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# **Review Paper**





# Mortality Rate of Acute Stroke in Iran: A Systematic **Review and Meta-Analysis**

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# **ABSTRACT**

Background: There is limited data about the short-term stroke mortality rates for patients in treatment

Objectives: This study aimed to estimate the short-term stroke (in hospital, one month, one year) mortality rates in Iran through a systematic review and meta-analysis.

Materials & Methods: We searched electronic databases, including three national (IranDoc, Megiran, SID) and four international (Scopus, PubMed, Web of Science, Google Scholar), from January 1990 to March 2020. We considered all observational studies on stroke mortality, such as cohort and crosssectional studies. Furthermore, the sub-group analyses were performed based on each province and metaregression analysis based on the study's year and patients' mean age.

Results: Among 143 studies, 28 were eligible (11 cohort and 17 cross-sectional studies). Based on the random model, the mortality rates for in-hospital, 1-month, and 1-year mortality were reported as 18.71% (95% CI: 15.09%-22.34%), 23.43% (95% CI: 20.08%-26.78%), and 34.44% (95% CI: 32.02%-36.85%), respectively. The results also revealed that mortality rates were neither related to the year studies conducted nor to the patient's age.

Conclusion: Approximately one-fifth of stroke patients in Iran die in the hospital after admission. The mortality rate increased in the one-month and one-year period, and about one-third of the patients died in the first year. Therefore, it is cardinal to focus on programs and solutions in which we can ameliorate mortality in the short-term period after stroke by performing primary specific treatments on patients.

Keywords: Stroke, Mortality, Systematic review, Meta-analysis, Iran

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# **Highlights**

- Stroke is the second leading cause of mortality worldwide.
- Mortality rates for in-hospital, one-month, and one-year mortality were reported as 18.71% (95% CI, 15.09%-22.34%), 23.43% (95% CI, 20.08%-26.78%), and 34.44% (95% CI, 32.02%-36.85%), respectively.
- Approximately one-fifth of stroke patients in Iran die in the hospital after admission.

#### Introduction

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troke is the second leading cause of mortality worldwide and the leading cause of acquired disability in adults. Also, two-thirds of the stroke-induced burden occurs in developing countries [1, 2]. Identify-

ing patients' mortality risk at admission can contribute to valuable clinical care modifications by identifying high-risk patients with poor outcomes who require more intensive resources. There is also an incremental course in the need to evolve well-validated models in predicting patients' mortality risk. The objective is to reduce the overall burden of stroke on developing societies and establish an organized and classified protocol in acute stroke management [3, 4].

Stroke has many personal and social consequences; hence, it has been recognized as one of the most prioritized non-communicable diseases by the World Health Organization, a specialized agency of the United Nations responsible for international public health [5]. Blood pressure, type 2 diabetes, and heart disease are the most cardinal yet modifiable risk factors for stroke [6]. Independent predictors of stroke's poor prognosis included the onset of stroke (whether acute or chronic), age over 70, deterioration during the first 48 hours of hospitalization, decreased consciousness, complete motor deficit, major cognitive syndrome, hyperglycemia, and female gender. Most ischemic strokes occur between 71 and 80, while most cases of hemorrhagic strokes occur between the age range of 60 and 70 [7, 8].

Recent estimates of the Global Burden of Disease Study clarified that the prevalence and incidence of stroke worldwide in 2016 were estimated to be 83 and 13.6 million, respectively [9]. Due to aging and population growth, the global burden of stroke is rising steadily [10]. The world has witnessed that the largest stroke burden pertains to low and middle-income countries [11]. In high-income countries, over the past two decades, the incidence of ischemic stroke has decreased by 13% and

the mortality rate by 37%. Moreover, DALY (the disability-adjusted life year) and the mortality ratio to incidence decreased by 34% and 21%, respectively [12].

There is no national stroke registry in Iran. Therefore, there was a discrepancy among the recorded stroke incidence from 22 to 140 strokes per 100000 people between different regions of the country [10]. Studies show that stroke resulted in 12.3% mortality with a median of 5.5 months after discharge, mostly due to recurrence or complications of stroke [13].

Stroke mortality can be an excellent indicator of stroke care and control. Several studies have been conducted to estimate the mortality rate of stroke in hospitals, including 30 days post-stroke [14, 15], six months post-stroke [16], and long periods with different sample sizes and different follow-up lengths in several provinces of Iran [17]. Identification of mortality predictors at the time of hospitalization can be beneficial in reducing post-stroke mortality rates. Therefore, the present study aimed to systematically review and meta-analysis the available evidence to assess the short-term mortality rate of stroke in Iran.

#### **Materials and Methods**

This review study is a systematic and meta-analysis of short-term stroke mortality rates in Iran. This study's reporting method is based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) checklist [18].

#### Search strategy

We applied the following terms, and our search was based on international electronic databases, including Scopus, PubMed, Web of Science, and national databases of Iranian Research Institute for Information Science and Technology (IranDoc), Magiran, Scientific Information Database (SID) Gray Literature, reference lists check, and manual journal searching from January 1990



to March 2020. The key search terms were "Stroke," or "Ischemic stroke," or" Hemorrhagic stroke," "Intracerebral hemorrhage," or "Intracerebral stroke," or "subarachnoid hemorrhage," or "Dead," or "Fatality Rate," or "Mortality Rate," or "Survival," or "Survival Analysis," or "Survival Rate" plus "Cohort Studies" or "Retrospective Studies" or "Prospective Studies" or "Longitudinal Studies" or "Cross-sectional studies" or "Observational studies" and "Iran."

We additionally examined resource references from retrieval articles to guarantee that none of the relevant articles were missed. The collected data were entered into EndNote, X7 software, and duplicate articles were automatically deleted. It is worth noting that two researchers reviewed the articles independently.

# Eligibility criteria

All observational studies (cross-sectional and cohort) referred to 1-month and 1-year stroke mortality related to Iran were entered into the review study without time limits. The included studies were necessitated to have a lethality rate or a mortality rate.

Death was defined as the permanent cessation of all vital signs, and its causes were classified according to the 10<sup>th</sup> version of the International Classification of Diseases (ICD-10). The causes of death in this study were stroke (ICD-10 I60-I69).

# Quality assessment

Newcastle-Ottawa's quality assessment checklist was utilized to evaluate the quality of the articles. This tool consists of three parts: selection (4 questions), comparison (1 question), and result (3 questions). Furthermore, based on the final score, the score was classified into three categories: good group (3 or 4 stars in the selection section, 1 or 2 stars in the comparison part, and 2 or 3 stars in the result section), fair (2 stars in the selection section, 1 or 2 stars in the comparison part and 2 or 3 stars in the result section), and poor (0 or 1 star in the selection section, 0 stars in the comparison part and 0 or 1 star in the result section) [2]. The results of the qualitative evaluation are presented in Appendix 1.

# Screening of studies

Two researchers conducted initial exploration and assessed the studies' qualities; in case of a discrepancy, the supervisor had the final word.

#### Data extraction form

A previously prepared checker extracted all ultimate articles that entered the study process. The checklist included the author's name, publication year, study timeframe, sample size, study location, gender, mean age, stroke type, and mortality rate at distinct intervals.

### Statistical analysis

Heterogeneity between studies was investigated by the Cochran test (with a significance level less than 0.1) and a combination employing I<sup>2</sup> statistics. In a case with heterogeneity, the random-effects model was applied by the inverse-variance method, and in the case of no heterogeneity, the fixed effects model was adopted. In the case of heterogeneity amidst studies, methods such as meta-regression and subgroup analysis were practiced. All analyses were performed by STATA software v. 13.

## Additional analysis

Due to the high heterogeneity of the studies, meta-regression analysis was practiced. Meta-regression analysis was conducted based on the year of the study and the mean age of the patients. Also, the subgroup analysis was performed only based on provinces to show more reliable stroke mortality status in the country for other variables such as stroke type, gender, the prevalence of hypertension, diabetes, etc. Due to the insufficient number of reports, meta-regression analysis and subgroup analysis were not preparatory.

### Publication bias

The random-effects model was utilized to lessen the chance of bias in studies [19, 20]. Egger emission bias assessment test was also practiced to estimate the risk of bias [21].

#### Results

#### Study selection

Of 143 retrieved records, 33 were withdrawn due to duplication, and 82 due to a lack of responses to the study questions. Finally, 28 articles were incorporated into the meta-analysis. The study design consisted of 11 cohort studies and 17 cross-sectional studies. It should be noted that the references of the entered articles were also reviewed to supplement relevant studies. The selection process of included studies is presented in Figure 1.



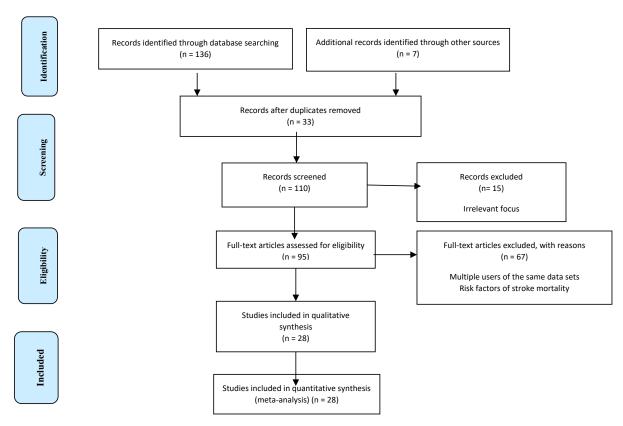


Figure 1. Flowchart of the included eligible studies in systematic review

#### **Study characteristics**

The incorporated studies were from 1998 to 2018, and only 13 provinces had at least one eligible study. Based on the geographical location of the province, out of 28 studies included, six were in Khorasan Razavi [22-27], 6 in East Azerbaijan [14, 16, 17, 28-30], 3 in Isfahan [31-33], 2 in Tehran [34, 35], 2 in Qom [13, 36], and 2 in Ardabil [34, 35, 37, 38]. Guilan [39], Kermanshah [40], South Khorasan [41], Mazandaran [42], Fars [15], Urmia [43], and Zahedan [44] Semnan [45] each had 1 study. One study was conducted on the entire population in Iran [46]. The characteristics of the studies are pitched in Table 1.

# Quality assessment

The articles' quality assessment results are shown in Appendixes 1 and 2. Based on our review using the relevant checklist, 18 studies had good quality, and ten articles had moderate quality.

# Heterogeneity

The results of the Chi-squared test and I<sup>2</sup> index revealed significant heterogeneity between studies in mortality

analysis for stroke and hospital mortality ( $I^2$ =99.1%, P<0.001) and monthly mortality ( $I^2$ =97.8%, P<0.001), so for these two, the random-effects model was adopted. The fixed-effects model was then used to analyze 1-year mortality ( $I^2$ =44.6%, P=0.125) because the studies were homogeneous.

# Results of the meta-analysis

First, the articles were classified based on the year of publication of the study. The obtained mortality rate was determined according to the following: hospital mortality rate, 1-month, and 1-year mortality rate. The mortality rates were conducted independently by provinces. Moreover, meta-regression was performed based on the study's year and the patients' mean age.

# Hospital mortality rate

Out of the ultimate articles, 17 studies published stroke hospital mortality. Based on the random-effect model, the study results recorded that the hospital mortality rate in Iran is 18.71% (95% CI: 15.09%-22.34%) among 47961 patients (Figure 2 and Appendix 3).



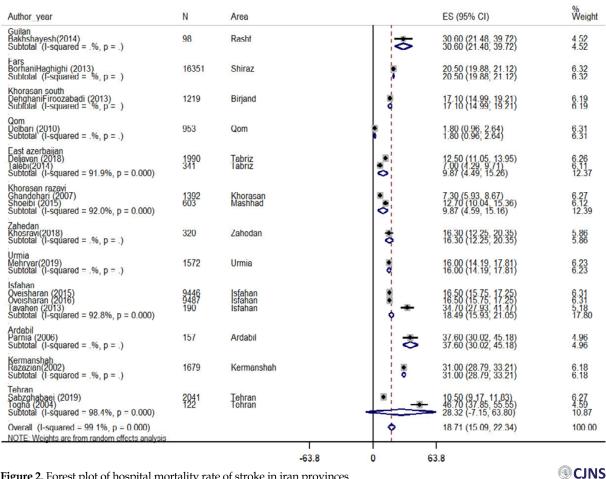


Figure 2. Forest plot of hospital mortality rate of stroke in iran provinces

Out of the final articles, 15 studies listed one-month-

long stroke mortality. Based on the random-effect model, the results revealed that the 1-month mortality rate in Iran was 23.43% (95% CI: 20.08%-26.78%) (Figure 3).

# One-year mortality

One-month mortality

Out of the final articles, five studies reported oneyear stroke mortality. The results revealed that one-year mortality in Iran based on the fixed-effects model was 34.44% (95% CI: 32.02%-36.85%) (Figure 4).

# Mortality rate based on provinces

Overall, the results of stroke mortality in 13 provinces in Iran, based on the studies included, are shown in Table 2. In general, 12 provinces reported at least one hospital mortality study, 7 reported one-month mortality rates, and three provinces proclaimed one-year mortality. Moreover, the highest and lowest prevalence in the provinces for hospital mortality was 37.60% (30.02%-45.18%) for Ardebil and 1.80% (0.96%-2.64%) for

Qom; for one month, the same index was for East Azerbaijan as 33.06% (13.63%-52.49%) and Mazandaran as 19.20% (14.32%-24.08%).

#### Meta-regression

The meta-regression results were based on the variables of the year of study and the mean age of the patients. There was no significant relationship between these two variables and mortality for years of study and mean age, although having risen in the year of study (Reg Coef=0.048, P=0.162 and increase in one unit mean age (Reg Coef=-0.017, P=0.585) and decrease hospital mortality, but these relationships were not statistically significant. Of course, although these two relationships were not statistically significant for one-month mortality, the results were somewhat different, with an increase in the year of the study (Reg Coef=0.025, P=0.260) and an increase in one unit of mean age (Reg Coef=0.030, P=0.232) and increased monthly mortality (Appendix 4).



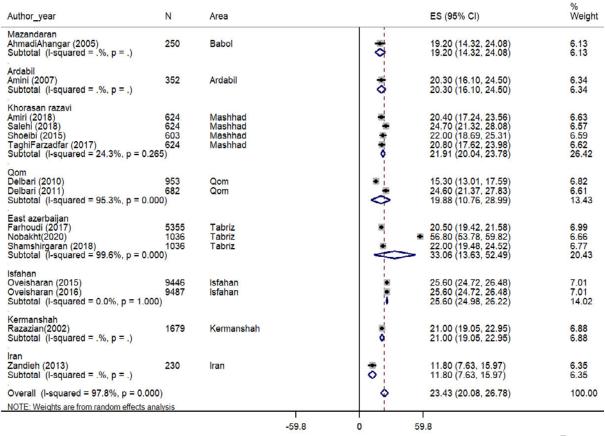


Figure 3. Forest plot of 1-month mortality rate of stroke in iran provinces

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#### **Publication bias**

Ultimately, we utilized funnel plots to check the propagation bias for stroke mortality; the Egger test results did not confirm this bias (P=0.479). These studies were scattered almost on both sides of the horizontal line, indicating the absence of publication bias (Appendix 5).

# Discussion

Based on our findings, the stroke in-hospital mortality rate in Iran was estimated to be 18.71%. This is the first study to determine the in-hospital mortality rate in Iran, and it provides a baseline figure to evaluate the subsequent changes in the trend of stroke mortality rate. Our results were lower than the seven countries that reported their stroke mortality rates to World Health Organization (WHO): Russian Federation, Ukraine, Belarus, Turkmenistan, Kazakhstan, Seychelles, and Oman. Their rates varied from 26 in Oman to 233 per 100000 population in Russian Federation [47]. The rate of hospital mortality in Germany reported by the stroke registry system in 2000 was estimated to be 4.9% [48]. In Mashhad, a province in Iran, the in-hospital stroke mortality rate from March 2018 to March 2019 was 14.2% [49]. This case fatality

rate was lower than reported in Tanzania, 33.3% [50]. Based on our data, age increased monthly mortality. The overall case fatality rate and reported case fatality rate in each gender demonstrated a non-significant increasing trend by age [51]. Furthermore, our study differed from a study in Tanzania, which described a significant increase of case fatality over the age of 65 [50].

Reedwong et al. [52] demonstrated that elderly patients have a higher mortality risk. This higher mortality risk is possibly due to transitional patients with medical emergencies and higher severity of stroke symptoms [53]. History of stroke, carotid stenosis, hypertension, dyslipidemia, and smoking are associated with low stroke mortality, probably because these risk factors are associated with non-cardioembolic stroke [54, 55]. Although significant studies have been published to predict stroke mortality, most have been convoyed when specific parts of stroke management and treatments have not yet been established or implemented on heterogeneous cohorts, such as ischemic and hemorrhagic strokes.



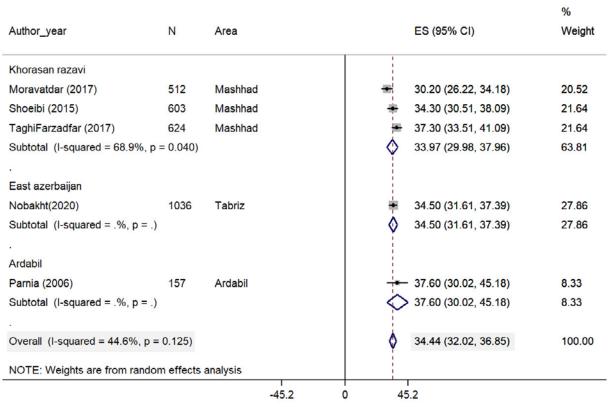


Figure 4. Forest plot of the 1-year mortality rate of stroke in iran provinces

In the Middle East, the results of a recent systematic review revealed a significant positive correlation between age and mortality rate [56]. Age is an important risk factor for death, and each additional year in age is correlated with a 3% relative increase in in-hospital stroke mortality [49]. Age seems to be the most important predictor of the 1-year mortality of stroke. According to several previous studies [57], age  $\geq 70$  years is associated with stroke risk (P<0.05) [58]. Although many studies have mentioned that increasing age is an important risk factor for in-hospital death, some studies have considered the effect of age more, especially for the elderly ( $\geq 65$  years). Also, it could not be independently correlated with poor outcomes (modified ranking scale  $\geq 3$ ) assessed through modified ranking scale at discharge [59, 60].

Based on our data, the 1-month stroke mortality rate in Iran was estimated to be 23.43%. The 30-day fatality rate in other demographic studies was estimated to be 23.43%, which was registered to be from 11.8% to 56.8% [61]. Recent studies have reported comparable results for 30-day lethality rates, such as ischemic stroke for 14.9% in Italy's Lazio regions in 2011-2012 [59] and 7.9% in Scotland in 2013 [62]. Moreover, in a review, the 28-day-old lethality rate varied from 17% to 33% and was estimated to be 22.9% [63]. Kumral reported that the overall 30-day mortality rate was 19.7%, which was higher for hemorrhagic stroke patients (29%) compared to ischemic

stroke (17%) [64]. The 28-day lethality rate for all types of stroke was 24%, while in the Oxfordshire Community Stroke project, the overall 30-day lethality rate was estimated at 19% [65]. Although in high-income countries, the lethality rate has decreased or remained steady for 28 days after stroke [66]. One of the reasons for this decline can be the improvement of care in the acute phase of the disease and management [67]. This finding might be relevant to Iran, which has undergone major political and socioeconomic changes after the Islamic revolution.

The 1-year mortality rate in Iran was 34.44%. In a separate study, independent predictors of stroke were considered age, pre-stroke functional status (MRS score more than 0), the severity of stroke (NIHSS), history of diabetes mellitus, heart disease, posterior circulation stroke syndrome (compared to anterior circulation stroke syndromes), and non-lacunar stroke causes [68]. In a population-based study in Greece on hemorrhagic patients, the 1-year mortality rate was estimated to be 36.8% [69]. The Danish MONICA study reported a 1-year mortality rate of 41% [70]. These mortality rates are considerably lower than those reported in previous older studies from Germany (58.3% between 1994 and 1996) [71] and New Zealand (57% between 1981-1982 and 1983) [72]. These differences may be associated with omitting cases that died before reaching the hospital.



Table 1. Basic information of included studies

Order	Audio (A)	la salta		N	Age, y	Мо	Mortality Rate		
Ö	Authors (y)	Location	Location Time		(Mean)	Hospital	One- Month	One- Year	
1	Razazian et al. (2003) [40]	Kermanshah City	1998-2000	1679	NR	31.00	21.00	NR	
2	Togha et al. (2004) [36]	Tehran City	1999-2002	122	66.00	46.70	NR	NR	
3	Tavahen et al. (2013) [32]	Isfahan City	2000-2001	190	NR	34.70	NR	NR	
4	AhmadiAhangar et al. (2005) [42]	Babol City	2001-2003	250	68.00	NR	19.20	NR	
5	BorhaniHaghighi et al. (2013) [15]	Shiraz City	2001-2010	16351	63.40	20.50	NR	NR	
6	Delbari et al. (2011) [13]	Qom City	2001-2002	682	69.60	NR	24.60	NR	
7	Ghandehari et al. (2007) [31]	Khorasan Province	2001-2005	1392	65.61	7.30	NR	NR	
8	DehghaniFiroozabadi et al. (2013) [41]	Birjand City	2002-2008	1219	69.60	17.10	NR	NR	
9	Parnia et al. (2006) [38]	Ardabil City	2003-2004	157	NR	37.60	NR	37.60	
10	Amini Sani et al. (2007) [37]	Ardabil City	2004-2005	352	69.10	NR	20.30	NR	
11	Delbari et al. (2010) [36]	Qom City	2006-2008	953	68.00	1.80	15.30	NR	
12	Oveisharan et al. (2015) [31]	Isfahan City	2006-2011	9446	69.98	16.50	25.60	NR	
13	Oveisharan et al. (2016) [33]	Isfahan City	2006-2010	9487	68.98	16.50	25.60	NR	
14	Salehi et al. (2018) [27]	Mashhad City	2006-2007	624	NR	NR	24.70	NR	
15	Shoeibi et al. (2015) [26]	Mashhad City	2006-2007	603	66.14	12.70	22.00	34.30	
16	TaghiFarzadfar et al. (2017) [23]	Mashhad City	2006-2010	624	64.60	NR	20.80	37.30	
17	Farhoudi et al. (2017) [28]	Tabriz City	2008-2013	5355	67.60	NR	20.50	NR	
18	Mehryar et al. (2019) [43]	Urmia City	2008-2015	1572	67.00	16.00	NR	NR	
19	Zandieh et al. (2013) [46]	Iran	2009-2010	230	NR	NR	11.80	NR	
20	Bakhshayesh et al. (2014) [39]	Rasht City	2010-2011	98	70.16	30.60	NR	NR	
21	Talebi et al. (2014) [30]	Tabriz City	2011-2011	341	68.80	7.00	NR	NR	
22	Nobakht et al. (2020) [17]	Tabriz City	2013-2015	1036	NR	NR	56.80	34.50	
23	Sabzghabaei et al. (2019) [35]	Tehran City	2013-2016	2041	66.50	10.50	NR	NR	
24	Shamshirgaran et al. (2018) [14]	Tabriz City	2013-2015	1036	69.06	NR	22.00	NR	
25	Moravatdar et al. (2017) [25]	Mashhad City	2014-2015	512	65.00	NR	NR	30.20	
26	Deljavan et al. (2018) [29]	Tabriz City	2015-2016	1990	65.80	12.50	NR	NR	
27	Khosravi et al. (2018) [44]	Zahedan City	2016-2016	320	63.20	16.30	NR	NR	
28	Amiri et al. (2018) [24]	Mashhad City	NR	624	64.55	NR	20.40	NR	

<sup>\*</sup> NR: Not Reported.



Table 2. Meta-analysis and heterogeneity of mortality rate of stroke in iran based on each province and time of mortality

	Total	Time of Mortality									
Area (Province)	Article		Hospital				One-Month				
	(Record)	N	Effect Estimate	l <sup>2</sup>	Р	N	Effect Estimate	l <sup>2</sup>	Р		
Khorasan Razavi	6(9)	2	9.87(4.59-15.16)	92.0	<0.001	4	21.91(20.04-23.78)	24.3	0.265		
East Azerbaijan	5(6)	2	9.87(4.49-15.26)	91.9	<0.001	3	33.06(13.63-52.49)	99.6	<0.001		
Isfahan	3(5)	3	18.49(15.93-21.05)	92.8	<0.001	2	25.60(24.98-26.22)	0.00	1.00		
Ardabil	2(3)	1	37.60(30.02-45.18)	-	-	1	20.30(16.10-24.50)	-	-		
Qom	2(3)	1	1.80(0.96-2.64)	-	-	2	19.88(10.76-28.99)	95.3	<0.001		
Tehran	2(2)	2	28.32(-7.15-63.80)	98.4	<0.001	-	NR	NR	NR		
Guilan	1(1)	1	30.60(21.48-39.72)	-	-	-	NR	NR	NR		
Kermanshah	1(2)	1	31.00(28.79-33.21)	-	-	1	21.00(19.05-22.95)	-	-		
South Khorasan	1(1)	1	17.10 (14.99-19.21)	-	-	-	NR	NR	NR		
Fars	1(1)	1	20.50(19.88-21.12)	-	-	-	NR	NR	NR		
Urmia	1(1)	1	16.00(14.19-17.81)	-	-	-	NR	NR	NR		
Zahedan	1(1)	1	16.30(12.25-20.35)	-	-	-	NR	NR	NR		
Mazandaran	1(1)	-	NR	NR	NR	1	19.20(14.32-24.08)	-	-		
Iran	1(1)	-	NR	NR	NR	1	11.80(7.63-15.97)	-	-		
Total	28(37)	17	18.71(15.09-22.34)	99.1	<0.001	15	23.43(20.08-26.78)	97.8	<0.001		

		Time of Mortality						
Area (Province)	Total	Article						
		(Record)	Effect Estimate	l <sup>2</sup>	P			
Khorasan Razavi	6(9)	3	33.97(29.98-37.96)	68.9	0.040			
East Azerbaijan	5(6)	1	34.50(31.61-37.39)	-	-			
Isfahan	3(5)	-	NR	NR	NR			
Ardabil	2(3)	1	37.60(30.02-45.18)	-	-			
Qom	2(3)	-	NR	NR	NR			
Tehran	2(2)	-	NR	NR	NR			
Guilan	1(1)	-	NR	NR	NR			
Kermanshah	1(2)	-	NR	NR	NR			
South Khorasan	1(1)	-	NR	NR	NR			
Fars	1(1)	-	NR	NR	NR			
Urmia	1(1)	-	NR	NR	NR			
Zahedan	1(1)	-	NR	NR	NR			
Mazandaran	1(1)	-	NR	NR	NR			
Iran	1(1)	-	NR	NR	NR			
Total	28(37)	5	34.44(32.02-36.85)	44.6	0.125			

\*NR; Not reported.

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# Limitations of the study

Among the constraints of this study are the type and quality of studies included in our study, the sample size of studies, and the number of studies conducted in each province that can affect this study's results. Another limitation of this review was that many studies had results based on critical variables such as gender, stroke typing, etc. Therefore, the researchers could not perform subgroup analysis and meta-regression based on these variables. These factors can also justify significant heterogeneity between studies. Moreover, it needs to be noted that the more distant cohort studies have higher mortality levels. It is inescapable to recognize the cohort effect and age in future research projects using demographic data and not look at cross-sectional data.

# Study suggestions

Lastly, the quantity of mortality for a time period and type of stroke was not plausible. A few studies reported this rate; however, there is a necessity for more prospective studies in this field in the future. Besides, no study was published in numerous geographic areas, and more studies are necessary, especially in deprived provinces, to have a more accurate approximation in the country.

#### Conclusion

Our study's findings revealed that the short-term mortality rate amongst stroke patients is about one-fifth in the hospital after death designation. This mortality rate increases in 1-month and 1-year periods, which increases by one-third in a 1-year mortality rate. Furthermore, it is essential to adjust programs to reduce mortality in short-term outcomes after stroke by performing specific primary treatments on these patients.

#### **Ethical Considerations**

#### Compliance with ethical guidelines

The research protocol was approved and supported by the Student Research Committee, Tabriz University of Medical Sciences (Code: IR.TBZMED.VCR. REC.1398.355).

#### Funding

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#### **Authors contributions**

Study conception and design: Hossein-Ali Nikbakht, Soheil Hassanipour, and Saber Ghaffari-fam; Acquisition of data: Hassan Soleimanpour, Layla Shojaieand, and Sohrab Heidari; Statistical analysis: Hossein-Ali Nikbakht, Soheil Hassanipour, Sima Afrashteh, and Ehsan Sarbazi; Interpretation of results: Hossein-Ali Nikbakht, Soheil Hassanipour, Layla Shojaie, and Saber Ghaffarifam; Drafting of manuscript, approval of the article's final version, including the authorship list: All authors.

#### Conflict of interest

The authors declared no conflict of interest.

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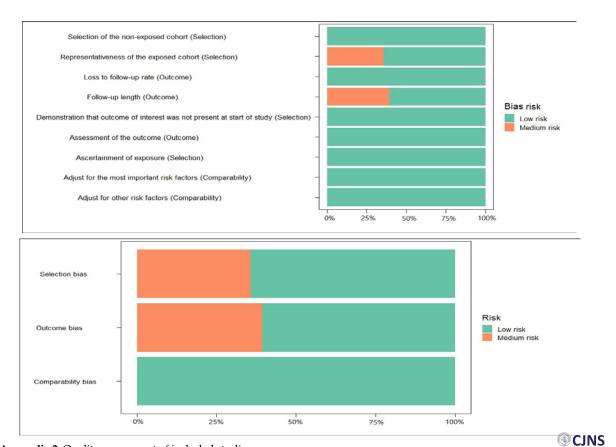
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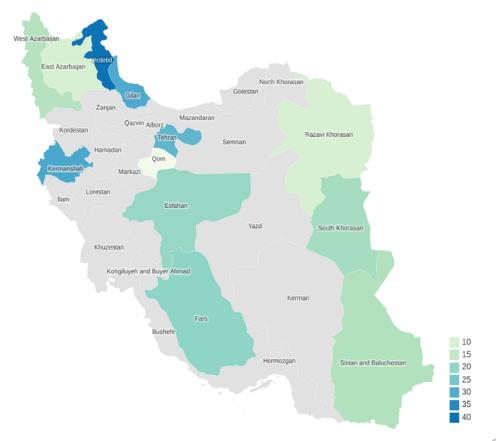
Appendix 1. Table of quality assessment of included studies

Author (y)	Selection	Comparability	Outcome	Total	Quality*
Oveisgharan et al. (2016) [31]	3	2	3	8	Good
Togha et al. (2004) [34]	2	2	2	6	Fair
Tavahen et al. (2013) [32]	2	2	2	6	Fair
Ghandehari et al. (2007) [22]	2	2	2	6	Fair
Zandieh et al. (2013) [46]	3	2	3	8	Good
Delbari et al. (2010) [36]	2	2	3	7	Fair
Delbari et al. (2011) [13]	3	2	3	8	Good
Ahangar et al. (2005) [42]	3	2	3	8	Good
Farzadfard et al. (2017) [23]	3	2	3	8	Good
Amiri et al. (2018) [24]	3	2	3	8	Good
Farhoudi et al. (2017) [28]	3	2	3	8	Good
Sabzghabaei et al. (2019) [35]	2	2	2	6	Fair
Dehghani Firoozabadi et al. (2013) [41]	3	2	2	7	Good
Borhani-Haghighi et al. (2013) [15]	3	2	2	7	Good
Morovatdar et al. (2017) [25]	2	2	3	7	Fair
Deljavan et al. (2018) [29]	3	2	3	8	Good
Shoeibi et al. (2015) [26]	3	2	3	8	Good
Salehi et al. (2018) [27]	3	2	3	8	Good
Oveisgharan et al. (2016) [31]	3	2	3	8	Good
Shamshirgaran et al. (2018) [14]	3	2	3	8	Good
Bakhshayesh et al. (2014) [39]	2	2	2	6	Fair
Talebi et al. (2014) [30]	2	2	2	6	Fair
Amini Sani et al. (2007) [37]	3	2	3	8	Good
Parnia et al. (2006) [38]	2	2	2	6	Fair
Razazian et al. (2003) [40]	3	2	3	8	Good
Mehryar et al. (2019) [43]	2	2	2	6	Fair
Khosravi et al. (2018) [44]	3	2	2	7	Good
Nobakht et al. (2020) [17]	3	2	3	8	Good





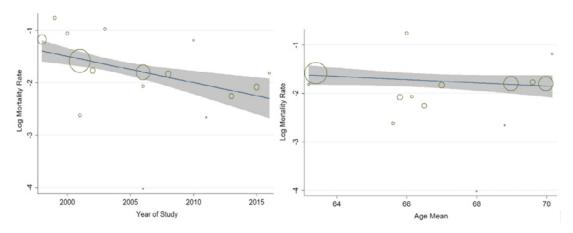
Appendix 2. Quality assessment of included studies



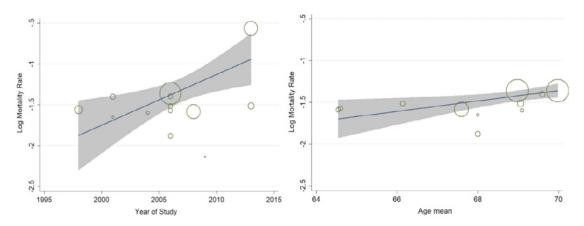
Appendix 3. Figure of hospital mortality rate of stroke in iran provinces



# A: Hospital mortality rate

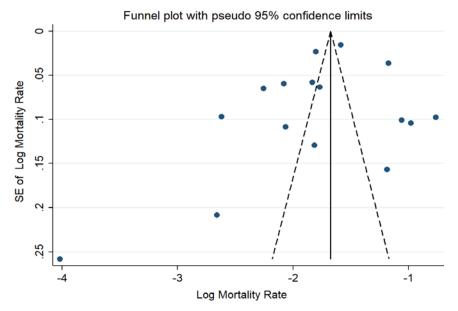


# B: One month mortality rate



Appendix 4. Meta-regression for time mortality rate of stroke based on age (Mean) and year of study





Appendix 5. Funnel plot of standard error by point estimate for the assessment of publication bias

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<sup>\*</sup> Newcastle-ottawa quality assessment form for cohort studies.