

# 實證醫學EBM應用競賽



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# 臨床情境

- 70歲陳伯伯是一位退休的公務人員，四個多月前左側中大腦動脈梗塞中風後併發右半邊偏癱、動作平衡明顯困難、失語症、中風後憂鬱症候群。最近三個月來不僅許多日常生活和行走活動能力仍需要家人協助，也因為憂鬱症的關係無法完成自行照顧。
- 聽說一種自費新穎的腦刺激療法「重複性跨顱磁刺激(repetitive transcranial magnetic stimulation, rTMS)」。

# 臨床問題

- 重複性跨顱磁刺激是否能改善梗塞型中風後之神經功能？
- 重複性跨顱磁刺激是否能改善梗塞型中風後之憂鬱程度？

# 背景知識-中風後合併症

UpToDate®

## Complications of stroke: An overview

Author: [Koto Ishida, MD](#)

Section Editor: [Scott E Kasner, MD](#)

Deputy Editor: [John F Dashe, MD, PhD](#)

[Contributor Disclosures](#)

All topics are updated as new evidence becomes available and our [peer review process](#) is complete.

Literature review current through: **Nov 2021**. | This topic last updated: **Nov 11, 2020**.

- ① 吞嚥困難、靜脈血栓、感染(肺炎、泌尿道感染)、心臟併發症(心肌梗塞、心律不整、心肌損傷)
- ② 與睡眠有關之呼吸障礙
- ③ 腸胃道出血、尿失禁、跌倒與骨折
- ④ 神經功能退化、癲癇發作
- ⑤ 疲勞、中風後憂鬱

Ask

問問題

**Depression** — Poststroke depression is common, although difficult to quantify precisely due to methodologic differences among studies. A 2013 meta-analysis, with pooled data from 43 studies and over 20,000 patients, found that the prevalence of depression observed at any time after stroke was 29 percent (95% CI 25-32 percent) [87]. There was no significant difference in prevalence rates of depression at different time points after stroke. In pooled data from 10 studies with over 16,000 patients, predictors of poststroke depression were disability, prestroke depression, cognitive impairment, stroke severity, and anxiety.

In a later case-control study that compared over 135,000 patients with stroke and no diagnosis of depression at baseline with 145,000 matched controls, the incidence of depression during the first two years after hospitalization was significantly higher for the group with stroke (25 versus 8 percent) [88].

Depression after stroke is correlated with poorer functional outcomes [89], although causation cannot be inferred from this. Nonetheless, when patients are matched for initial functional outcome, remission of depression is associated with a better functional outcome at three and six months than continued depression [90]. There appears to be a relationship between depression and 12- and 24-month mortality, but confounders likely exist [91].

Ask

問問題

# 背景知識-中風後憂鬱

UpToDate®

- ① 中風後憂鬱症之比例為29%(2013年超過20000名受試者之研究)
- ② 危險因子：身體活動功能障礙、中風嚴重度、中風前憂鬱程度、認知功能障礙、家庭與社會支持度
- ③ 預防：目前尚不清楚(2020年系統性文獻回顧49篇試驗，包含3342名受試者，非常低的證據可確定藥物或心理治療可降低中風後憂鬱的比率)
- ④ 評估：Montgomery-Asberg憂鬱評分量表(sensitivity-86%、specificity-78%)或其他憂鬱量表
- ⑤ 治療：目前尚無法確定藥物、心理治療或合併療法是否有效

# 根據臨床問題形成第一個 PICO

	英文關鍵字/Mesh	同義字	中文關鍵字
P	<p>Stroke [Mesh term]</p> <p>Poststroke [Mesh term]</p>	<p>Poststroke depression*</p> <p>PDS</p> <p>ischemic stroke</p> <p>cerebral bleed</p> <p>brain bleed</p> <p>intracerebral bleed</p> <p>intracranial bleed</p> <p>cerebral haemorrhage</p> <p>brain haemorrhage</p> <p>intracerebral haemorrhage</p> <p>Cerebral Infarction</p> <p>Intracranial Embolism</p> <p>Cerebrovascular Stroke</p> <p>Cerebral Stroke</p> <p>Intracranial Vascular Disease</p> <p>Brain Vascular Disorder</p>	<p>梗塞型中風</p> <p>缺血性中風</p> <p>中風後憂鬱 症候群</p>

**Ask**  
問問題

# 根據臨床問題形成第一個 PICO

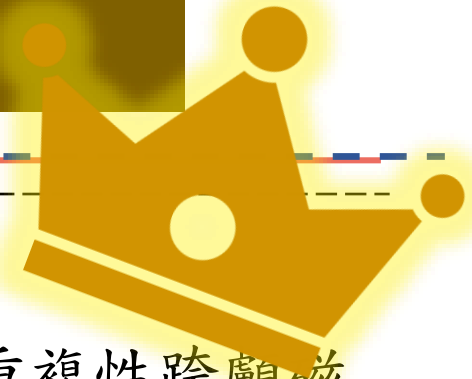
I	Repetitive transcranial magnetic stimulation [Mesh term]	transcranial magnetic stimulation, repetitive transcranial magnetic stimulation, paired pulse rTMS TMS r-TMS	重複性跨顱磁刺激
C	placebo	-	安慰劑
O	Neurologic Function [Mesh term]	functional neurological symptom disorder functional movement disorder	神經功能

Ask  
問問題

- 治療/預防型問題
  診斷型問題
  預後型問題
  傷害/病因型問題



# 根據臨床問題形成第二個 PICO



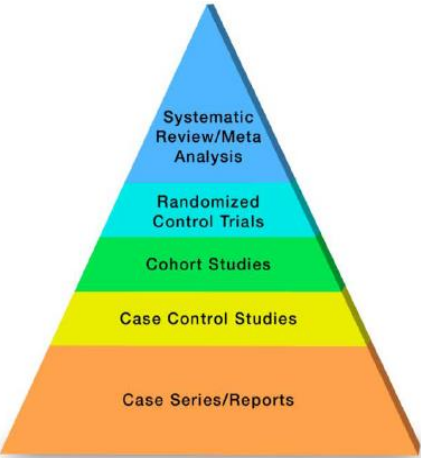
I	Repetitive transcranial magnetic stimulation [Mesh term]	transcranial magnetic stimulation, repetitive transcranial magnetic stimulation, paired pulse rTMS TMS r-TMS	重複性跨顱磁刺激
C	placebo	-	安慰劑
O	Depression [Mesh term]	Mood disorder Mental disease Affective disorder	憂鬱程度 Ask 問問題

- 治療/預防型問題
- 診斷型問題
- 預後型問題
- 傷害/病因型問題

### The New Evidence Pyramid

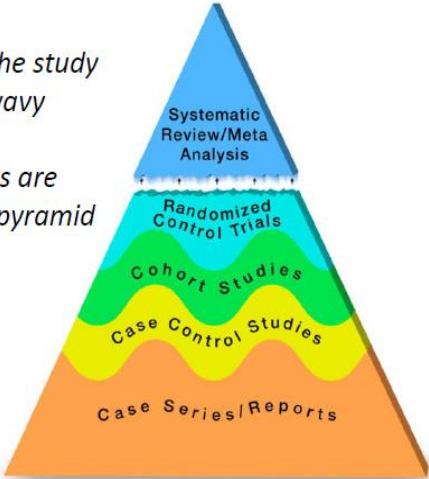
*(The Evidence Trapezoid)*

#### The traditional pyramid

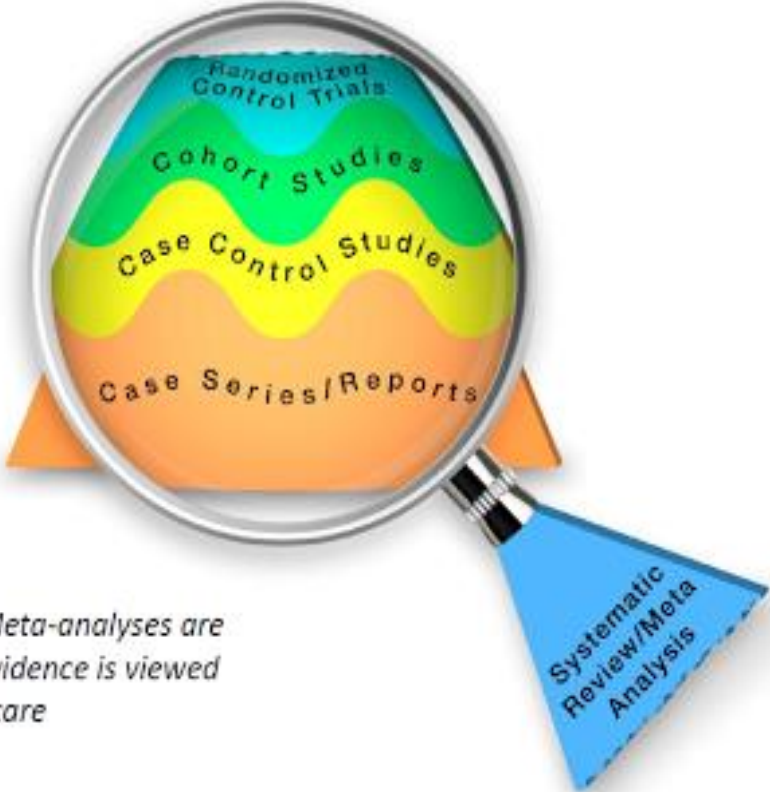


#### Revising the pyramid

- (1) Lines separating the study designs become wavy (GRADE)
- (2) Systematic reviews are 'chopped off' the pyramid



### The revised pyramid



*Systematic reviews & Meta-analyses are a lens through which evidence is viewed and applied to patient care*

# 檢索策略 - 搜尋Cochrane Library - 提升檢索效率



## Advanced Search

Search

Search manager

Medical terms (MeSH)

PICO search

Save search

View saved searches

Search help

Title Abstract Keyword

AND Title Abstract

AND Title Abstract

"Stroke" or "ischemic stroke" or "cerebral bleed" or "brain bleed" "intracerebral bleed" or "intracranial bleed" or "cerebral haemorrhage" or "brain haemorrhage" or "intracerebral haemorrhage" or "Cerebral Infarction" or "Intracranial Embolism" or "Cerebrovascular Stroke" or "Cerebral Stroke" or "Intracranial Vascular Disease" or "Brain Vascular Disorder"

AND

"Repetitive transcranial magnetic stimulation" or "transcranial magnetic stimulation, repetitive" or "transcranial magnetic stimulation, paired pulse" or "rTMS" or "TMS" or "r-TMS"

AND

"Depression" or "Mood disorder" or "Mental disease" or "Affective disorder"

關鍵字

技巧

■ 使用Advanced Search、Search manager、布林邏輯、無限制年份

Acquire  
找資料

# 檢索策略 - 搜尋Cochrane Library - 提升檢索效率



Cochrane Reviews  
1

Cochrane Protocols  
0

Trials  
97

Editorials  
0

Special Collections  
0

Clinical Answers  
0

More  
▼

1 Cochrane Review matching "**Stroke**" or "**ischemic stroke**" or "**cerebral bleed**" or "**brain bleed**" or "**intracerebral bleed**" or "**intracranial bleed**" or "**cerebral haemorrhage**" or "**brain haemorrhage**" or "**intracerebral haemorrhage**" or "**Cerebral Infarction**" or "**Intracranial Embolism**" or "**Cerebrovascular Stroke**" or "**Cerebral Stroke**" or "**Intracranial Vascular Disease**" or "**Brain Vascular Disorder**" in Title Abstract Keyword AND "**Repetitive transcranial magnetic stimulation**" or "**transcranial magnetic stimulation, repetitive**" or "**transcranial magnetic stimulation, paired pulse**" or "**rTMS**" or "**TMS**" or "**r-TMS**" in Title Abstract Keyword AND "**Depression**" or "**Mood disorder**" or "**Mental disease**" or "**Affective disorder**" in Title Abstract Keyword - (Word variations have been searched)

Cochrane Database of Systematic Reviews  
Issue 12 of 12, December 2021

[Select all \(1\)](#)    [Export selected citation\(s\)](#)    [Show all previews](#)

Order by

Results per page

1  **Repetitive transcranial magnetic stimulation for improving function after stroke**

Zilong Hao, Deren Wang, Yan Zeng, Ming Liu

[Intervention](#) [Review](#) [31 May 2013](#) [Free access](#)

[Show PICOs](#) [Show preview](#)

# 檢索策略 - 搜尋EMBASE-提升檢索效率

Embase®

Quick **PICO** PV Wizard Medical device Advanced Drug Disease Device Citation information

Find best term

Emtree

- anatomical concepts
- biological functions
- biomedical disciplines, sci
- chemical, physical and ma
- groups by age and sex
- health care c

**關鍵字**

"Stroke" or "ischemic stroke" or "cerebral bleed" or "brain bleed" "intracerebral bleed" or "intracranial bleed" or "cerebral haemorrhage" or "brain haemorrhage" or "intracerebral haemorrhage" or "Cerebral Infarction" or "Intracranial Embolism" or "Cerebrovascular Stroke" or "Cerebral Stroke" or "Intracranial Vascular Disease" or "Brain Vascular Disorder"

AND

"Repetitive transcranial magnetic stimulation" or "transcranial magnetic stimulation, repetitive" or "transcranial magnetic stimulation, paired pulse" or "rTMS" or "TMS" or "r-TMS"

AND

"Depression" or "Mood disorder" or "Mental disease" or "Affective disorder"

- PICO search
- 使用 Emtree，增加精確性
- 使用內建 synonyms 系統，增加搜尋廣度

**技巧**

Acquire  
找資料

# 檢索策略 - 搜尋EMBASE-提升檢索效率

Embase®

"Stroke" or "ischemic stroke" or "cerebral bleed" or "brain bleed" intracerebral bleed" or "intracranial bleed" or "cerebral haemorrhage" or "brain haemorrhage" or "intracerebral haemorrhage" or "Cerebral Infarction" or "Intracranial Embolism" or "Cerebrovascular Stroke" or "Cerebral Stroke" or "Intracranial Vascular Disease" or "Brain Vascular Disorder" AND "Repetitive transcranial magnetic stimulation" or "transcranial magnetic stimulation, repetitive" AND "transcranial magnetic stimulation, paired pulse" or "rTMS" or "TMS" or "r-TMS" AND "Depression" or "Mood disorder" or "Mental disease" or "Affective disorder"

Search > Mapping Date Sources Fields Quick limits EBM Pub. types Languages Gender Age Animal

## Quick limits

- Humans
- Animals
- Clinical studies

## Age

- Adolescent (13-17 years)
- Adult (18-64 years)
- Young adult (18-24 years)

"Stroke" or "ischemic stroke" or "cerebral bleed" or "brain bleed" "intracerebral bleed" or "intracranial bleed" or "cerebral haemorrhage" or "brain haemorrhage" or "intracerebral haemorrhage" or "Cerebral Infarction" or "Intracranial Embolism" or "Cerebrovascular Stroke" or "Cerebral Stroke" or "Intracranial Vascular Disease" or "Brain Vascular Disorder"

AND

"Repetitive transcranial magnetic stimulation" or "transcranial magnetic stimulation, repetitive" or "transcranial magnetic stimulation, paired pulse" or "rTMS" or "TMS" or "r-TMS"

AND

"Depression" or "Mood disorder" or "Mental disease" or "Affective disorder"

關鍵字

- Very elderly (80+ years)

## Gender



技巧

■ Similar records

■ 使用 Limit: Human

■ Filter : sources, studytype Systematic review → randomized controlled trial → controlled trial → cohort

# 檢索策略 - 搜尋PubMed-提升檢索效率



## TEXT AVAILABILITY

- Abstract
- Free full text
- Full text

## ARTICLE ATTRIBUTE

- Associated data

## ARTICLE TYPE

- Books and Documents
- Clinical Trial
- Meta-Analysis
- Randomized Controlled Trial
- Review
- Systematic Review

## PUBLICATION DATE

- 1 year
- 5 years
- 10 years
- Custom Range

Search	Actions	Details	Query	Results	Time
#4	...	>	Search: (("Stroke" or "ischemic stroke" or "cerebral bleed" or "brain bleed" "intracerebral bleed" or "intracranial bleed" or "cerebral haemorrhage" or "brain haemorrhage" or "intracerebral haemorrhage" or "Cerebral Infarction" or "Intracranial Embolism" or "Cerebrovascular Stroke" or "Cerebral Stroke" or "Intracranial Vascular Disease" or "Brain Vascular Disorder" AND (y_5[Filter])) AND ("Repetitive transcranial magnetic stimulation" or "transcranial magnetic stimulation, repetitive" or "transcranial magnetic stimulation, paired pulse" or "rTMS" or "TMS" or "r-TMS" AND (y_5[Filter]))) AND ("Depression" or "Mood disorder" or "Mental disease" or "Affective disorder" AND (y_5[Filter])) Filters: in the last 5 years	2	21:01:26
#3	...	>	Search: "Depression" or "Mood disorder" or "Mental disease" or "Affective disorder" Filters: in the last 5 years	123,981	21:01:11
#2	...	>	Search: "Repetitive transcranial magnetic stimulation" or "transcranial magnetic stimulation, repetitive" or "transcranial magnetic	6,578	21:01:00

技巧

- Advanced search, Truncation,
- 布林邏輯
- My NCBI: 建置 Clinical Queries
- 自然語言，同步 MeSH 檢索

Acquire  
找資料

# 檢索策略 - 搜尋PubMed-提升檢索效率



## TEXT AVAILABILITY

- Abstract
- Free full text
- Full text



1

Cite

Share

## ARTICLE ATTRIBUTE

- Associated data

## ARTICLE TYPE

- Books and Documents
- Clinical Trial
- Meta-Analysis
- Randomized Controlled Trial
- Review
- Systematic Review

## PUBLICATION DATE

- 1 year
- 5 years
- 10 years
- Custom Range



2

Cite

Share



**Repetitive transcranial magnetic stimulation for depression** after basal ganglia ischaemic **stroke**: protocol for a multicentre randomised double-blind placebo-controlled trial.

Tang Y, Chen A, Zhu S, Yang L, Zhou J, Pan S, Shao M, Zhao L.

BMJ Open. 2018 Feb 3;8(2):e018011. doi: 10.1136/bmjopen-2017-018011.

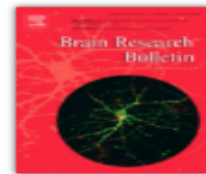
PMID: 29431126



Free PMC article.

Clinical Trial.

INTRODUCTION: Studies suggest that **repetitive transcranial magnetic stimulation (rTMS)** is effective for the treatment of **depression** and promotes the repair of white matter. This study aims to assess the effectiveness of **rTMS** in tre ...



**Different combinations of high-frequency rTMS and cognitive training improve the cognitive function of cerebral ischemic rats.**

Hong J, Chen J, Zeng Y, Zhang X, Xie M, Li C, Wen H.

Brain Res Bull. 2021 Oct;175:16-25. doi: 10.1016/j.brainresbull.2021.07.012. Epub 2021 Jul 16.

PMID: 34280480

Similar articles for PMID: 29431126

34 results

- Similar article 反覆檢索文獻
- 利用“研究設計”增加篩選效率 Systematic review → randomized controlled trial → cohort

Filters applied: Full text in the last 5 years. Clear all



# 檢索策略 - 搜尋華藝線上圖書館 - 提升檢索效率

## 技巧

### ■ 進階檢索、中文關鍵字

| 一般檢索 | 全文檢索 | 出版品檢索 |

重複性跨顱磁刺激



更多選項



查詢歷史



書目匯出



加入收藏



加入購物車

相關程度最高

法醫學雜誌

16卷4期 (2000 / 11 / 01)

P196 - 197

醫藥衛生 > 基礎醫學

社會科學 > 法律學

訂閱目次



1

上肢運動誘發電位研究

朱廣友(Guang-You Zhu) ; 沈彥 ;

法醫學雜誌 16卷4期 (2000/11), 196-197

上肢運動 ; 磁刺激 ; 誘發電位 ; upper limbs ; magnetic stimulation ; motor evoked potentials

預覽摘要



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全文下載



書目匯出



加入收藏



加入購物車

相關程度最高

## 關鍵字

重複性跨顱磁刺激

Acquire  
找資料



搜索  
結果

(98)

(25)

(2)

(1)

符合  
場景

(7)

(6)

(2)

(0)

(5)

(4)

(2)

(0)

Pubmed,  
Embase  
(2)SR

Exclusion criteria-1

- 有全文可供閱讀
- 與PICO相符
- 近五年

Exclusion criteria-2

- 最佳證據等級
- 刪除重複文章

# 比較收納文獻 - 選出最佳文獻，並提出我們的理由

文章	S	P	I	C	O
Efficacy and Safety of High-Frequency Repetitive Transcranial Magnetic Stimulation for Poststroke Depression: a Systematic Review and Meta-analysis(2019)	●	●	●	●	●
Efficacy of repetitive transcranial magnetic stimulation for post-stroke depression: a systematic review and meta-analysis of randomized clinical trials(2021)	●	●	●	●	●

# 比較收納文獻 - 選出最佳文獻，並提出我們的理由



## 文章

S

P

I

C

O

Efficacy and Safety of High-Frequency Repetitive Transcranial Magnetic Stimulation for Poststroke Depression: a Systematic Review and Meta-analysis (2019)



Efficacy of repet...  
for post-stroke...  
meta-analysis of...

■ 文章為SR-META

■ 符合PICO

■ 2019年

■ 最符合臨床情境



# 正確使用文獻評讀指南工具



## CASP Systematic Review Checklist

PDF Form

Print & Fill

Word

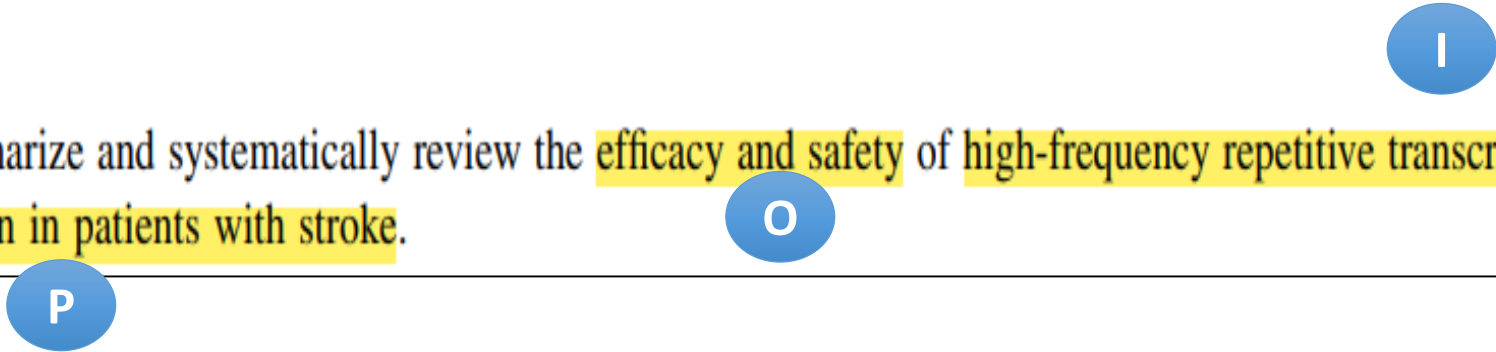
- 國際廣泛運用
- 簡單扼要
- 可適用於多種研究設計

Section A: Are the results of the review **valid**?

1. Did the review address a clearly focused question?  
 此研究是否問了一個清楚明確的問題?

**Abstract**

**Objective:** To summarize and systematically review the efficacy and safety of high-frequency repetitive transcranial magnetic stimulation (HF-rTMS) for depression in patients with stroke.



P	Depression in patients with stroke
I	HF-rTMS(重複性跨顱磁刺激)
C	Sham, blank
O	Efficacy 、 safety

YES    Can't tell    NO

## 2. Did the authors look for the right type of papers? 作者是否收納適當的研究類型？

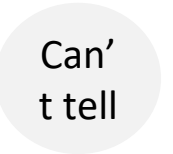
### Inclusion criteria and trial selection

The selected studies met the subsequent inclusion criteria: (1) **randomized controlled trial (RCT) published in a peer-reviewed journal**; (2) all patients underwent head **computed tomography**

or magnetic resonance imaging **and met the criteria for depression caused by stroke according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition**; (3) the **HF-rTMS group received rTMS alone or in combination with conventional treatment (such as vasodilators, nutritional supplements for the nervous system, and antidepressants)**; (4) the primary outcome was evaluated according to specific Hamilton Depression Rating Scale **(HAM-D, 17, 21, or 24 items) scores**; and (5) the stimulus frequencies in the HF-rTMS groups were greater than or equal to 10 Hz. Previous studies have shown the HAM-D scale to have

outcomes may or may not have been included, and we **excluded case reports, abstracts, comments, reviews, animal experiments, and duplicates.**

- 收錄符合治療型問題之RCT文章
- 說明**納入**條件
- 說明**排除**條件

YESCan't  
tellNO

Section A: Are the results of the review **valid**?

3. Do you think all the important, relevant studies were included?  
作者有沒有可能遺漏掉重要、相關的研究？(1/3)

搜尋日期：截至2018年11月15日

大型資料庫				
Pudmed	Cochrane	EMBASE	MEDLINE	
專業領域資料庫			中文資料庫	
PSYCINFO			CNKI	萬芳數據庫
其他				
引用檢索	臨床試驗	學會發表	碩博論文	國際會議摘要
非英美系	手檢資料	未發表文章	聯繫作者	

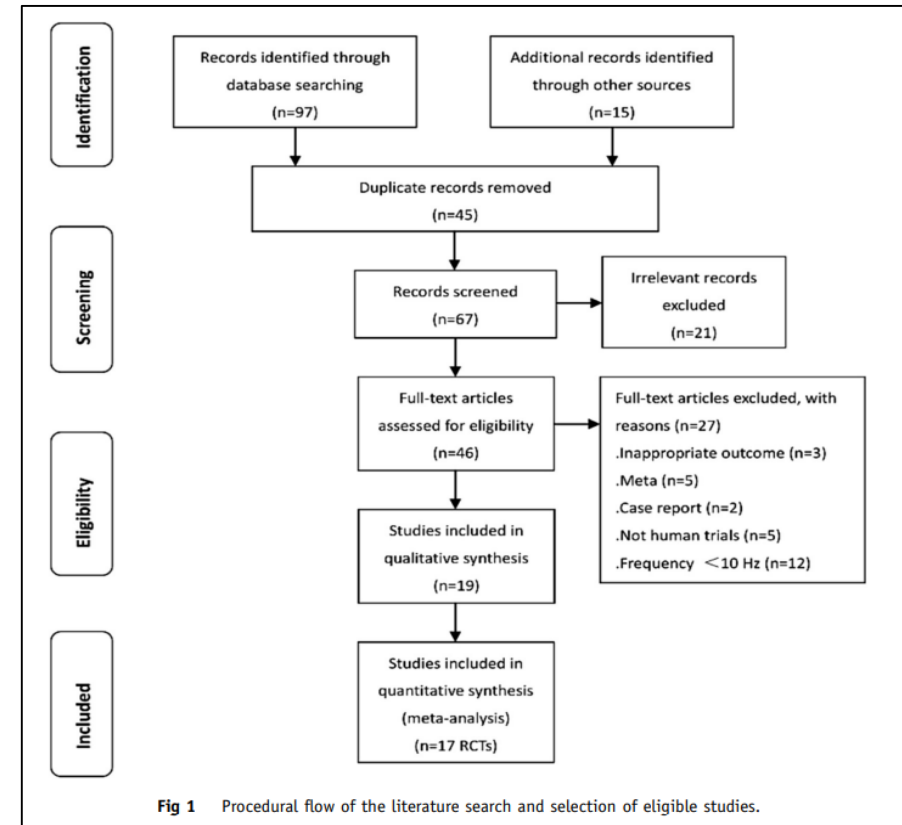


### 3. Do you think all the important, relevant studies were included? 作者有沒有可能遺漏掉重要、相關的研究？(2/3)

#### Search methods

The first 3 authors independently and systemically searched both Chinese (Wanfang and the China National Knowledge Infrastructure) and English (PubMed, Embase, Cochrane Library, and Web of Science) databases for eligible studies. To include as many studies as possible, no publication dates were excluded (from database inception until November 15, 2018). We used the following search terms: (“Stroke” or “Apoplexy” or “Cerebrovascular Disease”) and (“Depression” or “Depressive Symptom”) and (“Repetitive Transcranial Magnetic Stimulation”) and

(“Randomized Controlled Trial” or “Randomized”). We also performed cross-referencing searches manually by examining the bibliographies of potential articles and previously published reviews.



Flow diagram

有提供且清楚具體，前後一致

Section A: Are the results of the review **valid**?

3. Do you think all the important, relevant studies were included?  
 作者有沒有可能遺漏掉重要、相關的研究？(3/3)

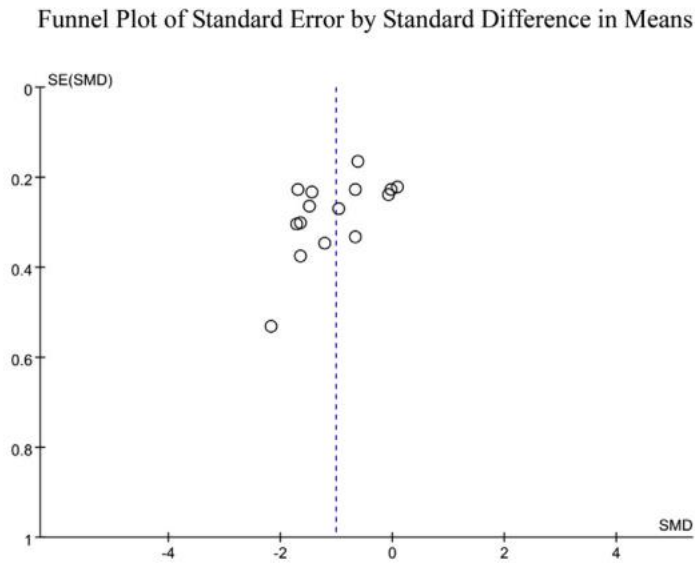


Fig 3 Funnel plot assessment of publication bias in RCTs that assessed use of HF-rTMS for treating depression in individuals with PSD.

<p><b>關鍵字</b></p>	<p>符合PICO且全面，無使用 MeSH term 搜尋              無詳述是否有語言限制</p>
<p><b>出版偏差分析</b></p>	<p><b>有</b>提供漏斗圖              Egger's test : X</p>

YES **Can't tell** NO

漏斗圖大致對稱  
 publication bias可接受

Section A: Are the results of the review **valid**?

# 4. Did the review's authors do enough to assess quality of the included studies?

## 作者是否有評估收納研究的品質？

**Table 2** Summary of methodological quality for all randomized controlled trials according to the modified Physiotherapy Evidence Database scale

Reference	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Sum Score
Chen et al <sup>17</sup>	1	1	0	1	0	1	1	1	1	1	8
Yang et al <sup>18</sup>	1	1	0	1	0	1	0	1	1	1	7
Gu et al <sup>19</sup>	1	1	0	1	1	1	0	1	1	1	8
Zhang et al <sup>20</sup>	1	1	0	1	0	1	0	1	1	1	7
Tang et al <sup>21</sup>	1	1	0	1	0	1	0	1	1	1	7
Li et al <sup>22</sup>	1	1	0	1	0	1	1	1	1	1	8
Wang et al <sup>23</sup>	1	1	0	1	0	1	0	1	1	1	7
Wang et al <sup>24</sup>	1	1	0	1	0	1	0	1	1	1	7
Liu et al <sup>25</sup>	1	1	0	1	0	1	0	1	1	1	7
Yang et al <sup>26</sup>	1	1	0	1	0	1	0	1	1	1	7
Li et al <sup>27</sup>	1	1	0	1	0	1	0	1	1	1	7
Zhang et al <sup>28</sup>	1	1	0	1	0	1	0	1	1	1	7
Yang et al <sup>29</sup>	1	1	0	1	0	1	0	1	1	1	7
Jin et al <sup>30</sup>	1	1	0	1	0	1	0	1	1	1	7
Yan et al <sup>31</sup>	1	1	0	1	1	1	0	1	1	1	8
Jorge et al <sup>32</sup>	1	1	0	1	1	1	0	1	1	1	8
Jorge et al <sup>12</sup>	1	1	0	1	1	1	0	1	1	1	8

NOTE. Item 1, eligibility criteria; item 2, randomization; item 3, concealed allocation; item 4, similar baseline; item 5, blinding of assessors; item 6, more than 85% retention; item 7, missing data management (intention-to-treat analysis); item 8, between-group comparison; item 9, point measure and measures of variability; item 10, cointervention (if cointervention was similar between the HF-rTMS and control groups, 1 point was awarded). A column designation of 1 indicates explicitly described and present in details. A column designation of 0 indicates absent, inadequately described, or unclear.

### Risk of bias for all selected RCTs

We adopted the **modified 10-item Physiotherapy Evidence Database scale** to assess the risk of bias for all selected RCTs in terms of the eligibility criteria, randomization, allocation concealment, similar baseline, blind evaluators, retention rate of more than 85%, management of missing data, between-group comparisons, point measurements and variability measures, and cointervention.<sup>13</sup> As

評估工具	modified Physiotherapy Evidence Database scale 評估項目完整
納入研究品質	7-9分

#### 4. Did the review's authors do enough to assess quality of the included studies?

作者是否有評估收納研究的品質？

...we conducted meta-analysis using Review Manager 5.0, Stata 14.0,<sup>b</sup> and Excel 2007<sup>c</sup> software. The 2 first authors independently identified the RCTs that met the inclusion criteria and the third author (who contributed material and analysis tools) was consulted in cases of disagreement. We calculated the

評讀人員	2位作者獨立評估
仲裁人員	評讀人員意見相左，會找第三位評審員進行討論。

YES

Can't tell

NO

Section A: Are the results of the review **valid**?

5. If the results of the review have been combined, was it reasonable to do so?  
 作者是否有把各個研究的結果合併起來？這樣的合併是合理的嗎？

Study or Subgroup	rTMS			Control			Weight	Std. Mean Difference	
	Mean	SD	Total	Mean	SD	Total		IV, Random, 95% CI	
Chen et al (2018)	-11.31	2.877	19	-6.42	2.995	20	5.9%	-1.63 [-2.37, -0.90]	
Yang et al (2018)	-15.79	5.521	38	-15.71	4.938	38	7.1%	-0.02 [-0.46, 0.43]	
Gu et al (2017)	-2.2	1.212	12	0.3	1.015	12	4.7%	-2.16 [-3.20, -1.12]	
Zhang et al (2017)	-11.57	4.868	40	-11.95	4.319	40	7.2%	0.08 [-0.36, 0.52]	
Tang et al (2017)	-20.84	5.094	53	-11.47	5.871	53	7.1%	-1.69 [-2.14, -1.25]	
Li et al (2016)	-10.81	3.44	31	-7.37	3.752	30	6.8%	-0.94 [-1.48, -0.41]	
Wang et al (2015) 12w	-13.13	7.799	75	-8.19	8.414	75	7.5%	-0.61 [-0.93, -0.28]	
Wang et al (2015) 6w	-15.95	3.378	35	-15.59	7.737	35	7.0%	-0.06 [-0.53, 0.41]	
Liu et al (2015)	-7.91	3.548	30	-2.17	3.379	30	6.6%	-1.64 [-2.22, -1.05]	
Yang et al (2014)	-15.33	6.144	37	-4.16	8.675	37	6.9%	-1.47 [-1.99, -0.95]	
Li et al (2014)	-21.07	3.516	47	-16.13	3.298	46	7.1%	-1.44 [-1.89, -0.98]	
Zhang et al (2013)	-11.73	3.284	41	-9.47	3.455	41	7.1%	-0.66 [-1.11, -0.22]	
Yang et al (2013)	-20.4	3.79	19	-18.1	3.02	19	6.3%	-0.66 [-1.31, -0.00]	
Jin et al (2013)	-8.06	3.869	30	-1.93	3.205	30	6.5%	-1.70 [-2.30, -1.11]	
Yan et al (2010)	-11.6	3.037	20	-6.45	5.018	20	6.2%	-1.22 [-1.90, -0.54]	
<b>Total (95% CI)</b>			<b>527</b>			<b>526</b>	<b>100.0%</b>	<b>-1.01 [-1.36, -0.66]</b>	

Heterogeneity: Tau<sup>2</sup> = 0.40; Chi<sup>2</sup> = 96.36, df = 14 (P < 0.00001); I<sup>2</sup> = 85%  
 Test for overall effect: Z = 5.67 (P < 0.00001)

=large heterogeneity) and Cochran Q test. If I-square < 50%, a fixed-effect model was adopted; if I-square > 50%, then we used a random effects model. We used forest plots to present the results of

異質性	12 : 85% : 高
效應模型	random-effects model

Section A: Are the results of the review **valid**?

5. If the results of the review have been combined, was it reasonable to do so?  
 作者是否有把各個研究的結果合併起來？這樣的合併是合理的嗎？

**Table 4** Regression analyses for the effect of mediator variables on the outcome of pretreatment and posttreatment HAM-D scores

Variable	Coefficient (SE)	95% CI (%)		P
		Lower	Upper	
Version of HAM-D 17 24	-0.162544 (-0.3595111)	-0.9635848	0.6384967	.661
Type of control intervention Sham rTMS Blank control	-0.1363385 (-0.7960555)	-1.910061	1.637384	.867
Total session ≥6 wk <6 wk	-1.023446 (-0.3485851)	-1.800143	-0.2467503	.015
Basic treatment Including antidepression Not including antidepression	0.1454299 (0.5900338)	-1.169247	1.460107	.810
Intercept	-0.3100672 (0.4952345)	-1.413518	0.7933842	.545

統合迴歸  
分析

有統合迴歸分析

Section A: Are the results of the review **valid**?

5. If the results of the review have been combined, was it reasonable to do so?  
 作者是否有把各個研究的結果合併起來？這樣的合併是合理的嗎？

**Table 3** Subgroup analyses for the effect of mediator variables on the outcome of pretreatment and posttreatment HAM-D scores

Subgroups	No. of Studies	Total Samples	SMD	95% CI (%)		Heterogeneity	
				Lower	Upper	<i>P</i>	<i>I</i> <sup>2</sup> , %
<b>Version of HAM-D</b>							
17	10	765	-1.06	-1.51	-0.61	<.00001	88
24	5	288	-0.92	-1.53	-0.31	<.0001	83
<b>Type of control intervention</b>							
Sham rTMS	3	136	-1.35	-2.1	-0.61	.03	70
Blank control	12	917	-0.94	-1.33	-0.55	<.00001	87
<b>Total session</b>							
≥6 wk	6	497	-0.43	-0.83	-0.03	.0003	78
<6 wk	9	556	-1.41	-1.66	-1.16	.10	40
<b>Basic treatment</b>							
Including antidepression	11	767	-0.97	-1.42	-0.53	<.00001	88
Not including antidepression	4	286	-1.12	-1.74	-0.51	.003	78

次組  
分析

1. HAM-D 17 versus 24
  2. Sharm rTMS versus blank control
  3. ≥6周 versus <6周
  4. 有抗憂鬱藥物 versus 無
- 次群組分析後I<sup>2</sup>未下降，仍藉由REM進行分析

YES

Can'  
t tell

NO

Section B: What are the **results**?

6. What are the overall results of the review?  
這篇回顧呈現了什麼結果？

7. How precise are the results?  
效果精準嗎？

主要結果

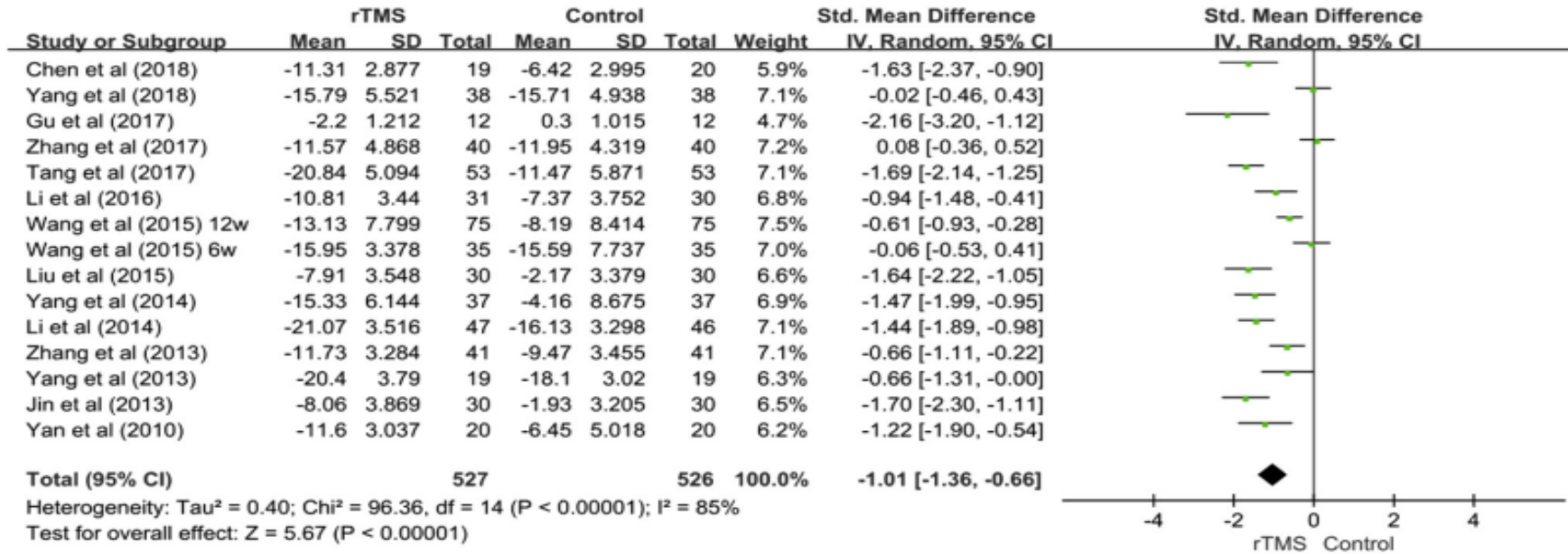


Fig 2 Effects of HF-rTMS on depression in individuals with PSD.

Intervention	rTMS
Comparison	control
Outcome	SMD -1.22[-1.90~-0.54](95%CI)
結論	PSD病人使用rTMS比控制組HAM-D分數有顯著性降低



Section B: What are the **results**?

6. What are the overall results of the review?  
這篇回顧呈現了什麼結果？

7. How precise are the results?  
效果精準嗎？

次要結果

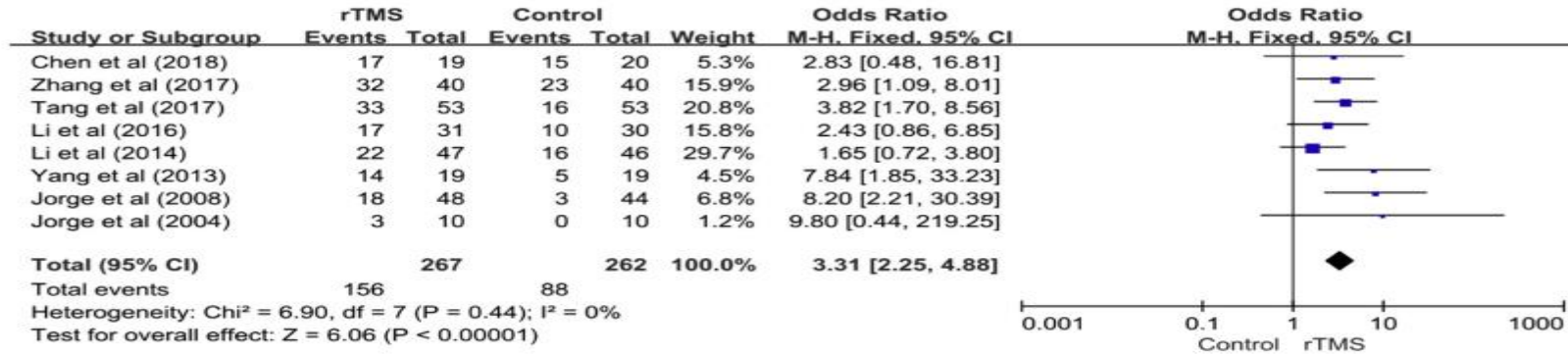


Fig 4 Response rates for HF-rTMS as a treatment for depression in individuals with PSD.

Intervention	rTMS
Comparison	control
Outcome	OR : 3.31, 95% CI, 2.25-4.88
結論	PSD病人治療反應率在使用rTMS比控制組有顯著性高

Section B: What are the **results**?

6. What are the overall results of the review?  
這篇回顧呈現了什麼結果？

7. How precise are the results?  
效果精準嗎？

次要結果

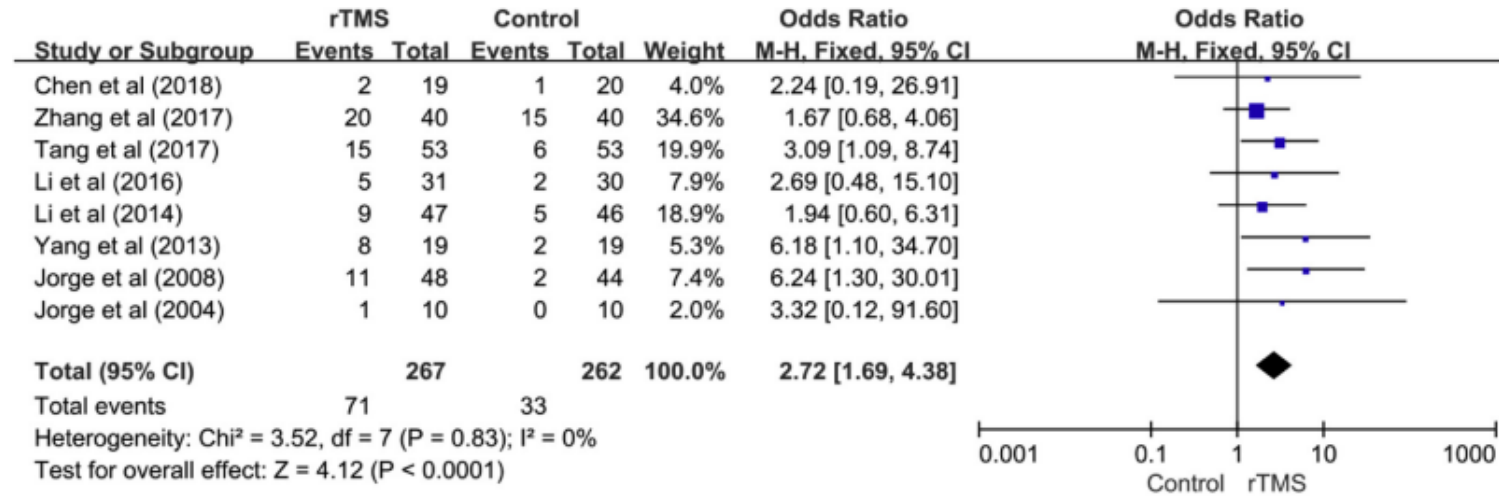


Fig 5 Remission rates for HF-rTMS as a treatment for depression in individuals with PSD.

Intervention	rTMS	
Comparison	control	
Outcome	OR : 2.72; 95% CI, 1.69-4.38	
結論	PSD病人緩解率在使用rTMS比控制組顯著性高	

Section B: What are the **results**?

6. What are the overall results of the review?  
這篇回顧呈現了什麼結果？

7. How precise are the results?  
效果精準嗎？

次要結果

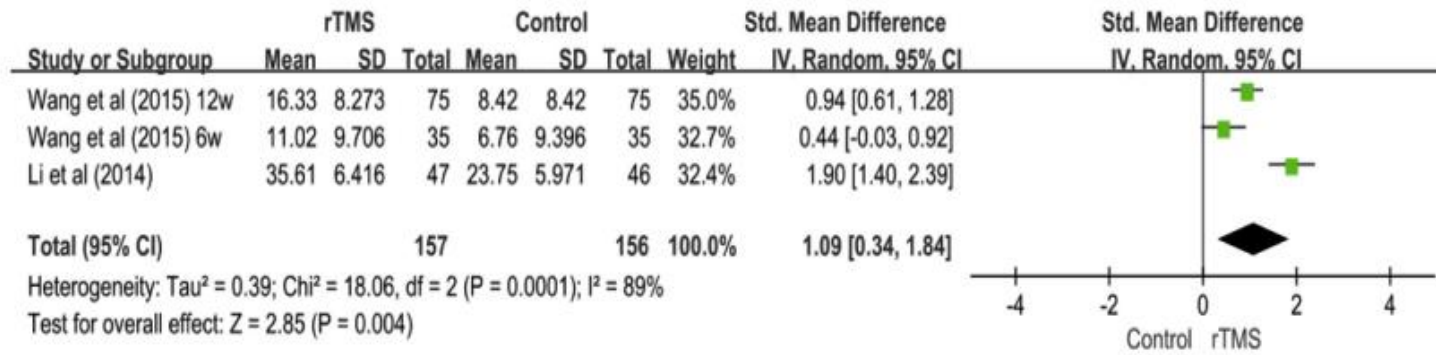


Fig 6 Effects of HF-rTMS on ADL on individuals with PSD.

Intervention	<b>rTMS</b>
Comparison	control
Outcome	SMD 1.09[0.34~1.84](95%CI)
結論	<b>PSD病人使用rTMS比控制組在ADL分數有顯著性增加</b>

Section B: What are the **results**?

6. What are the overall results of the review?  
這篇回顧呈現了什麼結果？

7. How precise are the results?  
效果精準嗎？

次要結果

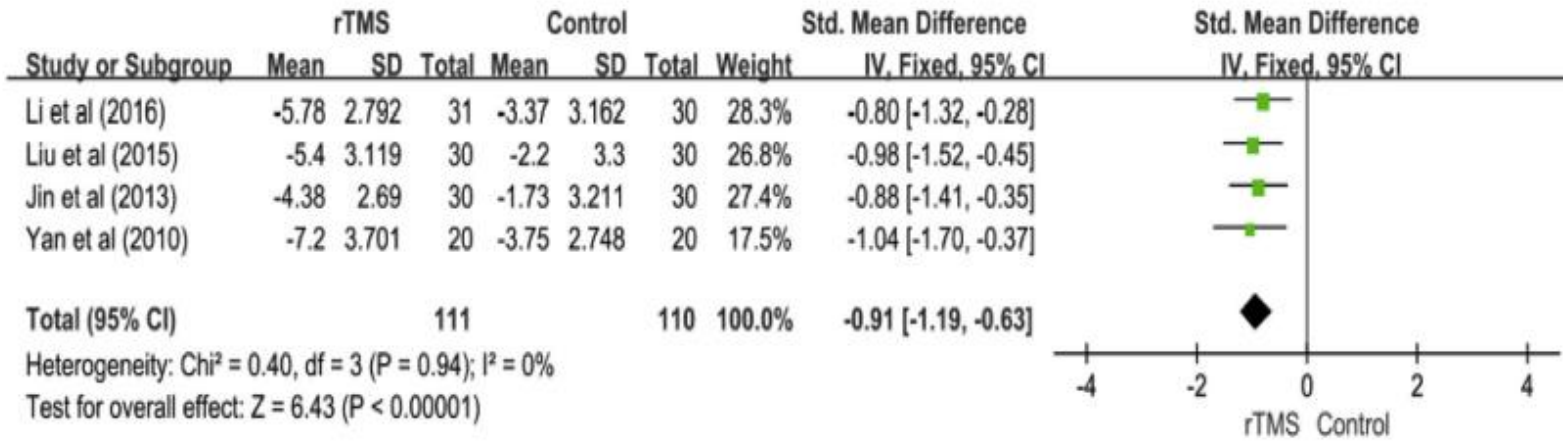


Fig 7 Effects of HF-rTMS on neurologic function in individuals with PSD.

Intervention	<b>rTMS</b>
Comparison	control
Outcome	SMD -0.91[-1.19~-0.63](95%CI)
結論	<b>PSD病人使用rTMS比控制組在NIHSS有顯著性降低</b>

Section B: What are the **results**?

6. What are the overall results of the review?  
這篇回顧呈現了什麼結果？

7. How precise are the results?  
效果精準嗎？

## 次要結果

**Table 5** Meta-analysis of adverse events, comparing HF-rTMS and control groups

Adverse Events	No. of RCTs	rTMS Groups		Control Groups		Heterogeneity			Meta-Analysis			
		Events	Total	Events	Total	<i>P</i>	<i>I</i> <sup>2</sup> , %	Model	<i>Z</i>	<i>P</i>	OR	95% CI
Headaches <sup>17,22,23,25,27,32</sup>	6	31	251	7	245	0.45	0	Fixed	3.53	.00	3.98	1.85-8.55
Loss of appetite <sup>27</sup>	1	1	47	2	46	-	-	-	0.59	.55	0.48	0.04-5.46
Local pain <sup>32</sup>	1	2	48	1	44	-	-	-	0.50	.61	1.87	0.16-21.37
Local discomfort <sup>32</sup>	1	7	48	6	44	-	-	-	0.13	.90	1.08	0.33-3.51
Anxiety <sup>32</sup>	1	2	48	0	44	-	-	-	1.00	.32	4.78	0.22-102.47

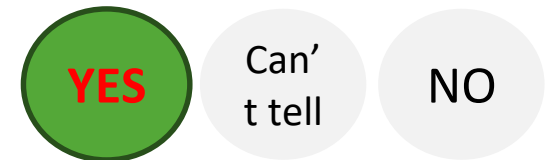
9. Were all important outcomes considered?  
是否所有重要的臨床結果都被考量到？

文獻研究以HAM-D分數作為評估工具，其結果聚焦、明確。

主要結果：HAM-D分數

次要結果：反應率、緩解率、ADL、神經功能(NIHSS)

副作用：頭痛、降低食慾、局部疼痛、局部不適、焦慮



Section C: Will the results **help locally**?

8. Can the results be applied to the local population?  
此研究是否可應用到你的病患？

Section C: Will the results **help locally**?

10. Are the benefits worth the harms and costs?  
這些好處隨之而來的傷害和花費是否值得？

此兩題在臨床之應用的部分會提及

# 此研究是否可應用於此病人？

**OK**

**OK**

**OK**

		評讀文獻	臨床情境
<b>P</b>	性別	無限制	男
	年齡	35.6-68.7	70歲
	共病	中風後憂鬱	失語症、中風後憂鬱症候群
	診斷	Poststroke Depression	左側中大腦動脈梗塞中風併發右半邊癱瘓
	其他	antidepressant	未服用藥物未明述
<b>I</b>		High-Frequency Repetitive Transcranial Magnetic Stimulation	rTMS
<b>O</b>		depression	中風後憂鬱程度



Risk of bias	
問題明確	●
蒐納適當	●
廣泛搜尋	●
品質評估	●
結果合併	●
顯著性	●
精準性	●

Risk of bias		如左
<b>Imprecision</b>	<b>-2</b>	<ul style="list-style-type: none"> <li>未進行TSA分析，不確定樣本數代表性</li> <li>降低MD太小</li> <li>缺乏時間分間追蹤</li> </ul>
<b>Inconsistency</b>	<b>-1</b>	<ul style="list-style-type: none"> <li>各研究結果有差異 未進行深入分析</li> <li>各研究間存在異質性 (族群、介入、結果)</li> </ul>
<b>Indirectness</b>		<ul style="list-style-type: none"> <li>無間接比較</li> <li>研究內容跟臨床執行無差異</li> </ul>
<b>Publication bias</b>	<b>-1</b>	<ul style="list-style-type: none"> <li>高估好處 低估壞處</li> <li>搜尋不詳盡，未發表報告</li> <li>企業贊助</li> <li>Antibiotic resistance was not adequately reported in the included</li> </ul>
<b>Plausible confounding</b>		干擾因子控制 (年齡性別抽菸酒精社經) 研究族群限制 (嚴重病人)
<b>Large effect</b>		<ul style="list-style-type: none"> <li>降低RR &gt; 200% 或 增加RR &lt; 200%</li> </ul>
<b>Dose effect</b>		

**證據等級**

⊕○○○

**極低**

# 醫療現況、治療利弊權衡

選擇	比較	
<b>Pharmacological therapy</b>	<ul style="list-style-type: none"> <li>- 證據等級：中</li> <li>- 治療次數：高</li> <li>- 療程：6個月以上的治療，再慢慢減藥</li> </ul>	<ul style="list-style-type: none"> <li>- 副作用：頭暈、感覺異常，手抖、焦慮、嘔吐、性功能異常、認知功能影響</li> <li>- 定期服用藥物</li> </ul>
<b>Psychological therapy</b>	<ul style="list-style-type: none"> <li>- 證據等級：中</li> <li>- 治療次數：中</li> <li>- 療程：6個月以上的治療，可透過遠距追蹤</li> </ul>	<ul style="list-style-type: none"> <li>- 副作用：無</li> <li>- 定期返診治療</li> </ul>
<b>Non-invasive brain stimulation (rTMS)</b>	<ul style="list-style-type: none"> <li>- 證據等級：低</li> <li>- 治療次數：中</li> <li>- 療程：每日進行20~40分鐘，約行20次療程，連續2-4週</li> </ul>	<ul style="list-style-type: none"> <li>- 副作用：頭痛，頭暈，耳鳴、癲癇</li> <li>- 定期返診治療</li> <li>- 長期效果不明</li> </ul>



**Cochrane**  
**Library**

Cochrane Database of Systematic Reviews

**Pharmacological, psychological, and non-invasive brain stimulation interventions for treating depression after stroke (Review)**

Allida S, Cox KL, Hsieh CF, Lang H, House A, Hackett ML

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with pharmacological interventions				
<b>Pharmacological interventions compared to placebo for treating depression after stroke</b>						
Depression: < 50% reduction in scale scores at end of treatment (Analysis 1.2)	Study population		RR 0.47 (0.32 to 0.69)	511 (6 RCTs)	⊕⊕⊕⊕ Very low <sup>a,c,d</sup>	
	821 per 1000	563 per 1000 (374 to 727)				
<b>Psychological therapy compared to usual care and/or attention control for treating depression after stroke</b>						
Depression: average change in scores between baseline and end of treatment (Analysis 3.3)		MD 6.20 lower (8.24 lower to 4.16 lower)	-	189 (3 RCTs)	⊕⊕⊕⊕ Very low <sup>a,c</sup>	
<b>Non-invasive brain stimulation compared to sham non-invasive brain stimulation and/or usual care for treating depression after stroke</b>						
Depression: mean scores at end of follow-up (Analysis 2.4)		MD 2.60 lower (3.33 lower to 1.87 lower)	-	170 (3 RCTs)	⊕⊕⊕⊕ Very low <sup>a,b</sup>	

**Summary of findings 4. Pharmacological intervention and a form of psychotherapy (combination) compared to pharmacological intervention and usual care or attention control (single) for treating depression after stroke**

**Pharmacological intervention and a form of psychotherapy (combination) compared to pharmacological intervention and usual care or attention control (single) for treating depression after stroke**

**Patient or population:** people with depression after stroke

**Setting:** inpatient, outpatient, or mixed

**Intervention:** pharmacological intervention and a form of psychotherapy (combination)

**Comparison:** pharmacological intervention and usual care or attention control (single)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with pharmacological intervention (single)	Risk with pharmacological intervention and psychotherapy (combination)				
Depression: meeting study criteria for depression at end of treatment (Analysis 4.1)	-	-	-	-	-	No data available
Depression: < 50% reduction in scale scores at end of treatment (Analysis 4.2)	-	-	-	-	-	No data available
Depression: mean scores at end of treatment (Analysis 4.3)	-	MD 1.53 lower (2.10 lower to 0.96 lower)	-	198 (2 RCTs)	⊕⊕⊕⊕ Very low <sup>a,b,c</sup>	
Activities of daily living: mean scores at end of treatment (Analysis 4.5)	-	MD 11.83 higher (0.27 higher to 23.40 higher)	-	198 (2 RCTs)	⊕⊕⊕⊕ Very low <sup>a,c,d</sup>	
Neurological function: mean scores at end of treatment (Analysis 4.6)	-	-	-	-	-	No totals
Adverse events: death - at end of treatment (Analysis 4.7)	-	-	-	-	-	No data available

# 成本效益考量：有形、無形

選擇	人力	時間	金錢	舒適度	臨床可行性
<b>Pharmacological therapy</b>	醫師 藥師 本人或家人	至少6個月不 間斷服藥	健保給付	藥物副作用 認知功能影響	已有相關治療指引 地區診所可行
<b>Psychological therapy</b>	醫師 心理治療師 本人	至少6個月， 每週一次30分 鐘	政府補助心理 諮商，掛號費 <b>250元/次</b>	佳	已有相關治療指引 地區診所可行
<b>rTMS</b>	醫師 本人、家人 陪同	2至4週，每天 每次20分鐘	完成全部療程 <b>10萬</b>	頭皮麻痛	已有相關治療指引 部分醫院可行

P	中風後憂鬱症候群
I	rTMS
C	無rTMS
O	憂鬱程度
證據等級	⊕○○○ 極低
治療利弊	<ul style="list-style-type: none"> <li>副作用：頭痛，頭暈，耳鳴、癲癇</li> <li>無法確認長期效益、復發後是否可繼續進行</li> </ul>
成本效益	費用高昂
價值觀與偏好	情境中無明述
臨床可行性	已有相關治療指引 部分醫院可行

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建議等級  
薄弱建議

# 臨床回覆

