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# A Review of Patient Related Barriers to Statin Adherence

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## Abstract

**Objective:** The effectiveness of statin therapy in primary and secondary prevention of cardiovascular (CV) disease as well as the reduction in CV related mortality is well-documented. However, with suboptimal adherence, the benefits of these medications cannot be fully realized. The purpose of this review was to summarize current literature that examines factors and barriers associated with statin adherence. These factors are important to consider when designing interventions to enhance adherence to statins.

**Methods:** A PUBMED search was conducted using the terms "statins" and "adherence", which generated 1,408 results. The most relevant studies which were found to exhaustively provide all the patient factors reported to affect adherence are summarized in this review.

**Results:** Patient factors which affected adherence included socio-demographic characteristics, factors relating to patient perceptions, adverse events of the medication or other disease conditions the patients suffered from. While some of the factors that were associated with better or worse adherence were patient characteristics which cannot be addressed, there are several prevalent reasons for non-adherence which can be targeted with interventions.

**Conclusion:** The extensive literature regarding factors positively or negatively influencing statin adherence reflects great research efforts. Interventions to address the identified barriers can help improve patient adherence and subsequent health outcomes.

## Introduction

3-hydroxy-3-methylglutaryl-coenzyme (HMG-CoA) reductase inhibitors, better known as statins, are an effective and widely prescribed class of drugs for lowering serum low-density lipoprotein (LDL) cholesterol concentrations. While the primary indication for statin use is hyperlipidemia, based on the 2013 ACC/AHA recommendations, statins are now also recommended and prescribed for patients at increased risk of atherosclerotic cardiovascular disease [1]. Medication adherence is defined by the World Health Organization as "the degree to which the person's behavior corresponds with the agreed recommendations from a health care provider" [2]. Poor adherence to medications is associated with increased morbidity and mortality as well as higher annual health care costs. In United States, 33 to 69 percent of medication-related hospital stays were found to be due to poor adherence to medications [3]. Enhancing adherence to statins has been shown to improve LDL levels and lower cardiovascular (CV) morbidity and mortality rates, [4] hospitalization and reduce costs associated with secondary prevention of cardiovascular disease [5]. However, due to asymptomatic as well as chronic nature of the disease, adherence to statins remains suboptimal [4]. As non-adherence leads to adverse outcomes and ultimately higher costs of care, all stakeholders are vested in improving adherence to such medications. Adherence to statins is also a part of the performance matrix used for reimbursement of provider organizations. Improvement of adherence to statins is the priority in quality improvement programs [6]. In order to design interventions to improve patient adherence, it is important to understand the patient related barriers to statins adherence as well as, factors which can positively influence statin adherence.

The purpose of this review was to summarize current literature that examines factors and barriers associated with patient adherence. Identifying such factors are the first step for designing influential interventions that can address the adherence problems among statin users.

## Methods

A PUBMED search was conducted using the terms "statins" and "adherence", which generated 1,408 results. The abstract of each result was reviewed and categorized as either irrelevant, patient related factors affecting adherence to statins, interventions to improve statin adherence, statin-based adherence studies and statin-based outcome studies as presented in Figure 1. There were no restrictions in including a certain type of publication and the included studies could be systematic reviews, meta-analysis, retrospective or survey based studies or interventions. Additionally, a study could fall into more than one category if it addressed factors from multiple categories.

The results from patient related factors which affect adherence are discussed in this review. The articles which have looked at risk factors or causes of statin non-adherence, surveys measuring attitudes and behaviors affecting statin adherence as well as studies looking at provider and environment-related factors (e.g. insurance status, copayments) which affect adherence were included. The 43 most relevant studies which were found to exhaustively provide all the patient factors affecting adherence have been referenced in this short review.

## Results

Table 1 presents all patient factors which were reported to affect adherence either positively or negatively. The barriers to adherence are elaborated below.

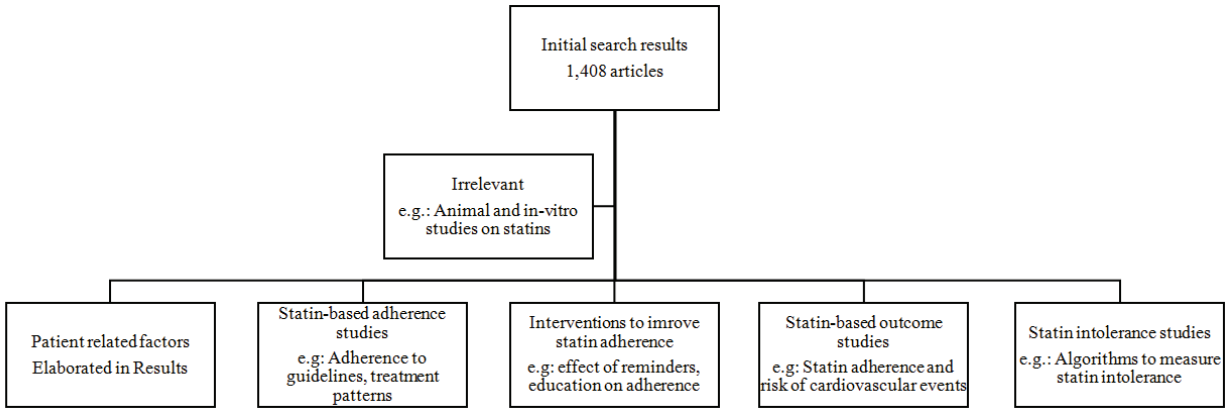


**Figure 1:** Flow chart for study-categorization and study-selection

**Table 1**: Patient factors which affect adherence to statins

| Key patient related factors affecting adherence | Key sociodemographic and clinical factors affecting adherence |
|---|---|
| **Negatively affecting adherence** | **Negatively affecting adherence** |
| High copayments/ cost related issues | Young age |
| New user | Very old age |
| Negative image through advertisements | Low socioeconomic status |
| Side effects/ Side effect perceptions | Low health literacy |
| Do not like remembering about disease condition | Depression |
| Do not like taking pills | Anxiety, anxiety related symptoms |
| Belief that the medication is not effective | No other disease |
| Communication issues with physician | Smoking |
| Dosing schedule | |
| Coverage gap | |
| Perception that condition not serious | |
| Trying lifestyle modifications | |
| **Positively affecting adherence** | **Positively affecting adherence** |
| Polypill/Fixed Dose Combinations | Hypertension |
| Mail order pharmacy | Diabetes |
| Patient's belief about treatment necessity | Obesity |
| Powerful others perception | Cardiovascular disease |
| Healthy behavior preference | |
| Visiting GP regularly for health issues | |
| Dietician counseling | |
| Family history of cardiovascular disease | |
| Getting regular lipid tests | |

## Sociodemographic patient related factors

New statin users, patients with lower socioeconomic background tend to have high discontinuation rates [7-10]. A meta-analysis revealed that the oldest (age>70) [11] and youngest (age<50) had lower adherence than middle age [12,13]. Low health literacy has been associated with poor adherence. Smokers are also predisposed to non-adherent behavior and medication discontinuation [14,15].

## Disease/ condition related factors

A meta-analysis about risk factors for statin non-adherence concluded that non-adherence is more common in patients who are asymptomatic for cardiovascular diseases i.e. who are using statins for primary prevention. While diagnosis of chronic diseases like diabetes and hypertension [7], obesity [15] or in general, greater number of co-morbidities [16] are associated with greater adherence, [12,17-19] depression was related to lower adherence.

## Occurrence of adverse events

Experiencing side effects or the perception of side-effects, especially muscle related were barriers to adherence [20,17]. Discontinuation is also a result of statin allergy, end stage renal disease or liver disease [21].

## Patient perceptions

There have also been studies which examined patient perceptions of statin adherence. A study by Wouters et al. [22] classified non-adherence as intentional and unintentional. While occurrence of adverse events leading to discontinuation or poor adherence is a separate issue, worrying about possible side-effects like stiffness, swelling of joints, muscle cramps lead to intentional non-adherence [22-26]. These side-effects about statin medication use are often disseminated through TV programs or internet [27,17]. Childhood adversity, which includes severe conflicts, fear of a family member, severe illness, financial difficulties were found to affect adherence in adult men, particularly if they had experienced multiple of these in their childhood [28]. Perceived risk of poor health, perceived benefit from taking medications affected the intent to take medications which in turn impacted the actual behavior [29]. Lack of perceived need for medications and perception that the disease is not life threatening promotes non-adherence [30,23]. Past behavior is also a significant predictor of adherence, including negative experiences from previous pharmacological treatments [29,17]. Certain groups of patients do not believe in efficacy of the medications [17,26]. This coupled with increased research of these medications online, medications reminding patients of their illness, making patients feel old and bad about themselves, not liking the idea of taking medications [17] and lack of satisfaction with physician's reasons for taking medications lead to discontinuation of medications [31]. Overall, patient beliefs do play an important role in predicting self-reported medication adherence and in achieving lipid goals [32,33]. The FDA warnings about potential adverse events related to statins such as memory loss and cognition, muscle damage with to high dose simvastatin and the increased risk of diabetes with statins [17] can all affect adherence by making patients perceive statin as high risk, low benefit drugs.

## Access limitations

High copayments or high costs are factors that have been proven to be a reason for non-adherence or discontinuation in multiple studies

and moving statins to low copayment tiers or generic substitution in the past have been found to have a positive effect on adherence [10,13,14, 23,30,34-41]. Patients enrolled in Medicare part D who are likely to reach coverage gap are also found to be poorly compliant before the gap itself in anticipation of hitting the gap [42]. A study based in Sweden reports retirement to be associated with decreased prevalence [43] but it is not known how it affects the US population.

### Other patient related factors

Practical causes like difficulty in getting refills, lack of information about dosage and intake, physical disability lead to unintentional non-adherence. While inconvenience to fill refills was negatively associated with adherence, use of a mail order pharmacy improved it [17,36,44]. Dosing schedule also has an effect on adherence as patients feel inconvenienced in taking the medication at the time directed by their physician [45]. Similarly patients taking multiple medications may feel inconvenienced and therefore fixed dose combinations or polypills have been known to improve adherence [46-50].

## Conclusion

Overall, there is extensive, rich literature about factors affecting adherence which reflects the research efforts in this area. There have been interventions which have targeted patient barriers to improve adherence, and future interventions should consider the factors and barriers described. It is however the combined efforts of patients, providers and the healthcare system which affect the overall adherence of patients, and there are continuous efforts directed towards improving patient adherence to medications, leading to improvement in subsequent patient outcomes.

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