



心腎共病的臨床照護實務經驗分享—— 以慢性腎臟病合併糖尿病為例

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大綱

- 糖尿病治療的挑戰與困境
- 個案分享: 慢性腎臟病合併糖尿病之治療經驗
- 從實證至臨床: 如何為患者提供糖心腎全方位保護
- 總結



糖尿病治療的挑戰與困境



2020年全台萬名糖尿病患心腎病變風險大普查 過半數T2D病患合併高血壓

中華民國糖尿病衛教學會

2020年【保腎護心 篩初健康】計畫
12家醫策會糖尿病照護品質認證機構

14,669名糖尿病患

96.65%

合併多重風險因子(MRF)

56%



合併有**高血壓**

37%



合併有**白蛋白尿**

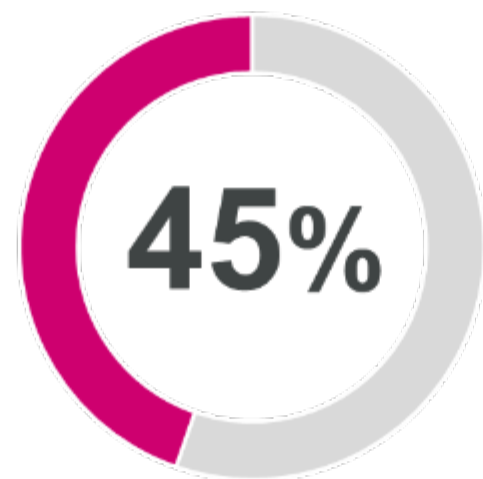


臺灣T2D照護的挑戰

糖尿病仍為
國人10大死因¹

110年度排名
第5位

超過4成患者未達
A1c個人化目標²



■ HbA1c個人化目標未達標率

T2D合併**CKD**
人數倍增³

2000-2014年間
+407%

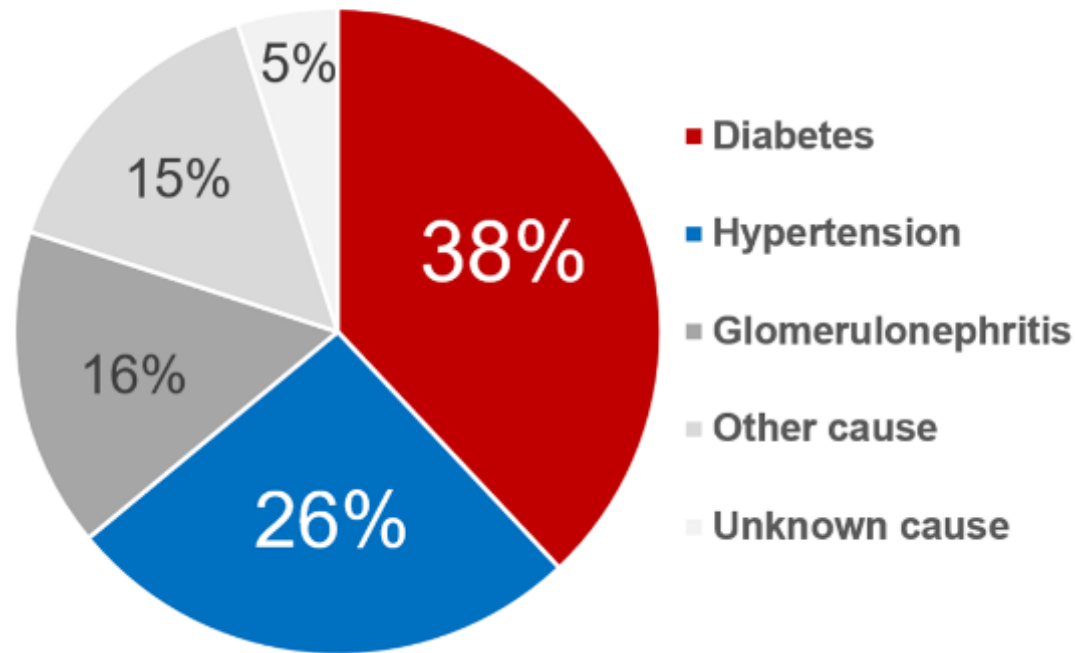
T2D合併**HF**
人數倍增³

2000-2014年間
+185%

HbA1c個人化目標：一般成年DM患者<7%、≥65歲以上患者<7.5%；CKD：Chronic Kidney Disease；HF：Heart Failure

糖尿病為最主要導致ESRD主因，高血壓佔第二位

Cause of ESRD



CKD risk



↑ **2.78倍**

Hyperglycemia is significantly associated with CKD (OR 2.78, 95%CI 1.59–4.88)



↑ **2.55倍**

Hypertension is significantly associated with CKD (OR 2.55, 95%CI 1.30–5.01)

ESRD: End-Stage Renal Disease

1. US CDC. Chronic Kidney Disease in the United States, 2019. 2. <https://www.researchsquare.com/article/rs-13718/v1>

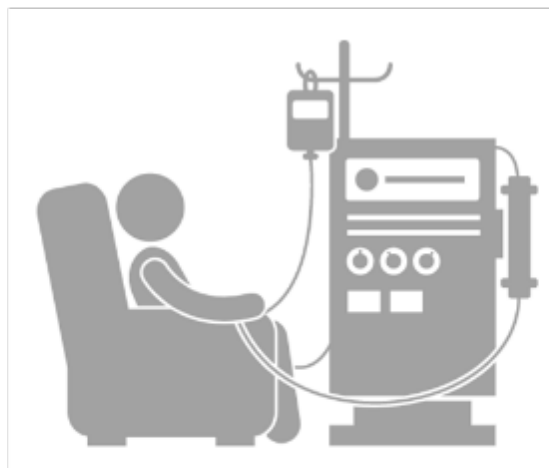
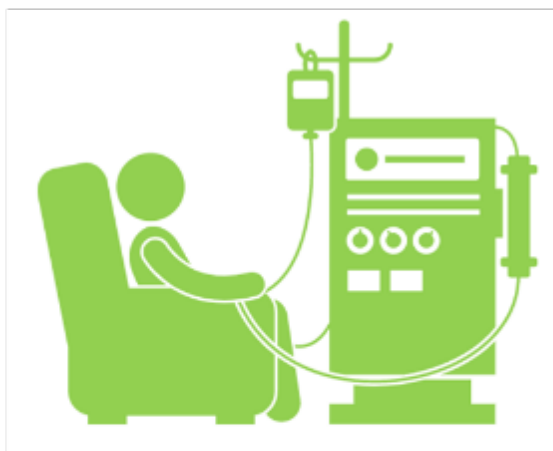


臺灣約每2位透析病患者有1位患有糖尿病

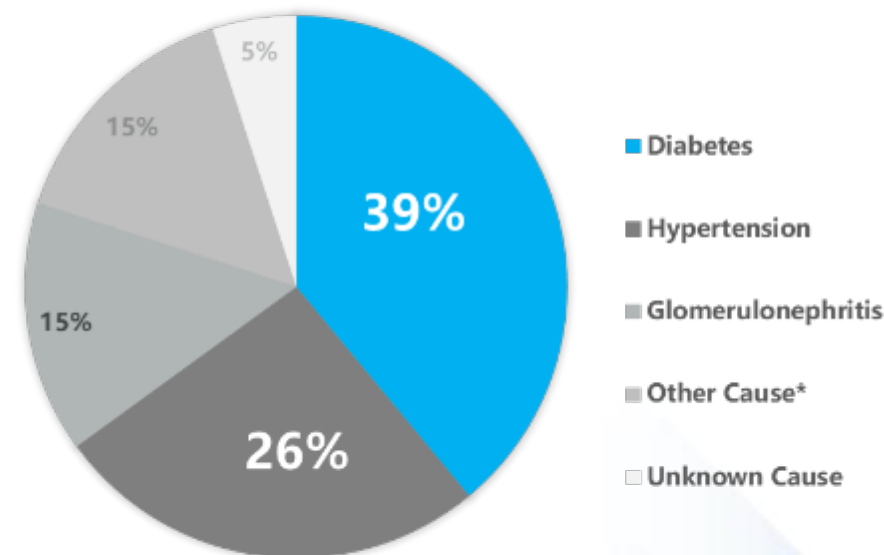


46.2% new dialysis patients'
principal diagnosis is diabetes

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



Cause of ESRD



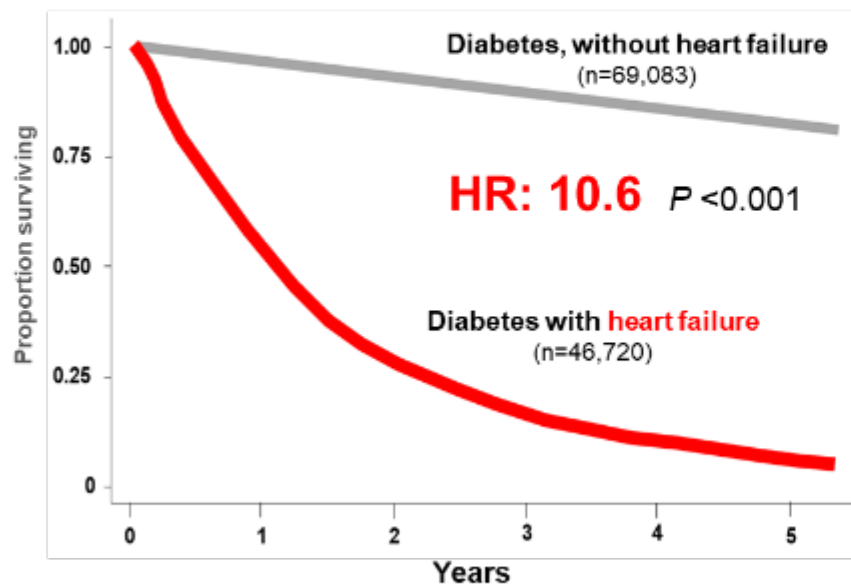
N=785,883(all age, 2018)

ESRD: End-Stage Renal Disease



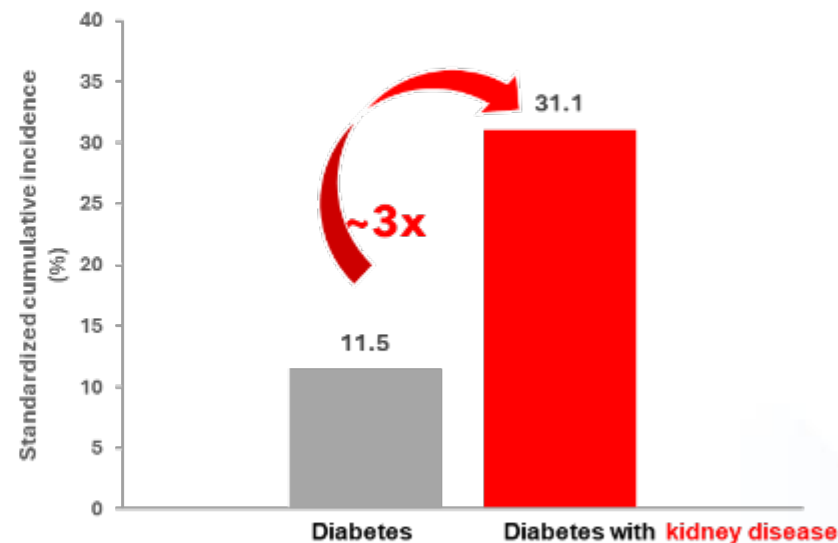
糖尿病患合併心衰竭或腎病變的死亡風險增加

糖尿病患罹患心衰竭，
死亡風險增加**10倍**



Study design:
A national, nonconcurrent
cohort study of U.S. elders with diabetes
by using data from the 5% standard analytical file, which contained Medicare
claims for 1,941,453 individuals in 1994

糖尿病患罹患腎病變，
死亡風險增加**3倍**



The NHANES is a population-based program of studies conducted by the National Center for Health Statistics of the US Centers for Disease Control and Prevention. This study uses data from NHANES III participants aged ≥ 20 years.

Ten-year standardized all-cause mortality, by diabetes and kidney disease status^{2,a}

a. Standardized according to a model adjusted for age, sex, and race

1. Diabetes Care 2004 Mar; 27(3): 699-703. ; 2. Afkarian M et al. *J Am Soc Nephrol* 2013;24:302-308



糖尿病患腎功能進程 CV風險隨腎功能惡化上升，早期治療是關鍵

及時拯救糖尿病患者生命
趁早做好糖心腎照護

糖尿病初期GFR正常或升高，腎臟病變恐已悄悄發生

0.9	0.8	0.8	Serum Creatinine (mg/dl)	1.0	>2.0	>10
120	150	150	GFR (ml/min)	90	60	<10
0	0	10	UACR (mg/g)	>30	>100	>300



DeFronzo教授：應自“**Silent Period 關鍵期**”
介入糖尿病腎病變照護



拯救未來的我

想讓未來站在自己這邊
就得先站在未來那邊！

拯救 未來的我

減少後悔、提升行動力的
自我調節心理學

邊池盈 (변지영) — 著
馮燕玲 — 譯



想讓未來站在自己這邊，
就得先站在未來那邊！

人很難總是深謀遠慮，只從從長遠來看有利的事，
但如果能把未來當成人生的指南針，
現在所做的事，就能成為拯救未來的契機；
未來的自己，也能成為推動現在的力量！

韓國網路書店「YES 24」讀者9.8分超高評價

讀者好評：「如果你覺得自己有點廢，推薦你讀這本書！」

臨床心理師 洪仲清

人生設計心理諮詢所共同創辦人，臨床心理師 盧美姣

心理學作家，「愛敬書院」版主 鍾 穎

韓國心理諮詢專家 尼克小姐

——拯救未來推薦



個案分享 慢性腎臟病合併糖尿病之治療經驗





個案分享: Baseline Characteristic



T2DM

蔡先生
75歲
豆腐店老闆

Biometric

T2DM duration	20
HbA1c (%)	8
eGFR (ml/min/1.73m ²)	87
UACR (mg/g)	195mg/g
BP (mm Hg)	136/78
LDL (mg/dL)	86

History (勾選)

Hypertension	V
Dyslipidemia	V
UACR \geq 30mg/g	V
Smoking	
HF	V
CAD	V
M \geq 55yrs, F \geq 60yrs	V
Others...	

Anti-diabetic Medication

Metformin	
Xigduo	1#QD
DPP4i	
SU	Glimet 2#QN
Insulin	Ryzodeg 30U BBF



經評估後須與讓患者了解多重風險因子、並針對蛋白尿情況進行藥物調整

CKD風險分期情況



蔡先生
75歲 豆腐店老闆
eGFR: 87 ml/min
UACR 195 mg/g

			Persistent albuminuria categories Description and range		
			A1	A2	A3
			<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min per 1.73m ²) Description and range	G1	≥90			
	G2	60-90			
	G3a	45-59			
	G3b	30-44			
	G4	15-29			
	G5	<15			

Green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red, very high risk.

DM foot and CAD



Wagner:Grade 1
No PAOD

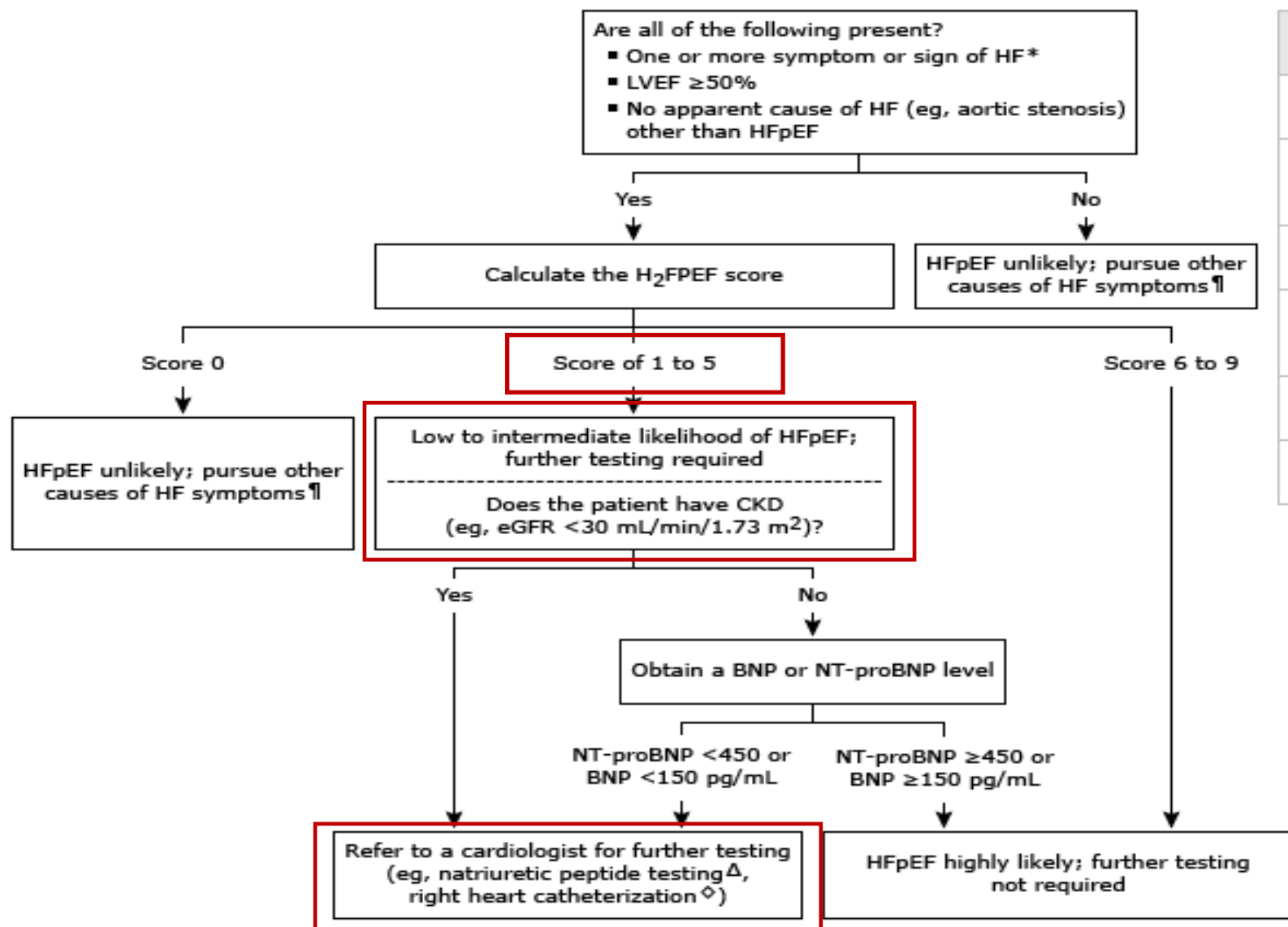
2024/03 CV ward admission

- Cardiac echo:
LEEF:57.9%
Diastolic dysfunction $E/A=0.59 (<1)$,
 $E/e'=12(>9)$
RVSP=31.2 mmHg (>30)
- PCI
CAD, 1VD, LAD diffuse disease lesion,
proximal to distal LAD 90~95% stenosis
LAD s/p stenting

H₂FPEF score

	Clinical Variable	Values	Points
H ₂	H heavy	BMI 27	1
	H ypertensive	exforge	
F	Atrial F ibrillation	N	
P	P ulmonary Hypertension	N	
E	E lder	>60	1
F	F illing Pressure	12	1
H ₂ FPEF score			Sum (0-9)
<div> <div>Total Points</div> <div> <div>0</div> <div>1</div> <div>2</div> <div>3</div> <div>4</div> <div>5</div> <div>6</div> <div>7</div> <div>8</div> <div>9</div> </div> </div> <div> <div>Probability of HFpEF</div> <div> <div>0.2</div> <div>0.3</div> <div>0.4</div> <div>0.5</div> <div>0.6</div> <div>0.7</div> <div>0.8</div> <div>0.9</div> <div>0.95</div> </div> </div>			

Approach to diagnosis of HFpEF

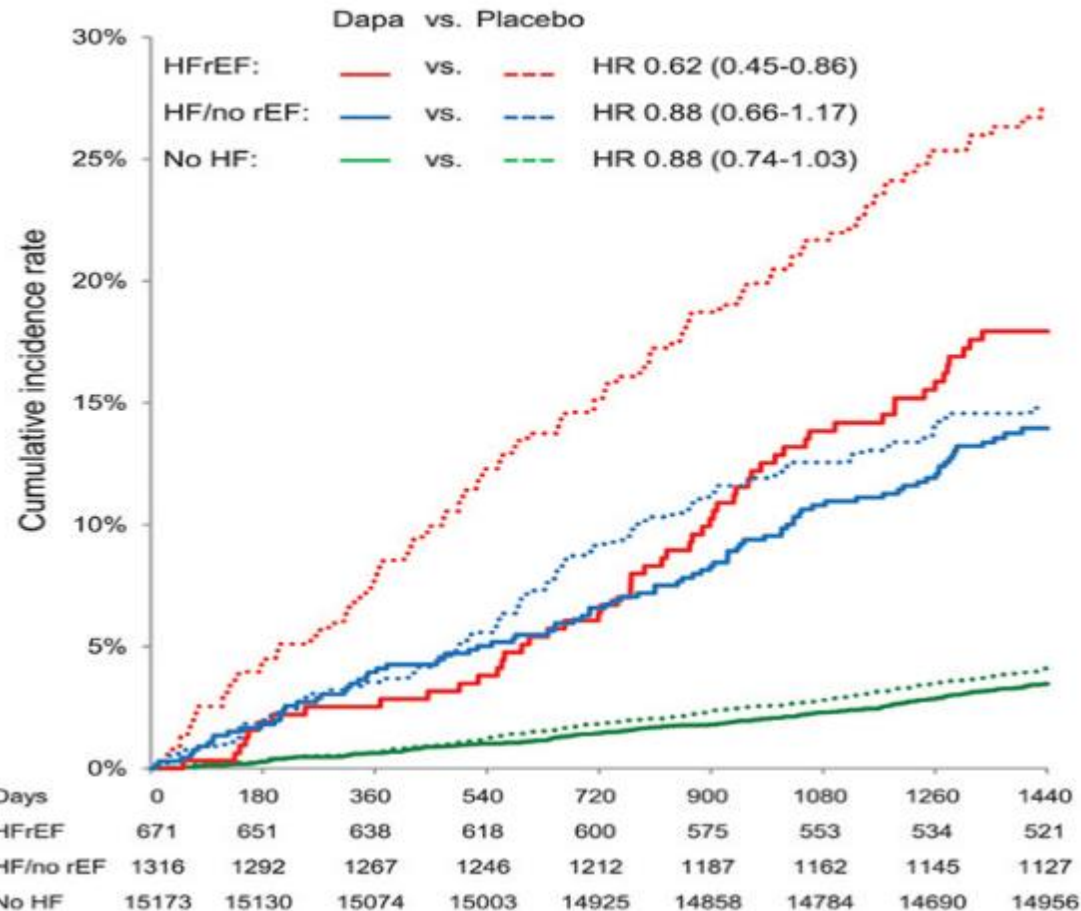


Calculation of the H₂FPEF score

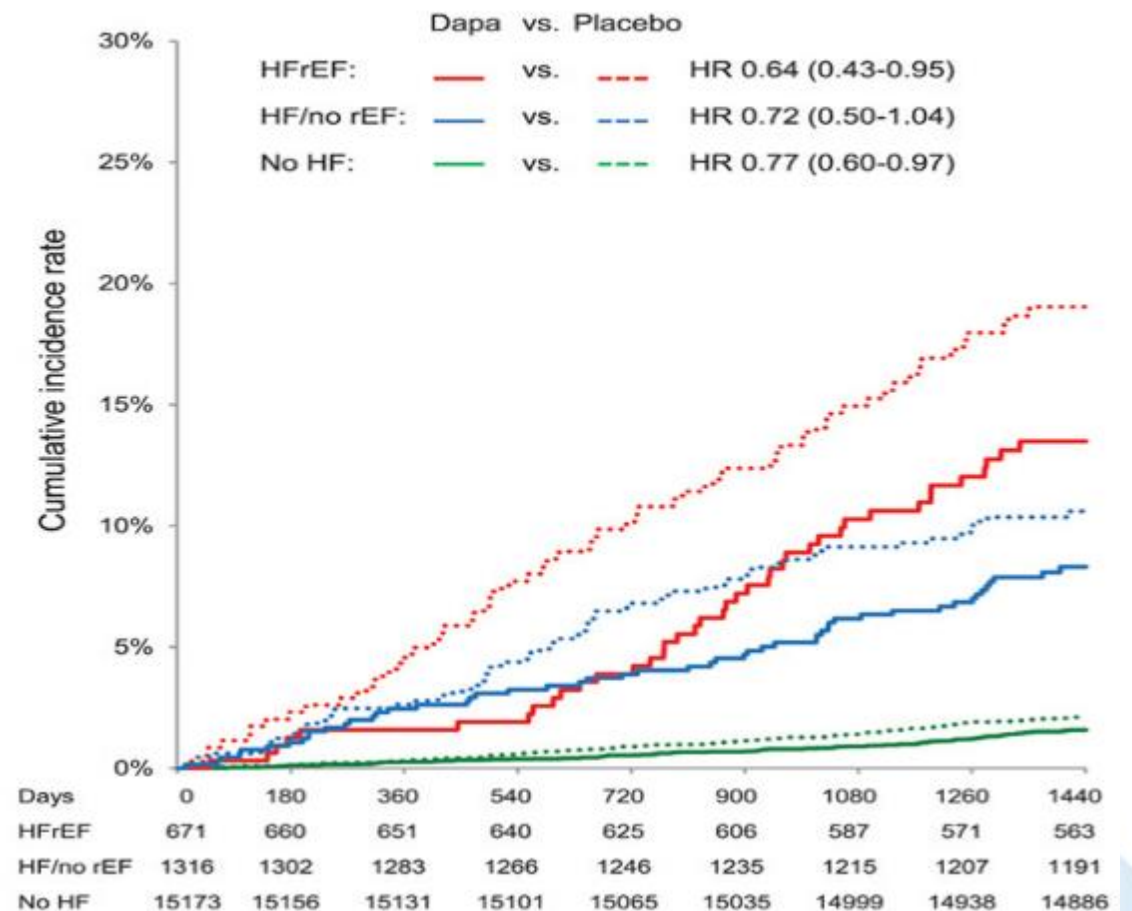
BMI ≥ 30 kg/m ²	2 points
Hypertensive or treated with ≥ 2 antihypertensive medications	1 point
Paroxysmal or persistent atrial fibrillation	3 points
Pulmonary artery systolic pressure > 35 mmHg by echocardiography	1 point§
Age > 60 years	1 point
E/e' > 9 by echocardiography	1 point§

Reduce HHF

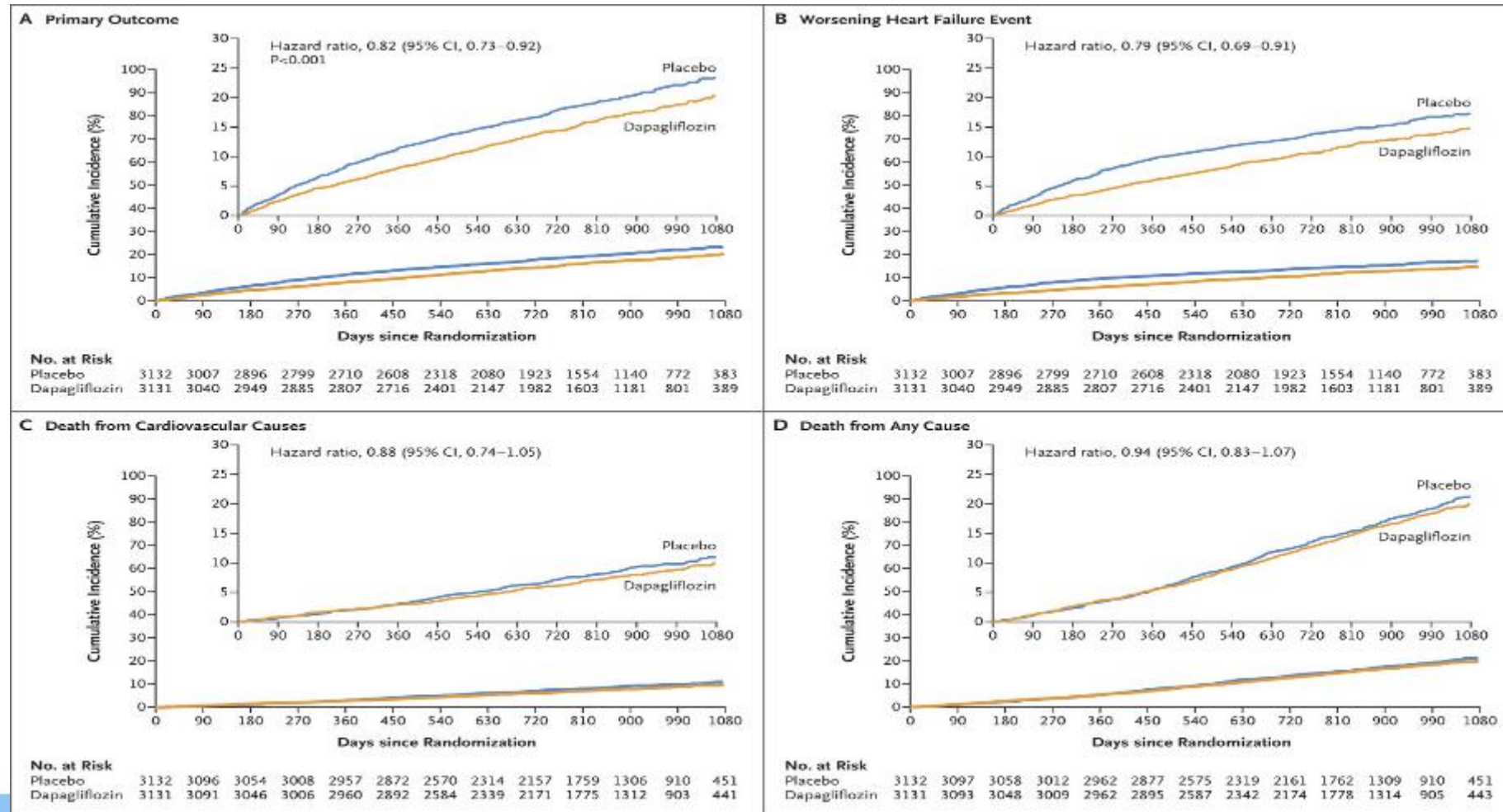
A Cardiovascular Death/Hospitalization for Heart Failure



B Hospitalization for Heart Failure



Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction





The risk of heart failure hospitalization after initiation of SGLT2i, GLP-1RA, DPP-4i, or SUs in patients with T2D and low-to-moderate CV risk

Helen Tesfaye, PharmD, MSc

ADA Scientific Sessions, 2024

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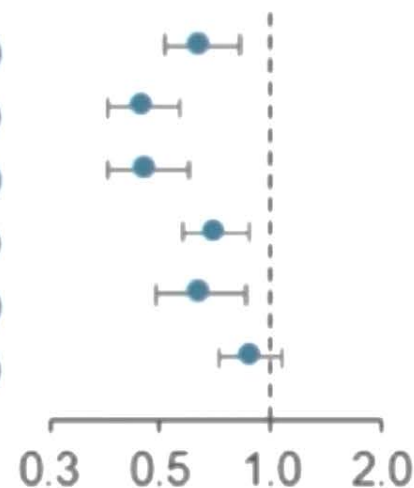
Study cohorts and data sources

- Study design: New-user, active-comparator cohort study with 6 pair-wise comparisons:
 - SGLT2i vs. GLP-1RA (cohort 1)
 - SGLT2i vs. DPP-4i (cohort 2)
 - SGLT2i vs. SU (cohort 3)
 - GLP-1RA vs. DPP-4i (cohort 4)
 - GLP-1RA vs. SU (cohort 5)
 - DPP-4i vs. SU (cohort 6)
- Data sources: Optum de-identified Clinformatics[®] Data Mart (CDM), IBM[®] MarketScan[®], and Medicare fee-for-service (FFS)

Results – Hospitalization for heart failure

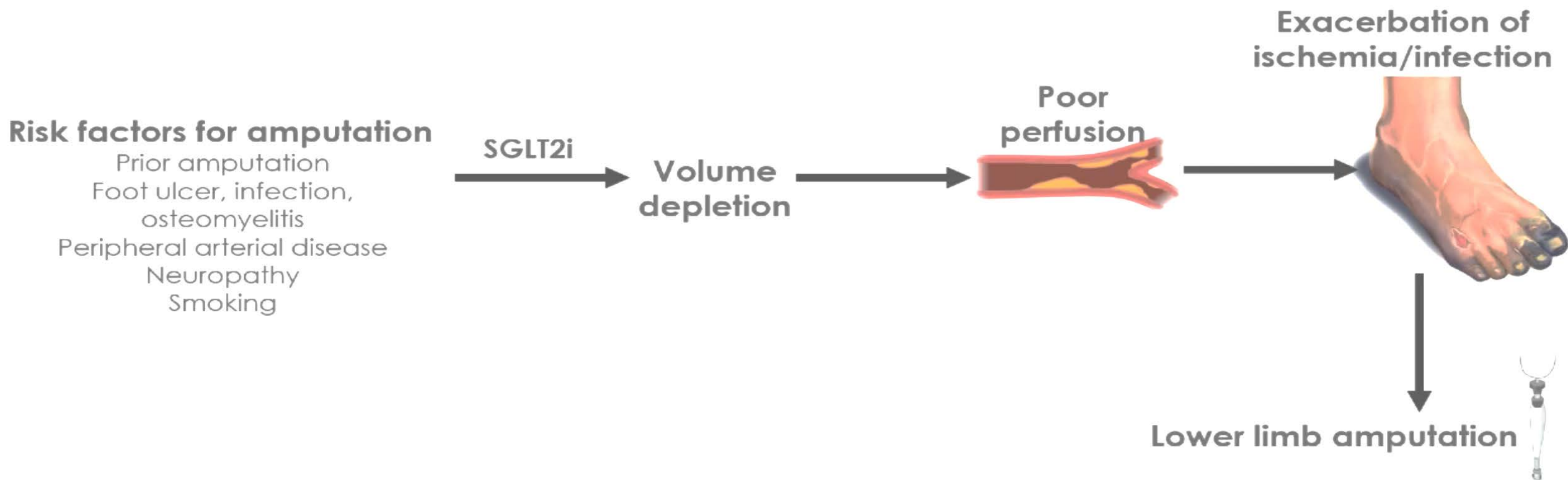
HHF (primary)

Exp. vs Ref.	No. of matched pairs	Exposure N events (IR/1000 PY)	Referent N events (IR/1000 PY)	HR (95% CI)
SGLT2i vs GLP-1RA	240,736	227 (0.98)	359 (1.61)	0.65 (0.51, 0.82)
SGLT2i vs DPP-4i	223,367	211 (0.91)	470 (2.17)	0.45 (0.36, 0.56)
SGLT2i vs SU	150,051	166 (1.05)	367 (2.25)	0.46 (0.36, 0.60)
GLP-1RA vs DPP-4i	191,724	306 (1.62)	440 (2.35)	0.71 (0.58, 0.87)
GLP-1RA vs SU	123,540	164 (1.38)	314 (2.42)	0.64 (0.49, 0.85)
DPP-4i vs SU	165,597	459 (2.72)	623 (3.25)	0.88 (0.72, 1.07)





Possible mechanism for SGLT2i associated lower limb amputation in T2D





Do diuretics increase risk of lower limb amputation? Meta-analysis of observational studies

Do diuretics increase the risk of limb events in patients with or at risk of LEAD ?



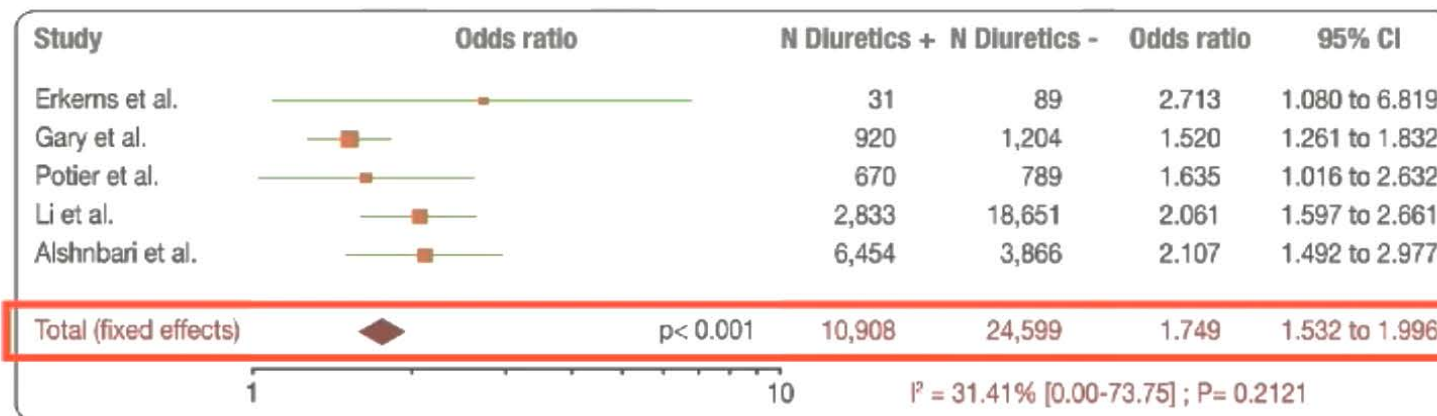
35,507 patients :



10,908
under diuretics



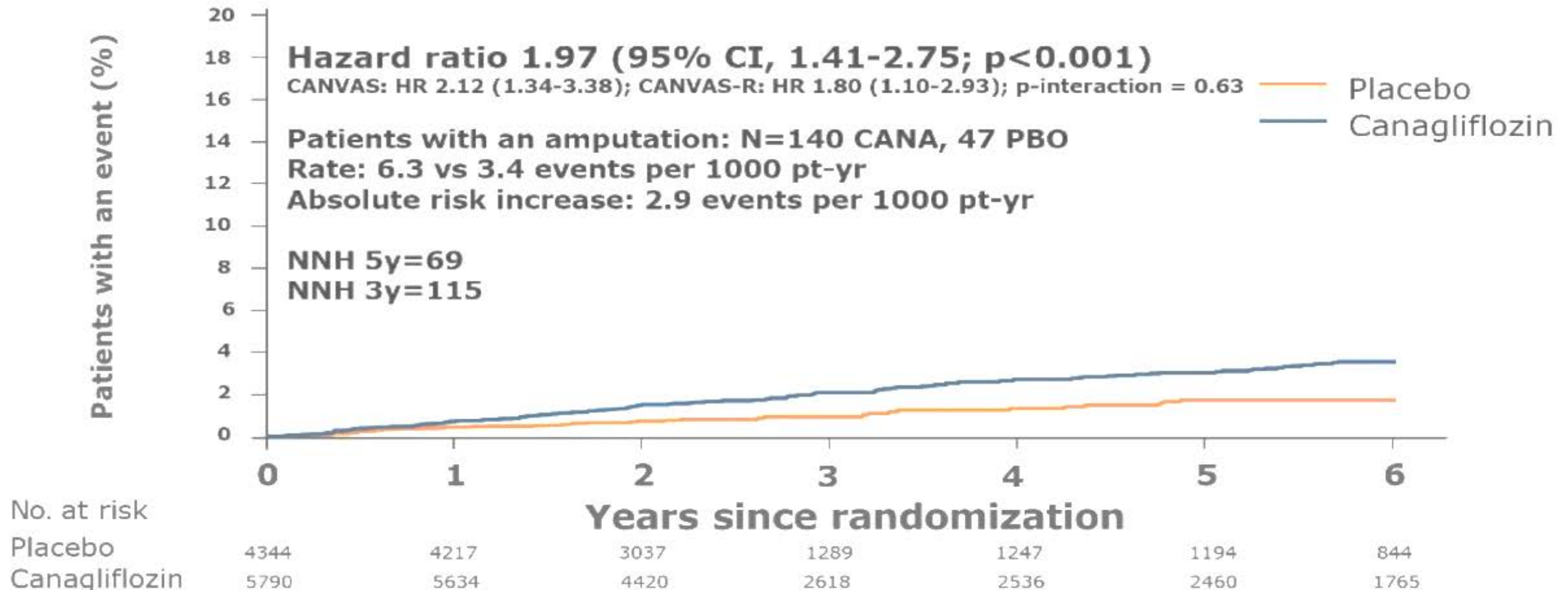
24,599
without diuretics



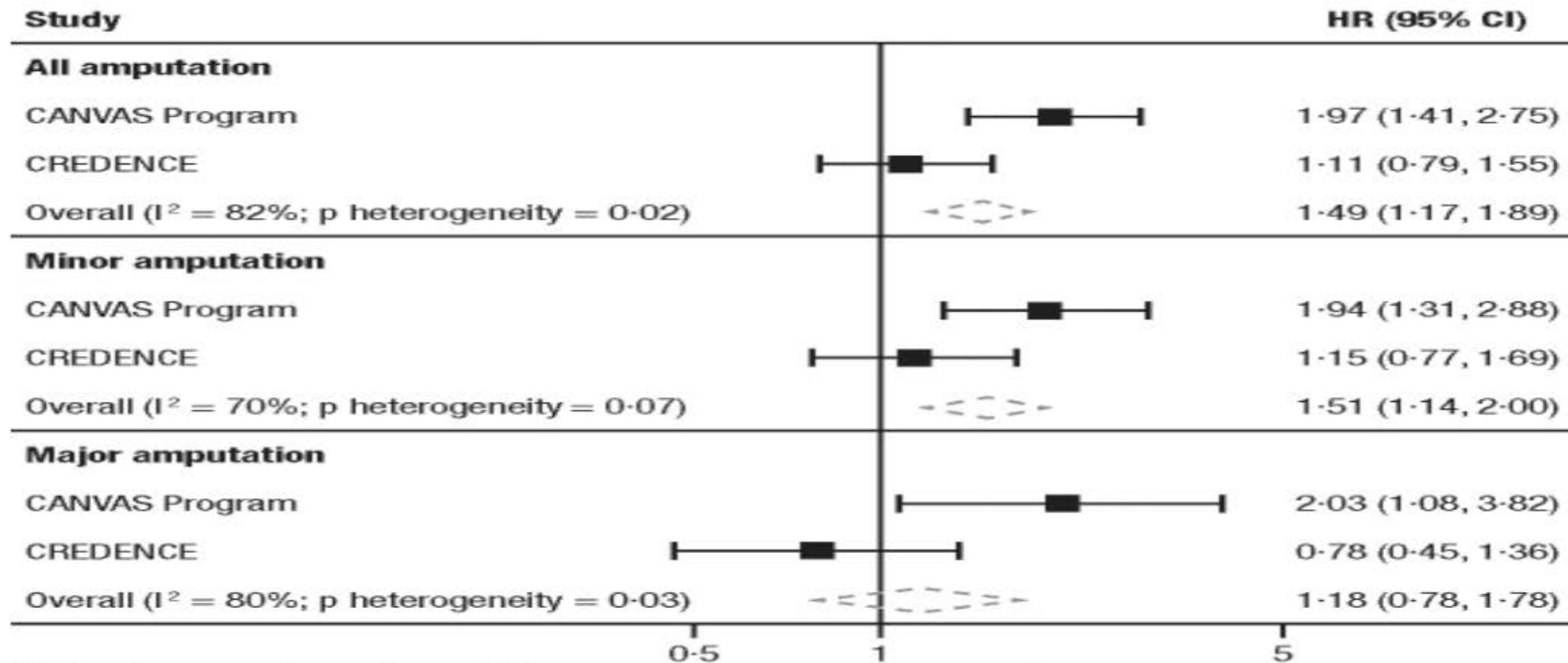
+74.9% increased risk of major adverse limb events under diuretics

LEAD, lower extremity arterial disease

CANVAS program: Lower extremity amputation



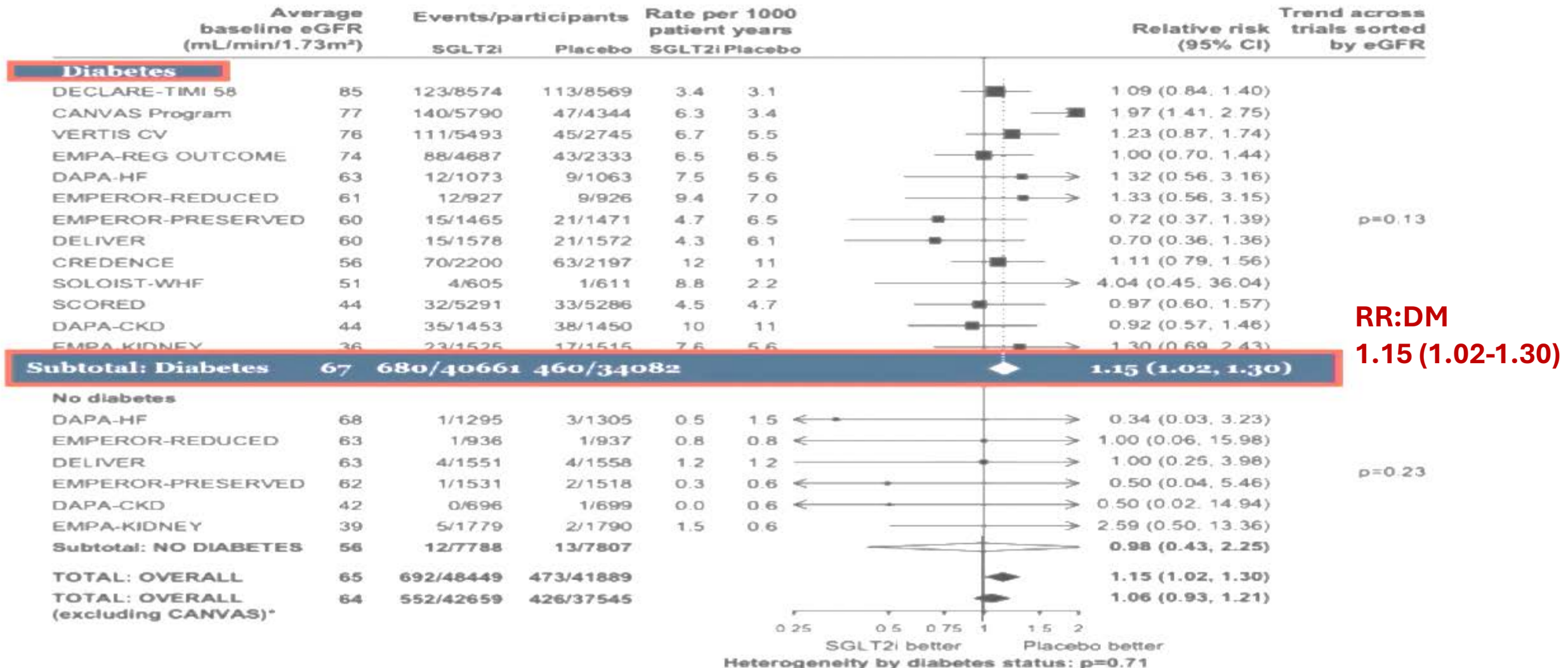
Risk of Amputation by Type of Amputation in the CANVAS program and the CREDENCE trial



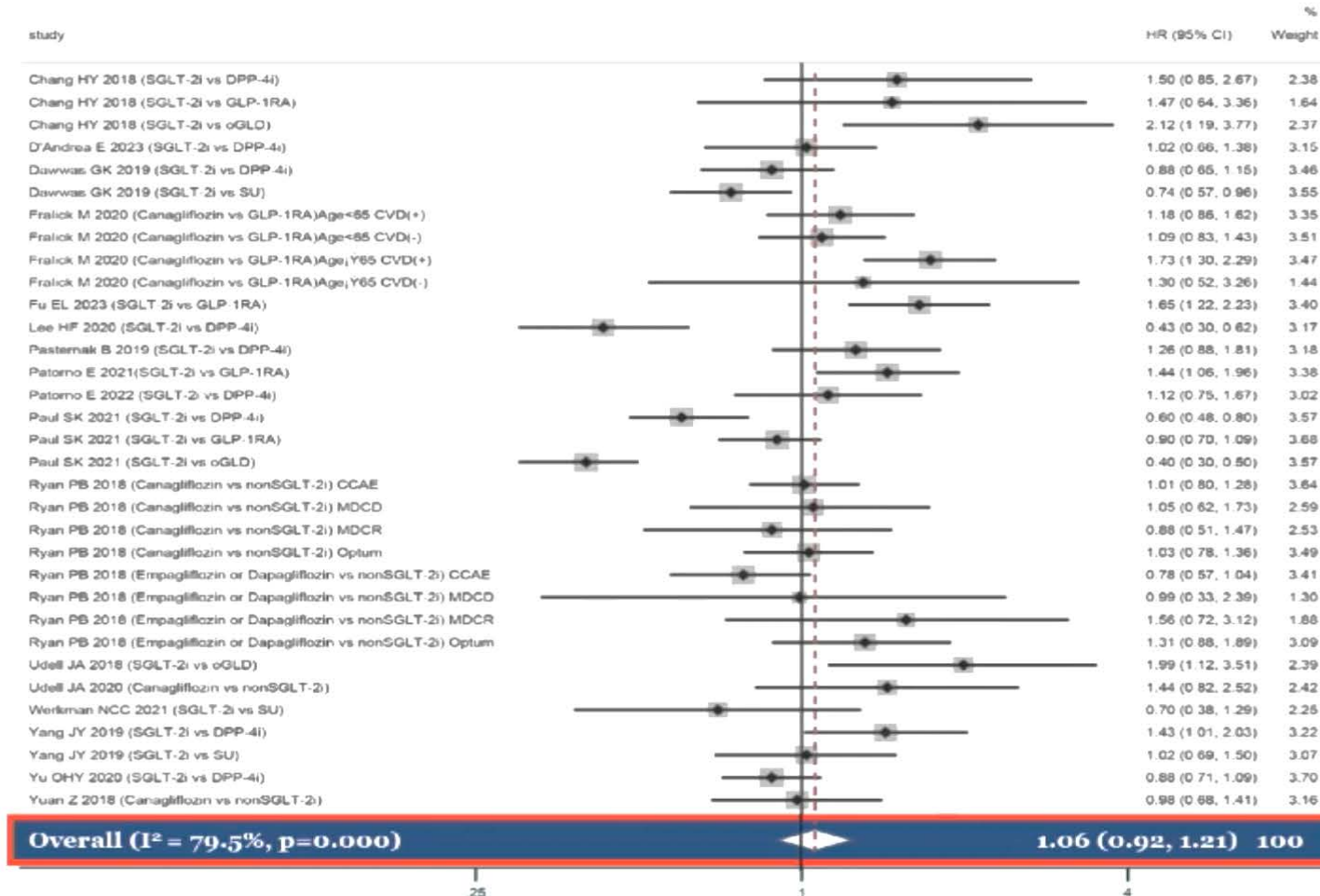
HR: hazard ratio; CI: confidence interval.

Effect of SGLT2i on lower limb amputation

Metaanalysis of 13 large placebo-controlled trials



Effect of SGLT2i on lower limb amputation in T2D: Metanalysis of cohort studies



HR
1.06 (0.92~1.21)

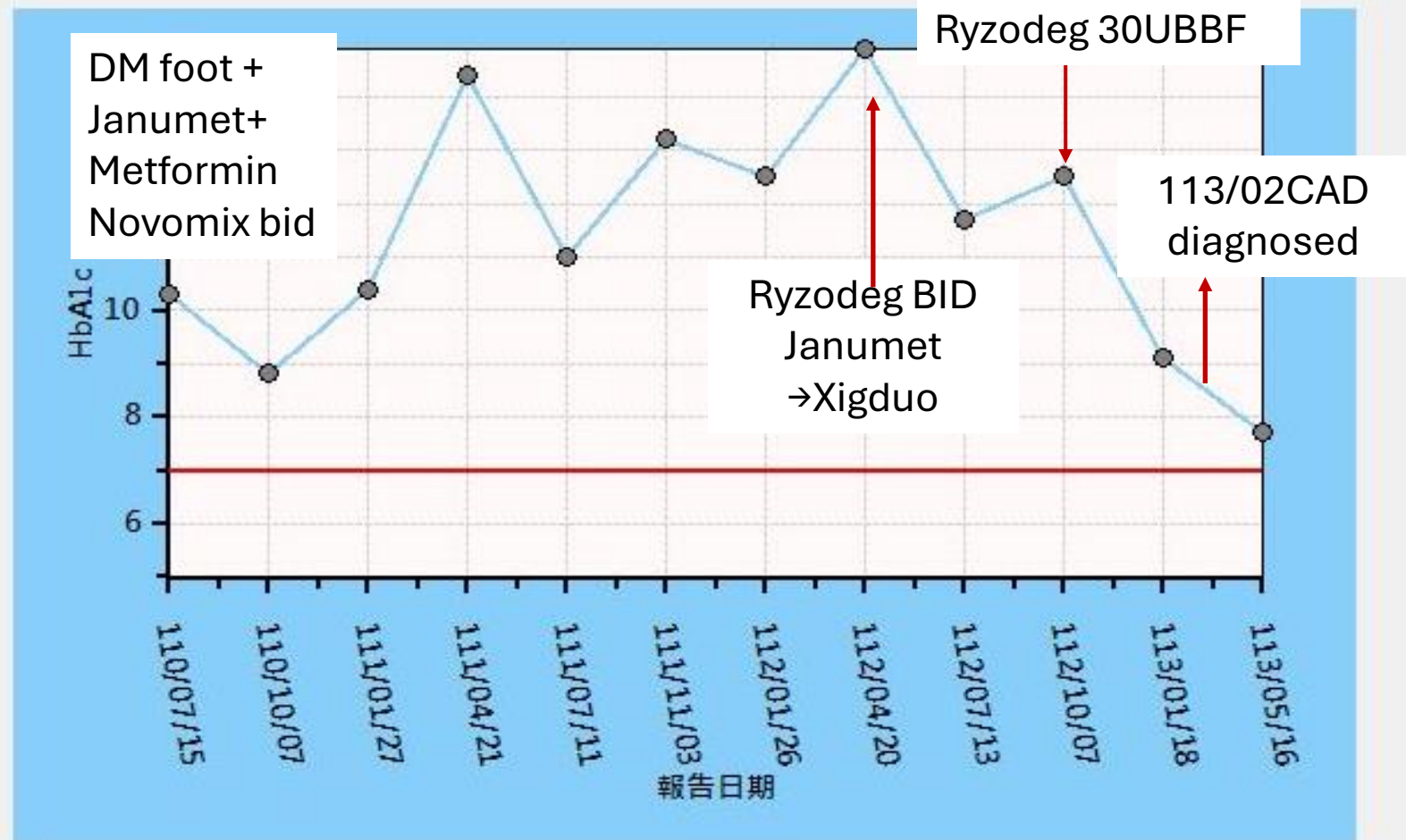
NOTE: Weights are from random-effects model



患者近三個月曾服用降血糖藥物，敬請持續注意患者的血

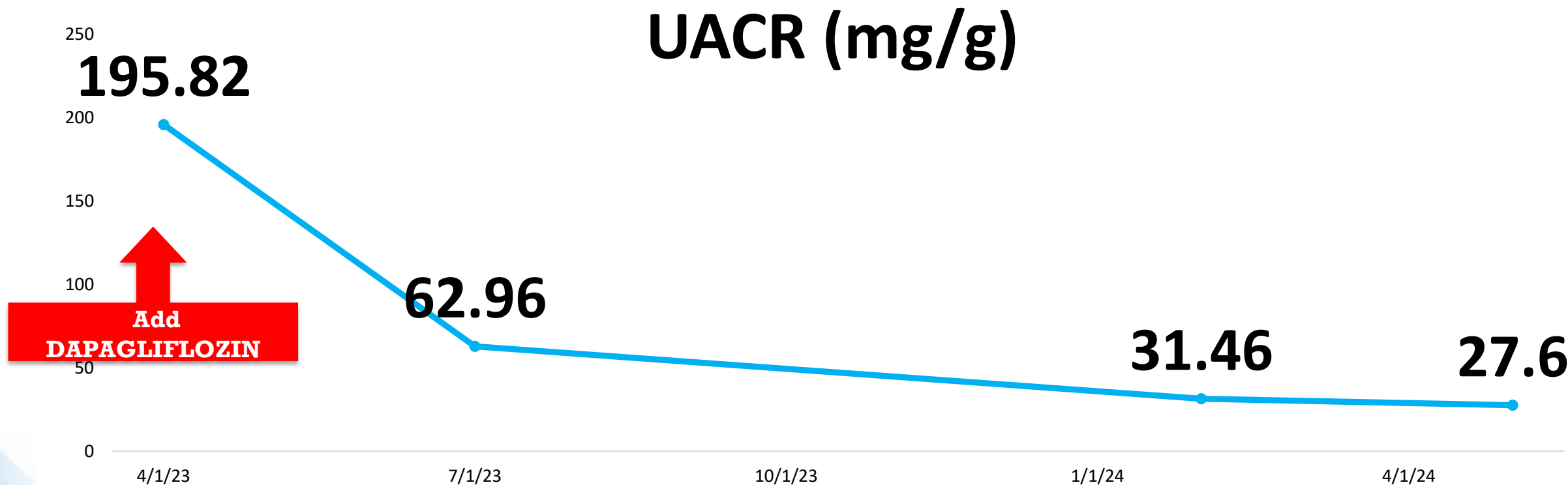
HbA1c :

報告日期	檢驗值
113/05/16	7.7
113/01/18	9.1
112/10/07	12.5
112/07/13	11.7
112/04/20	14.9
112/01/26	12.5
111/11/03	13.2
111/07/11	11.0
111/04/21	14.4
111/01/27	10.4
110/10/07	8.8
110/07/15	10.3

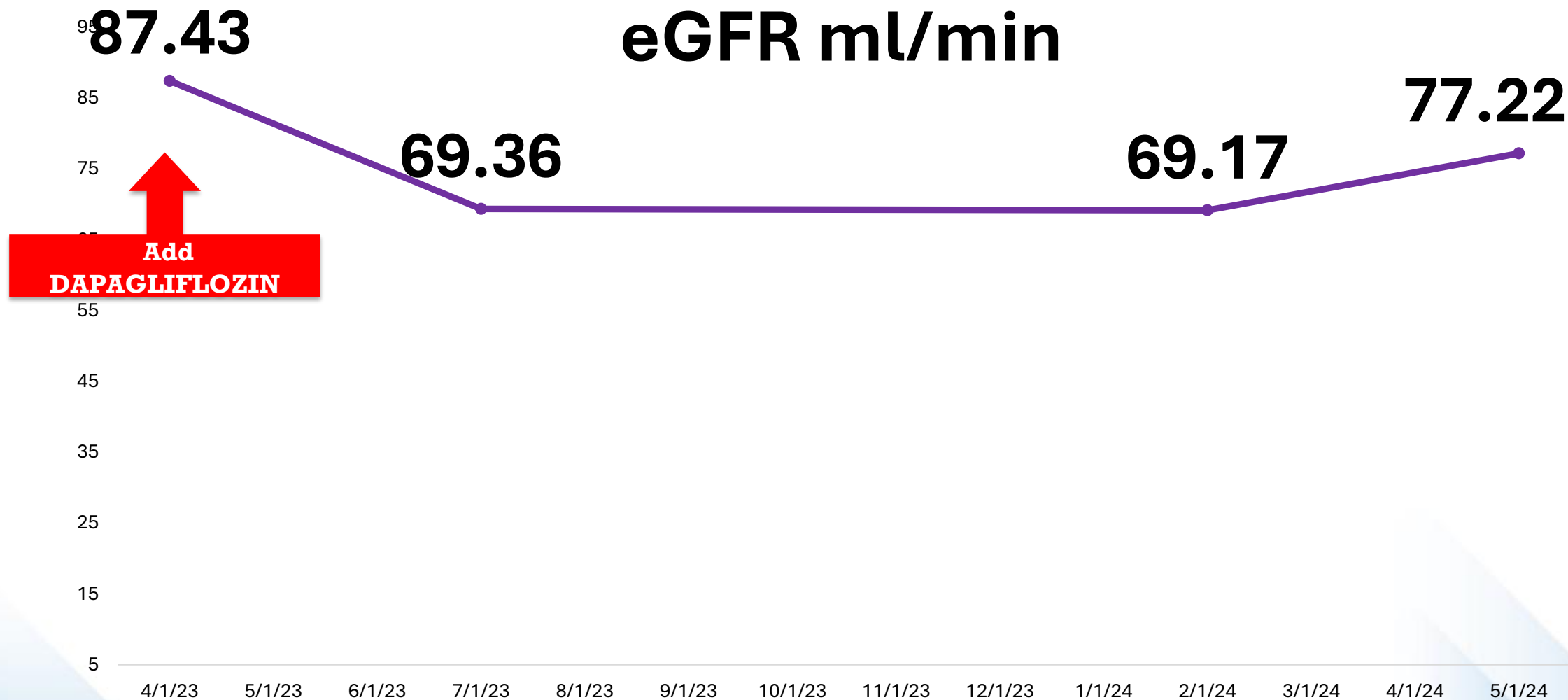




藥物介入後患者變化



藥物介入後患者變化





個案分享: Baseline Characteristic



林先生
39歲
傳產第二代

Biometric

T2DM duration	112/07
HbA1c (%)	9.4
eGFR (ml/min/1.73m ²)	
UACR (mg/g)	38 mg/g
BP (mm Hg)	130/87
LDL (mg/dL)	148

History (勾選)

Hypertension	
Dyslipidemia	V
UACR \geq 30mg/g	V
Smoking	
HF	
MI	
M \geq 55yrs, F \geq 60yrs	
Others...	

Anti-diabetic Medication

Metformin	Xigduo 1#QD
FORXIGA	
Contrave	2#BID for 3 months
Ozempic	2024/05



經評估後須與讓患者了解多重風險因子、並針對蛋白尿情況進行藥物調整

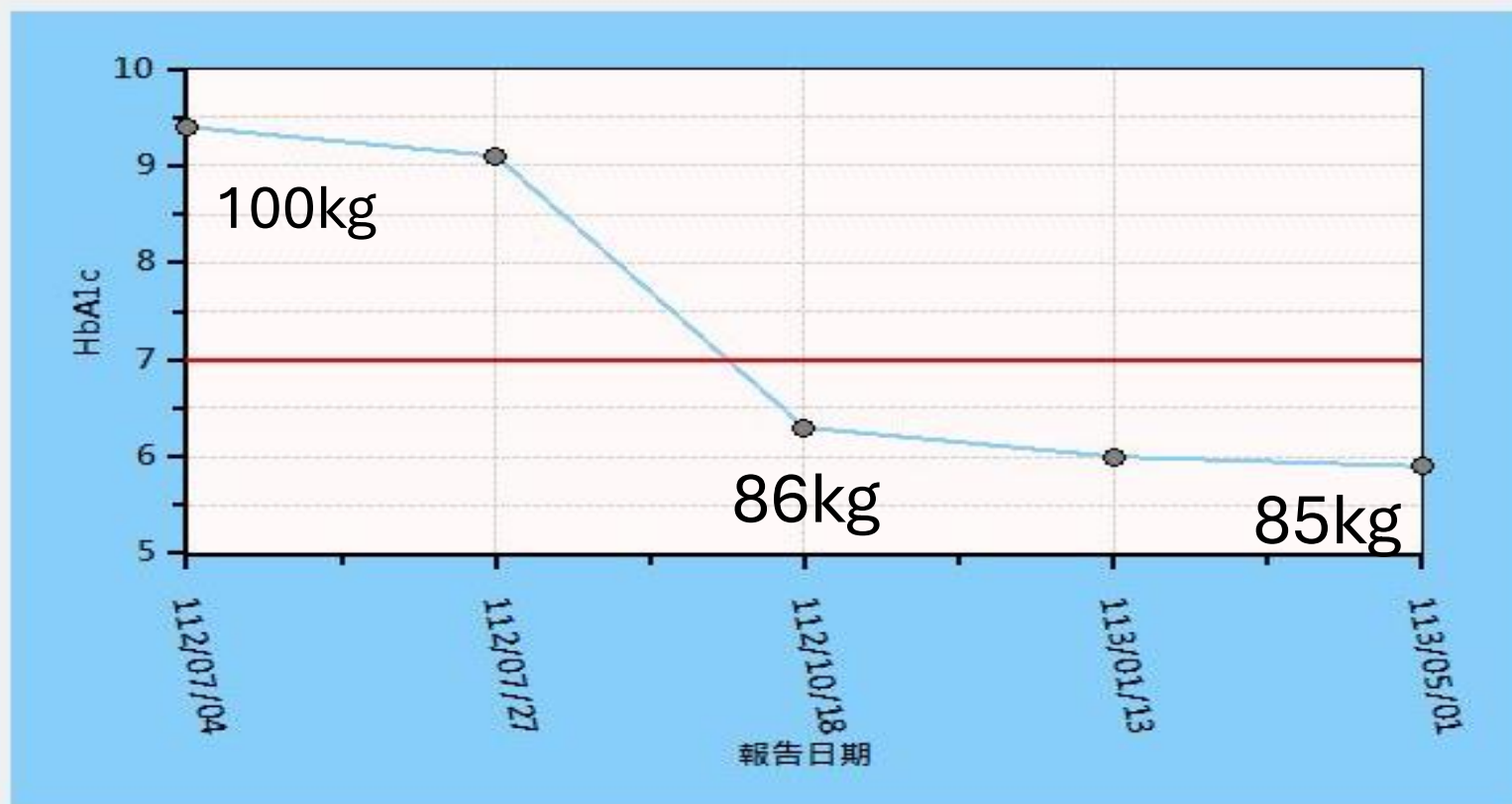


HbA1c

患者近三個月曾服用降血糖藥物，敬請持續注意患者的血糖變化。

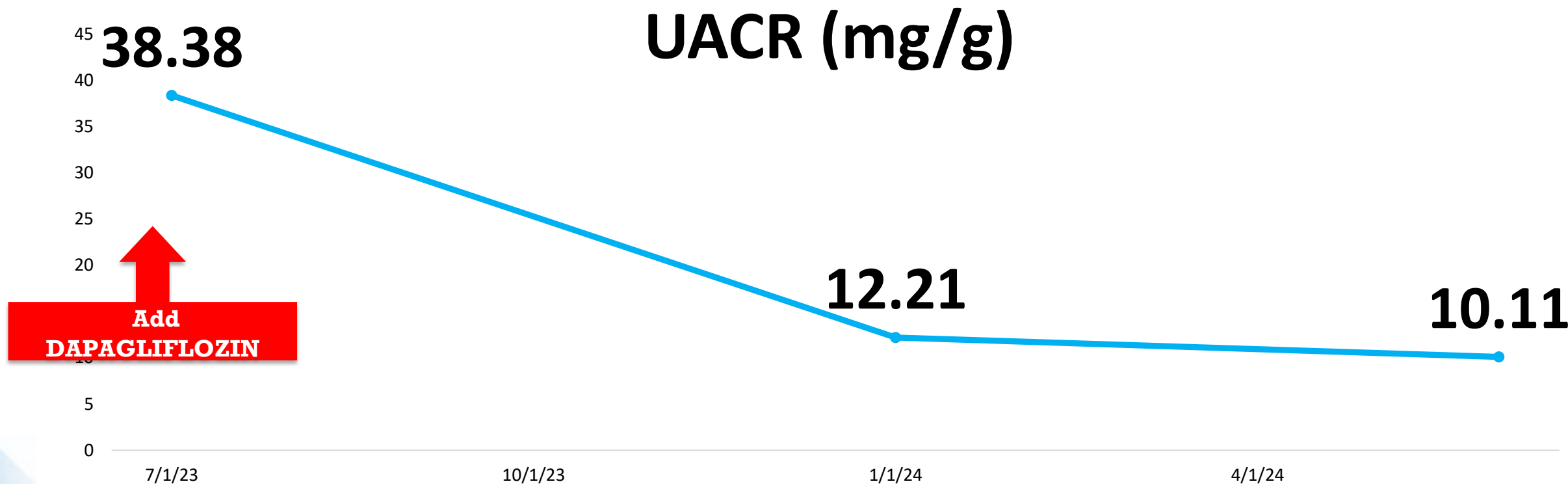
HbA1c :

報告日期	檢驗值
113/05/01	5.9
113/01/13	6.0
112/10/18	6.3
112/07/27	9.1
112/07/04	9.4





藥物介入後患者變化

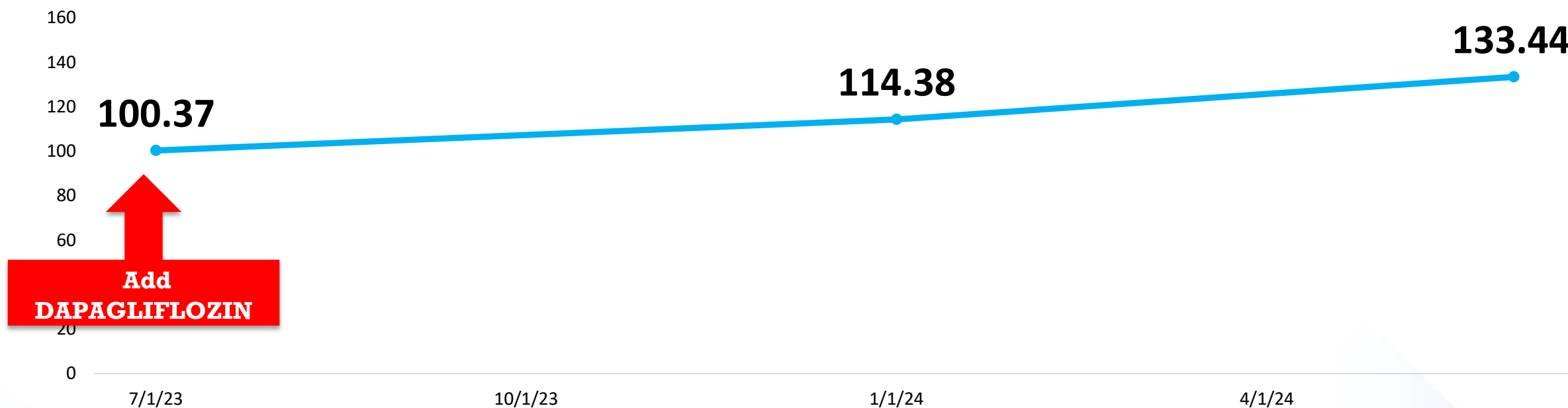




藥物介入後患者變化



eGFR (ml/min/1.73m²)



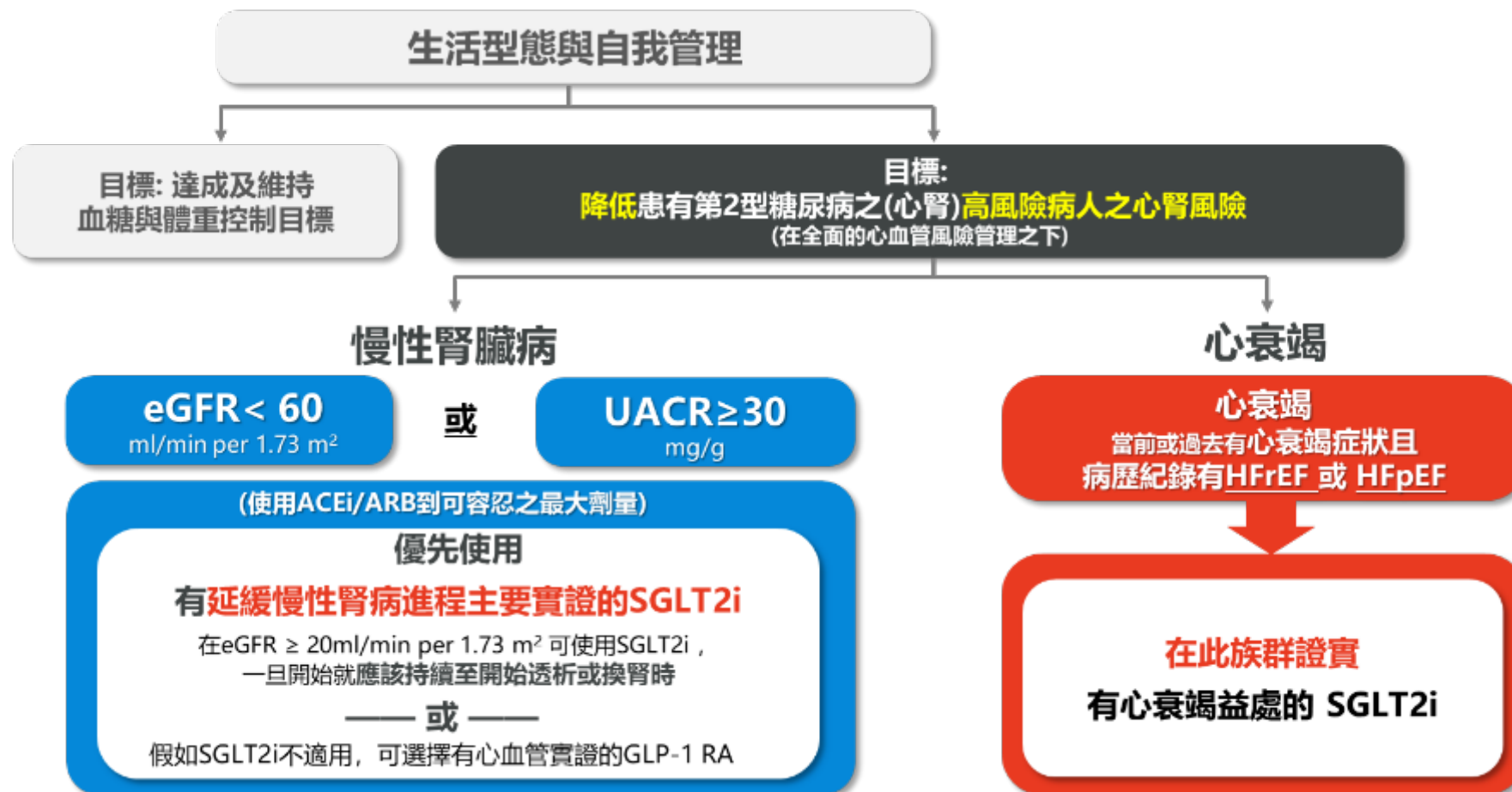


從實證至臨床： 如何為患者提供糖心腎全方位保護





2023 ADA糖尿病照護指引： 首選具CKD、心衰竭實證的SGLT2i





2024年ADA指引: **SGLT2i**建議使用於 4類T2D合併症患者以**降低心腎風險**

慢性腎臟疾病 	eGFR < 60 ml/min per 1.73 m ² 或 白蛋白尿(UACR ≥ 30 mg/g)	建議使用 有實證的 SGLT2i	A
心臟衰竭 	當前或過去有心衰竭症狀且 病歷紀錄有HFrEF 或HFpEF		
ASCVD高風險 	年齡≥55歲合併≥ 2個以下風險因子: 肥胖、高血壓、血脂異常、白蛋白尿、 抽菸		
ASCVD 	心肌梗塞、中風、任何血管重建手術、 短暫性缺血性發作、不穩定性心絞痛、 截肢、症狀性或無症狀的冠狀動脈疾病		



最新2023台灣腎臟醫學會慢性腎臟病照護指引建議： CKD高風險族群應每年eGFR&UACR篩檢

表A4-2-1：慢性腎臟病風險族群之建議篩檢頻率及方式¹

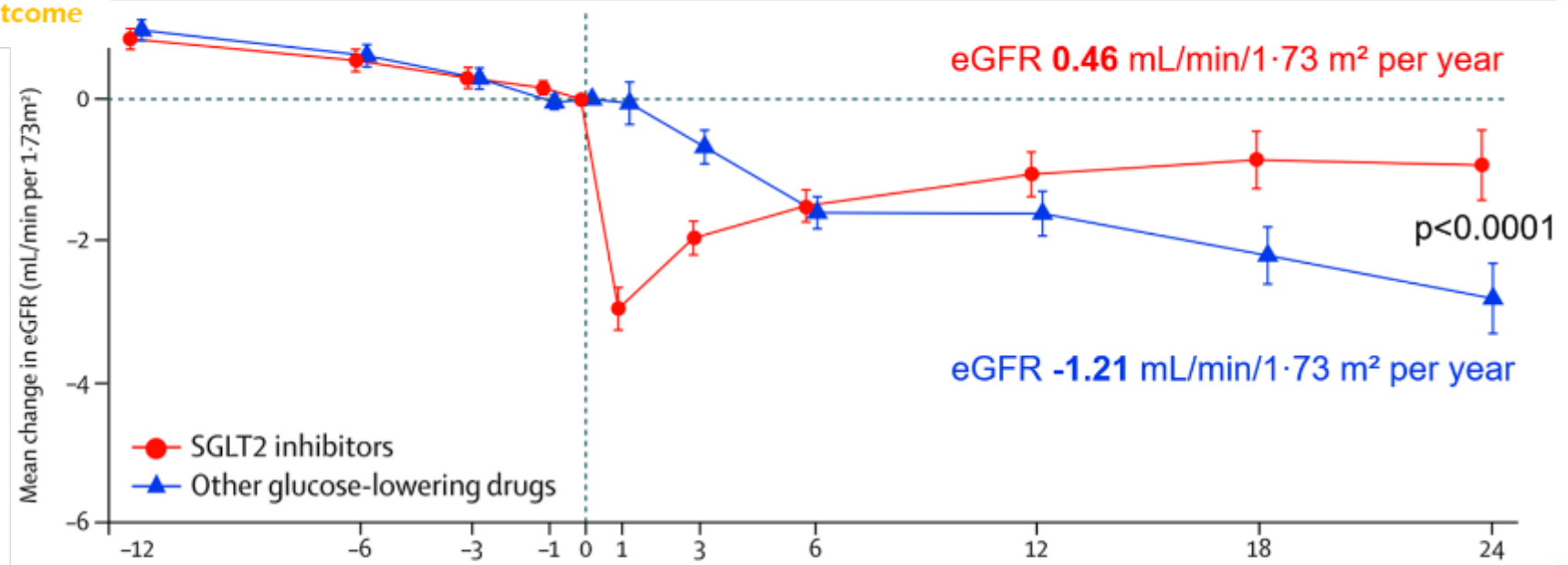
族群	篩檢頻率	篩檢方式	建議強度	證據等級
第1型糖尿病	初診斷五年後及往後每年	eGFR及UACR	1	A
第2型糖尿病	初診斷及往後每年	eGFR及UACR	1	A
高血壓	初診斷及往後每年	eGFR及UACR	1	A
心血管疾病	初診斷及往後每年	eGFR及UACR	1	A
高膽固醇血症	初診斷及往後每年	UACR	1	A
急性腎臟病病史	初診斷及往後每年	eGFR或UACR	1	A
仍在抽菸者	初診斷及往後每年	UACR	1	A
抗凝血劑使用者	初診斷及往後每年	UACR	1	A
>65歲者	初診斷及往後每年	eGFR及UACR	Good practice point	
肥胖	初診斷及往後每年	eGFR及UACR	Good practice point	



初期腎臟病變缺乏特異性症狀，
糖尿病、高血壓、心衰竭高風險族群定期篩檢非常重要！

1. https://tsnorgtw.gitbook.io/2022_taiwan_chronic_kidney_disease_clinical_guidelines/

SGLT2i較其他降糖藥物更能維持腎功能



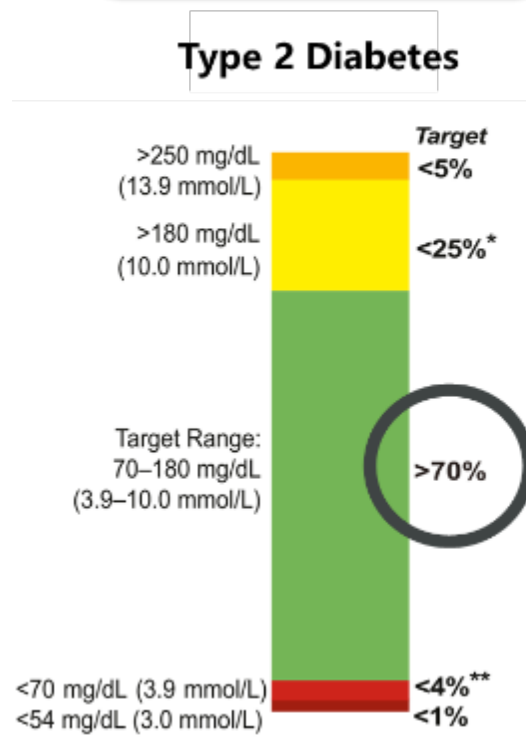
*35,561 patients with SGLT-2i vs. 35,561 patients with oGLD (other glucose-lowering drugs)

SGLT-2i vs. oGLD	40% eGFR decline	ESKD
	↓ 44% (p<0.0001)	↓ 67% (p=0.0024)

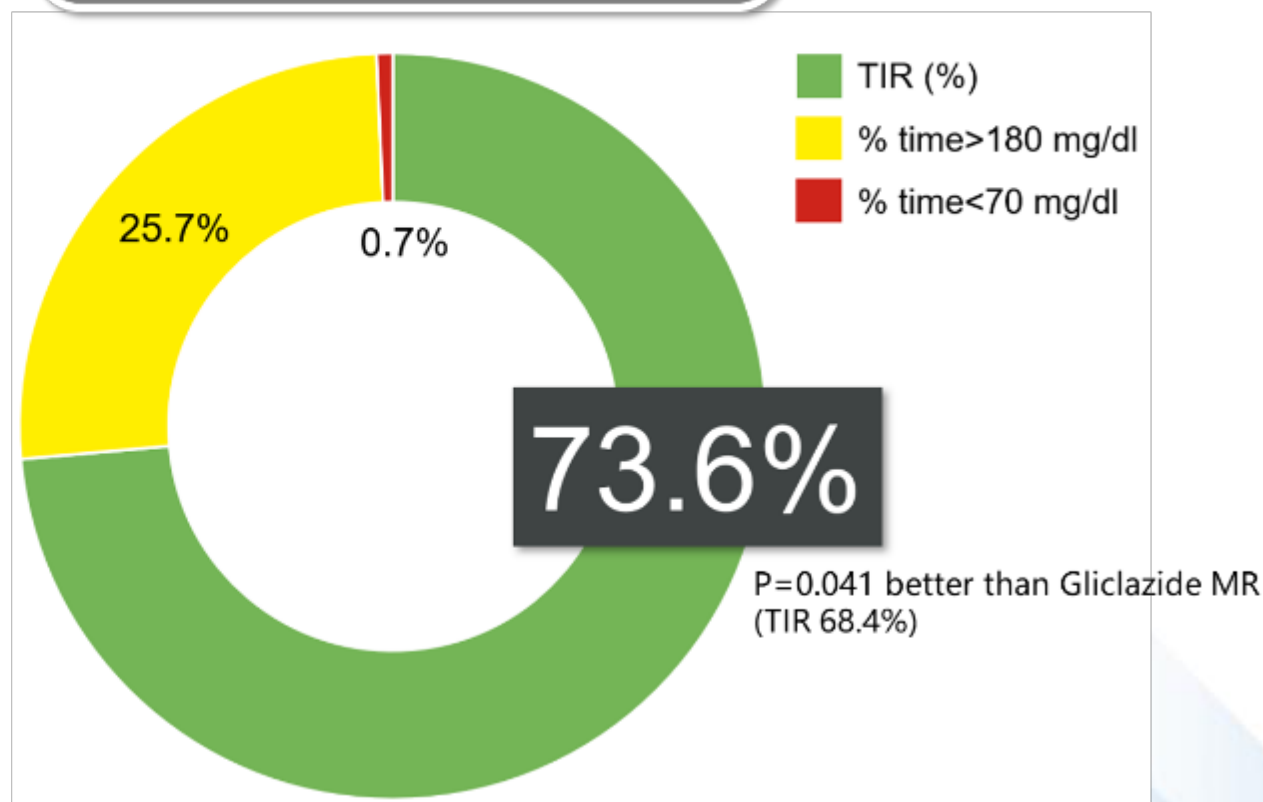


Dapagliflozin控糖效果：幫助T2D病患達到TIR>70%目標

ADA建議TIR目標



使用FORXIGA 12週後TIR表現



*Includes percentage of values >250 mg/dL ** Includes percentage of values <54 mg/dL TIR: time in range (70-180 mg/dL)

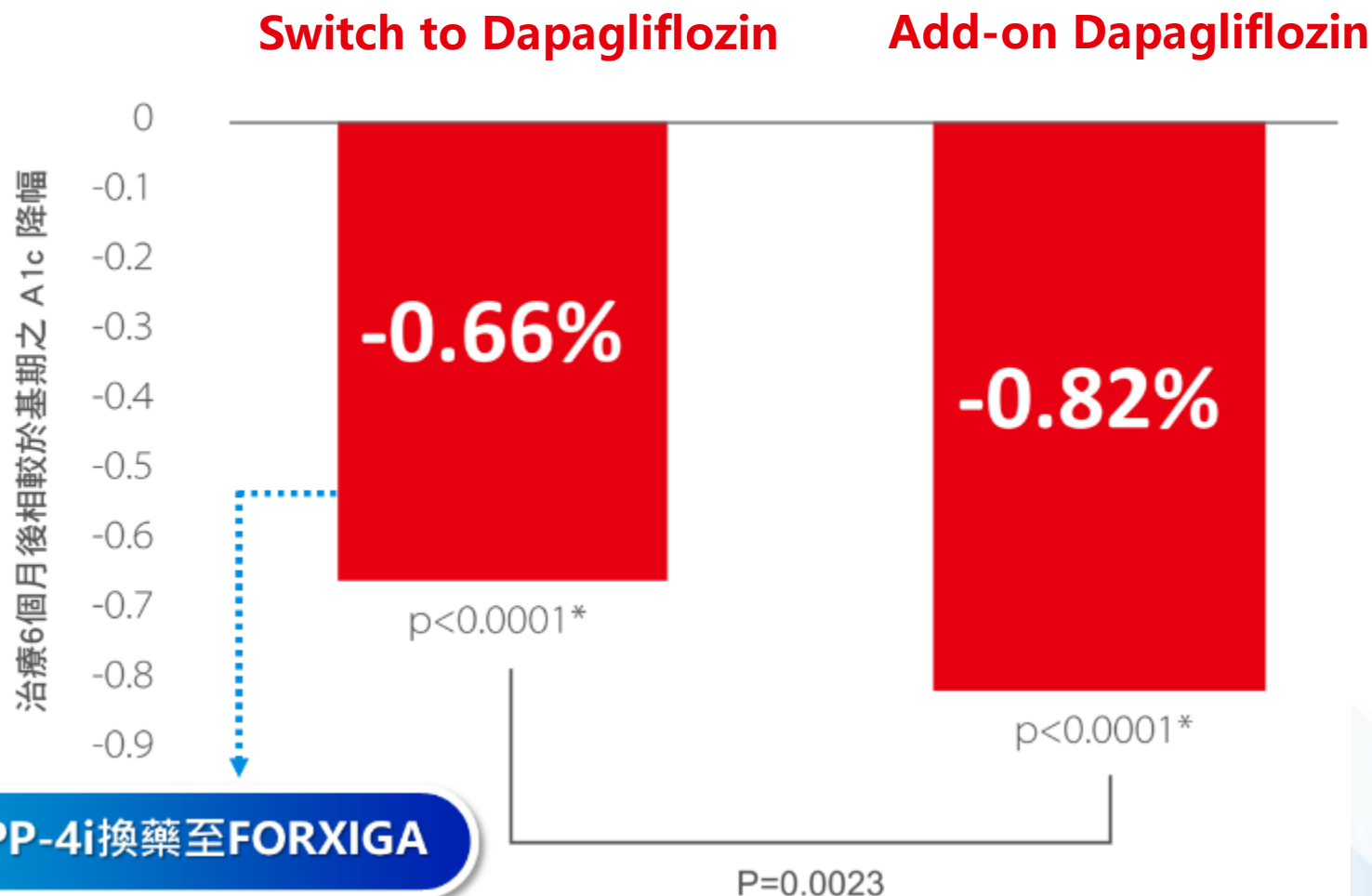
1. Diabetes Care. 2019 Aug;42(8):1593-1603. 2. Diabetes Obes Metab. 2020 Apr;22(4):501-511.



針對血糖控制不佳的患者 台灣研究：添加Dapagliflozin有效降低A1c 0.8%



N=1960
19家醫學中心/醫院
平均A1c 8.8%

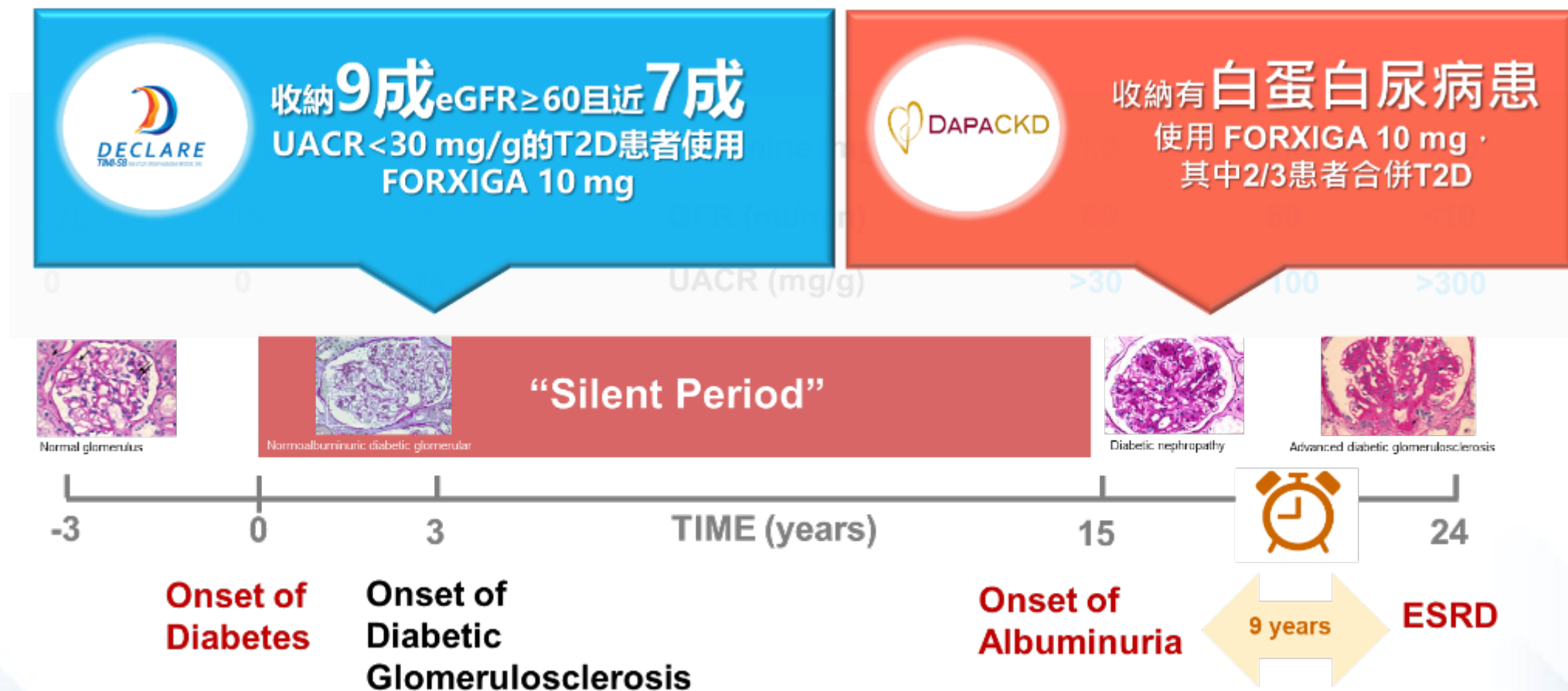


*vs baseline PeerJ 8:e9998 <https://doi.org/10.7717/peerj.9998>

The data is based upon Real World Evidence (RWE) data and is subject to potential confounding bias usually associated with observational research.



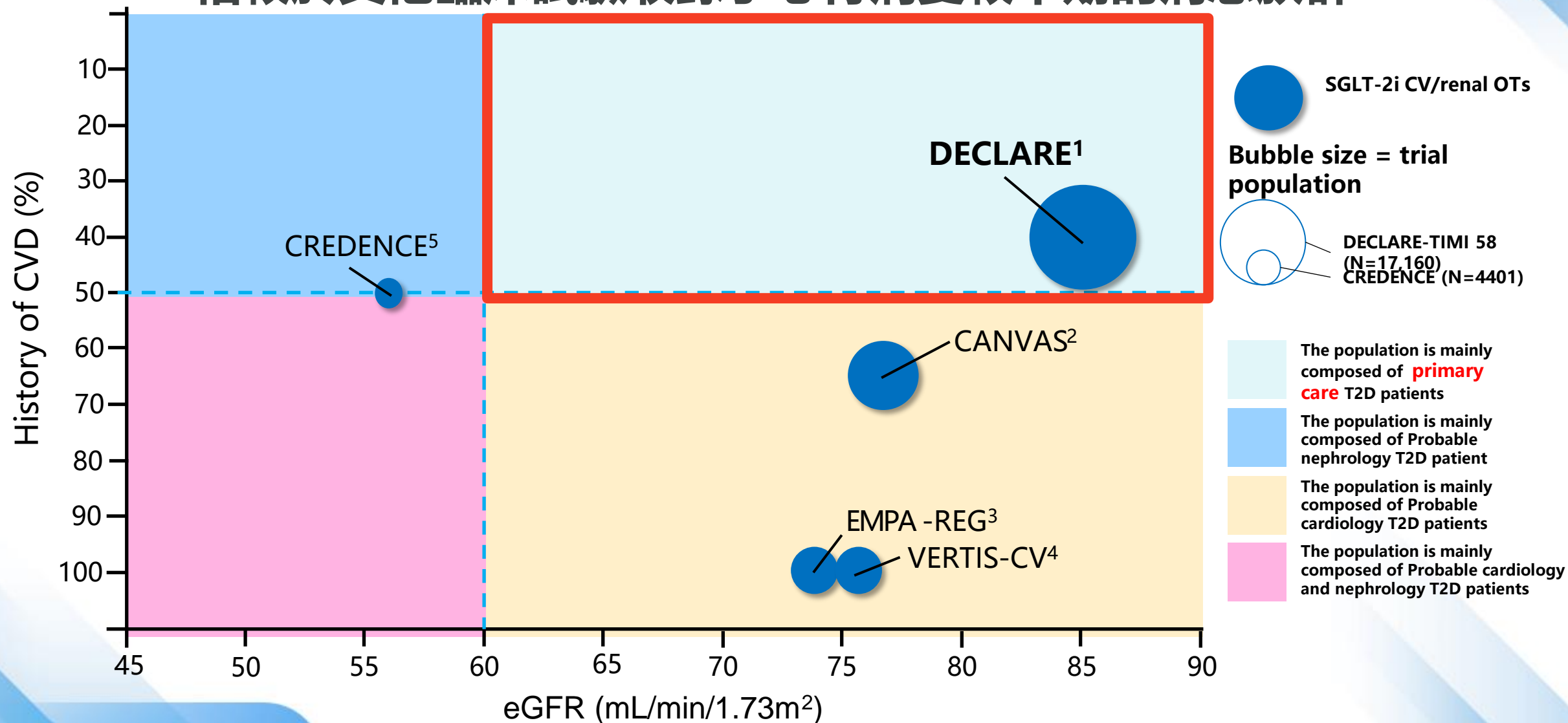
Dapagliflozin提供T2D患者 從預防到治療CKD完整實證





DECLARE

相較於其他臨床試驗收錄了心腎病變較早期的病患族群

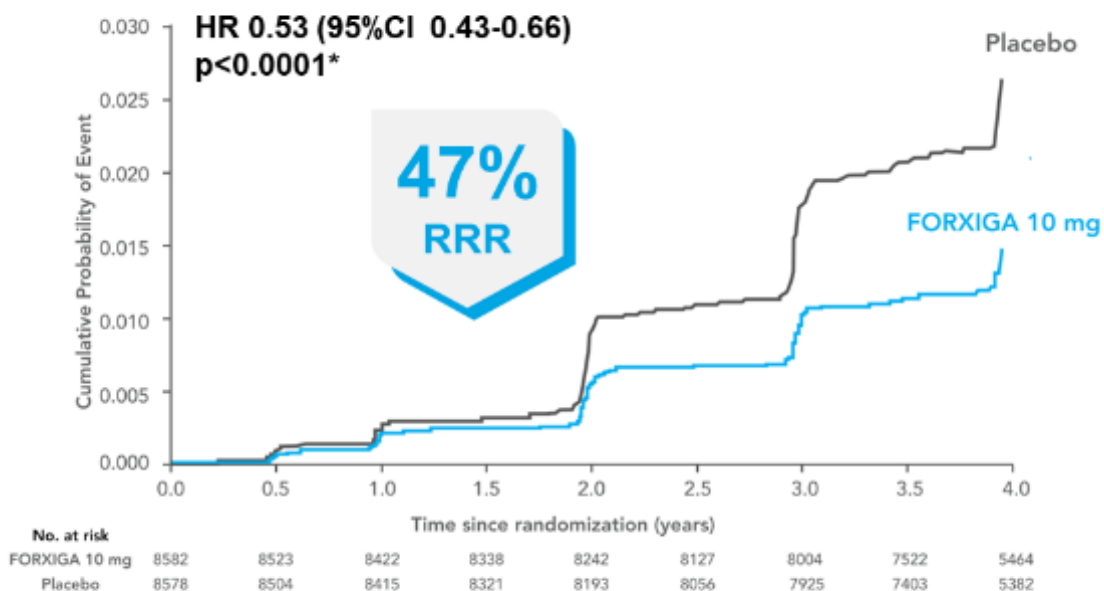




Dapagliflozin有效減少T2D患者 腎功能惡化、ESRD或腎因性死亡風險



Renal composite outcome*



	Dapagliflozin group (N=8574)		Placebo group (N=8569)			Hazard ratio (95% CI)	P value
	n	%	n	%			
腎臟複合終點	127	1.5%	238	2.6%	■	0.53(0.43-0.66)	<0.0001
eGFR減少40%以上 至<60 ml/min/1.73m ²	120	1.4%	221	2.5%	■	0.54(0.43-0.67)	<0.0001
ESRD	6	0.1%	19	0.2%	■	0.31(0.13-0.79)	0.013
ESRD或腎因死亡	11	0.1%	27	0.3%	■	0.41(0.20-0.82)	0.012
AKI	125	1.5%	175	2.0%	■	0.69(0.55-0.87)	0.002

ESRD ↓ 69%

HR 0.31 (0.13-0.79), p=0.013

*Nominally significant, prespecified exploratory outcome; Renal composite outcome: sustained ≥40% eGFR decline to <60 mL/min/1.73 m², ESKD, or renal death

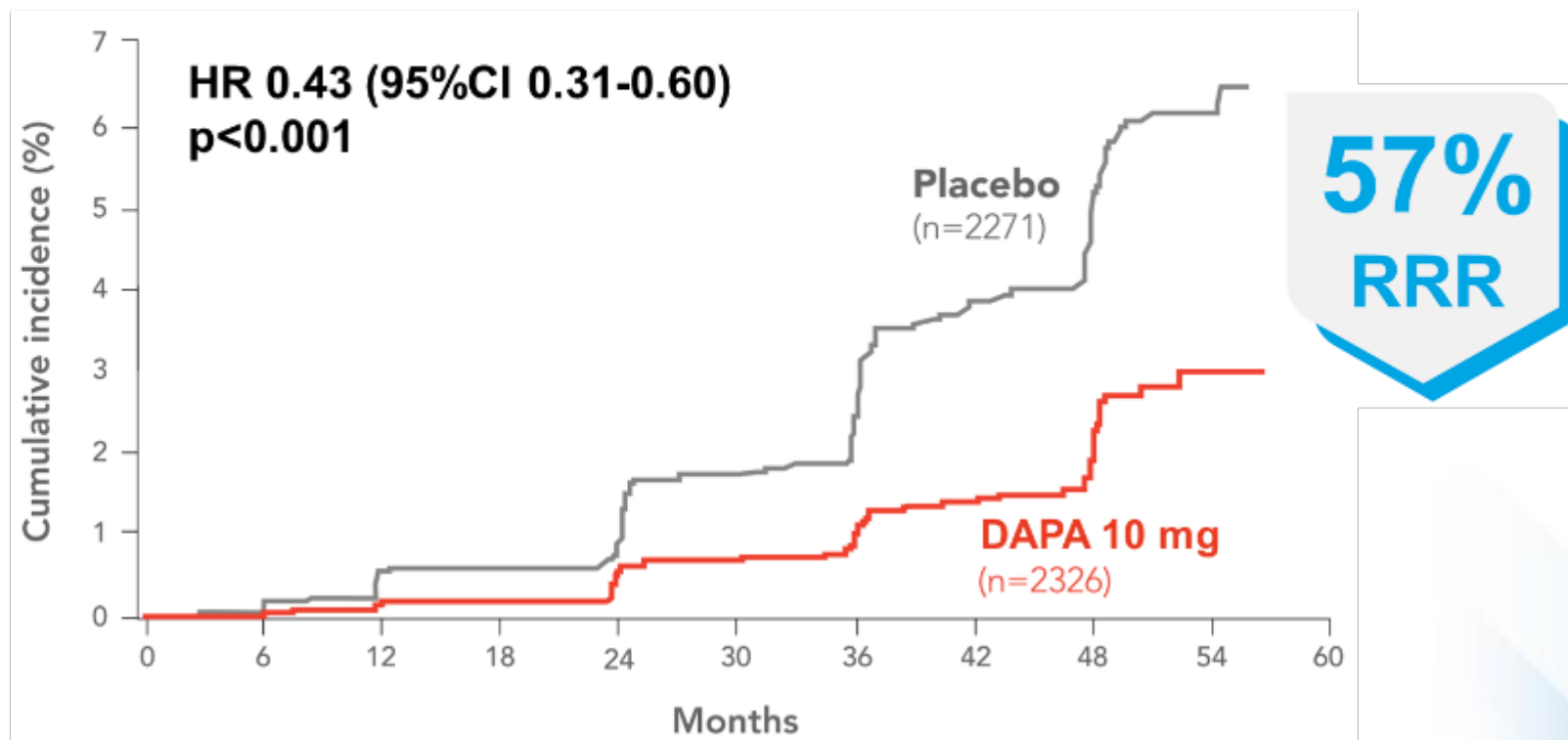
1. N Engl J Med. 2019 Jan 24;380(4):347-357. 2. Lancet Diabetes Endocrinol. 2019 Aug;7(8):606-617. 3. Diabetes Obes Metab. 2020 Aug;22(8):1357-1368.



Dapagliflozin 針對 T2D 合併 $eGFR \geq 60$ 但有微量白蛋白尿 顯著減少腎功能惡化、ESRD、腎因性死亡風險



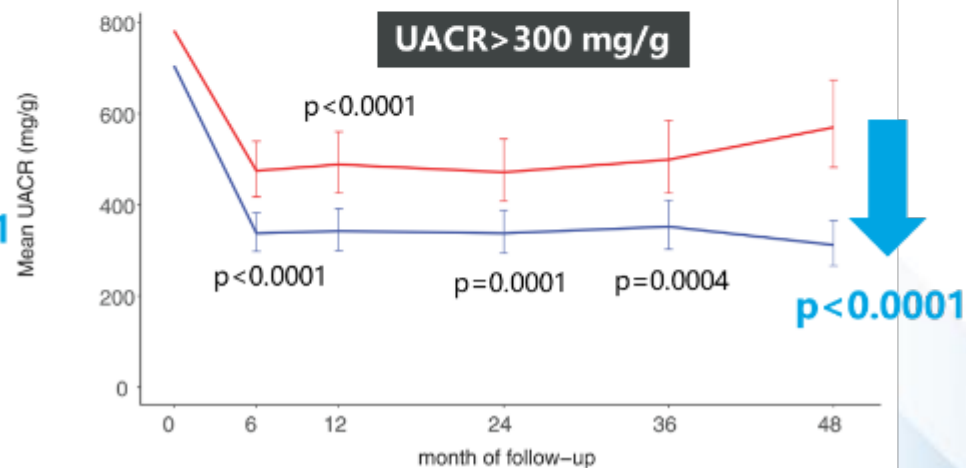
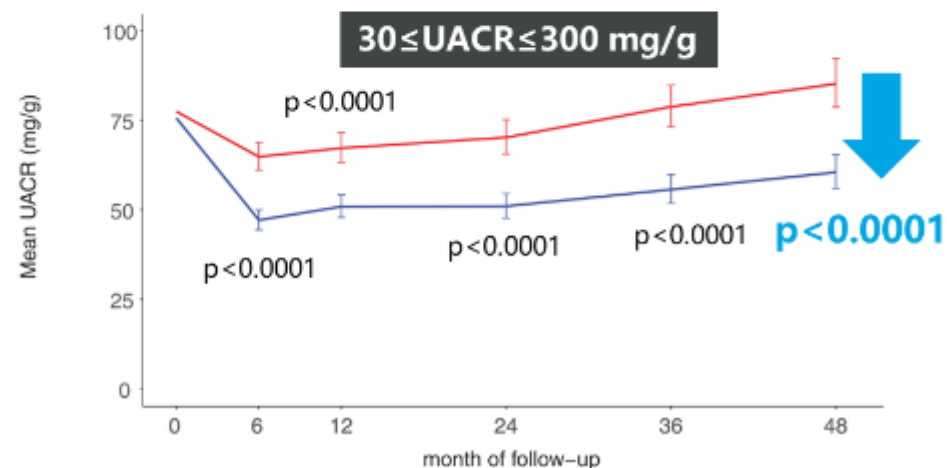
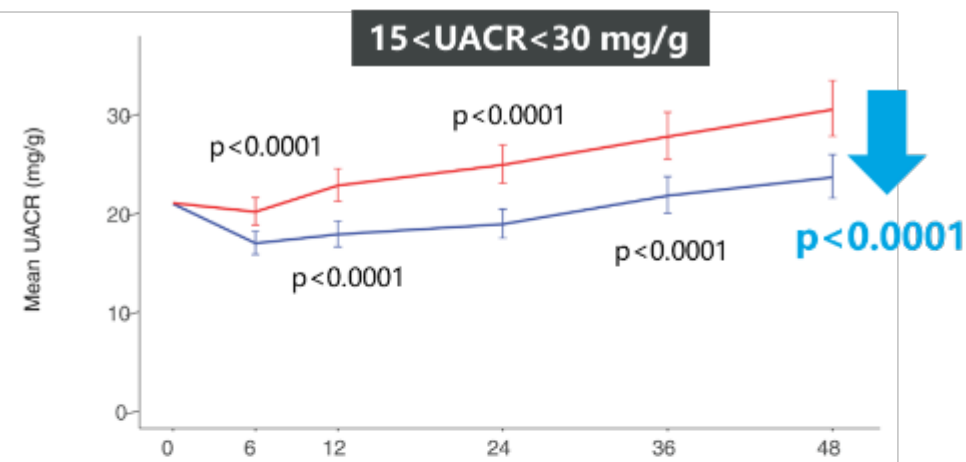
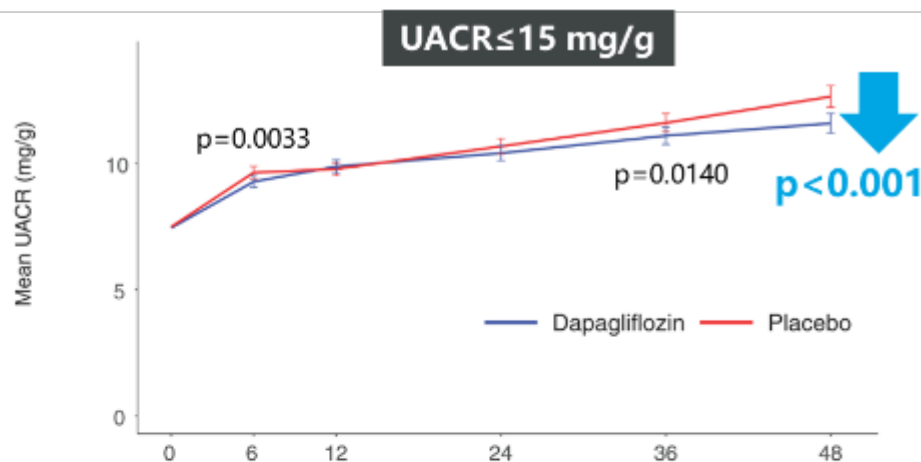
DECLARE post hoc analysis: 3-point renal composite in a subgroup of 4597 patients with $eGFR > 60$ mL/min/1.73 m² and UACR ≥ 30 mg/g



Composite renal-specific outcome: sustained $\geq 40\%$ eGFR decline to < 60 mL/min/1.73 m², ESKD, or renal death
Data on file, REF-107851, AstraZeneca Pharmaceuticals LP.

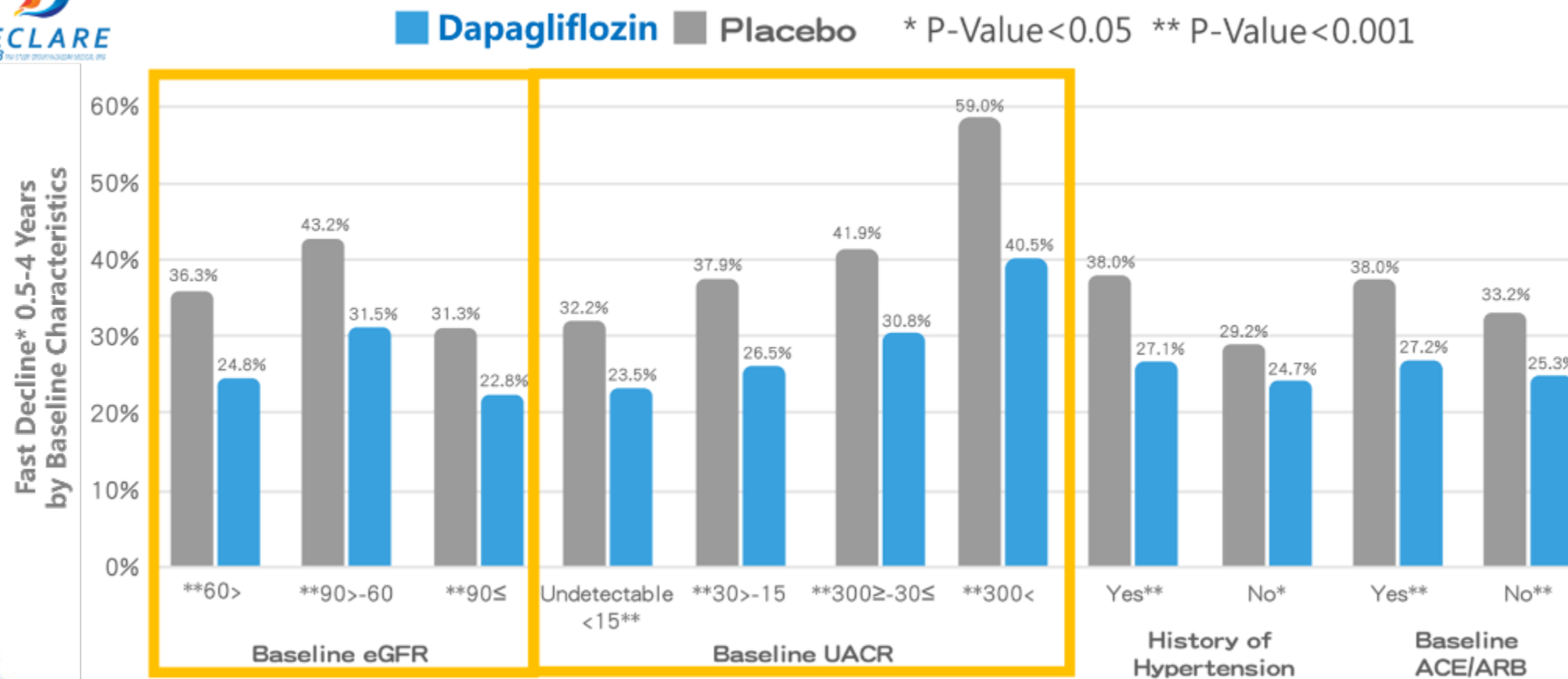


Dapagliflozin治療T2D減少UACR，無論白蛋白尿分級





無論 Baseline eGFR、UACR， Dapagliflozin組別eGFR快速下降的比率顯著低於安慰劑組

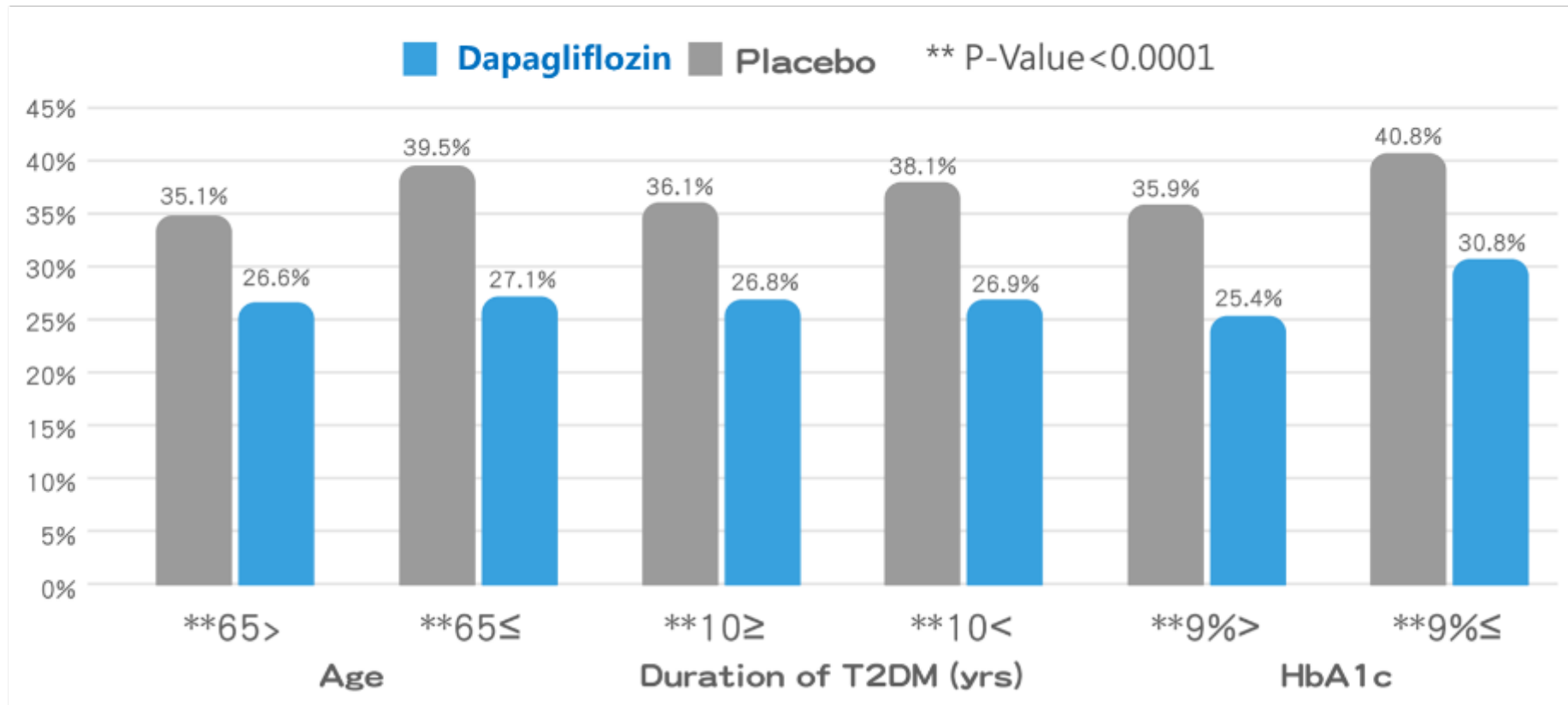


*Fast decline (FD) in eGFR can be defined as a reduction of ≥ 3 ml/min/1.73m²/year and is associated with poor long-term renal prognosis.

無論年齡、診斷時間、HbA1c, Dapagliflozin組別eGFR快速下降的比率顯著低於安慰劑組

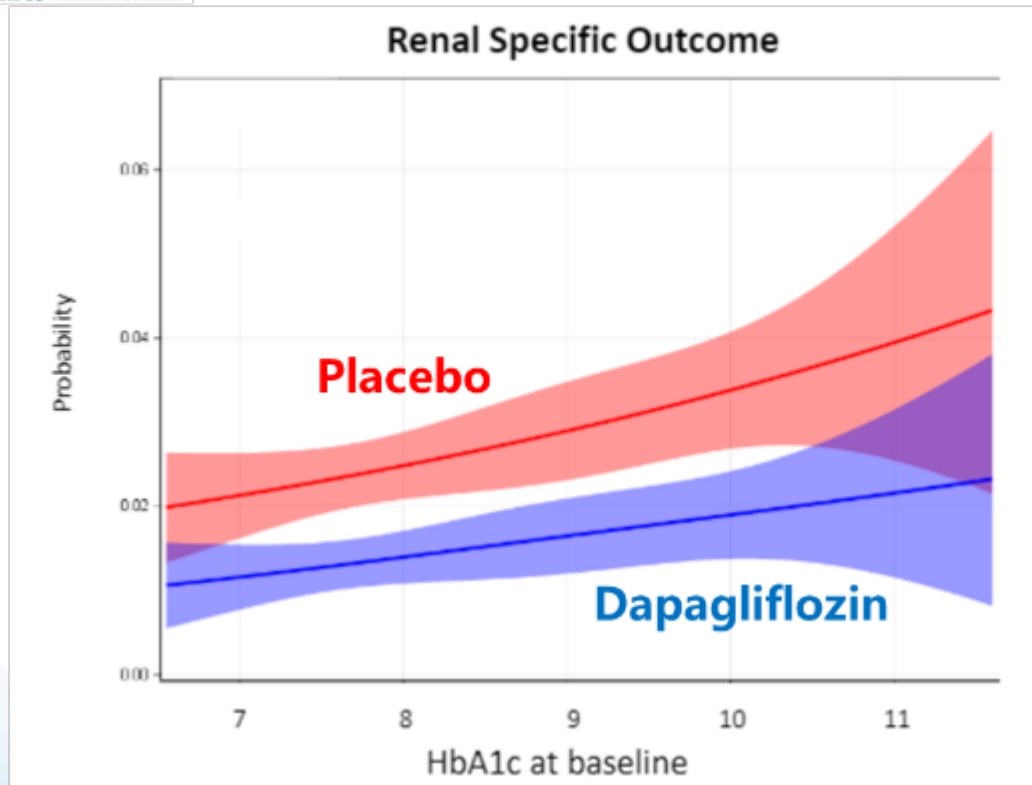


Fast Decline* 0.5-4 Years
by Baseline Characteristics



*Fast decline (FD) in eGFR can be defined as a reduction of ≥ 3 ml/min/1.73m²/year and is associated with poor long-term renal prognosis.

DECLARE次分析: T2D患者無論血糖高低 Dapagliflozin一致有效降低腎臟惡化事件風險



The renal specific outcome included a sustained decrease of 40% or more in eGFR to <60 mL/min/1.73 m², end-stage renal disease, or death from renal cause

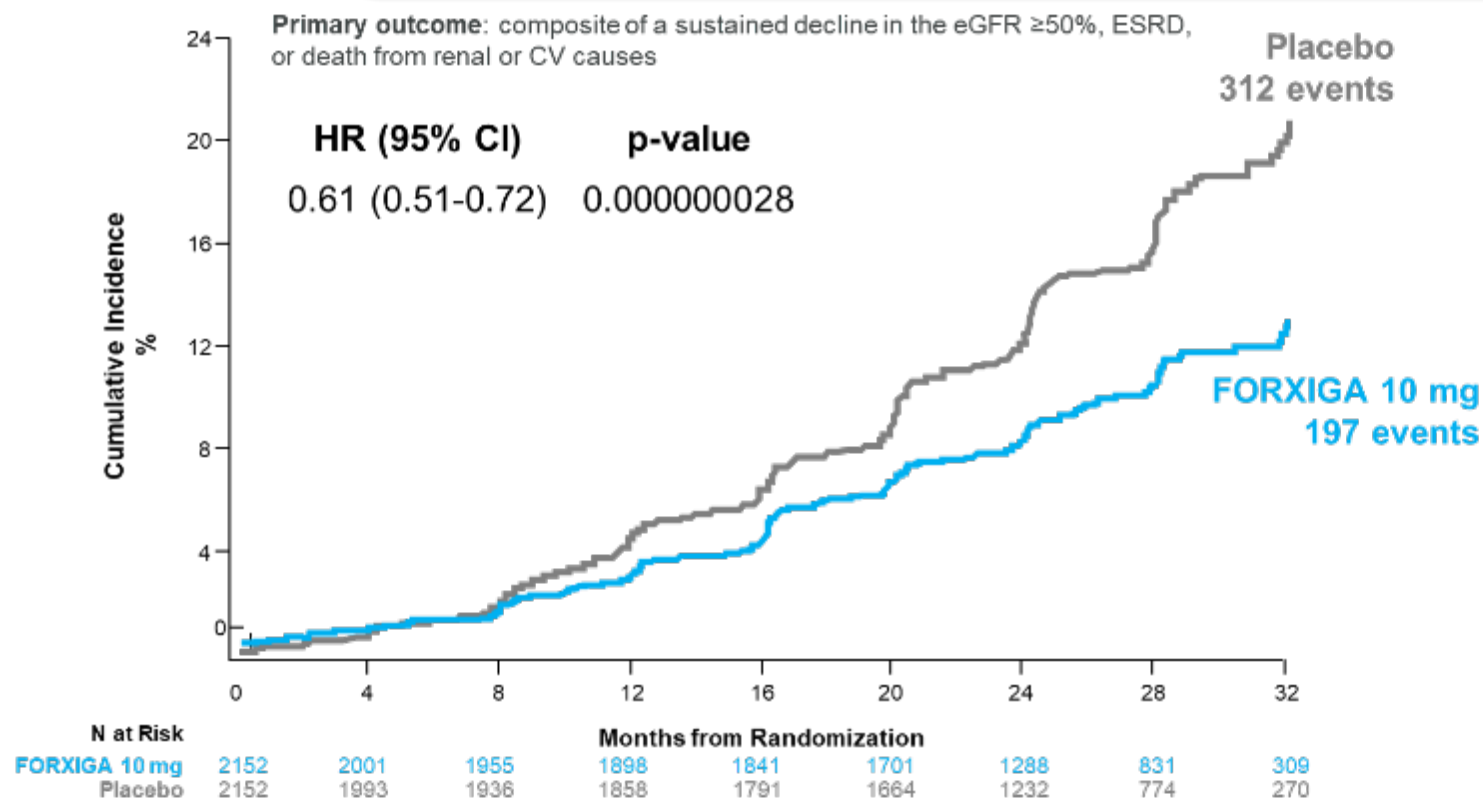
	Dapagliflozin (%)	Placebo (%)		Hazard Ratio	Interaction p-value
Renal-specific outcome					
Overall	1.5%	2.8%		0.53 (0.43-0.66)	
<7%	1.2%	2.7%		0.42 (0.19-0.91)	0.2596
7-<8%	1.1%	2.5%		0.45 (0.31-0.66)	
8-<9%	1.9%	2.5%		0.73 (0.49-1.09)	
≥9%	1.7%	3.5%		0.48 (0.32-0.70)	



Dapagliflozin治療CKD延緩腎臟惡化



顯著減少腎功能惡化、ESRD、心血管或腎因性死亡

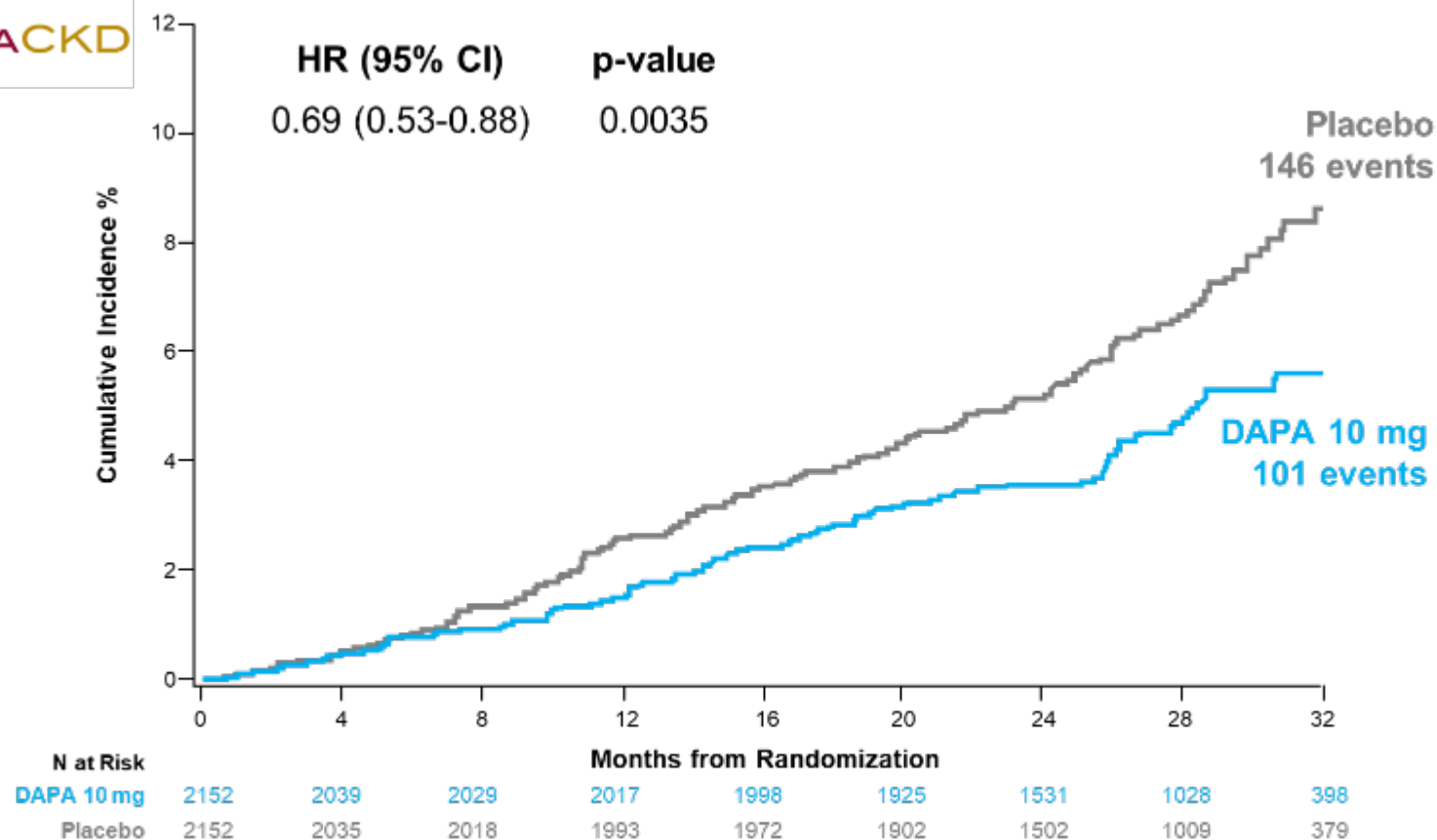


39%
RRR

ESRD ↓ 36%
HR 0.64 (0.50-0.82),
p=0.0004



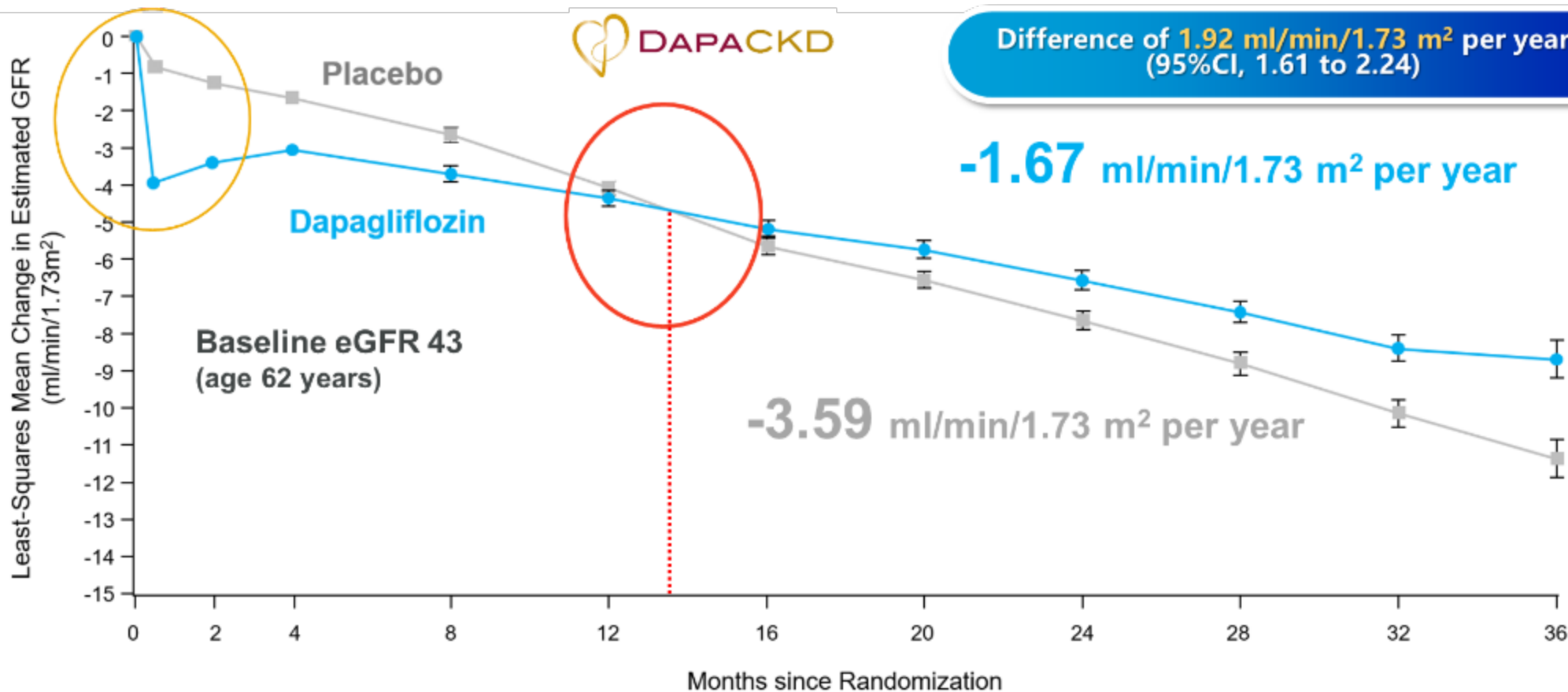
Dapagliflozin治療CKD顯著降低總死亡風險



31%
RRR



Dapagliflozin治療CKD減緩eGFR下降速度54%

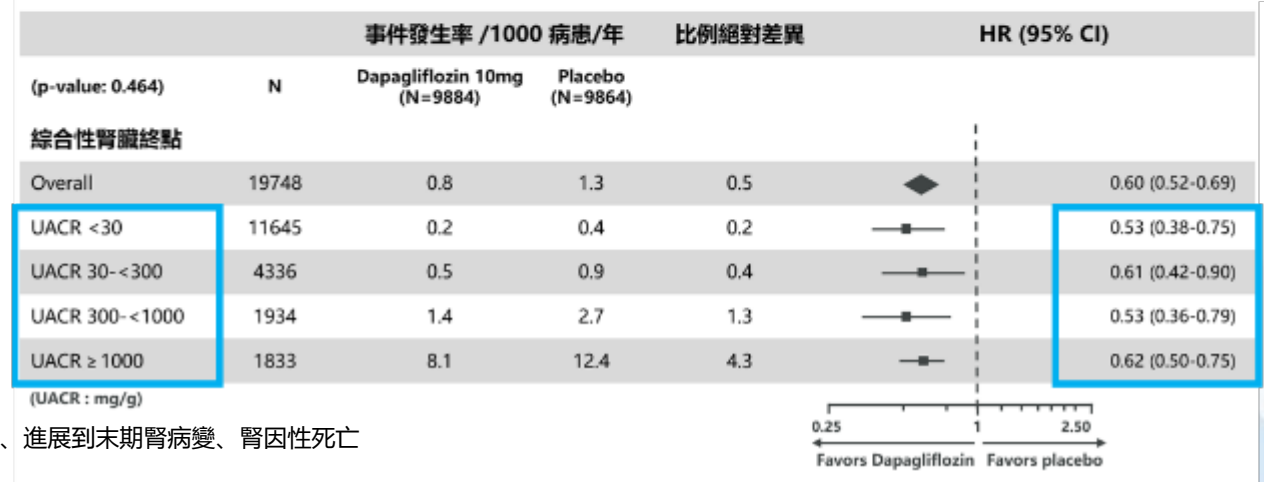
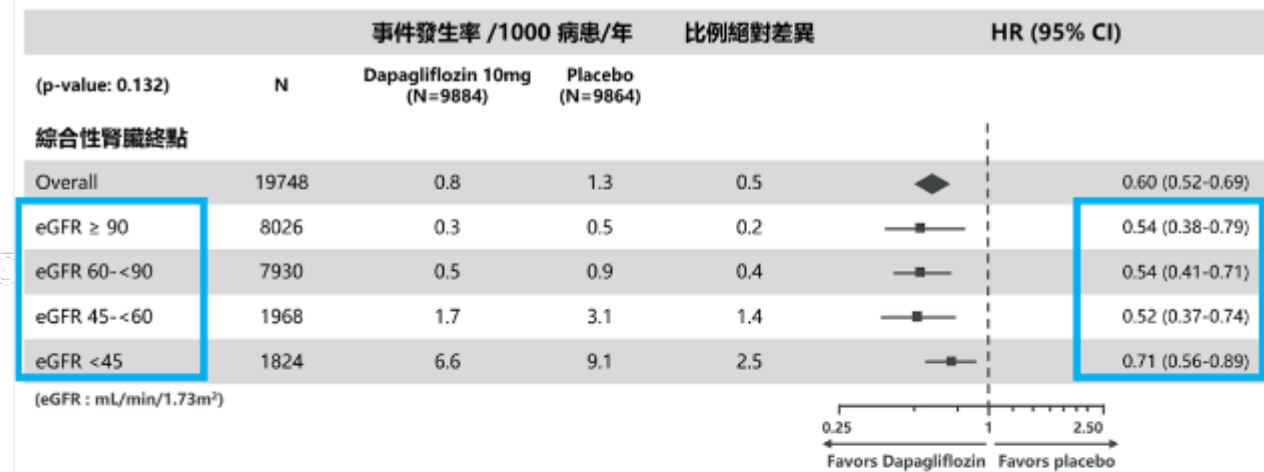


DAPA-CKD & DECLARE pooled analysis: Dapagliflozin減少腎臟惡化無差別eGFR及蛋白尿高低



eGFR ml/min/1.73m ²	DECLARE N	DAPA-CKD N	Total N (%)
<45	184	1640	1824 (9)
45-<60	1050	918	1968 (10)
60-<90	7582	348	7930 (40)
≥90	8026	0	8026 (41)

UACR mg/g	DECLARE N	DAPA-CKD N	Total N (%)
<30	11644	1	11645 (59)
30-<300	4029	307	4336 (22)
300-<1000	809	1125	1934 (10)
≥1000	360	1473	1833 (9)



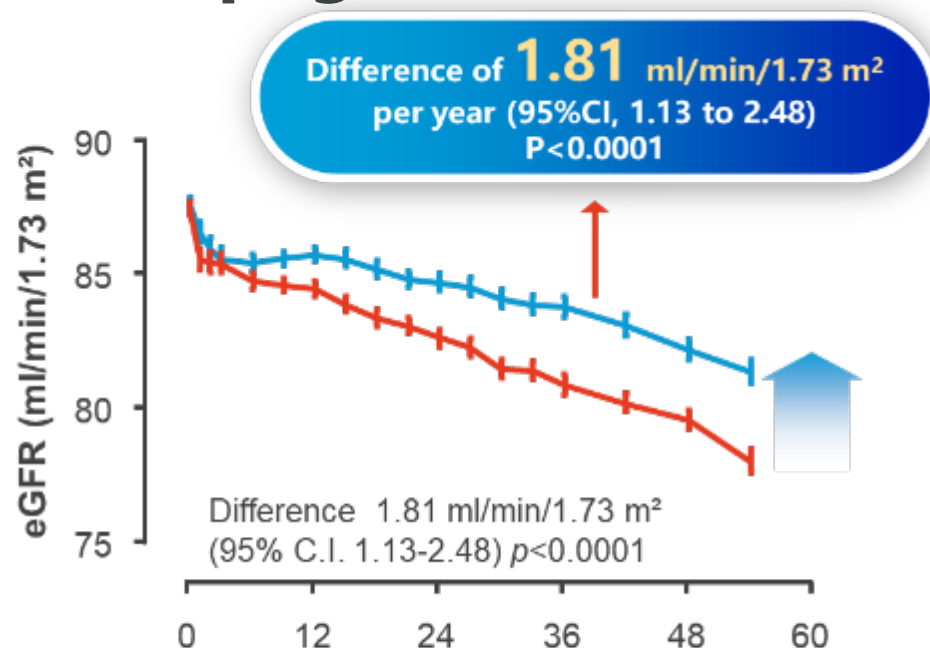
腎臟終點為 eGFR 持續減少 ≥ 40%、進展到末期腎病變、腎因性死亡

1. Moura F, et al. Presented at: ESC Congress 2022; August 26-29, 2022; Barcelona, Spain. 2.

https://academic.oup.com/eurheartj/article/43/Supplement_2/ehac544.2407/6745929?login=false



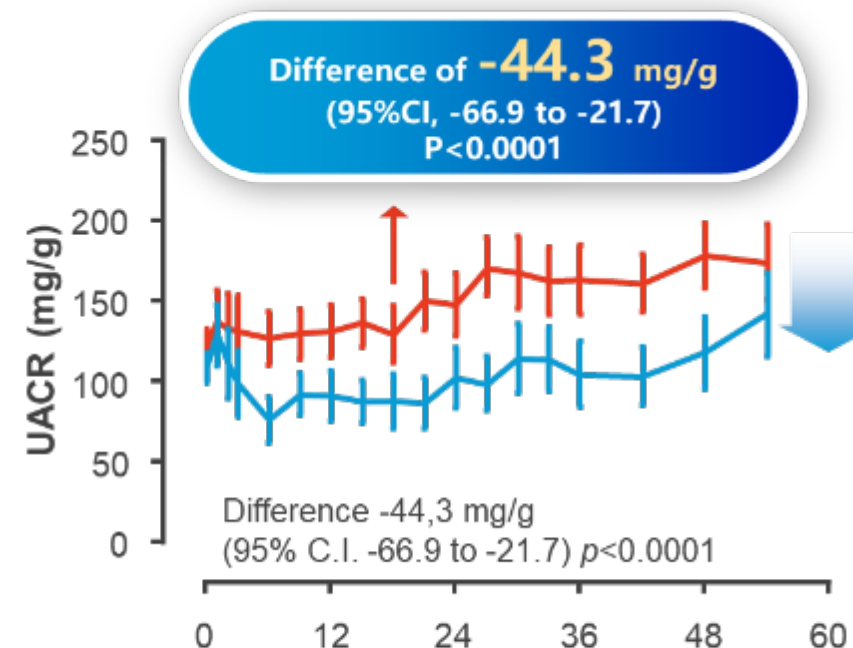
針對腎功能相對良好的T2D族群⁺，真實世界研究顯示： Dapagliflozin觀察到延緩eGFR下降與降低蛋白尿



No. of patients		Months after index date				
FORXIGA	4547	1988	1418	919	1058	699*
Comparators	4241	1997	1530	1197	1486	1139*

*54 months

— FORXIGA — Comparators



No. of patients		Months after index date				
FORXIGA	2660	695	467	358	382	264*
Comparators	2577	739	520	400	545	437*

*54 months

— FORXIGA — Comparators

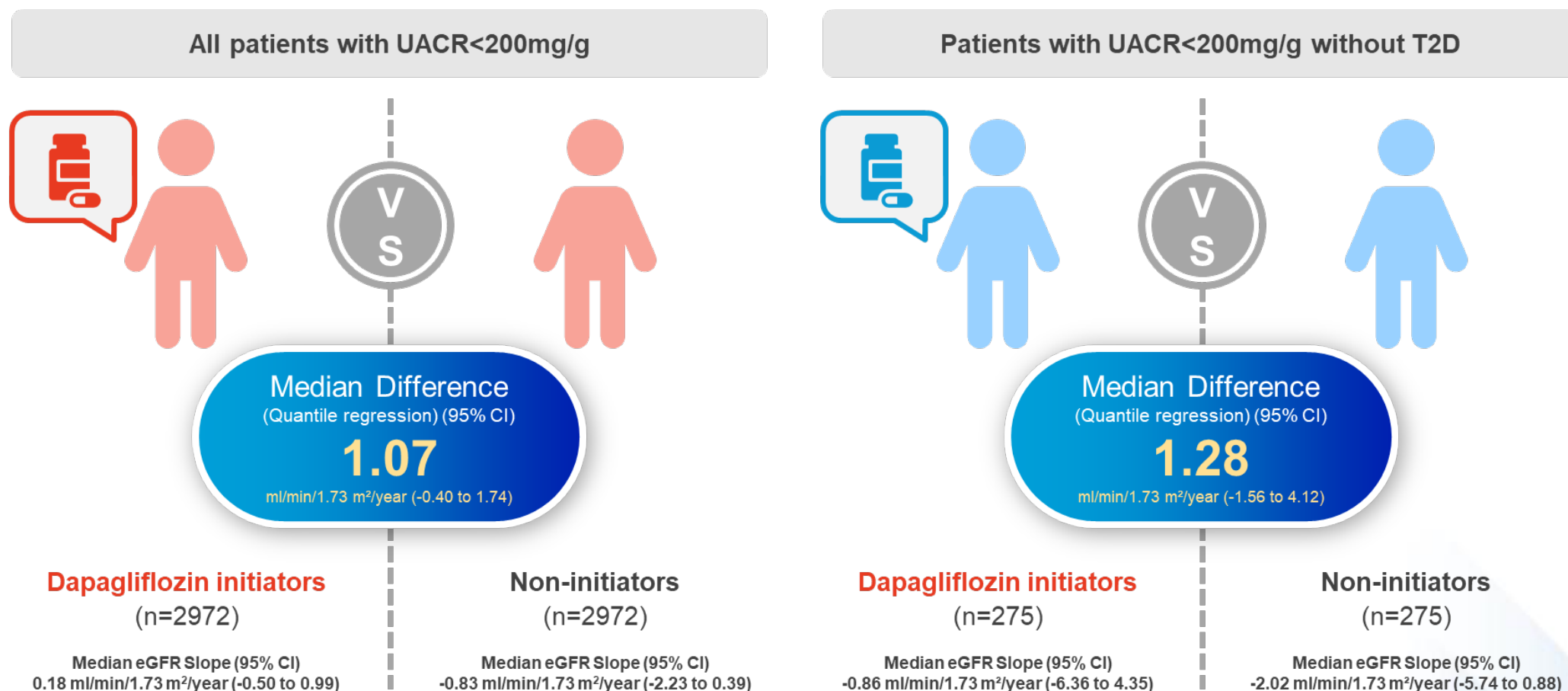
⁺此試驗納入族群，超過 93% 患者之 eGFR ≥60 ml/min/1.73 m²，85% 患者之 UACR ≤30 mg/g.

The Lancet Regional Health – Europe 2024;38: 100847 Published Online 1 February 2024

<https://doi.org/10.1016/j.lanepe.2024.100847>



最新RWE研究:不論有無T2D Dapagliflozin 針對UACR<200mg/g族群皆觀察到可延緩eGFR下降



Tangri, N., Rastogi, A., Nekeman-Nan, C. et al. Dapagliflozin Utilization in Chronic Kidney Disease and Its Real-World Effectiveness Among Patients with Lower Levels of Albuminuria in the USA and Japan. *Adv Ther* (2024). <https://doi.org/10.1007/s12325-023-02773-x>

Claims data from the USA and Japan were used to describe patients with CKD and UACR < 200 mg/g who were eligible for dapagliflozin 10 mg treatment (initiators and untreated) following its approval for CKD. A quantile regression analysis was performed to evaluate the effect of dapagliflozin 10 mg initiation versus no initiation on estimated glomerular filtration rate (eGFR) slope in a propensity score-matched cohort, using a prevalent new-user design



總結

- 糖尿病與心腎病變風險:糖尿病合併高血壓、蛋白尿會增加ESRD、心衰竭風險外，更增加死亡風險，隨著糖尿病患腎功能進程，CV風險隨腎功能惡化上升，早期治療是關鍵
- 最新國內外糖尿病照護指引建議: T2D治療需控糖與心腎保護，建議首選具有心腎實證的SGLT2i
- **Dapagliflozin 提供T2D患者從預防到治療CKD完整實證**
 - 針對T2D患者的早期護腎實證，從DECLARE Study到2024最新真實世界研究均顯示，Dapagliflozin使用在**腎功能相對較好的T2D患者族群**，觀察到能**保護腎臟，延緩eGFR下降，降低蛋白尿**
 - SGLT2i用於低蛋白尿族群，仍有腎臟保護療效， DECLARE與DAPA-CKD合併研究顯示，Dapagliflozin減少腎臟惡化無差別eGFR及蛋白尿高低，最新RWE研究也指出，不論有無T2D，**Dapagliflozin針對UACR<200mg/g族群皆觀察到可延緩eGFR下降**

Thanks for listening !

