Evidence-based medicine 實證醫學競賽

徐千雅[1]、黃子琳[1]、呂一寶[2]

- 一般科PGY醫師[1]
- 影像醫學科醫事放射師[2]

-臨床情境-

小莊是一位30出頭的年輕醫療工作者,由於工作的性質,常常需要長時間在電腦前坐著。忙碌的醫院生活讓 他幾乎沒有時間運動,下班後總是覺得身心疲憊,只想吃點鹹酥雞來犒賞自己,然後早早洗洗睡。然而,隨 著年齡增長,小莊漸漸感受到體力的下降和代謝的變慢。最近的公司健檢報告顯示出讓他頗為擔心的結果 :體重已屬於肥胖範疇,還出現了脂肪肝的跡象,血脂也有異常——HDL 偏低,三酸甘油 酯居高不下。雖然血 糖還在正常範圍,HAIC 也僅有5.3%,但這些指標讓小莊覺得自己必須採取一些行動。 看著周遭朋友開始嘗試各種方法減重 ,如間歇性斷食、生 酮飲食,甚至還有開始使用健身房會員的 ,小莊不 免感到壓力,心想:「難道我也該改變一下生活方式了?」在查閱資料的過程中,他注意到一些新的降血糖 藥物,如GLP-1 類的liraglutide 和 semaglutide,以及SGLT2 抑制劑,這些藥物似乎不僅能控制血糖 , 對減重也有良好的效果。對於不常運動的他來 說,這些藥物看起來相當吸引人。另外 ,他也考慮一些傳統療法,如中藥或針灸,希望能在改變生活習慣前 ,嘗試看看其他的治療選擇。 因此,小莊找到您這位熱愛實證醫學的同事,想知道是否有研究支持這些藥物和療法在肥胖、脂肪肝患者中 的減重效果,以及它們和運動或飲食控制相比的優劣之處。他希望能 夠了解哪一種方式最適合他的情況,以 便做出更有科學依據的選擇。

–背景知識–

What is GLP-1 ?

- **GLP-1** – GLP-1 is produced from the proglucagon gene in L cells of the small intestine. It binds to a specific GLP-1 receptor, which is expressed in various tissues, including pancreatic beta cells, pancreatic ducts, gastric mucosa, kidney, lung, heart, skin, immune cells, and the hypothalamus [4,6]. GLP-1 exerts its main effect by stimulating glucose-dependent insulin release from the pancreatic islets [4]. It has also been shown to slow gastric emptying [7], inhibit inappropriate post-meal glucagon release [8,9], and reduce food intake (table 1 and figure 1) [9]. In patients with type 2 diabetes, there is an impaired insulin response to GLP-1, possibly related to a reduction in postprandial GLP-1 secretion (figure 2A-C) [10] or to other mechanisms [11,12].

UpToDate®

Ask 5A-1

提出問題

-PICO 1-

P	NAFLD
I	GLP-1 receptor agonist 、semaglutide、SGLT-2 inhibitor
C	Placebo
O	Weight loss、nausea

治療型問題

問題設計：■治療型 □傷害型 □診斷型 □篩檢型 □預後型

-PICO 2-

P	Obesity、Non-Diabetes mellitus、fatty liver
I	傳統(中藥、針灸) (traditional)Chinese medicine/drug、acupuncture
C	GLP-1
O	Weight loss、drug intoxication

治療型問題

問題設計： ■治療型 □傷害型 □診斷型 □篩檢型 □預後型

Acquire

5A-2

搜尋資料

–搜尋資料–

	PICO關鍵字	MeSH同義字	中文關鍵字
P	NAFLD	Non-alcoholic Fatty Liver Disease	非酒精性脂肪性肝病
I	GLP-1 receptor agonist 、semaglutide	Glucagon-Like Peptide-1 Receptor Agonists 、semaglutide [Supplementary Concept]	類升糖素胜肽-1受體促效劑
C	SGLT-2 inhibitor	Sodium-Glucose Transporter 2 Inhibitors	司美格魯肽
O	Weight loss、nausea	Weight loss 、nausea	體重下降、噁心

選擇理由

1. 符合PICO
2. 2023發表
3. 為SR of RCT

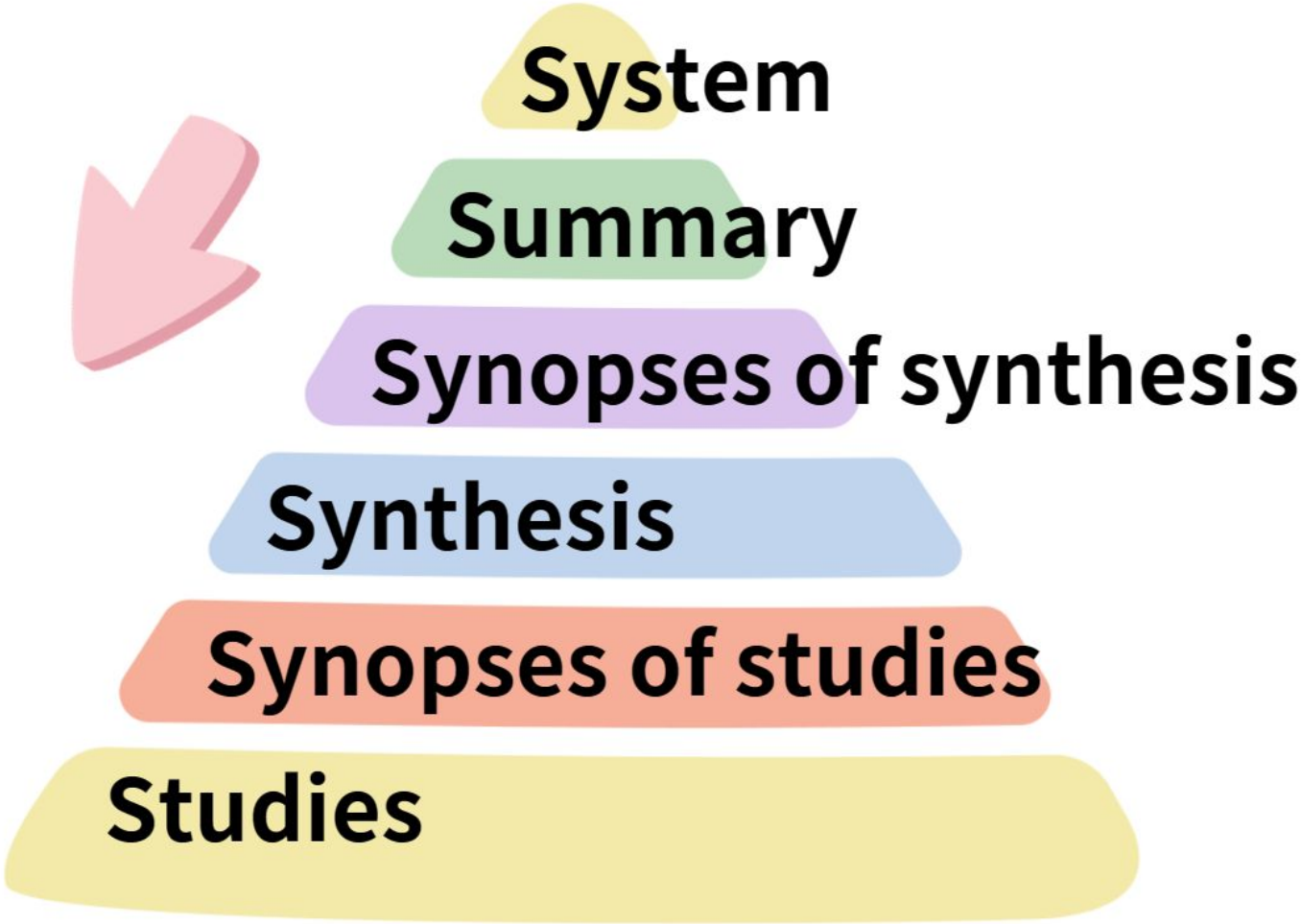
-搜尋資料-

首選
Level1：SR of RCT

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

–搜尋資料–



DynaMed Powered by EBSCOhost
UpToDate®
PubMed
Embase
Cochrane Library
airiti Library
華藝線上圖書館

–搜尋資料–

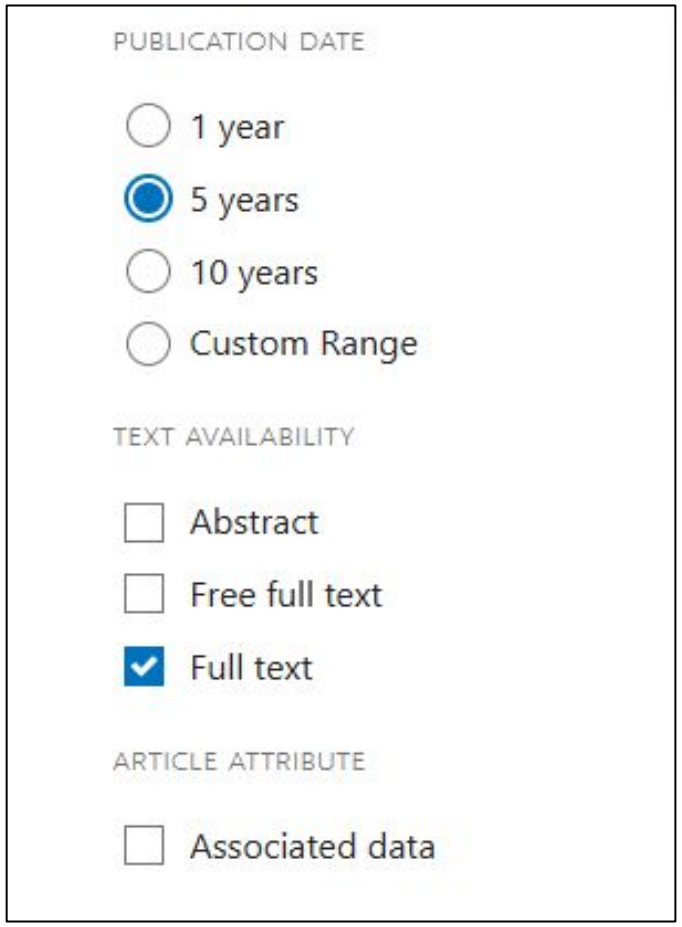
臨床問題

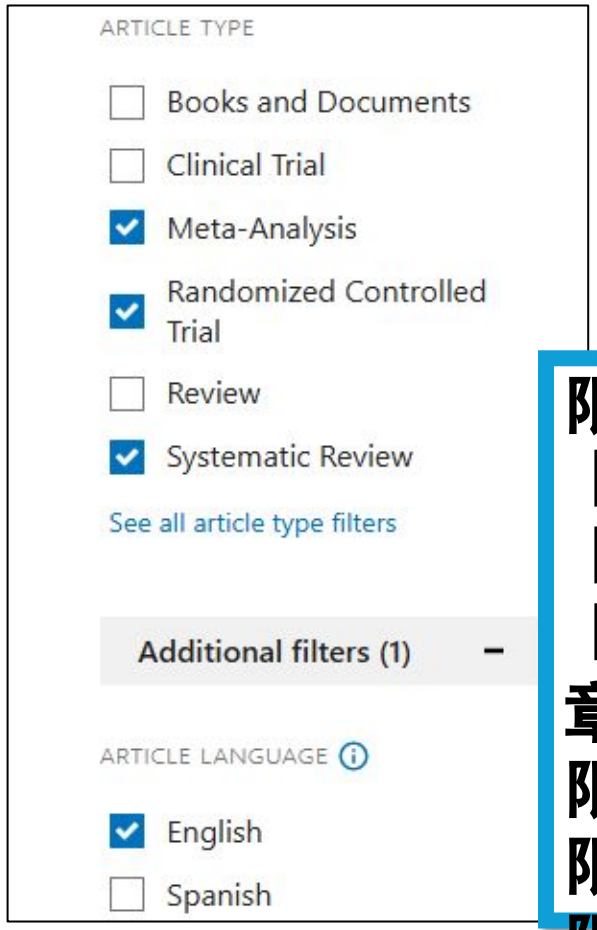
Systematic Review 、Meta-Analysis[Major]
Randomized Controlled Trial/Cohort Study

限定5年內、 full text
English、

Meet Our 『PICO』

–搜尋資料–





輸入關鍵字
『NAFLD、GLP-1 receptor agonist、Semaglutide、GLT-2 inhibitor 』
適當使用布林運算『 AND 』、『 OR』

限定適當文章類型
『Meta-Analysis 』文章
『Systematic Reviews 』 文章
『Randomized controlled Trial 』文章

限定搜尋範圍
限定『5年』 文章
限定『Full text 』全文可供評讀

–搜尋資料–

PubMed

SR作為filters
篩選level 1文獻
P AND I AND C

SR作為filters
篩選level 1文獻
使用MeSH terms

Search	Actions	Details	Query	Results	Time
#23	•••	⌄	Search: **(NAFLD) AND ((glp-1 receptor agonist) or (Semaglutide) or (SGLT-2 inhibitor))** Filters: **in the last 5 years, Full text, Meta-Analysis, Randomized Controlled Trial, Systematic Review, English** (("nafld"[All Fields] OR "non alcoholic fatty liver disease"[MeSH Terms] OR ("non alcoholic"[All Fields] AND "fatty"[All Fields] AND "liver"[All Fields] AND "disease"[All Fields]) OR "non alcoholic fatty liver disease"[All Fields] OR "nafld"[All Fields]) AND ("glucagon like peptide 1 receptor agonists" [Pharmacological Action] OR "glucagon like peptide 1 receptor agonists" [MeSH Terms] OR ("glucagon like"[All Fields] AND "peptide 1"[All Fields] AND "receptor"[All Fields] AND "agonists"[All Fields]) OR "glucagon like peptide 1 receptor agonists"[All Fields] OR "glp 1 receptor agonist"[All Fields] OR ("semaglutide"[Supplementary Concept] OR "semaglutide"[All Fields]) OR ("sodium glucose transporter 2 inhibitors"[Pharmacological Action] OR "sodium glucose transporter 2 inhibitors"[MeSH Terms] OR "sodium glucose transporter 2 inhibitors"[All Fields] OR "sglt 2 inhibitor" [All Fields]))) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR randomizedcontrolledtrial[Filter] OR systematicreview[Filter]) AND (fft[Filter]) AND (english[Filter])) **Translations** **NAFLD:** "nafld"[All Fields] OR "non-alcoholic fatty liver disease"[MeSH Terms] OR ("non-alcoholic"[All Fields] AND "fatty"[All Fields] AND "liver" [All Fields] AND "disease"[All Fields]) OR "non-alcoholic fatty liver disease" [All Fields] OR "nafld"[All Fields] **glp-1 receptor agonist:** "glucagon-like peptide-1 receptor agonists" [Pharmacological Action] OR "glucagon-like peptide-1 receptor agonists" [MeSH Terms] OR ("glucagon-like"[All Fields] AND "peptide-1"[All Fields] AND "receptor"[All Fields] AND "agonists"[All Fields]) OR "glucagon-like peptide-1 receptor agonists"[All Fields] OR "glp 1 receptor agonist"[All Fields] **Semaglutide:** "semaglutide"[Supplementary Concept] OR "semaglutide" [All Fields] **SGLT-2 inhibitor:** "sodium-glucose transporter 2 inhibitors" [Pharmacological Action] OR "sodium-glucose transporter 2 inhibitors" [MeSH Terms] OR "sodium-glucose transporter 2 inhibitors"[All Fields] OR "sglt 2 inhibitor"[All Fields]	111	21:54:06

–搜尋資料–

Cochrane Library

Access provided by: **National Taiwan University**

Advanced Search

Search | Search manager | Medical terms (MeSH) | PICO search

Save this search | View/Share saved searches | ? Search help

Print search history

#1	MeSH descriptor: [Non-alcoholic Fatty Liver Disease] explode all trees	MeSH	1987
#2	MeSH descriptor: [Glucagon-Like Peptide-1 Receptor Agonists] explode all trees	MeSH	36
#3	Any MeSH descriptor in all MeSH products	MeSH	0
#4	Any MeSH descriptor in all MeSH products	MeSH	0
#5	#1 AND (#2 OR #3 OR #4)	Limits	1
#6	Type a search term or use the S or MeSH buttons to compose	S MeSH Limits	N/A

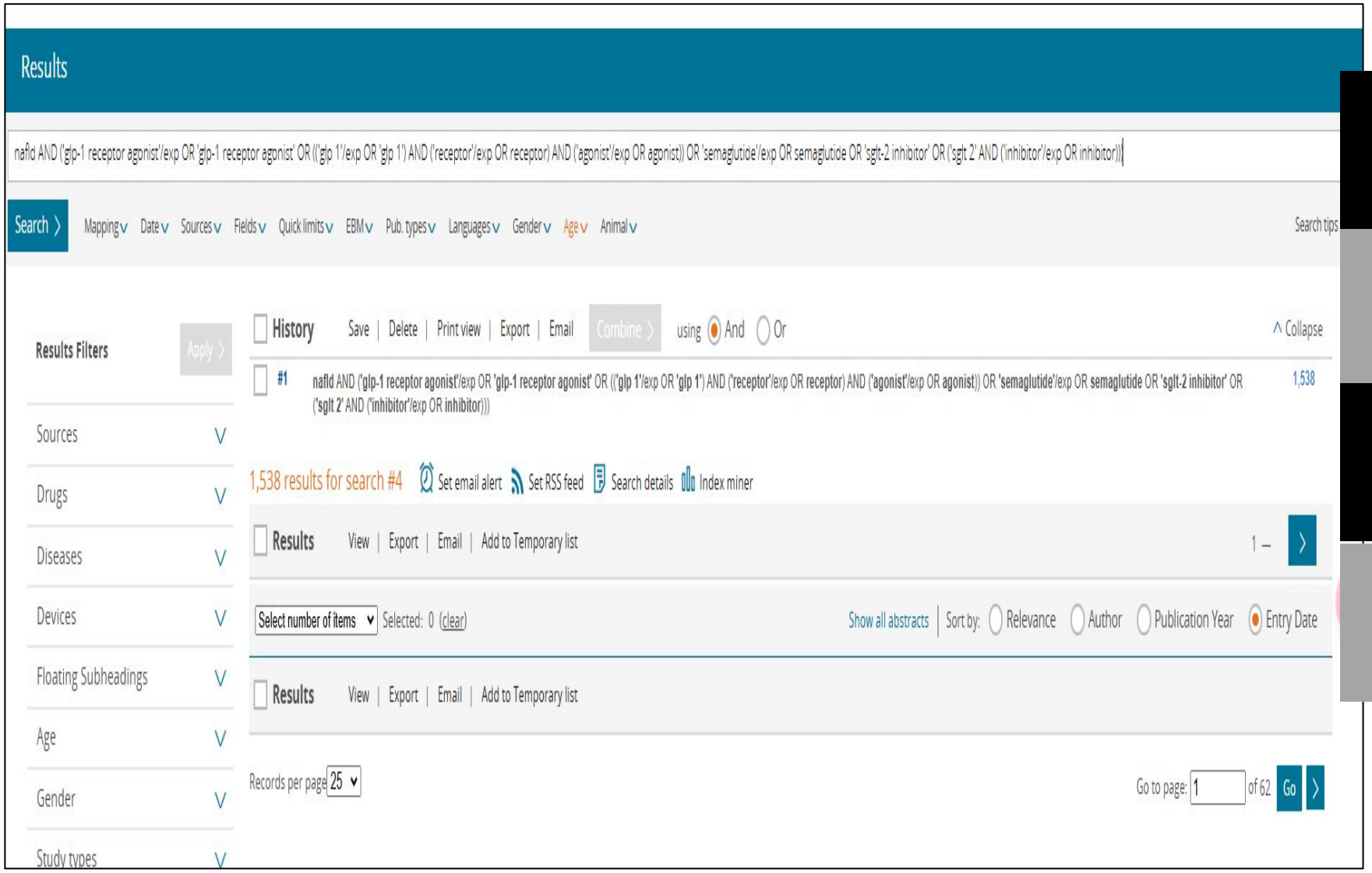
Clear all

輸入關鍵字

『NAFLD、GLP-1 receptor agonist、Semaglutide、GLT-2 inhibitor 』

適當使用布林運算『 AND 』、『 OR 』

–搜尋資料– Embase

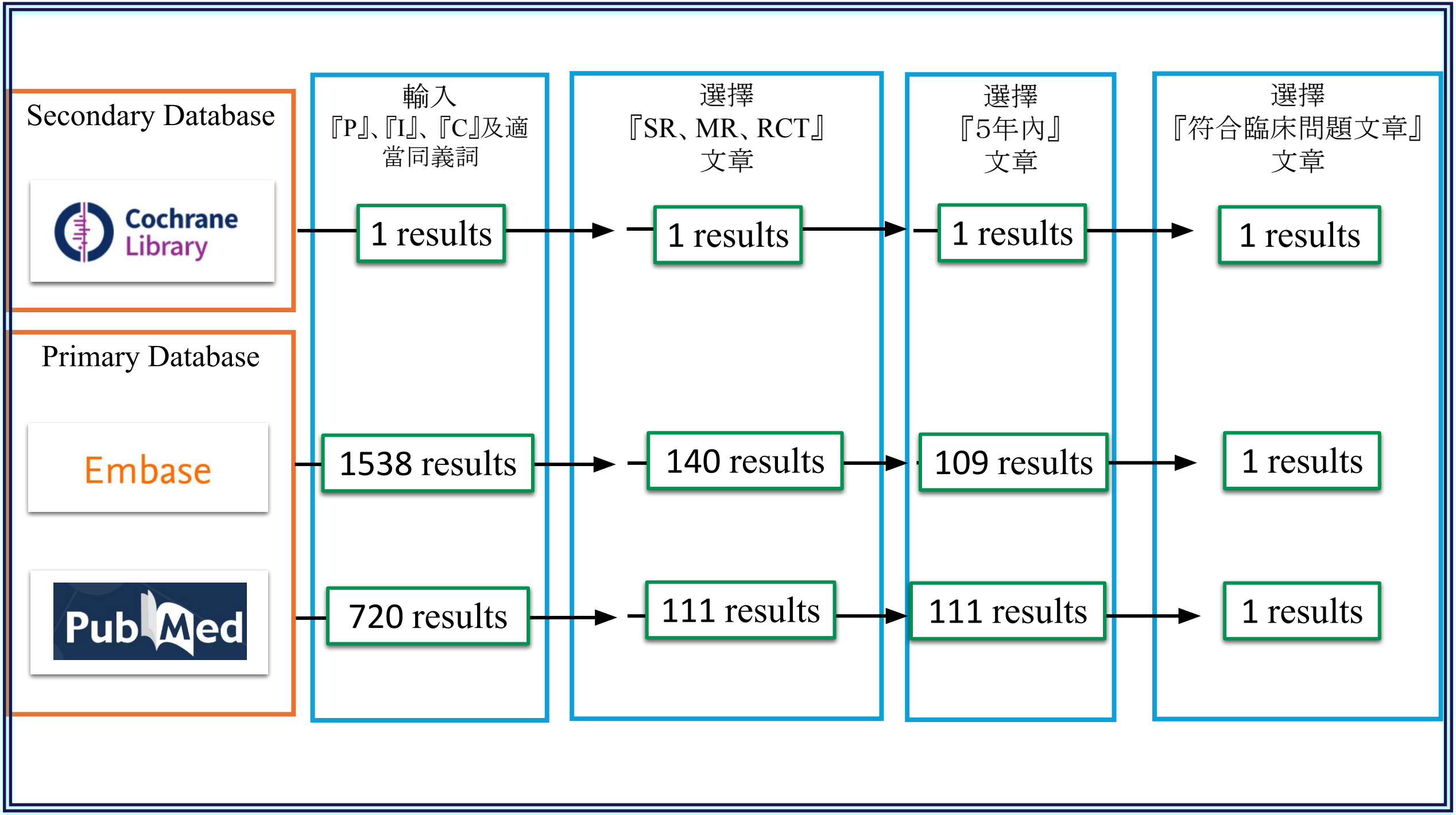


搜尋策略使用/br
搜尋all fields

比對emtree term
去掉不相關的詞

確認synonyms
包含所有可能

SR作為filters
篩選level 1文獻


Secondary Database
Cochrane Library
Primary Database
Embase
PubMed
輸入
『P』、『I』、『C』及適當同義詞
選擇
『SR、MR、RCT』文章
選擇
『5年內』文章
選擇
『符合臨床問題文章』文章
1 results
1 results
1 results
1 results
1538 results
140 results
109 results
1 results
720 results
111 results
111 results
1 results

–選擇最佳文獻

NIH National Library of Medicine
National Center for Biotechnology Information

PubMed®

› Front Pharmacol. 2023 Mar 13:14:1102792. doi: 10.3389/fphar.2023.1102792. eCollection 2023.

Comparative efficacy of 5 sodium–glucose cotransporter protein–2 (SGLT–2) inhibitor and 4 glucagon–like peptide–1 (GLP–1) receptor agonist drugs in non–alcoholic fatty liver disease: A GRADE–assessed systematic review and network meta–analysis of randomized controlled trials

Yunpeng Gu [1], Lei Sun [2], Wei Zhang [1], Tingting Kong [3], Run Zhou [3], Yining He [2], Chaohua Deng [2], Luping Yang [4], Jianing Kong [2], Yutong Chen [3], Junping Shi [5], Yalan Hu [6]

Affiliations + expand

PMID: 36992825 PMCID: PMC10040540 DOI: 10.3389/fphar.2023.1102792

✔ 最佳研究設計 SR of RCT
✔ 較新的發表年份
✔ 最符合臨床情境 PICO

Appraise

5A-3

評讀文獻

–評讀文獻–

CASP
Critical Appraisal Skills Programme

Validity（可信性）

Importance（重要性）

Practice（適用性）

CASP Checklist: 10 questions to help you make sense of a **Systematic Review**

How to use this appraisal tool: Three broad issues need to be considered when appraising a systematic review study:

- Are the results of the study valid? (Section A)
- What are the results? (Section B)
- Will the results help locally? (Section C)

✔ 針對效度直觀分析
✔ 針對結果直觀分析
✔ 共10個問題探討各面向

問題一：此研究是否問了一個清楚明確的問題?

frontiers | Frontiers in Pharmacology

TYPE Systematic Review
PUBLISHED 13 March 2023
DOI 10.3389/fphar.2023.1102792

OPEN ACCESS

EDITED BY
Runping Liu,
Beijing University of Chinese Medicine, China

REVIEWED BY
Sandhiya Selvarajan,
Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), India
Chang-Hai Liu,
Sichuan University, China
Gayatri Vishwakarma,
Indian Spinal Injuries Centre, India

*CORRESPONDENCE
Junping Shi,
20131004@hznu.edu.cn
Yanli Hu,
huyanli2022@126.com

Comparative efficacy of 5 sodium-glucose cotransporter protein-2 (SGLT-2) inhibitor and 4 glucagon-like peptide-1 (GLP-1) receptor agonist drugs in non-alcoholic fatty liver disease: A GRADE-assessed systematic review and network meta-analysis of randomized controlled trials

The following criteria were used to include studies in the systematic review and network meta-analysis: 1) Randomized controlled trials that compared, SGLT-2 inhibitors or GLP-1 receptor agonists against placebo or other active control drugs in NAFLD patients were included; and 2) Eligible studies must have

Results: The criteria were satisfied by 37 RCTs with 9 interventions (5 SGLT-2 inhibitors and 4 GLP-1 receptor agonists). Based on high certainty evidence, in patients with NAFLD (or comorbid with type 2 diabetes), semaglutide could lower alanine aminotransferase as well as aspartate aminotransferase, γ-glutamyl transferase, controlled attenuation parameter, liver stiffness measurement, body weight systolic blood pressure, triglycerides, high-density lipoprotein-cholesterol, glycosylated hemoglobin. Liraglutide could lower alanine aminotransferase as well as subcutaneous adipose tissue, body mass index, fasting blood glucose, glycosylated hemoglobin, glucose and homeostasis model assessment, while dapagliflozin could lower alanine aminotransferase as

☑️ Yes ⬜ No ⬜ Can't tell

PICO (+)

問題二：作者是否尋找適當研究型態的文獻?

Comparative efficacy of 5 sodium-glucose cotransporter protein-2 (SGLT-2) inhibitor and 4 glucagon-like peptide-1 (GLP-1) receptor agonist drugs in non-alcoholic fatty liver disease: A GRADE-assessed systematic review and network meta-analysis of randomized controlled trials

P

☑️ Yes ⬜ No ⬜ Can't tell

RCT (+)
PICO (+)

問題三：你認為所有重要且相關的研究都被納入?

☑️ Yes ⬜ No ⬜ Can't tell

We used predefined keywords to systematically search four large electronic databases (PubMed, Embase, Web of Science, and Cochrane Library) for relevant papers published through

PubMed
Embase
Web of Science
Cochrane Library

問題四：作者是否評估所納入研究文獻的品質?

The grading of recommendations assessment, development, and evaluation (GRADE) technique was used to assess the certainty of evidence (Atkins et al., 2004; Brignardello-Petersen et al., 2018; Brignardello-Petersen et al., 2020). Including specific guidance for network meta-analyses (Puhan et al., 2014). Two investigators with GRADE expertise assessed each domain individually for each comparison and outcome, and any conflicts were addressed through discussion. Criteria for classifying the certainty of each comparison and outcome as high, moderate, low, or very low, included considerations of risk of bias (failure to conceal random allocation or blind participants in randomized controlled trials or failure to adequately control for confounding in observational studies), inconsistency (heterogeneity of estimates of effects

☑ Yes ☐ No ☐ Can't tell

GRADE(+)
RoB (+)
兩人評讀(+)

問題四：作者是否評估所納入研究文獻的品質?

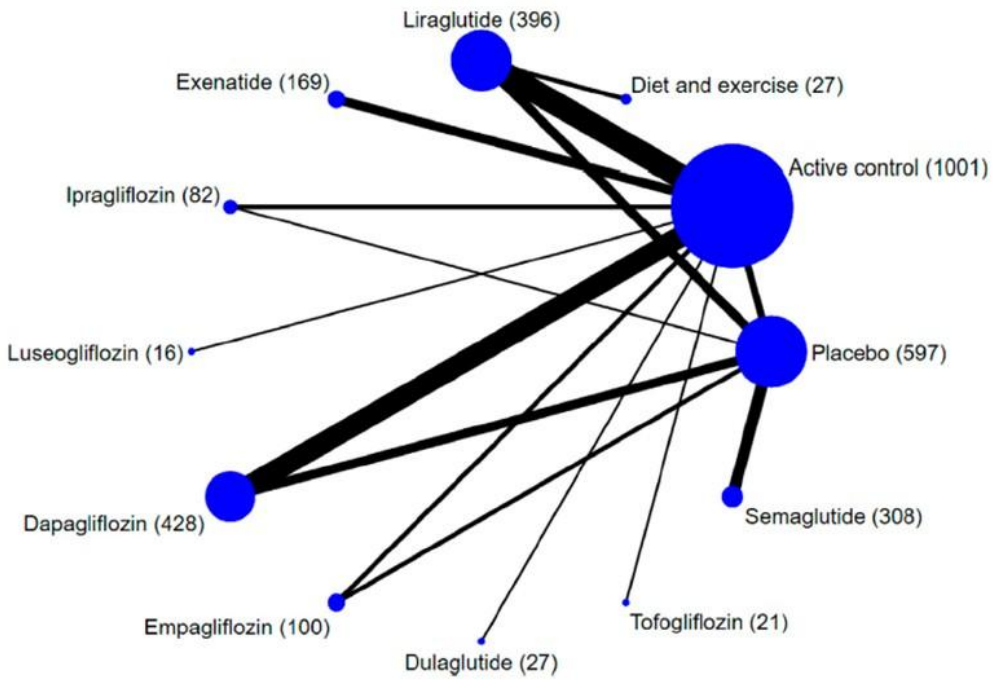


FIGURE 2
Network plot of trials evaluating the effects of sodium-glucose cotransporter protein-2 inhibitors and glucagon-like peptide-1 receptor agonists for patients with NAFLD. Network shows the number of participants assigned to each treatment class with the size of each circle proportional to the number of randomly assigned participants in the treatment comparisons (sample size for the specific treatment shown in brackets). Line thickness is proportional to the number of patients that contributed to the comparison.

☑️ Yes ⬜ No ⬜ Can't tell

RoB (+)

問題四：作者是否評估所納入研究文獻的品質?

☑ Yes ☐ No ☐ Can't tell

Anthropometric measures	Body weight (BW)	Body mass index (BMI)	Waist circumference (WC)	Systolic blood pressure (SBP)	Diastolic blood pressure (DBP)
	⊕⊕⊖⊖	⊕⊕⊖⊖	⊕⊕⊖⊖	⊕⊖⊖⊖	⊕⊖⊖⊖
Liraglutide	−3.75 kg (−6.34,-1.15)	−1.49 kg/m² (−2.39,-0.59)	−4.53 cm (−7.37,−1.69)	−3.27 mmHg (−7.45,0.91)	0.24 mmHg (−2.76,3.24)
	⊕⊕⊕⊖	⊕⊕⊕⊕	⊕⊕⊕⊖	⊕⊕⊕⊕	⊕⊕⊕⊕
Semaglutide	−8.14 kg (−11.45,−4.84)	NR	NR	−2.24 mmHg (−4.20,-0.27)	−0.38 mmHg (−1.41,0.64)
	⊕⊕⊕⊕			⊕⊕⊕⊕	⊕⊕⊕⊕

GRADE(+)

問題五：如果作者將研究結果進行合併，是否合理?

⬜ Yes ⬜ No ⬜ ☑️ Can't tell

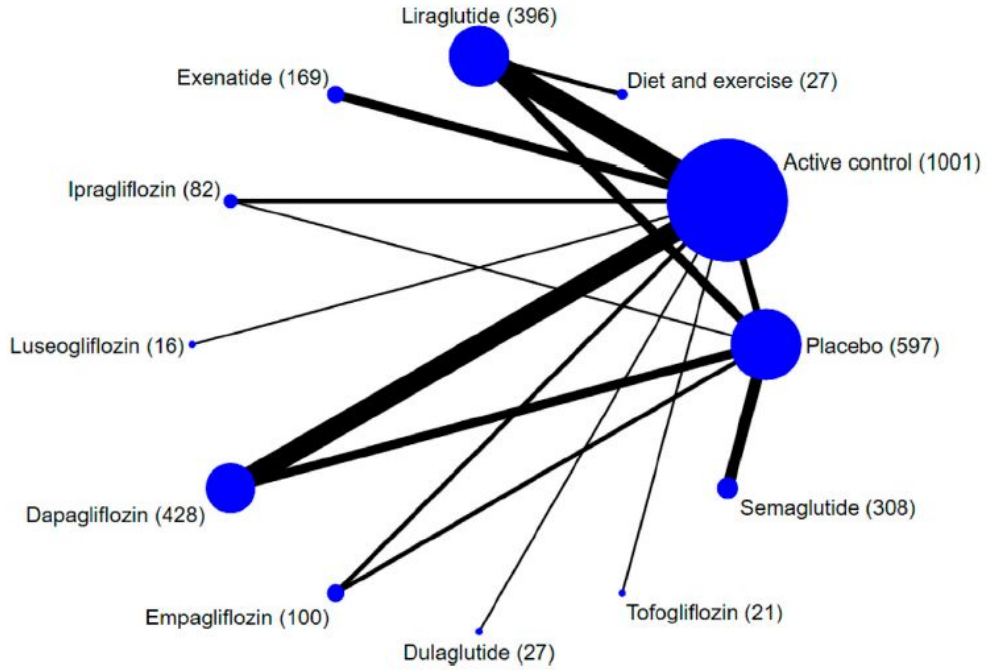


FIGURE 2
Network plot of trials evaluating the effects of sodium-glucose cotransporter protein-2 inhibitors and glucagon-like peptide-1 receptor agonists for patients with NAFLD. Network shows the number of participants assigned to each treatment class with the size of each circle proportional to the number of randomly assigned participants in the treatment comparisons (sample size for the specific treatment shown in brackets). Line thickness is proportional to the number of patients that contributed to the comparison.

The network structure **reveals potential biases** due to **uneven sample sizes**, **sparse data** for some treatments, and reliance on **indirect comparisons**.

問題六：這篇系統性文獻回顧的整體結果為何？

Primary outcome

SGLT2-I

TABLE 1 Summary of anticipated absolute differences in outcomes comparing sodium-glucose cotransporter-2 inhibitor and glucagon-like peptide-1 receptor agonist treatment with placebo treatment.

Liver enzymes parameters	Alanine aminotransferase (ALT)	Aspartate aminotransferase (AST)	γ-glutamyl transferase (GGT)
Dapagliflozin	−9.94 U/L (−18.42,−1.46)	−6.70 U/L (−12.03,−1.37)	−13.82 U/L (−31.20,3.57)
	⊕⊕⊕⊕	⊕⊕⊕⊖	⊕⊕⊖⊖
Empagliflozin	−5.37 U/L (−17.17,6.43)	−5.08 U/L (−12.07,1.92)	−16.60 U/L (−49.74,16.53)
	⊕⊕⊕⊕	⊕⊕⊕⊕	⊕⊕⊕⊖
Ipragliflozin	−8.09 U/L (−20.72,4.54)	−7.08 U/L (−14.76,0.60)	−10.37 U/L (−26.04,5.31)
	⊕⊕⊖⊖	⊕⊕⊖⊖	⊕⊕⊕⊖
Luseogliflozin	0.69 U/L (−20.37,21.75)	NR	NR
	⊕⊕⊖⊖		
Tofogliflozin	6.69 U/L (−19.27,32.65)	8.06 U/L (−7.03,23.14)	23.80 U/L (−7.21,54.80)
	⊕⊕⊕⊖	⊕⊕⊕⊖	⊕⊕⊕⊖

GLP-1 agonist

Dulaglutide	−16.31 U/L (−40.22,7.60)	−13.34 U/L (−28.22,1.53)	−18.70 U/L (−45.13,7.73)
	⊕⊕⊕⊖	⊕⊕⊕⊖	⊕⊕⊕⊖
Exenatide	−9.65 U/L (−21.65,2.35)	−8.50 U/L (−15.70,-1.29)	−7.29 U/L (−26.43,11.85)
	⊕⊕⊖⊖	⊕⊕⊖⊖	⊕⊕⊖⊖
Liraglutide	−8.30 U/L (−16.16, −0.43)	−4.60 U/L (−9.48,0.29)	−7.29 U/L (−19.88,5.30)
	⊕⊕⊕⊕	⊕⊕⊕⊕	⊕⊕⊕⊕
Semaglutide	−14.70 U/L (−24.79,−4.61)	−9.32 U/L (−15.12,−3.52)	−16.56 U/L (−27.30,−5.82)
	⊕⊕⊕⊕	⊕⊕⊕⊕	⊕⊕⊕⊕

☑️ Yes ⬜ No ⬜ Can't tell

Both SGLT-2 inhibitors and GLP-1 RAs **may offer hepatic benefits**, but **Semaglutide** may be preferred in patients with significant liver enzyme abnormalities

問題六：這篇系統性文獻回顧的整體結果為何？

Secondary outcome

SGLT2-I

Anthropometric measures	Body weight (BW)	Body mass index (BMI)
Dapagliflozin	−3.48 kg (−5.88,-1.08)	−1.13 kg/m² (−2.14,-0.11)
	⊕⊕⊕⊕	⊕⊕⊕⊖
Empagliflozin	−2.60 kg (−7.31,2.12)	−1.07 kg/m² (−2.45,0.31)
	⊕⊕⊕⊕	⊕⊕⊕⊕
Ipragliflozin	−3.04 kg (−7.54,1.47)	−1.07 kg/m² (−2.64,0.50)
	⊕⊕⊕⊖	⊕⊕⊕⊖
Luseogliflozin	NR	−0.83 kg/m² (−2.83,1.16)
		⊕⊖⊖⊖
Tofogliflozin	1.60 kg (−4.71,7.90)	NR
	⊕⊕⊕⊖	

GLP-1 agonist

Anthropometric measures	Body weight (BW)	Body mass index (BMI)
	⊕⊕⊖⊖	⊕⊕⊖⊖
Liraglutide	−3.75 kg (−6.34,-1.15)	−1.49 kg/m² (−2.39,-0.59)
	⊕⊕⊕⊖	⊕⊕⊕⊕
Semaglutide	−8.14 kg (−11.45,−4.84)	NR
	⊕⊕⊕⊕	
Dulaglutide	−2.14 kg (−8.45,4.16)	−1.00 kg/m² (−3.10,1.09)
	⊕⊕⊕⊖	⊕⊕⊕⊖
Exenatide	−4.40 kg (−8.12,−0.69)	−1.86 kg/m² (−3.12,-0.59)
	⊕⊕⊖⊖	⊕⊕⊖⊖

☑️ Yes ⬜ No ⬜ Can't tell

Both SGLT-2 inhibitors and GLP-1 receptor agonists are **effective** in reducing **BW and BMI**, with **GLP-1 receptor agonists**, particularly **semaglutide**, demonstrating **greater efficacy** in weight management.

問題六：這篇系統性文獻回顧的整體結果為何？

Secondary outcome

SGLT2-I

Blood lipids	Total cholesterol(TC)	Triglycerides (TG)	High density lipoprotein-cholesterol (HDL-C)	Low density lipoprotein-cholesterol (LDL-C)
Dapagliflozin	0.30 mmol/L (−0.19,0.78)	−0.23 mmol/L (−0.46,-0.01)	0.14 mmol/L (0.06,0.21)	−0.03 mmol/L (−0.37,0.31)
	⊕⊖⊖⊖	⊕⊕⊖⊖	⊕⊕⊖⊖	⊕⊕⊕⊕
Empagliflozin	−0.23 mmol/L (−0.76,0.30)	−0.09 mmol/L (−0.60,0.42)	0.03 mmol/L (−0.07,0.14)	−0.09 mmol/L (−0.55,0.37)
	⊕⊕⊕⊕	⊕⊕⊕⊕	⊕⊕⊕⊕	⊕⊕⊕⊕
Ipragliflozin	0.05 mmol/L (−0.28,0.38)	−0.26 mmol/L (−0.48,-0.04)	0.08 mmol/L (0.01,0.14)	0.06 mmol/L (−0.33,0.46)
	⊕⊕⊖⊖	⊕⊕⊕⊖	⊕⊕⊕⊖	⊕⊕⊕⊖
Luseogliflozin	NR	NR	NR	NR
Tofogliflozin	−0.01 mmol/L (−0.81,0.79)	0.52 mmol/L (−0.12,1.16)	NR	NR
	⊕⊕⊕⊖	⊕⊕⊕⊖		

GLP-1 agonist

Dulaglutide		−0.35 mmol/L (−2.76,2.07)	−0.02 mmol/L (−0.58,0.54)	0.10 mmol/L (−2.11,2.31)
		⊕⊕⊕⊖	⊕⊕⊕⊖	⊕⊕⊕⊖
Exenatide	−0.33 mmol/L (−0.74,0.07)	−0.21 mmol/L (−0.48,0.06)	0.07 mmol/L (−0.02,0.17)	−0.28 mmol/L (−0.73,0.18)
	⊕⊕⊖⊖	⊕⊕⊖⊖	⊕⊕⊕⊖	⊕⊕⊕⊖
Liraglutide	−0.24 mmol/L (−0.55,0.06)	−0.20 mmol/L (−0.43,0.03)	0.08 mmol/L (0.02,0.15)	−0.05 mmol/L (−0.35,0.25)
	⊕⊕⊕⊖	⊕⊕⊕⊖	⊕⊕⊕⊖	⊕⊕⊕⊖
Semaglutide	0.13 mmol/L (−0.13,0.39)	−0.25 mmol/L (−0.40,−0.10)	0.05 mmol/L (0.01,0.09)	0.16 mmol/L (−0.16,0.48)
	⊕⊕⊕⊕	⊕⊕⊕⊕	⊕⊕⊕⊕	⊕⊕⊕⊕

☑️ Yes ⬜ No ⬜ Can't tell

1.SGLT-2 inhibitors have mild effects on improving lipid profiles, with modest TG reduction and HDL-C improvement.

2. **GLP-1** receptor agonists are more **consistent in lowering TG** and have beneficial effects on HDL-C and LDL-C.

問題七：結果精準嗎？

⬜ Yes ⬜ No ☑️ Can't tell

Conclusion

In summary, this network meta-analysis provided evidence for the effects of SGLT-2 inhibitors and GLP-1 receptor agonists on NAFLD. Based on high confidence evidence of indirect comparisons, semaglutide, liraglutide and dapagliflozin all have a definite effect on NAFLD (or comorbid with type 2 diabetes) and semaglutide appears to have a therapeutic advantage over other included drugs. The effects of included medication therapy on various indicators differ, and clinical selection should be based on the specific condition of the patient. Although the majority of the SGLT-2 inhibitors and GLP-1 receptor agonists included in this analysis were effective for the treatment of NAFLD, there was no sufficient evidence to evaluate the impact of SGLT-2 inhibitors and GLP-1 receptor agonists on the liver structure. Head-to-head studies are required to provide more confidence in clinical decision-making.

The study provides reasonably precise evidence about the therapeutic effects of the drugs on NAFLD. However, its **reliance on indirect comparisons** introduces **limitations to its precision**.

問題八：此研究結果是否可應用到當地的族群？

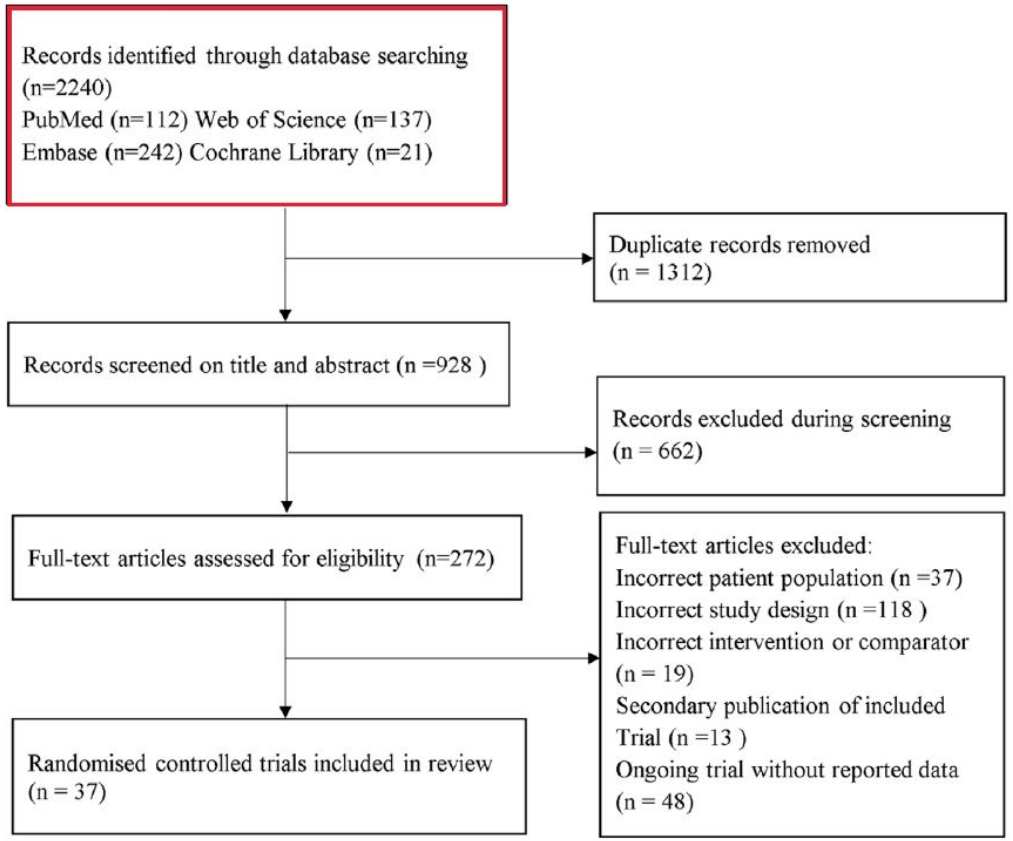


FIGURE 1
PRISMA flow diagram.

☑️Yes ⬜ No ⬜Can't tell

取自全世界 database

問題九：是否所有重要的臨床結果都有被考量到？

Outcomes

Primary outcomes were improvements in liver enzymes [alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyl transferase (GGT)] and liver fat parameters [subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), liver fat fraction (LFF), controlled attenuation parameter (CAP), liver stiffness measurement (LSM)]; secondary outcomes included anthropometric measures [body weight (BW), body mass index (BMI), waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP)], blood lipids [total cholesterol (TC), triglycerides (TG), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C) and serum adiponectin], glycemic parameters [fasting blood glucose (FBG), postprandial blood glucose (PBG), glycosylated hemoglobin (HbA1c), glucose and homeostasis model assessment (HOMA-IR)].

☑️ Yes ⬜ No ⬜ Can't tell

ALT, AST, r-GGT

Subcutaneous adipose tissue
Visceral adipose tissue

Body weight, BMI, waist circumference,

SBP/DBP,

TC,TG, HDL-C, LDL-C, FBG, HbA1c

問題九：是否所有重要的臨床結果都有被考量到？

☑ Yes ☐ No ☐ Can't tell

Liver fat parameters	Subcutaneous adipose tissue (SAT)	Visceral adipose tissue (VAT)	Liver fat fraction (LFF)	Controlled attenuation parameter (CAP)	Liver stiffness measurement (LSM)
Dapagliflozin	−0.26 cm^2 (−0.36,−0.17)	−6.96 cm^2 (−18.37,4.46)	−0.95% (−2.52,0.62)	−38.86 db/m (−73.39,-4.33)	−1.67 kPa (−4.49,1.16)
	⊕⊕⊕⊖	⊕⊕⊖⊖	⊕⊕⊕⊖	⊕⊕⊖⊖	⊕⊕⊕⊖

Liver fat parameters	Subcutaneous adipose tissue (SAT)	Visceral adipose tissue (VAT)	Liver fat fraction (LFF)	Controlled attenuation parameter (CAP)	Liver stiffness measurement (LSM)
Dapagliflozin	−0.26 cm^2 (−0.36,−0.17)	−6.96 cm^2 (−18.37,4.46)	−0.95% (−2.52,0.62)	−38.86 db/m (−73.39,-4.33)	−1.67 kPa (−4.49,1.16)
	⊕⊕⊕⊖	⊕⊕⊖⊖	⊕⊕⊕⊖	⊕⊕⊖⊖	⊕⊕⊕⊖

Anthropometric measures	Body weight (BW)	Body mass index (BMI)	Waist circumference (WC)	Systolic blood pressure (SBP)	Diastolic blood pressure (DBP)
Dapagliflozin	−3.48 kg (−5.88,-1.08)	−1.13 kg/m^2 (−2.14,-0.11)	−2.78 cm (−5.61,0.06)	−3.61 mmHg (−9.84,2.61)	−1.59 mmHg (−5.41,2.23)
	⊕⊕⊕⊕	⊕⊕⊕⊖	⊕⊕⊕⊕	⊕⊕⊕⊖	⊕⊕⊕⊖

Blood lipids	Total cholesterol(TC)	Triglycerides (TG)	High density lipoprotein-cholesterol (HDL-C)	Low density lipoprotein-cholesterol (LDL-C)	Serum adiponectin
Dapagliflozin	0.30 mmol/L (−0.19,0.78)	−0.23 mmol/L (−0.46,-0.01)	0.14 mmol/L (0.06,0.21)	−0.03 mmol/L (−0.37,0.31)	−1.61 μg/mL (−5.02,1.81)
	⊕⊖⊖⊖	⊕⊕⊖⊖	⊕⊕⊖⊖	⊕⊕⊕⊕	⊕⊕⊕⊖

Glycemic parameters	Fasting blood glucose (FBG)	Postprandial blood glucose (PBG)	Glycosylated hemoglobin (HbA1c)	Glucose and homeostasis model assessment (HOMA-IR)
Dapagliflozin	−0.75 mmol/L (−1.12,−0.39)	−2.14 mmol/L (−3.67,-0.61)	−0.72% (−1.01,−0.42)	−0.84 (−1.53,−0.15)
	⊕⊕⊕⊕	⊕⊕⊕⊕	⊕⊕⊕⊕	⊕⊕⊕⊕

ALT, AST, r-GGT

Subcutaneous adipose tissue
Visceral adipose tissue

Body weight, BMI, waist circumference,

SBP/DBP,

TC,TG, HDL-C, LDL-C, FBG, HbA1c

問題十：傷害和花費換得介入所產生益處是否值得?

☑ Yes ☐ No ☐ Can't tell

information regarding the safety of the nine interventions. Most adverse events were mild to moderate in severity, and no deaths were reported during the trial of the nine interventions. Gastrointestinal disorders were the most commonly reported AEs of GLP-1 receptor agonists. Urogenital infections, including urinary tract infections,

on NAFLD. Based on high confidence evidence of indirect comparisons, semaglutide, liraglutide and dapagliflozin all have a definite effect on NAFLD (or comorbid with type 2 diabetes) and semaglutide appears to have a therapeutic advantage over other included drugs. The effects of included medication therapy on various indicators differ, and clinical selection should be based on the specific condition of the patient. Although the majority of the SGLT-2 inhibitors and GLP-1 receptor agonists included in this analysis were effective

Semaglutide

- **Mild to moderate adverse events**
- **Therapeutic advantage over other included drugs**

Apply

5A-4

臨床應用

–臨床應用–

給付規定
5.1.3.2. Liraglutide (如Victoza)、dulaglutide (如Trulicity)、lixisenatide(如Lyxumia) semaglutide（如Ozempic）
1.限用於已接受過最大耐受劑量的metformin及/或sulfonylurea類藥物，且併用下列藥品之一持續6個月之後，HbA1c仍高於8.5%以上之第二型糖尿病患者 (1)SGLT-2抑制劑 (2)DPP-4抑制劑 (3)SGLT-2抑制劑合併DPP-4抑制劑複方藥品 (4)Insulin
2.當患者已接受前述口服降血糖藥物，及/或基礎胰島素治療仍未達理想血糖控制時，與口服降血糖藥物及/或基礎胰島素併用。
3.發生重大心血管事件，如心肌梗塞、接受冠狀動脈或其他動脈血管再通術(revascularization)、動脈硬化相關之缺血性腦中風等之病人，於接受過最大耐受劑量的metformin後，仍無法理想控制血糖之第二型糖尿病患者，可考慮不須使用其他口服降血糖藥品而考慮使用liraglutide或dulaglutide。
4.本藥品不得與DPP-4抑制劑、SGLT-2抑制劑併用。
5. 109年5月1日前已依生效前之給付規定使用本類藥物之病人，得繼續使用原藥物至醫師更新其處方內容（109/8/1）。

- **健保給付規定：非第二型糖尿病患者須自費**

–臨床應用–

商品名		劑量	廠商	單支單週藥價
Ozempic solution for injection	Semaglutide 1.34 MG/ML	1.5ML	台灣諾和諾德藥品股份有限公司	3,585
Ozempic solution for injection	Semaglutide 1.34 MG/ML	3ML	台灣諾和諾德藥品股份有限公司	3,585

藥物施打:一週施打一次
藥物費用: 3585元 (依照各家醫院彈性調整)

Audit 5A-5

執行決策

-執行決策-

醫療現況(實證醫學)

證據等級：CEBM(Level 1)
建議等級：Weak Recommendation

病人的治療偏好

希望可以藉由瘦瘦針達到在有肥胖，脂肪肝的情況下達到減重效果。

利弊平衡

使用瘦瘦針(Semaglutide)治療可預期體重減輕8.14公斤，效果十分顯著。

除了常見的腸胃道副作用如噁心嘔吐，但目前研究指出並無致死之風險。

費用資源

注射瘦瘦針(Semaglutide)，一週需注射一次，注射費用為3500-3800元/劑，可顯著減少使用者之體重。而過重會造成心血管疾病和中風風險提高，所產生之住院和介入/手術處置花費和醫療成本將遠大於預防。

-回答病人問題－以去學術化術語方式-

莊先生您好，經過我們團隊縝密的實證搜尋後，目前現有最佳證據是由 **系統性回顧文獻** 的研究支持，使用瘦瘦針(Semaglutide)治療可預期有效的協助體重減輕，且花費是 **一週3500-3800元** ，因為您的體重落於肥胖族群， **肥胖族群在心肌梗塞，血管硬化等慢性疾病中屬高危險族群** ，所以建議您接受一週施打一次的瘦瘦針(Semaglutide)的治療。另外平常仍須注重 **飲食控制和養成合適的運動習慣** ，這樣才能達成長期性的體重控制效果噢！

多謝
聆聽