REVIEW
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Intervention effect of telemedicine on ischemic stroke: a systematic review and meta-analysis

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Author contributions

Determined the direction of the topic: XO, DL and JY. Literature search: DZ and HC. Evaluation of research quality: DZ and HC. Data curation: DZ, HC, DL and WH. Drafting of the manuscript: DZ and HC.

Competing interests

The authors declare no conflicts of interest.

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Abbreviations

IS, ischemic stroke; RCT, randomized controlled trial; NIHSS, National Institutes of Health Stroke Scale; FMA, Fugl-Meyer motor function assessment; ADL, activity of daily living; RR, relative risk; MD, mean difference; FEM, fixed effect model; CI, confidence interval; REM, random effect model.

Citation

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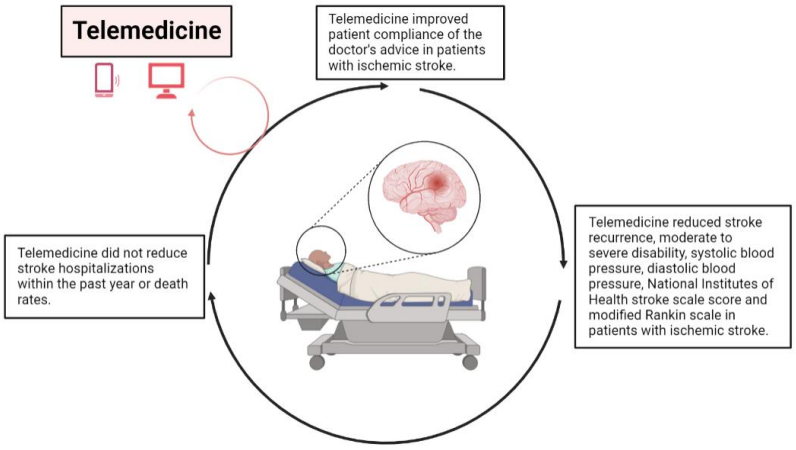
Abstract

Background: Telemedicine refers to the use of information technology by medical institutions to directly provide diagnostic and therapeutic services to patients outside the healthcare facility. It encompasses various aspects such as remote diagnosis, remote monitoring, remote consultation, and remote outpatient services. Numerous articles have evaluated its role in controlling diseases like hypertension, diabetes, atrial fibrillation, and ischemic stroke. However, the existing literature exhibits varying quality and sample sizes, lacking robust convincing power and systematic effectiveness evaluation. **Methods:** Following The Preferred Reporting Items for Systematic reviews and Meta-Analyses 2020 guidelines, we identified articles on remote medical intervention in ischemic stroke through databases including Web of Science, PubMed, EMBASE, Cochrane Library, CNKI, Weipu, and Wanfang. The search spanned from the inception of the databases to June 30, 2022. Two researchers independently assessed literature quality, extracted data, and conducted meta-analysis using RevMan 5.3 software. **Results:** Ten articles, involving 5092 patients, were included. Meta-analysis results indicate that telemedicine can effectively enhance compliance with doctors' advice in ischemic stroke patients. Telemedicine is also associated with reduced stroke recurrence, moderate to severe disability, systolic and diastolic blood pressure, National Institutes of Health Stroke Scale scores, and Modified Rankin Scale scores. Additionally, telemedicine demonstrates effectiveness in improving Fugl-Meyer motor function assessment and the Barthel Index of activity of daily living in ischemic stroke patients. However, telemedicine does not significantly reduce stroke hospitalization in the past year and the death rate. **Conclusion:** In comparison to traditional healthcare, telemedicine exhibits advantages in improving compliance and enhancing functionality in ischemic stroke patients. It is worth promoting telemedicine for better management of ischemic stroke patients. However, this study does not explain how telemedicine improves the functionality of ischemic stroke patients, indicating a need for further research.

Keywords: ischemic stroke; telemedicine; systematic review; meta-analysis



Introduction

Due to the increasing incidence of population aging, stroke is currently the second largest cause of death worldwide [1]. 5.5 million people died of stroke in 2016 alone [2]. Up to 50% of survivors become disabled. Ischemic stroke brings great pain to patients and is a heavy burden to society. The improvement and development of ischemic stroke (IS) treatment has become a global medical problem [3].

Ischemic stroke is a preventable disease, and its risk is closely related to factors such as blood pressure, blood lipid, blood glucose and obese homocysteine level [4]. Early screening and timely intervention can prevent disease occurrence and improve prognosis. Under the background of the national action plan to promote 'Internet +', telemedicine has developed rapidly. Telemedicine refers to the ability of medical institutions to directly provided medical services to patients outside of the medical institution using information technology. This includes remote diagnosis, remote monitoring, remote consultation, remote outpatient services and other aspects [5]. Telemedicine has great advantages in optimizing the allocation of medical resources, promoting the development of primary medical institutions, reducing patient medical costs, and improving patient medical experiences. At present, it has gradually become an important modality for early diagnosis, intervention and real-time monitoring of IS.

Nonetheless, there exists a paucity of clinical investigations focusing on telemedicine interventions for IS, and a consensus regarding its impact on IS remains elusive. In this research, a meta-analysis was employed to assess the utility of telemedicine in overseeing patients with IS and preventing complications associated with IS. Additionally, the study aimed to offer guidance on anticoagulant drug administration, thereby furnishing substantiation for the provision of clinical telemedicine services.

Information and methodology

Research registration

The protocol of this meta-analysis was registered using the PROSPERO with the registration number of CRD42022348357. Used 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, meta-analysis was strictly carried out.

Search methods and strategies

Retrieved database: PubMed, Web of Science, EMBASE, Cochrane library, CNKI, WANFANG, and WEIPU. Key words searched were telemedicine, mobile health, remote monitoring, telemonitoring, + telemedicine, telemedicine monitor, telehealth, remotely medical, telemetric, distance medical, remote consultation, distance counseling, cerebral infarction, ischemic stroke, and randomized controlled trial (RCT). Time of retrieval included from establishment of the database to June 30, 2022. The retrieval formula for the Web of Science database is as follows:

#1 Telemedicine or mobile health or remote monitoring or telemonitoring or telemedicine or telemedicine monitor or telehealth or remotely medical or telemetric or distance medical or remote consultation or distance counseling
#2 Cerebral infarction or ischemic stroke
#3 Randomized controlled trial
#4 #3 AND #2
#5 #4 AND #1

Inclusion criteria

1) Only RCTs with full-text remote medical intervention for ischemic stroke were included. Articles included are not restricted to languages and countries. 2) Individuals presenting with general clinical manifestations indicative of ischemic stroke and other medical conditions were excluded [6]. The delineation of specific stages of ischemic stroke was not restricted. 3) The treatment group intervention occurred by telemedicine that was not limited to the telephone, network, or small procedures. The control group intervention was via routine medical processes. 4) Outcome indicators included: mainly extracted medical advice compliance, stroke recurrence, stroke hospitalization in the past year, moderate to severe disability, death, systolic blood pressure changes, diastolic blood pressure changes, National Institutes of Health Stroke Scale (NIHSS) score changes, Fugl-Meyer motor function assessment (FMA) changes, the Barthel index of activity of daily living (ADL) changes, and Modified Rankin Scale changes. The amount of change is calculated by referring to previous article [7].

Exclusion criteria

Exclusion criteria included: 1) the article includes interventions that are not telemedicine; 2) the article contains repeated data; and 3) the article without outcome indicators.

Literature screening and data extraction

Two researchers independently screened articles and extracted data according to the inclusion and exclusion criteria. Dissenting articles were discussed with a third researcher. The articles retrieved from each database were input into CNKI-Estudy software for picking and repeating. According to the principle of PICOS, articles were screened and included in the study. Data extracted included: 1) basic information of the article, such as publication time, country, and first author; 2) baseline data of patients in different groups, including the number of cases, age, and gender; 3) intervention methods in different group, and follow-up time; and 4) observed indicators.

Quality evaluation of literature

The quality evaluation and data extraction were carried out by two staff. In instances of disparities, deliberation took place with a third researcher. The assessment of RCT quality was conducted referencing the Cochrane risk bias assessment tool, encompassing seven evaluation criteria.

Statistical analysis

Data analysis was performed using RevMan 5.3. Odds ratio and relative risk (RR) were used for the binary variables. The standard deviation mean differences (MD) was used as the effect indicator for the continuous variable. The heterogeneity between studies was statistically analyzed by t^2 and Chi^2 tests. An I^2 value of $\leq$ 50% and a P value $>$ 0.05 signified minimal heterogeneity, prompting the utilization of the fixed-effect model for analysis. Conversely, the random-effect model was applied. Subgroup analysis and sensitivity analysis were undertaken in the presence of an ample number of studies. In cases where studies were scarce and exhibited high heterogeneity, a descriptive analysis was conducted. Begger or Egger's test were used to assess and evaluate publication bias. If the number of articles was $<$ 10, a descriptive analysis was performed.

Results

Retrieval process and characteristics of included studies

A total of 532 articles were searched from seven databases, including 133 articles from the PubMed database, 102 articles from the Web of Science database, 115 articles from the EMBASE database, 171 articles from the Cochrane library database, zero articles from the CNKI database, 11 articles from the WANFANG database, and zero articles from the WEIPU database. Using CNKI-Estudy software, results showed that 114 articles were repeated. After reading the remaining 418 articles, 388 unrelated articles were excluded. After reading the abstract of each remaining article, nine additional unrelated articles were excluded. After reading the full text, four articles in which the full text was unavailable and seven articles without relevant outcome indicators were excluded. Ten articles were finally included [8–17], and the retrieval process was shown in Figure 1. Among the 10 articles included, six studies were from China [9, 10, 12–14, 17], one was from the United States [16]. The earliest research was published in

2008, and the latest research was published in 2021 [16, 17]. A total of 5,092 patients were included, as shown in Table 1.

Quality evaluation of included articles

This study included ten articles [8–17]. One article did not describe the random method used [8], but the other nine articles did [9–17]. Only two articles referred to allocation concealment methods and blinding methods [11, 17]. One article had incomplete data. There were no selective reports in ten articles [8–17]. It was unclear within the ten articles whether there were additional risks [8–17], as shown in Figure 2.

Meta-analysis results

Main outcomes. Two articles mentioned patient compliance to the doctor's advice [12, 14]. There was no heterogeneity between the two articles (P = 0.87, I^2 = 0%), so the fixed effect model (FEM) was used for meta-analysis. The results showed that telemedicine significantly improved patient compliance to the doctor's advice (RR = 1.34, 95% confidence interval (CI) (1.23, 1.47)). Three articles reported stroke recurrence [12, 15, 17]. There was no heterogeneity among these articles (P = 0.14, I^2 = 49%), so the FEM was used for meta-analysis. The results showed that telemedicine significantly reduced stroke recurrence in patients (RR = 0.42, 95% CI (0.29, 0.61)). Three articles reported stroke hospitalization in the past year [11, 16, 17]. There was heterogeneity among these articles (P = 0.06, I^2 = 64%), so the random effect model (REM) was used for meta-analysis. The results showed that telemedicine did not significantly reduce the stroke in the past year (RR = 0.7, 95% CI (0.43, 1.14)). Two articles reported moderate to severe disability [8, 17]. There was no heterogeneity among these articles (P = 0.77, I^2 = 0%), so the FEM was used. Meta-analysis showed that telemedicine significantly reduced the moderate to severe disability of patients (RR = 0.71, 95% CI (0.62, 0.8)). Four articles reported the death rate [8, 13, 16, 17]. There was no heterogeneity among these articles (P = 0.17, I^2 = 41%), so the FEM was used. Meta-analysis showed that telemedicine did not significantly reduce the death rate of patients (RR = 0.9, 95% CI (0.79, 1.03)), as shown in Table 2.

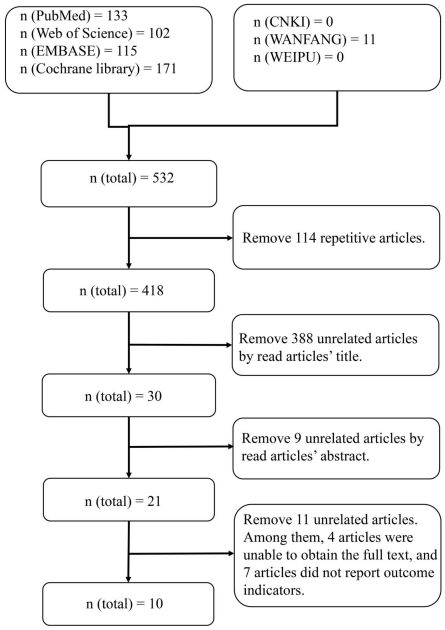


Figure 1 Flow chart of document retrieval

Table 1 Basic characteristics of included articles

Reference	Country	Experimental group	Age	Sample size	Control group	Age	Sample size
Audebert 2008 [8]	Germany	Remote medical consultation	/	1883	Routine care	/	1085
Li 2011 [9]	China	Remote rehabilitation guidance	65.69 ± 11.32	51	Conventional drugs	65.51 ± 13.02	50
Zheng 2014 [10]	China	Remote rehabilitation guidance	68.51 ± 8.31	41	Routine rehabilitation	70.07 ± 7.85	39
Hanley 2015 [11]	United Kingdom	Remote monitoring care	69.90 ± 12.60	40	Routine care	73.50 ± 11.70	15
Rao 2019 [12]	China	WeChat platform remote guidance	57.40 ± 9.60	100	Routine medical procedures	58.20 ± 9.40	100
Gou 2020 [13]	China	Remote medical consultation	62.00 ± 13.00	32	Routine medical procedures	64.00 ± 12.00	28
Liu 2020 [14]	China	WeChat platform remote guidance	66.00 ± 3.62	100	Routine medical procedures	65.00 ± 4.36	100
Kim 2020 [15]	South Korea	Remote monitoring care	60.00 ± 12.00	30	Routine care	56.00 ± 10.00	30
Sobhani 2021 [16]	United States of America	Post with teleStroke Rounds	73.10 ± 13.80	55	Post without telestroke round	79.20 ± 11.60	87
Yan 2021 [17]	China	Mobile phone program	66.20 ± 8.20	611	Routine care	65.20 ± 8.20	615

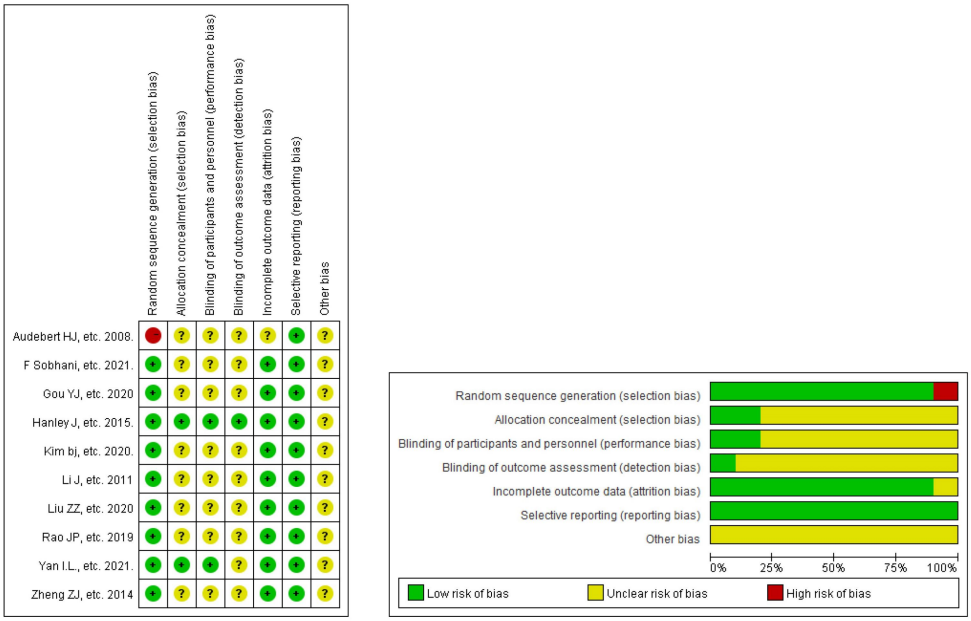


Figure 2 Quality evaluation of literature. (A) Risk of bias graph of included articles. (B) Risk of bias summary of included articles.

Table 2 Summary of meta-analysis results

Outcome indicators	Articles included	Heterogeneity test		Effects model	Meta-analysis results	
		P	I^2		Effective dose (95% CI)	*P* value
Main outcomes						
Patient compliance to the doctor's advice	2 [12, 14]	0.51	0%	FEM	RR = 1.34, (1.23, 1.47)	< 0.00001
Stroke recurrence	3 [12, 15, 17]	0.14	49%	FEM	RR = 0.42, (0.29, 0.61)	< 0.00001
Stroke hospitalization in the past year	3 [11, 16, 17]	0.06	64%	REM	RR = 0.70, (0.43, 1.14)	0.15
Moderate to severe disability	2 [8, 17]	0.77	0%	FEM	RR = 0.71, (0.62, 0.80)	< 0.00001
Death rate	4 [8, 13, 16, 17]	0.17	41%	FEM	RR = 0.90, (0.79, 1.03)	0.13
Blood pressure						
Systolic blood pressure	2 [11, 17]	0.38	0%	FEM	MD = –3.04, (–5.06, –1.02)	0.003
Diastolic blood pressure	2 [11, 17]	0.55	0%	FEM	MD = –1.96, (–2.89, –1.03)	< 0.0001
Additional outcomes						
National Institutes of Health Stroke Scale	2 [12, 14]	0.41	0%	FEM	MD = –1.92, (–2.37, –1.47)	< 0.00001
Fugl-Meyer motor function assessment	4 [9, 10, 12, 14]	< 0.00001	96%	REM	MD = 10.25, (2.03, 18.48)	0.01
The Barthel index of ADL	4 [9, 10, 12, 14]	< 0.00001	98%	REM	MD = 13.62, (2.63, 24.61)	0.02
Modified Rankin Scale	2 [12, 14]	0.15	53%	REM	MD = –1.03, (–1.30, –0.76)	< 0.00001

CI, confidence interval; RR, relative risk; MD, mean difference; FEM, fixed effect model; REM, random effect model; ADL, activity of daily living.

Blood pressure. Two articles reported blood pressure [11, 17], including diastolic blood pressure and systolic blood pressure. The heterogeneity test showed that there was no heterogeneity between the two articles, so the FEM was used. Meta-analysis results showed that telemedicine significantly reduced systolic blood pressure (MD = –3.04, 95% CI (–5.06, –1.02)) and diastolic blood pressure (MD = –1.96, 95% CI (–2.89, –1.03)), as shown in Table 2.

Additional outcomes. Two articles reported the NIHSS score [12, 14]. There was no heterogeneity between the two articles (P = 0.41, showed that telemedicine significantly increased the Barthel index of ADL in patients (MD = 13.62, 95% CI (2.63, 24.61)). Two articles reported results of the Modified Rankin Scale [12, 14]. There was heterogeneity between the two articles (P = 0.15, I^2 = 53%), so the REM was used. Meta-analysis results showed that telemedicine may significantly reduce the Modified Rankin Scale of patients (MD = I^2 = 0%), so the FEM was used. Meta-analysis showed that telemedicine significantly reduced the NIHSS score of patients (MD = –1.92, 95% CI (–2.37, –1.47)). Four articles reported the FMA score [9, 10, 12, 14]. The four articles had heterogeneity (P < 0.00001, I^2 = 96%), so the REM was used. Meta-analysis showed that telemedicine significantly increased the FMA score of patients (MD = 10.25, 95% CI (2.03, 18.48)). Four articles reported the Barthel index of ADL [9, 10, 12, 14]. There was heterogeneity among the four articles (P < 0.00001, I^2 = 98%), so the REM was used. Meta-analysis –1.03, 95% CI (–1.3, –0.76)), as shown in Table 2.

Subgroup analysis

We conducted a subgroup analysis to explore the causes of the heterogeneity of Fugl-Meyer motor function assessment and the Barthel index of ADL. The results of subgroup analysis showed that

heterogeneity was not related to region, sample size, intervention measures, published year, as shown in Table 3.

Publication bias

Due to the small number of included articles, funnel plots could not be used to assess publication bias. However, within the included articles, the effects of the different indicators were heterogeneous, suggesting that there may be publication bias.

Discussion

This study found that telemedicine can effectively improve patient compliance to the doctor's advice for patients with IS. This result is consistent with the research results of Shang et al. [18]. Ischemic stroke is an acute cerebrovascular disease with high incidence, high recurrence rate, high disability rate, and high mortality [1]. Control of risk factors is an important measure to prevent recurrence of ischemic stroke. Active lifestyle intervention, active drug control, and active rehabilitation therapy play an important role in reducing the risk of IS [19]. However, the implementation of these methods often requires long-term adherence by patients, so good patient compliance to the doctor's advice can ensure secondary prevention. Some IS patients have an insufficient understanding of the importance of risk control, lack relevant knowledge, and exhibit poor active coordination. Zhou et al. showed that the compliance rates of antihypertensive drugs, hypoglycemic drugs, and lipid-lowering drugs were 66.5%, 77.1%, and 39.3%, respectively, in patients with IS after 12 months of discharge [20]. Telemedicine refers to the medical service directly provided by medical institutions to patients outside of the medical institution by using information technology. Telemedicine includes remote diagnosis, remote monitoring, remote consultation, remote outpatient, and other remote aspects. Doctors can inform patients about the risk of disease through the internet, telephone, or software messages, and strengthen patients' understanding of IS. It can also remind patients to take medicines on time and remind patients of the correct dosages of medicines to ensure that the patient's condition is controlled. Thus, telemedicine is worth popularizing.

This study found that telemedicine can effectively reduce stroke recurrence, moderate to severe disability, systolic blood pressure, diastolic blood pressure, National Institutes of Health Stroke Scale scores, and Modified Rankin Scale scores in patients with IS. Telemedicine can effectively increase Fugl-Meyer motor function assessment and the Barthel index of ADL in patients with IS. These results have proved the important role of telemedicine in the control of IS. Patients with IS generally require long-term medication for stroke prevention. Previous studies have demonstrated that patient self-compliance is not high when there is a lack of clarity in disease awareness [20]. Remote telemedicine, however, can provide alerts and reminders for these patients, encouraging better adherence to medical advice. This aspect of work is akin to extending clinical care into the homes of IS patients [21]. Sun et al. believe that the function of telemedicine system should be further improved, and the construction of the telemedicine team should be accelerated to promote its sustainable and healthy development [5]. This is consistent with Fang et al. [22]. However, telemedicine did not reduce stroke hospitalization in the past year or death rates in patients with IS. With the continuous development of technology, the interventions in telemedicine are becoming increasingly diverse, especially with the development and application of intelligent programs through mobile applications. This further promotes the advancement of telemedicine. Typically, applications possess messaging capabilities and offer a wider range of applications and services compared to general information push/online communication. Moreover, over 50% of hypertensive patients are willing to accept such services through applications [23]. It can be widely utilized among IS patients.

Limitations

This study has certain limitations. This study identified some therapeutic effects of remote healthcare for IS patients, but the mechanisms underlying these effects were not thoroughly investigated. This lack of clarity may be associated with the relatively poor quality of studies included in this research. To address this issue, future relevant clinical studies are hoped to uncover more detailed data. The methodological quality of the articles included in this paper is generally poor. Only two articles referred to allocation concealment methods and blinding methods [11, 17]. One article had incomplete data. The present study included a small number of studies, one of which did not involve randomization [8]. There are some mixed factors, such as specific telemedicine methods, intervention courses, and regions. The sample size was small, including only 5,092 patients. Finally, the results of some meta-analyses were heterogeneous. The sources of heterogeneity were not identified through subgroup analysis or sensitivity analysis.

Table 3 Subgroup analysis results

Subgroup	Articles included	Fugl-Meyer motor function assessment				The Barthel index of ADL			
		I^2	*P* value	MD (95% CI)	*P* value	I^2	*P* value	MD (95% CI)	*P* value
Region									
Northern China	1 [9]	NA	NA	8.10 (3.10, 12.92)	0.001	NA	NA	6.21 (3.37, 9.05)	< 0.00001
Southern China	3 [10, 12, 14]	97%	< 0.00001	11.0 (0.38, 21.61)	0.04	99%	< 0.00001	16.20 (–1.39, 33.79)	0.07
Sample size									
< 100	2 [9, 10]	83%	0.02	2.48 (0.54, 4.43)	0.01	82%	0.02	4.00 (–0.07, 8.07)	0.05
≥ 100	2 [12, 14]	0%	0.51	15.51 (13.00, 18.02)	< 0.00001	93%	0.0002	23.43 (11.28, 35.58)	0.0002
Intervention measures									
Internet guidance	2 [9, 10]	83%	0.02	2.48 (0.54, 4.43)	0.01	82%	0.02	4.00 (–0.07, 8.07)	0.05
WeChat software guidance	2 [12, 14]	0%	0.51	15.51 (13.00, 18.02)	< 0.00001	93%	0.0002	23.43 (11.28, 35.58)	0.0002
Published year									
Before 2019	2 [9, 10]	83%	0.02	2.48 (0.54, 4.43)	0.01	82%	0.02	4.00 (–0.07, 8.07)	0.05
After 2019	2 [12, 14]	0%	0.51	15.51 (13.00, 18.02)	< 0.00001	93%	0.0002	23.43 (11.28, 35.58)	0.0002

ADL, activity of daily living; CI, confidence interval; MD, mean difference.

Conclusion

In summary, the effect of telemedicine on the prevention and treatment of IS needs a large number of rigorous randomized double-blind trials to continue to verify its usefulness. However, this study comprehensively collected all studies that met the standard of telemedicine intervention for IS and objectively and systematically evaluated the effect of telemedicine intervention for IS. Therefore, the results of this study may provide clinical guidance.

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