REVIEW

Delivery of patient adherence support: a systematic review of the role of pharmacists and doctors

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submit your manuscript | www.dovepress.com Dovepress http://dx.doi.org/10.2147/PI.S46647 Abstract: We conducted a systematic review of adherence support programs involving doctors and pharmacists. We searched MEDLINE®, Embase, International Pharmaceutical Abstracts, PsycINFO®, and CINAHL using the keywords "pharmacist" or "doctor" and "adhere*" or "compli*" and "randomized controlled trials". We found 89 studies involving pharmacists; in contrast, only 14 studies involved doctors. The roles of pharmacists and doctors ranged from providing education and counseling to adjusting treatment. Most interventions that specified a patient group were carried out with patients with chronic conditions (n=79) and only six included short-term treatments. The majority of interventions improved adherence and clinical outcomes to some extent, although the size of effect size was sometimes small. Resource utilization (eg, hospitalization rates, visits to doctors) did not change in the majority of studies that reported it. Few studies included cost analyses. All but one study had high risk of performance bias due to the nature of the interventions, which made it impossible to blind the participants. The majority of studies did not report tailoring the interventions to patient needs and the vast majority of papers did not report taking a concordant patient-centered approach or considering patients' own views and experiences when providing adherence support. In addition, the majority of studies did not describe training for the health care professionals involved in providing adherence support. Providing training for doctors and pharmacists to take a more patient-centered concordant approach would be expected to increase the effectiveness of adherence support further.

Keywords: interventions, patient views, patient experiences, patient-centered approach, resource utilization

Introduction to patient adherence support and programs

One of the biggest challenges in health care worldwide is to ensure that patients are both willing and able to take their treatments as prescribed, and that they persist in doing so over the designated amount of time. When they do not do this, it is most often referred to as "treatment nonadherence" or "treatment noncompliance", and the consequences can be severe. Nonadherence to appropriately prescribed treatments may lead to reduced clinical benefit and increased risk of morbidity and mortality.¹ For example, it has been estimated that nonadherence is responsible for 48% of asthma deaths, an 80% increased risk of death in diabetes and a 3.8-fold increased risk of death in the year following a heart attack.² The related economic burden on health care systems is significant. In the UK, the cost of unused and unwanted medicines has been estimated to cost the US health care system US\$310 billion (note US billion =10⁹) annually.⁴

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Nonadherence is prevalent in all disease categories and similar rates of nonadherence are found in chronic conditions such as diabetes (33%) and skin disorders (23%) as in lifethreatening conditions such as cancer (20%) and end-stage renal disease (30%).⁵ However, rates may vary between patients as well as within individual patients across different treatments and over time. The rate of nonadherence that is clinically significant also varies between diseases. Typically, lifestyle recommendations such as diet (average percentage of patients that were nonadherent across studies 41%) and exercise (average percentage of patients nonadherent 28%) display more adherence challenges than pharmaceutical medicines (average percentage of patients that were nonadherent 21%).⁵ Asymptomatic patients have been found to be less adherent than symptomatic patients in, for example, HIV.⁶ It is important to point out that differing adherence definitions and measurements used across studies also influence the adherence rates captured.

The reasons for nonadherence are numerous and multifaceted, and the patients' relationship and communication with their health care providers are key factors that influence both their motivation and their ability to adhere.¹ The patient may decide not to take their treatment as prescribed ("intentional nonadherence") for several different reasons. For example, the patient may experience side-effects that they are not prepared to tolerate or may have concerns over the long-term effects of taking the medication, while other patients may not fully appreciate the necessity or effectiveness of the medication to manage their condition.¹ Other patients may not be able to take their treatment as prescribed, even though they intend to do so ("unintentional nonadherence"). Forgetting is the most common reason patients' give for missing doses unintentionally, but problems such as difficulties with dexterity and swallowing, reduced access to medication, and high prescription co-payments can also hinder treatment adherence.¹ It is worth bearing in mind that forgetting is an example of unintentional nonadherence that might be influenced by intentional factors, such as perceived need for treatment and concerns about treatment.7

Both international and national policy drivers, such as the World Health Organization⁸ and National Institute for Health and Care Excellence¹ in the UK, have called for increased patient involvement in treatment decisions to improve adherence and health care outcomes. The term "concordance" can be used to emphasize the shared decision-making process between patient and health care provider that should ideally be achieved when prescribing treatments. A scoping review of concordance, adherence, and compliance in medicine taking noted that concordance initially focused on the consultation process, in which doctor and patient agree therapeutic decisions that incorporate their respective views and moved to a wider concept that stretches from prescribing communication to patient support in medicine taking. In the concordance model, a decision not to take a medicine is an acceptable and good outcome.^{9,10}

In addition, numerous adherence support programs have been developed over the years. Key criteria for success are that interventions are appropriate for implementation in practice and that they are cost-effective. To ensure robust development, implementation, and evaluation of interventions, it has been recommended that development is theory driven¹¹ and that the behavioral-change techniques (BCTs) that are used is clearly defined.¹²

A number of large-scale reviews have evaluated the evidence around adherence support programs. For example, Haynes et al¹³ and Kripalani et al¹⁴ reviewed randomized controlled trials that measured both adherence and clinical outcome. Haynes et al¹³ found 44% and Kripanali et al¹⁴ found 54% of interventions successful at increasing adherence. However, Haynes et al¹³ noted that "even with the most effective methods for long-term treatments, improvements in drug use or health were not large". Kripalani et al14 and Haynes et al¹³ concluded that complex interventions were more likely to be effective, for example, by including combinations of more convenient care, information, reminders, self-monitoring, reinforcement, counseling, family therapy, psychological therapy, crisis intervention, manual telephone follow-up, and supportive care (although they could not determine the relative importance of the individual components). There was also no consensus regarding whether motivational, behavioral, or combined approaches were preferable.

The literature has not been able to provide guidance regarding what specific theoretical models and BCTs are needed to improve the effectiveness of adherence interventions, but there are some indications of factors that may increase effectiveness. Kripalani et al¹⁴ concluded that behavioral interventions that reduced the dosing demands of therapies consistently improved adherence with a large effect size. Haynes et al¹³ argued that interventions delivered by allied health care professionals (HCPs) such as nurses and pharmacists were worthy of future research. In addition, others have found that tailoring interventions to individual patients' needs, rather than using a "one-size-fits-all" approach, is likely to be more effective.¹⁵ Interventions that are tailored to individual needs can, for example, distinguish

between a patient's lack of motivation to take medication and practical barriers to taking medication, as well as address an individual's unique mix of factors in order to improve adherence. Lastly, a recent meta-analysis found that cognitive-based BCTs are effective at improving adherence, can be effectively delivered by routine HCPs, and can have effects that go beyond those achieved by educational or behavioral interventions.¹⁶

Some more recent reviews have focused on particular modes of delivery. For example, Rubio-Valera et al¹⁷ and Morgado et al¹⁸ reviewed pharmacist-led adherence support programs for patients prescribed antidepressants and antihypertensives, respectively, and these interventions were deemed promising and worthy of further study. Pharmacists may be considered particularly suited to deliver adherence interventions given their responsibility to monitor and optimize patients' pharmacological treatment as part of providing pharmaceutical care.¹⁹ Cutrona et al²⁰ reviewed interventions for cardiovascular medication in which the patient's doctor was involved, but the interventions appeared to be less effective when a doctor was involved than when other HCPs were involved.²⁰

Due to the promising findings regarding pharmacist-led interventions from these disease-specific reviews, one of the aims of the current review was to expand the scope and review the evidence regarding pharmacist-led adherence support programs across diseases categories. Second, despite the negative impact of physician involvement in adherence support programs for cardiovascular medications found by Cutrona et al,²⁰ it was deemed important to include a wider search for evidence from such interventions in other populations. The role of nurses was beyond the scope of this project.

Methods

Search strategy

We carried out a systematic review to evaluate delivery of patient adherence support involving pharmacists and/or doctors. We included evidence related to all aspects of patient adherence (eg, adherence to medication, diet, lifestyle changes, screening procedures).

SG and LE developed a search strategy and performed an electronic search of the following databases: MEDLINE[®] (1946 to September 6, 2013), Embase (1980 to August 2013), International Pharmaceutical Abstracts (1970 to August 2013), PsycINFO[®] (1806 to the first week of September 2013), and CINAHL (September 9, 2013). We used the keywords "pharmacist" or "doctor" or "physician" and "adhere*" or "compli*" and "randomized controlled trials". MA also hand searched the bibliographies of included papers and obtained the full text of any original studies that potentially met the inclusion criteria.

Inclusion and exclusion criteria Inclusion criterion

The inclusion criterion was RCTs of interventions to improve adherence in which pharmacists and/or doctors had a defined role in terms of delivery. All countries and settings were included.

Exclusion criteria

The exclusion criteria were: study designs other than RCTs, interventions without a defined role for pharmacists and/or doctors, papers not published in English, conference abstracts, and protocols only.

Screening and data extraction

All database search results were combined into a Reference Manager[®] (v 11; Thomson Reuters, New York, NY, USA) database. An electronic duplicate search was conducted using Reference Manager followed by a manual duplicate search. All duplicate papers were removed. MA then screened each title and abstract to determine whether the full research paper should be retrieved or whether it was evident it did not meet the inclusion criterion at that stage. SG independently screened a random 10% sample of abstracts to check the reliability of the screening process (agreement level 90%). All discrepancies were resolved through discussion. MA then reviewed all retrieved and screened full manuscripts to determine whether each article met the inclusion criterion and SG independently reviewed a further random 10% sample of full papers to check reliability (agreement level 96%). MA then extracted data from the included articles regarding pharmacists' and/or doctors' delivery of support on patient adherence. SG then independently reviewed a random 10% of the data extraction table to check reliability (agreement level 90%).

The following data were extracted directly into electronic tables: study author and year, the country in which the research was carried out, sample size, clinical diseases of interest, the nature of the intervention (including whether it was tailored to each patient or fixed for all participants), the setting and the HCP involved, training for HCP, the HCP's involvement in the intervention, measured outcomes, and the effectiveness of the intervention.

To assess the quality and the risk of biases of the included papers, the Cochrane Collaboration's tool for assessing risk of

bias in randomized trials was used.²¹ MA performed a quality assessment of the included papers, and SG conducted a 10% reliability check (agreement level 94%). All discrepancies were resolved through discussion.

Results

Overview

A total of 1,031 abstracts were screened and 219 full-text articles were obtained. Of these, 103 met the inclusion criterion²²⁻¹²⁴ (Figure 1). Details of the included studies are shown in <u>Supplementary Table S1</u> and <u>Table S2</u>.

Quality assessment

The full quality-assessment results are found in <u>Supplemen-tary Table S2</u>. Of the 103 studies, 13 were found to have low risk of bias in all domains (selection bias, detection bias, attrition bias, selective reporting bias, and other bias) except for the risk of performance bias. Only three studies had high risk of bias in at least four of the six domains.^{25,78,83}

Performance bias

All but one study had high risk of performance bias. The high risk of performance bias was due to the nature of the interventions, which made it impossible to blind the participants. The only study that did not have high risk of performance bias had an unclear risk, because the patients were blinded but the physicians were not.²⁹

Selection bias

The risk of bias when generating the random sequence was low in 50 studies and high in 14 studies. In 39 papers, the method of generating a random sequence was not described, making the risk of selection bias unclear. The risk of selection bias when concealing the allocation was low in 44 studies, high in 47 studies, and unclear in 12 studies.

Detection bias

In 26 studies, the risk of detection bias was low. In 69 studies, information regarding blinding of outcome measurements was insufficient, making the risk of detection bias unclear, and, in eight of the studies, the risk was high.

Attrition bias

The majority of studies had a low risk of attrition bias. Conversely, 17 studies were found to have a high risk of attrition bias, and, in 14 studies, the information provided was insufficient to decide the risk of attrition bias.

Selective reporting bias

In 99 studies, no selective reporting could be identified, indicating low risk of reporting bias. However, in one study, some results were only compared within the groups and not between them.¹⁰⁹ In three studies (3%), data were incomplete.^{42,58,103}



Figure I Flow chart of papers identified, screened and evaluated. Abbreviation: RCT, randomized controlled trial.

Other bias

Other risks of bias occurred when there were differences between the intervention group and control group at baseline. This type of bias occurred in 29 studies. Examples were difference in age of patients declining to participate and those who consented,³⁹ dropout rate,²⁶ adherence,^{41,94} blood pressure,^{48,106,113} and comorbidity.^{48,63}

Key findings

The HCP delivering the intervention

Only 14 of the interventions were delivered by doctors.^{29,35,38,53,61,64,72,87,95,96,98,110} The rest of the interventions were delivered by different types of pharmacists (clinical, hospital, community, research, senior, or unspecified).

Settings

In 52 papers, the setting was described as special clinics or practices, and, in 24 papers, the studies were carried out at hospitals. Eighteen studies were carried out at community pharmacies.

A total of 44 studies were carried out in the USA, with the remaining studies having been conducted in a range of international countries, including those in Europe, Africa, Asia, Canada, and Australia.

Clinical diseases

The most common diseases targeted in the interventions were hypertension (16 studies), type II diabetes (eleven studies) and heart failure (seven studies). In eleven studies, there was no specific disease group studied. Most interventions were carried out with patients with chronic conditions and only a few included short-term treatments – for instance, *Helicobacter pylori*-infected ulcers or other infections.^{24,34,57,78,108}

Training received by the HCP

In the majority of studies, no additional training for the HCP was described (63%). However, when additional training was reported (37% of the studies), it included educational workshops on the specific disease, training on the intervention protocol or relevant guidelines, or interview training. In 5% of the studies, the authors described providing specific training in patient-centered approaches, respecting patients' wishes, or helping patients set goals for their treatment.^{30,65,82,90,96} In one study, the authors explicitly stated that the HCP did not receive additional training.⁴²

The role of the HCP in the intervention

When pharmacists were involved in the delivery of the intervention, in 93% of cases, they carried out the full intervention. In contrast, it was more common for doctors to deliver only part of the intervention (64% of the studies in which doctors were involved), when compared with interventions delivered by pharmacists. The pharmacists often had a role as a patient educator, providing either tailored or fixed patient education, as well as making treatment recommendations. In the studies in which the doctors delivered the intervention, they gave advice and adjusted patients' treatments, and also provided patient education. In four studies, the doctor delivered the intervention in collaboration with other HCPs.^{53,64,77,87}

Tailored versus fixed interventions

Fifteen of the interventions were fixed. These included structured education,^{97,38} written information,⁹⁶ mailed letters,^{77,95,111} videotapes, or telephone calls.⁵¹ In six studies, several methods were used.^{25,29,31,35,45} In one study, the patients were given a blood-pressure measuring device to take home and instructions on how to use it.⁸⁴ Another study included a demonstration dose of sublingual nitroglycerin, for which the physician was present.⁷²

Forty percent of the interventions were tailored. These included tailored patient counseling,^{22,58} education,40,75,87,92,101,118 assessment and instructions,35,48,57 or a combination of different approaches.^{67,78,109} In the studies in which the interventions were tailored, the HCP tailored the interventions based on patients' needs, giving tailored information and advice^{36,46,50,120} and prioritizing the recommendations based on the patients' medical records. 62,107 Hederos et al⁶⁴ used the concept of "concordance" (defined as reaching an agreement with parents of pediatric patients on how to look upon asthma and its management). They used this approach with the hypothesis that the parents would understand the advice and education better. Personalized medication adherence plans, individual goal values, and identification of adherence barriers were evaluated and used in five studies.^{28,48,52,61,82} In total, 14 studies explicitly reported using some method of tailoring the intervention by taking the patients' own views into account rather than simply the HCP's viewpoint.^{28,30,36,47,48,50,52,61,64,65,82,90,96,120}

In 46% of the studies, it was unclear to what extent the interventions were tailored, as the interventions were not described in sufficient detail.

A greater proportion of studies carried out in the last 15 years than older studies reported being tailored to patients' needs (46% versus [vs] 6%). All the studies reporting the use of a more patient-centered concordant approach were carried out in the last 15 years. However, in the last 15 years, there was still a higher proportion of studies that did not describe

tailoring the intervention to individual patients' needs than those that did.

Effectiveness of the patient adherence support provided by pharmacists and doctors Short-term versus long-term treatments

The effectiveness of interventions for studies focusing on short- and long-term treatments were similar. For short-term treatments, interventions showed benefits in five studies,^{24,34,45,57,78} and one paper failed to show any benefits other than patient satisfaction with pharmacy service.¹⁰⁸ For research focusing on long-term treatments, interventions showed benefits in 64 out of 79 (81%) studies. Consequently, 15 studies failed to show any improvement.

A range of different outcomes was used in measuring the effectiveness of the adherence support provided. These included medication adherence, attending screening appointments, clinical outcomes, quality of life (QoL), medication knowledge, patient satisfaction, resource utilization, and cost analyses. The effects of the adherence intervention on these outcomes are summarized in Table 1.

Medication adherence

Medication adherence was measured in several different ways, including pill counts, serum concentrations, Medication Event Monitoring System, self-report, questionnaires, and pharmacists' refill records. The interventions statistically significantly enhanced adherence in 68 studies. However, 35 interventions failed to show statistically significant improvement in adherence. Some interventions did not result in a statistically significant change in adherence but did result in a statistically significant improvement in clinical outcomes – for example, blood pressure⁸⁴ and fasting blood glucose.⁸⁵ When differences in adherence were significant, a range of effect sizes was seen.

Table I Effectiveness of	of the	interventions
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Where adherence was measured dichotomously and patients classified as either adhering or not adhering to treatment, in 16 of 41 (40%) studies, the number of patients in the intervention group adhering was double or more than double the number in the control group, with the remaining studies (25/41, 60%) showing more modest effects. When adherence was measured as an adherence rate, the mean adherence rates were between 3% and 20% greater in the intervention group than in the control group.

Inhaler technique was measured in six out of eleven studies regarding asthma, with improvement being demonstrated in five of them.^{22,47,56,74,86} Inhaler technique was not measured in any of the studies regarding chronic obstructive pulmonary disease.

Screening appointments

Seven studies concerned adherence to cancer screenings. The authors recorded patients' adherence to screening appointments to evaluate the effectiveness of the interventions. One study measured attitude toward the screening tests and did not find any statistically significant difference between the intervention group and control group.³⁸ Of the six remaining, five showed a statistically significant improvement in screening rates,^{29,35,77,110,111} and only one paper failed to show any improvement.⁹⁵

Clinical outcomes

A range of clinical outcomes was assessed including: blood pressure, lipid levels, HbA_{1c} levels, severity of symptoms, and adverse drug events (ADEs).

Blood pressure was an outcome measure in 21 papers. Blood pressure was statistically significantly improved in 16 (76%) of them.^{10,32,36,41,48,61,67,69,71,84,87,88,96,107,113,120} Only five failed to show any statistically significant improvement.^{42,52,65,99,106}

Outcome	Papers measuring the outcome (n=103)	Papers showing statistically significant benefits/improvements, n (%)	Papers failing to show statistically significant benefits/improvements, n (%)
Medication adherence	103	68 (66)	35 (34)
Cancer screening rates	6	5 (83)	l (17)
Quality of life	23	16 (70)	7 (30)
Blood pressure	21	16 (76)	5 (24)
Lipid values	13	7 (54)	6 (46)
HbA	9	8 (89)	1 (11)
Severity of symptoms	15	2 (13)	13 (87)
Adverse drug reactions	8	I (I3)	7 (87)
Medication knowledge and understanding	27	20 (74)	7 (26)
Resource utilization	19	3 (16)	16 (84)
Cost analyses	5	4 (80)	I (20)

Abbreviation: HbA_{1c}, hemoglobin A_{1c}.

Thirteen papers measured patients' lipid levels, but the majority (seven) failed to show any significant difference.^{33,51,52,65,82,93,106}

Nine papers measured HbA_{1c} levels.^{42,44,65,68,70,85,94,106} All but one of them⁶⁵ demonstrated a statistically significant improvement in the intervention group.

Severity of symptoms was measured in 15 papers, and only two studies (13%) showed statistically significant changes in this outcome.^{83,89}

Eight interventions used ADEs as an outcome measure. Seven (87%) of them failed to show any statistically significant benefit, and the other one detected a statistically significant improvement in one arm of the study.⁸⁹ Murray et al⁸⁹ investigated the effect of adherence support on patients with complicated and uncomplicated heart failure and/or hypertension, and found a statistically significant reduction in ADEs in the complicated stratum but not in the uncomplicated stratum.

QoL

QoL was used as an outcome measure in 24 of the studies. Improvement was noted in nine (38%) of them^{27,67,68,83,99,100,104,109,112} and 15 (62%) failed to show any improvement.^{30,37,47,62,66,70,72,84,86,87,90,113,114,117,118}

Medication knowledge and understanding

Medication knowledge and medication understanding were used as measures in 27 studies. Medication knowledge was statistically significantly improved in 20 (74%) of the studies that used it as an outcome measure^{22,25–27,30,31,57,62,68,70,74,80,81,83,86,88,91,97,99,102,103,109,112,119} and seven (26%) failed to show statistically significant improvement.^{26,30,62,86,103,109,119}

Patient satisfaction

Sixteen papers measured patient satisfaction. In nine of the studies (56%), satisfaction increased as a result of the intervention,^{25,26,36,52,75,90,108,112,118} and, in seven studies (44%), patient satisfaction did not statistically significantly change.^{34,40,58,62,67,91,113}

Resource utilization

A number of outcome measures were related to resource utilization, including hospitalization rates, visits to doctors, and visits to emergency rooms. Nineteen papers investigated patients' resource utilization; a decrease was found in three (16%) studies,^{22,112,121} with the remaining 16 (84%) studies not finding any change.

Cost analysis

Six studies also did some form of cost analysis as a part of evaluating the effectiveness and feasibility of the interventions. One study⁴² was cost-effective and another showed a gain of 42.2 working days.⁶⁴ Beaucage et al calculated that each intervention would cost US\$3.74.³⁴ Another study aimed to calculate total direct health care costs, but the variation in costs was too large for a comparison to be possible.⁹⁰ In a fifth study, an economic evaluation of the intervention was conducted, determining that the intervention group had a statistically significantly lower cost to the National Health Service (NHS) than the control.⁵⁰ Zhang et al did not find any difference in cost of drugs or hospitalization between the intervention and control group.¹²⁴

Discussion

Evaluation: effectiveness of the role played by pharmacists and doctors in providing patient adherence support

Involving pharmacists and doctors in adherence support appears to improve outcomes to some extent, although the size of effect is sometimes small. Of the interventions involving pharmacists and doctors, 66% led to some improvements in clinical outcomes. These findings need to be viewed in the context of a high possibility of performance bias, because the nature of the interventions made it impossible to blind the participants. In addition, there is a possibility of reporting bias and of a higher proportion of interventions showing an effect being published than those not doing so.

The percentage of adherence interventions showing improvements in medication adherence and clinical outcomes in this review was higher than in a Cochrane review of medication adherence interventions¹³ in which 44% were found to lead to improvements in medication adherence and 31% to improvements in clinical outcomes. In addition, improvement in adherence was higher than that found in another large-scale review.14 Our review focused on interventions involving doctors and pharmacists, while the other two reviews13,14 included all adherence interventions. This indicates that involving pharmacists and doctors in adherence interventions may make them more effective. However, we are cautious with the interpretation of this finding, because the inclusion and exclusion criteria were not identical in the reviews. In addition, the studies covered by the reviews used many different types of interventions and different methods of measuring adherence and clinical outcomes, making direct comparisons impossible.

It is of interest that in both our review and that of Morgado et al,¹⁸ who reviewed pharmacy interventions to enhance blood-pressure control and adherence to antihypertensive therapy, more studies showed improvement in clinical outcomes than showed improvement in adherence. This contrasts with reviews of general adherence support programs^{13,14} (not necessarily involving a pharmacist), in which adherence was found to improve more frequently than clinical outcomes. The difference may be due to the multifaceted nature of interventions and the fact that pharmacists may make clinical recommendations as well as provide adherence support. The difference may also be due to the nonlinear relationship between adherence and clinical outcome in some conditions, and because some clinical outcomes, such as high blood pressure, are affected by factors that may not have been part of the intervention (such as exercise or diet).

Recommendations: ways to improve the delivery of patient adherence support Recommendations for practice

Our review demonstrates that while the majority of adherence support provided by pharmacists and doctors leads to some improvements in outcomes, there is room to improve the provided support further. The successful features of adherence interventions that have been identified by previous research were not reported as being present in the majority of adherence interventions provided by pharmacists and doctors.

Previous research has suggested that adherence support involving pharmacists that is tailored to individual needs, rather than being fixed, is more likely to be effective.¹⁵ In our review, while there was a trend toward more tailored approaches being used in the last 15 years, less than 50% of adherence support programs in the last 15 years were tailored to individual needs, with the remainder either being fixed or not reported in sufficient detail to determine if they had been tailored. We would therefore recommend increasing the level of tailoring of interventions to improve the delivery of patient adherence support.

In addition, taking a more concordant approach, where the aim is to formulate an agreed treatment plan between the HCP and patient rather than expecting the patient to follow the HCP's instructions, has been shown to improve treatment outcomes.¹ In our review, out of the 41 studies in which tailoring to patient need was reported, only 14 described a concordant approach whereby patients' individual goal values and identification of adherence barriers were evaluated and agreement reached. In the rest of the studies, the tailoring appeared to be a result of the HCP's own view of the patient's needs. We therefore recommend using a patient-centered approach and involving patients in decisions when tailoring adherence support.

Finally, the majority of studies did not describe any training for the HCPs involved. When training was reported, it was sometimes more focused on the specific clinical diseases involved rather than on how to give adherence support. We would recommend that HCPs receive specific training on how to develop a concordant approach with patients and formulate a joint treatment plan that meets patients' own identified needs and that therefore may be more likely for patients to adhere to.

Recommendations for research

The majority of interventions were delivered by pharmacists rather than doctors. Evaluation of more adherence support programs involving doctors would inform this area of research, particularly as a previous review of adherence support in patients with cardiovascular problems and diabetes suggested doctors were less effective than other HCPs in providing effective adherence support in these disease groups.²⁰

A cost analysis economic evaluation was provided by very few of the studies. Cost analyses are important to evaluate the cost-effectiveness of interventions and would be helpful to incorporate into evaluations. The outcomes used in the studies included adherence to medication and adherence to attending screening appointments. However, use of these outcome measures makes the assumption that increased adherence is always a positive outcome. Nonadherence may be an appropriate decision by the patient. None of the studies included a measure of concordance or patient involvement in decision making. It would be appropriate to include such outcome measures – for example, the Leeds Attitude to Concordance scale¹²⁵ – in future studies.

Limitations of the review

Due to the large volume of literature on adherence support strategies, our review only focused on the role of pharmacists and doctors in providing adherence support. Further reviews are needed on the role of other HCPs, especially nurses, in providing adherence support.

The search strategy for this review was broad and included adherence support for all treatments and preventive

health care. This meant that we did not include search terms for specific treatments and preventive strategies such as "cancer screening" and may have missed some relevant studies in these areas. In addition, we excluded studies not written in English and did not use alterative names for "pharmacist", such as "chemist".

As with all reviews of adherence interventions, the definition of what is acceptable adherence is problematic. It is defined differently by different researchers and will vary from condition to condition. Relatedly, the differentiation between people who miss occasional doses and those who take drug "holidays" is often not made. Again, as for all such reviews, the measurement of adherence in studies presents difficulties, as there is no gold standard for such measurement.

Conclusion

Adherence support programs involving pharmacists and doctors appear to improve outcomes to some extent, although the size of effect is not always large. Their effectiveness may be increased by working with patients to tailor adherence strategies according to individual patient needs. A much greater volume of studies have evaluated the role of pharmacists than the role of doctors; therefore, more research is needed to evaluate the role of doctors in providing adherence support.

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References

- National Institute for Health and Clinical Excellence (NICE). Medicines Adherence: Involving Patients in Decisions about Prescribed Medicines and Supporting Adherence. London: NICE; 2009. Available from: http://www.nice.org.uk/nicemedia/pdf/CG76NICEGuideline.pdf. Accessed May 9, 2014.
- Elliot R. Non-adherence to medicines: not solved but solvable. J Health Serv Res Policy. 2009;14(1):58–61.
- Trueman P, Lowson K, Blighe A, et al; York Health Economics Consortium, School of Pharmacy, University of London. *Evaluation of the Scale, Causes and Costs of Waste Medicines: Final Report*. London: York Health Economics Consortium and School of Pharmacy, University of London; 2010. Available from: http://eprints.pharmacy.ac.uk/2605/1/ Evaluation_of_NHS_Medicines_Waste_web_publication_version. pdf. Accessed May 12, 2014.
- Capgemini Consulting. Patient Adherence: The Next Frontier in Patient Care; Vision and Reality. 9th ed. Paris: Capgemini Consulting; 2011. Available from: http://www.capgemini.com/resource-file-access/ resource/pdf/Patient_Adherence__The_Next_Frontier_in_Patient_ Care.pdf. Accessed May 12, 2014.
- 5. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care*. 2004;42(3):200–209.
- Gao X, Nau DP, Rosenbluth SA, Scott V, Woodward C. The relationship of disease severity, health beliefs and medication adherence among HIV patients. *AIDS Care*. 2000;12(4): 387–398.
- Gadkari AS, McHorney CA. Unintentional non-adherence to chronic prescription medications: how unintentional is it really? *BMC Health Serv Res.* 2012;12:98.
- World Health Organization (WHO). Adherence to Long-Term Therapies: Evidence for Action. Geneva: WHO; 2003. Available from: http://www. who.int/chp/knowledge/publications/adherence_full_report.pdf?ua=1. Accessed May 12, 2014.
- Horne R, Barber N, Weinman J, Elliott RA, Morgan M, Cribb A. Concordance, adherence and compliance in medicine taking: a scoping exercise. London: National Co-ordinating Centre for NHS Service Delivery and Organisation NCCSDO; 2006. Available from: http://www. nets.nihr.ac.uk/__data/assets/pdf_file/0007/81394/ES-08-1412-076.pdf. Accessed June 4, 2014.
- Horne R, Keller I. Interventions to facilitate adherence. In: Horne R, Weinman J, Barber N et al (eds). *Concordance, adherence and compliance in medicine taking: a conceptual map and research priorities*. National Co-ordinating Centre for NHS Service Deliver and Organisation NCCSDO: London; 2006.
- 11. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci.* 2011;6:42.
- Abraham C, Michie S. A taxonomy of behavior change techniques used in interventions. *Health Psychol.* 2008;27(3):379–387.
- Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev.* 2008;(2):CD000011.
- Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: a systematic review. *Arch Intern Med.* 2007;167(6):540–550.
- Clifford S, Garfield S, Eliasson L, Barber N. Medication adherence and community pharmacy: a review of education, policy and research in England. *Pharm Pract (Granada)*. 2010;8(2):77–88.
- Easthall C, Song F, Bhattacharya D. A meta-analysis of cognitive-based behaviour change techniques as interventions to improve medication adherence. *BMJ Open*. 2013;3(8).
- Rubio-Valera M, Serrano-Blanco A, Magdalena-Belio J, et al. Effectiveness of pharmacist care in the improvement of adherence to antidepressants: a systematic review and meta-analysis. *Ann Pharmacother*. 2011;45(1):39–48.

- Morgado MP, Morgado SR, Mendes LC, Pereira LJ, Castelo-Branco M. Pharmacist interventions to enhance blood pressure control and adherence to antihypertensive therapy: Review and meta-analysis. *Am J Health Syst Pharm*. 2011;68(3):241–253.
- Foppe van Mil JW, Schulz M. A review of pharmaceutical care in community pharmacy in Europe. *Harvard Health Policy Rev.* 2006;7:155–168.
- Cutrona SL, Choudhry NK, Stedman M, et al. Physician effectiveness in interventions to improve cardiovascular medication adherence: a systematic review. J Gen Intern Med. 2010;25(10):1090–1096.
- 21. Higgins JP, Altman DG, Sterne JA, editors; Cochrane Statistical Methods Group and the Cochrane Bias Methods Group. Assessing risk of bias in included studies. In: Higgins JP, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions*. V 5.1.0. Oxford: Cochrane Collaboration; 2011 [updated March]. Available from: http://handbook.cochrane.org/chapter_8/8_assessing_risk_of_bias_ in_included_studies.htm. Accessed May 12, 2014.
- 22. Abdelhamid E, Awad A, Gismallah A. Evaluation of a hospital pharmacy-based pharmaceutical care services for asthma patients. *Pharm Pract (Granada).* 2008;6(1):25–32.
- Adler DA, Bungay KM, Wilson IB, et al. The impact of a pharmacist intervention on 6-month outcomes in depressed primary care patients. *Gen Hosp Psychiatry*. 2004;26(3):199–209.
- Al-Eidan FA, McElnay, JC, Scott MG, McConnell JB. Management of Helicobacter pylori eradication – the influence of structured counselling and follow-up. *Br J Clin Pharmacol.* 2013;53(2):163–171.
- Al-Saffar N, Abdulkareem A, Abdulhakeem A, Salah AQ, Heba M. Depressed patients' preferences for education about medications by pharmacists in Kuwait. *Patient Educ Couns.* 2008;72(1):94–101.
- Al-Saffar N, Deshmukh AA, Carter P, Adib SM. Effect of information leaflets and counselling on antidepressant adherence: open randomised controlled trial in a psychiatric hospital in Kuwait. *Int J Pharm Pract*. 2005;13(2):123–131.
- Al Mazroui NR, Kamal MM, Ghabash NM, Yacout TA, Kole PL, McElnay JC. Influence of pharmaceutical care on health outcomes in patients with Type 2 diabetes mellitus. *Br J Clin Pharmacol*. 2009;67(5): 547–557.
- Alsabbagh MW, Lemstra M, Eurich D, Wilson TW, Robertson P, Blackburn DF. Pharmacist intervention in cardiac rehabilitation: a randomized controlled trial. *J Cardiopulm Rehabil Prev.* 2012;32(6): 394–399.
- Aragones A, Schwartz MD, Shah NR, Gany FM. A randomized controlled trial of a multilevel intervention to increase colorectal cancer screening among Latino immigrants in a primary care facility. *J Gen Intern Med.* 2010;25(6):564–567.
- Armour CL, Reddel HK, LeMay KS et al. Feasibility and effectiveness of an evidence-based asthma service in Australian community pharmacies: a pragmatic cluster randomized trial. *Journal of Asthma*. 2013;50(3):302–309.
- Ascione FJ, Shimp LA. The effectiveness of four education strategies in the elderly. *Drug Intell Clin Pharm.* 1984;18(11):926–931.
- Ashok KM, Elayaraja J, Shailaja K, Ramasamy C. Improving medication adherence and clinical outcomes of hypertensive patients through patient counseling. *Res J Pharm Biol Chem Sci.* 2011;2(3): 231–241.
- Aslani P, Rose G, Chen TF, Whitehead PA, Krass I. A community pharmacist delivered adherence support service for dyslipidaemia. *Eur J Public Health*. 2011;21(5):567–572.
- Beaucage K, Lachance-Demers H, Ngo TT, et al. Telephone follow-up of patients receiving antibiotic prescriptions from community pharmacies. *Am J Health Syst Pharm*. 2006;63(6):557–563.
- Bejes C, Marvel MK. Attempting the improbable: offering colorectal cancer screening to all appropriate patients. *Fam Pract Res J*. 1992;12(1):83–90.
- 36. Blenkinsopp A, Phelan M, Bourne J, Dakhil N. Extended adherence support by community pharmacists for patients with hypertension: a randomised controlled trial. *Int J Pharm Pract.* 2000;8(3): 165–175.

- Bouvy ML, Heerdink ER, Urquhart J, Grobbee DE, Hoes AW, Leufkens HG. Effect of a pharmacist-led intervention on diuretic compliance in heart failure patients: a randomized controlled study. *J Card Fail*. 2003;9(5):404–411.
- Braun KL, Fong M, Kaanoi ME, Kamaka ML, Gotay CC. Testing a culturally appropriate, theory-based intervention to improve colorectal cancer screening among Native Hawaiians. *Preventive Med.* 2005;40(6):619–627.
- Calvert SB, Kramer JM, Anstrom KJ, Kaltenbach LA, Stafford JA, Allen LaPointe NM. Patient-focused intervention to improve longterm adherence to evidence-based medications: a randomized trial. *Am Heart J.* 2012;163(4):657–665.
- Capoccia KL, Boudreau DM, Blough DK, et al. Randomized trial of pharmacist interventions to improve depression care and outcomes in primary care. *Am J Health Syst Pharm.* 2004;61(4):364–372.
- Carter BL, Bergus GR, Dawson JD, et al. A cluster randomized trial to evaluate physician/pharmacist collaboration to improve blood pressure control. *J Clin Hypertens*. 2008;10(4):260–271.
- 42. Chan CW, Siu SC, Wong CK, Lee VW. A pharmacist care program: positive impact on cardiac risk in patients with type 2 diabetes. *J Cardiovasc Pharmacol Ther.* 2012;17(1):57–64.
- Chisholm MA, Mulloy LL, Jagadeesan M, DiPiro JT. Impact of clinical pharmacy services on renal transplant patients' compliance with immunosuppressive medications. *Clin Transplant*. 2001;15(5):330–336.
- 44. Choe HM, Mitrovich S, Dubay D, Hayward RA, Krein SL, Vijan S. Proactive case management of high-risk patients with type 2 diabetes mellitus by a clinical pharmacist: a randomized controlled trial. *Am J Manag Care*. 2005;11(4):253–260.
- Clark PM, Karagoz T, Apikoglu-Rabus S, Izzettin FV. Effect of pharmacist-led patient education on adherence to tuberculosis treatment. *Am J Health Syst Pharm.* 2007;64(5):497–506.
- Clifford S, Barber N, Elliott R, Hartley E, Horne R. Patient-centred advice is effective in improving adherence to medicines. *Pharm World Sc.* 2006;28(3):165–170.
- Cordina M, McElnay JC, Hughes CM. Assessment of a community pharmacy-based program for patients with asthma. *Pharmacotherapy*. 2001;21(10):1196–1203.
- Criswell TJ, Weber CA, Xu Y, Carter BL. Effect of self-efficacy and social support on adherence to antihypertensive drugs. *Pharmacotherapy*. 2010;30(5):432–441.
- 49. De Tullio PL, Kirking DM, Arslanian C, Olson DE. Compliance measure development and assessment of theophylline therapy in ambulatory patients. *J Clin Pharm Ther.* 1987;12(1):19–26.
- Elliott RA, Barber N, Clifford S, Horne R, Hartley E. The cost effectiveness of a telephone-based pharmacy advisory service to improve adherence to newly prescribed medicines. *Pharm World Sc.* 2008;30(1): 17–23.
- Eussen SR, van der Elst ME, Klungel OH, et al. A pharmaceutical care program to improve adherence to statin therapy: a randomized controlled trial. *Ann Pharmacother*. 2010;44(12):1905–1913.
- Evans CD, Eurich DT, Taylor JG, Blackburn DF. The Collaborative Cardiovascular Risk Reduction in Primary Care (CCARP) study. *Pharmacotherapy*. 2010;30(8):766–775.
- Farber HJ, Oliviera L. Trial of an asthma education program in an inner-city pediatric emergency department. *Pediatr Asthma Allergy Immunol*. 2004;17(2):107–115.
- Faulkner MA, Wadibia EC, Lucas BD, Hilleman DE. Impact of pharmacy counseling on compliance and effectiveness of combination lipid-lowering therapy in patients undergoing coronary artery revascularization: a randomized, controlled trial. *Pharmacotherapy*. 2000;20(4):410–416.
- 55. Finley PR, Rens HR, Pont JT, et al. Impact of a collaborative care model on depression in a primary care setting: a randomized controlled trial. *Pharmacotherapy*. 2003;23(9):1175–1185.
- García-Cárdenas V, Sabater-Hernández D, Kenny P, Martínez-Martínez F, Faus MJ, Benrimoj SI. Effect of a pharmacist intervention on asthma control. A cluster randomised trial. *Respiratory Medicine*. 2013;107(9):1346–1355.

- Garnett WR, Davis LJ, McKenney JM, Steiner KC. Effect of telephone follow-up on medication compliance. *Am J Hosp Pharm.* 1981;38(5): 676–679.
- Geurts MM, Pot JL, Schepers EH, et al. The evaluation of an intervention based on the application of patient self-completion concordance forms in Dutch community pharmacies and the effect on adherence to chronic medication. *Patient Educ Couns.* 2010;78(1):85–90.
- Grant RW, Devita NG, Singer DE, Meigs JB. Improving adherence and reducing medication discrepancies in patients with diabetes. *Ann Pharmacother*. 2003;37(7–8):962–969.
- Grymonpre RE, Williamson DA, Montgomery PR. Impact of a pharmaceutical care model for non-institutionalised elderly: results of a randomised, controlled trial. *Int J Pharm Pract.* 2001;9(4)235–241.
- Hamann J, Cohen R, Leucht S, Busch R, Kissling W. Shared decision making and long-term outcome in schizophrenia treatment. *J Clin Psychiatry*. 2007;68(7)992–997.
- Hanlon JT, Weinberger M, Samsa GP, et al. A randomized, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy. *Am J Med.* 1996;100(4):428–437.
- Hawkins DW, Fiedler FP, Douglas HL, Eschbach RC. Evaluation of a clinical pharmacist in caring for hypertensive and diabetic patients. *Am J Hosp Pharm.* 1979;36(10):1321–1325.
- 64. Hederos C. Group discussions with parents have long-term positive effects on the management of asthma with good cost-benefit. *Acta Paediatr*. 2005;94(5):602–608.
- 65. Heisler M, Hofer TP, Schmittdiel JA, et al. Improving blood pressure control through a clinical pharmacist outreach program in patients with diabetes mellitus in 2 high-performing health systems: the adherence and intensification of medications cluster randomized, controlled pragmatic trial. *Circulation*. 2012;125(23):2863–2872.
- Holland R, Brooksby I, Lenaghan E, et al. Effectiveness of visits from community pharmacists for patients with heart failure: HeartMed randomised controlled trial. *BMJ*. 2007;334(7603):1098.
- Hunt JS, Siemienczuk J, Pape G, et al. A randomized controlled trial of team-based care: impact of physician-pharmacist collaboration on uncontrolled hypertension. J Gen Intern Med. 2008;23(12):1966–1972.
- Iram M, Shobha Rani RH, Pais N. Impact of patient counseling and education of diabetic patients in improving their quality of life. *Arch Pharm Pract.* 2010;1(2):18–22.
- Jacobs M, Sherry PS, Taylor LM, Amato M, Tataronis GR, Cushing G. Pharmacist Assisted Medication Program Enhancing the Regulation of Diabetes (PAMPERED) study. *J Am Pharm Assoc.* 2012;52(5): 613–621.
- Jarab AS, Alqudah SG, Khdour M, Shamssain M, Mukattash TL. Impact of pharmaceutical care on health outcomes in patients with COPD. *Int J Clin Pharm.* 2012;34(1):53–62.
- Jarab AS, Alqudah SG, Mukattash TL, Shattat G, Al-Qirim T. Randomized controlled trial of clinical pharmacy management of patients with type 2 diabetes in an outpatient diabetes clinic in Jordan. *J Manag Care Pharm*. 2012;18(7):516–526.
- 72. Kelly JM. Sublingual nitroglycerin: improving patient compliance with a demonstration dose. *J Am Board Fam Pract*. 1988;1(4):251–254.
- Klein A, Otto G, Krämer I. Impact of a pharmaceutical care program on liver transplant patients' compliance with immunosuppressive medication: a prospective, randomized, controlled trial using electronic monitoring. *Transplantation*. 2009;87(6):839–847.
- 74. Kumar DS, Adepu R, Parthasarathi G, Mahesh PA. Impact of community pharmacist provided patient education in asthma patients on treatment outcomes – a study. *Indian Journal of Pharmaceutical Education and Research*. 2009;43(2):125–133.
- López Cabezas C, Falces Salvador C, Cubí Quadrada D, et al. Randomized clinical trial of a postdischarge pharmaceutical care program vs regular follow-up in patients with heart failure. *Farm Hosp.* 2006;30(6):328–335. English and Spanish.
- Lai PS, Chua SS, Chew YY, Chan SP. Effects of pharmaceutical care on adherence and persistence to bisphosphonates in postmenopausal osteoporotic women. *J Clin Pharm Ther.* 2011;36(5):557–567.

- 77. Lantz PM, Stencil D, Lippert MT, Beversdorf S, Jaros L, Remington PL. Breast and cervical cancer screening in a low-income managed care sample: the efficacy of physician letters and phone calls. *Am J Public Health.* 1995;85(6):834–836.
- Lee M, Kemp JA, Canning A, Egan C, Tataronis G, Farraye FA. A randomized controlled trial of an enhanced patient compliance program for Helicobacter pylori therapy. *Arch Intern Med.* 1999;159(19): 2312–2316.
- Lee SS, Cheung PY, Chow MS. Benefits of individualized counseling by the pharmacist on the treatment outcomes of hyperlipidemia in Hong Kong. *J Clin Pharmacol.* 2004;44(6):632–639.
- Lim WS, Low HN, Chan SP, Chen HN, Ding YY, Tan TL. Impact of a pharmacist consult clinic on a hospital-based geriatric outpatient clinic in Singapore. *Ann Acad Med Singapore*. 2004;33(2):220–227.
- Lipton HL, Bird JA. The impact of clinical pharmacists' consultations on geriatric patients' compliance and medical care use: a randomized controlled trial. *Gerontologist*. 1994;34(3):307–315.
- Ma Y, Ockene IS, Rosal MC, Merriam PA, Ockene JK, Gandhi PJ. Randomized Trial of a Pharmacist-Delivered Intervention for Improving Lipid-Lowering Medication Adherence among Patients with Coronary Heart Disease. *Cholesterol.* 2010;2010:383281.
- McLean W, Gillis J, Waller R. The BC Community Pharmacy Asthma Study: A study of clinical, economic and holistic outcomes influenced by an asthma care protocol provided by specially trained community pharmacists in British Columbia. *Can Respir J.* 2003;10(4): 195–202.
- Mehos BM, Saseen JJ, MacLaughlin EJ. Effect of pharmacist intervention and initiation of home blood pressure monitoring in patients with uncontrolled hypertension. *Pharmacotherapy*. 2000;20(11): 1384–1389.
- Mehuys E, Van BL, De BL et al. Effectiveness of a community pharmacist intervention in diabetes care: a randomized controlled trial. *J Clin Pharm Ther.* 2011;36(5):602–613.
- Mehuys E, Van Bortel L, De Bolle L, et al. Effectiveness of pharmacist intervention for asthma control improvement. *Eur Respir J*. 2008;31(4): 790–799.
- Mohammadi E, Abedi HA, Jalali F, Gofranipour F, Kazemnejad A. Evaluation of 'partnership care model' in the control of hypertension. *Int J Nurs Pract.* 2006;12(3):153–159.
- Morgado M, Rolo S, Castelo-Branco M. Pharmacist intervention program to enhance hypertension control: a randomised controlled trial. *Int J Clin Pharm*. 2011;33(1):132–140.
- Murray MD, Ritchey ME, Wu J, Tu W. Effect of a pharmacist on adverse drug events and medication errors in outpatients with cardiovascular disease. *Arch Intern Med.* 2009;169(8):757–763.
- Murray MD, Young J, Hoke S, et al. Pharmacist intervention to improve medication adherence in heart failure: a randomized trial. *Ann Intern Med.* 2007;146(10):714–725.
- Nazareth I, Burton A, Shulman S, Smith P, Haines A, Timberal H. A pharmacy discharge plan for hospitalized elderly patients – a randomized controlled trial. *Age Ageing*. 2001;30(1):33–40.
- Noureldin M, Plake KS, Morrow DG, Tu W, Wu J, Murray MD. Effect of health literacy on drug adherence in patients with heart failure. *Pharmacotherapy*. 2012;32(9):819–826.
- Peterson GM, Fitzmaurice KD, Naunton M, Vial JH, Stewart K, Krum H. Impact of pharmacist-conducted home visits on the outcomes of lipidlowering drug therapy. *J Clin Pharm Ther.* 2004;29(1):23–30.
- Phumipamorn S, Pongwecharak J, Soorapan S, Pattharachayakul S. Effects of the pharmacist's input on glycaemic control and cardiovascular risks in Muslim diabetes. *Prim Care Diabetes*. 2008;2(1):31–37.
- 95. Pierce M, Lundy S, Palanisamy A, Winning S, King J. Prospective randomised controlled trial of methods of call and recall for cervical cytology screening. *BMJ*. 1989;299(6692):160–162.
- 96. Pladevall M, Brotons C, Gabriel R, et al; Writing Committee on behalf of the COM99 Study Group. Multicenter cluster-randomized trial of a multifactorial intervention to improve antihypertensive medication adherence and blood pressure control among patients at high cardiovascular risk (the COM99 study). *Circulation*. 2010;122(12): 1183–1191.

- Polack J, Jorgenson D, Robertson P. Evaluation of different methods of providing medication-related education to patients following myocardial infarction. *Can Pharm J.* 2008;141(4):241–247.
- Qureshi NN1, Hatcher J, Chaturvedi N, Jafar TH; Hypertension Research Group. Effect of general practitioner education on adherence to antihypertensive drugs: cluster randomised controlled trial. *BMJ*. 2007;335(7626):1030.
- 99. Ramanath K, Balaji D, Nagakishore Ch, Kumar SM, Bhanuprakash M. A study on impact of clinical pharmacist interventions on medication adherence and quality of life in rural hypertensive patients. *J Young Pharm.* 2012;4(2):95–100.
- 100. Ramanath KV, Venkappa KR. Study the impact of clinical pharmacist provided patient counseling on hypertension management in rural Indian population. *Arch Pharm Pract.* 2013;4(1):28–34.
- 101. Rathbun RC, Farmer KC, Stephens JR, Lockhart SM. Impact of an adherence clinic on behavioral outcomes and virologic response in treatment of HIV infection: a prospective, randomized, controlled pilot study. *Clin Ther.* 2005;27(2):199–209.
- 102. Rickles NM, Svarstad BL, Statz-Paynter JL, Taylor LV, Kobak KA. Improving patient feedback about and outcomes with antidepressant treatment: a study in eight community pharmacies. *JAm Pharm Assoc*. 2006;46(1):25–32.
- Rickles NM, Svarstad BL, Statz-Paynter JL, Taylor LV, Kobak KA. Pharmacist telemonitoring of antidepressant use: effects on pharmacist-patient collaboration. J Am Pharm Assoc. 2005;45(3): 344–353.
- Sadik A, Yousif M, McElnay JC. Pharmaceutical care of patients with heart failure. Br J Clin Pharmacol. 2005;60(2)183–193.
- Sathvik BS, Karibasappa MV, Nagavi BG. Self-reported medication adherence pattern of rural Indian patients with hypertension. *Asian Journal of Pharmaceutical and Clinical Research*. 2013;6(Suppl 1): 49–52.
- 106. Shah M, Norwood CA, Farias S, Ibrahim S, Chong PH, Fogelfeld L. Diabetes transitional care from inpatient to outpatient setting: pharmacist discharge counseling. J Pharm Pract. 2013;2(2):120–124.
- 107. Sookaneknun P, Richards RM, Sanguansermsri J, Teerasut C. Pharmacist involvement in primary care improves hypertensive patient clinical outcomes. *Ann Pharmacother*. 2004;38(12):2023–2028.
- 108. Stevens VJ, Shneidman RJ, Johnson RE, Boles M, Steele PE, Lee NL. Helicobacter pylori eradication in dyspeptic primary care patients: a randomized controlled trial of a pharmacy intervention. *West J Med*. 2002;17(2):92–96.
- Sturgess IK, McElnay JC, Hughes CM, Crealey G. Community pharmacy based provision of pharmaceutical care to older patients. *Pharm World Sci.* 2003;25(5):218–226.
- Thompson RS, Michnich ME, Gray J, Friedlander L, Gilson B. Maximizing compliance with hemoccult screening for colon cancer in clinical practice. *Med Care*. 1986;24(10):904–914.

- Turner KM, Wilson BJ, Gilbert FJ. Improving breast screening uptake: persuading initial non-attenders to attend. *J Med Screen*. 1994;1(3): 199–202.
- Varma S, McElnay JC, Hughes CM, Passmore AP, Varma M. Pharmaceutical care of patients with congestive heart failure: interventions and outcomes. *Pharmacotherapy*. 1999;19(7):860–869.
- Vivian EM. Improving blood pressure control in a pharmacist-managed hypertension clinic. *Pharmacotherapy*. 2002;22(12):1533–1540.
- Volume CI, Farris KB, Kassam R, Cox CE, Cave A. Pharmaceutical care research and education project: patient outcomes. *J Am Pharm Assoc (Wash)*. 2001;41(3):411–420.
- 115. Vuong T, Marriott JL, Kong DC, Siderov J. Implementation of a community liaison pharmacy service: a randomised controlled trial. *Int J Pharm Pract*. 2008;16(3):127–135.
- Wandless I, Whitmore J. The effect of counseling by a pharmacist on drug compliance in elderly patients. *J Clin Hosp Pharm.* 1981;6(1): 51–56.
- 117. Wang KY, Chian CF, Lai HR, Tarn YH, Wu CP. Clinical pharmacist counseling improves outcomes for Taiwanese asthma patients. *Pharm World Sci.* 2010;32(6):721–729.
- Weinberger M, Murray MD, Marrero DG, et al. Effectiveness of pharmacist care for patients with reactive airways disease: a randomized controlled trial. *JAMA*. 2002;288(13):1594–1602.
- 119. Williford SL, Johnson DF. Impact of pharmacist counseling on medication knowledge and compliance. *Mil Med.* 1995;160(11):561–564.
- 120. Wong MC, Liu KQ, Wang HH, et al. Effectiveness of a pharmacist-led drug counseling on enhancing antihypertensive adherence and blood pressure control: a randomized controlled trial. *J Clin Pharmacol.* 2013;53(7):753–761.
- 121. Wu JY, Leung WY, Chang S, et al. Effectiveness of telephone counselling by a pharmacist in reducing mortality in patients receiving polypharmacy: randomised controlled trial. *BMJ*. 2006; 333(7567):522.
- 122. Young HN, Havican SN, Griesbach S, Thorpe JM, Chewning BA, Sorkness CA. Patient and phaRmacist telephonic encounters (PARTE) in an underserved rural patient population with asthma: results of a pilot study. *Telemed J E Health*. 2012;18(6):427–433.
- 123. Zerafa N, Zarb Adami M, Galea J. Impact of drugs counselling by an undergraduate pharmacist on cardiac surgical patient's compliance to medicines. *Pharmacy Practice (Granada)*. 2011;9(3):156–161.
- 124. Zhang C, Zhang L, Huang L, Luo R, Wen J. Clinical pharmacists on medical care of pediatric inpatients: a single-center randomized controlled trial. *PLoS ONE*. 2012;7(1):e30856.
- 125. Knapp P, Raynor DK, Thistlethwaithe JE, Jones MB. A questionnaire to measure health practitioners' attitudes to partnership in medicine taking: LATCon II. *Health Expect*. 2009;12(2):175–186.

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