

Primary Nonadherence to Medication among Patients with Chronic Illnesses

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Abstract

Introduction: Patients cooperation in taking prescribed medications is crucial for achieving targeted clinical outcomes. Non-adherence remains prevalent despite that healthcare systems are capable of providing affordable medications. Primary medication non-adherence can have major negative clinical and economic consequences.

Aim of Work: This aims to assess the prevalence of primary medication non-adherence (PMN) reported in the literature in chronic diseases. These diseases namely include asthma and chronic obstructive pulmonary disease (COPD), depression, hyperlipidemia, diabetes mellitus, hypertension and osteoporosis. Such chronic diseases contribute directly and indirectly towards most of deaths worldwide attributed to non-communicable diseases.

Methodology: A comprehensive and systematic search was conducted regarding aspects of non-adherence to medication. PubMed, Embase and Google Scholar search engines were the mainly used database.

Conclusion: The prevalence of primary medication non-adherence was 17%. Further, the prevalence for each of the six diseases-osteoporosis 25%, hyperlipidemia 25, hypertension 16, asthma/COPD 14, depression, and diabetes mellitus 10%. Age, gender and baseline health status were the frequently reported factors. A lack of involvement in shared decision-making had the strongest association with PMN. Recent app has been showed a considerable contribution towards patients primary adherence to medication. Among young individuals who had type 1 diabetes, medication non-adherence was linked to increased likely to admission for diabetes complications, such as diabetic ketoacidosis.

Keywords: Primary Medication Non-Adherence (PMN); Chronic Diseases

Introduction

Medication non-adherence is an incessant problem that compromises the effectiveness of healthcare systems [1]. Patients cooperation in taking prescribed medications is crucial for achieving targeted clinical outcomes. Non-adherence remains prevalent despite that healthcare systems are capable of providing affordable medications [2]. A recent analysis on statin prescriptions in the United States reported that nearly 15.4% of patients did not have their medications within 90 days of the order date [3]. Another study in France found persistence rates to be 1.5% among new users of inhaled corticosteroids [4]. Therefore, such warning rates of non-adherence to medication have been linked to poor outcomes and unnecessary healthcare expenses [2].

Vrijens and his colleagues proposed a classification divided medication adherence into three categories: primary adherence, implementation and discontinuation [5]. Secondary non-adherence has been addressed in several studies [6]. In contrast, there has been a lack of research focusing widely on primary medication non-adherence [7,8].

Primary medication non-adherence can have major negative clinical and economic consequences. In chronic illnesses, primary medication non-adherence has been associated with greater mortality rates in patients with a history of cardiovascular diseases [9]. Also, primarily non-adherent patients to anti-hyperlipidaemic medications were 1.25 times more liable to be encountered in the emergency department, unnecessarily affecting ended healthcare resources [10].

To tackle these aspects, we aimed to assess the prevalence of primary medication non-adherence (PMN) reported in the literature in chronic diseases. These diseases namely include asthma and chronic obstructive pulmonary disease (COPD), depression, hyperlipidemia, diabetes mellitus, hypertension and osteoporosis. Such chronic diseases contribute directly and indirectly towards most of deaths worldwide attributed to non-communicable diseases [11]. In addition, depression is a rising cause of disability that leads widely to disease and medication prescription burden globally [13]. Further, osteoporosis has become a major public health problem due to its negative effect on quality of life and mortality [14]. Medications are corner stone in the management of these chronic diseases, it is essential to study their prevalence of and correlated factors associated with primary medication non-adherence. Finally, we grouped factors associated with PMN according to medication, patient among other characteristics in order to provide an extensive analysis of proposed risk factors.

Materials and Methods

Search strategy and data source

We ran a systematic search in MEDLINE, Google Scholar, Cochrane Library, and Embase. Using each database's internal thesaurus (e.g. [MeSH] in MEDLINE), we designed the search approach into three aspects for ease of search-prevalence, primary medication non-adherence (PMN) and chronic diseases with their medications.

Terminology

Adapting the terminologies suggested by the International Society for Pharmaco-economics and Outcomes Research (ISPOR) [15], primary medication non-adherence is determined based on two components: a newly initiated medication and exact period of time to fill the prescription. In order to be newly initiated, we included medication had not been given to the patient for a certain period of time prior to prescription. Thus, patients failed filling a prescription for a newly initiated drug within an exact timetable were marked as primary non-adherent.

Eligibility criteria

We included studies that assessed primary medication non-adherence in the six chronic conditions. Studies published in English within the last decade in order to achieve a considerable comparability and relevance. Clinical trials and observational studies were included. Subjects ages were ≥ 18 years old and received a recent prescription for any of the mentioned chronic conditions.

Prevalence of primary medication non-adherence

The retrieved prevalence of primary medication non-adherence was 17%. Further, the prevalence for each of the six diseases-osteoporosis 25%, hyperlipidaemia 25, hypertension 16, asthma/COPD 14, depression, and diabetes mellitus 10%.

Factors associated with primary medication non-adherence

Factors that were significantly associated with primary medication non-adherence were extracted and sub-grouped them based on the five dimensions of adherence framework recommended by World Health Organization. These dimensions were patient related, social and economic, therapy related and healthcare environment related factors [16].

Age, gender and baseline health status were the frequently reported factors. A lack of involvement in shared decision-making had the strongest association with PMN. Being naïve to a new medication class had the strongest association with PMN (OR: 5.13). The prescriber's specialty was the most frequently reported prescriber-related factor. Having a physician who prescribed more prescriptions during the study period had the strongest association with PMN (OR: 1.58). Many of the healthcare system-related factors studied were related to cost (e.g. type of insurance).

One of the significant factor in the observed variation of PMN rates is using different follow-up timeframe. Therefore, this lack of standardization of the follow-up time augments challenges for stakeholders to measure the true magnitude of primary medication non-adherence. In view of this, a standardized follow-up timeframe to determine PMN would enhance a better comparability through studies. The ISPOR recommends using a time to filling of 15 - 30 days as the follow-up period account for possible therapy modifications that occur shortly after the prescription [17].

Factors related to type of chronic disease

Despite that definitions of primary medication non-adherence used in these studies still varied substantially, there have been improvement in quality and including larger number of patients and prescriptions. Though the progress in the management of chronic illness and advances in healthcare systems, PMN remains yet a major problem.

It was estimated that one in six patients were primarily non-adherent to new chronic condition medications. This finding is consistent with a US study, where the prevalence of primary medication non-adherence was 18% in patients aged ≥ 65 years with new prescriptions. Also, Lemstra and his colleagues reported a lower primarily non-adherence rate of 14.6% [12]. This difference could be attributed to the fact that we included osteoporosis in our review, which contributed to the overall higher PMN rate, having PMN rate of 25%.

Significant variation of PMN prevalence was observed between chronic diseases. Primarily non-adherence rates differ according to diseases, particularly, osteoporosis and hyperlipidemia which had the highest primarily non-adherence rate of 25%. The nature of these diseases is suggested to be contributing to the high PMN rate reported. These studies included patients with newly diagnosed osteoporosis. Thus, patients may not have experienced serious clinical symptoms, which leads to a low engagement to primary chronic treatment [18]. In regards to low rates of PMN in hyperlipidaemia, Jackevicius, *et al.* included patients with prior hospitalization for acute myocardial infarction [10]. These patients were found to be more adherent as they are worried about a consequence, resulting in the low primarily non-adherence rates [19]. However, diabetes mellitus, depression and asthma/ COPD had the lowest prevalence of PMN in this study (10, 12%, 14% respectively). These diseases usually present with symptoms when poorly controlled that patients are anticipated to be more adherent to new medications to ease their symptoms.

Age

Younger patients with osteoporosis showed more treatment adherence as they are more aware of the sequel compared with the older patients. On the other hand, patients with hyperlipidemia from the same age group are unaware of possible consequences, leading them

to being less primarily adherent [20,21]. This differences between chronic diseases highlights that a one-size-fits-all measures to improve primary adherence to medication is effective and efficient. Recognizing that primary medication non-adherence is more prevalent among younger patients, interventional measures are recommended to be delivered early in order to keep them adherent in their treatment.

Addressing the importance of behavioral factors, Shrank, *et al.* reported that patients who were prescribed new medications were three times less likely to be adherent to their prescriptions than patients refilling their medications [22].

Role of mobile and web-based apps

Patient education enhances the development of self-management skills. The recent accessibility of illness-specific educational features in electronic devices helps patients to easily obtain reliable information. Adding features, such as alarms, rewards, and interaction with peers, may induce better outcomes [23]. However, relying on education alone is insufficient to increase medication adherence [23,24].

Two mobile apps provided a new feature that allowed subjects to share their experiences with other peers through social media to enhance reassurance of common lived experiences [25,26]. Also, two other apps offered gamification tools, and several other apps added graphical features for disease-specific control measures [27,28]. Patients expressed their tendency towards the new gaming aspects of these mobile apps and felt that collecting prizes served as motivation for medication adherence. In addition, this feature would account considerably to future app development.

Medication non-adherence in pediatrics

Medication non-adherence and ED Visits

Two studies found that children who had asthma and did not fill prescriptions for anti-inflammatory medications had a greater risk for an ED visit than those who filled at least one prescription [29,30]. Also, lower percentage of time during which children and adolescents had anti-inflammatory medications was related to higher risks of an emergency department visit [31]. Consistently, a lower amount of doses administrated, as assessed via electronic devices, was linked to increased ED visits [32].

In a study comparing sets of adolescent who had asthma seen in the ED to those seen in asthma clinic, those seen in the ED were more likely to report non-adherence [33]. Similarly, health care providers report of more non-adherence was linked to more emergency department visits for children who had asthma [34].

Medication non-adherence and outpatient visits

Examining medication non-adherence and outpatient visits, Herndon and his colleagues reported that non-adherence was associated with fewer asthma-related office visits. In a population of children with asthma, a child possessed inhaled corticosteroids or leukotriene inhibitors was associated with lower rates of office visits [31].

Medication non-adherence and hospitalizations

Five studies examined the relation between medication non-adherence and hospitalizations. Out of the pooled studies, four of them studies included children with type 1 diabetes and adolescents had asthma. For youth who had asthma, a greater risk for hospitalization was reported in those failing to fill any prescriptions for anti-inflammatory medication [29]. However, when medication non adherence for inhaled corticosteroids were calculated, those with 20% to 49% MPR had increased likelihood to a hospital admission when compared with those with an medication non adherence of 0% to 19% [31].

Self-reports by healthcare provider of non-adherence to corticosteroids were linked to higher rates of hospitalizations in children who had asthma [34]. However, in another study, a composite score constituted of giving caregivers yes/no questions that are related to their

adherence to filling prescriptions. Also, the questionnaire assessed giving more/less medication than prescribed, and having suggested devices implied no relation to whether the child was admitted to the hospital in the past 9 months [35]. Further, among young individuals who had type 1 diabetes, medication non-adherence was linked to higher likelihood of admission for diabetes complications, such as diabetic ketoacidosis [36].

Conclusion

The prevalence of primary medication non-adherence was 17%. Further, the prevalence for each of the six diseases—osteoporosis 25%, hyperlipidemia 25, hypertension 16, asthma/COPD 14, depression, and diabetes mellitus 10%. Significant variation of PMN prevalence was observed between chronic diseases. Primarily non-adherence rates differ according to diseases, particularly, osteoporosis and hyperlipidemia which had the highest primarily non-adherence rate of 25%. The nature of these diseases is suggested to be contributing to the high PMN rate reported. Age, gender and baseline health status were the frequently reported factors. A lack of involvement in shared decision-making had the strongest association with PMN. One of the significant factors in the observed variation of PMN rates is using different follow-up timeframe. Therefore, this lack of standardization of the follow-up time augments challenges for stakeholders to measure the true magnitude of primary medication non-adherence. Recent app has been showed a considerable contribution towards patients' primary adherence to medication.

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