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The interventions to improve medication adherence in coronary heart disease patient: A systematic review

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Abstract

Objective: **The clinical outcome and quality of life of CHD patients are greatly influenced by medication adherence. Non-adherence of CHD patients to treatment results in sub-optimal clinical outcomes and increasing costs. This study aims to describe effectiveness of the intervention to improve the medication adherence in CHD patients.**

Methods: **Systematic review methodology was used in this study. Scopus and PubMed were used to search the relevant article systematically. The outcome measured was medication adherence in coronary heart disease patients.**

Results: **Final screening was 31 articles that met the inclusion criteria in this study of 788 articles. Selection processes the article used the PRISMA guideline. Most of the articles (15 articles) use interventions that utilize information technology (IT) as known with m-health in the form of text messages, website, and smartphone-based applications in increasing medication adherence in CHD patients. The non m-health interventions developed are in the form of self-efficacy programs, monitoring and education by health workers or care workers, pharmacy care by clinical pharmacists, and the use of drugs in the form of multi-capsules. The results of most intervention with m-health can improve the medication adherence in CHD patient effectively. Education and motivation program by professional health care and multi-capsules also increasing the medication adherence in the intervention control. There was a decrease of medication adherence in some articles with long time follow-up that can be attention for the professional health care to manage the patient adherent.**

Conclusion: **Th medication adherence in CHD patient can be improve by various program. Modification of m-health and non m-health intervention can be resolved to increase the communication, motivation, and knowledge about medication adherence in CHD patients.**

Keywords: Artery disease, Cardiovascular, Education, Medication management, m-health

1. Introduction

One of the biggest causes of death in the world is cardiovascular disease, and it causes not only a large mortality rate but also a high rate of disability for sufferers. In 2019, 32 % or 17.9 million deaths in the world was caused by cardiovascular disease and 85 % was due to heart attack and stroke. There was 17 million premature death (under 70 years old) that related to noncommunicable disease; 38 % was caused by cardiovascular disease [1]. The most common type of cardiovascular disease is coronary heart disease (CHD), including myocardial infarction and angina. The mortality caused by CHD is greater than that from other chronic disease likely cancer and diabetes [2]. Treatment of CHD patients includes the treatment of chronic diseases in the form of drug use and lifestyle changes, where most CHD patients undergo secondary prevention treatment by minimizing the risk factors for recurring

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events. The problems, not achieving therapeutic targets for blood pressure and cholesterol levels in CHD patients, are caused by patients not complying with lifestyle change recommendations. As many as 20 % of CHD patients also stop using drugs, thereby increasing the risk factors for hospitalization as well as mortality and morbidity [3].

Antihypertensive, antiplatelet, anticoagulant and statin are classes of drugs used in the treatment of CHD. In addition, invasive procedures such as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) can also be an option for CHD treatment according to the patient's clinical condition. Healthy lifestyle support is very important as a form of non-pharmacological therapy in CHD patients. The clinical outcome and quality of life of CHD patients are strongly influenced by patient adherence to pharmacological and non-pharmacological treatment [4]. Medication adherence can be defined as measures or levels of adherence with treatment recommendations or prescriptions [5]. Another definition of medication adherence according to WHO is individual behaviour including taking medication, following diet and/or lifestyle changes by recommendations and agreements with health care providers. The level of medication adherence is influenced by five related aspects, namely the patient, disease, treatment, health care system and team and social economy [6].

Increasing medication adherence can be done in several ways through education and counselling by professional health workers. Each health worker can play a role according to their competence in a patient treatment management team. The use of information technology which is currently developing rapidly can also support monitoring patient treatment, for example mobile health (m-health). According to the Global Observatory for eHealth (GOe), the definition of m-health is the practice of medical and public health through the support of mobile devices such as cell phones, patient monitoring devices, personal digital assistants (PDAs) or similar wireless devices. Bluetooth technology, 3G and 4G telecommunications systems, global positioning system (GPS) and short message services (SMS) are also involved in the use of m-health [7]. Services of m-health have a broad scope in providing health services which includes electronic prescribing, patient medical records to text messages that remind patients to take medication [8].

This study aims to determine the programs to increase medication adherence in CHD patients and to see the effectiveness of these programs based on the results of the previous research using a systematic review method. A well-organized systematic review can provide good evidence for a variety of disciplines including health and drug use. The stages in a systematic review include preparation of research questions, determination of inclusion and exclusion criteria, search methods in databases, quality assessment, and statistical analysis up to the preparation of articles so that the manuscript of a systematic review can be published [9].

Abbreviation list

CHD	Coronary Heart Disease
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
IT	Information Technology
JBI	Joanna Briggs Institute
PICO	Patient, Intervention, Comparison, Outcome
MMAS	Morisky Medication Adherence Scale
MPR	Medication Possession Ratio
MEMS	Medication Event Monitoring System
PCI	Percutaneous Coronary Intervention
CABG	Coronary Artery Bypass Graft

2. Methods

This study was compiled in the form of a systematic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Evaluation of the results of health interventions is one of the purposes of a review that can be carried out using the PRISMA guide [10]. The results of the research or journals reviewed in this study are articles published between 2012–September 2023 with a search date of September 27, 2023. The article was identified by combining Medical Subject Headings (MeSH) and Boolean operators. The search keywords are “medication adherence” AND “coronary heart disease”. This review uses the PubMed and Scopus databases for an electronic systematic literature search. The language used in the reviewed articles is English. Processing of articles in this review uses the Mendeley reference manager to store article data and duplicate selection.

2.1. Study selection and quality assessment

The inclusion and exclusion criteria were used to select the articles in this study. The articles published in 2012–2023, measuring medication adherence as the outcome, can be assessed in full text, were written in English language, and free of charge are the inclusion criteria. The articles published less than period 2012–2023, qualitative study, incomplete data, protocol article, review article, clinical

guidelines, book chapter, letter to the editor, and economic evaluation study were excluded. The articles that met the inclusion criteria will include as the samples in this study. The articles were searched on electronic database and checked the duplicate by the two authors (AM and LA), then they screened the title, abstract, or both independently to determine which article would be assessed further. The discussion would be carried out if there was a different on the perception to decide whether the article was relevant to the purpose with the study or not. The assessment by the third author (LKD) used if there were discrepancies in the procedure. The critical appraisal tool was used to help to assess the quality of the article by the Joanna Briggs Institute (JBI). The tool was chosen because it was valid instrument to assess the quality of cohort and randomized controlled trial research methodologies [11]. The result of the JBI appraisal given by score that categorized article for high quality (>70%), medium quality (50–70%), and low quality (<50%) [12].

2.2. Data extraction

The team researchers extracted the data used the PICO method (patient or participant, intervention, comparison, outcome) [13]. The patient is an adult patient with a diagnosis of coronary heart disease, including myocardial infarction and acute coronary syndrome. The intervention used is the provision of therapy or treatment by health workers such as pharmacists, doctors, and nurses manually or by utilizing certain technologies that aim to increase adherence to the treatment of coronary heart disease patients. The outcome seen in this review is treatment adherence both in the form of primary and secondary outcomes. Outcome measurement can be carried out using medication adherence questionnaires, self-care, or databases in a technology system. The presentation of data extraction can be seen in Table 4.

3. Results

The total number of articles obtained from the results of literature searches through PubMed and Scopus was 789 articles. After screening for duplication as well as titles and abstracts, 154 full articles were reviewed according to predetermined inclusion criteria. The results were 31 articles that met the inclusion criteria. Figure 1 PRISMA diagram illustrates the entire article selection procedure. The result of article quality using JBI critical appraisal tool give score range 61,54–92,31 % for RCT design, 72,73–90,91 % for cohort design, and 100 % for quasi experimental design, so the article methodology was medium and high quality. Tables 1–3 represent the result of article quality assessment.

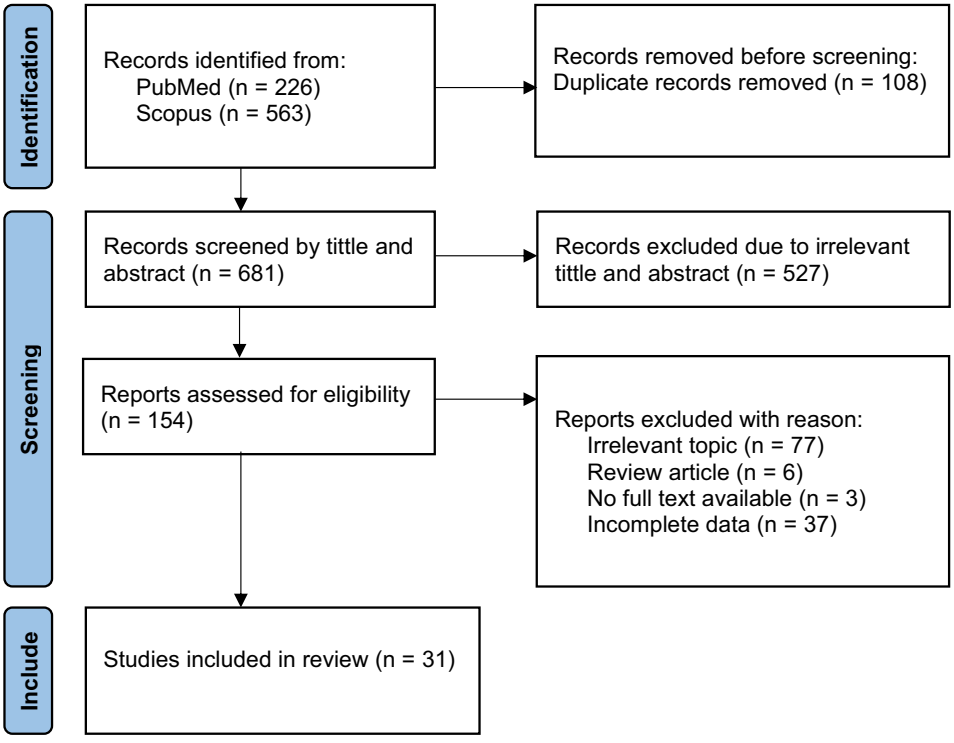

Fig. 1. PRISMA flow diagram of the screening and selection process.

Table 1. Quality assessment of randomized controlled trial design.

Author	Was true randomization used for assignment of participants to treatment groups?	Was allocation to treatment groups concealed?	Were treatment groups similar at the baseline?	Were participants blind to treatment assignment?	Were those delivering treatment blind to treatment assignment?	Were outcomes assessors blind to treatment assignment?
Ni et al., 2022	Yes	Yes	Yes	No	No	No
Gaudel et al., 2022	Yes	Yes	Yes	No	Yes	No
Park et al., 2014	Yes	Yes	Yes	No	No	No
Santo et al., 2018	Yes	Yes	Yes	No	Yes	Yes
Li et al., 2022	Yes	Yes	Yes	No	No	No
Ostbring et al., 2021	Yes	Yes	Yes	No	No	Yes
Bae et al., 2021	Yes	Yes	Yes	No	Yes	Yes
Maddison et al., 2021	Yes	Yes	Yes	No	Yes	Yes
Mariani et al., 2020	Yes	Yes	Yes	No	No	No
Xavier et al., 2016	Yes	Yes	Yes	No	No	No
Cao et al., 2017	Yes	Yes	Yes	No	Yes	Yes
Bruggmann et al., 2021	Yes	Yes	Yes	No	No	No
Calvert et al., 2012	Yes	Yes	Yes	No	No	Yes
Casper et al., 2019	Yes	Yes	Yes	No	No	No
Castellano et al., 2022	Yes	Yes	Yes	No	No	No
Chow et al., 2022	Yes	Yes	Yes	No	Yes	Yes
Ivers et al., 2020	Yes	Yes	Yes	No	No	Yes
Khonsari et al., 2014	Unclear	Unclear	Yes	No	No	Yes
Krackhardt et al., 2022	Yes	Yes	Yes	No	No	No
Lourenco et al., 2013	Yes	Yes	Yes	Yes	No	No
Putra et al., 2022	Unclear	Unclear	Yes	No	No	No
Rinfret et al., 2013	Yes	Yes	Yes	No	No	No
Wang et al., 2020	Yes	Yes	Yes	No	No	No
Wu et al., 2019	Yes	Yes	Yes	Yes	No	No
Xu et al., 2019	Yes	Yes	Yes	No	Yes	Yes
Yin et al., 2021	Yes	Yes	Yes	No	No	No
Yu et al., 2020	Yes	Yes	Yes	No	No	No
Sharma et al., 2016	Yes	Yes	Yes	No	No	No

Most of the research designs carried out were randomized controlled trials (RCT), only 3 articles with designs other than RCT, one article with quasi-experimental designs and two cohort articles design. Most of the research sites are in Asian countries, namely China, India, Nepal, Republic of Korea, Indonesia, Malaysia, and Thailand. Other data were also obtained from research in America, Australia, and Europe. Only one articles settings in Africa. The mapping number of studies in each country can be seen in Fig. 2.

Most articles that were obtained used information technology (IT) or mobile health in the form of sending interventions via website, text messages or mobile applications. Fifteen articles (48,39%) used the m-health program as a form of intervention. Other interventions are in non-IT form in the form of one article (3,26%) providing a self-efficacy program, nine articles (29,03%) with educational programs and follow-up by health workers and care workers, four articles (12,90%) in the form of providing pharmaceutical care by a clinical or community pharmacists and two articles (6,45%) providing several drugs in one form capsule (multi-capsules or polypill program).

There are several methods used to evaluate the outcome of medication adherence in this study. Nine articles used the Morisky Medication Adherence Scale 8 (MMAS-8) method to measure medication adherence, and of the nine articles there was two article that compare MMAS-8 with another method. The percentage of drug use and the electronic monitoring device Medication Event Monitoring System (MEMS) were used as comparison [14,15].

Another medication adherence evaluation method implemented was the percentage of drug use by comparing the number of drugs taken with the number of drugs prescribed. Six articles used the percentage method of drug use as an evaluation procedure. One article used a drug non-adherence score in the form of the Voils Medication Non-Adherence Extent Scale as a form of evaluation [16].

Were treatment groups treated identically other than the intervention of interest?	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?	Were participants analysed in the groups to which they were randomized?	Were outcomes measured in the same way for treatment groups?	Were outcomes measured in a reliable way?	Was appropriate statistical analysis used?	Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?	Total score (%)
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	84.62
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	92.31
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	84.62
Yes	Yes	Yes	Yes	Yes	Yes	Yes	92.31
Yes	Yes	Yes	Yes	Yes	Yes	Yes	92.31
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	92.31
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	No	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	92.31
Yes	Yes	Yes	Yes	Yes	Yes	Yes	84.62
Yes	Yes	Yes	Yes	Yes	Yes	Yes	69.23
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	84.62
Yes	Yes	Yes	Yes	Yes	Yes	Yes	61.54
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	84.62
Yes	Yes	Yes	Yes	Yes	Yes	Yes	92.31
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92
Yes	Yes	Yes	Yes	Yes	Yes	Yes	76.92

One article used data recorded in the system to determine patient medication adherence [17]. The Morisky scale used is not only MMAS-8, but there is one article that uses the Morisky Levin Green Scale [18] and Modified Morisky Scale [19] to evaluate medication adherence. The use of a self-report questionnaire can also be used to determine medication adherence as one of the variables, in this study the questionnaire Self-Care Coronary Heart Disease Inventory [20] and Self-Efficacy for Appropriate Medication Use Scale [21]. Recording made by health care workers on drug use sheets can also be an alternative in measuring medication adherence used in one article [22]. Medication Possession Ratio (MPR) which compares the number of drugs prescribed with the number of days missed and the day of obtaining the last drug can also be used to measure the level of medication adherence, where there are three articles in this study that use the MPR [23]. The medication adherence also can be measured by the medication refill that used in three articles [24–26]. All the instrument that used to measure the medication adherence as the outcome was reliable based on article quality assessment.

The size of the samples used in each article is very diverse, starting from the smallest (36 patients) and the largest (2632 patients). The total sample used from all articles was 13.527 patients, with an average sample size of 437 patients. The shortest medication adherence measurement endpoint was performed at 15 days and the longest was measured at 24 months after the intervention. The results of measuring medication adherence obtained using the percentage of drug use in all articles obtained more than 80 % for the intervention group. Articles that use the MMAS-8 score show that after being given the intervention the patient's medication adherence score is in the score range of 6–8 in all articles that fall into the medium adherence category. The proportion of high adherence score

Table 2. Quality assessment of quasi experimental design.

Author	Is it clear in the study what is the 'cause' and what is the 'effect' (i.e., there is no confusion about which variable comes first)?	Were the participants included in any comparisons similar?	Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Was there a control group?	Were there multiple measurements of the outcome both pre and post the intervention/exposure?	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Was appropriate statistical analysis used?	Total score (%)
Polsook et al., 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100

MMAS-8 was 48,5−88,2 % for the intervention group.

The result from the intervention that used m-health show that intervention group has medication adherence higher than control group in nine articles, but three articles show that the patients in control group have medication adherence higher than intervention group. Two articles show that the patients in intervention group same as the control group. The polypill or multi-capsules program show the effectiveness of improvement the medication adherence that was the intervention group has the higher adherence to the control group. The self-efficacy program not effectively because the intervention group has same adherence to the control group. Education program with follow-up by the health professional or care worker was effective to improve the patient medication adherence. All articles show that the intervention group has higher adherence to the control group. Pharmaceutical care by clinical pharmacists also effective to improve medication adherence in CHD patients. All the intervention group from four article has the higher adherence than the control group.

The duration of intervention is one of the things that affect medication adherence found in this study. The average patient's medication adherence will increase in the short term, but the longer the patient's medication adherence intervention will decrease. The results in the article that measured medication adherence at two time points were obtained at the second point measurement with a longer period there was a decrease in medication adherence. The result of five articles shows that medication adherence in the intervention group can improve with the program but in second time point that longer the scale of adherence will decrease. Medication adherence decrease on 12 months follow-up in two article [26,27]. The other result show that medication adherence decreases on 90 days, 6 months, and 24 months with each one article [28−30]. This needs to be a concern for health care professionals considering that CHD patients need long-term treatment, even for the rest of their lives. Summary of identified studies can be seen on Table 4.

4. Discussion

4.1. Medication adherence instrument

In this study, medication adherence was assessed using a variety of techniques, including the percentage of drug use, the MMAS-8 score, the MPR, and other self-efficacy instruments. Measurements

Table 3. Quality assessment of cohort design.

Author	Were the two groups similar and recruited from the same population?	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Was the exposure measured in a valid and reliable way?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Were the outcomes measured in a valid and reliable way?	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	Were strategies to address incomplete follow up utilized?	Was appropriate statistical analysis used?	Total score (%)
Gao et al., 2023	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	72.73
Livori et al., 2023	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	90.91

using the MMAS-8 were carried out by filling out a questionnaire developed by Doctor Morisky and colleagues containing eight question items with answers using a Likert scale. The results of the MMAS-8 score were categorized into three categories of compliance levels, namely high compliance (score 8), moderate compliance (score 6-<8), and low compliance (score <6) [31]. The use of MMAS-8 must comply with ethics related to the ownership license of the questionnaire owned by Doctor Morisky, where all articles using MMAS-8 in this study have obtained permission to use the questionnaire from Doctor Morisky.

The percentage of drug use is calculated by comparing the number of drugs prescribed with the number of drugs taken by the patient, so this method is the easiest to use to measure patient medication adherence. The MPR parameter is obtained by calculating the ratio of drug possession using the formula for the number of days the drug was obtained divided by the number of days the patient missed taking the drug plus the last number of days the drug was received. This method is specific for identifying non-adherence with patient medication, easy to use, inexpensive and does not require invasive procedures that only require documentation of medication use data so that patients are not worried about being monitored [23]. Medication refill can describe the medication adherence because CHD patient must take the medicine daily and must refill the prescription as scheduled. Patient who is not adherence will identify by prescription record the proportion of days covered [26].

4.2. Effectiveness of interventions

Interventions provided to increase medication adherence in CHD patients are generally divided into two major parts, namely using IT and non-IT. Most of the articles utilize IT in the interventions provided to patients in the form of text messages and mobile applications, which are part of mobile health (m-health). The purpose of using m-health is to provide safe and effective electronic health services so that increased collaboration between health professionals, health care units and patients is urgently needed in achieving the objectives of using m-health [8].

In this study, most of the use of mobile health show the improvement for medication adherence in CHD patient effectively. Text message, website, and smartphone-based application were the form of m-health that used as a patient intervention. There were several studies that show ineffective result.

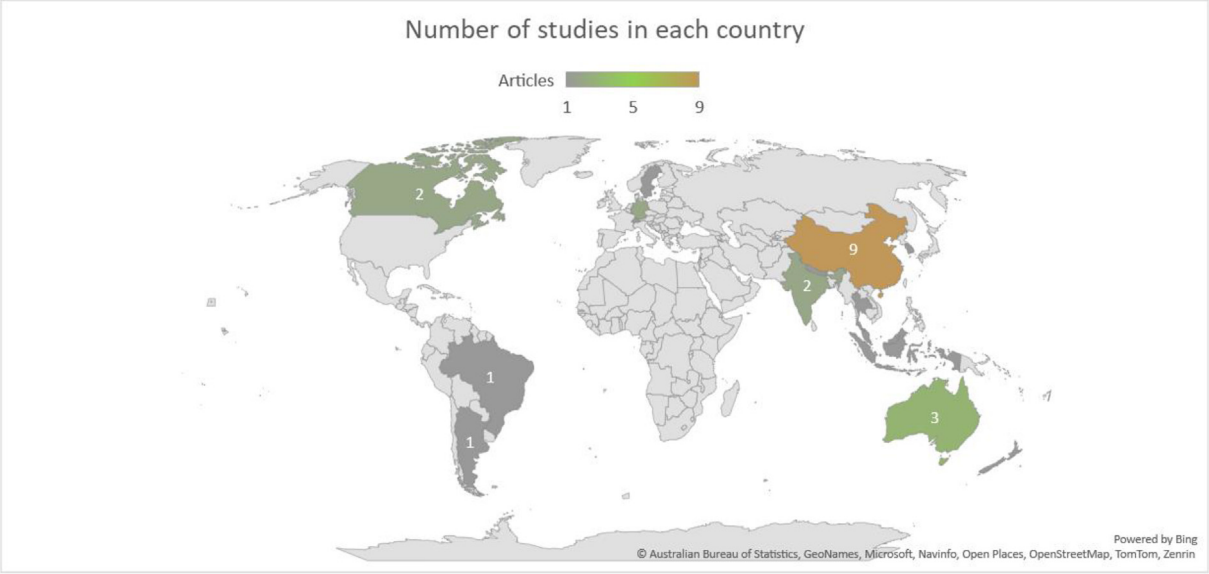

Fig. 2. Number of studies in each country.

Study by Chow et al. (2022) that use the text message as an intervention show the intervention group have lower medication adherence than control group. This study uses self-reported questionnaire as the instrument to measure the medication adherence. The method of self-reported can be overestimate data and have the high risk of bias [32]. Other study by Maddison et al. (2021) with text message education also has the result that the MPR rate in intervention group lower than the control group. There were many lifestyles change and medication adherence education that must be carried out by the patient become unfocussed. The content of the message that is less interesting also the reason for patient to not adherence with the education [33].

Study in CHD patient with post CABG use the smartphone-based application as the intervention group show that there was no difference of medication adherence between intervention and control group. Patient feasibility is the important thing to increase the patient engagement with the application. Software update, system error, and reminder setting must be solved so the patient can use the application easily. Short term follow-up in 6 month also caused the any significant outcome measure cannot detected [34]. The m-health intervention can be considered effective in increasing medication adherence in cardiovascular patients, although not all m-health programs have good results when compared to the control group [35].

The study by Mariani et al. (2020) using multicapsules does not have an additional impact on patient medication adherence, but in terms of formulation these preparations have a good therapeutic effect at a low additional cost. The weakness of this intervention is the possibility of adverse events for certain patients due to the use of several types of drugs in one capsule [29]. Other study with a polypill containing aspirin, ramipril, and atorvastatin was effective to increase the medication adherence in CHD patients with low risk adverse event in both intervention and control group [36].

Most of the studies using education intervention with follow-up by health care professionals or care workers were effectively to improve the medication adherence in CHD patients. Study by Calvert et al. (2012) with community pharmacist counselling as the intervention show the difference result between two medication adherence instruments. First instrument use self-reported questionnaire that show no significant difference on medication adherence score between intervention and control group. Prescription refill record was used as comparison show that medication adherence in the intervention group higher than control group [25]. Other study with education program intervention by Lourenco et al. (2013) use two instruments to measure the medication adherence which one was MMAS-8 and percentage drug use as the other. The intervention and control group have similar percentage adherent on baseline. Two months follow-up result was the intervention group has higher percentage adherent than control group. The baseline of MMAS-8 score was higher in the intervention group than control group, but the control group have MMAS-8 score same as the intervention group after two months follow-up [15]. One of the instruments that used was

Table 4. Summary of identified study.

Author and Study design	Patient	Intervention	Comparative	Outcome
Ni et al., 2022 [16] Randomized controlled trial	Patients in the Cardiology Department of a university-affiliated hospital in southern China (n = 36)	Providing education and reminders to take medication through the WeChat messaging application.	Standard care	Medication non-adherence score baseline 6,28 both on intervention and control group. Second endpoint on 15 days evaluation the non-adherence score decreases 1,00 on intervention group and decrease 1,44 at control group from the baseline score. After 30 days the non-adherence score decreases 1,35 at intervention group and decrease 0,69 on control group from the baseline score.
Sharma et al., 2016 [28] Randomized controlled trial	Patients with acute coronary syndrome who are hospitalized in India (n = 100)	Follow up visit care by non-physician health workers in providing education and information to patients.	Standard care	Medication adherence (>80%) 12 months Control group = 77,1% Intervention group = 92%. 24 months Control group = 40,9% Intervention group = 83,3%.
Gaudel et al., 2022 [42] Randomized controlled trial	Coronary artery disease patients in Sahid Gangalal National Heart Centre in Kathmandu, Nepal (n = 224)	Nurse-led counselling about coronary artery disease, lifestyle-related risk factors and their modification, and the importance of lifestyle changes.	Standard care	Baseline Intervention group: High adherence = 9,8% Medium adherence = 62,5% Low adherence = 7,1% Control group: High adherence = 32,1% Medium adherence = 40,2% Low adherence = 8,1% 1 month Intervention group: High adherence = 86,7% Medium adherence = 13,3% Control group: High adherence = 42,9% Medium adherence = 51% Low adherence = 6,1% 6 months Intervention group: High adherence = 88,2% Medium adherence = 10,7% Low adherence = 1,1% Control group: High adherence = 54,8% Medium adherence = 41,8% Low adherence = 3,4%

(*continued on next page*)

Table 4. (continued)

Author and Study design	Patient	Intervention	Comparative	Outcome
Park et al., 2014 [14] Randomized controlled trial	Participants are the coronary heart disease patients from community hospital in Northern California (n = 90)	There are two intervention group that one group will be receive education text message with reminder text message, and the other group only receive education text message.	Standard care	MMAS-8 score Baseline Test message and education group = 6,20 Only education group = 5,85 Control group = 6,01 Follow-up 30 days Test message and education group = 6,43 Only education group = 6,73 Control group = 6,96 MEMS Percent doses taken on schedule Antiplatelets Test message and education group = 86,2% Only education group = 85,7% Control group = 69% Statins Test message and education group = 84,1% Only education group = 79,7% Control group = 74,4%
Santo et al., 2019 [43] Randomized controlled trial	Coronary heart disease patients in a large urban tertiary hospital in Sydney, Australia (n = 152)	Two intervention group which the first group for basic reminder application and the second group for advanced reminder with additional interactive and customisable features.	Standard care	MMAS-8 score (mean) Control group = 6,63 Basic application group = 7,19 Advanced application group = 7,02 Percent patients MMAS-8 score Control group Low score (<6) = 29,4% Medium score (6-<8) = 27,5% High score (=8) = 43,1% Application group Low score (<6) = 18,8% Medium score (6-<8) = 32,7% High score (=8) = 48,5%
Li et al., 2022 [27] Randomized controlled trial	Patients coronary heart disease that hospitalized in Peking University First Hospital China between April 2016 and June 2017 (n = 300)	Self-management mobile application named DTx.	Standard care	Percent of drug use 6 months Control group = 69,2% Intervention group = 86,4% 12 months Control group = 53,7% Intervention group = 72%

Östbring et al., 2021 [39] Randomized controlled trial	Patients with CHD from the cardiology unit at the County Hospital in Kalmar, Sweden (n = 316)	Intervention group patient received follow-up program by two clinical pharmacies in motivational interviewing and medication reviews.	Standard care	MMAS-8 score Control group = 7,4 Intervention group = 7,6 Percent medium and high score Control group = 89,8% Intervention group = 93,8%
Bae et al., 2021 [19] Randomized controlled trial	Coronary heart disease patients with first percutaneous coronary intervention in Chungcheongbuk-Do and Incheon, Republic of Korea (n = 879)	Lifestyle modification supporting by website and text message for 6 months.	Standard care	Drug use percentage >80% Control group = 92,1% Intervention group = 98,2% Modified Morisky Scale (maximal score 5) Control group = 5 Intervention group = 5
Maddison et al., 2021 [33] Randomized controlled trial	Patients with acute coronary syndrome after underwent percutaneous coronary intervention in two large metropolitan hospitals in Auckland, New Zealand (n = 306)	Personalized automated program of self-management by short text message for 24 weeks.	Standard care	MPR >80% 24 weeks Control group = 46,4% Intervention group = 36,6% 52 weeks Control group = 45,7% Intervention group = 36,6%
Mariani et al., 2020 [29] Randomized controlled trial	Patients with a myocardial infarction in public hospital in Buenos Aires, Argentina (n = 100)	Patients received multi-capsules containing aspirin (100 mg), atenolol (50 or 100 mg), ramipril (5 or 10 mg), and simvastatin (40 mg) taken once daily.	Control group patients taken aspirin, atenolol, ramipril, and simvastatin in separate pills once daily	MPR mean Baseline Control group = 93,5% Intervention group = 98% 6 months Control group = 94,2% Intervention group = 89,6%
Polsook et al., 2016 [21] Quasi-experimental design	Patient with post-acute myocardial infarction from the in-patient department, Police General Hospital Bangkok Thailand (n = 44)	Self-efficacy program included health education, lifestyle modification, and medication adherence.	Standard care	Medication adherence score Control group = 29,23 Intervention group = 30
Xavier et al., 2016 [22] Randomized controlled trial	Patients with acute coronary syndrome from 14 hospitals across India (n = 750)	Community health worker trained patient on the method patient diary and calendar to reminder and record of drug intake at home.	Standard care	Medication adherence Control group = 92% Intervention group = 97%
Cao et al., 2017 [30] Randomized controlled trial	Patients diagnosed with coronary heart disease and admitted for the first time in a general tertiary-level hospital in Chengdu, China (n = 236)	Transitional care program delivered by hospital-community partnership.	Standard care	MMAS-8 score (mean) Control group Baseline = 5,81 30 days = 6,32 90 days = 6,46 Intervention group Baseline = 5,9 30 days = 6,86 90 days = 6,77

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Table 4. (continued)

Author and Study design	Patient	Intervention	Comparative	Outcome
Bruggmann et al., 2021 [44] Randomized controlled trial	Patients with STEMI or NSTEMI myocardial infarction treated with PCI in University Hospital of Lausanne, Switzerland (n = 60)	Web-based video and short interview with the pharmacist.	Standard care	ARMS score (mean) 1 month Intervention group = 13,15 Control group = 13,24 3 months Intervention group = 12,54 Control group = 13,75 6 months Intervention group = 13,52 Control group = 13,68
Calvert et al., 2012 [25] Randomized controlled trial	Patients hospitalized with coronary artery disease and discharge on aspirin, beta-blocker, and statin in Duke University Hospital, New Castle (n = 115)	Standard counselling by community pharmacists about cardiovascular medication include a pocket medication card, tips for remembering to take medication, and pillbox.	Standard care	Patient self-reported Intervention group = 91% Control group = 94% Prescription refill records Intervention group = 53% Control group = 38%
Casper et al., 2019 [38] Randomized controlled trial	Patients diagnosed with acute coronary syndrome and follow the cardiac rehabilitation program in Ain Shams University Hospital, Cairo, Egypt (n = 40)	Clinical pharmacist-provided services include drug related problem management, clinical assessment, and education.	Standard care	MMAS-8 score Baseline Intervention group: High adherence = 0 Moderate adherence = 35% Low adherence = 65% Control group: High adherence = 30% Moderate adherence = 40% Low adherence = 30% 3 months Intervention group: High adherence = 50% Moderate adherence = 50% Low adherence = 0 Control group: High adherence = 15% Moderate adherence = 20% Low adherence = 65%

Castellano et al., 2022 [36] Randomized controlled trial	Patients had history of myocardial infarction within the previous six months at 113 centres in Spain, Italy, France, Germany, Poland, The Czech Republic, and Hungary (n = 2499)	The polypill treatment consist of aspirin (100 mg), ramipril (2,5; 5; or 10 mg), and atorvastatin (20 or 40 mg).	Standard care	MMAS-8 score 6 months Intervention group: High adherence = 70,6% Medium adherence = 24% Low adherence = 5,5% Control group: High adherence = 62,7% Medium adherence = 27,8% Low adherence = 9,5% 24 months Intervention group: High adherence = 74,1% Medium adherence = 21,7% Low adherence = 4,2% Control group: High adherence = 63,2% Medium adherence = 29,8% Low adherence = 6,9%
Chow et al., 2022 [32] Randomized controlled trial	Patients with acute coronary syndrome were recruited from 13 urban and 5 rural centres across 3 times zones and 5 (of 8) states and territories of Australia (n = 1424)	Supportive and motivational text messages on medications and healthy lifestyle weekly (TEXTMEDS)	Standard care	Proportion of medication taken was>80% both at 6 and 12 months Intervention group = 50,4% Control group = 54,3%
Gao et al., 2023 [45] Cohort	Patients diagnosed with coronary heart disease in Aerospace Centre Hospital Beijing, China (n = 228)	Continuous pharmaceutical care program which was focused on patient-centre disease management and risk factor control	Standard care	Mean of medication adherence score Intervention group: Baseline = 79,54 1 month = 93,89 3 months = 95,58 6 months = 97,18 Control group: Baseline = 79,22 1 month = 88,13 3 months = 89,27 6 months = 89,94
Ivers et al., 2020 [46] Randomized controlled trial	Patients with obstructive coronary artery disease after a myocardial infarction in 9 cardiac centres in Ontario, Canada (n = 2632)	Telephone call and a series of mailed booklet education	Standard care	Proportion of medication adherence Mail only group = 37% Mail and phone call group = 35% Control group = 36%

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Table 4. (continued)

Author and Study design	Patient	Intervention	Comparative	Outcome
Khonsari et al., 2015 [47] Randomized controlled trial	Patients diagnosed acute coronary syndrome in a tertiary teaching hospital in Kuala Lumpur, Malaysia (n = 62)	Text message reminder for taking medication after discharge from hospital	Standard care	MMAS-8 score Intervention group: High adherence = 64,5% Medium adherence = 19,4% Low adherence = 16,1% Control group: High adherence = 12,9% Medium adherence = 29% Low adherence = 58,1%
Krackhardt et al., 2023 [48] Randomized controlled trial	Patients with acute coronary syndrome treated with ticagrelor co-administered with low dose acetylsalicylic acid in Germany (n = 676)	Smartphones-based support tool application for medication intake reminder and motivational message	Standard care	Mean adherence rate 1 month Intervention group = 98,7% Control group = 96,5% 3 months Intervention group = 91,5% Control group = 96,4% Twelve months Intervention group = 93,4% Control group = 87,0%
Lourenco et al., 2014 [15] Randomized controlled trial	Patients with coronary artery disease with clinical manifestation of angina or myocardial infarction in the state of Sao Paulo, Brazil (n = 115)	Action and coping planning strategies by telephone call and face-to-face meetings about patient medication	Standard care	Mean of MMAS-8 score Intervention group: Baseline = 7,3 2 months = 6,4 Control group: Baseline = 6,5 2 months = 6,4 Percentage of adherence mean Intervention group: Baseline = 93% 2 months = 98% Control group: Baseline = 94% 2 months = 96%
Livori et al., 2023 [49] Cohort	Patients diagnosed with acute coronary syndrome who received percutaneous coronary intervention in a large public regional health service in Victoria, Australia (n = 156)	Telehealth education by cardiology pharmacist clinic	Standard care	Percentage of medication adherence at 12 months Intervention group = 44% Control group = 31%

Putra et al., 2022 [50] Randomized controlled trial	Patients with coronary heart disease in Sidoarjo Regional General Hospital, Indonesia (n = 56)	Mobile health application for patient education	Standard care	Percentage of medication adherence Baseline Intervention group: High adherence = 0% Moderate adherence = 80% Low adherence = 20% Control group High adherence = 0% Moderate adherence = 80% Low adherence = 20% 30 days Intervention group: High adherence = 12% Moderate adherence = 88% Low adherence = 0% Control group: High adherence = 0% Moderate adherence = 76% Low adherence = 24%
Rinfret et al., 2013 [26] Randomized controlled trial	Patients underwent drug-eluting stent implantation with dual antiplatelet therapy in tertiary care university cardiovascular centre and community in Canada (n = 300)	Physician and pharmacist counselling by telephone calls after stent implantation procedure	Standard care	Median refill adherence 3 months Clopidogrel Intervention group = 100% Control group = 95,6% Acetylsalicylic acid Intervention group = 100% Control group = 90,1% Statin Intervention group = 100% Control group = 93,4% 12 months Clopidogrel Intervention group = 99,3% Control group = 91,5% Acetylsalicylic acid Intervention group = 99,2% Control group = 90,2% Statin Intervention group = 99,2% Control group = 92,1%

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Table 4. (continued)

Author and Study design	Patient	Intervention	Comparative	Outcome
Wang et al., 2020 [51] Randomized controlled trial	Patients post coronary artery bypass graft in a medical centre in North China (n = 164)	WeChat-based follow up service of cardiac health education and medication reminder	Standard care	Percent adherent >80% 6 months Statin Intervention group = 98,7% Control group = 94,7% Aspirin Intervention group = 98,8% Control group = 92,6% Beta-blocker Intervention group = 97,4% Control group = 97,4% Renin-angiotensin system inhibitor Intervention group = 90,4% Control group = 86,2% 12 months Statin Intervention group = 98,6% Control group = 75,0% Aspirin Intervention group = 98,8% Control group = 87,8% Beta-blocker Intervention group = 93,4% Control group = 69,3% Renin-angiotensin system inhibitor Intervention group = 89,3% Control group = 67,7%
Wu et al., 2019 [52] Randomized controlled trial	Patients with acute myocardial infarction after percutaneous coronary intervention in Teaching Hospital in Suzhou, China (n = 140)	Handbook of transitional health management after percutaneous coronary intervention and follow-up method by telephone and home visit from health professional	Standard care	Percentage of medication adherence Baseline Intervention group = 25,7% Control group = 27,1% 6 months Intervention group = 91,4% Control group = 78,6&
Xu et al., 2019 [53] Randomized controlled trial	Patients diagnosed with coronary heart disease in Department of Cardiology at a university teaching hospital in China (n = 240)	Education and medication assessment by clinical pharmacist and telephone follow-up after discharge from hospital	Standard care	Percentage of medication adherence 6 months Intervention group = 48,3% Control = 45,8% 12 months Intervention group = 47,9% Control group = 46,6%

Yin et al., 2022 [54] Randomized controlled trial	Patients with coronary heart disease and received percutaneous coronary intervention in The Central Hospital of Wuhan, China (n = 100)	Omaha system-based care which were nursing practice developed by American Omaha Visiting Nurse Association	Standard care	Morisky-Green score mean Intervention group = 3,56 Control group = 2,28 Percentage of medication adherence Intervention group = 92% Control group = 48%
Yu et al., 2020 [34] Randomized controlled trial	Patients after coronary artery bypass graft in five teaching hospitals in China (n = 987)	Smartphone application focused medication reminder, cardiac health education, health questionnaire, and personal data	Standard care	Proportion of low adherence by MMAS-8 score 3 months Intervention group = 6,3% Control group = 5,8% 6 months Intervention group = 11,8% Control group = 11,7%

MPR: medication possession ration; MMAS: Morisky Medication Adherence Scale; MMES: Medication Event Monitoring System.

patients self-reported as the questionnaire, maybe the patient know that they were investigated so they answer with the good condition not the actual condition. The change of behaviour as a motivational respond to the interest care or attention received through observation or assessment was known with the Hawthrone effect. This effect was the result of the study in the workplace at the Hawthorne Plant of the Western Electric Company in Cicero, Illinois, during the 1920s. The received attention made the behaviour change to the research participants which can influence the study result [37].

Pharmaceutical care program by clinical pharmacist can improve the medication adherence in CHD patients effectively. Four study involved the clinical pharmacist show the higher improvement of medication adherence in the intervention control than the control group. Pharmacists collect the clinical data from patient's medical record, assessed the drug related problem and drug therapy management and make the interview to give the education. The communication and medication adherence barrier can be resolve by the interview session [38]. Study by Ostbring et al. (2021) with the counselling by clinical pharmacy show that the intervention can improve the medication adherence in CHD patient but not positive effect on CHD risk factor. Interprofessional collaboration between cardiologist and clinical pharmacist was occurred to support the patient's clinical needs and medicine beliefs [39]. Patients need information and knowledge that can motivate drug use so that it will increase patient medication adherence. Patient knowledge is key with the support of the involvement of all professional health workers needed in increasing medication adherence [40].

Factors that influence medication adherence are social and economic, health care system, disease-related, patients-related, and therapy-related. Support from family, friends or caregivers who can assist in providing drug use rules can provide good medication adherence. Good relationships and communication between patients and health workers will have a positive impact on medication adherence. Patient medication adherence can significantly decrease in chronic disease conditions that require long-term treatment. The absence of complaints or symptoms experienced by patients is the cause of non-compliance. Poor adherence is caused by a low level of knowledge about the disease and the purpose of using the drug as well as a lack of motivation or understanding about the possibility of side effects and drug use errors [41]. The development of appropriate programs or interventions for CHD patients is still urgently needed

to increase medication adherence so that clinical outcomes can be achieved and improve the patient's quality of life. The results of this review can be a reference in increasing new knowledge about medication adherence in CHD patients.

4.3. Limitation

The limitation of this study is that the criteria for CHD patients are still not specific considering that there are several classifications of CHD disease with different types of action and therapy. In addition, this study only observed the effectiveness of the program on the patient's medication adherence level. In further studies, the impact of program administration on patient medication expenses can be added.

5. Conclusion

There were various instruments used to measured medication adherence in CHD patients. The percentage of drug use and MMAS-8 were the most familiar instruments. Medication adherence rate measured by the percentage of drug use was higher 80 % in all articles. The results of MMAS-8 score were in score range 6–8 depicting the medium adherence in all articles. All the article used the valid and reliable instrument to measure the medication adherence in CHD patients.

Many interventions to increase medication adherence in CHD patients, in the form of m-health, education and follow-up by care workers or professional health care, the use of multi-capsules preparations, self-efficacy, and pharmaceutical care by clinical pharmacy. The text message, website, and smartphone-based application as known by m-health were the most program as the intervention in many articles. Effectiveness of m-health intervention can be seen from the increasing of the medication adherence score in the intervention group than the control group in most of the articles. The others education program and pharmaceutical care studies also provided effective impact to improve the medication adherence in CHD patients. Education and consultation given by professional health workers as a form of interprofessional collaboration could be reinforced using technology (m-health) as a form of program to increase medication adherence in CHD patients. Mobile health becomes an instrument for providing up-to-date health services to patients in accordance with the health science and technology rapid developments. The patient's clinical outcome could be achieved optimally if the patients have good medication adherence so that it would also give an impact on the effectiveness of treatment costs.

Author contribution

Conception: AM, LA. Literature review: AM, LA, LKD. Methodology: LA, LKD. Software: AM, LKD. Analysis and/or interpretation: AM, LKD. Investigation: AM, LA. Resources: AM, LA. Data collection and/or processing: AM, LA, LKD. Writer-original draft: AM, LA. Writing- review & editing: AM, LA, LKD. Visualization: AM, LKD. Supervision: LA, LKD. Project administration: AM, LA. Fundings: AM, LA, LKD.

Conflict of interest

There is no conflict of interest in this study.

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