

# A Randomized Controlled Study on the Application of LEARNS Health Education Combined with Intelligent Follow-up Management in Secondary Prevention of Ischemic Stroke and Its Impact on Patient Compliance and Neurological Function

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**Objective:** This randomized controlled study aimed to evaluate the effectiveness of LEARNS health education combined with intelligent follow-up management in the secondary prevention of ischemic stroke (IS), focusing on patient compliance and neurological function outcomes. The LEARNS model is a structured patient education framework encompassing Listen, Establish, Adopt, Reinforce, Name, and Strengthen, aiming to support individualized and interactive patient learning.

**Methods:** A total of 120 first-episode IS patients admitted to the Neurology Department of our hospital from April to June 2024 were enrolled and randomly assigned to either a control group (n = 60), receiving conventional health education plus intelligent follow-up, or an observation group (n = 60), receiving LEARNS health education combined with intelligent follow-up management. Patient outcomes were assessed using the General Medication Adherence Scale (GMAS), secondary prevention control measures (including blood glucose, blood pressure, lipid control, smoking/alcohol cessation, obesity control, and exercise adherence), the Barthel Index (BI) for neurological function, and ischemic stroke recurrence. Evaluations were conducted at discharge and at all follow-up time points within six months post-discharge.

**Results:** Compared to the control group, the observation group showed significantly higher medication adherence rates, better control in all secondary prevention measures, and higher neurological function recovery rates at all follow-up time points ( $P < 0.05$ ). Additionally, the 6-month recurrence rate was significantly lower in the observation group (1.67%) than in the control group (13.33%) ( $P < 0.05$ ).

**Conclusion:** LEARNS health education combined with intelligent follow-up management effectively enhances patient compliance, improves secondary prevention outcomes, supports neurological recovery, and reduces recurrence risk in patients with ischemic stroke.

**Keywords:** LEARNS model, health education, intelligent follow-up, ischemic stroke, secondary prevention, medication adherence, neurological recovery

## Introduction

Ischemic stroke (IS), an acute cerebrovascular event resulting from the obstruction of cerebral blood flow, remains one of the primary global causes of death and long-term disability.<sup>1</sup> In China, recent epidemiological studies<sup>2</sup> reveal that stroke has emerged as the leading health burden, with IS comprising over 70% of all stroke cases. Although substantial progress

has been made in acute-phase treatments, IS patients are still highly susceptible to recurrent strokes, sustained neurological deficits, and compromised quality of life after discharge—posing significant burdens on both families and society. Consequently, preventing IS recurrence through effective secondary prevention has become a major priority in clinical and public health contexts.

Secondary prevention includes a range of strategies: blood pressure, glucose, and lipid control; smoking cessation and alcohol moderation; adherence to healthy dietary and exercise habits; strict medication compliance; and engagement in neurorehabilitation programs.<sup>3</sup> Despite their proven effectiveness, these measures are often inadequately implemented in real-world settings. Many patients experience poor adherence and unhealthy lifestyle behaviors due to a lack of disease-specific education and structured guidance post-discharge.<sup>4</sup> Factors such as fragmented follow-up systems, insufficient patient education, and weak self-management capabilities significantly undermine secondary prevention efforts.<sup>5</sup> Therefore, the development of structured, integrated, and patient-centered intervention models is essential to bridge this gap and enhance long-term outcomes for IS patients.

The LEARNS health education model—comprising Listen, Establish, Adopt, Reinforce, Name, and Strengthen—is a patient-centered framework rooted in social constructivist theory. It emphasizes interaction, individualized learning, and empowerment, aiming to promote health literacy, self-efficacy, and disease-specific knowledge. Recent studies have demonstrated the model's clinical utility: Zhang et al<sup>6</sup> reported that LEARNS-based perioperative education significantly improved disease understanding and compliance in patients with laryngeal tumors; Zhao et al<sup>7</sup> summarized high-level evidence supporting LEARNS-based rehabilitation guidance for post-stroke motor dysfunction; and Martin et al<sup>8</sup> validated learner-centered strategies—aligned with the LEARNS principles—for enhancing communication and patient engagement in chronic disease management.

Meanwhile, intelligent follow-up management systems, enabled by mobile health (mHealth) technologies and data analytics, offer tools for personalized care planning, remote monitoring, and behavioral reinforcement.<sup>9–11</sup> These systems can help overcome traditional limitations in continuity of care and improve patient engagement. While both LEARNS education and intelligent follow-up have shown individual promise, their synergistic application in IS secondary prevention remains underexplored.

Therefore, this study investigates whether the combined use of LEARNS health education and intelligent follow-up management yields superior outcomes in medication adherence, neurological function, and recurrence prevention compared to conventional management. We hypothesize that IS patients receiving this integrated intervention will demonstrate significantly improved adherence, clinical indicators, neurological recovery, and reduced recurrence. A randomized controlled trial involving 120 first-episode IS patients is conducted to provide evidence-based guidance for long-term secondary prevention practices in stroke care.

## Materials and Methods

### Study Design

This was a single-center, prospective, randomized controlled trial (RCT) conducted to evaluate the effect of LEARNS health education combined with intelligent follow-up management on secondary prevention outcomes in patients with IS.

### Participants and Inclusion Criteria

A total of 120 patients who were first-time inpatients at the Neurology Department of our hospital between April and June 2024, and diagnosed with IS, were recruited. Inclusion criteria were as follows: (1) Met the diagnostic criteria of the Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke in China (2022);<sup>12</sup> (2) Completed a 6-month follow-up with complete and valid clinical data; (3) Aged between 18 and 80 years; (4) Possessed basic communication ability (verbal or assisted), sufficient to complete the intervention and follow-up assessments; (5) Provided informed consent and voluntarily agreed to participate in the study. Exclusion criteria were as follows: (1) Diagnosed with severe cognitive impairment, as assessed by a Mini-Mental State Examination (MMSE)<sup>13</sup> score < 18; (2) Severe comorbidities such as congenital heart disease or uncontrolled hypertension; (3) Severe visual or auditory impairment that could not be

corrected or compensated for and would hinder participation in education or follow-up activities; (4) Substance or alcohol dependence; (5) Active malignant tumors; (6) Autoimmune diseases; (7) Pregnancy or lactation.

## Sample Size Calculation

The sample size was estimated using G\*Power 3.1.9.7 software. Assuming a medium effect size (Cohen's  $d = 0.5$ ), an  $\alpha$  level of 0.05, and a power ( $1-\beta$ ) of 0.80 for a two-tailed test, the minimum sample size required per group was calculated as 51. Considering a potential 15% dropout rate, we enrolled 60 participants in each group (total 120).

## Randomization and Blinding

Randomization was conducted using a computer-generated random number sequence created by an independent statistician. Participants were randomly assigned in a 1:1 ratio into either the control group ( $n = 60$ ) or the observation group ( $n = 60$ ) using block randomization with a block size of 4 to ensure group balance throughout the enrollment period.

Although stratified randomization based on baseline stroke severity (eg, NIHSS score) was considered, it was not implemented due to the relatively small sample size and the similar distribution of baseline characteristics in the study population.

To ensure allocation concealment, group assignments were placed in sequentially numbered, sealed, opaque envelopes, which were prepared and opened by a third-party research coordinator who was not involved in the intervention delivery or outcome evaluation.

Due to the nature of the health education intervention, neither participants nor the healthcare providers could be blinded to the treatment allocation. However, outcome assessors and data analysts were blinded to group assignments to minimize observer bias and analysis bias.

## Ethical Considerations

This study was reviewed and approved by the Medical Ethics Committee of The First Affiliated Hospital of Qiqihar Medical College (Approval No. 2024-005-01). All patients and their families were fully informed of the study objectives, procedures, potential risks, and benefits. Written informed consent was obtained from all participants. The study complied with the principles of the Declaration of Helsinki (as revised in 2013).

## Methods

Secondary prevention strategies were implemented in accordance with the Chinese Guidelines for Secondary Prevention of Cerebrovascular Diseases.<sup>14</sup> Data were collected via electronic medical records and semi-structured interviews, including demographics, neurological recovery, blood pressure, blood glucose and lipid levels, and health behavior metrics. Personalized patient health records were established.

**Control group (routine health education + intelligent follow-up):** Patients received standard hospital-based health education on disease knowledge, medication use, lifestyle modification, and warning signs, delivered through brochures and in-person nurse counseling during hospitalization. After discharge, intelligent follow-up was conducted using the “3+1” model, which included regular reminders and check-ins via WeChat, SMS, intelligent voice system, and monthly manual phone calls. The frequency and interaction time were matched with those of the observation group to control for attention bias.

**Observation group (LEARNS health education + intelligent follow-up):** In addition to the above, patients received the LEARNS-based intervention. The intervention consisted of six modules: (1) Listen: Upon admission, semi-structured interviews explored patients' individualized needs, preferences for health education formats, and expectations. (2) Establish: After consent, personal recovery plans were created collaboratively with patients and caregivers, emphasizing patient-provider partnership. (3) Adopt: The hospital information center maintained the intelligent follow-up system. Educational materials (videos, audio, text, infographics) were pushed at scheduled intervals post-discharge. Patients were required to complete at least 80% of the assigned educational content, and system logs were used to track engagement and adherence. (4) Reinforce: Encouragement messages and peer support via WeChat groups were offered weekly. Family members were also invited to participate, reinforcing knowledge and behavioral change. (5) Name: Patient responses to follow-up questionnaires were automatically categorized. Based on the feedback, staff adjusted education

strategies and follow-up intensity. (6) Strengthen: Key areas of misunderstanding or noncompliance were addressed through individualized coaching and reinforced during follow-up contacts.

To reduce the “contact effect”, both groups received an equal number of interactions, similar communication formats, and contact duration over the 6-month intervention period.

## Observation Indicators and Evaluation Criteria

**(1) Medication Adherence:** At discharge (T0), and at 1 month (T1), 3 months (T2), and 6 months (T3) post-discharge, patients’ medication adherence was assessed using the General Medication Adherence Scale (GMAS).<sup>15</sup> The GMAS is a validated tool that comprehensively evaluates medication-taking behaviors, beliefs, and barriers, and has demonstrated good reliability and construct validity in chronic disease populations, including stroke patients. Scores were categorized into high (29–33), moderate (17–28), and low (0–16) adherence. The medication adherence rate was calculated as: Medication adherence rate = (number of patients with high adherence + number with moderate adherence) / total number of patients × 100%.

**(2) Secondary Prevention Control:** At T0, T1, T2, and T3, the following indicators were assessed: ① Blood glucose: Fasting 4.4–6.1 mmol/L, 2-hour postprandial 6.1–11.1 mmol/L, HbA1c <7%. ② Blood pressure: SBP <140 mmHg, DBP <90 mmHg. ③ Blood lipids: TC <5.2 mmol/L, LDL-C <3.12 mmol/L. ④ Smoking and alcohol: Non-smoking and alcohol <25 g/day. ⑤ Obesity control: Overweight/obese patients aimed to reduce weight by 10%; others maintained a normal BMI. ⑥ Exercise: Aerobic activity 3–4 times/week, about 40 minutes/session.

**(3) Neurological Recovery:** Neurological function was assessed using the Barthel Index (BI)<sup>16</sup> at T0, T1, T2, and T3. The BI is a widely used and validated scale that assesses the performance of activities of daily living (ADL) and reflects the degree of functional independence. It is recommended in stroke rehabilitation guidelines due to its sensitivity to changes in functional status over time. Patients scoring at Level 1 or Level 2 were considered to have good neurological recovery.

**(4) IS Recurrence:** During the 6-month follow-up, medical staff monitored recurrence of ischemic stroke through clinical reexamination and patient/family reporting.

**Data Completeness:** No participants were lost to follow-up, and all outcome data were complete; therefore, no imputation or special handling for missing data was required.

## Statistical Analysis

GraphPad Prism 8 was used for charting, and SPSS 22.0 software for data analysis.

Categorical data: Expressed as percentages (%) and analyzed using the  $\chi^2$ -test. Continuous data: Expressed as ( $\bar{x} \pm s$ ), with independent sample t-tests for comparisons between groups. A p-value <0.05 was considered statistically significant.

## Results

### Comparison of Baseline Information

The baseline information, including gender, age, body mass index (BMI), comorbidities, neurological function, and education level, was compared between the two groups ( $P > 0.05$ ), indicating comparability. See [Tables 1](#) and [2](#).

### Comparison of Medication Adherence

In the control group, the numbers of patients adhering to medication at T0, T1, T2, and T3 were 48 (80.00%), 45 (75.00%), 42 (70.00%), and 40 (66.67%), respectively. In the observation group, the numbers were 56 (93.33%), 54 (90.00%), 53 (88.33%), and 51 (85.00%), respectively. The medication adherence rates at T0, T1, T2, and T3 in the observation group were significantly higher than those in the control group ( $P < 0.05$ ). See [Figure 1](#).

**Table 1** Barthel Index (BI) Evaluation Standards

Self-Care Ability	Level	Criteria	Care Dependency
Severe dependency	Level 4	Total score <40	Fully dependent on others
Moderate dependency	Level 3	Total score 41–60	Mostly dependent on others
Mild dependency	Level 2	Total score 61–99	Partially dependent on others
No dependency	Level 1	Total score 100	Independent

**Table 2** Comparison of Clinical Data ( $\bar{x} \pm s$ , n [%])

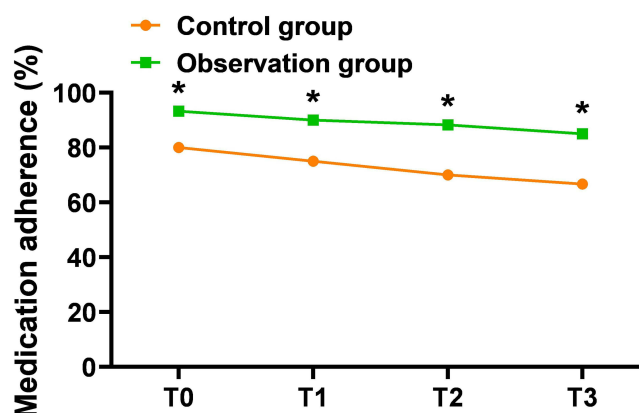
	Control (n=60)	Observation (n=60)	t/x <sup>2</sup>	P
Gender	–	–	0.306	0.579
Male	33 (55.00)	36 (60.00)	–	–
Female	27 (45.00)	24 (40.00)	–	–
Age (years)	65.27±7.84	64.79±8.13	0.329	0.742
BMI (kg/m <sup>2</sup> )	23.87±3.24	23.56±3.17	0.529	0.597
Comorbidities	–	–	–	–
Hypertension	41 (68.33)	46 (76.67)	1.044	0.306
Diabetes	27 (45.00)	31 (51.67)	0.533	0.465
Dyslipidemia	32 (53.33)	36 (60.00)	0.543	0.461
Neurological Function (BI Score)	55.43±9.82	54.91±9.56	0.293	0.769
Education Level	–	–	0.454	0.500
High school or below	49 (81.67)	46 (76.67)	–	–
College or above	11 (18.33)	14 (23.33)	–	–

## Comparison of Secondary Prevention Control

The rates of glucose control, blood pressure control, lipid control, smoking cessation/alcohol restriction, obesity control, and exercise compliance at T0, T1, T2, and T3 in the observation group were significantly higher than those in the control group ( $P < 0.05$ ). See [Table 3](#).

## Comparison of Neurological Function Recovery

In the control group, the numbers of patients with good neurological recovery at T0, T1, T2, and T3 were 32 (53.33%), 35 (58.33%), 37 (61.67%), and 38 (63.33%), respectively. In the observation group, the numbers were 43 (71.67%), 47 (78.33%), 50 (83.33%), and 51 (85.00%), respectively. The rates of good neurological recovery at T0, T1, T2, and T3 in the observation group were significantly higher than those in the control group ( $P < 0.05$ ). See [Figure 2](#).



**Figure 1** Comparison of Medication Adherence [n (%)].

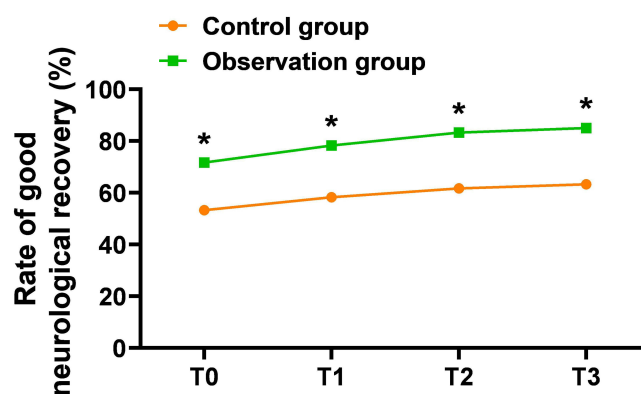
**Note:** Comparison between groups at the same time points, \* $P < 0.05$ .

**Table 3** Comparison of Secondary Prevention Control [n (%)]

Secondary Prevention Control Status	Control (n=60)	Observation (n=60)	$\chi^2$	P
Blood Glucose Control Compliance Rate	—	—	—	—
T0	39 (65.00)	52 (86.67)	7.684	0.005
T1	37 (61.67)	48 (80.00)	4.880	0.027
T2	33 (55.00)	47 (78.33)	7.350	0.006
T3	29 (48.33)	42 (70.00)	5.829	0.015
Blood Pressure Control Compliance Rate	—	—	—	—
T0	40 (66.67)	52 (86.67)	6.708	0.009
T1	38 (63.33)	51 (85.00)	7.350	0.006
T2	35 (58.33)	48 (80.00)	6.603	0.010
T3	31 (51.67)	44 (73.33)	6.008	0.014
Blood Lipid Control Compliance Rate	—	—	—	—
T0	38 (63.33)	51 (85.00)	7.350	0.006
T1	36 (60.00)	47 (78.33)	4.728	0.029
T2	32 (53.33)	45 (75.00)	6.125	0.013
T3	28 (46.67)	42 (70.00)	6.720	0.009
Smoking and Alcohol Restriction Compliance Rate	—	—	—	—
T0	35 (58.33)	50 (83.33)	9.075	0.002
T1	33 (55.00)	46 (76.67)	6.261	0.012
T2	30 (50.00)	44 (73.33)	6.909	0.008
T3	25 (41.67)	40 (66.67)	7.552	0.006
Obesity Control Compliance Rate	—	—	—	—
T0	33 (55.00)	48 (80.00)	8.547	0.003
T1	30 (54.55)	44 (73.33)	6.909	0.086
T2	27 (45.00)	40 (66.67)	5.711	0.016
T3	24 (40.00)	37 (61.67)	5.634	0.017
Exercise Compliance Rate	—	—	—	—
T0	35 (58.33)	50 (83.33)	9.075	0.002
T1	32 (53.33)	47 (78.33)	8.335	0.003
T2	29 (48.33)	41 (68.33)	4.937	0.026
T3	26 (43.33)	38 (63.33)	4.821	0.028

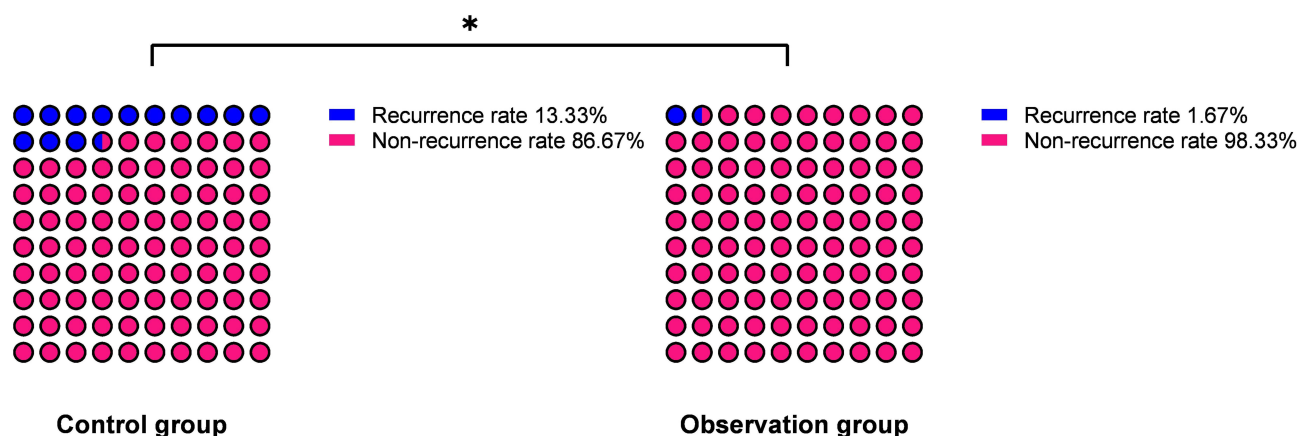
## Comparison of Recurrence Rates

Among the 60 patients in the control group, 8 experienced recurrence; in the observation group, only 1 experienced recurrence. The 6-month recurrence rate in the observation group (1.67%) was significantly lower than that in the control group (13.33%) ( $P < 0.05$ ). See Figure 3.

**Figure 2** Comparison of Neurological Function Recovery [n (%)].

**Note:** Comparison between groups at the same time points, \* $P < 0.05$ .





**Figure 3** Comparison of Recurrence Rates [n (%)].

**Note:** Comparison between groups at the same time points, \*P < 0.05.

## Discussion

IS, as a prevalent neurological disease, is characterized by a high disability and recurrence rate, making secondary prevention a critical aspect of long-term management.<sup>17</sup> However, in clinical practice, secondary prevention management of patients faces numerous challenges, including poor medication adherence, inadequate control of risk factors, and insufficient patient awareness of disease management. These issues not only limit the effectiveness of secondary prevention but also significantly increase the risk of recurrence and disability.<sup>18,19</sup> Therefore, exploring more efficient and comprehensive intervention strategies has become a crucial task to enhance the effectiveness of secondary prevention for IS. The combination of LEARNS health education and intelligent follow-up management provides an innovative intervention pathway. LEARNS health education is patient-centered and aims to enhance patients' awareness of disease and self-management ability through targeted health education and behavioral change support.<sup>20</sup> Intelligent follow-up management, leveraging real-time and intelligent features of information technology, provides personalized feedback support for patients.<sup>21</sup> The combination of these approaches not only addresses the limitations of single interventions but also forms a multidimensional, comprehensive management model, offering robust theoretical support for improving the effectiveness of secondary prevention in patients.

Studies<sup>22</sup> have shown that medication adherence is a key factor influencing the long-term management outcomes of IS patients. This study revealed that patients receiving the combined intervention of LEARNS health education and intelligent follow-up management (observation group) demonstrated significantly higher medication adherence rates across all four time points compared to the control group ( $P < 0.05$ ). This result highlights the effectiveness of the combined intervention in improving patients' medication behaviors through innovative measures. Firstly, LEARNS health education adopts personalized strategies in medication education by engaging in-depth communication with patients to identify their concerns and doubts about pharmacological treatment, thereby developing tailored educational content. This educational approach emphasizes two-way interaction, enhancing patients' understanding of the necessity of medication and reducing the likelihood of treatment discontinuation due to misunderstandings.<sup>23</sup> Secondly, intelligent follow-up management uses technological tools to push medication reminders and monitor patients' medication behaviors through data feedback, enabling timely corrections and fostering regular medication habits. Finally, the intervention also emphasizes family involvement, further consolidating patients' medication adherence through family support. Regarding improvements in secondary prevention control, this study demonstrated that the observation group showed significantly better control rates in blood glucose, blood pressure, blood lipids, smoking cessation, alcohol limitation, obesity control, and physical activity compared to the control group ( $P < 0.05$ ). These findings underscore the unique advantages of the combined intervention model in risk factor management. LEARNS health education systematically educates patients on the potential impact of various risk factors on stroke recurrence. For instance, in blood glucose control, the educational content emphasizes the importance of monitoring glucose levels

and provides specific dietary and pharmacological adjustment plans. Similarly, for blood lipid and blood pressure management, the approach illustrates the risks of hyperlipidemia and hypertension through examples and offers practical intervention suggestions. Moreover, the combined intervention focuses on guiding healthy behaviors, such as creating exercise plans tailored to patients' conditions and highlighting the positive effects of smoking cessation and alcohol limitation on health.

The scheduled monitoring function of intelligent follow-up management provides assurance for the control of risk factors, enabling healthcare professionals to promptly adjust intervention strategies based on the data, thereby achieving individualized management. This closed-loop health management model effectively enhances patients' control over risk factors, laying a foundation for reducing recurrence risks.

Neurological function recovery is an essential metric for evaluating rehabilitation outcomes in IS patients.<sup>24</sup> The study demonstrated that the Barthel Index scores for neurological recovery in the observation group were significantly higher than those in the control group ( $P < 0.05$ ), indicating that the combined intervention significantly promotes functional recovery, consistent with previous research.<sup>25,26</sup> This effect is attributed to several factors. LEARNS health education provides scientific guidance to help patients better complete rehabilitation training. Additionally, psychological support, as part of the education, helps patients build confidence in rehabilitation and mitigates the adverse effects of anxiety and depression on recovery processes.<sup>27</sup> Intelligent follow-up systems support rehabilitation training by sending reminders, recording patients' training progress, and adjusting training content based on feedback data, ensuring the scientific validity and feasibility of rehabilitation plans. Previous studies<sup>28</sup> have shown that dynamic management models improve patients' training adherence and promote sustained improvements in functional recovery, corroborating the findings of this study. Stroke recurrence is a critical issue affecting patient prognosis. This study found that the recurrence rate within six months in the observation group was 1.67%, significantly lower than the control group's 13.33% ( $P < 0.05$ ). This result demonstrates that the combined intervention model effectively reduces the risk of stroke recurrence. Effective control of risk factors is fundamental to reducing recurrence rates.<sup>29,30</sup> The integration of LEARNS health education and intelligent follow-up management significantly improved patients' indicators such as blood pressure, blood glucose, and blood lipids. Moreover, the long-term adherence to healthy behaviors (eg, smoking cessation, alcohol limitation, physical activity) further reduced recurrence risk. Mechanistically, LEARNS health education enhances patients' comprehensive understanding of the disease and its management, increasing their willingness to actively participate in health management. Intelligent follow-up, through dynamic monitoring and data analysis, provides real-time decision-making support for patients and healthcare providers, ensuring timely adjustments to interventions. This bidirectional mechanism effectively lowers recurrence risks.

The results of this study offer new insights into secondary prevention management models for IS patients. The combined intervention of LEARNS health education and intelligent follow-up management significantly improved medication adherence, enhanced risk factor control, promoted functional recovery, and reduced recurrence rates, providing robust support for optimizing post-stroke care. The intervention's comprehensive and individualized characteristics make it highly suitable for clinical use. However, this study has some limitations. First, the relatively small sample size and single-center design may limit the generalizability of the findings. Furthermore, while this study evaluated outcomes over a 6-month follow-up period, it is worth noting that the behavioral foundation established through the LEARNS-based intervention may exert a more enduring impact. The LEARNS model fosters long-term behavior change by promoting patient engagement, empowering individuals with disease-related knowledge, and reinforcing goal-oriented self-management strategies. These changes are not merely temporary improvements but may be internalized into patients' daily routines, leading to sustained medication adherence, regular monitoring, and healthier lifestyles. The intelligent follow-up component further enhances this process by providing continuous feedback and adaptive support, helping patients maintain behavioral momentum and prevent relapse. Therefore, the integrated approach is not only effective in the short term but also has the potential to support long-term secondary prevention. Future studies with extended observation periods are needed to verify these long-term effects.



## Conclusion

The combined LEARNS health education and intelligent follow-up management model demonstrates significant benefits in the secondary prevention of ischemic stroke. It offers an innovative, feasible, and patient-centered strategy for improving post-stroke recovery, medication adherence, and recurrence control. This approach shows promise not only for hospital-based management but also for integration into community and home-based care settings. In future research, this model may be adapted and tested in the management of other chronic diseases, potentially broadening its scope and impact in chronic care.

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An unauthorized version of the Chinese MMSE was used by the study team without permission, however this has now been rectified with PAR. The MMSE is a copyrighted instrument and may not be used or reproduced in whole or in part, in any form or language, or by any means without written permission of PAR ([www.parinc.com](http://www.parinc.com)).

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## Disclosure

The authors report no conflicts of interest in this work.

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