



REVIEW PAPER

Taking medicine in the right way – most important but most neglected

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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. 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.

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

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

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 centers for disease control and prevention (CDC) estimates that medication non-adherence accounts for 30 to 50% of chronic disease treatment failures. Poor adherence can lead to treatment failure, worsening symptoms, and health deterioration.³

Aim

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.

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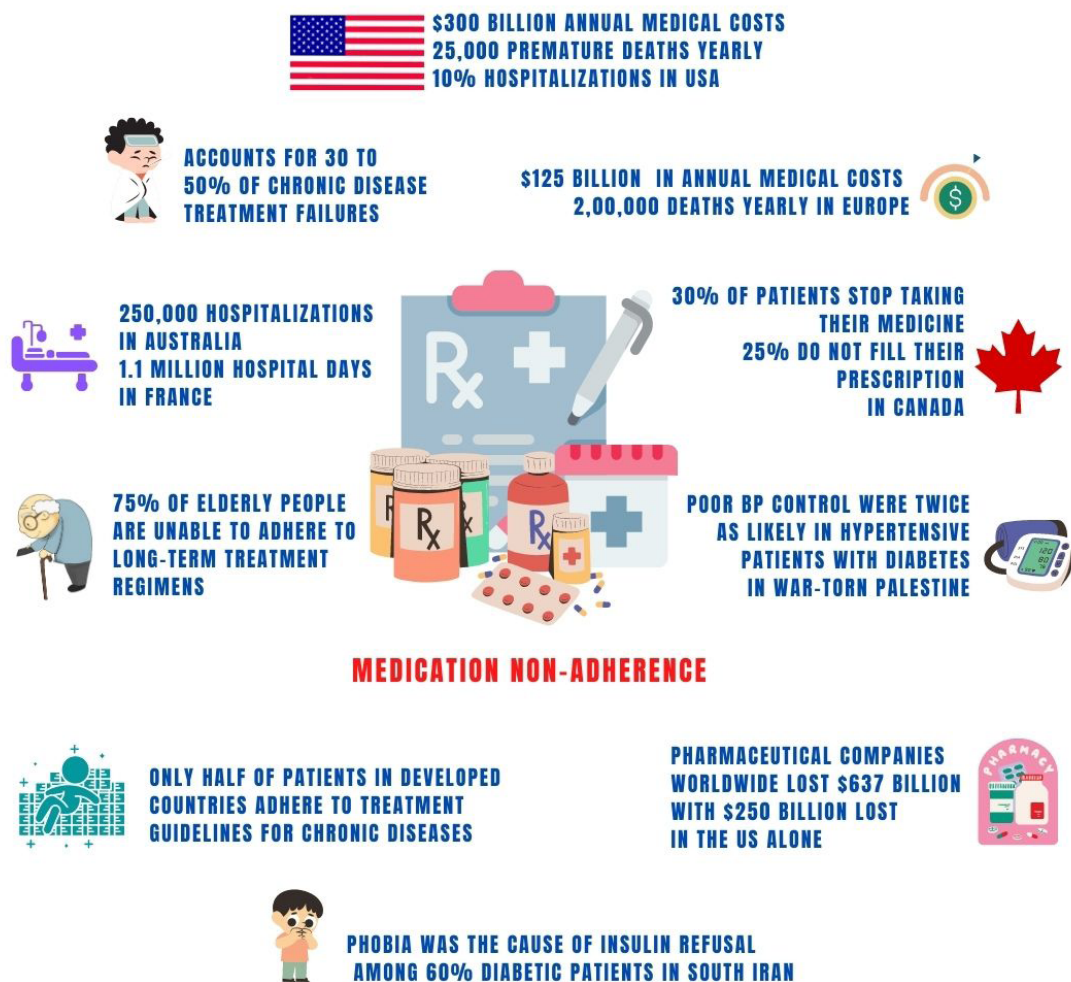


Fig. 1. Medication non-adherence and possible outcomes

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 on-line sources, journals from Elsevier, Springer, Willey On-line Library, and Wolters Kluwer were thoroughly searched.

Analysis of the literature

A literature review demonstrates that, even in highly privileged populations from developing countries, medication treatment protocols are not consistently followed. The primary causes that are not excusable include negligence, poor health literacy, and forgetfulness, the cost of medications, poly pharmacy, and patient perception of the repercussions of non-adherence, among many other factors. The main findings of the current study are that despite millions of hours of similarly conducted research conducted all over the world, the problem of non-adherence still exists. This is because the research is only published in journals and not conducted on the general public, who are victims of recklessness

with regard to their own health, whether intentionally or unintentionally. The solution to changing their health-seeking behavior is thorough patient education.

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); 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.^{8,10-12} Furthermore, two-thirds of medication-related hospitalizations in Australia are potentially avoidable.⁹ Ac-

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 2050¹⁸. 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 non-steroidal anti-inflammatory drugs in patients with COVID-19, Dengue, and Chikungunya

Non-steroidal anti-inflammatory drugs (NSAIDs) are responsible for at least 650,000 hospitalizations, 165,000 deaths, and 30% of adverse drug reactions (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, approximately 300 metric tons of morphine-type analgesics are used worldwide each year, with less than 1% distributed to low- and middle-income countries.³³ 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

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.

Humanitarian crisis: poor blood pressure control among cardiac patients

A recent study by the American Heart Association revealed that patients with high blood pressure (BP) 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 be-

lieve 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

Table 2. Interventions to improve treatment guideline adherence

Interventions	Details
Psychological adaptation training – ABC taxonomy	The first stage, initiation, 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, implementation, 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 discontinuation, denotes the end of therapy, when the next dose is skipped and no additional doses are given after that. The term "persistence," 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}

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

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).

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.

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Conflicts of interest

The author declares that he has no competing interests.

References

1. Grissinger M. The Five Rights: A Destination Without a Map. *Physical Therapy-Oxford Academic*. 2010;35(10):542.
2. Brown MT, Bussell JK. Medication adherence: WHO cares? *Mayo Clinic Proceedings*. 2011;86(4):304-314. doi: 10.4065/mcp.2010.0575.
3. Center for Drug Evaluation and Research. Why you need to take your medications as prescribed or instructed. U.S. Food and Drug Administration. <https://www.fda.gov/drugs/special-features/why-you-need-take-your-medications-prescribed-or-instructed>. Accessed November 5, 2022.
4. Barnett NL. Medication adherence: where are we now? A UK perspective. *Eur J Hosp Pharm*. 2014;21:181-184. doi: 10.1136/ejhpharm-2013-000373.
5. Record 6.8M people waiting for hospital treatment in England. *The Guardian*. <http://www.theguardian.com/society/2022/sep/08/waiting-lists-for-routine-hospital-treatment-in-england-break-record>. Published September 8, 2022. Accessed November 5, 2022.
6. Andrews L. 60% of NHS patients have waited 18 weeks for treatment at worst-performing hospital trust. *Daily Mail Online*. <http://www.dailymail.co.uk/news/article-10577387/60-NHS-patients-waited-18-weeks-treatment-worst-performing-hospital-trust.html>. Published March 7, 2022. Accessed November 5, 2022.
7. Mohiuddin AK. Chapter 14. Patient Compliance. *The Role of the Pharmacist in Patient Care: Achieving High Quality, Cost-Effective and Accessible Healthcare Through a Team-Based, Patient-Centered Approach*. Universal-Publishers; 2020:250-270.
8. <https://www.universal-publishers.com/book.php?method=ISBN&book=1627343083>
9. Cutler RL, Torres-Robles A, Wiecek E, et al. Pharmacist-led medication non-adherence intervention: reducing the economic burden placed on the Australian health care system. *Patient Preference and Adherence*. 2019;13:853-862. doi: 10.2147/PPA.S191482.
10. Lim R, Ellett LM, Semple S, Roughead EE. The extent of medication-related hospital admissions in Australia: A review from 1988 to 2021. *Drug Safety*. 2022;45(3):249-257. doi: 10.1007/s40264-021-01144-1.
11. Medication Nonadherence: Medicine's Weakest Link. Wolters Kluwer, Health/Experts Insight, <https://www.wolterskluwer.com/en/expert-insights/medication-nonadherence-medicines-weakest-link>. Accessed February 3, 2020.
12. Kardas P, Bago M, Barnestein-Fonseca P, et al. Reimbursed medication adherence enhancing interventions in 12 European countries: Current state of the art and future challenges. *Front Pharmacol*. 2022;13:944829. doi:10.3389/fphar.2022.944829
13. van Boven JF, Tsiligianni I, Potočnjak I, et al. European Network to Advance Best Practices and Technology on Medication Adherence: Mission Statement. *Front Pharmacol*. 2021;12:748702. doi: 10.3389/fphar.2021.748702.
14. Bonsu KO, Young S, Lee T, Nguyen H, Chitsike RS. Adherence to Antithrombotic Therapy for Patients Attending a Multidisciplinary Thrombosis Service in Canada – A Cross-Sectional Survey. *Patient Preference and Adherence*. 2022;16:1771-1780. doi: 10.2147/PPA.S367105.
15. Zhang Y, Flory JH, Bao Y. Chronic Medication Nonadherence and Potentially Preventable Healthcare Utilization and Spending Among Medicare Patients. *J Gen Intern Med*. 2022;37(14):3645-3652. doi: 10.1007/s11606-021-07334-y.

16. Bulik BS. Nonadherence costs pharma \$600B-plus in annual sales: Study. Fierce Pharma. <https://www.fiercepharma.com/marketing/non-adherence-costs-healthcare-system-patient-outcomes-and-pharma-bottom-line>. Published November 22, 2016. Accessed November 24, 2022.
17. Bahta M, Tesfamariam S, Weldemariam DG, et al. Dispensing of antibiotics without prescription and associated factors in drug retail outlets of Eritrea: A simulated client method. *PLoS One*. 2020;15(1):e0228013. doi: 10.1371/journal.pone.0228013.
18. Improve antibiotic use. Centers for Disease Control and Prevention. <https://www.cdc.gov/sixteen/hai/index.htm>. Published March 9, 2022. Accessed November 18, 2022.
19. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*. 2022;399(10325):629-655. doi: 10.1016/S0140-6736(21)02724-0.
20. Rawson TM, Moore LSP, Zhu N, et al. Bacterial and Fungal Coinfection in Individuals With Coronavirus: A Rapid Review To Support COVID-19 Antimicrobial Prescribing. *Clinical Infectious Diseases-Oxford Academic*. 2020;71(9):2459-2468. doi:10.1093/cid/ciaa530.
21. Clancy CJ, Nguyen MH. Coronavirus disease 2019, superinfections, and antimicrobial development: what can we expect? *Clinical Infectious Diseases-Oxford Academic*. 2020;71:2736-2743.
22. Daria S, Islam MR. Indiscriminate Use of Antibiotics for COVID-19 Treatment in South Asian Countries is a Threat for Future Pandemics Due to Antibiotic Resistance. *Clinical Pathology - SAGE Journals*. 2022;15:2632010X221099889. doi: 10.1177/2632010X221099889.
23. Langford BJ, So M, Raybardhan S, et al. Antibiotic prescribing in patients with COVID-19: Rapid review and meta-analysis. *Clinical Microbiology and Infection*. 2021;27:520-531. doi: 10.1016/j.cmi.2020.12.018.
24. Cong W, Poudel AN, Alhusein N, Wang H, Yao G, Lambert H. Antimicrobial Use in COVID-19 Patients in the First Phase of the SARS-CoV-2 Pandemic: A Scoping Review. *Antibiotics*. 2021;10(6):745. doi: 10.3390/antibiotics10060745.
25. Kamara IF, Kumar AMV, Maruta A, et al. Antibiotic Use in Suspected and Confirmed COVID-19 Patients Admitted to Health Facilities in Sierra Leone in 2020-2021: Practice Does Not Follow Policy. *Int J Environ Res Public Health*. 2022;19(7):4005. doi: 10.3390/ijerph19074005.
26. Usman M, Farooq M, Hanna K. Environmental side effects of the injudicious use of antimicrobials in the era of COVID-19. *Sci Total Environ*. 2020;745:141053. doi: 10.1016/j.scitotenv.2020.141053.
27. Kasciūškevičiūtė S, Gumbrevičius G, Vendzelytė A, Ščiupokas A, Petrikonis K, Kaduševičius E. Impact of the World Health Organization Pain Treatment Guidelines and the European Medicines Agency Safety Recommendations on Nonsteroidal Anti-Inflammatory Drug Use in Lithuania: An Observational Study. *Medicina*. 2018;54(2):30. doi: 10.3390/medicina54020030.
28. Davis A, Robson J. The dangers of NSAIDs: look both ways. *Br J Gen Pract*. 2016;66(645):172-173. doi: 10.3399/bjgp16X684433.
29. Lucas GNC, Leitão ACC, Alencar RL, Xavier RMF, Daher EF, Silva Junior GBD. Pathophysiological aspects of nephropathy caused by non-steroidal anti-inflammatory drugs. *Brazilian Journal of Nephrology*. 2019;41(1):124-130. doi: 10.1590/2175-8239-JBN-2018-0107.
30. Mohiuddin AK. Medication adherence: Fact or fictions? *Current Research in Public Health*. 2022;2(1):18-21. doi: 10.31586/crph.2022.533.
31. Jahrami H, BaHammam AS, Bragazzi NL, Saif Z, Faris M, Vitiello MV. Sleep problems during the COVID-19 pandemic by population: a systematic review and meta-analysis. *J Clin Sleep Med*. 2021;17(2):299-313. doi: 10.5664/jcsm.8930.
32. Ostuzzi G, Papola D, Gastaldon C, et al. Safety of psychotropic medications in people with COVID-19: evidence review and practical recommendations. *BMC Medicine-Springer Nature*. 2020;18(1):215. doi: 10.1186/s12916-020-01685-9.
33. Sarangi A, McMahan T, Gude J. Benzodiazepine Misuse: An Epidemic Within a Pandemic. *Cureus*. 2021;13(6):e15816. doi: 10.7759/cureus.15816.
34. Bhadelia A, De Lima L, Arreola-Ornelas H, Kwete XJ, Rodriguez NM, Knaul FM. Solving the Global Crisis in Access to Pain Relief: Lessons From Country Actions. *Am J Public Health*. 2019;109(1):58-60. doi: 10.2105/AJPH.2018.304769.
35. Lopez G. Marijuana Majority/ Americans support marijuana legalization, but many of their political leaders do not. *The New York Times*. <https://www.nytimes.com/2022/11/23/briefing/legal-weed-marijuana.html>. Accessed November 23, 2022.
36. Oltermann P. Germany announces plan to legalise cannabis for recreational use. *The Guardian*. <https://www.theguardian.com/world/2022/oct/26/germany-to-legalise-cannabis-for-recreational-use>. Published October 26, 2022.
37. Mohiuddin AK. Our low health literacy needs urgent fixing. <https://www.thedailystar.net/opinion/views/news/our-low-health-literacy-needs-urgent-fixing-3193246>. Published December 11, 2022.
38. Alam MM, Melhim LKB, Ahmad MT, Jemmali M. Public Attitude Towards COVID-19 Vaccination: Validation of COVID-Vaccination Attitude Scale (C-VAS). *J Multidiscip Healthc*. 2022;15:941-954. doi: 10.2147/JMDH.S353594.
39. Danabal KGM, Magesh SS, Saravanan S, Gopichandran V. Attitude towards COVID 19 vaccines and vaccine hesitancy in urban and rural communities in Tamil Nadu, India - a community based survey. *BMC Health Services Research*. 2021;21(1):994. doi: 10.1186/s12913-021-07037-4.

40. Leelavathy M, Messaline S, Ramachandran D, Sukumaran A, Jose R, Noufel AN. Attitude towards COVID-19 vaccination among the public in Kerala: A cross sectional study. *Fam Med Prim Care Rev*. 2021;10(11):4147-4152. doi: 10.4103/jfmpc.jfmpc_583_21.
41. Paul E, Steptoe A, Fancourt D. Attitudes towards vaccines and intention to vaccinate against COVID-19: Implications for public health communications. *Lancet Reg Health Eur*. 2021;1:100012. doi: 10.1016/j.lanepe.2020.100012.
42. Chauke GD, Nakwafila O, Chibi B, Sartorius B, Mashamba-Thompson T. Factors influencing poor medication adherence amongst patients with chronic disease in low-and-middle-income countries: A systematic scoping review. *Heliyon*. 2022;8(6):e09716. doi: 10.1016/j.heliyon.2022.e09716.
43. Chong E, Wang H, King-Shier KM, Quan H, Rabi DM, Khan NA. Prescribing patterns and adherence to medication among South-Asian, Chinese and white people with type 2 diabetes mellitus: a population-based cohort study. *Diabetic Medicine*. 2014;31(12):1586-1593. doi: 10.1111/dme.12559.
44. Sohal T, Sohal P, King-Shier KM, Khan NA. Barriers and Facilitators for Type-2 Diabetes Management in South Asians: A Systematic Review. *PLoS One*. 2015;10(9):e0136202. doi: 10.1371/journal.pone.0136202.
45. Alsairafi ZK, Taylor KM, Smith FJ, Alattar AT. Patients' management of type 2 diabetes in Middle Eastern countries: review of studies. *Patient Preference and Adherence*. 2016;10:1051-62. doi: 10.2147/PPA.S104335.
46. Almigbal TH, Almutairi KM, Vinluan JM, et al. Association of health literacy and self-management practices and psychological factor among patients with type 2 diabetes mellitus in Saudi Arabia. *Saudi Medical Journal*. 2019;40(11):1158-1166. doi: 10.15537/smj.2019.11.24585.
47. Nair SC, Sreedharan J, Satish KP, Ibrahim H. Health literacy in a high income Arab country: A nation-wide cross-sectional survey study. *PLoS One*. 2022;17(10):e0275579. doi: 10.1371/journal.pone.0275579.
48. Hashim SA, Barakatun-Nisak MY, Abu Saad H, Ismail S, Hamdy O, Mansour AA. Association of Health Literacy and Nutritional Status Assessment with Glycemic Control in Adults with Type 2 Diabetes Mellitus. *Nutrients*. 2020;12(10):3152. doi: 10.3390/nu12103152.
49. Hussein SH, Albatineh AN, Almajran A, Ziyab AH. Association of health literacy and other risk factors with glycemic control among patients with type 2 diabetes in Kuwait: A cross-sectional study. *Primary Care Diabetes*. 2021;15(3):571-577. doi: 10.1016/j.pcd.2021.01.011.
50. Khatiwada B, Rajbhandari B, Mistry SK, Parsekar S, Yadav UN. Prevalence of and factors associated with health literacy among people with Noncommunicable Diseases (NCDs) in South Asian countries: A systematic review. *Clin Epidemiology Glob Health*. 2022;18:101174. doi: 10.1016/j.cegh.2022.101174.
51. Rajah R, Hassali MAA, Murugiah MK. A systematic review of the prevalence of limited health literacy in Southeast Asian countries. *Public Health*. 2019;167:8-15. doi: 10.1016/j.puhe.2018.09.028.
52. Saleh A, Wirda W, Irwan AM, Latif AI. The relationships among self-efficacy, health literacy, self-care and glycemic control in older people with type 2 diabetes mellitus. *Working with Older People*. 2021;25(2):164-169. doi: 10.1108/wwop-08-2020-0044.
53. Choudhry NK, Kronish IM, Vongpatanasin W, et al. Medication Adherence and Blood Pressure Control: A Scientific Statement From the American Heart Association. *Hypertension*. 2022;79(1):e1-e14. doi: 10.1161/HYP.0000000000000203.
54. Elnaem MH, Mosaad M, Abdelaziz DH, et al. Disparities in Prevalence and Barriers to Hypertension Control: A Systematic Review. *Int J Environ Res Public Health*. 2022;19(21):14571. doi: 10.3390/ijerph192114571
55. Keasley J, Oyebo O, Shantikumar S, et al. A systematic review of the burden of hypertension, access to services and patient views of hypertension in humanitarian crisis settings. *BMJ Glob Health*. 2020;5(11):e002440. doi: 10.1136/bmjgh-2020-002440.
56. Alawneh IS, Yasin A, Musmar S. The Prevalence of Uncontrolled Hypertension among Patients Taking Antihypertensive Medications and the Associated Risk Factors in North Palestine: A Cross-Sectional Study. *Adv Med Sci*. 2022;2022:5319756. doi: 10.1155/2022/5319756
57. Rahman A, Biswas J, Banik PC. Non-communicable diseases risk factors among the forcefully displaced Rohingya population in Bangladesh. *PLOS Global Public Health*. 2022;2(9). doi: 10.1371/journal.pgph.0000930.
58. Lossius MI, Alfstad KÅ, Aaberg KM, Nakken KO. Discontinuation of antiepileptic drugs in seizure-free patients - when and how? *Journal of the Norwegian Medical Association*. 2017;137(6):451-454. doi: 10.4045/tidsskr.16.0957.
59. Caqueo-Urizar A, Urzúa A, Mena-Chamorro P, Bravo de la Fuente J. Effects of Adherence to Pharmacological Treatment on the Recovery of Patients with Schizophrenia. *Healthcare*. 2021;9(9):1230. doi: 10.3390/healthcare9091230.
60. Banerjee S, Varma RP. Factors affecting non-adherence among patients diagnosed with unipolar depression in a psychiatric department of a tertiary hospital in Kolkata, India. *Depress Res Treat*. 2013;2013:809542.
61. Graeupner D, Coman A. The dark side of meaning-making: How social exclusion leads to superstitious thinking. *J Exp Soc Psychol*. 2017;69:218-222.
62. Puckree T, Mkhize M, Mgbhozi Z, Lin J. African traditional healers: what health care professionals need to know. *Int J Rehabil Res*. 2002;25(4):247-251. doi: 10.1097/00004356-200212000-00001.
63. Taher M, Pashaeypoor S, Cheraghi MA, Karimy M, Hoseini ASS. Superstition in health beliefs: Concept exploration and development. *Fam Med Prim Care Rev*. 2020;9(3):1325-1330. doi: 10.4103/jfmpc.jfmpc_871_19.
64. Grim BJ, Grim ME. Belief, Behavior, and Belonging: How Faith is Indispensable in Preventing and Recovering from

- Substance Abuse. *J Relig Health*. 2019;58(5):1713-1750. doi: 10.1007/s10943-019-00876-w.
65. Mirahmadizadeh A, Delam H, Seif M, Banihashemi SA, Tabatabaee H. Factors Affecting Insulin Compliance in Patients with Type 2 Diabetes in South Iran, 2017: We Are Faced with Insulin Phobia. *Iran J Med Sci*. 2019;44(3):204-213.
66. Félix IB, Henriques A. Medication adherence and related determinants in older people with multimorbidity: a cross-sectional study. *Nursing Forum*. 2021;56:834-843. doi: 10.1111/nuf.12619.
67. Chippa V, Roy K. Geriatric Cognitive Decline and Polypharmacy. *National Library of Medicine*. <https://www.ncbi.nlm.nih.gov/books/NBK574575/>. Published January 2022. Accessed November 18, 2022.
68. Varghese D, Ishida C, Koya HH. Polypharmacy. *National Library of Medicine*. <https://www.ncbi.nlm.nih.gov/books/NBK532953/>. Published January 2022. Accessed November 18, 2022.
69. Santer M, Ring N, Yardley L, Geraghty AW, Wyke S. Treatment non-adherence in pediatric long-term medical conditions: systematic review and synthesis of qualitative studies of caregivers' views. *BMC Pediatrics*. 2014;14:63. doi: 10.1186/1471-2431-14-63.
70. Al-Hassany L, Kloosterboer SM, Dierckx B, Koch BC. Assessing methods of measuring medication adherence in chronically ill children—a narrative review. *Patient Preference and Adherence*. 2019;13:1175-1189. doi: 10.2147/PPA.S200058.
71. Wu YY, Luo YY, Huang LF, et al. Prevalence and risk factors of medication non-adherence in children with inflammatory bowel disease. *Zhonghua Er Ke Za Zhi*. 2022;60(11):1191-1195. doi:10.3760/cma-j.cn112140-20220110-00036
72. Jin J, Sklar GE, Min Sen Oh V, Chuen Li S. Factors affecting therapeutic compliance: A review from the patient's perspective. *Ther Clin Risk Manag*. 2008;4(1):269-86. doi: 10.2147/tcrm.s1458.
73. Wilder ME, Kulie P, Jensen C, et al. The Impact of Social Determinants of Health on Medication Adherence: a Systematic Review and Meta-analysis. *J Gen Intern Med*. 2021;36(5):1359-1370. doi: 10.1007/s11606-020-06447-0.
74. Kardas P, Lewek P, Matyjaszczyk M. Determinants of patient adherence: a review of systematic reviews. *Front Pharmacol*. 2013;4:91. doi: 10.3389/fphar.2013.00091.
75. Bosworth HB, Blalock DV, Hoyle RH, Czajkowski SM, Vols CI. The role of psychological science in efforts to improve cardiovascular medication adherence. *Am Psychol*. 2018;73(8):968-980. doi: 10.1037/amp0000316
76. Correia S, Correia A, Videira I, et al. Health gains of telephone follow-up nursing intervention to patient with heart disease. *Gerontechnology*. 2019:107-113. doi:10.1007/978-3-030-16028-9_10
77. Tan CS. The Need of Patient Education to Improve Medication Adherence Among Hypertensive Patients. *Malays J Pharm Sci*. 2020;6(1):1-5. doi: 10.52494/moel1486.
78. Michie S, Richardson M, Johnston M, et al. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. *Ann Behav Med*. 2013;46(1):81-95. doi: 10.1007/s12160-013-9486-6.
79. Howren MB, Gonzalez JS. Treatment adherence and illness self-management: introduction to the special issue. *J Behav Med*. 2016;39(6):931-934. doi: 10.1007/s10865-016-9804-0.
80. Bahri P, Harrison-Woolrych M. Focusing on risk communication about medicines: why now?. *Drug Safety*. 2012;35(11):971-975. doi: 10.1007/BF03261984.
81. Fukuda Y, Ando S, Saito M. Risk awareness, medication adherence, and driving behavior as determined by the provision of drug information to patients. *Patient Educ Couns*. 2020;103(8):1574-1580. doi: 10.1016/j.pec.2020.02.037.