



# 心腎共病的臨床照護實務經驗分享—— 以慢性腎臟病合併心衰竭為例

林口長庚紀念醫院 腎臟科  
陳冠興 醫師

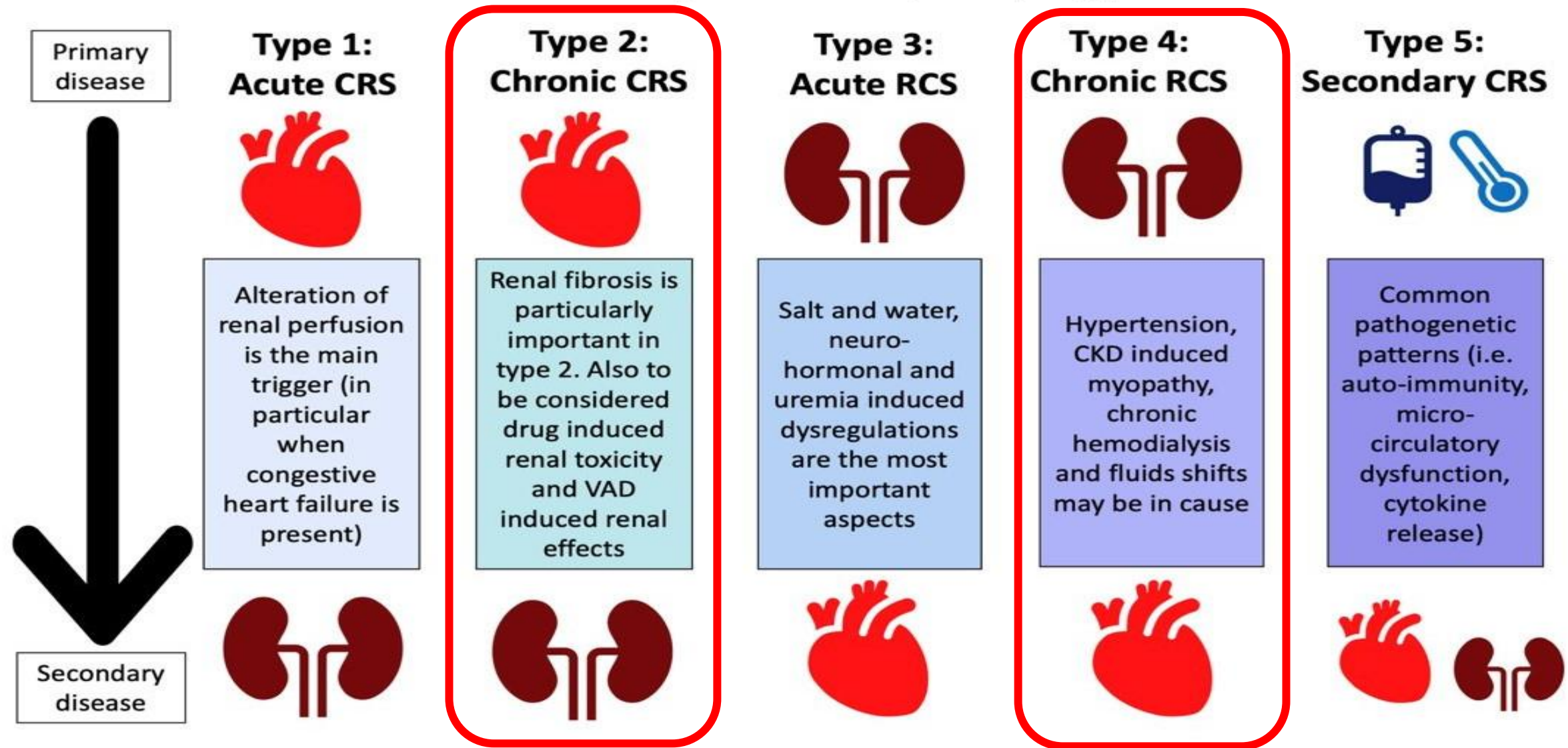
2024.06



# 大綱

- 心衰竭治療的挑戰與困境
- 個案分享: 慢性腎臟病合併心衰竭之治療經驗
- 從實證至臨床: 如何為患者提供全方位心腎保護
- 總結

# Cardiorenal Syndrome (CRS) Types

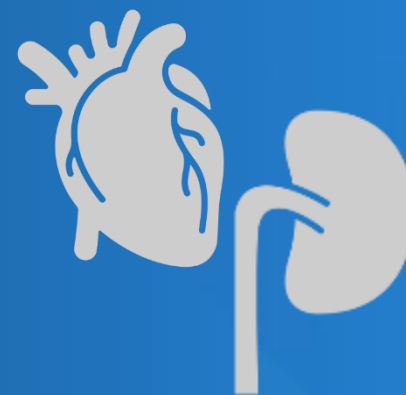


Schematic representation of the five Cardiorenal syndrome (CRS) types according to the organ direction (primary > secondary disease) and the time window (acute or chronic). According to this classification, two CRS (acute and chronic), two renocardiac (acute and chronic) syndromes, and one secondary CRS are depicted.

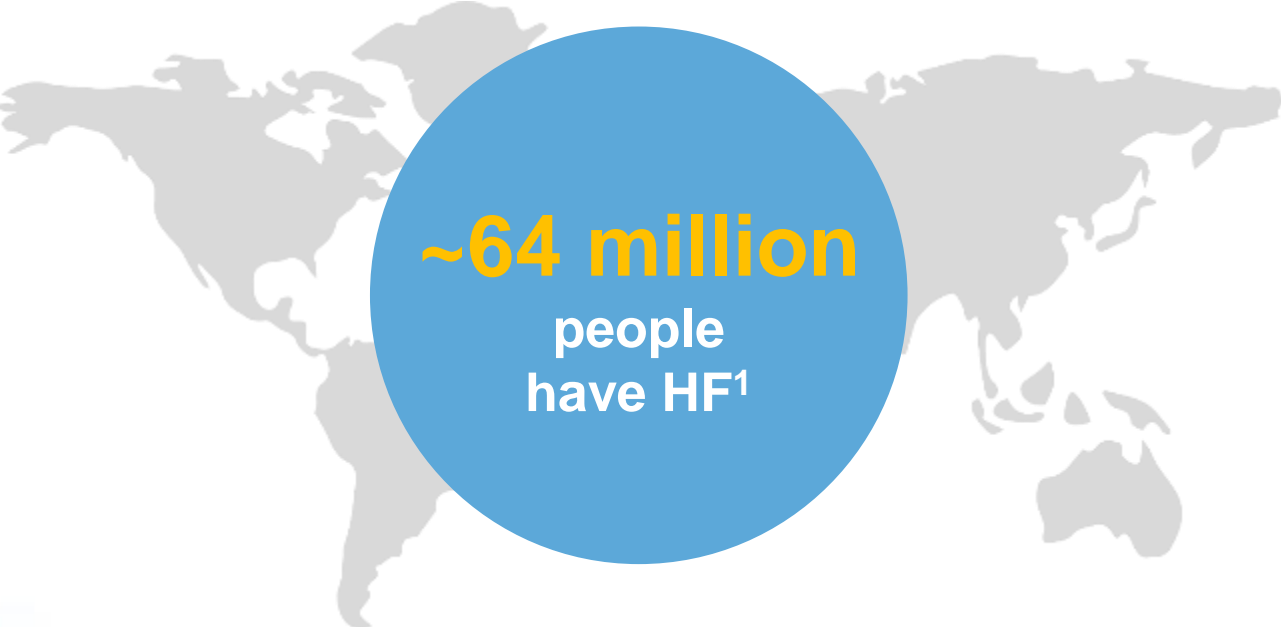
CKD, chronic kidney disease; RCS, renocardiac syndrome; VAD, ventricular assist device.



# 心衰竭治療的挑戰與困境



# 心衰竭影響全球近6400萬人，患者五年內死亡率高達50%



**~64 million**  
people  
have HF<sup>1</sup>



Projected **~24% rise in cases** between 2012 and 2030<sup>2</sup>



5-year **mortality rate ~50%**<sup>3</sup>



HF **mortality risk is similar** to some of the common **cancers (Cardiac cancer !)** in both men and women<sup>4</sup>



Economic burden **~350 billion US dollars**<sup>2</sup>



**Over 50%** of patients with HF have **HFpEF**<sup>5</sup>

HF = heart failure; HFpEF = heart failure with preserved ejection fraction; US = United States.

1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. *Lancet*. 2018;392:1789-1858; 2. Lippi G et al. *AME Med J*. 2020;5:15; 3. Jones NR et al. *Eur J Heart Fail*. 2019;21:1306-1325; 4. Mamas AM et al. *Eur J Heart Fail*. 2017;19:1095-1104; 5. Omote K et al. Online ahead of print. *Annu Rev Med*. 2021.





## 心衰竭為住院主要原因，造成全球嚴重醫療負擔



**1<sup>st</sup> cause of hospitalizations** in people over 65 years of age<sup>1,a</sup>



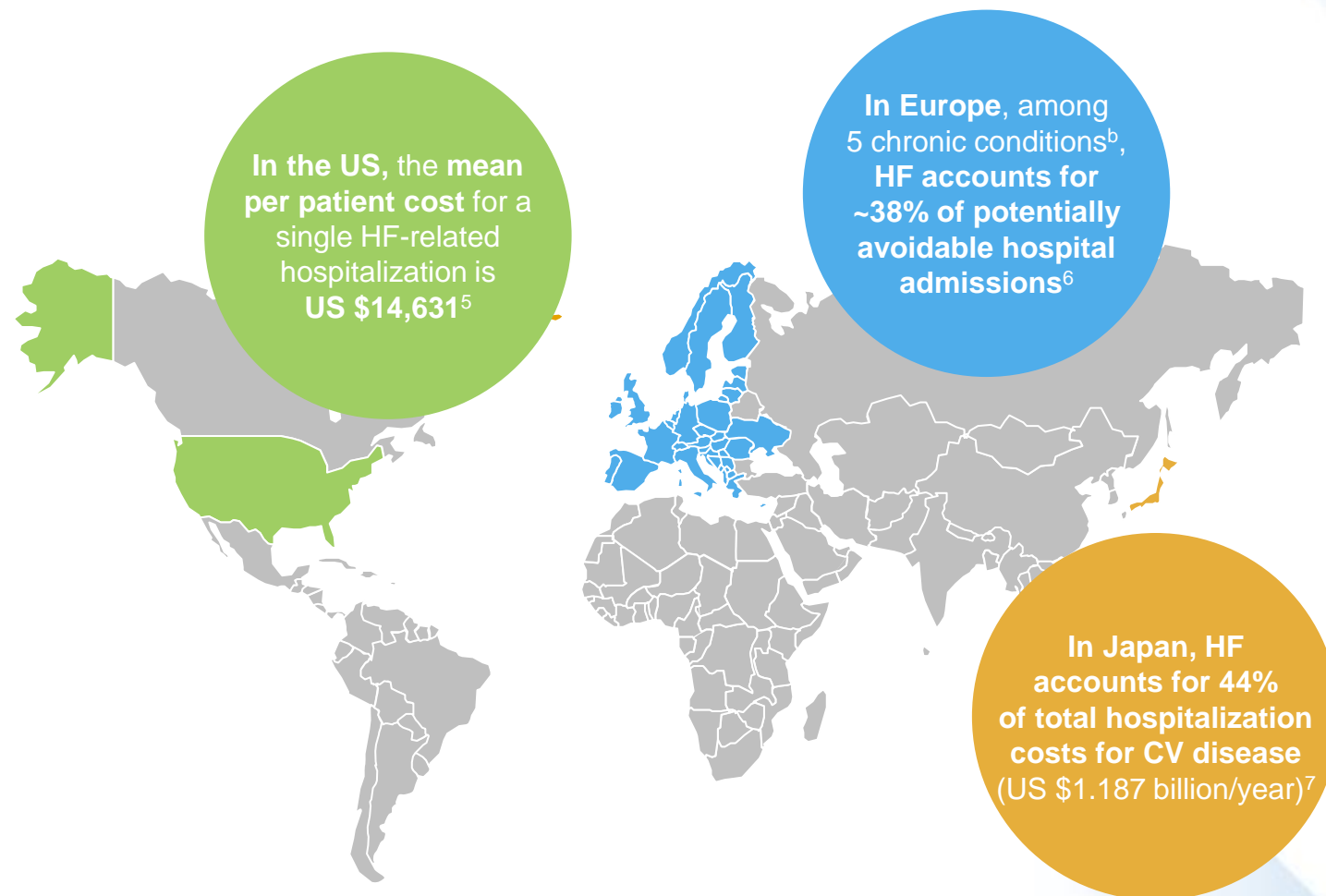
**1<sup>st</sup> cause of unplanned hospital readmission<sup>2</sup>**



**Global direct cost of HF,** which includes hospitalizations, is **~\$65 billion<sup>3</sup>**



Hospital admissions for HF are **projected to rise by ~50%** over the next 25 years<sup>4</sup>



aIn developed countries; bOther chronic conditions include diabetes, hypertension, COPD/bronchiectasis, and asthma.

COPD = chronic obstructive pulmonary disease; CV = cardiovascular; HF = heart failure; US = United States.

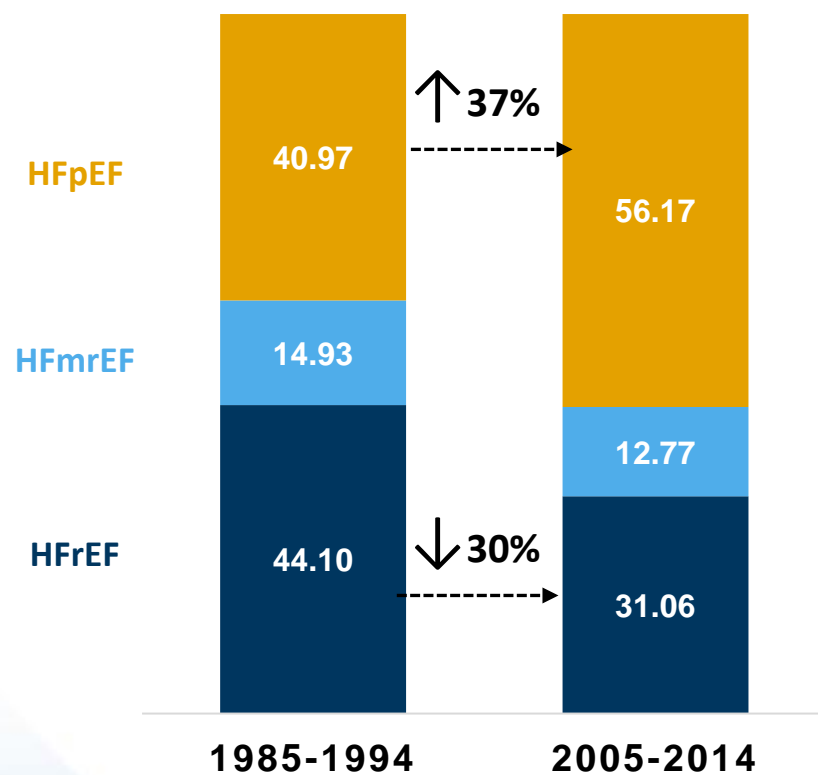
1. Cowie MR et al. ESC Heart Fail. 2014;1:110-145; 2. Gheorghiade M et al. J Am Coll Cardiol. 2013;61:391-403; 3. Cook C et al. Int J Cardiol. 2014;171:368-376; 4. Groenewegen A et al. Eur J Heart Fail. 2020;22:1342-1356; 5. Kilgore M et al. Risk Manag Healthc Policy. 2017;10:63-70; 6. Health at a glance: Europe 2018: state of health in the EU cycle. [https://doi.org/10.1787/health\\_glance\\_eur-2018-en](https://doi.org/10.1787/health_glance_eur-2018-en). Accessed August 6, 2021; 7. Kanaoka K et al. Circ J. 2019;83:1025-1031.

## New HF classification

	LVEF	Other parameter(s) needed for the definition
<b>HFrEF</b>	$\leq 40\%$	-
<b>HFimpEF</b>	$> 40\%$	previous LVEF $\leq 40\%$
<b>HFmrEF</b>	41-49%	evidence of spontaneous or provokable increased LV filling pressures*
<b>HFpEF</b>	$\geq 50\%$	evidence of spontaneous or provokable increased LV filling pressures*

# 心衰竭盛行率逐年上升，其中56%為HFpEF病患

Percentage of Patients Within Each LVEF Category<sup>1,a</sup>



Reasons for Increased HFpEF Prevalence<sup>2</sup>

## Increasing Life Expectancy and Aging of the Population

- Global population is rapidly aging
- Rate of HFpEF among patients with HF increases with age
- Increase in comorbidities associated with aging

## Epidemic of Cardiac and Non-cardiac Comorbidities

- Improved survival after onset of CAD
- Rate of AF increasing due to an aging general population and increased longevity
- Increasing incidence of obesity, metabolic syndrome, and diabetes

## Increased Clinical Recognition

- Improved diagnostic techniques
- Development of diagnostic guidelines

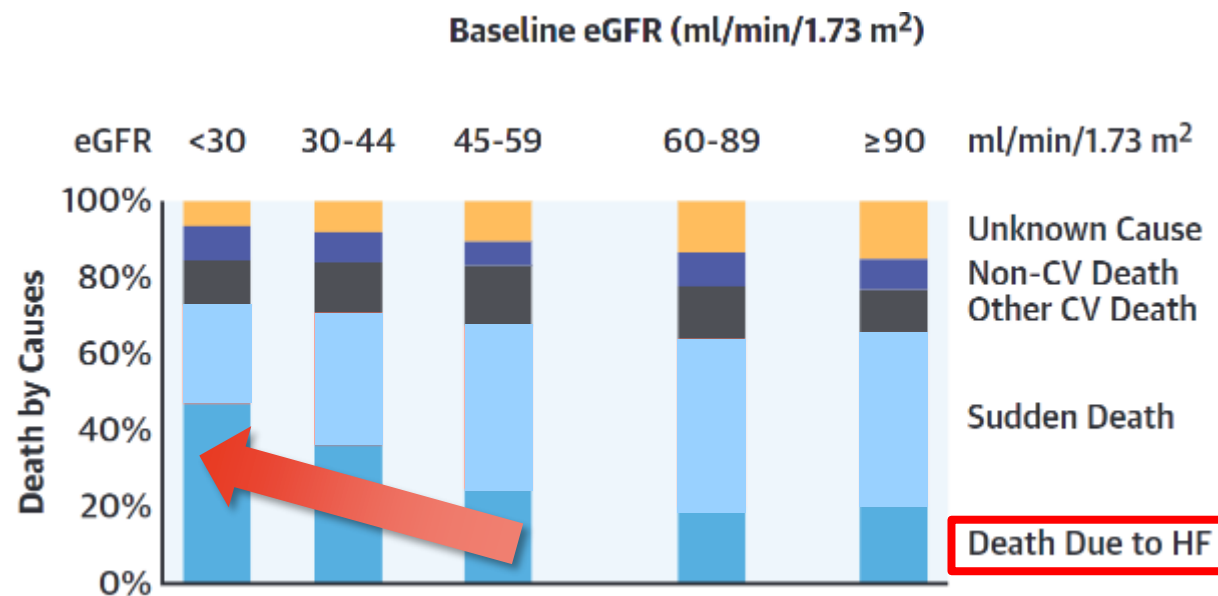
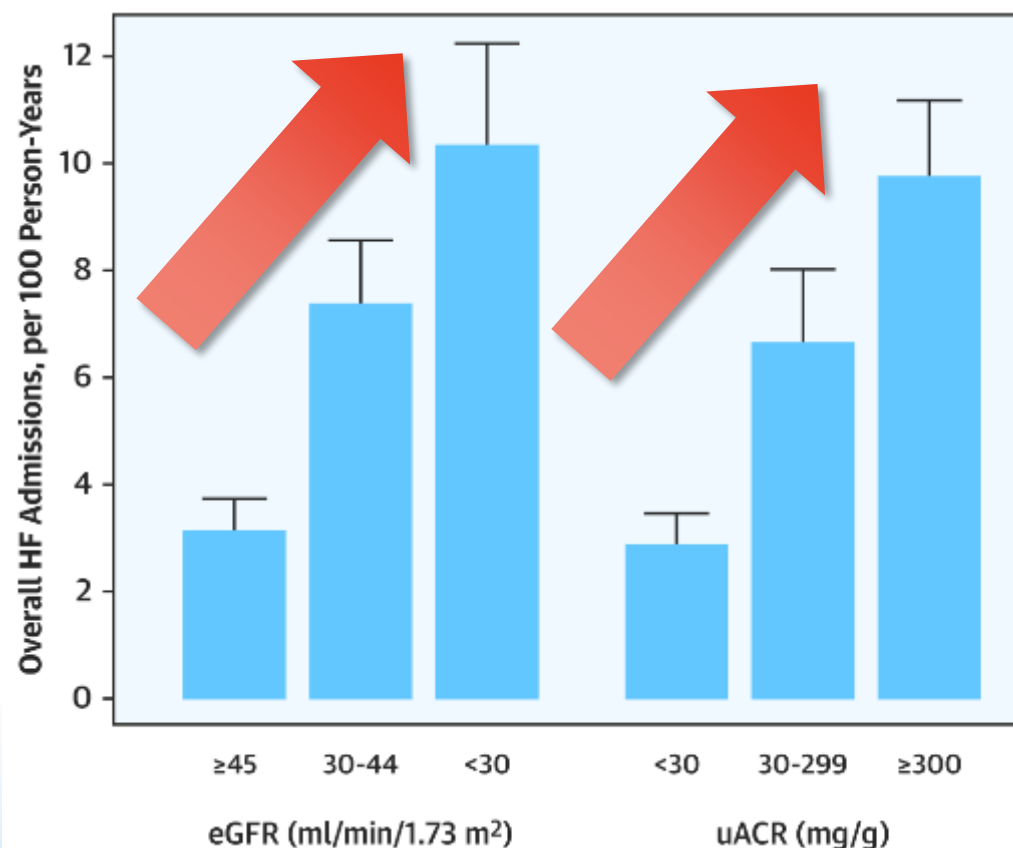
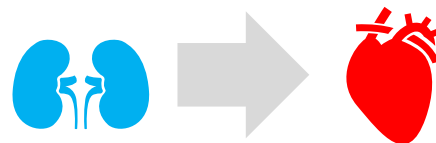
aHF prevalence data for 894 outpatients with new onset HF from the community based, Framingham Study over 3 decades (1985-2014). LVEF categories were defined as HFrEF (EF <40%), HF with mid-range EF (EF 40-<50%), and HFpEF (EF ≥50%).

AF = atrial fibrillation; CAD = coronary artery disease; EF = ejection fraction; HF = heart failure; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction.

1. Vasan RS et al. JACC Cardiovasc Imaging. 2018;11:1-11; 2. Oktay AA et al. Curr Heart Fail Rep. 2013;10:401-410.



## 腎功能越差，HF患者的住院與死亡風險越高

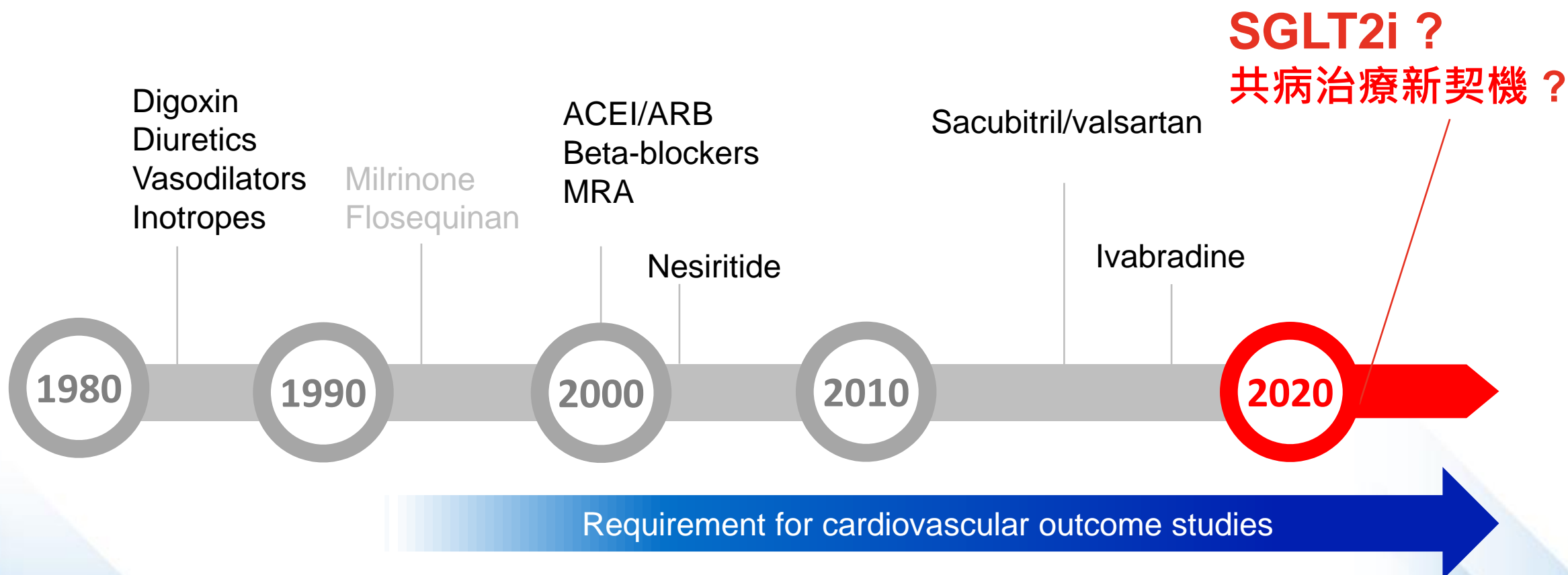


### Cause of Death in patients with HF by eGFR

Analysis of 16,740 individual patients with left ventricular ejection fraction <50% from 10 double-blind, placebo-controlled trials



# The History of Heart Failure Medicine





## 心衰竭治療目標典範轉移：強調心腎共護概念

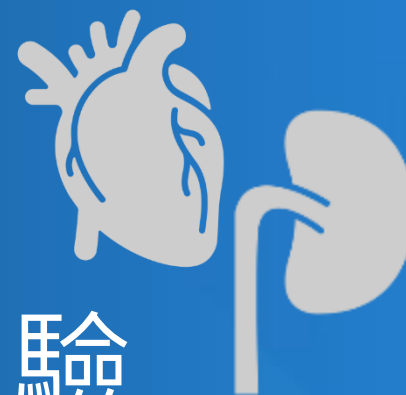
- ✓ 提升存活率
- ✓ 減少心衰住院事件
- ✓ 改善症狀並預防惡化
- ✓ 預防或延緩腎臟功能惡化



PROFESSOR JOHN MCMURRAY



# 個案分享： 慢性腎臟病合併心衰竭之治療經驗





## 個案簡介



黃先生  
61歲 工廠員工

### History

DM	V
Hypertension	V
Dyslipidemia	V
Smoking	x
CKD	V
MI	V
Gout	V

最近一次就診發現

### 症狀描述:

最近數週發生較容易累，爬樓梯會喘，晚上躺平會覺得不舒服，腳有水腫等現象....

### Biometric

HbA1c (%)	7.5
eGFR (ml/min/1.73m <sup>2</sup> )	43 (IIIb)
UACR (mg/g)	1200
Serum Creatinine (mg/dl)	1.9
BP (mm Hg)	136/92
LDL (mg/dL)	70
Uric acid (mg/dL)	5.6



# CKD風險分期情況



			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 <sup>2</sup> ) Description and range	G1	≥90	Green	Yellow	Orange
	G2	60-90	Green	Yellow	Orange
	G3a	45-59	Yellow	Orange	Red
	G3b	30-44	Orange	Red	Red
	G4	15-29	Red	Red	Red
	G5	<15	Red	Red	Red



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

## 治療經驗分享



### 目前用藥

#### Current Medication

- ARB (Sevikar)
- Linagliptin / Metformin
- Stain (Rosuvastatin)
- Diuretics
- Febuxostat
- Pentoxifylline
- Aspirin

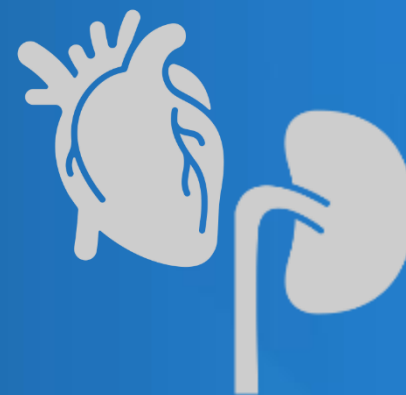


#### 本次藥物調整的治療目標

**降低蛋白尿、改善心衰竭、  
減少腎病變風險、穩定血糖**



# 從實證至臨床： 如何為患者提供全方位心腎保護





# 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

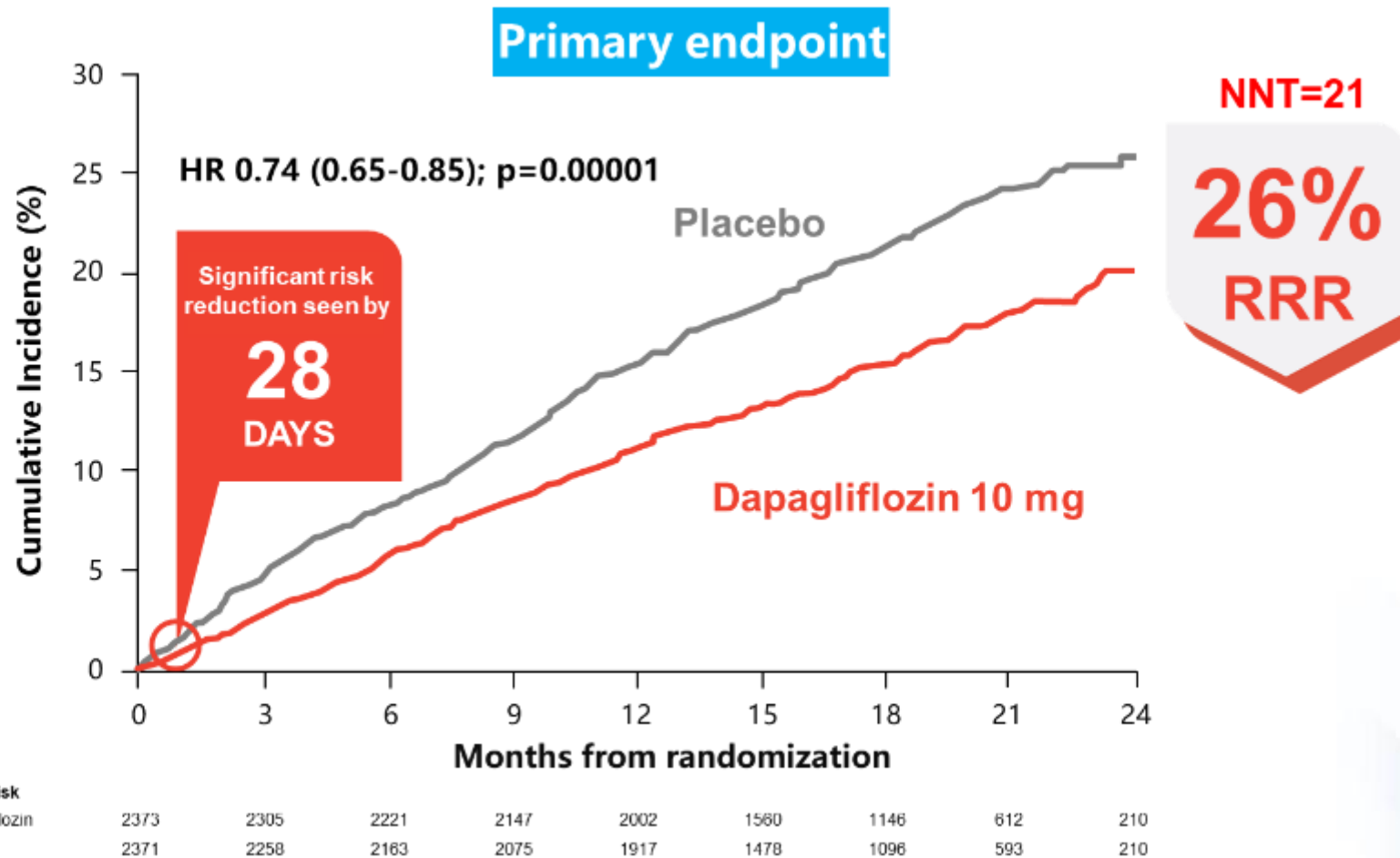
SGLT2i (1)

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

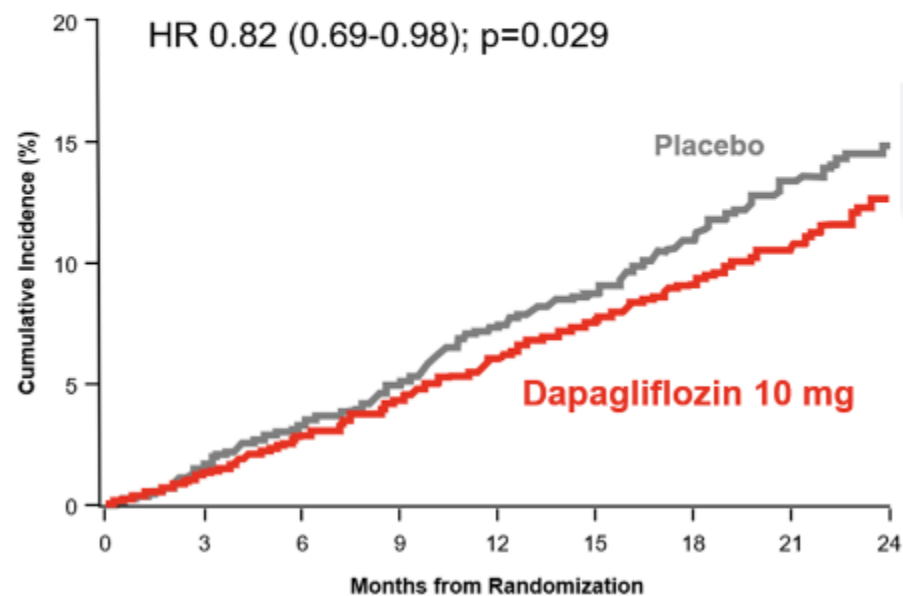




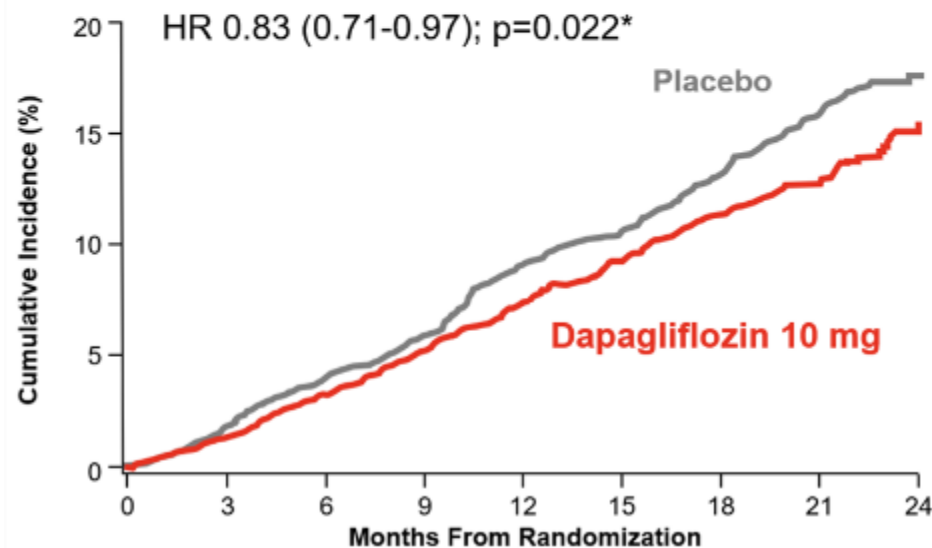
# Dapagliflozin 針對HFrEF，顯著減少心血管死亡、總死亡



## CV Death



## All-cause Mortality



# DAPA-HF 亞洲次族群分析：

亞洲vs其他地區，減少心血管死亡或心衰竭惡化減少程度一致

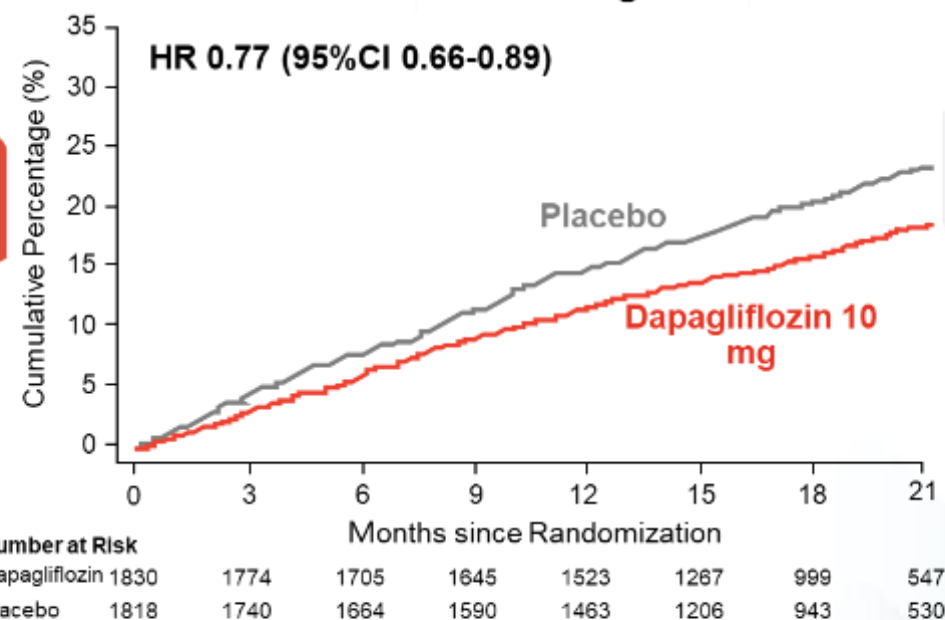
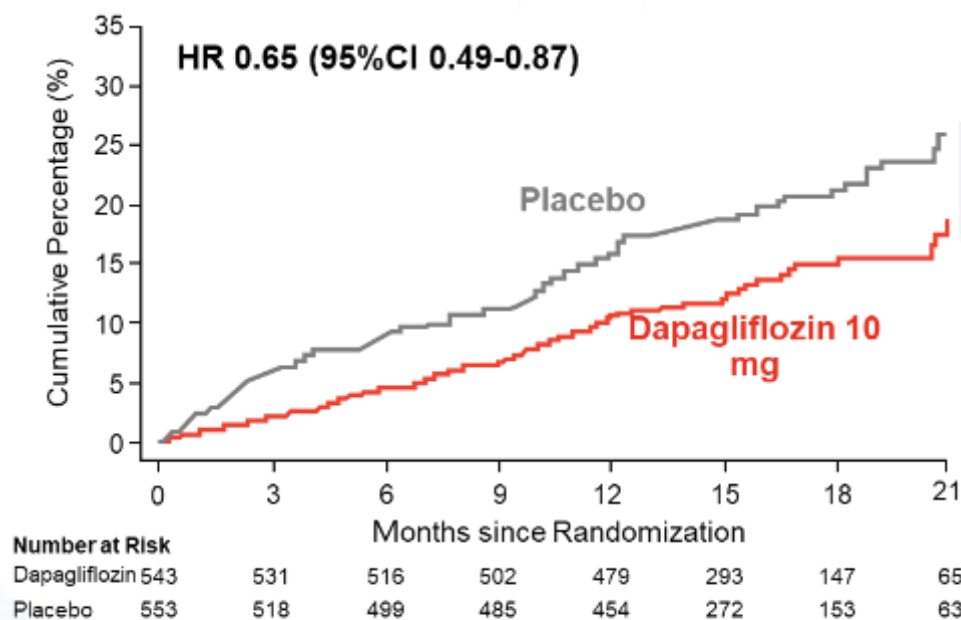


Primary endpoint

Worsening heart failure or CV death

Asia

Other Regions



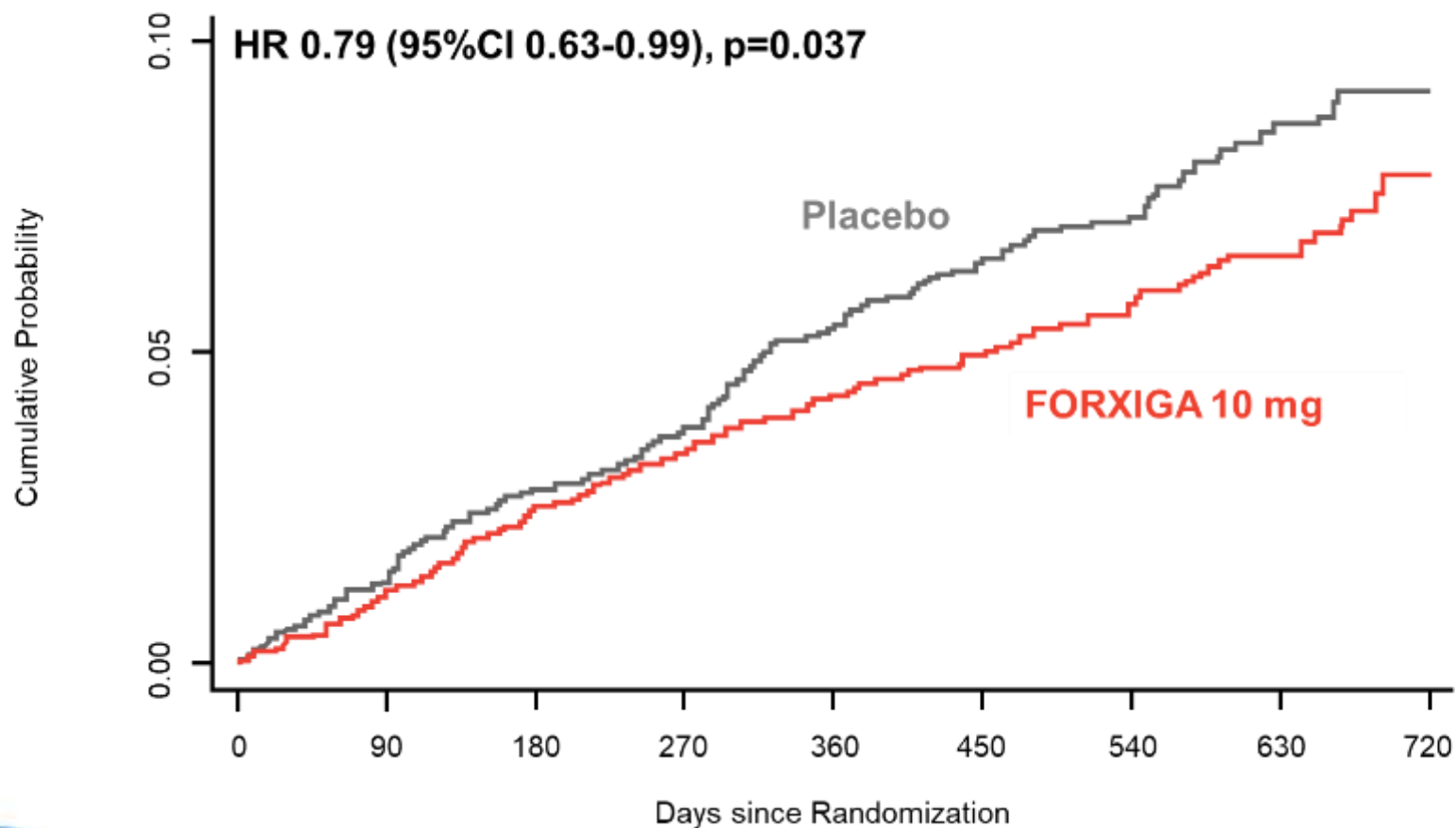
Interaction p-value = 0.32



# Dapagliflozin治療HFrEF 觀察到 心室性心律不整、心臟驟停或猝死風險較低

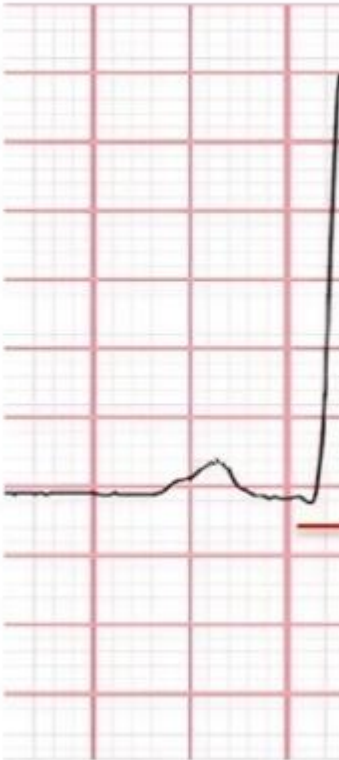


## Serious Ventricular Arrhythmia/Resuscitated Cardiac Arrest / Sudden Death



# Effect of Empagliflozin Treatment on Ventricular Repolarization Parameters

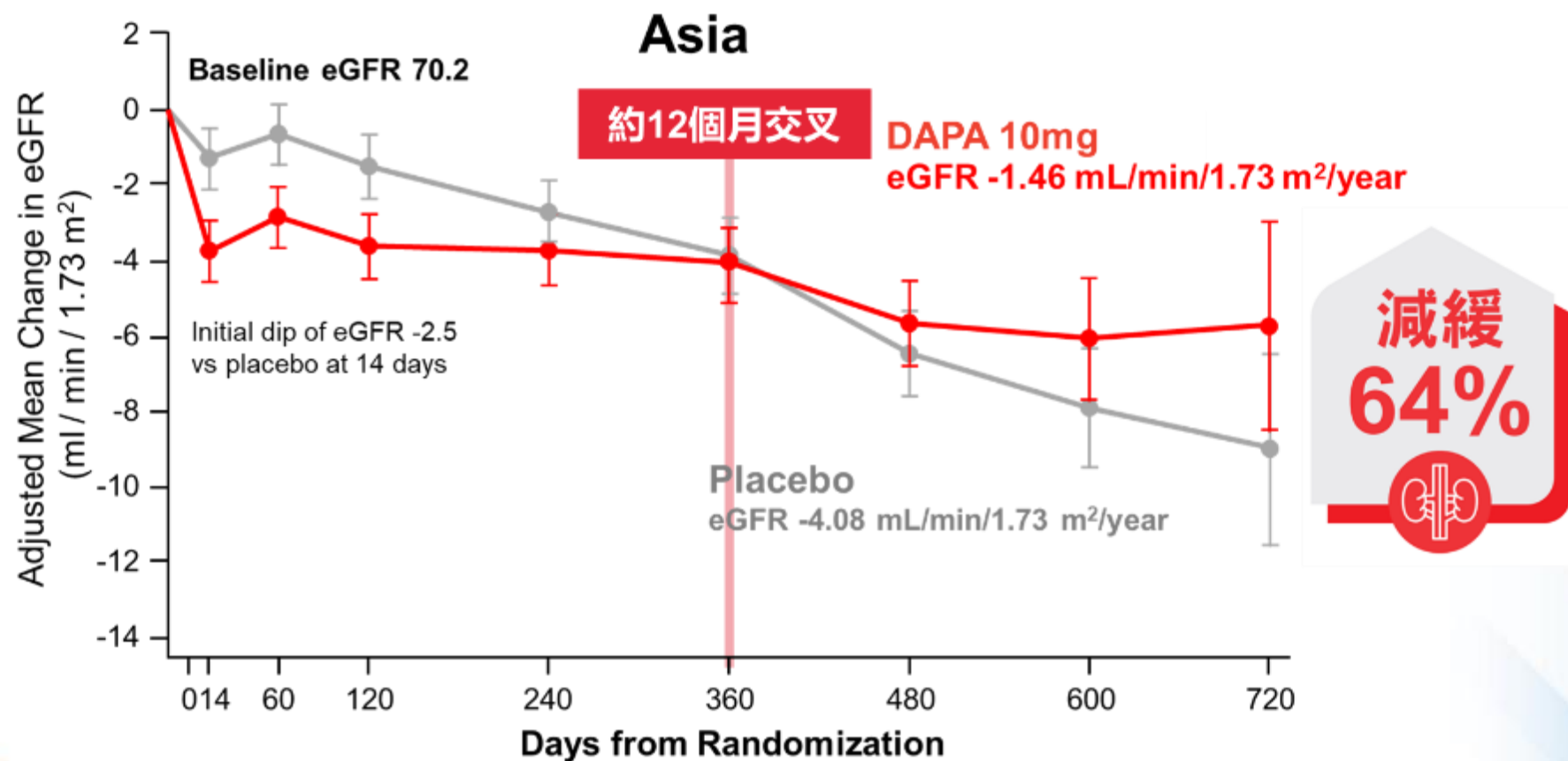
Rev. Cardiovasc. Med. 2024; 25(2): 64



Echocardiographic parameters	Before the treatment	After the treatment	<i>p</i>
LVEF (%)	58.6 ± 8.0	59.8 ± 8.5	0.254
LVEDD (mm)	47.2 ± 4.4	46.6 ± 3.6	0.287
LVESD (mm)	30.7 ± 2.2	30.1 ± 2.9	0.139
IVS (mm)	9.6 ± 1.5	9.6 ± 1.3	0.916
PW (mm)	9.6 ± 1.4	9.5 ± 1.4	0.683
LA (mm)	32.4 ± 4.7	32.3 ± 3.5	0.080
E (cm/s)	76.0 ± 14.9	72.6 ± 14.3	0.105
A (cm/s)	68.2 ± 14.3	66.9 ± 14.6	0.503
E/A ratio	1.1 ± 0.3	1.0 ± 0.4	0.097
Electrocardiography parameters			
HR (beat/min)	71.8 ± 11.1	74.2 ± 10.6	0.174
QT (msec)	408.5 ± 22.9	378.8 ± 14.1	<0.001
QTc (msec)	427.0 ± 20.5	404.7 ± 13.8	<0.001
QTd (msec)	52.1 ± 1.2	47.8 ± 1.7	<0.001
Tp-e (msec)	82.3 ± 8.7	67.1 ± 5.1	<0.001
Tp-e/QTc ratio	0.19 ± 0.01	0.17 ± 0.01	<0.001



# SGLT2i延緩腎功能惡化: 亞洲HFrEF患者使用Dapagliflozin eGFR下降減少64%







## 如何進行藥物搭配與調整以達到治療目標？

Date	2022/8/11	2022/8/18	2022/12/14	2023/8/24
Biometric	<ul style="list-style-type: none"><li>• A1C 7.5</li><li>• eGFR: 43</li><li>• UACR: 1200</li><li>• Cr. 1.9</li><li>• BP 142/72</li></ul>	<ul style="list-style-type: none"><li>• OPD 回診</li></ul>	<ul style="list-style-type: none"><li>• A1C 6.7</li><li>• eGFR: 39</li><li>• UACR: 700</li><li>• Cr. 2.0</li><li>• BP 128/65</li></ul>	<ul style="list-style-type: none"><li>• A1C 6.5</li><li>• eGFR: 41</li><li>• UACR: 610</li><li>• Cr. 1.95</li><li>• BP 130/66</li></ul>
Description			<ul style="list-style-type: none"><li>• 泡泡尿有減少, 喘的狀況有改善, 血糖自我監測也有比較好</li></ul>	<ul style="list-style-type: none"><li>• 狀況穩定且有進步</li></ul>
Medication	<ul style="list-style-type: none"><li>• Lina 1# qd</li><li>• Metformin 1# bid</li><li>• Sevika 1# qd</li></ul>	<ul style="list-style-type: none"><li>• Dapa 1# qd</li><li>• Metformin 1# bid</li><li>• Sevika 1# qd</li></ul>	<ul style="list-style-type: none"><li>• Dapa 1# qd</li><li>• Metformin 1# qd</li><li>• Sevika 1# qd</li></ul>	<ul style="list-style-type: none"><li>• Dapa 1# qd</li><li>• Metformin 1# qd</li><li>• Sevika 1# qd</li></ul>

## 藥物介入後患者變化(續)

Before Treatment



After Treatment



## 2023 ESC 治療指引更新



**2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure ESC Clinical Practice Guidelines**  
25 Aug 2023



**HFpEF & HFmrEF  
治療建議**



**HF 共病管理建議**

## 2023 ESC 治療指引更新



**2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure ESC Clinical Practice Guidelines**  
25 Aug 2023



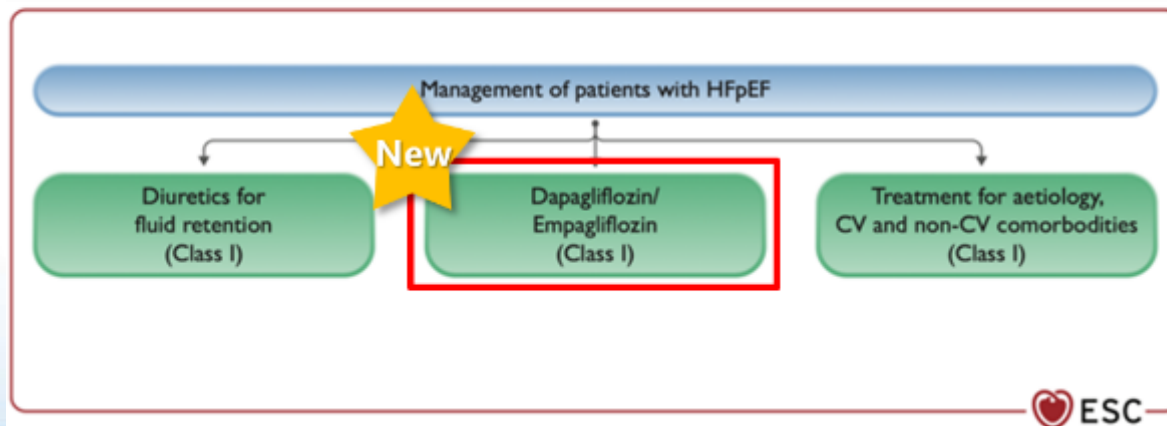
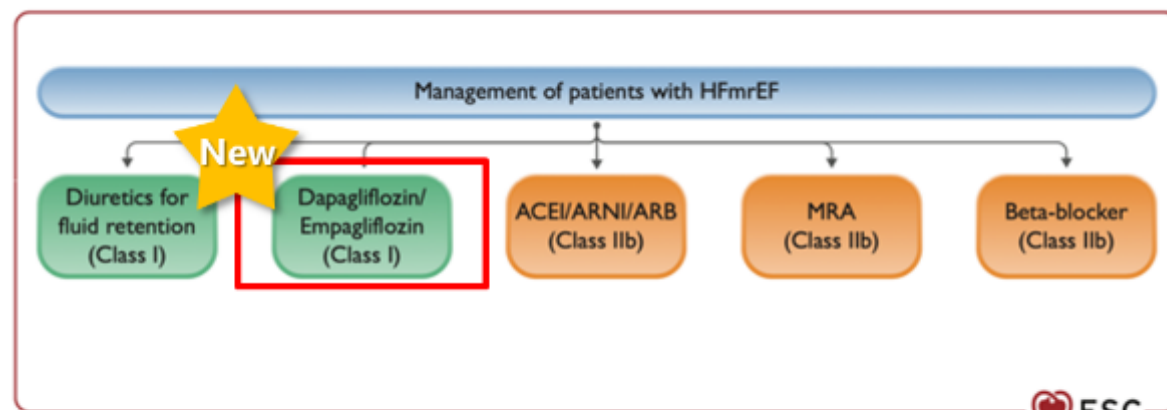
**HFpEF & HFmrEF  
治療建議**



**HF 共病管理建議**



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

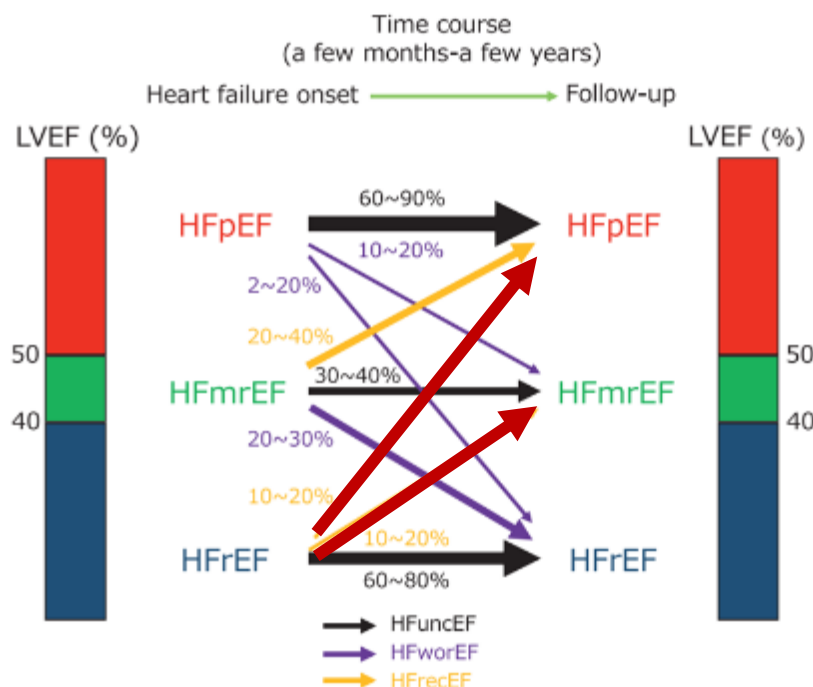


An SGLT2 inhibitor (**dapagliflozin** or **empagliflozin**) is recommended in patients with **HFmrEF/HFpEF** to reduce the risk of HF hospitalization or CV death.



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>

HFpEF 族群中: 約四成的心衰患者為HFrEF進展為HFimpEF  
許多心衰臨床試驗排除此類患者



### HFimpEF Definition

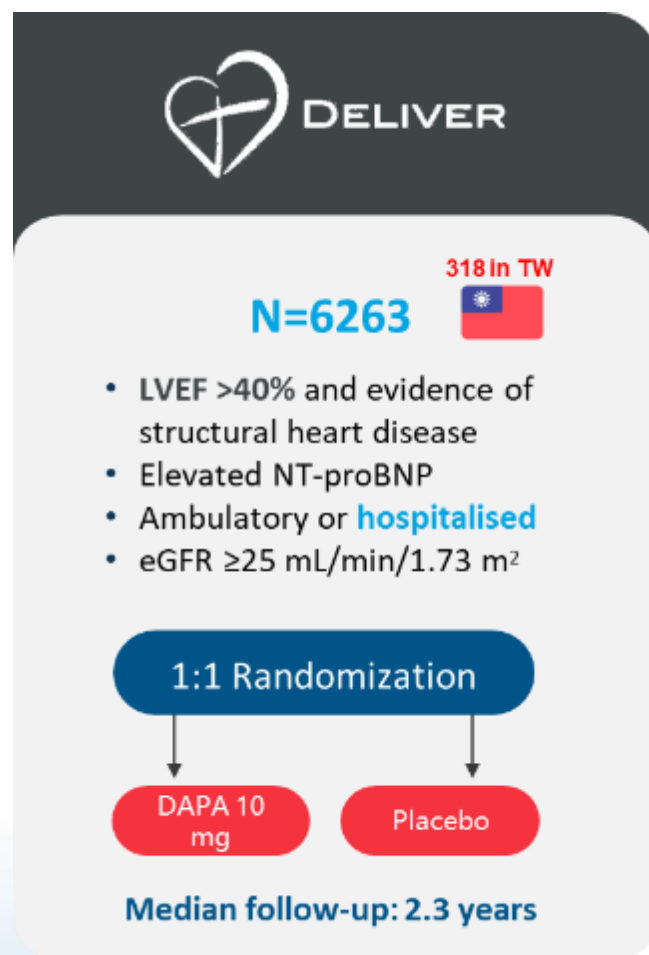
- **ESC:** HF with a second measurement of LVEF > 40% and a **≥10% increase** from baseline LVEF of ≤ 40% was defined as HFimpEF
- **AHA/ACC/HFSA:** Previous LVEF ≤40% and a follow-up measurement of LVEF >40%

*Excluded by both HFrEF and HFpEF trials*

**DELIVER唯一收錄 HFimpEF (18%) 的 HFpEF 試驗**



# DELIVER試驗設計: 符合臨床上常見的LVEF>40%心衰患者



## PRIMARY ENDPOINT<sup>2</sup>

Composite of CV death or worsening HF (hHF or an urgent HF visit)



- Full patient population
- Patients with LVEF <60%

## SECONDARY ENDPOINTS<sup>2</sup>

- Total number of hHF (first and recurrent) and CV death
- Change in KCCQ-TSS from baseline to 32 weeks
- CV death
- All-cause mortality

## BASELINE CHARACTERISTICS<sup>1,2</sup>

**1011 pg/mL**  
Median NT-proBNP

**54%**  
Average LVEF

**55%**  
Without T2D

**50%**  
With an eGFR <60 mL/min/1.73 m<sup>2</sup>

**10%**  
Hospitalized or recently discharged

**18%**  
With prior LVEF  $\leq 40\%$  (HFimpEF Patient)

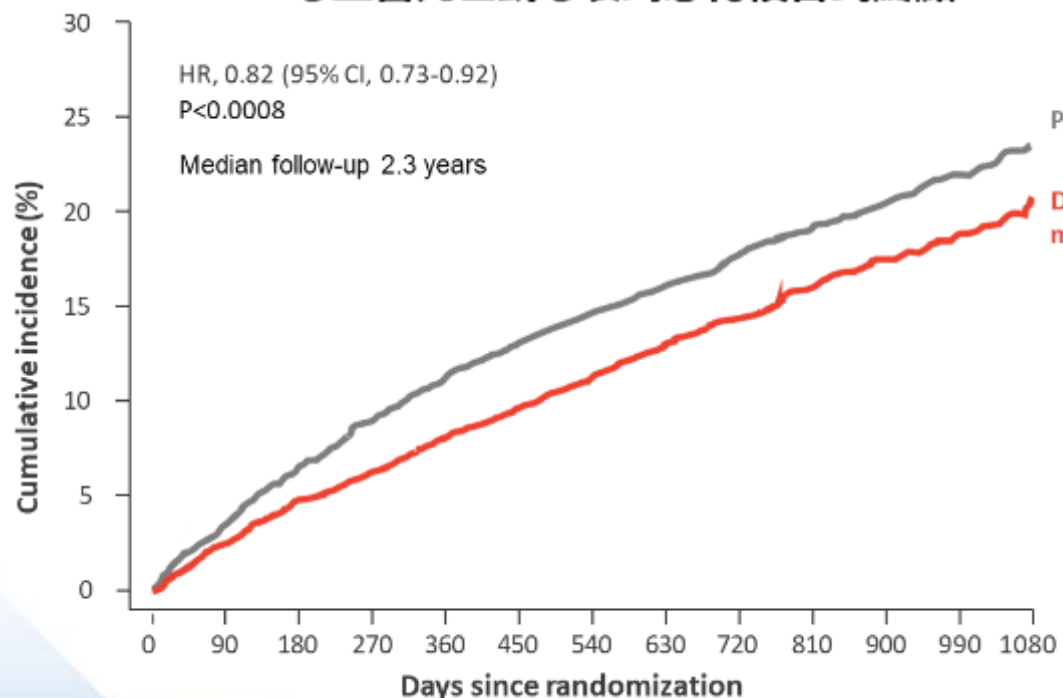


# DELIVER試驗: Dapagliflozin 顯著減少心血管死亡或心衰竭惡化



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

心衰住院或  
心血管死亡

20%  
RRR

95% CI 0.71, 0.91  
P <0.001

心衰惡化和心血  
管死亡事件數

23%  
RRR

95% CI 0.67, 0.89  
P <0.001

<sup>a</sup>hHF or an urgent HF visit. 1. Solomon, S.D. et al. J Am Coll Cardiol HF. 2022;10(3):184–197. 2. N Engl J Med. 2022 Sep 22;387(12):1089-1098

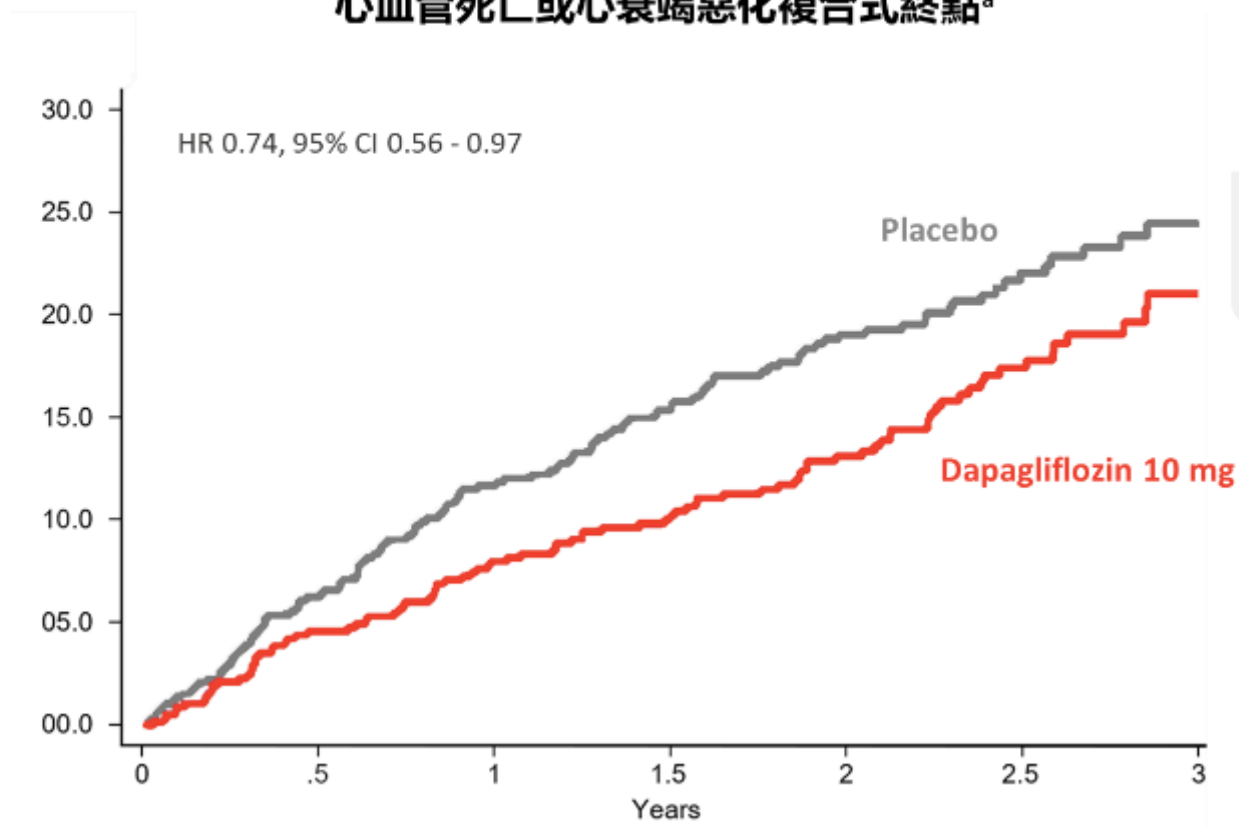


# 針對HFimpEF患者 Dapagliflozin同樣顯著下降主要試驗終點



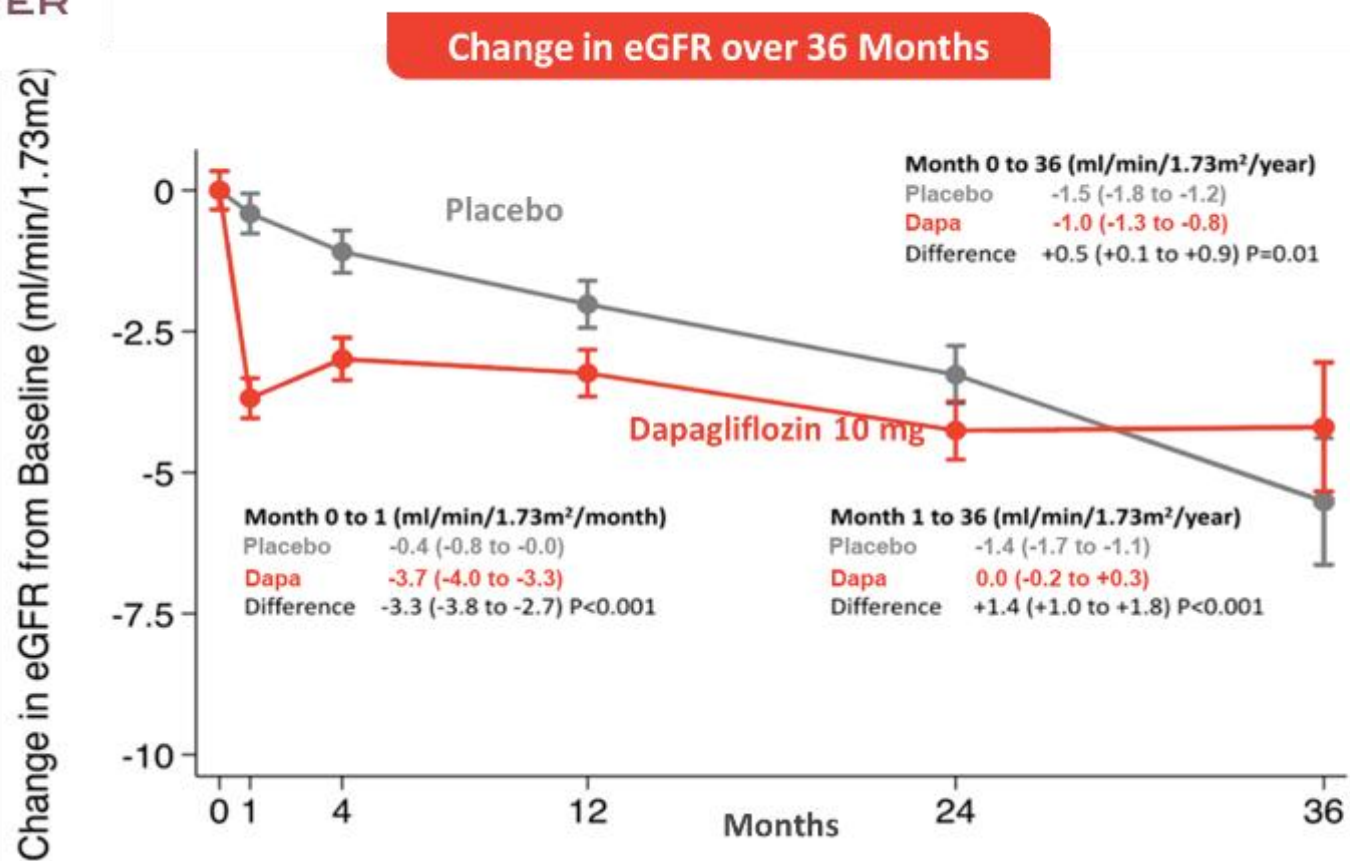
## 主要試驗終點

心血管死亡或心衰竭惡化複合式終點<sup>a</sup>



26%  
RRR

# Dapagliflozin延緩腎功能惡化 無論HFpEF或HFimpEF，eGFR下降減少33%



減緩  
33%

# DAPA-HF and DELIVER pooled dataset

Dapagliflozin 10mg once daily vs placebo

Median follow-up = 22 (IQR 17-30) months

收錄超過 11,000 位心衰竭病患<sup>1,2</sup>



<sup>a</sup>hHF or an urgent HF visit.

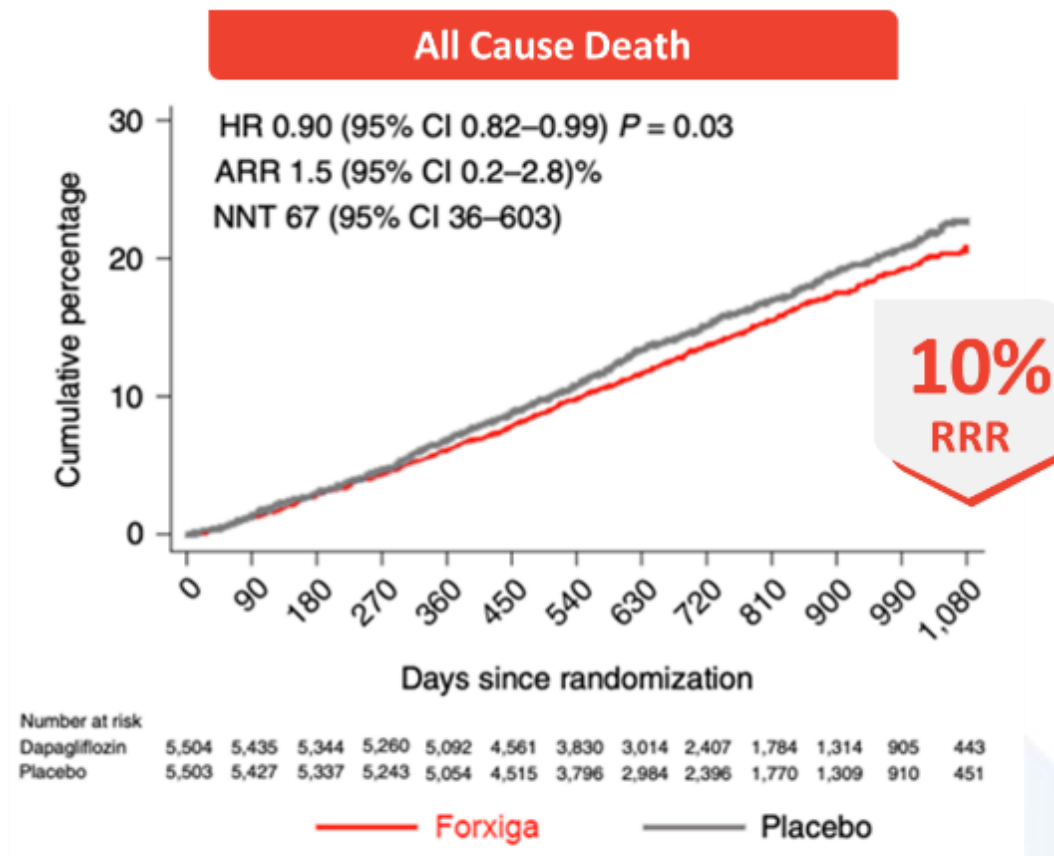
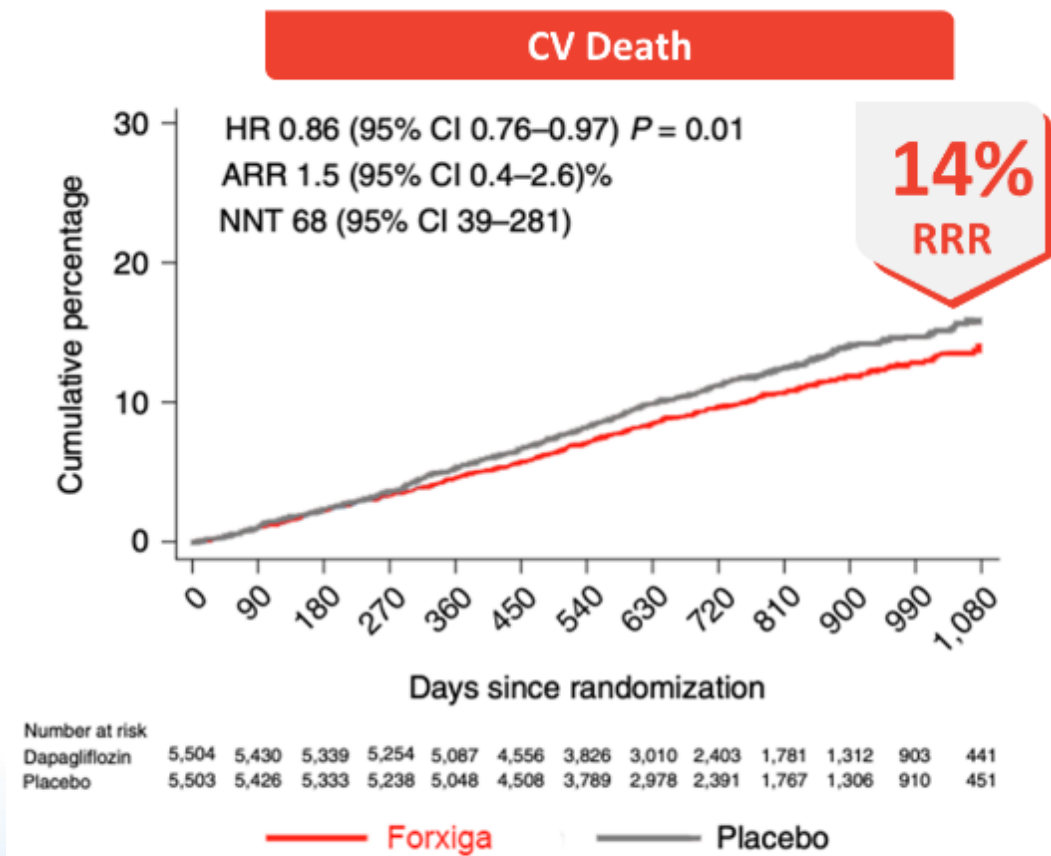
CV, cardiovascular; EF, ejection fraction; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; hHF, hospitalisation for heart failure; LVEF, left ventricular ejection fraction.

1. McMurray JJV, et al. *N Engl J Med*. 2019;381(21):1995-2008. 2. Solomon SD, et al. *JACC Heart Fail*. 2022;10(3):184-197. 3. Solomon SD, et al. *N Engl J Med*. 2022;387(12):1089-1098.



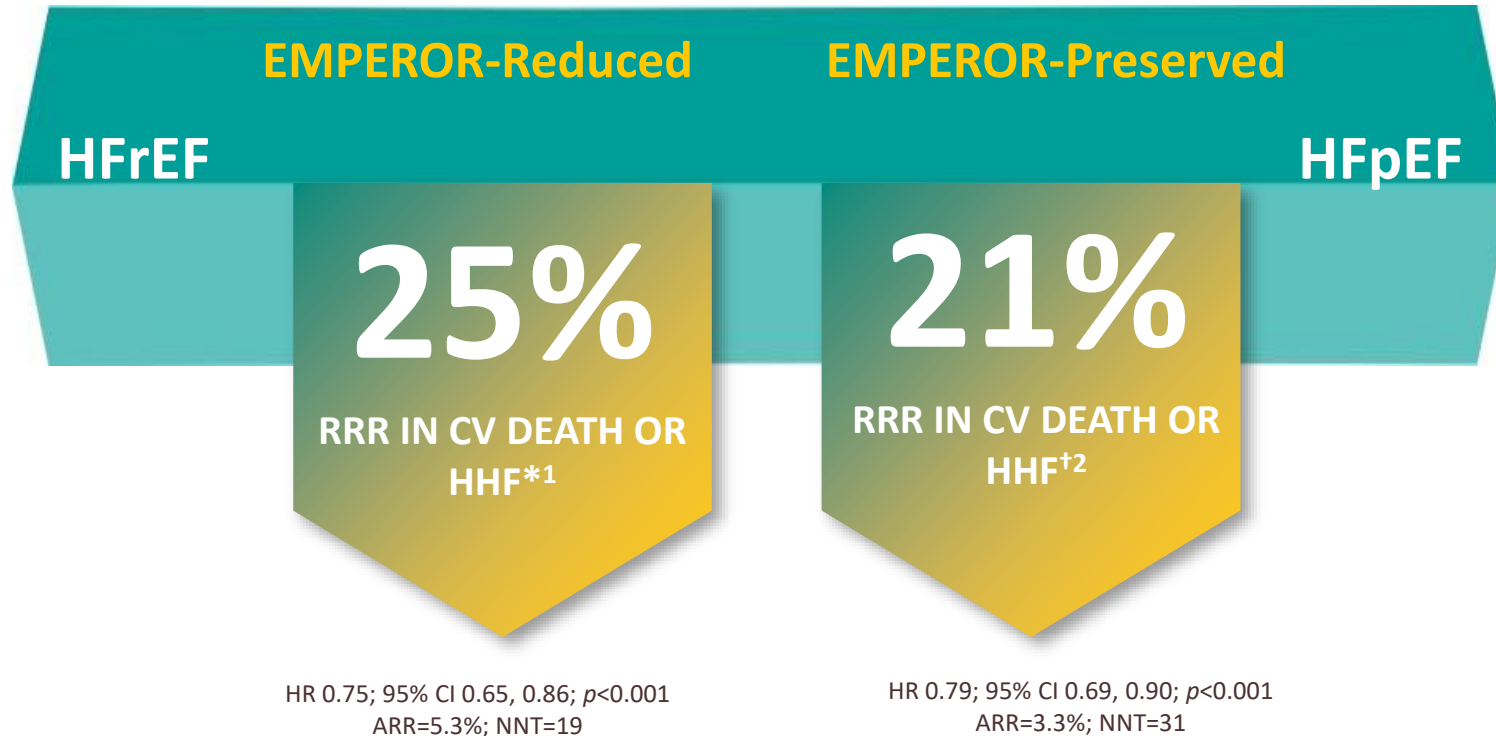


# DAPA-HF & DELIVER合併分析: 不論LVEF高低, Dapagliflozin顯著下降CV死亡和全死亡風險





# Jardiance® provides protection for people with HF across the LVEF spectrum by reducing the risk of CV death or HHF



Consistent efficacy across subgroups including<sup>1-3</sup>:

- With or without T2D
- With or without CKD

**Jardiance®** 恩排糖  
(empagliflozin)

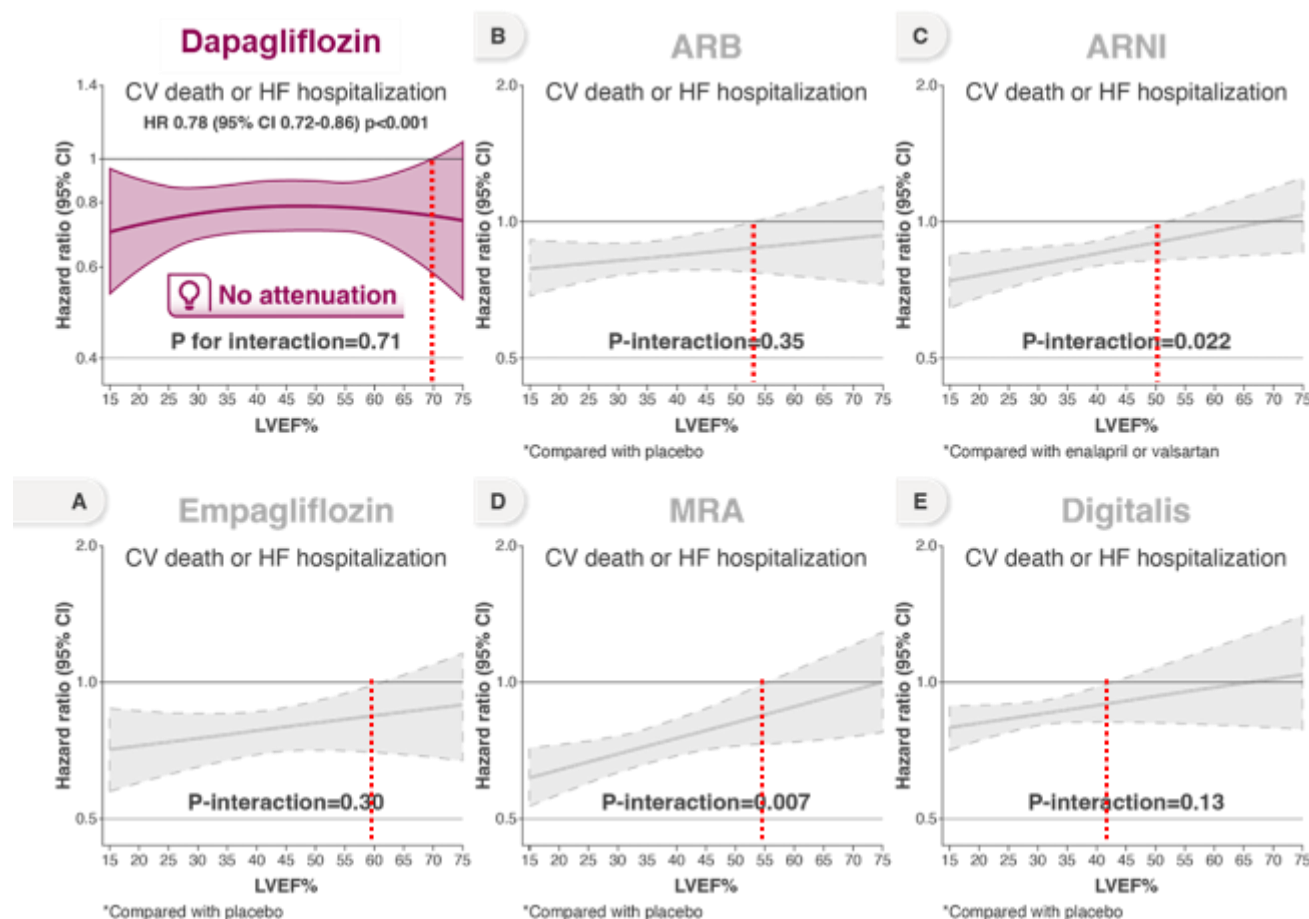
ARR, absolute risk reduction; CKD, chronic kidney disease; CV, cardiovascular; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HHF, hospitalisation for heart failure; LVEF, left ventricular ejection fraction; NNT, number needed to treat; RRR, relative risk reduction; T2D, type 2 diabetes

See notes for footnotes

1. Packer M et al. *N Engl J Med* 2020;383:1413; 2. Anker SD et al. *N Engl J Med* 2021;385:1451; 3. Zannad F et al. *Circulation* 2021;143:310

相較於其他藥物的試驗結果

Dapagliflozin CV死亡和HF住院風險減緩不受LVEF高低影響



1. Eur Heart J. 2022 Feb 3;43(5):427-429. doi: 10.1093/eurheartj/ehab828.
2. Jhund PS et al. Nat Med. 2022 Aug 27. doi: 10.1038/s41591-022-01971-4.

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

Recommendation	Class <sup>a</sup>	Level <sup>b</sup>
An SGLT2 inhibitor ( <b>dapagliflozin</b> or empagliflozin) is recommended in patients with <b>HFmrEF</b> to reduce the risk of HF hospitalization or CV death. <sup>c 6,8</sup>	I	A

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CV, cardiovascular; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; SGLT2, sodium-glucose co-transporter 2.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

<sup>c</sup>This recommendation is based on the reduction of the primary composite endpoint used in the EMPEROR-Preserved and DELIVER trials and in a meta-analysis. However, it should be noted that there was a significant reduction only in HF hospitalizations and no reduction in CV death.

Recommendation	Class <sup>a</sup>	Level <sup>b</sup>
An SGLT2 inhibitor ( <b>dapagliflozin</b> or empagliflozin) is recommended in patients with <b>HFpEF</b> to reduce the risk of HF hospitalization or CV death. <sup>c 6,8</sup>	I	A

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CV, cardiovascular; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; SGLT2, sodium-glucose co-transporter 2.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

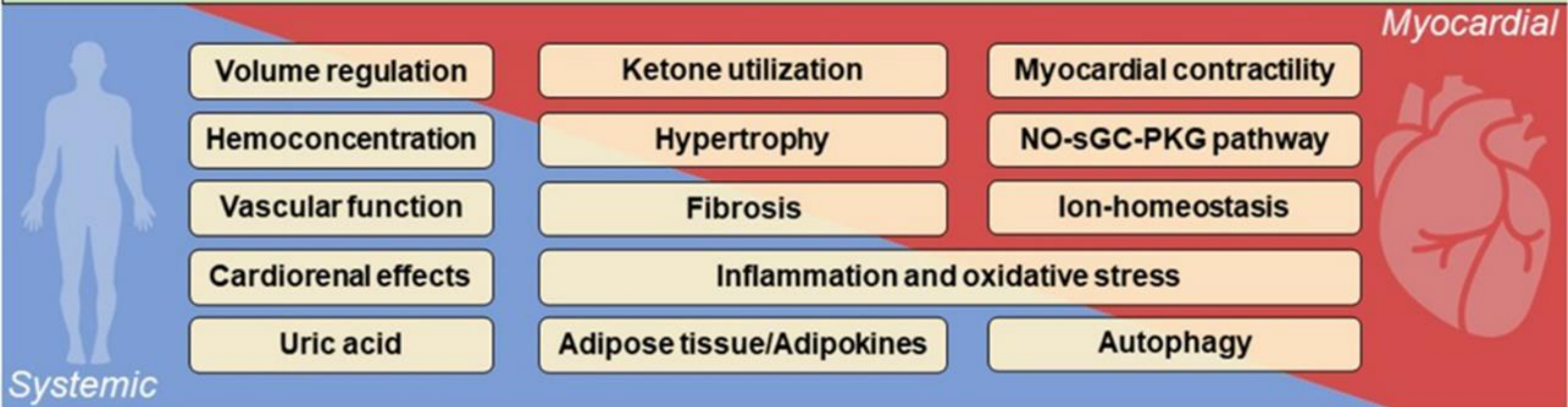
### ESC European Society of Cardiology

A subsequent aggregate data meta-analysis of the two trials confirmed a 20% reduction in the composite endpoint of CV death or first hospitalization for HF (HR 0.80, 95% CI 0.73–0.87;  $P < .001$ ). CV death was not reduced significantly (HR 0.88, 95% CI 0.77–1.00;  $P = .052$ ). HF hospitalization was reduced by 26% (HR 0.74, 95% CI 0.67–0.83;  $P < .001$ ). There were consistent reductions in the primary endpoint across the LVEF range studied.<sup>24</sup> Another individual patient data meta-analysis that incorporated data from DAPA-HF (Dapagliflozin And Prevention of Adverse outcomes in Heart Failure) in HFrEF with DELIVER confirmed that there was no evidence that the effect of dapagliflozin differed by ejection fraction.<sup>22</sup> This also showed that dapagliflozin reduced the risk of death from CV causes (HR 0.86, 95% CI 0.76–0.97;  $P = .01$ ).<sup>22</sup>

**DAPA-HF & DELIVER pooled analysis:**  
**DAPA護心效果不受LVEF高低影響，唯一SGLT2i顯著降CV死亡**



## Possible effects of SGLT2i on the heart





## 2023 ESC 治療指引更新



**2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure ESC Clinical Practice Guidelines**  
25 Aug 2023



**HFpEF & HFmrEF  
治療建議**



**HF 共病管理建議**

# 2023 ESC Focused Update HF合併CKD或T2D，建議使用SGLT2i降低hHF和CV死亡(Class 1A)

**ESC**  
European Society of Cardiology



## Recommendation Table 4 - Recommendations for the prevention of heart failure in patients with type 2 diabetes mellitus and chronic kidney disease

Recommendation	Class <sup>a</sup>	Level <sup>b</sup>
In patients with <b>T2DM and CKD</b> , SGLT2 inhibitors ( <b>dapagliflozin</b> or empagliflozin) are recommended to reduce the risk of HF hospitalization or CV death. <sup>5,7,35</sup>	I	A
In patients with T2DM and CKD, <sup>c</sup> finerenone is recommended to reduce the risk of HF hospitalization. <sup>10,11,34,40</sup>	I	A

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(11%) had a history of HF. During a median follow-up of 2.4 years, a reduction in the primary outcome, a composite of sustained decline in eGFR of  $\geq 50\%$ , end-stage kidney disease, or kidney-related or CV death, was reduced by 39% by dapagliflozin compared with placebo (HR 0.61, 95% CI 0.51-0.72;  $P < .001$ ). Also, the risk of the secondary outcome of HF hospitalization or CV death was decreased by dapagliflozin compared with placebo (HR 0.71, 95% CI 0.55-0.92;  $P = .009$ ) with, however, a relatively small absolute risk reduction (4.6% vs. 6.4% with dapagliflozin vs. placebo).<sup>5</sup>

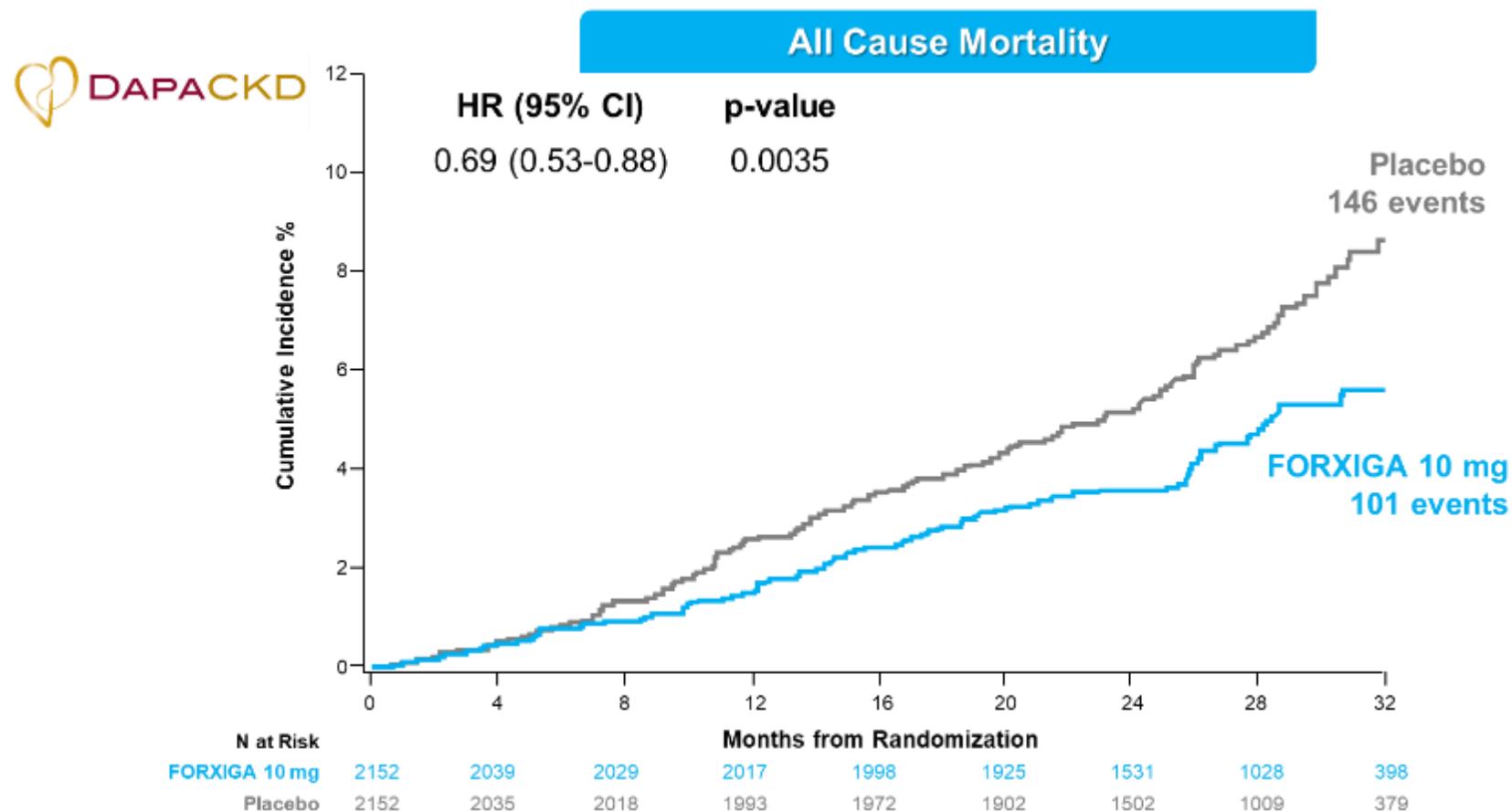
## EMPA-Kidney

EMPA-KIDNEY enrolled a broader group of patients with CKD, compared with DAPA-CKD, including patients with eGFR 20-45 mL/min/1.73 m<sup>2</sup>, even in the absence of albuminuria, or with an eGFR of 45-90 mL/min/1.73 m<sup>2</sup> and a urinary albumin-to-creatinine ratio  $< 200$  mg/g. Patients were randomized 1:1 to empagliflozin 10 mg once daily or placebo. Overall, 658 of the 6609 patients enrolled (10%) had a history of HF. During a median follow-up of 2.0 years, a reduction in the primary composite endpoint of progression of kidney disease or CV death was observed.<sup>7</sup> The risk of HF hospitalization or death for CV causes was not reduced significantly (HR 0.84, 95% CI 0.67-1.07;  $P = .15$ ).<sup>7</sup>





## 針對CKD患者，Dapagliflozin顯著減少總死亡風險



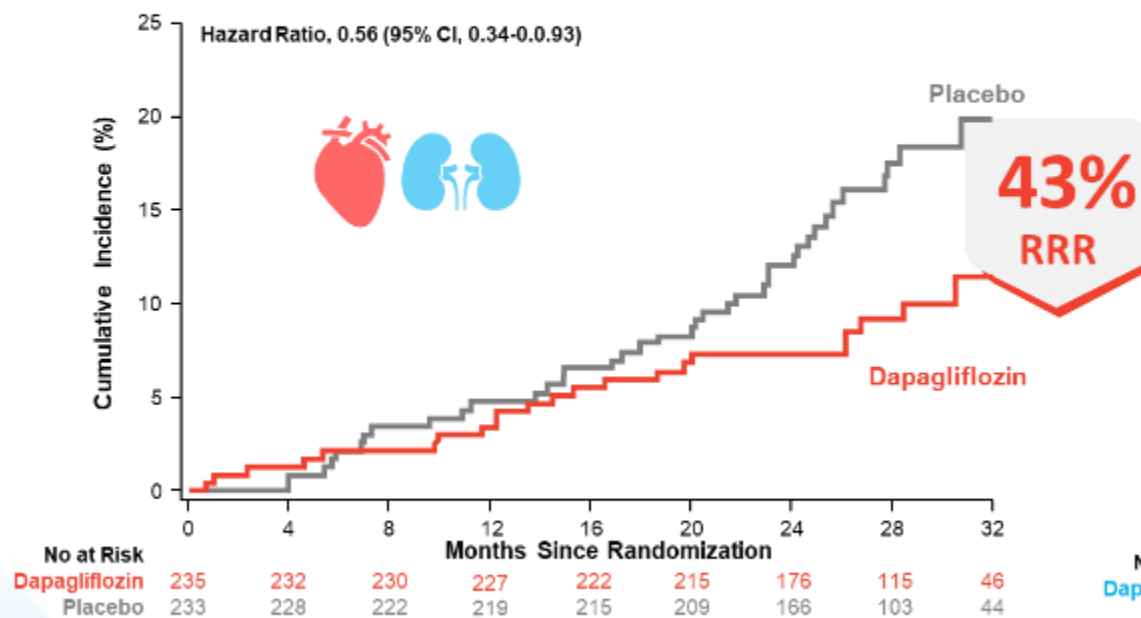


# CKD患者無論有無HF 使用Dapagliflozin皆能顯著下降全因死亡

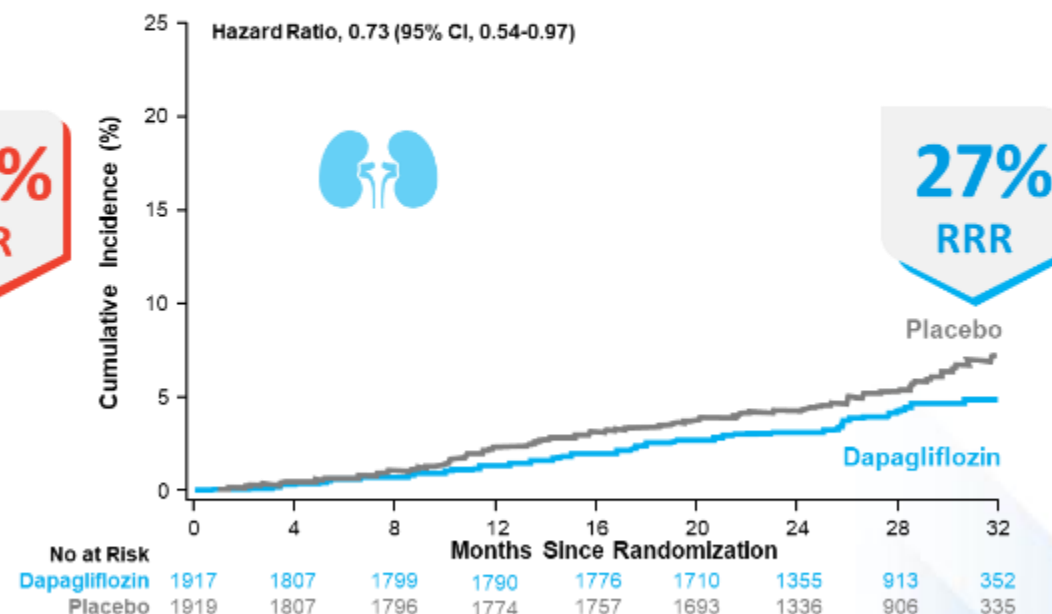


## All-Cause Mortality by Baseline History of HF

### Patient with HF (10.8% in DAPA-CKD)



### Patient without HF (89.2% in DAPA-CKD)



p-interaction=0.39

Dapagliflozin 仿單安全性資料更新 (2024.4.2)

**透析患者可持續使用FORXIGA 救心保命**

2024/4/2起心腎保護族群再擴增



**及時開始預防，一錠守護到底**



eGFR 25 起始使用



持續使用



洗腎免停  
救心保命

UPDATED

T2D

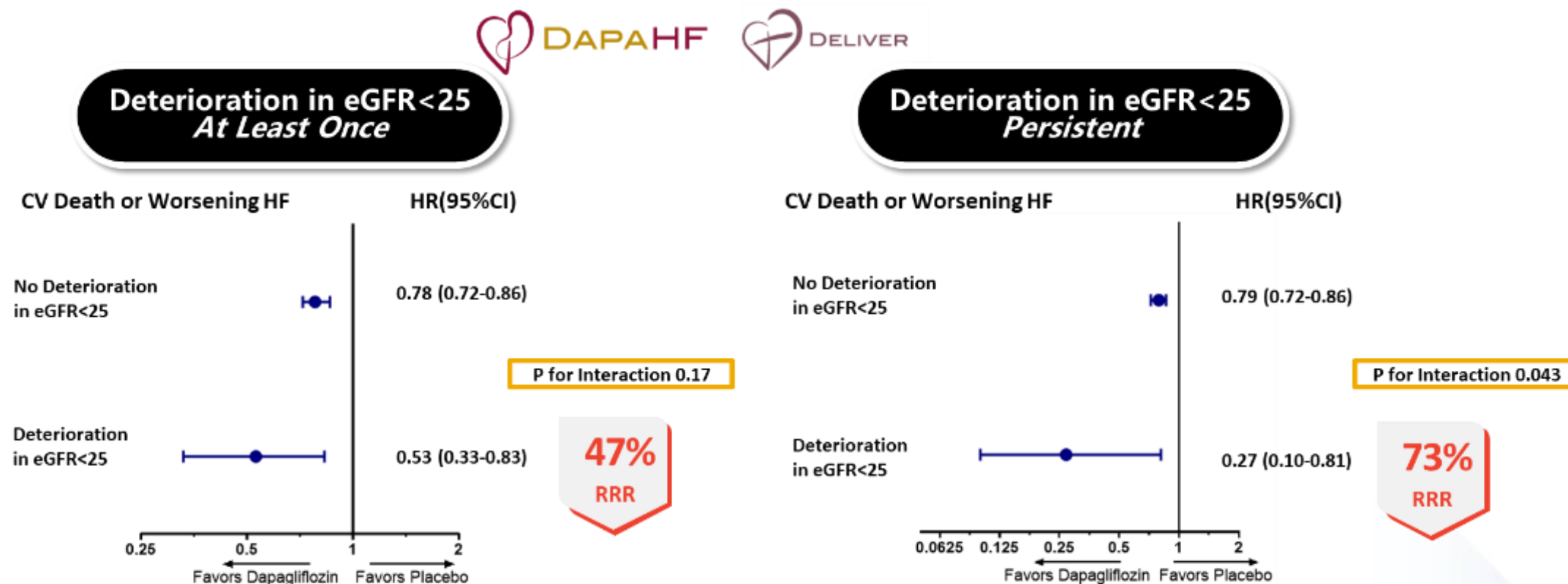
CKD

HFrEF

HFpEF

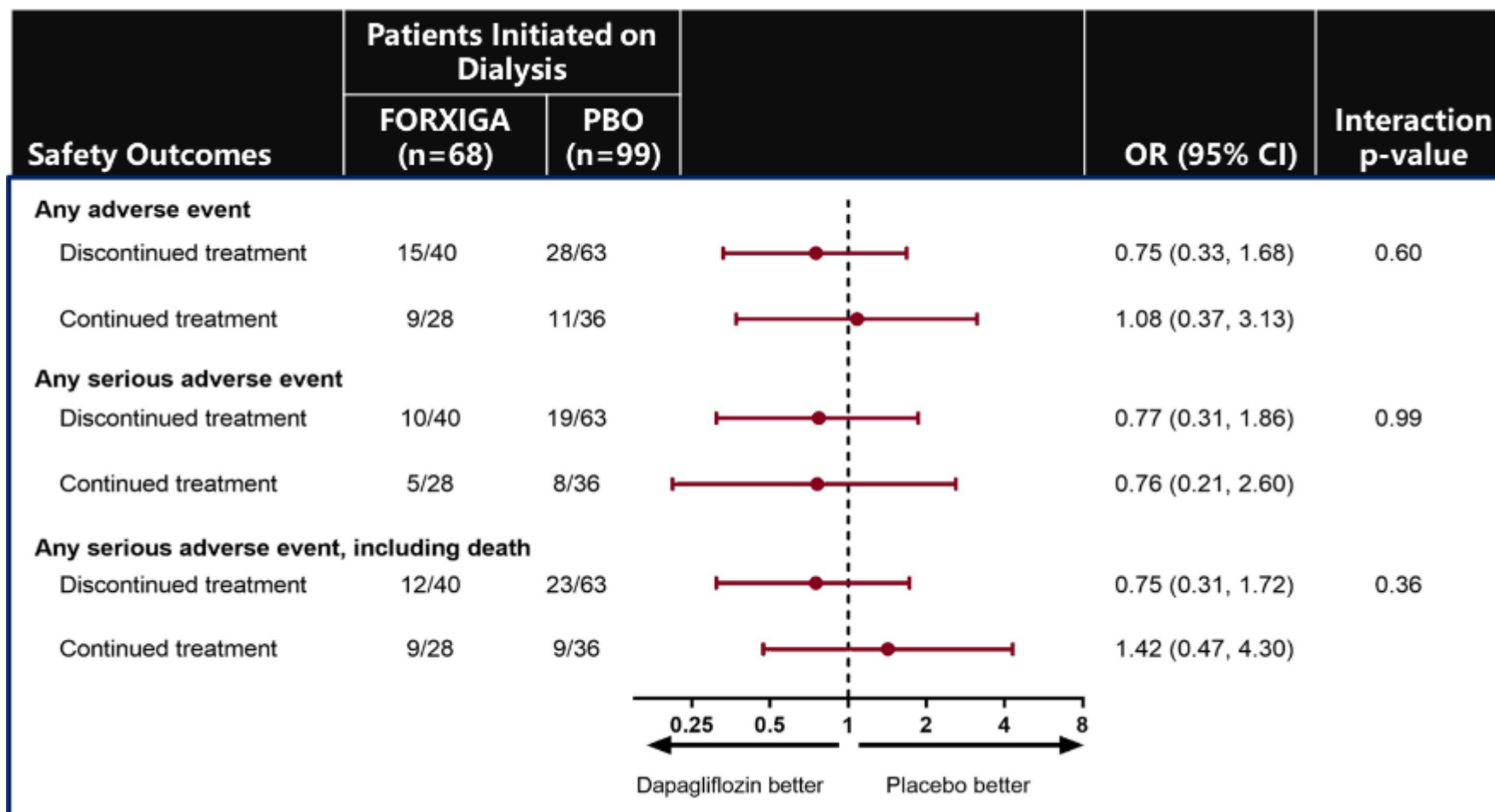
# DAPA-HF and DELIVER Pooled Analysis

eGFR<25持續使用，Dapagliflozin可降低心血管死亡或心衰竭惡化



Treatment with FORXIGA was associated with lower rates of the CV death or worsening HF regardless of deterioration of eGFR to <25ml/min/1.73m<sup>2</sup>

## 透析病人持續使用Dapagliflozin，不良事件發生率與安慰劑組相當



aChronic dialysis defined as the need for dialysis for at least 28 days.

CI = confidence interval; DAPA = dapagliflozin; OR = odds ratio; PBO = placebo.

Heerspink HJL et al. Presented at: 60th ERA Congress; June 15-18, 2023; Milan, Italy and Virtual.





# 台灣SGLT2i eGFR適用範圍及劑量

SGLT2i 臺灣核准eGFR 劑量用法(2024.4.2)

		eGFR 45	eGFR 25	ESRD 續用
Dapagliflozin 10 mg	糖尿病	開始使用 控糖+ 心腎保護	持續使用，洗腎免停 <sup>2</sup>	✓
	心衰竭	開始使用	持續使用，洗腎免停 <sup>2</sup>	✓
	腎臟病	開始使用	持續使用，洗腎免停 <sup>2</sup>	✓
Empagliflozin 10 mg	糖尿病	開始使用	eGFR 30 心腎保護使用時劑量不可提升 <sup>3,4</sup>	✓
	心衰竭	開始使用	eGFR 30 使用時劑量不可提升 <sup>4</sup>	✓
	腎臟病	開始使用	eGFR 30 使用時劑量不可提升 <sup>4</sup>	✓
Empagliflozin 25 mg	糖尿病	開始使用	eGFR 30 eGFR < 30 禁用	✗
Canagliflozin	糖尿病	開始使用	eGFR 30 審慎評估是否繼續給藥 <sup>5</sup>	✗

1.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 2.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。 3.對於eGFR低於30 的第二型糖尿病成人病人，不建議使用Empagliflozin改善其血糖控制。根據其作用機制，Empagliflozin在此情況下可能無療效。 4.若 eGFR 低於 30，則 empagliflozin 建議劑量限於 10 mg；  
參考資料: 衛福部食藥署仿單 (更新至2024.4.2) 5.請勿對該病人新處方本藥





## 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**



# 總結

- 心腎功能交互影響，腎功能越差，心衰及死亡風險越高，過往心臟衰竭治療可降低死亡，但未能滿足腎臟保護，**SGLT2i提供共病治療的新契機**
- 2023 ESC治療指引更新: CKD合併心衰竭，建議首選SGLT2i治療降低**hHF**和**CV死亡風險**
- **Dapagliflozin 提供T2D從預防到治療的心腎實證，減少心衰竭惡化風險**
  - 治療 HFrEF 病患：Dapagliflozin治療HFrEF 減少心血管死亡或心衰竭惡化、延緩亞洲族群腎功能下降
  - 治療 HFmrEF & HFpEF 病患：Dapagliflozin 顯著下降心衰患者總死亡、心衰竭住院風險、心衰竭惡化風險、延緩腎功能下降
  - 針對共病管理，Dapagliflozin治療CKD，下降UACR及減少腎功能惡化、有效減少心血管死亡或心衰竭惡化，顯著降低總死亡提供一致的心腎保護療效

# Thanks for listening !

