

Adherence to Medication and Treatment Guidelines: Most Important but Mostly Despised

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ABSTRACT

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.

Keywords: Medication Non-Adherence, Patient Non-Compliance, Avoidable Medical Costs.

ABBREVIATIONS

Adverse Drug Reactions (ADR)

Blood Pressure (BP)

Non-steroidal anti-inflammatory drugs (NSAIDs)

The Centers for Disease Control and Prevention (CDC)

World Health Organization (WHO)

INTRODUCTION

To cure any disease, proper use of medicine or taking medicine in the correct order is required. According to the WHO, noncompliance with treatment regimens causes major problems in patients, particularly those with chronic illnesses. “Right administration” depends on at least 5 right factors--right patient, right drug, right time, right dose and right route [1]. “Medicines simply will not work if you don’t take it right”—This simple fact is not understood by most people around the world, and as a result, more than half of chronic disease patients in the developed world do not take their medicine correctly, according to WHO [2]. Patients suffering from chronic diseases may have a particularly difficult time adhering because their medications must frequently be taken for an extended period of time, sometimes for the rest of their lives. Patients may struggle to stick to treatment regimens for a variety of reasons, and the CDC estimates that medication non-adherence accounts for 30 to 50% of chronic disease

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treatment failures. Poor adherence can lead to treatment failure, worsening symptoms, and health deterioration [3].

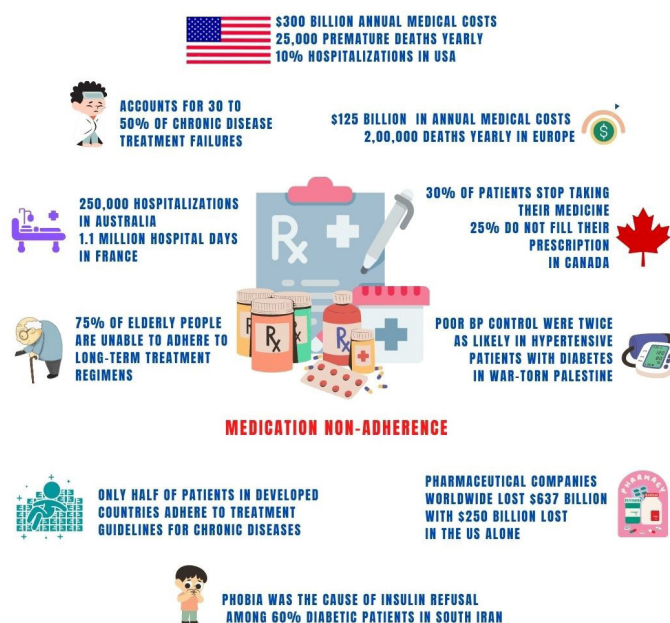


Figure 1. Medication non-adherence and possible outcomes.

Non-Adherence in the so-called Developed Countries

In the United Kingdom, up to 50% of medicines are not taken as prescribed, and 60% of NHS patients were unable receive the appropriate treatment within 18 weeks [4-6]. In patients with chronic diseases, noncompliance with medications leads to poorer health outcomes, higher healthcare costs, increased hospitalizations, and even higher mortality rates [7]. Medication non-adherence alone accounts for at least 10% of hospitalizations in the United States, 250,000 hospitalizations in Australia, and 1.1 million hospital days in France (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 [8,11,12]. Furthermore, two-thirds of medication-related hospitalizations in Australia are potentially avoidable [9]. According to a recent Canadian study, 30% of patients stop taking their medicine before it is recommended, and 25% do not fill their prescription or take less than prescribed [13]. Medication non-adherence attributed to \$679-\$898 more preventable spending among patients who had at least one preventable encounter [14]. However, pharmaceutical companies worldwide lost \$637 billion in potential sales due to non-adherence, with \$250 billion lost in the United States alone last year (Figure 1) [15].

Misuse of Antibiotics

More than half of all antibiotics sold in the world are sold without a prescription, and the CDC reports that 30-50% of antibiotics prescribed in hospitals are inappropriate or unnecessary [16,17]. According to a recent Lancet study funded by the Bill and Melinda Gates Foundation and the Wellcome Trust, nearly 5 million deaths worldwide in 2019 were caused by bacterial resistance, which is expected to double by 2050 [18]. In South Asia, nearly 70% of hospitalized patients received one or more antibiotics, whereas 100% of ICU patients received antibiotics [19,20]. However, 70% to 80% of COVID-19 patients received various antibiotics for COVID-19 treatment [21-23]. The antibiotics most commonly prescribed were azithromycin, ceftriaxone, amoxicillin, metronidazole, and amoxicillin-clavulanic acid [24]. In addition, it has been reported that about 90% of patients with COVID-19 are being unnecessarily treated with antibiotics and close to 100% of these prescriptions were empiric [25].

Abuse of NSAIDs in patients with COVID-19, Dengue, and Chikungunya

NSAIDs are responsible for at least 650,000 hospitalizations, 165,000 deaths, and 30% of ADR-related hospital admissions worldwide each year [26,27]. Overuse of this class of drugs can result in kidney damage, and their side effects can be three to four times more severe in patients with kidney disease [28].

Many studies have found that these drugs are widely abused in Dengue, Chikungunya, and Covid-19 patients. It is even more important to keep the body hydrated than to reduce the fever with pain relievers, especially in Dengue or Covid-19 patients. Excessive use of Paracetamol syrup or suppositories in children can cause gastric irritation, which can lead to vomiting and hospitalization. With a few exceptions, most hospitalizations or ICU admissions among those patients could be avoided simply by halting dehydration at residence with saline and fruit juice or simply by drinking more water [29].

A New Era of Uncontrolled Use of Prescription Only and Recreational Drugs

Sleep disturbances are reported by approximately 40% of Covid-19 patients. Benzodiazepines increase the risk of delirium in Covid-19 patients, depress the system in patients with compromised breathing functions, and are contraindicated with some anti-viral medications [30,31]. Surprisingly, benzodiazepine dispensing increased dramatically in Canada between 2020 and 2021, while abuse of similar drugs more than doubled in Italy [32]. According to the American Journal of Public Health [33], approximately 300 metric tons of morphine-type analgesics are used worldwide each year, with less than 1% distributed to low- and middle-income countries. As a result, the developed world retains their misuse and associated side effects. Prior to the US midterm elections, an announcement from authorities on “simple possession of cannabis” to thousands of convicted citizens exploded recreational drug abuse in both the US and the EU [34,35].

Negative Attitude towards Covid-19 Vaccine

A cross-sectional study of 259 school leaders in Hong Kong carried out during the COVID-19 pandemic between April 2021 and February 2022 shows that more than 50% of participants had limited health literacy, which was strongly associated with a negative attitude towards vaccination, confusion about COVID-19-related information and secondary symptoms [36]. Earlier, a US-based study in 2020 concluded that two-thirds of the Americans will not get the COVID-19 vaccine when it is first available, while 25% report that they do not have any intention to get vaccinated at any time [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].

Medical Cost and Low-Health-Literacy: The Two Major Barriers of Adherence among Diabetes Patients

A strange similarity can be found in under-developed, developing countries and the so-called developed world in the West or the Middle-East when it comes to not taking medicine properly. According to a WHO report, only half of patients in developed countries adhere to treatment guidelines for chronic diseases, which is much less in developing countries [41]. Several studies among diabetic patients in South Asian countries have shown that nearly half of patients do not adhere to their prescribed medication and are at risk of acute and long-term complications, resulting in increased hospitalization rates and medical costs [42, 43]. “Medical costs are barriers to adherence to proper clinical guidelines for chronic diseases in poor countries”-- although discussed in many forums but forgetfulness, confusion about the duration required for medication use and mistrust about the overall efficacy of medication are among the reasons for non-adherence to diabetes management protocols in Middle Eastern countries [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].

Humanitarian crisis: Poor BP Control among Cardiac Patients

A recent study by the American Heart Association revealed that patients with high blood pressure do not follow treatment guidelines because of--(a) suboptimal dosing or prescribing the wrong medication (b) lack of insurance or lack of health care access and (c) patient failure to comply prescribed medication or other lifestyle guidelines [52]. Among hypertensive patients, less than 50% have persistent control over BP, even though more patients have received treatment over time. Furthermore, inadequate BP control was reported among those with elevated total cholesterol, LDL, and uric acid levels in both high, low and middle income countries [53]. Humanitarian crisis is associated with increased short-term and long-term cardiac morbidity and mortality and increases in BP [54]. For example, hypertensive patients with diabetes mellitus were twice as likely to exhibit poor BP control, found in war-torn Palestine [55]. Also, a US-based survey on re-settled Rohingya refugees from Myanmar shows

a higher trend of chronic diseases like diabetes, hypertension and obesity [56].

Superstitions: An Elephant in the Room

Epilepsy and schizophrenia still seen in most countries of the world as an evil spirit --although two-thirds of patients can become seizure-free with adequate treatment, poor adherence to proper guidelines is a major problem for effective recovery [57, 58]. In a study conducted in India, 60% of the patients believed in luck and superstition with regard to illnesses [59]. Superstitions also reported in close to 40% men and 70% women in Northern Germany [60]. In Africa, 70% of people turn to indigenous treatments such as charms and witchery to treat their illness [61]. Surprisingly, more than 40% of Americans believe in spiritual treatments and researchers found that 73% of addiction treatment programs in the USA include a spirituality-based element [62, 63]. Phobia was the cause of insulin refusal among 60% diabetic patients, despite

physician recommendations—found in a study conducted in South Iran [64].

Pediatric and Geriatric Complications to Non-Adherence

Due to multiple physical complications and additional medication burden, three-quarters of geriatric persons worldwide are unable to adhere to appropriate long-term treatment regimens (Figure 1) [65]. 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, while ADRs are estimated to account for 5% to 28% of acute geriatric medical admissions [66, 67]. For children, common non-adherences are related to family routines, child-raising issues, and to social issues such as poverty. Long-term disease conditions like asthma, cystic fibrosis, HIV, diabetes, inflammatory bowel disease and juvenile arthritis—are attributable to around 60% of non-adherence among children [68-70].

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

No.	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

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. Interventions to improve Treatment Guideline Adherence.

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 [74].
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 [75].
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 [76].
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 [77].
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 [78].
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. [79, 80].

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. Healthcare providers should explore more effective health-education methods for identifying patients' attitudes toward disease, medicine trust, psychological stressors, and increasing adherence to medication.

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CONFLICT OF INTEREST

The author declares that he has no competing interests.

INFORMED CONSENT

N/A.

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