REVIEW ARTICLE



Physician-pharmacist collaborative practice and telehealth may transform hypertension management

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Abstract

Community pharmacists play a crucial role in hypertension management and their intervention, mainly including education, medication monitoring, and reviewing, blood pressure (BP) measurement and cardiovascular risk factors tracking, have proved to enhance BP control and adherence to antihypertensive treatment. A multidisciplinary collaborative approach with the referring physician and a patient-centered model of care have been proved to be particularly effective for improving control of hypertension and promoting patients' health. The inclusion of telehealth in such model (the so-called telepharmacy) may expand the reach of the pharmacist's intervention and provide pharmacy operations and patient care at a distance with further benefits for hypertensive patients and their managing physicians. Very few randomized controlled studies have evaluated the clinical efficacy of the implementation of telepharmacy services in the management of hypertension, with the strongest evidence limited to physician–pharmacist collaborative interventions based on home BP telemonitoring plus patient education on lifestyle, drug therapy, and cardiovascular risk factors control. The results of these trials documented a benefit of telehealth mainly in terms of improvement of BP control consequent to antihypertensive medication intensification and optimization. Although promising, these results need to be corroborated through larger, prospective, and long-term studies, which should also evaluate additional long-term benefits of telepharmacy services in hypertension management.

Introduction

Community pharmacists are integral members of the hypertension team management and may support the patient's referring physician in the effort of improving blood pressure (BP) control and adherence to antihypertensive drug treatment [1]. Team-based care practices including a pharmacist may help expand patient access to screening of hypertension, improve efficiency of hypertension management, and assure quality of care [2, 3]. Telehealth may help make this collaboration working particularly effective and implement an efficient

physician-pharmacist collaborative practice for hypertension management [4].

In the present review, we will discuss the current evidence of effectiveness of hypertension management in community pharmacies, focusing on the benefit, which can be achieved when a team-based healthcare model relying on telehealth is applied.

Current model of a community pharmacy-based hypertension management

The current model of a community pharmacy-based hypertension management includes three levels of intervention [5]. These levels consist in (i) the promotion of a healthy lifestyle in the population for cardiovascular prevention through health education; (ii) the contribution to early detection of hypertension by measuring BP and referring possible hypertensive patients to the primary care doctor, and (iii) the management of treated hypertensive individuals with regular BP measurement in the pharmacy, the counseling and provision of information on drug

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Table 1 Goals to be achieved by the community pharmacist at the three different levels of intervention for hypertension management

Level of the intervention	Main goal	Operational goal
1	Primary prevention of hypertension	Verbal advice and/or educational material (leaflets, flyers, posters, videos, websites) with information on the following modifiable risk factors for hypertension: • Excessive intake of calories • High intake of salt • Excessive intake of alcohol • Inadequate physical activity • Smoking • High intake of saturated fatty acids • Regular use of contraceptives • Psychosocial stress
2	Early detection of hypertension	Development of referral protocols between the pharmacists and the general practitioners BP measurement and assessment Possible screening for other risk factors Implementation of educational programs about BP measurement including home self-measurement
3	Management of hypertensive patients on treatment	 To monitor BP and other relevant health parameters in treated hypertensive patients and to refer the general practitioner those who do not achieve an adequate BP control To identify possible drug-related problems To obtain and reinforce therapeutic compliance To provide health education to patients with hypertension about necessary lifestyle modifications and cardiovascular risk factors control To advise on treatment regimen to hypertensive patients To teach about self-measurement of BP

BP blood pressure (adapted from ref. 5)

treatment and drug safety, the reporting of possible drugrelated problems to the general practitioner (Table 1).

The services that can be offered to potential or established hypertensive patients consists in educational activities directed at patients, those directed at healthcare professionals and services provided within the frame of a multidisciplinary teamwork. A summary of such services is presented in Table 2.

There are several benefits when a pharmacy service is included in the hypertension management model. The pharmacy is usually at a walking distance from home or workplace, is open 6-7 days a week, no appointment is generally required to be seen for a BP measurement, and basic services are usually delivered at lower costs compared with other primary care settings such as general practitioner clinics. Proper pharmacist's training ensures that BP measurement, a pivotal procedure for screening and detection of uncontrolled hypertension, is carried out according to current guidelines. For all these reasons, pharmacies may help to expand patient access to screening of hypertension, improve efficiency of hypertension management and assure continuity of care in the community, in collaboration with the general practitioner, hypertension specialist, and other healthcare professionals.

Table 2 Pharmacy services for hypertension management

Pharmacist-led interventions directed at patients

- Education on hypertension and healthy lifestyle
- · Counseling on medication and therapeutic regimens

Pharmacist-led interventions directed at healthcare professionals

- Drug safety management and documentation of adverse drug reactions occurring to the patients
- · Monitoring patient's adherence to physician's prescription

Pharmacist's interventions directed at patients and healthcare professionals in a multidisciplinary collaborative practice:

- Medication management (including medication administration, review, dose adjustment or titration, monitoring, and reconciliation)
- Definition and application of disease management pathways and protocols
- Office BP measurement (based on validated and calibrated devices)
- Out-of-office BP measurements (home and ambulatory BP monitoring, also with telemonitoring)
- Monitoring of cardiovascular risk factors (e.g. lipid, blood glucose, etc.)
- · Monitoring of patients' outcomes
- Post-hospital discharge follow-up and home visits (in case of critical patients)

Implementation of such services would not increase medical workload appreciably, a major concern of general practitioners when evaluating pharmacy services. In a large cohort of 131,419 patients presenting to a community

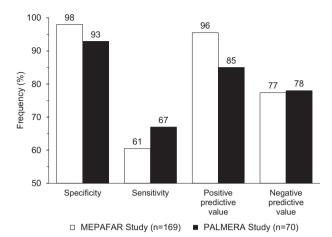


Fig. 1 Agreement between community pharmacy and home blood pressure measurements in the MEPAFAR (MEdida de la Presion Arterial en FARmacia) and PALMERA Study in 239 treated hypertensive patients (redrawn from 13 to 15 by permission)

pharmacy in England with a newly prescribed antihypertensive medication, only 4.5% were referred back by a pharmacist to a general practitioner within the first 2 weeks of starting a new antihypertensive medication [6]. The most common patient-reported factors associated with referral were the occurrence of a side effect, uncertainty regarding the efficacy of the medication, and negative feelings toward the newly prescribed antihypertensive drugs.

BP measurement in the pharmacy: is it accurate, reliable and useful?

BP measurement is the most popular procedure and direct intervention carried out in the pharmacy for the evaluation of suspected or established hypertension. However, obtaining an accurate BP measurement in a sometimes not cosy and often uncomfortable environment like the community pharmacy is not always an easy task. To guarantee accurate BP measurements, the pharmacists must be trained to monitor BP properly and to regularly check the accuracy of the sphygmomanometers in use in their facilities. Only devices validated according to the current validation protocols must be used [7, 8]. The issue of validated devices is not a minor one, because evidence is provided by a number of studies that when BP measuring devices used in the pharmacy are compared with reference validated devices, they often generate inaccurate BP values; up to 30% of devices fail to provide reliable values, either because they are not clinically validated or because the required annual calibration of the device is disregarded [9–12].

Notwithstanding such disappointing premises, some studies proved that BP measured in community pharmacies may have some clinical value, provided that (i) calibrated and validated devices are used, (ii) BP control is estimated with several readings collected on different occasions, and (iii) the pharmacist is trained to proper BP measurement. In two of these studies, the MEPAFAR (MEdida de la Presion Arterial en FARmacia) and PAL-MERA Study, including in total 239 treated hypertensive patients, the BP measurement in the pharmacy showed high specificity and positive predictive value using home BP monitoring as the reference, and thus it may be considered accurate to confirm the occurrence of a lack of BP control (Fig. 1) [13–15]. This means that treated hypertensive patients with elevated BP measured in the pharmacy on repeated occasions should be reasonably referred to a physician because they may require adjustments in the medication regimen. Conversely, BP measured in a pharmacy setting showed low sensitivity and negative predictive value, indicating that this approach could have limitations in patients with adequate BP control. Namely, they might require treatment intensification despite normal BP in the pharmacy.

An open-question regarding BP measured in the pharmacy is whether in this setting the same hypertension threshold (<140/90 mmHg) recommended for BP measured in the doctor's office applies. In fact, a recent metaanalysis of eight studies including 4157 individuals showed that BP measured in a pharmacy setting is similar to daytime average BP (+1.55 mmHg for systolic BP, SBP, and + 2.96 mmHg for diastolic BP, DBP), but higher than 24hour average BP (+7.75 mmHg SBP and + 6.52 mmHgDBP). The comparison between BP measured in the pharmacy and that measured in the doctor's office was inconclusive, with no evidence of a difference between the two modalities (-0.89 mmHg for SBP and -0.24 mmHg for DBP), but high heterogeneity. This study suggests that BP measured in the pharmacy should be best interpreted using the 135/85 mmHg threshold for day-time BP rather than that for office BP (140/90 mmHg). Although further studies are needed to confirm these cutoff values, an approach based on lower thresholds may have the effect of increasing the sensitivity for detecting hypertension when referring patients to their general practitioner with borderline elevated BP, albeit at the expense of specificity [16]. Realistically, these studies tell the story that integrating BP measurement in the pharmacy with out-of-office BP measurement could be the best solution to identify true hypertensive referred to community pharmacies.

Evidence of effectiveness of pharmacist's intervention in hypertension management

In randomized controlled studies clinical pharmacy services offered to hypertensive patients have been found to enhance



Table 3 Design and outcomes of main systematic reviews assessing the effectiveness of the pharmacist's intervention on BP control and secondary outcomes in hypertensive patients

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Author year [ref.]	Author No. of studies year [ref.] and subjects included	Type of pharmacist's intervention	Length of follow-up (months)	Effect of the intervention
Machado [17]	Machado 13 (2246) [17]	Medication management and education about high BP	7.6	• Larger SBP reduction with the intervention $(-6.9 \pm 12.0 \text{ mmHg vs.}]$ control; $p = 0.047$) • No effect on DBP (intervention vs. control $-3.6 \pm 3.8 \text{ mmHg; } p = 0.06$) • Eight out of 13 studies assessing adherence to antihypertensive treatment reported sensitive outcomes following pharmacist's management • Only one out of eight studies categorized as sensitive the pharmacist's intervention on quality of life
Morgado [18]	8 (2619)	Medication management, educational interventions, BP measurement, medication reminders, improved administration systems, personal contacts	6.7	• Larger SBP and DBP reductions with the intervention than with the control $(-4.9\pm0.9 \text{ and } -2.6\pm0.9 \text{ mmHg; } p < 0.001 \text{ for both})$ • Improved BP control with the intervention $(62.8\% \text{ vs. } 32.6\% \text{ control, } p < 0.001)$ • Medication adherence was increased only in patients with a significant BP reduction
Santschi [19]	39 (14,224)	Patient education and counseling about lifestyle, medication and medication adherence, BP measurement, medication management, reminder system, and healthcare professional training	v	• Larger BP reductions were observed following pharmacist's intervention vs. control (-7.6 (-9.0 , -6.3) mmHg for SBP and -3.9 (-5.1 , -2.8) mmHg for DBP; $p < 0.001$ for both) • The SBP reduction was particularly effective if the intervention was led directly by the pharmacist, without co-management (-8.5 (-10.0 , -7.0 mmHg vs. -6.3 (-8.0 , -4.5) under collaborative care, $p = 0.046$) • The efficacy tended to be larger if the intervention was administered at least monthly compared with less frequently than once a month both for SBP (-9.1 (-11.4 , -6.7) vs. -6.7 (-9.1 , -4.4) mmHg, $p = 0.140$) and DBP reduction (-4.5 (-6.1 , -2.9) vs. -1.9 (-3.5 , -0.3) mmHg, $p = 0.08$)
Cheema [20]	16 (3034)	Patient education on hypertension, management of prescribing and safety 6.5 problems associated with medication, and advice on lifestyle	6.5	• Pharmacist-led intervention was associated with a significantly ($p < 0.00001$) larger reduction in SBP (6.1 (3.8, 9.8) mmHg) and DBP (2.5 (1.5, 3.4) mmHg) than standard care • The BP reduction observed with the intervention vs. usual care was smaller in hypertensive patients with comorbidities (1.9 (3.1, 6.9) mmHg for SBP and 1.5 (0.4, 3.4) mmHg for DBP; $p = 0.460$ and 0.127, respectively) • The pharmacist's intervention improved medication adherence (odds ratio 12.1 (4.2, 34.6), $p < 0.001$)
BP blood	pressure, SBP s	BP blood pressure, SBP systolic blood pressure, DBP diastolic blood pressure		



Fig. 2 Factors influencing sustainability of pharmacist-led interventions in primary-care settings (redrawn from 22 by permission)

BP control and improve adherence to antihypertensive therapy as compared with usual care (Table 3).

Machado and co-workers [17] put together 13 studies carried out in mixed pharmacy settings (hospital, outpatient clinic, or community) with an overall sample size of 2246 patients. After a follow-up of almost 8 months the pharmacist's intervention, based on medication management (82% of cases) and hypertension education (68%), was associated with a larger SBP reduction than the standard care group, but not with an improved DBP control, adherence to the therapy, and quality of life. Morgado and coworkers [18] published a systematic review including 2619 patients recruited in eight studies (hospital, outpatient clinic, or community pharmacy setting). The pharmacist's intervention significantly reduced BP and improved the rate of BP control more than usual care. A positive effect on medication adherence was observed, but only when the intervention significantly reduced BP. A larger and more recent meta-analysis of 39 randomized controlled trials performed in outpatient clinic or community pharmacies and including 14,224 patients, showed that not only the pharmacist's intervention was associated with larger BP reductions compared with standard care, but also that the effect tended to be larger if the intervention was led by the pharmacist and was done at least monthly [19].

Cheema and co-workers [20] examined 16 randomized controlled trials encompassing 3032 hypertensive patients with or without cardiovascular comorbidities followed-up in community pharmacies. The authors observed that community pharmacist-led interventions were associated with significant reductions in BP and increased adherence to

treatment compared with usual care, thus contributing to improve clinical management of hypertension. A trend was observed for a smaller BP reduction from community pharmacist's interventions in patients with cardiovascular comorbidities in comparison with those without comorbidities (SBP mean difference and 95% confidence interval: 1.9 (-3.1, -6.9) mmHg and DBP difference: 1.5 (-0.4, -3.4) mmHg; p = 0.460 and 0.127, respectively).

Collaborative practice for an efficient management of hypertensive patients in the pharmacy

In the studies presented above the interventions were provided by the pharmacist independently of other healthcare professionals' supervision. However, the multidisciplinary approach is currently regarded as ideal in order to improve patients' outcomes rather than unilateral interventions. In recent years, specific researches and models of care have been oriented toward the primary care setting and home care, with a progressive involvement of community rather than hospital pharmacies [21]. This research highlighted that the multidisciplinary approach based on a collaborative and patient-centered model of care may be beneficial for improving control of chronic diseases, and in particular hypertension, and for appropriateness of medications use or for promotion of health and wellness.

Team-based care interventions involving pharmacists were associated with improved BP control compared with usual care in a meta-analysis of 37 studies [3]. The effectiveness of the BP control was larger for studies involving community pharmacies (odds ratio and 95% confidence interval: 2.89 (1.83, 4.55)) than for those involving pharmacists within primary care clinics (2.17 (1.75, 2.68)). The inclusion of a nurse rather than a pharmacist in the team did not change the effect of the intervention. In another review of 52 studies [2], a team-based care approach predominantly including pharmacists, nurses or both, collaborating with hypertensive patients and primary care providers was effective in improving BP outcomes during a median follow-up of 12 months. Patients receiving team-based care were more likely to have BP at target compared with usual care (+12%) and displayed larger SBP and DBP reductions during follow-up (5.4 and 1.8 mmHg, respectively). In this meta-analysis, the extent of the improvement in BP control was larger when pharmacists rather than nurses were added to the team. No difference in the effect was observed between interventions provided in the healthcare or in the community settings. More recently, the same research groups updated the review of the literature with studies published since 2014 [22], confirming that team-based care strategies involving a pharmacist improve BP management.



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Guideline	Type of document	Year of issue	Specific for the pharmacy	Main recommendations
American College of Cardiology (ACC) [25]	Health policy statement	2015	Yes	• The document describes the characteristics of the cardiovascular team-based care and provides background information on the clinical pharmacist's role, training, certification, and potential utilization in a variety of practice models • Examples of effective cardiovascular team-based care are provided, including hypertension clinics with the advantage of improved BP control, better use of evidence-based therapies and reliable documentation of lifestyle education
Canadian Hypertension Education Program (CHEP) [26]	Guideline	2016	Yes	 Automatic office BP measurements obtained in a pharmacy and physician's office are likewise comparable and are the preferred method for measuring BP in an office setting The main laboratory tests for the investigation of patients with hypertension, which may be carried out in the pharmacy are indicated: the lipid panel is a recommended laboratory testing Health behavior management is recommended, with emphasis on the recommendation to increase dietary potassium in patients who are not at risk of hyperkalaemia Indication on the new BP targets and thresholds for high-risk patients is provided Update of antihypertensive treatment approach is discussed
American Association of Colleges of Pharmacy (AACP) [27]	Health policy statement	2010	Yes	• AACP should collaborate with health professionals associations and other key stakeholders to facilitate and influence the expansion of pharmacists' contributions in primary care service delivery • AACP should partner to facilitate or support the development and maintenance of a registry that documents the clinical, humanistic, and economic outcomes of pharmacists practicing in primary care • Colleges and schools should design or expand experiential education in such a way as to permit students to train in practice environments with a future model of interprofessional, interdisciplinary, patient-centered care
Spanish Society of Hypertension (SHE) and Spanish Guideline Society of Community Pharmacy (SEFAC) [28]	Guideline	2011	Yes	• The document is particularly addressed to the community pharmacist and is intended to provide current knowledge on hypertension with the aim of a better shared management of patients with hypertension and cardiovascular risk • Specific information on methodology of BP measurement and classification is provided • The document serves as a tool for developing programs, supporting the involvement of the community pharmacy in the care of patients with hypertension and cardiovascular risk
American College of Cardiology (ACC) and American Heart Association (AHA) [29]	Guideline	2017	°	• A team-based care approach is recommended for adults with hypertension • Follow-up and monitoring after initiation of drug therapy for hypertension control should include systematic strategies to help improve BP, including use of home BP monitoring, team-based care (including a pharmacist), and telehealth strategies • The clinical pharmacist is an individual hypertension team member in charge of comprehensive medication management, involving identification and documentation of medication-related problems, initiating, modifying, and discontinuing medication to address identified problems, and educating patients on their medication regimen
European Society of Cardiology (ESC) and European Guideline Society Hypertension (ESH) [30]	Guideline	2018	No	• The important role of nurses and pharmacists in the education, support, and follow-up of treated hypertensive patients is emphasized as part of the overall strategy to improve BP control and drug adherence • The Health System should financially support the collaboration between pharmacists and doctors and the development of national databases, including prescription data, available for physician and pharmacists, in order to improve drug adherence

Thus, there is growing evidence that multidisciplinary approaches, and particularly those including a community pharmacist, may improve high BP detection, enhance BP control, increase adherence to therapy and improve outcomes in hypertensive patients [19, 20]. Team-based care such as a physician–pharmacist collaboration appears also to be a cost-effective strategy for managing hypertension, particularly for high-risk patients [22, 23].

In spite of proof of effectiveness, the implementation and sustainment of a team-based care model in primary care settings remains a substantial challenge. As shown in Fig. 2, a number of factors may be related to a program's ability to sustain its activities and benefits over time. Such factors must be taken into account by public health decision makers when developing and implementing prevention and intervention programs managed by community pharmacists [22, 24].

To allow implementation of the hypertensive management model in the pharmacy and to best integrate pharmacists into specialized care of hypertensive patients, adequate training on guidelines and on practical aspects of disease management must also be guaranteed as well as achievement of adequate expertize verified. Accreditation programs should be established in individual countries, taking into account education, licensing requirements, regulatory issues, scope of practice, and responsibilities [25]. Defining clear tasks and roles pertinent to the respective educational backgrounds and establishing an efficient communication between the various team members may help to improve the quality and effectiveness of care and integration between various healthcare professionals involved in the management of the hypertensive patient.

Pharmacist-based hypertension management: guidelines and policy statements

The growing relevant role played by pharmacists in a patient-centered model of care of hypertension requires pharmacist's ability, time, and willingness to change professional attitude. The pharmacist needs a specific training and certification under the supervision of the physician in order to acquire or update competencies and skills on hypertension management and related comorbidities. Recommendations on the management of the hypertensive patients by pharmacists and specific guidelines on the education and training process that the pharmacist should follow, have been published in recent years by some professional associations (Table 4). The American College of Cardiology has published a guide to a training pathway and certification process that US clinical pharmacists need to follow in order to deliver high-quality patient care within

the context of a cardiology practice [25]. The Canadian Hypertension Education Program has published a set of guidelines on hypertension management, specifically dedicated to the pharmacists [26]. These guidelines highlight in particular the importance of using automated BP measurement as a reference. They also provide a diagnostic algorithm-based on BP measurement in the pharmacy. The American Association of Colleges of Pharmacy has published a document with recommendations on potential delivery care models with integration of pharmacists in primary care practice in the community in the context of partnership with patients and healthcare service providers [27]. The Spanish Hypertension Society has published specific recommendations for community pharmacists in order to properly evaluate BP in hypertensive patients, focusing on the use of calibrated and validated devices, proper methodology and promotion, and supervision of outof-office BP methods [28].

Finally, the European and American hypertension guidelines have recently given emphasis on the multidisciplinary approach to hypertension management, though they did not provide any specific recommendation [29, 30].

Telehealth in hypertension management

The use of health information technologies may help in creating telehealth networks, involving various healthcare professionals and providing "whole person" comprehensive disease management and preventive care, according to the novel concept of patient-centered model. The minimum team should be constituted by a physician, a nurse, and a pharmacist and an electronic communication system that ensures a constant relationship between the healthcare team with provision of specific diagnostic tests and facilitating information exchange. In the context of such model, the pharmacist may share some tasks with the doctor, reducing the general practitioner workload and inappropriate referral of patients to doctors.

Through telehealth technology, pharmacists may expand the reach of their intervention and provide pharmacy operations and patient care at a distance with substantial benefit for hypertensive patients and their managing physicians [31]. Several pharmacy-based telehealth or telepharmacy services are currently available, ranging from phone calls to medication dispensing, educational activities, digital pill counts to track adherence and telemonitoring, the majority of them involving the pharmacist in more professional activities within a multidisciplinary healthcare team [31]. Examples of some of these services are reported in Table 5.

As discussed in the next section the evaluation of the clinical impact of telepharmacy services for the



Table 5 The most common currently available telepharmacy services for hypertension management

- Pharmacist-led telephonic clinics
- · Medication counseling
- Drug review/monitoring (including adverse events and adherence)
- Provision of drug information
- · Remote medication dispensing
- · Medication therapy management
- Patient assessment and counseling (including teleconsultation)
- Virtual management within a multidisciplinary team
- Telemonitoring of BP and lab values (e.g. blood lipids, blood glucose)
- · Automated text message reminders or phone calls
- · Instructional and educational videos
- · Educational websites

BP blood pressure

management of hypertensive patients has been primarily focused on home BP telemonitoring (HBPT) and the intervention of the pharmacist under the supervision of a physician. Few studies reported on the evaluation of telephone interventions for improving adherence and BP control.

In a retrospective study the effect of motivational interviewing conducted by pharmacists in improving adherence to treatment in patients with both diabetes mellitus and hypertension was tested [32]. A total of 186 non-adherent patients were identified: 87 received the intervention, based on a single initial phone call and 5 monthly follow-up calls, and 99 served as controls. Patients completing the initial call and at least two follow-ups were less likely to discontinue (odds ratio and 95% confidence interval: 0.29 (0.15, 0.54), p < 0.001) and more likely to be adherent (odds ratio and 95% confidence interval: 1.53 (1.02, 2.28), p = 0.009). The most commonly identified patient barriers to adherence were forgetfulness (25.3%), issues with their physician (16.8%), and adverse effects (6.9%).

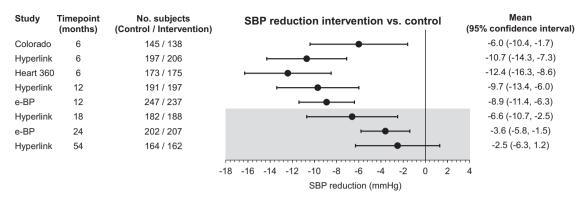
The effect of 3 months of counseling about medication and lifestyle issues by a pharmacist and health coach over the phone was evaluated in 156 patients with uncontrolled hypertension and compared with 400 patients under usual care [33]. Patients in the intervention groups were asked to complete questionnaires online and to submit at least one BP reading per week. After 3 months, 71% of patients allocated to the intervention vs. 31% of controls had achieved target BP values. Patients who were diabetic, depressed, had issues affording medications at baseline and had low health capability were less likely to reach their goal BP with the intervention.

Clinical effectiveness of home BP telemonitoring delivered through the pharmacy

The strongest evidence for effectiveness of telepharmacy for hypertensive patients is restricted to four randomized controlled studies based on HBPT, including 1565 patients, of which 787 randomized to usual care and 778 to a pharmacist's intervention, consisting of HBPT, in-person or remote visits, and education under the physician supervision [34–40]. The primary study endpoints were the office BP reduction and/or the rate of BP control (< 140/90 mmHg or < 130/80 mmHg in case of diabetes or chronic kidney disease) during the trial. Common secondary endpoints included adherence to treatment, changes in the use of antihypertensive medications, and acceptability of the intervention. In three studies (Electronic Communications and Home BP Monitoring or e-BP, Improving BP in Colorado and Hyperlink) the primary endpoints were evaluated also at 6-42 months, following the withdrawal of the intervention. As shown in Figs. 3 and 4 BP reductions and proportions of patients at target following a pharmacist's intervention were significantly larger than those in the usual care group. The only exception was office DBP reduction and BP response in the Improving BP in Colorado study. Interestingly, the benefit of the pharmacist's intervention was markedly reduced or abolished months after its withdrawal, highlighting the importance of the sustainability of the intervention on the long-term (Figs. 3 and 4).

The studies provided additional interesting results. Antihypertensive medication intensification was the main mover to improved BP control in all the four studies. In the economic analyses of three of the four studies, the improved BP control was achieved at a relatively low cost compared with the usual care approach [41–43]. In e-BP study barriers to the implementation into the community practices of the intervention included an unfamiliar pharmacist into the healthcare team, lack of information technology resources, and provider resistance to use a single-management protocol [44]. Facilitators included the intervention's perceived potential to improve quality of care, patients' empowerment and staff time saving. In two studies (Hyperlink and Improving BP in Colorado) evaluating adherence to treatment no difference was found between the two study groups [34, 45]. The satisfaction rate and adherence to HBPT was high (73% in the Hyperlink study and 58% in the Heart 360 Study, respectively), as well as the acceptability (86% of patients in the Improving BP in Colorado). In the Hyperlink Study the effect of the intervention was larger in patients who were younger, did not suffer from diabetes, had high DBP, added salt less than daily in food preparation and took less-antihypertensive medication drugs at entry [46].





Study	Timepoint (months)	No. subjects (Control / Intervention)	DBP reduction intervention vs. control	Mean (95% confidence interval)
Colorado	6	145 / 138	· · · · · ·	-2.3 (-4.9, -0.2)
Hyperlink	6	197 / 206	⊢	-6.0 (-8.6, -3.4)
Heart 360	6	173 / 175		-5.7 (-7.8, -3.6)
Hyperlink	12	191 / 197	⊢	-5.1 (-7.4, -2.8)
e-BP	12	247 / 237		-3.5 (-4.9, -2.1)
Hyperlink	18	182 / 188	· · · · · · · · · · · · · · · · · · ·	-3.0 (-6.3, 0.3)
e-BP	24	202 / 207	-	-1.0 (-1.9, -0.2)
Hyperlink	54	164 / 162		-1.0 (-3.2, 1.2)
				-
		-	18 -16 -14 -12 -10 -8 -6 -4 -2 0 2	4
			DBP reduction (mmHg)	

Fig. 3 Differential change from baseline between the intervention and the usual care group for office systolic blood pressure (SBP) and diastolic blood pressure (DBP) in four different randomized controlled

studies. Differences are shown as mean and 95% confidence interval at different time points. The gray insert in the graph denotes the period of the study following the withdrawal of the intervention [34–37, 39, 40]

Conversely, in the Heart 360 Study the impact of the intervention was larger in the subgroup of patients with diabetes or chronic kidney disease [36].

The consistent evidence provided by these studies suggests that the synergy between HBPT and pharmacist case management of hypertensive patients may improve hypertension screening and control.

Conclusions

According to the current evidence from the scientific literature, a greater involvement of pharmacists in activities directed to hypertensive patients and collaboration with other healthcare professionals, and in particular with the primary care physician, all seem to provide an enhanced effect on various outcomes. Few randomized or observational controlled studies suggest that carefully organized, structured physician-pharmacist collaborative intervention, particularly when based on telehealth, including HBPT plus patient education on lifestyle, drug therapy, and cardiovascular risk factor control, may be effective for improving BP control. Further large and well-conducted studies, addressing additional outcomes

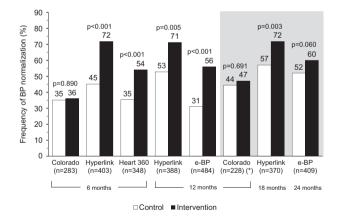


Fig. 4 Proportion of patients with controlled office blood pressure (BP < 140/90 mmHg in all patients except < 130/80 mmHg in case of diabetes or chronic kidney disease) in four different randomized controlled studies in patients randomized to usual care (open bars) and in those randomized to home BP telemonitoring plus pharmacist's care (full bar). Results are shown according to study and time point. The gray insert in the graph denotes the period of the study following the withdrawal of the intervention. P values of the differences between the two study groups are shown on top of the bars. The asterisk indicates that normalization was defined as systolic BP < 140 mmHg in all patients except < 130 mmHg in case of diabetes or chronic kidney disease [34-40]

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beyond BP control, including cost-effectiveness of the intervention, are needed in order to fully demonstrate the long-term benefits of pharmacy services in hypertension management.

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Author contributions SO devised the original idea of the work, made the search of the literature, and wrote the manuscript. MT and CC critically revised the manuscript. All authors met the ICMJE criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval to the version to be published.

Compliance with ethical standards

Conflict of interest SO is scientific consultant of Biotechmed Ltd, provider of telemedicine services. The remaining authors declare no conflicts of interest regarding the publication of this paper.

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