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RESISTANT HYPERTENSION (L DRAGER, SECTION EDITOR)

The Potential of mHealth Applications in Improving Resistant Hypertension Self-Assessment, Treatment and Control

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Abstract

Purpose of Review To review the evidence supporting the use of mobile health (mHealth) apps to improve resistant hypertension self-assessment, treatment and control.

Recent Findings mHealth apps have been used to directly measure blood pressure (BP) levels, either using the oscillometric method with automated inflatable cuffs or using pulse wave signals detected by smartphone technology without the need for cuffs. These app-based BP monitors tend to over or underestimate BP levels when compared to a gold standard aneroid sphygmomanometer. However, the differences in BP measurements are within the acceptable range of 5 mmHg pre-defined by the European Society of Hypertension International Protocol Revision 2010. mHealth apps are also used as tools to support physicians in improving hypertension treatment. App-based clinical decision support systems are innovative solutions, in which patient information is entered in the app and management algorithms provide recommendations for hypertension treatment. The use of these apps has been shown to be feasible and easily integrated into the workflow of healthcare professionals, and, therefore particularly useful in resource-limited settings. In addition, apps can be used to improve hypertension control by facilitating regular BP monitoring, communication between patients and health professionals, and patient education; as well as by reinforcing behaviours through reminders, including medication-taking and appointment reminders. Several studies provided evidence supporting the use of apps for hypertension control. Although some of the results are promising, there is still limited evidence on the benefits of using such mHealth tools, as these studies are relatively small and with a short-term duration.

Summary Recent research has shown that mHealth apps can be beneficial in terms of improving hypertension self-assessment, treatment and control, being especially useful to help differentiate and manage true and pseudo-resistant hypertension. However, future research, including large-scale randomised clinical trials with user-centred design, is crucial to further evaluate the potential scalability and effectiveness of such mHealth apps in the resistant hypertension context.

Keywords mHealth · Mobile technology · Apps · Applications · Digital health · Hypertension · Self-assessment · Treatment · Control

The Burden of Hypertension

Hypertension is the global leading risk factor for cardiovascular diseases (CVDs), disability and death. Approximately 218 million disability-adjusted life years (DALYs) and 10.4 million deaths worldwide were attributed to hypertension in 2017 [1]. The global prevalence of hypertension has increased from 25.9 to 31.1% between 2000 and 2010 [2]. Importantly, hypertension is most prevalent in low- and middle-income countries (LMICs), where there is combination of overpopulation, increasing industrialisation and weaker health systems (distance, financial constraints, reduced capacity). An estimated

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1.39 billion people have hypertension, with approximately 75% of those living in LMICs [2]. The estimated prevalence of hypertension has decrease in high-income countries (HICs), while it has increased in LMICs, being estimated to be 28.5% and 31.5%, respectively in 2010 [2].

Uncontrolled hypertension is associated with subclinical and clinically manifested CVDs, such as coronary, cerebrovascular and peripheral artery disease. The risk of CVDs doubles for every 20 mmHg and 10 mmHg increase in systolic and diastolic blood pressure (BP), respectively [3]. Prevention and management of hypertension are essential to reduce the CVD morbidity and mortality. Some of the major challenges related to hypertension are improving its awareness, treatment and control, which are generally low, especially in LMICs. The global rates of hypertension awareness, treatment and control were estimated to be 46.5%, 36.9% and 13.8%, respectively [2]. Importantly, hypertension awareness, treatment and control rates are substantially lower in LMICs compared to HICs: 37.9% compared to 67.0%, 29.0% compared to 55.6% and 7.7% compared to 28.4%, respectively [2].

Resistant hypertension is defined as elevated BP above the goal for a hypertensive patient despite the concomitant use of three anti-hypertensive medications of different classes, including a diuretic, a renin-angiotensin system blocker and a long-acting calcium channel blocker [4, 5]. Resistant hypertension is a real challenge in clinical practice, and it is important to differentiate true resistant hypertension, which usually needs to be further investigated, from pseudo or apparent resistant hypertension. The diagnosis of true resistant hypertension has three main pre-requisites: (1) the elevated BP to be confirmed in an out-of-office setting, excluding the diagnosis of white-coat hypertension; (2) the anti-hypertension medications to be at maximally tolerated doses; and (3) the confirmation that the patient is adherent to the treatment.

Confirming medication adherence is of particular importance before diagnosing a patient with resistant hypertension, as a high proportion of those with poorly controlled BP, between 14.1 and 40.4%, are pseudo-resistant due to poor adherence to the anti-hypertensive medications. Therefore, especially in those patients with suspected resistant hypertension, improving medication adherence alongside with reinforcing healthy lifestyle changes, including weight loss, a healthy diet, reduced sodium and alcohol intake, and regular physical activity, is essential to improve BP control [4, 5]. However, to date, the available strategies were ineffective in improving hypertension management and control, as most hypertensive patients fail to achieve long-term behavioural changes and approximately 50% of hypertensive patients have suboptimal medication adherence [5, 6].

Overall, the increasing hypertension global burden of disease is alarming, and resistant hypertension remains a major public health challenge globally. Thus, we are challenged with the need for scalable solutions that address hypertension prevention and ongoing management. Such solutions need to overcome the barriers of distance, capacity and financial limitations, while being simple and meaningful to people.

The Potential of mHealth

According to the World Health Organization, mobile health or mHealth has the potential to transform healthcare across the globe [7•]. mHealth is defined as the use of mobile wireless technologies to support the achievement of health objectives, especially for public health purposes [7•]. In the early 2000s, the first types of mobile devices used in mHealth interventions included personal digital assistants (PDAs) and mobile phones with basic features; and, more recently, newer technologies were added to the pool of mHealth devices, such as smartphones, tablets, wearable devices and smartwatches [8].

The continued growth in mobile networks has enabled the widespread of mHealth interventions in the last two decades. According to a report from the International Communications Union, the number of mobile phone subscriptions now exceeds the global population, with an estimated 7.74 billion subscriptions worldwide in 2017 [9]. In addition, the total number of mobile broadband subscriptions has increased more than 15 times in the last 10 years, now accounting for more than 50% of the mobile phone subscriptions and enabling millions of people to have access to the internet and online services through their phones [9]. This increase in mobile broadband subscriptions was accelerated in the last decade by the advent of smartphones and tablets, as well as the growing availability of wireless networks worldwide.

Given the current broad availability, use of mobile wireless technologies in healthcare is particularly relevant, due to the wide reach, broad acceptance and ease-of-use of these technologies [10]. Therefore, there has been an increasing interest in studying the use of such technologies to improve health outcomes. Importantly, mHealth research has evolved over time with the advances in mobile wireless technologies. Before 2007, PDAs dominated mHealth research; then, between 2007 and 2012, mobile phones with basic features, such as text-messaging, were the main types of devices used in mHealth research; finally, from 2012 onwards, smartphones, tablets and wearable devices started to be increasingly used in mHealth interventions [8].

Over the last decade, there has been a proliferation of mobile applications (apps) available for download in smartphones and tablets through the online app stores. Currently, there are 2.1 and 1.8 million apps available in the Google Play and Apple App stores, respectively [11]. Of those, at least 325,000 are health-related apps, with an estimated 3.7 billion app downloads in 2017 [12]. Mobile health or mHealth apps have been previously categorised into (i) information apps, in which individuals can find, view and read medical information; (ii) diagnostic apps, in which a calculation or analysis is performed based on information entered in the app and a result/diagnosis is provided; (iii) control apps, in which remote monitoring can be performed to help disease management; and (iv) adapter apps, which are used alongside accessories that transform the app into a medical device [13•]. Many of these types of mHealth apps are used to support the achievement a wide variety of health objectives, including those related to hypertension. Therefore, mHealth strategies offer an opportunity to address the widespread burden of hypertension through scalable interventions that can be accessed on mobile devices such as apps on smartphones.

mHealth Applications in the Hypertension Context

mHealth apps have been increasingly used in the hypertension context. From the patients'/users' perspective, mHealth technology can positively transform hypertension self-management [14•]. A qualitative study has identified key aspects that were found to be important for patients when developing mHealth interventions to improve hypertension self-management; these are individualisation options/system flexibility to accommodate patient needs; trustful relationship with healthcare professionals who recommend the self-management tool, ensuring the quality and security of this tool; motivation for self-management through automated feedback and rewards systems; and the ability to communicate with health professionals [14•]. From the physicians' perspective, using mHealth technologies in hypertension management can have benefits, such as readily available out-of-office BP measurements data and increased patient engagement in self-management [15•]. However, some concerns were raised related to unmanageable quantity of health information and possible increase in patient anxiety, the 'worried-well' phenomenon.

In this section, we outline how apps can be used to achieve three main objectives of extreme importance in the hypertension context: (1) improving self-assessment; (2) improving treatment; and (3) improving control.

Improving Self-Assessment

mHealth apps can improve self-assessment by facilitating BP measurements. Apps have been used to directly measure BP levels, either using the oscillometric method with automated inflatable cuffs or using pulse wave signals detected by smartphone technology without the need for cuffs. Apps, such as the iHealth BP, Withings BP and Qardio, measure BP using the oscillometric method connected to inflatable cuffs via Bluetooth. The iHealth models BP5 and Track (upper arm inflatable cuffs) and model BP7 (wrist inflatable cuff) [16•, 17•, 18•], as well as the Withings BP-800 have been tested and shown to accurately measure BP [19•]. Another app called the Accutension was also found to measure BP with good accuracy using an electronic auscultatory method [20]. Comparisons of four different wireless app-based BP monitors were made and the results found that these devices tend to overestimate both systolic BP (SBP) and diastolic BP (DBP) when compared to a gold standard aneroid sphygmomanometer [21••]. However, the differences in BP measurements were within the acceptable range of 5 mmHg pre-defined by the European Society of Hypertension (ESH) International Protocol Revision 2010.

Several apps have also claimed to accurately measure BP levels without an inflatable cuff. One of the most popular apps was the Instant Blood Pressure (IBP) app, which utilised pulse wave signals using the smartphone camera to measure BP. Users were instructed to place the right index finger over the smartphone's rear camera lens while placing the smartphone's bottom edge in direct and firm contact with the chest. The IBP app was launched in June 2014 and was one of the top best-selling apps until it was removed from the app stores in July 2015 [22•]. However, a study with 85 individuals conducted by researchers from the John Hopkins University has demonstrated that the IBP app was inaccurate in measuring BP, usually underestimating higher BP levels and overestimating lower BP levels [22•].

Other researchers from Michigan University have reported the development of a mHealth app to measure BP without an inflatable cuff [23••]. For the app to work, it needs a special case to be attached to the smartphone, where the user presses the index finger on a sensor while holding the phone at the heart level. This device uses photoplethysmography and force transducers to measure the blood volume oscillations and the applied pressure. Researchers tested the usability and accuracy of this app-based BP monitoring device in 30 individuals and found that the device was easy to use, as 90% of the users only required one or two trials to learn how to use the device. In terms of accuracy, however, the results demonstrated that this app-based device yielded bias and precision errors when compared to a validated automated arm cuff BP monitor.

Given the wide availability and ease-of-use of smartphones and mHealth apps, these app-based BP monitoring devices could facilitate and encourage patients to perform regular BP self-assessment. In the context of resistant hypertension, the BP self-assessment done using these app-based BP monitors could be useful in confirming an elevated BP in an out-of-office setting, helping to differentiate patients with true and pseudo-resistant hypertension.

Improving Treatment

mHealth apps are also used as tools to support physicians in improving hypertension treatment. App-based clinical decision support systems are innovative solutions, in which patient information is entered in the app and management algorithms provide recommendations for hypertension treatment. The use of these apps is feasible and easily integrated into the workflow of healthcare professionals, and, therefore particularly useful in resource-limited settings [24].

The SmartHealth trial in India tested this app-based clinical decision support tool to improve hypertension treatment and cardiovascular disease management [25]. Non-physician healthcare workers entered patient information on the app, which through risk assessment algorithms, provided the patient's cardiovascular risk status. High-risk patients were then referred to primary healthcare physician. The app also provided decision support to the physicians for medication prescription. Although a promising tool, the trial failed to improve anti-hypertensive medications prescription [26••].

Another app for clinical decision support, called Tele-HAS, was developed in Brazil to support family physicians in improving hypertension treatment [27••]. Similarly, in the Brazilian app, the patient's clinical and laboratory data were entered in the app, which provided guideline-based treatment recommendations to the physicians. This app was also found to be easily integrated into the daily routine of the primary healthcare setting, either at the facility or during home visits. Most physicians found that the app was easy to use and user-friendly; they also reported that, by using the app, they had access to new knowledge in hypertension and that it had the potential to improve patients' treatment.

These app-based clinical decision support tools can be particularly useful in LMICs, where there are low numbers of physicians, making it difficult for patients to have access to them, and usually overburdening the available physicians. These app-based tools could facilitate the work of physicians by providing point-of-care readily available recommendations on hypertension treatment, as well as by reducing some of the physicians work load, which could be done by trained non-physician healthcare workers using this reliable tool. In addition, such tools can help physician uptitrate the anti-hypertensive medications to the maximally tolerated doses before confirming the diagnosis of resistant hypertension.

Improving Control

mHealth apps can also be used to improve hypertension control by facilitating regular BP monitoring, communication between patients and health professionals, and patient education; as well as by reinforcing behaviours through reminders, including medication-taking and appointment reminders. A recent review evaluated hypertension-related apps available in online app stores and found that the majority of 107 apps found in the Apple and Google Play stores were targeted at patients. The most common app features were BP tracking/monitoring, which was present in 69.1% of the apps, analytical tools and feedback on BP trends in 66.3%, and heart rate tracking in 61.7% [28••]. In addition, 43.9% of those apps had the ability to export and share the data with health professionals and others, 37.0% had educational information on hypertension, and 22.4% had medication adherence tools. Of note, only three apps had documented expert and healthcare agency involvement in the app development. Similar results were found in a later review [29•]. Meanwhile, a more recent review found that the educational component was the most frequent feature found in hypertension-related apps, followed by BP tracking and self-monitoring [30•].

Another review has evaluated apps specifically aimed at improving medication adherence through daily medication reminders and found that about 55% of them had a medication-taking tracking feature [31]. Furthermore, another way that apps could improve hypertension control is through healthy behaviour support, particularly recommending an effective diet, such as the Dietary Approaches to Stop Hypertension (DASH). A mHealth app, the DASH Mobile, has been developed with this aim and is yet to be tested [32].

Although hundreds of hypertension-related apps are now available for download in the app stores, only a small number of apps have been or are currently being tested in research studies, for example the BPcontrol app [33], the BPMAP [34], the mWellcare app [35], the Medisafe app [36] among others. Studies with pre-post design have shown promising results, demonstrating that these apps produced significant reductions in both SBP and DBP and improvements in medication adherence, over 4 weeks to 9 months [37•, 38•, 39•, 40•, 41•]. However, only a few studies with more robust design, such as randomised clinical trials (RCTs), have tested the impact of mHealth apps on BP control and medication adherence in hypertensive patients. The mHealth intervention details and the results of these RCTs are presented in Table 1.

Two studies have shown improvements in BP levels and BP control in the app-based intervention group compared to the control group [42••, 43••], while one study did not find improvements in BP levels, but found improvements in medication adherence [36]. Another study also found improvements in medication adherence, as well as in patients' self-integration, self-regulation, self-monitoring and total self-management scores [44••]. In addition, a further study using the same app used in the study by Morawski et al., but conducted in patients with coronary heart disease, also found improvements in medication adherence, also not being able to demonstrate a significant reduction in BP levels. However, both studies had a short-term follow-up of only 3 months that might not have been a long enough period to demonstrate the impact of the app intervention on BP.

These studies add to the pool of evidence supporting the use of apps for hypertension control. Although some of the results are promising, there is still limited evidence on the benefits of using such mHealth tools, as these studies are relatively small and with a short-term duration. In addition, as previously discussed, medication adherence is a major issue in the context of resistant hypertension. The mHealth apps discussed in this section can be used not only as a strategy

Table 1 Randomised clinical trials of app-based interventions to improve hypertension control in hypertensive patients

Author, year Country	Number of participants	Duration	Interventions	Outcomes	*P* value
Albini [42••], 2016 Italy	690	6 months	Intervention: Eurohypertension app - BP data monitoring twice a week - Daily medication reminders - Education—general information about hypertension Control: Usual care	SBP at FUP—mean (SD) I: 137.8 mmHg (12.8) C: 139.3 mmHg (12.3)	0.13
				DBP at FUP—mean (SD) I: 85.4 mmHg (7.5) C: 85.4 mmHg (7.9)	0.96
				Change in SBP—mean (SD) I: − 10.5 mmHg (6.3) C: − 6.1 mmHg (6.9)	< 0.0001
				Change in DBP—mean (SD) I: − 6.2 mmHg (3.8) C: − 3.4 mmHg (4.5)	< 0.0001
				SBP/DBP < 140/90 mmHg at FUP—*n* (%) I: 219 (72.3) C: 119 (39.9)	< 0.0001
Kim [43••, 45], 2016 USA	95	6 months	Intervention: HealthCycles app and website - Monitoring BP with Withings BPM twice a day three times a week - BP graphs - Reminders for monitoring - Education on hypertension - General healthy behaviours recommendations + HealthComp disease management program Control: HealthComp disease management program - Nurse-delivered patient education including wellness and disease prevention information and chronic disease management	SBP at FUP—mean (SD) I: 133.4 mmHg (12.9) C: 140.2 mmHg (18.4)	NP
				DBP at FUP—mean (SD) I: 82.8 mmHg (11.2) C: 85.3 mmHg (12.1)	NP
				SBP/DBP < 140/90 mmHg at FUP—*n* (%) I: 34 (65) C: 22 (51)	NP
				Medication adherence MMAS-8 score—mean (SD) I: 6.7 (1.4) C: 6.5 (1.5)	NP
				Exercise units per week—mean (SD) I: 39.8 (23.8) C: 41.3 (29.5)	NP
				Cigarettes per day—mean (SD) I: 2.6 (7.3) C: 0.3 (1.6)	NP
				Frequency of drinking per month—mean (SD) I: 7.6 (7.9) C: 5.8 (6.8)	NP
				Patient Activation Measure score—mean (SD) I: 79.4 (21.9) C: 72.1 (18.7)	NP
Morawski [36], 2018 USA	412	12 weeks	Intervention: Medisafe app - BP monitoring/tracking - Medication list - Medication reminders	SBP at FUP—mean (SD) I: 140.8 mmHg (15.7) C: 141.2 mmHg (17.3)	0.78
				Change in SBP—mean (SD)	

Table 1 (continued)

Author, year Country	Number of participants	Duration	Interventions	Outcomes	*P* value
			- Medication adherence weekly reports - Medfriend feature, in which the user would allow app access to a family member or friend to view the medication-taking history, receive alerts when the user would miss a medication dose and provide peer-support Control: Usual care	I: − 10.6 mmHg (16.0) C: − 10.1 mmHg (15.4)	
				SBP/DBP < 140/90 mmHg at FUP—*n* (%) I: 67 (35.8) C: 69 (37.9)	0.68
				Medication adherence MMAS-8 score—mean (SD) I: 6.3 (1.6) C: 5.7 (1.8)	0.01
Najafi [44••], 2018 Iran	100	6 weeks	Intervention 1: Telegram app - Educational information about hypertension and advice in the form of key tips using educational images and videos on a weekly basis - Questions about health status, medication adherence and health behaviours on a weekly basis Intervention 2: Self-management with phone follow-up - Face-to-face education sessions about self-management behaviours in hypertension, such as adherence to a healthy diet, regular exercise and medications, medications side effects and how to measure BP - Weekly phone follow-up to encourage self-management strategies, providing tips and reminders and answering questions Intervention 3: Self-management without phone follow-up - Face-to-face education sessions about self-management behaviours in hypertension, such as adherence to a healthy diet, regular exercise and medications, medications side effects and how to measure BP - No phone follow-up Control: Patient general education session at the hospital	Self-integration score*—mean (SD) I1: 3.64 (0.29) I2: 3.56 (0.36) I3: 2.84 (0.93) C: 1.99 (0.33)	< 0.0001
				Self-regulation score*—mean (SD) I1: 3.61 (0.39) I2: 3.64 (0.38) I3: 2.58 (1.10) C: 1.48 (0.48)	< 0.0001
				Self-monitoring*—mean (SD) I1: 3.85 (0.27) I2: 3.83 (0.37) I3: 2.95 (0.99) C: 1.96 (0.43)	< 0.0001
				Medication adherence*—mean (SD) I1: 3.95 (0.10) I2: 3.96 (0.20) I3: 2.78 (1.12) C: 1.79 (0.43)	< 0.0001
				Total self-management behaviours*—mean (SD) I1: 3.73 (0.22) I2: 3.70 (0.29) I3: 2.81 (1.01) C: 1.83 (0.33)	< 0.0001

BP, blood pressure; *C*, control; *DBP*, diastolic blood pressure; *FUP*, follow-up; *I*, intervention; *MMAS-8*, Morisky Medication Adherence Scale 8-item; *NP*, not provided; *SBP*, systolic blood pressure; *SD*, standard deviation

*Measured using the Hypertension Self-Management Behavior Questionnaire (HSMBQ) to improve adherence to anti-hypertensive medications, but also as a potential tool to measure adherence. Future studies could assess and validate how these apps can be used as a tool to measure adherence, identifying those patients with low versus high medication adherence; and, therefore, helping to differentiate those with pseudo versus true resistant hypertension. Importantly, researchers should focus on conducting large-scale RCTs with longer follow-up and sufficient power to detect a statistically significant improvement on BP levels.

mHealth Regulations and Implications to Practice

Regulations on mHealth tools are still an unclear and evolving space. The US Food and Drug Administration (FDA) has previously provided guidance on mHealth apps oversight and determined that it would only regulate those apps that were considered medical devices [46••], such as those app-based BP monitor devices to improve hypertension self-assessment. More recently, in 2017, a new regulation released by the FDA has increased the regulatory oversight on apps intended to provide clinical decision support [47••], such as those apps used to help physicians to improve hypertension treatment. As the mHealth landscape is always rapidly changing, regulatory agencies need to constantly revise its regulatory guidance and adapt to this ever-changing technology-based healthcare delivery strategies.

Another important aspect of the mHealth scenario is the current lack of a quality assessment and certification process of mHealth apps. The online app stores have a quality-rating system that is only based on users' feedback, but it does not take into account several important aspects that should be considered when evaluating if an app is of high quality. A previous review has attempted to design a stepwise process to assess the quality of mHealth apps by systematically reviewing available apps in the online app stores, identifying desirable features to be present in the apps to achieve a particular health objective, and assessing the app quality through download, testing and rating of the apps using a validated quality assessment tool [31].

Regulations and certification of mHealth apps are complex and standard processes are still lacking. A formal app certification approach was proposed, in which apps would be assessed whether they comply with basic standards in three areas: (i) accessibility, ensuring that mHealth apps have a clear language, are easy to use, affordable and available in all online app stores; (ii) data security privacy, ensuring that personal data in mHealth apps are secure and that data sharing with third parties is prohibited; and (iii) content, ensuring that the app content is accurate and developed with expert involvement [48•].

Finally, for mHealth strategies to have an impact on public health, mHealth apps need to be simple and user-friendly, but functional, as well as affordable, secure and with proven efficacy. The more the use of mHealth apps become common practice in healthcare, the more patients and healthcare providers need guidance on how to evaluate and be confident that recommended apps are high-quality tools. A concept of prescribable apps has emerged and should be further developed in the future [49].

Conclusion

Hypertension is the global leading risk factor for CVDs, disability and death with LMICs disproportionately impacted. Resistant hypertension remains a challenge in clinical practice. With advancements in mobile technology, there is an opportunity to implement mHealth strategies that can overcome barriers associated with reach, distance and a scarcity of human resources while also being meaningful to patients. Recent research has shown that mHealth apps can be beneficial in terms of hypertension self-assessment, treatment and control, being especially useful to help differentiate and manage true and pseudo-resistant hypertension. However, further research, including large-scale RCTs with user-centred design, is crucial to evaluate the potential scalability and effectiveness of such mHealth apps in the resistant hypertension context.

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Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

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- •• Of major importance

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