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Interventions for improving adherence to treatment in patients with high blood pressure in ambulatory settings (Review)

Schroeder K, Fahey T, Ebrahim S

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[Intervention Review]

Interventions for improving adherence to treatment in patients with high blood pressure in ambulatory settings

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ABSTRACT

Background

Lack of adherence to blood pressure lowering medication is a major reason for poor control of hypertension worldwide. Interventions to improve adherence to antihypertensive medication have been evaluated in randomised trials but it is unclear which interventions are effective.

Objectives

To determine the effectiveness of interventions aiming to increase adherence to blood pressure lowering medication in adults with high blood pressure

Search methods

All-language search of all articles (any year) in the Cochrane Controlled Trials Register (CCTR), MEDLINE, EMBASE, and CINAHL in April 2002.

Selection criteria

RCTs of interventions to increase adherence to blood pressure lowering medication in adults with essential hypertension in primary care, with adherence to medication and blood pressure control as outcomes

Data collection and analysis

Two authors extracted data independently and in duplicate and assessed each study according to the criteria outlined by the Cochrane Collaboration Handbook.

Main results

We included 38 studies testing 58 different interventions and containing data on 15519 patients. The studies were conducted in nine countries between 1975 and 2000. The duration of follow-up ranged from two to 60 months. Due to heterogeneity between studies in terms of interventions and the methods used to measure adherence, we did not pool the results. Simplifying dosing regimens increased adherence in seven out of nine studies, with a relative increase in adherence of 8 per cent to 19.6 per cent. Motivational strategies were

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successful in 10 out of 24 studies with generally small increases in adherence up to a maximum of 23 per cent. Complex interventions involving more than one technique increased adherence in eight out of 18 studies, ranging from 5 per cent to a maximum of 41 per cent. Patient education alone seemed largely unsuccessful.

Authors' conclusions

Reducing the number of daily doses appears to be effective in increasing adherence to blood pressure lowering medication and should be tried as a first line strategy, although there is less evidence of an effect on blood pressure reduction. Some motivational strategies and complex interventions appear promising, but we need more evidence on their effect through carefully designed RCTs.

PLAIN LANGUAGE SUMMARY

What interventions improve adherence to treatment in patients with high blood pressure in ambulatory settings

High blood pressure is a major risk factor for heart attack and stroke, and drug treatment of high blood pressure can substantially reduce this risk. However, the control of high blood pressure in the community is far from optimal. One of the major reasons for this is that patients with high blood pressure often fail to take their medication as prescribed. A number of interventions have been tested that aim to help patients take their medication but it is still uncertain how effective they are.

This review evaluates the effectiveness of interventions aiming to help patients with taking blood pressure lowering medication. We included studies in adult patients with a diagnosis of high blood pressure in a community setting and assessed interventions that aimed to increase adherence to blood pressure lowering medication. The outcomes assessed were adherence to medication and blood pressure changes.

For many interventions it is difficult to draw any real conclusions due to weaknesses of the included studies. However, reducing the number of daily doses appears to be effective in increasing adherence to blood pressure lowering medication and should be tried as a first line strategy although there is little evidence of an effect on blood pressure reduction. Some motivational strategies and complex interventions appear promising but we need more evidence on their effect through carefully designed randomised controlled trials to confirm these findings.

BACKGROUND

Hypertension is a major risk factor in the development of cardiovascular disease and poses a significant public health problem (MacMahon 1990). Randomized trials have demonstrated that treating high blood pressure with medication can substantially reduce the risk of stroke by 31 to 45 per cent and myocardial infarction by 8 to 23 per cent (Collins 1994). There is evidence that intensification of medication by means of treatment with two or more antihypertensive drugs is associated with improved blood pressure control (HDFP 1986, HDFP 1984). Despite the availability of effective treatments, the control of high blood pressure in the community is far from optimal, with lack of adherence to blood pressure lowering medication being a major factor (Burt 1995, Colhoun 1994, Sackett 1975). Adherence in treated hypertensives is estimated to be between 50 to 70 per cent (Psaty 1990, Caro 1995), and the importance of improving adherence to long-term therapies has recently been addressed by the World Health Organization in a major report (Sabate 2003).

A variety of interventions aiming to improve adherence to antihypertensive medication have been evaluated in randomized controlled trials (RCTs), and five systematic reviews have tried to summarize the evidence in this field (Dunbar-Jacob 1991; Ebrahim 1998, Morrison 2000, McDonald 2002, Roter 1998). The searches in three of these reviews were limited to studies indexed only in MEDLINE (Dunbar-Jacob 1991, Ebrahim 1998, Morrison 2000), thereby lacking in sensitivity and specificity (Dickersin 1994) and only included English language publications. None of these reviews could recommend any single approaches that increase adherence to blood pressure lowering medication. The most recent and more general review used a more comprehensive literature search and included six studies in hypertension (McDonald 2002).

Because more trials in this area have emerged recently (

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Blenkinsopp 2000, Andrejak 2000, Mehos 2000), this prompted us to carry out a new systematic review of the literature to establish which types of interventions to increase adherence are most effective, using a more comprehensive search strategy and including publications in languages other than English. We also aimed to investigate and report the effect of individual interventions used in factorial trials.

OBJECTIVES

- To locate and describe studies evaluating interventions aimed at improving adherence to antihypertensive medication
- To undertake a critical review of the quality of the study methods looking in particular at study design and validity
- To summarise the effectiveness of the above interventions
- To indicate areas for future research

METHODS

Criteria for considering studies for this review

Types of studies

RCTs of interventions to increase adherence to blood pressure lowering medication.

Types of participants

Adults with a diagnostic label of essential hypertension (as defined in individual studies) in a primary care, outpatient or other community setting.

Types of interventions

Any intervention designed to enhance medication adherence, including the following:
1. Education of caregivers and patients (e.g. counselling, health education)
2. Simplification of dosage regimens
3. Involvement of allied health professionals (e.g. nurses, pharmacists)
4. Special monitoring (e.g. vial caps, blood pressure self-measurement)
5. Motivation (e.g. financial incentives, reminder packages, reminder aids including diaries or follow-up appointments)
Control groups should either have received no intervention or "usual care" and have similar characteristics as the intervention groups.

Types of outcome measures

1. Adherence to medication (including any definition of adherence and noting how this was defined and measured in each study)
2. Blood pressure change in mmHg or change in blood pressure control according to the criteria used in each individual RCT. A 'net reduction' of blood pressure refers to the 'net' difference between the changes of blood pressure between baseline and follow-up in the intervention and control group.
Exclusion criteria:
1. Interventions not designed to increase adherence
2. Participants suffering from secondary hypertension
3. Participants hospitalised as opposed to ambulatory
4. Study design not RCT
5. Results already reported in another publication
6. Full results not reported and further information not available from study authors

Search methods for identification of studies

We identified original RCTs by an all-language search of all articles (any year) in the Cochrane Controlled Trials Register (CCTR), which now includes all RCTs that can be found in the MEDLINE and EMBASE databases, in April 2002. We applied a systematic search strategy using a series of topic terms to define the condition of interest (see below). We screened the references of all retrieved articles to identify additional publications. We contacted 25 study authors and experts in the field about other relevant trials or unpublished material and obtained responses from 17 individuals .
Search strategy:
1 HYPERTENS*
2 BLOOD-PRESSURE*:ME
3 (BLOOD:TI near PRESSURE:TI)
4 BLOOD-PRESSURE-DETERMINATION*:ME
5 BLOOD:TI next PRESSURE:TI near MONITOR*:TI
6 #1 or #2 or#3 or #4 or #5
7 PATIENT near COMPLIANCE
8 COMPLIANCE and :TI or ADHERENCE:TI
9 PATIENT next EDUCATION
10 ADHER* or MOTIVAT*
11 AMBULATORY-CARE*:ME
12 AMBULATORY:TI
13 COUNSEL*
14 FEEDBACK
15 REMINDER-SYSTEMS*:ME
16 REMIND*
17 DRUG-INFORMATION-SERVICES*:ME
18 ATTITUDE-TO-HEALTH*:ME
19 EDUCATION* next METHODS
20 EDUCATION* next MATERIAL*
21 PUBLICATIONS*:ME
22 PAMPHLET* or BROCHURE* or LEAFLET* or POSTER*

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23 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22
24 #6 and #23
This search strategy was amended slightly for further searches of MEDLINE, EMBASE and CINAHL.

Data collection and analysis

Study Identification
We assessed studies according to the Cochrane Handbook. Two investigators (KS, TF) assessed lists of citations and abstracts independently. Each reviewer indicated whether a citation was potentially relevant (i.e. appearing to meet the inclusion criteria), was clearly not relevant, or gave insufficient information to make a judgement. We resolved differences by discussion and attempted to obtain printed copies of all potentially relevant citations or full paper versions of those where insufficient information was available. Both investigators assessed copies of all presumably relevant articles independently according to the above criteria. To be included in the review, a study had to meet all our selection criteria.
Study Selection
We independently extracted data in duplicate concerning study design, methods, clinicians and patients, interventions, outcomes and potential sources of bias using a structured data collection form. As there is only a small amount of evidence available that masking reviewers reduces the risk of bias, we were not blinded to the source and the authors of publications.(Berlin 1997) A third rater (SE) verified the data extraction, and corrections were made where necessary.
Study evaluation
Due to the limited evidence on applying quality scores for individual RCTs we have presented RCT characteristics in a descriptive format, thereby providing a more accessible and more objective summary.(Juni 1999) Two reviewers provided data for the table independently and in duplicate, which were verified by the third reviewer. Disagreements were handled in the same way as for study identification and selection. We contacted 25 corresponding authors of studies to request missing data and verification of study details.
Quantitative data analysis
Due to heterogeneity between studies in terms of interventions and the various methods that were used to measure adherence, we felt that pooling of the results was inappropriate. We grouped and reported the individual arms of factorial trials separately in the respective groups.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.
We screened 1929 citations and included 38 studies that met all our predefined criteria, involving a total of 15519 patients and testing 58 different interventions. The table 'Characteristics of included studies' summarizes the characteristics of included RCTs, which were conducted between 1975 and 2000. We chose to report the interventions tested in factorial trials separately and treated these like individual studies.
The majority of trials were performed in the USA (n equals 21) and Canada (n equals 8) with the remainder located in Europe (n equals 8), Australia (n equals 1) and South Africa (n equals 1). Study participants fell into a number of different categories that included newly diagnosed patients, patients with established hypertension on medication, patients with controlled or uncontrolled hypertension, patients adherent or non-adherent to medication or infrequent attendees at clinic.
In view of a lack of a generally accepted categorization, we grouped studies arbitrarily into the following four pragmatic categories: (i) simplification of dosing regimens, (ii) patient education, (iii) patient motivation, support and reminders and (iv) complex health and organizational interventions including interventions in combination.
Adherence was measured in different ways, including self-report, direct questioning, pill counts, and the medication event monitoring system (MEMS®), which logs the time and date of each opening of a medication container. Various criteria for adherence were used in the different studies. All studies examined both men and women in varying proportions, and the duration of follow-up ranged from two to 60 months.

Risk of bias in included studies

The methodological quality of included studies was generally low (see Table 1). The randomization process was reported and provided adequate concealment of allocation in only 10 out of the 38 studies (26 per cent). The outcome assessors were blind to treatment allocation in 12 studies (31 per cent). Losses to follow-up were well documented in 33 studies (85 per cent). Only eight trials (21 per cent) reported a power calculation, and most of the remaining trials appeared too small to detect clinically important differences. None of the included studies fulfilled all the quality criteria.

Effects of interventions

EFFECT ON ADHERENCE AND BLOOD PRESSURE
Individual RCTs reported results on adherence in many different ways, making a pooled analysis inappropriate. Nineteen studies reported an improvement in adherence alone, of which 13 also

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reported blood pressure changes. Seven RCTs found an improvement in adherence combined with a reduction in blood pressure, and in seven studies a reduction in blood pressure occurred without an increase in adherence. Fifteen of the included studies (26 per cent) did not report a blood pressure outcome, and none of the studies examined major clinical endpoints.

Please note that in the following section, the total number of RCTs (i.e. interventions) is 58 rather than 38. This is because some studies reported the results of factorial trials testing two or more different interventions, which we have evaluated separately.

(i) SIMPLIFICATION OF DOSING REGIMENS (nine study interventions)

Interventions evaluated in this category included once daily versus twice daily preparations of metoprolol, amlodipine, or enalapril. One study tested transdermal clonidine plus placebo tablets versus verapamil and a transdermal placebo (Burris 1991). Asplund and colleagues compared pindolol and clopamide combined in one tablet versus both drugs in separate tablets.

Simplifying dosing regimens improved adherence in seven out of nine studies (Andrejak 2000, Baird 1984, Boissell 1996, Detry 1995, Leenen 1997, Mounier-Veh. 1998, Girvin 1999), with relative improvement in adherence ranging from 8 to 19.6 per cent. All five studies in this category that used objective outcome measurement (MEMS®) showed an improvement in adherence through the use of once-daily instead of twice-daily dosage regimens, although four of these compared two different drugs. Seven studies also reported blood pressure changes. Only one study showed an increase in adherence (90 versus 82 per cent, p less than 0.01) together with a reduction in systolic blood pressure of 6 mmHg systolic (p less than 0.01) (Leenen 1997). However, the changes in diastolic blood pressure in this study were insignificant.

(ii) PATIENT EDUCATION (six study interventions)

Educational interventions in the included studies consisted of an educational programme via slides, audiotape and booklet (Sackett 1975), group education (Webb 1980; Pierce 1984; Marquez-Contr. 1998), written educational material (Kirscht 1977), and education via visual aids, lecture, discussion and knowledge test (Kerr 1985).

Patient education seemed largely unsuccessful. Only a single and relatively small trial (n=110) improved adherence (93 versus 69 per cent, p less than 0.002) with no reported effect on blood pressure (Marquez-Contr. 1998). This study used group education in groups of 15 people over 90 minutes and additional postal information leaflets at one, three and five months.

(iii) PATIENT MOTIVATION, SUPPORT AND REMINDERS (24 study interventions)

In this category, we included interventions such as special compliance dispensers (Becker 1986; Eshelman 1976; Rehder 1980; McKenney 1992; Skaer 1993), drug reminder charts (Gabriel 1977), self-recording of blood pressure (Johnson 1978; Kirscht 1977; Kerr 1985; Zarnke 1997), monthly home visits (Johnson 1978), teaching on self-determination (Nessman 1980), counseling (Rehder 1980; Webb 1980; Morisky 1985; Park 1996), nurse phone calls (Kirscht 1977), social support (Kirscht 1977; Morisky 1985), small group training (Morisky 1985), postal reminders (Skaer 1993), and telephone-linked computer counselling (an interactive computer based telecommunications system that converses with patients in their homes between office visits to their physicians) (Friedman 1996).

Motivational strategies were successful in 10 out of 24 study interventions with mostly small increases in adherence up to a maximum of 23 per cent (Kirscht 1977, Gabriel 1977, Nessman 1980, Friedman 1996, McKenney 1992, Morisky 1985, Skaer 1993, Kirscht 1977). All of these studies used methods of measuring adherence, such as pill counts, self-report, direct questioning, and prescription refill records, which are less reliable than electronic monitoring (Urquhart 1997). Successful interventions included daily drug reminder charts (mean adherence score 82.4 versus 70.4 per cent, p=0.002) (Gabriel 1977), training on self-determination (4.6 out of 7 weeks adherent versus 3.3 weeks in the control group, p less than 0.001) (Nessman 1980), reminders and packaging (increase in adherence between 8 per cent for reminders alone and 23 per cent for reminders and packaging in combination, p less than 0.05) (Skaer 1993), social support (98 per cent achieved maximum adherence score versus 93 per cent, p less than 0.05) (Kirscht 1977), nurse phone calls (96 per cent achieved maximum adherence score versus 91 per cent, p less than 0.05) (Kirscht 1977), family member support (53 per cent high adherers versus 40 per cent low adherers, p less than 0.05) (Morisky 1985), electronic medication aid cap (mean adherence 95 per cent versus 78 per cent, p=0.0002) (McKenney 1992), and telephone-linked computer counseling (18 per cent adherent versus 12 per cent in the control group, p=0.03) (Friedman 1996).

(iv) COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS INCLUDING INTERVENTIONS IN COMBINATION (19 study interventions)

The interventions in this category consisted mainly of complex combined interventions or structured hypertension management (see table of included studies for further details).

Complex interventions increased adherence in eight out of 18 study interventions (Blenkinsopp 2000, Burrelle 1986, Logan 1979, Sclar 1991, Solomon 1998, Haynes 1976, Saunders 1991), ranging from five per cent to a maximum of 41 per cent. Worksite care through specially trained nurses improved adherence (67 per cent versus 49 per cent, p less than 0.005) and led to a net reduction in diastolic blood pressure of 4 mmHg between intervention and control groups (p less than 0.001) (Logan 1979). A combination of home visits, education and special dosing devices improved adherence in a small trial of 16 patients (92 per cent versus 71 per cent, p less than 0.001) (Burrelle 1986). A strategy involving an educational leaflet, a telephone reminder, a mailed reminder and an educational newsletter was successful in both previously treated hypertensives ('medication possession ratio' 82 per cent versus 48 per cent, p less than 0.05) and those who were newly diagnosed

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(93 per cent versus 52 per cent, p less than 0.05) (Sclar 1991). Two fairly recent trials reported weak evidence of an effect of a patient-centered pharmaceutical care model in which pharmacists either used a structured, brief questioning protocol to identify patients' medication related problems and their information needs relating to hypertension and its treatment (compliance score 0.23 versus 0.61, p less than 0.05) (Solomon 1998), or a combination of structured brief questioning protocol with advice, information and referral to the family practitioner (62 per cent adherent versus 50 per cent, p less than 0.05) (Blenkinsopp 2000). In this study, blood pressure was also better controlled (i.e. blood pressure readings of 159/89 mmHg or below) in the intervention group (35.7 per cent became controlled versus 17.1 per cent, p less than 0.05), although blood pressure data were available only for a subset of participants.

DISCUSSION

Summary of key findings

In this systematic review we found RCTs that evaluated a number of strategies to improve adherence to blood pressure lowering medication, including simplification of dosing regimens, patient education, motivation, support, and reminders as well as complex health and organizational interventions including interventions in combination. Simplification of dosing regimens increased adherence in seven out of nine studies, with improvement in adherence ranging from 8 to 19.6 per cent. Adherence in these studies was mainly measured with electronic monitors and these results confirm findings from past research. There was inconclusive evidence for the effect of motivational and more complex interventions. Education alone appeared largely unsuccessful. An effect on both adherence and blood pressure was only observed in seven out of 58 interventions (18 per cent). While an effect on both adherence and blood pressure was only observed for a minority of interventions, not all studies reported blood pressure outcomes.

INTERPRETATION OF THE RESULTS IN THE LIGHT OF PREVIOUS RESEARCH

This review differs from previously published reviews in that we used a more comprehensive search strategy and different methodology. Compared to the latest reviews on adherence enhancing strategies (Morrison 2000; McDonald 2002), we found and included considerably more studies (nine and 32 more studies respectively). The review by Morrison extracted categorical data in preference to continuous data and ignored evidence from trials where data could not be converted. This may have been particularly relevant for the results in the group with changes in medication dosing, where we come to the opposite conclusion. This review is also different in that we have reported the results from individual arms of factorial trials separately.

We agree with the review by McDonald et al that for complex interventions it is often difficult to estimate the independent effects of individual interventions (McDonald 2002). It also remains difficult to disentangle specific adherence effects as opposed to non-specific effects of increased attention. Our findings confirm that even the most effective interventions do not appear to lead to large improvements in adherence and blood pressure reductions. However, clinical outcomes were not measured and BP measurements were not included in all of the studies.

An earlier review of research on adherence reported benefits of educational interventions in improving adherence (Dunbar-Jacob 1991). However, we were unable to confirm this finding, perhaps because our review was limited to evidence from randomised trials only.

LIMITATIONS OF THIS REVIEW

Comparing the RCTs included in this review was difficult. Many RCTs showed marked heterogeneity in terms of participants, interventions and outcomes. Study authors also measured and reported adherence inconsistently. Individual RCTs demonstrated variable and often poor methodological quality, particularly with regard to randomization, blinding of outcome assessment and losses to follow-up, whilst the sample sizes of many trials were too small to detect clinically relevant differences. Rather surprisingly, 15 out of the included 38 studies (39%) did not report a blood pressure outcome, and none reported major clinical endpoints.

There are also some difficulties in interpreting the results of this systematic review. Adherence was measured (e.g. self-report, pill counts, direct questioning, electronic monitoring, drug blood levels) and calculated in different ways (e.g. using arbitrary cut-off points to define adherence such as 80%), and in addition was usually assessed unblinded to allocation status, which made the comparison of RCTs difficult. Levels of adherence in the control groups of the trials studied ranged from 12% to 94%, which is indicative of the heterogeneity in both criteria for defining adherence and the participants studied. With no agreed definitions on how adherence should be measured and defined, it is not surprising that for most interventions the impact on adherence and blood pressure appears to be variable. Because of the different definitions for adherence that have been adopted in individual RCTs, it has not been possible to examine the relationship between adherence to medication and subsequent blood pressure control. Our categorization and grouping of trials was arbitrary, and the group allocation of some trials might be debatable.

It is possible that the interventions tested in the factorial trials were not independent from each other. Particularly in the case of complex interventions evaluated in factorial trial designs, interactions are likely, and the results have therefore to be interpreted with caution.

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AUTHORS' CONCLUSIONS

Implications for practice

Our findings suggest that introducing simpler dosing regimens can be effective in improving adherence, but the effect on subsequent blood pressure reduction has not been established and may not be clinically important. The results of various motivational and more complex interventions are promising, although there is insufficient evidence to suggest a single approach.

We suggest that innovative approaches should be introduced in the context of further RCTs. It is important that physicians are aware of the various reasons for poor adherence and aim to simplify dosing regimes as far as possible.

Different health professionals were involved in delivering the interventions in the studies included in this review. In many countries, the role of allied health professionals such as nurses or physician assistants is expanding, which may lead to new management opportunities for tackling adherence-related problems in patients with high blood pressure.

Implications for research

The results of this review highlight a number of problem areas in adherence related research. Many studies used unreliable methods of measuring adherence such as self-report and pill counts. It appears that electronic monitoring provides more objective and reliable results and, in addition, produces data on medication taking patterns (Urquhart 1997). Although a large number of studies have been conducted in this area, larger trials of higher quality are needed that use reliable methods of measuring adherence and that also investigate the relationship between adherence and blood pressure reduction. We feel this is particularly important in the context of an increasing elderly population of people who often take multiple medications.

Hypertensive patients may fail to take their medication due to the long duration of therapy, the symptomless nature of the condition, side effects of medication, complicated drug regimens, lack of understanding about hypertension management, lack of motivation and the challenge to individual patients' health beliefs (Ebrahim 1998; Dowell 2002). It would seem logical that future studies should try and adopt a 'tailored' approach aimed at individual patients and addressing the above mentioned barriers to adherence (Working Party 1997). Combinations of strategies that include simpler dosage regimens, patient motivation and that involve other health professionals in a patient-centered approach should be further investigated. In addition, patients' views should be taken into account when piloting interventions, and the interventions themselves should be based on shared decision-making in a partnership between patient and practitioner (Bowling 2001; Sieber 2000; Thomson 2001; Rand 2000).

It is paramount that every study that evaluates an intervention to increase adherence to blood pressure lowering medication should also measure blood pressure as a second outcome to help examine the relationship between adherence and blood pressure control.

Finally, only one RCT underwent an economic evaluation, which showed that nurse-led work-site care was not cost-effective, with an incremental cost-effectiveness ratio almost double that of usual care (Logan 1983). It is important that future studies include economic analyses because adherence interventions will generally have cost implications. Adherence to blood pressure lowering medication must persist long-term to show a clinically relevant benefit. Many studies included in this review had a follow-up period of less than six months (see table of Characteristics of Studies). We therefore suggest that interventions in future studies should be tested over a period of at least six months.

We conclude that simplification of dosing regimens appears to be the most promising intervention to increase adherence to blood pressure lowering medication. The results of this review should be interpreted with caution due to the poor methodological quality and heterogeneity of trials included in this review. Our findings emphasize the need for further RCTs with sufficient power and of rigorous methodology.

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* *Indicates the major publication for the study*

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Andrejak 2000

Methods	Parallel trial, study duration six months, follow -up at six months
Participants	162 participants with mild to moderate hypertension, 45 per cent men, mean age 57 years, multi-centre, France
Interventions	SIMPLIFICATION OF DOSING REGIMENS: once daily trandolapril 2mg versus twice daily captopril 25mg
Outcomes	ELECTRONIC MONITORING: percentage of correct dosing 94 per cent in intervention group compared to 78. 1 per cent among controls, p less than 0.0001
Notes	Study compared two different drugs.

Asplund 1984

Methods	Cross-over trial, intervention four months on each regimen, follow-up at eight months
Participants	160 participants with treated and controlled hypertension, 61 per cent men, mean age 51 years, hospital outpatients in Sweden
Interventions	SIMPLIFICATION OF DOSING REGIMENS: pindolol 10mg and clopamide 5mg once daily in one combination tablet versus two tablets
Outcomes	PILL COUNT AND SELF REPORT: 40.8 per cent never forgot a tablet in the experimental group versus 69 per cent in the control group (not statistically significant, but no exact p-value reported) Net increases of 2.8 mmHg systolic and 3.0 mm Hg diastolic (not statistically significant, no exact p-value reported)
Notes	Dropouts not clearly reported

Baird 1984

Methods	Parallel, study duration eight weeks, follow-up at 10 weeks
Participants	389 participants with treated and controlled hypertension, 70 per cent men, mean age 54 years, primary care, Canada
Interventions	SIMPLIFICATION OF DOSING REGMENS: Metoprolol 200mg once daily versus metroprolol 100mg twice daily
Outcomes	PILL COUNT: 96 per cent took more than 80 per cent of medication in the intervention group (once-daily regimen) compared to 90 per cent in the control group (p equals 0.059). 93 per cent took more than 90 per cent of medication in the intervention group compared to 82 per cent in the control group (p equals 0.009). 1 mmHg net reduction in systolic blood pressure and no net reduction for diastolic blood pressure (not statistically significant, no exact p-value reported)

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Baird 1984 (*Continued*)

Notes	Detailed reasons for loss to follow-up reported. Randomisation procedure and blinding to outcome assessment unclear

Becker 1986

Methods	Parallel, study duration one year, follow-up at one year
Participants	180 participants with treated and uncontrolled hypertension, primarily middle aged black women, less than 20 per cent employed, primary care in USA
Interventions	PATIENT MOTIVATION, SUPPORT AND REMINDERS: special unit dose reminder packaging versus usual medication vials
Outcomes	PILL COUNT AND SELF REPORT: 84 per cent adherent in the intervention group compared to 75 per cent among the controls (not statistically significant, no exact p-value reported). Net reduction in diastolic blood pressure 0.2 mmHg (not statistically significant)
Notes	Physicians blinded to treatment allocation, aware that compliance study was in progress but unaware of the aims of the study

Blenkinsopp 2000

Methods	Cluster-randomised parallel, study duration six months
Participants	180 participants with treated hypertension, 62 per cent age 60 or over, 20 community pharmacy sites, UK
Interventions	COMPLEX HEALTH AND ORGANISATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: structured brief questioning protocol on medication problems, including advice, information and referral to general practitioner by pharmacists three times at two-month intervals
Outcomes	SELF REPORT: 62 per cent adherent in the intervention group compared to 50 per cent in the control group (p less than 0.05). 35.7 per cent of uncontrolled patients became controlled in the intervention group compared to 17. 1 per cent in the control group (p less than 0.05)
Notes	Complete data on blood pressure only available on 100 participants, high likelihood of bias

Boissell 1996

Methods	Parallel, study duration three months, follow up at three months
Participants	7272 participants, 50 per cent men, mean age 61 years, primary care, France
Interventions	SIMPLIFICATION OF DOSING REGIMENS: nicardipine 20 mg thrice daily versus nicardipine SR 50 mg twice daily

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Boissell 1996 (*Continued*)

Outcomes	SELF REPORT: 82 per cent of participants in intervention group reported excellent adherence compared to 76 per cent among controls (p less than 0.001). Net reduction in blood pressure 0.2 mmHg (systolic) and 0.3 mmHg (diastolic). Not statistically significant, no exact p-value reported
Notes	No differential loss to follow-up reported, high participant number due to large number of participating general practitioners, bias likely

Burrelle 1986

Methods	Parallel, study duration eight weeks, follow-up at eight weeks
Participants	16 participants with treated hypertension and non-adherent, 75 per cent black, 75 per cent female, mean age 69 years, hospital outpatients and primary care, USA
Interventions	COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: Home visits, education, special dosing devices versus usual care
Outcomes	PILL COUNT AND SELF REPORT: Percent of pills taken: 92 per cent in the intervention group compared to 71 per cent in the control group (p less than 0.0001). Net reduction in blood pressure 7 mmHg (systolic) and net increase of 7 mmHg in diastolic blood pressure (p greater than 0.05)
Notes	Small study, likelihood of bias.

Burris 1991

Methods	Parallel, study duration eight weeks, follow up at eight weeks
Participants	58 participants with treated and uncontrolled hypertension, mean age 67/68 years (intervention/control), 76/66 per cent male (intervention/control), hospital outpatients, USA
Interventions	SIMPLIFICATION OF DOSING REGIMENS: transdermal clonidine 0.1mg per day with placebo tablets versus verapamil SR 120mg daily plus transdermal placebo
Outcomes	PILL COUNT, VISUAL ASSESSMENT: 96 to 100 per cent of participants wore the active patch at every visit compared to 100 per cent using the placebo patch. 68 to 88 per cent had optimal tablet counts in the verapamil SR group compared to 11 to 37 per cent in the control group (p-values not reported). Net reduction 5 mmHg (systolic) and 1 mmHg (diastolic), p less than 0.05
Notes	No probability values reported for adherence outcome. Study compared different drugs. Different methods used to assess adherence in both groups. High likelihood of bias

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Detry 1995

Methods	Crossover, study duration 12 weeks, follow-up at 12 weeks
Participants	320 participants with uncontrolled hypertension, age under 70 years, mean age 60 years, 52 per cent male, hospital outpatients, Belgium
Interventions	SIMPLIFICATION OF DOSING REGIMENS: amlodipine 5mg daily versus nifedipine 20mg twice daily
Outcomes	PILL COUNTS AND ELECTRONIC MONITORING: therapeutic coverage 93.7 per cent in the intervention group versus 75.9 per cent in the control group (p less than 0.001). Blood pressure changes not reported
Notes	Crossover RCT, patients double-counted. Randomisation procedure not reported. Study compared two different drugs

Eshelman 1976

Methods	Parallel, study length and timing of follow-up not reported
Participants	100 participants with treated hypertension, no baseline data reported, hospital outpatients and pharmacy department, USA
Interventions	PATIENT MOTIVATION, SUPPORT AND REMINDERS: compliance dispenser versus usual medication bottle
Outcomes	PILL COUNT AND SELF REPORT: 63 per cent adherent in the intervention group compared to 61 per cent in the control group (not statistically significant, no exact p-value reported)
Notes	Dropouts at least 33 per cent with no differential loss to follow-up reported. Bias likely

Friedman 1996

Methods	Parallel, study duration six months, follow-up at six months
Participants	267 participants with treated hypertension, 90 per cent white, 77 per cent women, mean age 76 years, primary care, USA
Interventions	PATIENT MOTIVATION, SUPPORT AND REMINDERS: telephone linked computer counselling versus usual care
Outcomes	PILL COUNT: 18 per cent adherent in the intervention group compared to 12 per cent in the control group (p equals 0.03). Net reduction in blood pressure 4.7 mmHg systolic (p equals 0.85) and 4.4 mmHg diastolic (p equals 0.09)
Notes	Treatment provider blinded until baseline measurement completed. Randomisation by 'paired randomisation protocol'

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Gabriel 1977

Methods	Parallel, 3 1/2 months follow-up
Participants	79 participants with treated hypertension, mean age 65 years, mainly black women, pharmacy at community health center, US
Interventions	PATIENT MOTIVATION, SUPPORT AND REMINDERS: daily drug reminder chart with pharmacist supervision
Outcomes	PILL COUNT AND SELF REPORT: mean compliance score 82.4 per cent in the intervention group compared to 70.4 per cent in the control group (p equals 0.002)
Notes	Small study, no power calculation reported, unreliable assessment of adherence

Girvin 1999

Methods	Cross over, three months follow -up
Participants	27 participants with controlled hypertension, 64 per cent men, mean age 62 years, general practices, Northern Ireland
Interventions	SIMPLIFICATION OF DOSING REGIMENS: enalapril 20mg once daily versus Enalapril 10mg twice daily
Outcomes	ELECTRONIC MONITORING: 92.2 per cent adherent in intervention group versus 72.6 per cent in the control group (p less than 0.001). 5.3 mmHg net reduction in systolic and 1.0 mmHg net reduction in diastolic blood pressure (p equals 0.068 and 0.086 respectively)
Notes	Patient selection with potential for selection bias.

Hamilton 1993

Methods	Parallel, six months follow up
Participants	34 participants with treated hypertension, mean age 54 years, white, married, high school educated, hypertension clinic in tertiary care teaching medical center, US
Interventions	COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: postcard reminder, nurse-led educational appointment and follow-up phone call compared with usual care
Outcomes	SELF REPORT: adherence score of 27.5 in intervention group compared to 24.5 in control group (p equals 0.12). Net reductions of blood pressure 17.3 mmHg systolic and 4.7 mmHg diastolic (p equals 0.03 and 0.22 respectively)
Notes	Small study.

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Hawkins 1979

Methods	Parallel study, 29 months follow -up
Participants	1148 participants with hypertension and diabetes, hospital outpatient clinic, mean age 60 years, 76 per cent women, USA
Interventions	COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: post-diagnostic management of patients with hypertension and diabetes by clinical pharmacist versus usual physician review
Outcomes	PRESCRIPTION RECORD: diuretic only: 60.5 per cent adherent in intervention group versus 52.9 per cent in the control group (p less than 0.7), diuretic plus methyldopa: 84.6 per cent adherent in intervention group versus 65.4 per cent among controls (p equals 0.2). Net reduction in blood pressure 4 mmHg systolic and 0 mmHg diastolic (p less than 0.001 and not significant with no exact p-value reported, respectively, for both groups combined)
Notes	High losses to follow-up (45 per cent)

Haynes 1976

Methods	Parallel, study duration one year, follow-up at one year
Participants	39 participants with treated and uncontrolled hypertension, male steel workers, work-site, Canada
Interventions	COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: Self-measurement of blood pressure, medication and blood pressure charting, tailoring to daily routines, fortnightly review and rewards (financial and praise) versus no intervention
Outcomes	PILL COUNT: 66 per cent adherent in the intervention group compared to 43 per cent among the controls (p less than 0.025). Net reduction in diastolic blood pressure 4 mmHg (p=0.12)
Notes	Small study. Potential sources of bias well reported. Study was underpowered to detect an effect on blood pressure

Johnson 1978

Methods	Factorial, study duration six months, follow-up at six months
Participants	204 participants with treated but uncontrolled hypertension, 60 per cent women, mean age 54/52 years (men/women), primary care, Canada
Interventions	COMPLEX HEALTH AND ORGANISATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: self-recording of blood pressure and monthly home visits, self-recording only, monthly home visits only versus no intervention
Outcomes	Increase in adherence 10 per cent (self-monitoring plus visits), 12 per cent (self-monitoring only) and ten per cent (home visits only) compared to one per cent decrease in the control group (not significant, no exact p-value reported) . Reductions in diastolic blood pressure 1mmHg (self-monitoring plus home visits), 2 mmHg (self-monitoring only) and 2 mmHg (home visits only), all not statistically significant, but no exact p-value reported

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Johnson 1978 (*Continued*)

Notes	Power calculation not reported but probability of type II error quantified in the discussion

Kerr 1985

Methods	Parallel, study duration one day, follow up at three months
Participants	235 employees, 57 per cent men, mean age 50.3 years, work-site, USA
Interventions	COMPLEX HEALTH AND ORGANISATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: Education and self-monitoring, self-monitoring only, education only versus no intervention
Outcomes	SELF REPORT: Per cent of pills taken: 100 per cent (education and self-monitoring), 84 per cent (self-monitoring only) and 81 per cent (education only) versus 100 per cent (control), not statistically significant. Reduction in diastolic blood pressure zero mmHg (education and monitoring) and increases in diastolic blood pressure of 1 mmHg (self-monitoring only) and 5 mmHg (education only), not statistically significant
Notes	Large dropouts in all groups, inconsistencies between denominators in tables and dropouts that vary for blood pressure and adherence outcomes

Kirscht 1977

Methods	Parallel, study duration one day, follow-up at three months
Participants	400 participants with treated hypertension, nearly all white, 78 per cent age over 50, primary care, USA
Interventions	COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: Four sequential interventions four months apart: Education, nurse phone calls, self-recording of blood pressure, social support versus usual care
Outcomes	SELF REPORT: Percentage of maximum adherence score achieved (intervention versus control): Educational material 91 versus 90 per cent (not significant), nurse phone calls 96 versus 91 per cent (not significant), self-monitoring 94 versus 94 per cent (not significant) and social support 98 versus 93 per cent (p less or equal to 0.05). Blood pressure changes not reported
Notes	Results difficult to interpret due to unclear reporting of adherence scores

Leenen 1997

Methods	Parallel, study duration 20 weeks, follow-up at 20 weeks
Participants	198 participants with newly diagnosed hypertension, 60 per cent men, mean age 55 years, primary care, Canada
Interventions	SIMPLIFICATION OF DOSING REGIMENS: Amlodipine 5mg daily versus diltiazem SR 60mg twice daily

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Leenen 1997 (*Continued*)

Outcomes	ELECTRONIC MONITORING (MEDICATION EVENT MONITORING SYSTEM): 90 per cent adherent in intervention group compared to 82 per cent in the control group (p less than 0.01). Net reduction in systolic blood pressure 6 mmHg (p less than 0.01) and diastolic blood pressure 1 mmHg (not statistically significant, no exact p-value reported)
Notes	Study compared two different drugs. Bias likely.

Logan 1979

Methods	Parallel, study duration six months, follow up at six months
Participants	457 volunteers from business, newly diagnosed hypertension, 88 per cent white, 79 per cent male, mean age 47 years, work-site, Canada
Interventions	COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: Nurse-led work-site care versus usual care
Outcomes	PILL COUNT: 67 per cent adherent in the intervention group compared to 49 per cent in the control group (p less than 0.005). Reduction in blood pressure 4 mmHg diastolic (p less than 0.001)
Notes	Differential loss to follow-up well reported

Logan 1983

Methods	Parallel, study duration one year, follow-up at one year
Participants	194 participants, uncontrolled hypertensive business employees, 84 per cent white, 73 per cent male, business employees, work site, Canada
Interventions	COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: nurse-led care versus usual care
Outcomes	PILL COUNT: 55 per cent adherent in the intervention group compared to 56 per cent in the control group (not statistically significant, no exact p-value reported). Net reduction in diastolic blood pressure 3 mmHg (not significant)
Notes	Randomisation process unclear

Marquez-Contr. 1998

Methods	Parallel, study duration six months, follow-up at six months
Participants	110 participants with newly diagnosed and established treated hypertension, 71 per cent women, mean age 59 years, primary care, Spain

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Marquez-Contr. 1998 (*Continued*)

Interventions	PATIENT EDUCATION AND COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: group sessions with information about blood pressure management and postal education (with information on blood pressure and the importance of compliance, sent at months one, three and five) versus usual care
Outcomes	PILL COUNT: 93 per cent adherent in the intervention group compared to 69 per cent in the usual care group (p less than 0.002). Reduction in blood pressure not reported
Notes	Differential loss to follow-up in both treatment arms not reported

McKenney 1992

Methods	Two-phase parallel, study duration two times 12 weeks, follow-up at 12 and 24 weeks
Participants	70 participants, 70 per cent white, 59 per cent women, mean age 73 years
Interventions	PATIENT MOTIVATION, SUPPORT AND REMINDERS: electronic medication aid cap with recording card and blood pressure cuff versus usual drug bottle
Outcomes	PILL COUNT: PHASE I: Mean adherence 95 per cent in the intervention group compared to 78 per cent among controls (p equals 0.0002) . Net reduction in blood pressure intervention versus control 4.8 mmHg systolic (p equals 0.0006) and 8.6 mmHg diastolic (p less than 0.001) PHASE II: Mean adherence rates 93.6 per cent for cap only (p equals 0.003), 98.7 per cent for cap and card (p less than 0.001) , 100.2 per cent for cap card and cuff (p less than 0.001) versus 79 per cent in the control group. Net blood pressure reduction 12.3 mmHg systolic (p less than 0.01) and 19.2 mmHg diastolic (p equals 0.0001) for cap and card. Net blood pressure reduction 19.5mmHg systolic (p equals 0.0006) and 12.7 mmHg diastolic (p=0.0006) for cap, card and cuff
Notes	Nine patients required change of medication during second phase, and their blood pressure measurements were not included in the analysis

Mehos 2000

Methods	Parallel, six months follow-up
Participants	41 participants with uncontrolled hypertension, mean age 59 years, 70 per cent women, single family medicine clinic, US
Interventions	COMPLEX HEALTH AND ORGANISATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: home blood pressure measurement, diary, instruction to measure blood pressure, information on hypertension and risk factor with subsequent evaluation by clinical pharmacist versus usual care

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Mehos 2000 (*Continued*)

Outcomes	PRESCRIPTION REFILL DATA: mean adherence 82 per cent in intervention group versus 89 per cent in the control group (p equals 0.29). Blood pressure net reduction 10.1 mmHg systolic (p equals 0.069) and 6.7 mmHg diastolic (p equals 0.02)
Notes	Patients randomised using a 'deck of cards'

Morisky 1985

Methods	Sequential factorial, study duration three years, follow-up at five years
Participants	193 participants with treated hypertension, 91 per cent black, 70 per cent women, median age 54 years, USA
Interventions	PATIENT EDUCATION: re-inforcement interview, family member support, small groups versus usual care
Outcomes	SELF REPORT: high adherers: 53 per cent (family support), 36 per cent (counselling) and 40 per cent (small group training) versus 40 per cent in the usual care group (p less than 0.05, not significant and not significant respectively) . Control of blood pressure (control being defined as equal or less than 140/90 mmHg in patients age 39 and under; equal or less than 150/95 mmHg for ages 40 to 59; equal or less than 160/100 age 60 or older) 75 per cent (family support), 54 per cent (counselling) and 46 per cent (small group training) in the intervention groups compared to 50 per cent in the control group (p less than 0.05, not significant and not significant, respectively)
Notes	No significant differences between dropouts and those who continued to receive care

Mounier-Veh. 1998

Methods	Parallel, study duration 12 weeks, follow-up at 12 weeks
Participants	103 participants with treated and uncontrolled hypertension, mean age 54 years, 27 per cent women, primary care, France
Interventions	SIMPLIFICATION OF DOSING REGIMENS: amlodipine 5mg once daily versus nifedipine 20mg twice daily
Outcomes	ELECTRONIC MONITORING: 92.5 per cent adherent in the intervention group compared to 74.8 per cent among the controls (p less than 0.001). net reduction in systolic blood pressure 0.8 mmHg and 1.1 mmHg net increase in diastolic blood pressure (not statistically significant, no exact p-value reported)
Notes	Treatment allocation according to 'enrollment order' and 'randomisation list', study compares two different drugs

Nessman 1980

Methods	Parallel, study duration eight weeks, follow-up at six months
Participants	52 non-adherent participants with treated but uncontrolled hypertension, 75 per cent white, 98 per cent male, mean age 55 years, hospital outpatients, USA

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Nessman 1980 (*Continued*)

Interventions	PATIENT MOTIVATION, SUPPORT AND REMINDERS: nurse and psychologist teaching self-determination versus nurse and protocol-run clinic (control)
Outcomes	PILL COUNT: intervention group compliant for 4.6 out of seven weeks versus 3.3 weeks in the control group (p less than 0.001). Reduction in systolic blood pressure 6 mmHg (p less than 0.05)
Notes	Only 10 per cent of eligible patients took part in the study which may have led to self-selection

Park 1996

Methods	Parallel, four months follow-up
Participants	64 participants, mainly white with treated hypertension, 50 per cent women, mean age 60 years, two chain pharmacies, US
Interventions	PATIENT MOTIVATION, SUPPORT AND REMINDERS: pharmacy-based education and counselling
Outcomes	PILL COUNT: mean adherence 86.6 per cent in the intervention group compared to 89.1 per cent in the control group (not statistically significant, no exact p-value reported)
Notes	Small sample size, method of randomisation unclear.

Pierce 1984

Methods	Factorial trial, six months follow-up
Participants	115 participants with uncontrolled hypertension, mean age 57 years, 60 per cent women, one general practice clinic, Western Australia
Interventions	COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: Self monitoring of blood pressure and health education alone and in combination versus usual care
Outcomes	PILL COUNT AND SELF REPORT: self-monitoring and education: 26 per cent good adherers versus 24 per cent in the control group (not significant, no exact p-value reported), self-monitoring only: 30 per cent versus 24 per cent (not significant, no exact p-value reported), education only: 28 per cent versus 24 per cent (not significant, no exact p-value reported). BLOOD PRESSURE: education: 83 per cent had blood pressure reduction versus 67 per cent among controls (p less than 0.05, effect size unclear), self monitoring: 74 per cent versus 78 per cent (not significant, no exact p-value reported, effect size unclear), both education and self monitoring combined: 74 per cent versus 78 per cent, no exact p-value reported, effect size unclear)
Notes	Randomisation procedure prone to bias. Reporting of outcomes inadequate

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Rehder 1980

Methods	Factorial, study duration three months, follow-up at six months
Participants	150 participants with treated hypertension, 92 per cent black, 75 per cent women, mean age 50 years, hospital outpatients, USA
Interventions	COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: Counselling with special medication container and special medication container only versus usual medication vials
Outcomes	PILL COUNT: 99 per cent (counselling and container), 94 per cent (container only) and 90 per cent (counselling only) versus 88 per cent among the controls, not statistically significant (no exact p-value reported)
Notes	High dropout rate and small sample size for a factorial trial

Sackett 1975

Methods	Factorial, study duration not reported, follow-up at six months
Participants	230 male steel workers, work site, Canada
Interventions	COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: doctor-led work site care, educational programme, both interventions versus neither intervention (control)
Outcomes	PILL COUNT: 54 per cent of those receiving augmented convenience adherent compared to 51 per cent receiving usual care (not statistically significant) 50 per cent adherent in education group compared to 56 per cent among controls (not statistically significant). Net increase of the percentage of participants with controlled blood pressure (diastolic blood pressure less than 90 mmHg) of 4 per cent for physician-led work site care and five per cent (physician-led work site care plus education), not statistically significant
Notes	No power calculation as such, but important effect size reported a priori

Saunders 1991

Methods	Parallel, study duration six months, follow-up at six months
Participants	224 participants, newly diagnosed or infrequently attending, black, 73 per cent women, about 65 per cent aged 40 to 59 years in two intervention groups, Soweto, South Africa
Interventions	COMPLEX HEALTH AND EDUCATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: written reminders, patient-held records, home visits versus usual care
Outcomes	PILL COUNT: 31 per cent (newly diagnosed) and 68 per cent (infrequent attenders) adherent in the intervention group versus 15 per cent (newly diagnosed) and 37 per cent (infrequent attenders) among the controls (p equals 0.19 and 0.009 respectively). Reduction in blood pressure 7 mmHg diastolic (not significant) for newly diagnosed participants and net increase in diastolic blood pressure 4.3 mmHg among infrequent attenders (not statistically significant, no exact p-value reported)

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Saunders 1991 (*Continued*)

Notes	Dropouts were lower in the intervention groups.

Sclar 1991

Methods	Parallel, study duration six months, follow up at six months
Participants	344 previously treated and 109 newly diagnosed hypertensive participants, mean age 57 years, hospital outpatients, USA
Interventions	COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: Prescription refill pack containing drugs and educational material versus usual supply of drugs
Outcomes	PILL COUNT: 34 per cent (newly diagnosed) and 41 per cent (established hypertensives) higher medication possession rates in the intervention groups compared to controls (p less than 0.05 for both groups). Reduction in blood pressure not reported
Notes	No drop-outs reported despite uneven number randomised

Skaer 1993

Methods	Factorial, study duration 12 months
Participants	304 participants, previously untreated for mild to moderate hypertension, mean age 56 years, 46 per cent women, pharmacy, US
Interventions	PATIENT MOTIVATION, SUPPORT AND REMINDERS: postal reminder, special unit dose reminder packaging and both combined versus usual care
Outcomes	PRESCRIPTION RECORD: increases in the 'medication possession ratio' of 8 per cent (postal reminder), 11 per cent (unit dose packaging) and 23 per cent (both combined) compared to usual care (p less than 0.05 for all interventions)
Notes	Potential sources of bias not fully reported.

Solomon 1998

Methods	Parallel, six months follow-up
Participants	133 participants with treated hypertension, 64 per cent caucasian, 28 per cent black, mean age 67 years, 10 departments of Veterans Affairs medical centers and one academic medical center, US
Interventions	COMPLEX HEALTH AND ORGANIZATIONAL INTERVENTIONS, INTERVENTIONS IN COMBINATION: patient-centred pharmaceutical care model by pharmacy residents versus usual care
Outcomes	PILL COUNT AND SELF REPORT: better compliance scores in intervention group (0.23) compared to controls (0.61, p less than 0.05). Net blood pressure reduction 6.9 mmHg systolic (p less than 0.05) and minus 0.6 mmHg

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Solomon 1998 (*Continued*)

	diastolic (not statistically significant)
Notes	Only results from self-report of adherence reported. Likelihood of bias

Webb 1980

Methods	Parallel three arm, study duration three months, follow-up at 18 months
Participants	123 participants with treated hypertension, black, 79 per cent women, mean age 55 years, primary care, USA
Interventions	PATIENT EDUCATION AND PATIENT MOTIVATION, SUPPORT AND REMINDERS: education or counselling versus usual care
Outcomes	PILL COUNT: differences in adherence scores minus 0.2 for education and plus 0.2 for counselling (p greater than 0.10). Net reduction in diastolic blood pressure 3.3 mmHg for education and 2.3 mmHg for counselling (p greater than 0.1, respectively)
Notes	Unclear on which outcome and treatment difference the power calculation was based on, unequal numbers due to drop-outs after randomisation but before start of intervention (no reasons given)

Zarnke 1997

Methods	Parallel, study duration eight weeks, follow-up at eight weeks
Participants	31 participants with treated and controlled hypertension, 65 per cent women, mean age 54 years, primary care and hospital outpatients, USA
Interventions	PATIENT MOTIVATION SUPPORT AND REMINDERS: home blood pressure monitoring and self-measurement of blood pressure versus usual care
Outcomes	NOT CLEARLY DEFINED, PROBABLY PILL COUNT: 0.3 doses missed per subject per week in the intervention group compared to 0.4 in the control group (not statistically significant, no exact p-value reported). Net reduction in mean arterial blood pressure 2.9 mmHg (p equals 0.039)
Notes	No power calculation but primary and secondary hypotheses stated

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Binstock 1988	No usual care control group
Casebeer 1995	Publication is a report of a study design only, not a study report. The study itself has to our knowledge not been published yet

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(*Continued)*

Eisen 1990	No contemporary control group
Gonzalez-Fern. 1990	Hospital setting
Powers 1982	Unable to interpret results
Strogatz 1983	No adherence outcome
Takala 1979	No adherence outcome
Zismer 1982	No adherence outcome

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DATA AND ANALYSES

This review has no analyses.

ADDITIONAL TABLES

Table 1. Quality assessment of included trials and potential sources of bias

Study	Random. appropriate?	Outcome ass. blind?	Losses to follow up	Comment
Sackett 1975	not reported	yes	10/144 (6.9 per cent)	No power calculation stated as such, but important differences stated a priori
Eshelman 1976	not reported	not reported	33/100 (33 per cent)	No differential loss to follow up reported.
Haynes 1976	yes	yes	5/39 (12.8 per cent)	Lacked statistical power. Power calculation was performed, but no exact figures reported
Gabriel 1977	not reported	not reported	none	No power calculation reported.
Johnson 1978	not reported	yes	4/140 (2.9 per cent)	Power calculation not reported, but probabilty of type II error quantified in discussion
Hawkins 1979	yes	no	519/1148 (45.2 per cent)	High losses to follow up
Logan 1979	not reported	yes	41/457 (9 per cent)	Differential loss to follow up well reported
Nessman 1980	not reported	no	not reported	Only 10 per cent of eligible patients took part in the study, which may indicate self selection
Rehder 1980	not reported	not reported	52/100 (52 per cent)	High losses to follow up ans small sample size for a factorial trial
Webb 1980	not reported	not reported	not reported	Unclear on what outcome and treatment difference the power calculation was based on

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Table 1. Quality assessment of included trials and potential sources of bias (*Continued*)

Kirscht 1981	not reported	not reported	66/417 (15.8 per cent)	Results difficult to interpret.
Logan 1983	yes	yes	9/194	Randomisation process seems adequate but is not entirely clear
Asplund 1984	not reported	not reported	30/160 (18.8 per cent)	Differential losses to follow up not clearly reported
Baird 1984	not reported	not reported	50/289 (17.3 per cent)	Detailed reasons for losses to follow up given
Pierce 1984	yes	yes	2/115 (1.7 per cent)	Outcomes poorly reported.
Kerr 1985	not reported	not reported	52/116 (44.8 per cent)	Large dropouts in all groups, inconsistencies between denominators in tables and dropouts, which vary for blood pressure and adherence outcomes
Morisky 1985	not reported	not reported	110/400 (27.5 per cent)	No significant differences between dropouts and those who continued to receive care
Becker 1986	not reported	not reported	15/180 (8.3 per cent)	Physicians were blinded to treatment allocation. They were aware that compliance study was in progress but unaware of the aims of the study
Burrelle 1986	not reported	not reported	None	Small study
Burris 1991	yes	yes	9/58 (15.5 per cent)	No p-values reported for adherence outcome
Saunders 1991	no	yes	33/224 (14.7 per cent)	Dropouts were lower in the intervention groups but much higher in the 'newly treated' group than among the 'infrequent attenders'

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Table 1. Quality assessment of included trials and potential sources of bias (*Continued*)

Sclar 1991	not reported	not reported	not reported	No dropouts reported despite uneven number randomised.
McKenney 1992	not reported	not reported	not reported	Nine participants required a change in medication during the second phase of the study
Hamilton 1993	not reported	not reported	4/34 (11.8 per cent)	Small sample size.
Skaer 1993	yes	yes	not reported	Losses to follow up not reported.
Detry 1995	not reported	no	18/640 (2.8 per cent)	Cross over RCT, patients were double counted
Boissell 1996	yes	no	253/7274 (3.5 per cent)	No differential loss to follow up reported. High number of participants due to large number of participating general practitioners
Friedman 1996	not reported	yes	34/267 (12.7 per cent)	Treatment provider blinded until baseline measurement was completed
Park 1996	not reported	no	11/64 (17.2 per cent)	Small study
Leenen 1997	yes	yes	21/198 (10.6 per cent)	Compared two different drugs. Only reported within group comparison
Zarnke 1997	yes	not reported	not reported	No power calculation but primary and secondary hypotheses were stated
Marquez-Contreras 1998	not reported	not reported	15/110 (13.6 per cent)	Differential loss to follow up in both treatment arms not reported
Mounier-Vehier 1998	not reported	not reported	18/103 (17.5 per cent)	Treatment allocation according to 'enrollment order' and 'randomisation list'

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Table 1. Quality assessment of included trials and potential sources of bias (*Continued*)

Solomon 1998	not reported	no	not reported	Multiple potential sources of bias
Girvin 1999	not reported	yes	2/27 (7.4 per cent)	Small study.
Andrejak 2000	yes	no	29/162 (17.9 per cent)	Differential loss to follow up well reported.
Blenkinsopp 2000	not reported	not reported	40/282 (14.2 per cent)	Randomisation at pharmacy level. Complete data on blood pressure available only on 100 patients
Mehos 2000	not reported	not reported	5/41 (12.2 per cent)	High likelihood of bias.

WHAT'S NEW

Last assessed as up-to-date: 25 February 2004.

Date	Event	Description
13 August 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 4, 1999

Review first published: Issue 2, 2004

Date	Event	Description
26 February 2004	New citation required and conclusions have changed	Substantive amendment

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CONTRIBUTIONS OF AUTHORS

All authors contributed to all stages of conducting this review.

DECLARATIONS OF INTEREST

None.

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Internal sources

- NHS Executive South West Research and Development, UK.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*Patient Compliance; Antihypertensive Agents [*administration & dosage]; Hypertension [*drug therapy; *psychology]; Patient Education as Topic; Randomized Controlled Trials as Topic

MeSH check words

Humans

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