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REVIEW

# Pharmacist-Led Digital Health Interventions to Improve Treatment Outcomes in Patients with Hypertension - A Systematic Review

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**Abstract:** With the advancement of digital technologies, pharmacist-led digital health interventions (DHI) have emerged as a promising strategy to improve hypertension management. This systematic review evaluated randomized controlled trials (RCTs) published from December 1996 to May 2024, identified via PubMed by incorporating key concepts including DHIs, pharmaceutical care, and hypertension. The review included RCTs assessed telephone-, web-, or mobile-based pharmacist-led DHI compared to usual care (UC). Primary outcomes included blood pressure (BP) reduction, medication adherence, and identification of drug-related problems (DRPs). Following the modified Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, fourteen RCTs met inclusion criteria, with interventions categorized as telephone monitoring (n = 6), web-based interventions (n = 5), and mobile-based interventions (n = 3). Eight studies (57.14%) showed significant BP reduction in the intervention group (IG), one (7.14%) reported diastolic blood pressure (DBP) reduction only, and one found no significant BP difference between IG and control group (CG). One study reported a higher BP control rate in the IG (OR = 3.64). All studies evaluating adherence (n = 5) showed improvements, and one reported enhanced DRP identification. We identified that interventions' effectiveness is influenced by frequency of the intervention, personalization, and patient engagement. Designing an intervention compatible with each patient and providing sufficient guidance may improve effectiveness. As most studies were conducted in high-income countries, further research is needed to ensure the applicability of DHIs in diverse settings. In conclusion, pharmacist-led DHIs demonstrate potential in improving hypertension outcomes, with further validation required to support their implementation across varied healthcare systems.

**Keywords:** pharmacist-led, hypertension, digital health intervention, patient treatment, clinical outcomes

## Introduction

The number of adults with hypertension worldwide increased from 594 million in 1975 to 1.28 billion in 2019, with most of the increase occurring in low- and middle-income countries.[1] However, only 21% of the 1.4 billion individuals aged 30 to 79 are able to effectively control their hypertension.[2] Hypertension is managed with pharmacological treatment and lifestyle modifications. Pharmacological treatment involves the administration of essential antihypertensive drugs, namely angiotensin receptor blockers (ARB), calcium channel blockers (CCB), angiotensin-converting enzyme inhibitors (ACEi), and thiazide diuretics.[3] Lifestyle modification to lower BP include weight loss, regular exercise, avoiding tobacco consumption, and maintaining a healthy, low-salt diet. However, several factors can affect the desired outcome of the therapy, including patient's medication adherence, drug-related problems, and the patient's overall health condition.[4]

Previous studies have demonstrated that interventions initiated by pharmacist can enhance patient's medication adherence and BP management in patients taking antihypertensive medication.[5,6] In this digital era, pharmacist-led



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DHI presents a promising approach to improve patient health. DHI refers to the use of digital equipment complemented with wireless systems such as text-messages reminders, telephone monitoring, and web-based intervention, to enhance healthcare outcomes.[7] However, there are currently no reviews specifically assessing digital interventions for hypertensive patients that are led by pharmacists, despite their numerous potential benefits for both patients and pharmacists. These interventions offer several advantages, including cost-effectiveness, resource efficiency, and improved accessibility.[8]

The aim of this study was to assess the characteristics of pharmacist-led digital health interventions for patients with hypertension from published articles of RCTs. Such understanding may help identify key features that make these interventions effective and inform future strategies to optimize hypertension management through digital pharmacist-led care.

# Material and Methods

## Search Strategy

This study adhered to the PRISMA guidelines to ensure full disclosure of methods and findings. Relevant studies were identified through PubMed Database, spanning publications from December 1996 to May 2024. The literature retrieval process incorporated key concepts including: i) digital health interventions; ii) pharmacist and pharmaceutical care; and iii) hypertension. The following keywords were used: (Telemedicine[MeSH] OR telepharmacy[tiab] OR clinical decision support[tiab] OR automated medication system[tiab] OR automated pharmacy system[tiab] OR bar coding[tiab] OR electronic medication order entry[tiab] OR electronic medication management system[tiab] OR automated dispensing[tiab] OR computerized reminder system[tiab] OR information technology[tiab] OR medication ordering entry[tiab] OR electronic medication ordering and administration system[tiab] OR remote consultation[MeSH] OR electronic consult*[tiab] OR digital technolog*[tiab] OR teleconsult*[tiab] OR mhealth[tiab] OR m-health[tiab] OR multimedia[tiab] OR virtual[tiab] OR mobile health[tiab] OR telemedicine[tiab] OR electronic health record[tiab] OR telehealth[tiab] OR telecare[tiab] OR telehealth care[tiab] OR mobile health intervention*[tiab] OR mobile applications[tiab] OR mobile telemedicine[tiab] OR mcare[tiab] OR m-care[tiab] OR mobile communication[tiab] OR mobile technolog*[tiab] OR multimedia technolog*[tiab] OR mobile devic*[tiab] OR app[tiab] OR apps[tiab] OR mobile app*[tiab] OR website*[tiab] OR internet consultation*[tiab] OR internet monitoring[tiab] OR video consultation*[tiab] OR video monitoring[tiab] OR telephone*[tiab] OR mobile phone*[tiab] OR smart phone*[tiab] OR smart-phone*[tiab] OR text messag*[tiab] OR text messaging[tiab] OR SMS[tiab] OR short messag*[tiab] OR multimedia messag*[tiab] OR multi-media messag*[tiab] OR website platform[tiab] OR web-based medication platform[tiab] OR web-based application[tiab] OR web-based tool[tiab] OR electronic health[tiab] OR ehealth[tiab] OR e-health[tiab]) AND (Pharmacist*[tiab] OR pharmaceutical care[tiab]) AND (hypertension[tiab] OR blood pressure management[tiab]).

## Inclusion and Exclusion Criteria

Inclusion to studies was done to RCTs conducted on adult patients with hypertension that assessed how pharmacist-initiated DHIs affect the wellbeing of the patients. The assessment focused on clinical outcomes, specifically on the reduction of BP, improvement in medication adherence, reduction in adverse drug reactions (ADRs) and medication errors. Exclusion criteria comprised trials that: (a) did not utilize DHI, (b) were not RCTs, (c) did not assess hypertension-related outcomes, (d) were not pharmacist-led, (e) had a different primary intervention method, (f) were not published in English, and (g) were literature reviews/systematic reviews, case reports/case series, or conference abstracts.

## Screening and Data Extraction

Two investigators (GS and A) independently screened and evenly divided all retrieved records, evaluating both titles and abstracts based on predefined criteria. Conflicting screening assessments were reconciled through consultation with WNI as a third reviewer. Following the title and abstract screening phase, a full-text review was conducted for eligible articles to proceed with the final inclusion assessment. A modified PRISMA flowchart was used to visualize the screening and selection methodology. Relevant data from qualifying studies were extracted using predefined form, documenting general study characteristics, study design, and key findings.

## Risk of Bias Assessment

Cochrane Risk of Bias (RoB) 2.0 tool was used to evaluate methodological quality and detect potential bias affecting internal validity. The assessment covered the following domains: (D1) Bias arising from the randomization process; (D1b) Bias arising from the timing of identification and recruitment of participants; (D2) Bias due to deviations from intended intervention; (D3) Bias due to missing outcome data; (D4) Bias due to measurement of the outcome; (D5) Bias in selection of the reported results. The assessment covered the following domains applicable to RCTs. However, D1b was only applied to cluster-RCTs, as this design involves participant recruitment after cluster allocation. Each domain was judged as having low, some concerns, or high risk, followed by an overall RoB judgment for each study. Studies with a low RoB were considered more methodologically robust and therefore preferable in the overall interpretation of findings.

# Results

## Literature Search and Selection Process

The process of article selection is displayed by Figure 1 through a flowchart. Two hundred and two articles retrieval from PubMed was done in the initial search. Only 21 articles proceeded to full-text assessment after titles and abstracts screening phase, while 181 studies did not. Seven studies were further excluded throughout the full-text review based on specific criteria, resulting in 14 articles that fulfilled the eligibility requirements and were included into the final analysis.

## Characteristic of the Study

Table 1 summarizes the findings from the 14 analyzed studies. The United States of America accounted for the majority of the studies (n = 10),[12,13,15–22] while the remaining were conducted in Ghana (n = 1),[9] Denmark (n = 1),[10] United Arab Emirates (n = 1),[11] and China (n = 1).[14] The population varies significantly in size, ranging from 31 to 4078 patients. The

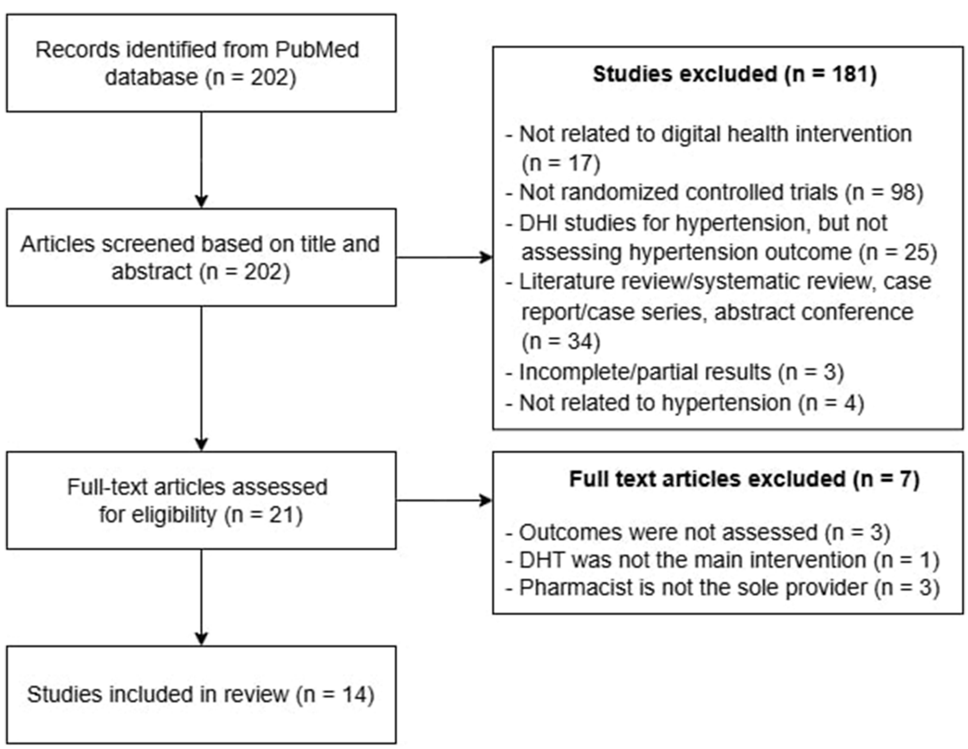


**Figure 1** Flow Diagram of Systematic Review.

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**Table 1** General Characteristics of the Studies

| No | Author, Publication Year | Setting | Country | Subject | Design | Outcome |
|---|---|---|---|---|---|---|
| Hypertension | | | | | | |
| 1 | Mozu et al, 2023[9] | 2 university hospitals | Ghana | Adults (Age ≥18) with an established hypertension diagnosis, phone accessibility, and signed informed consent | RCT[a] | Adherence and BP[b] |
| 2 | Hedegaard et al, 2015[10] | Odense University Hospital | Denmark | Adults (Age ≥18), were prescribed at least one antihypertensive agent | RCT | Adherence and BP |
| 3 | Ibrahim et al, 2022[11] | 16 community pharmacies | United Arab Emirates | Adults with hypertension at their latest pharmacy visit (BP >140/90 mmHg for patients diagnosed with diabetes or CKD[c]) | 2-arm RCT | BP, Adherence, and DRP[d] |
| 4 | Green et al, 2008[12] | 10 Medical Centers within Group Health | United States of America | Adults aged 25 to 75 who were diagnosed solely with hypertension and undergoing antihypertensive therapy | 3-arm RCT | BP |
| 5 | Asche et al, 2016[13] | 16 Study Clinics at HealthPartners Medical Group | United States of America | Adult patients with BP >140/90 mmHg at their 2 latest visits were identified from electronic medical records. These patients' uncontrolled BP were then confirmed by remeasurements amounting to 3 times | 2 Group Cluster RCT | BP |
| 6 | Wang et al, 2022[14] | Department of Endocrinology of Dongying People's Hospital | China | Adults aged 18–65 with diagnosed type 2 diabetes and hypertension who were hospitalized for uncontrolled blood glucose or BP. They were included if their conditions were well-controlled at discharge, received pharmaceutical care during hospitalization, and continued antidiabetic and antihypertensive medications after discharge | RCT | Adherence and BP |
| 7 | Bosworth et al, 2018[15] | Durham Veterans Affairs Medical Center (VAMC) clinics | United States of America | Adults aged at least 40, had a diagnosis of either uncontrolled hypertension (average BP ≥150/100 mmHg) or hypercholesterolemia (LDL[e] ≥130 mg/dL), based on electronic medical record data | 2-arm RCT | BP |
| 8 | Margolis et al, 2022[16] | 21 primary care clinics | United States of America | Patients who were at the age of 18 to 85, diagnosed with hypertension twice or more in the last 2 years, visited PCP[f] within the last year, made an appointment in the same clinic where their PCP practice, had persistent elevated BP readings on both of their latest and current appointment (≥150/95 mmHg) | Pragmatic Cluster RCT | BP |
| 9 | Gupta et al, 2023[17] | 6 primary care clinics | United states of America | Patients who aged ≥65 years with uncontrolled hypertension, had multiple comorbidities, frailty, and mobility limitations | Pilot Study-RCT | BP |
| 10 | Magid et al, 2013[18] | 10 clinics | United states of America | Hypertension patients with the age range of 18–79, 2 latest BP readings were persistently elevated, prescribed with ≤3 antihypertensive drugs, had accessibility to internet (registered on KPCO[g] My Chart Web site) | Pragmatic RCT | BP |

(*Continued*)

**Table 1** (Continued).

| No | Author, Publication Year | Setting | Country | Subject | Design | Outcome |
|---|---|---|---|---|---|---|
| 11 | Margolis et al, 2013[19] | 2 clinics | United States of America | Adult patients whose BP readings for the 2 latest primary care visits were persistently elevated (≥140/ 90 mmHg) | Cluster RCT | BP |
| 12 | Beran et al, 2018[20] | 16 primary care clinics | United States of America | Adult patients whose BP readings for the 2 latest primary care visits were persistently elevated (≥140/ 90 mmHg). | 2-arm Cluster RCT | BP |
| 13 | Choudhry et al, 2018[21] | 14 primary care practice sites | United States of America | Patients who were at the age of 18 to 85 who had suboptimal hyperlipidemia, hypertension or diabetes, and medication non-adherence | 2 arm Pragmatic Cluster RCT | Adherence |
| 14 | Mehos et al, 2000[22] | 1 training clinic | United States of America | Patients who aged ≥35 year with stage 1 or 2 hypertension, current therapy with at least one antihypertensive drugs, ability to measure BP with a home monitor | Prospective RCT | BP |

**Notes**: [a]RCT, Randomized Controlled Trial; [b]BP, Blood Pressure; [c]CKD, Chronic Kidney Disease; [d]DRP, Drug-related Problem; [e]LDL, Low-density Lipoprotein; [f]PCP, Primary Care Professional; [g]KCPO, Kaiser Permanente Colorado.

DHI used in these studies included telephone-based (n = 6), web-based (n = 5), and mobile-based intervention (n = 3). Five studies used combination of these methods. The majority of the studies focused on assessing BP (n = 13)[9–20,22] and medication adherence (n = 4),[9,11,14,21] while one study assessed DRPs.[11]

Table 2 presents a detailed analysis of the 14 studies that were part of this review. It outlines key aspects of each study, including the comparison of DHI, the follow-up period, and the main findings of the studies.

## Telephone-Based Intervention

Out of fourteen studies reviewed, six studies utilized telephone-based monitoring as an intervention.[9,10,15,16,21,22] Five of the studies employed combined methods, either telephone and web-based or telephone and mobile-based interventions.[13,14,17,19,20] However, telephone calls were used less frequently compared to web or mobile interventions. Two studies found that telephone-based interventions significantly decreased SBP and DBP.[9,22] One study found that BP was effectively lowered, but comparative analysis revealed that the result among intervention group (IG) and control group (CG) did not differ substantially.[16] Another study showed no significant decrease except for DBP.[10] However, three studies show a significant improvement in medication adherence.[9,10,21] Besides that, this method also effective in promoting therapeutic lifestyle modifications, as evidenced by the significant increase in participants adopting healthier habits.[9]

## Web-Based Intervention

Throughout the analysis, we found five studies that used web-based interventions.[12,13,18–20] While three out of five studies were combined with other methods, the entirely web-based studies allow the patients to receive training in utilizing not only the home blood pressure monitor (HBPM) but also the website in order to fulfill their health-related necessities.[12] All of the studies showed that web-based interventions led to a significantly greater result in reaching the controlled BP state compared to UC or the CG. These results are also related to some key factors including medication adjustments, patient–pharmacist relationship, and treatment plans.[20]

**Table 2** Main Findings of the Studies

| No | Author, Publication Year | Intervention (n, Mean Age, % Female, Frequencies) | Control (n, Mean Age, %Female) | Follow-up Period | Main Findings |
|---|---|---|---|---|---|
| 1 | Mozu et al, 2023[9] | Pharmacist-initiated phone calls (n = 57, 62.2 ± 10.9, 50%, monthly) | Routine clinical care which included monthly or bimonthly visit to clinic (n = 59, 62.8 ± 10.5, 44%) | 6 months | Significant decrease in SBP[a] (mean of 148.1 + 23.6 to 134.8 + 13.7) and DBP[b] (mean of 85.8 + 9.8 to 79.5 + 8.7) in the IG[c] |
| | | | | | Significant improvement of medication adherence from 85.7% to 96.5% in the IG |
| 2 | Hedegaard et al, 2015[10] | Pharmacist-led collaborative care, medication review, tailored adherence counselling including motivational interviewing and telephone follow-ups (n = 231, 62, 40.3%, 2 or more follow-up telephone calls to the patient within the first 6 months) | Usual Care (n = 285, 60, 40%) | 12 months (6 months of pharmacist intervention and 6 months of follow-up) | No significant difference, except in DBP of the IG (mean of 76.4 (11.1)) compared to UC[d] (mean of 76.7 (10.1)) |
| | | | | | 20.3% of patients (n = 231) were nonadherent in the IG (MPR[e] < 0.80), compared to 30.2% in the CG[f] (n = 285), with a risk difference of 9.8% (95% CI[g]: 17.3, 2.4) and a statistically significant difference in median MPR (P = 0.02). |
| 3 | Ibrahim et al, 2022[11] | Virtual meeting with pharmacist (n = 115, 60.8 (11.5), 45.4%, every 2 weeks within the first 6 months and monthly for the remaining 6 months) | Usual Care (n = 118, 61.0 (12.3), 44.2%) | 3, 6, 9, and 12 months | Mean SBP in the IG decreased from 145.9 mmHg at baseline to 124.5, 123.2, 123.5, and 124.9 mmHg while in the CG decrease from 146.7 mmHg at baseline to 135.9, 133.8, 133.7, and 132.4 mmHg at every 3-month follow-up from 3 to 12 months.<br>Mean DBP in the IG dropped from 84.3 mmHg at baseline to 77.6, 76.2, 76.1, and 77.8 mmHg while the CG decreased from 85.1 mmHg at baseline to 82.3, 81.5, 81.5, and 81.9 mmHg at the same intervals |
| | | | | | Participants in the IG demonstrated significantly enhanced medication adherence and hypertension-related knowledge (4.9 at first measurement to 7.3, 7.9, 7.9, and 7.6 at every 3-month follow-up from 3 to 12 months) |
| | | | | | The incidence and identification of DRPs[h] by pharmacists for each subject in the IG and CG were 2.1% and 1.0% (p = 0.002) and 0.6 compared to 0.3 (p = 0.001) |

(*Continued*)

**Table 2** (Continued).

| No | Author, Publication Year | Intervention (n, Mean Age, % Female, Frequencies) | Control (n, Mean Age, %Female) | Follow-up Period | Main Findings |
|---|---|---|---|---|---|
| 4 | Green et al, 2008[12] | BPM-Web[i] (n = 259, 59.5 (8.3), 45.9%, twice in a week accompanied with measurements)<br>BPM-Web-Pharm[j] (n = 261, 59.3 (8.6), 55.9%, BPM used twice in a week accompanied with measurement. Communication with pharmacists conducted every 2 weeks until BP is controlled followed by a reduced frequency during the maintenance phase | Usual Care (n = 258, 58.6 (8.5), 54.7%) | 12 months | BPM-Web-Pharm achieved significantly better BP control, with 56% of patients achieving controlled BP compared to 31% in UC and 36% in BPM-Web (P < 0.001). It also resulted in greater reductions in SBP (−8.9 mmHg compared to UC, −6.0 mmHg compared to BPM-Web) and DBP (−3.5 mmHg compared to UC), all with P < 0.001. |
| 5 | Asche et al, 2016[13] | Patients used home BP monitors to transmit data and received pharmacist-led management including an initial in-person education session and regular phone consultations (n = 177, 61.8 (11.5), 43.5%, 6 BP measurements weekly and phone consultation every 2 weeks within the first 6 months until BP control was sustained for 6 weeks, then consultation was reduced to monthly) | Usual Care (n = 174, 59.9 (12.3), 44.8%) | 12 months | The IG was significantly more likely to achieve BP control than the UC group, with odds 3.64 times higher. This positive effect was especially strong patients who were younger (p = 0.02), did not have diabetes (p = 0.005), had higher initial DBP (p = 0.02), used salt infrequently in meal preparation (p = 0.007), and those taking fewer (0–2 rather than 3–6) antihypertensive medications at the start of the study (p = 0.02) |
| 6 | Wang et al, 2022[14] | Pharmacist consultations, individualized medication education using varied media, online follow-up via WeChat, and continuous telephone follow-up (n = 40, 42, 42.5%, 2 pharmacist consultations every week; 1 answer daily via WeChat; phone consultations every 2 weeks) | Routine clinical care (n = 40, 43, 40%) | 3 months | BP control rates was higher in the IG than the CG (92.5% vs 62.5%, P < 0.001)<br>Medication adherence was higher in the IG than the CG (90.0% vs 52.5%, P < 0.001) |
| 7 | Bosworth et al, 2018[15] | Phone consultations (n = 215, 60.9 (8.4), 25.3%, monthly) | Primary care and generic printed educational material on CVD[k] and how to reduce CVD risk at baseline and 6 months (n = 213, 61.5 (8.9), 25%) | 6 and 12 months | SBP and DBP decreased at 6 and 12 months, but there was no significant difference compared to the CG |
| 8 | Margolis et al, 2022[16] | Telehealth Care for systematic home-based BP monitoring via phone calls (n = 1423, 62.4 (14.2), 56.6%, once in 2–4 weeks) | Usual Care/Clinic-based Care (n = 814, 58.3 (14.2), 50.6%) | 12 months | Both Telehealth and Clinic-Based Care were effective in lowering BP by 18–19/10 mmHg with no statistically significant BP difference between groups. |
| 9 | Gupta et al, 2023[17] | Mobile-based Intervention (vCCC[l]) for monitoring and counseling (n = 17, 71.5 ± 4.3, 64.7%, at least once in a month) | Usual Care (n = 14, 70.1 ± 3.8, 64.3%) | 3 months | Patients in the vCCC arm demonstrated a reduction in mean BP between baseline and 12-week follow-up (P = 0.01), but patients in UC arm did not (P = 0.45) |
| 10 | Magid et al, 2013[18] | Web-based Intervention (Heart360 Web Site) for monitoring and counseling (n = 175, 60 (11.3), 38.3%, BP measurement 3 times a week) | Usual Care (n = 173, 59.1 (10.9), 41%) | 6 months | A greater percentage of patients in the HBPM[m] group reached target BP levels (54.1%) compared to the UC group (35.4%; P<0.001) |

(*Continued*)

**Table 2** (Continued).

| No | Author, Publication Year | Intervention (n, Mean Age, % Female, Frequencies) | Control (n, Mean Age, %Female) | Follow-up Period | Main Findings |
|---|---|---|---|---|---|
| 11 | Margolis et al, 2013[19] | Telemonitoring through a web-enabled oscillometric BP monitor connected to a secure website via modem (n = 228, 61.1 (12), 45.2%, BP measurement 6 times a week and one phone every 2 weeks) | Usual Care (n = 222, 60.2 (12.2), 44.1%) | 6 months | The proportions of patients with controlled BP at all visits were 50.9% (95% CI, 36.9%–64.8%) in Telemonitoring Intervention and 21.3% (95% CI, 14.4%–30.4%) in UC (P=0.002). |
| 12 | Beran et al, 2018[20] | Telemonitoring through a web-enabled oscillometric BP monitor connected to a secure website via modem (n = 228, 61.1 (12), 45.2%, BP measurement 6 times a week and one phone call every 2–4 weeks) | Usual Care (n = 222, 60.2 (12.2), 44.1%) | 12 months | The intervention resulted in improved BP control compared with UC at both 6 (72% vs 45%, P < 0.001) and 12 months (71% vs 53%, P =0.005) |
| 13 | Choudhry et al, 2018[21] | Telephone consultation (n = 2038, 60.4 (11.7), 45.3%, 3 or more calls with frequency not mentioned) | Usual Care (n = 2040, 59.2 (11.5), 45%) | 12 months | Medication adherence of the hypertension disease subgroups was higher in the IG than the UC group (42.7% vs 35.9%) |
| 14 | Mehos et al, 2000[22] | Telephone consultation with homebased BP monitoring (n = 18, 60.0 ± 14.8, 77.8%, once a month) | Usual Care (n = 18, 57.6 ± 13.5, 61.1%) | 6 months | Mean absolute reductions in SBP and DBP were significantly reduced from baseline in IG (17.0 and 10.5 mmHg, both p<0.0001) while participants in CG showed less reductions (7.0 and 3.8 mmHg, p=0.12 and p=0.09) |

**Notes**: [a]SBP, Systolic Blood Pressure; [b]DBP, Diastolic Blood Pressure; [c]IG, Intervention Group; [d]UC, Usual Care; [e]MPR, Medication Possession Ratio; [f]CG, Control Group; [g]CI, Confidence Interval; [h]DRPs, Drug-related Problems; [i]BPM-Web, Home blood pressure monitoring and secure patient website training; [j]BPM-Web-Pharm, BPM-Web and pharmacist care management via web communication; [k]CVD, Cardiovascular Disease; [l]vCCC, Virtual Collaborative Care Clinic; [m]HBPM, Home Blood Pressure Monitoring.

### Mobile-Based Intervention

We found three studies that used mobile-based interventions in which all of them are combined with telephone-based method.[11,14,17] The interventions were not done purely with one mobile application. Communication with the patients were mostly done with phone calls, while data collection such as the BP readings, demographic information, medical history, antihypertensive medications, and laboratory values are obtained through mobile application and/or electronic health record (HER). All of the studies showed that mobile-based interventions led to the greater decrease of BP compared to the CG. Two of the studies also showed that not only medication adherence, but also the knowledge of the patients were significantly improved.[11,14]

### Risk of Bias

Cochrane RoB tool was used to ensure the validity or quality of the included RCT and cluster-RCT studies. Among five RCTs, two studies[9,10] showed a low overall risk of bias, while one study[14] exhibited some concerns, and two studies[17,22] demonstrated high overall risk of bias. Three biases comprised bias arising from the randomization process (D1), bias due to deviations from intended intervention (D2), and bias due to missing outcome data (D3) occurred the most, observed in 60% of RCTs. Bias due to measurement of the outcome (D4) was low in all RCTs. From nine cluster-RCTs, seven studies[11–13,15,18,20,21] exhibited low overall risk of bias, while two[16,19] posed some concerns. All bias generally demonstrated low risk of bias, with bias arising from the randomization process (D1) as observed in 22,22% of the cluster-RCTs. Further details on bias assessment are available in Tables 3 and 4.

## Discussion

To our knowledge, this is the first systematic review examining the impact of pharmacist-led DHI on treatment outcomes in hypertensive patients. Overall, the findings are predominantly positive. Eight DHI studies (57.14%) reported both SBP

**Table 3** Risk of Bias Assessment of RCT Studies

| Study | Judgement | | | | | |
|---|---|---|---|---|---|---|
| | D1[a] | D2[b] | D3[c] | D4[d] | D5[e] | Overall |
| Mozu et al, 2023[9] | Low | Low | Low | Low | Low | Low |
| Hedegaard et al, 2015[10] | Low | Low | Low | Low | Low | Low |
| Wang et al, 2022[14] | Some concern | Low | Low | Low | Low | Some concern |
| Gupta et al, 2023[17] | High | Some concern | Some concern | Low | Some concern | High |
| Mehos et al, 2000[22] | Some concern | Some concern | Some concern | Low | Low | High |

**Notes**: [a]D1, Bias arising from the randomization process; [b]D2, Bias due to deviations from intended intervention; [c]D3, Bias due to missing outcome data; [d]D4, Bias due to measurement of the outcome; [e]D5, Bias in selection of the reported results.

**Table 4** Risk of Bias Assessment of Cluster-RCT Studies

| Study | Judgement | | | | | | |
|---|---|---|---|---|---|---|---|
| | D1[a] | D1b[b] | D2[c] | D3[d] | D4[e] | D5[f] | Overall |
| Ibrahim et al, 2022[11] | Low | Low | Low | Low | Low | Low | Low |
| Green et al, 2008[12] | Low | Low | Low | Low | Low | Low | Low |
| Asche et al, 2016[13] | Low | Low | Low | Low | Low | Low | Low |
| Bosworth et al, 2018[15] | Low | Low | Low | Low | Low | Low | Low |
| Margolis et al, 2022[16] | Some concerns | Low | Low | Low | Low | Low | Some concerns |
| Magid et al, 2013[18] | Low | Low | Low | Low | Low | Low | Low |
| Margolis et al, 2013[19] | Some concerns | Low | Low | Low | Low | Low | Some concerns |
| Beran et al, 2018[20] | Low | Low | Low | Low | Low | Low | Low |
| Choudhry et al, 2018[21] | Low | Low | Low | Low | Low | Low | Low |

**Notes**: [a]D1, Bias arising from the randomization process; [b]D1b, Bias arising from the timing of identification and recruitment of participants; [c]D2, Bias due to deviations from intended intervention; [d]D3, Bias due to missing outcome data; [e]D4, Bias due to measurement of the outcome; [f]D5, Bias in selection of the reported results.

and DBP were reduced significantly over conventional therapy.[9,11,12,17–20,22] One study (7.14%) found a significant improvement only in DBP, with no meaningful change in SBP.[10] One study (7.14%) showed the methods can effectively lower BP, but results of IG and CG did not differ substantially.[15] One study (7.14%) also finds that odds ratio (OR) of BP control in IG is 3.64 times higher than in CG.[13] All of the studies that assessing medication adherence (n = 5, 35.71%) showed an increase in the IG compared to CG.[9,11,14,21] One study (7.14%) showed enhanced DRP identification by pharmacists in the IG, eg, unnecessary drug therapy, drug–drug interaction, and ADR than in CG.[11]

Telephone-based intervention that is used in six out of fourteen studies (35.71%) were shown to be the most common method. This is consistent with previous systematic reviews evaluating pharmacist-led digital health interventions for patients with diabetes, which found that telephone intervention methods were more frequently utilized compared to web- and mobile-based interventions.[23] Despite being the most commonly used, telephone-based interventions are highly flexible and can be effectively combined with other approaches, such as web- and mobile-based platforms. This combination provides a more flexible and thorough approach, adapting to the most compatible approach for the patients.

For instance, telephone-based interventions provide direct human interaction, which can enhance patient engagement and trust, while web and mobile platforms offer convenience and real-time monitoring capabilities.[24]

While most of the studies with telephone-based interventions (n = 4, 66.7%) showed notable reductions in SBP and DBP, one of them showed no significant decrease in SBP, with only DBP showing improvement. A potential explanation for this discrepancy is that unlike other studies, this particular study included patients who had already achieved their target BP levels.[8] This limited the potential for further improvement, as there was a smaller margin for change.[23] One study also reported a decrease in BP but no significant difference compared to CG. This could be attributed to the reduced intervention frequency, as delays in replacing and training clinical pharmacy specialists led to fewer patient encounters. Moreover, many participants had well-controlled risk factors at baseline, which may have minimized the intervention's measurable impact similar to the previous study.[13]

Compared to the telephone-based intervention method, both web-based and mobile-based interventions are more effective, as all studies using these methods successfully achieved the BP goal or maintained controlled BP. Although not as straightforward as telephone-based monitoring, these methods have been proven effective, provided that patients receive initial training on using the website and/or mobile application and are willing to engage with the pharmacist. A few of the studies also elaborated that through websites and mobile applications, pharmacists can conveniently provide patients with more personalized medication adjustments and/or frequent reminders.[11,17] Thus, the patient's clinical outcomes can be significantly improved without the need for frequent visits to clinics or hospitals. Meanwhile, pharmacists have a greater opportunity to identify DRPs for each patient.[11]

After a year of intervention, the results of IG and CG's mean SBP did not differ substantially in one of the studies. While this suggests a higher control difficulty for SBP compared to DBP, it may also be influenced by the frequency of virtual meeting between the pharmacists and the patient. The virtual meeting's frequency decreased from once every two weeks in the first six months to once a month for the remaining six months, which might affect patients' medication adherence. This issue can be solved by maintaining a consistent follow-up schedule and/or tailoring treatment plans to specifically address SBP control.[11]

A study by Wang et al reported an interesting finding, where medication adherence in the IG reached 90% after three months.[14] In comparison, another study conducted over six months achieved a slightly higher adherence rate of 96.5%, indicating that the three-month adherence rate was already quite high.[25] However, a different study reported a significantly lower adherence rate of 42.7% after twelve months of intervention.[26] The total sample sizes for these studies were 80, 116, and 4,078 participants, respectively. These findings suggest that shorter intervention periods may lead to high adherence rates initially, but maintaining adherence over longer durations, especially in larger populations, presents a greater challenge. Such results highlight the essential role of intervention design that not only can achieve high initial adherence but also sustain it over time, particularly in a real-world, large-scale settings. This is crucial as low adherence to hypertension treatment raises the potential of damaged organs and adverse cardiac issues.[27]

The results of this study underscore the potential of pharmacists' involvement in DHI exclusively to hypertensive patients. While our findings indicate that most pharmacist-led DHI benefit patients, other studies have also explored the outcomes of these methods in populations with different diseases. Goldfien et al revealed that of patients with gout of IG attained a higher percentage compared to CG in reaching target serum uric acid (sUA) level ≤6.0 mg/dL (35% vs 13%, $p = 0.03$).[28] However, Adams et al demonstrated that tobacco cessation attempts of IG and the CG did not differ substantially.[29] Eldeib et al also found that medication adherence of IG and the CG for all cycles of metastatic colorectal treatment are not notably distinct.[30] There are several factors that contributed to the lack of contrast between the IG and CG's results, including the brief duration of the counseling session that led to patients' lack of motivation in adhering to the designed therapy and the standard care's quality for the CG. When the standard care is considered good enough for the patients, it would be difficult for the IG to demonstrate greater results.[29,30] Compared to a review by Christy et al which focuses on the diabetes mellitus (DM) disease, our review has several differences. Most of the digital health intervention methods from both studies are the same, but one additional intervention method, text-message reminder, is not found in our study. The follow-up periods from the review by Christy et al are larger in variety, from 2 to 24 months, while ours are from 3 to 12 months. Apart from the hypertension and DM-specific clinical outcomes, patient's knowledge is addressed only in our study. Additionally, the pharmacist-led DHI for hypertension has shown greater results compared to DM's because most of the included studies indicated positive results. Meanwhile, only around half of the studies from Christy et al indicated positive results.[23]

While the included studies primarily focused on conventional DHI, recent advances in digital health technologies present exciting opportunities to complement existing pharmacist-led interventions. Emerging innovations like artificial intelligence (AI)-driven tools and wearable devices may further enhance hypertension care. For instance, AI-powered chatbots for medication reminders and machine learning algorithms to analyze blood pressure trends could help personalize care while reducing pharmacist workload.[31] These tools can optimize resource allocation by automating routine monitoring tasks and identifying patients who require more intensive support. Moreover, the interactive nature of AI-powered platforms may help increase patient engagement and encourage sustained adherence to therapy. Likewise, wearable technologies capable of real-time BP monitoring may support more timely and proactive interventions. Although these tools were not featured in the studies included in this review, they represent promising directions for future research and integration into pharmacist-led care models.[32,33]

In addition to technological advancements, the global applicability of pharmacist-led DHI could be strengthened by expanding research beyond high-income countries. Most of the included studies (10 out of 14) were conducted in the United States, reflecting insights from well-resourced healthcare systems. Future investigations in low- and middle-income countries (LMICs) could explore how pharmacist-led DHI perform in different healthcare environments, particularly those with varying levels of digital infrastructure, literacy, and access. Adapting interventions with offline-capable platforms or incorporating community health workers could enhance feasibility and effectiveness in these settings.[34,35] Such efforts would broaden the evidence base and support the global scalability of pharmacist-led DHI for hypertension management.

This study showcases its strengths through the use of comprehensive keywords and a thorough analysis of pharmacist-led DHI for hypertension. Our review highlights the potential benefits of these interventions, including improved BP control and reduction, as well as enhanced medication adherence. Additionally, Cochrane RoB tool was used to evaluate the potential of bias. While the primary focus is on pharmacist-led DHI, the study also considers various clinical outcomes, such as BP levels, medication adherence, and the identification of DRPs. There are several limitations to this study. First, the heterogeneity of the included studies, including variations in DHI and follow-up durations, prevented direct comparisons through meta-analysis. Secondly, the inclusion of only English-language articles may introduce selection bias. Lastly, most of the studies are conducted in United States of America, which is a developed country, thus further studies in developing countries are surely encouraged to improve generalizability.

## Conclusion

This review of 14 RCTs found that pharmacist-led DHI for patients with hypertension, utilizing telephone, web, and mobile-based interventions, yielded predominantly positive outcomes. Most of these studies (57.1%) demonstrated improvements in BP control, while 35.7% showed enhanced medication adherence, and one study highlighted better identification of DRPs. Web and mobile-based interventions are recommended to be implemented in future enhanced service that is led by pharmacist, as all studies using these methods achieved the BP goal or maintained controlled BP. Interventions' effectiveness is influenced by several factors, including intervention frequency, patient engagement, and personalized communication. However, generalizability may be limited, as majority of the studies (n = 10) were conducted in developed countries. Further research is needed to refine these approaches, ensuring their scalability and sustainability in diverse, real-world settings to enhance patient's state of health.

## Abbreviations

ACEi, Angiotensin-Converting Enzyme inhibitors; ADR, Adverse Drug Reaction; AI, Artificial Intelligence; ARB, Angiotensin Receptor Blockers; BP, Blood Pressure; CCB, Calcium Channel Blockers; CG, Control Group; CI, Confidence Interval; CKD, Chronic Kidney Disease; CVD, Cardiovascular Disease; DBP, Diastolic Blood Pressure; DHI, Digital Health Interventions; DM, Diabetes Mellitus; DRPs, Drug-related Problems; HBPM, Home Blood Pressure Monitoring; IG, Intervention Group; KCPO, Kaiser Permanente Colorado; LDL, Low-density Lipoprotein; LMICs, Low- and Middle-Income Countries; mmHg, Millimeters of Mercury; MPR, Medication Possession Ratio; OR, Odds Ratio;

PCP, Primary Care Professional; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT, Randomized Controlled Trial; RoB, Risk of Bias; SBP, Systolic Blood Pressure; sUA, Serum Uric Acid; UC, Usual Care; vCCC, Virtual Collaborative Care Clinic.

## Disclosure

The authors report no conflicts of interest in this work.

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