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# Strategies to Improve Statin Medication Adherence Among Patients at Risk of Cardiovascular Disease Identified Through Electronic Health Records: A Literature Review

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**Abstract.** Statin is a group of lipid/cholesterol-lowering medications that is commonly used for primary and secondary prevention of cardiovascular diseases (CVD). In Australia, this is the first line of pharmacological therapy for CVD risk management. High-risk patients who do not adhere to lipid-modifying medicines have an increased risk of CVD mortality, hospitalization, and revascularization. However, studies show that 67% of patients are non-adherent to statins. As such, improving statin adherence through various strategies is very important. This literature review delves into the studies from the past 10 years to identify the various strategies used and their effectiveness to improve statin adherence. The initial search results on PubMed showed 157 articles and based on the inclusion and exclusion criteria, 7 articles were finally used for this review. The patients in the studies were identified through electronic health records. The findings suggest that education, counselling and motivation through face-to-face interaction, phone calls or text messages, reminder messages and frequent follow-up visits are good strategies to improve statin adherence. Alongside these, simplifying regimens, switching combinations of medicines, or using alternate dosing have also been shown to improve statin adherence. In summary, counselling and face-to-face interaction are effective methods for improving statin adherence. The use of electronic health record (EHR) systems combined with targeted interventions delivered to patients identified to be non-adherent to statin may further improve statin adherence.

**Keywords.** Statin, adherence, cardiovascular disease, intervention, review

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## 1. Introduction

Cholesterol is known to be related to atherosclerosis, a condition leading to various cardiovascular diseases depending on the presence or absence of associated risk factors such as age, gender, presence of diabetes and/or hypertension, LDL-C level, people with chronic kidney disease, as well as smoking status, family history, ethnic background, obesity and sedentary lifestyle [1]. Inflammation is a part of the atherosclerosis process or the blocking of blood vessels. Acute myocardial infarction is caused by acute disruption of an atherosclerotic plaque, activating the thrombotic process and blockage of the artery, bringing about myocardial necrosis. Statins are a group of lipid/cholesterol-lowering medications with anti-inflammatory effects, commonly used for primary and secondary prevention of cardiovascular disease (CVD) [2]. Varieties of statins differ in biological properties, chemical structures, adverse effects, safety, and efficacy [3].

In Australia, about 1.2 million people (4.8%) have one or more cardiac or vascular conditions, attributing to 27% deaths [4]. Statin is a commonly used first line of pharmacological therapy for CVD risk management. The AusHEART study showed that statin is prescribed to 30% of patients aged more than 55 who are at low absolute CVD risk, and statin is taken by over 40% of Australian patients who are more than 65 [5,6].

The balance between benefits and the risk of adverse effects of statin such as myopathy or impaired cognition is not well understood [6]. Statins are generally well tolerated, but statin intolerance can be presented as muscle aches, weakness, or cramps [7]. Non-adherence to statins may lead to an increased risk of CVD mortality, hospitalization, and the need for revascularization [5]. About 55% of individuals had good adherence (>80%) to statin in South-Western Sydney [8]. Statin adherence is higher for secondary prevention of CVD compared to its use in primary prevention [1].

Statin adherence can be measured by either direct observation or drug concentration in blood or urine. Indirect methods to measure statin adherence include pill counts, self-reported use of statin, statin dispensation and refills, and measurement of physiological markers (LDL-C levels). However, the most common indirect methods are medication possession ratio (MPR), and proportion of days covered (PDC) [9].

There have been many strategies used to improve statin adherence, most of which were quite successful. In this review, we aim to identify the studies from the past 10 years and synthesize the strategies for the improvement of statin adherence. Therefore, the objective of this review was to: 1) identify various strategies used to improve statin adherence among patients identified through electronic health records; 2) determine the effectiveness of these strategies in terms of the various measurements used in each study.

## 2. Methods

This review was based on the five stages of literature review (formulation of research questions, identification of relevant studies, selection of studies, charting the data, and reporting results) as described by Arksey and O'Malleys [10]. Articles published in peer-reviewed journals from 2012 to 2022 were included in this review. The search was performed on 17 November 2022, using PubMed. Search terms were related to adherence ("adherence strategies" OR "improving adherence") and prescription drug ("statin").

Studies that measured the effect of interventions on improving adherence to statin medications for primary or secondary prevention of CVD were included. Studies with adults of age ≥18 years in outpatient and/or inpatient settings, identified through

electronic health records (EHR) were included. Studies were excluded if the intervention was limited to specific populations, such as patients with Alzheimer's Disease, and if not written in English. The initial search results showed 157 articles. After title, abstract and full text screening, 7 articles (Table 1) were found to meet the selection criteria.

**Table 1.** Intervention studies investigating the various strategies for improving adherence to statin medications.

| Citation | Place and duration | Participants | Intervention | Adherence measure | Outcomes |
|---|---|---|---|---|---|
| Taitel et al. (2012) | Midwest USA. Sept 2010 and Oct 2011 | <6 months gap in 1st and 2nd supplies of statin. Identified through pharmacy digital system | Patients received 1st face-to-face counselling sessions and 2nd statin prescription. | Adherence was measured using MPR | Intervention group had significantly greater MPR than control |
| Thom et al. (2013) | India, Ireland, England, Netherlands. July 2010-12 | ≥18 years with high CVD risk identified through a web-based clinical data management system | FDC-based strategies containing combinations of aspirin, simvastatin, lisinopril, atenolol, and hydrochlorothiazide | Adherence to self-reported use of statin, and changes in LDL-C levels at the end | FDC group (86%) had better adherence than usual care group (65%) |
| Derose et al. (2013) | Southern California. Apr to mid-Jun 2010 | ≥ 24 years, new statin users which was not filled after 1-2 weeks. Data from existing electronic records | Automated telephone calls 1 week after the letters for continued nonadherence; the control group received no outreach | Statin supplies distributed for 2 weeks after delivering the letter, and statin refills for a year | Statins supplied to 42.3% of intervention population and 26.0% of control population. |
| Leslie et al. (2016) | USA. Apr 2012 to Mar 2014 | Beneficiaries of a health plan, identified through MedImpact Healthcare Systems | 2 components intervention: a 90-day statin refill and a statin refill reminder at retail pharmacies. | Adherence was calculated as PDC. Threshold was PDC ≥ 80% | Statin adherence was 1.2 times more in the intervention than control groups |
| Wu et al. (2018) | Auckland. 2011 to 2015 | ≥ 2 statin prescriptions, with ≥ 90 days of statin treatment, from electronic records | Vitamin $D_3$ (2.5 mg) or placebo oral capsules were mailed to participants' homes in this randomized trial | Adherence was measured by PDC. The threshold was PDC ≥ 80% | Improved statin (especially simvastatin) persistence over 24 months |
| Byrne et al. (2020) | Northampton-shire region of England. May 2016 to Apr 2018 | 40-74 years, total cholesterol ≥ 5 mmol/l, no preexisting CVD, and no inherited lipid disorder, from electronic database | Two group education sessions, as well as 44 weeks of motivational texts, medication reminders, and phone calls (at 2 weeks and 6 months) | Urine samples were analysed for biochemical assay, for the presence of atorvastatin and rosuvastatin | No significant difference of statin adherence was found between the groups |
| Wang et al. (2022) | North China. Jan 2019 to Dec 2019 | ≥18 years, who had coronary artery bypass graft, from electronic medical records | Social media-based intervention (WeChat) along with follow-up care (at 1, 6 and 12 months) | Statin adherence and composite medication adherence score at 12 months | Intervention had greater statin adherence, and lower LDL-C at 12 months |

## 3. Results

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram below (Figure 1) shows the selection of the 7 articles. All the selected studies included participants that were identified through digital systems.

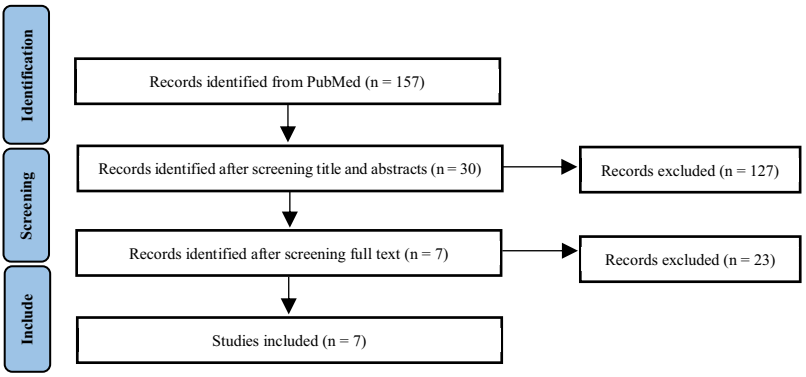


**Figure 1.** The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for study selection of this literature review

Different types of interventions are used to improve statin adherence among patients. Counselling and motivating through face-to-face interaction, phone calls or text messages have been identified as modes of intervention that had a significantly greater effect on increasing statin adherence among patients [11].

Through counselling, benefits of the medication based on evidence and patients' freedom of choice can be reinforced. This is supported by a study of intervention and non-intervention groups that show an MPR difference of 4.9% [11,12]. In contrast, the Ready to Reduce Risk (3R) intervention did not lead to differences among the two groups which may have been because the adherence levels at baseline were already much higher among the intervention group [13].

Reminder messages and frequent follow-up visits appear to be effective in ensuring a high level of statin adherence. Reminders sent out by telephone calls increased adherence by 16.3% [14]. In a study on 164 participants, the intervention group, who received reminders and follow-up services via the online WeChat platform, was found to have greater statin adherence (98.6%) than the control group (75.0%) [15].

Other methods explored include simplifying regimens (e.g., fixed-dose combination), switching from multiple medications, and using alternate dosing show improvement in adherence by 20% [16]. Medication refills and refill reminders at retail pharmacies increased the odds of adherence by 1.25 [17]. Vitamin D supplementation has also been shown to improve persistence in statin use among older adults, phenomenon that calls for further investigation [18].

## 4. Discussion

In this review, we identified and summarized several strategies to improve statin adherence. Our review suggests that effective counselling/face-to-face interaction between patients and healthcare providers is a crucial strategy in improving statin adherence.

## 5. Conclusions

The use of EHR helps in identifying patients who are not adherent to statin and can also be used to provide targeted interventions to improve adherence. Different strategies work in different populations. As such, study designs must be patient-centric and contextualized to the population setting.

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