



# 心腎共病的治療策略 及指引更新

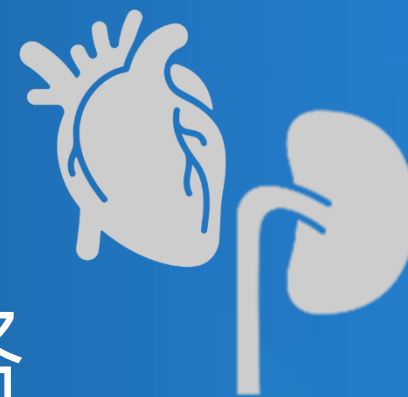
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# 大綱

- 心腎共病的臨床挑戰及治療策略
- 心腎共病治療的臨床實證及指引更新
- 總結



# 心腎共病的臨床挑戰及治療策略

# AHA: Cardiovascular-Kidney-Metabolic (CKM) Syndrome



## Circulation

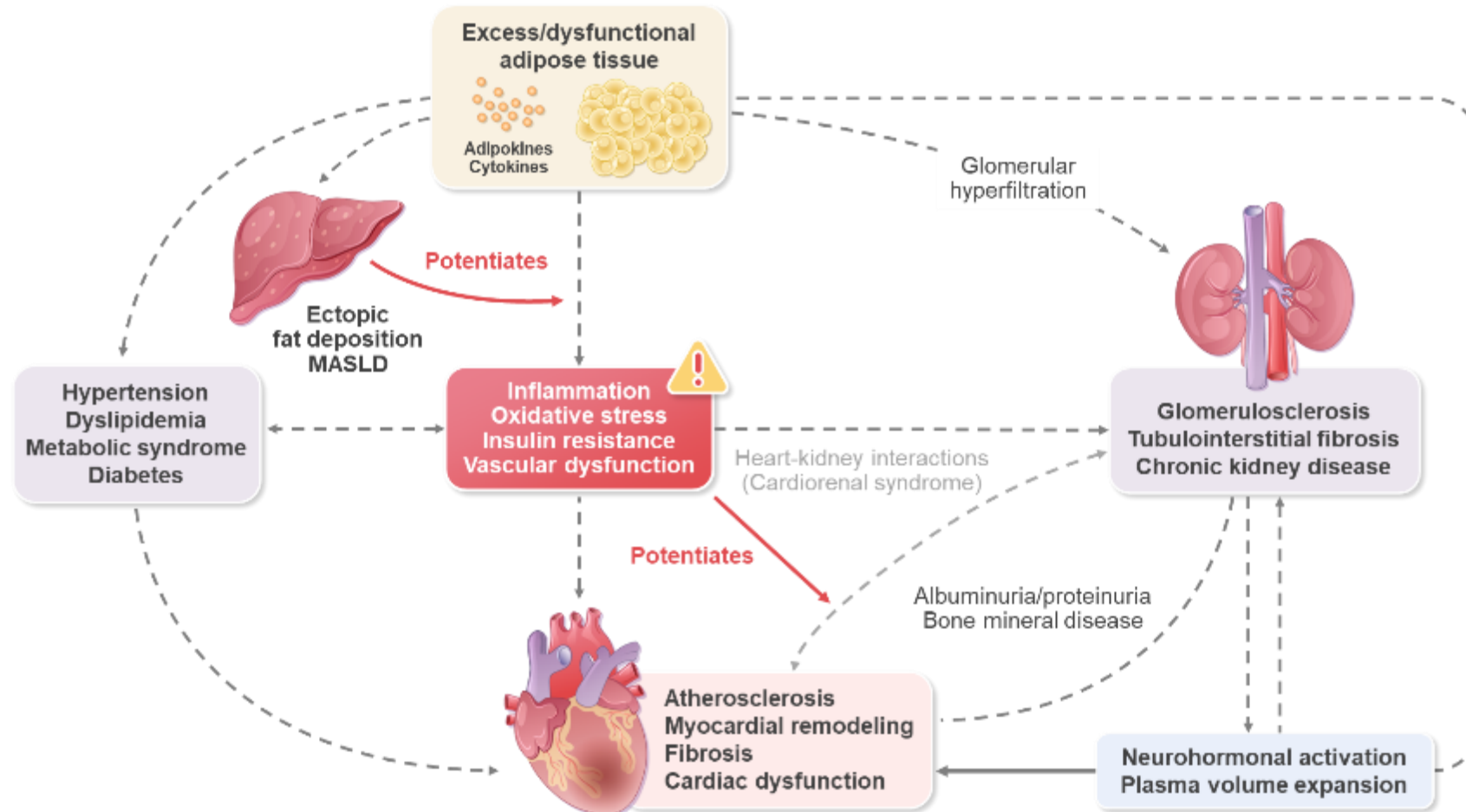
### **A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association**

Chiadi E. Ndumele, Ian J. Neeland, Katherine R. Tuttle, Sheryl L. Chow, Roy O. Mathew, Sadiya S. Khan, Josef Coresh, Carissa M. Baker-Smith, Mercedes R. Carnethon, Jean-Pierre Després, ... **See all authors** ✓

Originally published 9 Oct 2023 | <https://doi.org/10.1161/CIR.0000000000001186> | Circulation. 2023;148:1636–1664

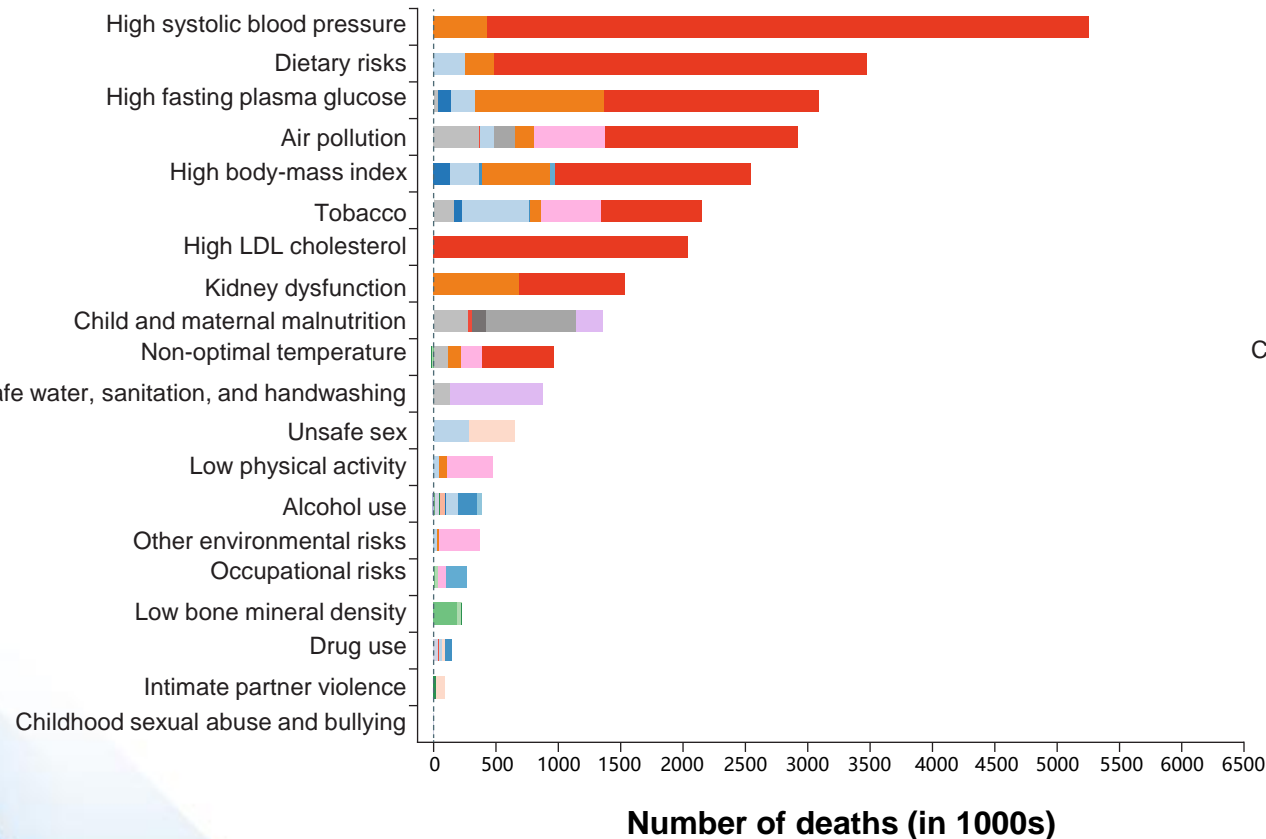
# Cardiovascular-Kidney-Metabolic (CKM) Syndrome

## 心、腎、代謝交互作用

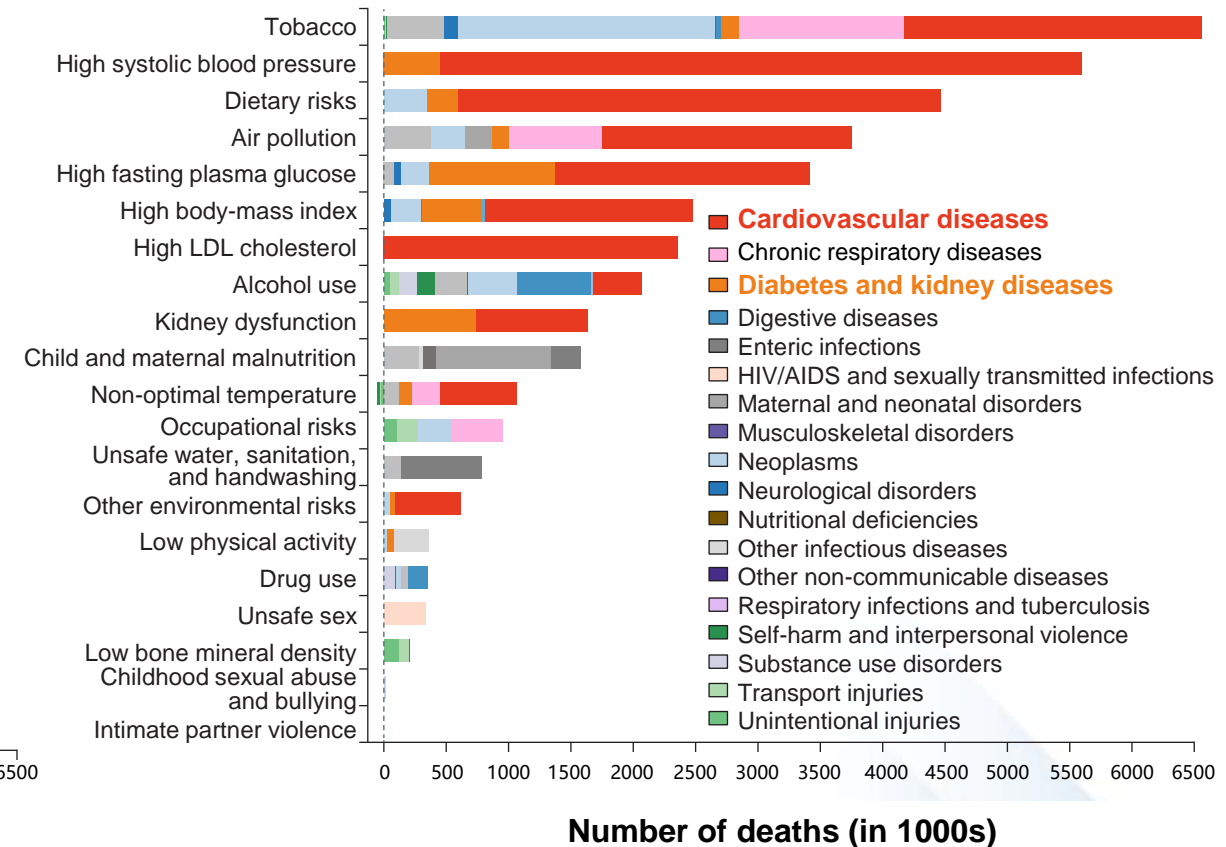


# 全球20大致死風險因素所對應死因：心腎病變死亡佔最大宗

**A Global attributable deaths from Level 2 risk factors for females in 2019**



**B Global attributable deaths from Level 2 risk factors for males in 2019**

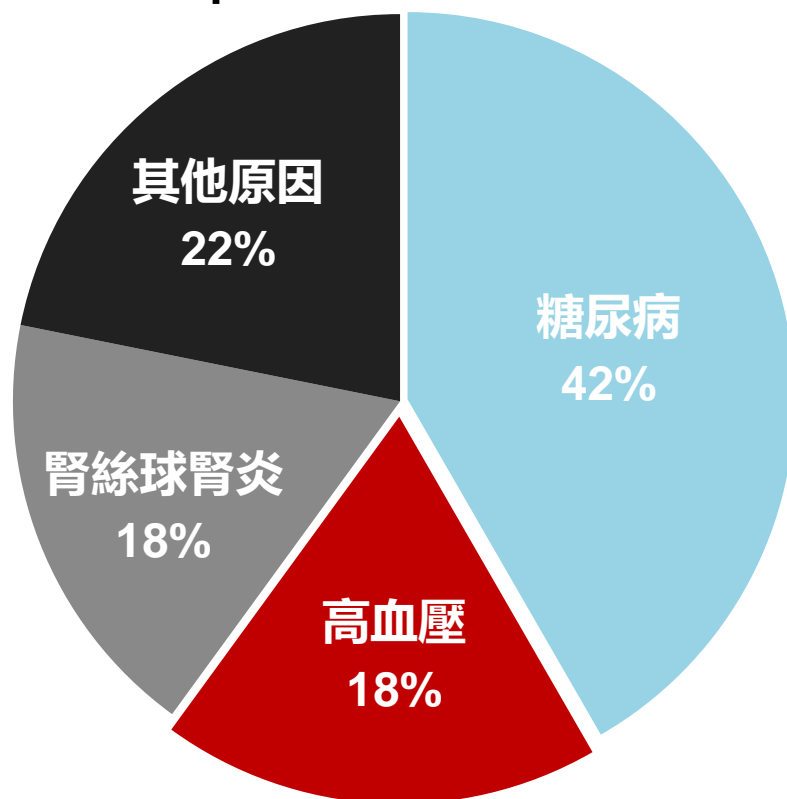




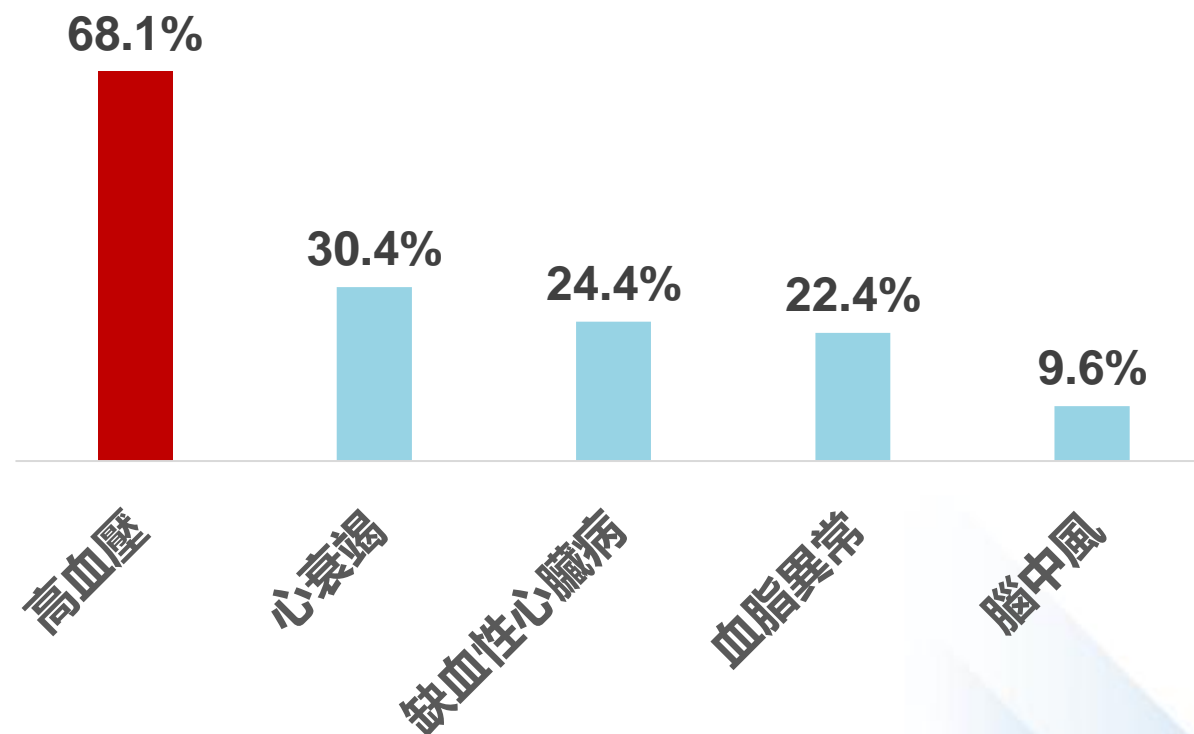


## 糖尿病、高血壓為末期腎臟病風險主要風險

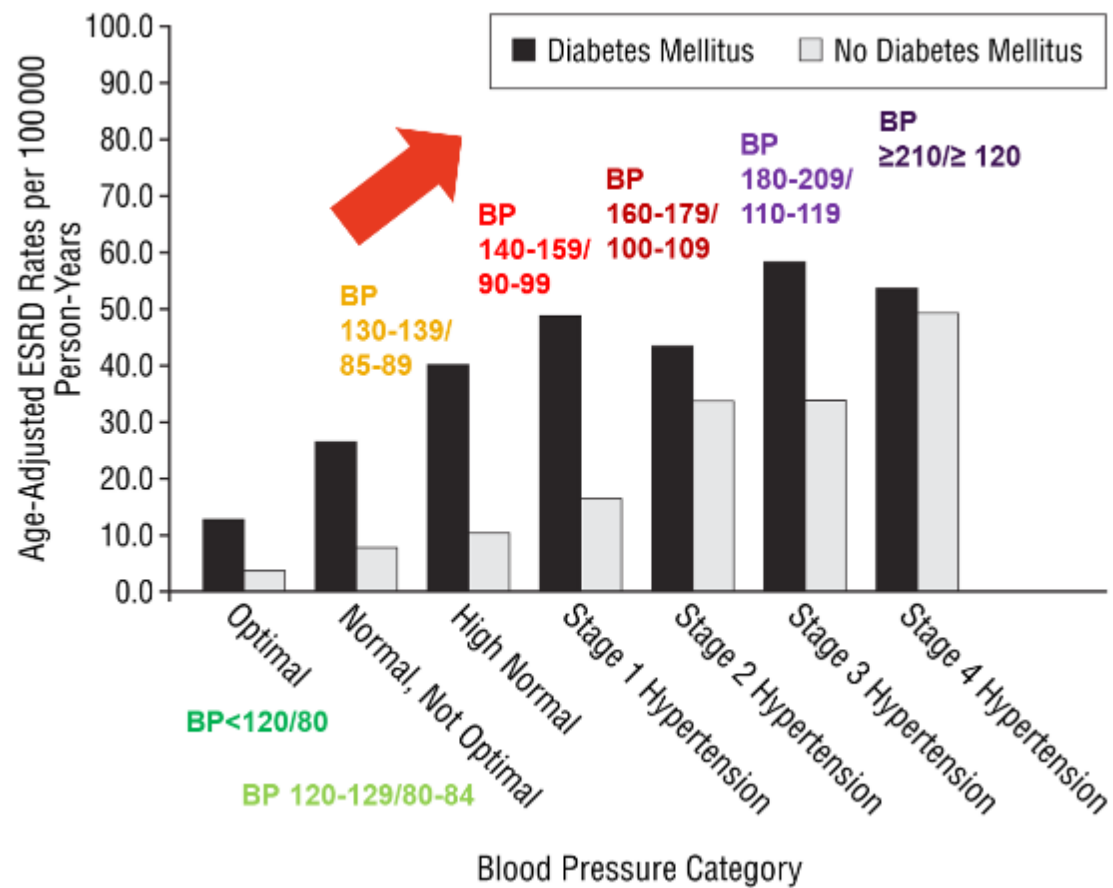
Age-standardized global prevalence rate of CKD by cause per 100,000 persons in 2016<sup>1</sup>



2021 台灣腎病年報伴隨相關共病情況



# Rate for ESRD by BP and DM







## 糖尿病與高血壓皆為HF高風險族群

### ACC/AHA心衰竭分級

#### Stage D: Advanced HF

Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT.

#### Stage C: Symptomatic HF

Structural heart disease with current or previous symptoms of HF.

#### Stage B: Pre-HF

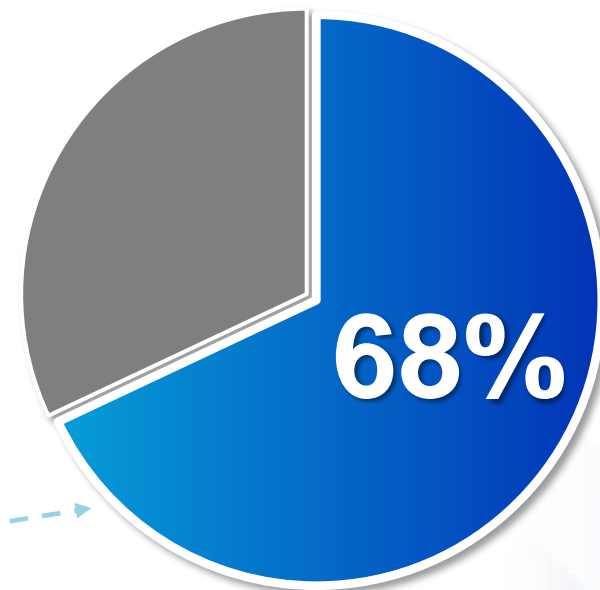
Structural heart disease, Evidence for increased filling pressures, patients with risk factors and Increased levels of B-type natriuretic peptides\* or persistently elevated cardiac troponin

#### Stage A: At Risk for HF

hypertension, ASCVD, diabetes, metabolic syndrome and obesity, exposure to cardiotoxic agents, genetic variant for cardiomyopathy, or positive family history of cardiomyopathy

糖尿病與高血壓

**68%** 無心臟病史的糖尿病患  
潛在左心室功能不全



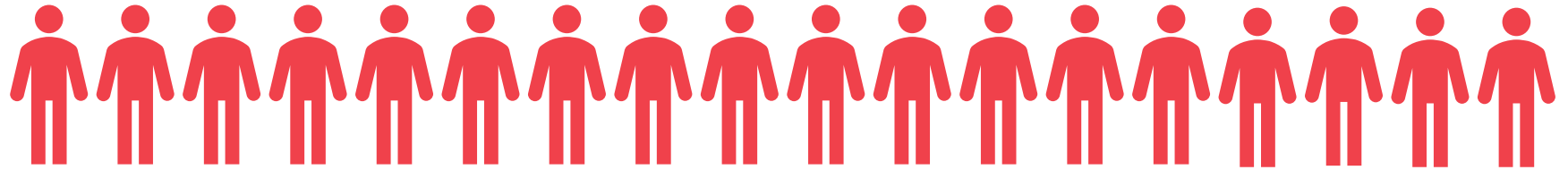
68% of T2D patients (n=386) without cardiac disease had **LV dysfunction** ~5 years after T2D diagnosis<sup>3</sup>

# Presence of CKD is commonly associated with the development of fatal CV comorbidities

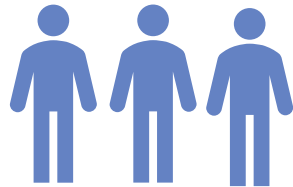
Older patients\* with CKD are 6 times more likely to die of CV disease than to advance to ESKD and dialysis†



Deaths due to  
CV disease



Progression to  
ESKD/RRT

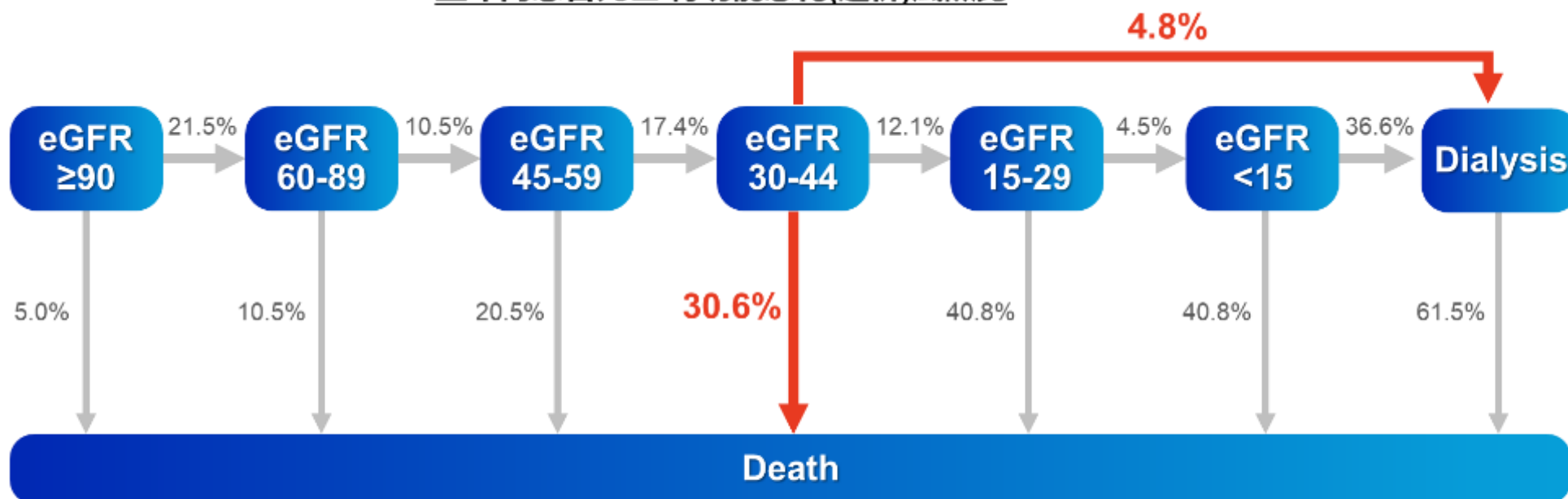


\*≥65 years of age; †During 9.7 years of median follow-up  
RRT, renal replacement therapy  
Dalrymple L *et al.* *J Gen Intern Med* 2011;26:379



針對台灣eGFR<60 T2D患者  
無論eGFR 分級，死亡風險皆遠高於洗腎風險

五年內患者死亡/腎功能惡化(透析)風險比



Stage 3B CKD患者  
死亡風險較透析發生高



# KDIGO 慢性腎臟病指引： CKD患者CV死亡風險隨疾病進程增加

Relative risk of **CV mortality**  
according to eGFR and ACR<sup>a</sup>

		UACR (mg/g)			
		<10	10–29	30–299	≥300
GFR categories (mL/min/1.73 m <sup>2</sup> ) description and range	>105	0.9	1.3	2.3	2.1
	90–105	Ref	1.5	1.7	3.7
	75–90	1.0	1.3	1.6	3.7
	60–75	1.1	1.4	2.0	4.1
	45–60	1.5	2.2	2.8	4.3
	30–45	2.2	2.7	3.4	5.2
	15–30	14	7.9	4.8	8.1

Relative risk of **all-cause mortality**  
according to eGFR and ACR<sup>a</sup>

		UACR (mg/g)			
		<10	10–29	30–299	≥300
GFR categories (mL/min/1.73 m <sup>2</sup> ) description and range	>105	1.1	1.5	2.2	5.0
	90–105	Ref	1.4	1.5	3.1
	75–90	1.0	1.3	1.7	2.3
	60–75	1.0	1.4	1.8	2.7
	45–60	1.3	1.7	2.2	3.6
	30–45	1.9	2.3	3.3	4.9
	15–30	5.3	3.6	4.7	6.6

Relative risk of **ESRD**  
according to eGFR and ACR<sup>a</sup>

		UACR (mg/g)			
		<10	10–29	30–299	≥300
GFR categories (mL/min/1.73 m <sup>2</sup> ) description and range	>105	Ref	Ref	7.8	18
	90–105	Ref	Ref	11	20
	75–90	Ref	Ref	3.8	48
	60–75	Ref	Ref	7.4	67
	45–60	5.2	22	40	147
	30–45	56	74	294	763
	15–30	433	1044	1056	2286

All results are adjusted for covariates and compared to the reference cell (Ref). Each cell represents a pooled RR from a meta-analysis; bold numbers indicate statistical significance at  $P < 0.05$ . Incidence rates per 1000 person-years for the reference cells are 7.0 for all-cause mortality, 4.5 for CV mortality, and 0.04 for kidney failure. Colors reflect the ranking of adjusted RR. The point estimates for each cell were ranked from 1 to 28 (the lowest RR having rank number 1, and the highest number 28). The categories with a rank number 1–8 are green, rank numbers 9–14 are yellow, the rank numbers 15–21 are orange and the rank numbers 22–28 are colored red.

ACR, albumin:creatinine ratio; CV, cardiovascular; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; GFR, glomerular filtration rate; RR, relative risk  
Kidney Disease Improving Global Outcomes Chronic Kidney Disease Work Group. *Kidney Int Suppl* 2013;3:1–150



## 糖、心、腎間交互影響密切 全方位照護是更好的治療策略



預防勝於治療，建議使用具有心腎保護療效的藥物  
及時護腎維持心臟功能

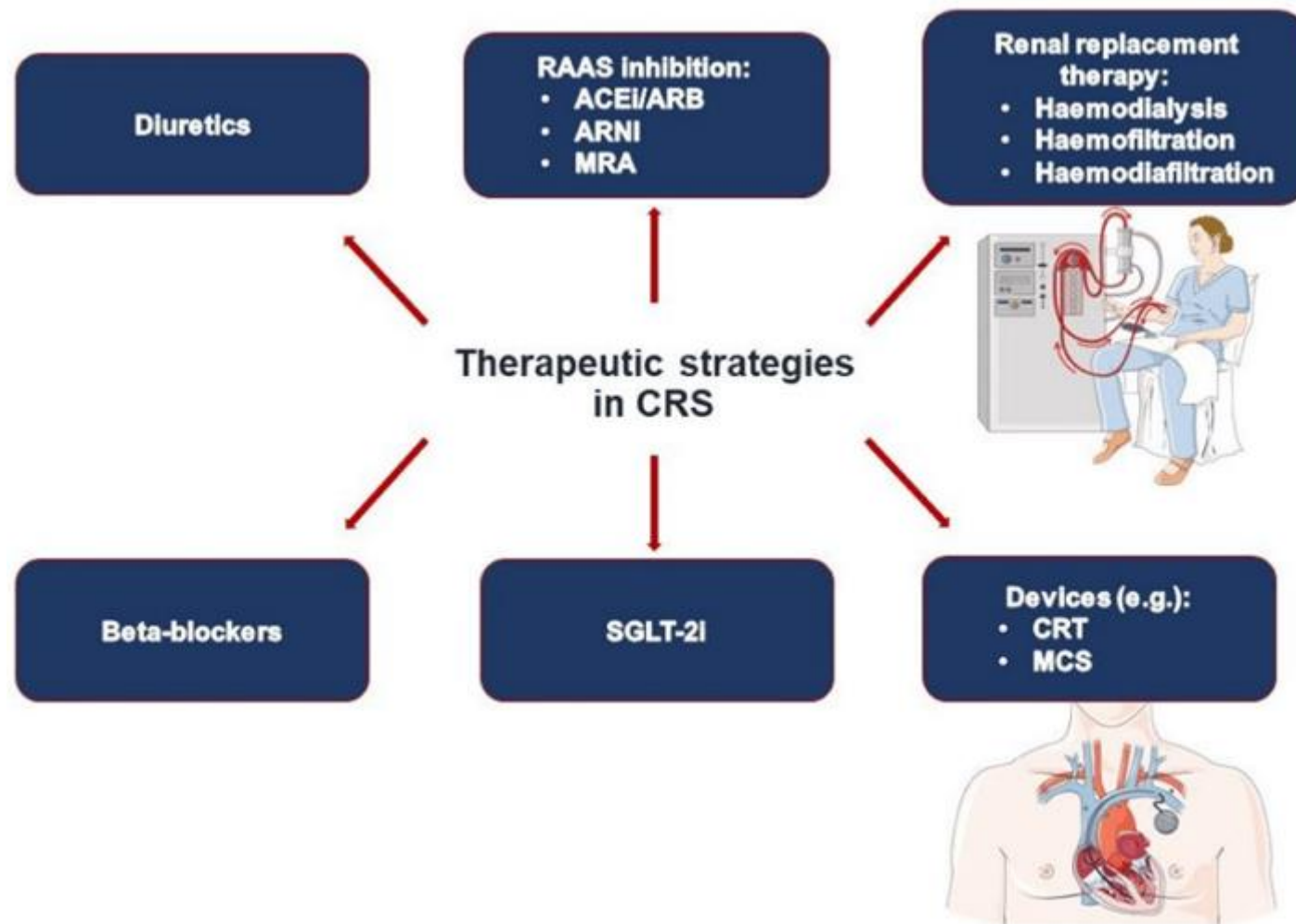


**Figure 2. Interaction of cardiovascular disease (CVD) and chronic kidney disease (CKD).**

Various mediators and mechanisms in vascular disease, heart failure, and CKD contribute to the progression of CVD and influence the prognosis of patients. PTM indicates post-translational modification.

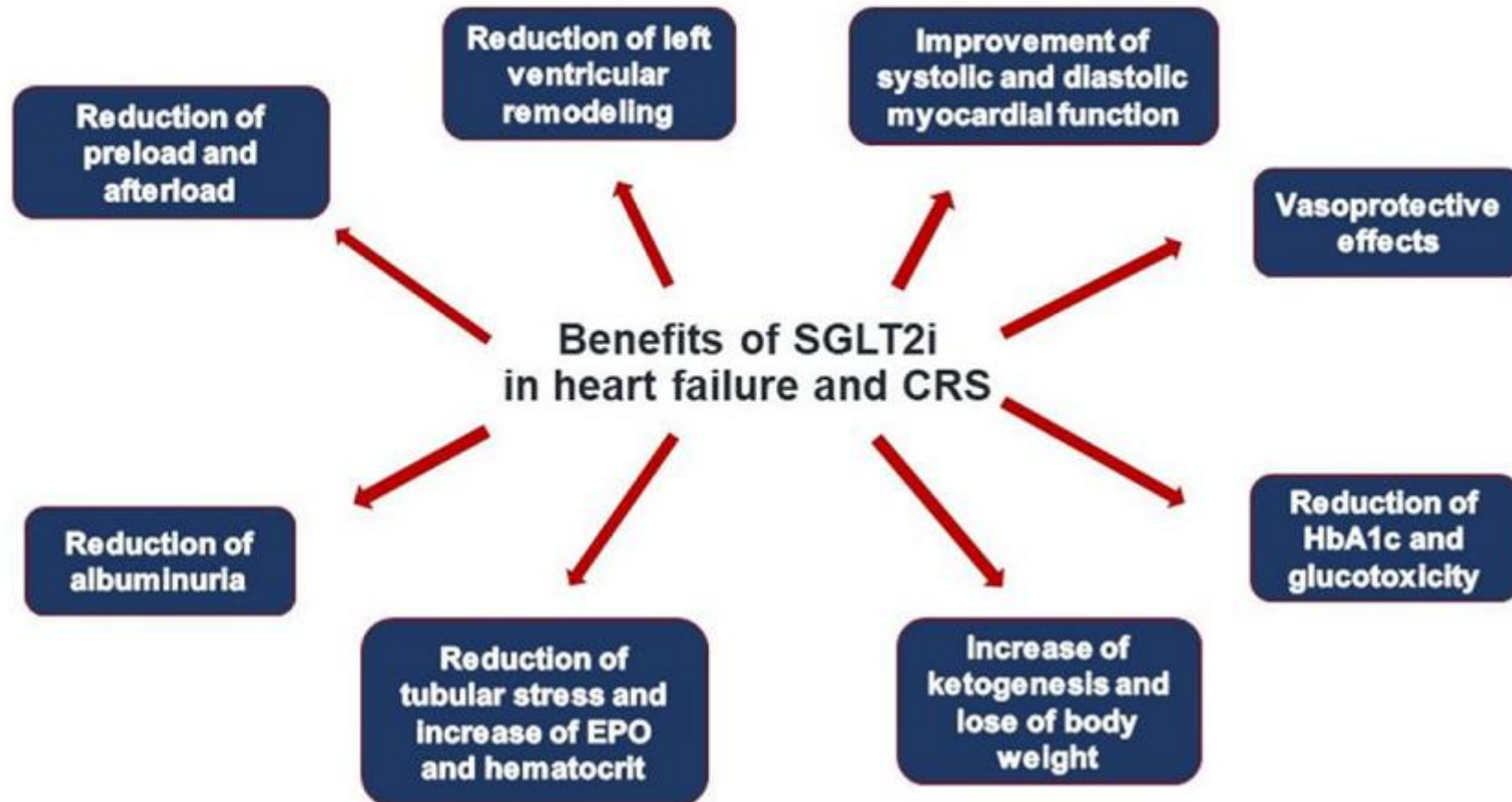


# Treatment Strategies in CRS



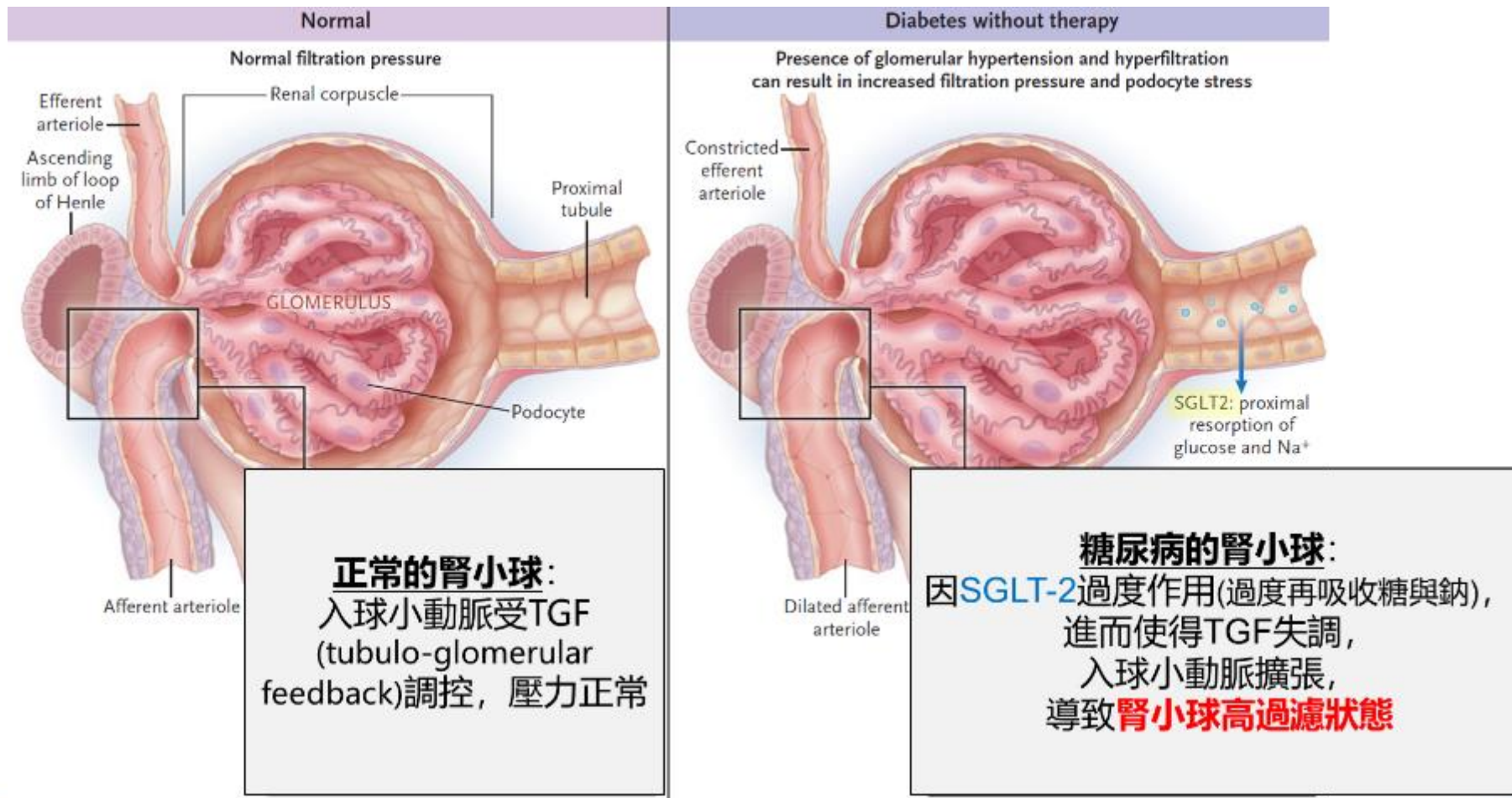


# SGLT2 Inhibitors: An Emerging Therapeutic Tool in CRS





# SGLT-2過度作用導致腎小球高過濾狀態





## Braunwald's Corner

# SGLT2 inhibitors: the statins of the 21<sup>st</sup> century

Eugene Braunwald  <sup>1,2\*</sup>

<sup>1</sup>TIMI Study Group, Division of Cardiovascular Medicine, Brigham and Women's Hospital, Hale Building for Transformative Medicine, Suite 7022, 60 Fenwood Road, Boston, MA 02115, USA; and <sup>2</sup>Department of Medicine, Harvard Medical School, Boston, MA, USA

A relatively small number of drugs have been responsible for major advances in medical practice. The discovery, development, and elucidation of the mechanisms of action of **aspirin, penicillin, and statins** are remarkable success stories, each with some surprises and each crowned by a Nobel Prize. The sodium glucose co-transporter inhibitors have been proven effective in the treatment of type 2 diabetes mellitus, various forms of heart failure, and kidney failure and represent *the, or one of the,* major pharmacological advances in cardiovascular medicine in the 21st century.

T2DM

HFrEF

CKD

HFpEF

CVOT

EMPA-REG  
CANVAS

**DECLARE-TIMI58**

**DAPA-HF**

EMPEROR-Reduced

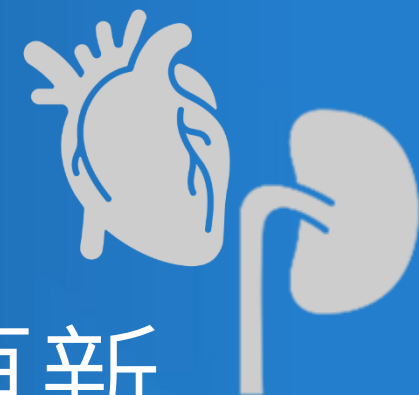
CREDENCE

**DAPA-CKD**

EMPA-KIDNEY

EMPEROR-Preserved

**DELIVER**

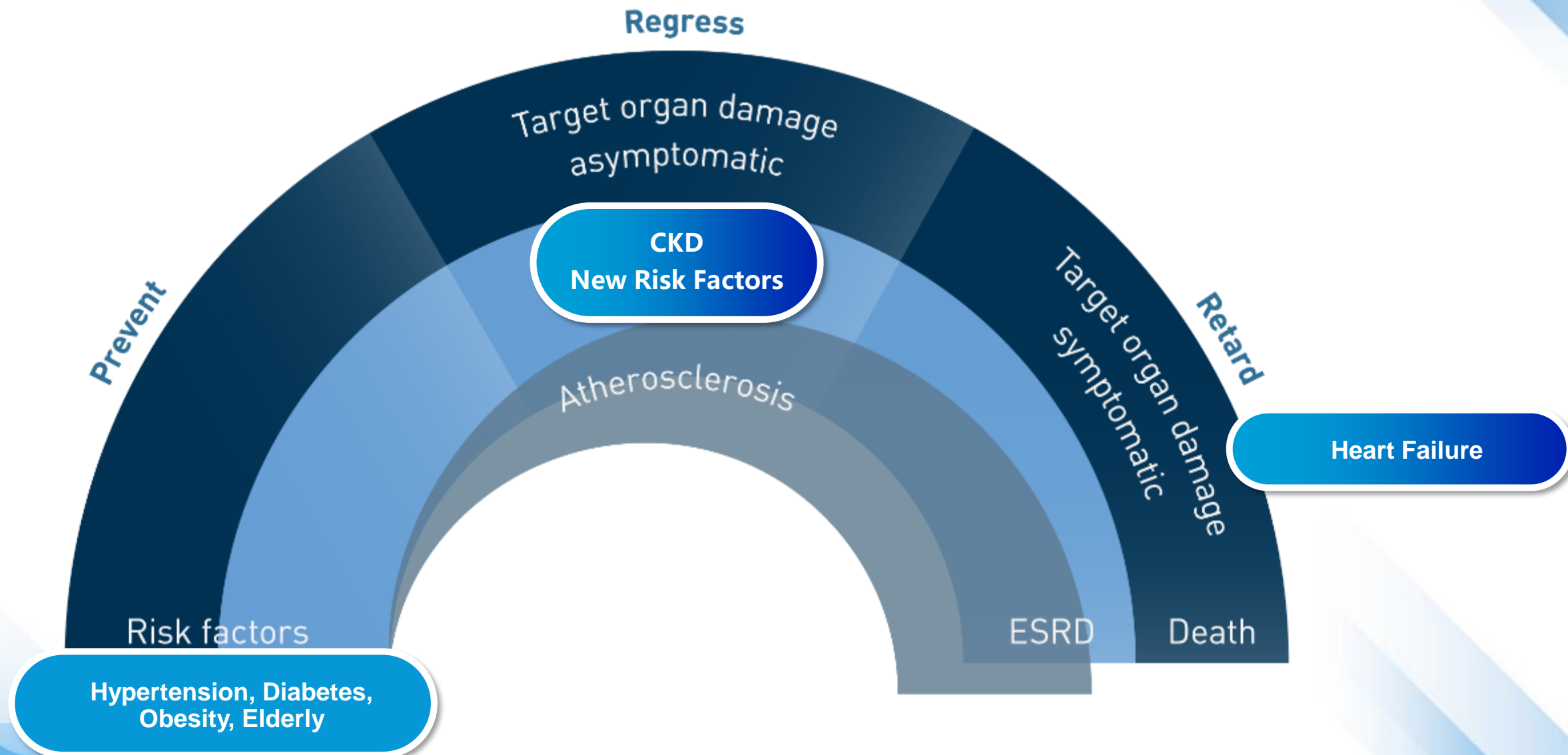


# 心腎共病治療的臨床實證及指引更新

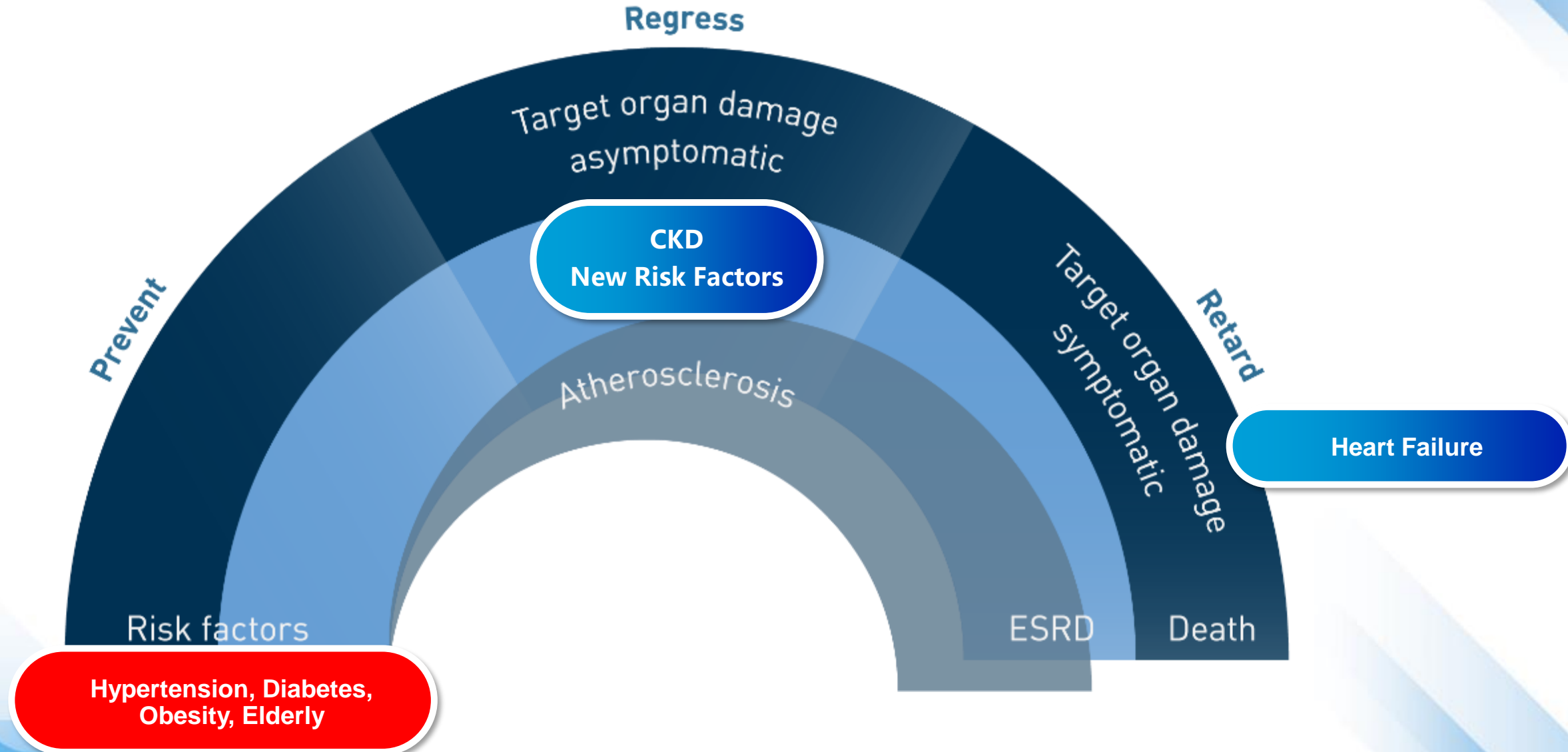




# Cardiorenal Continuum



# Cardiorenal Continuum





# 最新2023 ESC/ESH 高血壓指引 HTN合併T2D/DKD/CKD，建議使用SGLT2i減少心腎風險 (Class 1A)



Recommendations and statements	CoR	LoE
BP should be monitored to detect hypertension in all patients with diabetes, because it is a frequent comorbidity associated with an increase CV risk and risk for kidney events.	I	A
Non-dipping or elevated night-time BP are frequent in type 2 diabetes and should be monitored by ABPM or HBPM.	I	B
Antihypertensive treatment in type 2 diabetes is recommended to protect against macrovascular and microvascular complications.	I	A
Immediate lifestyle interventions and antihypertensive drug treatment are recommended for people with type 2 diabetes when office SBP is $\geq 140$ mmHg and DBP is $\geq 90$ mmHg.	I	A
Drug treatment strategies in patients with type 2 diabetes should be the same as for patients without diabetes and the primary aim is to lower BP below $<130/80$ mmHg.	I	A
<u>SGLT2is are recommended to reduce cardiac and kidney events in type 2 diabetes.</u>	I	A
The non-steroidal MRA finerenone can be used, because of its nephroprotective and cardioprotective properties in patients with diabetic CKD and moderate to severe albuminuria.	I	A
There are only limited data on the potential benefits of combining SGLT2is and finerenone.	II	C

Dual combination of an ACEi with an ARB is not recommended.	III	A
<u>SGLT2is inhibitors are recommended for patients with diabetic and non-diabetic nephropathies CKD if eGFR is at least 20 ml/min/1.73<sup>2</sup>.<sup>a</sup></u>	I	A
The non-steroidal MRA finerenone is recommended in patients with CKD and albuminuria associated with type 2 diabetes mellitus if eGFR is at least 25 ml/min/1.73 <sup>2</sup> and serum potassium $<5.0$ mmol/L.	I	A
In CKD patients with hyperkalemia a potassium binder can be used to maintain normal or near normal serum potassium levels ( $<5.5$ mmol/L) in order to allow optimal treatment with a RAS-blocker or a MRA to continue.	II	B

<sup>a</sup>Additional eGFR and albuminuria criteria apply for initiation of treatment with different SGLT2is according to their respective approval.

2022 AHA/ACC/HFSA 治療指引建議

# 強調 SGLT2i 從HF預防到治療的全光譜角色

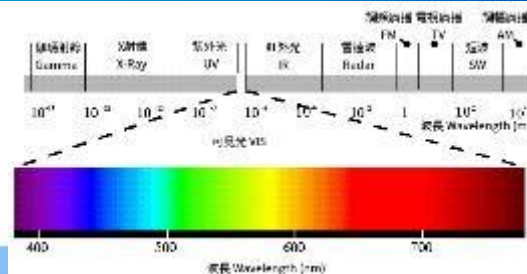
CLINICAL PRACTICE GUIDELINE: FULL TEXT

## 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines



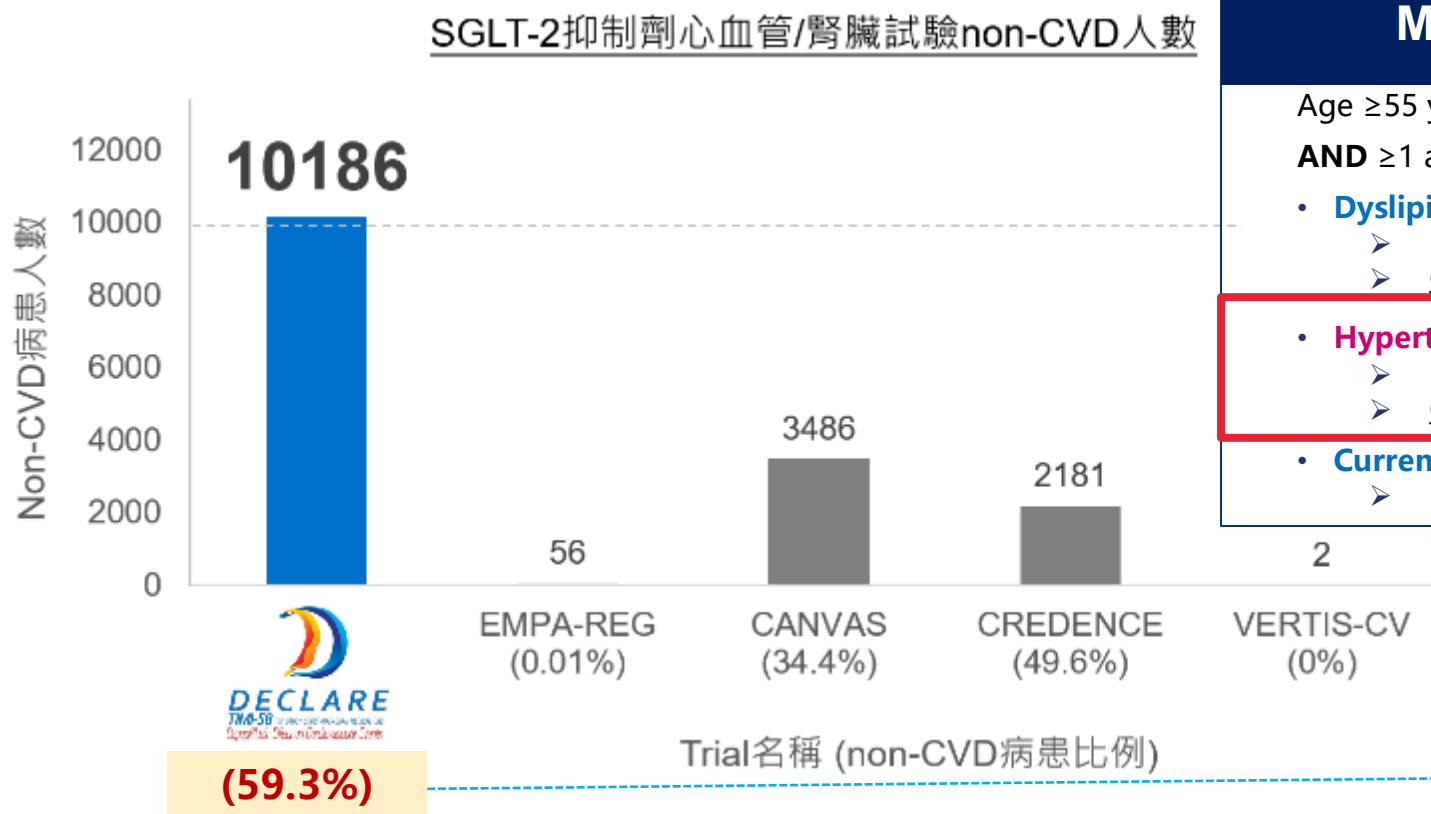
## SGLT2i從HF預防到治療的全光譜角色



GDMT of major medication classes	Stage A At-Risk for Heart Failure	Stage B Pre-Heart Failure	Stage C & D Stage C: Symptomatic Heart Failure & Stage D: Advanced Heart Failure		
			HFrEF LVEF $\leq 40\%$	HFmrEF LVEF 41-49%	HFpEF LVEF $\geq 50\%$
	SGLT2i in pts with DM (1)	SGLT2i in pts with DM (1)	ARNi in NYHA II-III; ACEi or ARB in NYHA II-IV (1)	Diuretics, as needed (1)	Diuretics, as needed (1)
		ACEi (1)	Beta blocker (1)	SGLT2i (2a)	SGLT2i (2a)
		ARB if ACEi intolerant (1)	MRA (1)	ACEi, ARB, ARNi (2b)	ARNi (2b)
		Beta blocker (1)	SGLT2i (1)	MRA (2b)	MRA (2b)
			Diuretics, as needed (1)	Beta blocker (2b)	ARB (2b)
			Hydral-nitrates for NYHA III-IV, in African American pts (1)		

# DECLARE

## 唯一non-CVD病患超過萬人的T2DM CVOT



### Multiple Risk Factors

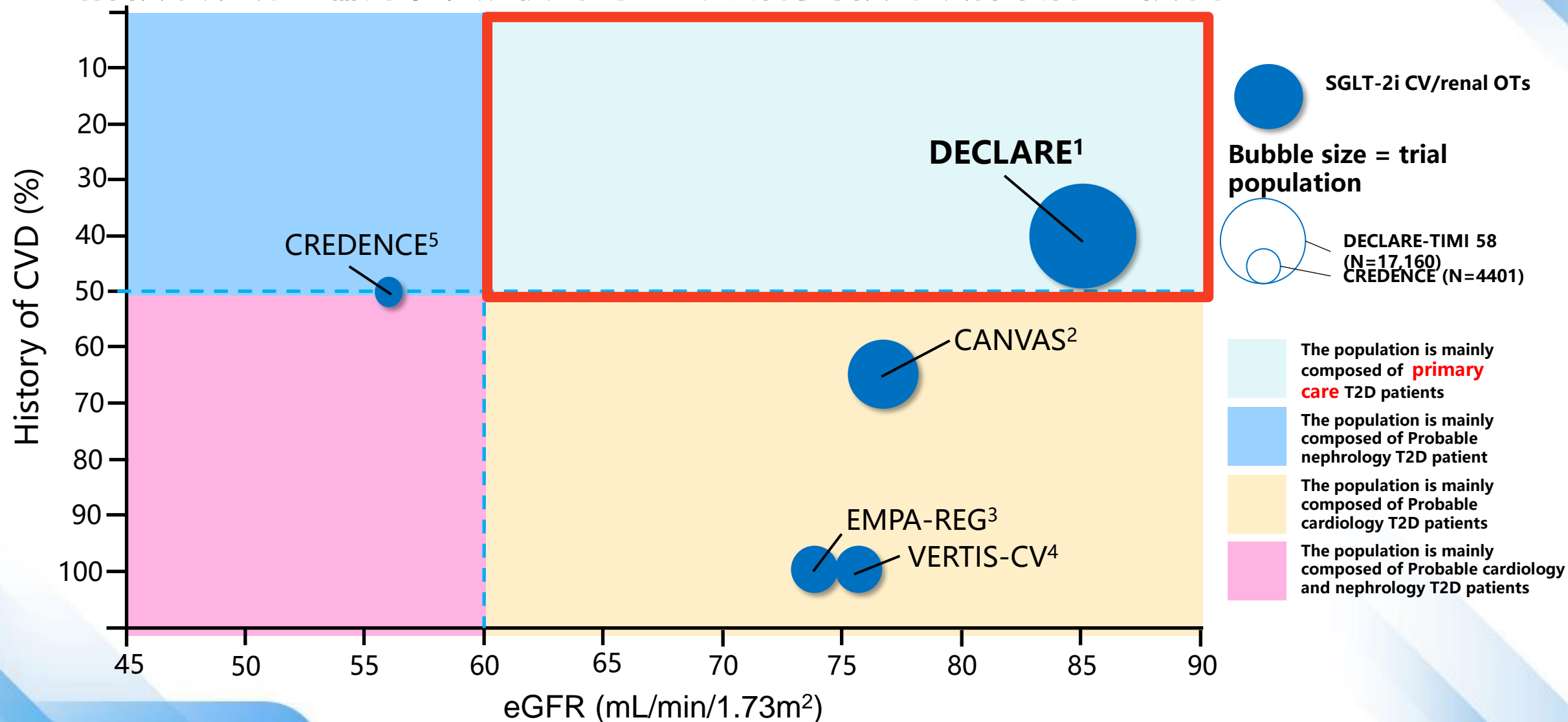
Age  $\geq 55$  years (men),  $\geq 60$  years (women)

**AND**  $\geq 1$  additional risk factors:

- **Dyslipidemia (73.9%)** ( $\geq 1$  of following)
  - LDL-C  $> 130$  mg/dL ( $> 3.36$  mmol/L)
  - On lipid-lowering therapy
- **Hypertension (91.2%)** ( $\geq 1$  of following)
  - BP  $> 140/90$  mm Hg at enrolment
  - On antihypertensive therapy
- **Current smoking (14.4%)**
  - $\geq 5$  cigarettes/day for  $\geq 1$  year

# 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



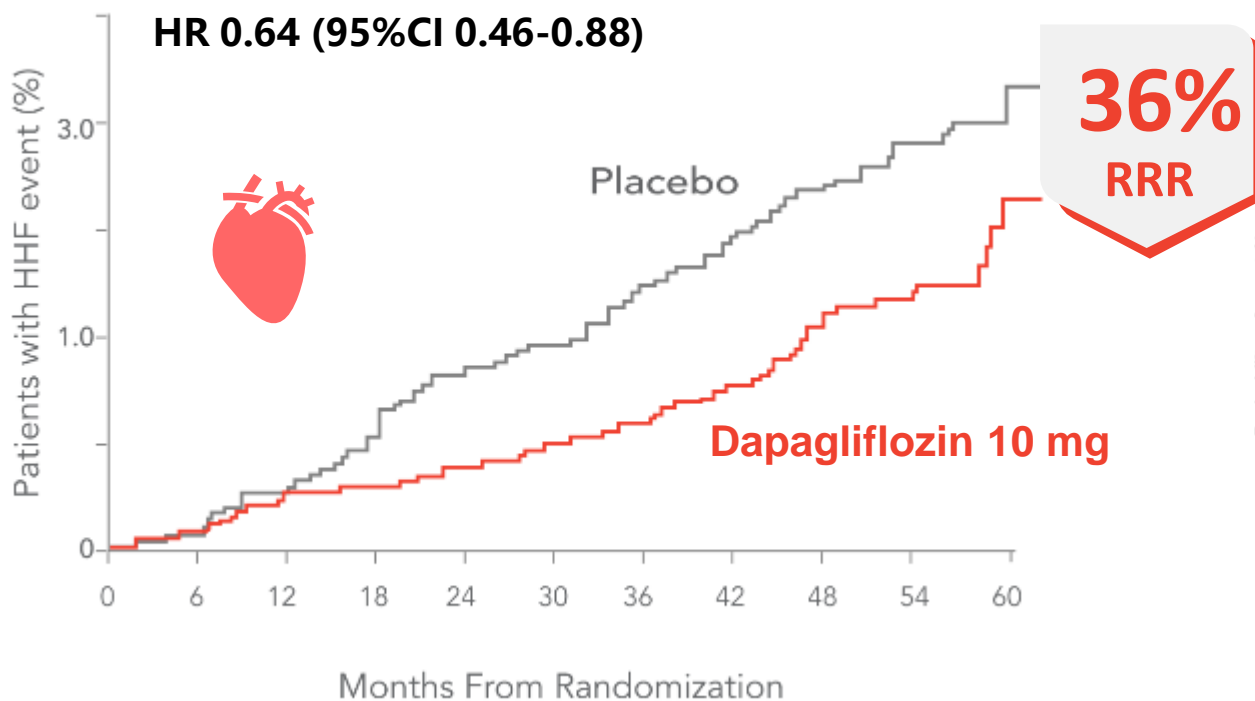


# Dapagliflozin 治療 T2D 合併風險因子患者 唯一 SGLT2i 預防心衰竭住院和腎臟惡化



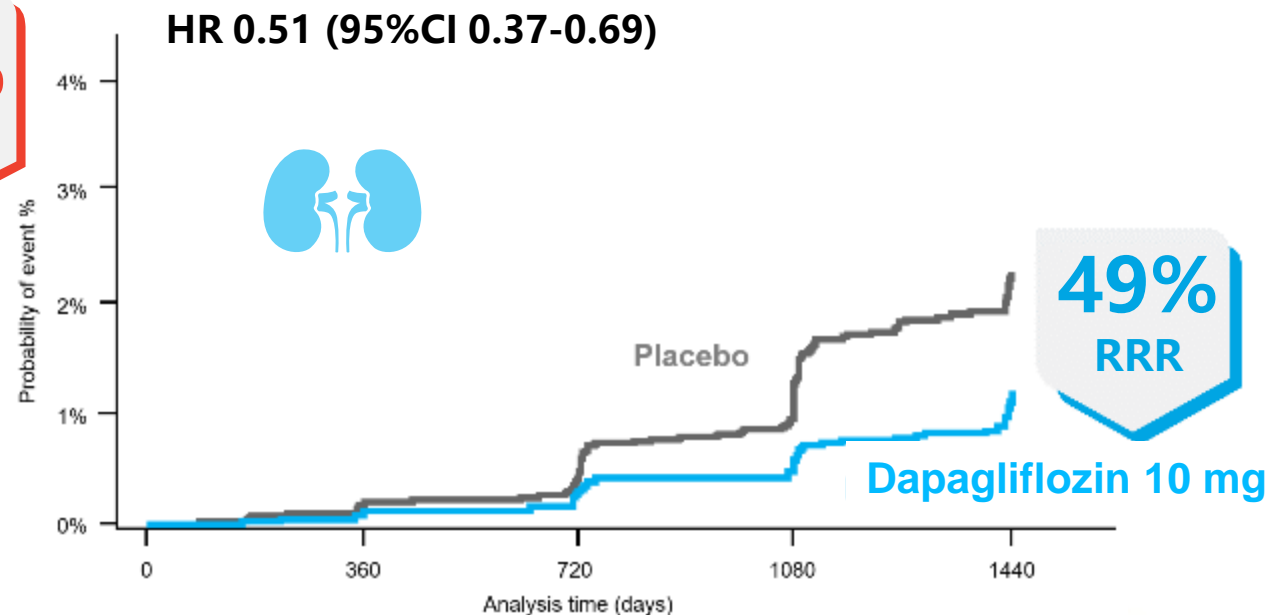
Analyses of **Primary Prevention** in patients with MRF From DECLARE-TIMI 58

## Reduction in hHF



## Reduction in renal-specific outcome

sustained  $\geq 40\%$  eGFR decline to  $< 60$ , ESKD, or renal death



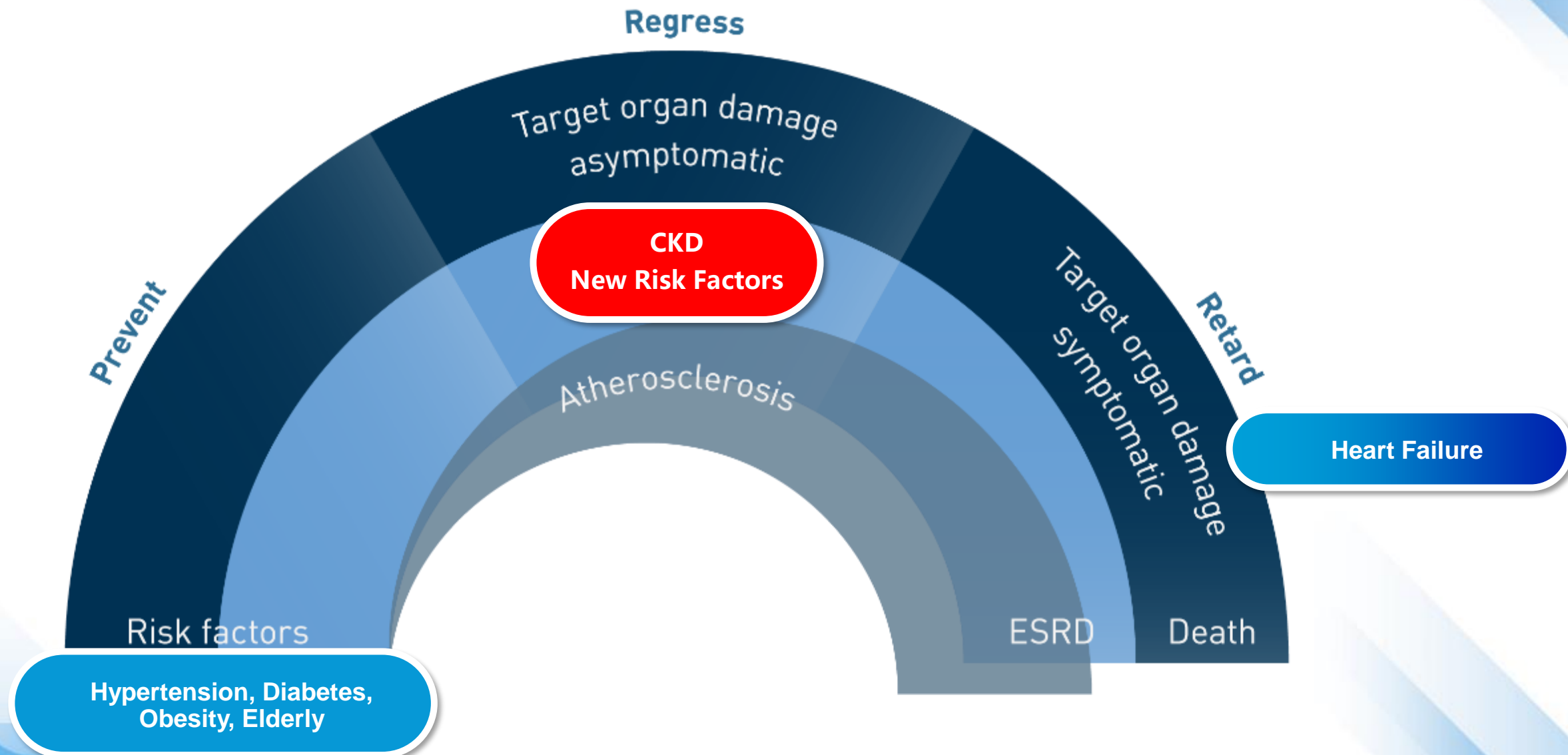
MRF: multiple risk factors, hHF: hospitalization for heart failure

Patients with MRF were men aged  $\geq 55$  and women aged  $\geq 60$  years with at least one additional cardiovascular risk factor including dyslipidemia, hypertension, or current tobacco use

Diabetes Care. 2021 May;44(5):1159-1167.



# Cardiorenal Continuum





# Recent clinical guidelines for the management of CKD in T2D recommend a combination of drug therapies



ADA KDIGO  
Consensus  
2022



ESC



European  
Society of  
Hypertension



最高可耐受劑量的**RAS blocker** 加上 **SGLT2 inhibitor** 及 **MRA** 可為CKD T2D病人治療的**三本柱(pillars of therapy)**，能夠最大化延緩DKD進程及降低心衰竭住院率等好處



There are now three distinctly different classes of drugs with a strong evidence base and level A guideline recommendations<sup>\*,1-6</sup>:

RASi

nsMRA  
(finerenone)

SGLT-2i

<sup>\*</sup>In addition to glucose and BP control

ESC, European Society of Cardiology; KDIGO, Kidney Disease: Improving Global Outcomes; RASi, renin-angiotensin system inhibitor; SGLT-2i, sodium-glucose co-transporter-2 inhibitor

1. Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2022;102:S1-S128; 2. American Diabetes Association. *Diabetes Care* 2023;46(Suppl 1):S191-S202;

3. de Boer IH, et al. *Diabetes Care* 2022;45:3075-3090; 4. Sarafidis PA, et al. *Clin Kidney J* 2023; doi:10.1093/ckj/sfad139; 5. Mancia G, et al. *J Hypertens* 2023; doi: 10.1097/HJH.0000000000003480;

6. Blazek O, et al. *Am Heart J Plus* 2022;19:100187



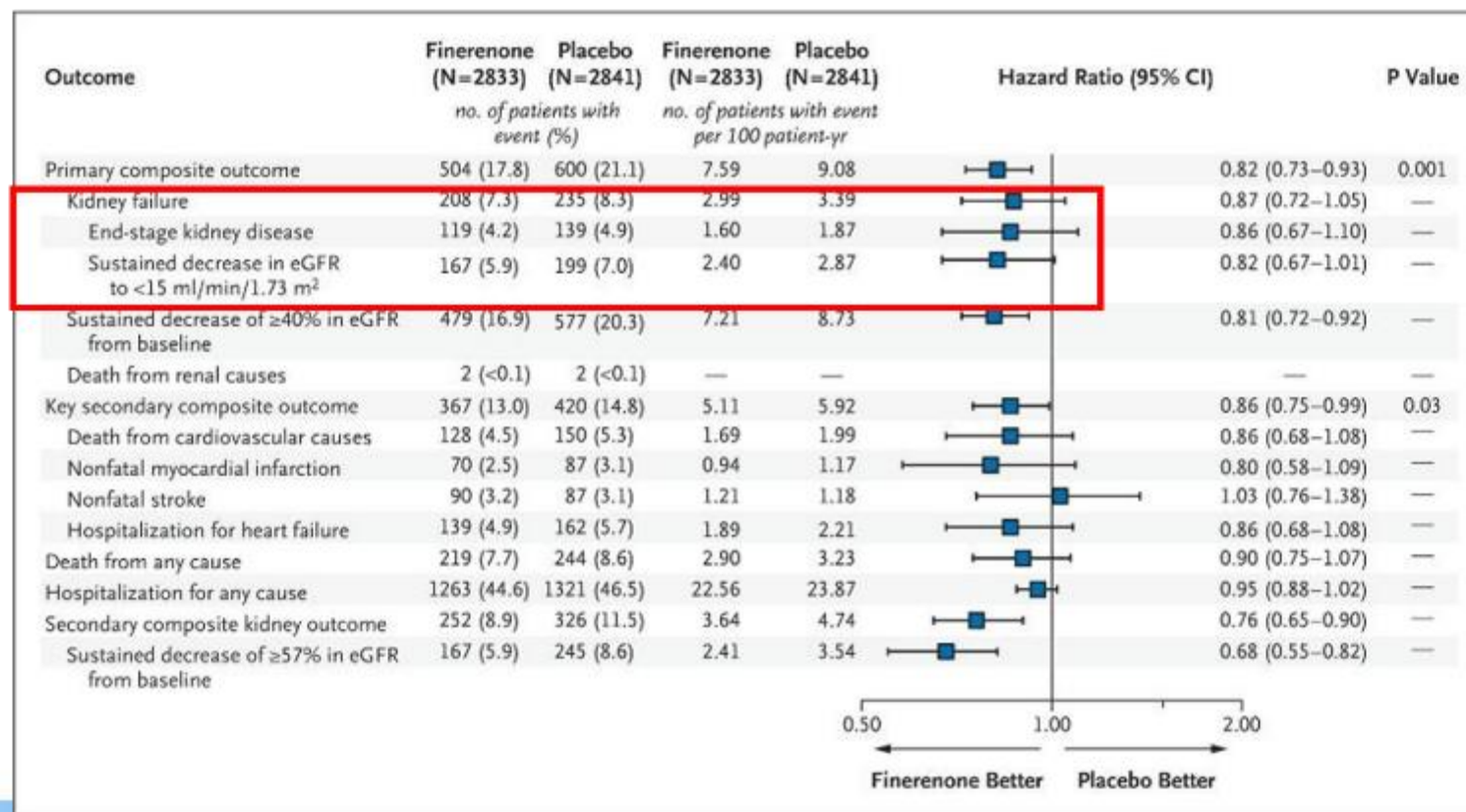
# FIDELIO-DKD

## The renal effect of finerenone on DKD patients

5734 patients with CKD and T2D treated with renin-angiotensin system blockade; median follow-up of 2.6 years

- diabetic retinopathy with eGFR 25-60, UACR 30-300 mg/g
- eGFR 25-75, UACR 300-5000 mg/g

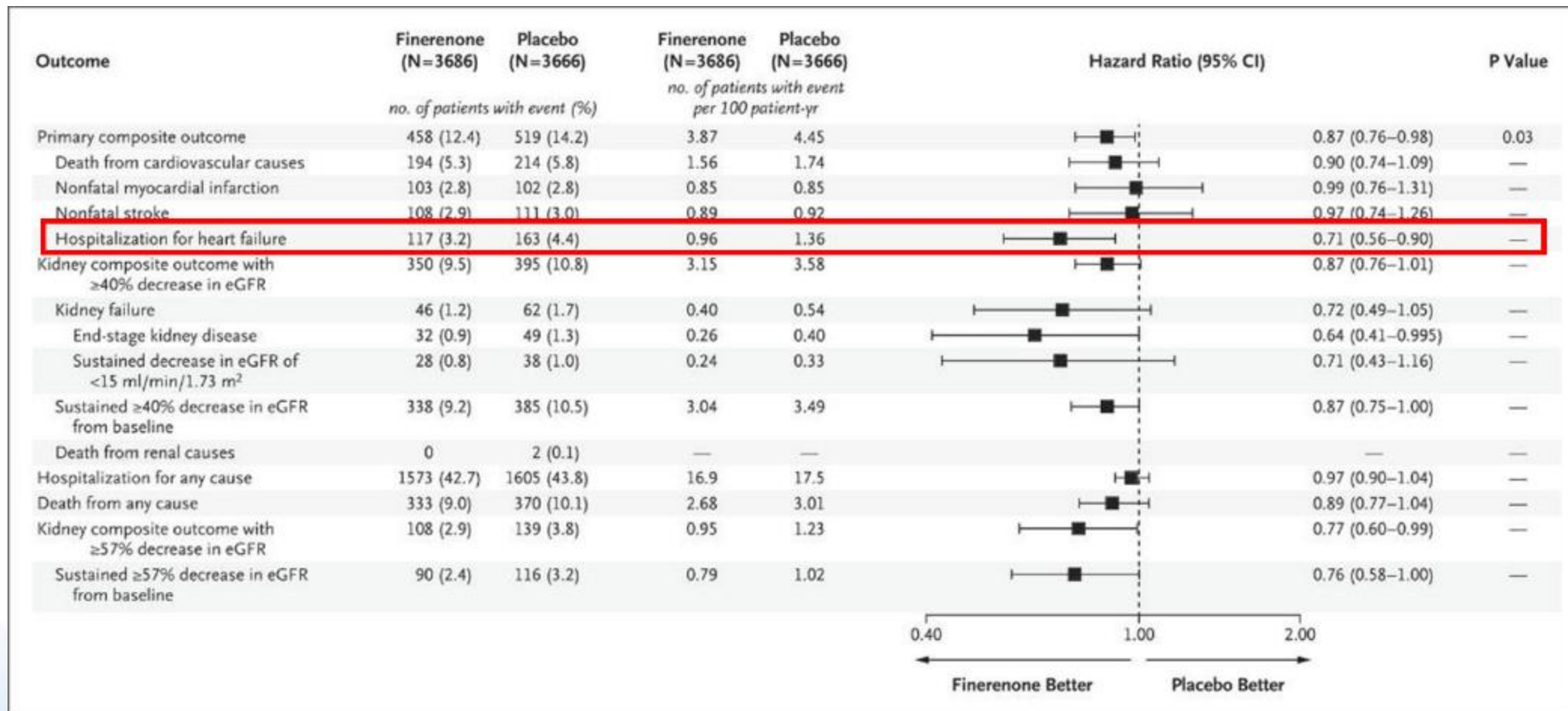
Finerenone is a first-in-class non-steroidal, selective mineralocorticoid receptor antagonist (MRA)



↓ 18%

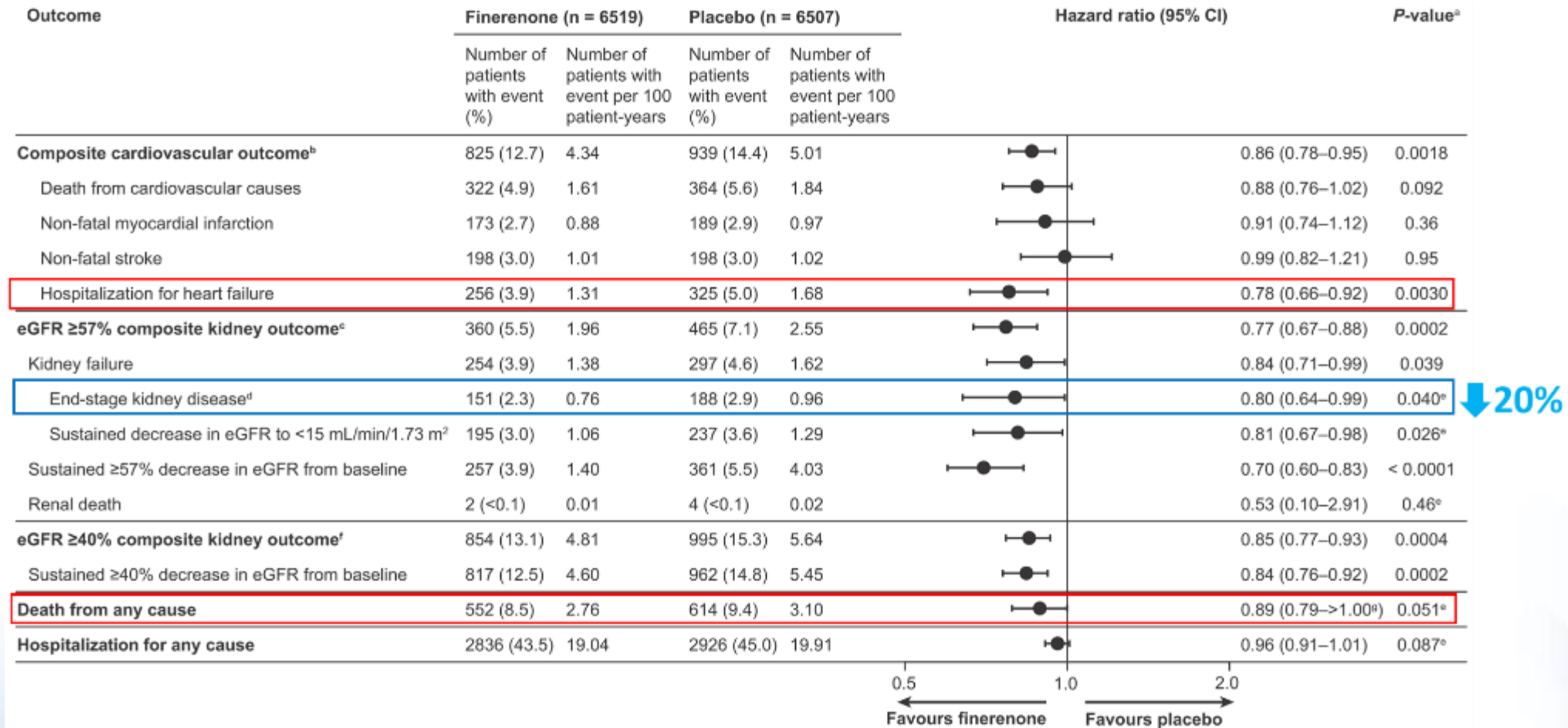
# FIGARO-DKD

## The cardiovascular effect of finerenone on DKD patients





# FIDELITY pooled analysis: FIDELIO-DKD + FIGARO-DKD (13,026 patients)



# 2024 KDIGO CKD治療指引更新: SGLT2i納入一線治療



2024 KDIGO治療指引  
建議等級/證據等級<sup>1</sup>

**CKD患者**



**建議3.7.1:**  
CKD合併T2D且eGFR $\geq$ 20ml/min/1.73m<sup>2</sup>的成人患者\*

證據等級

**1A**

治療建議

**建議3.7.2:**  
CKD合併心衰(無論蛋白尿狀態)  
或  
eGFR $\geq$ 20ml/min/1.73m<sup>2</sup>+UACR  $\geq$  200 mg/g 的成人患者\*\*

**1A**

**推薦使用  
SGLT2i**

**建議3.7.3:**  
成人eGFR $\geq$ 20- 45ml /min /1.73m<sup>2</sup>+UACR < 200 mg/g

**2B**

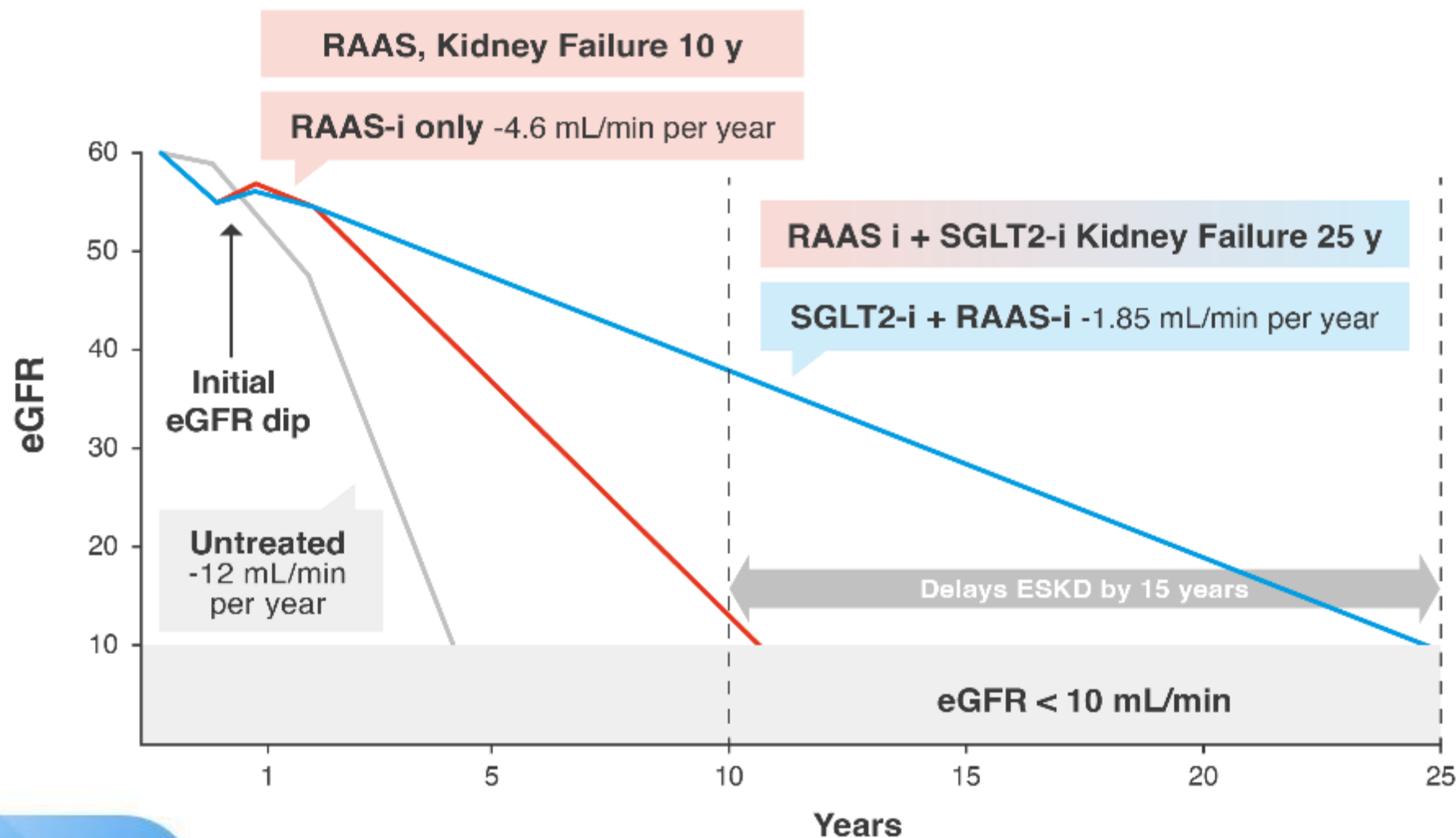
\*臨床觀點 3.7.1: 一旦起始使用SGLT2i，即使eGFR < 20 ml/min per 1.73 m<sup>2</sup>，繼續使用也是合理的，除非患者無法耐受或開始使用腎臟替代治療(透析)

臨床觀點 3.7.2: 在長時間禁食、手術或身處重大醫療疾病治療期間，暫停SGLT2i是合理的 (患者可能有較高的酮症風險)

\*\*臨床觀點 3.7.3: 使用SGLT2i並不需要改變CKD監測的頻率，而起始治療時可逆的eGFR下降通常並不能視為停止治療的指標

eGFR小於25: Dapagliflozin針對此類病人不建議起始治療，然而Forxiga治療後，eGFR降低至小於25 mL/min/1.73 m<sup>2</sup>的透析前病人，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。

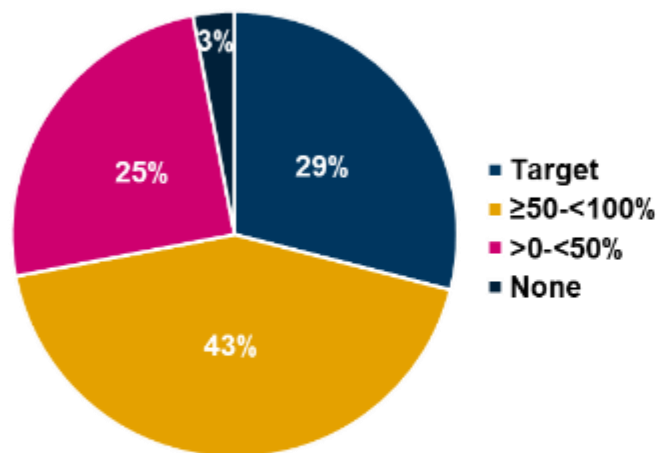
## SGLT2i併用RAASi，可延緩進入ESKD近15年



















# Dapagliflozin皆能提供腎臟保護效果，無差別RAASi使用劑量

Patient Distribution by ACEi/ARB Target Dose<sup>a</sup> Level



	Events/100 patient-years			Hazard ratio (95% CI)	P-value for interaction
	Dapagliflozin	Placebo			
Primary outcome: eGFR decline ≥50%, ESKD, or kidney or CV death					
Target dose	4.9	7.1		0.67 (0.49, 0.94)	0.76
≥50 to <100% target dose	4.6	8.1		0.56 (0.43, 0.73)	
>0 to <50% target dose	4.2	6.0		0.68 (0.46, 1.01)	
None	6.0	13.2		0.54 (0.20, 1.46)	
Secondary outcome: eGFR decline ≥50%, ESKD or kidney death					
Target dose	3.6	5.6		0.61 (0.42, 0.90)	0.86
≥50 to <100% target dose	3.3	6.3		0.52 (0.38, 0.70)	
>0 to <50% target dose	2.8	4.3		0.61 (0.38, 0.97)	
None	6.0	11.6		0.68 (0.24, 1.93)	
Secondary outcome: Hospitalization for heart failure or CV death					
Target dose	2.1	3.4		0.60 (0.38, 0.97)	0.38
≥50 to <100% target dose	2.1	3.0		0.72 (0.48, 1.06)	
>0 to <50% target dose	2.5	2.5		1.02 (0.60, 1.75)	
None	0.9	4.5		NC	
Secondary outcome: All-cause mortality					
Target dose	2.1	2.5		0.81 (0.49, 1.32)	0.77
≥50 to <100% target dose	2.0	3.5		0.59 (0.40, 0.86)	
>0 to <50% target dose	2.4	3.3		0.76 (0.46, 1.26)	
None	2.7	3.6		NC	

0.20.30.512

←Dapagliflozin BetterPlacebo Better→

<sup>a</sup>Maximum recommended target antihypertensive ACEi/ARB dose.

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin-receptor blocker; CV = cardiovascular; ESKD = end-stage kidney disease; NC = not calculable.

J Am Heart Assoc. 2023;12(9):e028739.

# 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 $\geq 30$ to $< 90$ mL/min/1.73 m <sup>2</sup> UACR $> 300$ to $\leq 5000$ mg/g	eGFR $\geq 25$ to $< 75$ mL/min/1.73 m <sup>2</sup> UACR $\geq 200$ and $\leq 5000$ mg/g	eGFR $\geq 20$ to $< 45$ mL/min/1.73 m <sup>2</sup> or eGFR $\geq 45$ to $< 90$ mL/min/1.73 m <sup>2</sup> with UACR $\geq 200$ mg/g (or protein:creatinine ratio $\geq 300$ mg/g)
Primary Endpoint	Doubling of serum creatinine, ESRD, renal or CV death	$\geq 50\%$ sustained decline in eGFR, ESRD, renal or CV death	Progression of kidney disease( $\geq 40\%$ sustained decline in eGFR, ESRD, sustained decline in eGFR to $< 10$ , renal death) or CV death

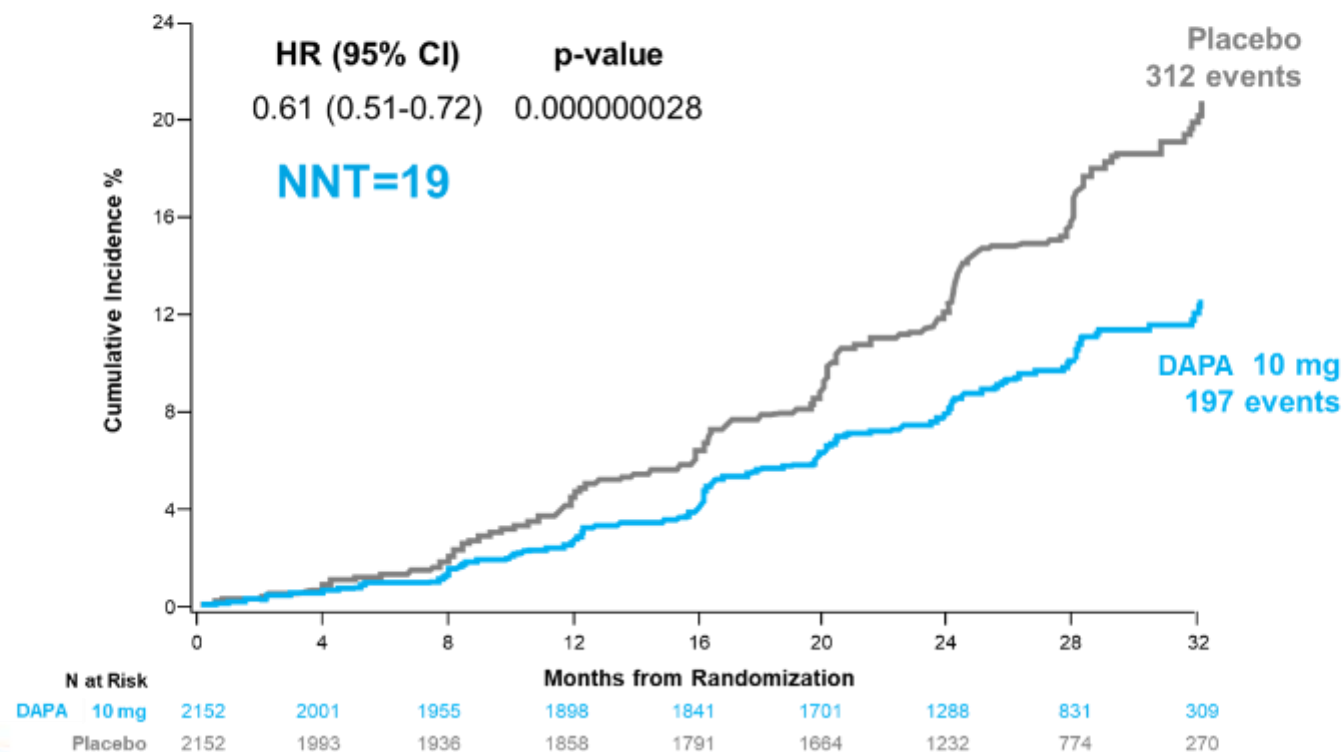


# Dapagliflozin治療CKD: 顯著減少腎功能惡化、ESRD、心血管或腎因性死亡



## Primary Outcome

Sustained decline in the eGFR  $\geq 50\%$ , ESRD, or death from renal or CV causes



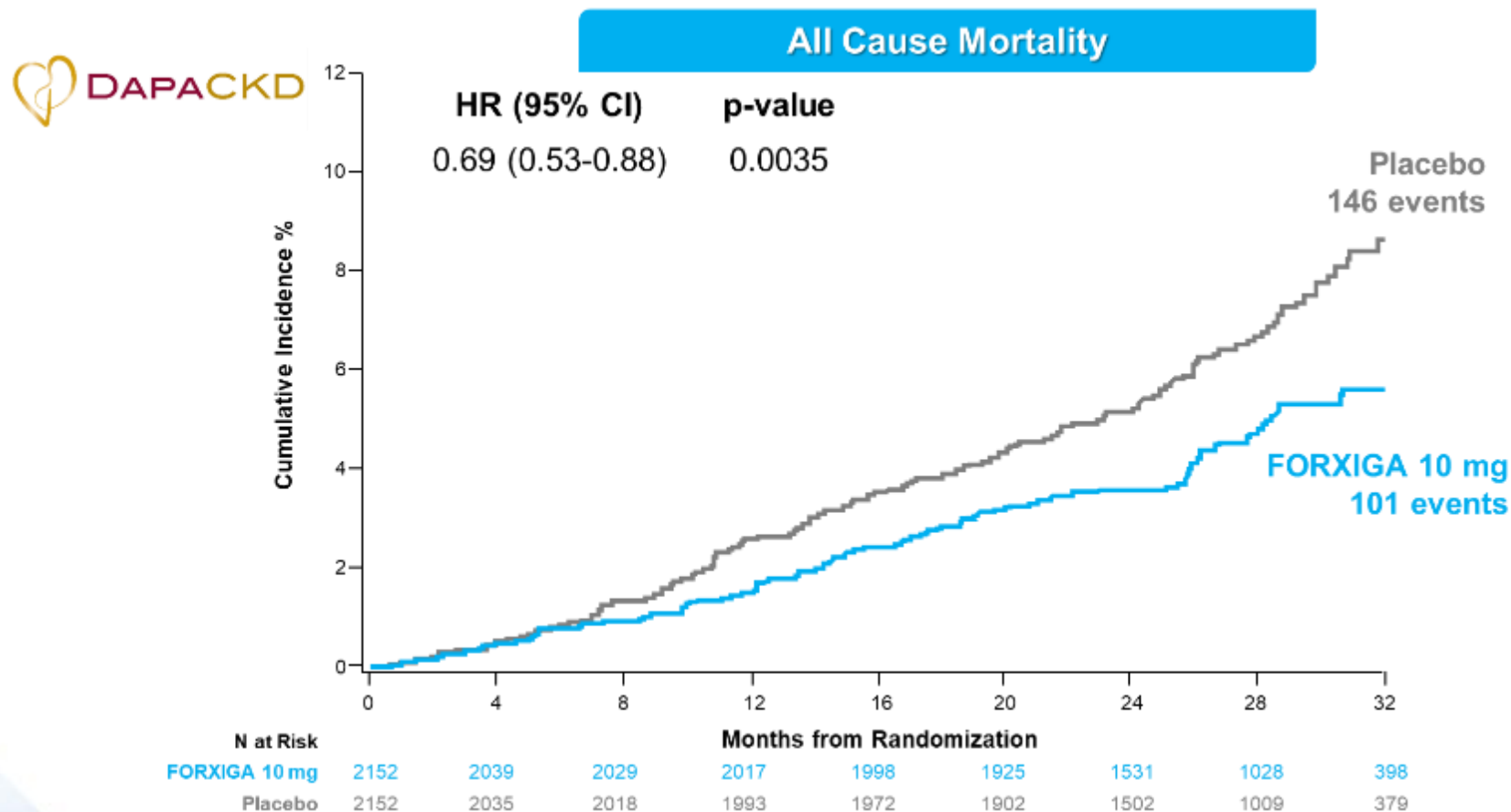
39%  
RRR

ESRD ↓ 36%

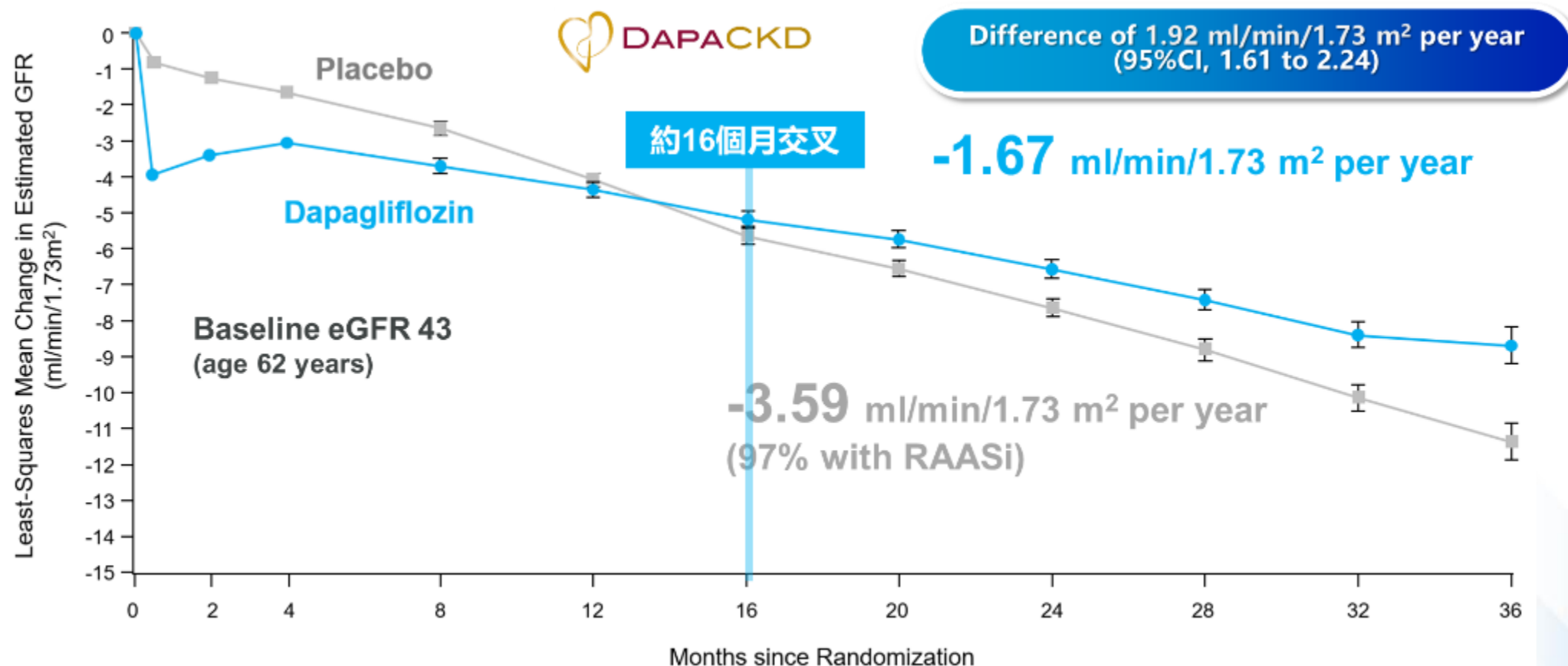
HR 0.64 (0.50-0.82),  
p=0.0004



## 針對CKD患者，Dapagliflozin顯著減少總死亡風險



# Dapagliflozin減緩CKD患者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



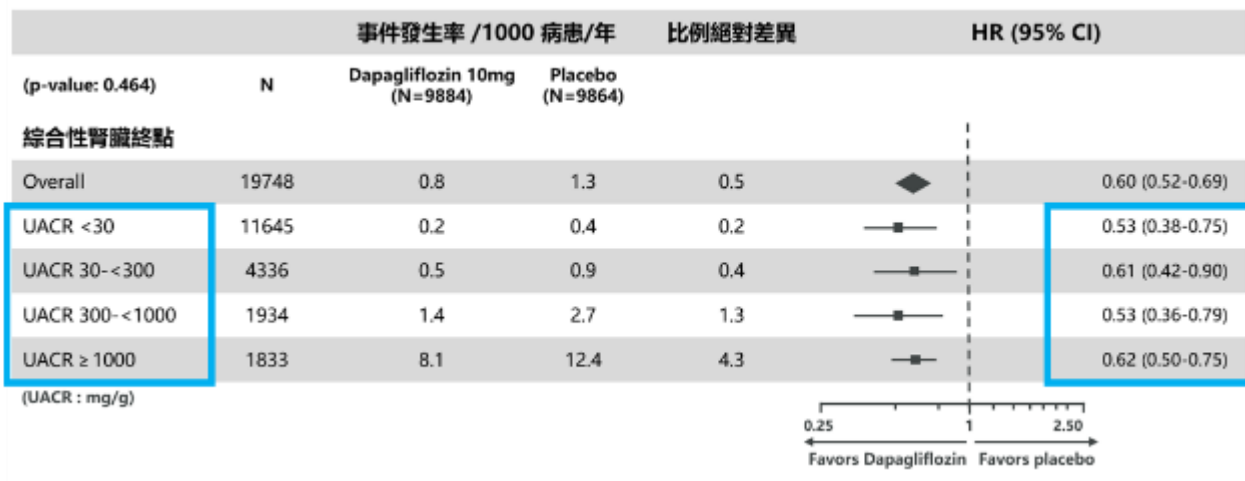
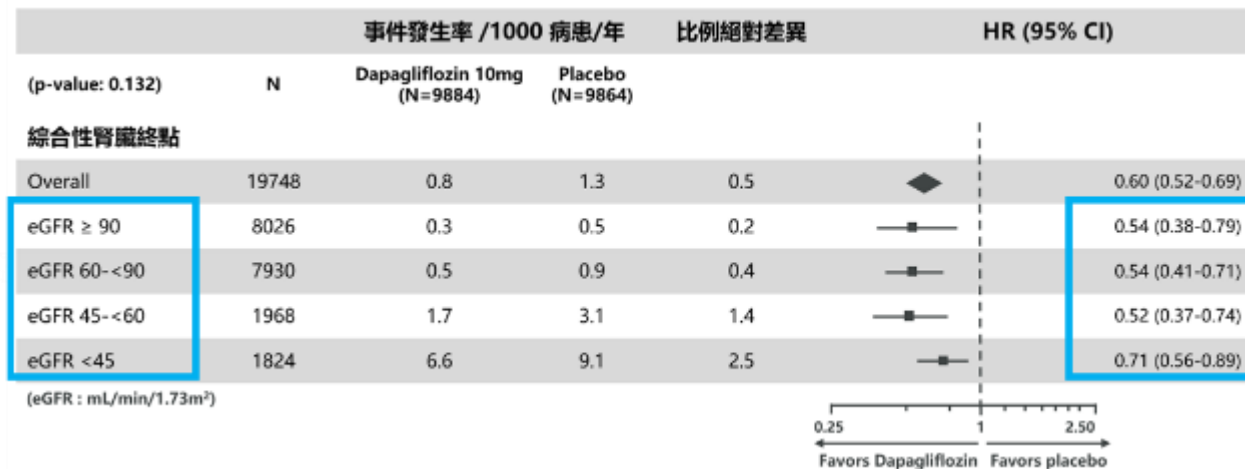
eGFR ml/min/1.73m <sup>2</sup>	DECLARE N	DAPA-CKD N	Total N (%)
<45	184	1640	1824 (9)
45-<60	1050	918	1968 (10)
60-<90	7582	348	7930 (40)
≥90	8026	0	8026 (41)

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

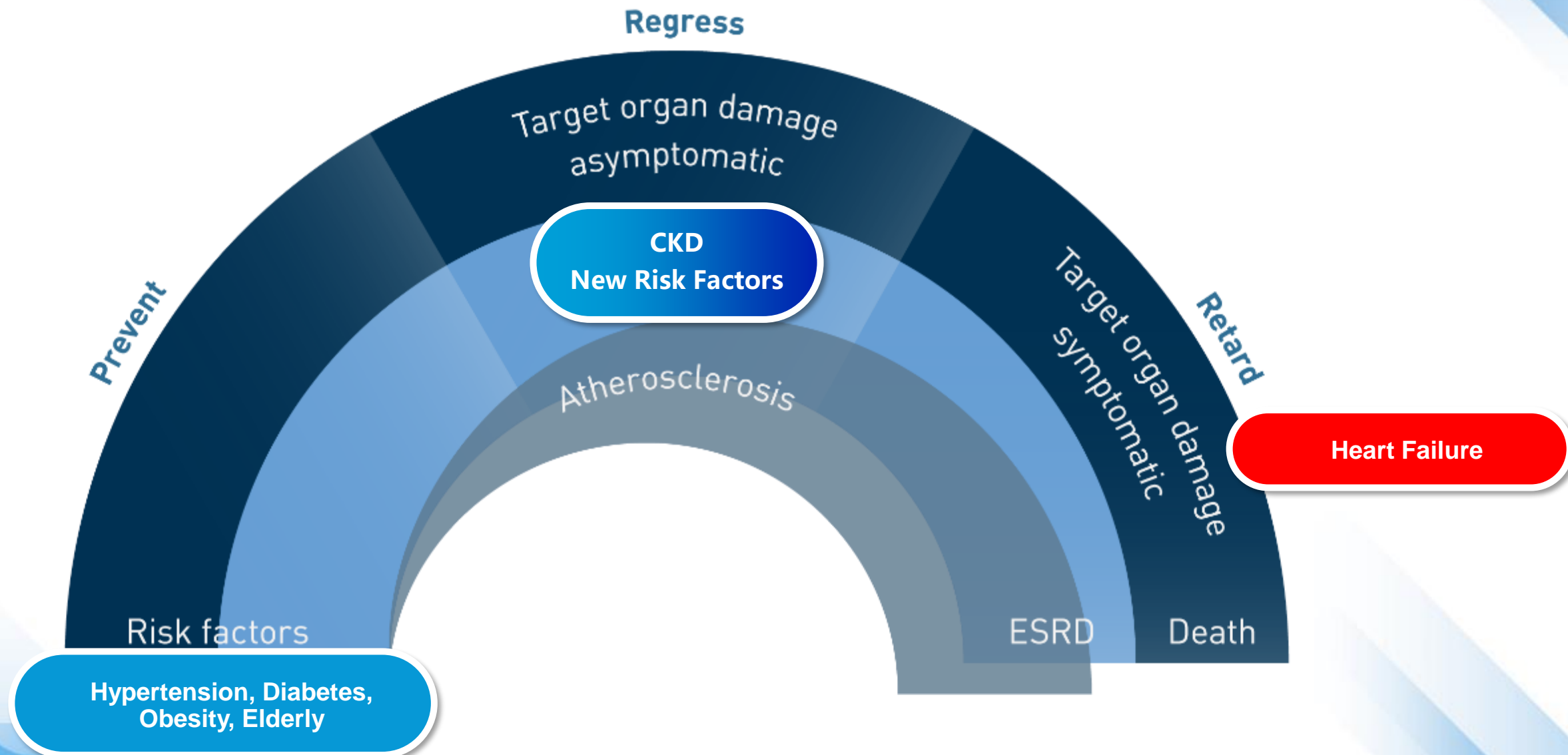
1. Moura F, et al. Presented at: ESC Congress 2022; August 26-29, 2022; Barcelona, Spain. 2.

[https://academic.oup.com/eurheartj/article/43/Supplement\\_2/ehac544.2407/6745929?login=false](https://academic.oup.com/eurheartj/article/43/Supplement_2/ehac544.2407/6745929?login=false)





# Cardiorenal Continuum





# 2021 ESC HF治療指引建議： SGLT2i為HFrEF一線用藥，證據等級1A

**ESC**  
European Society of Cardiology

2021 ESC Guidelines for the  
diagnosis and treatment of acute  
and chronic heart failure

ESC Clinical Practice Guidelines

27 Aug 2021

**SGLT-2i為一線用藥，  
為HFrEF患者降低死亡**

## Management of HFrEF

To reduce mortality – for all patients

ACE-I/ARNI

BB

MRA

SGLT2i (1)

Recommendations	Class	Level
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death	I	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death	I	A

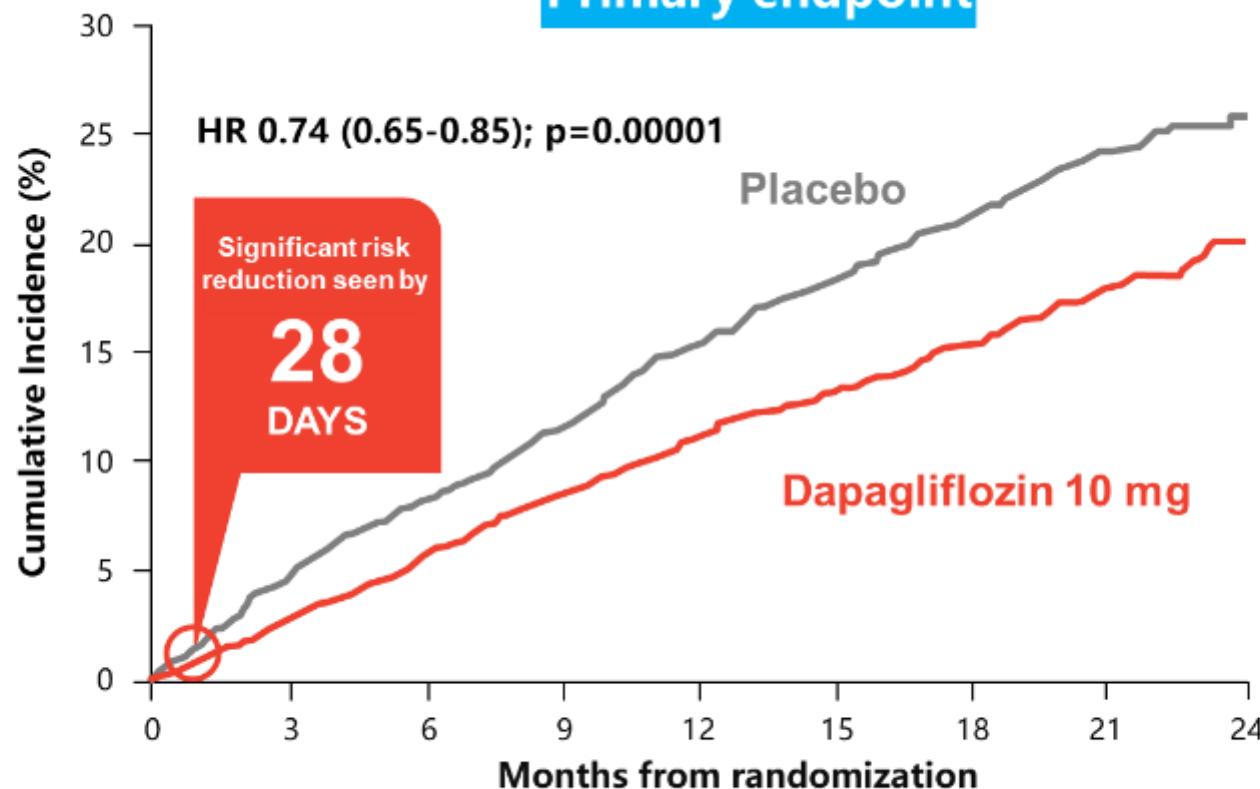


# Dapagliflozin 治療 HFrEF 減少心血管死亡或心衰竭惡化

## DAPA-HF : 28天 顯著減少主要試驗終點



Primary endpoint



NNT=21

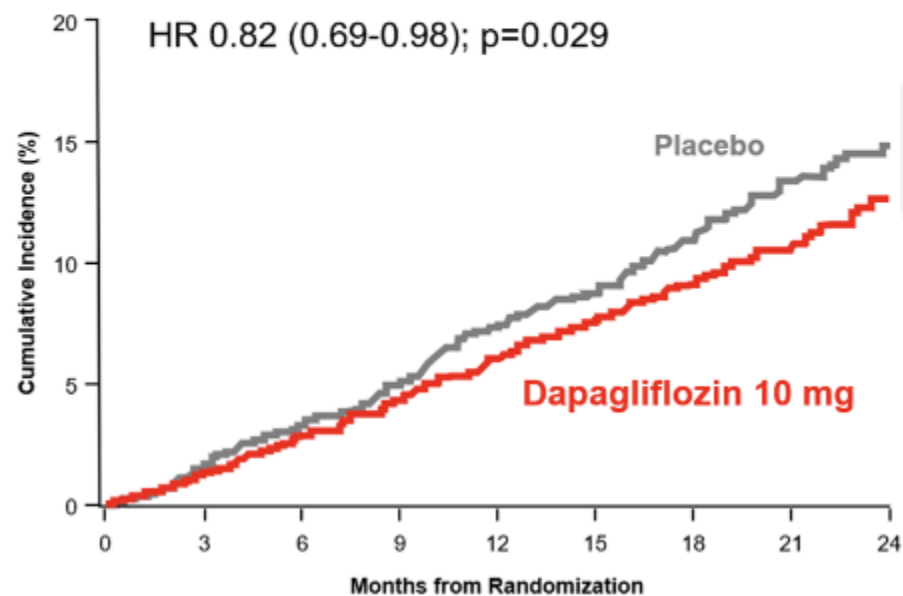
26%  
RRR

No. at risk									
Dapagliflozin	2373	2305	2221	2147	2002	1560	1146	612	210
Placebo	2371	2258	2163	2075	1917	1478	1096	593	210

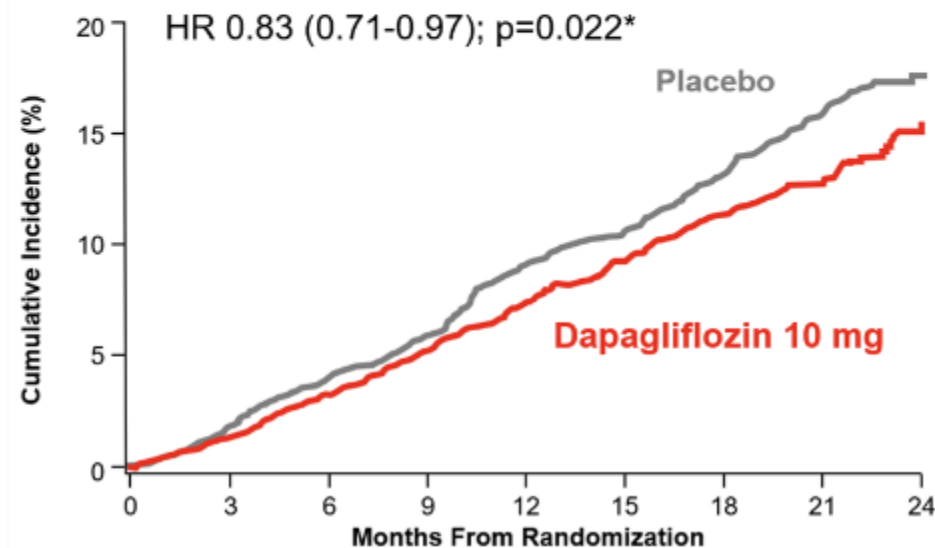
# Dapagliflozin 針對HFrEF，顯著減少心血管死亡、總死亡



## CV Death



## All-cause Mortality







# 2021 ESC Heart Failure Guideline

## HFmrEF/HFpEF治療仍存在未滿足的需求



- **ACEI/ARB, Beta-blockers, MRA, ARNI (Class IIb)**
- Similar with HFrEF treatment

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Diuretics are recommended in patients with congestion and HFmrEF in order to alleviate symptoms and signs. <sup>137</sup>	I	C
An <b>ACE-I</b> may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. <sup>11</sup>	IIb	C
An <b>ARB</b> may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. <sup>245</sup>	IIb	C
A <b>beta-blocker</b> may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. <sup>12,119</sup>	IIb	C
An <b>MRA</b> may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. <sup>246</sup>	IIb	C
<b>Sacubitril/valsartan</b> may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. <sup>13,247</sup>	IIb	C

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- **Diuretics**

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Screening for, and treatment of, aetiologies, and cardiovascular and non-cardiovascular comorbidities is recommended in patients with HFpEF (see relevant sections of this document).	I	C
<b>Diuretics</b> are recommended in congested patients with HFpEF in order to alleviate symptoms and signs. <sup>137</sup>	I	C

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# HFpEF照護新契機—SGLT2i



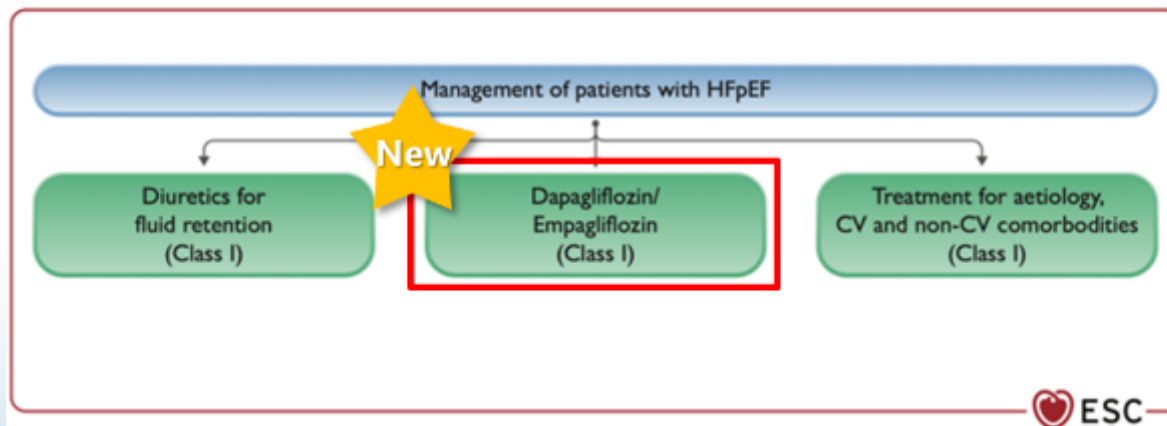
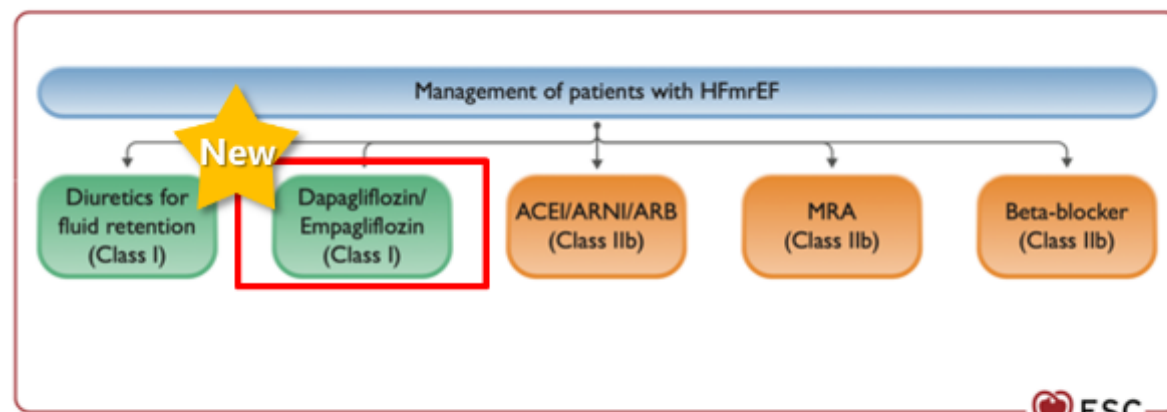
**Table 3 Comparison of DELIVER and other trials in heart failure with left ventricular ejection fraction >40%**

	CHARM-Preserved <sup>22</sup>	PEP-CHF <sup>23</sup>	I-PRESERVE <sup>24</sup>	TOPCAT <sup>25</sup>	PARAGON-HF <sup>17</sup>	EMPEROR-Preserved <sup>26</sup>	DELIVER
Patients, n	3023	850	4128	3445	4800	5988	6200
Treatment arms	Candesartan vs. placebo	Perindopril vs. placebo	Irbesartan vs. placebo	Spironolactone vs. placebo	Sacubitril/valsartan vs. valsartan	Empagliflozin vs. placebo	Dapagliflozin vs. placebo
Key inclusion criteria	NYHA class II–IV, prior CV hospitalization	Clinical diagnosis of DHF with ≥ signs/symptoms of HF, ≥ 2 of the following: LAE/LVH/impaired left ventricular filling/AF	NYHA class II–IV + any corroborating evidence (e.g. HF sign), LVH or LAE considered optional corroborating evidence, HFH required unless in NYHA class III–IV	≥ 1 HF symptom + ≥ 1 HF sign, elevated NP or HFH	NYHA class II–IV, elevated NT-proBNP (adjusted for AF and higher if no recent HF hospitalization), structural heart disease (LAE or LVH)	NYHA class II–IV, elevated NT-proBNP	NYHA class II–IV, elevated NT-proBNP (adjusted for AF), structural heart disease (LAE or LVH)
LVEF cutpoint	>40%	>40%	≥45%	≥45%	≥45%	>40%	>40%
Endpoint	First of either CV death or HFH	First of either all-cause death or HFH	First of either all-cause death or hospitalization for a CV cause	First of either CV death, HFH, or RSD	CV death and total HFH (first and recurrent)	CV death or HFH	CV death or HFH either in the full population or in patients with LVEF <60%

AF, atrial fibrillation; CV, cardiovascular; DHF, diastolic heart failure; HF, heart failure; HFH, heart failure hospitalization; LAE, left atrial enlargement; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; NP, natriuretic peptide; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association.



## 2023 ESC Focused Update HFmrEF & HFpEF建議使用SGLT2i (Class 1A)



An SGLT2 inhibitor (**dapagliflozin** or **empagliflozin**) is recommended in patients with **HFmrEF/HFpEF** to reduce the risk of HF hospitalization or CV death.



Dapagliflozin reduced the primary endpoint of CV death or worsening HF (HF hospitalization or urgent HF visit) (HR 0.82, 95% CI 0.73–0.92;  $P < .001$ ). Once again, the principal effect was due to a reduction in worsening HF and there was no reduction in CV death. Dapagliflozin also improved symptom burden. The effects were independent of T2DM status.<sup>6</sup> The efficacy of dapagliflozin was consistent in those who remained symptomatic, despite **improved LVEF**, suggesting that these patients may also benefit from SGLT2 inhibition.<sup>6,22</sup> The benefit of dapagliflozin was also consistent across the range of LVEF studied.<sup>6,23</sup> The background use of therapies for concomitant CV disease was high: 77% were on a loop diuretic, 77% were on an ACE-I/ARB/ARNI, 83% were on a beta-blocker, and 43% were on an MRA.<sup>6</sup>

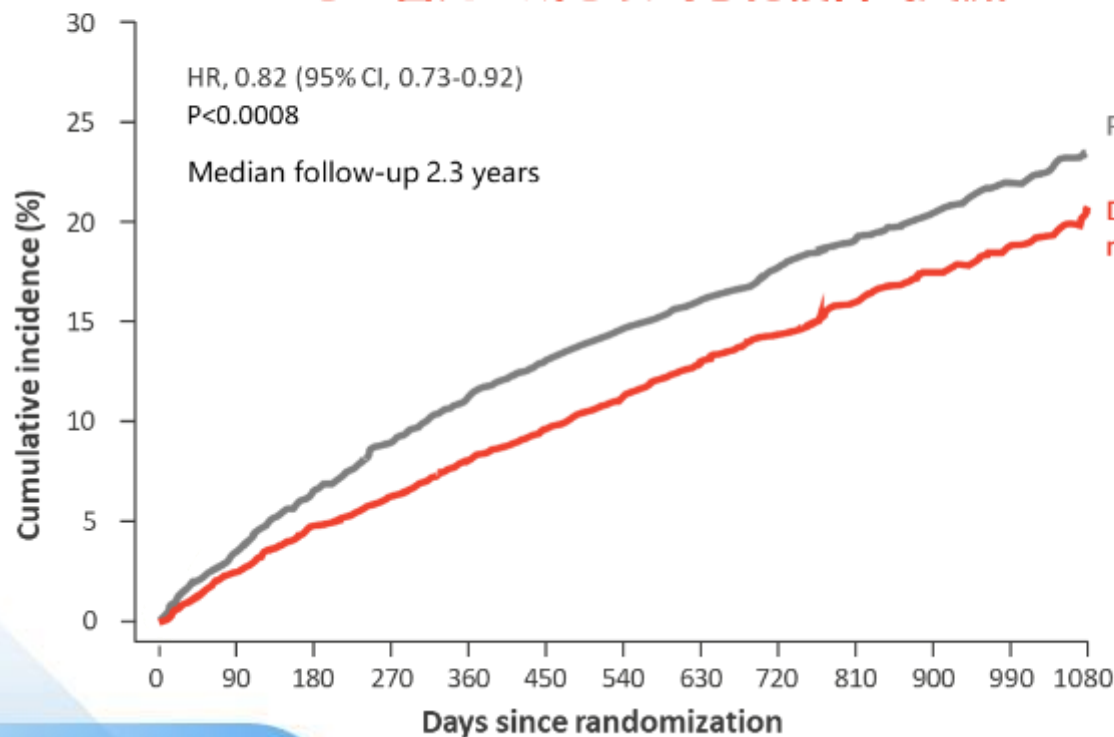


# Dapagliflozin 減少心血管死亡或心衰竭惡化 13天 顯著減少主要試驗終點



主要試驗終點

心血管死亡或心衰竭惡化複合式終點<sup>a</sup>



18%  
RRR

HFimpEF族群

26%  
RRR

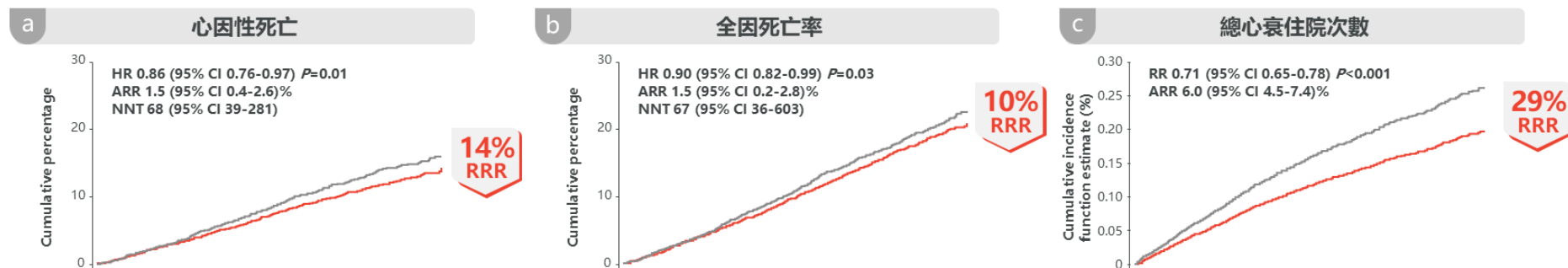
HR 0.74, 95% CI 0.56 - 0.97

\*包含 HFpEF或HFimpEF <sup>a</sup>心衰竭住院與心衰竭緊急就醫

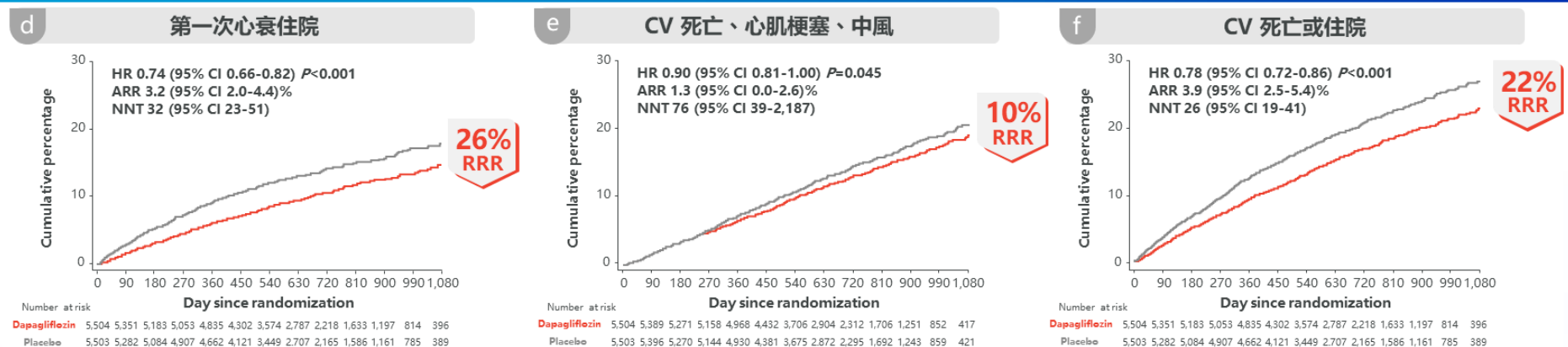
1. Solomon, S.D. et al. J Am Coll Cardiol HF. 2022;10(3):184-197. 2. Solomon SD et al. Online ahead of print. N Engl J Med. 2022



# DAPA-HF & DELIVER: 不論LVEF高低， 總死亡率、CV死亡、心衰竭住院風險等皆下降



## Consistency across LVEF spectrum





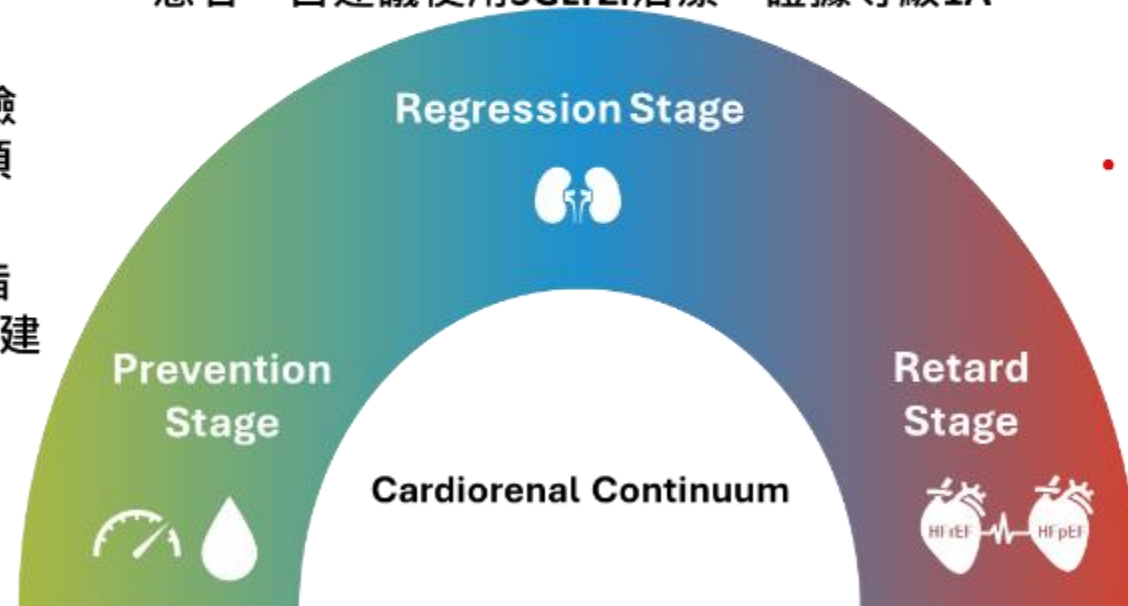


# 總結

腎臟和心臟的急性或慢性功能變化導致另一器官功能惡化，SGLT2i提供心腎雙護療效，  
從預防到治療，**針對高風險族群應及早治療，降低心腎風險**

- 腎功能越差，心衰及死亡風險越高，及時護腎維持心臟功能、降低死亡
- 2024 KDIGO CKD治療指引更新：CKD合併T2D、CKD合併心衰或 $\text{eGFR} \geq 20 \text{ ml/min/1.73m}^2 + \text{UACR} \geq 200 \text{ mg/g}$  的成人患者，皆建議使用SGLT2i治療，證據等級1A

- **高血壓與糖尿病**為HF高風險族群，及早透過共病管理預防心腎風險
- 2023 ESC/ESH 高血壓治療指引：高血壓合併T2D患者，建議使用SGLT2i降低心腎風險



- 2023 ESC 高血壓與心衰竭治療指引：HF患者無論是否合併HTN、CKD或T2D，一致建議使用SGLT2i降低心腎風險和CV死亡

# Thanks for listening !

