Meta-analysis of pharmacist-led and pharmacist-physician intervention on blood pressure control

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ABSTRACT

Effective intervention is a significant component in the improvement of blood pressure control and patient adherence. Blood pressure control includes different self-monitoring techniques, mobile health monitoring, or healthcare professionals' interventions. This study aims to compare, analyze, and interpret the effectiveness of pharmacist-physician collaboration and pharmacist-led interventions. Meta-analysis was performed using MEDLINE via PubMed, EMBASE, EBSCO, Web of Science, Scopus, and the Cochrane Library databases between 2008-2018. Of the 51 relevant systematic reviews identified, 15 were of sufficient quality and included in the data synthesis. The breakdown of the 15 included 7 (n=2026) pharmacist and 8 pharmacist-physician interventions (n=2361). The impact of pharmacist-physician collaboration and pharmacist-led interventions on Systolic Blood Pressure was –8.22 (–11.01; –5.42) (P<0.01) and –7.68 (–9.30; –6.06) (P=0.35), respectively. On the other hand, similar correlation for Diastolic Blood Pressure for the impact of pharmacist-physician collaboration and pharmacist-led interventions was –3.55 (–4.54; –2.55) (P=0.49) and –2.58 (–3.76; –1.39) (P=0.24), respectively. These results suggest that both interventions are effective for blood pressure control. However, when two meta-analyses were compared, it was found that pharmacist-physician collaboration was more effective than pharmacist-led interventions. This finding highlights the importance of multidisciplinary approaches during blood pressure control procedures. When a holistic view is considered; especially cost-effectiveness, future studies must be diversified to encompass a broader context and impact analysis.

Introduction

According to the World Health Organization (WHO), hypertension is described as a 'silent killer' that can cause heart disease, stroke and kidney failure, premature death and disability.[1] and the aging population increases hypertension.[2] Forecasters estimate that by 2025, over 1.5 billion people are expected to suffer from hypertension, which is a severe public health concern.[3] However, the WHO also reports that it will be both preventable and treatable if all stakeholders such as governments, health workers, civil society, and individuals cooperate to reduce hypertension.[1] This notification supports the necessity of pharmacist and pharmacist-physician interventions, which are the main topic of our study.

For well-controlled blood pressure, systolic blood pressure and diastolic blood pressure should be less than 140/90 mm Hg. Otherwise, high blood pressure increases the risk of ischemic heart disease 3- to 4-fold, of overall cardiovascular disease by 2- to 3-fold,[4] and the incidence of stroke increases 3- to 8-fold in patients with borderline and definite hypertension, respectively.[5]

Many factors such as race/ethnicity, socio-economical, and health literacy affect the quality of communication with the patient with hypertension.[6] Therefore, blood pressure management requires the participation of all stakeholders, such as patients, families, and in particular, health care professionals. This management includes enhancing awareness, lifestyle modifications, access to treatment, evidence-based medicine, increasing medical adherence, and monitoring.[7]

Several studies have shown that physician-pharma-

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Contributions: the authors contributed equally. Each contribution was detailed in the *Materials and Methods* section.

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Ethical statement: no approval was needed from the University's Institutional Review Board since this study was a meta-analysis.

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cist collaborative management (PPCM) has a remarkable impact on blood pressure control and other chronic diseases.[8-10] Others have also shown the importance of Home Blood Pressure Tele-monitoring as another technique. The same studies have underlined the effectiveness of Web-Based Home Blood Pressure Monitoring with Pharmacist Support.[11-15] In addition to meta-analysis related to the impact of the pharmacist on patient care,[16] certain studies have emphasized the necessity of pharmacist-led interventions as pharmacists are the most accessible healthcare professionals - and highly capable of the management of hypertension.[17-21]

Meanwhile, other studies have reported that team-based health care delivery models such as physician-pharmacist collaboration are important in meeting patient needs, improving health care quality[22] and, in particular, in effective blood pressure management. However, they have also stressed the comparatively higher cost of care.[23]

For this reason, our study aims to evaluate the intervention of the pharmacist and pharmacist-physician cooperation by meta-analyses and interprets the effectiveness of these interventions in view of all available literature.

Materials and Methods

We have followed preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines for reporting meta-analysis.[24,25]

Data sources and search strategy

Primary data sources used are; MEDLINE via PubMed, EMBASE, EBSCO, Web of Science, Scopus, and the Cochrane Library, systematically searched by two independent authors (M.M. and Y.C.). These databases were searched for the period from 2008 to May 2018. Search terms included: 'Pharmacist intervention' OR 'Pharmacist care intervention' OR 'Pharmacist' OR 'Pharmacist-physician collaboration management' OR 'Pharmacist-physician intervention' OR 'Pharmacist-physician' OR 'Blood pressure control' AND 'Blood pressure' OR 'High blood pressure' OR 'Hypertension.' We also scanned the references of included studies that met the eligibility criteria.

Study selection

The inclusion criteria are listed below:

- Randomized controlled trial (RCT);
- Articles published between 2008-2018;
- Articles in the English language;
- Articles with full texts;
- At least 3-month duration of the study;
- A control group;
- Focused on patients with hypertension, but where patients with specific conditions (Diabetes, asthma, *etc*.) were excluded;
- Described and evaluated the type of intervention and outcomes;
- A pharmacist or a pharmacist in collaboration with a physician for the intervention.

The study screening was made in tandem by two authors (M.M. and Y.C.) independently. One of the researchers was blind to the authors of the articles. Conflicts in evaluating articles for inclusion were resolved by consensus.

Studies were screened for inclusion by reviewing the title and abstract. The screening was limited by publication date and the English language. Meta-analysis was also screened as potentially relevant studies. The last screening, which reviewed full-text articles was performed by two authors (M.M. and Y.C.). The remaining articles were divided into two groups as pharmacist-physician intervention and pharmacist intervention.

Data extraction and quality assessment

The extraction process was performed by one of our authors and checked for accuracy by another. Data were collected from full texts that extracted the following descriptive information: First author, publication year, country, study design, study duration, sample size, and characteristics of intervention. Our study has no restrictions on age, gender, and ethnicity.

The quality of the selected papers was independently scored, and all data were coded by two researchers (M.M. and Y.C.). Any disagreements between the two authors were resolved by consensus. Otherwise, any disagreement was to be resolved by a third reviewer (T.D.). However, there was no disagreement in our study to require such support.

Data synthesis and analysis

We used the Cochrane Collaboration tool from the Cochrane Handbook[26] to assess the risk of bias and the PRISMA statement. The RCTs were graded based on sequence generation, allocation concealment, incomplete outcome data, selective reporting, blinding of participants and personnel, and blinding of the outcome assessment. We categorized these judgments as 'low risk,' 'high risk' or 'unclear risk' of bias. All meta-analyses were conducted using 'RStudio Version 1.2.1335, 2019 RStudio, Inc.' for Windows version 10.0 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014), at the 5% significance level.

Results

A total of 19,412 articles were identified during the initial search (Figure 1). From that group, 109 articles

were written in different languages. Thus, the initial search revealed 877 potentially relevant studies, and those were selected for our database search. After reviewing the abstract and removing duplicate publications, 51 full-text articles were reviewed for a more detailed evaluation. From that group, 15 studies met the inclusion criteria (pharmacist intervention 7, PPCM intervention 8). 36 were excluded for the following reasons:

- not an interventional study;
- studied participants with a different disease not relevant to review;
- did not include pharmacists in the study interventions;
- presented pharmaceutical interventions and outcomes investigating neither adherence nor blood pressure;
- presented pharmaceutical interventions and outcomes investigating blood pressure but not adherence;
- investigated medication adherence outcome in the intervention group only, and baseline adherence was not measured.

Each study intervention was categorized as pharmacist-directed care or pharmacist collaborative care.

Studies into PPCM intervention included 2361 participants (1305 interventions and 1056 control studies), and studies on pharmacist intervention included 2026 participants (990 interventions and 1036 control studies).

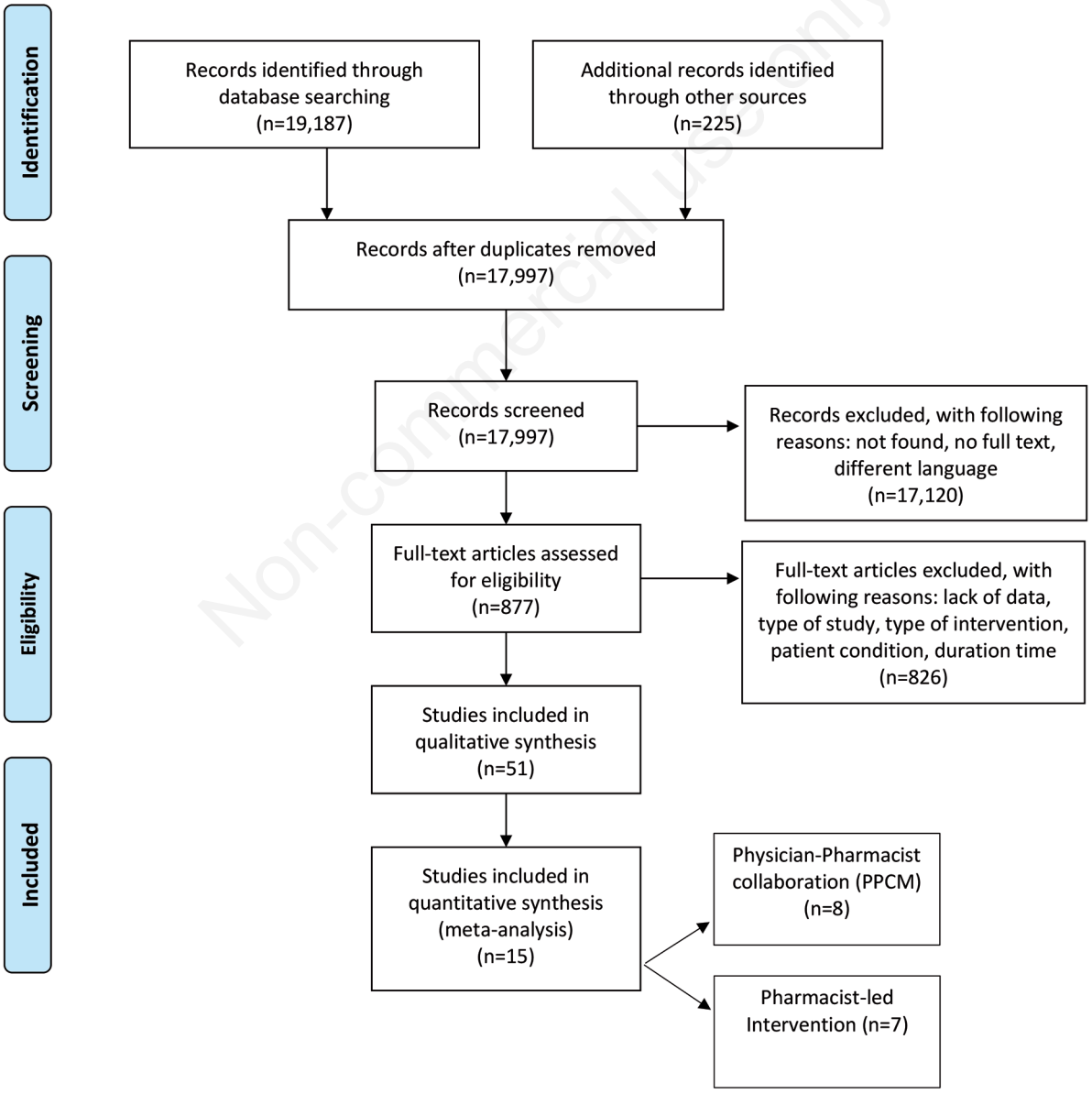

Figure 1. Flow chart of data extracting according to PRISMA.[24,25]

The publication years ranged from Jan 2008 to May 2018. Regarding patient characteristics, the mean age of all studies was 48.8 to 68. Regarding physician-pharmacist collaboration (PPCM), most studies were conducted in the US (n=7), and 1 in Jordan. Regarding pharmacist-led interventions, 2 of the studies were conducted in the US, 1 in Australia, 1 in China, 1 in Japan, 1 in Portugal, and 1 in Canada. Study duration ranged from 3 months to 30 months, with most lasting no longer than 12 months. The sample size in each trial ranged from 104 to 723 participants.

Overall, 15 randomized control trials with combined interventions were analyzed where Tables 1 and 2 show the summary of the included study characteristics.[10,27-39] The mean intervention duration was 11 months for PPCM and 12 months for pharmacist-led intervention. Six of the studies were relatively short-term (<9 months), and 9 of the studies were long-term (9-30 months). It was found that time of duration was not directly related to blood pressure control (Figures 2-5). However, we can state that the extension of the duration may increase the effectiveness of blood pressure control in pharmacist-led interventions.

According to the random effects model, the correlation between article quality scores and the impact of PPCM and pharmacist-led interventions on SBP were –8.22 (–11.01; –5.42) (P<0.01) and –7.68 (–9.30; –6.06) (P=0.35), respectively (Figures 2 and 3). On the other hand, similar correlation for DBP for the impact of PPCM and pharmacist-led interventions was –3.55 (–4.54; –2.55) (P=0.49) and –2.58 (–3.76; –1.39) (P=0.24), respectively (Figures 4 and 5). The mean reduction from baseline to endpoint in PPCM intervention was more than in pharmacist-led interventions.

Discussion

Hypertension is one of the leading causes of mortality. Therefore, to control high blood pressure, the quality of intervention plays a critical role. For this reason, it is essential to investigate what kind of intervention is more effective in combating this disease.

The findings of Morgado, who performed a meta-analysis between 1999 and 2009, showed that pharmacist interventions improved medication adherence significantly.[40] Morgado's study was similar to our research except for the different period used (time interval

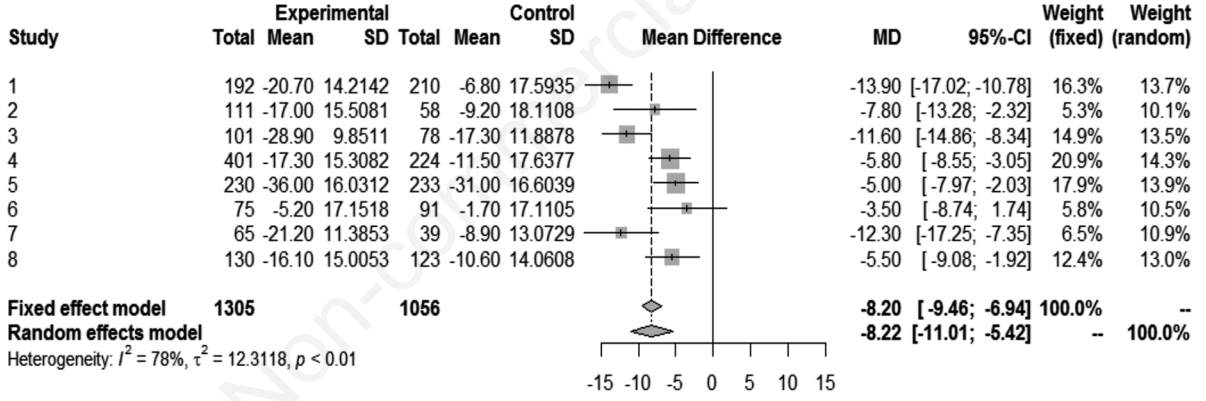

Figure 2. Improvement of systolic blood pressure of physician-pharmacist collaboration intervention.

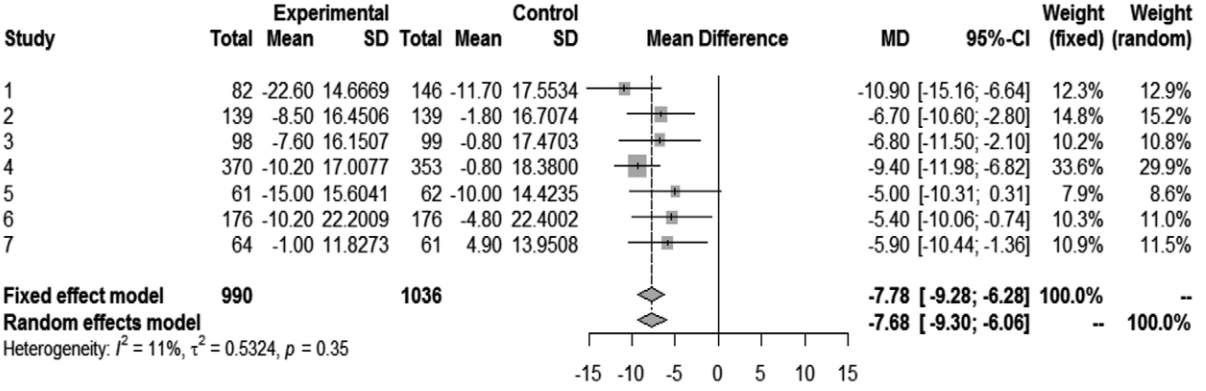

Figure 3. Improvement of systolic blood pressure of pharmacist intervention.

Table 1. Characteristics of the included studies related to physician-pharmacist collaborative management intervention.

Study No./Ref No.	Year/Country	Duration time	Study design	Study population (No.)	Population ages	SBP intervention	SBP control	DBP intervention	DBP control
1/10 (Carter, 2009[10])	2009/US	6 Months	Prospective, cluster-randomized, controlled clinical trial	Total: 402 Control: 210 Intervention: 192	Control 59.2 (13.8) Intervention 57.3 (14.3) Mean: 58.3	Baseline 153.6±12.8 Endpoint 132.9±15.5	Baseline 150.6±14.1 Endpoint 143.8±20.5	Baseline 87.4±11.9 Endpoint 77.7±11.2	Baseline83.6±12.3 Endpoint 79.1±14.3
2/27 (Smith, 2016[27])	2016/US	9 Months	Prospective, cluster randomized, multicentre clinical trial CAPTION	Total: 169 Control: 58 Intervention: 111	Control 65.2 (11.2) Intervention 62.9 (11.7) Mean: 64.05	Baseline 149.0±15 Endpoint 132±16	Baseline 150.2±16 Endpoint 141±20	Baseline 83.5±13 Endpoint 75±12	Baseline 78.9 (12) Endpoint 73±13
3/28 (Carter, 2008[28])	2008/US	9 Months	Prospective, cluster randomized controlled trial	Total: 179 Control:78 Intervention: 101	Control 61.9 (11.3) Intervention 59.6 (13.7) Mean: 60.75	Baseline 153.1±10.0 Endpoint 124.2±9.7	Baseline 150.3±9.0 Endpoint 133.0±14.2	Baseline 84.9±12.0 Endpoint 74.7±9.6	Baseline 85.4±11.0 Endpoint 78.5±10.9
4/29 (Polgreen, 2015[29])	2015/US	9 Months	Prospective, cluster-randomized, controlled trial	Total: 625 Control: 224 Intervention: 401	Mean: 61 (1.01)	Baseline 148.9±14.8 Endpoint 131.6±15.8	Baseline 149.7±15.3 Endpoint 138.2±19.7	Baseline 85.1±12.1 Endpoint 76.3±11.1	Baseline 84.3±12.6 Endpoint 78 .0±14.5
5/9 (Hunt, 2008[9])	2008/US	12 Months	Prospective, single-blind, randomized, controlled trial	Total: 463 Control: 233 Intervention: 230	Control 68 (13) Intervention 68 (12) Mean: 68	Baseline 173±15 Endpoint 137±17	Baseline 174±15 Endpoint 143±18	Baseline 92±14 Endpoint 75±9	Baseline 90±14 Endpoint 78±11
6/30 (Hirsch, 2014[30])	2014/US	9 Months	Randomized, pragmatic, clinical trial	Total: 166 Control: 91 Intervention: 75	Control 69.6 (11.4) Intervention 65.4 (13.0) Mean: 67.5	Baseline 134.8±17.4 Endpoint 129.6±16.9	Baseline 134.4±16.5 Endpoint 132.7±17.7	Baseline 75.1±12.5 Endpoint 72.6±10.2	Baseline 75.7±13.4 Endpoint 75.4±13.8
7/ 31 (Carter, 2010[31])	2010/US	27 Months	Prospective, cluster randomized controlled efficacy trial	Total: 104 Control: 39 Intervention: 65	Control 62.77 (11.1) Intervention 58.94 (13.2) Mean: 60.85	Baseline 152.5±9.5 Endpoint 131.3±13	Baseline 150.1±9.6 Endpoint 141.2±15.8	Baseline 85.5±12.2 Endpoint 76.3±11.7	Baseline 85.4±10.7 Endpoint 77.1±11.3
8/32 (Albsoul-Younes, 2011[32])	2011/Jordan	6 Months	Randomized controlled clinical trial	Total: 253 Control:123 Intervention: 130	Control 57.5 (11.9) Intervention 56.3 (9.6) Mean: 56.9	Baseline 137.5±15.4 Endpoint 121.4±14.6	Baseline 134.8±14.6 Endpoint 124.2±13.5	Baseline 85.2±9.7 Endpoint 74.7±12.9	Baseline 83.7±8.1 Endpoint 76.5±13.11
			Overall	**Total no: 2361**					

of our study: 2008-2018). In addition, though Morgado's findings only mention pharmacist interventions, the same study covers both methods. Therefore, Morgado's study[40] was not included in part of our study.

Another previous meta-analysis conducted by Santschi *et al*. shows that intervention by the pharmacist or pharmacist in collaboration with physicians or nurses improves the risk factor in cardiovascular disease management.[41] Both studies highlight similar results within our study.

According to our meta-analysis, the pharmacist-physician collaborative intervention increased blood pressure control more than pharmacist-led interventions. However, it should also be noted that team-based care can also increase the cost of care. Additionally, 'Collaboration among Pharmacists and Physicians to Improve Blood Pressure Now' (CAPTION) was known as an effective study to implement PPCM for hypertensive patients in the United States. However, recent data show that no improvement is visible in the blood pressure control rate in the US.[42]

Despite these conflicting data, we can still say that the pharmacist plays a critical role in managing blood pressure.[40,41,43-47] However, regarding pharmacist-led intervention, an extension of duration can be essential to improve blood pressure control. Therefore, as evidenced by our study, the most reasonable approach would be to adopt pharmacist-physician collaboration and interventions to achieve effective patient care.

On the other hand, this study covers several limitations related to heterogeneity, such as interventions, duration of follow-up, and study population. Many studies could not be included in the meta-analysis because they did not meet specific inclusion criteria such as language or publication date. As more studies were conducted in the USA, the heterogeneity of the population, such as ethnicity, was affected. In the near future, studies should be diversified by incorporating different backgrounds such as regional, urban, *vs* rural, and the inclusion of other advanced techniques.

Limitation

This meta-analysis was performed using several databases between 2008-2018. One of the limitations of our research is that the data of the last years (2019-2020) were not reviewed. Another limitation was that

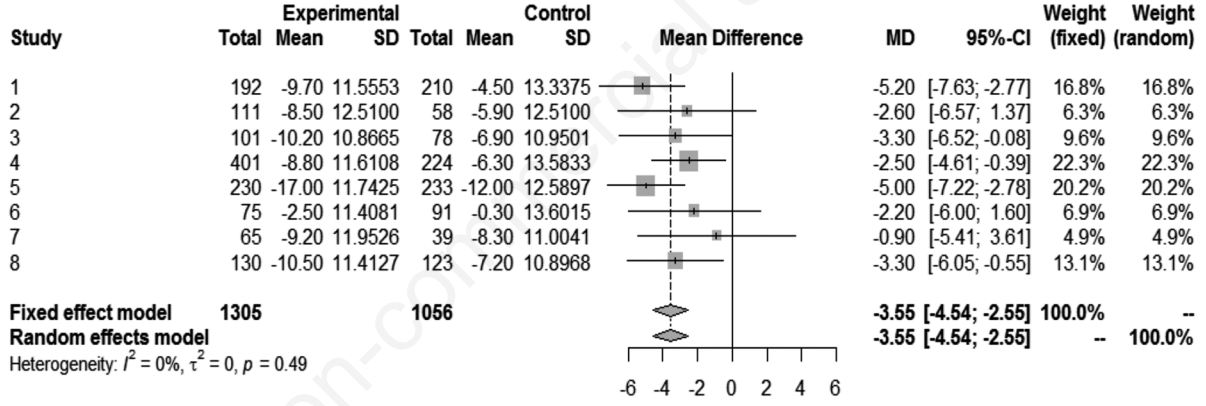

Figure 4. Improvement of diastolic blood pressure for physician-pharmacist collaboration intervention.

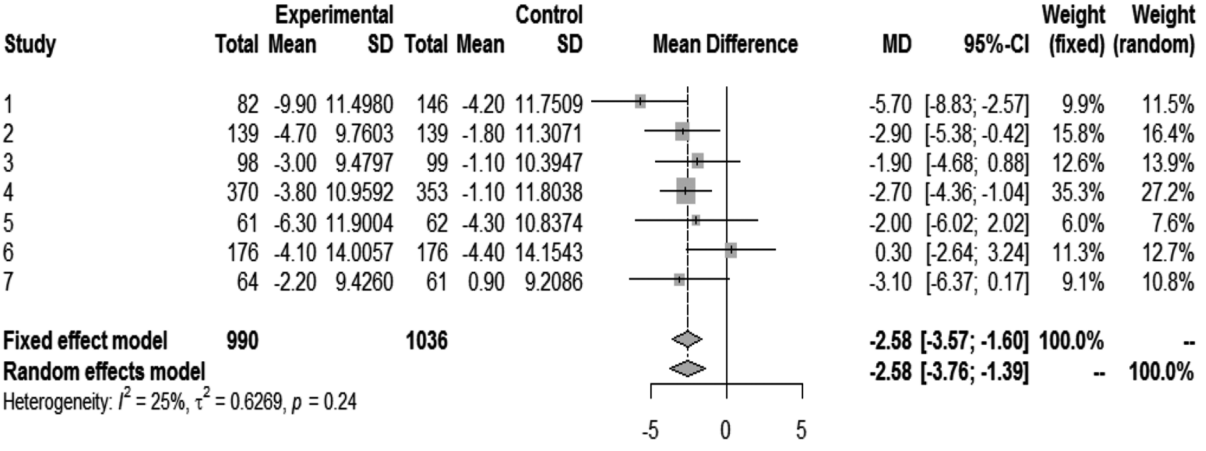

Figure 5. Improvement of diastolic blood pressure for pharmacist intervention.

Table 2. Characteristics of the included studies related to pharmacist-led intervention.

Study No./Ref No.	Year/Country	Duration time	Study design	Study population (No.)	Mean age	SBP intervention	SBP control	DBP intervention	DBP control
1/33 (Wentzlaff, 2011[33])	2011/US	24 Months	Prospective, cluster randomized, controlled trial	Total: 228 Control: 146 Intervention: 82	Control 59.8 (13.2) Intervention 56.07 (14.3) Mean: 57.93	Baseline 152.6±13.2 Endpoint 130.0±16.0	Baseline 149.8±14.0 Endpoint 138.1±20.4	Baseline 87.3±12.5 Endpoint 77.4±10.4	Baseline 83.0±11.9 Endpoint 78.8±11.6
2/34 (Zhao, 2012[34])	2012/China	6 Months	Prospective, randomized, controlled study	Total: 278 Control: 139 Intervention: 139	Control 65.6 (18.8) Intervention 62.4 (19.1) Mean: 64	Baseline 142.5±16.6 Endpoint 134.0±16.3	Baseline 143.9±17.2 Endpoint 142.1±16.2	Baseline 85.2±10.2 Endpoint 80.5±9.3	Baseline 86.4±11.7 Endpoint 84.6±10.9
3/35 (Morgado, 2011[35])	2011/Portugal	9 Months	Randomized controlled study	Total: 197 Control: 99 Intervention: 98	Control 60.7 (11.8) Intervention 58.3 (11.6) Mean: 59.5	Baseline 141.6±16.3 Endpoint 134.0±16.0	Baseline 141.9±16.8 Endpoint 141.1±18.0	Baseline 85.2±10.2 Endpoint 82.2±8.7	Baseline 86.4±11.7 Endpoint 85.3±8.9
4/36 (Tsuyuki, 2016[36])	2016/Canada	3 Months	Multicenter, randomized controlled trial	Total: 723 Control: 353 Intervention: 370	Control 61 (12) Intervention 62 (12) Mean: 61.5	Baseline 137.4±19.7 Endpoint 127.2±13.8	Baseline 137.1±19.4 Endpoint 136.3±17.3	Baseline 80.8±11.4 Endpoint 77±10.5	Baseline 81.1±12.1 Endpoint 80±11.5
5/37 (Carter, 2015[37])	2015/US	30 Months	Randomized controlled trial	Total: 123 Control: 62 Intervention: 61	Control 66.0 (10.4) Intervention 63.6 (11.2) Mean: 64.8	Baseline 147±13.7 Endpoint 132±17.3	Baseline 147±11.7 Endpoint 137±17.7	Baseline 79.9±11.8 Endpoint 73.6±12	Baseline 78.8±9.9 Endpoint 74.5±11.7
6/38 (Stewart, 2014[38])	2014/Australia	6 Months	Prospective, non-blinded, cluster-randomized, controlled trial	Total: 352 Control: 176 Intervention: 176	Control 66.6 (11.7) Intervention 66.8 (12.1) Mean: 66.7	Baseline 141.9±22.4 Endpoint 131.7±22	Baseline 140.1±22.5 Endpoint 135.3±22.3	Baseline 84.3±14.4 Endpoint 80.2±13.6	Baseline 83.2±14.5 Endpoint 78.8±13.8
7/39 (Okada, 2017[39])	2017/Japan	3 Months	Cluster-randomized controlled trial	Total: 125 Control: 61 Intervention: 64	Control 66.6 (9.0) Intervention 61.6 (9.9) Mean: 64.1	Baseline 135.2±13.1 Endpoint 134.2±10.4	Baseline 131.8±14.1 Endpoint 136.7±13.8	Baseline 81.6±8.7 Endpoint 79.4±10.1	Baseline 76.6±9.6 Endpoint 77.5±8.8
			Overall	**Total no: 2026**					

36 studies were excluded from the data synthesis due to not meeting the inclusion criteria. As a result, future studies need to be diversified to encompass a larger sample size and impact analysis.

Conclusions

Our meta-analysis has revealed that pharmacist-physician collaboration was relatively more effective than pharmacist-led interventions.

This finding highlights the importance of multidisciplinary approaches during blood pressure control procedures. However, when a holistic view is considered, especially including the cost-effectiveness, future studies must be diversified to encompass a broader context and impact analysis. To improve blood pressure control, it is crucial to examine how pharmacists could be more effective within a shorter timeframe, and their precise role in the team.

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