糖尿病治療的器官保護新觀念
應用在腎臟病變防治

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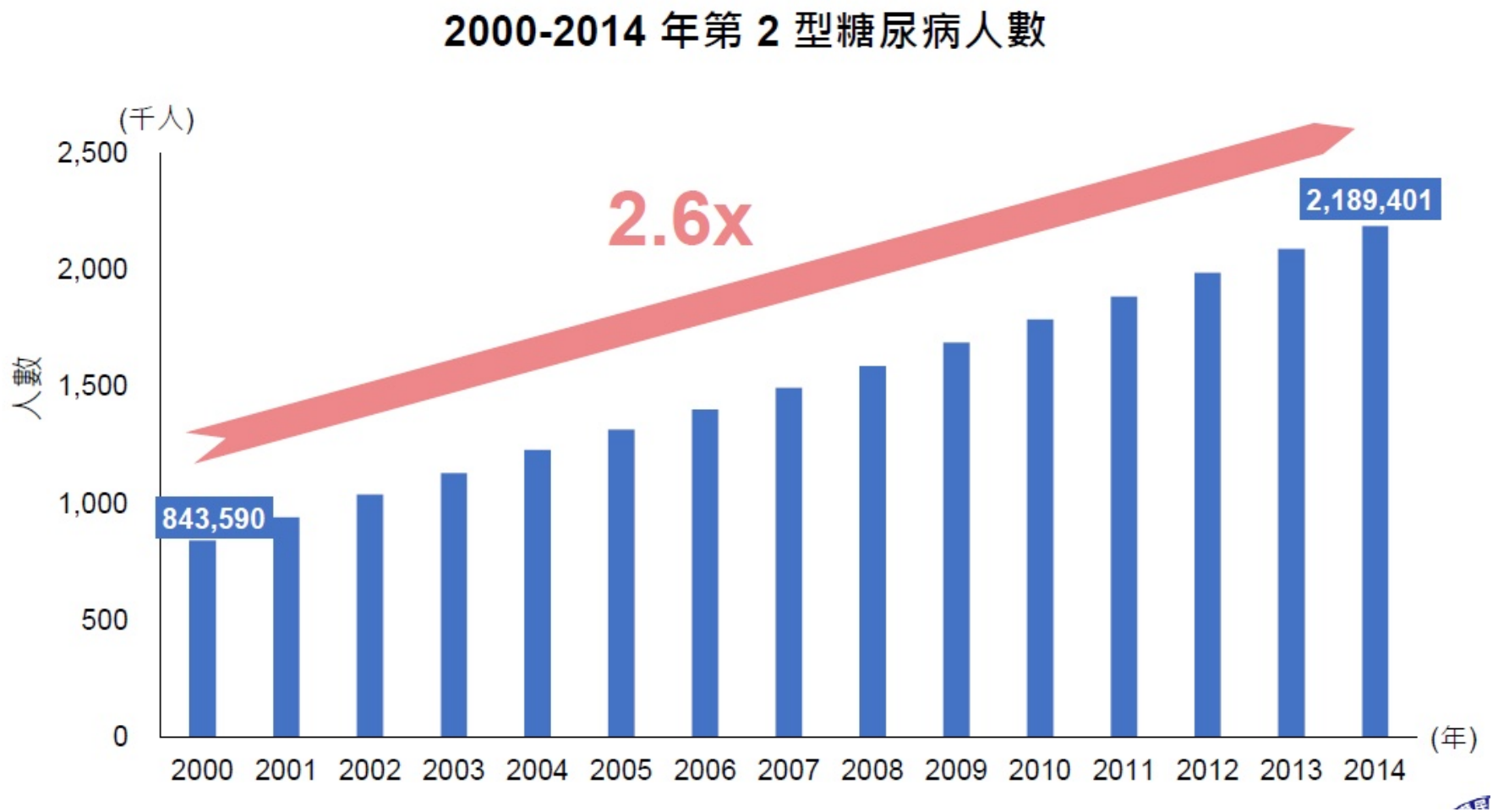
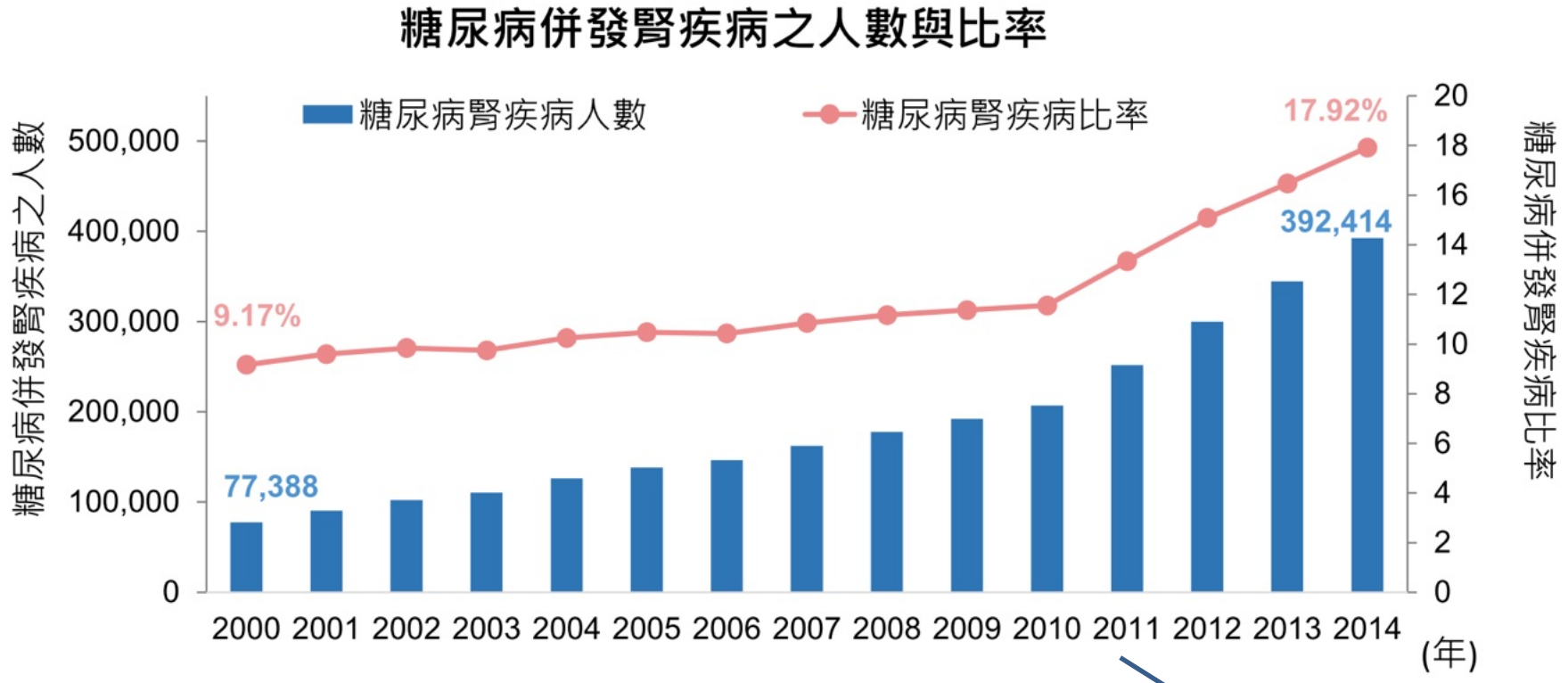
暨藥物治療工作小組委員

臺灣糖尿病人數持續增加
每10位就有1位為T2D患者



1. 中華民國糖尿病衛教學會, 台灣糖尿病年鑑 2019 第2型糖尿病

台灣第2型糖尿病患合併腎病變人數及比率皆逐年攀升



2000-2014臺灣T2D合併CKD
比率+95.4%，人數+407%

2011 年啟動初期慢性腎臟病給付改善方案

中華民國糖尿病衛教學會, 臺灣糖尿病年鑑 2019第2型糖尿病 簡報
http://www.endo-dm.org.tw/DB/book/73/%E8%87%BA%E7%81%A3%E7%B3%96%E5%B0%BF%E7%97%85%E5%B9%B4%E9%91%91%202019%E7%AC%AC2%E5%9E%8B%E7%B3%96%E5%B0%BF%E7%97%85%20%E7%B0%A1%E5%A0%B1.pdf

糖尿病腎臟疾病的發生率和盛行率

發生率：3%/每年：已知罹患糖尿病約10-20年患者

盛行率：美國的糖尿病患者: microalbuminuria約43%, macroalbuminuria約8%

TADE 2006糖尿病腎臟疾病調查

n=3415	比率(%)
正常	50.3
微量白蛋白尿	23.8
巨量白蛋白尿	25.9

DEMAND study 2003 亞洲

n=8561	比率(%)
正常	44
微量白蛋白尿	44
巨量白蛋白尿	12

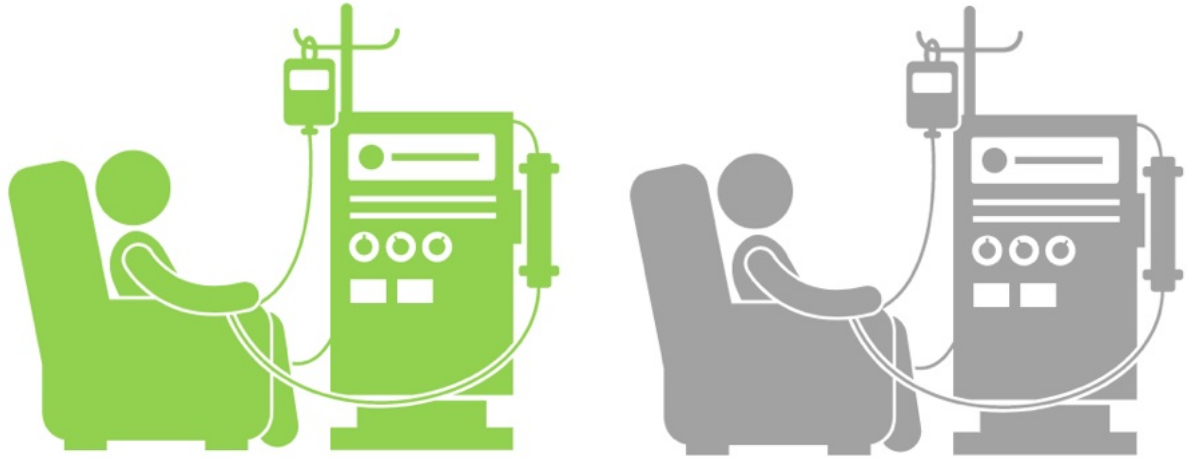
Without prior known proteinuria and/or kidney disease duo to diabetes
Duration: 7.3 yrs, A1C: 7.8 %

Diabetes technology and therapeutics. 2008; Vol 10, No 5:397-403

臺灣約每2位透析病患有1位患有糖尿病

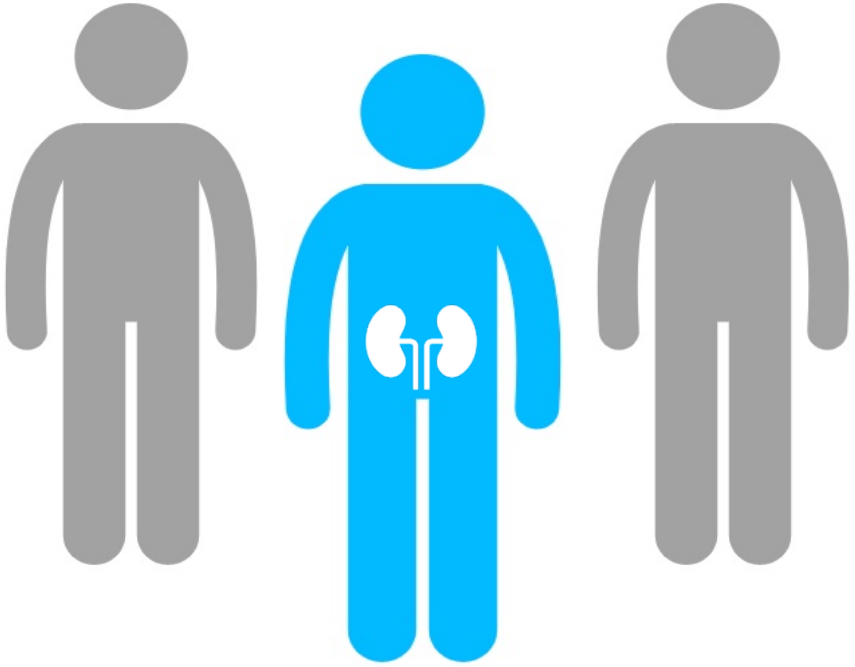
46.2% **new dialysis patients' principal diagnosis is diabetes**

In 2020 Kidney Disease in Taiwan Annual Report (data in 2018)



33.24% **patients with diabetes have nephropathy**

In Taiwan P4P program (data in 2014)



P4P: pay-for-performance

1. 2020 Kidney Disease in Taiwan Annual Report (p.56, p71) 2.. J Formos Med Assoc. 2019 Nov;118 Suppl 2:S122-S129. (Participants in P4P)

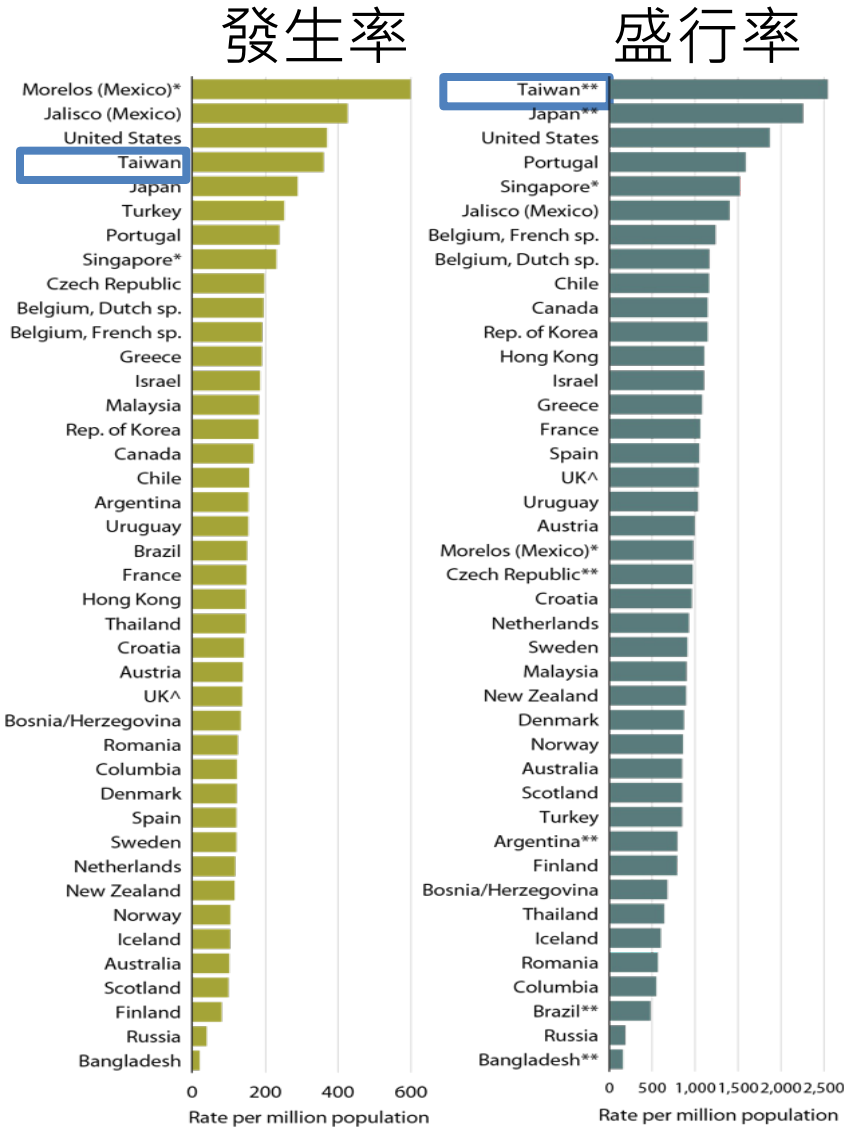
2010台灣接受透析治療之末期臟病患數與模式

盛行病患數 59,856
2010-12-31尚存活者

血液透析 53,631
腹膜透析 6,225

2010年全年
新發病患數 8,362

2010
盛行率: 2,584/百萬人口
發生率: 361/百萬人口
台灣人口數: 約2300萬

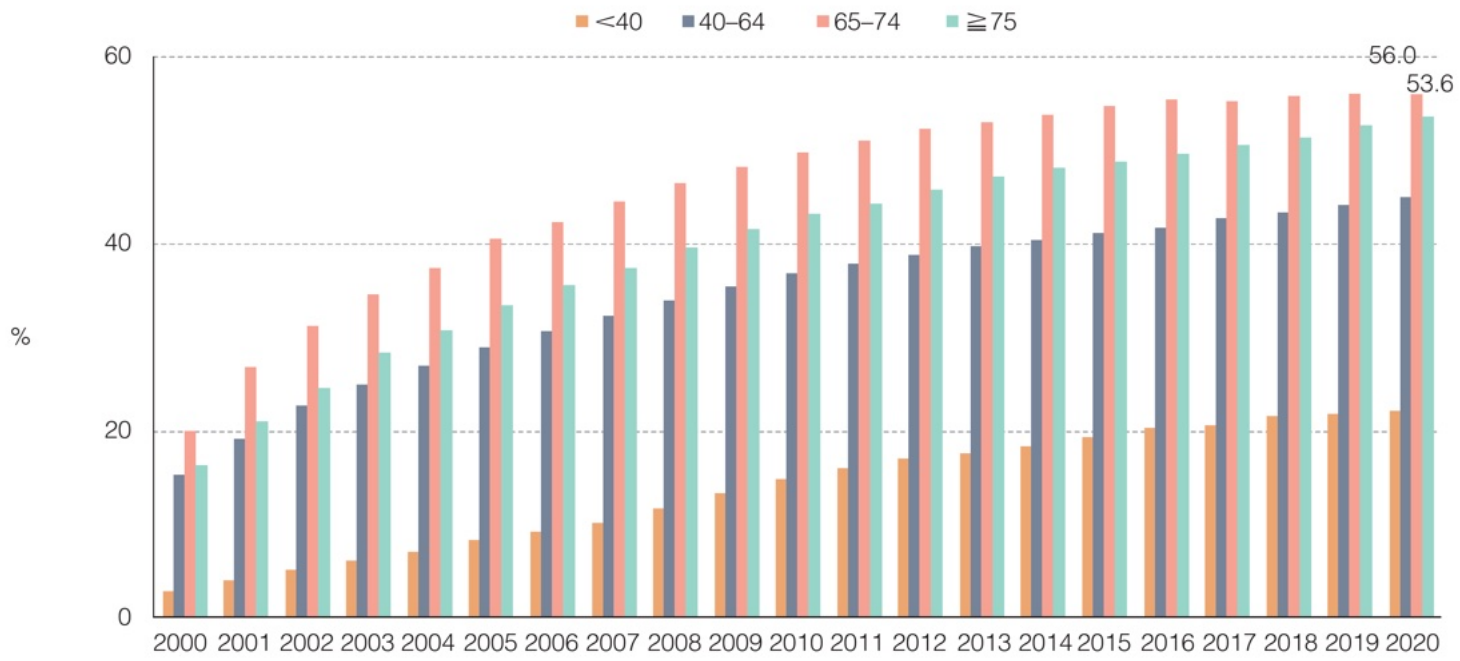


TSN Renal Registry, 2012；USRDS 2013

2022台灣腎病年報

透析患者有糖尿病比率逐年增加，2020年達49.6%

透析盛行患者有糖尿病比率（%）（依年齡別）



註：糖尿病以盛行前一年度之門、住診任一診斷欄位為判斷依據，且符合住院1次或門急診2次以上的定義。糖尿病之ICD-9-CM與ICD-10-CM碼請參考方法學。

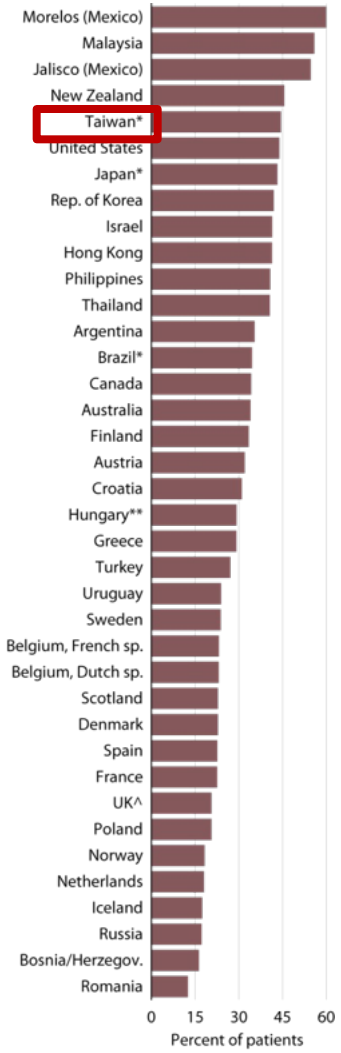
2020透析患者有糖尿病比率: 49.6%

2000透析患者有糖尿病比率: 15.0%

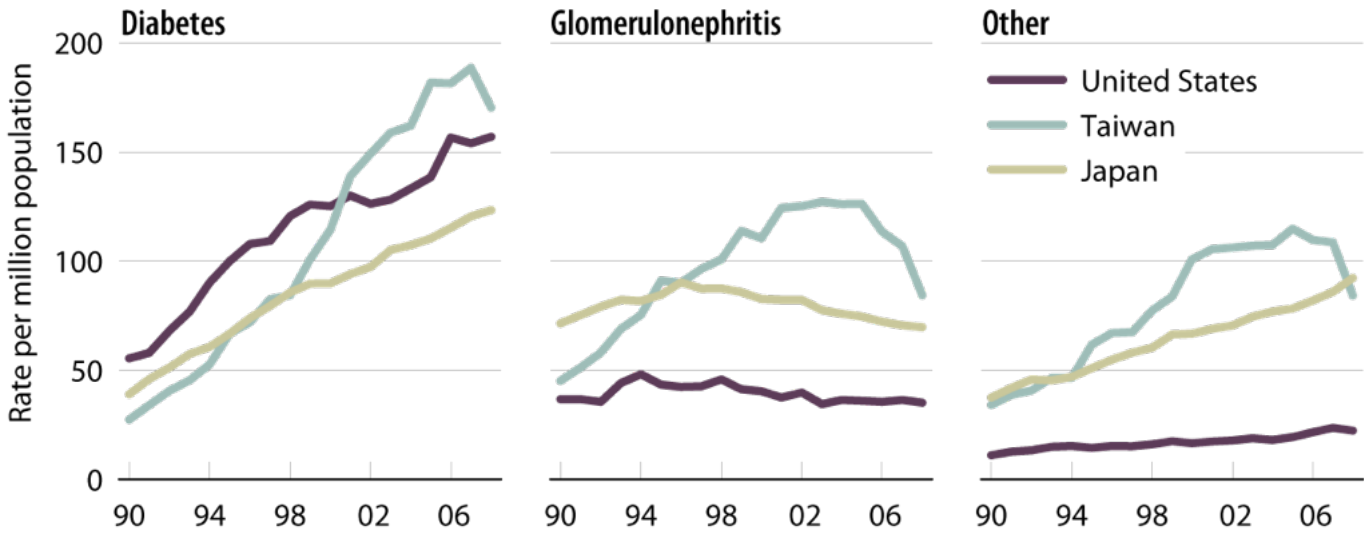
2022 台灣腎病年報: https://library.nhri.org.tw/ebook/

糖尿病是台灣、美國、日本
ESRD最主要的原因

糖尿病



Percentage of incident patients with ESRD due to diabetes, 2008 (USDR)

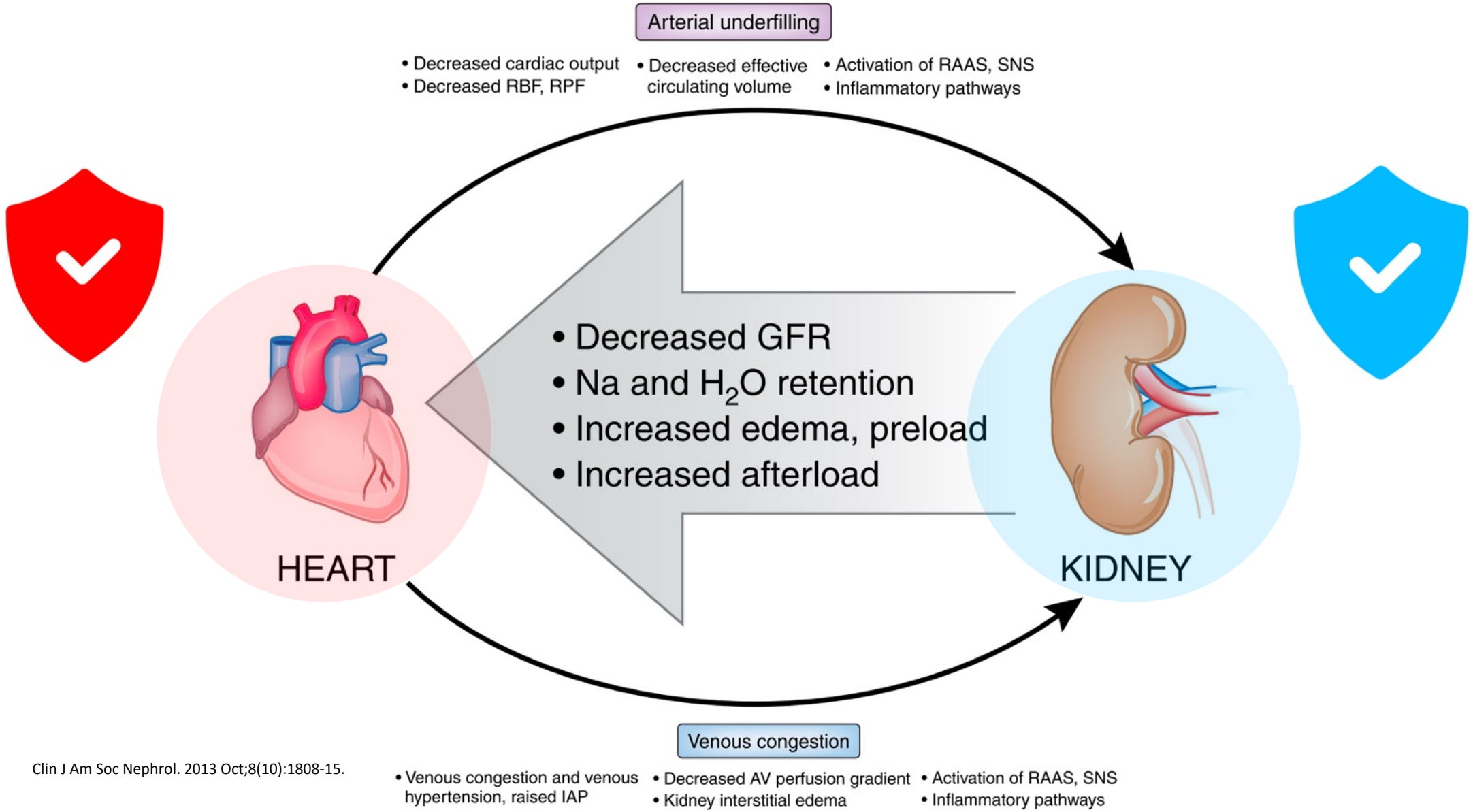


Year	Taiwan	Japan	US
2005	42%	41.6%	44.1%
2006	43.5%	42.5%	44.3%
2007	44.7%	43.2%	43.9%

Year	Taiwan	Japan	US
2008	44.6%	43.2%	43.9%
2009	43.8%	44.6%	43.8%
2010	45.7%	43.9%	44.1%

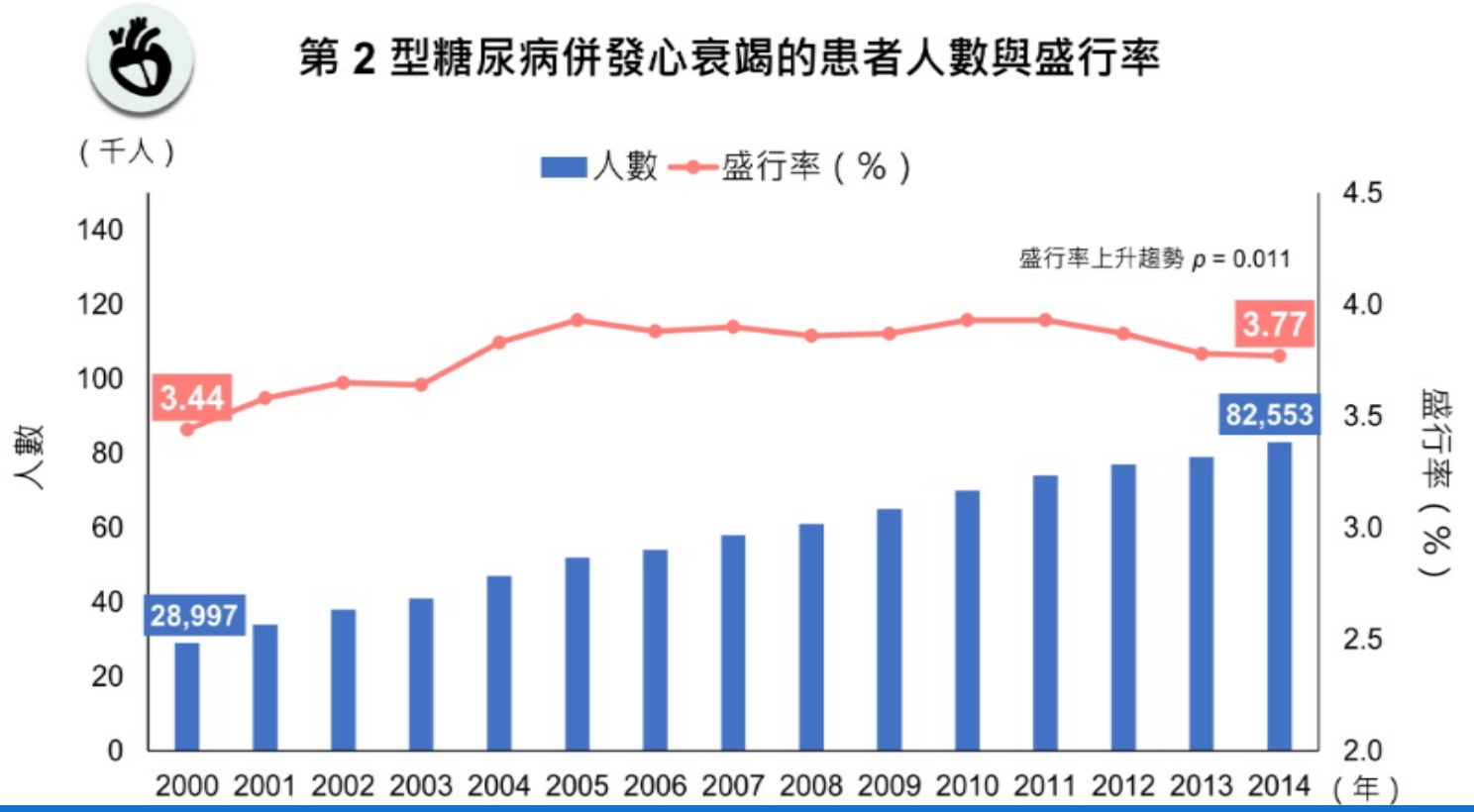
2013 ANNUAL DATA REPORT
USRDS

腎臟不好會連帶影響心臟，增加心衰竭風險



Clin J Am Soc Nephrol. 2013 Oct;8(10):1808-15.

台灣第2型糖尿病患合併心衰竭人數及比率皆逐年攀升



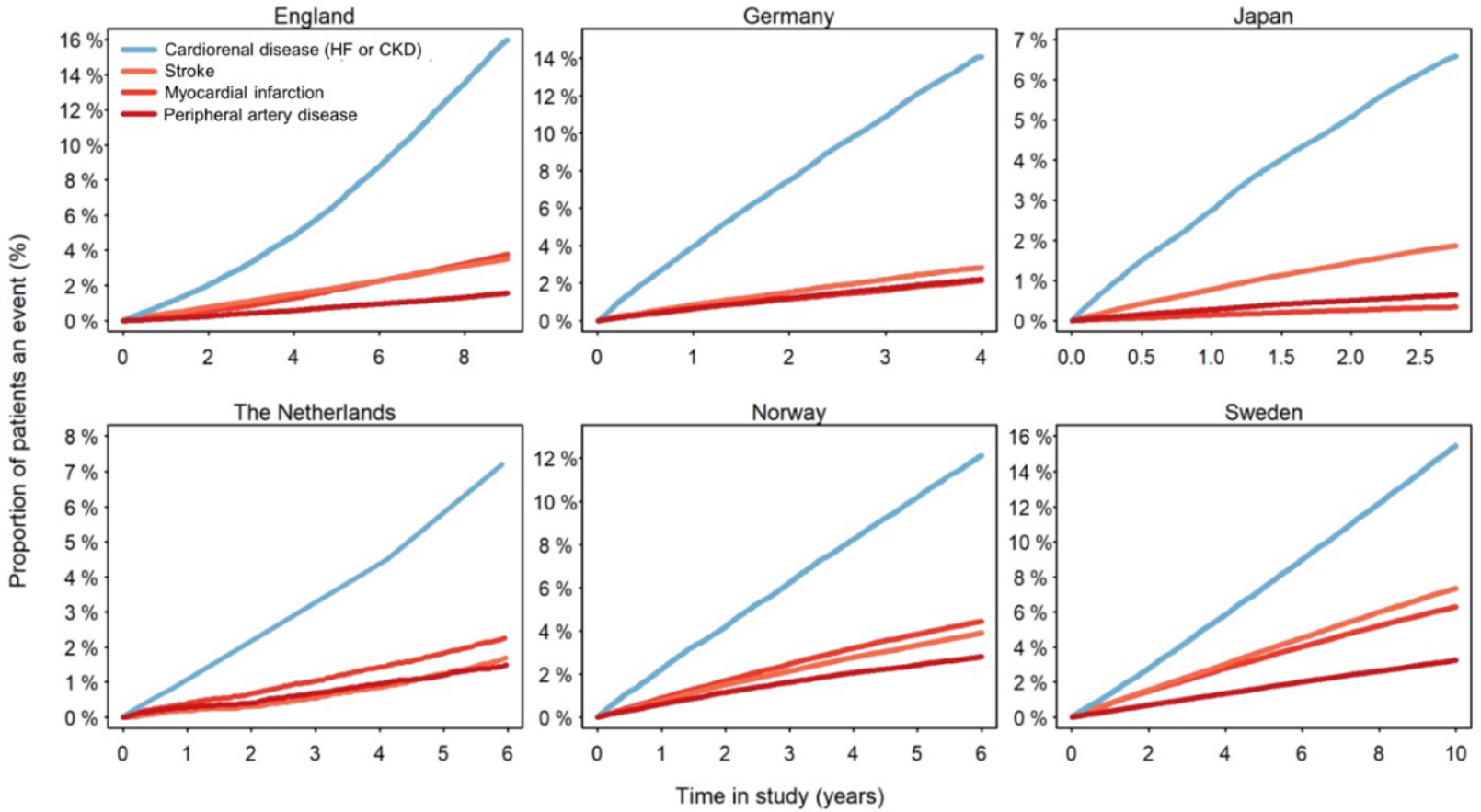
2000-2014臺灣T2D合併HF

比率+9.6%，人數+185%

中華民國糖尿病衛教學會, 臺灣糖尿病年鑑 2019第2型糖尿病 簡報
http://www.endo-dm.org.tw/DB/book/73/%E8%87%BA%E7%81%A3%E7%B3%96%E5%B0%BF%E7%97%85%E5%B9%B4%E9%91%91%202019%E7%AC%AC2%E5%9E%8B%E7%B3%96%E5%B0%BF%E7%97%85%20%E7%B0%A1%E5%A0%B1.pdf

6個國家~77萬T2D病患追蹤4.5年結果:

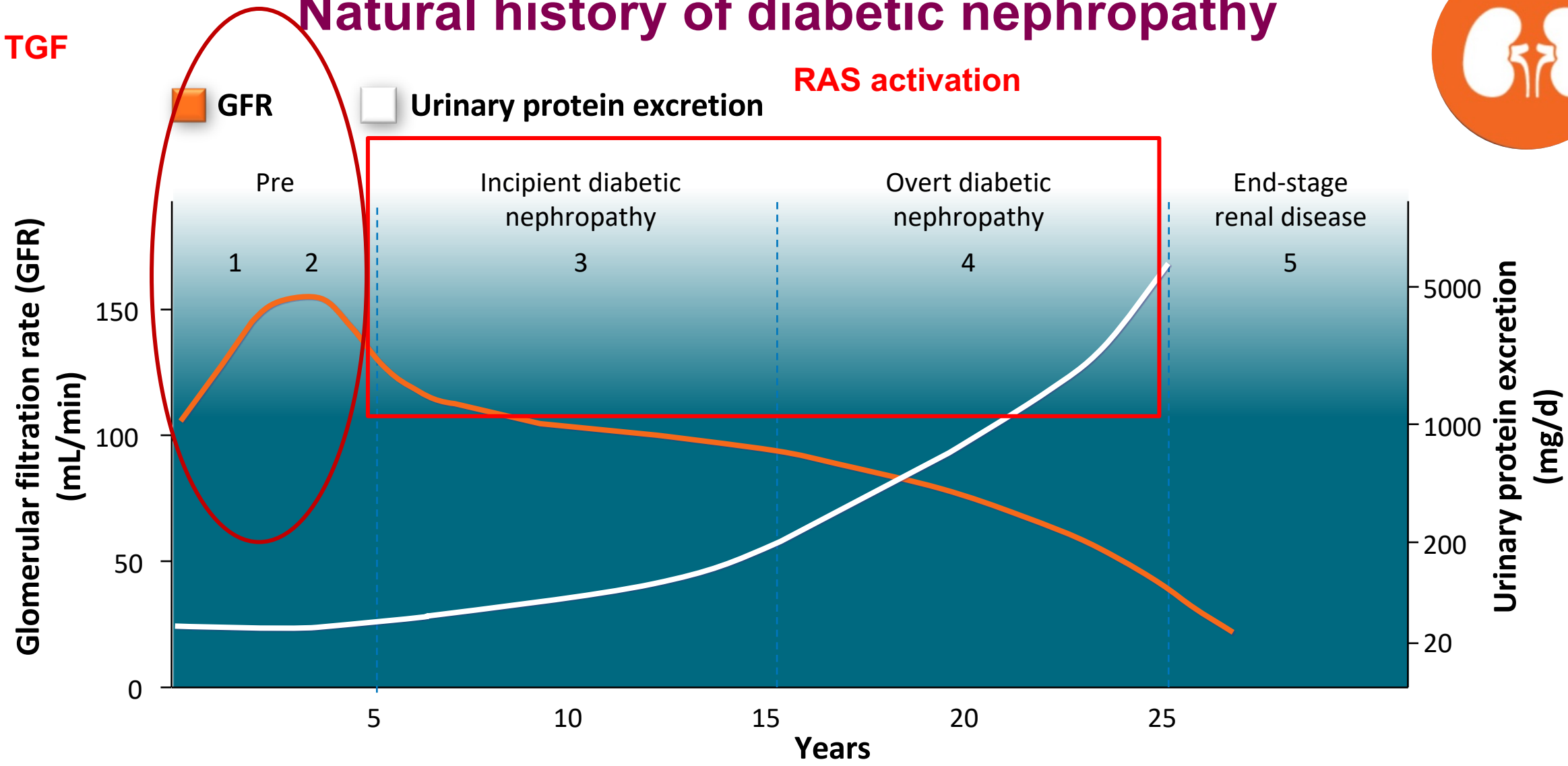
心腎病變: CKD(36%)、HF(24%)為最常見的第一個共病症



137,081 (18%) developed a **first CVRD manifestation**,
represented by **CKD** (36%), **HF** (24%), stroke (16%), MI (14%) and PAD (10%).

CVRD: cardiovascular- and renal disease; Diabetes Obes Metab. 2020 Sep;22(9):1607-1618.

Natural history of diabetic nephropathy



Functional	Hyperfiltration	Microalbuminuria, hypertension	Albuminuira, declining GFR

Vora JP, et al. In: Johnson RJ, Feehally J, eds. Comprehensive Clinical Nephrology. New York: Mosby; 2000.

糖尿病腎臟疾病
(diabetic kidney disease; DKD)
病理機轉、診斷及分期

- 如何確認腎臟已受糖尿病傷害
- 如何診斷
- 何謂白蛋白尿
- 糖尿病腎臟疾病分期

糖尿病腎臟疾病之白蛋白尿分期

CKD 的白蛋白尿分期				
期別	AER（mg/24 h）	ACR（mg/mmol）	（mg/g）	描述
A1	<30	<3	<30	正常或輕度升高
A2	30-300	3-30	30-300	中度升高 *
A3	>300	>30	>300	重度升高 **

AER 白蛋白排泄率；ACR 白蛋白 - 血清肌酸酐比值；CKD 慢性腎臟病

* 相對於年輕成年人的水平；

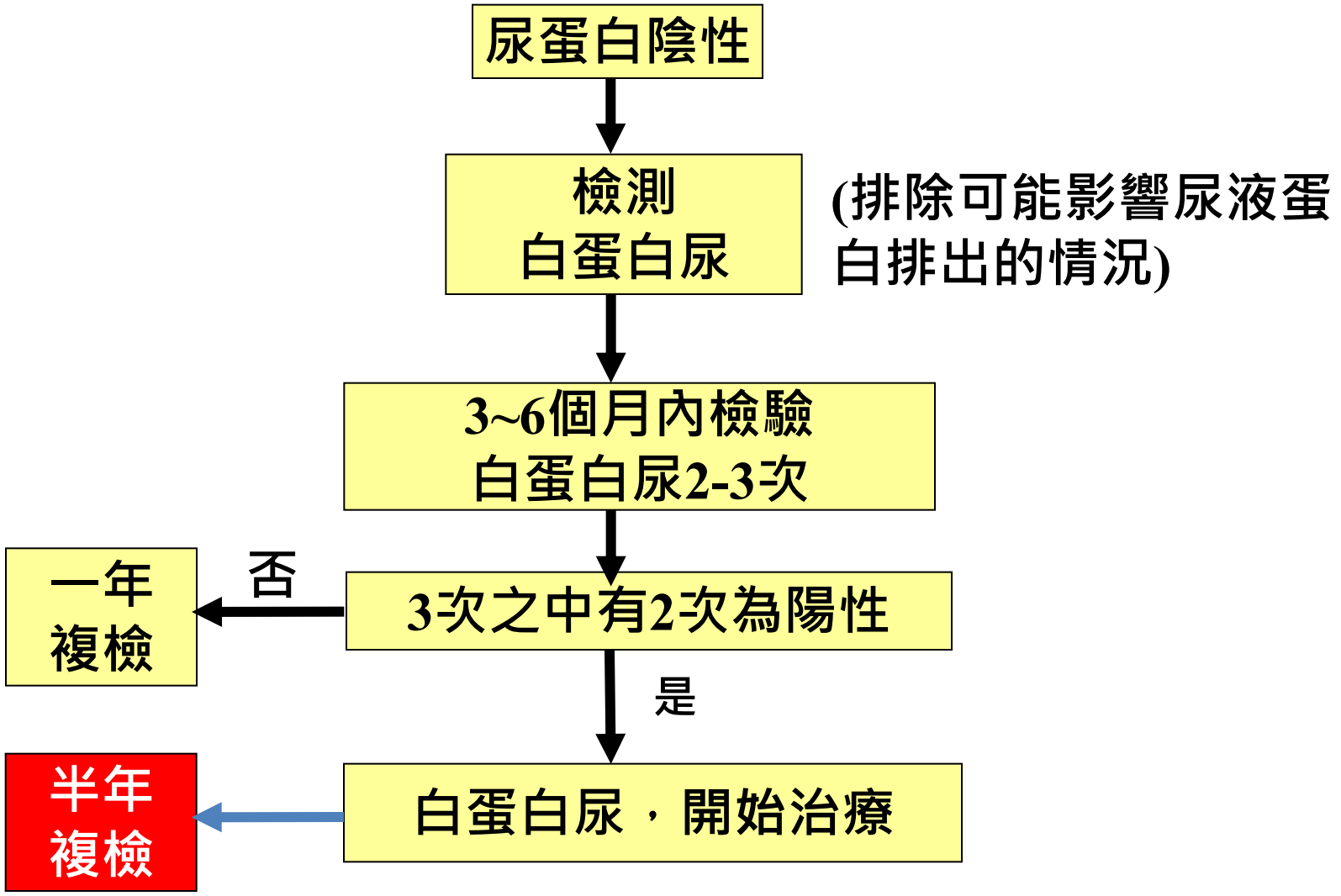
** 包括腎病症候群（白蛋白排泄通常 >2200 mg/24h [ACR>2220 mg/g；>220 mg/mmol]）

Chronic kidney disease classification by estimated glomerular filtration rate and albuminuria
2019 ESC Guidelines

eGFR (mL/min/1.73 m²)	Albuminuria categories (albumin:creatinine ratio spot urine)			
	A1 <30mg/g	A2 30-300 mg/g	A3 >300 mg/g	
G1 (≥90)	No CKD	G1 A2	G1 A3	Increasing risk↓
G2 (60–89)	No CKD	G2 A2	G2 A3	
G3a (45–59)	G3a A1	G3a A2	G3a A3	
G3b (30–44)	G3b A1	G3b A2	G3b A3	
G4 (15–29)	G4 A1	G4 A2	G4 A3	
G5 (<15)	G5 A1	G5 A2	G5 A3	
	Increasing risk→			

Green = low risk; yellow = medium risk; orange = high risk; red = very high risk.
CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate.

白蛋白尿的篩檢


尿蛋白陰性
檢測
白蛋白尿
(排除可能影響尿液蛋白排出的情況)
3~6個月內檢驗
白蛋白尿2-3次
3次之中有2次為陽性
否
一年
複檢
是
白蛋白尿，開始治療
半年
複檢

糖尿病腎臟疾病的危險因子

可以治療的	不可治療的
高血糖	遺傳
高血壓	糖尿病罹病期
高血脂	糖尿病罹病年齡
吸煙	高血壓家族史
高蛋白質攝取	糖尿病腎臟疾病家族史

高血壓的控制及目標

臨床建議	證據等級	臨床建議強度	華人資料
糖尿病患將收縮壓控制於140 mmHg 以下，舒張壓控制於90 mmHg 以下可延緩腎臟疾病的發生和惡化	高	強烈建議	
糖尿病患合併蛋白尿，而有腎臟疾病惡化的危險性者，建議收縮壓控制於130 mmHg以下，舒張壓控制於80 mmHg 以下	中	中等建議	有[176; 227]
糖尿病患合併白蛋白尿或腎臟疾病者，建議第一線降血壓藥物使用ACEi 或ARB	高	強烈建議	

2019台灣糖尿病腎臟疾病臨床照護指引

Optimizing lipid control in Taiwanese diabetic patients: A collaborative consensus by the Diabetes Association of the Republic of China (Taiwan) and the Taiwanese Association of Diabetes Educators

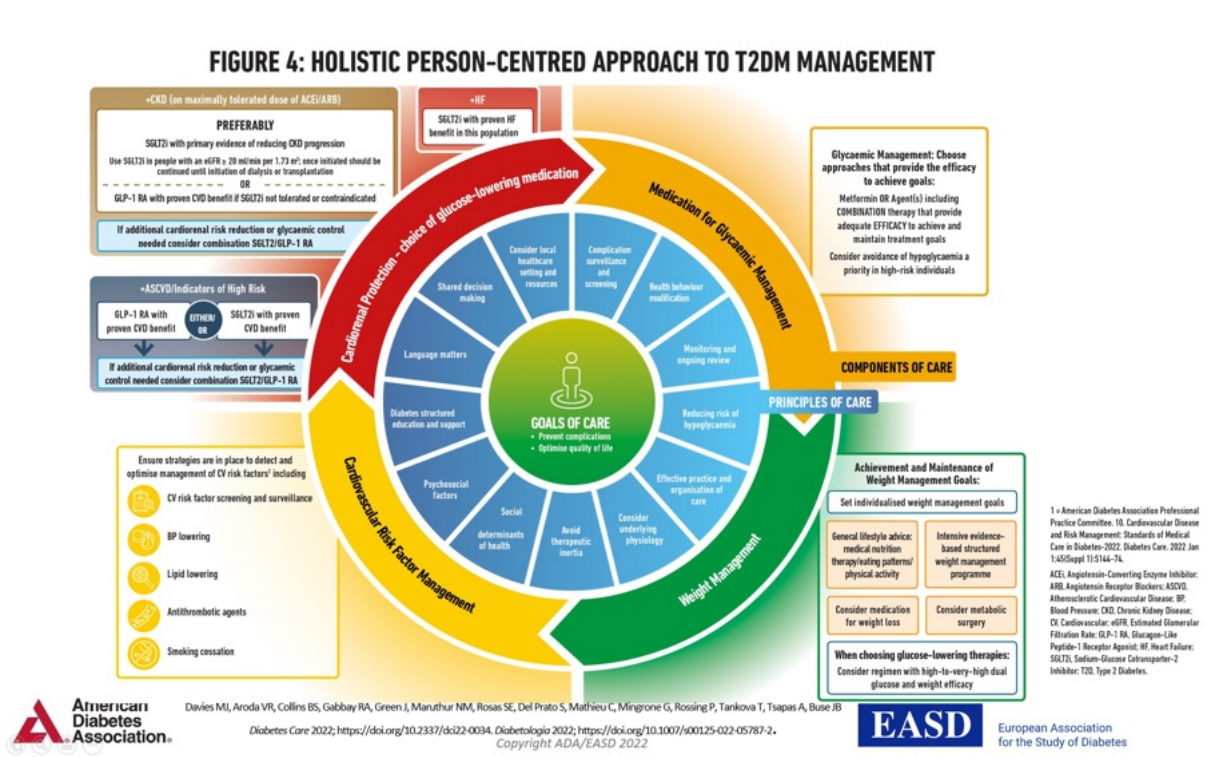
Feng-Chih Shen[1,2], Chih-Hsun Chu[3], Jung-Fu Chen[1,2], Chin-Sung Kuo[4,5], Chih-Yao Hsu[6], Ching-Han Lin[7], Yi-Jing Sheen[8,9,10], Sheng-Chiang Su[11], Kai-Jen Tien[12], Chieh-Hua Lu[11], Chun-Chuan Lee[13,14], Yi-Sun Yang[15,16], Shih-Te Tu[17], Po-Tsang Chen[18], Ching-Chu Chen[19,20], Ming-Nan Chien[13,14], Hung-Yuan Li[21], Wayne Huey-Herng Sheu[9,22], Chien-Ning Huang[15,16]*†, Chih-Yuan Wang[21,23]*†, Horng-Yih Ou[7]*†

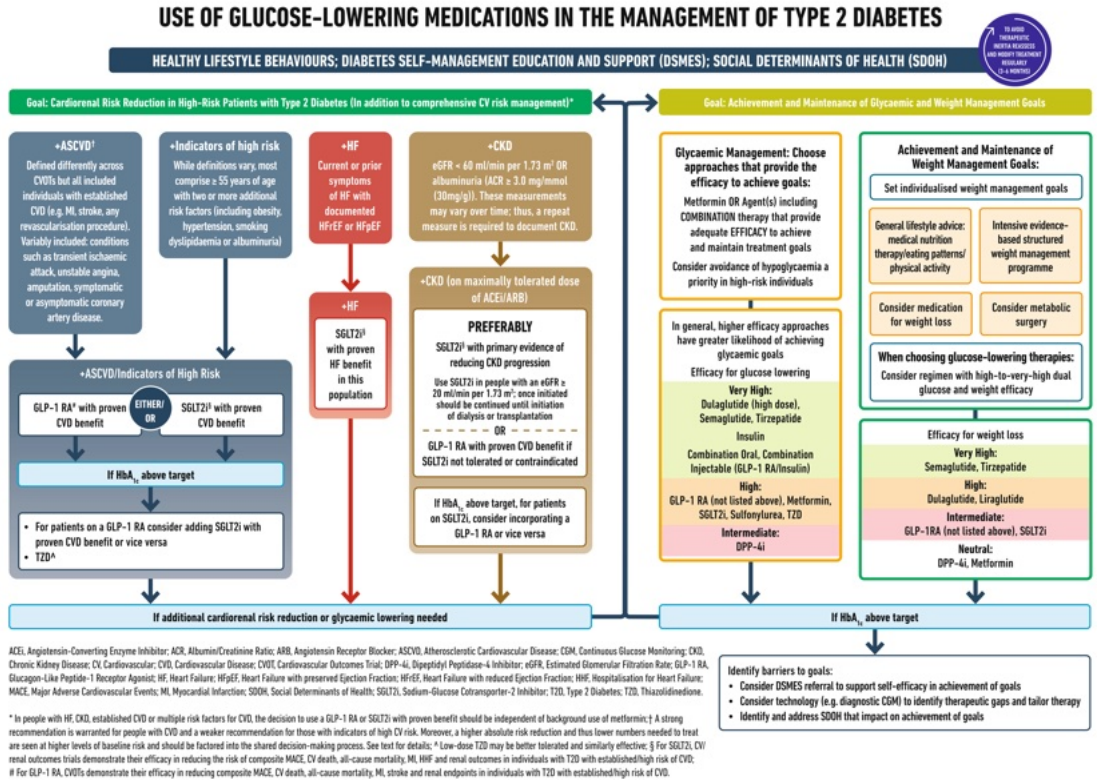
Table 1 | Recommendations for treatment goals for LDL-C, non-HDL-C, triglyceride, and ApoB according to the cardiovascular risk in patients with type 2 diabetes mellitus

	Classifications	LDL-C	Non-HDL-C (mg/dL)	TG (mg/dL)	ApoB (mg/dL)
Primary prevention	DM aged 40–75 years	<100 mg/dL or decrease of 30–40%	<130	<150	<90
	DM with ≥2 ASCVD risk factors† and specific comorbidities‡	<70 mg/dL or decrease of 50%	<100	<150	<80
Secondary prevention	DM with ASCVD	<55 mg/dL and decrease of 50%	<85	<150	<65

†Age (≥45 for males, ≥55 for females), family history of early ASCVD, hypertension, smoking, and low HDL-C (≤40 mg/dL). ‡Albuminuria, chronic kidney disease (eGFR ≤60 mL/min/1.73 m^2), retinopathy, neuropathy, and an ankle-brachial index (ABI) <0.9. ASCVD, atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride.

2022年11月ADA/EASD Consensus:
全方位血糖管理與器官保護





強調全方位血糖管理與心腎保護

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB
Diabetes Care 2022; https://doi.org/10.2337/dci22-0034. *Diabetologia* 2022; https://doi.org/10.1007/s00125-022-05787-2. https://professional.diabetes.org/content-page/management-hyperglycemia-type-2-diabetes-ada-easd-consensus-report-2022

USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

Goal: Cardiorenal Risk Reduction in High-Risk Individuals with Type 2 Diabetes (in addition to comprehensive CV risk management)*

+ASCVD†

Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, any revascularization procedure). Variably included: conditions such as transient ischemic attack, unstable angina, amputation, symptomatic or asymptomatic coronary artery disease.

+Indicators of high risk

While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria)

+ASCVD/Indicators of High Risk

GLP-1 RA# with proven CVD benefit **EITHER/OR** SGLT2i§ with proven CVD benefit

If A1C above target

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit or vice versa
- TZD^

+HF

Current or prior symptoms of HF with documented HFrEF or HFpEF

+HF

SGLT2i§ with proven HF benefit in this population

+CKD

eGFR <60 mL/min per 1.73 m² OR albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). These measurements may vary over time; thus, a repeat measure is required to document CKD.

+CKD (on maximally tolerated dose of ACEi/ARB)

PREFERABLY

SGLT2i§ with primary evidence of reducing CKD progression

Use SGLT2i in people with an eGFR ≥20 mL/min per 1.73 m²; once initiated should be continued until initiation of dialysis or transplantation

OR

GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated

If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA or vice versa

If additional cardiorenal risk reduction or glycemic lowering needed

Goal: Achievement and Maintenance of Glycemic and Weight Management Goals

Glycemic Management: Choose approaches that provide the efficacy to achieve goals:

Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals

Prioritize avoidance of hypoglycemia in high-risk individuals

In general, higher efficacy approaches have greater likelihood of achieving glycemic goals

Efficacy for glucose lowering

Very High:
Dulaglutide (high dose), Semaglutide, Tirzepatide

Insulin

Combination Oral, Combination Injectable (GLP-1 RA/Insulin)

High:
GLP-1 RA (not listed above), Metformin, SGLT2i, Sulfonylurea, TZD

Intermediate:
DPP-4i

Achievement and Maintenance of Weight Management Goals:

Set individualized weight management goals

General lifestyle advice: medical nutrition therapy/eating patterns/ physical activity

Intensive evidence-based structured weight management program

Consider medication for weight loss

Consider metabolic surgery

When choosing glucose-lowering therapies:

Consider regimen with high-to-very-high dual glucose and weight efficacy

Efficacy for weight loss

Very High:
Semaglutide, Tirzepatide

High:
Dulaglutide, Liraglutide

Intermediate:
GLP-1 RA (not listed above), SGLT2i

Neutral:
DPP-4i, Metformin

If A1C above target

Identify barriers to goals:

- Consider DSMES referral to support self-efficacy in achievement of goals
- Consider technology (e.g., diagnostic CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact achievement of goals

* In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

最新2024年ADA第2型糖尿病藥物治療流程圖
延續ADA/EASD共識

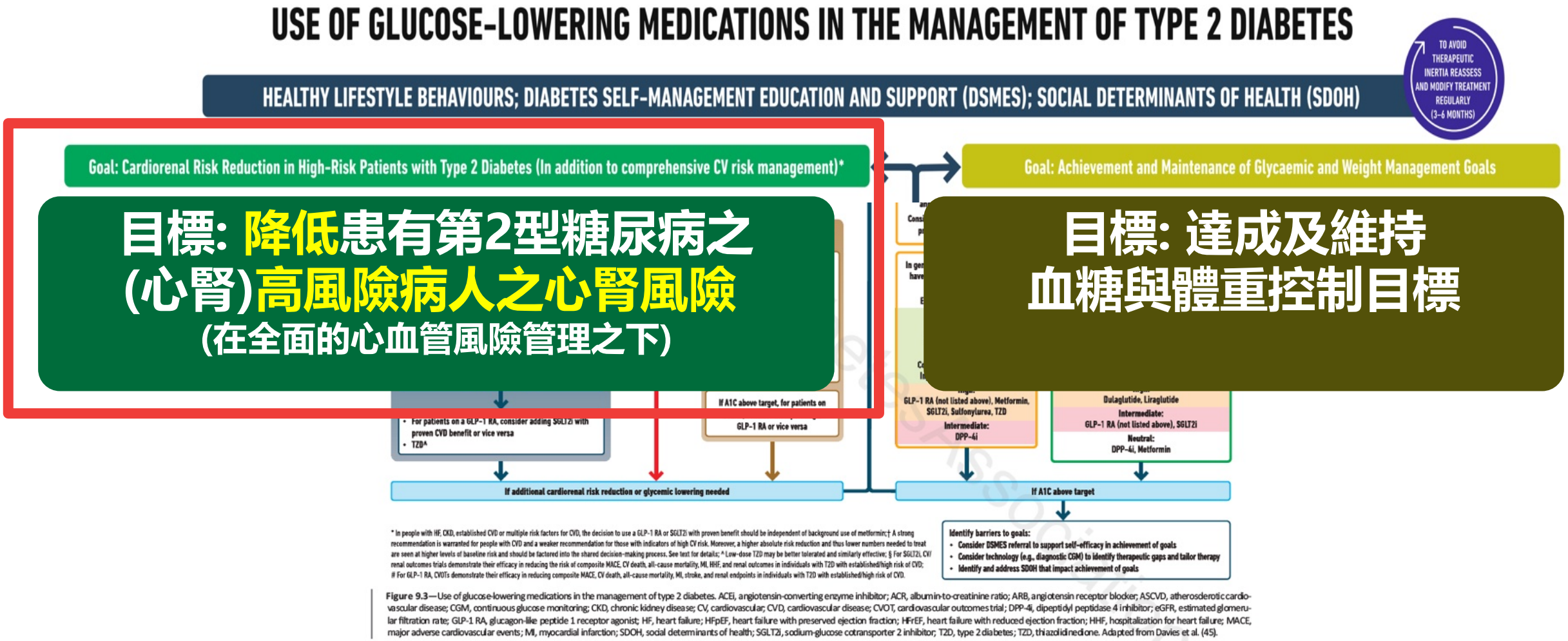
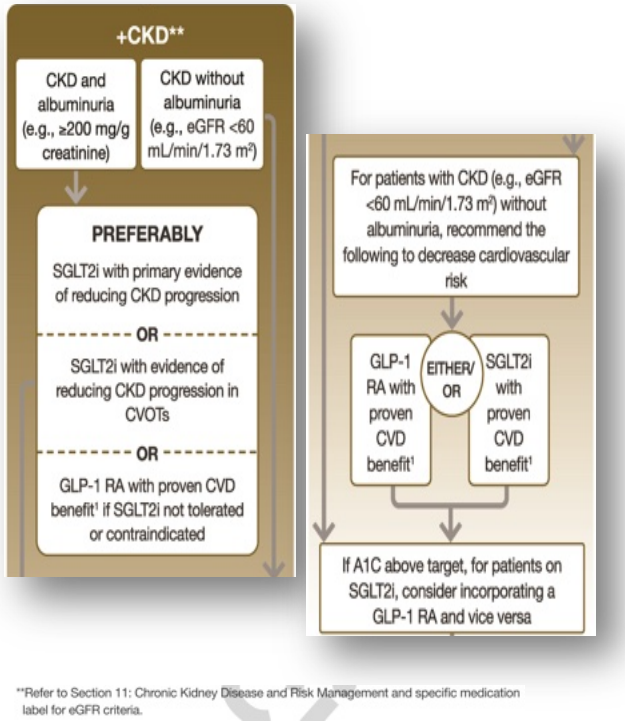


Figure 9.3—Use of glucose-lowering medications in the management of type 2 diabetes. ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin-to-creatinine ratio; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; CGM, continuous glucose monitoring; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; CVOT, cardiovascular outcomes trial; DPP-4i, dipeptidyl peptidase 4 inhibitor; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalization for heart failure; MACE, major adverse cardiovascular events; MI, myocardial infarction; SDOH, social determinants of health; SGLT2i, sodium-glucose cotransporter 2 inhibitor; T2D, type 2 diabetes; TZD, thiazolidinedione. Adapted from Davies et al. (45).

Diabetes Care Volume 46, Supplement 1, January 2023,S147

2023-2024 ADA Guideline:
T2D合併CKD治療，唯一首選SGLT2i

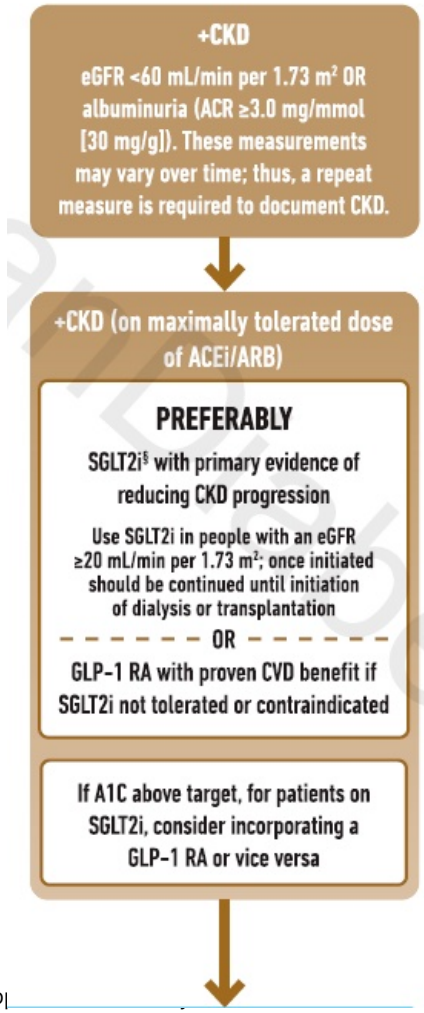
2022 ADA guideline



**Refer to Section 11: Chronic Kidney Disease and Risk Management and specific medication label for eGFR criteria.

2023 ADA guideline

1. 蛋白尿標準放寬
2. 強調ACEI/ARB使用
3. 路線圖簡化，SGLT2i唯一首選
4. SGLT2i 啟用及續用條件



UACR≥30 mg/g 或 **eGFR < 60** 起始使用

(使用ACEi/ARB到可容忍之最大劑量)

優先使用

有延緩慢性腎病進程主要實證的SGLT2i

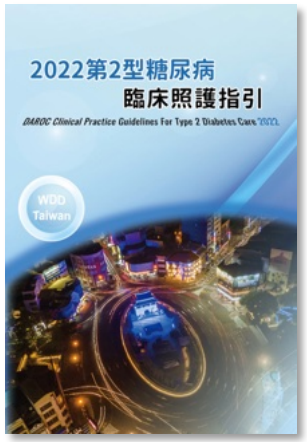
在eGFR ≥ 20ml/min per 1.73 m² 可使用SGLT2i，一旦開始就**應該持續至開始透析或換腎時**

或

假如SGLT2i不適用，可選擇有心血管實證的GLP-1 RA

1. Diabetes Care Volume 45, Supplement 1, January 2022 2. Diabetes Care Volume 46, Sup

中華民國糖尿病學會
2022第2型糖尿病臨床照護指引



藥物	SGLT2i	GLP1-RA	DPP4i	TZD	SU/ Glinide	AGI	Insulin
腎疾病	有 (指腎絲球過濾率，透析及腎因性或心因性死亡終點)	有 (指蛋白尿之改善)	有 (指蛋白尿之改善)				中立

http://www.endo-dm.org.tw/dia/

臨床建議

UACR≥30 mg/g

或

eGFR<60 ml/min/1.73m²

建議優先使用SGLT-2抑制劑 (建議強度: 強烈)

http://www.endo-dm.org.tw/diahttp://www.endo-dm.org.tw/DB/book/88/2022%20DAROC%20T2DM%20guideline-core%20slide.pdf p.261

Renal outcome trial of SGLT2i

	Canagliflozin 100 mg	Dapagliflozin 10 mg	Empagliflozin 10 mg
Study	CREDENCE	DAPA-CKD	EMPA-KIDNEY
Publish date	April 14, 2019 (NEJM)	Sep. 24, 2020 (NEJM)	Nov. 4, 2022 (NEJM)
Status	stopped early on demonstration of efficacy	stopped early for overwhelming efficacy	stop early due to clear positive efficacy
N	4401	4304	6609
Medium duration	2.6 years	2.4 years	2 years
Patient population	T2D	with or without T2D	with or without T2D
Renal population inclusion criteria	eGFR ≥30 to <90 mL/min/1.73 m^2 UACR >300 to ≤5000 mg/g	eGFR ≥25 to <75 mL/min/1.73 m^2 UACR ≥200 and ≤5000 mg/g	eGFR ≥20 to <45 mL/min/1.73 m^2 or eGFR ≥45 to <90 mL/min/1.73 m^2 with UACR ≥200 mg/g (or protein:creatinine ratio ≥300 mg/g)
Primary Endpoint	Doubling of serum creatinine, ESRD, renal or CV death	**≥50%** sustained decline in eGFR, ESRD, renal or CV death	Progression of kidney disease(**≥40%** sustained decline in eGFR, ESRD, sustained decline in eGFR to <10, renal death) or CV death

1. N Engl J Med. 2019 Jun 13;380(24):2295-2306. 2. N Engl J Med. 2020 Oct 8;383(15):1436-1446. 3. https://clinicaltrials.gov/ct2/show/NCT03594110

臺灣SGLT2i糖尿病、腎病相關適應症

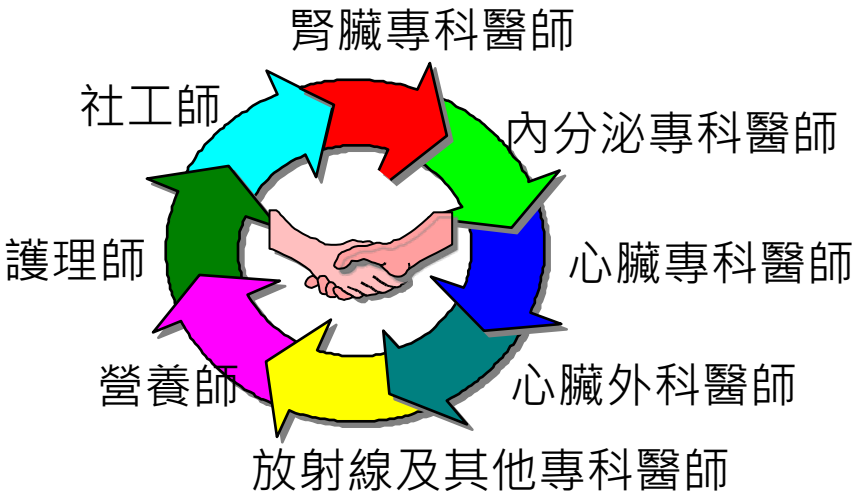
	Dapagliflozin	Canagliflozin	Empagliflozin 10 mg	Empagliflozin 25 mg	Ertugliflozin
腎病相關適應症	第二型糖尿病 預防腎臟病：降低慢性腎臟病(CKD)新發生或惡化的風險 慢性腎臟病：用於治療有惡化風險之慢性腎臟病的成人病人時，可降低持續性腎絲球過濾率(eGFR)下降、末期腎病(ESKD)、心衰竭住院和心血管死亡的風險。	糖尿病腎病變(巨量蛋白尿期)	針對心臟衰竭患者(紐約心臟學會(NYHA)第二級至第四級的心臟衰竭成年病人)：減緩預估腎絲球過濾率(eGFR)下降。	無	無
蛋白尿限制	無	巨量蛋白尿期	無	-	-
eGFR限制	eGFR≥25：每日一次10 mg eGFR<25：不建議開始治療，然而Forxiga治療後，eGFR降低小於25的病人，可持續使用以降低eGFR下降、ESKD、心血管死亡和心衰竭住院的風險。 透析病人：禁止使用	eGFR≥30：每日一次 eGFR<30：不建議使用 透析病患：禁止投藥	第二型糖尿病 eGFR≥30：無需調整劑量 eGFR<30：不建議使用 透析：禁用 心臟衰竭 eGFR≥20：無需調整劑量 eGFR<20：不建議使用 透析：禁用	第二型糖尿病 eGFR≥30：無需調整劑量 eGFR<30：禁用 ESRD或透析：禁用	第二型糖尿病 eGFR≥45: 不須調整劑量 eGFR 30-45: 不建議，如果血糖控制維持穩定，且eGFR介於30-45之間，病人可繼續使用 eGFR<30: 禁用 ESRD/透析: 禁用 確定患有CVD之T2DM eGFR≥30: 不須調整劑量 eGFR<30: 資料不足，無法據以作出給藥建議 ESRD/透析: 禁用

T2DM: 第二型糖尿病 CVD: 心血管疾病; eGFR低於45的第二型糖尿病病人使用Forxiga可預防心血管事件及預防腎臟病，不建議血糖控制

https://info.fda.gov.tw/MLMS/H0001.aspx

糖尿病腎臟疾病轉介至腎臟科時機

- 進入第4期臨床糖尿病腎臟疾病時，建議轉介至腎臟專科做進一步的衛教與治療。
  - 延長患者不需要透析的時間
  - 降低花費，改善照護品質
  - 適當的提供有關腎臟疾病治療的資訊，有助於病患及家屬正確的選擇治療方式。
  - 讓Pre-ESRD病患安全且平順地進入透析或移植



Conclusion

1. 2023-2024 ADA Guideline糖尿病之血糖與體重控制建議:

- 使用Metformin、複方或其他藥物提供足夠療效幫助患者達標
- SGLT2i控糖療效等級高，優於DPP4-I

2. 針對糖尿病合併CKD:

- 2023-2024 ADA guideline 、中華民國糖尿病學會第2型糖尿病臨床照護指引建議:

eGFR<60 或 UACR≥ 30的T2D患者建議優先使用SGLT-2抑制劑

謝謝聆聽