



三軍總醫院
Tri-Service General Hospital

實證醫學競賽

109/05/22

內科部

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臨床情境 Clinical Scenario

45歲黃先生，平常除了抽煙外，無其他嗜好。三年前公司體檢意外發現的第二型糖尿病，也在飲食控制及口服降血糖藥物的使用下，控制得不錯。

黃先生一直有健走的習慣，最近一個月來他發現自己健走的時候越來越容易累，走的距離也沒有之前長，經過ABI檢查後，其結果是0.6，懷疑是周邊動脈阻塞疾病(peripheral arterial disease, PAD)，由於是下肢動脈狹窄引起的，需要吃cilostazol治療，也建議吃aspirin預防血栓。也可以考慮做心導管手術，將狹窄的動脈撐開，改善下血流循環情況。

黃先生對於自己的病情有疑問，他想知道

1.光靠測量血壓診斷PAD準確嗎？有沒有更確定的診斷方法呢？

超音波可以嗎？還是要做到血管攝影？

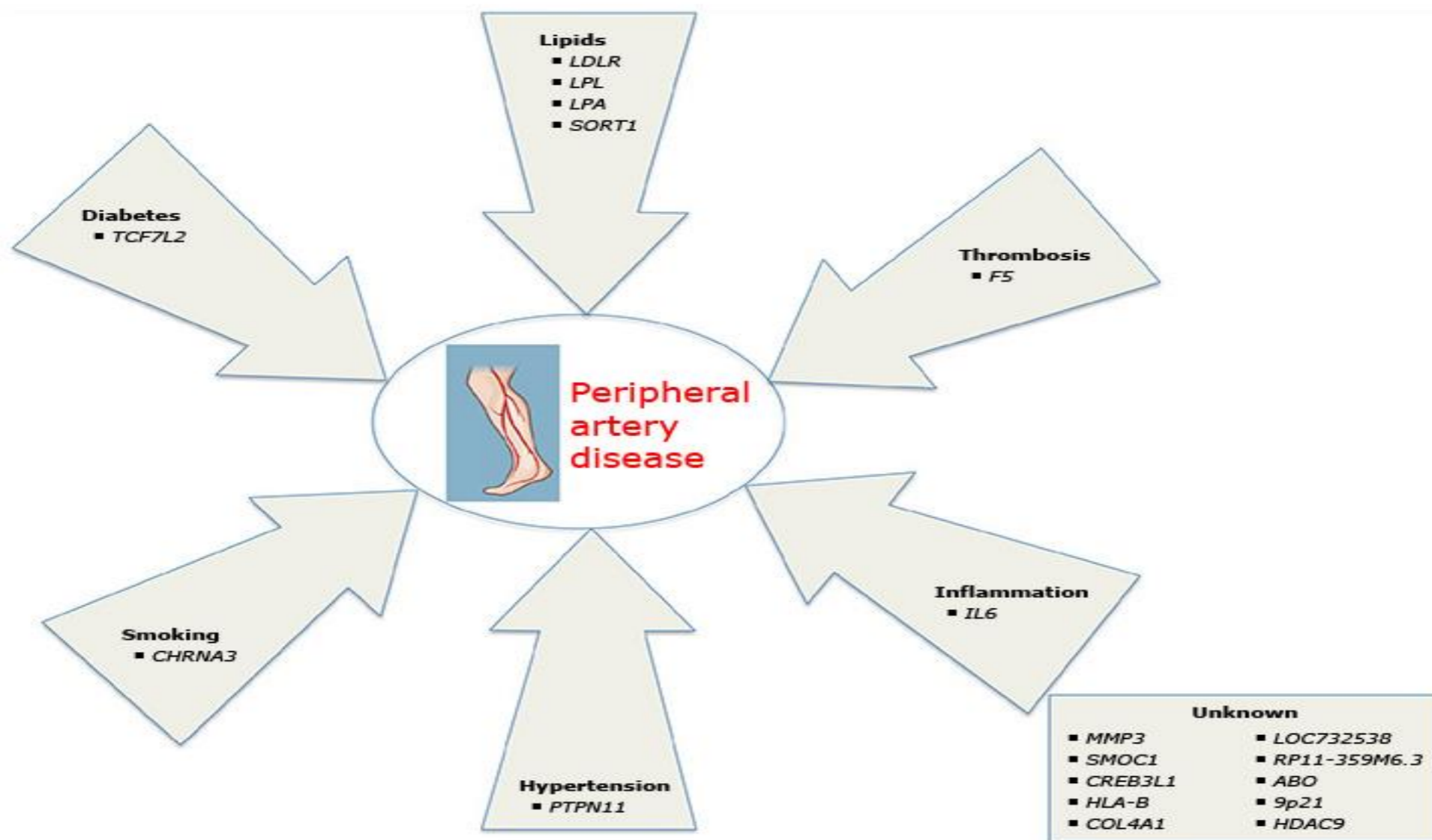
2.他也想知道，是不是一定要吃cilostazol，效果如何？如果不吃藥有其他替代的方法？光吃aspirin預防血栓夠嗎？運動可以嗎？醫師建議的心導管血管擴張手術，效果怎樣呢？會不會有風險

Background knowledge

- PAD results from an **atherosclerotic process**
 - Silent or present with a variety of symptoms
 - Signs indicative of extremity ischemia
 1. Claudication
 2. Rest pain
 3. Ulceration
 4. Gangrene

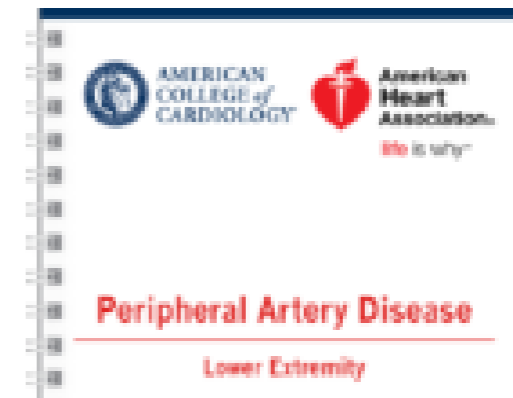
Background knowledge

Peripheral artery disease risk loci and known causal risk factors

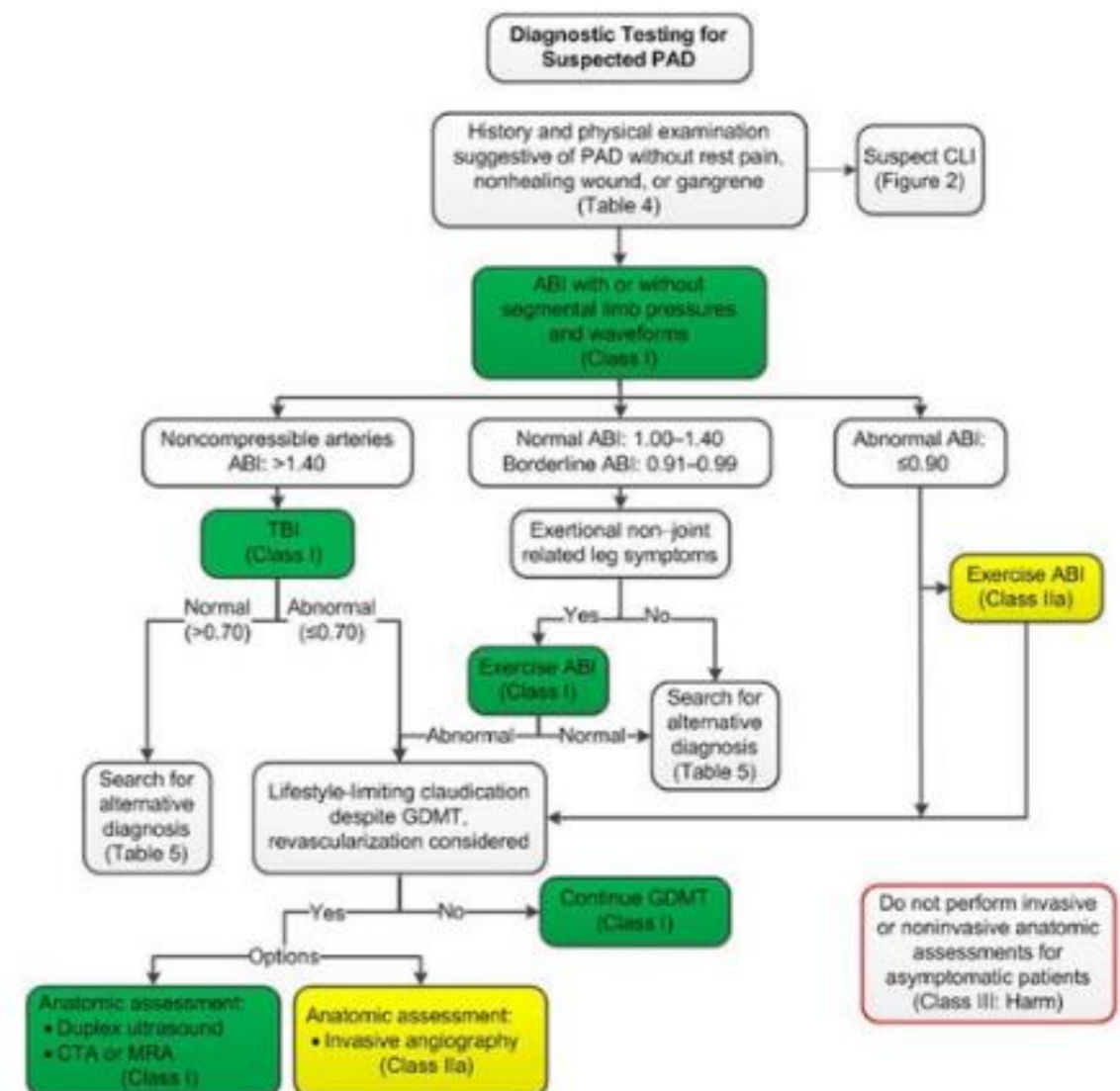


Background knowledge

- The measurement of an ankle-brachial index (ABI) ≤ 0.9 .
- For patients with appropriate symptoms, but a normal ABI, we obtain **an ABI following exercise testing**.
- Duplex ultrasonography is commonly used in conjunction with the ABI to **identify the location and severity of arterial obstruction**
- **Advanced vascular imaging** (computed tomographic [CT] angiography, magnetic resonance [MR] angiography, catheter-based arteriography) is usually reserved for patients in whom there remains uncertainty following noninvasive testing



COR	LOE	Recommendations
I	B-NR	In patients with history or physical examination findings suggestive of PAD (Table 4), the resting ABI, with or without segmental pressures and waveforms, is recommended to establish the diagnosis. ⁶⁰⁻⁶⁵



Background knowledge

Risk factor modification



1. Antithrombotic therapy

COR	LOE	Recommendations
I	A	Cilostazol is an effective therapy to improve symptoms and increase walking distance in patients with claudication. ^{119,163}

COR	LOE	Recommendations
Antiplatelet Agents		
I	A	Antiplatelet therapy with aspirin alone (range 75–325 mg per day) or clopidogrel alone (75 mg per day) is recommended to reduce MI, stroke, and vascular death in patients with symptomatic PAD. ^{120–124}

2. Smoking cessation

3. Lipid-lowering therapy

4. Glycemic control

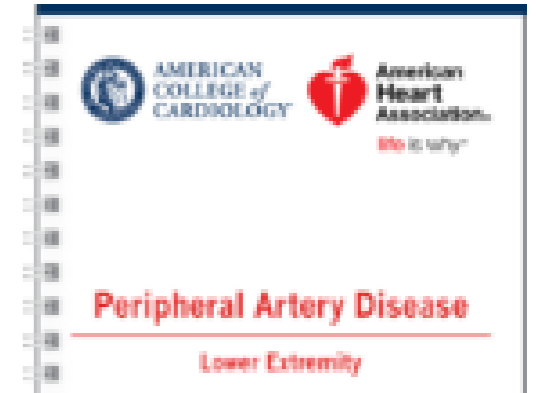
5. Antihypertensive therapy

6. Diet and exercise

7. Obesity

Background knowledge

Revascularization



*.For those with significant or disabling symptoms of claudication **unresponsive to lifestyle adjustment and pharmacologic therapy**

→Consider intervention treatment

*.In the absence of limb-threatening ischemia, symptoms of PAD tend to remain stable with medical therapy.

*.Performing prophylactic intervention, whether percutaneous or surgical, **in patients with minimal claudication provides little benefit**, may cause harm, and is not indicated.

I	A	Endovascular procedures are effective as a revascularization option for patients with lifestyle-limiting claudication and hemodynamically significant aortoiliac occlusive disease. ^{13,25,26,190,194,196,201}
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臨床問題

P Peripheral artery disease

I ABI

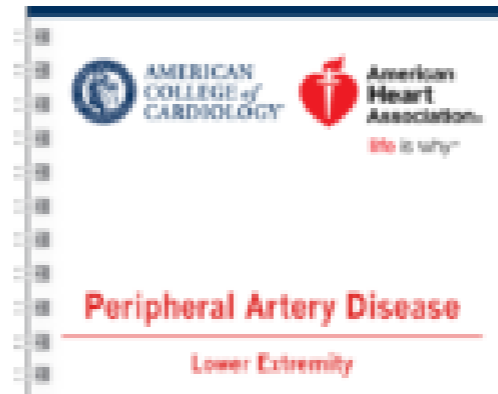
C Duplex ultrasonography ; Angiography

O Accuracy of disease diagnosis

Type

診斷型問題

AHA guideline 2016



COR	LOE	Recommendations
I	B-NR	In patients with history or physical examination findings suggestive of PAD (Table 4), the resting ABI, with or without segmental pressures and waveforms, is recommended to establish the diagnosis. ^{60–65}
I	C-LD	Resting ABI results should be reported as abnormal (ABI ≤ 0.90), borderline (ABI 0.91–0.99), normal (1.00–1.40), or noncompressible (ABI > 1.40). ^{46,63–66}
I	B-NR	Duplex ultrasound, CTA, or MRA of the lower extremities is useful to diagnose anatomic location and severity of stenosis for patients with symptomatic PAD in whom revascularization is considered. ^{100–103}
I	C-E0	Invasive angiography is useful for patients with CLI in whom revascularization is considered.
IIa	C-E0	Invasive angiography is reasonable for patients with lifestyle-limiting claudication with an inadequate response to GDMT for whom revascularization is considered.

- ◆ ABI檢查為AHA guideline 建議的第一線檢查
- ◆ 血管超音波以及血管攝影用於定位以及病情嚴重建議進行侵入性治療的病人。
- ◆ 侵入性治療用於Critical limb ischemia的病人會有益處。

臨床問題

P 周邊動脈阻塞疾病

I 不吃藥以外其他治療

C 傳統藥物治療

O 行走距離、生活品質

Type 治療型問題 (搜尋目標→ SR、RCT)

關鍵字

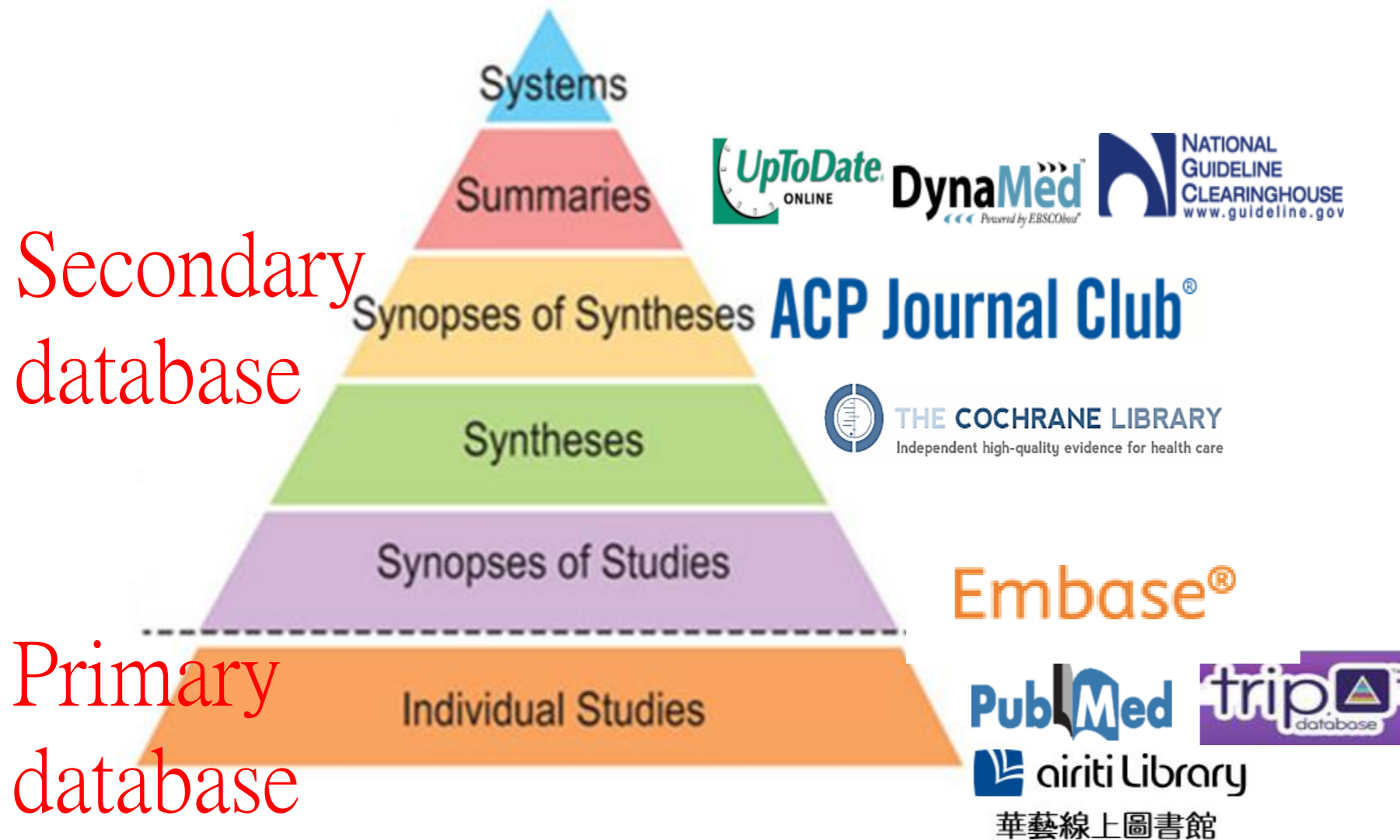
Ask

	中文關鍵字	英文關鍵字	同義字/MeSH/Emtree
P	周邊動脈阻塞疾病	Peripheral artery disease	Peripheral arteries disease PAOD Intermittent claudications
I	不吃藥以外其他治療	Exercise, percutaneous angioplasty	exercise, PTA
C	傳統藥物治療	Medications	medical therapy, medical treatment
O	行走距離、生活品質	Walking distance, quality of life	MWD, QoL

資料搜尋 Acquire

• 6S EBM Resources

- 以「P & I」搜尋，再依結果調
- 整納入之
關鍵字與同義字
- 本情境為
治療型問題
故會先查找符合
臨床情境SR再找
RCT的文章





Advanced Search

Search

Search manager

Medical terms (MeSH)

PICO search^{BETA}

Filter: within 1 year

Save this search

View saved searches

Search help

View fewer lines

Print

+										
-	+	#1	MeSH descriptor: [Peripheral Arterial Disease] explode all trees							
-	+	#2	PAOD							
-	+	#3	MeSH descriptor: [Intermittent Claudication] explode all trees							
-	+	#4	#1 or #2 or #3							
-	+	#5	medications	Limits	32834					
-	+	#6	medical therapy	Limits	146853					
-	+	#7	medical treatment	Limits	149357					
-	+	#8	#5 or #6 or #7	Limits	213129					
-	+	#9	#4 and #8	Limits	356					

**搜索: 3篇Cochrane Review
15篇 Clinical trail**

關鍵字: Peripheral artery disease, PAOD,
Medical treatment, Medications,
Intervention, Quality of life, walking
distance, MWD

技巧

1. 使用 **Cochrane Library search Manager** 搜尋
加入 **布林邏輯 AND, OR** 作搜尋連結
2. **未限制年份**

Primary database

關鍵字: Peripheral artery disease, PAOD, Medical treatment, Medications, Intervention, Quality of life, walking distance, MWD

acquire

The screenshot shows the PubMed.gov search interface. At the top left is the PubMed.gov logo. The search bar contains the query: (((PAOD[MeSH Terms]) OR (peripheral arterial disease[MeSH Terms]))) OR (cl...). Below the search bar are links for 'Advanced', 'Create alert', and 'Create RSS'. To the right of the search bar is a 'Search' button and a 'User Guide' link. Below the search bar are buttons for 'Save', 'Email', and 'Send to'. To the right of these buttons is 'Sorted by: Best match' and a 'Display options' button. On the left side, there is a 'MY NCBI FILTERS' section with a refresh icon. Below that is a 'RESULTS BY YEAR' section with a bar chart showing search results from 2010 to 2020. The bar chart has a 'Reset' button and a 'Download' icon. To the right of the bar chart, there is a message: 'Filters applied: Meta-Analysis, Systematic Reviews, in the last 1 year. Clear all'. Below that is another message: 'The following term was not found in PubMed: PAOD'. The search results list one result: 'Global vascular guidelines on the management of chronic limb-threatening ischemia.' with 1 result. The authors listed are Conte MS, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, Mills JL, Ricco JB, Suresh KR, Murad MH; CVC Writing Group.

1. 將關鍵字輸入，使用自然語言，自動搜索MeSH
2. 利用布林邏輯“AND”“OR”等語法以免遺漏文獻搜尋分類
3. 將Clinical Queries檢索分類建入 My NCBI，建立有效率的Filter
4. 使用 Filter 功能以提升篩選效率，限定文章類型meta-analysis，systematic review, RCT, Full text, Humans

關鍵字: Peripheral artery disease, PAOD, Medical treatment, Medications, Intervention, Quality of life, walking distance, MWD

#8 AND (2019:py OR 2020:py) AND ('meta analysis'/de OR 'systematic review'/de)

Search > Mapping ▾ Date ▾ Sources ▾ Fields ▾ Quick limits ▾

Results Filters

+ Expand — Collapse all Apply >

Sources ▾

Drugs ▾

Diseases ▾

Devices ▾

Floating Subheadings ▾

Age ▾

Gender ▾

Study types ▲

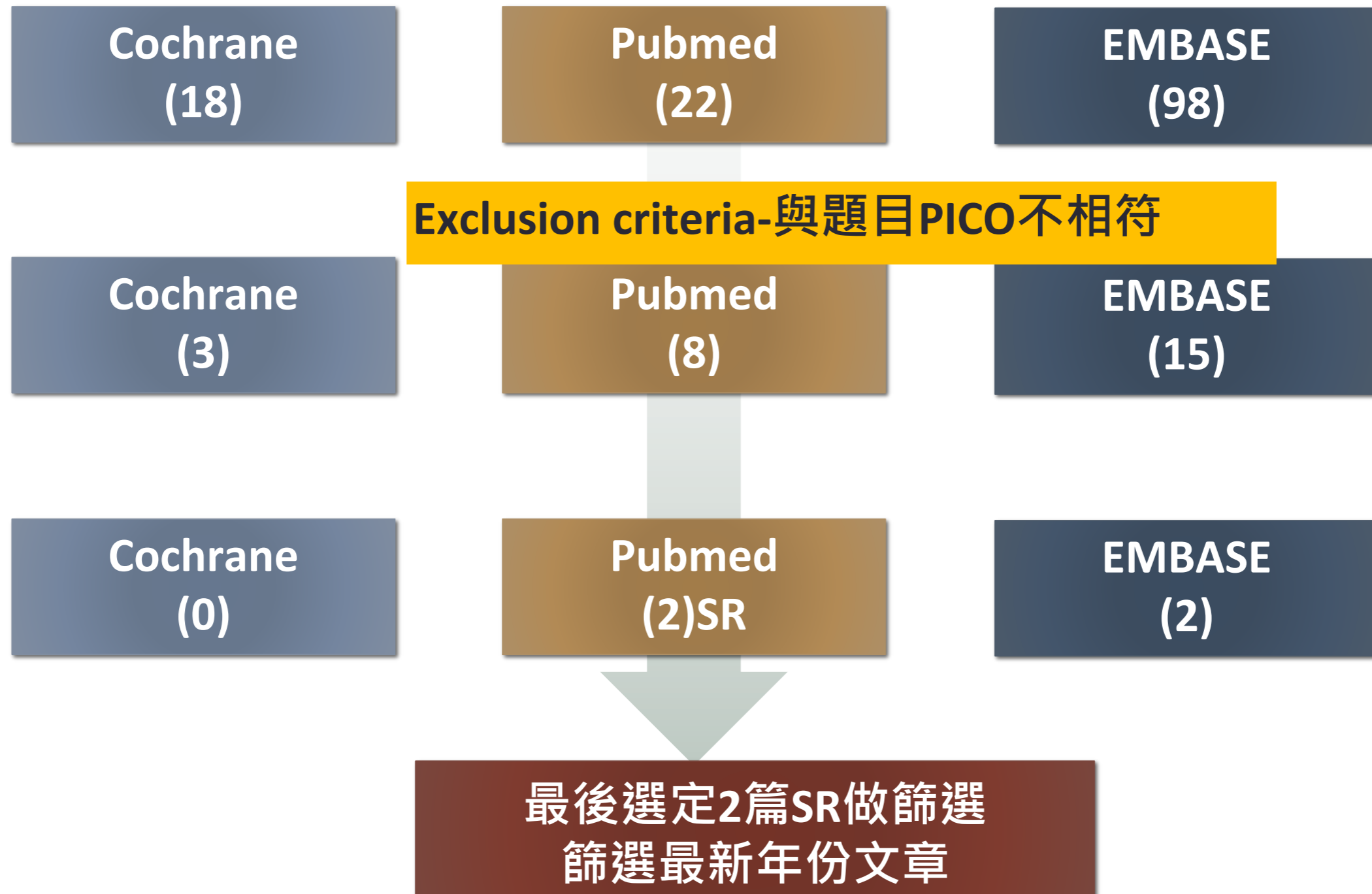
 human 97 systematic review 89 meta analysis 53 randomized 22 History Save | Delete | Print view | Export | Email Combine > using And Or ^ Collapse

<input type="checkbox"/>	#9	#8 AND (2019:py OR 2020:py) AND ('meta analysis'/de OR 'systematic review'/de) AND ('article'/it OR 'review'/it)	98
<input type="checkbox"/>	#8	#4 AND #7	27,712
<input type="checkbox"/>	#7	#5 OR #6	2,709,035
<input type="checkbox"/>	#6	medical AND treatment	2,538,002
<input type="checkbox"/>	#5	medications	232,283
<input type="checkbox"/>	#4	#1 OR #2 OR #3	175,333
<input type="checkbox"/>	#3	'intermittent claudication'	12,277
<input type="checkbox"/>	#2	paod	1,285
<input type="checkbox"/>	#1	'peripheral occlusive artery disease'/exp OR 'peripheral occlusive artery disease'	174,281

98 results for search #9 [Set email alert](#) [Set RSS feed](#) [Search details](#) [Index miner](#) Results View | Print | Export | Email | Order | Add to Clipboard 1 — 25 >Select number of items ▾ Selected: 0 (clear) Show all abstracts | Sort by: Relevance Publication Year Entry Date 1 Statin treatment and accrual of covert cerebral ischaemia on neuroimaging: a systematic review and meta-analysis of randomized trials

1. 將關鍵字輸入，使用自然語言，自動搜索MeSH
2. 利用布林邏輯“AND”“OR”等語法以免遺漏文獻搜尋分類
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4. 使用 Filter 功能以提升篩選效率，限定文章類型meta-analysis，systematic review, RCT, Full text, Humans

搜索結果





Supervised Exercise Therapy and Revascularization for Intermittent Claudication

Network Meta-Analysis of Randomized Controlled Trials

Athanasios Saratzis, MBBS, PhD,^a Ioannis Paraskevopoulos, MD, PhD,^b Sanjay Patel, BSc (HONS), MBC_HB, MD (RES),^a
Tommaso Donati, BSc, MD,^a Lukla Biasi, MD,^a Athanasios Diamantopoulos, MD, PhD,^a Hany Zayed, MD, MSc,^{a,*}
Konstantinos Katsanos, MSc, MD, PhD^{c,*}

2019 .11. 12

Journal of the American College of Cardiology: Cardiovascular Interventions

Impact factor:9.544

文獻納入理由：

最符合臨床問題 最佳的研究設計 年份最新

評讀工具：

CASP SR critical appraisal tool

Did the review address a clearly focused question?

此研究是否問了一個清楚明確的問題？

OBJECTIVES The aim of this study was to perform a comprehensive meta-analysis comparing all therapeutic modalities for intermittent claudication (IC), including best medical therapy (BMT) alone, percutaneous angioplasty (PTA), supervised exercise therapy (SET), and PTA combined with SET, to establish the optimal first-line treatment for IC.

BACKGROUND IC is a common health problem that limits physical activity, results in decreased quality of life (QoL) and is associated with poor cardiovascular outcomes. Previous meta-analyses have attempted to combine data from randomized trials; however, none have combined data from all possible treatment combinations or synthesized QoL outcomes.

P	Ischemic intermittent claudication
I	Medical therapy, PTA, exercise, PTA + exercise
C	Comprehensive meta-analysis comparing all therapeutic modalities
O	Quality of life, walking distance

Yes

Can't Tell

No

Did the authors look for the right type of papers?

作者是否收納適當的研究類型？

STUDY SELECTION. Upon completion of the electronic search, a list of all relevant abstracts was collated and reviewed to identify published clinical trials comparing the efficacy of any form of contemporary treatment (SET, BMT, PTA, or surgical intervention) in patients presenting with ischemic IC. All abstracts were screened independently by 2 authors. The senior author was advised in case of disagreement regarding potential inclusion of a study. Studies included in this analysis were required to have: 1) a randomized controlled trial design; 2) data on the baseline symptom status of study participants; 3) clearly defined intervention and control groups; and 4) objective measures of exercise capacity at the end of the study. The references cited in all the trials that fulfilled the inclusion criteria were also examined to identify additional studies. No anatomic exclusion criteria were applied. Trials presented at conferences that had not published full results in the form of peer-reviewed papers were not included. All identified trials that fulfilled the 4 aforementioned criteria were included in the final synthesis.

評讀結果

- 收錄符合問題的**RCT**文章
 - 說明 **納入**條件
 - 說明 **排除**條件

Yes	<input checked="" type="checkbox"/>
Can't Tell	<input type="checkbox"/>
No	<input type="checkbox"/>

Do you think the important, relevant studies were included?

作者有沒有可能遺漏掉重要、相關的研究？

SEARCH STRATEGY. An electronic search of MEDLINE, Embase, Allied and Complementary Medicine Database, and Scopus was performed in December 2018 using the following key terms: claudication OR “peripheral arterial disease” OR “peripheral artery disease,” exercise. The search was limited to human studies published after 1970; no language restrictions were applied.

評讀結果

- 盡可能搜尋各種一、二級資料庫
 - 搜尋文獻參考資料
 - 聯繫文章作者及專家
- 進一步取得尚未發表的文章和資料
 - 無語言限制

Yes	<input checked="" type="checkbox"/>
Can't Tell	<input type="checkbox"/>
No	<input type="checkbox"/>

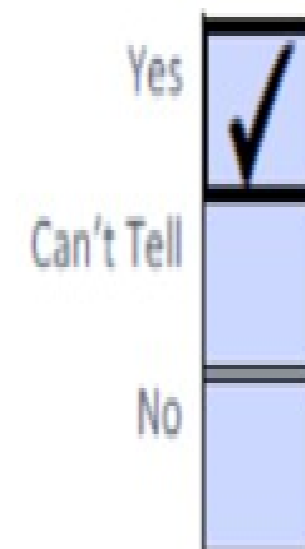
Did the review's authors do enough to assess the quality of the included studies?

作者是否有評估收納研究的品質？

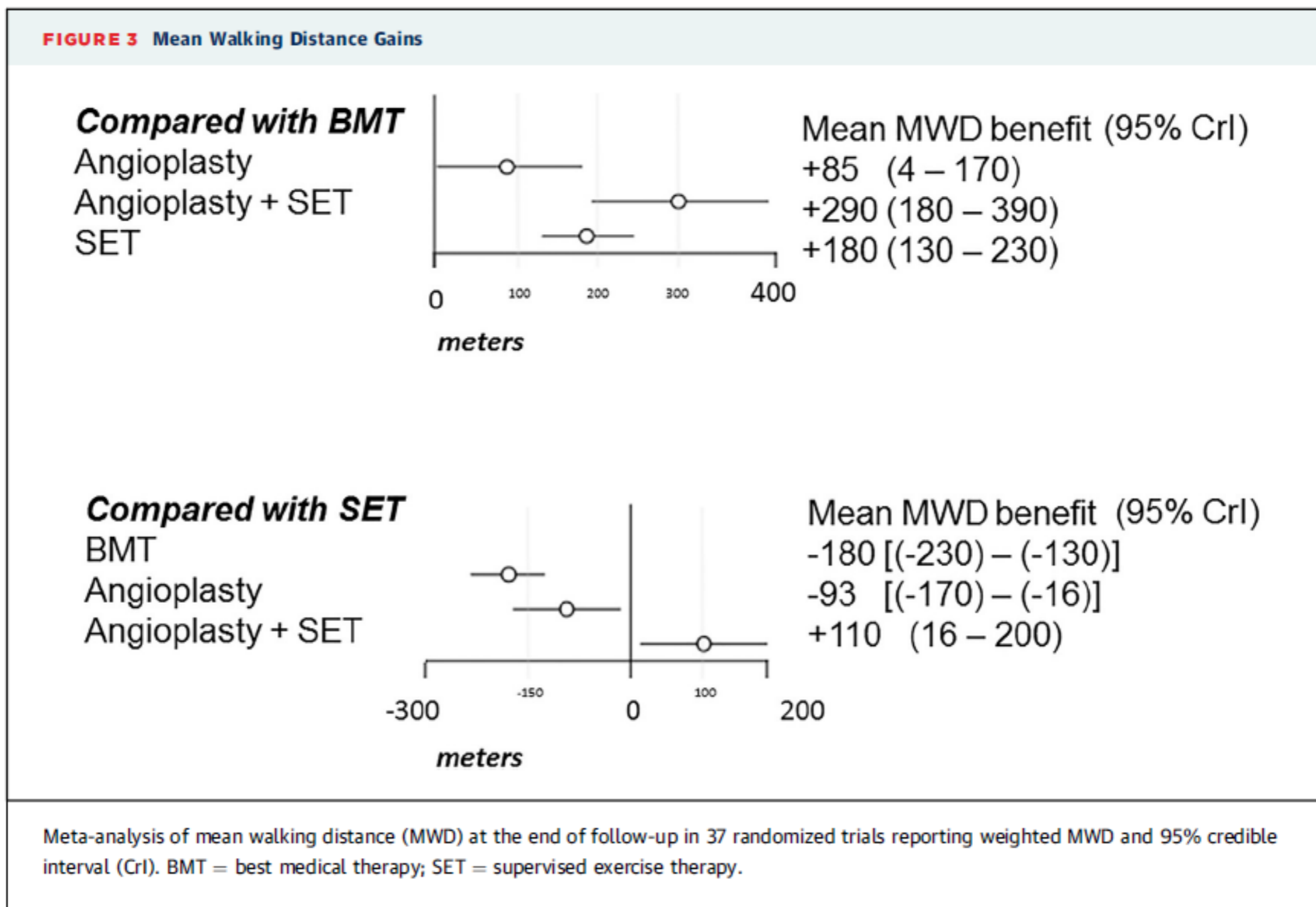
DATA EXTRACTION AND ASSESSMENT OF RISK FOR BIAS. Data extraction was performed independently by 2 authors. Presentation, clinical characteristics, target lesion location, type of intervention offered, outcomes measured at baseline and end of study, follow-up duration, and clinical events were extracted from individual studies into an electronic database. Discrepancies were resolved through discussion with the senior author. Risk for bias was assessed using the Cochrane risk for bias assessment tool, and the relevant studies were classified as exhibiting low, moderate, or high risk (12). Publication bias was assessed using a funnel plot. Quantitative quality assessment was performed using the PEDro scale, a validated tool in the context of clinical trials (13). The PEDro scale provides 11 different criteria (potential scores of 0 to 11) to assess whether a trial is likely to be internally valid and could have sufficient statistical information to make the results interpretable.

評讀結果

- 兩位作者獨立評讀，意見相左時諮詢第三位作者
- 使用 **Cochrane Handbook for Systematic Reviews of Interventions** 去評估品質及bias

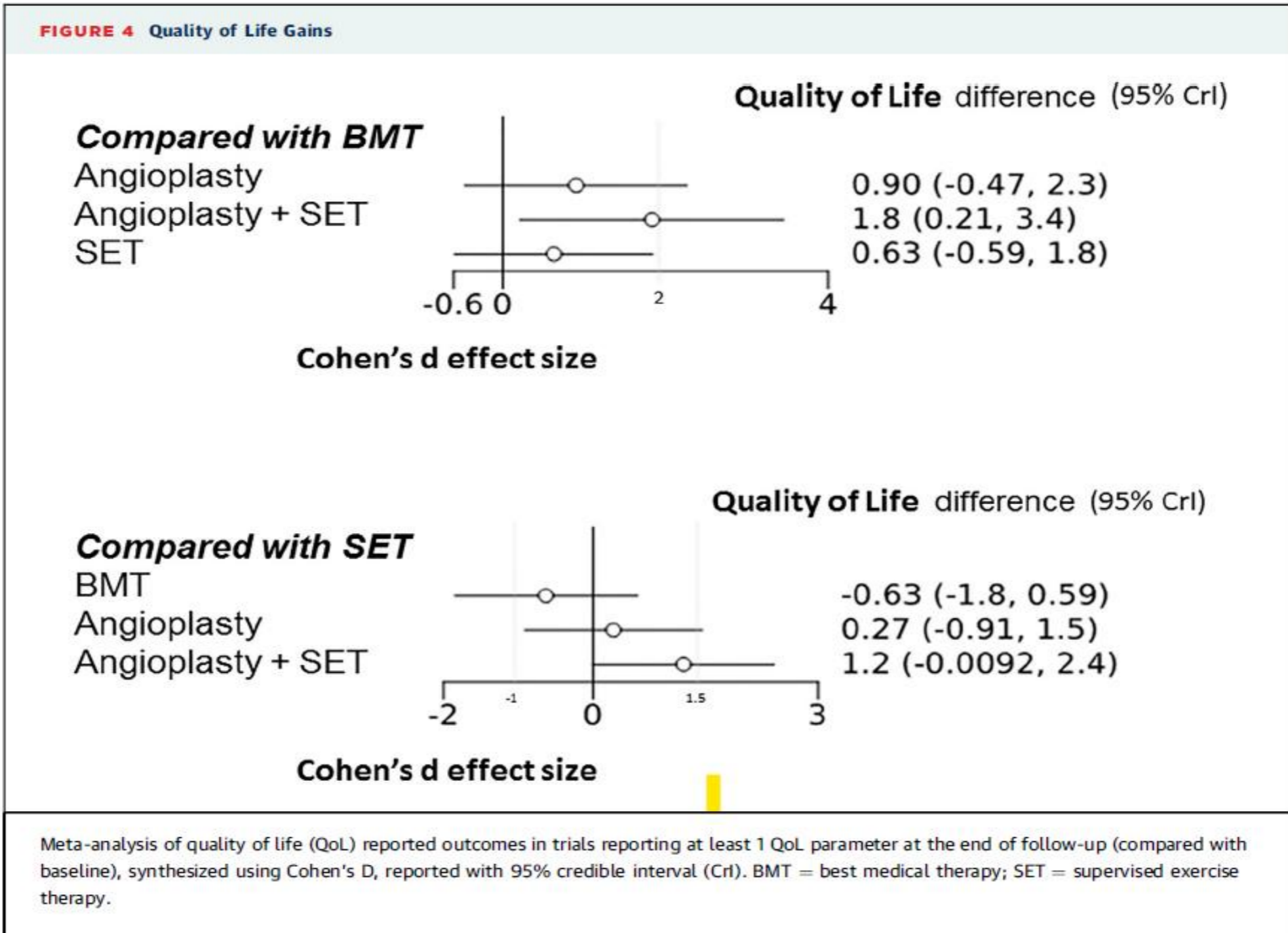


What are the overall results of the review? 這篇回顧呈現了什麼結果?



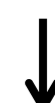
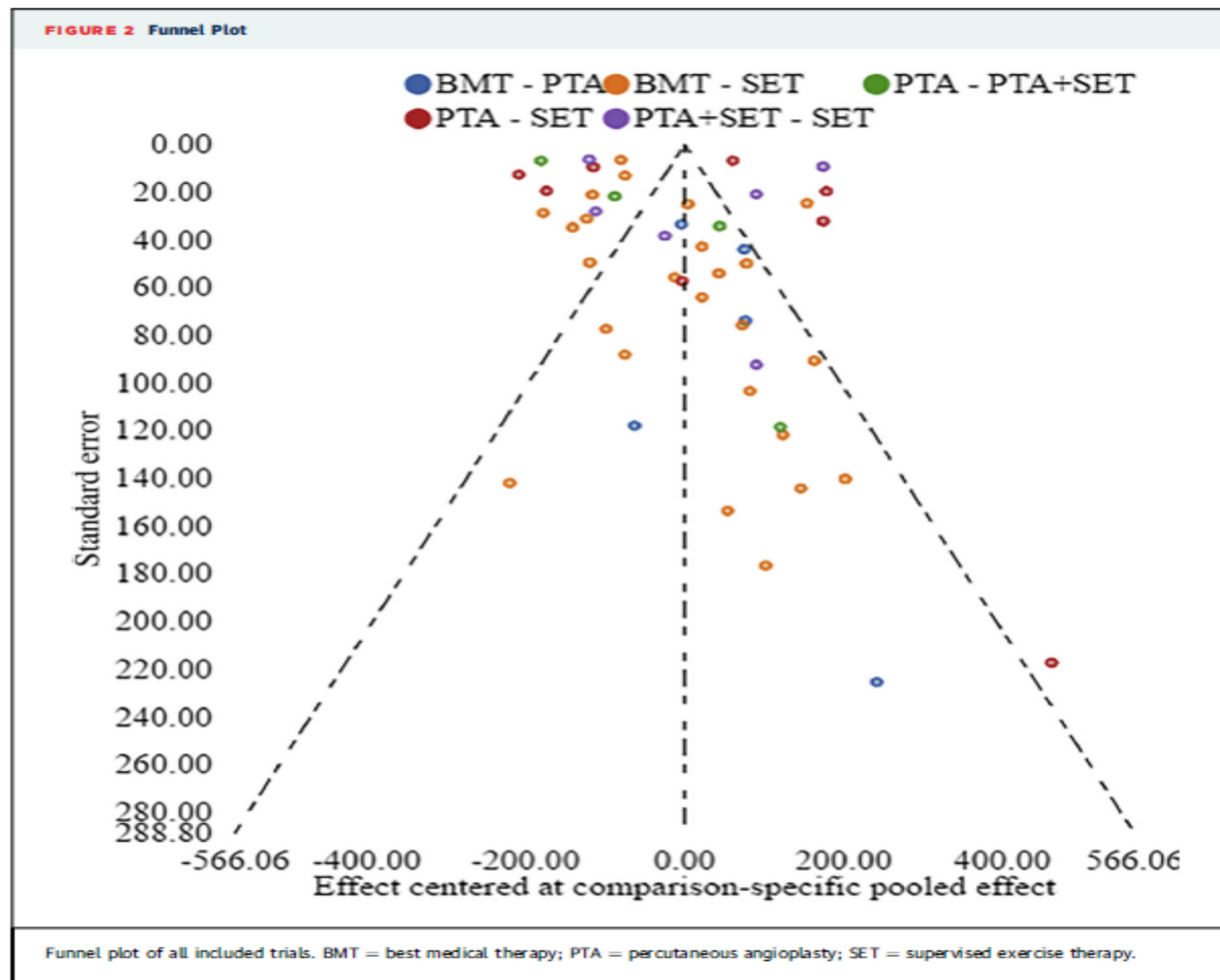
What are the overall results of the review? 這篇回顧呈現了什麼結果？

麼結果？



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

果?



Levels of Evidence

Oxford Centre for Evidence-Based Medicine

2011 Levels of Evidence

Question	Step 1 (Level 1 ⁺)	Step 2 (Level 2 ⁺)	Step 3 (Level 3 ⁺)	Step 4 (Level 4 ⁺)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances ^{**}	Local non-random sample ^{**}	Case-series ^{**}	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards ^{**}	Case-control studies, or "poor or non-independent reference standard" ^{**}	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial [†]	Case-series or case-control studies, or poor quality prognostic cohort study ^{**}	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or n-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study ^{**}	Case-series, case-control studies, or historically controlled studies ^{**}	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, n-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.) ^{**}	Case-series, case-control, or historically controlled studies ^{**}	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or n-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non-randomized controlled cohort/follow-up study ^{**}	Case-series, case-control, or historically controlled studies ^{**}	Mechanism-based reasoning

本臨床情境為治療型問題，為收納 RCT之SR，故等級為level 1

臨床回覆

Evidence

最佳證據等級
現有臨床研究資料

根據目前團隊所搜尋到的最佳證據顯示，ABI為最合適的診斷工具，而侵入型治療以及運動是最能改善預後的治療方式，其證據等級為 level 1。

Expectation

病人期望
偏好、顧慮、期待

擔心手術風險以及藥物治療的效果

Environment

臨床情況
病患的病情及醫院的醫療環境

ABI檢查的安排相較血管攝影以及超音波易於安排，且侵入性為低；藥物治療花費比較低，但是預後比較不佳，而手術雖然能改善預後，但也要考慮相關併發症。

Experience

臨床經驗
本身的臨床技能、經驗、判斷

依據黃先生目前的情況，建議以ABI的結果為優先，但在治療的部份，除了藥物治療之外，可以考慮使用侵入性治療加上運動，能使得預後更好