Intervention Enhancing Medication Adherence in Stroke Patients: An Integrative Review

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ABSTRACT

Objective: This review aimed to systematically identify and analyze randomized controlled trials (RCTs) reported in the literature that were related to interventions targeted at enhancing medication adherence in stroke patients.

Materials and Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) system was applied to present the process flow, including study identification, screening, exclusion, and inclusion. The PubMed electronic database was searched, and the reference lists of relevant studies were reviewed from 2015 until 2020 to identify relevant RCTs.

Results: The results identified nine relevant RCTs, which included a medication-taking reminder mobile application (Medisafe), health empowerment interventions, telehealth education, and motivational interviews as the medication adherence enhancement interventions that have been most often used in the past five years. Furthermore, these RCTs mainly aimed to improve patients' medication adherence, physical activity, and clinical outcome, such as blood pressure and high-density lipoprotein cholesterol.

Conclusion: This integrative review has implications for the heightened recognition of the necessity for interventions aimed at enhancing patients' adherence to their medication, and that could be applied in clinical practice.

Keywords: Integrative Review; Medication Adherence Intervention; Stroke; Nurse (Siriraj Med J 2021; 73: 429-444)

INTRODUCTION

Stroke is a leading cause of mortality and disability globally.[1] In 2016, there were 5.5 million deaths and 116.4 million Disability-Adjusted Life Years (DALYs) lost due to stroke. Although age-standardized mortality rates have significantly fallen from 1990 to 2016, the stroke burden remains high.[2] Patients with a history of stroke have a risk of recurrence, ranging from 1.8% within one month to 43% within 5 years.[1] The mortality rate in the beginning stage of recurrent stroke is 56.2%, which is higher than for the first stroke.[1] Hence, critical improvements in the secondary prevention of stroke are required to decrease these risks, and there is a particular need to reduce the severity and mortality from stroke.[3,4] Adherence to stroke medication is considered critical to preventing the recurrence of stroke[5], but is often sub-optimal in many stroke survivors. Antihypertensive therapy, cholesterol reduction with statins, antiplatelet agents, or the treatment of atrial fibrillation with oral anticoagulants are all instances of evidence-based secondary stroke prevention medication.[6] Previous research has stated that management in combination with preventive medication could reduce the recurrence of ischemic events by about 75%.[7,8] However, approximately 50% of chronic disease patients do not adhere to their medical therapy[9,10], and this lack of adherence to medication

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dramatically impacts their health outcomes.[11] In the United States, general medication nonadherence is estimated to be responsible for roughly 125,000 deaths per year, at least 10% of hospitalizations, 23% of nursing-home admissions[11], and a substantial increase in morbidity and mortality.[12-14] For stroke patients, a previous study showed that about one-third of stroke survivors are considered to be nonadherent to their medication.[15]

Various interventions have been proposed and implemented to enhance patient adherence to medication, such as behavior therapy and the dissemination of information materials related to the importance of medication adherence.[16-20] Moreover, a previous study suggested that utilizing functional interventions in daily practice and management for both professionals and patients could be most promising for facilitating greater medication adherence.[21] Nevertheless, research, including stroke patients' preferences for medication adherence intervention, is profoundly lacking. A literature review was conducted on this subject, but we found no reported studies in which stroke patients were participants among the five meta-analyses and systematic reviews that we found and that covered 217 innovative studies.[9,11,14,18] Therefore, it was decided to perform an integrative review to identify and analyze medication adherence interventions in stroke patients. Specifically, it was decided to concentrate on summarizing these studies and the effect of different medication adherence interventions on the medication adherence of stroke patients. The following questions were identified to drive this integrative review:

1) What kinds of interventions and theoretical frameworks used for medication adherence interventions in stroke patients are reported across studies?

2) What effects do the different types of interventions have on the medication adherence of stroke patients?

MATERIALS AND METHODS

Identification of relevant studies

In this review, the PubMed electronic database was searched, and the reference lists in relevant studies were reviewed to identify randomized controlled trials (RCTs) reporting interventions for enhancing medication adherence in stroke patients. The following combined search terms were utilized: (***Stroke OR cerebrovasc* disorders OR cerebrovasc* disease OR cerebrovasc* accident OR brain isch?emi* OR isch?emi* cerebral attack OR brain attack OR intracranial h?emorrhage* OR CVA) AND (Medication Adherence OR Medication Nonadherence OR Medication Noncompliance OR Medication Persistence OR Medication Compliance OR Medication Non-Compliance)***. The detailed search strategy is shown in Table 1. The search phrases were used according to the fundamental guidelines of the database. Moreover, the authors reviewed the reference lists of the relevant literature, and one additional article was identified. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[22] system was applied for the process flow, including the identification, screening, exclusion, and inclusion of the literature studies (Fig 1). The inclusion criteria, as well as exclusion criteria for eligible studies, are shown in Table 2.

Study selection

First, the researcher screened the titles and abstracts of the qualified studies. Subsequently, the full text was also assessed to decide whether or not it was relevant to the present study. Inclusion criteria were implemented to guarantee that only studies considered relevant to the study objective were included. Similarly, exclusion criteria were utilized to screen out literature not affiliated with a review (Table 2). A literature review paper matrix was designed (Supplementary Table 1), which included the following data for each study: references, countries, and duration of intervention, target population, sample size, problem and purpose, theoretical framework, intervention details, medication adherence measures (reliability, validity), methodological problems, key findings, and implications.

RESULTS

Search results and description of the studies

Fig 1 shows that 25 references were classified throughout the initial search (one was included through a list of references searched because of the study's relevance[23]), of which 17 articles were excluded in the title and abstracts screening phase by following the inclusion and exclusion criteria (Table 2), leaving 9 articles that qualified for the full-text screening.

Table 3 shows the included RCTs, which were published between 2015 and 2018 and were conducted in 4 countries, namely China (n = 3), United States (n = 3), Pakistan (n = 2), and New Zealand (n = 1). The research duration reported varied across the studies (from the enrollment to the final assessment of one participant), whereby 4 studies were performed over 3 months, 3 studies had a duration of between 3 months and 6 months, and 2 RCTs involved studies over more than 6 months. The target populations in the included studies were individuals with stroke, including ischemic stroke (n = 5), non-specified subtypes of stroke (n = 3), hemorrhagic stroke (n = 1), transient ischemic attack (n = 1), and hypertensive patients (n = 1), which were

TABLE 1. Search strategies.

Database	Search	Search String
PubMed	1	(((((((("Stroke"[MeSH Terms] OR "Stroke"[Text Word] OR "cerebrovascular"[All Fields]) AND ("disease"[MeSH Terms] OR "disorders"[Text Word])) OR "cerebrovascular"[All Fields]) AND ("disease"[MeSH Terms] OR "disease"[Text Word])) OR "cerebrovascular"[All Fields]) AND ("accidents"[MeSH Terms] OR "accident"[Text Word])) OR ("brain"[MeSH Terms] OR "brain"[Text Word])) AND (("cerebrum"[MeSH Terms] OR "brain"[MeSH Terms] OR "cerebral"[Text Word]) AND ("attack"[All Fields] OR "attacked"[All Fields] OR "attacker"[All Fields] OR "attacker s"[All Fields] OR "attackers"[All Fields] OR "attacking"[All Fields] OR "attacks"[All Fields]))) OR "Stroke"[MeSH Terms] OR ("intracranial"[All Fields] OR "intracranially"[All Fields]) OR ("Stroke"[MeSH Terms] OR "CVA"[Text Word])
	2	("medication adherence"[MeSH Terms] OR Medication Adherence[Text Word]) OR ("medication adherence"[MeSH Terms] OR Medication Nonadherence[Text Word]) OR ("medication adherence"[MeSH Terms] OR Medication Noncompliance[Text Word]) OR ("medication adherence"[MeSH Terms] OR Medication Persistence[Text Word]) OR ("medication adherence"[MeSH Terms] OR Medication Compliance[Text Word]) OR ("medication adherence"[MeSH Terms] OR Medication Non-Compliance[Text Word])
	3	1 AND 2

TABLE 2. Study criteria.

	Inclusion	Exclusion
1	Adult patients (18 years or older)	Stroke as a complication
2	Diagnosis of stroke (including ischemic stroke, hemorrhagic stroke, or transient ischemic attack)	Studies including children or adolescents under 18 years old, adults living in a nursing home, or the hospital who received the assistance with the medication adherence intervention
3	A randomized controlled trial aimed at improving medication adherence published from January 1, 2015, to December 31, 2020	Conference proceedings, abstracts, protocol, pilot study, and review articles
4	Described in the English language	Targeted only caregivers of stroke patients
5	Included an outcome measure of medication adherence such as adherence to combination therapy guide, elicitation of compliance and adherence behaviors questionnaire, medication adherence rating scale, medication event monitoring system, or patient medication adherence questionnaire	

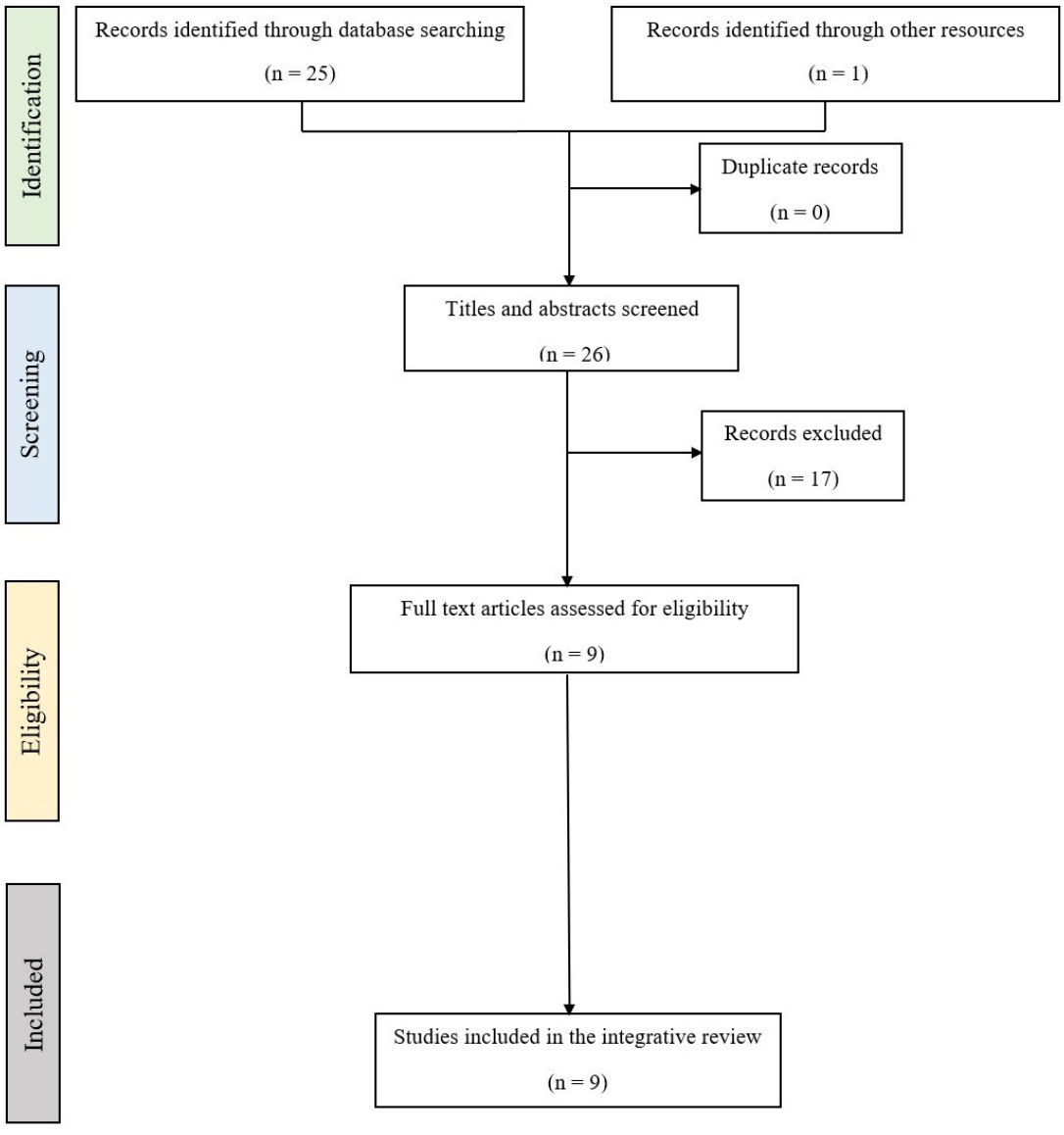

Fig 1. Flow chart diagram displaying the selection method of qualified studies.

included because of the study relevance from the bibliography search. The most commonly reported control and the experimental group sample sizes were >50 to 100 (n = 3).

Interventions enhancing medication adherence in stroke patients

Intervention and purpose

Medication-taking reminder mobile applications (e.g., Medisafe), health empowerment interventions, telehealth education, and motivational interviews are the medication adherence enhancement intervention that has been most often used in the past five years. Nevertheless, Medisafe has never been used in stroke patients before.[23] Furthermore, this review found that interventional studies mainly aim to improve medication adherence, physical activity, and clinical outcomes (blood pressure, high-density lipoprotein cholesterol, etc.).[23-31]

Theoretical framework

In this review, the theory of health empowerment[24], self-efficacy theory[24], guidelines for the secondary prevention of ischemic stroke and transient ischemic attack[25,26], the health belief model[27,30], and social cognitive theory[30] were applied to guide the interventions for enhancing medication adherence in stroke patients (Table 3), while 4 out of the 9 RCTs did not specify a theoretical framework.[23,28,29,31] The health belief model (2 out of 2) and guidelines for the secondary prevention of ischemic stroke and transient ischemic attack (2 out of 2) were identified as the most prominent and significant determinants of medication adherence compared to the other frameworks. Only 1 study used the social cognitive theory as a framework, and medication adherence and blood pressure as the clinical outcomes in this study were significantly improved after the intervention.[30] Regarding the theory of health

TABLE 3. Overall characteristics of the included studies.

Variables		Count	
Year			
2018[23,27,29,31]		4	
2017[26]		2	
2016[24,25]		1	
2015[28,30]		2	
Countries			
China[25-27]		3	
United States[23,24,31]		3	
Pakistan[29,30]		2	
New Zealand[28]		1	
Duration of intervention			
0 – 3 months[23,27,29,30]		4	
> 3 – 6 months[24,25,31]		3	
> 6 – 12 months[26,28]		2	
Target population#			
Ischemic stroke[24-27,30]		5	
Non-specified subtype of stroke[28,29,31]		3	
Hemorrhagic stroke[24]		1	
Transient ischemic attack[31]		1	
Hypertension*[23]		1	
Theoretical Framework##			
Unspecified[23,28,29,31]		4	
Health Belief Model[27,30]		2	
Guidelines for the Secondary Prevention of Ischemic Stroke and Transient Ischemic Attack[25,26]		2	
The theory of health empowerment[24]		1	
Social Cognitive Theory[30]		1	
Self-efficacy Theory[24]		1	
Medication adherence measures			
The 8-item Morisky medication adherence scale (MMAS-8)[23,29,30]		3	
The 4-item Morisky medication adherence scale (MMAS-4)[24]		1	
Modified health behavior scale[25]		1	
The proportion of medication-taking was compared between the control and intervention groups[26]		1	
The Health Promoting Lifestyle Profile II[27]		1	
The Tablets Routines Questionnaire (TRQ)[31]		1	
Asking whether (in the past seven days) participants had taken all of their medication as prescribed. Moreover, patients were asked to indicate the number of doses/pills missed, if they just forgot (yes/no), the reason for the missed dose(s), and to provide detail if side effects were noted[28]		1	
Sample (n)			
Control (C)	**Experimental (E)**	**C**	**E**
0 – 25[31]	0 – 25[31]	1	1
> 25 – 50[25]	> 25 – 50[25]	1	1
> 50 – 100[27,29,30]	> 50 – 100[27,29,30]	3	3
> 100 – 200[24,28]	> 100 – 200[24,28]	2	2
> 200 – 300[23]	> 200 – 300[23]	1	1
> 300[26]	> 300[26]	1	1

#One study may consist of > 1 target populations
##One study may apply > 1 theoretical framework
*This study was included through other resources because of the study's relevance

empowerment and self-efficacy theory, although there was no statistical difference in medication adherence between the intervention and control groups in the studies that used these frameworks, other components, such as self-efficacy in illness management and self-management behaviors, were reported to be statistically significant.[24]

Medication adherence measurements

Six studies used different medication adherence report scales with acceptable reliability and validity to measure the medication adherence, while the other 3 RCTs did not provide this information (Table 3). The 8-item Morisky medication adherence scale (MMAS-8) (reliability: α = 0.83, validity: 93% sensitivity, 53% specificity) (n = 3) was often used to evaluate the medication adherence[23,29,30], followed by the 4-item Morisky medication adherence scale (MMAS-4) (reliability: α = 0.55, average item-test correlation: 0.65) (n =1)[24], modified health behavior scale (content validity index: 0.85, reliability: α = 0.878, the split-half reliability: 0.801) (n = 1)[25], and the Health Promoting Lifestyle Profile II scale (reliability: α = 0.853, split-half reliability: 0.781, test-retest reliability: 0.845) (n = 1)[27], respectively.

DISCUSSION

Although the prevalence of stroke is on the rise globally, medication can help prevent future strokes, and hence medication adherence is critical for preventing future strokes. However, the medication adherence rate is not at a satisfactory level.[28,29] The present integrative review found that medication-taking reminder mobile applications, such as Medisafe, have, to the best of our knowledge, not yet been used to improve medication adherence and clinical outcome in stroke patients.[23] Although the literature review revealed a previous interventional study that proposed the use of short message service (SMS) reminders to improve patients' medication adherence, there were limitations reported with this system; for example, SMS messages may not be received by patients if they provide an incorrect contact phone number, and also, as SMS is a one-way communication system, there is no guarantee that patients will rigorously comply with the treatment.[32,33] The use of reminders can though, provide a solution for some patients, mostly those with unintentional nonadherence, such as patients willing to take medicine but who may forget or miss the proper time.[34] The research explained that 22% - 73% of patients in diverse populations regularly reported forgetting to take medication, which is the most frequently cited reason for nonadherence in a number of studies.[35-44] Accordingly, a simple intervention such as Medisafe seems to perform well in daily practice and is comfortable for both patients and healthcare professionals to handle and adapt this intervention to prevent instances of nonadherence to medication.

The included studies' key strengths, namely for the RCTs, in this review, need to be reported. First, in this integrative review, a total of 9 RCTs were included. These studies had followed the design principles for randomized controlled trials, including randomly assigning participants to each group to ensure an equal chance of participation (minimized selection bias and sampling error). Moreover, RCTs display a higher degree of confidence in causal relationships than other research designs, thus increasing such a study's internal validity.[45-48]

Furthermore, the previous literature suggested that dropout rates can be expected to be less than 15% to 20% for RCTs.[49] In this review, 7 out of the 9 RCTs showed dropout rates of <20%, with the reasons and time of dropping out varying, including during the intervention (e.g., dead, declined to continue) and during the study assessment period (e.g., lost to follow-up). The dropout rate is an essential issue because it can threaten a study's' internal validity (e.g., by changing the random composition of the groups and their equivalence), external validity (e.g., by decreasing the generalizability of the RCT findings to only those who remained in the study), and statistical validity (e.g., by diminishing the sample size and the statistical power to detect differences between the intervention and control groups). Accordingly, most RCTs in this review seemed to have minimized these threats as acceptable dropout rates were reported.[50,51] However, another 2 RCTs had dropout rates of 39.38%.[28] and 26.32%[31], so improving the retention rates by following the appropriate guideline for additional investigation is required.

Nevertheless, there were also some limitations found in the included RCTs in this review that need to be noted. Self-reporting, the generalizability of the findings, and study recruitment issues need to be considered. First, 6 of the RCTs used various different medication adherence report scales with the reliability and validity reported, while the other 3 RCTs used medication adherence report scales without reporting the reliability and validity. Most of the included medication adherence reported scales in this review showed acceptable reliability and validity. However, most of them involved self-reporting, which is simple, inexpensive, and practically useful in the clinical setting, but is subject to certain limitations, such as being susceptible to errors, with the increase in time between visits particularly needing to be considered as this can threaten the study's internal validity.[52] On the other hand,

direct methods of measuring medication adherence, such as measuring medication concentration in the blood or urine and detecting biological markers in the blood, have several disadvantages too, such as typically being expensive and labor-intensive. Nevertheless, in some situations, this approach is practical; for instance, evaluating the serum level of antiepileptic drugs (phenytoin, valproic acid).[52] In summary, there is no gold standard to measure medication adherence[53,54], and the choice may depend on the research objective, funding, study population, and setting. Researchers need to consider the measurement carefully, and importantly, any error or bias that threatens the study validity should be minimized.

Second, the generalizability of the RCTs' findings should also be considered as a limitation since most of the RCTs were carried out in a specific unit and specific stroke population. For example, Wan et al.'s study[25] performed RCTs in 3 units of 2 major hospitals, thus limiting the generalizability of the findings to the whole population. Moreover, another study included only patients diagnosed with mild ischemic stroke, while severe stroke patients were excluded, which could have led to selection bias, thus limiting the generalizability of the results.[27]

Finally, study recruitment issues also need to be mentioned as a limitation of the included RCTs. With the ongoing development of technology, more people can now access the internet; however, some people still cannot or do not. In this regard, one study recruited participants entirely online[23], citing literature that indicated that more than 50% of patients use the internet for medical information.[23] Hence, the significant improvement in medication adherence or other related outcomes in either the control or intervention group may have been due to the interventional design itself or extraneous variables, like information obtained from the internet, and so this study's results may not be generalizable to other populations with different sociodemographic characteristics, such as those who cannot access the internet.

LIMITATIONS

There are several limitations in this integrative review itself to note. First, the researcher searched only the PubMed electronic database and relevant bibliographies, which could possibly lead to a limitation of this study's findings and generalizability. Additionally, this review's primary purpose was to systematically identify and analyze reported randomized controlled trials (RCTs) for interventions aimed at enhancing medication adherence in stroke patients. Therefore, the researcher solely included RCTs involving a medication adherence intervention. As it included only one type of study design, this may lead to a limitation of the research findings. In any further study, it is suggested that other types of study design that involve this kind of intervention should be included, such as quasi-experimental studies, which may increase the integrative review's uniqueness. Moreover, since the researcher did not include studies from the "gray" literature, such as conference proceedings or abstracts, this may introduce a publication bias. Finally, only English-language studies were included. Because of this, RCTs reported in other languages that also aimed to improve medication adherence in stroke patients may have been missed and hence omitted.

CONCLUSION

Medication adherence can lead to diminished healthcare service use, improved patient quality of life, and decreased healthcare expenses.[55-57] The present integrative review has implications for the heightened recognition of the necessity of interventions aimed at enhancing patients' adherence to their medication, and that could be applied in clinical practice. For example, there is the possibility of using medication-taking reminder mobile applications (such as Medisafe) to improve medication adherence and clinical outcomes among stroke patients, yet this innovation has never been used before among stroke patients. In the future, health care providers may utilize this innovation to promote high-quality stroke care in clinical practice. A previous systematic review revealed that four studies used such a reminder system, three of which reported a significant positive impact on medication adherence.[18] One study into the medication adherence of HIV patients receiving message reminders found a significant difference in favor of those receiving message reminders.[18] Likewise, one asthmatic study found that the adherence rate of asthma patients who received daily message reminders was higher than those who were not reminded.[58] Therefore, the use of Medisafe appears to be a potential tool for assisting medication adherence in patients with stroke, albeit some questions arise as an outcome of this integrative literature review related to its use, specifically: 1) Can Medisafe improve medication adherence in stroke patients? 2) Can Medisafe improve clinical outcomes, such as blood pressure, in stroke patients?

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Supplementary Material: Supplementary materials (Supplementary Table 1) related to this article can be accessed by contacting the corresponding author (suebsarn25@gmail.com).

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SUPPLEMENTARY TABLE 1. The literature review paper matrix.

References, countries, and duration of RCTs	Target population, sample size (n)*	Problem & Purpose	Theoretical Framework	Intervention details	Medication adherence measures (reliability, validity)	Methodological problems: Threats to study validity (Critical Analysis)	Key Findings	Implications
(**1**)[1] The United States 3 months	Hypertensive **Experimental (E):** 209 **Control (C):** 202 **Note:** the author included hypertensive patients because it is the most relevant study; Medisafe never used in stroke patients. **- Dropout rate of 12%**	- Medication non-adherence estimates for 50% of uncontrolled hypertension. Smartphone applications (apps) that aim to improve adherence are broadly available but have not been rigorously evaluated. - This study aimed to determine if the Medisafe smartphone application increases self-reported medication adherence and blood pressure control.	Unspecified (Study protocol provided)	**E:** In this group, participants were guided to download and use the Medisafe application, including medication-taking reminder alerts, adherence reports, and optional peer support. **C:** N/A **Randomly assigned** The author attempted to enroll at least 390 patients to have 80% power to detect a 5 mmHg. the difference in systolic blood pressure between treatment arms, with an α of 0.05 (even with a 20% loss to follow up or a standard deviation of up to 17 mm Hg)	The 8-item Morisky medication adherence scale (MMAS-8) **Reliability:** Chronbach's alpha 0.83 **Validity:** (93% sensitivity, 53% specificity)	- The recruitment was performed entirely online, in which the literature showed that more than 50% of patients use the internet for medical information. These RCT results may not be generalizable to other populations of individuals with poorly controlled hypertension, who may have different sociodemographic and comorbidity characteristics than the patients in our study participants. - The researcher used home blood pressure monitors to evaluate blood pressure outcomes, in which different participant may measure their blood pressure differently. This can threaten internal validity (measurement). - Self-management	- After 12 weeks, the mean (SD) score on the **MMAS improved by 0.4 (1.5) among intervention participants** and remained unchanged among controls (between-group difference: 0.4; 95% CI, 0.1-0.7; P = 0.01). ^ - After 12 weeks, the mean (SD) systolic blood pressure decreased by 10.6 (16.0) mm Hg among intervention participants and 10.1 (15.4) mm Hg among controls (between-group difference: −0.5; 95% CI, −3.7 to 2.7; P = 0.78). ≠	- Patients randomized to use a smartphone application had a small improvement in self-reported medication adherence among poorly controlled hypertension patients but no change in systolic blood pressure than controls. Hence, its advantage and other mobile health interventions on clinical outcomes remain to be established. - The recruitment method should be improved. - The way of blood pressure measuring should be improved.
(**2**)[2] The United States 6 months	Ischemic stroke, Hemorrhagic stroke **E:** 105 **C:** 105 **- Dropout rate of 16.7%**	- After a stroke, self-management is a challenge because of multifaceted care needs and complex disabling consequences that further barrier patient participation.	- The theory of health empowerment - Self-efficacy Theory	**E:** Usual care (the ambulatory rehabilitation schedule) + small group sessions (establish a partnership with the nurse facilitator for stroke self-management to begin personal goal setting and action planning) +	The 4-item Morisky medication adherence scale (MMAS-4) **Reliability:** Chronbach's alpha 0.55 **Average item-test correlations:** 0.65	behavior was assessed using self-report. This might have led to over-reporting of what was seen as desired behavior by the participants. - The baseline characteristics between	**- Medication adherence. ≠** - Self-efficacy in illness management 3-month and 6-month. ^ - Self-management behaviors at all follow-up time points. ^	Stroke patient empowerment intervention could be combined into the ambulatory rehabilitation phase. It would become more plausible for continuing professional support

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References, countries, and duration of RCTs	Target population, sample size (n)*	Problem & Purpose	Theoretical Framework	Intervention details	Medication adherence measures (reliability, validity)	Methodological problems: Threats to study validity (Critical Analysis)	Key Findings	Implications
		- This study aimed to investigate the effects of the Health Empowerment Intervention for Stroke Self-management (HEISS) on stroke patients' self-efficacy, self-management behavior, and functional recovery.		biweekly telephone follow-up calls (encourage and commend participants on their actions for positive changes and to provide problem-solving skills to overcome any perceived barriers that participants encountered). **C:** Usual care only. **Randomly assigned**	(internal consistency reliability) **Validity:** good sensitivity and moderate specificity in identifying nonadherent individuals	those who have completed data collection and those who have dropped-out were nearly similar. The intervention's effects might be overestimated if dropped out cases had better outcome measures or vice versa.		to aid stroke patients in understanding responsibility for and participating in stroke self-management in a home setting.
(**3**)[3] China 6 months	Ischemic stroke **E:** 40 **C:** 40 **- Dropout rate of 12.1%**	- Adopting healthy behaviors is critical for secondary stroke prevention. However, compliance often decreases with time after hospital discharge, yet few studies have investigated programs promoting long-term adherence to health behaviors. - This research proposed to evaluate the effectiveness of a guideline-based, goal-setting telephone follow-up program for patients with ischemic stroke.	Guidelines for the Secondary Prevention of Ischemic Stroke and Transient Ischemic Attack	**E:** The intervention group consisted of predischarge education and three goal-setting follow-up sessions conducted by telephone. **C:** The control group gained the usual stroke education, including freely available educational brochures on understanding stroke and cutting stroke risk. **Randomly assigned**	Modified health behavior scale **Content validity index:** 0.85 **Cronbach's α (reliability):** 0.878 **The split-half reliability:** 0.801 (a measure of internal consistency — how well the test components contribute to the construct that's being measured)	- The information regarding health behaviors and medication adherence was self-reported, so memory errors and expectation bias may have influenced the result. - The study was carried in 3 units of 2 major hospitals, limiting the generalizability of findings to the whole population. - Eleven patients meeting the inclusion criteria declined to participate, suggesting that better recruitment methods are expected.	- Six months after discharge, patients in the intervention group exhibited **significantly higher medication adherence** than patients in the control group. ^ - Physical activity, nutrition, low-salt diet adherence, blood pressure monitoring, smoking abstinence, unhealthy alcohol use, and modified Rankin Scale (mRS). ≠	The intervention improved only medication adherence at six months post-discharge. These results indicate a need for more effective strategies to help stroke patients achieve guideline-recommended targets for health behaviors

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(**4**)[4] China 1 year	Ischemic stroke **E:** 613 **C:** 574 **- Dropout rate of 6.9%**	- Antiplatelet is the treatment of the first choice for long-term secondary prevention of vascular events. Although ischemic stroke patients are still at significant risk for recurrence; roughly one-third of stroke survivors will have a recurrent vascular event within five years. - This RCT proposes to evaluate a health promotion program on medication adherence to antiplatelet therapy among ischemic stroke patients.	Guidelines for the Secondary Prevention of Ischemic Stroke and Transient Ischemic Attack	**E:** The daily 30 minutes of training sessions for three days aimed to develop patients' awareness and improve their medication adherence. The physicians called the patients at one, three, and six months after hospital discharge to monitor progress and offer secondary prevention guidance. **C:** Usual stroke management programs. **Randomly assigned**	The proportion of medication-taking was compared between the control and intervention groups. **Reliability:** N/A **Validity:** N/A	- The data collected are self-reported; participants likely over or underrated their skills and knowledge when responding to survey items. - No reliability and validity of medication adherence measurement were reported.	- After a one-year follow-up, **the proportion of patients who took the antiplatelet therapy increased significantly** in the intervention group, reaching 73.2%, with a pre-post difference between two arms of 22.9% ($P < 0.01$). ^ - The proportion of patients with an awareness of antiplatelet therapy significantly increase (24.4%, $P < 0.01$). ^	The health promotion program showed a positive impact on awareness of and adherence to antiplatelet therapy, which can be scaled up to other resource-limited areas.
(**5**)[5] China 3 months	Ischemic stroke **E:** 80 **C:** 78 **- Dropout rate of 9.2%**	- The health behaviors of hypertensive stroke patients in China are not satisfactory. Because unimodal programs were inefficient for improving blood pressure control in stroke patients, recent efforts are directed at multi-modal interventions.	Health Belief Model	**E:** Usual care + face-to-face and telephone health belief education, a patient calendar handbook, and weekly automated short-message services. **C:** Usual care only (health education during hospitalization, a stroke prevention handout, follow-up by doctors	The Health Promoting Lifestyle Profile II **Cronbach's α (reliability):** 0.853 **The split-half reliability:** 0.781 **Test-retest reliability:** 0.845	- The program is considered proper only for patients diagnosed with mild ischemic stroke. Severe stroke patients were excluded; this can lead to selection bias. - Health behavior information was self-reported and subject to expectation bias (Hawthorne effect).	**- Medication adherence. ^** - Better health behaviors for physical activity, nutrition, low-salt diet. ^ - Decreased systolic blood pressure and increased blood pressure control rate. ^	At three months, the Comprehensive Reminder System's use based on the Health Belief Model produced a positive outcome of most health behaviors and blood pressure control. Continued implementation of this intervention protocol

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		- This study aimed to test the effect of a Health Belief Model Comprehensive Reminder System on health behaviors and blood pressure control in hypertensive ischemic stroke patients after the occurrence and hospital discharge.		at the outpatient department, and telephone follow-up by nurses at one week and one month after discharge). **Randomly assigned**				is guaranteed to determine the long-term effect.
(**6**)[8] New Zealand 12 months	Unspecified (excluding subarachnoid hemorrhage) **E:** 119 **C:** 115 **- Dropout rate of 39.38%**	- The literature shows that stroke recurrence rates are high (20%–25%) and have not declined over the past three decades. - This study aimed to examine the effectiveness of motivational interviewing (MI) for reducing stroke recurrence. Medication adherence and lifestyle change will be measured.	Unspecified	**E:** The intervention group received four motivational interview sessions at 28 days, 3, 6, and 9 months post-stroke. Sessions were audio-recorded. The primary interview was administered face-to-face; subsequent interviews were conducted by telephone. **C:** Usual care only. **Randomly assigned**	- Asking whether (in the past seven days) they had taken all of their medication as pre-scribed. - Patients were asked to indicate the number of doses/pills missed, if they just forgot (yes/no), the reason for the missed dose(s), and to provide detail if side effects were noted. **Reliability: N/A** **Validity:** The validity of self-reports was cross-checked with electronic medication dispense records where available, which suggests accurate reporting.	- Although medication adherence measured by self-reports is inexpensive and straightforward, and validated for use in clinical settings, it may have led to an overestimation of adherence. - The motivational interview's nature was not plausible to blind participants, which may have influenced self-report outcomes.	**- Self-reported medication adherence** at six months and nine months post-stroke. ^ - The change measures blood pressure and cholesterol. ≠	Motivational interview (MI) developed self-reported medication adherence. Other effects were nonsignificant, though in the direction of a treatment effect. Additional research is required to determine whether MI leads to improvement in other essential functioning (e.g., caregiver burden).

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(**7**)[7] Pakistan 3 months	Unspecified (stroke) + coronary artery disease **E:** 99 **C:** 98 **- Dropout rate of 9.64%**	- Medications can diminish stroke risk by 30% and Myocardial Infarction (MI) by 15%. Nevertheless, adherence, even in developed countries, is only around 50%. Health-based procedures can be an inexpensive and efficiently accessible tool to increase compliance and bridge the communication gap between health care providers and users. - This RCT aimed to develop and examined the effectiveness of a tailored health information technology-driven intervention: "Talking Prescriptions" to increase medication adherence in patients.	Unspecified	**E:** This group received daily Interactive Voice Response (IVR) call services regarding specific statin and antiplatelet, daily tailored medication reminders for statin and antiplatelet, and weekly lifestyle modification messages. **C:** N/A **Randomly assigned**	The 8-item Morisky medication adherence scale (MMAS-8) **Reliability:** (α = 0.83) **Validity:** (93% sensitivity, 53% specificity)	- Medication adherence was assessed using self-report; this might have led to overreporting. - This RCT did not study the effect of an intervention on improving patient clinical outcomes targeted for future larger-scale clinical trials.	The 8-item Morisky **medication adherence** scale. ≠	A phone-based medication adherence program was possible in settings with high volume clinics and low patient knowledgeability. Due to limited follow-up, the program did not achieve any statistically significant differences in adherence behavior as self—reported by the MMAS-8 Scale.

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(**8**)[8] Pakistan 2 months	Ischemic stroke **E:** 83 **C:** 79 **- Dropout rate of 19%**	- Mobile technology's effectiveness in improving medication adherence via customized Short Messaging Service (SMS) reminders for stroke has not been tested in low resource areas. - This study aimed to test the effectiveness of SMS on developing medication adherence in stroke survivors.	- Health Belief Model - Social Cognitive Theory	**E:** Usual care + received reminder SMS for two months that contained personalized, prescription tailored daily medication reminder(s), and twice-weekly health information SMS. **C:** Usual care only. **Randomly assigned**	The 8-item Morisky medication adherence scale (MMAS-8) **Reliability:** (α = 0.83) **Validity:** (93% sensitivity, 53% specificity)	- Medication adherence was assessed using self-report; this might have led to overreporting. - Participants who only have a telephone can participate in this study. Those who do not have may underrepresent, and this leads to selection bias.	**- The mean medication adherence score ^** - The mean diastolic blood pressure ^	The SMS intervention seems possible for clinical use in stroke survivors for improving adherence. Further investigations are needed to report on meaningful biologic outcomes like recurrent stroke, death, and disability.
(**9**)[9] The United States 6 months	Unspecified (stroke) + Transient Ischemic Attack **E:** 14 **C:** 14 **- Dropout rate of 26.32%**	- Stroke is the leading cause of disability, death, and health resource use among Americans. Self-management is a caring procedure that allows individuals to solve problems as they arise, practice new health behaviors, and gain emotional stability. Although several articles support self-management training for stroke survivors, there is limited data specific to young African Americans men.	Unspecified	**E:** Participants obtain self-management training, delivered in 1 individual and 4 group sessions (over three months). **C:** Usual care only. **Randomly assigned**	The Tablets Routines Questionnaire (TRQ) **Reliability:** N/A **Validity:** N/A	- Small sample size, limited duration, and research staff were not blind to the intervention assignment. - Using a one-time blood pressure assessment, including the possibility of elevation when a measurement is done in a clinical setting (white-coat hypertension) and underdetection (masked hypertension).	**- Medication adherence ≠** - High-density lipoprotein cholesterol ^ - Glycosylated hemoglobin ^ - Systolic blood pressure ^	The intervention was not capable of engaging all patients. Qualitative findings suggest that while the group format was highly acceptable, aspects of the program might be improved. More sessions might have been accommodating, supporting telephone attendance for those with travel or logistic difficulties.

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		- This study proposed to compare a self-management intervention (TargetEd MAnageMent Intervention [TEAM]) versus treatment as usual (TAU) to reduce stroke risk in African American (AA) men.						

RCTs Randomized Controlled Trials
N/A Not applicable
*Final analyzed
^ Outcome significantly improved after the intervention
v Outcome significantly worsened after the intervention
≠ Outcome unchanged after the intervention

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