. The pharmacist could make changes in the prescribed drugs and dosages and provided medication counselling centred around the discussion of side effects, recommending lifestyle changes and an assessment of compliance at each visit.

Comparisons Pharmacist-managed hypertension clinic care (intervention) vs traditional PCP care (control). Intervention vs control.

Length of Study/ Follow-up 6 months.

Outcome measures studied Adherence: 1/ self report questionnaire (monthly measured in intervention group, at baseline and 6 months for control group) 2/ drug refill information from pharmacy.

Results Note: None compliance: defined as missing more than 3 doses of drug in 1 week or having pharmacy records indicate failure to refill drugs within 2 weeks after the scheduled refill date.

Adherence: There were no significant differences in compliance (from the self report measure) between ($p > 0.25$, mean, sds not given for adherence) or within ($p > 0.07$) the two groups at baseline or the end of the study. 68% of patients in the intervention group admitted forgetting to taking there drug at least once a week vs 48% in the control group ($p = 0.253$). 92% of patients in both the intervention group and control group took there drugs as directed by their healthcare professional and did not take more than prescribed ($p = 1.00$). Pharmacy records indicated the 85% of patients in

	the intervention group received their refills within 2 weeks of the next refill date vs 93% of patients in the control group (p > 0.42). Blood pressure control: 81% of patients in the intervention group obtained a blood pressure below 140/90 mm Hg at the end of the study vs 30% of patients in the control group (p = 0.001). Mean changes in systolic blood pressure for the intervention and control groups were -18.4 (95% CI -26.3, 10.5) and 3.98 (95% CI -11.8, 3.79) respectively (p = 0.001). Mean changes in diastolic blood pressure for the intervention and control groups were -12.38 (95% CI -16.49, -8.28) and 2.54 (95% CI -1.49, 6.57) respectively (p = 0.001). Of the eleven patients in the diabetes group in the intervention group 91 % attainted the goal blood pressure of below 130/80 mm Hg versus only 12% of 16 patients with diabetes in the control group (p = 0.001). Patient satisfaction and quality of life: no statistically significant differences noted between groups.
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention did not significantly increase adherence.
Effect due to factor in study?	Unsure, potential problems (see above).
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	

Vrijens B;Belmans A;Matthys K;de K;Lesaffre E;

Effect of intervention through a pharmaceutical care program on patient adherence with prescribed once-daily atorvastatin

Ref ID 2554 2006

Study Type Randomised Controlled Trial **Funding** Pfizer Belgium.

Number of participant	392 patients total. Intervention group: 194, control group: 198.
Inclusion/Exclusion Criteria	Inclusion/exclusion: aged 18 years or above, who had been taking atorvastatin for at least 3 months, and who had no contraindications to continuation of the treatment, could be included in the study provided they usually got their medication in one of the pharmacies participating in the study. Three months of administration of atorvastatin was necessary to preclude recruiting newly diagnosed patients.
Patient Characteristics	Male n (%): Intervention group: 106 (55%), control group: 91 (46%). Age (yrs): Mean (std): Intervention group: 61.9 (9.9), control group: 60.4 (10.2). Significant differences between groups at baseline in terms of age and HDL (addressed in analysis).
Recruitment	Patients who usually visited one of the participating pharmacies were asked to enrol in the study.
Setting	35 pharmacies in Belgium.
Interventions/ Test/ Factor being investigated	The supportive intervention program consisted of review by the patients' pharmacist, jointly with the patient, of the electronically compiled dosing history, a 'beep-card' that reminds patient of the dosing time, and educational reminders. In the intervention group, the pharmacist delivered an educational message at each follow-up visit, updated the 'compliance passport' and analyzed, together with the patient, the electronically compiled dosing history of the past month/3 months. The pharmacist was trained on how to communicate with, and teach the patient to read the MEMS graphics.

Comparisons	Support intervention program vs usual care. Intervention v control.
Length of Study/ Follow-up	12 months.
Outcome measures studied	Adherence: Medication Electronic Monitoring System (mems). The primary outcome parameter is 'post-baseline adherence' to prescribed therapy defined as the proportion of days during which the MEMS record showed that the patient had opened the container.
Results	Adherence: The average duration of the baseline and post baseline periods were respectively 90 and 215 days. Baseline adherence in the intervention group showed a small but statistically significantly higher value than that observed in the non-intervention group ($p<0.003$). Post-baseline adherence results were 6.5% higher for the intervention group than for the non-intervention group. Results were similar for both language regions. A Wilcoxon test stratified for language region and baseline adherence shows that post-baseline adherence is significantly different for both groups ($p<0.001$), indicating that for similar levels of baseline adherence, intervention had a beneficial effect on post-baseline adherence. In the intervention group, 25 (13%) subjects discontinued medication prior to 300 days, in contrast to 51 (26%) subjects in the non-intervention group. After 300 days, persistence was significantly ($p<0.002$) higher in the intervention group (87%) compared to the non-intervention group (74%).
Safety and adverse effects	None.
Does the study answer the question?	Yes. The intervention led to a significant increase in adherence and medication persistence.
Effect due to factor in study?	Fairly although some concerns (see above).
Consistency of results with other studies?	
Directly applicable to guideline population?	Yes.
Internal Validity	

Wagner GJ;Kanouse DE;Golinelli D;Miller LG;Daar ES;Witt MD;Diamond C;Tilles JG;Kemper CA;Larsen R;Goicoechea M;Haubrich RH;

Cognitive-behavioral intervention to enhance adherence to antiretroviral therapy: a randomized controlled trial (CCTG 578)

Ref ID 371 1909

Study Type	Randomised Controlled Trial	**Funding**	National Institute of Mental Health; University wide AIDS Research Program of the University of California.

Number of participant	230 Total sample - 199 started ART (enhanced 75; cognitive-behavioural 79; control, 76).
Inclusion/Exclusion Criteria	Inclusion: Eligible patients were adults (age >/- 18 years) in stable health (no active opportunistic infection) and planning to begin, restart, or switch to a new ART regimen containing a protease inhibitor (PI) or non-nucleotide reverse transcriptise inhibitor (NNRTI). ART-experienced patients had to report either having had problems with adherence or a belief that they could benefit from the intervention. Other eligibility criteria included HIV-1 RNA >/- 3000 copies/ml, no active substance abuse, and English or Spanish speaking.
Patient Characteristics	Mean age 39 (range 21-70). Female 20%; 30% Caucasian, 14% African American, 49% Latino, 2% Asian-Pacific Islander. Patients who were planning to begin, restart or switch to a new ART regimen.

Recruitment	Not mentioned.
Setting	5 HIV primary care clinics. California.
Interventions/ Test/ Factor being investigated	Five-session adherence interventions to increase adherence to antiretroviral treatment, given as: cognitive-behavioural alone or enhanced with two weeks practice trial, and thirdly no intervention at all but usual clinical care.
Comparisons	Group 1: Cognitive behavioral (CB) Practice Trial group v Group 2: CB No practice Trial group v Group three: Usual care group. Further within group randomization (2.1 ratio) to therapeutic drug monitoring or standard care (these groupings not addressed).
Length of Study/ Follow-up	Interviewer and self-administered questionnaires administered at screening (week -4), weeks 4, 12, 24 and 48; Blood drawn at -4, -2, 0, 1, 2, 4, 6, 12, 18, 24, 32, 40 and 48 weeks. Control group received follow-up visits every 3 months (or more).
Outcome measures studied	Adherence was the primary outcome and week 4 the primary test point; virologic response was the secondary outcome.
Results	No difference in adherence between the enhanced and cognitive-behavioural groups up to week 24. Adherence increased for the enhanced group at week 48, but declined for the cognitive behavioural group, although there was a lot of drop out in all groups by the end. The difference between interventions and the control group for % with 90% of prescribed doses taken was significant in week 4 with more adherence in the intervention group (82% vs 65%;, p=0.01). This reduced to 66% for the intervention and 55% of the control by week 24 (p=0.28) but by week 48 the control group adhered more than the intervention groups (65% versus 57%, p=0.52).
Safety and adverse effects	None reported.
Does the study answer the question?	The effects of the interventions on adherence were modest and short-term and no effects with virologic and immunologic outcomes. There is need for ongoing adherence monitoring and maintenance training. This does help answer the question as it suggests that cognitive interventions do not drastically increase adherence.
Effect due to factor in study?	Yes
Consistency of results with other studies?	Yes
Directly applicable to guideline population?	Relevant as it is aimed to find out whether the intervention will increase adherence, and also uses a practice trial condition to see if this helps adherence. Only cognitive-behavioural intervention used. Population is people with HIV to start ART.
Internal Validity	Concealment bias; no blinding;