

Interventions to Enhance Medication Adherence in Hypertensive Patients: A Systematic Review

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ABSTRACT

Hypertension being a major risk factor for Cardio- and Cerebro-Vascular diseases could be termed as silent killer that has affected over 1.56 billion patients per annum. It is a silent killer in both the developed as well as developing nations of the world. Currently about half of people with hypertension (HTN) have uncontrolled blood pressure due to Lack of medication adherence. This paper elaborates the different interventions intended to enhance medication adherence in Hypertensive patients by means of systematic review, thereby broadening the scope of knowledge associated with Medication adherence interventions. In this systematic review authors have tried to collect research evidences of various popular approaches which are being used in the current practices namely, Self- monitoring, Patient counselling/ Patient education (Personalized telephone counselling sessions with health educators), Medication regimen management (Using combination pills to reduce number of pills patients taken daily), Medication taking reminders such as refill reminder calls or use of electronic drug monitors for monitoring and reminding, Pill count, Pill box, Smart app, Audio and Video tape. Traditional self-monitoring patients showed lower medication adherence, tele-nursing was originating to be further effective compared to self-monitoring method. Triple combination pill and fixed dose achieved a target BP. Cost of the monitors and the challenges of integrating their adherence data into clinical care are the barriers to their routine use outside of the research setting in electronically monitored adherence. The use of

pill boxes resulted in clinically considerable reductions in systolic BP as well as an increased number of patients meeting prescribed BP goals.

Keywords: Hypertension, Enhancement of Medication adherence, Interventions, Clinical outcomes.

INTRODUCTION

Hypertension is a major risk factor for cardiovascular disease, cerebrovascular disease and renal diseases. It is estimated that 1.56 billion patients suffer from hypertension by the year 2025. ^[1] Currently about half of people with hypertension (HTN) have uncontrolled blood pressure due to Lack of medication adherence. ^[2] Medication adherence is defined as "the degree to which the person's behaviour corresponds with the agreed recommendations from a health care provider". Both direct and indirect measures can be used to assess the medication adherence. ^[4]

Medication adherence is an ambidextrous issue and comprised of three components: inception, implementation, and persistence. A combination of methods is recommended to measure adherence, with electronic monitoring and drug measurement being the most accurate. ^[5] Several problems attributed for non-adherence to medical regimens, such as poor instructions, symptomless nature of the condition, the long continuance of therapy,

concomitant effects of medication, complex drug regimens, lacking in knowing about hypertension management and risks, and costs of medication. Patient self-management, electronic drug monitors (MEMS.E-CAP) Medication regimen management (using combination pills), Mobile phone apps, Pill box or Pill count methods are commonly used to identify the non-adherence risk of patients.^[6, 7]

Adherence to medication is a use full component of health outcome,^[8, 9] we can increase medication adherence by improved patient outcomes.^[10] Patients may fail to take their medication leads to considerable degeneration of disease, increased healthcare costs and death. In other words, non-adherence affects the individual patients and the healthcare system.^[8, 12] WHO states, ‘increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments.’^[11]

INTERVENTIONS FOR MEDICATION ADHERENCE

1. Self-monitoring

In research and clinical care, self-monitoring is the mainly regular approach for assessing adherence behaviour. Assessing of medication adherence of self-management range from single simple questions regarding missed doses to composite multi-item assessments. It can fluctuate substantially in their questions phrasing, recall periods, and response items in an exertion to facilitate the training settings. It may too serve clinicians in identifying barriers in patients to allocate sufficient compliance.^[13]

A study developed medication adherence survey (MAS), a multi-item counselling to increase adherence (outcome).^[14] Another study reported that a entirety of 67.1% participants had insignificant BP influence and was much connected with low self-management skills. 21.3% participants had controlled BP and was better in those who were adherent to medication.^[15] It was also found that stronger beliefs in barriers to compelling medications such as medications’ side effects, prohibitive cost, bad taste, and unsafe effects, were notably allied with reduced pills.^[16, 17]

Table1: Studies involving Self-Monitoring of Medication Adherence

Authors/Year	Design	Sample size(n)	Mean Age Gender	Medication Adherence Measure	Outcome
Qu Z et al., 2019 ^[14]	Cross-sectional	873	360 men and 513 women	Morisky medication adherence scale	About 67.1% were non adherent to Their regimens. Adherence of patients using self management in hypertension was low
Adidja,et al., 2018 ^[15]	Cross-sectional	183	60 men and 120 male	Self management	About two- thirds(66.7%)of the study participants were non adherent to their medication mainly by forgetfulness, lack of funds, and multiple dosing.
Hallberg et al.,2015 ^[16]	Cross sectional	49	26 male and 23 female	Self-management was assessed by reporting through phones	Patients perceived the benefits of the awareness of factors effecting the blood pressure (between the blood pressure and daily life routine) which resulted increased motivation to adhere to treatment
Schoenthaleet al., 2016 ^[17]	Longitudinal study	815	589 male, 226 female	Self management included self efficacy, depressive and social support, patient-provider communication	High efficacy in medication adherence was seen with low depressive symptoms, collaborative patient-provider communication.

2. Patient counseling/ Patient education (Personalized telephone counseling sessions with health educators)

Telephone counseling is a appropriate and more effective tool in achieving medication adherence. A cluster-randomized clinical trial as well as 30

Community Health Centers was randomly assigned to the intrusion condition. Patients at the intrusion restriction sites acknowledged patient education, home BP monitoring, and monthly lifestyle counseling, at that interval physicians attended monthly hypertension case rounds,

and acquired feedback on their patients' home BP readings and chart audits. Patients and physicians at the usual prerequisite sites acknowledged in print enduring teaching items and hypertension treatment guidelines respectively. The major outcome was BP control and consequential outcomes were changes in systolic and diastolic BP at 12 months. Further investigation on implementation of behavioral modification strategies for hypertension have power over in low-resource settings be supposed to focus on the promotion of other economical and tailored interventions in high-risk population^[18]. In addition to other tests the effectiveness of motivational interviewing compared with the routine treatment for Chinese hypertensive patients. 120 eligible participants were randomly assigned to control group (usual care group) or the intervention group (motivational

interviewing group). It was found that the requisition of motivational interviewing for hypertensive patients is a shows potential appeal for sustaining the clinical benefits of adherence behavior.^[20]

A convenient sample of 100 subjects, who attended the outpatient clinics of the aforementioned setting were, divided equally into study and control groups 50 subjects each. The intrusion group (tele-nursing intervention) was followed by follow-up handset calls throughout the duration of the study. There were statistically substantial differences between both groups regarding mean arterial blood pressure scores after tele-nursing intervention. The mean level of arterial blood pressure & BMI was significantly lower in the study group than the control after intervention.^[21]

Table 2: Studies involving Patient counselling as the means of intervention.

Authors/ Year	Designs	Participants intervention	Intervention	Outcome
Ogedegbe et al., 2014 ^[18]	Cluster randomized clinical trial	N=1058 Duration:12months	Intervention group:patient education ,self BP monitoring and lifestyle counseling and printed material regarding patient education	Implementation of multi level intervention did not improve BP control in patients
Beuneet et al.,2014 ^[19]	Cluster randomised trial	N=146 intervention n=75, control =71 Duration:6months by trained practiced nurses	intervention group :3 sessions of education at 2, 8 and 20 weeks with hypertension care Control group: hypertension care and education	This intervention led to an improved adherence to lifestyle recommendations, and hypertension care.
Mac et al.,2014 ^[20]	randomised controlled trial	N=120 Duration:6months	control group: usual care group intervention group: motivational interviewing group.	the adherence were increased in the motivational interviewing counselling group.
Magdaetal.,2020 ^[21]	A quasi experimental	N=50 24 male, 26 female	Tele-Nursing(30 mins per call) and control group received outpatient teaching	The level of arterial blood pressure and BMI was significantly lower in the study group than control group after intervention

3. Medication regimen management (Using combination pills to reduce number of pills patients taken daily)

Four trials examined the effect of adjusting medication regimens (using combination pills to reduce the number of pills patients take daily).^[22] A study reported that there was no significant difference between groups in the on-treatment analysis and in intention-to treat analysis. Free Triple Combination Therapy of Atorvastatin, Perindopril, Amlodipine in Hypertensive Patients could effectively

improve adherence which was calculated to be low in the free combination cohort.^[23] It is also implied that there is possible advantage of the fixed combination regarding this outcome. The results of the pooled analysis of the three trials showed a non significant trend towards better blood pressure control favouring the fixed combination group.^[24] Randomized trial shows that ODF combination of perindopril, indapamide and amlodipine is as safe as free combination of the 3 drugs, but is associated with a larger effectiveness in BP control,

acquiescence and, accompanying with statin, in cholesterol reduction. A better cardiovascular risk control is achieved with

ODF combination than with a free administration.^[25]

Table 3: Studies involving Medication regimen management as the means of intervention.

Authors/Year	Designs	Participants intervention	Intervention	Outcome
Webster et al., 2018 ^[22]	Randomized clinical trial	N=700 Meanage:56 42%men,58% women	A once-daily fixed dose triple combination pill(20mg of telmisartan, 2.5mg of amlodipine and 12.5mg of chlorthalidone)	Triple combination pill led to an Increased proportion of patients achieving their target BP at 6months by adhering to their regimen.
Pecherina et al., 2014 ^[23]	Random sample method	N=124 Intervention group:61% Controlgroup:56.5%	Nebivolol+Amlodipine as fixed combination Nebivolol 2.5mg/5mg in free combination with Amlodipine2.5mg or 5mg	Fixed combination is more effective than free combination
Valentina Perrone et al., 2019 ^[24]	Cohort analysis	N= 2292	triple fixed-dose atorvastatin/perindopril/amlodipine (CTAPA) free combination atorvastatin/perindopril/ amlodipine	Fixed-dose CTAPA could effectively improve adherence compare to free combination
Marazzi G et al., 2016 ^[25]	Randomized trial	12weeks	ODFC of perindopril 10mg indapamide 2.5 mg/amlodipine 5 or 10 mg Free combination of of perindopril/indapamide /amlodipine plus atorvastatin 20 mg	Fixed combination is associated with a greater efficacy in BP control, compliance and, associated with statin,in cholesterol reduction

4. Medication taking reminders such as refill reminder calls or use of electronic drug monitors for monitoring and reminding

Electronic monitoring provides additional dependable and meticulous records about substantial patient adherence. It accomplishes times and dates (‘time stamping’) of medicine events. It includes smart phone app, pagers, and pill bottles with alarm characteristics. Studies of commercially accessible data intimate that the most successful interventions were delivered by qualified counselors and concerned multitude sessions’ studies of successful interventions.^[26] Computerized clinical result sustain systems (TeleHAS)

are advantage with easy completion and responsive edge and the impending to enhance patients’ treatment. Through the app recommendations, more than 90% of physicians had get into to new perception about cardiovascular risk and hypertension.^[27] A study also showed that there was consequential enhancement in the intervention but on the whole of these gains were preoccupied after 5 months. Even with the correlation between electronically monitored adherence and clinical outcomes, the expense of the monitors and the challenges of integrating their obedience records into clinical care may be barriers to their regime use of outside of the research setting.^[28]

Table 3: Studies involving Medication Reminders as the means of intervention.

Authors/Year	Designs	Participants intervention	Intervention	Outcome
Inselet et al., 2016 ^[26]	Two-group longitudinal randomized control trial.	N=128 Age : 65 Duration : 5 months	4 training sessions in cognitive behavioural techniques to promote habitual medication-taking, delivered by trained nurses	No difference in adherence at 6 months
Silveira et al., 2019 ^[27]	Randomized controlled trials	N=535	TeleHAS app consisted of integrating clinical and lab data which performs cardiovascular risk calculation and for the management of BP	Feasible, Usability and utility of computerised clinical decision support system (CDSSs) was easy to incorporate into daily routine in context of primary care setting.
Patel s et al., 2013 ^[28]	Automated medication reminder system-phone based	N=50 duration:7months	Pill phone application Pre activation phase Activation Post activation phase	There was a significance increase in adherence between pre activation and activation phases

5. Pill Count

Pill count may perhaps be a advantageous tool for exploring faithfulness patterns in mutually intervention and control group, and their consequences on blood pressure reduction.^[29, 31] A statistical analysis carried out in a primary health care in Renteria-Beraun (Guipuzcoa), Basque Health tune yielded analogous observance for men and women, and for identical age groups via Morisky-Green and pill count. Approximately 50% of the patients had sufficient acquiescence according to at least one of the 3 tests. A better affiliation was originated between Morisky-Green's test and the pill count method, and medication adherence was better at what time familiarity of the disease increased, and what time the numeral of prescribed pills became smaller.^[30] In a study,

antihypertensive medicine adherence was evaluated by pill counts at baseline and at the cessation of the study. The percentage of adherence for intervention group patients was greater between baselines at the cessation of the study despite the fact that it didn't amend in the control group.

The relative amount of patient adherence at the completion of the study was greater in the intrusion group compared to the control group. The chances of compliance to antihypertensive drug therapy in the intervention group were 4.07 times privileged than the control group. This shows that in treated hypertensive patients, the pharmacist interference was allied with conspicuous enhancement in antihypertensive medications adherence, compared to usual care.^[32]

Table5: Studies involving Pill Countas the means of intervention.

Authors/ year	Designs	Participant intervention	Interventions	Effects/ Outcomes
Granger et al, 2015 ^[29]	cross-sectional	N=86 Duration : 1 year	pre discharge education by nurses on medication goals	Pill counts Proportion of patients who took >80% of their pills increased from 32%to70% in intervention group vs 28%to33%in control groupat1 year.
Gutiérrez ^[30]	Descriptive, transversal study	N=100 7 months	Morisky-Green's test (men and women), Batalla'stest,Pill count method(different age groups)	A significant correlation was found between Morisky-Green's test and the pill count method and similar consent was found between patients of both genders and different age groups
Hein A.W. van Onzenoortet al., 2010 ^[31]	parallel-group design	N= 228 patients Duration 1 year	Pill count and Medication event monitoring system	Patients reachedComparable improvement in blood pressure values and reductionsby using Pill count and electronic monitoring.
Fikri-benbrahim n et al., 2013 ^[32]	Controlled study	Control-89, Intervention -87	Pill counts, and education on hypertension	Adherence was increased in I: 86%-96.5% and in C: 86.5%-85.4% it did not differ.

6. Pill box

Smart pillboxes that emphasize patients to take medications may help to evade unintentional non-adherence to medicine regimens. Smart pillboxes can keep track of patients' schedules and remember them to take the right medication, at the same time some can forward alert notifications to caregivers. The use of smart pillboxes is an alternate to make progress drug acquiescence in the non-adherent patients.^[33, 34] A systematic review make another study of of randomized trials evaluated the effectiveness of certain measures suggested to enhance adherence exhibited that adherence to medication

regimen was improved after initiation of pill boxes^[35] but low-priced medication standard pillbox did not enhance medication adherence.^[38] Anti-hypertensive medication adherence shows consequential difference between the intervention and control group. Intervention group showed compliance to drug regimens greater than in the control group. Systolic blood pressure was differing between two groups as diastolic blood pressure was statistically important unusual between two groups at three months post intervention.^[39] Participant's perception and satisfaction on functionality and features, as well as the pattern and size, were affirmative amongst participants. Advance

studies evaluated the effectiveness of smart pill boxes in enhancing medication adherence showed that foremost concern patients who reported missing a dose by

accident were 2.4 times likely to assistance a smart pillbox, while those with heart disease were almost 4times as likely to want to use a smart pillbox. [37]

Table6: Studies involving Pill Box as the means of intervention.

Authors/ year	Designs	Participant intervention	Interventions	Effects/ Outcomes
Porter A. K et al., 2014 ^[36]	A chi-square	each patient was provided two 7-day pill boxes duration : 2- 4 weeks	Pill box	refill of pill boxes, BP measurement, and adherence was assessed by pill boxes of those, achieved at least a 10 mmHg reduction in BP
Choi et al., 2019 ^[37]	Random sample	N= 500 Age =>40 Duration: 7days	Technology and associate factors can keep track of patients' schedules and remind them to take the right medication	Patients willingness to use smart pillboxes reduced unintended non-adherence
Niteeshet al., 2017 ^[38]	randomized clinical trial	N= 53480 Age = 45 Digital timer cap 15.1%, pill bottle strip: 16.3%, control 15.1%	Patients was randomized to receive in the mail a pill bottle strip with toggles, digital timer cap, or standard pillbox	Low-cost reminder devices did not improve adherence among non adherent patients
Woodhanet al., 2017 ^[39]	Randomisedcontrolled trial	N= 30, 10 person dropout Duration = 2 week	Researcher explained how to fill in all antihypertensive medication into the intelligent pill box and provide manual and explain how to use the pill box to participants	Intelligent pill box improved medical adherence among Thai elderly hypertension patients in rural area.

7. Smart App

Currently, nearly over 1, 50,000 health apps accessible for download in different app Stores.^[40]The consequences with regard to usability of a commercially accessible app for hypertension was originate to be of bad condition as of high

risk of bias or the not have of in sequence regarding the sampling procedure and collection and closure to clearly report the investigate aims, design, duration, and outcome rate as well as high attenuation rate.^[41]

Table7: Studies involving Smart appas the means of intervention.

Authors/ year	Designs	Participant intervention	Interventions	Effects/ Outcomes
Guo et al., 2017 ^[41]	cluster randomized design pilot study	N=113 Mean age= 67.4 years; 57.5% were male, Duration: 69 days	mAF App	Quality of life scores were significantly increased in the mAF App versus usual care
Emilio Marquez et al., 2017 ^[42]	Randomized controlled trial	Duration 12months	AlerHTAApp Adherence was measured by MEMS	Patients favour the pharmacological therapeutic adherence and improve the percentage of hypertensive patient control.
Morrissey et al., 2018 ^[43]	Qualitative descriptive study	Focus groups centred on usability and acceptability	MiBP app	Patients perspective on smart phone apps were development of digital competence, rules of engagement and sustainability of these technologies were identified

8. Audio and Video Tape

Studies conceded out on pharmacist-run interventions via low health literacy flashcards and smart phone-activated reply (QR) bar-coded educational flashcard tape to enhance adherence to medication regimen and disease state understanding. Low health literacy prescription and disease limitation flashcards, which were furthermore untaken as QR-coded online videos, were intended

for the intervention patients. The outcome was the discrepancy in medication compliance at 180 days after pharmacist intervention compared with the control group, who were matched on the basis of co morbidity conditions, besieged medications, and medication class. Medication compliance was measured by means of a personalized Pharmacy superiority Alliance percentage of days covered (PDC) calculation. This conclude

that the manager of flashcards and QR-coded prescription bottles for drug and disease state education is an innovative tactic of improving adherence to diabetes, hypertension, and heart failure medications in a low-health literacy serene population.^[44] Internet-based interventions (e-counselling) also have the potential to deliver a wide range of preventive counselling services. The peak enormity

of blood pressure reduction has been found for interventions that lasted 6 months or longer which used 5 or further behaviour modification techniques and delivered health messages proactively. Imminent studies are desired to evaluate the contribution of specific intervention components in order to begin a superlative training e-counselling protocol that is effective in reducing blood pressure.^[45]

Table8: Studies involving Audio and Video Tapes the means of intervention.

Authors/Year	Designs	Participants intervention	Intervention	Outcome
Denise L. Yeung et al., 2017 ^[44]	Prospective, matched, quasi-experimental design	N=68 Duration:180 days	QR-coded online videos, flash cards.	In a low health literacy use of flash cards and QR coded online videos are innovation way increasing adherence
Sam Liu et al., 2013 ^[45]	randomised control trials	6months	Internet-based e-counselling	Internet based interventions was associated with significant decrease in blood pressure SBP-3.8mmHg and DBPBY 2.1mmHg with an 8% reduction in stroke mortality and 5%reduction in coronary heart disease

CONCLUSION

In this review authors have tried to collect research evidences of various popular approaches which are being used in the current practices. Traditional self-monitoring patients showed lower medication adherence, tele-nursing was originating to be further effective compared to self-monitoring method. Triple combination pill and fixed dose achieved a target BP. Cost of the monitors and the challenges of integrating their adherence data into clinical care are the barriers to their routine use outside of the research setting in electronically monitored adherence. The use of pill boxes resulted in clinically considerable reductions in systolic BP as well as an increased number of patients meeting prescribed BP goals.

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