

MEDICATION AND TREATMENT GUIDELINE COMPLIANCE: MOST IMPORTANT BUT MOSTLY DESPISED

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ABSTRACT

Introduction and aim: To cure any disease, proper use of medicine or taking medicine in the correct order is required. Even patients from developed countries struggle to maintain their drug compliance. There is an odd parallel between underdeveloped, emerging nations and the so-called developed world in the West when it comes to improper medicine use. The understanding and perception of the disease is the most important factor influencing whether patients stick to their treatment plan.

Material and methods: Non-systematic review.

Analysis of the literature: There is a thorough discussion of medication non-adherence issues and a few adherence-improving methods.

Conclusion: Adherence to treatment guidelines is essential in the treatment of any disease.

Keywords: medication non-adherence, patient non-compliance, avoidable medical costs, low health literacy, vaccine negligence.

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INTRODUCTION

Any disease must be treated with medicine in the right way or in the right sequence. According to the WHO, patients who have chronic illnesses, in particular, suffer greatly when treatment regimens are not followed. At least five elements must be present for "right administration" to occur: the appropriate patient, the appropriate drug, the appropriate time, the appropriate dose, and the appropriate route [1]. Most people around the world do not understand that "medicines simply will not work if you do not take them correctly," and as a result, more than half of chronic disease patients in the civilized countries do not take their medicine correctly, according to the WHO [2]. Because their medications must be regularly taken for a lengthy period of time, sometimes for the rest of their lives, patients with chronic diseases may struggle to adhere to them. The Centers for Disease Control and Prevention (CDC) estimate that medication non-adherence accounts for 30 to 50% of chronic disease treatment failures. Patients may find it difficult to adhere to treatment regimens for a variety of reasons. Poor adherence may result in treatment failure, deteriorating health, and worsening symptoms [3].

OBJECTIVE OF THE STUDY

To demonstrate that the most important issues of treatment guidelines compliance are despised in the majority of cases around the world, and to discuss a few reasons for this.

MATERIAL AND METHODS

Prioritized databases for public health topics included PubMed, ALTAVISTA, Embase, Scopus, Web of Science, and the Cochrane Central Registers. Along with other online sources, journals from Elsevier, Springer, Willey Online Library, and Wolters Kluwer were thoroughly searched.

LITERATURE REVIEW

- A. **Non-adherence in the so-called developed countries**
Up to 50% of medications in the United Kingdom are not taken as directed, and 60% of NHS patients were unable to receive the necessary care within 18 weeks [4-6]. Noncompliance with medication regimens results in worse health outcomes, higher healthcare costs, more hospitalizations, and even higher mortality rates in patients with chronic diseases [7].

At least 10% of hospitalizations in the United States, 250,000 hospitalizations in Australia, and 1.1 million hospital days in France are solely attributable to medication non-adherence (Figure 1) [8-10]; causes \$300 billion in annual medical costs in the United States and \$125 billion in the European Union; and causes more than 1,25,000 premature deaths in the United States and 2,00,000 deaths in the European Union(Figure 1)[8, 11, 12]. Additionally, two-thirds of hospitalizations in Australia related to medication may be prevented [9]. A recent Canadian study found that 25% of patients do not fill their prescription or take it less frequently than directed, and 30% of patients stop taking their medication before it is advised [13]. For patients who had at least one avoidable encounter, medication non-adherence led to \$679–\$898 more in avoidable spending [14]. However, non-adherence cost pharmaceutical companies \$637 billion in lost potential sales globally last year, \$250 billion of which occurred in the United States alone (Figure 1) [15].

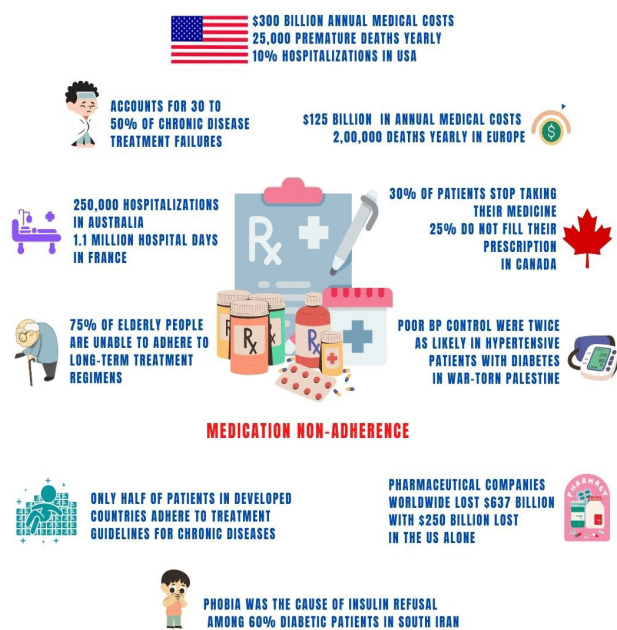


Figure 1: Medication non-adherence and possible outcomes

B. Misuse of antibiotics

The CDC reports that 30-50% of antibiotics prescribed in medical facilities are inappropriate or unnecessary, and more than half of all antibiotics sold worldwide are sold without a prescription [16, 17]. A recent Lancet study supported by the Bill and Melinda Gates Foundation and the Wellcome Trust found that bacterial resistance contributed to nearly 5 million deaths globally in 2019 and is predicted to double by 2050 [18]. In South Asia, 100% of patients in intensive care units received antibiotics, compared to nearly 70% of hospitalized patients who did [19, 20]. However, different antibiotics were prescribed for 70% to 80% of COVID-19 patients [21–23]. Azithromycin, ceftriaxone, amoxicillin, metronidazole, and amoxicillin-clavulanic acid were the antibiotics that were most frequently prescribed [24].

Additionally, it has been reported that close to 100% of the prescriptions for antibiotics given to COVID-19 patients were empiric and that about 90% of those patients were receiving unnecessary treatment [25].

C. Abuse of non-steroidal anti-inflammatory drugs in patients with COVID-19, Dengue, and Chikungunya

Every year, non-steroidal anti-inflammatory drugs (NSAIDs) cause at least 650,000 hospital admissions, 165,000 fatalities, and 30% of hospital admissions resulting from adverse drug reactions (ADRs) worldwide [26, 27]. Overuse of this class of medications can harm the kidneys, and patients who already have kidney disease may experience side effects that are three to four times more severe [28]. Numerous studies have revealed that COVID-19, Dengue, and Chikungunya patients frequently abuse these medications. In patients with COVID-19 or dengue, maintaining body hydration is even more crucial than lowering fever with painkillers. Children who use Paracetamol syrup or suppositories excessively may experience vomiting and hospitalization due to gastric irritation. With a few rare exceptions, most hospitalizations or ICU admissions among those patients could be prevented by simply drinking more water or saline at home to prevent dehydration [29].

D. A new era of uncontrolled use of prescription only and recreational drugs

About 40% of COVID-19 patients report having sleep disturbances. Benzodiazepines are contraindicated with some antiviral medications and raise the risk of delirium in COVID-19 patients as well as depress the system in patients with impaired breathing functions [30, 31]. Surprisingly, between 2020 and 2021, benzodiazepine dispensing rose sharply in Canada, while abuse of comparable drugs more than doubled in Italy [32]. Around 300 metric tons of morphine-type analgesics are used annually worldwide, with less than 1% going to low- and middle-income nations, according to the American Journal of Public Health [33]. As a result, their misuse and related side effects persist in the developed world. An announcement from authorities on "simple possession of cannabis" to thousands of convicted citizens prior to the US midterm elections exploded recreational drug abuse in both the US and the EU[34, 35].

E. Negative attitude towards COVID-19 vaccine

More than 50% of participants in a cross-sectional study of 259 school leaders in Hong Kong conducted during the COVID-19 pandemic between April 2021 and February 2022 had limited health literacy, which was strongly associated with a negative attitude toward vaccination, a lack of clarity regarding COVID-19-related information, and secondary symptoms [36]. An earlier study conducted in the US in 2020 found that 25% of Americans report having no intention to get vaccinated at any time, and that two-thirds of Americans will not get the COVID-19 vaccine when it is first made available [37]. In India, vaccine hesitancy was high in Tamil Nadu, more than 40% and willingness for vaccine uptake was found to be close to 90% in Kerala [38, 39]. Another vaccine hesitancy survey by University College London,

UK finds mistrust among 16% respondents, and 23% were confused [40].

F. Medical cost and low-health-literacy: the two major barriers of adherence among diabetes patients

When it comes to improper medication use, there is an odd parallel between underdeveloped, developing nations and the so-called developed world in the West or the Middle East. In developed countries, only half of patients follow recommendations for treating chronic illnesses, compared to much lower rates in developing nations, according to a WHO report (Figure 2) [41]. Numerous studies on diabetic patients in South Asian nations have revealed that almost half of patients do not take their medication as directed and are at risk of both short-term and long-term complications, which raises hospitalization rates and medical costs [42, 43]. Despite being widely discussed, "Medical costs are barriers to adherence to proper clinical guidelines for chronic diseases in poor countries." But among the reasons for non-adherence to diabetes management protocols in Middle Eastern countries are forgetfulness, confusion about the duration required for medication use, and mistrust about the overall efficacy of medication [44]. Health literacy and medication adherence are strongly associated (Table 1). Poor glycemic control due to low-

health-literacy among diabetes patients reported to both South-East Asian and Middle Eastern countries [45-51].

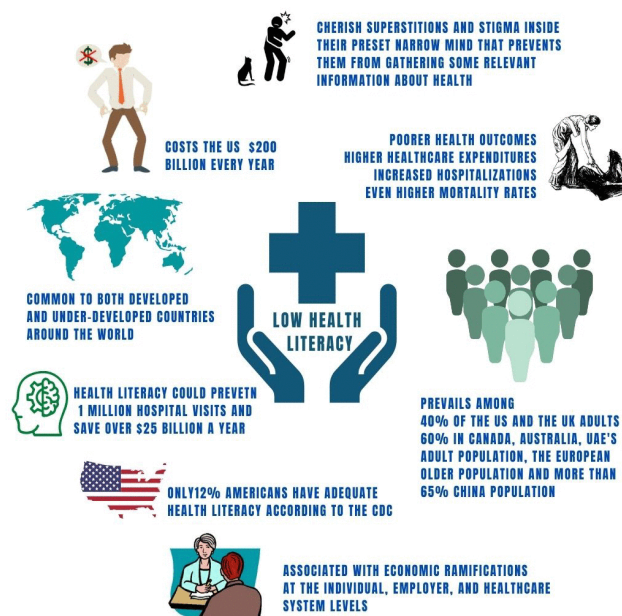


Figure 2: Low Health Literacy Facts

Table 1: Several identified reasons for non-adherence to treatment guidelines for chronic diseases [7, 71-73]

Status	Factors
Patient's socio-economic status	Low health literacy, lack of family or social support network, unstable living or homelessness, financial insecurity
Treatment-related	Complexity and duration of treatment procedures, frequent changes in medication regimen, lack of immediate results, real or perceived unpleasant side effects, interference with lifestyle
Health system-related	High treatment costs, limited health system for patient education and follow-up, doctor-patient relationship, patient trust in health care, long waits, lack of patient information materials
Patient-related	Visual-hearing and cognitive impairment, mobility and dexterity, psychological and behavioral factors, perceived risk of disease susceptibility, superstitions and stigmatization by disease, etc.

G. Humanitarian crisis: poor blood pressure control among cardiac patients

According to a recent American Heart Association study, patients with high blood pressure (BP) do not adhere to treatment recommendations because of the following factors: a) suboptimal dosage or prescribing the incorrect medication; b) lack of insurance or access to care; and c) patients' refusal to adhere to prescribed medication or other lifestyle recommendations [52]. Despite the fact that more patients with hypertension have received treatment over time, less than 50% of them consistently have stable blood pressure. Additionally, in high, low, and middle income countries, individuals with elevated levels of total cholesterol, LDL, and uric acid reported having inadequate blood pressure

control [53]. Increased short- and long-term cardiac morbidity and mortality as well as increases in blood pressure are all linked to humanitarian crises [54]. For instance, in the conflict-torn country of Palestine, hypertensive patients with diabetes mellitus were twice as likely to have poor blood pressure control [55]. Additionally, a study conducted in the US on newly settled Rohingya refugees from Myanmar reveals an increase in the prevalence of chronic diseases like diabetes, hypertension, and obesity [56].

H. Superstitions: an elephant in the room

Although two-thirds of patients could become seizure-free with proper care, poor adherence to proper guidelines is a major problem for effective recovery (Table 1) [57, 58]. Epilepsy and schizophrenia are still

viewed in the majority of the world as an evil spirit. In an Indian study, 60% of the participants thought that illnesses were the result of luck or superstition [59]. In Northern Germany, superstitions were also reported in nearly 40% of men and 70% of women [60]. 70% of people in Africa use folk remedies like charms and witchcraft to treat their illnesses [61]. Surprisingly, researchers found that 73% of addiction treatment programs in the USA include a spirituality-based element and that more than 40% of Americans believe in spiritual therapies [62, 63]. According to a South Iranian study, 60% of diabetic patients refused insulin despite doctor recommendations due to phobia [64].

I. Pediatric and geriatric complications to non-adherence

Three-quarters of elderly people worldwide are unable to follow recommended long-term treatment regimens because of numerous physical issues and an increased medication burden (Figure 1) [65]. ADRs are estimated to account for 5% to 28% of acute geriatric medical admissions, and patients over the age of 65 who take at least five medications are at an increased risk of mild cognitive impairment, memory loss, falls, frailty, impairment, and death [66, 67]. Common non-adherences among kids involve family rituals, parenting concerns, and social issues like poverty. About 60% of children's non-adherence is caused by chronic diseases like juvenile arthritis, cystic fibrosis, HIV, diabetes, inflammatory bowel disease, and asthma [68-70].

RESULTS AND DISCUSSION

According to the literature review, even in highly privileged populations in developing nations, treatment protocols are not always adhered to. Negligence, poor health literacy, forgetfulness, the cost of medications, polypharmacy, and patient perception of the consequences of non-adherence are among the main causes that are not excusable, among many other elements. The main conclusions of the current study are that the issue of non-adherence persists despite the millions of similar studies that have been conducted throughout the world. This is because the research is only published in journals and is not communicated to the general population, who are frequently careless about their own health, whether on purpose or unintentionally. Patient education is essential for changing their health-seeking behavior.

Tools to improve medication and treatment guideline adherence

There is evidence that the number of chronic diseases and drugs increases non-adherence. Chronic disease management necessitates ongoing psychological adaptation through behavioral, educational, integrated care, self-management, and risk-communication interventions, which may result in significant changes in therapeutic indications. In addition, several newer technologies that may improve medication and treatment guideline adherence have been incorporated (Table 2).

Table 2: Interventions to improve treatment guideline adherence [74-80]

Interventions	Details
Psychological adaptation training - ABC taxonomy	The first stage, <i>initiation</i> , is measured as a time-to-event variable and refers to the interval between prescription and the patient taking the first dose of a prescribed medication. The second phase, <i>implementation</i> , is a continuous measurement of the difference between the amount of medication prescribed and actually taken. It covers the time from the first dose until the last one is taken. The third stage, known as <i>discontinuation</i> , denotes the end of therapy, when the next dose is skipped and no additional doses are given after that. The term " <i>persistence</i> ," which is frequently used, refers to a time-to-event variable that measures how long a patient spends in the implementation phase.
Behavioral interventions	Four steps are involved in the modeling of behavior: attention, retention, reproduction, and motivation. Telephone follow-up and home visits, particularly in associations with educational components, seem to have a positive impact, providing planning and support, and integrated pre and post discharge interventions.
Patient education	Health promoters typically have credibility to conduct patient education programs due to their expert knowledge and appropriate training. However, knowledge by itself does not guarantee success as a health educator. The following three guidelines must be followed in patient education programs: In order to change patients' health-related behaviors, it is important to address the following factors: (a) establishing a relationship between patients and healthcare providers; (b) delivering and evaluating the education program's goals to patients; and (c) paying attention to low self-esteem and non-verbal patients.
Integrated care interventions	An interdisciplinary approach relies on health professionals from different disciplines, along with the patient, working collaboratively as a team. The physician, pharmacist, or nurse invites the patient to take part in the program, but in practice, the physician is often

the best person to invite the patient to participate in the program because of the established patient-provider relationship.

Self-management Interventions	The medication self-management intervention consists of two weekly phone calls and three in-person education sessions spread out over six weeks. To identify the factors that affect adherence, as well as how and why these factors contribute to poor adherence, a thorough assessment of adherence problems will first be conducted. Depending on each patient's condition and potential adherence issues, medication-related knowledge and skills will be offered. For a better understanding of patients' cognitive factors influencing adherence behavior, motivational interviewing techniques will be used.
Risk-communication interventions	Patients and healthcare professionals exchange information about risks in both directions. The key to reducing the risks of drug-related car accidents is verbal communication of information and the use of straightforward documents. Providing patients with accurate information can improve their sense of self-efficacy and satisfaction, which can lead to behavioral changes and risk reduction.

CONCLUSION

Finally, it can be stated that patients' knowledge and interpretation of the disease are the primary factors influencing their adherence to the treatment regimen. Health-care providers should explore more effective health-education methods for identifying patients' attitudes toward disease, medicine trust, psychological stressors, and increasing adherence to medication.

The list of abbreviations:

ADR –adverse drug reactions

BP – blood pressure

NSAIDs – non-steroidal anti-inflammatory drugs

CDC – centers for disease control and prevention

WHO – World Health Organization

DECLARATIONS

The current research was carried out exclusively to look into problems associated with medication non-adherence. With time and the availability of newer investigation in the same field, the statistical evidence or variables presented here may transform.

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Author contributions

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Conflicts of interest

The author declares that he has no competing interests.

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