三軍總醫院
Tri-Service General Hospital

實證醫學競賽

110 / 5 / 11

組別：第 2組

組員：陳怡文、潘蒼嬉、簡潔藥師

臨床場景

- 臨床情境：50yr林先生，HT 175cm，wt 92kg，History:Diabetes。醫師檢查其抽血報告發現林先生的Hb1Ac=10.2%，因此為他加開立Sitagliptin以控制血糖。林先生上網查詢資料，看到Sitagliptin (Januvia®)在網上有造成胰臟炎甚至是胰臟癌的疑慮，並在電視節目上也聽聞肉桂(Cinnamon)有控制血糖的功效。

- 病人詢問藥師：

1. 請問Sitagliptin(Januvia®)真的會造成胰臟炎或胰臟癌嗎？
2. 肉桂(Cinnamon)真的可以降低糖化血色素嗎？
3. 能不要吃醫師加開的Januvia嗎，改吃其他藥物或其他血糖控制方法？

背景資訊

UpToDate®

§ 糖尿病(Diabetes Mellitus type II)（這邊僅討論第二型）

1. 定義：
   由於胰島素抗性不足以及和胰島素相對分泌不足有關，特徵為高血糖。
2. 診斷：
   - 8小時空腹血糖值(FPG)＞126mg/dl
   - OGTT後兩小時血糖值＞200mg/dl
   - Hb1Ac＞6.5%
3. 治療：
   - 口服藥物治療（ex.Metformin, SGLT2i, Sufonylureas……等）
4. 風險因子：
   - 種族/肥胖/飲食習慣（高油高糖）/長期久坐

臨床問題

PICO 1：傷害型問題

	中文	英文
P	糖尿病	Diabetes Mellitus
I	Sitagliptin	
C	Placebo	
O	胰臟炎	Pancreatitis

臨床問題

PICO 2：治療型問題

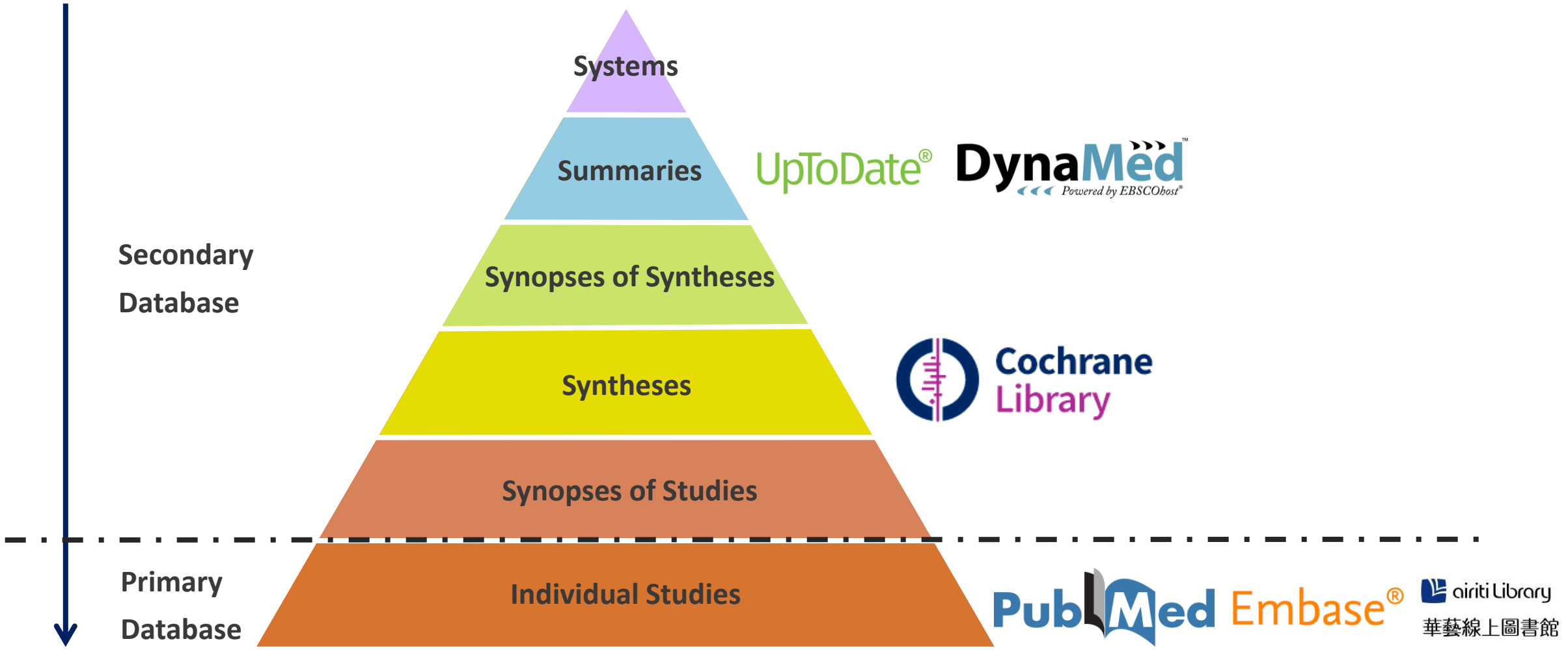
	中文	英文
P	糖尿病	Diabetes Mellitus
I	肉桂	Cinnamon
C	Placebo	
O	糖化血色素	Glycosylated hemoglobin

搜尋策略：關鍵字

選擇PICO 2，原因：我組對於仿間保健食品，並不像一般藥物相對熟悉，希望透過實證資料佐證增進這方面的理解

	中文	關鍵字	同義字
P	糖尿病	Diabetes Mellitus	Diabetes/Diabetic
I	肉桂	Cinnamon/Cinnamon Extract	ceylon cinnamon cinnamomi cortex cinnamomi vericortex
C	Placebo		
O	糖化血色素	Glycosylated hemoglobin	glycated haemoglobin glycated hemoglobin A glycohaemoglobin glycosyl hemoglobin

搜尋策略：資料庫


Systems
Summaries
Synopses of Syntheses
Syntheses
Synopses of Studies
Individual Studies
Secondary Database
Primary Database
UpToDate®
DynaMed
Powered by EBSCOhost
Cochrane Library
PubMed
Embase®
airiti Library
華藝線上圖書館

搜尋策略：布林邏輯

P	I	C	O
Diabetes Mellitus	Cinnamon OR Cinnamon Extract	Placebo	Glycosylated hemoglobin

搜尋策略：總論

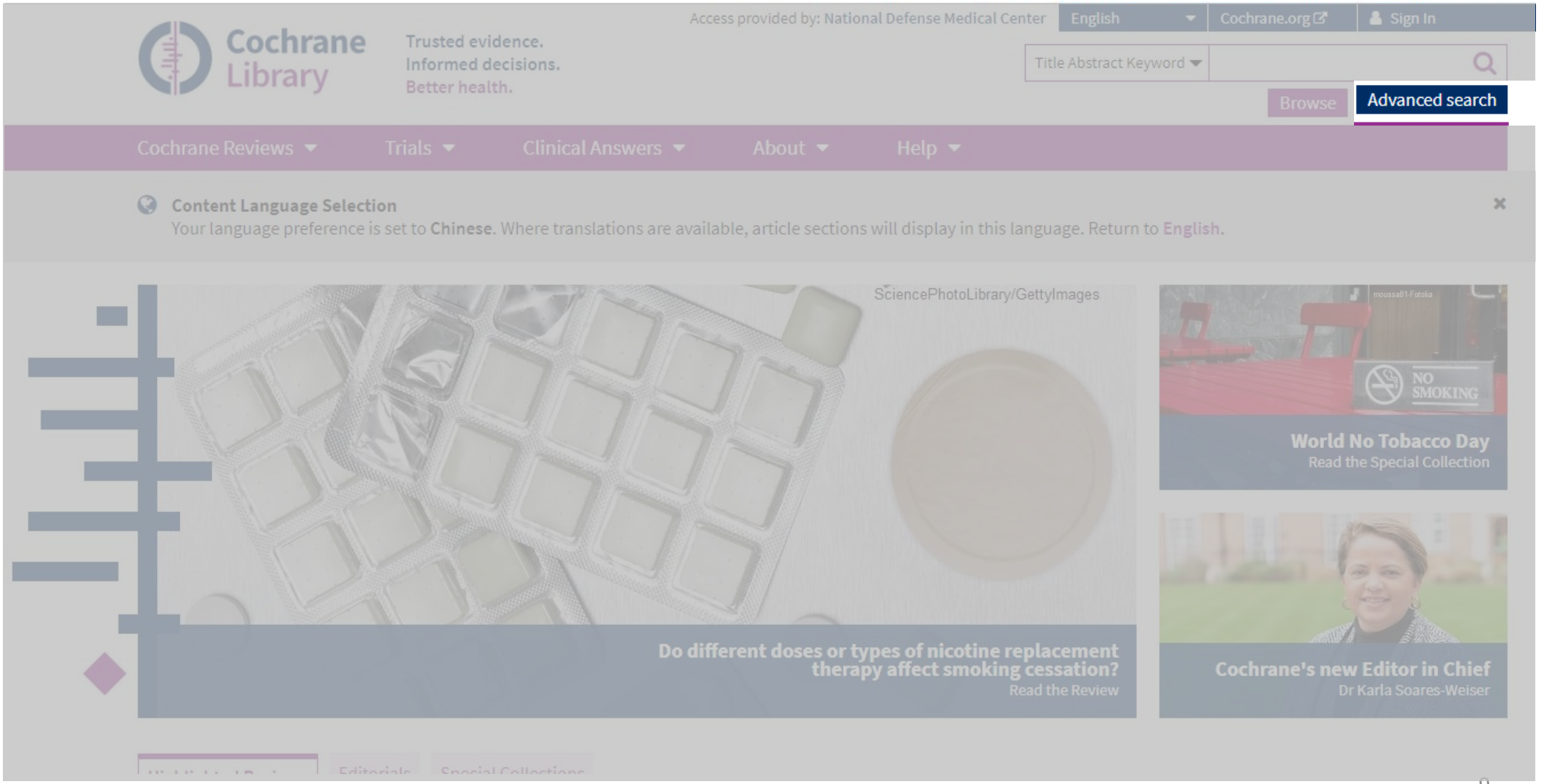
- 關鍵字

布林邏輯　　P&I搜尋　　依結果搜尋其他關鍵字

- 順序：列為欲評讀文獻

1. Systematic Review
2. Randomized Controlled Trial
3. Cohort Study

Secondary Database: Cochrance Library

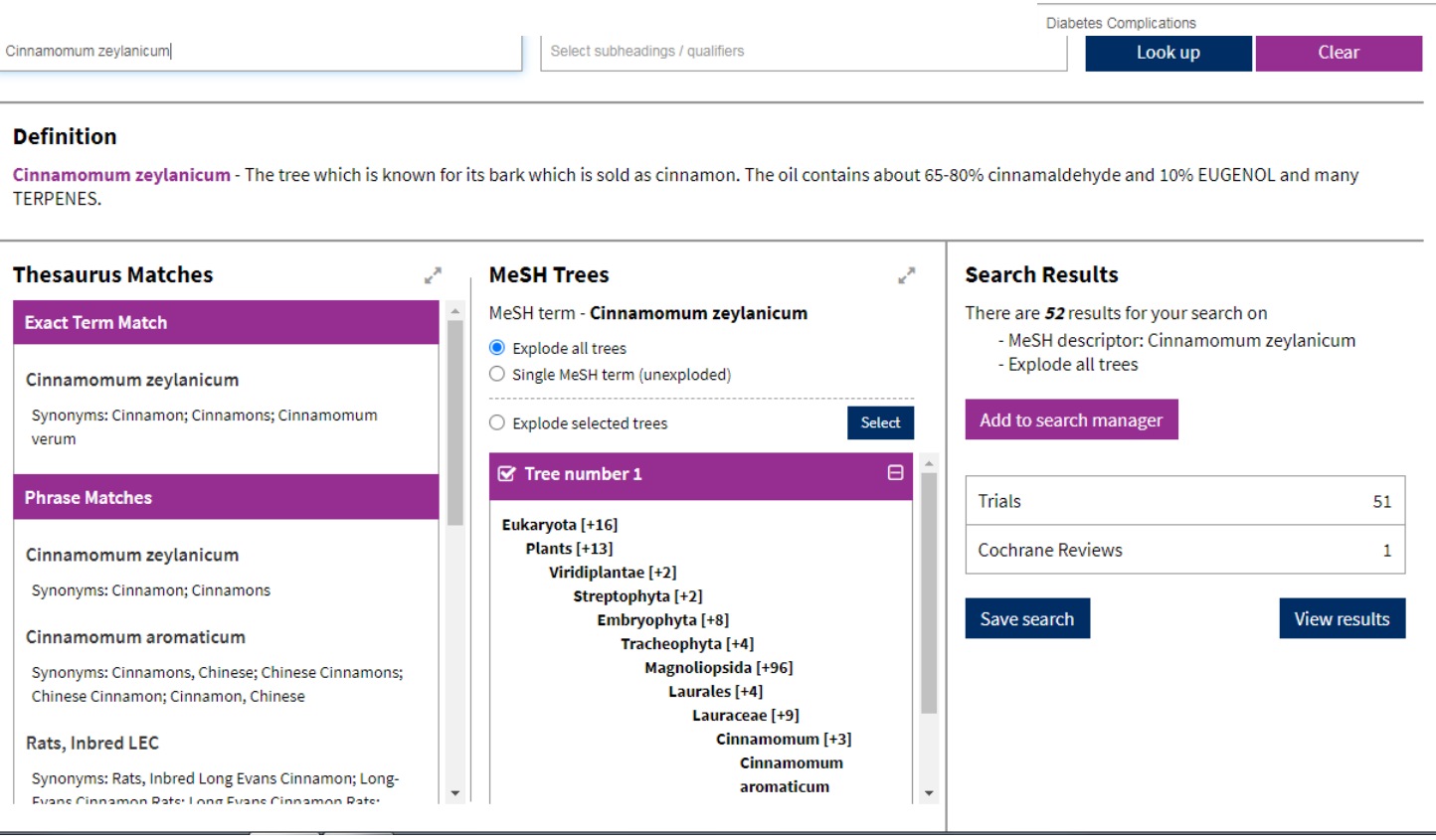


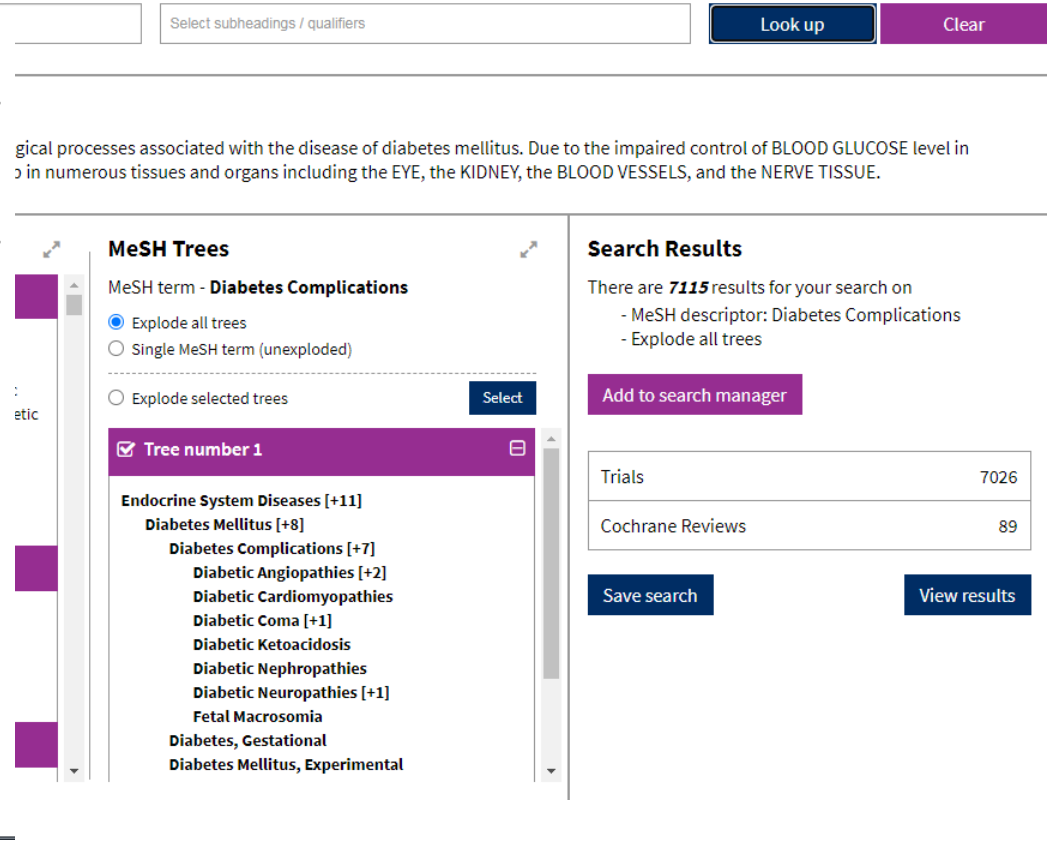
檢索
ACQUIRE

Secondary Database: Cochrance Library

關鍵字：cinnamon. diabetss

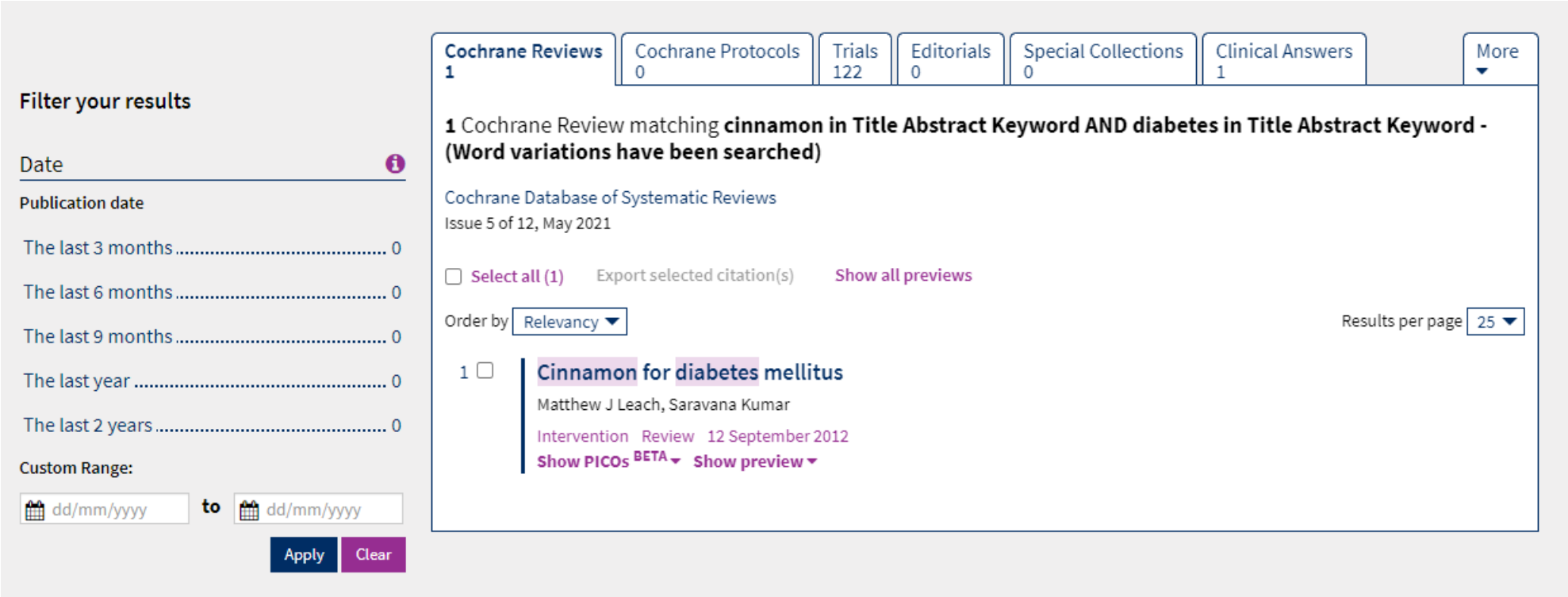
1. 使用Search Manager 搜尋
2. 加入布林邏輯 AND與OR 作搜尋連結
3. Search limit：未限制年份、語言



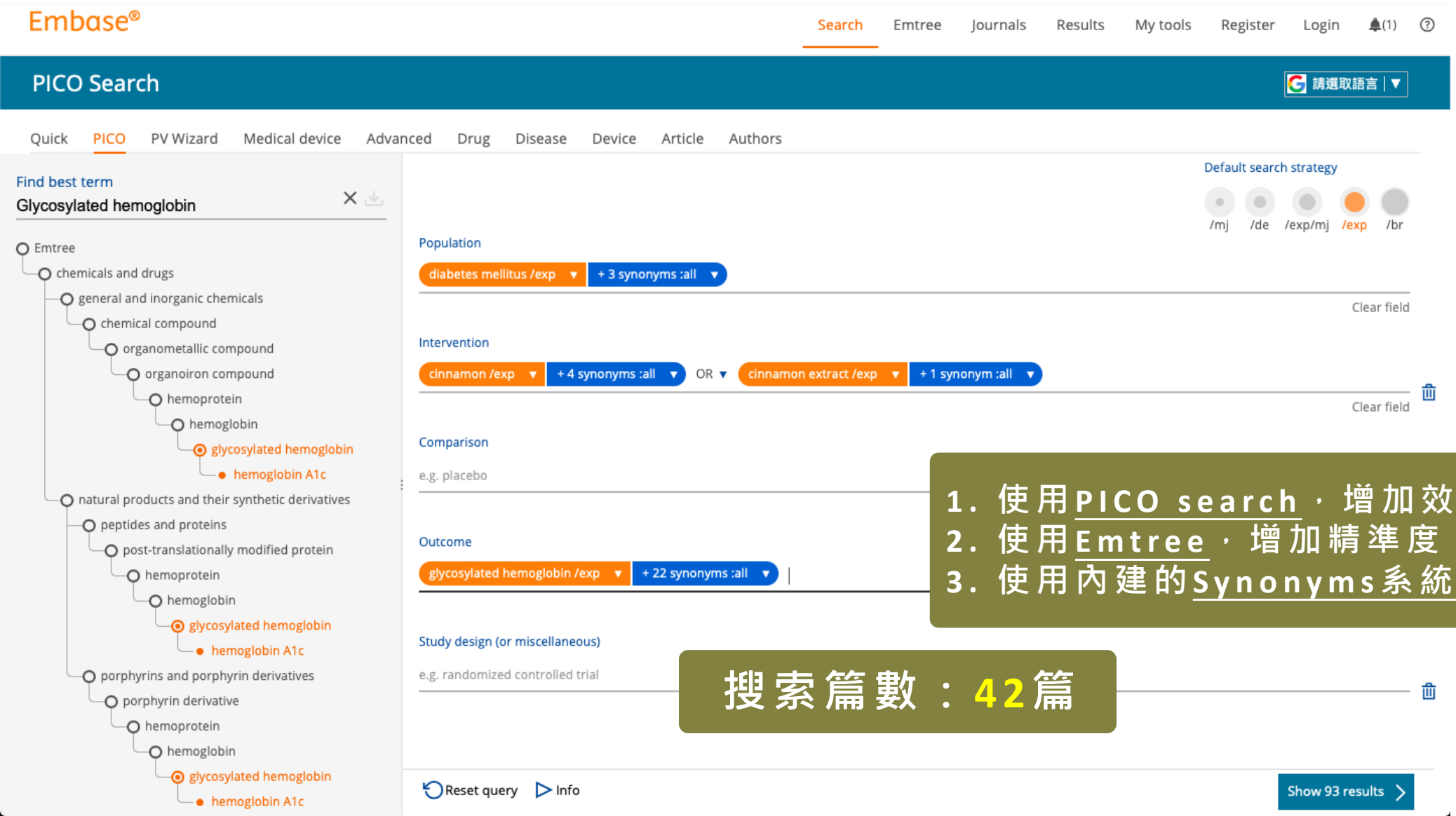


Secondary Database: Cochrance Library

搜索結果：



Primary Database: Embase



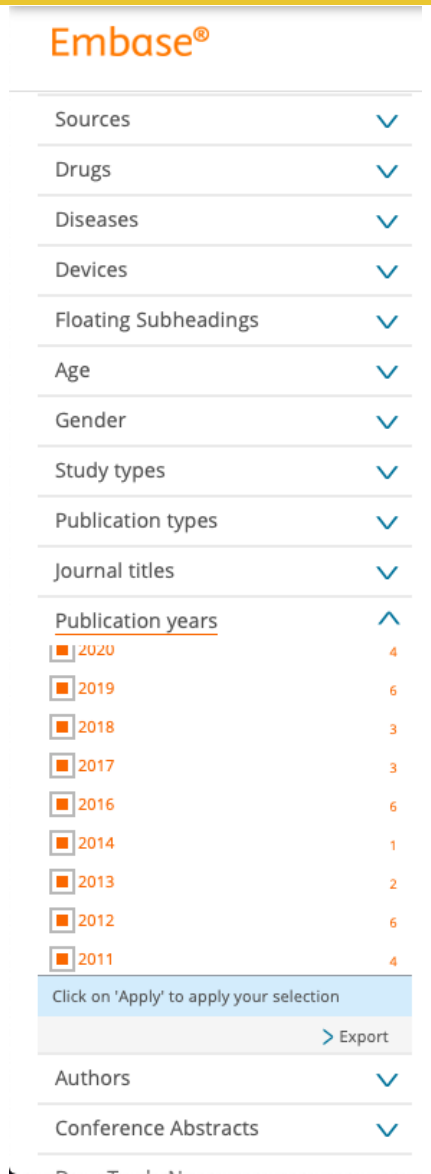
1. 使用PICO search，增加效率
2. 使用Emtree，增加精準度
3. 使用內建的Synonyms系統，增加搜尋廣度

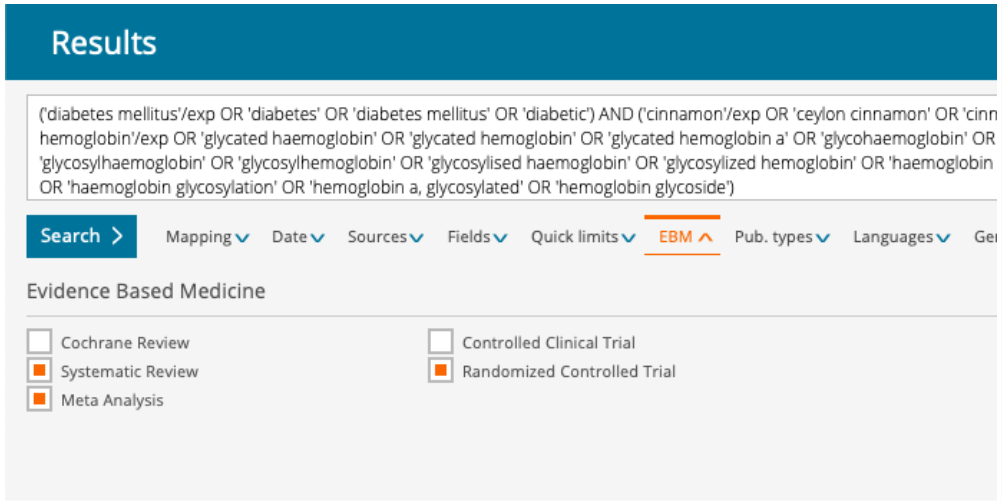
搜索篇數：42篇

檢索
ACQUIRE

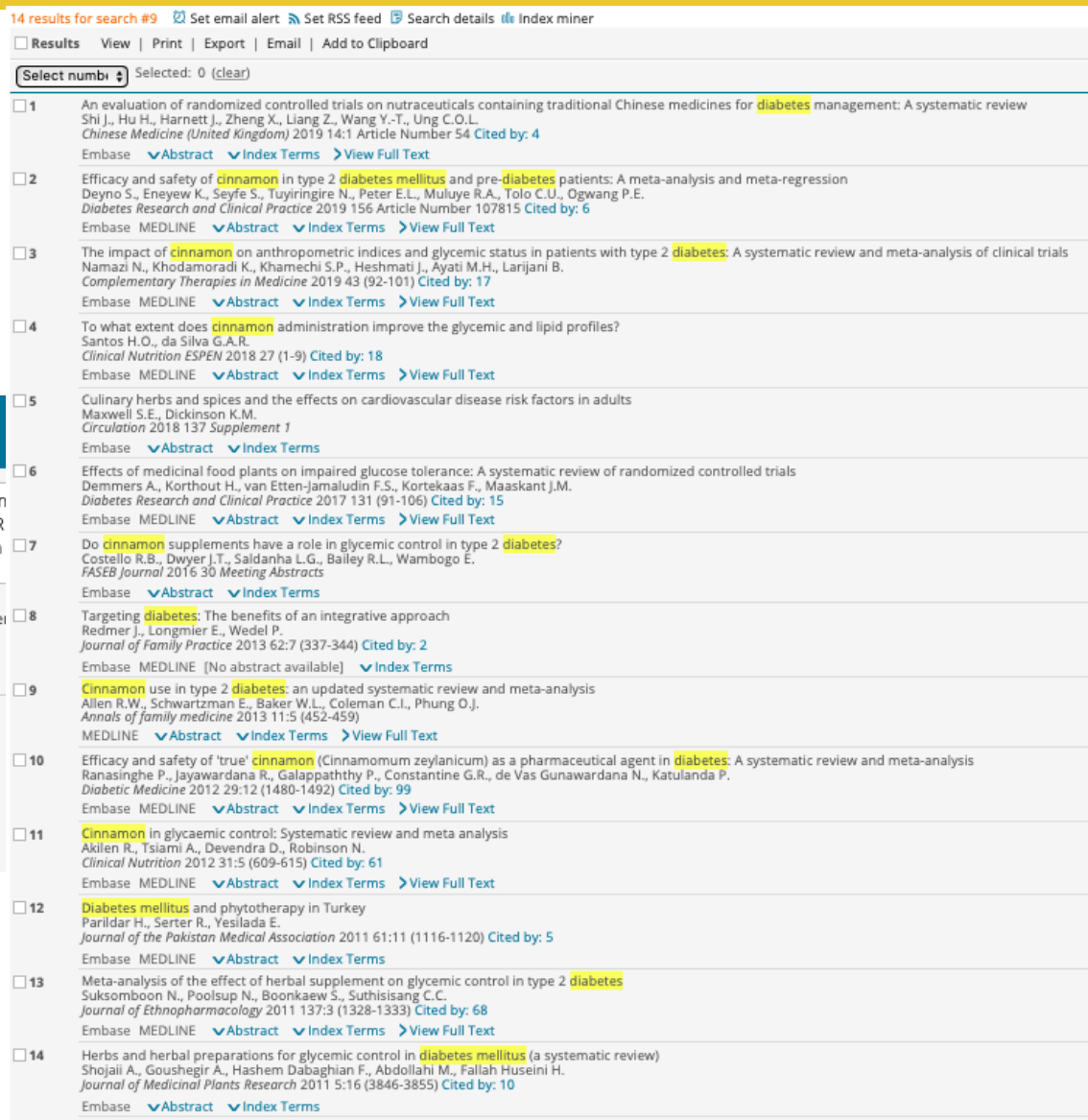
Primary Database: Embase

1. 使用Filter和Limit
   - 限縮文獻種類
   - 限縮年份為10年內

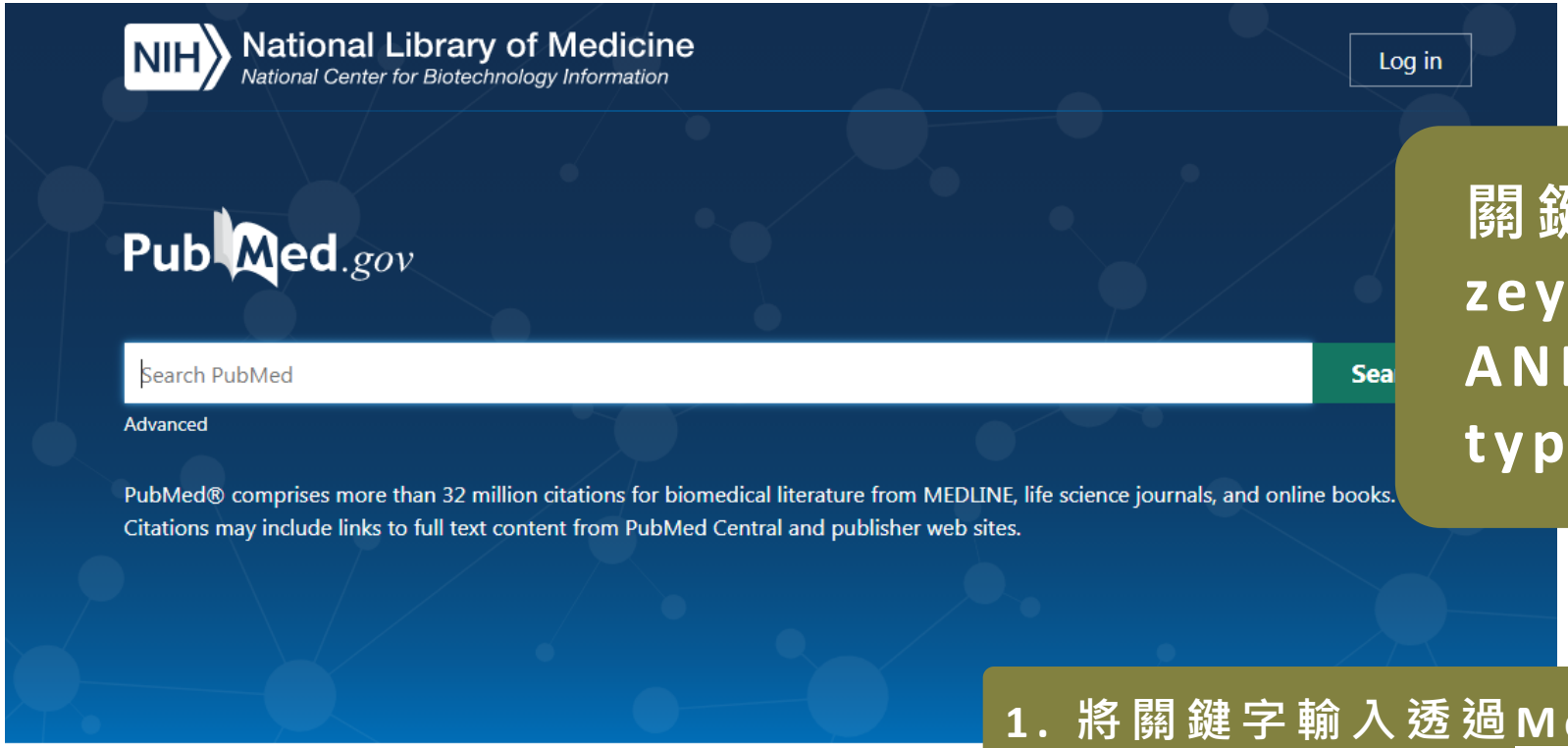




搜索篇數：14篇



Primary Database: PubMed

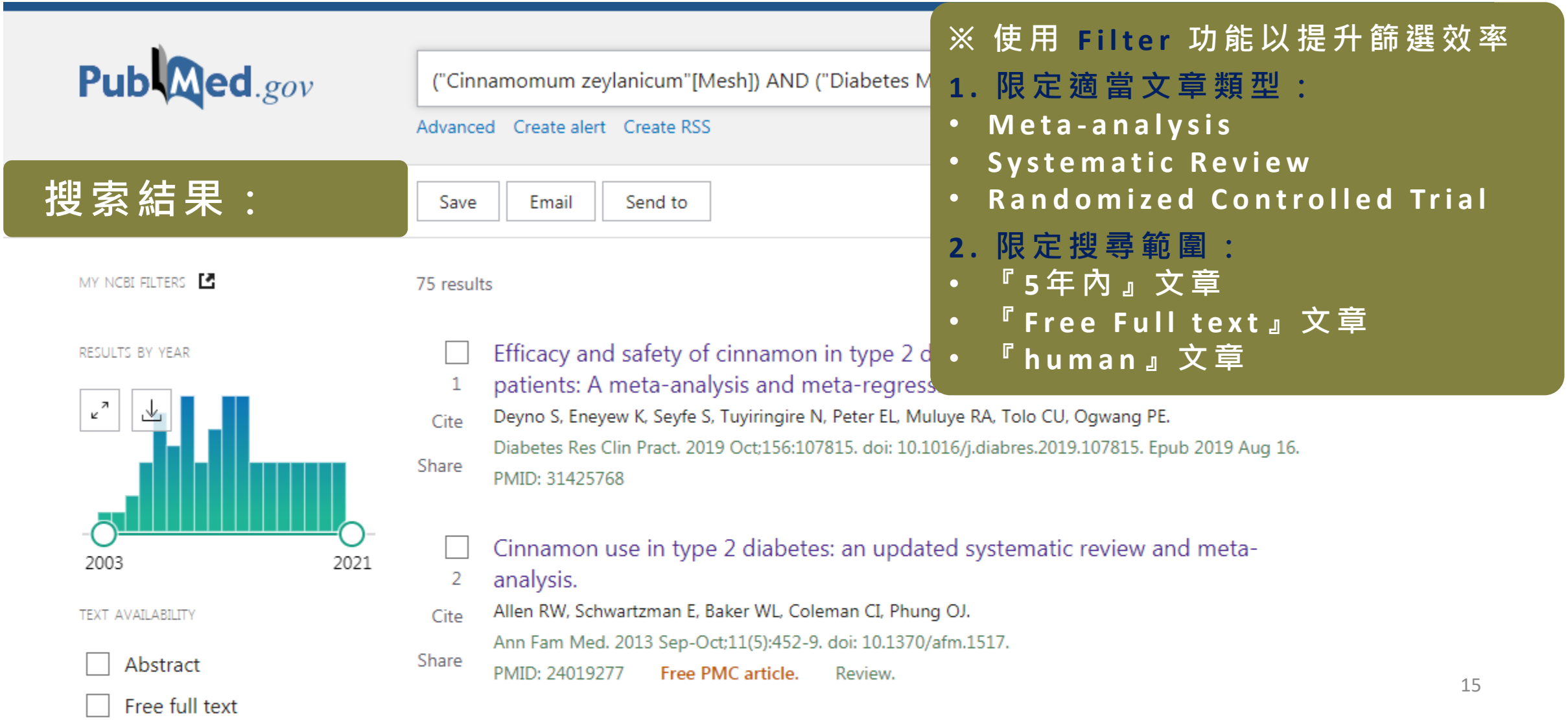


關鍵字：
"Cinnamomum zeylanicum"[MeSH Terms] AND "diabetes mellitus, type 2"[MeSH Terms]

1. 將關鍵字輸入透過MeSH找出最適當之Medical Terms
2. 利用布林邏輯篩選文獻搜尋分類
3. 使用Clinical Queries檢索分類

Primary Database: PubMed

搜索結果：



※ 使用 Filter 功能以提升篩選效率

1. 限定適當文章類型：
   - Meta-analysis
   - Systematic Review
   - Randomized Controlled Trial
2. 限定搜尋範圍：
   - 『5年內』文章
   - 『Free Full text』文章
   - 『human』文章

Primary Database: 華藝線上圖書館

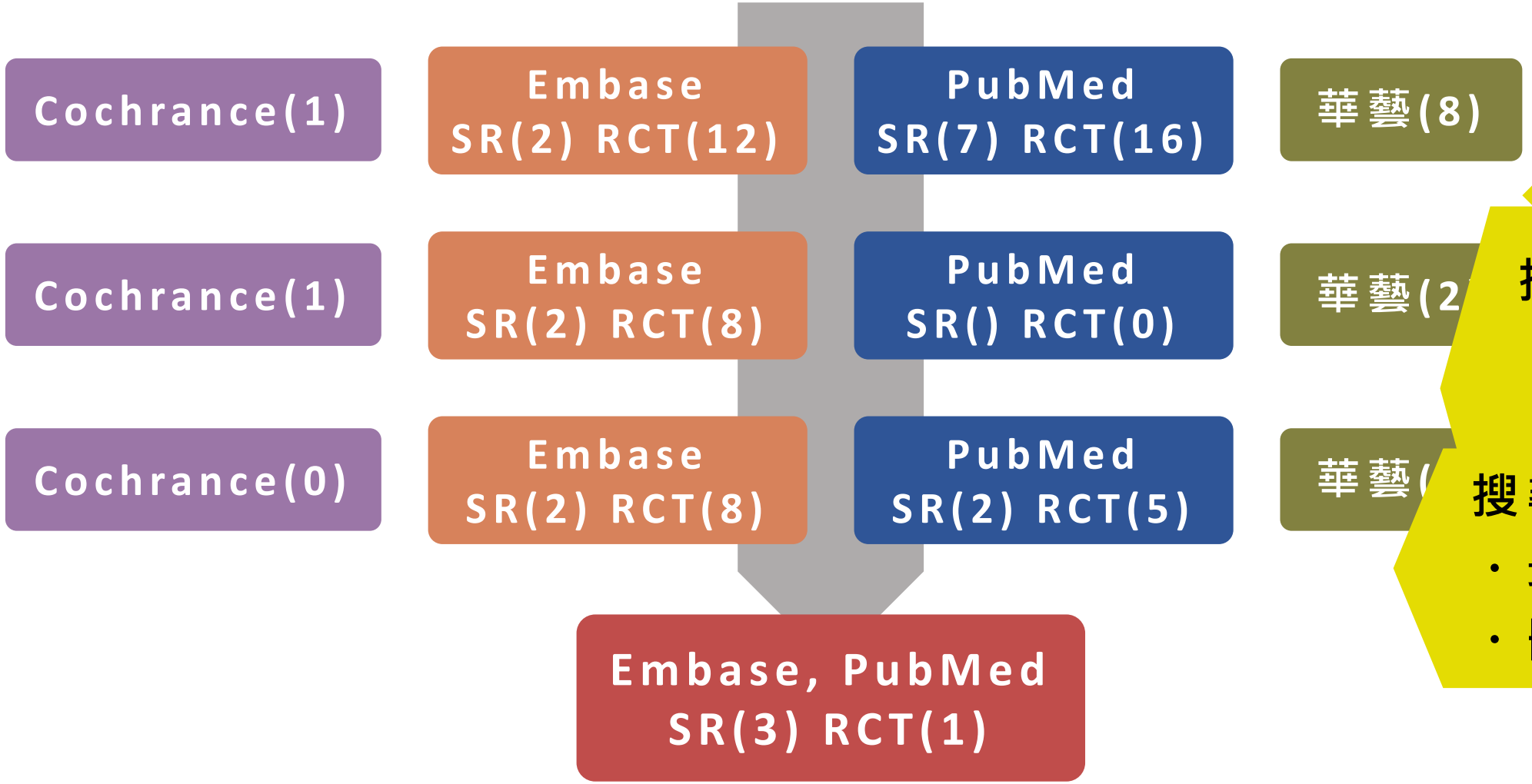
關鍵字：

1. 進階檢索、中文關鍵字
2. 布林邏輯連接關鍵字
3. 限定十年內

Primary Database: 華藝線上圖書館

搜索結果：

篩選結果



符合場景

搜尋條件1：

- 有全文
- 與PICO相符

搜尋條件2：

- 最佳證據等級
- 刪除重複文章

文章篩選

標題	年份
Efficacy and safety of cinnamon in type 2 diabetes mellitus and pre-diabetes patients: A meta-analysis and meta-regression	2019
The impact of cinnamon on anthropometric indices and glycemic status in patients with type 2 diabetes: A systematic review and meta-analysis of clinical trials	2019
Cinnamon use in type 2 diabetes: an updated systematic review and meta-analysis	2013
Controlling type 2 diabetes mellitus with herbal medicines: a triple-blinded randomized controlled trial of efficacy and safety	2016

文章篩選

標題	P	I	C	O
Efficacy and safety of cinnamon in type 2 diabetes mellitus and pre-diabetes patients: A meta-analysis and meta-regression	●(部分)	●	●	●
The impact of cinnamon on anthropometric indices and glycemic status in patients with type 2 diabetes: A systematic review and meta-analysis of clinical trials	●	●	●	●
Cinnamon use in type 2 diabetes: an updated systematic review and meta-analysis	●	●	●	●
Controlling type 2 diabetes mellitus with herbal medicines: a triple-blinded randomized controlled trial of efficacy and safety	●	●	●	×

篩選結果

Contents lists available at ScienceDirect

Complementary Therapies in Medicine

journal homepage: www.elsevier.com/locate/ctim

The impact of cinnamon on anthropometric indices and glycemic status in patients with type 2 diabetes: A systematic review and meta-analysis of clinical trials

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[b] Department of Nursing, Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran
[c] School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran
[d] Department of Nutrition, School of Public Health, Iran University of Medical Sciences, Tehran, Iran
[e] Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Keywords:
Cinnamon
T2DM
Glycemic parameters
Metabolic status

ABSTRACT

Background and aims: There is some evidence regarding the positive effects of cinnamon on metabolic status in patients with type 2 diabetes (T2DM). However, they are conflicting. In the present study, we aimed to systematically review the effects of cinnamon on glycemic status and anthropometric indices in patients with T2DM.

Methods: Five electronic databases including PubMed/Medline, SCOPUS, Web of Sciences, EMBASE, and the Cochrane library were searched until 31 February 2018 with no language limitation. Randomized clinical trials that examined the effects of cinnamon on at least fasting blood sugar (FBS) were included. Other glycemic parameters and anthropometric indices were also extracted. A random effects model with DerSimonian and Laird method was used for pooling the effect sizes.

Results: Finally, 18 studies were included in the meta-analysis. Supplementation with cinnamon reduced FBS by −19.26 mg/dL (95% CI: −28.08, −10.45; I^2:96.5%; p = 0.0001) compared to placebo. However, the effects of cinnamon on HbA1C (−0.24%; 95% CI: −0.48, −0.01; I^2: 76.8%, p = 0.0001), body weight (−0.46, 95%CI: −1.87, 2.30; I^2:0%; p = 0.79), body mass index (WMD: −0.05 kg/m2; 95% CI: −0.52, 0.42; I^2: 0%; p = 0.91), and waist circumference (WMD: −0.53 cm; 95% CI: −3.96, 2.81; I^2: 0%; p = 0.66) were not significant. Additionally, cinnamon did not change the serum levels of insulin and insulin resistance significantly.

Conclusion: Supplementation with cinnamon can reduce serum levels of glucose with no changes in other glycemic parameters and anthropometric indices. However, due to high heterogeneity findings should be interpreted with great caution.

《文獻納入理由》

- 年份
- 族群
- 符合PICO

我們的文獻工具是CASP SR Critical Appraisal Tool 2018

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

● YES ● NO ● CAN'T TELL

Table 1
PICO criteria for the present systematic review.

PICO	Descriptors
Participants:P	Adult subjects with type 2 diabetes
Intervention: I	Cinnamon OR Cinnamons OR Cinnamomum verum OR Cinnamomum zeylanicum OR Cinnamomum OR Ceylon cinnamon
Comparision: C	Placebo group
Outcome: O	Weight OR "BMI" OR Body mass index OR Quetelet OR Glucose OR Sugar OR FBS OR Insulin OR HOMA-IR OR "insulin resistance" OR QUICKI OR "insulin sensitivity" OR HbA1c OR Diabetes OR Diabetic OR DM

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

● YES ○ NO ○ CAN'T TELL

	此篇研究	臨床情境	是否相符
P	Adult subjects with type 2diabetes	55 y/o Male ,DM ,overweight(BMI=30), Poor blood sugar control	● YES ○ NO
I	Cinnamon OR Cinnamons OR Cinnamomum verum OR Cinnamomum zeylanicum OR Cinnamomum OR Ceylon cinnamon	cinnamon	● YES ○ NO
C	Placebo group	Placebo group	● YES ○ NO
O	Weight OR "BMI" OR Body mass index OR Quetelet OR Glucose OR Sugar OR FBS OR Insulin OR HOMA-IR OR "insulin resistance" OR QUICKI OR "insulin sensitivity" OR HbA1c OR Diabetes OR Diabetic OR DM	HbA1c. FBG.	● YES ○ NO

文章之PICO搜尋，與病人之PICO相符合

Table 1
PICO criteria for the present systematic review.

PICO	Descriptors
Participants:P	Adult subjects with type 2 diabetes
Intervention: I	Cinnamon OR Cinnamons OR Cinnamomum verum OR Cinnamomum zeylanicum OR Cinnamomum OR Ceylon cinnamon
Comparision: C	Placebo group
Outcome: O	Weight OR "BMI" OR Body mass index OR Quetelet OR Glucose OR Sugar OR FBS OR Insulin OR HOMA-IR OR "insulin resistance" OR QUICKI OR "insulin sensitivity" OR HbA1c OR Diabetes OR Diabetic OR DM

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

● YES ● NO ● CAN'T TELL

Inclusion	Exclusion
The primary outcome for the present study was the effects of supplementation with cinnamon on FBS concentrations. Therefore, when any paper did not report this parameter, even if it reported other glycemic status and anthropometric indices, it was not included. Other inclusion criteria were as follows: (i) randomized clinical trials (parallel or cross-over design), (ii) existence of a placebo group, (iii) included adult subjects, (iv) examined the effects of cinnamon on at least FBS at baseline and at the end of the trial in both intervention and placebo groups, (v) examined T2DM, and (vi) examined any form of cinnamon (whole herb not effective components). Additionally, papers reported sufficient information including mean or mean differences with standard deviation (SD), standard error (SE) or 95% confidence intervals (95% CI) were included. Papers were excluded if they had any study	(95% CI) were included. Papers were excluded if they had any study design other than clinical trials such as animal or in vitro/In vivo studies, (ii) before-after studies, (iii) examined other types of diabetes, diseases or healthy subjects, (iv) examined effective components of cinnamon or food/beverages with added cinnamon, (v) in combination with other herbal or non-herbal ingredients, (vi) include children/adolescent (younger than 18 years old), and (vii) athletes.
欲探討肉桂cinnamon對糖尿病之功效，屬於介入型問題，本篇文獻有包含RCT的文章 包含之項目如type 2 DM. FBG. Hb1AC均與討論之個案相關	排除之項目如: 含有動物實驗、其他類型的糖尿病等等

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

● YES ● NO ● CAN'T TELL

Table 2
Characteristics of the included papers in the systematic review.

Author/ Year	Location	Study design	Gender (Male/ Female)	Mean age	Sa
Zare et al (2018)	Iran	R/P triple	both	52.6	1:
Zahedifar et al (2018)	Iran	R/P double	Both	54.6	5:
Talaei et al (2017)	Iran	R/P double	Both	57	3:
Sengsuk et al (2016)	Thailand	R/P double	Both	57	9:
Tangvarasittichai et al (2015)	Thailand	R/P double	Both	57	1(
Azimi et al (2014)	Iran	R/P Single	Both	53.8	7:
Mirfeizi et al (2014)	Iran	R/P triple	Both	> 18	7:
Hasanzadeh et al (2013)	Iran	R/P double	Both	54.3	7(
Vafa et al (2012)	Iran	R/P double	Both	55	3:
Lu et al (2012)	China	R/P double	Both	61	4:
Zahmatkesh et al (2012)	Iran	R/P double	Both		5:
Haghighian et al (2011)	Iran	R/P double	Both	56.8	6(
Akilen et al (2010)	England	R/P Single	Both	55	5:
Otto et al (2010)	USA	R/P double	Both	46	2:
Blevins et al (2007)	USA	R/P double	Both	60.8	5:
Mang et al (2006)	Germany	R/P double	Both	63	6:
Vanschoonbeek et al (2006)	Netherland	?R/P double	Female	62.5	2:
Khan et al (2003)	Pakistan	R/P/ double	Both	> 40 years	2(

R/P: Randomized placebo.

Table 2
Characteristics of the included papers i

Author/ Year	Location		Adjustment	Side effects	Type of Cinnamon	Quality score
Zare et al (2018)	Iran					
Zahedifar et al (2018)	Iran					
Talaei et al (2017)	Iran	er	No	No	Not clear	3
Sengsuk et al (2016)	Thailand	er	No	No	Not clear	2
Tangvarasittichai et al (2015)	Thailand	er	No	No	C. cassia	4
Azimi et al (2014)	Iran	er	No	No	Not clear	5
		er	No	No	c.cassia	5
Mirfeizi et al (2014)	Iran	er				
Hasanzadeh et al (2013)	Iran					
Vafa et al (2012)	Iran	er	No	No	c.cassia	3
Lu et al (2012)	China	er	No	No	Not clear	2
Zahmatkesh et al (2012)	Iran	t	No	No	Not clear	2
Haghighian et al (2011)	Iran	er	No	No	Not clear	3
Akilen et al (2010)	England	er	No	No	Not clear	2
		er	Yes, covariates were not clear	No	C. cassia	5
Otto et al (2010)	USA	us	Not clear	Not clear	Not clear	2
Blevins et al (2007)	USA	t				
Mang et al (2006)	Germany	er	No	Not clear	c.cassia	2
Vanschoonbeek et al (2006)	Netherlan	er	No	No	Not clear	2
			No		C. cassia	3
Khan et al (2003)	Pakistan	er	No	No	C. cassia	1

R/P: Randomized placebo.

有包含各種國家之研究
亞洲(伊朗. 中國.泰國. US. UK. 德國等等)

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

● YES ● NO ● CAN'T TELL

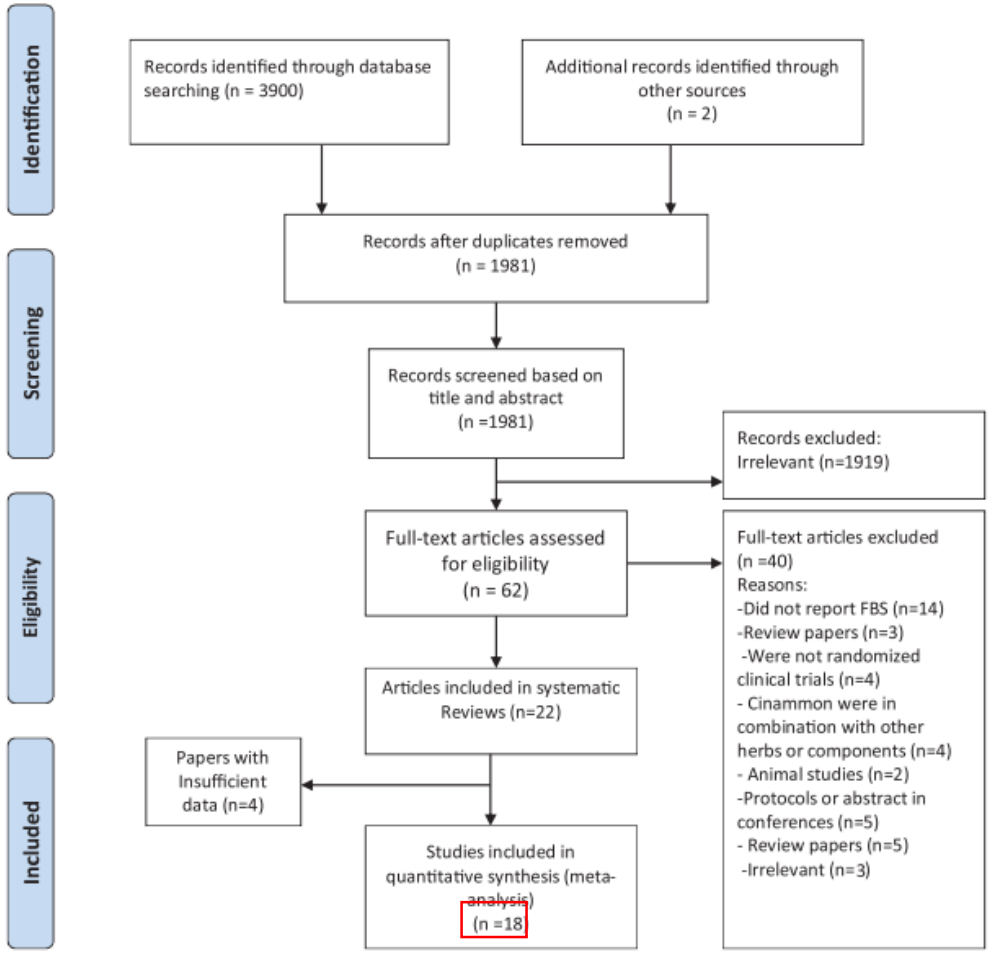

Fig. 1. Procedures of study selection.

依 PRISMA statement，作者只收納證據等級較高的 SR 文章，共有18篇。

優點：

- 作者排除非RCT為主軸之文章
- 作者搜尋了重要一級和二級資料庫。
- 有清楚列出納入及排除文章之理由
- 沒有研究設計限制。

2.1. Search strategy

The current systematic review and meta-analysis was designed and conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.[27]

At the first step, PICOS criteria were defined as represented in Table 1. In the next step, five main electronic databases including PubMed/Medline, SCOPUS, Web of Sciences, EMBASE, and the Cochrane library were searched by two independent reviewers (N.N, J.H). Search was restricted to papers published between January 2000 and 31 February 2018 with no language limitation. Details of search strategies containing both medical subject headings (MeSH) and non-medical subject heading key terms for each database are provided in Appendix S1.

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

● YES ● NO ● CAN'T TELL

2.1. Search strategy

The current systematic review and meta-analysis was designed and conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.[27]

At the first step, PICOS criteria were defined as represented in Table 1. In the next step, five main electronic databases including PubMed/Medline, SCOPUS, Web of Sciences, EMBASE, and the Cochrane library were searched by two independent reviewers (N.N, J.H). Search was restricted to papers published between January 2000 and 31 February 2018 with no language limitation. Details of search strategies containing both medical subject headings (MeSH) and non-medical subject heading key terms for each database are provided in Appendix S1.

1. 搜尋的資料庫(大於2個)
- PubMed/Medline
- SCOPUSWeb of Sciences
- EMBASE
- the Cochrane library

2. 有使用MeSH term
3. 搜尋時沒語言限制

4. 未收錄未發表或是會議相關的文章

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？

● YES ● NO ● CAN'T TELL

After identification of eligible papers, the two reviewers (P.Kh, K.Kh) independently extracted the following characteristics based on the pre-defined form: first author's name, publication year, country, study design, randomization, blinding, sample size (after drop out), gender, mean age, dosage, form of supplement (extract, powder, etc) and placebo, duration of the intervention, participant's status,

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were considered, not other intervention groups. Any discrepancies in the extracted characteristics were resolved by the third investigator (H.A).

1. 全文由兩位評審員（P.Kh和K.Kh）獨立評估
2. 若以上兩者意見相左，則諮詢第三評審員（H.A)來解決分歧

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？

● YES ● NO ● CAN'T TELL

2.4. Quality assessment

The methodological quality assessment of the eligible papers was examined using the Jadad checklist [28] using two reviewers independently (N.N, K.KH). The Jaded scale contains items relevant to random assignment (2 items), blindness (2 items), and the flow of participants (1 item). The maximum score is five. Papers with at least 3 scores considered as high quality papers. Any discrepancies were also resolved by the third reviewer (B.L).

用Jadad score評估文章品質(quality)，其總分為5分
至少要3分以上才算品質好，本篇SR有達到其分數

3.4. Publication bias & sensitivity analysis

Funnel plot showed no publication bias for FBS and HbA1c that was confirmed with Begg's test. Based on Begg's test, there was no publication bias for FBS concentrations (p = 0.28) and HbA1c (p = 0.78). Besides, no publication bias was existed for body weight (p = 0.51) and BMI (p = 0.52) (Egger's regression test). Based on sensitivity analysis, excluding no clinical trial changed the pooled effect sizes.

本篇Funnel plot及Begg's tests 計算publication bias，然p值均>0.05
[FBS concentrations (p = 0.28) and HbA1c (p = 0.78).]

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？

● YES ○ NO ○ CAN'T TELL

Heterogeneity was assessed by Cochran's Q test and the I^2 test. I^2 > 50% was assumed as high heterogeneity. To find the parameters induced heterogeneity, subgroup analysis was conducted, if possible. The possibility of subgroup analysis means the existence of at least two trails in each category of age, gender, adjustment, dosage, duration of the intervention, location, quality, and species of cinnamon. To assess the effect of each study on the pooled effect estimate, sensitivity analysis was conducted.

Potential publication bias was identified using the funnel plot, Begg's rank correlation (existence of more than 10 studies) and Egger's regression tests (existence of fewer than 10 studies). When there was a publication bias, "trim and fill" methods were used to correct the pooled estimates. All statistical analysis was performed using STATA version 11.0 (Stata Corp, College Station, TX). P values less than 0.05 were considered statistically significant.

parameters and anthropometric indices were also extracted. A random effects model with DerSimonian and Laird method was used for pooling the effect sizes.

1. 使用Cochrane Q's test & I^2 test來分析研究間的異質性 (heterogeneity)。
2. 整體結果異質性大，本篇採用random-effects model進行meta-analysis是合理的(異質性 >25%)。

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？

● YES ● NO ● CAN'T TELL

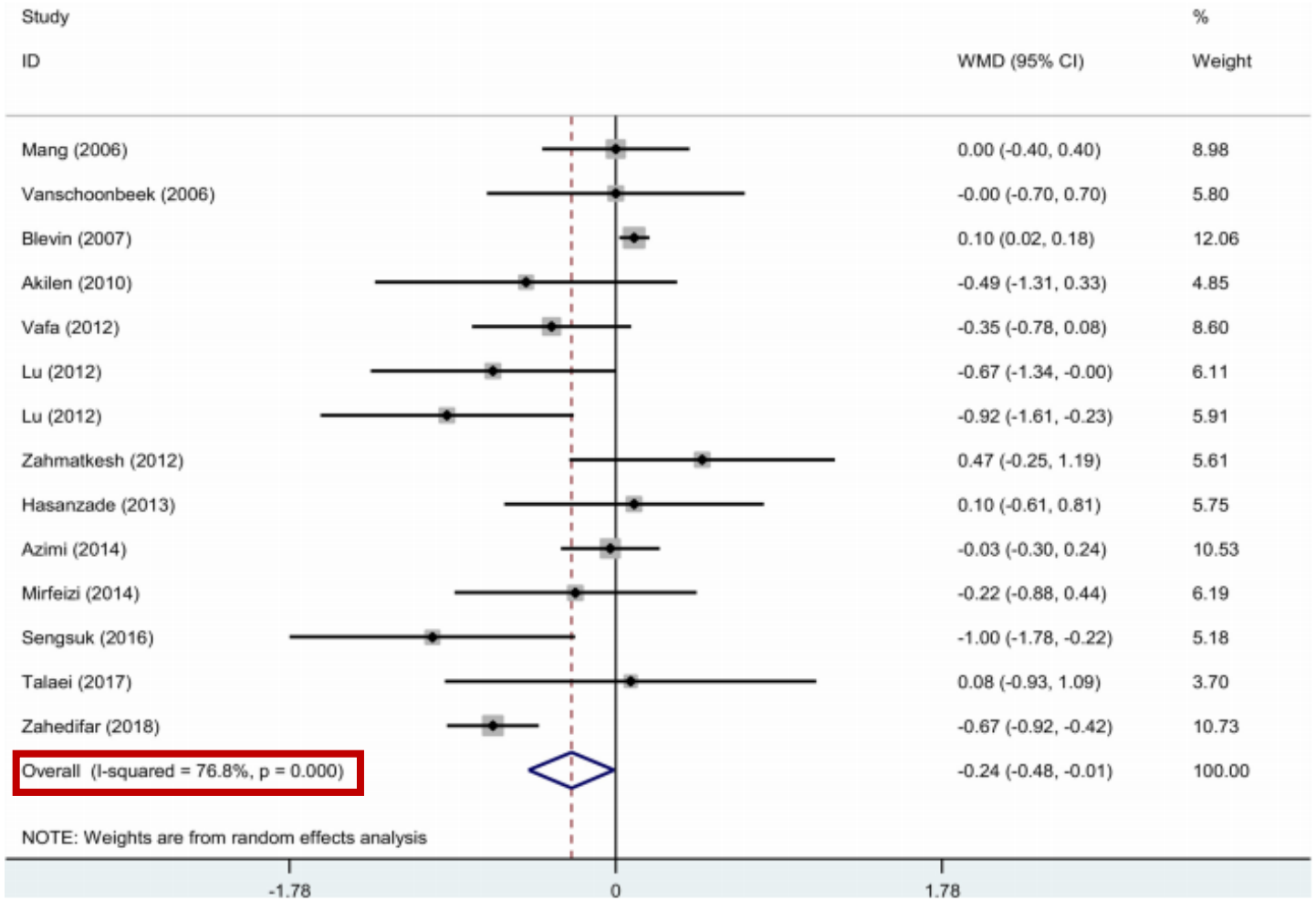


Fig. 3. Forest plot for the effects of supplementation with cinnamon on HbA1c.

<cinnamon on Hb1Ac>
I^2=76.8%, p=0.000
異質性高

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？

● YES ● NO ● CAN'T TELL

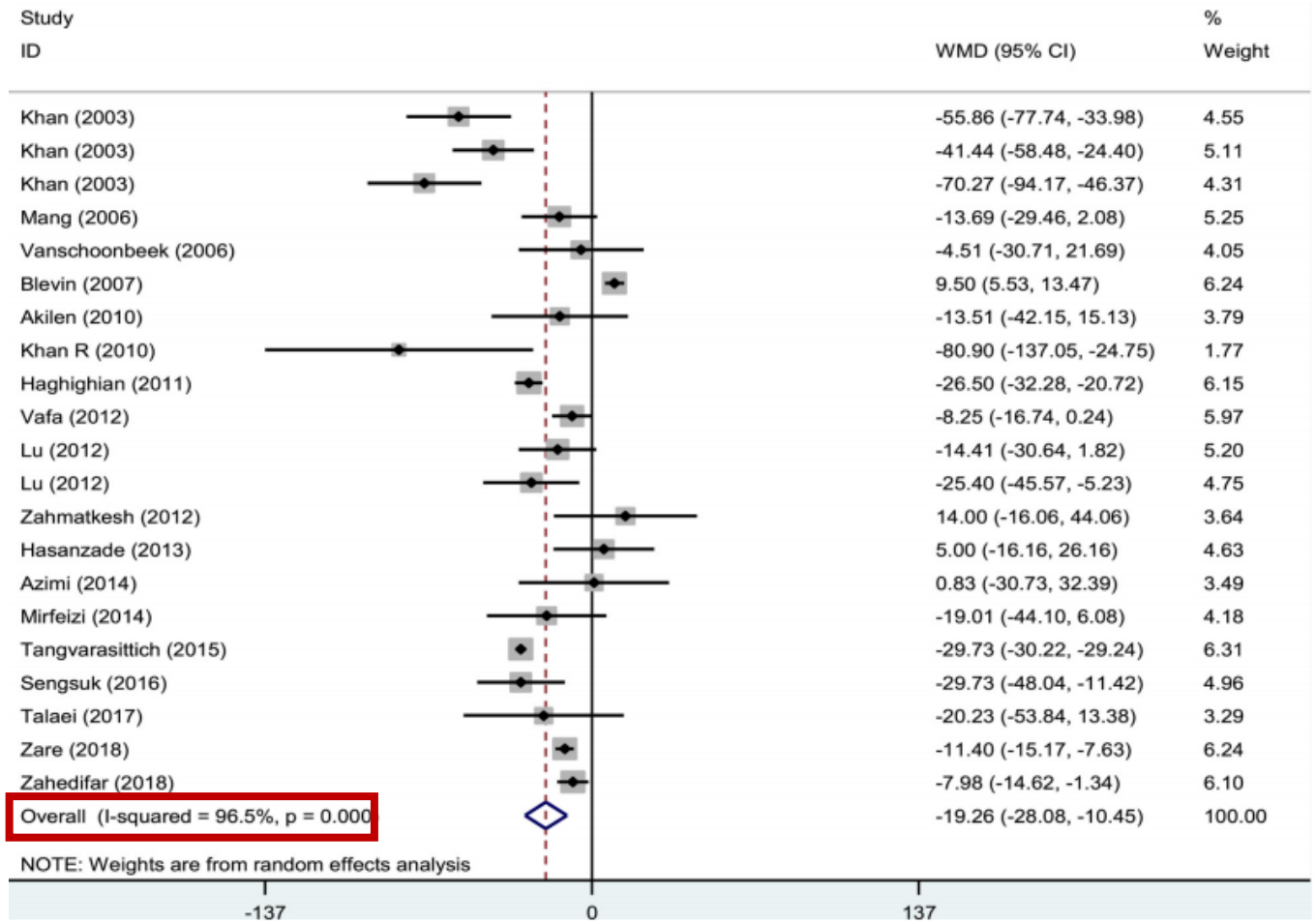


Fig. 2. Forest plot for the effects of supplementation with cinnamon on fasting blood sugar.

<cinnamon on FBS>
I^2=96.5%, p=0.000
異質性高

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？

● YES ● NO ● CAN'T TELL

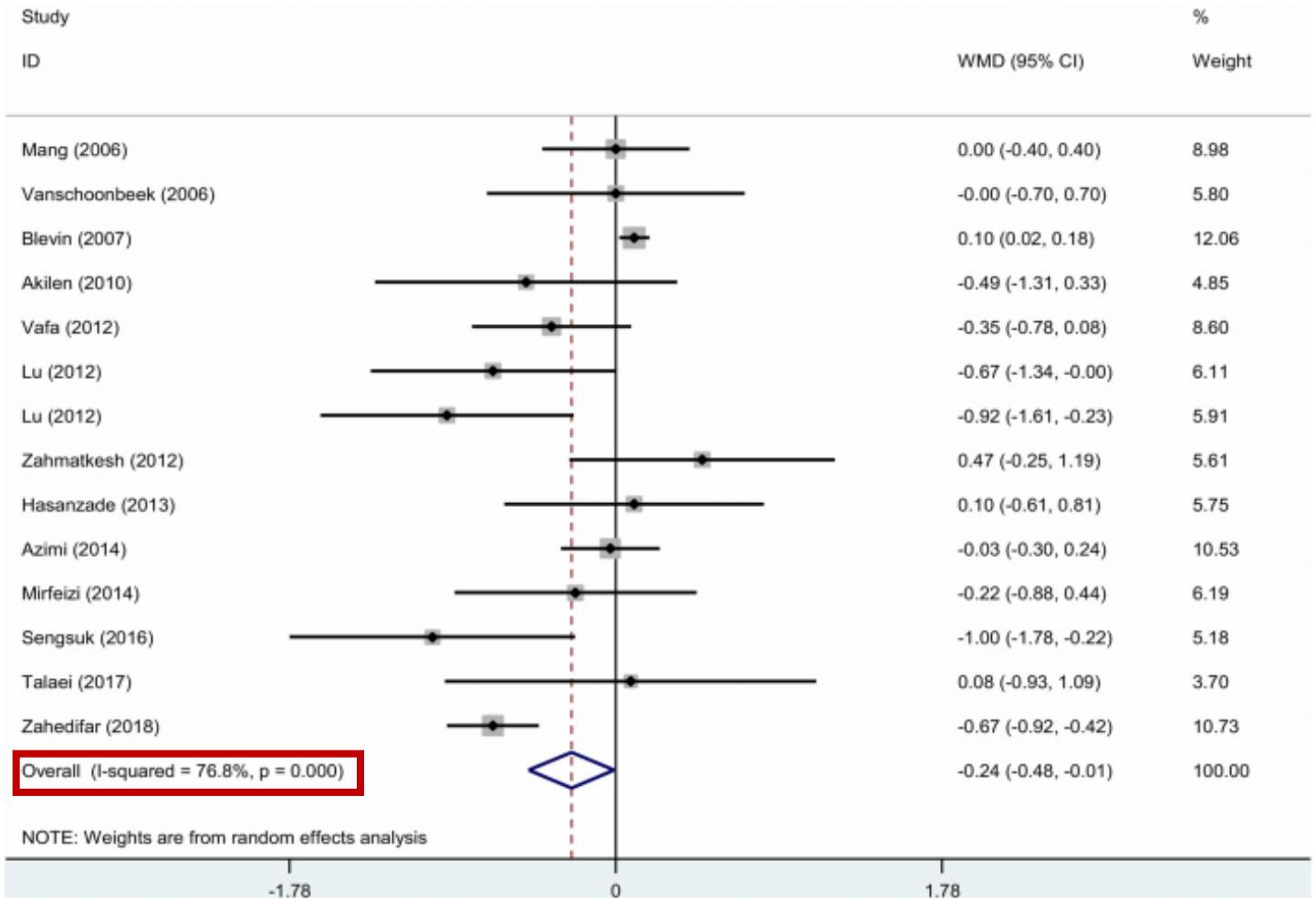


Fig. 3. Forest plot for the effects of supplementation with cinnamon on HbA1c.

<cinnamon on Hb1Ac>
I^2=76.8%, p=0.000
異質性高

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

Results: Finally, 18 studies were included in the meta-analysis. Supplementation with cinnamon reduced FBS by −19.26 mg/dL (95% CI: −28.08, −10.45; I^2:96.5%; p = 0.0001) compared to placebo. However, the effects of cinnamon on HbA1C (−0.24%; 95% CI: −0.48, −0.01; I^2: 76.8%, p = 0.0001), body weight (−0.46, 95%CI: −1.87, 2.30; I^2:0%; p = 0.79), body mass index (WMD: −0.05 kg/m2; 95% CI: −0.52, 0.42; I^2: 0%; p = 0.91), and waist circumference (WMD: −0.53 cm; 95% CI: −3.96, 2.81; I^2: 0%; p = 0.66) were not significant. Additionally, cinnamon did not change the serum levels of insulin and insulin resistance significantly.
Conclusion: Supplementation with cinnamon can reduce serum levels of glucose with no changes in other glycemic parameters and anthropometric indices. However, due to high heterogeneity findings should be interpreted with great caution.

7. How precise of the results?
結果精準嗎？

Cinnamon 在降低糖尿病指標如 FBS及Hb1Ac均有顯著差異，
然因為異質性高且信賴區間大，所以還需要更深入的研究探討

見以下之投影片

Cinnamon 降低 FBS
−19.26 mg/dL (95% CI: −28.08, −10.45; I^2:96.5%; p = 0.0001)
整體來看，在95%信賴區間p值達顯著差異；在分組分析中有特別列出亞洲族群其信賴區間為17.63，寬度較寬

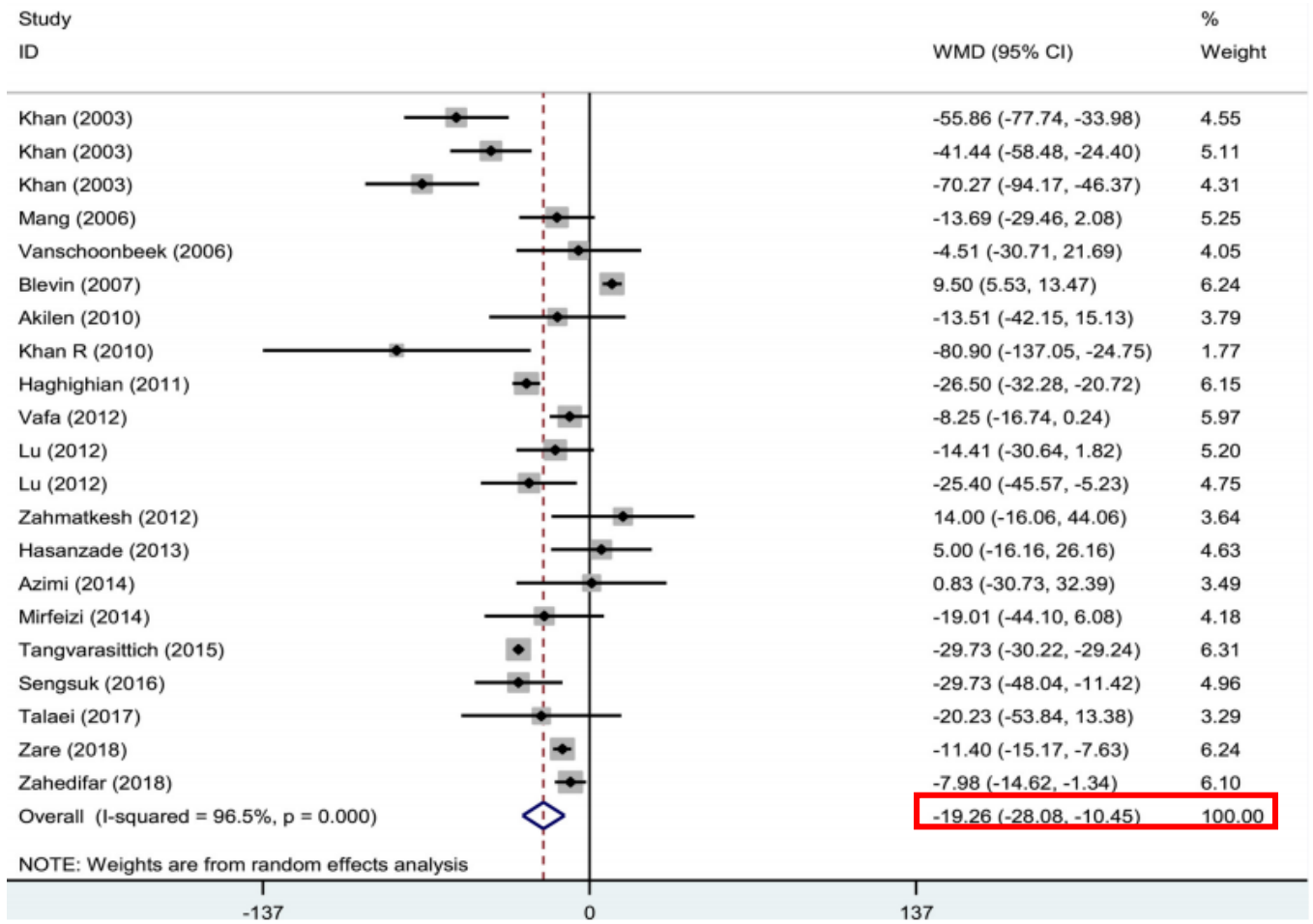


Fig. 2. Forest plot for the effects of supplementation with cinnamon on fasting blood sugar.

Table 3
Subgroup analysis for the effects of cinnamon on fasting blood sugar in patients with type 2 diabetes.

Variables	No. study	Pooled effect size (95% CI)	I^2 (%)	$P_{heterogeneity}$
Fasting blood sugar				
Blindness				
Double	13	−13.83 (-25.29, -2.37)	97.1	0.0001
Single	3	−16.75 (-55.64, 22.13)	75	0.01
Adjustment				
Yes	5	−14.42 (-29.33, 0.49)	45.1	0.12
No	13	−19.89 (-29.83, -9.95)	97.2	0.0001
Diet				
Yes	4	−19.86 (-35.47, -4.26)	67.9	0.02
No	14	−19.21 (-28.13, -10.29)	91.6	0.0001
Location				
Asia	14	−22.32 (-29.75, -14.89)	92.1	0.0001
Non-Asia	3	−11.66 (-23.8, 0.56)	0	0.83
Age (year)				
≤56	7	−20.57 (-32.73, -8.42)	86	0.0001
> 56	9	−16.15 (-29.97, -2.33)	97.8	0.0001
Dosage (g/day)				
≤1.8	5	−13.56 (-27.92, 0.79)	94.2	0.0001
> 1.8	14	−21.55 (-29.37, 13.73)	86.5	0.0001
		Form		
Powder	15	−18.98 (-29.06, -8.90)	97.2	0.0001
Extract	2	−16.76 (-26.6, -6.89)	0	0.62
BMI at baseline (kg/m^2)				
≤29	7	−9.95 (-24.19, 4.28)	95.7	0.0001
> 29	6	−15.81 (-28.53, -3.09)	84.8	0.0001
		Study quality		
< 3	8	−23.48 (-36.75, 10.20)	94.9	0.0001
≥3	10	−15.21 (-26.17, -4.26)	92.5	0.0001

Cinnamon 降低 Hb1Ac
−0.24%; (95%CI: −0.48, −0.01; I^2: 76.8%, p = 0.0001)
整體來看，在95%信賴區間p值達顯著差異

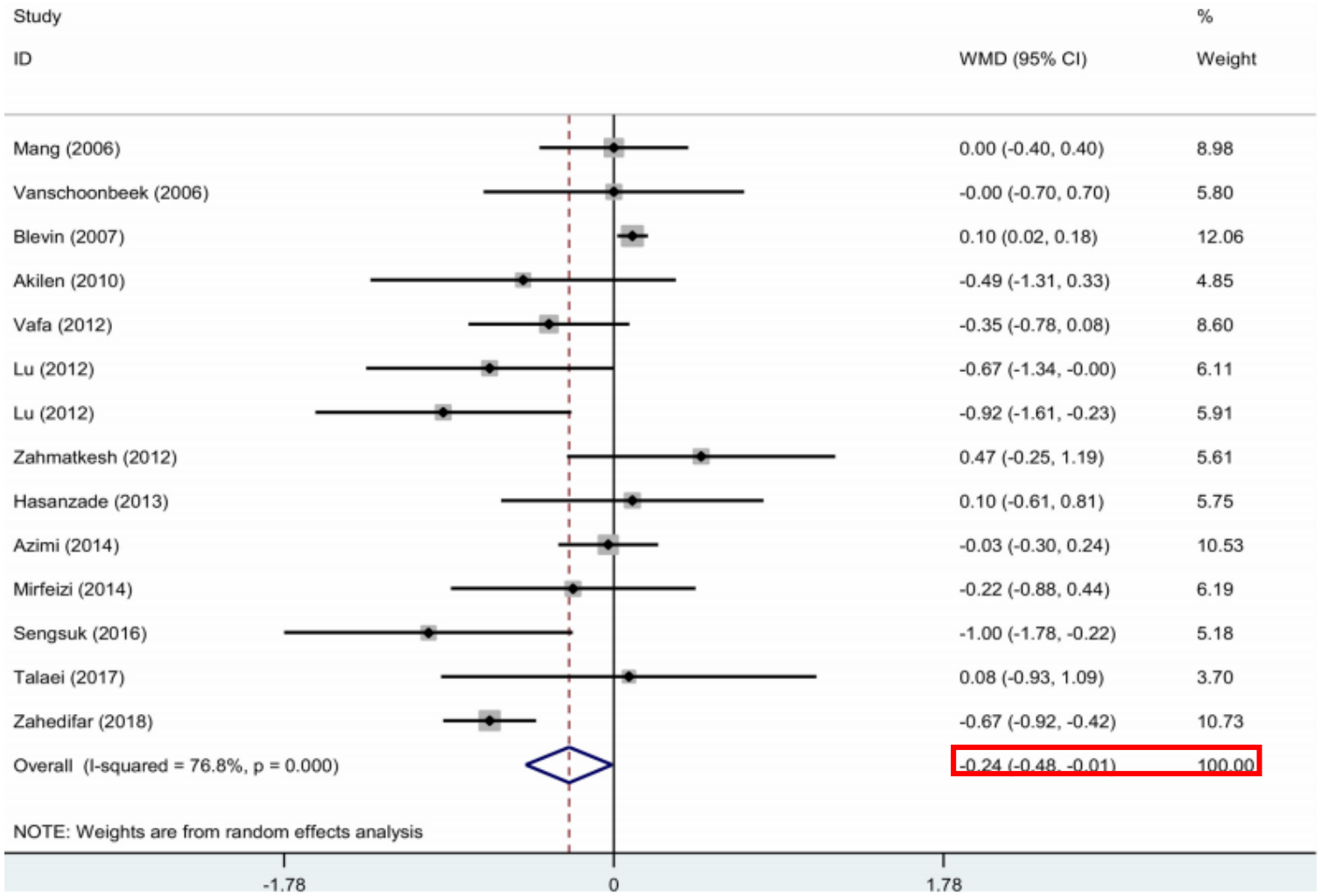


Fig. 3. Forest plot for the effects of supplementation with cinnamon on HbA1c.

然而整體而言，Cinnamon 在降低 BMI(−0.46, 95%CI: −1.87, 2.30; I2 :0%; p = 0.79)
及 腰圍(−0.05 kg/m2; 95% CI: −0.52, 0.42; I2 : 0%; p = 0.91)
均沒有達顯著差異

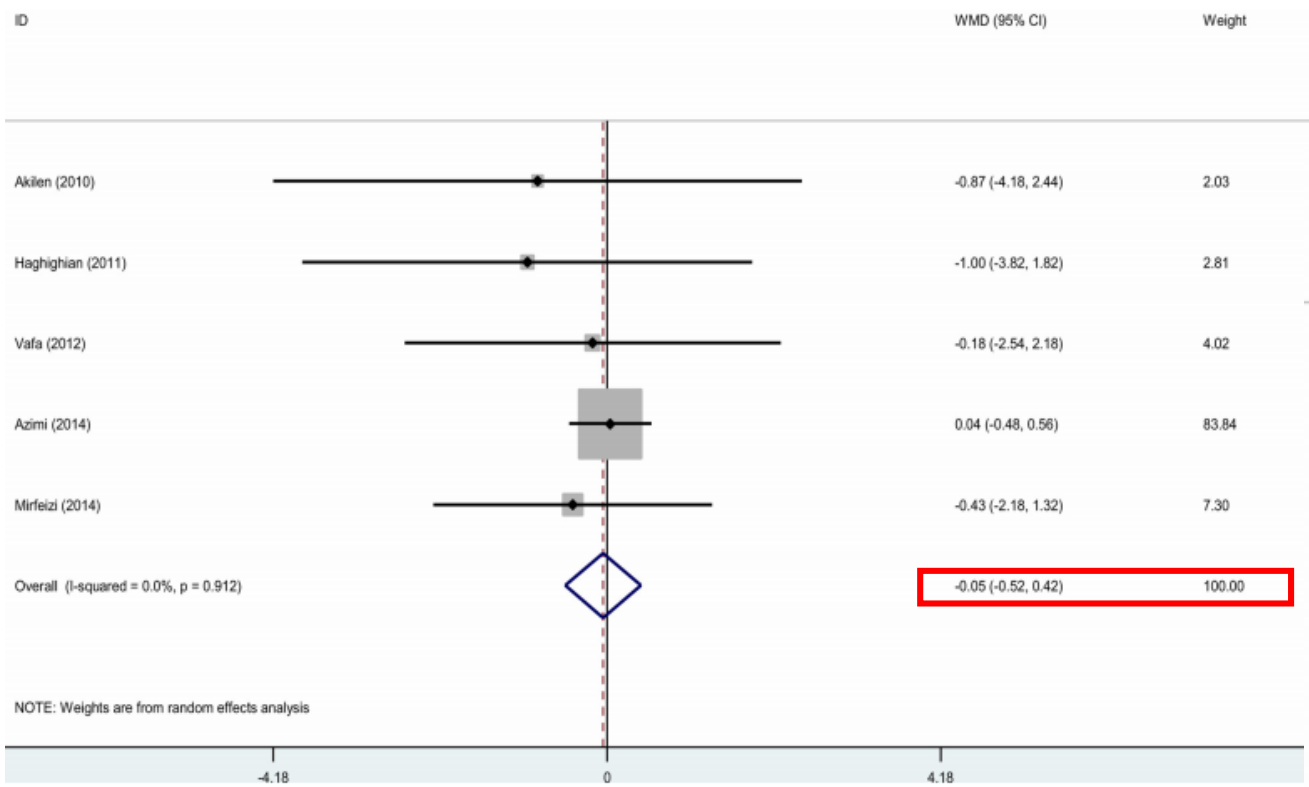


Fig. 5. Forest plot for the effects of supplementation with cinnamon on body mass index.

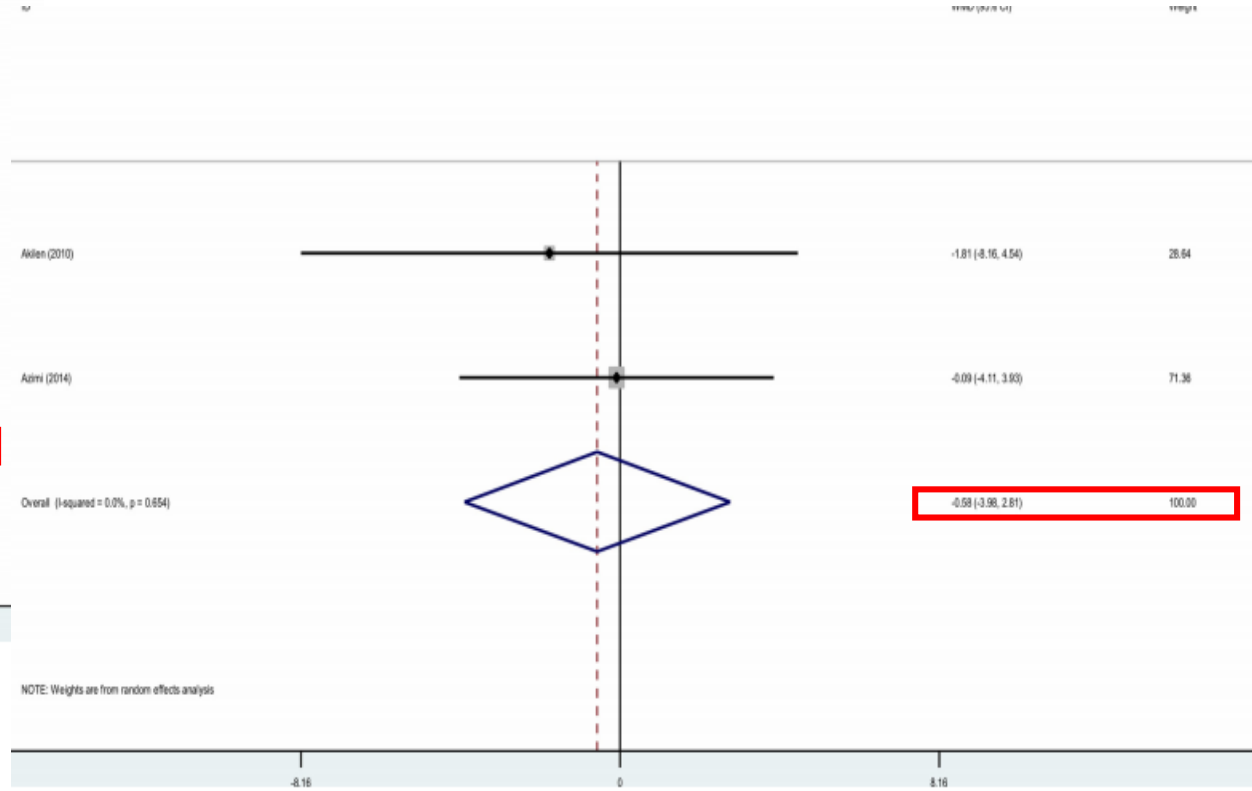


Fig. 6. Forest plot for the effects of supplementation with cinnamon on waist circumference.

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

● YES ● NO ● CAN'T TELL

- 文獻研究分析是討論糖尿病病人給肉桂的影響、且收錄的內容平均年齡層介於 40~60 歲且亞洲族群佔多數(13篇)。大致符合本題目的背景，故可應用到病患身上。

Characteristics of the included papers in the systematic review.

Author/ Year	Location	Study design	Gender (Male/ Female)	Mean age	Sample size	Dosage (g/ day)	Duration (day)	Form	Adjustment	Side effects	Type of Cinnamon	Quality score
Zare et al (2018)	Iran	R/P triple	both	52.6	138	1	90	powder	No	No	Not clear	3
Zafarkhani et al (2016)	Iran	R/P double	both	54.6	2	2	56	powder	No	No	Not clear	2
Talaei et al (2013)	Iran	R/P double	both	57	2	3	56	powder	No	No	c.cassia	4
Sengsuk et al (2016)	Thailand	R/P double	both	57	1	1.5	60	powder	No	No	Not clear	5
Tangvarasittichai et al (2015)	Thailand	R/P double	Both	57	106	1.5	60	powder	No	No	c.cassia	5
Azimi et al (2014)	Iran	R/P Single	Both	53.8	79	3	56	powder	Yes/ covariates were not mentioned	No	Not clear	3
Mirfeizi et al (2014)	Iran	R/P triple	Both	> 18	72	1	90	powder	Yes/ Baseline value	Yes/ Skin Allergy (n = 1)	Not clear	4
Hasanzadeh et al (2013)	Iran	R/P double	Both	54.3	70	1	60	powder	No	No	c.cassia	3
Vafa et al (2012)	Iran	R/P double	Both	55	37	3	56	powder	No	No	Not clear	2
Lu et al (2012)	China	R/P double	Both	61	43	0.12	91	extract	No	No	Not clear	2
Zahmatkesh et al (2012)	Iran	R/P double	Both		55	2	56	powder	No	No	Not clear	3
Haghighian et al (2011)	Iran	R/P double	Both	56.8	6	1.5	56	powder	No	No	Not clear	2
Akilen et al (2010)	England	R/P Single	Both	55	5	3	84	powder	Yes, covariates were not clear	No	C. cassia	5
Otto et al (2010)	USA	R/P double	Both	46	22	0.5	84	Aqueous extract	Not clear	Not clear	Not clear	2
Blevins et al (2007)	USA	R/P double	Both	60.8	57	1	90	powder	No	Not clear	c.cassia	2
Mang et al (2006)	Germany	R/P double	Both	63	65	3	120	powder	No	No	Not clear	2
Vanschoonbeek et al (2006)	Netherland	?R/P double	Female	62.5	25	1.5	42		No		C. cassia	3
Khan et al (2003)	Pakistan	R/P/ double	Both	> 40 years	20	1 3 6	40	powder	No	No	C. cassia	1

● 年齡 ● 性別 ● 種族 ● 共病 ● 疾病嚴重度

● 在台灣可行 ● 符合 ● 不符合

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

● YES ● NO ● CAN'T TELL

- ● Adverse effects
- ● FBS
- ● HbA1c
- ● body weight
- ● BMI
- ● waist circumference
- ● cost

● 有評估 ● 無評估

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？

● YES ● NO ● CAN'T TELL

項目	優點	缺點	沒顯著影響
Cinnamon	• Adverse effects • FBS	• cost (以漢方養身堂為例 特級135元/50克 每天補充2克為例 每日花費5.4元)	• HbA1c • body weight • BMI • waist circumference

綜合評讀結果

	問題		結果
有效性	1	清楚明確的問題？	● YES ○ NO ○ UNCLEAR
	2	收納適當的研究類型？	● YES ○ NO ○ UNCLEAR
	3	包含所有重要、相關的研究？	● YES ○ NO ○ UNCLEAR
	4	評估收納研究的品質？	● YES ○ NO ○ UNCLEAR
	5	是否合併？合併的合理性？	● YES ○ NO ○ UNCLEAR
重要性	6	適當的呈現結果？	● YES ○ NO ○ UNCLEAR
	7	結果精準嗎？	● YES ○ NO ○ UNCLEAR
應用性	8	是否可以應用到你的病患？	● YES ○ NO ○ UNCLEAR
	9	所有重要的臨床結果都被考量到？	● YES ○ NO ○ UNCLEAR

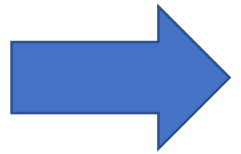
證據等級

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

評定證據等級 GRADE Online

		outcome
研究設計		RCT
降階	1. 存在誤差風險	-
	2. 結果不一致	+++
	3. 證據不具直接性	-
	4. 結果不精準	++
	5. 存在發表誤差	-
升階	1. 效果顯著	-
	2. 降低干擾因素	-
	3. 具劑量—反應效果	-
證據等級		低



SDM

病人考量

考量因素	不重要(0)	普通(1)	重要(2)	非常重要(3)
經濟(費用)	●			
治療有效性				●
副作用				●
生活品質			●	
方便性	●			

每項選擇之優缺點、風險

● 較佳 ● 普通 ● 較差

		治療方式
		補充肉桂
考量因素	經濟(費用)	●
	治療有效性	●
	副作用	●
	生活品質	●
	方便性	●

其他糖尿病藥物治療


第 2 型糖尿病人高血糖的處理流程圖
(2020年修訂版)
健康生活型態的飲食和運動及醫病共享決策
糖化血色素<7.5%
糖化血色素 ≥ 7.5%或高於個別化目標值1.5%以上
建議使用一種抗糖尿病藥
合併高血糖症狀
建議使用兩種抗糖尿病藥
合併高血糖症狀
初診斷建議首選：Metformin
• 效果：佳
• 低血糖：低
• 體重：稍下降
• 副作用：腸胃道/乳酸血症
建議先以 Insulin 治療
建議 Metformin +
以下不同機轉的抗糖尿病
建議先以 Insulin 治療
若單一治療未達控制目標時，宜評估心腎風險及共病，加上以下不同機轉的抗糖尿病藥
SGLT2i
心血管實證：有(建議使用)
心衰竭實證：強(建議使用)
腎病變實證：強(建議使用)
控制血糖效果：中等
體重：下降
低血糖：低
副作用：糖尿病酮酸中毒、生殖泌尿道感染、骨折、截肢、脫水
GLP1-RA
心血管實證：部分有(建議使用)
心衰竭實證：中立
腎病變實證：有(蛋白尿)
控制血糖效果：佳
體重：下降
低血糖：低
副作用：腸胃道
TZD
心血管實證：有
心衰竭實證：不建議使用
腎病變實證：缺
控制血糖效果：佳
體重：增加
低血糖：低
副作用：水腫、心衰竭、骨折
DPP4i
心血管實證：中立
心衰竭實證：部分中立
腎病變實證：有(蛋白尿)
控制血糖效果：中等
體重：無影響
低血糖：低
副作用：少見
AGI
心血管實證：中立
心衰竭實證：缺
腎病變實證：缺
控制血糖效果：中等
體重：稍下降
低血糖：低
副作用：腸胃道
SU/Glinide
心血管實證：缺
心衰竭實證：缺
腎病變實證：缺
控制血糖效果：佳
體重：增加
低血糖：中
副作用：低血糖
Insulin
心血管實證：中立
心衰竭實證：中立
腎病變實證：中立
控制血糖效果：最佳
體重：增加
低血糖：高
副作用：低血糖
未達控制目標
再加上另一種不同機轉的抗糖尿病藥 (SU 和 Glinide 不建議合併，DPP4i 和 GLP1-RA 不建議合併)

佳糖維 胰臟炎疑慮

Pancreatic events

Cases of **acute pancreatitis** (including hemorrhagic and necrotizing with some fatalities), chronic pancreatitis, and pancreatic cancer have been reported with use of incretin-based therapies (eg, dipeptidyl peptidase-4 [DPP-4] inhibitors, glucagon-like peptide 1 [GLP-1] receptor agonists), including sitagliptin (Ref).

Mechanism: Causality has not been firmly established (Ref). DPP-4 inhibitors indirectly stimulate GLP-1 receptors in pancreatic islet beta cells and exocrine duct cells which may cause an overgrowth of the cells that cover the smaller ducts, thereby resulting in hyperplasia, increased pancreatic weight, duct occlusion, back pressure, and subsequent acute or chronic pancreatic inflammation (Ref).

Risk factors:

- Patients with a prior history of pancreatitis may be at an increased risk for acute pancreatitis.
- Patients with acute pancreatitis due to any cause are at an increased risk for progression to recurrent acute pancreatitis and then to chronic pancreatitis; patients with chronic pancreatitis are at an increased risk for pancreatic cancer (Ref).
- Risk factors for pancreatitis due to any cause include, but are not limited to, hypertriglyceridemia, cholelithiasis, alcohol use, and obesity.

臨床回覆

- 根據林先生所好奇的問題

經過我們謹慎的文獻查找後可以知道

- 在高證據等級的文章，但證據品質低的文獻可以知道

目前搜尋到的證據看到雖然使用肉桂的補充沒有副作用，不論在控制空腹血糖、糖化血色素、降低體重、腰圍、BMI都沒有顯著的差異。

- 在肉桂的補充方面，可能需要自行購買。
- 在不想改變飲食和運動習慣之下，建議還是以藥物治療為主。

THANK YOU!