

# The Non-adherence Scope in Stroke: A Narrative Review

Jamunarani Appalasamy<sup>1,\*</sup>, Amutha Selvaraj<sup>1</sup>, Siva Seeta Ramaiah<sup>2</sup>

<sup>1</sup>School of Pharmacy, Monash University, Bandar Sunway, Subang Jaya, MALAYSIA.

<sup>2</sup>Subang Jaya Medical Centre, SS12, Subang Jaya, MALAYSIA.

## ABSTRACT

Stroke is among the most significant disease burden globally, with upper middle-income countries having the highest prevalence. Worldwide stroke burden is credited to modifiable risk factors related to underlying comorbidities and the patients' lifestyle. Non-adherence to medication is an added liability which cause substantial loss in terms of money, time, and effort of various stakeholders. There is a lack of behavioural interventions with significant results to overcome intentional non-adherence to stroke preventative medication. A narrative review was selected for analysis to gain a general understanding and defining of intentional non-adherence. The results of this review identified several criteria of perception, belief, and attitude of stroke patients' intrinsic and extrinsic characteristics of

medication taking and treatment behaviour which are potential modifiable factors to sustain stroke prevention.

**Key words:** Stroke, Non-adherence, Behaviour, Belief, Intrinsic and Extrinsic factors, Medication taking behaviour.

## Correspondence

**Dr. Jamunarani Appalasamy,**

School of Pharmacy, Monash University, MALAYSIA.

Email id: jamuna.rani@monash.edu

DOI: 10.5530/jyp.2022.14.4

## INTRODUCTION

Annually, a substantial number of people end with moderate to severe long-term disability after stroke.<sup>1</sup> Up to one third of all people who experience a stroke will proceed to another stroke (recurrent stroke) within weeks or months.<sup>2</sup> The morbidity rate of stroke could paralyse economic growth caused by incurring treatment expenses and loss of workforce.<sup>3</sup> According to the INTERSTROKE study, about 90% of the worldwide stroke burden are credited to modifiable risk factors related to underlying comorbidities and the patients' lifestyle.<sup>4,5</sup> Furthermore, these modifiable recurrent stroke risk factors are added-on with a heavy burden; non-adherence to medication which cause substantial loss in terms of money, time and effort of various stakeholders.<sup>6,7</sup>

Ultimately, adherence to medication and treatment management is a main key-action towards treatment optimisation despite all the barriers. Thus, extensive research was done past decades to understand adherence in stroke especially prevention via modifiable risk factors. For example, high adherence to antihypertensive medications was associated with higher odds of blood pressure control than those with low adherence levels.<sup>8</sup> Whereas, a meta-analysis of 23 randomized trials on antihypertensive medication compared with no drug therapy resulted in a 32% reduction in stroke risk.<sup>9</sup> Similarly, each 25% increment of increased adherence to statin medications for hyperlipidaemia was associated with a 3.8-mg/dL reduction in LDL cholesterol.<sup>10</sup> Moreover, cessation of smoking with adherence to interventions such as nicotine replacement and oral smoking-cessation medications helped to reduce the risk of stroke.<sup>11</sup>

Healthcare prescribers continuously find it a challenge to tailor adherence interventions to patients' needs and understanding complexity of non-adherence characteristics is a test by its own.<sup>12-14</sup> This article narrates a glimpse of medication non-adherence adversity with illustration of scenario solely from neurologists' experiences with stroke patients.

## Primary and secondary medication non-adherence in recurrent stroke prevention

Primary non-adherence to medication occurs when the patient never collects or starts a new prescribed medication.<sup>15</sup> Personal negative perception, attitude and belief towards the stroke preventative medication hinders the patient's adherence. For example, a stroke survivor may not believe that he needs to take aspirin because he does not physically 'feel' the effects of blood thickening or atherosclerosis. He may deny ingesting the medication based on his benefit over risk ratio justification, in this case, whether taking aspirin would cause him harm.

Whereas secondary non-adherence to medication occurs when the patient does not take the prescribed medication according to instruction which causes suboptimal therapy.<sup>15</sup> As in the case above, stopping aspirin ingestion could result from the patient experiencing unwanted gastro-intestinal disturbances or otherwise, self-medicating with other alternative herbal supplements for blood thinning effect.

## Intentional and unintentional medication non-adherence in recurrent stroke prevention

Medication adherence is defined as the extent of a patient continuing his prescribed medication to a certain degree accepted and agreed by both the prescriber and patient.<sup>16,17</sup> Intentional non-adherence to medication is based on personal justification of treatment and disease whereby the patient actively decides to stop taking his medications at the beginning or during various stages of his or her treatment phase. Certain patient related factors such as belief, attitude or dissatisfaction with the prescriber could cause his non-adherence. Hence, the patient's 'loyalty' to adhere to medication regimen and treatment advice depends heavily on his confidence and motivation.<sup>18</sup> For instance, a stroke survivor who learned about the side-effects of warfarin would probably anticipate the fear of bleeding and may decide to ignore the importance of continuing

warfarin or quit even before starting the medication. However, this event would be reversed if the prescriber notified, discussed, and convinced the patient regarding the information which eventually creates a mutual trust between both. For example, smoking cessation treatment which require motivation to quit. Under the same circumstances, a stroke patient with paralysis may require a longer personalised consultation followed-up with intermittent care from rehabilitation compared to another non-paralysed stroke patient.

Unintentional non-adherence to medication is not strongly related to personal belief and attitude of the patient but rather depends on physical, socioeconomic, and cognitive capability in continuing the medication regimen.<sup>18</sup> This type of non-adherence commonly affects elderly stroke patients who are prescribed several types of medication for underlying comorbidities such as diabetes or hypertension. Forgetfulness could be a core factor of medication negligence making these patients to be classified as vulnerable.<sup>19,20</sup> Therefore, it is vital to assess patients' type of non-adherence and their level of concordance to avoid suboptimal stroke prevention medication therapy. However, oral adherence assessment and feedback from this group of patients would be inaccurate as most of them tend to please the prescriber and produce false positive responses.<sup>21</sup> In this way, resolving unintentional non-adherence to medication is hardly modifiable with behavioural intervention alone and would certainly require aid from caregiver, support groups and health system management. This article would elaborate further on causal factors of intentional non-adherence to stroke preventative medication with distinctive attention of its intrinsic and extrinsic characteristics affecting medication taking behaviour among stroke survivors.

## METHODS

A literature search was conducted using Google Scholar, Ovid, Medline, PubMed and Cochrane databases, with most articles covering the time period from 2000 to 2020. Keywords and phrases related to medication non-adherence, medication taking behaviour and recurrent stroke were used. Search terms included "intentional medication non-adherence," "stroke preventative medication non-adherence," "intentional non-adherence characteristics" and "extrinsic and intrinsic of non-adherence." We excluded non-English articles, letters, editorials and comments. Only studies, reports or reviews which significantly link intentional non-adherence factors with recurrent stroke were accepted for analysis.

## OUTCOME

Upon discharge from the inpatient ward within two weeks or more depending on physical and cognitive improvement, a patient with TIA or stroke would be expected to meet their physician for a few follow-ups on health and medication adherence assessment. Recurrent stroke therapeutic management includes lifestyle modification in terms of physical exercise, diet plan, rehabilitation involvement, knowledge enhancement, adherence to an appropriate medication regime and self-care management such as smoking cessation. These key components are based on personalized strategies to improve the patient's ability to self-manage their morbidity with a belief that it would lead the individual to a perceived quality of life. However, a follow-up study reported a substantial drop-out at outpatient stroke facilities within few months of stroke admission and medication recollection post discharge.<sup>22</sup>

Table 1 and the following sections further elaborates how do these intrinsic and extrinsic characteristics of intentional non-adherence critically affect medication taking behaviour among stroke survivors. As we may notice, intrinsic factors originate from the doer itself; the stroke patient, whereas extrinsic factors derive from external effect affecting the doer's action.

**Table 1: Intentional nonadherence factors affecting medication taking behaviour of stroke preventative medication.<sup>23</sup>**

Intrinsic factors	Extrinsic factors
Personal attitude, perception and belief about the prescriber, the prescribed medication, the disease.	Family and community support Cultural health practice diversity Clinician relationship Medication effect Functional health literacy
Self-motivation, depression and readiness to follow prescribed medication	Natural environment Media influence
Self-care management and medication practice	Access to alternative medication

## Personal attitude, perception and belief about the prescriber, the prescribed medication, and the disease

A successful stroke care and prevention management depends on enthusiastic patients with psychological readiness who trust their care providers' support for health improvement. On the other hand, patients who develop negative thoughts or misconceptions about their condition and incline away from their treatment efforts set a barrier for any improvement.<sup>24</sup> According to Necessity and Concerns framework, the patients' belief is built on common-sense evaluations of prescribed medicines which involves perceptions of personal need for treatment and interest of potential adverse events.<sup>25</sup>

A recent meta-analysis done on eighteen studies supported the concept of medication beliefs as an integral part of the self-regulation of illness theory.<sup>26</sup> Cultural variations such as language differences were noted across patients and society, or country predominantly influences the belief about the disease. Furthermore, their family and society influence, knowledge about the disease, their prescriber's belief and confidence about the treatment and delivery system of the medication eventually mould specific individual attitude towards recovery and the meaning of quality of life.<sup>27</sup>

As an illustration, a newly diagnosed patient with TIA who is obese would assume increased weight and lack of exercise as main cause of the disease compared to a smoker who would conclude smoking as the leading cause of TIA. Depending on their past experiences with these symptoms and influence from their physician, family, friends, society perspectives and the media; the illness representation is concerning the individual's lifestyle before and after diagnosis of TIA. Most stroke patients would link their lifestyle habits as the main cause of recurrent stroke as an illness compared to other factors such as uncontrolled diabetes, hypertension, or stress. Based on their own benefit outweighing risk and health belief justification, these patients would modify their lifestyle whether to exercise more or to stop smoking or vice versa.

Disease awareness or functional health literacy depends on the stroke patients' knowledge level.<sup>28-30</sup> The depth of knowledge and readiness to accept the ability depends on exposure, and it differs between individuals. For instance, a person who works with the healthcare would be aware of recurrent stroke because of the nature of the job compared to a construction worker unless the latter had different exposure to stroke knowledge. In addition, family or society environment that evolves with food preparation and self-care practice would also contribute to their understanding of stroke. In other words, these patients would have their own prognosis of their diagnosed disease regarding quitting or continuing the perceived lifestyle.

To add on, positive clinician relationship between patients and prescribers enhances a better disease management. In other words, choice of a medication regime, delivery system and consideration of adverse

effect depends on in-depth understanding of belief and perception of the patient. In this case, the patient could choose between a nicotine patch or gum based on self-understanding about smoking cessation and capability of maintaining a good adherence level or a choice between a combination of an oral anti-obesity e.g., orlistat and exercise for weight management. But to keep in mind, periodic monitoring is essential to avoid 'the white-coat adherence syndrome' whereby patients start to please and continue to report positive medication efficacy to the prescriber for the sake of maintaining a good clinician relationship.<sup>6</sup>

### Self-motivation, depression, and readiness to follow the prescribed medication

Self-motivation, also known as self-efficacy, is perceived as the ability to overcome changes or undertake a task of self-management.<sup>31,32</sup> High self-motivated person has a positive outlook of life and coping capability in managing their disease compared to the low motivated person.<sup>33</sup> Self-determination theory developed by Edward L. Deci and Richard M. Ryan explains the association between human motivation and personality characteristics with basic needs satisfaction of these patients without external influences.<sup>34,35</sup> Self-motivation is classified into; intrinsic and extrinsic motivation.<sup>34</sup>

Intrinsic motivation causes a person engaging in a behaviour for its own sake as they enjoy it or finds the activity enjoyable. Whereas, extrinsic motivation causes engagement in an activity to earn a reward or to avoid negative consequences.<sup>34-38</sup> As the case in point, an intrinsically motivated patient with TIA who is obese but loves to exercise would willingly engage in the activity without expecting if the exercise would decrease their weight and would have had the same rigor even before the TIA event. In comparison, an extrinsic motivated patient with TIA and obese would start to engage in some physical activity to reduce weight based on past learning experience that obesity is a hindrance to wellness.<sup>34</sup> Similarly, 'healthy adherer effect'; a perception of wellness also depends on the patients' inner being and will to strive compared to trusting 100% effect of the preventative medication.<sup>38</sup> Hence, a highly motivated, adhering to a certain medication regime would be a simple routine otherwise it would be a burden affecting their quality of life.

Family and society ongoing support motivate stroke survivors to improve their condition. Yet, surprisingly, a huge percentage of moderate to severe condition stroke patients especially with debilitating physical symptoms experience depression due to loneliness and inability to maintain a stable relationship with loved one. In addition, patients who has lost their income due to physical disability or lack of medical insurance support also face depression and low self-motivation.<sup>39,40</sup>

There have been studies on the natural environment on self-motivation, which we believe plays a role in influencing medication-taking behaviour. However, a recent systematic review reported that good nature, managed and clean dwelling or conducive working environment gives positive personal inner self-esteem and less stress, which stroke survivors crucially require for quality life satisfaction.<sup>41</sup> Moreover, active communication with prescriber with high-intensity treatment has shown vast improvement among low self-esteem and depressed patients.<sup>42</sup>

### Self-medication and treatment management practice

Self-medication is defined as health-seeking behaviour in which the individual self-administers substances perceived as safe to improve one's ailment without medical supervision.<sup>43</sup> Self-medication involves food, caffeine, alcohol or over the counter (OTC) medication such as opioids, painkillers, and supplements. Self-medicating behaviour begins when there is a doubt on medication efficacy or added on factors as mentioned earlier e.g., culture, media, awareness, and experience. Hence, self-medication unknowingly could cause intentional non-adherence to

prescribed medication. For instance, antiplatelet and anticoagulant are known as 'silent saver' thus its significant importance could not be physically felt or seen except by parameter monitoring. Although it causes some discomfort, physicians prescribe it based on its benefit over risk properties. Nevertheless, the rise of 'blood thinner herbs' has generated a barrier against the potency of those medications.

The disparity of belief about prescribed medication is very much affected by cultural self-care practice and misconception, media information misinterpretation, low awareness of the medical benefit and abundance of alternative medication.

For example, herbal or homeopathy practitioners would recommend ginkgo biloba, danshen, cinnamon, turmeric or cayenne pepper for blood thinning effect compared to aspirin.<sup>44</sup> These herbs have been recommended as blood thinners yet, they are not well documented with recommended dosage as stroke preventative agents and therefore, are potentially hazardous. In addition, naturopathies recommend these supplements as alternatives or adjunct treatment for stroke symptoms which is one root cause of drug interactions. Self-medication practice has become a norm whereby patients meet various health practitioners when they do not 'feel' results within their perceived 'healing time'. In response to advanced information technology, it's a growing trend that stroke patients pursue for various treatment practice without seeking advice from their prescriber accounting to another dilemma; 'problematic polypharmacy'.<sup>45</sup>

## FUTURE DIRECTIONS

### Acknowledging intrinsic and extrinsic factors of medication taking and treatment management behaviour

It is a prerequisite to recognize the needs of every individual, physical and emotional prior to prescribing stroke preventative medication therapy. Before starting a medication regimen, we need to explore the stroke survivor's background, experiences, attitude, capability, and readiness to adhere. Patients' perception regarding stroke and its treatment, their readiness to accept changes includes motivation level, belief, awareness, and their willingness to share information with prescribers are the challenges we would face in modifying medication taking behaviour among stroke patients.<sup>30,43,47</sup> In addition, social cognitive behavioural theory that describes human motivation and action are controlled by anticipation that shapes personal competency has to be well understood.<sup>31,32</sup> Hence, strong focus on intrinsic and extrinsic factors with continuity of assessment is the current requirement for preventing stroke recurrence.

## ACKNOWLEDGEMENT

The APC of this article was supported by the School of Pharmacy, Monash University Malaysia [ECR grant /000006].

## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

## REFERENCES

1. American Heart Association. Heart disease and stroke statistics. Dallas: American Heart Association; 2020. Update. Available from: [https://www.heart.org/HEARTORG/General/Heart-and-Stroke-Association-Statistics\\_UCM\\_319064\\_SubHomePage.jsp](https://www.heart.org/HEARTORG/General/Heart-and-Stroke-Association-Statistics_UCM_319064_SubHomePage.jsp). [accessed 5.12.21].
2. Johnston SC, Gress DR, Browner WS, Sidney S. Short-term prognosis after emergency department diagnosis of TIA. *JAMA*. 2000;284(22):2901-6. doi: 10.1001/jama.284.22.2901, PMID 11147987.
3. Dele A, Anderson S. An estimation of the economic impact of chronic non-communicable diseases in selected countries. Geneva: World Health Organization Department of Chronic Diseases and Health Promotion; 2006.

- Available from: <http://www.who.int/chp>. [accessed 5.12.21].
4. O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, et al. INTERSTROKE investigators. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): A case-control study. *Lancet*. 2016;388(10046):761-75. doi: 10.1016/S0140-6736(16)30506-2, PMID 27431356.
  5. Hughes S. INTERSTROKE highlights urgent need for stroke prevention. *Medscape medical news*; 2016. Available from: <http://www.medscape.com/viewarticle/866640>. [accessed 5.12.21].
  6. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005;353(5):487-97. doi: 10.1056/NEJMra050100, PMID 16079372.
  7. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care*. 2005;43(6):521-30. doi: 10.1097/01.mlr.0000163641.86870.af, PMID 15908846.
  8. Bramley TJ, Gerbino PP, Nightengale BS, Frech-Tamas F. Relationship of blood pressure control to adherence with antihypertensive monotherapy in 13 managed care organizations. *J Manag Care Pharm*. 2006;12(3):239-45. doi: 10.18553/jmcp.2006.12.3.239, PMID 16623608.
  9. Psaty BM, Lumley T, Furberg CD, Schellenbaum G, Pahor M, Alderman MH, et al. Health outcomes associated with various antihypertensive therapies used as first-line agents: A network meta-analysis. *JAMA*. 2003;289(19):2534-44. doi: 10.1001/jama.289.19.2534, PMID 12759325.
  10. Ho PM, Rumsfeld JS, Masoudi FA, McClure DL, Plomondon ME, Steiner JF, et al. Effect of medication non-adherence on hospitalization and mortality among patients with diabetes mellitus. *Arch Intern Med*. 2006;166(17):1836-41. doi: 10.1001/archinte.166.17.1836, PMID 17000939.
  11. Fagerström K. The epidemiology of smoking: Health consequences and benefits of cessation. *Drugs*. 2002;62;Suppl 2:1-9. doi: 10.2165/00003495-200262002-00001, PMID 12109931.
  12. Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev*. 2008;2(2):CD000011. doi: 10.1002/14651858.CD000011.pub3, PMID 18425859.
  13. McDonald HP, Garg AX, Haynes RB. Interventions to enhance patient adherence to medication prescriptions: scientific review [scientific review]. *JAMA*. 2002;288(22):2868-79. doi: 10.1001/jama.288.22.2868, PMID 12472329.
  14. Kim JY, Wineinger NE, Steinhubl SR. The influence of wireless self-monitoring program on the relationship between patient activation and health behaviors, medication adherence, and blood pressure levels in hypertensive patients: A substudy of a randomized controlled trial. *J Med Internet Res*. 2016;18(6):e116. doi: 10.2196/jmir.5429, PMID 27334418.
  15. Deroose SF, Green K, Marrett E. Medication adherence increased by automated phone and mail notices. *Arch Intern Med*. 2012;172:1-6.
  16. Delamater AM. Improving patient adherence. *Clin Diabetes*. 2006;24(2):71-7. doi: 10.2337/diaclin.24.2.71.
  17. Meichenbaum D, Turk DC. Facilitating treatment adherence: A practitioner's guidebook. New York: Plenum Press; 1987.
  18. Wroe AL. Intentional and unintentional non-adherence: A study of decision making. *J Behav Med*. 2002;25(4):355-72. doi: 10.1023/A:1015866415552, PMID 12136497.
  19. Mufson EJ, Binder L, Counts SE, DeKosky ST, DeToledo-Morrell L, Ginsberg SD, et al. Mild cognitive impairment: Pathology and mechanisms. *Acta Neuropathol*. 2012;123(1):13-30. doi: 10.1007/s00401-011-0884-1, PMID 22101321.
  20. Forgetfulness: Knowing when to ask for help | National Institute on Aging. NIA. 2012.
  21. Pickering TG, Eguchi K, Kario K. Masked hypertension: A review. *Hypertens Res*. 2007;30(6):479-88. doi: 10.1291/hypres.30.479, PMID 17664850.
  22. Faridi KF, Peterson ED, McCoy LA, Thomas L, Enriquez J, Wang TY. Timing of first post discharge follow-up and medication adherence after acute myocardial infarction. *JAMA Cardiol*. 2016;1(2):147-55. doi: 10.1001/jamacardio.2016.0001, PMID 27437885.
  23. Rodriguez KM. Intrinsic and extrinsic factors affecting patient engagement in diabetes self-management: Perspectives of a certified diabetes educator. *Clin Ther*. 2013;35(2):170-8. doi: 10.1016/j.clinthera.2013.01.002, PMID 23411000.
  24. Reeve E, To J, Hendrix I, Shakib S, Roberts MS, Wiese MD. Patient barriers to and enablers of deprescribing: A systematic review. *Drugs Aging*. 2013;30(10):793-807. doi: 10.1007/s40266-013-0106-8, PMID 23912674.
  25. Horne R, Chapman SCE, Parham R, Freemantle N, Forbes A, Cooper V. Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: A meta-analytic review of the necessity-concerns framework. *PLOS ONE*. 2013;8(12):e80633. doi: 10.1371/journal.pone.0080633, PMID 24312488.
  26. Diefenbach MA, Leventhal H. The common-sense model of illness representation: Theoretical and practical considerations. *J Soc Distress Homeless*. 1996;5(1):11-38. doi: 10.1007/BF02090456.
  27. Hofstede G. Culture's consequences, comparing values, behaviors, institutions, and organizations across nations. Thousand Oaks, CA: SAGE; 2001.
  28. Bardel A, Wallander MA, Svärdsudd K. Factors associated with adherence to drug therapy: A population-based study. *Eur J Clin Pharmacol*. 2007;63(3):307-14. doi: 10.1007/s00228-006-0246-4, PMID 17344769.
  29. Hyre AD, Krousel-Wood MA, Muntner P, Kawasaki L, DeSalvo KB. Prevalence and predictors of poor antihypertensive medication adherence in an urban health clinic setting. *J Clin Hypertens (Greenwich)*. 2007;9(3):179-86. doi: 10.1111/j.1524-6175.2007.06372.x, PMID 17344769.
  30. Kirsch I, Jungeblut A, Jenkins L, Kolstad A. Adult literacy in America. A first look at the results of the national adult literacy survey. Washington, DC: National Center for Education Statistics, US Department of Education; 1993.
  31. Bandura A. Social foundations of thought and action. Englewood Cliffs, NJ: Prentice Hall; 1986.
  32. Bandura A. Self-efficacy mechanism in psychobiologic functioning. *Thought control of action*. Washington, DC: Hemisphere; 1992:355-94.
  33. Locke EA, Latham GP. A theory of goal setting and task performance. Englewood Cliffs, NJ: Prentice Hall; 1990.
  34. Ryan RM, Deci EL. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. *Am Psychol*. 2000;55(1):68-78. doi: 10.1037//0003-066x.55.1.68, PMID 11392867.
  35. Deci EL, Ryan RM. Motivation, personality, and development within embedded social contexts: An overview of self-determination theory. In: Ryan RM, editor, *Oxford handbook of human motivation*. Oxford, UK: Oxford University Press; 2012. p. 85-107.
  36. Myers DG. *Modules. Psychology*. 8th ed. New York: Worth Publishers; 2010.
  37. Plotnik R, Kouyoumjian H. *Introduction to psychology*. Wadsworth, CA: Belmont; 2011.
  38. Ho PM, Bryson CL, Rumsfeld JS. Medication adherence: Its importance in cardiovascular outcomes. *Circulation*. 2009;119(23):3028-35. doi: 10.1161/CIRCULATIONAHA.108.768986, PMID 19528344.
  39. Cacioppo J, Patrick W. *Loneliness: Human nature and the need for social connection*. New York: W.W. Norton and Company; 2008.
  40. Hawkey LC, Cacioppo JT. Loneliness matters: A theoretical and empirical review of consequences and mechanisms. *Ann Behav Med*. 2010;40(2):218-27. doi: 10.1007/s12160-010-9210-8, PMID 20652462.
  41. Bowler DE, Buyung-Ali LM, Knight TM, Pullin AS. A systematic review of evidence for the added benefits to health of exposure to natural environments. *BMC Public Health*. 2010;10:456. doi: 10.1186/1471-2458-10-456, PMID 20684754.
  42. Stewart M, Brown J, Weston, McWhinney I, McWilliam C, Freeman T. *Patient-centred medicine: Transforming the clinical method*. London: SAGE; 1995.
  43. Brunner R, Dunbar-Jacob J, Leboff MS, Granek I, Bowen D, Snetselaar LG, et al. Predictors of adherence in the Women's Health Initiative calcium and Vitamin D Trial. *Behav Med*. 2009;34(4):145-55. doi: 10.3200/BMED.34.4.145-155, PMID 19064373.
  44. Abebe W. Herbal medication: Potential for adverse interactions with analgesic drugs. *J Clin Pharm Ther*. 2002;27(6):391-401. doi: 10.1046/j.1365-2710.2002.00444.x, PMID 12472978.
  45. Martin D, Tony A, Rupert P. *Polypharmacy and medicines optimisation. Making it safe and sound The King's Fund*; 2013. Available from: <https://www.kingsfund.org.uk/publications/polypharmacy-and-medicines-optimisation>. [accessed 5.4.21].
  46. Steiner JF, Earnest MA. The language of medication-taking. *Ann Intern Med*. 2000;132(11):926-30. doi: 10.7326/0003-4819-132-11-200006060-00026, PMID 10836931.
  47. Brown MT, Bussell JK. Medication adherence: WHO cares? *Mayo Clin Proc*. 2011;86(4):304-14. doi: 10.4065/mcp.2010.0575, PMID 21389250.

**Article History:** Received: 30-11-2021; Revised: 09-12-2021; Accepted: 10-01-2022

**Cite this article:** Appalasaamy J, Selvaraj A, Ramaiah SS. The Non-adherence Scope in Stroke- A Narrative Review. *J Young Pharm*. 2022;14(1):21-4.