



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

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<p>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.</p>	<p>Short Communication</p>
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INTRODUCTION

Proper use of medicine or taking medicine in correct order is essential to cure any disease. According to the WHO, lack of adherence to treatment regimens leads to major problems among patients, mostly 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 won't work if you don't take it right"--This simple fact is not understood by most people in the world, as a result still more than half of the patients with chronic diseases in the developed world do not take their medicine correctly--says WHO [2]. Patients with chronic diseases may find it especially difficult to adhere because their medications must frequently be taken for an extended period of time, sometimes for the rest of their lives. There are a variety of reasons why patients may struggle to stick to treatment regimens, and the CDC estimates that medication noncompliance accounts for 30 to 50% of chronic disease treatment failures. Poor adherence may result in treatment outcomes not being met, symptoms worsening, and health deterioration [3].

Non-Adherence in the so-called Developed Countries

In the UK, up to 50% of medicines are not taken as intended and 60% of NHS patients failed to receive the right treatment within 18 weeks [4-6]. Lack of medication adherence leads to poorer health outcomes, higher healthcare expenditures, increased hospitalizations, and even higher mortality rates in patients with chronic diseases [7]. Medication non-adherence alone accounts for at least 10% of hospitalizations in US, 250,000 hospitalizations in Australia and 1.1 million hospital days in France [8-10]; induces \$300 billion in annual medical costs in US, and \$125 billion in EU; causes more than 1,25,000 premature deaths in the US and 2,00,000 deaths in EU [8, 11, 12]. Also, two-thirds of medication-related hospital admissions in Australia are potentially preventable [9]. A recent Canadian study found that 30% of patients stop taking their medication before it is instructed, and 25% patients do not fill their prescription or take less than prescribed [13]. Among patients with at least one preventable encounter, medication non-adherence was associated with \$679-\$898 increased preventable spending [14]. However, pharmaceutical companies around the globe lost \$637 billion in potential sales annually due to non-adherence,

with \$250 billion lost for the same in the U.S. alone last year [15].

Misuse of Antibiotics

More than half of the antibiotics worldwide are sold without a prescription and CDC stated, 30-50% of antibiotics prescribed in hospitals are inappropriate or unnecessary [16, 17]. A recent study published by The Lancet, funded by the Bill & Melinda Gates Foundation, Wellcome Trust, states that nearly 5 million deaths worldwide in 2019 were related to bacterial resistance, which is expected to double by 2050 [18]. In south Asia, about 70% of hospitalized patients have been administered a minimum of one or more antibiotics, whereas 100% of ICU patients received antibiotics [19, 20]. However, 70% to 80% of COVID-19 patients got different types of antibiotics for their COVID-19 treatment [21-23]. The most frequently prescribed antibiotics 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

Globally, NSAIDs are responsible for at least 650,000 hospitalizations and 165,000 deaths and 30% of ADR related hospital admissions around the globe annually [26, 27]. Overuse of this class of drugs can cause kidney injury, and their side effects can be 3 to 4 times higher in kidney compromised patients [28]. Many studies have reported widespread misuse of these drugs in Dengue, Chikungunya and Covid-19 patients. Especially in Dengue or Covid-19 patients, it is more important to maintain the hydration level of the body than to bring down the fever with the pain killers. In children, the use of excess Paracetamol syrup or suppositories may cause stomach irritation, which hampers digestion and led to vomiting and ended up with hospitalization. Most hospitalizations or ICU admissions among those patients could be prevented, with few exceptions, simply by preventing dehydration at home with saline and fruit juice or simply by drinking more water [29].

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

More or less 40% of Covid-19 patients report sleep disturbances—use of Benzodiazepines in Covid-19 patients increases the incidence of delirium, depresses the system in patients with compromised respiratory functions, and contraindicated with some anti-viral medications [30, 31]. Surprisingly, between 2020-2021, a huge increase in benzodiazepine dispensing is reported in Canada and abuse of similar drugs doubled in Italy [32]. Around 300 metric tons of morphine-type

painkillers are used worldwide each year, less than 1% of which distributed to low-and-middle income countries, says the American Journal of Public Health [33]. So their misuse and related side effects are also retained by the developed world. 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. 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

Three-quarters of elderly patients worldwide are unable to adhere to appropriate long-term treatment regimens—due to multiple physical complications and additional medication burden [65]. Elderly patients taking at least 5 medications are at increased risk of mild cognitive impairment, dementia, falls, frailty, disability, and mortality, while ADRs are estimated to be 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, IBD and juvenile arthritis—are attributable to around 60% of non-adherence among children [68-70].

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

No.	Status	Factors
1.	Patient's socio-economic status	Low health literacy, lack of family or social support network, unstable living or homelessness, financial insecurity
2.	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
3.	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
4.	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

CONCLUSION

Finally, it can be said that patients' knowledge and perception of the disease is the main driving force in determining their adherence to the treatment regimen. Health care providers should explore providing more effective health-education to identify patients' attitudes toward disease, trust in medications, psychological stressors, and increase medication adherence.

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)

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