

## Characteristics Early versus Late Recurrent Ischemic Stroke: A Scoping Review on Timing and Predictors

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### LITERATURE REVIEW

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### Keywords:

*Early Recurrence, Late Recurrence, Recurrent Ischemic Stroke, Stroke Recurrence, Time of Recurrence*



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### ABSTRACT

Recurrent ischemic stroke (RIS) is a major global health issue due to its high morbidity, mortality, and economic burden. While numerous studies have explored the timing and pattern of RIS globally, there is a limited understanding of this issue within the Indonesian context. In the absence of sufficient local data, synthesizing global evidence becomes crucial to inform clinical practice and policy development in regions like Indonesia. This review aimed to explore timing patterns of RIS especially early and late phases and estimate risks based on follow-up, to inform evidence-based interventions. A scoping review based on Arksey & O'Malley framework and PRISMA-ScR guidelines. Literature search (2014–2024) in PubMed, Scopus, ScienceDirect, and CINAHL. Nine studies were included and analyzed thematically. From 2,987 articles, 9 met inclusion criteria. RIS risk ranged 4.3–23.4%, with median recurrence time 21–25 days. Early RIS (<90 days) had distinct risk factors (e.g. hypertension, prior stroke, heart disease) compared to late RIS. Modified Rankin Scale (mRS) and National Institutes of Health Stroke Scale (NIHSS) were key instruments; follow-ups done via clinics, registries, or surveys. Early (<90 days) and late recurrent ischemic strokes differ in both risk factors and clinical implications. Early post-stroke monitoring is critical to reducing recurrence. To address long-term prevention and support adherence to secondary prevention strategies, technology-assisted monitoring or broader digital health solutions should be considered as potential interventions, particularly in overcoming challenges related to long-term follow-up and patient engagement.

### Key Messages:

- RIS frequently occurs within the first year, requiring intensive early secondary prevention.
- Variations in recurrence patterns and risk factors necessitate individualized risk assessment and long-term monitoring.
- Lack of standardized definitions and follow-up durations limits data comparability and synthesis.

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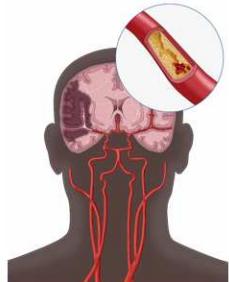


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## GRAPHICAL ABSTRACT

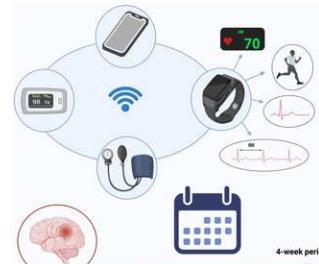
### Timing and Pattern of Recurrent Ischemic Stroke

Recurrent ischemic stroke (RIS) is a major global health issue due to its high morbidity, mortality, and economic burden. Despite global research, understanding of RIS timing and pattern in Indonesia remains limited. This review aims to explore timing patterns of RIS—especially early and late phases—and estimate risks based on follow-up, to inform evidence-based interventions.



**Recurrent Ischemic Stroke**

- **Early RIS (<90 days):** Hypertension, prior stroke, heart disease
- **Late RIS (>90 days):** Different risk factors
- **Tools:** mRS, NIHSS
- **Follow-up via clinics, registries, surveys**



#### Recommendations:

- Early vs late RIS → different risks & strategies
- Early monitoring is critical
- mHealth integration for long-term prevention

## INTRODUCTION

Stroke remains one of the leading causes of long-term disability and mortality worldwide, with ischemic stroke accounting for the majority of cases. The global burden of ischemic stroke is particularly profound in low- and middle-income countries, where health systems face challenges in delivering long-term care and follow-up (1,2). Among stroke survivors, recurrent ischemic stroke (RIS) is a critical issue, affecting approximately 20–30% of patients within five years of the initial event. Notably, the risk is highest during the first year post-stroke (3,4). RIS is associated with worsened neurological outcomes, increased premature mortality (2,5) higher healthcare costs, and diminished quality of life for both patients and caregivers (5–7).

In Indonesia, stroke is the leading cause of death, responsible for nearly one-fifth of all national deaths (8,9). Stroke prevalence rose from 7 per 1,000 people in 2013 to 10.9 per 1,000 in 2018, with ischemic stroke comprising over 60% of all stroke cases (10,11,12). National hospital data indicate that about one-third of ischemic stroke patients had a history of previous stroke (13), highlighting the importance of understanding the timing and pattern of recurrence. Yet, longitudinal data from Indonesia are scarce, so insights from global studies are needed for evidence-based intervention development(14–16).

Although national data emphasize RIS control, the global understanding of relapse dynamics remains incomplete. Timing patterns of relapse are key in determining clinical monitoring intensity, rehab resource allocation, and intervention planning (17). However, lack of consistent recurrence time mapping and reliance on local registries limit personalized post-stroke follow-up and global research integration (18). Attention to RIS timing and patterns is essential, as these inform secondary prevention strategies and personalized interventions (17,19).

A key but often under-recognized aspect of RIS is the timing of recurrence. Evidence shows that most recurrent events do not occur uniformly over time; instead, they cluster within specific periods—especially within the first 30–90 days after the initial stroke, which is widely recognized as the early high-risk window. Studies report recurrence rates of up to 8.6% within the first 30 days, with significant variation based on stroke subtype (20–22). Large artery atherosclerosis (LAA) and cardioembolic stroke are frequently associated with early recurrence, while small vessel disease (SVD) is more often linked to delayed recurrence (23,24). Risk factors for RIS also vary by timing and include advanced age, hypertension, diabetes, male gender, dependency at discharge, and poor adherence to secondary prevention (23,25,26).

Despite growing attention to these time-dependent patterns, there is a lack of systematic synthesis mapping the timing of RIS recurrence and its associated predictors. Most existing studies report recurrence as a single cumulative figure, without distinguishing early and late phases. This gap hampers the ability of clinicians and policymakers to tailor post-stroke interventions according to patients' evolving risk profiles. In addition, while some global data have begun to explore this issue, research from Indonesia remains sparse despite the fact that stroke is the leading cause of death in the country, responsible for nearly one-fifth of all national deaths (8,9), with ischemic stroke comprising over 60% of cases (10,11)1,12). National hospital data also show that one in three ischemic stroke patients has a history of previous stroke, yet longitudinal and risk-stratified data are still lacking (27,28).

This scoping review aims to systematically identify and map the timing patterns of recurrent ischemic stroke (early vs. late) and explore their associated risk and protective factors across global studies. By synthesizing existing evidence, the review seeks to inform more targeted secondary prevention strategies and guide future research, especially in resource-limited settings such as Indonesia.

## METHODS

### Study Design

This study design used a scoping review according to the framework of Arksey and O'Malley and reported using the PRISMA Extension for Scoping Reviews (PRISMA-ScR) guide (29). A scoping review was chosen because it can map the main concepts, range of evidence, and gaps in available research in the topic of timing and patterns of recurrent ischemic stroke (RIS), which until now has not been documented systematically. The steps taken in this review are identify the research question, identify relevant studies, conduct study selection, record and classify data, and combine, summarize, and report findings (30).

### Eligibility Criteria

This scoping review employed the PCC (Population, Concept, Context) framework to guide the formulation of research questions and the selection of relevant articles. The Population (P) refers to adult patients who have experienced recurrent ischemic stroke. The Concept (C) focuses on the timing and pattern of ischemic stroke recurrence. The Context (C) includes studies that explore or report on the timing and pattern of ischemic stroke recurrence in any healthcare or geographical setting. Based on this framework, the selection of articles was conducted by three independent reviewers following the PRISMA-ScR guidelines (Figure 1).

Inclusion criteria in this review were original full-text accessible articles, written in English, published within the last 10 years (2014–2024), using a prospective or retrospective cohort study design, and addressing the timing or pattern of recurrent ischemic stroke recurrence. The restriction to the last decade was chosen to guarantee the relevance of the findings to recent developments in clinical practice, diagnostic technology, and stroke management approaches. Excluded studies included non-English articles, inaccessible full-text, case reports, literature reviews, editorials, as well as studies that did not address the timing or pattern of ischemic stroke recurrence.

### Search Strategy

The literature search was conducted systematically by three authors (M.C, C.E.K, and A.P.P) using four major databases: PubMed, Scopus, ScienceDirect, and CINAHL Plus with Full Text. The search focused on articles published in the last 10 years (2014–2024) and was organized based on a predefined PCC (Population, Concept, Context) framework. Keyword combinations used in the search were: ("recurrent ischemic stroke" OR "stroke recurrence") AND ("time to recurrence" OR "recurrence interval"). The Boolean operators "AND" and "OR" were used to expand or narrow the search results according to the needs of the topic. In addition, the search results were also expanded using snowballing techniques, which traced references from the selected articles to find additional relevant studies. This review did not use keywords based on measured outcomes as this tends to limit the number of articles found in the search.

### Study Selection and Quality Appraisal

Three authors (M.C, C.E.K, and A.P.P) independently selected studies that met the eligibility criteria. At the initial stage, duplication of articles was checked using Mendeley's reference manager. Next, the authors selected articles based on title, abstract, and full text to assess the suitability of the topic and the

predefined inclusion and exclusion criteria. In the final stage, all articles that passed the selection were quality assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Cohort Studies (31).

This checklist consists of 11 statements with answer options: Yes, No, Unclear, and Not Applicable. Each "Yes" answer was given a score of 1, while the others were given a score of 0. The final score was calculated as a percentage. Articles with a JBI score below 70% were eliminated from the analysis process. In case of discrepancies in the selection or assessment results, all authors discussed the differences until they reached an agreement. In this process, no disagreement was found among the authors regarding the eligibility of the analyzed studies.

### Data Extraction and Analysis

Data were systematically extracted by one author (M.C) and independently reviewed by two other authors (C.E.K and A.P.P) to ensure accuracy and consistency. Information from studies that met the inclusion criteria was organized into two main tables. Table 1 includes study characteristics of recurrent ischemic stroke (RIS), including author name, year of publication, study location, design, recruitment period, sample size, mean age of participants, follow-up method and duration, post-stroke functional status, and special population characteristics. Table 2 contains patterns of recurrence time, estimated cumulative risk of RIS, and significant risk or protective factors. The variables collected include the operational definition of recurrence, time distribution of RIS events, and results of predictor analysis.

Analysis was thematic and exploratory descriptive, beginning with the organization of data in summary tables, followed by synthesis of differences in recurrence definitions, follow-up methods and population characteristics. All authors were actively involved in the interpretation and discussion of results and reviewed all included studies to minimize errors and ensure compliance with inclusion criteria.

## RESULTS

### Study Selection

The literature search process was conducted systematically and transparently to ensure that only relevant articles that met the inclusion criteria were analyzed in this scoping review. The literature search was conducted through four main databases, namely EBSCO-hosted Medline Ultimate (n = 285), PubMed (n = 1,881), ScienceDirect (n = 813), and Scopus (n = 7), as well as one additional article with snowballing technique, resulting in a total of 2,987 articles found. In the initial stage, duplicate articles were identified using the check for duplicates feature in the Mendeley Reference Manager application. As a result, 452 duplicate articles were identified and excluded, leaving 2,535 articles.

Next, screening was conducted based on the title and abstract, which resulted in 2,495 articles being excluded due to irrelevance to the review topic, such as not addressing ischemic stroke recurrence, or not explicitly reporting the timing of recurrence. A total of 40 articles were then analyzed at the full-text review stage. From this stage, 31 articles were excluded with the following details: the population was not exclusively ischemic stroke patients (n = 10), the outcome was inappropriate or irrelevant (n = 9), and did not explicitly report recurrence time (n = 12). Finally, 9 articles met all criteria and passed the JBI critical appraisal tools (see Table 1).

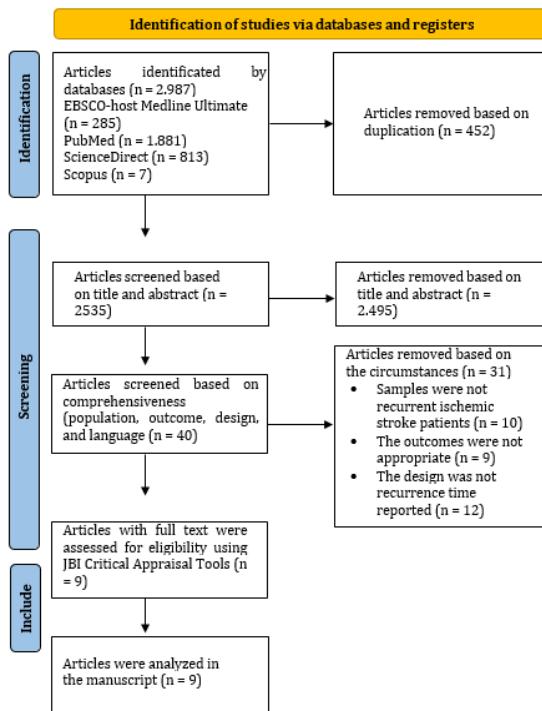
**Table 1. JBI Critical Appraisal Results**

No	Study and Year	Study Design	JBI Score	Percentage	Status
1	Wang et al., 2016	Prospective cohort	9/11	81.8%	Eligible
2	Kumar et al., 2023	Prospective cohort	8/11	72.7%	Eligible
3	Uzuner et al., 2023	Retrospective cohort	9/11	81.8%	Eligible
4	Zhang et al., 2019	Prospective cohort	10/11	90.9%	Eligible
5	Elnady et al., 2020	Prospective cohort	8/11	72.7%	Eligible
6	Verburgt et al., 2024	Retrospective cohort	9/11	81.8%	Eligible
7	Zhao et al., 2019	Prospective cohort	10/11	90.9%	Eligible
8	Khanevski et al., 2019	Prospective cohort	11/11	100%	Eligible
9	Giang et al., 2015	Retrospective cohort	10/11	90.9%	Eligible

### Characteristics of the Selected Studies

Nine studies were included in this scoping review, comprising five prospective cohort studies,

three retrospective cohort studies, and one prospective observational study (see Table 2). The studies were conducted in various countries, including China, India, Egypt, Turkey, the Netherlands, Norway and Sweden. The number of participants varied from 75 to 17,149, with a predominant age range of 18 to 75 years. The duration of follow-up ranged from 3 months to more than 5 years, with tracking methods as diverse as clinical visits, telephone monitoring, community surveys, medical record keeping, as well as the use of national registries. Post-stroke functional status was assessed using the NIHSS, mRS, or other scales, although not all studies explicitly reported this.



**Figure 1. PRISMA Flow Diagram adapted from Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372: n71. Creative Commons (32).**

All studies evaluated the timing of ischemic stroke recurrence with varying definitions, including early (<3 months), moderate (3–12 months), to long-term (>1 year) recurrence. The cumulative risk of stroke recurrence ranged from 4.3% to 23.4%, with peak recurrence generally occurring within the first 3 to 12 months. The most consistently reported risk factors include hypertension, heart disease, history of stroke/TIA, and poor functional status (mRS ≥3). Some studies also identified protective factors such as improved secondary therapy adherence and primary prevention. The diversity of designs, geographic locations, and analytic approaches enrich the understanding of the time dynamics and patterns of ischemic stroke recurrence in the global population.

**Table 2. Characteristics Studies of Recurrent Ischemic Stroke (RIS)**

No	Study and Year	Location	Study Design	Recruitment Period	N	Mean Age (years)	Follow-up Duration	Follow-up Method	Post-Stroke Functional Status	Specific Population Notes
1	Wang et al., 2016	China	Prospective cohort	2007–2008	7,593	64 (median)	3, 6, 12 months	Clinical & telephone	NIHSS at baseline; mRS not specified	Focused on in-hospital complications as main predictors
2	Uzuner et al., 2023	Turkey	Retrospective cohort	2017–2020	521	Not reported	3 months	Medical records & clinical	TOAST + OCSP classification	Studied early recurrence within 3 months
3	Zhang et al., 2019	China	Prospective cohort	2010–2016	641	61.8 ± 12.6	3 years	Telephone & routine surveys	mRS ≥3 as predictor	Assessed adherence to medication & mRS on recurrence timing

No	Study and Year	Location	Study Design	Recruitment Period	N	Mean Age (years)	Follow-up Duration	Follow-up Method	Post-Stroke Functional Status	Specific Population Notes
4	Verburg et al., 2024	Netherlands	Retrospective cohort	2006–2020	6,447	70 (median)	1 year	National medical registry	NIHSS at admission; mRS at discharge	Analyzed recurrence timing and etiology via ICD codes
5	Zhao et al., 2019	China (rural)	Prospective cohort	1992–2017 (phased)	5,121	Not reported	5 years	Community-based follow-up	Not explicitly reported	Investigated decadal recurrence trends
6	Khanevski et al., 2019	Norway	Prospective cohort	2007–2013	1,872	73.2 (mean)	Mean 5.6 years	Regional medical records	mRS at discharge	Included IS/TIA; evaluated recurrence and mortality risks
7	Giang et al., 2015	Sweden	National retrospective cohort	1987–2006	17,149	18–54 years	4 years	National inpatient registry	Not specified	Young adults; analyzed long-term recurrence trends
8	Elnady et al., 2020	Egypt	Prospective cross-sectional	Apr–Aug 2017	122	65.4 ± 10.1	1 year	Inpatient follow-up	NIHSS & Scandinavian Stroke Scale	Compared early vs late RIS based on TOAST
9	Kumar et al., 2023	India	Prospective observational study	Jan–Dec 2021	75	64.8 ± 9.5	1 year	mRS monthly checks	mRS monitored monthly	First-ever IS patients; identified recurrence by mRS worsening

Abbreviation: NIHSS (*National Institutes of Health Stroke Scale*); mRS (*Modified Rankin Scale*); TOAST (*Trial of Org 10172 in Acute Stroke Treatment*); OCSP (*Oxfordshire Community Stroke Project*); ICD (*International Classification of Diseases*); IS (*Ischemic Stroke*); TIA (*Transient Ischemic Attack*).

## Study Outcome

All studies in this scoping review reported the primary outcome of RIS, with variations in the duration of follow-up ranging from 3 months to more than 5 years. Several studies have reported the incidence of recurrent ischemic stroke at various time intervals. One study reported a 14% recurrence rate within 3 months (26), another documented 14.7% within 12 months (25), while a cumulative incidence of 20.1% over a 3-year period was also observed (33). Recurrent ischemic stroke rates have been reported at varying intervals across several studies. One study observed recurrence rates of 4.3% within 30 days, 6.7% within 90 days, and 8.8% within 1 year (34). Another reported a 14.2% recurrence over 4 years (35). A cumulative risk of 5.4% within 1 year and 11.3% within 5 years was also documented (23). Additionally, recurrence rates of 14.7% at 3 months and 21.3% at 1 year were found in a more recent investigation (36).

Some studies have emphasized additional outcomes beyond the incidence of recurrent ischemic stroke. One study evaluated the long-term risk of RIS over a 5-year period, reporting a cumulative rate of 11.3%, along with the risk of mortality associated with baseline stroke characteristics (23). One study focused on a young adult population and recorded patterns of RIS over a 4-year period, including differences in incidence between males and females (35). Another highlighted the declining trend of RIS incidence between decades as a reflection of successful prevention efforts (37). Two studies assessed the outcomes of RIS based on the timing of recurrence (early vs late), as well as the factors that influence such differences (24,36). In addition, one study also utilized the change in mRS score as a clinical outcome indicator indicating functional stroke recurrence (36).

## Patterns and Timing of Recurrence

The timing pattern of recurrent ischemic stroke (RIS) recurrence in the nine reviewed studies showed significant variation, both in the definition of “early” and “late” timing and the period of highest risk (see Table 3). Several studies have categorized the timing of recurrence into distinct phases, as demonstrated in a study that differentiated between early (<1 year) and late ( $\geq 1$  year) RIS, where the type of stroke and patient comorbidities appeared to differ between phases (24). Early RIS is more commonly associated with Large Artery Atherosclerosis (LAA) etiology and cardioembolic embolism, while late RIS is associated with small vessel disease and high systolic hypertension.

Another study presented the median time to recurrence. One study reported a median recurrence time of 21 days (26), while another recorded a median time of 25 days, suggesting that most RIS occurred

within the first month post-stroke (34). Other studies also reflect this trend, reporting higher rates of RIS in the first 3 months compared to later periods (26,36).

Some studies observed long-term time trends. Two studies show the accumulation of RIS incidence from year to year, which emphasizes the importance of continuous monitoring and prevention (23,33). Another study even reviewed the decadal pattern of recurrence and noted a trend of decreasing RIS over time, likely due to increased access to preventive therapy (38). Meanwhile, one study found that the highest risk of RIS occurred in the first 6 months and decreased progressively thereafter (35).

**Table 3. Patterns, Risks, and Predictors of Recurrent Ischemic Stroke (RIS)**

No	Study and Year	Definition of Recurrence	Temporal Pattern	Cumulative RIS Risk (%)	Significant Risk/Protective Factors	Statistical Analysis Results	
						p-value	95% CI
1	Wang et al., 2016	New or worsening neurological deficit post-discharge	3, 6, 12 months	14.7% at 12 months	In-hospital complications: UTI RTI CHF	0.016 0.011 0.041	1.14-4.23 1.18-3.52 1.03-3.42
2	Uzuner et al., 2023	New stroke within 3 months	Median 21 days	14.0% at 3 months	CAD CHF CKD	0.009 0.016 0.012	1.30-6.51 1.21-6.27 1.27-7.03
3	Zhang et al., 2019	Clinically confirmed new ischemic stroke	1, 2, 3 years	11.5% (1 yr), 16.7% (2 yr), 20.1% (3 yr)	Prior stroke mRS ≥3 Poor medication adherence AF NIHSS ≥5 Dyslipidemia	0.002 0.008 0.016 0.020 0.043 0.019	1.62-7.82 1.18-2.89 1.11-2.84 1.06-2.30 1.07-2.36 1.07-2.09
4	Verburgt et al., 2024	New stroke diagnosis in ICD	Median 25 days	4.3% (30d), 6.7% (90d), 8.8% (1 yr)	Minor stroke LAA subtype	0.025 <0.001	1.05-1.95 1.51-3.35
5	Zhao et al., 2019	Any recurrent stroke within 5 years	Assessed per 5-year period	23.4% (2012-2017); declining trend	Age ≥75 Prior ischemic stroke AF	0.034 0.005 0.002	1.03-1.92 1.12-1.88 1.20-2.35
6	Khanevski et al., 2019	New IS/TIA >28 days post-index	1 & 5 years (mean 5.6 yrs)	5.4% (1 yr), 11.3% (5 yr)	HTN Prior IS/TIA Chronic infarcts LAA subtype Smoking	0.030 0.026 0.043 <0.001 0.045	1.05-2.59 1.06-2.50 1.01-2.18 1.41-3.33 1.01-2.32
7	Giang et al., 2015	Hospitalization for new IS after 28 days	1-6 mo, 6-12 mo, 1-4 years	14.2% (4 yrs); 11.8% men, 9.8% women	HTN DM AF Male gender Younger age (<45)	0.010 0.040 0.009 0.009 0.010	1.11-2.20 1.02-2.13 1.16-2.86 0.25-0.82 0.21-0.81
8	Elnady et al., 2020	New stroke ≥24h post-improvement of prior stroke	<1 year = early; ≥1 year = late	Not reported	Early RIS: LAA Cardioembolism Late RIS: SVD ↑SBP Afasia	0.008 0.013 0.040 0.026 0.047	1.28-5.31 1.19-4.41 1.04-5.37 1.004-1.065 1.02-6.27
9	Kumar et al., 2023	mRS worsening from prior status	3, 6, 9, 12 months	14.7% (3 mo), 21.3% (1 yr)	Age >75 Male gender HTN DM Dyslipidemia	0.021 0.036 0.025 0.014 0.048	Not reported

Abbreviation: RIS (Recurrent Ischemic Stroke); OR (Odds Ratio); CHF (Congestive Heart Failure); mRS (Modified Rankin Scale); LAA (Large Artery Atherosclerosis); HTN (Hypertension); HR (Hazard Ratio); DM (Diabetes Mellitus); MRI (Magnetic Resonance Imaging); ICD (International Classification of Diseases); IS/TIA (Ischemic Stroke / Transient Ischemic Attack).

### Risk and Protective Factors

Studies showed that the main risk factors for RIS include hypertension, history of stroke, and other cardiovascular conditions. Hypertension, history of previous stroke or TIA, and chronic ischemic lesions on MRI were significantly associated with an increased risk of RIS within five years (23). Hypertension and DM have been identified as dominant factors in young patients, with the highest risk occurring within the initial 6 months post-stroke (35). Coronary artery disease and congestive heart failure have also been shown to significantly increase the risk of early recurrence (26). On the other hand, complications during

hospitalization such as pneumonia have been shown to increase the risk of RIS (25). Risk was also increased in patients with high functional disability (mRS  $\geq 3$ ) and low adherence to stroke therapy (33). Age  $>75$  years, male sex, hypertension, DM, and dyslipidemia were identified as risk factors, although not all were statistically significant (36). Mild stroke and LAA subtype were associated with recurrence within the initial 30–90 days (34). Dominant factors in early RIS included LAA, cardioembolism, and valve disease, while late RIS was more strongly associated with SVD and high systolic blood pressure (24). Interestingly, recurrence rates have decreased in the last decade due to improvements in primary and secondary prevention in rural China (38).

### **Measurement Tools and Follow-Up Approaches**

Functional measurement tools and follow-up methods differ between studies, with mRS and NIHSS being the most frequently used instruments. One study used mRS as a predictor of risk and noted that an mRS score  $\geq 3$  increased the likelihood of RIS within three years (33), while another monitored mRS on a monthly basis and interpreted worsening of mRS as an indication of clinical relapse (36). In a different study, the mRS score at discharge was recorded as an initial functional assessment to correlate it with long-term risk (23). Additionally, NIHSS at baseline and mRS at hospital discharge were recorded, and data from a national ICD-based registry were used to detect relapse (34). NIHSS at admission was also used to evaluate baseline severity and matched with recurrence outcomes (25), and both NIHSS and the Scandinavian Stroke Scale were employed during hospitalization to compare early and late RIS characteristics (24). In terms of follow-up methods, hospital medical records were utilized in one study (26), while another combined telephone and routine surveys in a 3-year follow-up (33). A 5-year community follow-up was conducted in a different study (38), and national inpatient registry data were used to assess relapse over 4 years (35). This combination of tools and methods reflects the need for consistent monitoring standards that are adaptive to local contexts.

## **DISCUSSION**

This scoping review aims to map the timing pattern of recurrence and identify the risk and protective factors that influence RIS. Findings from the selected studies provide a dynamic picture of the timing and frequency of recurrence, while supporting the development of more targeted RIS prevention strategies in the critical post-stroke period.

### **The Primacy of the Early Recurrence Window**

The majority of studies show that RIS tends to occur in the early phase after the first stroke, with a peak of recurrence within the first three months. Median recurrence times of 21 and 25 days were recorded in two separate studies (26,34), consistent with a meta-analysis reporting that two-thirds of relapses occur within the first 90 days (21). Supporting this, data also showed a 7.9% relapse rate within the first 30 days (20). This concept of an "early high-risk period" underscores the importance of more intensive identification and management in the early post-stroke phase to lower the risk of recurrence.

The early post-stroke period is a critical window for preventive intervention. Treatment immediately after TIA or minor stroke has been shown to reduce the risk of recurrence by 80% in the first 90 days (39,40), and non-lacunar strokes are also at high risk of recurrence within the first two weeks (41). Physiological mechanisms in this phase, such as inflammation and thrombus formation, add urgency to intensive management, including blood pressure control and drug titration (42). Intervention in this early phase is believed to not only prevent short-term recurrence, but also contribute to the reduction of long-term morbidity and mortality (42,43).

In addition to the high risk in the early phase, RIS recurrence also persists in the intermediate and long-term phases. A cumulative increase in recurrence up to 12 months post-stroke has been observed in several studies (25,33,36). Early recurrence ( $<1$  year) is predominantly associated with LAA and cardioembolism subtypes, whereas late recurrence ( $\geq 1$  year) is more linked to small vessel disease and systolic hypertension (24). The risk persists for more than 5 years (23,35,38), and may extend up to a decade, particularly in older adults with vascular comorbidities (44). Moreover, even young patients remain at long-term risk for up to two decades (45), highlighting the importance of long-term prevention strategies based on risk stratification (46).

### **Profiles of Early versus Late Recurrence**

The timing of RIS recurrence reflects pathophysiological variation and clinical management post-stroke (33,36). Patients with poor risk factor control, severe carotid stenosis, smoking, hypertension, and a history of stroke have a high risk of recurrence (47,48). DM is also an independent risk factor for RIS (33), and patients with DM and hypertension tend to experience slow but cumulative recurrence (26,47). Early recurrence (<1 year) is often associated with acute embolization and thrombus instability (50,51), whereas late recurrence (≥1 year) is more related to the progression of atherosclerosis and vascular remodeling (52). Factors at the time of first stroke, such as hospitalization complications and low functional status, are also predictors of early recurrence (18,33).

Based on these findings, stroke recurrence prevention strategies should be dynamic and multi-layered. Early interventions, such as antiplatelet combinations in the hyperacute phase, have been shown to decrease recurrence rates within the first 90 days (25). However, long-term effectiveness relies heavily on the ongoing control of risk factors, such as blood pressure, blood lipid profile, and patient lifestyle (48). Multidisciplinary approaches that include patient education, long-term pharmacological support, and technology-based blood pressure monitoring such as telemonitoring are beginning to show promising results, as found in recent studies (53,54). One study specifically showed that utilizing mobile health can reduce relapse by 15% in patients with low adherence (48). Meanwhile, the study of Kolmos et al. underlines the importance of continuity of care, which is proven to reduce the risk of recurrence in patients who receive education and intensive monitoring after ischemic stroke (18). Thus, RIS management does not only rely on early intervention, but also requires ongoing planning that considers clinical risk profiles as well as recurrence time patterns, where a combination of medical and technological factors must go hand in hand to maximize long-term outcomes (18,53).

### **Methodological Considerations and Heterogeneity**

Discussions on the timing of RIS recurrence still face methodological challenges that impact data consistency between studies (23). One of the main obstacles is the lack of a standardized definition of early and late recurrences (26). For example, Kang et al. categorize early recurrence as new lesions appearing within 30 days post-thrombolysis, whereas Uzuner et al. and Verburgt et al. only reported the median time to recurrence without explicit classification (20,26,34). This inconsistency makes comparative analysis difficult and may obscure the interpretation of risk, especially in the early phase which is crucial in secondary prevention.

In addition to definitional issues, most studies only focus on describing the timing of recurrence without using a predictive approach based on the chronology of events (55). Yet, understanding the different pathophysiological dynamics between early and late phases is crucial in mapping individualized risk. One study emphasize the need for the development of prediction models that consider the temporal aspects of relapse (34). Therefore, there is a need for standardization of time classification and integration of predictive approaches to improve the precision of interventions, especially in the high-risk post-stroke phase (20).

### **Implications of Study**

Given the high burden of stroke in Indonesia and the limited availability of longitudinal data on recurrent ischemic stroke (RIS), the findings of this global scoping review offer important implications for clinical and public health practices in the country. The identification of early (<90 days) as a high-risk period for recurrence emphasizes the urgent need for structured post-discharge monitoring systems within Indonesian hospitals and primary care networks. Moreover, the consistent use of tools such as the Modified Rankin Scale (mRS) and National Institutes of Health Stroke Scale (NIHSS) found in international studies could serve as a reference for standardizing post-stroke evaluations in Indonesia. In the absence of a national stroke registry, leveraging digital health platforms tailored to local infrastructure may support patient follow-up, improve therapy adherence, and reduce recurrence rates. This underscores the importance of integrating global evidence into local policy frameworks, including the development of risk-based secondary prevention protocols and investment in digital health innovations suited to Indonesia's diverse healthcare settings.

### **Strengths and Limitations of Study**

The strength of this scoping review is the use of a systematic and transparent research design based on the Arksey and O'Malley framework and PRISMA-ScR guidelines, which ensures reliability and replicability. The literature search strategy included four major databases (PubMed, Scopus, ScienceDirect, and CINAHL) as well as snowballing techniques to expand coverage. Article selection was conducted by three independent reviewers using the JBI Critical Appraisal Checklist, with a cross-validation process in data extraction. The exploratory thematic and descriptive approach used allowed in-depth mapping of variations in relapse time and RIS risk factors. In addition, the diversity of population, geographical setting, and duration of follow-up in the analyzed studies enriches the interpretation of RIS dynamics in a global context.

However, there are a number of limitations to this study. Heterogeneity in the definition of relapse, duration of follow-up, and data collection methods between studies makes it difficult to consolidate findings consistently. The number of studies that met the inclusion criteria was only nine, which may limit generalizability especially to underrepresented populations. Not all studies explicitly reported protective factors, resulting in uneven risk mapping. In addition, the lack of standardized definitions of early and late relapse and the absence of a formal assessment of the risk of bias may limit interpretation of the internal validity of the analyzed results. These methodological inconsistencies highlight the need to harmonize definitions and study designs in future RIS research.

## **CONCLUSION**

This scoping review affirms that recurrent ischemic stroke (RIS) demonstrates a clear temporal distinction between early and late recurrence phases, each underpinned by differing pathophysiological mechanisms and clinical risk profiles. Early RIS, occurring within the first 90 days post-index stroke, is primarily driven by acute risk factors such as hypertension, diabetes, prior stroke history, and etiologies like large artery atherosclerosis and cardioembolism. In contrast, late RIS manifesting beyond 90 days is more frequently associated with progressive vascular pathology, including small vessel disease, hyperlipidemia, and poorly controlled systolic blood pressure.

Recognizing these temporal differences is crucial, as it enables the implementation of phase-specific preventive strategies. The early high-risk window necessitates intensive secondary prevention through proactive monitoring, rapid therapeutic optimization, and individualized care plans. Conversely, late recurrence requires long-term commitment to risk factor control, continuity of care, and patient engagement.

To enhance the effectiveness of these strategies, the integration of digital health innovations such as remote monitoring, mobile health (mHealth), or telehealth should be considered to support sustained adherence and reduce the risk of recurrence. These findings reinforce the need for time-sensitive, risk-adjusted stroke care models, particularly in settings where structured long-term follow-up remains a challenge. Ultimately, a temporally informed approach to RIS can transform post-stroke care by aligning prevention efforts with the dynamic nature of recurrence risk.

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## **CONFLICTS OF INTEREST**

The authors declare no conflict of interest.

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