



## Original Article



## Factors Affecting Non Compliance to Medication in Epileptic Patients

Mamoona Tanwir Rana<sup>1</sup>, Madiha Malik<sup>2</sup>, Muhammad Imran<sup>3</sup>, Imran Ahmed Moinuddin<sup>4</sup>, Hafiz Muhammad Imtiaz Afzal<sup>5</sup>, Qurat Ul Ain Zulfi<sup>6</sup>, Nayab Zahid<sup>7</sup>, Sara Aleem<sup>8</sup> and Razi<sup>8</sup>

<sup>1</sup>Akhtar Saeed Medical and Dental College, Akhtar Saeed Trust Hospital, Lahore, Pakistan

<sup>2</sup>Department of Neurology, University of Lahore Teaching Hospital, Lahore, Pakistan

<sup>3</sup>Department of Neurology, Lahore General Hospital, Lahore, Pakistan

<sup>4</sup>Department of Medicine, University College of Medicine and Dentistry, Lahore, Pakistan

<sup>5</sup>Department of Psychiatry and Behavioral Sciences, Pak Red Crescent Medical and Dental College, Lahore, Pakistan

<sup>6</sup>Department of Community Medicine, Sialkot Medical College, Sialkot, Pakistan

<sup>7</sup>Department of Surgery, Idrees Hospital, Sialkot, Pakistan

<sup>8</sup>Department of Medicine, Idrees Hospital, Sialkot, Pakistan

## ARTICLE INFO

**Keywords:**

Epilepsy, Non Compliance, Poor Seizure Control, Cost Reduction

**How to Cite:**

Rana, M. T., Malik, M., Imran, M., Moinuddin, I. A., Afzal, H. M. I., Zulfi, Q. U. A., Zahid, N., Aleem, S., & Razi, . (2025). Factors Affecting Non Compliance to Medication in Epileptic Patients : Medication Noncompliance in Epilepsy. *Pakistan Journal of Health Sciences*, 6(5), 217-223. <https://doi.org/10.54393/pjhs.v6i5.2679>

**\*Corresponding Author:**

Qurat Ul Ain Zulfi

Department of Community Medicine, Sialkot Medical College, Sialkot, Pakistan  
[quratbilal@outlook.com](mailto:quratbilal@outlook.com)

Received Date: 20<sup>th</sup> December, 2024

Revised Date: 3<sup>rd</sup> May, 2025

Acceptance Date: 17<sup>th</sup> May, 2025

Published Date: 31<sup>st</sup> May, 2025

## ABSTRACT

Non-compliance with antiepileptic medications is a significant concern, leading to poor seizure control, increased hospitalization, and higher healthcare costs. **Objective:** To identify factors contributing to non-compliance among epileptic patients. **Methods:** A cross-sectional study was conducted at Akhtar Saeed Trust Hospital, Lahore, from July 2023 to March 2024, including 200 epileptic patients aged 18-60 years identified as non-compliant using the Morisky Medication Adherence Scale (MMAS-4). Patients with psychiatric illnesses, hearing problems, or those pregnant/lactating were excluded. Data on demographics and contributing factors (e.g., high costs, forgetfulness, unemployment) were collected via structured proformas. Statistical analysis using SPSS version 25.0 included descriptive statistics and stratified analyses to explore relationships between factors and demographics, with significance at  $p < 0.05$ . **Results:** Of 200 patients, 67.5% were male. High cost (57.5%) was the leading factor, followed by forgetfulness (55.0%), prolonged treatment duration (32.5%), unemployment (29.5%), and medication complexity (16.5%). Monthly household income significantly influenced these factors; high costs and prolonged treatment duration were predominant in low-income groups ( $p < 0.001$ ). Forgetfulness was uniformly reported across socio-economic strata ( $p = 0.094$ ). **Conclusions:** High medication costs and forgetfulness are primary contributors to non-compliance among epileptic patients. Strategies like cost reduction, simplified regimens, and reminder interventions are essential to enhance adherence and improve clinical outcomes.

## INTRODUCTION

Epilepsy, a chronic neurological disorder characterized by recurrent, unprovoked seizures, affects over 65 million individuals worldwide. Epilepsy affects approximately 50 million individuals globally, with a prevalence of 9.99 per 1,000 people in Pakistan, translating to about 2 million individuals nationwide. [1, 2]. Antiepileptic drugs (AEDs) are the mainstay of epilepsy treatment, offering the potential for seizure freedom in nearly two-thirds of patients when

adhered to correctly [3]. However, non-compliance with medication regimens among epileptic patients is a critical issue that continues to undermine effective treatment outcomes. [4]. The World Health Organization (WHO) classifies medication non-compliance as a major public health concern, particularly in chronic conditions like epilepsy [5]. Understanding the multifaceted factors that affect adherence is therefore crucial in improving



outcomes for patients suffering from epilepsy [6]. Adherence to AEDs remains suboptimal due to patient-related and socioeconomic factors, highlighting the need to identify underlying causes and design targeted interventions [7]. Medication non-compliance in epileptic patients arises from patient-related, treatment-related, socioeconomic, and healthcare system factors. [8]. Cognitive impairments and forgetfulness also contribute significantly, particularly among elderly patients who may be managing multiple comorbidities and medications simultaneously [9]. Treatment-related factors also play an essential role in adherence. The complexity of the prescribed regimen like polypharmacy, the frequency of dosing, and the occurrence of adverse effects are critical determinants of compliance [10]. Many AEDs are associated with side effects, ranging from mild drowsiness to severe mood and cognitive changes, significantly impact adherence; with an Ethiopian study showing patients experiencing adverse effects were 13.68 times more likely to be non-compliant (aOR: 13.68; 95% CI: 3.27–56.97) [11]. Socioeconomic factors like financial constraints, low health literacy, and limited healthcare access hinder AED adherence, with a Bangladeshi study showing a strong positive correlation between AED costs and adherence levels [12]. Cultural beliefs and stigma in societies like India hinder epilepsy treatment adherence, as fear of ostracization deters care. Despite 87% awareness and 83.7% identifying it as neurological stigma remains a barrier [13]. A study conducted in Pakistan showed that 44.4% exhibited non-compliance to AED and was more prevalent among patients with longer illness duration and those on polypharmacy [10]. Another study suggested that the primary reasons for non-compliance among epilepsy patients were the high cost of treatment (54%) in self-paying patients, while uncontrolled seizures (33.3%) and misleading by local quacks (25%) were major factors among those receiving free treatment [14]. According to Awan *et al.*, among epilepsy patients 26.7% were non-compliant with AED treatment, with forgetfulness being the most common reason (72.5%), followed by affordability issues (12.5%) and symptom relief (7.5%) [15]. Non-adherence was significantly associated with poor seizure control (77.5% vs. 49.1%,  $p = 0.001$ ) and a higher frequency of convulsive seizures in the past year ( $p = 0.006$ ), highlighting the critical impact of adherence on treatment outcomes [9].

The study aimed to determine the frequency of contributing factors leading to non-compliance with antiepileptic medications in patients diagnosed with epilepsy.

## METHODS

A cross sectional study was conducted at Akhtar Saeed Trust Hospital, Department of Medicine and Allied, Lahore. The study was approved by the Ethical Review Committee of Akhtar Saeed Trust Hospital, in accordance with the ethical principles for medical research involving human subjects outlined in the Declaration of Helsinki (IRB no.2023/ASTH/687). The study was conducted from July 15, 2023 to March, 2024 (for 8 months). Patients were required to have been taking antiepileptic drugs (AEDs) for more than three months and were identified as non-compliant using the Morisky Medication Adherence Scale (MMAS-4) the scale was translated in local language as well [15, 16]. The MMAS-4 was employed to assess medication adherence among epileptic patients in this study [17]. Sample size of 200 was calculated at 95% confidence level and 5% margin of error and taking an expected percentage of noncompliance as 44.4% [10]. A non-probability convenience sampling method was used for patient selection. Patients with Epilepsy who were taking AED for more than three months and were non-compliant to medication were enrolled from the Outpatient Department after taking informed consent. A patient answering YES to  $\leq 2$  questions on the Morisky Medication Adherence Scale (MMAS-4) was deemed non-compliant i.e., (a) Patient has ever forgotten to take medication; (b) Patient has ever had problems remembering to take medication; (c) Patient has stopped medication due to worsening symptoms; (d) Patient has stopped medication due to alleviating symptoms. Patient's self-reports were cross checked with prescription records to validate adherence to reduce recall bias. Bio data was entered in a pre-designed structured proforma. Various contributing factors determining compliance like unemployment, income per month in PKR high cost, forgetfulness, complexity of medicine, prolonged duration of treatment were noted [17, 18]. All information was kept confidential and all patients were managed as per hospital protocol. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 25.0. Chi-square test was used for categorical variable comparisons. Qualitative data like gender and contributing factors were presented as frequencies and percentages. Quantitative data i.e., age was presented as means and standard deviations. Data were stratified for age, gender, socio-economic status and educational status and a p-value of less than 0.05 was considered statistically significant. Specifically employing the chi-square test to analyze relationships between categorical variables such as household income, educational levels, and medication adherence outcomes. This method was selected due to its appropriateness for categorical data, which does not require normality tests that are necessary for continuous data analyses like t-tests or ANOVA. Additionally, we checked that the sample size was adequate to provide expected frequencies in the

contingency tables, requiring that each cell have a minimum expected count of five to uphold the chi-square test's accuracy; where this criterion was not met, Fisher's exact test was utilized, suitable for smaller sample sizes.

## RESULTS

A total of 200 patients with diagnosis of Epilepsy were included. Age range in this study was from 18 to 60 years with a mean age of  $39.5 \pm 12.5$  years. Most of the patients 73 (36.5%) were in 46-60 years of age group, while 57 (28.5%) and 70 (35.0%) were in 18-30 years and 31-45 years of age groups respectively (Table 1). According to household income 74 (37.0%) had monthly income <25,000 per month, while 66 (33.0%) and 60 (30.0%) had monthly income 25,000-50,000 and >50,000 per month respectively (Table 1). According to educational status, 44 (22.0%) were illiterate, while 80 (40.0%) and 76 (38.0%) did middle and matriculation or higher respectively. According to contributing factors of non-compliance to medications in epileptic patients, high cost 115 (57.5%) was the most common factor followed by forgetfulness in 110 (55.0%), prolonged duration of treatment in 65 (32.5%), unemployment in 59 (29.5%) and complexity of medicine in 33 (16.5%). Table 1 illustrated the socio-demographic characteristics of a study population totaling 200 individuals, categorized by gender, age groups, and socio-economic status. Gender-wise, males were predominant, constituting 67.5% (n=135) of the participants, while females accounted for 32.5% (n=65). The age distribution showed a spread across three defined groups: 18-30 years (n=57, 28.5%), 31-45 years (n=70, 35.0%), and 46-60 years (n=73, 36.5%). In terms of monthly income, participants were divided into (<25,000; 37.0%, n=74) (26,000-50,000; 33.0%, n=66), and (>51,000; 30.0%, n=60) income brackets.

**Table 3:** Stratification of Contributing Factors with Respect to Socio-Economic Status

Contributing Factors	Socio-Economic Status			p-Value
	<25,000 Frequency (%)	26-50,000 Frequency (%)	>51,000 Frequency (%)	
Complexity of Medicine	16 (21.6)	15 (22.7)	2 (3.3)	0.004
Unemployment	29 (39.2)	28 (42.4)	2 (3.3)	0.0001
High Cost	68 (91.9)	39 (59.1)	8 (13.3)	0.000001
Forgetfulness	44 (59.5)	40 (60.6)	26 (43.3)	0.094
Prolonged Duration of Treatment	32 (43.2)	29 (43.9)	4 (6.7)	0.000001

The findings in table 4 suggest that the complexity of medicine, which increased across the age groups (from 10.5% in 18-30 years to 21.9% in 46-60 years), did not reach statistical significance (p-value of 0.216). Unemployment and high cost showed slight variations in percentages across the age groups but remained statistically non-significant with p-values of 0.416 and 0.956, respectively. Forgetfulness and prolonged duration of treatment also exhibited minor percentage differences across age groups but without statistical significance (p-values of 0.812 and 0.434, respectively).

**Table 4:** Stratification of Contributing Factors with Respect to Age

Contributing Factors	18-30 Years Frequency (%)	31-45 Years Frequency (%)	46-60 Years Frequency (%)	p-Value
Complexity of Medicine	6 (10.5)	11 (15.7)	16 (21.9)	0.216
Unemployment	13 (22.8)	22 (31.4)	24 (32.9)	0.416
High Cost	33 (57.9)	41 (58.6)	41 (56.2)	0.956
Forgetfulness	32 (56.1)	40 (57.1)	38 (52.1)	0.812
Prolonged Duration of Treatment	15 (26.3)	23 (32.9)	27 (37.0)	0.434

**Table 1:** Socio-Demographic Profile of study participants

Variables	Frequency (%)
<b>Gender</b>	
Male	135 (67.5)
Female	65 (32.5)
<b>Age Groups</b>	
18-30 Years	57 (28.5)
31-45 Years	70 (35.0)
46-60 Years	73 (36.5)
<b>Household Income per Month (PKR)</b>	
<25,000	74 (37.0)
26-50,000	66 (33.0)
>51,000	60 (30.0)
Total	200 (100.0)

Table 2 shows that high cost was the most frequently occurred issue, reported by 115 participants (57.5%),

**Table 2:** Frequency of Contributing Factors

Factors	Frequency (%)
Complexity of Medicine	33/200 (16.5)
Unemployment	59/200 (29.5)
High Cost	115/200 (57.5)
Forgetfulness	110/200 (55.0)
Prolonged Duration of Treatment	65/200 (32.5)

The table 3 reveals significant differences based on monthly household income: complexity of medicine and unemployment exhibited notable decreases in frequency as monthly income increased, with p-values of 0.004 and 0.0001, respectively, indicating strong statistical significance.

## DISCUSSION

Poor medication compliance is a widespread issue, even among patients with epilepsy who understand the risks of seizures and death. Indicators of non-compliance in epilepsy include inconsistent requests for repeat prescriptions of antiepileptic drugs (AEDs), lack of improvement with appropriate treatment, and increased seizure frequency. However, identifying all non-compliant patients remains challenging [18, 19]. According to the current study among 200 patients, 135 (67.5%) were males and 65 (32.5%) were females showing bias in healthcare access or a higher frequency of diagnosed epilepsy in males. Literature often shows mixed results regarding gender differences. Some studies find no significant disparity, while others, like Hauser WA and Hesdorffer DC observed a slight male predominance, possibly due to higher exposure to risk factors such as head injuries and strokes in adulthood [20]. In this study, the age group of older adults (46-60 years) emerged as the most prominent, suggesting a possible higher occurrence of epilepsy or enhanced diagnostic rates within this demographic. A demographic study by Lezaic indicated that while epilepsy can begin at any age, there was a notable incidence peak in the population over 60 years. This reflects an increased risk due to age-associated conditions like stroke and Alzheimer's disease [21]. The current results revealed that among the epilepsy patients studied, 37.0% of the sample belonged to the category, with a monthly income of less than 25,000 PKR. Mandorf S *et al.*, found that in their study, 24% of patients couldn't consistently afford medications, 49% had medical insurance, and 78% of low-income patients sought free drugs or financial aid, contributing to non-adherence to AEDs [8]. The study highlighted the primary reasons for non-compliance with medication among epileptic patients, identifying high medication costs as the most significant factor, affecting 115 out of 200 patients (57.5%). This is contrasting with findings by Govil *et al.*, who reported that only 8.2% of their cohort cited economic constraints as a major barrier to epilepsy treatment, patients were unable to afford to purchase medicines [22]. Despite both studies being conducted in low-income settings, it suggested that local economic factors and healthcare system efficiencies might significantly influence patient experiences and perceptions of affordability in epilepsy treatment. According to Peroni *et al.*, despite similar retail prices globally, over 80% of people with epilepsy in LICs and MICs face substantial financial burdens due to low per capita income and inadequate reimbursement systems, whereas less than 20% in HICs experience better affordability due to higher incomes and stronger reimbursement mechanisms, underscoring the inequity in access to antiseizure medications worldwide [23]. In this study, 55% of participants reported forgetfulness as a key factor in medication non-compliance, closely aligning with a study

conducted in Indonesia which found a similar impact in 50% of their cohort. This highlights the critical role of cognitive dysfunction in adherence, emphasizing the need for interventions like reminder technologies or cognitive support to mitigate its effects and improve patient outcomes [24]. In the current study, 32.5% of patients identified the prolonged duration of treatment as a barrier to medication adherence, while 16.5% reported challenges related to the complexity of their medication regimens. These rates are notably higher than those reported in a study conducted in India, where 20.0% of patients experienced fatigue from taking medication over an extended period. Additionally, the Indian study found that 8.2% of patients attributed non-adherence to managing multiple medications, and 2.5% cited the complexity of the drug regimen. The combined complexity-related non-compliance in the reference study amounted to 10.7%, which remains significantly lower than the findings of the present study [22]. In the present study, the influence of household income on non-compliance with antiepileptic medications reveals significant disparities in contributing factors across different income groups the complexity of medicine was found to be a significant barrier to medication adherence among patients from different groups, with a p-value of 0.004. This disparity may be due to limited resources, lower health literacy, or inadequate support, whereas higher income patients likely benefit from better access to mitigating resources. In comparison, the Saudi Arabian study reported that 24% of patients cited complexity as a major barrier to adherence, with a p-value of 0.034 [25]. Unemployment was significantly linked to non-compliance, particularly in the low (39.2%) and middle (42.4%) income groups, compared to the high income group (3.3%) ( $p = 0.0001$ ). Employment status seems crucial for medication adherence; likely due to the affordability it provides. A study conducted in Malaysia revealed that employment status was significantly associated with ASM adherence ( $p = 0.012$ ), with adherence being higher among employed participants or students (56.3%) compared to unemployed, pensioners, or housewives (43.7%). Non-adherence was also more prevalent in unemployed participants (36.0%) compared to employed individuals (64.0%), emphasizing the role of employment in improving adherence [7]. These international findings support the notion that improving employment opportunities and providing financial support could positively impact adherence rates. The high cost of medication was also a major barrier, especially among the PKR < 25000 group, where 91.9% reported cost as a reason for non-compliance, and similarly in the PKR 26-50000 (59.1%), but far less in the group earning PKR > 51000 (13.3%) ( $p = 0.000001$ ). Monthly income was significantly associated with adherence status ( $p = 0.008$ ), with adherence rates increasing from 26.2% in participants earning less than \$18 (999 birrs) to 58.3% in those earning above \$55 (3000 birrs). Conversely, non-



adherence was highest in the PKR<25000 income group 39.77 (95% CI: 32.44, 47.10) and lowest in the PKR>51000 income group (41.7%), highlighting the impact of financial stability on compliance [26]. This highlighted the financial burden on lower-income patients, stressing the need for cost-reduction strategies to enhance adherence. Forgetfulness appears to be a notable factor across all income groups, with similar percentages reported among PKR<25000 group (59.5%) and PKR 26-50000 (60.6%) groups, and a lower proportion in the PKR>51000 group (43.3%). The lack of statistical significance ( $p=0.094$ ) suggests that forgetfulness is a universally common issue, irrespective of income status. This aligns with findings from a study conducted in Norway where forgetfulness emerged as a significant factor contributing to non-compliance. Approximately 40% of participants reported sometimes or often forgetting to take their AEDs, highlighting unintentional non-compliance. Forgetfulness was independently associated with non-compliance due to memory problems, with an odds ratio (OR) of 1.529 (95% CI: 1.137–2.053,  $p = 0.005$ ) [27]. These findings underscore the need for interventions like medication reminders to enhance adherence. The prolonged duration of treatment is also highlighted as a contributing factor, with 43.2% of patients from PKR<25000 household income, 43.9% from PKR26-50000 income, and only 6.7% from PKR>51000 income reporting it as a reason for non-compliance. The statistically significant  $p$ -value ( $p=0.000001$ ) underscores the challenges of long-term treatment, particularly for those from lower income backgrounds. Studies from international settings, such as the UAE indicated that prolonged duration of treatment did not have a statistically significant association with non-compliance ( $p = 0.396$ ), as adherence rates remained relatively consistent across treatment durations, with slight variations: 73.7% for  $\leq 1$  year, 66.4% for  $>1-5$  years, and 70.0% for  $>5$  years [28]. This suggests that interventions focused on simplifying treatment plans and providing long-term support are crucial, especially for economically disadvantaged patients. The cross-tabulation of age groups influenced contributing factors to non-compliance with antiepileptic medications among the patients revealed varying levels of influence for factors such as the complexity of drugs, unemployment, high cost, forgetfulness, and prolonged duration of treatment. The complexity of medication was reported by 21.9% of patients aged 46-60, 15.7% aged 31-45, and 10.5% aged 18-30 ( $p=0.216$ ). These findings align with those of Permatananda *et al.*, they found that patients under 40 years old had higher adherence rates compared to those aged 40 and above ( $p=0.001$ ), suggesting that younger patients may manage complex regimens more effectively [24]. Unemployment affected 32.9%, 31.4%, and 22.8% in these age groups, respectively, with no significant difference ( $p=0.416$ ). The higher rates in older age groups may reflect greater employment challenges

among older adults with epilepsy. However, the absence of a significant difference suggests that unemployment affects medication adherence similarly across ages. Teh *et al.*, (2020) reported that being employed or a student was significantly associated with non-adherence ( $p=0.012$ ), indicating that employment status can impact adherence behaviors [7]. High cost was cited by 57.9% (18-30), 58.6% (31-45), and 56.2% (46-60), showing no age-related disparity ( $p=0.956$ ). Similarly, in the study conducted in Saudi Arabia, high cost was reported as the second most common cause of non-adherence following forgetfulness, though specific age stratification was not provided. Forgetfulness, on the other hand, was the most prevalent factor contributing to non-compliance in the study, affecting 56.1% to 57.1% of participants across all age groups, with no significant differences observed ( $p = 0.812$ ). This finding aligns with a study conducted by Mahmoud MR, where forgetfulness was identified as the leading cause of non-adherence, affecting 69.6% of patients and showing a significant association with non-compliance ( $p < 0.05$ ) [29]. These results underscore the consistency of forgetfulness and high cost as universal barriers to medication adherence, irrespective of age stratification or geographic location. Prolonged treatment duration was more common among older patients: 37.0% (46-60), 32.9% (31-45), and 26.3% (18-30), though differences were non-significant ( $p=0.434$ ) also seen in Indonesian study where patients with a treatment duration of less than 10 years exhibited better adherence than those with longer treatment durations ( $p=0.023$ ) [22]. This study has several limitations that should be considered when interpreting the findings. The reliance on self-reported data introduces the possibility of recall and social desirability bias, as patients may underreport or overestimate their medication adherence. Second, the study is limited to a specific population within Pakistan, which may restrict the generalizability of the findings to other regions with different healthcare infrastructures, socioeconomic conditions, and cultural perceptions of epilepsy. Moreover, another limitation of this study is the absence of a formal validation study of the MMAS-4 for the Urdu-speaking population in Pakistan. While the scale is respected and validated internationally, different cultural nuances and language interpretations could potentially affect the accuracy of the results in this context. Future research could focus on conducting a validation study of the MMAS-4 in local languages to confirm its reliability and validity in Pakistan, enhancing the robustness of adherence assessments in this population, the absence of confidence intervals in the statistical analysis is another notable limitation of the study. Confidence intervals are essential for assessing the precision and reliability of estimated effects, offering insights beyond the statistical significance indicated by  $p$ -values. Their inclusion helps contextualize the strength and variability of observed

associations, providing valuable information for clinical and policy decision-making. The initial analytical focus was primarily on identifying statistically significant associations, which led to the exclusion of confidence intervals. Recognizing this limitation, we recommend that future research includes confidence intervals to furnish a fuller statistical picture. Additionally, the study does not account for potential confounding factors such as comorbid conditions, cognitive impairments, or psychological disorders like depression and anxiety, which may independently influence adherence. The cross-sectional design also limits the ability to establish causality between non-compliance and its associated factors, making it difficult to assess long-term adherence patterns.

## CONCLUSIONS

Medication non-compliance in epilepsy is driven more by socioeconomic and behavioral factors than by clinical ones. In this study, high out-of-pocket medication costs (57.5%) and forgetfulness (55.0%) were the leading causes, followed by unemployment (29.5%), regimen complexity (16.5%), and side effects (8.3%). Clinical factors like seizure type or polytherapy showed no significant association. These findings highlight the need for both financial support (e.g., subsidies, insurance coverage) and behavioral interventions (e.g., app reminders, simplified regimens, patient education) to improve adherence, seizure control, and quality of life for epileptic patients in Pakistan.

## Authors Contribution

Conceptualization: MTR

Methodology: MM, IAM

Formal analysis: MI, IS

Writing, review and editing: MM, IAM, HMIA, QUA, NZ, SA, R

All authors have read and agreed to the published version of the manuscript

## Conflicts of Interest

All the authors declare no conflict of interest.

## Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

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