Pharmacist interventions to enhance blood pressure control and adherence to antihypertensive therapy: review and meta-analysis
Morgado MP, Morgado SR, Mendes LC, Pereira LJ, Castelo-Branco M

CRD summary
This review concluded that pharmacist interventions to improve medication adherence in people with essential hypertension could significantly improve adherence, systolic and diastolic blood pressure and blood pressure control. The interventions were complex, multifaceted and included medication management. In view of questionable quality of included data and methods of synthesis, and large difference between interventions, the reliability of conclusions is uncertain.

Authors’ objectives
To assess the effects of pharmacist interventions that targeted antihypertensive medication adherence and blood pressure control in adults with essential hypertension.

Searching
MEDLINE, The Cochrane Library and ISI Web of Knowledge were searched from 1999 to June 2009; search terms were reported. The bibliographies of retrieved articles were checked for additional studies. Articles had to be written in English, French, Spanish, German, Portuguese or Italian.

Study selection
Studies in adults with essential hypertension who were being treated with blood pressure (BP) lowering medication in primary care, outpatient or community settings were eligible for inclusion. The intervention of interest had to be delivered by a pharmacist and aimed at improving adherence to antihypertensive medication or BP control. Studies that described multidisciplinary interventions were only included if the pharmacist’s role was clearly described. Studies had to report on medication adherence, and at least one of systolic BP (SBP), diastolic BP (DBP) and BP control.

The included studies were randomised controlled trials (RCTs) and non-RCTs. In the included studies mean baseline SBP ranged from 140mmHg (standard deviation, SD, 18) to 173mmHg (SD 15), and mean baseline DBP from 71.7mmHg (SD 9.1) to 90mmHg (SD 14). The interventions were generally varied and complex and included one or more of the following: medication management, patient education, self-monitoring and recording of BP, medication reminders, improved administration systems or use adherence aids (such as blister packs), more frequent follow-up, education and/or alerts directed at health care personnel, pharmacist clinical visits to clinics. Frequency of intervention varied being generally between monthly and two-monthly, but in one very short term study was two-weekly. Settings for studies included primary care clinics and hospital clinics, pharmacies, army clinics and aircraft carrier personnel. Adherence was measured in varying ways (self-report, prescription refills, pill counts, plasma drug levels).

Two authors independently selected studies for inclusion. Disagreements were resolved by discussion and consensus, or with a third author.

Assessment of study quality
Quality was assessed using the Downs and Black scale. This scored items related to quality of reporting, external validity, internal validity (bias), confounding variables, power and rater’s overall opinion on quality. Maximum score was 42 (taken as 100%). Scores below 50% were considered weak, 50 to 69% fair, 70 to 79% good and 80 to 100% very good.

Two reviewers independently assessed quality. Disagreements were resolved by consensus.

Data extraction
Data were extracted in order to calculate: levels of adherence to medication, SBP and DBP at baseline and end of study; the percentages of participants with controlled BP, and odds ratio and 95% confidence intervals for blood pressure under control, at end of study; and net differences in SBP and DBP between intervention and control, before and after
intervention. For each study interventions were classified as "sensitive" (i.e. positive intervention from a clinical point of view, and that had a statistically significant positive result) or "non-sensitive".

Data were extracted by two reviewers independently. Disagreements were resolved by discussion and consensus, or with a third author. Authors were contacted for missing data.

Methods of synthesis
Results were described in tables and narrative discussion. Vote counting was used to summarise the numbers of studies with positive results. Mann-Whitney U test was used to investigate any influence of quality scores on outcomes.

Where there were sufficient data, and it was considered appropriate, a fixed-effect method was used to calculate pooled mean difference (MD) and standard deviations (SD) for SBP and DBP. Heterogeneity was assessed using $\chi^2$.

Publication bias was investigated using funnel plots and the Begg-Mazumdar statistic.

Results of the review
Fifteen studies (3,280 participants) were included. Of these eight were randomised controlled trials (RCTs; 1,432 participants) two were cluster RCTs (1,520 participants), four were single group controlled trials (217 participants; participants served as own controls) and one a non-RCT (111 participants). Study size ranged from 26 to 1341 participants. Most studies were undertaken in USA; other settings included Brazil, Nigeria, UK and Thailand.

Quality scores ranged from 50% to 82%, with nine considered fair, four good and two very good. Losses to follow-up ranged from 3.4% to 48.5% with five studies losing more than 20% of participants. Length of follow-up ranged from two weeks to 12 months.

The Begg-Mazumdar test suggested no significant publication bias.

Baseline medication adherence ranged from 35% to 88.6% and at end of study from 50% to 95.8%. Overall 61% of outcomes were classified as significantly improved by pharmacist intervention. Compared to control, seven out of 16 comparisons showed a significant improvement in medication adherence. Out of 13 comparisons, seven showed a significant improvement in both SBP and DBP, four a significant improvement in SBP alone and one in DBP alone (range for SBP -5.0 to -18.6 mm HG, for DBP -1.0 to -12.2mmHg). Compared with control, seven out of 12 studies showed a significant increase in the percentage of participants with BP control (range 17.5% to 51%).

When results were analysed according to study quality there appeared to be a correlation between study quality and impact on SBP and DBP with higher quality trials showing less positive effect on BP control and on medication adherence.

When results were formally meta-analysed, compared to control pharmacist interventions statistically significantly reduced SBP (MD -4.9mm Hg SD 0.9, nine comparisons) and DBP (MD -2.6 mm Hg SD 0.9, seven studies).

Authors' conclusions
Pharmacist interventions could significantly improve medication adherence, SBP, DBP and blood pressure control in people with essential hypertension.

CRD commentary
The inclusion criteria in terms of participants and intervention were clearly described. However, criteria for study design were not given, which implied that the review was not restricted to the best evidence to answer the review question. The search covered several databases, but was limited in terms of dates covered, languages included and a lack of a search for unpublished studies. It was possible that publication bias or language bias may have affected the review. Authors’ test for publication bias may have been unreliable given the limited number of available studies. The review methods were aimed at reducing reviewer error or bias.

The quality of included studies was assessed using a scoring system. Only the composite scores were reported and this made it difficult to comment on the reliability of the evidence presented. The authors’ decision not to statistically combine some results may have been appropriate given the differing nature of interventions and reported outcomes.
However "vote counting" positive results did not take into account differences between sizes of studies or of effect size of outcomes. For those outcomes that were statistically pooled a description of the methods used was limited, so it was not clear whether pooling of results was undertaken appropriately. Little information was given about the included participants so it may be difficult to generalise from the results. The length of follow-up was relatively short in some studies, and overall losses to follow up were relatively high. In view of the questionable quality of included data, limitations of the synthesis and, as the authors acknowledge, large differences between interventions, the reliability of authors' conclusions is uncertain.

**Implications of the review for practice and research**

The authors did not state any implications for practice or research.

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