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Publication details

Post-print of: Newell, S, Bowman, JA & Cockburn JD 1999, 'A critical review of interventions to increase compliance with medication-taking, obtaining medication refills, and appointment-keeping in the treatment of cardiovascular disease', *Preventive Medicine*, vol. 29, pp.535-548.
Published version available from:
http://dx.doi.org/10.1006/pmed.1999.0579

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Running Title: Compliance with Cardiovascular Disease Treatments

A Critical Review of Interventions to Increase Compliance with Medication-Taking, Obtaining Medication Refills and Appointment-Keeping in the Treatment of Cardiovascular Disease.

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Word count: 2,240 (introduction - conclusion)

Acknowledgments: This review was undertaken on behalf of and funded by the National Heart Foundation of Australia. The authors would like to thank Professor Brian Haynes and Dr Denise Ruth for reviewing the list of located studies, Kathy Rainbird for double-coding references, Rosemary Omwandho for her tireless tracking down of the numerous references, Anna Di Legge for her substantial assistance with preparing earlier versions of this manuscript and the many individuals and organisations who assisted in the search for studies.

Abstract

Background*:* To critically review the literature regarding interventions to improve cardiovascular patients' compliance with medication-taking, obtaining medication refills or appointment keeping.

Methods*:* The search for relevant randomised trials involved searching the Medline, Healthplan and Psychlit databases were searched from 1985 to 1996; searching the bibliographies of located studies; contacting Australian government departments, non-government organisations and pharmaceutical companies; and ultimate review of the resulting list by two field experts. The 33 located trials were critically appraised and classified as of good, fair or poor methodological quality. Descriptive and effectiveness data were then extracted from the 20 good and fair quality trials. Inter-rater reliability was high on the 20% of references double-coded.

Results*:* The 20 studies reviewed evaluated the effectiveness of 18 intervention strategies. Tentative recommendations were made for many patient-focussed and structural strategies across all three target behaviours. Physician-focussed strategies, tested only for appointment keeping, were all tentatively recommended against.

Conclusions*:* The methodological quality of many of the located trials was less than optimal, prohibiting strong recommendations. Therefore, further good quality, randomised trials are necessary in order to clarify the effectiveness of those strategies identified as potentially useful in this review.

Keywords: Cardiovascular, pharmacological interventions, patient compliance, review.

Introduction

Many factors have been linked to low compliance with cardiovascular treatments, including various characteristics of the patient, the physician, the patient-physician relationship, the treatment, the setting and the disease.[1-3] Consequently, numerous interventions have been tested in attempts to counteract these factors and, thereby, to maximise patients' compliance with recommended treatments.[4-6] While the results have been rather varied, there appears a consensus that multiple strategy interventions are consistently more effective than single strategy interventions at increasing levels of compliance, especially with long-term treatments.[3; 5; 7; 8] However, there is little evidence to indicate whether all strategies of these complex interventions are required or which strategies, if any, are the most effective. Similarly, many of the trials conducted, and included in subsequent literature reviews, have not been randomised trials, making it difficult to draw firm conclusions from either the studies or the reviews.[4; 6; 9] In addition, most of the more rigorous reviews of this literature were conducted some time ago, leading to questions about their current relevance.[1; 5; 10]

Therefore, this review aimed to summarise the recent literature regarding the effectiveness of individual intervention strategies, whether trialed alone or in complex interventions, at increasing cardiovascular patients' compliance with medication-taking, obtaining medication refills and appointment keeping.

Review Methodology

Data Sources

Medline, Healthplan and Psychlit were searched, from January 1985 to March 1996, for English-language papers including the terms (cardiovascular or heart or hypertens*) and (interven* or study or trial*) and (patient-compliance in MeSH). The resulting large number of citations (1,310 in total) was searched manually for articles investigating, or reviewing, interventions to increase cardiovascular patients' compliance with medication-taking, obtaining medication refills or appointment keeping. The

bibliographies of all relevant papers were also searched for additional potentially relevant studies. Health-related government and non-government bodies were also contacted, along with any additional organisations and companies suggested, in an attempt to locate unpublished studies. Finally, a list of the studies identified was sent to an expert on compliance literature and an expert on cardiovascular literature with requests for details of potentially relevant omitted studies.

Study Selection

For inclusion, a study must have: involved people with cardiovascular disease (eg: angina) or elevated levels of cardiovascular risk factors (eg: high blood pressure); implemented an intervention aimed at increasing their compliance with medication-taking, obtaining medication refills or appointment keeping; reported results on patient compliance; and randomly allocated patients to treatment conditions.

Data Extraction: Study Quality

The methodological quality of the studies located was assessed in relation to eight criteria, largely based on those of Haynes et al (1979):[1] selection and description of the sample, specification of the illness or condition, type of compliance measures, description of the therapeutic regimen, definition of compliance, description of the intervention, consent and loss to follow-up rates. Table 1 summarises the points achievable within each criteria. Twenty per cent of papers were double-coded.

INSERT TABLE 1 HERE

Assigning Quality Percentages to the Studies

As studies could obtain up to 35 points, actual scores were divided by 35 and multiplied by 100 to give "Quality Percentages", which classified each study as follows: ***Good Quality*** studies with quality percentages of 66.7 or higher; ***Fair Quality*** studies with percentages of between 50 and 66.6; and ***Poor Quality*** studies with percentages of less than 50.

Data Extraction: Study Results

Data were extracted from only good and fair quality studies regarding the patient groups targeted, samples achieved and the nature and effectiveness of the strategies trialed. Where control groups received some intervention strategies, the effectiveness of only additional strategies received by the intervention group was assessed.

Data Synthesis

Wide variations in the nature of interventions, outcome measures, length of follow-ups and presentation of results prohibited using meta-analyses. Therefore, results were summarised across studies exploring each intervention strategy, within each target behaviour, using the decision tree shown in Figure 1, resulting in one of five outcomes: a strong or tentative recommendation for, strong or tentative recommendation against or no recommendation for or against the strategy.

FIGURE 1 HERE

Briefly, strong recommendations were made only where at least three studies, including at least one of good quality, had investigated the strategy; consistent evidence from numerous fair quality studies resulted in tentative recommendations; and inconsistent evidence resulted in no recommendation about the strategy. In this paper, the number of references cited may be less than the number of studies discussed, as some papers discussed two separate studies[11-14] or tested multiple interventions.[15-21]

Review Results

Coding Quality Assurance

Two independent reviewers assigned identical quality classification codes for seven of the eight papers double-coded, giving a kappa of 0.82. There was also almost total agreement regarding the sample, intervention and results information extracted from the included studies.

Study Quality and Inclusion

A total of 45 relevant intervention studies were located.[11-51] Of these, 12 (27%) non-randomised trials were excluded.[13; 24; 28; 30; 34; 37; 39; 40; 43; 45; 47] Table 1 summarises how the 33 randomised trials scored on each quality criteria. The best performances were seen in the definition of compliance and description of intervention criteria but performances on the remaining criteria were sub-optimal. Subsequently, another 13 (29%) studies were excluded for having quality percentages less than 50%.[12; 26; 33; 35; 38; 41; 42; 44; 46; 48-50] The results of the remaining 20 studies, exploring interventions to increase compliance with medication-taking,[22; 25; 27; 29; 36; 51] obtaining medication refills[14; 21] and appointment keeping[11; 15-20; 23; 31; 32] are reviewed in this paper.

Intervention Effectiveness

Interventions Targeting Medication-Taking

Six papers discussed four fair quality studies exploring interventions aimed at increasing compliance with medication-taking.[22; 25; 27; 29; 36; 51] Two studies employed single strategy interventions: reduced dose frequency[25] and supplying the medication as confectionery.[36] Three papers reported the results from different follow-up points for one multiple strategy intervention, involving tailored behavioural and educational counselling for patients.[22; 27; 29] The last paper discussed another multiple strategy intervention involving home visits, behavioural, educational and personal counselling, written medication schedules, education materials for patients and compliance-enhancing packaging.[51] Table 2 briefly describes each study's intervention and sample and summarises the effectiveness of each intervention. The only interventions that improved patients' medication-taking were reducing dose frequency[25] and one of the multiple strategy interventions.[51]

INSERT TABLE 2 HERE

Interventions Targeting Obtaining Medication Refills

Two papers discussed three fair quality studies exploring interventions aimed at increasing compliance with obtaining medication refills.[14; 21] They employed two single strategy interventions: sending reminder letters to patients[21] and supplying medications in compliance-enhancing packaging,[21] and three multiple strategy interventions involving either or both of the above, in conjunction with making telephone reminder calls or providing written education materials to patients.[14; 21] Table 3 briefly describes each study's intervention and sample and summarises the effectiveness of each intervention. As shown, all the trialed interventions increased patients' compliance with obtaining medication refills.

INSERT TABLE 3 HERE

Interventions Targeting Appointment Keeping

Ten papers discussed 10 fair quality studies[11; 15; 16; 18-20; 23; 31; 32] and one good quality study[17] exploring interventions aimed at increasing compliance with appointment keeping. They employed seven single strategy interventions and 16 multiple strategy interventions, involving 15 different intervention strategies: sending patient reminder letters;[11; 15-17; 19; 23; 31] giving patients written educational materials;[11; 16; 19; 20; 31] offering patients financial incentives;[19; 20] sending patients' physicians prompt letters;[15; 17] behavioural counselling for patients;[18] behavioural contracting with patients;[32] giving patients free pre-prepared food;[20] providing patient-held records;[11] visiting patients at home;[11] giving patients prompting devices;[15] giving patients' physicians prompting devices;[15] and sending patients' physicians written educational materials.[15] Table 4 briefly describes each study's intervention and sample and summarises the effectiveness of each intervention. As shown, most interventions improved patient compliance. However, interventions aimed solely at patients' physicians were consistently ineffective.

INSERT TABLE 4 HERE

Review Recommendations

A total of 18 intervention strategies were trialed in the 20 studies reviewed: sometimes as single strategy interventions but, more often, as part of multiple strategy interventions. The types of strategies trialed were divided into three types: patient-focussed (56%), health care provider-focussed (17%), and structural interventions (28%). Table 5 summarises the recommendations for or against each strategy, within each of these intervention types, across the three target behaviours explored.

INSERT TABLE 5 HERE

For medication-taking, tentative recommendations were made for patient-focussed strategies, such as providing personal counselling, written education materials and prompting devices, and for structural strategies, such as making home visits, using compliance-enhancing packaging and prescribing drugs with reduced dose frequency. However, providing medication in confectionery form was tentatively recommended against.

Similarly, for obtaining medication refills, tentative recommendations were made for patient-focussed strategies, such as providing written education materials and reminder letters and telephone calls, and for the structural strategy of using compliance-enhancing packaging.

Again, a number of patient-focussed and structural strategies were also tentatively recommended for increasing compliance with appointment keeping, with behavioural counselling and providing written education materials, reminder letters and financial incentives among the most promising. However, behavioural contracting with patients and giving prompting devices were tentatively recommended against, as were all the physician-focussed strategies tested for this target behaviour.

Discussion

This review aimed to summarise the evidence and make recommendations regarding the effectiveness of intervention strategies aimed at increasing patient compliance with behaviours related to treating their cardiovascular disease: taking prescribed medications, obtaining medication refills and keeping appointments. Unfortunately, the ability to make confident recommendations was hampered by a number of limitations within the studies located.

Limitations of the Studies Located

First, the overall methodological quality of the studies located was poor: almost a third were immediately excluded as they were not randomised trials.[13; 24; 28; 30; 34; 37; 39; 40; 43; 45; 47] A similar proportion were excluded for failing to reach the 50% methodological quality cut-off.[12; 26; 33; 35; 38; 41; 42; 44; 46; 48-50] Furthermore, only one of the 20 reviewed studies attained a quality percentage considered to indicate a "good" quality study.[17] The generally low quality of the studies in this area was particularly disappointing as similar criticisms have been raised in previous reviews of this literature.[5; 6; 9]

Second, the reviewed studies showed a heavy reliance on indirect outcome measures, such as pill counts and patients' self-reported compliance.[15; 16; 19; 22; 25; 27; 29; 31; 36; 51] It is disappointing to see these measures still so widely used, as numerous studies and reviews have outlined the problems with their sensitivity and specificity for at least 20 years.[1; 8] Third, the reviewed studies tended to employ small samples: more than half with less than 50 patients per experimental group, increasing the likelihood of Type II errors.[15; 17; 18; 20; 22; 23; 25; 27; 32; 36; 51] Fourth, the reviewed studies tended to employ relatively short follow-up periods: only six (30%) studies followed patients for twelve months or longer.[15; 16; 20-22; 27] While acknowledging the difficulties of obtaining funding for and conducting long term follow-ups, their absence prohibits recommendations about interventions likely to prove effective in the longer term.

Limitations of this Review

First, we included all studies stating random allocation of patients to experimental groups although little information was given about the randomisation processes employed. Therefore, it is possible that some included studies may have used less than optimal methods of randomising patients to treatment groups.

Second, as with all reviews, there may be some relevant studies which we failed to locate. However, it is hoped that the multi-faceted search strategy employed has kept such omissions to a minimum.

Third, the scale used to assess the methodological quality of located studies has not been validated and arbitrary cut-points were used to classify the studies as of poor, fair or good quality. However, given the wide variation in study quality, some additional weighting element was considered necessary when interpreting the results. All criteria and cut-points were specified a priori and 20% of references were double-coded by independent reviewers to help ensure objectivity and reliability in classifications.

Overview of Review Findings

Despite the above limitations, we believe this review represents one of the most rigorous conducted of the recent literature. A number of patient-focussed strategies, such as sending reminders or distributing written education materials, and structural strategies, such as supplying medication in compliance-enhancing packaging, were tentatively recommended for across all three target behaviours. Although only explored in relation to appointment keeping, physician-focussed strategies, such as distributing reminders and educational materials to patients' physicians, were tentatively recommended against. These findings are largely in keeping with those of previous reviews.[2-6; 10] However, it was not possible to make strong recommendations due to the relatively poor methodological quality of many of

the studies located. Therefore, further rigorous trials are needed to confirm or refute these tentative recommendations.

Recommendations for Future Research

It is considered important that future trials should try to overcome the methodological flaws of the existing studies discussed above. Therefore, it is strongly recommended that any future trials should: be randomised, controlled trials, with the randomisation protocol detailed in publications; have follow-up periods of at least 6 months, where appropriate; involve no-intervention control groups; employ adequate sample sizes to detect feasible and meaningful significant increases in compliance; employ direct, objective measures, wherever possible; and, if direct measures are unavailable or not feasible, employ multiple outcome measures or assess the used measure's validity in a sub-group of patients.

Conclusion

Despite the rigorous methods employed and the recent studies included in this review, we could make limited strong recommendations about the effectiveness of the various intervention strategies trialed. Hopefully, our findings will assist in the design of future trials and encourage the adoption of higher methodological standards and reporting in these future studies.

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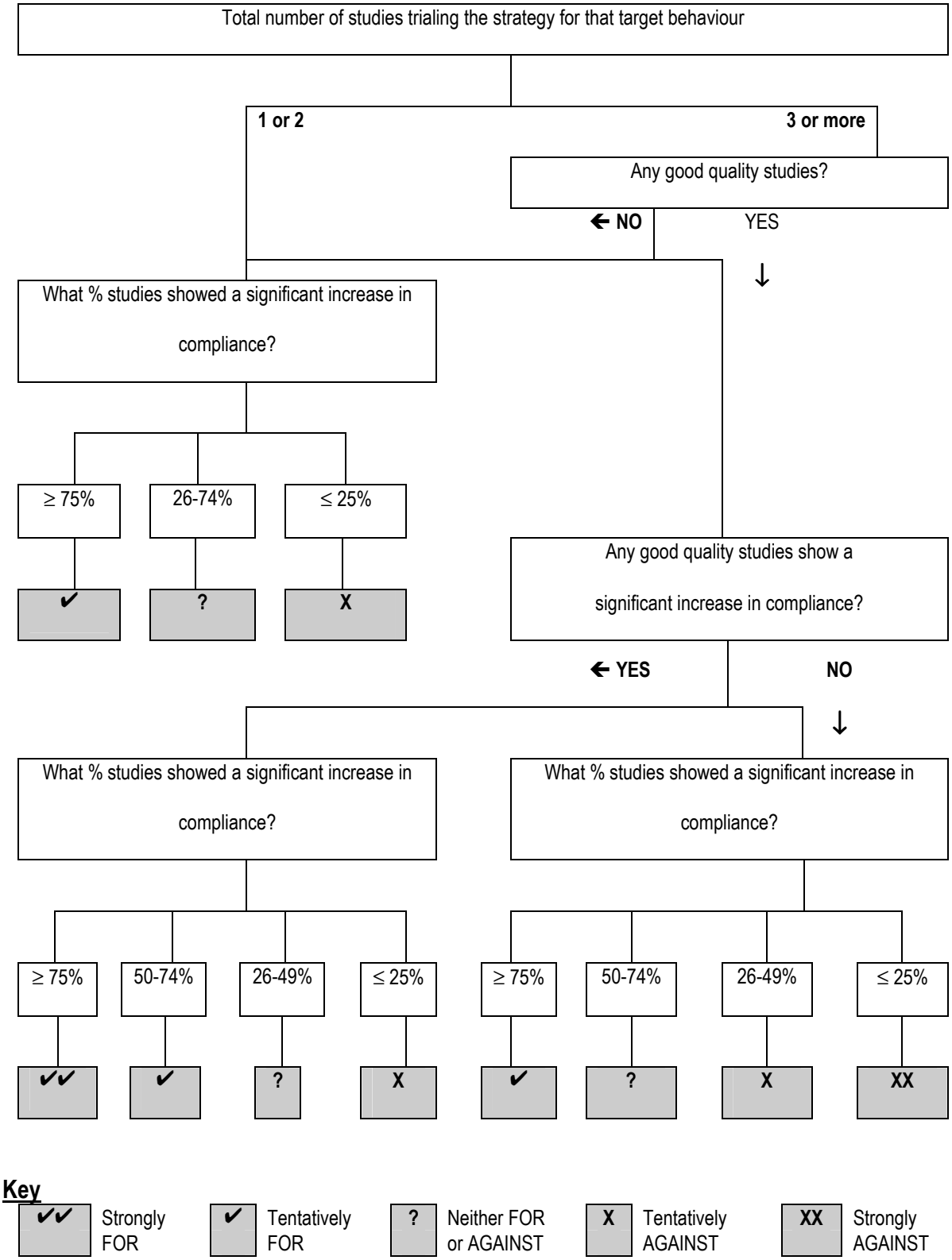
Figure 1: **The decision tree used in developing recommendations based on the number, quality and results of the studies reviewed.**



Key

✔✔	Strongly FOR	✔	Tentatively FOR	?	Neither FOR or AGAINST	X	Tentatively AGAINST	XX	Strongly AGAINST

Table 1: **The quality criteria coding schedule and the proportion of the 33 trials obtaining each score.**

Points awarded	Sample*	Definition of illness	Measure of compliance#	Description of intervention	Description of regimen	Definition of compliance	Consent rate	Loss to follow-up
Basic Points 4	-	-	Objective, direct & longitudinal OR Immediate & direct taken 3+ times for ≥ 80% patients **0%**	-	-	-	-	-
3	Adequate demographic description AND Random pop'n sample OR Patients from ≥ 3 clinics OR Patients from regional program/ referral centre **24%**	Replicable diagnostic criteria AND Inclusion and/or exclusion criteria **41%**	Immediate & direct **35%**	-	-	-	> 80% **38%**	< 10% OR Drop-outs counted as non-compliers **35%**

Points awarded	Sample*	Definition of illness	Measure of compliance#	Description of intervention	Description of regimen	Definition of compliance	Consent rate	Loss to follow-up
2	As 3 points, but inadequate demographic description **3%**	Replicable criteria but no inclusion or exclusion criteria **24%**	Objective & indirect **24%**	Replicable **76%**	Replicable **41%**	Replicable cut-point OR Continuous **88%**	70 - 80% **0%**	10 - 20% **29%**
1	Adequate demographic description AND Non-random sample OR Patients from 1-2 clinics **56%**	Non-replicable diagnoses only **29%**	Subjective **41%**	Non-replicable **24%**	Non-replicable **24%**	Non-replicable cut-point **6%**	< 70% **3%**	>20% **21%**
0	As 1 point, but inadequate demographic description **18%**	None / could only be inferred **6%**	Not stated **0%**	None **0%**	None / could only be inferred **35%**	None **6%**	Not reported OR Volunteers **59%**	Not reported **15%**

Points awarded	Sample*	Definition of illness	Measure of compliance#	Description of intervention	Description of regimen	Definition of compliance	Consent rate	Loss to follow-up
Bonus Points 1	% patients excluded reported **12%**	Co-morbidity described **9%**	*(codes 2 & 3 only)* Taken at random & patient unaware why **30%**	-	Co-intervention precluded or noted **9%**	-	Reported by group OR Randomised after consent **29%**	Reported by group **53%**
1	Consecutive patients OR Random sample with ≥80% follow-up **74%**	-	*(all codes)* Follow-up ≥ 6 months **44%**	-	-	-	-	-
1	Groups' demographics compared at baseline **68%**	-	*(code 1 only)* Measure's validity assessed/ referenced **36%**	-	-	-	-	-
1	Groups' outcomes compared at baseline **65%**	-	*(all codes)* Per extra measure **21% (1 extra)** **3% (2 extra)**	-	-	-	-	-

* Adequate demographic description required at least age and gender information for recruited patients.

Direct measures included appointment records (for attendance), biochemical markers and drug metabolites. Indirect measures included pill counts. Subjective measures included patient self-report.

Table 2: **The samples, interventions and results of the studies targeting compliance with medication-taking.**

Study Ref, Country & Quality %	Target Group#	Experimental Groups & Brief Intervention Summary#	Subjects			Length of follow-up (months)	Compliance Ratesϕ
			N	Age (years)	% male		
Burrelle (1986)[51] USA **Q% = 62.9**	Elderly hypertensives with poor compliance (DBP>90 or SBP>160mmHg)	I- Home visits involving tailored education about disease & treatment & personal counselling + educational AHA brochure + written medication planner + 7 day dose packaging + referrals to other support agencies. C- Usual care.	I - 8 C - 8	Imean=68 Cmean=70	I=13% C=38%	2	I>C, p<0.001
Miller et al (1988)[29] USA **Q% = 54.3**	Patients suffering their 1st myocardial infarction	I- 1 nurse-delivered, individual, face-to-face intervention at a 1 month follow-up visit: assessed compliance, discussed physical & psychosocial adjustments & developed health plan regarding target behaviours. C- Usual care.	I - 56 C - 47	Range:30-65	I=73% C=89%	1	I<C, ns
Miller et al (1989)[27] USA **Q% = 51.4**			I - 39 C - 42	Range:36-68 Mean=54	81%	12	I>C, ns
Miller et al (1990)[22] USA **Q% = 51.4**			I - 29 C - 22	Range:37-68 Mean=55	78%	24	I<C, ns

Study Ref, Country & Quality %	Target Group#	Experimental Groups & Brief Intervention Summary#	Subjects			Length of follow-up (months)	Compliance Ratesϕ
			N	Age (years)	% male		
Burris et al (1991)[25] USA **Q% = 51.4**	Patients with mild hypertension (DBP=90-104 mmHg)	I1 -Patients prescribed transdermal clonidine patches to be changed once a week. I2 -Patients prescribed oral verapamil-SR to be taken once daily. *Dosage strengths tailored to patient's needs.*	I1 - 29 I2 - 29	I1 mean=67 I2 mean=68	I1=76% I2=66%	2	I1>I2, p<0.01
Sweeney et al (1991)[36] USA **Q% = 51.4**	People with LDL or total cholesterol > 90th percentile & not respond to AHA diet.	I1 -Cholestyramine powder: 2*4g packets twice daily. I2 -Cholestyramine confectionery bars: 2*4g bars twice daily.	I1 - 38 I2 - 45	I1 mean=56 I2 mean=55	I1=17% I2=24%	2	I1<I2, ns

AHA = American Heart Association, C = control group, DBP = diastolic blood pressure, I = intervention group, LDL = low density lipoproteins, SBP = systolic blood pressure.

ϕ Indicates the direction and the strength (p value) of any difference between the experimental groups (ns = no significant difference).

Table 3: **The samples, interventions and results of the studies targeting medication refill compliance.**

Study Ref, Country & Quality %	Target Group#	Experimental Groups & Brief Intervention Summary#	Subjects			Length of follow-up (months)	Compliance Ratesϕ
			N	Age (years)	% male		
Skaer et al (1993)[21] USA **Q% = 62.9**	Previously untreated mild-moderate hypertensives	*All patients prescribed 240mg verapamil once daily.* I1 - Patients mailed refill reminder 10 days before due. I2 - Patients given specially packaged medication - each dose separately. I3 - Patients given refill reminder & specially packaged medications. C - No intervention.	I1 - 73 I2 - 85 I3 - 68 C - 78	I1 mean=54 I2 mean=57 I3 mean=57 C mean=56	I1=37% I2=38% I3=41% C=40%	12	I1>C, p<0.05 I2>C, p<0.05 I3>C, p<0.05 I3>I2, p<0.05 I3>I1, p<0.05
Sclar et al (1991)[14] USA Study A **Q% = 57.1**	Patients with newly-diagnosed hypertension.	I - Patients given special kit with initial prescription (30 days atenolol, letter explaining the educational program, educational newsletter) + phone check-up/reminder 1 week before first refill due + mailed reminders each subsequent month + monthly mailed educational newsletters. C - No intervention.	I - 50 C - 59	I mean=58 C mean=54	I=62% C=59%	6	I>C, p<0.05
Sclar et al (1991)[14] USA Study B **Q% = 57.1**	Patients with previously-diagnosed hypertension.		I - 163 C - 181	I mean=55 C mean=56	I=81% C=63%	6	I>C, p<0.05

C = control group, I = intervention group.

ϕ Indicates the direction and the strength (p value) of any difference between the experimental groups (ns = no significant difference).

Table 4: **The samples, interventions and results of studies targeting compliance with appointment-keeping.**

Study Ref, Country & Quality %	Target Group#	Experimental Groups & Brief Intervention Summary#	Subjects			Length of follow-up (months)	Compliance Ratesϕ
			N	Age (years)	% male		
Velez et al (1985)[17] USA **Q% = 80.0**	People with high screened blood pressure (DBP=95-120 mmHg)	C - Verbally advised to see their GP about BP within 2-3 weeks. I1 - As C + patients mailed personalised reminder letter, sent the day after the screening visit. I2 - As C + letter, including result, sent to patient's physician notifying them patient been advised to visit. I3 - C + I1 + I2.	C - 21 I1 - 13 I2 - 18 I3 - 22	C mean=58 I1 mean=52 I2 mean=55 I3 mean=56	99%	1½	I1>C, p<0.05 I2>C, ns I3>C, p<0.05
Jones et al (1987)[18] USA **Q% = 62.9**	Patients with hypertension identified in Emergency Dept (ED). (DBP>90 mmHg)	C - Referred (to various agencies) for follow-up care for their BP. I1 - As C + patients given face-to-face, nurse-delivered Health Belief Model-based intervention, tailored individually, while in ED. I2 - As C + patients given, by phone, similar briefer, nurse-delivered intervention 1-2 days after ED visit. I3 - C + I1 + I2.	C - 17 I1 - 30 I2 - 16 I3 - 9 *I2 & I3 lost 6 people each - complied before being phoned.*	<u>overall</u> 6% aged 18-29 28% aged 30-39 24% aged 40-49 21% aged 50-59 22% aged 60+	47%	Not reported	<u>Made appt</u> I1>C, p<0.001 I2>C, p<0.001 I3>C, p<0.001 <u>Kept appt</u> I1>C, p<0.01 I2>C, p<0.01 I3>C, p<0.01

Study Ref, Country & Quality %	Target Group#	Experimental Groups & Brief Intervention Summary#	Subjects			Length of follow-up (months)	Compliance Ratesϕ
			N	Age (years)	% male		
Hamilton et al (1993)[23] Study A USA **Q% = 62.9**	Patients with primary hypertension (SBP>159 or DBP>90mmHg)	I - Patients mailed postcard reminder 1 week before appointment. C - No intervention.	I - 17 C - 13	I mean=57 C mean=52	Not reported	1 - 2	I>C, p<0.05
Leslie et al (1991)[32] USA **Q% = 60.0**	Patients referred to a cardiac rehabilitation program	C - 8 nurse-delivered, 1-hour, weekly group education sessions (medications, dietary changes & exercise guidelines). I - As C + patients negotiated weekly contracts (heart rate goals & frequency & duration of exercise), choosing own reward.	C - 14 I - 14	C mean=54 I mean=57	C=64% I=79%	2	I>C, ns
Murray et al (1988)[16] USA **Q% = 57.1**	People with high BP at screening (DBP>89mmHg or on BP medication)	I1 - Patients mailed 1 personalised letter & educational newsletter from the six developed as part of the National High Blood Pressure Education Program. I2 - Patients mailed all six newsletters from above program over 10 week period, each accompanied by a personalised letter. C - No intervention. *But part of Minnesota Heart Health Program.*	I1 - 250 I2 - 250 C - 250	Range:25-74 Mean=52	≅50%	9 - 30	<u>Discussed BP with physician</u> I1>C, p<0.05 I2>C, p<0.05

Study Ref, Country & Quality %	Target Group#	Experimental Groups & Brief Intervention Summary#	Subjects			Length of follow-up (months)	Compliance Ratesϕ
			N	Age (years)	% male		
Lefebvre et al (1991)[31] USA **Q% = 57.1**	People with 2 high screening cholesterol levels (>6.21 mmol/l)	I - Patient sent reminder letter from Chief of Cardiology, including their results & information about the increased chance of CVD. Sent 2 weeks after 2nd screening. C - No intervention. *But part of Pawtucket Heart Health Program.*	I - 198 C - 188	I mean=64 C mean=65	I=27% C=33%	3	I<C, ns
Gans et al (1994)[15] USA **Q% = 57.1**	People with high (>239 mg/dL) or borderline (200-239 mg/dL) screening cholesterol & 2 other CVD risk factors	C - Brief one-on-one counselling session: dietary & referral recommendations + self-help nutrition kit + results form, including referrals + pocket cholesterol record card. *Also in Pawtucket Heart Health Program.* I1 - As C + patient sent personalised, reminder letter (including lifestyle goals & referral reminder) + fridge magnet within 4 weeks of visit. I2 - As C + patient's physician sent letter with patient's results, recommendations made + national cholesterol guidelines + pre-addressed reminder postcard to send the patient. I3 - C + I1 + I2.	C - 45 I1 - 42 I2 - 39 I3 - 47	C mean=50 I1 mean=54 I2 mean=51 I3 mean=50	C =56% I1=56% I2=55% I3=53%	4 - 12	I1<C, ns I2<C, ns I3<C, ns

Study Ref, Country & Quality %	Target Group#	Experimental Groups & Brief Intervention Summary#	Subjects			Length of follow-up (months)	Compliance Ratesϕ
			N	Age (years)	% male		
Murray et al (1988)[16] USA **Q% = 57.1**	People with high BP at screening (DBP>89mmHg or on BP medication)	I1 - Patients mailed 1 personalised letter & educational newsletter from the 6 for the National High BP Education Program. I2 - Patients mailed all six newsletters from above program over 10 week period, each accompanied by a personalised letter. C - No intervention. *But part of Minnesota Heart Health Program.*	I1 - 250 I2 - 250 C - 250	Range:25-74 Mean=52	≅50%	9 - 30	Discussed BP with physician I1>C, p<0.05 I2>C, p<0.05
Saunders et al (1991)[11] Study A South Africa **Q% = 57.1**	Newly diagnosed hypertensives (DBP>119mm Hg or >1 test >105 mmHg)	I - Patient sent reminder letter prior to next visit + 2 recall letters if appointment missed + home visit if still not attend + given patient-held record, including education section & space to monitor medication-taking, BP levels, weight, drugs prescribed and appointment dates & times + education about how to use the patient-held record. C - No intervention.	I - 59 C - 56	61% aged 40-59	I=34% C=30%	6	I>C, p<0.001
Saunders et al (1991)[11] Study B South Africa **Q% = 57.1**	Poor attending hypertensives (DBP>119mm Hg or >1 test >100mmHg)		I - 54 C - 55	69% aged 40-59	I=19% C=25%	6	I>C, p<0.0001

Study Ref, Country & Quality %	Target Group#	Experimental Groups & Brief Intervention Summary#	Subjects			Length of follow-up (months)	Compliance Ratesϕ
			N	Age (years)	% male		
Maiman et al (1992)[19] USA **Q% = 54.3**	People with moderate-high risk screening cholesterol levels & no prior history of high cholesterol - age & sex specific cut-offs used.	C1 - Brief counselling session about result, interpretation, possible consequences of high cholesterol, benefits of diet & drug therapy (from health professional) + given leaflet summarising session + referred to own GP for re-testing. C2 - As C1 but delivered by layperson. I1 - As C1 + mailed brief reminder letter 3 days after screening + financial incentive if attend their GP. I2 - As C2 + brief reminder + financial incentive. I3 - As C1 + mailed detailed reminder letter 3 days after screening - restating session information. I4 - As C2 + detailed reminder letter.	C1 - 223 C2 - 174 I1 - 202 I2 - 187 I3 - 215 I4 - 177	<u>Overall</u> 30% aged 20-44 23% aged 45-54 47% aged 55-65	38½%	5	I1+I2>C1+C2, p<0.0001 I3+I4>C1+C2, p<0.0001 I1>C1, p<0.05 I3>C1, ns I2>C2, p<0.0001 I4>C2, p<0.0001

Study Ref, Country & Quality %	Target Group#	Experimental Groups & Brief Intervention Summary#	Subjects			Length of follow-up (months)	Compliance Ratesϕ
			N	Age (years)	% male		
Jeffery et al (1993)[20] USA **Q% = 54.3**	People 14-32 kg overweight	C - 20 weekly group counselling sessions (n=20) led by behavioural scientist & nutritionist: weigh-in, review exercise & food diaries, info from leader & group discussion. Then monthly sessions with weekly individual weigh-ins. I1 - As C + given free pre-prepared food for 5 dinners & breakfasts per week + meal plans & recipes for other meals. I2 - As C + cash payment ($2.50 - $25) each week based on amount of weight lost. I3 - As C + I1 + I2.	C - 40 I1 - 40 I2 - 41 I3 - 41	C mean=37½ I1 mean=38½ I2 mean=38 I3 mean=38	C=50% I1=50% I2=50% I3=50%	6, 12 & 18	<u>6 months</u> I1>C, p<0.0001 I2>C, p<0.001 I3>C, p<0.0001 <u>12 months</u> I1>C, p<0.0001 I2>C, p<0.001 I3>C, p<0.0001 <u>18 months</u> I1>C, p<0.0001 I2>C, ns I3>C, p<0.0001

BP = blood pressure, C = control group, CVD = cardiovascular disease, DBP = diastolic blood pressure, GP = general physician, I = intervention group, SBP = systolic blood pressure.

ϕ Indicates the direction and strength (p value) of any difference between the experimental groups (ns = no significant difference).

Table 5: **Summary recommendations for and against each trialed intervention strategy, by target behaviour.**

Intervention Strategy	Target Behaviour					
	Medication taking		Obtaining medication refills		Appointment keeping	
	Recommendation*	Proportion studies where p<0.05	Recommendation*	Proportion studies where p<0.05	Recommendation*	Proportion studies where p<0.05
Patient-focussed Strategies						
• Behavioural counselling	?	1/2			✔	4/4
• Educational counselling	?	1/2				
• Personal counselling	✔	1/1				
• Sending reminder letters			✔	4/4	✔	11/14
• Behavioural contracting					X	0/1
• Giving written education materials	✔	1/1	✔	2/2	✔	7/9
• Giving financial incentives					✔	4/4
• Making telephone reminders			✔	2/2		
• Giving patient held records					✔	2/2
• Giving prompting devices	✔	1/1			X	0/2

Intervention Strategy	Target Behaviour					
	Medication taking		Obtaining medication refills		Appointment keeping	
	Recommendation*	Proportion studies where p<0.05	Recommendation*	Proportion studies where p<0.05	Recommendation*	Proportion studies where p<0.05
Structural Strategies						
• Providing free pre-prepared food					✔	2/2
• Making home visits	✔	1/1			✔	2/2
• Using compliance-enhancing packaging	✔	1/1	✔	2/2		
• Using drugs with reduced dose frequency	✔	1/1				
• Giving medication as confectionery	**X**	0/1				
Physician-focussed Strategies						
• Sending prompt letters					**X**	1/4
• Sending written education materials					**X**	0/2
• Sending prompting devices					**X**	0/2

✔ = Tentatively FOR **X =** Tentatively AGAINST **?** = Neither FOR or AGAINST

Appendix A: Potentially relevant references with insufficient or incorrect source information

1. Ramirez R. Patient compliance: strategies for improvement. Pharmacy, 1992;5:26-30.
2. Rubin I. Rx-OTC buckling: another chance to encourage patient compliance. Pharmacy Times, 1994;60:58-59.
3. Rudd P. Maximising compliance with antihypertensive therapy. Drug Therapeutics, 1992;22:25-32.
4. Van der Stichele RH et al. Measuring patient compliance with electronic monitoring: lisinopril versus atenolol in essential hypertension. Post Market Surveillance, 1992;6:77-90.

Précis: Despite a lack of rigorous trials, this critical review tentatively recommends for or against intervention strategies to increase patient compliance and makes some concrete suggestions for future research.