實證醫學競賽

內科NP 雷麗碧
藥劑科 何睿凱 林姝芸

臨床情境

一位68歲糖尿病第二型合併慢性腎病(腎絲球濾過率約45mL/min/1.73m^2)的男性病人，因有蛋白尿(每日蛋白排>0.5g)且血壓控制不佳，現正使用ACE抑制劑(氯沙坦)控制血壓。主治醫生考慮在此病人加入一項新的腎保護藥物(例如SGLT-2抑制劑)來降低進一步惡化為末期腎病或需洗腎的風險。

在這樣的病人族群中，加入SGLT-2抑制劑與單純維持ACE抑制劑治療相比，是否能有效減少腎功能惡化、洗腎啟動或死亡率的發生?並評估其適用性於該病人。

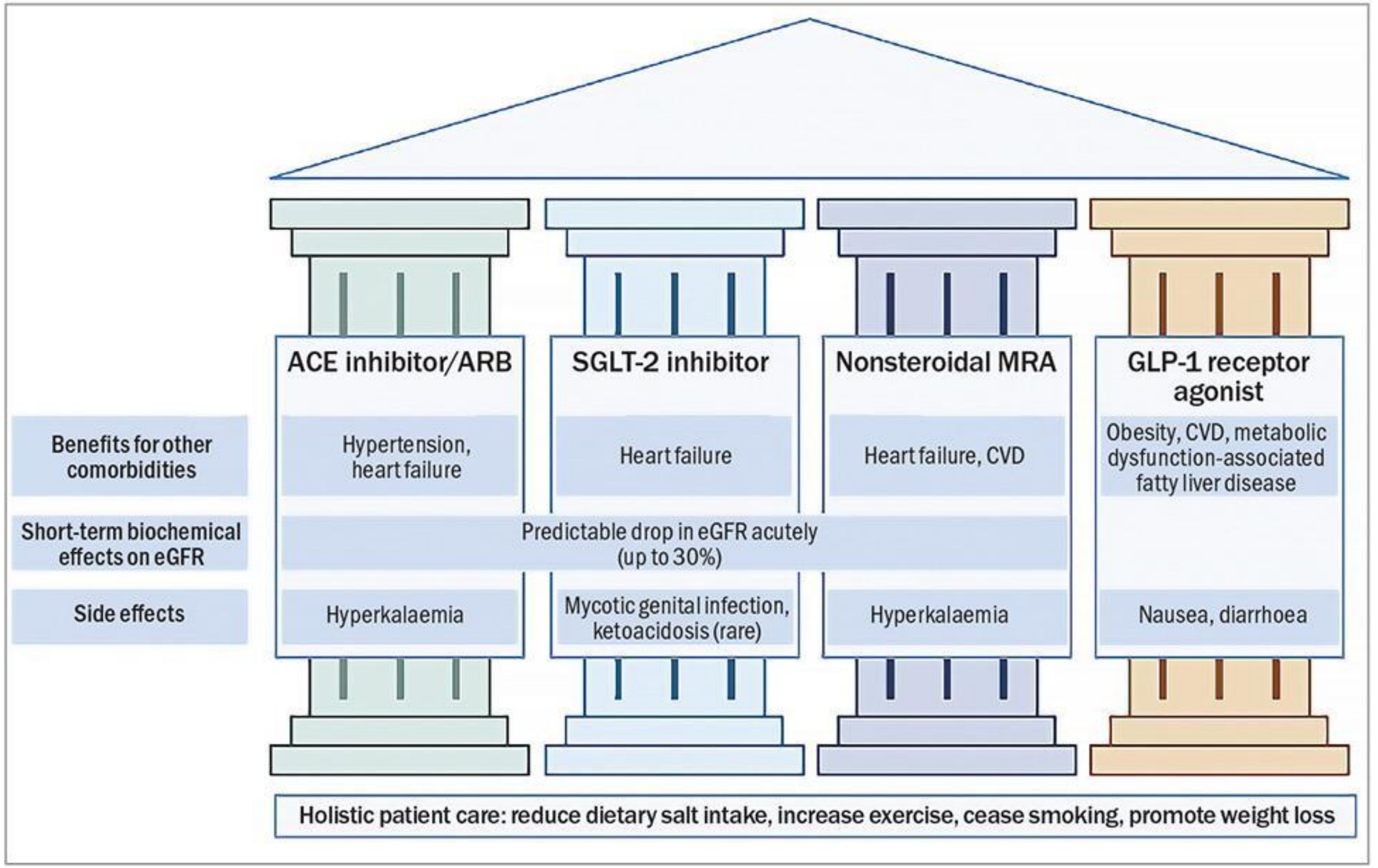
背景資訊-Diabetic Kidney Disease (DKD)

1. DKD can be classified by renal function trajectories into 4 types
    1. classical DKD
    2. albuminuria regression
    3. rapid eGFR decline
    4. non-proteinuric or non-albuminuric DKD
2. National Nutrition and Health Survey in Taiwan revealed：
   a rising DKD prevalence from 9.17 % in 2000 to 17.92 % in 2014 was also recorded, pervasive across both sexes and all age groups but elderly were most affected .
3. Taiwan ranked the top on incidence of treated end-stage renal disease (ESRD) globally (525 per million population in 2020), with DKD constituting 49.6 % of all dialysis-dependent patients reflecting its public health significance.

J Formos Med Assoc. 2025 Aug 20:S0929-6646(25)00439-5.

背景資訊

The pillars of therapy for diabetic kidney disease

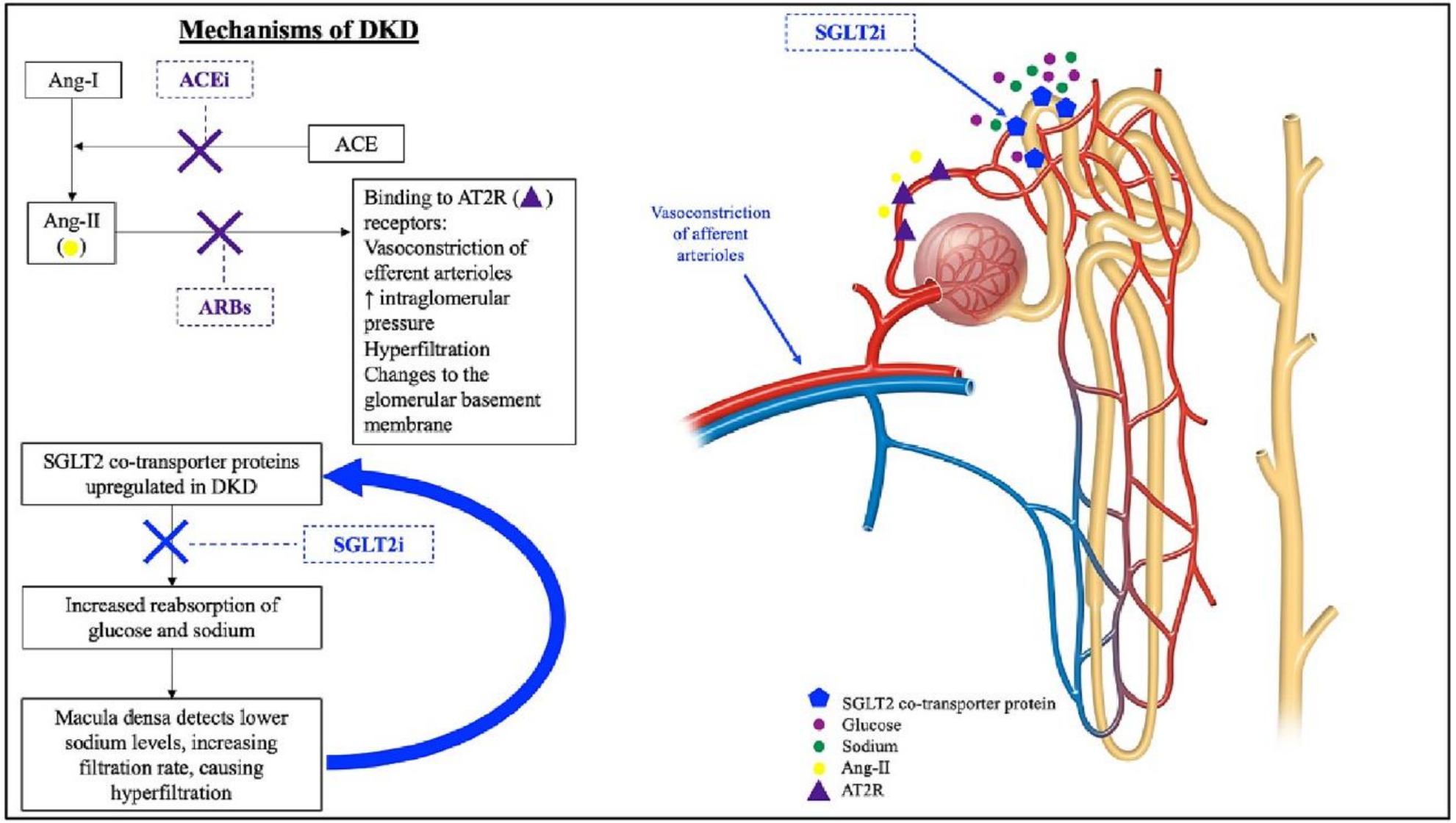


Medicine Today 2024; 25(12): 10-17

背景資訊

SGLT-2 inhibitors mechanism

1. increase distal sodium delivery→restoring tubuloglomerular feedback
2. afferent arteriolar vasoconstriction→reduction in intraglomerular pressure
3. modestly lower blood pressure and reduce albuminuria



J Diabetes Complications. 2023 Jun;37(6):108456.

Five Steps to Practice EBM (5 As)

1 Asking - 提出問題

2 Acquiring - 搜尋證據

3 Appraising - 評讀文獻

4 Applying - 臨床應用

5 Assessing - 執行決策

Asking-提出問題

PICO-1

	Free-Text	Synonyms
P	Patient with Type 2 DM, Chronic kidney disease, Hypertension, Proteinuria	Hypertension, chronic kidney disease, proteinuria, diabetes mellitus
I	sodium glucose co-transporters 2 inhibitor	Dapagliflozin, Empagliflozin, Canagliflozin, sodium glucose co-transporters 2, SGLT2 inhibitor
C	Angiotensin Converting Enzyme Inhibitors, or angiotensin receptor blockers	Ramipril, fosinopril, monopril, lisinopril, perindopril, captopril, losartan, valsartan, telmisartan, irbesartan, Olmesartan, candesartan, eprosartan, Angiotensin Converting Enzyme Inhibitors, ACEI, angiotensin receptor blockers, ARB
O	Renal function, Dialysis, Death	estimated Glomerular Filtration Rate , estimated GFR, renal function, dialysis, death

問題設計：■治療型 □傷害型 □ 診斷型 □ 篩檢型 □預後型

PICO-2

	Free-Text	Synonyms
P	Patient with Type 2 DM, Chronic kidney disease	chronic kidney disease, diabetic kidney disease, diabetic nephropathy
I	sodium glucose co-transporters 2 inhibitor	Dapagliflozin, Empagliflozin, Canagliflozin, sodium glucose co-transporters 2, SGLT2 inhibitor
C	Angiotensin Converting Enzyme Inhibitors, or angiotensin receptor blockers	Ramipril, fosinopril, monopril, lisinopril, perindopril, captopril, losartan, valsartan, telmisartan, irbesartan, Olmesartan, candesartan, eprosartan, Angiotensin Converting Enzyme Inhibitors, ACEI, angiotensin receptor blockers, ARB
O	Renal function, Dialysis, Death	estimated Glomerular Filtration Rate , estimated GFR, renal function

問題設計：■治療型 □傷害型 □ 診斷型 □ 篩檢型 □預後型

Acquiring-搜尋文獻

Acquiring Electronic Databases

PubMed

Cochrane

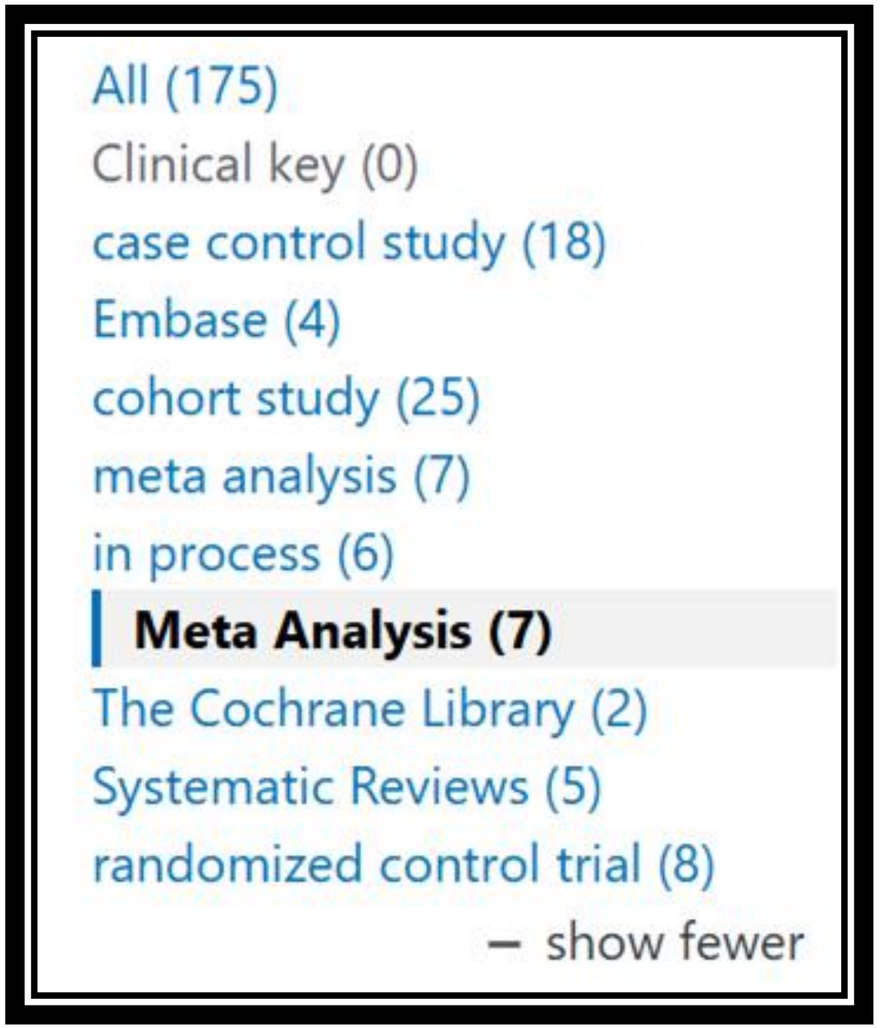
airiti Library
華藝線上圖書館

Search Query – Pubmed (

Search	Query	Items found
5	(((#1) AND (#2)) AND (#3)) AND (#4)	175
4	(estimated Glomerular Filtration Rate) OR ((estimated GFR) OR (renal function))	535,901
3	((((((((((Ramipril) OR (fosinopril)) OR (monopril)) OR (lisinopril)) OR (perindopril)) OR (captopril)) OR (losartan)) OR (valsartan)) OR (telmisartan)) OR (irbesartan)) OR (olmesartan)) OR (candesartan)) OR (eprosartan)) OR ((((Angiotensin Converting Enzyme Inhibitors) OR (ACEI)) OR (angiotensin receptor blockers)) OR (ARB))	98,543
2	(((Dapagliflozin) OR (Empagliflozin)) OR (Canagliflozin)) OR ((sodium glucose co-transporters 2) OR (SGLT2 inhibitor))	16,422
1	(estimated Glomerular Filtration Rate) OR ((estimated GFR) OR (renal function))	535,901

Search Query – Pubmed

使用Filter
☑篩選MA, RCT, SR
☑不限期間



Search Query – Pubmed-Meta analysis

1 Cite

Finerenone in type **2** diabetes and **renal** outcomes: A random-effects model **meta-analysis**.

Ghosal S, Sinha B.

Front Endocrinol (Lausanne). 2023 Jan 20;14:1114894. doi: 10.3389/fendo.2023.1114894. eCollection 2023.

PMID: 36742404 **Free PMC article.**

BACKGROUND: The nonsteroidal mineralocorticoid antagonist finerenone is a new addition to the list of agents (**angiotensin converting enzyme inhibitors** and **sodium glucose** cotransporter **2 inhibitors**) conferring **renal** pr ...

檢視 PDF

Mismatch the PICO

2 Cite

Sodium-Glucose Cotransporter **2 Inhibitors** and Risk of Hyperkalemia in People With Type **2** Diabetes: A **Meta-Analysis** of Individual Participant Data From Randomized, Controlled Trials.

Neuen BL, Oshima M, Agarwal R, Arnott C, Cherney DZ, Edwards R, Langkilde AM, Mahaffey KW, McGuire DK, Neal B, Perkovic V, Pong A, Sabatine MS, Raz I, Toyama T, Wanner C, Wheeler DC, Wiviott SD, Zinman B, Heerspink HJL.

Circulation. 2022 May 10;145(19):1460-1470. doi: 10.1161/CIRCULATIONAHA.121.057736. Epub 2022 Apr 8.

PMID: 35394821 **Free article.**

BACKGROUND: Hyperkalemia increases risk of cardiac arrhythmias and death and limits the use of renin-**angiotensin**-aldosterone system **inhibitors** and mineralocorticoid **receptor antagonists**, which improve clinical outcomes in people with **chronic** ...

檢視 PDF

Mismatch the PICO

Search Query – Pubmed-Meta analysis

3

Cite

Efficacy of Modern Therapies for Heart Failure with Reduced Ejection Fraction in Specific Population Subgroups: A Systematic Review and Network **Meta-Analysis**.

Lavalle C, Mariani MV, Severino P, Palombi M, Trivigno S, D'Amato A, Silvetti G, Pierucci N, Di Lullo L, Chimenti C, Summaria F, Ronco C, Badagliacca R, Miraldi F, Vizza CD.

Cardiorenal Med. 2024;14(1):570-580. doi: 10.1159/000541393. Epub 2024 Sep 16.

PMID: 39284285 **Free article.**

We compared randomized clinical trials for HFrEF emerging therapies focusing on the elderly (patients >65 years old and >75 years old), **chronic kidney disease** (CKD) (**estimated glomerular filtration rate** (eGFR) &lt ...

檢視 PDF

Mismatch the PICO

4

Cite

A **meta-analysis** of randomized controlled clinical trials for implications of acute treatment effects on **glomerular filtration rate** for long-term **kidney** protection.

Heerspink HJL, Eddington D, Chaudhari J, Estacio R, Imai E, Goicoechea M, Hannedouche T, Haynes R, Jafar TH, Johnson DW, van Kruijsdijk RCM, Lewis JB, Li PKT, Neuen BL, Perrone RD, Ruggenenti P, Wanner C, Woodward M, Xie D, Greene T, Inker LA.

Kidney Int. 2024 Oct;106(4):688-698. doi: 10.1016/j.kint.2024.05.024. Epub 2024 Jun 18.

PMID: 38901604

Pharmacologic interventions to slow **chronic kidney disease** progression, such as ACE-**inhibitors**, **angiotensin receptor blockers**, or **sodium glucose co**-transporter **2 inhibitors**, often produce acute tr ...

Mismatch the PICO

Search Query – Pubmed-Meta analysis

5

Cite

Efficacy and safety of **sodium glucose** cotransporter **2 inhibitors** plus standard care in **diabetic kidney disease**: A systematic review and **meta-analysis**.

Woodhams LM, Chalmers L, Sim TF, Yeap BB, Schlaich MP, Schultz C, Hillis GS.

J Diabetes Complications. 2023 Jun;37(6):108456. doi: 10.1016/j.jdiacomp.2023.108456. Epub 2023 Mar 18.

PMID: 37127001

INTRODUCTION: Many people with type **2** diabetes progress to end-stage **diabetic kidney disease** (DKD) despite blockade of the renin-**angiotensin** system, suggesting the need for innovative treatment options for DKD. To capture the findings of recent ...

6

Cite

Benefits of **SGLT2 inhibitors** combining with renin-**angiotensin**-system **blockers** on cardiovascular outcomes in **chronic kidney disease** patients: A systemic review and **meta-analysis**.

Liu T, Li R, Wang X, Gao X, Zhang X.

Med Clin (Barc). 2022 Jul 22;159(2):65-72. doi: 10.1016/j.medcli.2021.09.031. Epub 2021 Dec 3.

PMID: 34872768 English, Spanish.

We conducted this **meta-analysis** to explore the effect of **SGLT2 inhibitors** combining with RAS **blockers** on cardiovascular outcomes in **chronic kidney disease** (CKD) patients. ...We included randomized controlled trials (RCTs) ba ...

Unavailable full text

Search Query – Pubmed-Meta analysis

☐ 7 Cite

Kidney Disease in Type **2** Diabetes Mellitus and Benefits of **Sodium**-**Glucose** Cotransporter **2 Inhibitors**: A Consensus Statement.

Roy A, Maiti A, Sinha A, Baidya A, Basu AK, Sarkar D, Sanyal D, Biswas D, Maisnam I, Pandit K, Raychaudhuri M, Sengupta N, Chakraborty PP, Mukhopadhyay P, Raychaudhuri P, Sahana PK, Chatterjee P, Bhattacharjee R, Dasgupta R, Saraogi RK, Pal SK, Mukhopadhyay S, Mukhopadhyay S, Goswami S, Chowdhury S, Ghosh S; Working Group of the Endocrine Society of Bengal.

Diabetes Ther. 2020 Dec;11(12):2791-2827. doi: 10.1007/s13300-020-00921-y. Epub 2020 Oct 6.

PMID: 33025397 **Free PMC article.** Review.

Patients with DKD have a higher risk of cardiovascular and all-cause mortality. **Angiotensin**-**converting enzyme inhibitors** or **angiotensin receptor blockers** and antihyperglycemic drugs form the mainstay of DKD management and aim to re ...

檢視 PDF

Mismatch the PICO

Search Query – Cochrane library

#1	(estimated Glomerular Filtration Rate) OR ((estimated GFR) OR (renal function))	S	MeSH	Limits	36037
#2	(((Dapagliflozin) OR (Empagliflozin)) OR (Canagliflozin)) OR ((sodium glucose co-transporters 2) OR (SGLT2 inhibitor))			Limits	6169
#3	((((((((((((Ramipril) OR (fosinopril)) OR (monopril)) OR (lisinopril)) OR (perindopril)) OR (captopril)) OR (losartan)) OR (valsartan)) OR (telmisartan)) OR (irbesartan)) OR (olmesartan)) OR (candesartan)) OR (eprosartan)) OR ((((Angiotensin Converting Enzyme Inhibitors) OR (ACEI)) OR (angiotensin receptor blockers)) OR (ARB))			Limits	21180
#4	((chronic kidney disease) OR (diabetic kidney disease)) OR (diabetic nephropathy)			Limits	24695
#5	#1 AND #2 AND #3 AND #4			Limits	91

Cochrane Reviews	Cochrane Protocols	Trials	Editorials	Special Collections	Clinical Answers
8	0	83	0	0	0

Search Query – Cochrane library

1 ☐

Sodium-glucose co-transporter protein 2 (SGLT2) inhibitors for people with chronic kidney disease and diabetes

Patrizia Natale, David J Tunnicliffe, Tadashi Toyama, Suetonia C Palmer, Valeria M Saglimbene, Marinella Ruospo, Letizia Gargano, Giovanni Stallone, Loreto Gesualdo, Giovanni FM Strippoli

Free access Intervention Review 21 May 2024

Show PICOs **Show preview**

Mismatch the PICO

2 ☐

Interventions for preventing the progression of autosomal dominant polycystic kidney disease

Kitty St Pierre, Brydee A Cashmore, Davide Bolignano, Carmine Zoccali, Marinella Ruospo, Jonathan C Craig, Giovanni FM Strippoli, Andrew J Mallett, Suetonia C Green, David J Tunnicliffe

Free access Intervention Review 2 October 2024 New search Conclusions changed

Show PICOs **Show preview**

Mismatch the PICO

3 ☐

Insulin and glucose-lowering agents for treating people with diabetes and chronic kidney disease

Clement Lo, Tadashi Toyama, Ying Wang, Jin Lin, Yoichiro Hirakawa, Min Jun, Alan Cass, Carmel M Hawley, Helen Pilmore, Sunil V Badve, Vlado Perkovic, Sophia Zoungas

Free access Intervention Review 24 September 2018

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Mismatch the PICO

4 ☐

Thiazolidinediones for people with chronic kidney disease and diabetes

Patrizia Natale, Suetonia C Green, David J Tunnicliffe, Giovanni Pellegrino, Tadashi Toyama, Pantelis Sarafidis, Giovanni FM Strippoli, supported by Cochrane Kidney and Transplant

Intervention Review 13 November 2025

Show PICOs **Show preview**

Mismatch the PICO

Search Query – Cochrane library

5 ☐ **Immunosuppressive therapy for IgA nephropathy in children**

Areefa Alladin, Deirdre Hahn, Elisabeth M Hodson, Pietro Ravani, Kenneth Pfister, Robert R Quinn, Susan M Samuel

Free access Intervention Review 12 June 2024

Show PICOs **Show preview**

Mismatch the PICO

6 ☐ **Metformin and second- or third-generation sulphonylurea combination therapy for adults with type 2 diabetes mellitus**

Kasper S Madsen, Pernille Kähler, Lise Katrine Aronsen Kähler, Sten Madsbad, Filip Gnesin, Maria-Inti Metzendorf, Bernd Richter, Bianca Hemmingsen

Free access Intervention Review 18 April 2019

Show PICOs **Show preview**

Mismatch the PICO

7 ☐ **Glucagon-like peptide 1 (GLP-1) receptor agonists for people with chronic kidney disease and diabetes**

Patrizia Natale, Suetonia C Green, David J Tunnicliffe, Giovanni Pellegrino, Tadashi Toyama, Giovanni FM Strippoli

Intervention Review 18 February 2025

Show PICOs **Show preview**

Mismatch the PICO

8 ☐ **Interventions for people with type 2 diabetes mellitus fasting during Ramadan**

Shaun Wen Huey Lee, Won Sun Chen, Renukha Sellappans, Shakirah Binti Md.Sharif, Maria-Inti Metzendorf, Nai Ming Lai

Free access Intervention Review 12 July 2023

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Mismatch the PICO

Search Query – 華藝線上圖書館

airiti Library

登入

進階查詢　查詢歷史

1. 文章篇名, 關鍵字, 摘要 — ((chronic kidney disease) OR (diabetic kidney disease)) OR (diabetic nephropathy)

2. AND — 文章篇名, 關鍵字, 摘要 — ((((((((((((Ramipril) OR (fosinopril)) OR (monopril)) OR (

3. AND — 文章篇名, 關鍵字, 摘要 — (((Dapagliflozin) OR (Empagliflozin)) OR (Canagliflozin)

4. AND — 文章篇名, 關鍵字, 摘要 — (estimated Glomerular Filtration Rate) OR ((estimated C

添加一行

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((([ALL3]=(((chronic kidney disease) OR (diabetic kidney disease)) OR (diabetic nephropathy)) AND [ALL3]=((((((((((((((Ramipril)
OR (fosinopril)) OR (monopril)) OR (lisinopril)) OR (perindopril)) OR (captopril)) OR (losartan)) OR (valsartan)) OR
(telmisartan)) OR (irbesartan)) OR (olmesartan)) OR (candesartan)) OR (eprosartan)) OR ((((Angiotensin Converting Enzyme
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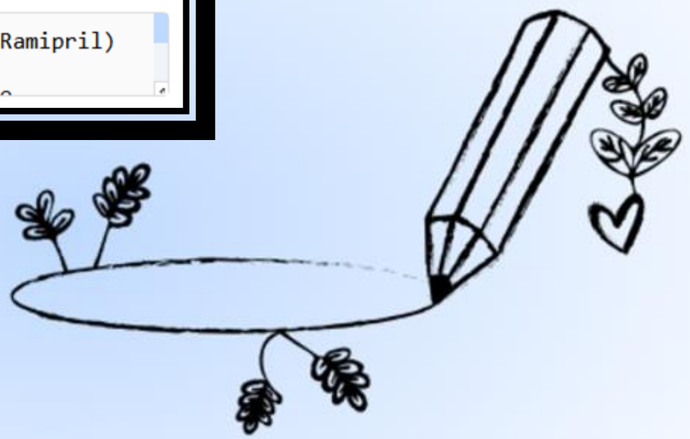
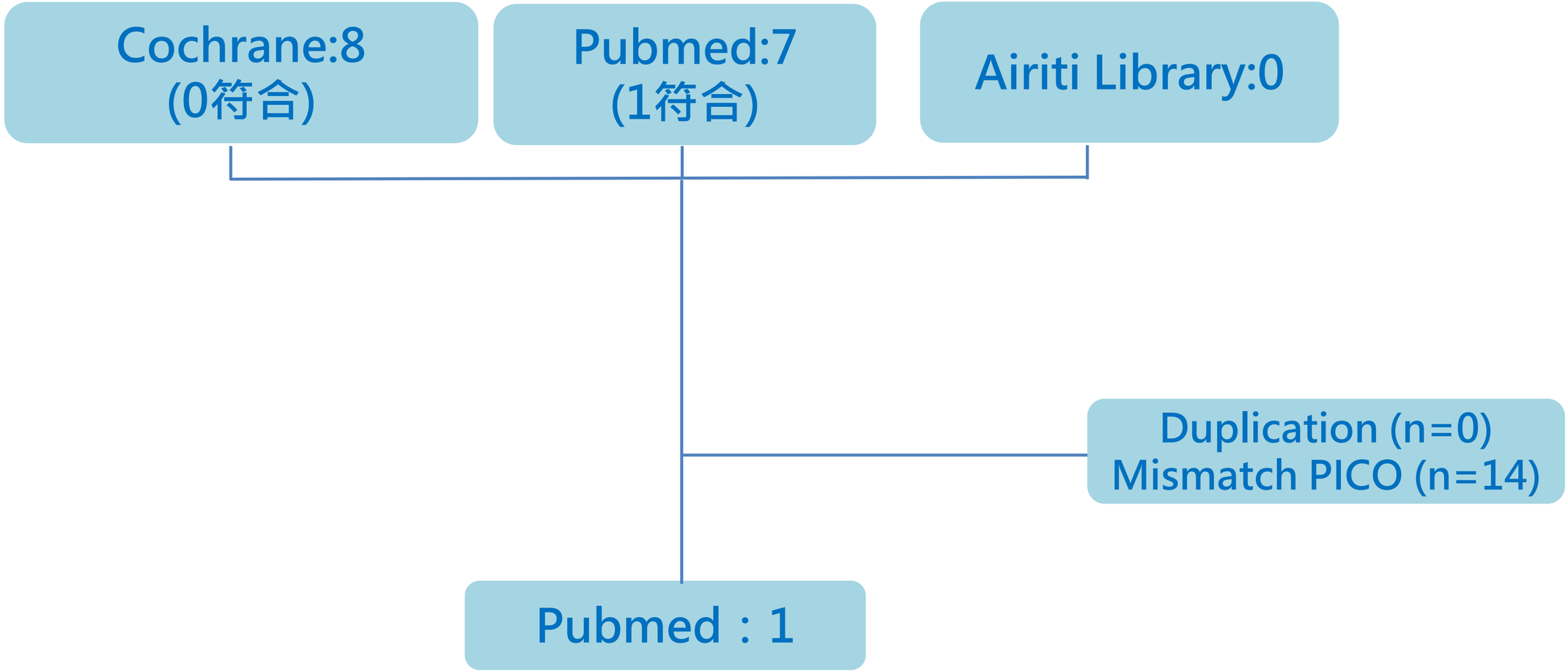


文章類型

出版日期

Search Query



選擇本篇的理由-PICO符合

Summarize article

文獻類型
- ■ Systematic Review
- ☐ Randomised Control Trial
- ☐ Cohort Study
- ☐ Case Control Study
- ☐ Case Report

Efficacy and safety of sodium glucose cotransporter 2 inhibitors plus

ABSTRACT

Introduction: Many people with type 2 diabetes progress to end-stage diabetic kidney disease (DKD) despite blockade of the renin-angiotensin system, suggesting the need for innovative treatment options for DKD. To capture the findings of recent studies, we performed an updated systematic review and meta-analysis of the efficacy and safety of sodium glucose co-transporter 2 (SGLT2) inhibitors combined with standard care involving angiotensin converting enzyme (ACE) inhibitors and/or angiotensin receptor blockers (ARBs) on the development and progression of DKD in people with type 2 diabetes compared with standard care alone.

Methods: The Cochrane Library, MEDLINE, EMBASE, PubMed and clinical trials registers were systematically searched for randomized controlled trials published before 1 September 2022. Primary outcomes were urine albumin-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR). Secondary outcomes were glycated hemoglobin (HbA1c) and systolic blood pressure (SBP). Relative risk was calculated for adverse events.

Results: Eight studies enrolling 5512 participants were included. In the meta-analysis ($n = 1327$), SGLT2 inhibitors were associated with a statistically significant reduction in UACR (weighted mean difference [WMD] -105.61 mg/g, 95 % CI -197.25 to −13.98, $I^2 = 99$ %, $p = 0.02$). There was no statistically significant difference in relation to eGFR ($n = 1375$; WMD -0.23 mL/min/1.73m^2, 95 % CI -4.34 to 3.89, $I^2 = 94$ %, $p = 0.91$).

Conclusions: SGLT2 inhibitors in addition to standard care including ACE inhibitors and/or ARBs significantly reduced albuminuria, HbA1c and SBP when compared to standard care alone, supporting their routine use in people with type 2 diabetes.

I

P

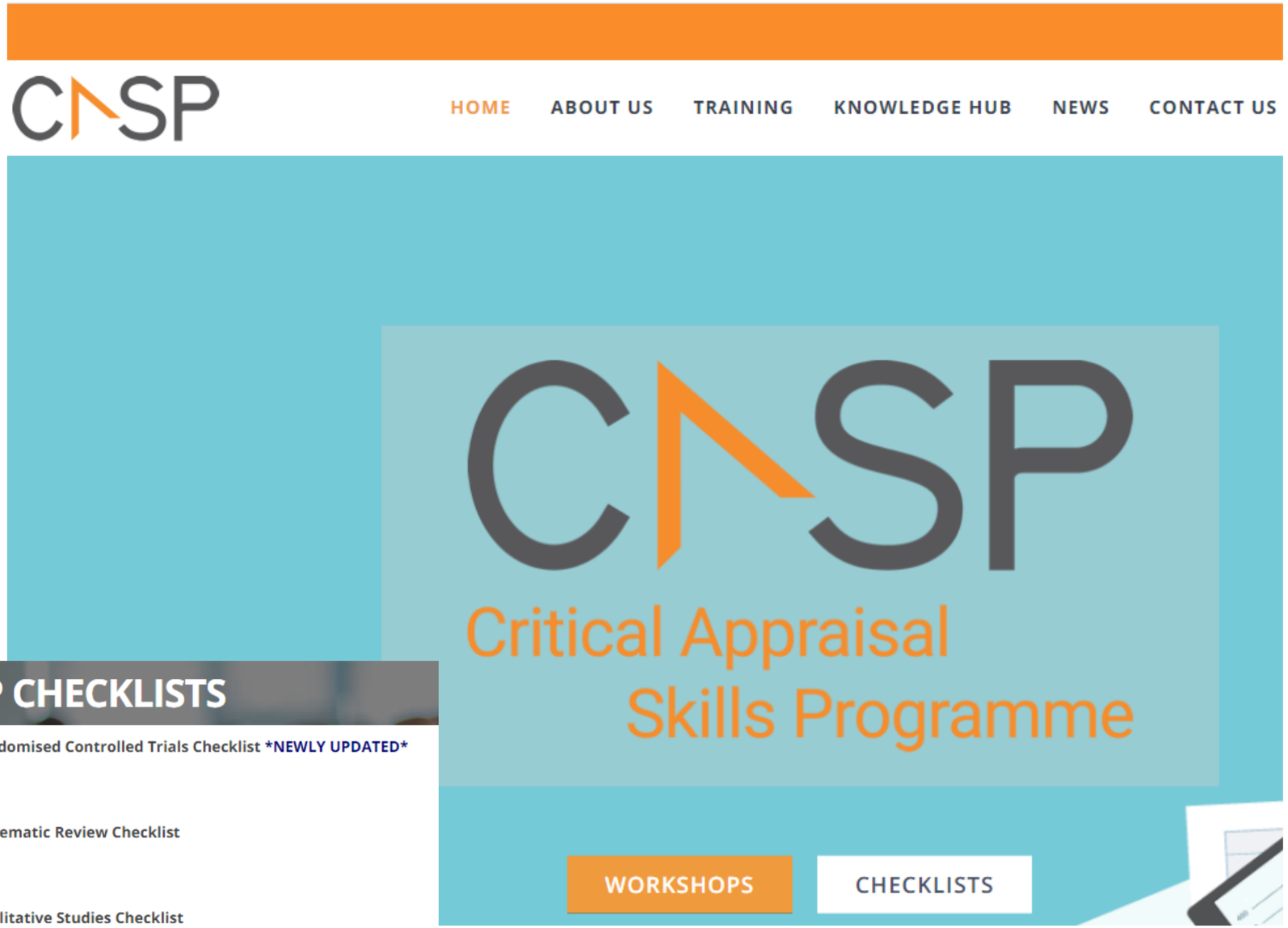
C

O

- ☑ 符合臨床問題
- ☑ 證據等級最高
- ☑ 研究族群相近
- ☑ 年份最新
- ☑ 作者為該領域專家

Appraising-評讀文獻

Selected Critical Appraisal Tools



Validity (可信性)

Importance (重要性)

Practice (適用性)

文獻評讀-SM/Meta analysis

Validity

1.此篇系統性文獻是否問了一個清楚、明確的問題?

☑ Yes ☐ No ☐ Can’ t tell

PICO都有涵蓋，此研究問了清楚明確的問題

ABSTRACT

Introduction: Many people with type 2 diabetes progress to end-stage diabetic kidney disease (DKD) despite blockade of the renin-angiotensin system, suggesting the need for innovative treatment options for DKD. To capture the findings of recent studies, we performed an updated systematic review and meta-analysis of the efficacy and safety of sodium glucose co-transporter 2 (SGLT2) inhibitors combined with standard care involving angiotensin converting enzyme (ACE) inhibitors and/or angiotensin receptor blockers (ARBs) on the development and progression of DKD in people with type 2 diabetes compared with standard care alone.

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Conclusions: SGLT2 inhibitors in addition to standard care including ACE inhibitors and/or ARBs significantly reduced albuminuria, HbA1c and SBP when compared to standard care alone, supporting their routine use in people with type 2 diabetes.

I

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文獻評讀-SM/Meta analysis

2.作者是否尋找適當研究型態的文獻?

☑ Yes ☐ No ☐ Can’ t tell

2.2. Study selection

This systematic review included RCTs involving people living with type 2 diabetes and albuminuria, who were randomized to either standard care (ACE inhibitors and/or ARBs) or a SGLT2 inhibitor in addition to standard care. Participants were required to be over 18 years old, and the primary endpoints, UACR and estimated glomerular filtration rate (eGFR), needed to be reported to determine changes in renal function.

文獻評讀-SM/Meta analysis

3.你認為所有重要且相關的研究都被納入?

☑ Yes ☐ No ☐ Can’ t tell

2.1. Data sources and searches

A systematic search of the literature was conducted in The Cochrane Library, MEDLINE, EMBASE and PubMed. Searches were also conducted in the World Health Organization (WHO) International Clinical Trials Registry Platform Search Portal, PROSPERO, ClinicalTrials.gov, and the EU Clinical Trials register. Searches through these databases and platforms were based on a combination of relevant Medical Subject Headings (MeSH) and free text terms for papers published before 1 September 2022. Duplicates were removed and reference lists were screened for other potentially eligible trials. There were no restrictions on publication date, however language filters were employed to obtain records

納入的研究來自4個資料庫,包含了Cochrane library,Medline,PubMed、Embase重要的初級資料庫,我們認為重要且相關的研究都被納入

文獻評讀-SM/Meta analysis

4.系統性文獻回顧的作者是否評估所納入研究文獻的品質?

☑ Yes ☐ No ☐ Can’ t tell

The quality of the studies included in this revie
review authors (LW, TFS) independently. This wa
Cochrane Risk of Bias Tool [18], and examined seq
lection bias), allocation concealment (selection b
ticipants (performance bias), blinding of outcome
bias) incomplete outcome data (attrition bias)
reporting (reporting bias) and other bias. Each di
either “high risk” or “low risk” and when there w
support an assessment, the term “unclear” was u
text were retrieved from the relevant sections to

made. Reporting bias was assessed through v
funnel plot and interpreted cautiously. Func
assessed under the “other bias” division. Th
assessment of the present meta-analysis accordi
2020 is shown in Supplementary Table 5.

2.4. Data synthesis and analysis

Review Manager (RevMan, The Cochrane Collaboration, London) was used to conduct a meta-analysis, using a random-effects model. Mean differences (MD) with SD were calculated for the continuous data, including UACR, eGFR, HbA1c and SBP. Weighted mean difference (WMD) was calculated as the sum of the differences in each study, weighted by the participants (n) for each study. The relative risk (RR) with a 95 % CI was calculated for reported adverse effects.

Heterogeneity was assessed using the I^2 statistic to quantify inconsistency and describe the level of variability in effect estimates due to heterogeneity rather than chance. Significant heterogeneity was defined as an I^2 value >50 % or a P value <0.1. In case of heterogeneity across the included studies, subgroup analyses were performed for the primary outcomes base on the type of SGLT2 inhibitor, the baseline level of albuminuria and eGFR. A sensitivity analysis to assess the robustness of our findings was not performed, due to unknown or high risk of bias found in each study in the risk of bias assessment.

文獻評讀-SM/Meta analysis

Validity

5.如果作者將研究結果進行合併，這樣的合併是否合理?

☑ Yes ☐ No ☐ Can’ t tell

2.3. Data extraction and quality assessment

Articles retrieved for this meta-analysis were screer
by two review authors (LW, TFS). Initially, titles and
tified studies were screened for eligibility. Potentiall
were screened at full text level to ensure they met t
included in the systematic review. Disagreements i
were resolved by a third review author (LC). Supple
lustrates the PRISMA flow diagram for the study selec

2.4. Data synthesis and analysis

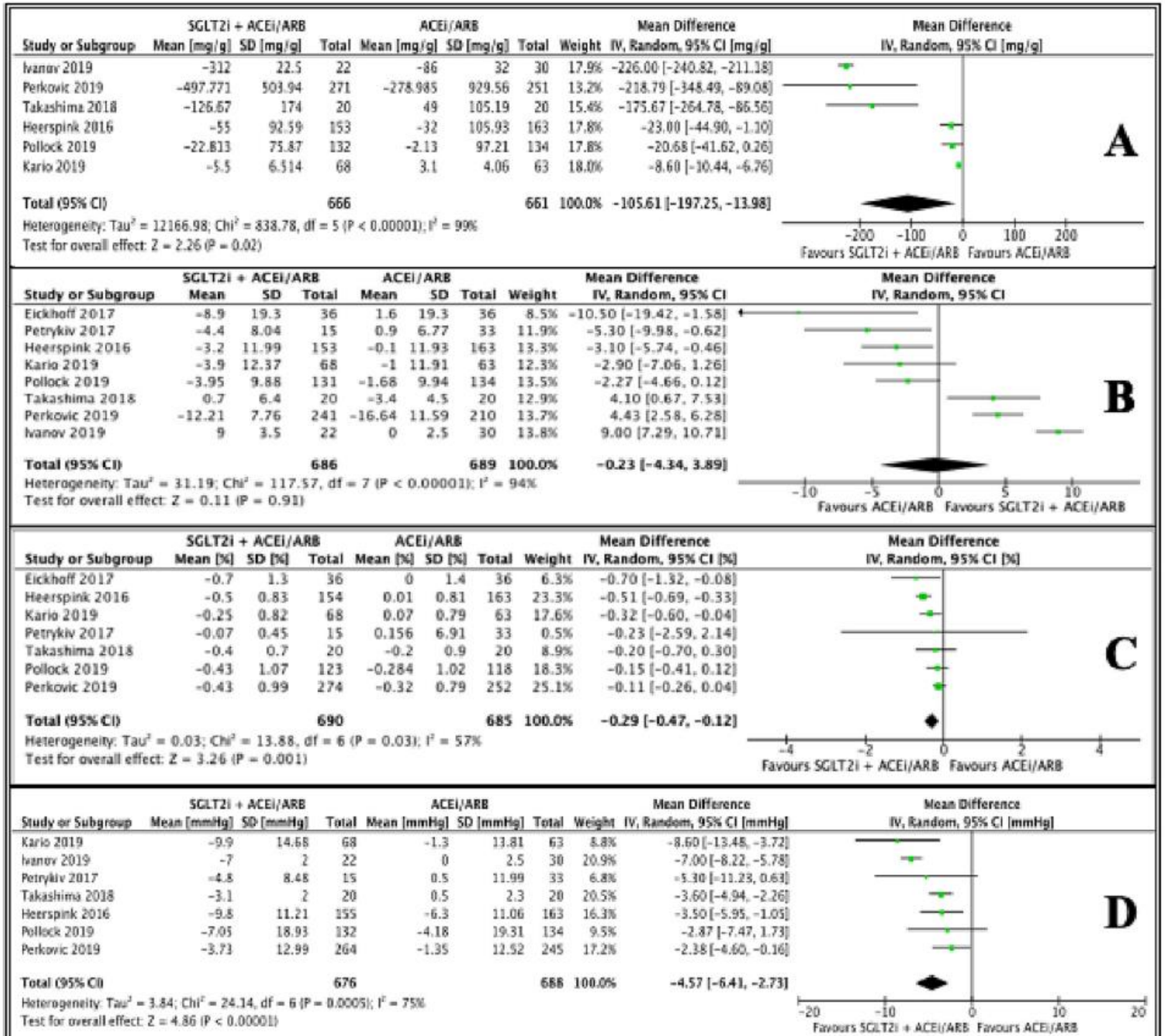
Review Manager (RevMan, The Cochrane Collaboration, London) was used to conduct a meta-analysis, using a random-effects model. Mean differences (MD) with SD were calculated for the continuous data, including UACR, eGFR, HbA1c and SBP. Weighted mean difference (WMD) was calculated as the sum of the differences in each study, weighted by the participants (n) for each study. The relative risk (RR) with a 95 % CI was calculated for reported adverse effects.

Heterogeneity was assessed using the I^2 statistic to quantify inconsistency and describe the level of variability in effect estimates due to heterogeneity rather than chance. Significant heterogeneity was defined as an I^2 value >50 % or a P value <0.1. In case of heterogeneity across the included studies, subgroup analyses were performed for the primary outcomes base on the type of SGLT2 inhibitor, the baseline level of albuminuria and eGFR. A sensitivity analysis to assess the robustness of our findings was not performed, due to unknown or high risk of bias found in each study in the risk of bias assessment.

文獻評

6.這篇系統

Importance



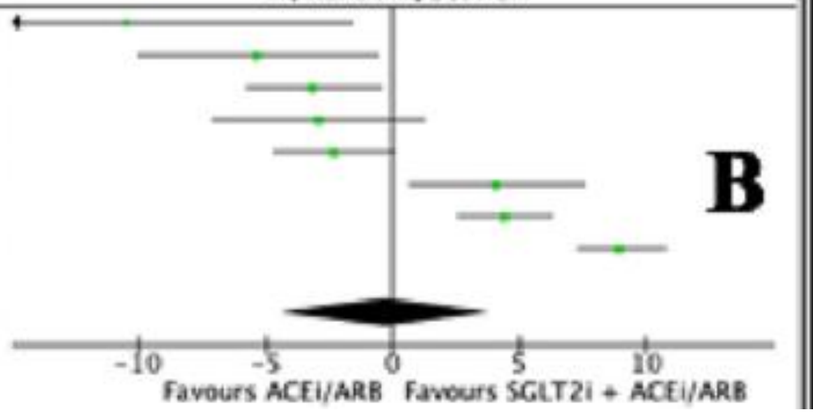
文獻評讀-SM/Meta analysis

7.結果精準嗎?

Study or Subgroup	SGLT2i + ACEi/ARB Mean	SD	Total	ACEi/ARB Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Eickhoff 2017	-8.9	19.3	36	1.6	19.3	36	8.5%	-10.50 [-19.42, -1.58]
Petrykiv 2017	-4.4	8.04	15	0.9	6.77	33	11.9%	-5.30 [-9.98, -0.62]
Heerspink 2016	-3.2	11.99	153	-0.1	11.93	163	13.3%	-3.10 [-5.74, -0.46]
Kario 2019	-3.9	12.37	68	-1	11.91	63	12.3%	-2.90 [-7.06, 1.26]
Pollock 2019	-3.95	9.88	131	-1.68	9.94	134	13.5%	-2.27 [-4.66, 0.12]
Takashima 2018	0.7	6.4	20	-3.4	4.5	20	12.9%	4.10 [0.67, 7.53]
Perkovic 2019	-12.21	7.76	241	-16.64	11.59	210	13.7%	4.43 [2.58, 6.28]
Ivanov 2019	9	3.5	22	0	2.5	30	13.8%	9.00 [7.29, 10.71]
Total (95% CI)			**686**			**689**	**100.0%**	**-0.23 [-4.34, 3.89]**

Heterogeneity: $Tau^2 = 31.19$; $Chi^2 = 117.57$, df = 7 ($P < 0.00001$); $I^2 = 94\%$

Test for overall effect: Z = 0.11 (P = 0.91)



文獻評讀-SM/Meta analysis

8.此研究是否可應用到當地的族群？

☑ Yes ☐ No ☐ Can’ t tell

研究對象包含亞洲人

文獻評讀-SM/Meta analysis

9.是否所有重要的臨床結果都有被考量到?

☐ Yes ☐ No ☑ Can’ t tell

A B S T R A C T

Introduction: Many people with type 2 diabetes progress to end-stage diabetic kidney disease (DKD) despite blockade of the renin-angiotensin system, suggesting the need for innovative treatment options for DKD. To capture the findings of recent studies, we performed an updated systematic review and meta-analysis of the efficacy and safety of sodium glucose co-transporter 2 (SGLT2) inhibitors combined with standard care involving angiotensin converting enzyme (ACE) inhibitors and/or angiotensin receptor blockers (ARBs) on the development and progression of DKD in people with type 2 diabetes compared with standard care alone.

Methods: The Cochrane Library, MEDLINE, EMBASE, PubMed and clinical trials registers were systematically searched for randomized controlled trials published before 1 September 2022. Primary outcomes were urine albumin-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR). Secondary outcomes were glycated hemoglobin (HbA1c) and systolic blood pressure (SBP). Relative risk was calculated for adverse events.

Results: Eight studies enrolling 5512 participants were included. In the meta-analysis (n = 1327), SGLT2 inhibitors were associated with a statistically significant reduction in UACR (weighted mean difference [WMD] -105.61 mg/g, 95 % CI -197.25 to −13.98, I^2 = 99 %, p = 0.02). There was no statistically significant difference in relation to eGFR (n = 1375; WMD -0.23 mL/min/1.73m^2, 95 % CI -4.34 to 3.89, I^2 = 94 %, p = 0.91).

Conclusions: SGLT2 inhibitors in addition to standard care including ACE inhibitors and/or ARBs significantly reduced albuminuria, HbA1c and SBP when compared to standard care alone, supporting their routine use in people with type 2 diabetes.

O

文獻評讀-SM/Meta analysis

9.是否所有重要的臨床結果都有被考量到?

☐ Yes ☐ No ☑ Can’ t tell

people with and without type 2 diabetes [36,37]. The DAPA-CKD trial found the renoprotective effects of dapagliflozin extended to people without diabetes [38,39]. The hazard ratio (HR) in participants with type 2 diabetes and those without diabetes was consistent for the primary endpoint; sustained decline in eGFR of at least 50 %, end-stage kidney disease, or kidney-related or cardiovascular death. The HR was 0.64, 95 % CI 0.52–0.79 and 0.50, CI 0.35–0.72 for people with and without diabetes, respectively. The median UACR for participants randomized to dapagliflozin with and without diabetes was 1024.5 mg/g (472.5–2111.0) and 870.5 mg/g (472.0–1533.5), respectively [39]. In addition, the EMPA-KIDNEY trial investigated the effects of empagliflozin in a variety of patients with CKD, including people with and without diabetes. The empagliflozin group had reductions in UACR by 19 %; 54 % of these participants did not have a diagnosis of diabetes [40]. These studies demonstrate the effectiveness of SGLT2 inhibitors in people without type 2 diabetes.

文獻評讀-SM/Meta analysis

10.付出的傷害和花費換得介入所產生益處是否值得?

☑ Yes ☐ No ☐ Can’ t tell

5. Conclusions

The present meta-analysis demonstrated that SGLT2 inhibitors in addition to standard care, with an ACE inhibitor and/or ARB, significantly reduced albuminuria when compared to standard care alone, in patients with type 2 diabetes. Greater reductions in UACR were seen with the studies utilizing canagliflozin, and in patients with higher baseline UACR values. Benefits were also seen in relation to glycemic and blood pressure control, with no persistent adverse effect on eGFR. Our findings corroborate existing evidence supporting the renoprotective role of SGLT2 inhibitors in DKD and suggest that these agents in combination with RAS blockade may become the new standard of care in this setting.

文獻評讀-SM/Meta analysis

Practice

10.付出的傷害和花費換得介入所產生益處是否值得?

☑ Yes ☐ No ☐ Can’ t tell

Meta-Analysis > Med Clin (Barc). 2022 Jul 22;159(2):65-72. doi: 10.1016/j.medcli.2021.09.031. Epub 2021 Dec 3.

Benefits of SGLT2 inhibitors combining with renin-angiotensin-system blockers on cardiovascular outcomes in chronic kidney disease patients: A systemic review and meta-analysis

[Article in English, Spanish]
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Affiliations + expand

PMID: 34872768 DOI: 10.1016/j.medcli.2021.09.031

Abstract

Background and objective: Efficacy of sodium-glucose cotransporter 2 (SGLT2) inhibitors in combination with renin-angiotensin-system (RAS) blockers for CKD remains controversial. We conducted this meta-analysis to explore the effect of SGLT2 inhibitors combining with RAS blockers on cardiovascular outcomes in chronic kidney disease (CKD) patients.

Methods: We searched Embase, PubMed, Web of Science, and Cochrane Library databases with the following keywords. "Renal Insufficiency, Chronic" or "Diabetic Nephropathies" and "Sodium-glucose cotransporter 2 inhibitors". We included randomized controlled trials (RCTs) based on angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB) therapy. The outcome events included cardiac and renal outcomes and other adverse events. This study is registered with PROSPERO: CRD42020218337.

Results: Ten RCTs including 16,983 CKD patients met the inclusion criteria. Compared with placebo plus RAS blockers, SGLT2 inhibitors plus RAS blockers significantly reduced cardiovascular mortality and heart failure-related hospitalization rates (RR=0.78, 95% CI: 0.66-0.91, p=0.002; RR=0.7, 95% CI: 0.61-0.8, p=0.000). We also performed trials sequential analysis (TSA) and the results indicated that our results are reliable. Additionally, it significantly reduced the 24-h urinary albumin excretion rate (24hUAE) and the creatinine elevation rate (WMD=-0.19, 95% CI: -0.24 to -0.14; RR=0.61, 95% CI: 0.51-0.74, p=0.000), delayed progression to end-stage renal disease (ESRD) (RR=0.69, 95% CI: 0.59-0.81, p=0.000). Further, it had no significant effect on the incidence of renal-related adverse events or renal-related mortality. Although it decreased the estimated glomerular filtration rate (eGFR) (WMD=-5.4, 95% CI: -7.24 to -3.57), this effect was reversible.

Conclusions: These data provide a well-document testimonial of the benefits of the combined use of SGLT2 inhibitors and RAS blockers for cardiovascular and renal outcomes in CKD patients.

文獻評讀-SM/Meta analysis

No	Examination	Yes/No/Can’ t tell
1	此篇系統性文獻回顧是否問了一個清楚、明確的問題?	Yes
2	作者是否尋找適當研究型態的文獻?	Yes
3	你認為所有重要且相關的研究都被納入?	Yes
4	系統性文獻回顧的作者是否評估所納入研究文獻的品質?	Yes
5	如果作者將研究結果進行合併，這樣的合併是否合理?	Yes
6	這篇系統性文獻回顧的整體結果為何？	Yes
7	結果精準嗎？	Yes
8	此研究結果是否可應用到當地的族群？	Yes
9	是否所有重要的臨床結果都有被考量到？	Can’ t tell
10	付出的傷害和花費換得介入措施所產生的益處是否值得？	Yes

Level of evidence & Grade of Recommendation

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

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

Applying-臨床應用

臨床應用—價格

Canaglu 100mg tab	CANAT	Antidiabetic agent-(Sodium-dependent glucose cotransporters inhibitor · SGLT2)	26.10
Forxiga 10mg tab	FORXT	Antidiabetic agent-(Sodium-dependent glucose cotransporters inhibitor · SGLT2) Heart failure preparations	25.40
Jardiance 10mg tab	JARDT	Antidiabetic agent-(Sodium-dependent glucose cotransporters inhibitor · SGLT2) Heart failure preparations	26.60

臨床應用—價格

Capoten 25mg tab	CAPOT	Hypotensive agents- Angiotension Converting Enzyme Inhibitors(ACEI)	1.50
Tritace 10mg tab	TRIT1	Hypotensive agents- Angiotension Converting Enzyme Inhibitors(ACEI)	4.08
Zestril 10mg tab	ZESTR	Hypotensive agents- Angiotension Converting Enzyme Inhibitors(ACEI)	2.00

臨床應用—價格

Diovan 160mg tab	DIOV1	Hypotensive agents- Angiotensin II Receptor Antagonists(ARB)	5.10
Edarbi 40mg tab	EDART	Hypotensive agents- Angiotensin II Receptor Antagonists(ARB)	8.40
Micardis 80mg tab	MICA8	Hypotensive agents- Angiotensin II Receptor Antagonists(ARB)	8.40

血液透析給付點數為4100(每月5萬);
腹膜透析每月成本約4萬5000元

Assessing-執行決策

給病人的建議...

符合健保給付的前提下，建議患者服用SGLT2 inhibitor並用ARB/ACEI，對於腎臟保護與預期後續心血管事件可能有維持效果，並持續觀察副作用(如泌尿道感染)

Thank You