

血脂衛教協會 2020年北、中、南學術研討會

●高雄場

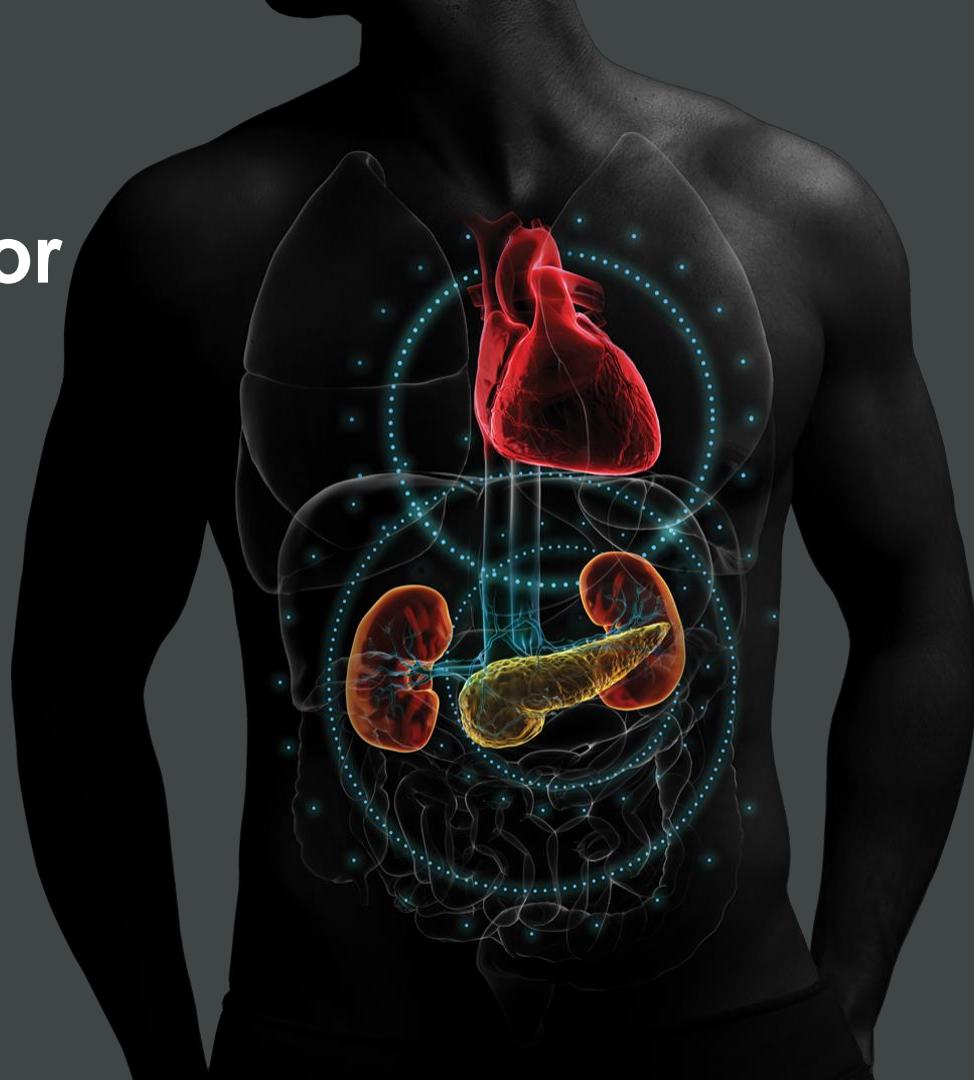
地點：高雄市政榮民總醫院 門診大樓第二會議室(高雄市左營區大中一路386號)

時間：2020/07/12 (星期日) 09:00 – 16:45

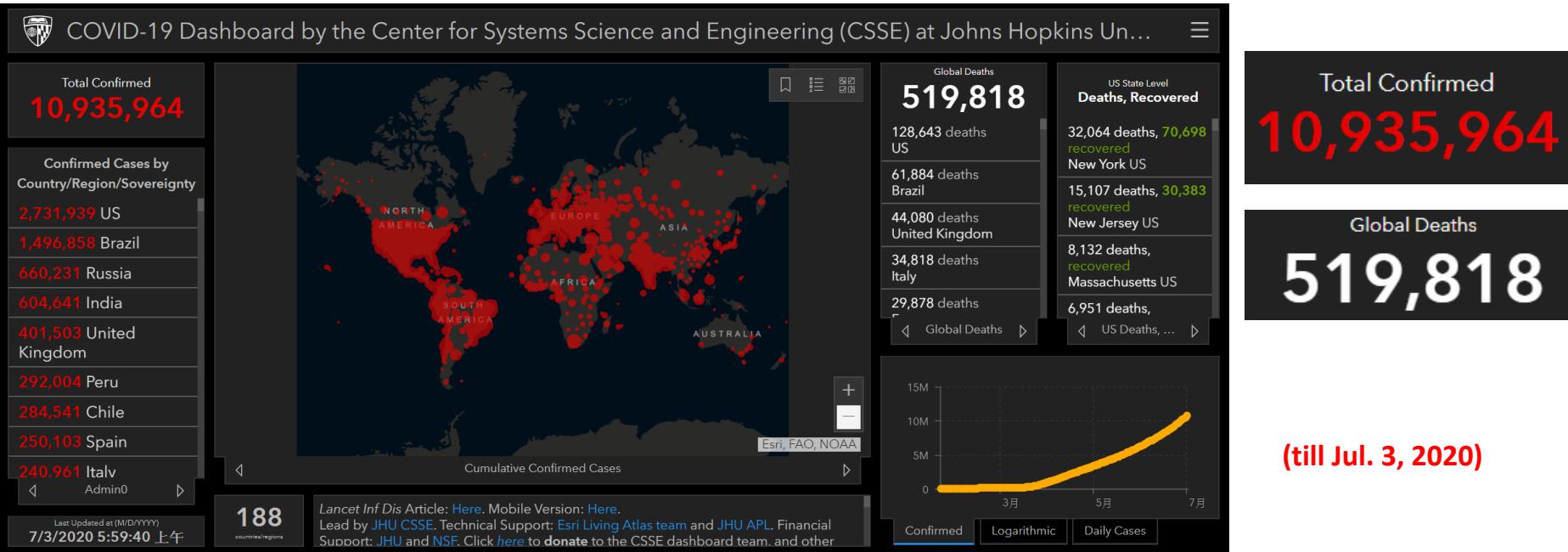
開始	結束	時間	講師	題目	主持人
09:00	09:05	00:05		Opening Remarks	吳造中 理事長
09:05	09:40	00:35	朱俊源 醫師	How to optimize statin therapy for very-high and high risk ASCVD patients in dyslipidemia?	
09:40	10:15	00:35	許栢超 醫師	Establish the Standard of Care for Dyslipidemia Treatment on High Risk Patient	
10:15	10:35	00:20		Break Time	
10:35	11:10	00:35	林宗憲 醫師	Single-Pill with CCB+Statin in SBP & LDL Control -- Lower Cardiovascular Risk, Increased Compliance, and Cost-effectiveness	許勝雄 理事
11:10	11:45	00:35	郭風裕 醫師	The need for urgency in treating hyperlipidemia in post-ACS patients	
11:45	12:45	01:00		Lunch Time	
12:45	13:20	00:35	趙庭興 醫師	For primary prevention – Balancing efficacy and safety	吳彥雯 秘書長
13:20	13:55	00:35	朱志生 醫師	Icosapent Ethyl(EPA) and Cardiovascular Outcomes: Insights From Recent Clinical Trials.	
13:55	14:30	00:35	楊智超 醫師	Beyond BP lowering CV-Renal protection effects of ARB in T2DM	
14:30	14:50	00:20		Break Time	
14:50	15:25	00:35	李美月 醫師	Complete the Cardio-renal syndrome Puzzle : New Era of SGLT2 inhibitors	賴文德 理事
15:25	16:00	00:35	田凱仁 醫師	Timely Treatment for High-Risk Patient with T2DM for Cardio-Renal Complication	
16:00	16:35	00:35	沈峰志 醫師	The Art of Fixed Ratio Combination in DM treatment	
16:35	16:45	00:10		Closing Remarks	

Timely Treatment for Patient with T2D for Renal-Cardio Complication

田凱仁 醫師
奇美醫院
內分泌新陳代謝科



全球Covid-19疫情仍在世界各地持續延燒

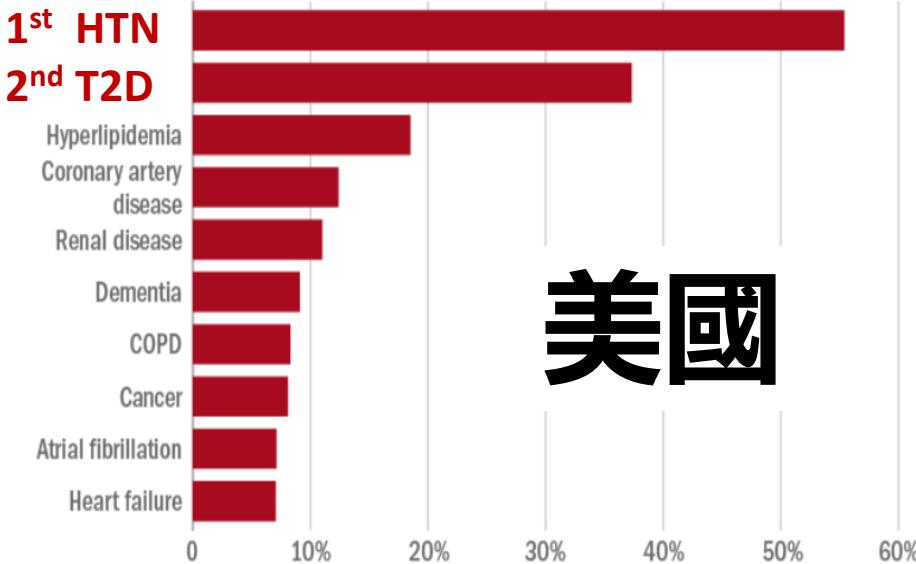


<https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html?fbclid=IwAR10MHQ40VqgE2Z02z2BzkgAeC6K2Afk7ia5Z3HN6kSDOWStUwYT3NuXzE#/bda7594740fd40299423467b48e9ecf6>

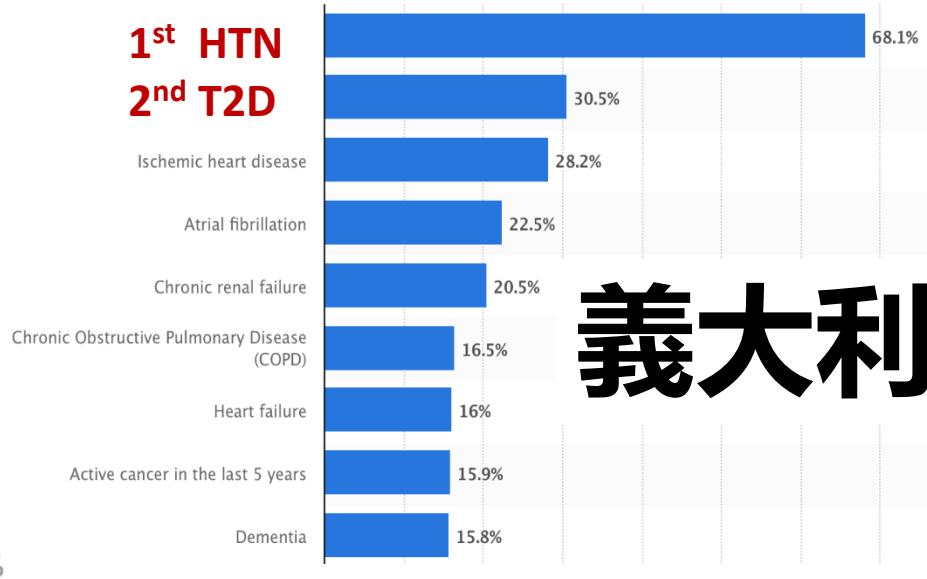
高血壓及糖尿病為新冠肺炎住院/死亡病患最常見的兩大共病

美國疾管署資料顯示，因病情嚴重住院的美國新冠肺炎病患，高達近50%有高血壓，40%有糖尿病

義大利近期發表在JAMA，更發現因疫情死亡的病患，高達2/3有高血壓，近1/3有糖尿病



<https://www.the-hospitalist.org/hospitalist/article/220457/coronavirus-updates/comorbidities-rule-new-yorks-covid-19-deaths>



<https://jamanetwork.com/journals/jama/fullarticle/2763667?widget=personalizedcontent&previousarticle=2763401>
<https://www.statista.com/statistics/1110949/common-comorbidities-in-covid-19-deceased-patients-in-italy/>

高血壓及糖尿病會增加新冠肺炎患死亡風險

CCDC共72314個案分析中，新冠肺炎伴有共病症的死亡率為糖尿病7.3%，高血壓6.0%，相較於沒有共病者的0.9%，糖尿病患者一旦感染新冠肺炎，死亡率恐高出8倍

TABLE 1. (continued)

Baseline characteristics	Confirmed cases, N (%)	Deaths, N (%)	Case fatality rate, %	Observed time, PD	Mortality, per 10 PD
Comorbid condition [†]					
Hypertension	2,683 (12.8)	161 (39.7)	6.0	42,603	0.038
Diabetes	1,102 (5.3)	80 (19.7)	7.3	17,940	0.045
Cardiovascular disease	873 (4.2)	92 (22.7)	10.5	13,533	0.068
Chronic respiratory disease	511 (2.4)	32 (7.9)	6.3	8,083	0.040
Cancer (any)	107 (0.5)	6 (1.5)	5.6	1,690	0.036
None	15,536 (74.0)	133 (32.8)	0.9	242,948	0.005
Missing	23,690 (53.0)	617 (60.3)	2.6	331,843	0.019

糖尿病患感染新冠肺炎共病風險高，尤其心腎的交互影響

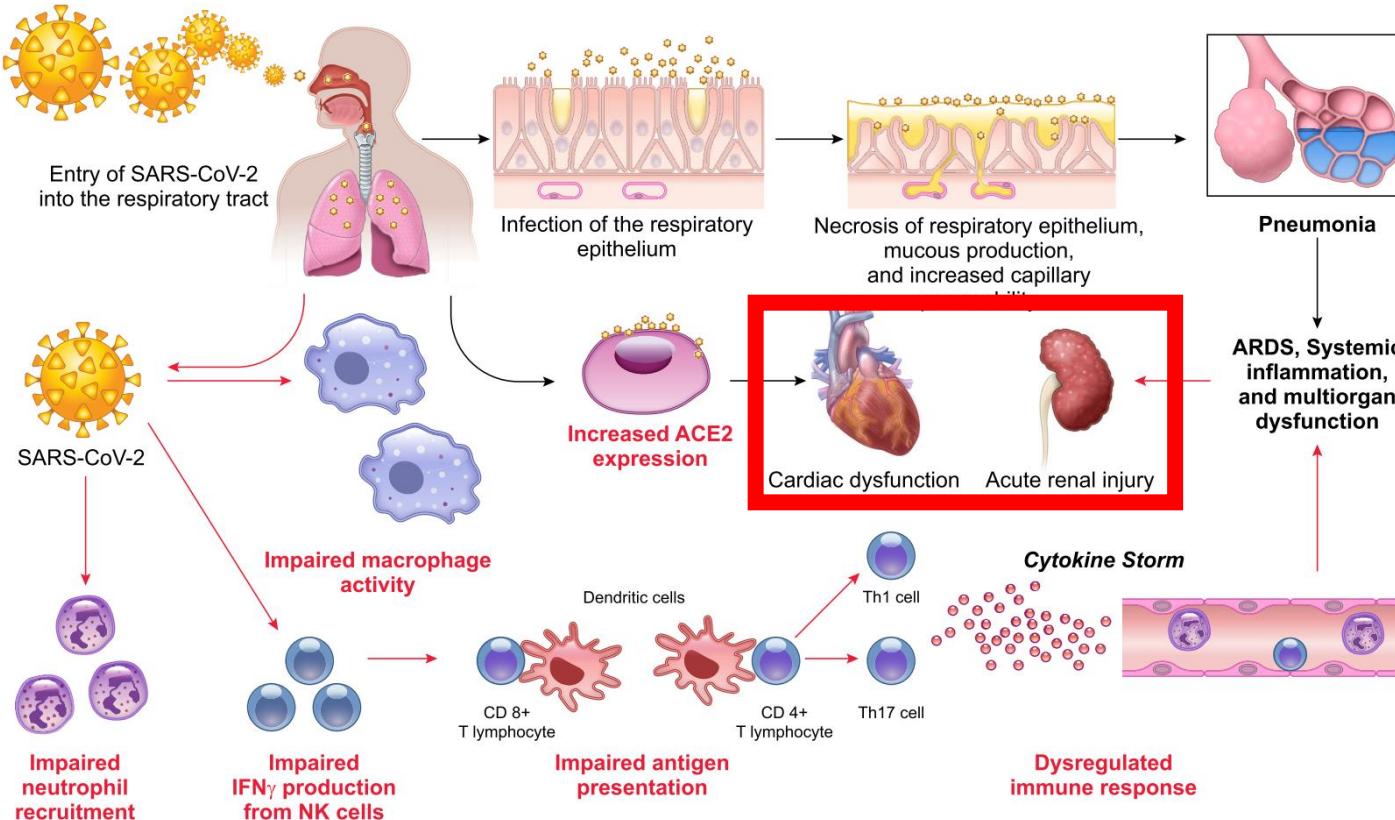


Fig. Putative mechanisms contributing to increased susceptibility for coronavirus disease (COVID-19) in patients with diabetes mellitus (DM).

糖尿病病患本身屬高感染風險族群，遭遇病原體感染如新冠肺炎，體內免疫系統不受控制時，便會引起細胞激素風暴(cytokine storm)，不僅會造成心臟及腎臟的損傷交互影響，更可能引發重症衰竭，甚至導致死亡。

在新冠肺炎的衝擊下迎接糖尿病治療新時代 控糖兼預防，心腎器官齊保護

糖尿病學會提出控糖新觀念「控糖三二一」



血糖監控3指標：
監測飯前& 飯後血糖、
HbA1c



腎臟功能2注意
監測微蛋白尿及檢測
eGFR(腎絲球過濾率)



心衰預防1(一)一定要
早期控制三高，預防心
衰竭合併症

佳佳姐 60歲



- **Medical history**

- Diagnosed with **T2D** 8 years ago
- **Hypertension**
- **Albuminuria**
- BW 52 kg, BMI of 21

- **Current treatment**

- Metformin+DPP-4i
- ARB

我需要新的治療嗎？

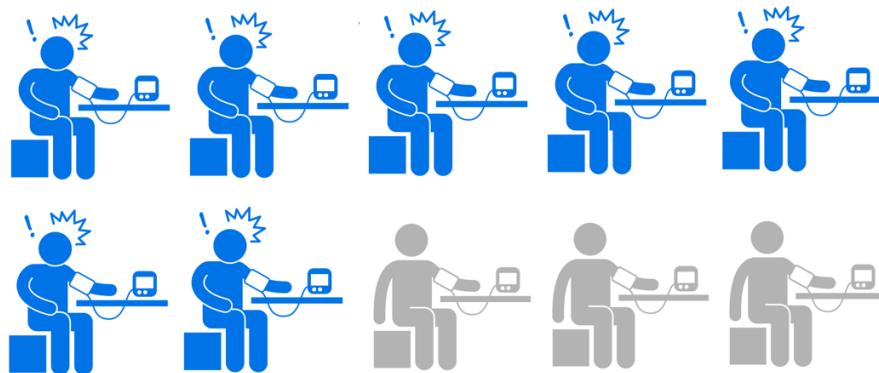
- **Status**

- HbA1c **7.6%**
- eGFR 72 ml/min/1.73 m²
- BP **133/81 mmHg**
- UACR **42 mg/g**

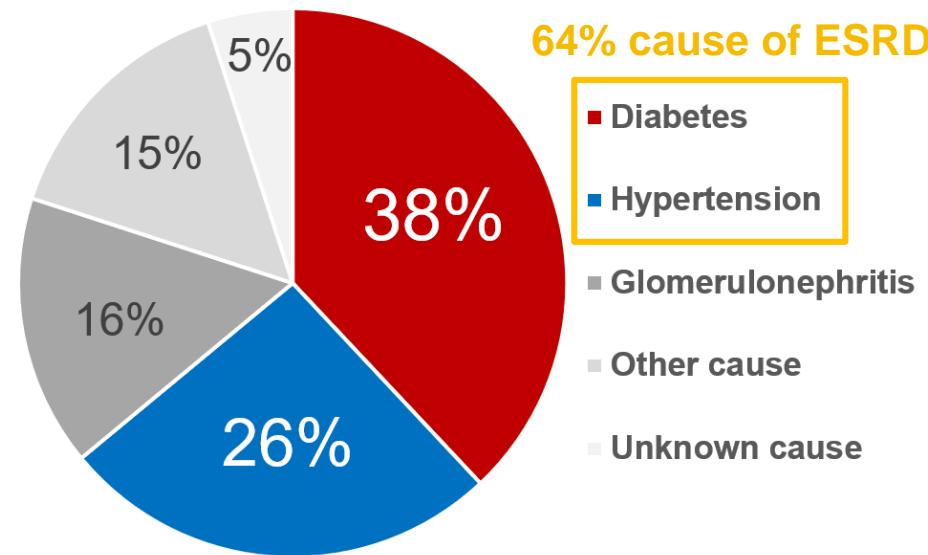
血糖控制不太好，這次抽血檢查出現**蛋白尿**紅字，腎臟功能一年比一年差，很害怕未來要洗腎...

像佳佳姐這樣的病患不在少數：台灣T2D病患有66%合併高血壓
糖尿病、高血壓即為導致ESRD兩大主因

66% T2D patients with hypertension
in Taiwan



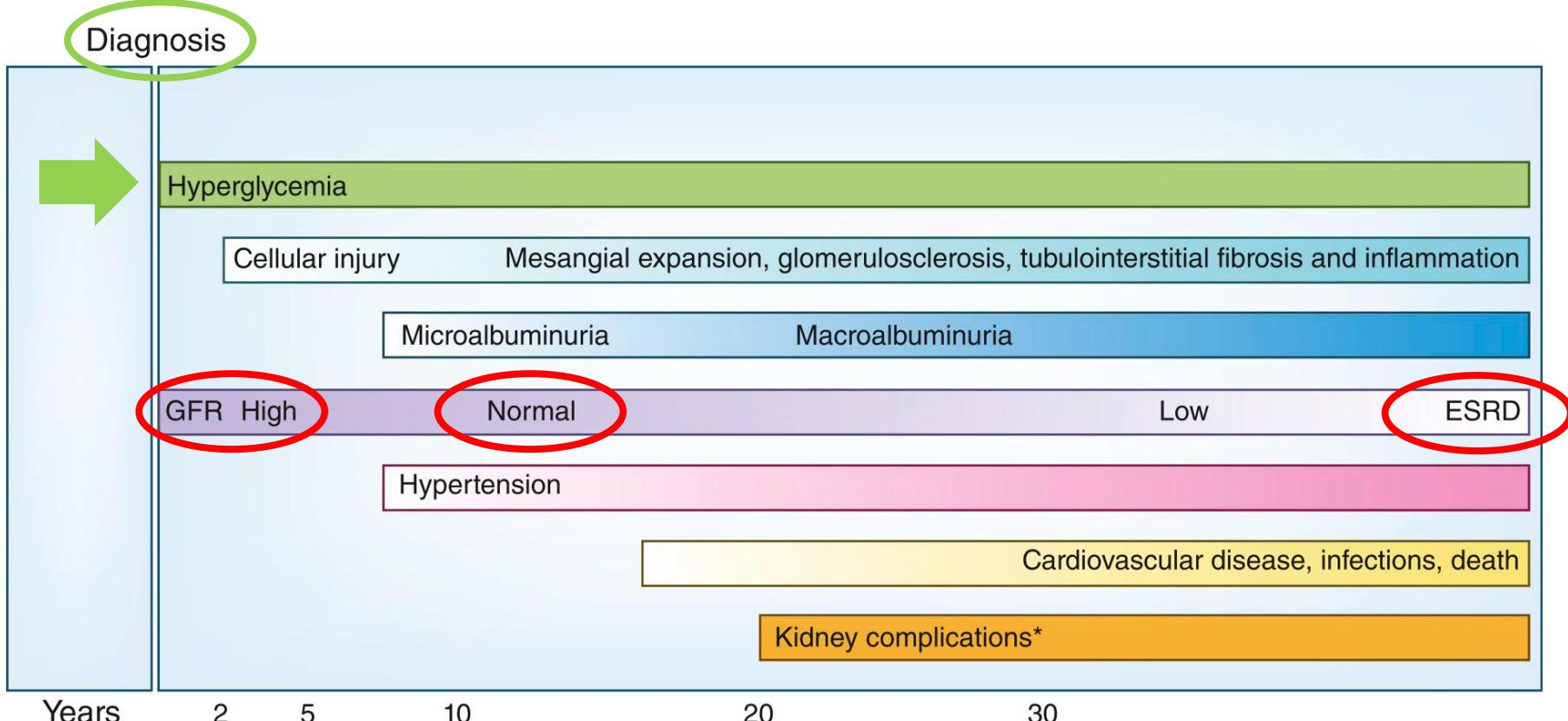
Diabetes & hypertension is No.1 and No.2
reported causes of ESRD



ESRD: End-Stage Renal Disease

1. 糖尿病衛教學會. 臺灣糖尿病年鑑-2019 第2型糖尿病(p.12) 2. US CDC. Chronic Kidney Disease in the United States, 2019

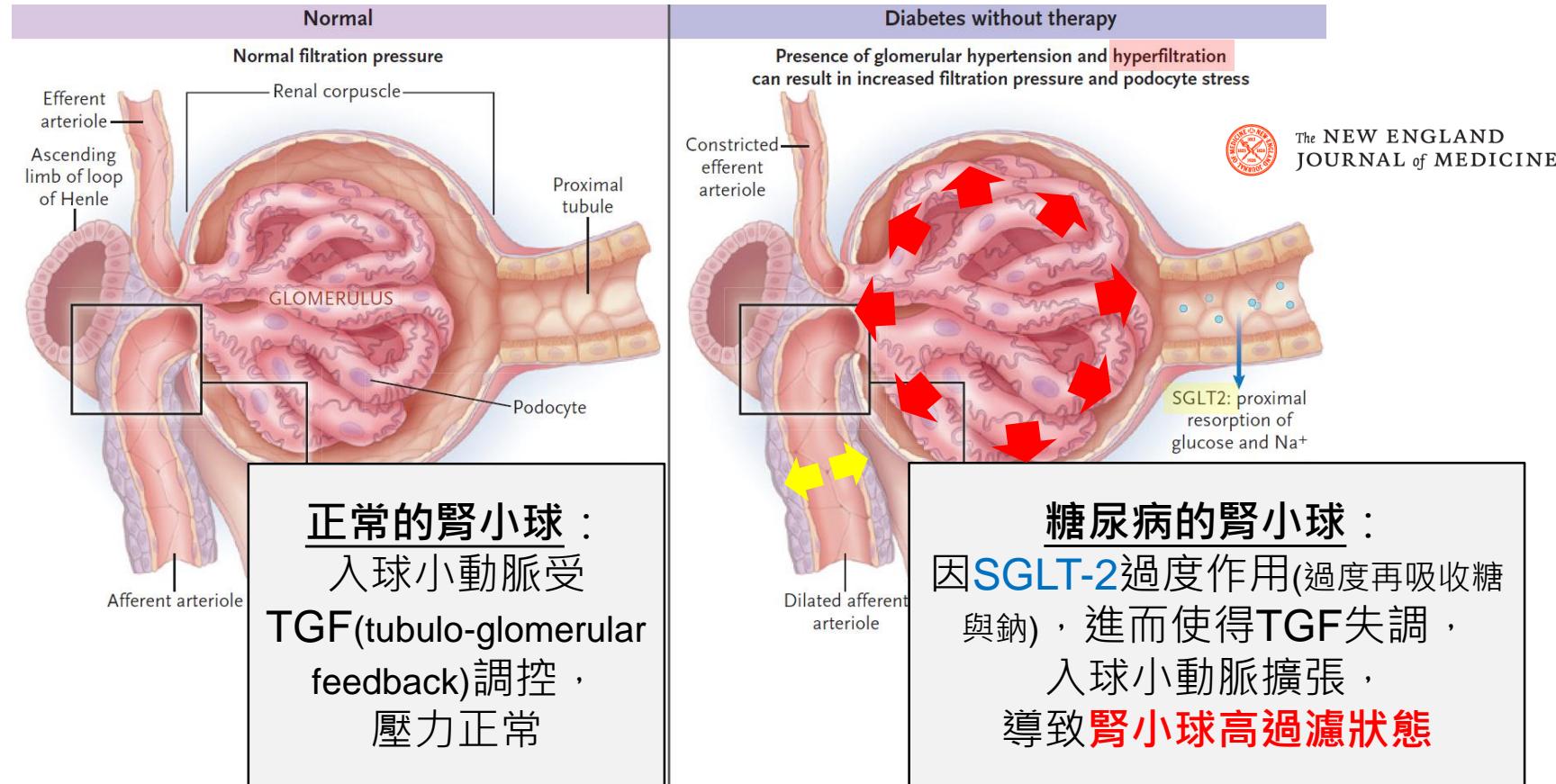
糖尿病初期 eGFR為升高或正常，但腎病變已悄悄在發生



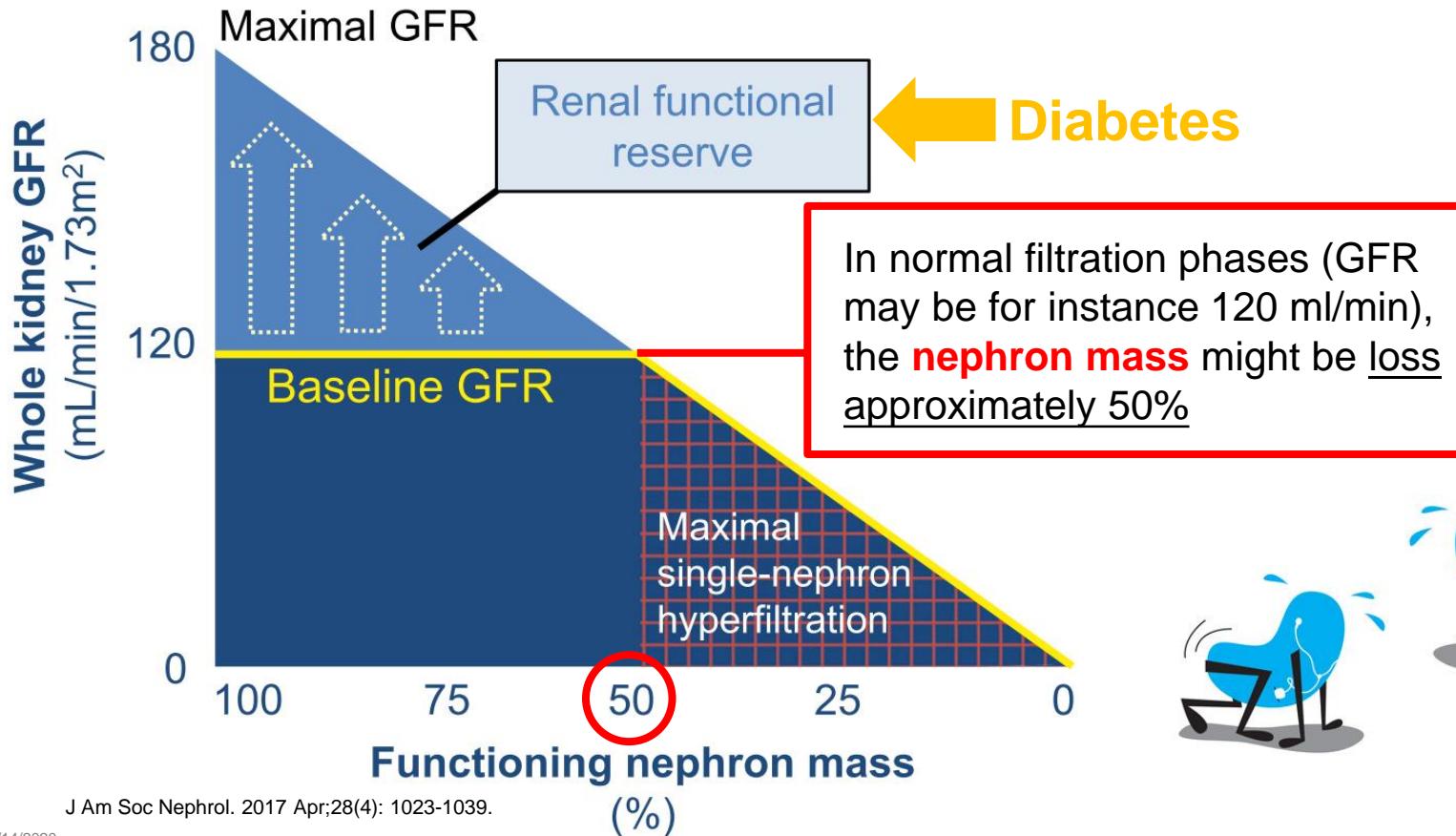
*Kidney complications: anemia, bone and mineral metabolism, retinopathy, and neuropathy

CJASN December 2017, 12 (12) 2032-2045

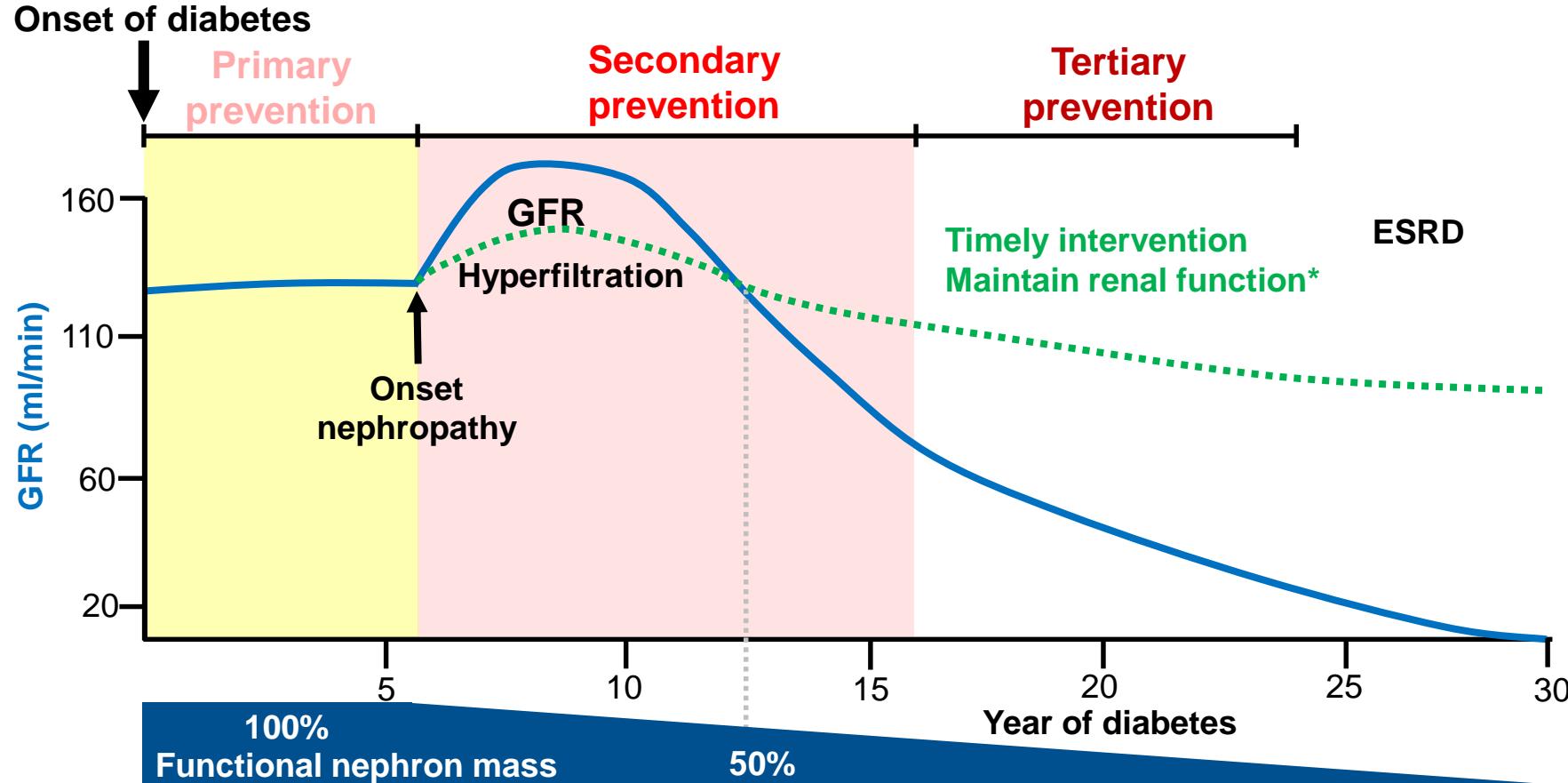
糖尿病腎病變：SGLT-2過度作用導致腎小球高過濾狀態為重要病因



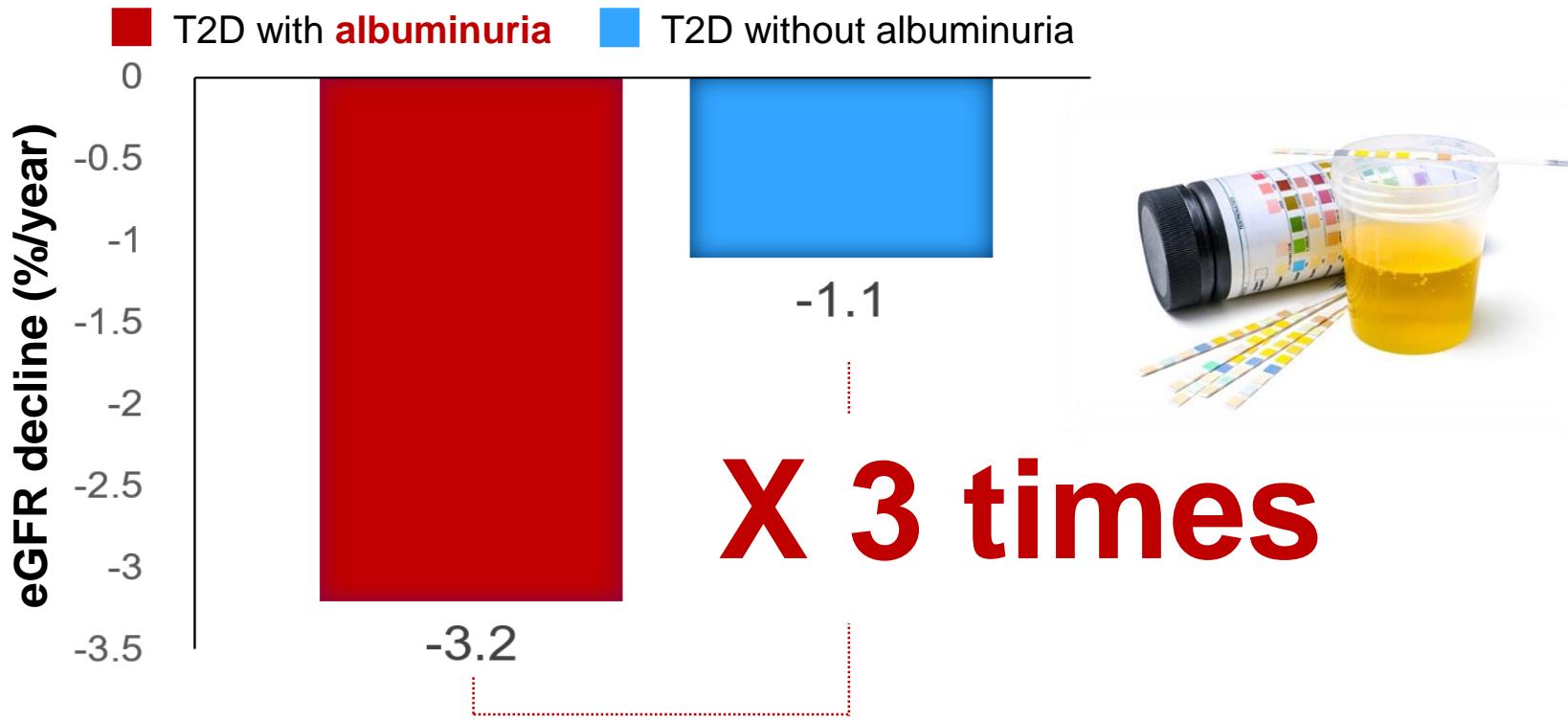
腎小球高過濾狀態：eGFR看似正常， 但腎元可能已受損50%



理想的糖尿病腎病變介入：及時降低高過濾狀態，維持eGFR

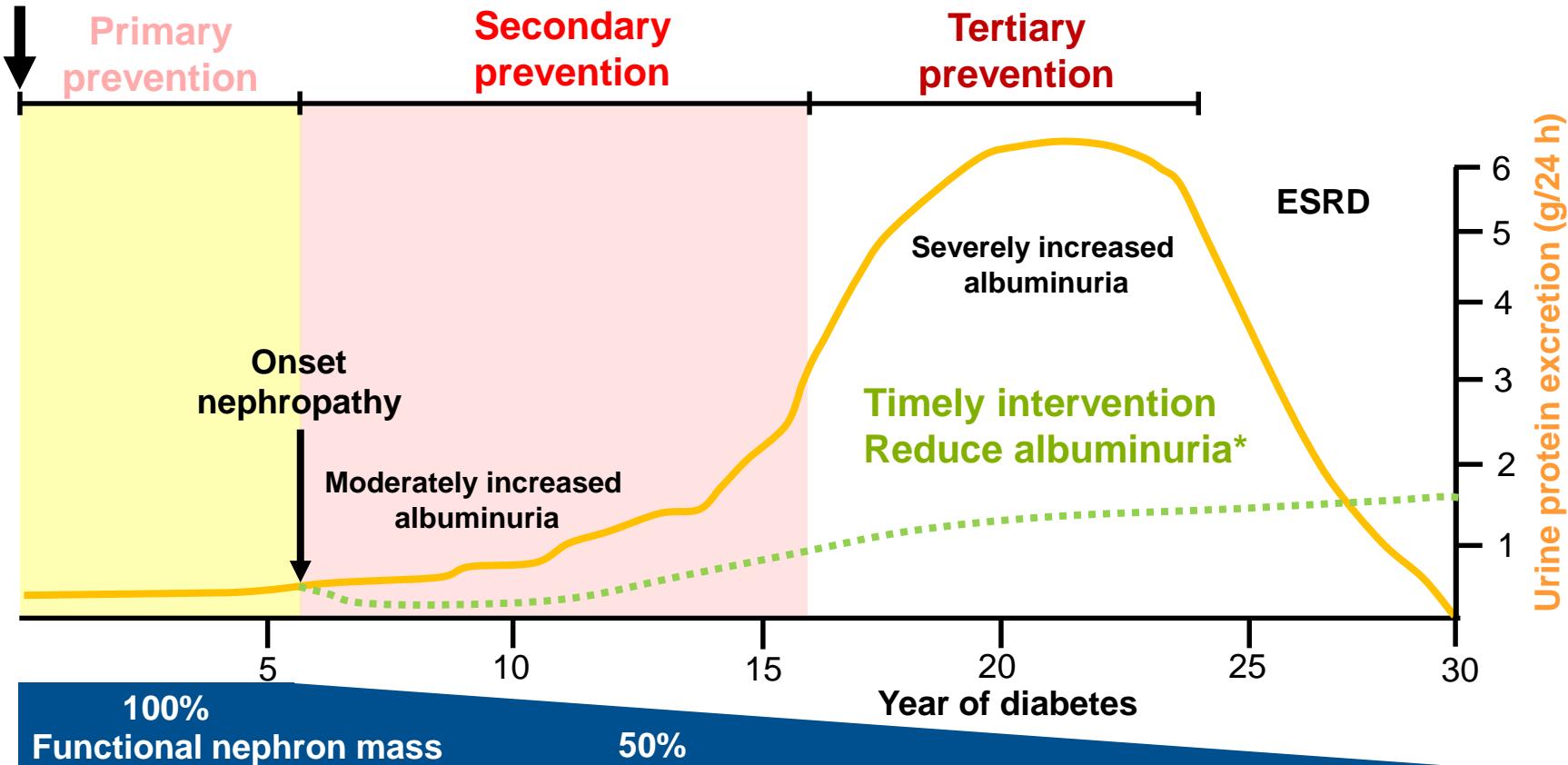


有蛋白尿的糖尿病病患，腎功能惡化速度快三倍

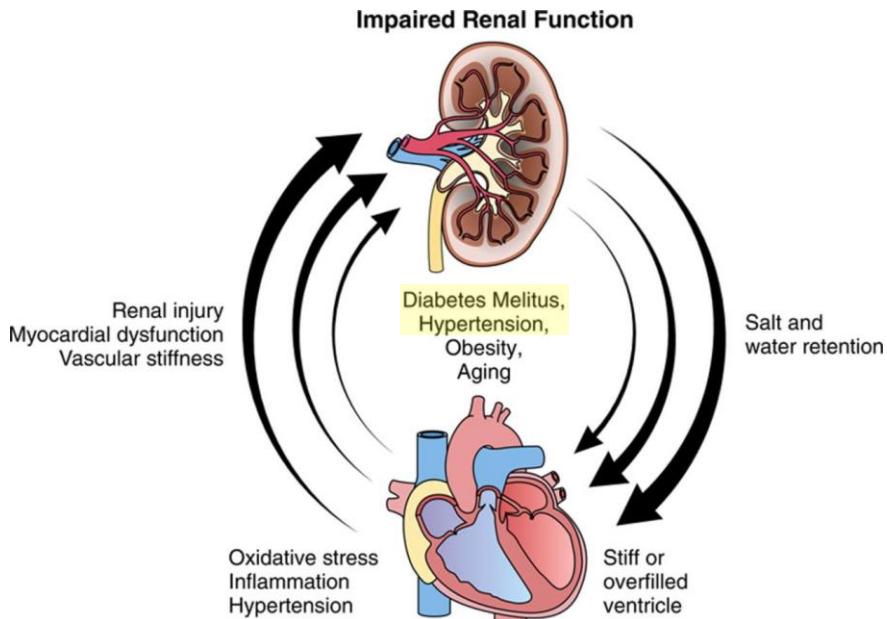


理想的糖尿病腎病變介入：及時減少蛋白尿，降低蛋白尿惡化風險

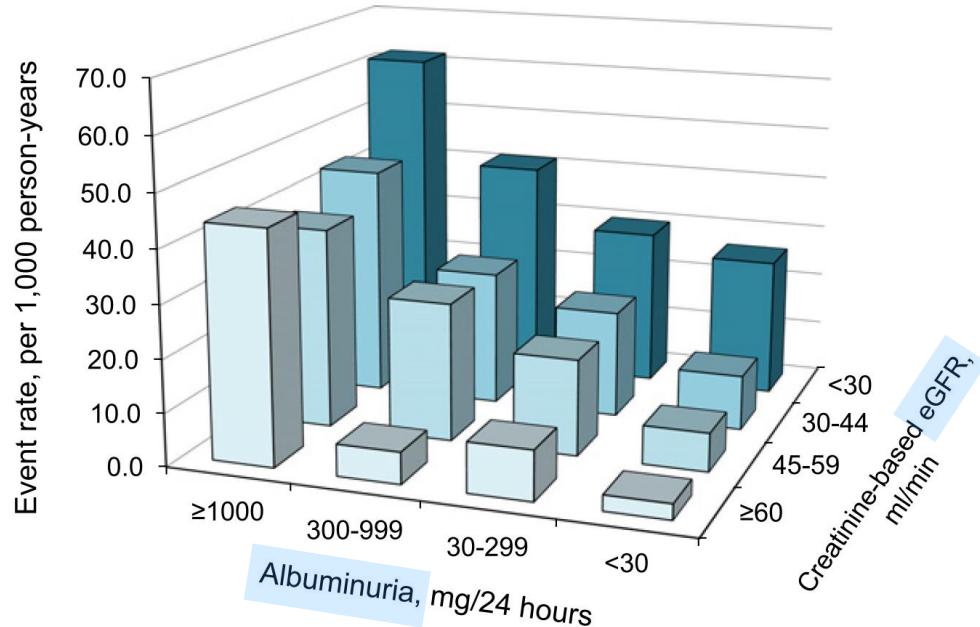
Onset of diabetes



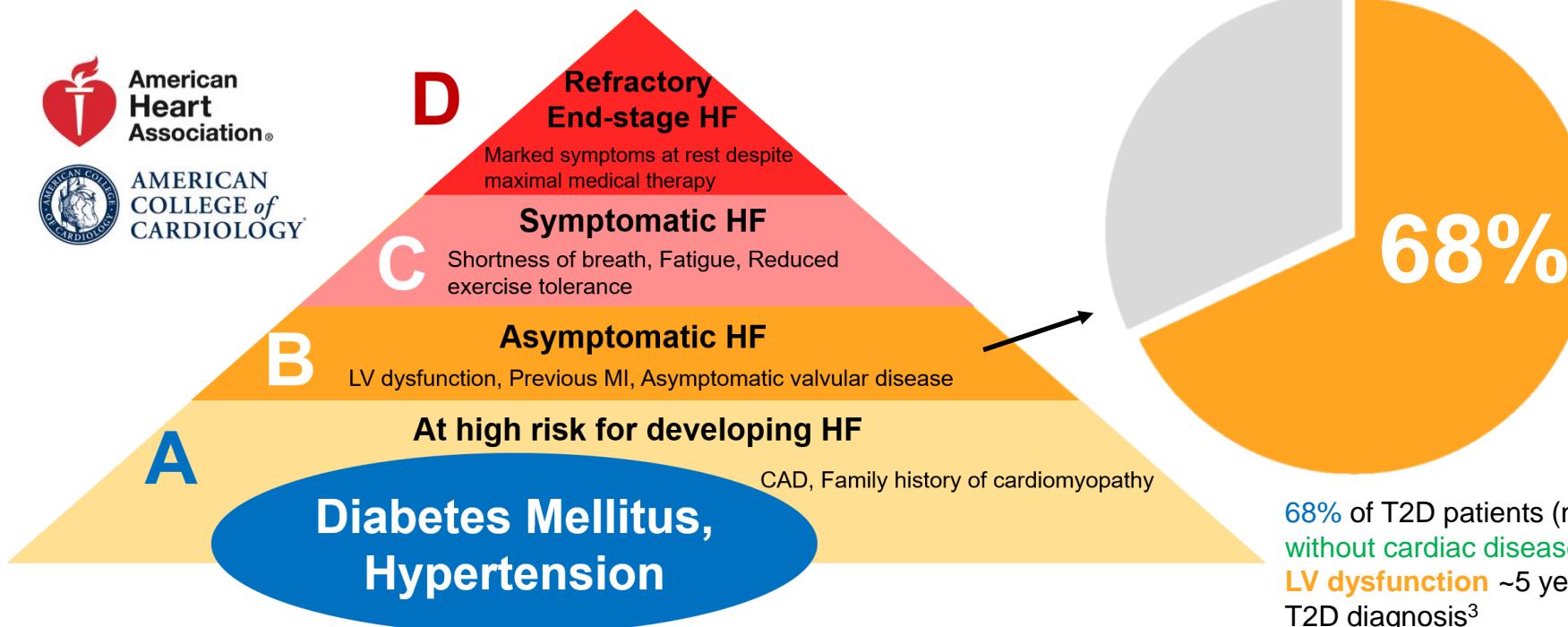
腎臟不好連帶會影響心臟：eGFR、蛋白尿越差，心衰竭風險越高



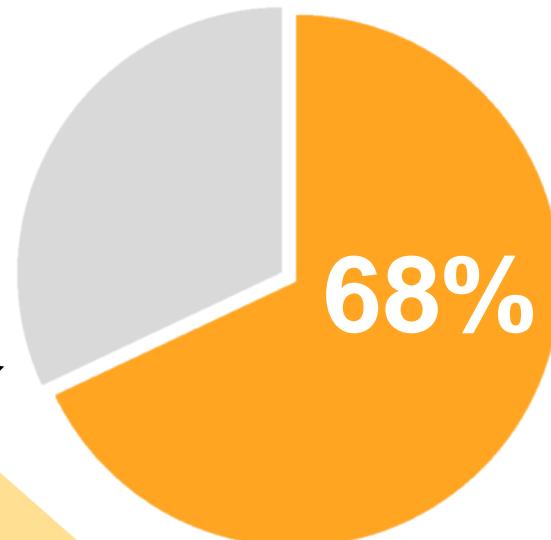
Worse eGFR and albuminuria links to higher incidence of **heart failure**



糖尿病、高血壓病患為 ACC/AHA心衰竭分級stage A

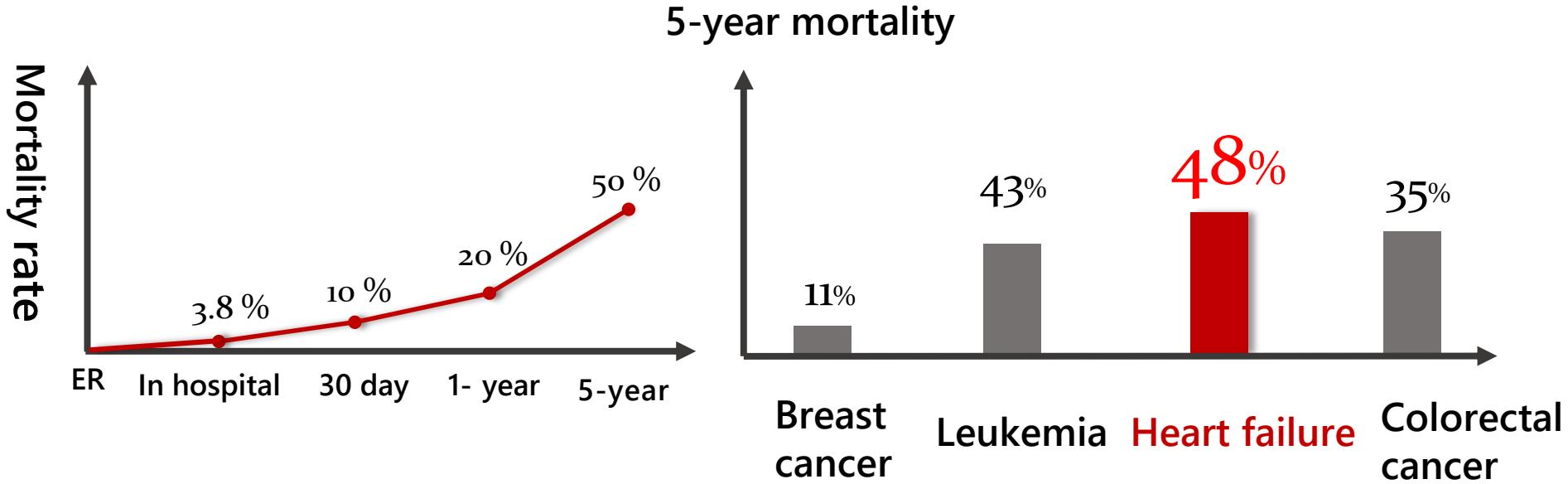


68%無心臟病史的糖尿病患
潛在左心室功能不全



68% of T2D patients (n=386)
without cardiac disease had
LV dysfunction ~5 years after
T2D diagnosis³

心衰竭(俗稱:心臟的癌症) 5年死亡率高達50% 高於乳癌、大腸直腸癌、白血病 預防應為更好的治療策略



National Cancer Institute. Surveillance, epidemiology, and end results program. Cancer stat fact sheet. <http://seer.cancer.gov/statfacts>. Accessed June 8, 2015

糖尿病患控制好血糖、血壓等風險因子，CVD風險得以控制， 但心衰竭風險仍上升

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes

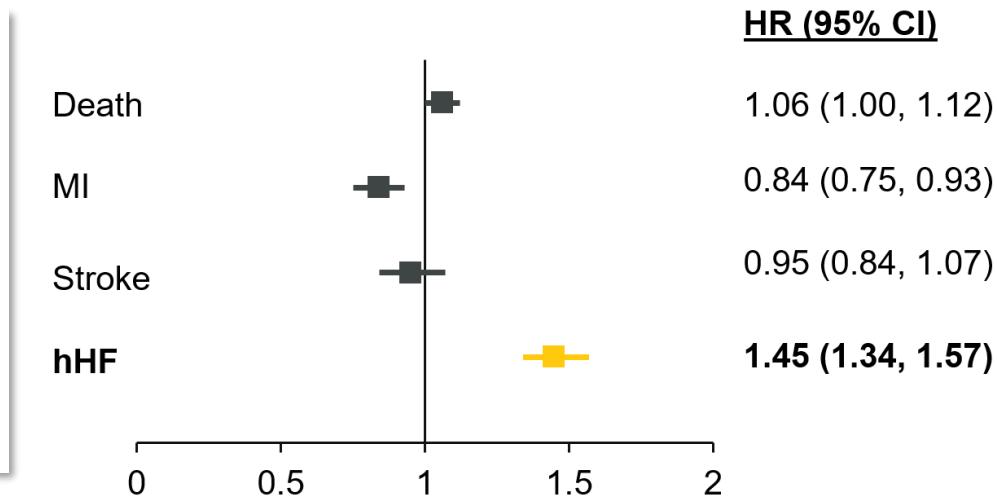
Aidin Rawshani, M.D., Araz Rawshani, M.D., Ph.D., Stefan Franzén, Ph.D., Naveed Sattar, M.D., Ph.D., Björn Eliasson, M.D., Ph.D., Ann-Marie Svensson, Ph.D., Björn Zethelius, M.D., Ph.D., Mervete Miftaraj, M.Sc., Darren K. McGuire, M.D., M.H.Sc., Annika Rosengren, M.D., Ph.D., and Sofia Gudbjörnsdóttir, M.D., Ph.D.

- A cohort study included 271,174 patients with T2DM
- Median follow-up 5.7 years
- Swedish National Diabetes Register



The NEW ENGLAND
JOURNAL of MEDICINE

N Engl J Med. 2018 Aug 16;379(7):633-644.



The risk of heart failure was consistently higher among T2D patients who had 5 risk factors within target range (A1c <7.0%, LDL <2.5 mmol; 97 mg/dl, BP<140/80 mmHg, albuminuria, current smoking) compared to patients without diabetes

MI: myocardial infarction, hHF: hospitalization for heart failure

再看一眼，佳佳姐



- **Medical history**

- Diagnosed with **T2D** 8 years ago
- **Hypertension**
- **Albuminuria**
- BW 52 kg, BMI of 21

- **Current treatment**

- Metformin+DPP-4i
- ARB

糖尿病+高血壓
左心室功能可能已經
出現異常

- **Status**

- HbA1c **7.6%**
- eGFR 72 ml/min/1.73 m²
- SBP **133 mmHg**
- UACR **42 mg/g**

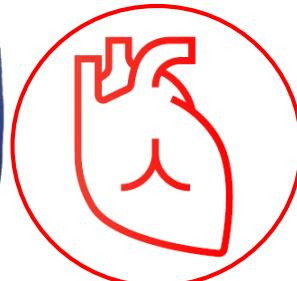
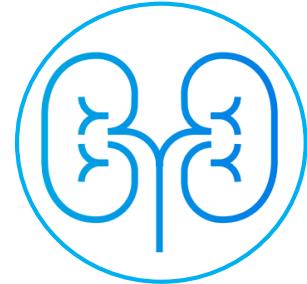
糖尿病+高血壓
腎元可能已經受損>50%；
有蛋白尿→腎功能3倍速惡化

今日的治療選擇將決定佳佳姐的未來



優質控糖

延緩
腎病變



心臟保護
↓ 心衰竭風險



第2型糖尿病病人高血糖的處理流程圖 (2020年修訂版)

健康生活型態的飲食和運動及醫病共享決策



2018糖尿病
臨床照護指引
DAROC Clinical Practice Guidelines
For Diabetes Care 2018



中華民國糖尿病學會
The Diabetes Association of the Republic of China (Taiwan)

1. DAROC Clinical Practice Guidelines for Diabetes Care-2018, Taiwan, Diabetes Association of the R.O.C., 2018
2. <http://www.endo-dm.org.tw/dia/>



評估心腎風險及共病



SGLT2i

心血管實證：有(建議使用)

心衰竭實證：強(建議使用)

腎病變實證：強(建議使用)

控制血糖效果：中等

體重：下降

低血糖：低

副作用：糖尿病酮酸中毒、
生殖泌尿道感染、骨折、
截肢、脫水



價值1.5%以上

高血糖症狀

可以 Insulin 治療

病藥

Insulin

心血管實證：中立

心衰竭實證：中立

腎病變實證：中立

控制血糖效果：最佳

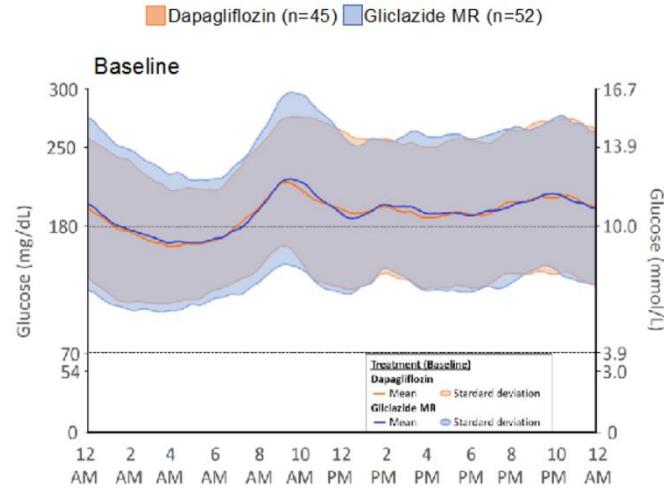
體重：增加

低血糖：高

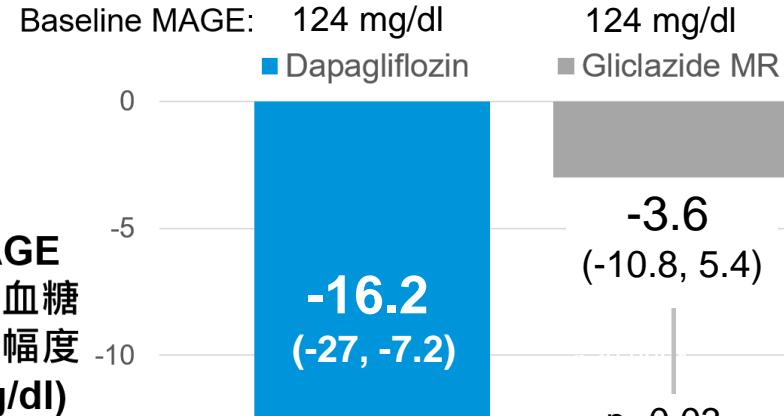
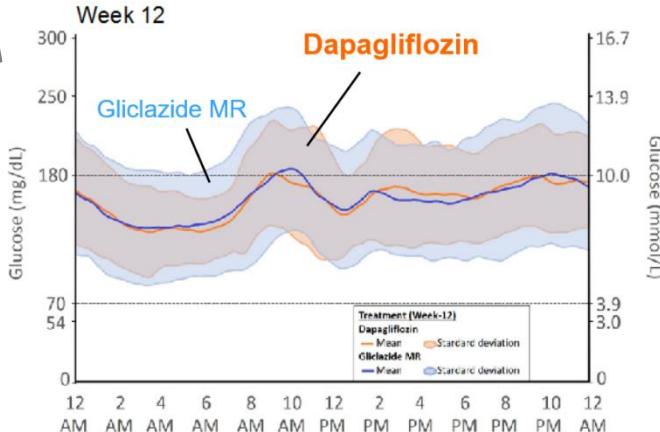
副作用：低血糖



Dapagliflozin 優質控糖：相較SU能降低血糖波動、提供病患更好的血糖平穩度

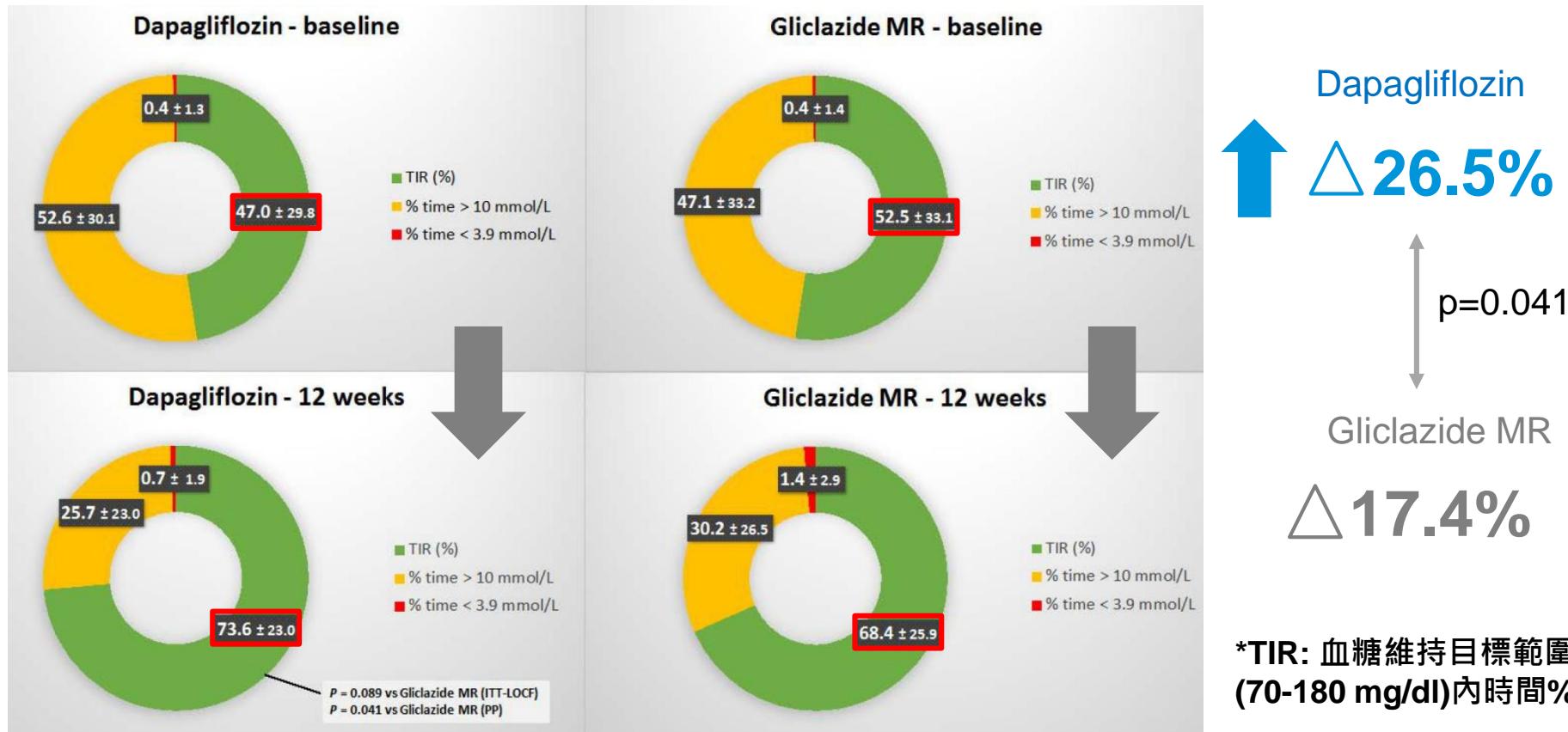


24-hour CGM



CGM: Continuous Glucose Monitoring
MAGE: Mean Amplitude of Glycemic Excursions.
Diabetes Obes Metab. 2020 Apr;22(4):501-511.

Dapagliflozin 優質控糖：相較SU更能維持24小時血糖在目標範圍時間



LEAD Study – Dapagliflozin在台灣的真實世界研究

Use and Effectiveness of Dapagliflozin in Patients with T2D: A Multicenter Retrospective Study in Taiwan

- 1960 patients with T2D from 19 medical centers/reginal hospitals in Taiwan
- Primary objective: A1c change after 6 months treatment with Dapagliflozin



Baseline

Age (years)	57.8 ± 11.5
HbA1c (%)	8.8 ± 1.4
Weight (kg)	75.2 ± 15.8
BMI (kg/m^2)	28.3 ± 4.9
SBP (mmHg)	136.6 ± 17.6
DBP(mmHg)	77.8 ± 11.3
Hypertension	60.5%
CVD	16.9%
Nephropathy	34.6%

1960位使用
Dapagliflozin
的T2D病患



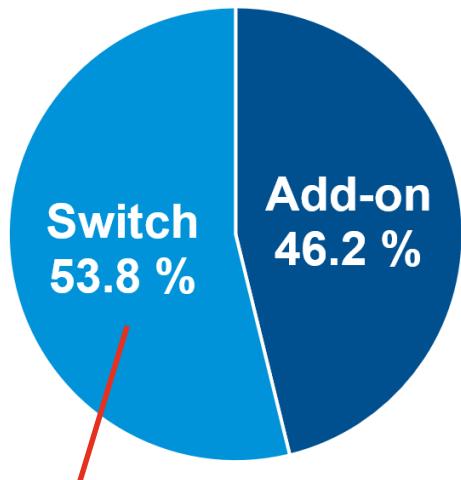
19家
醫學中心/
醫院

針對血糖控制不佳的患者

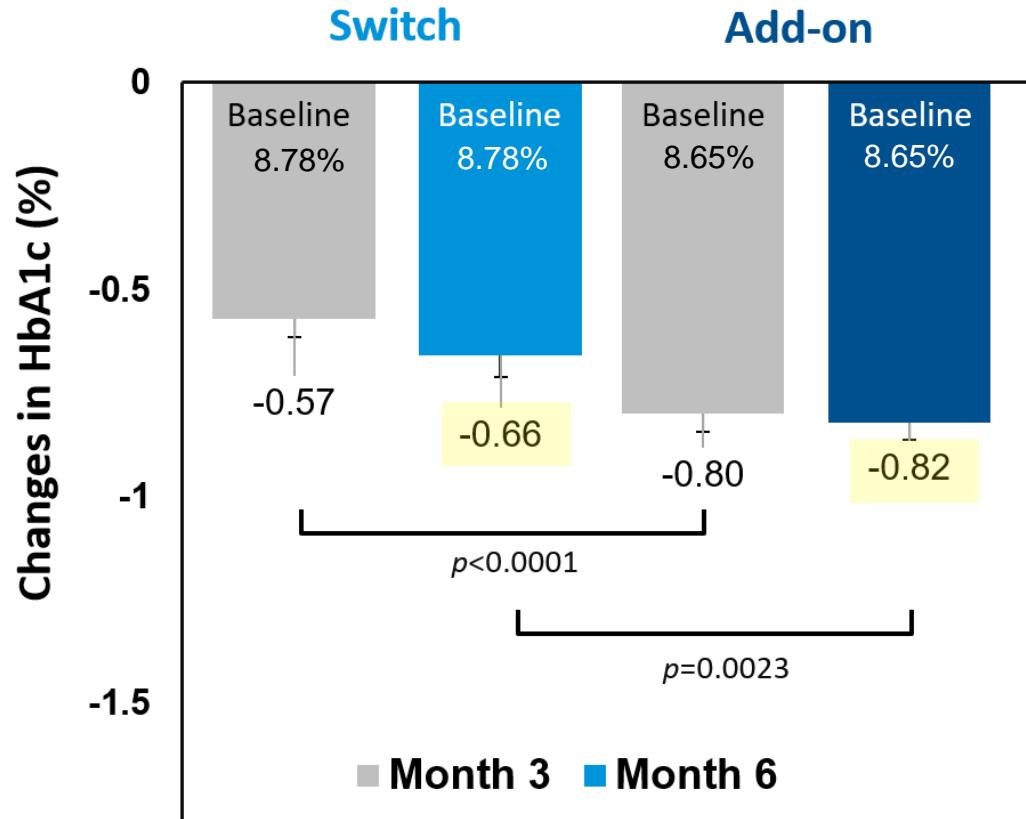
Add-on或switch成Dapagliflozin皆能有效降糖



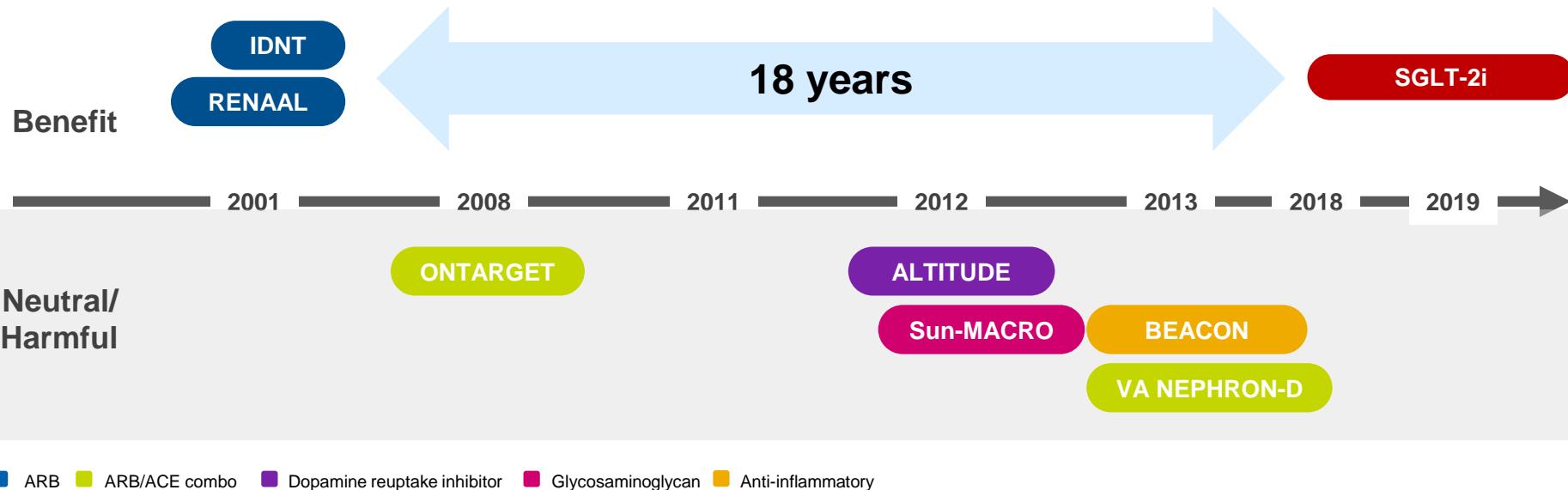
Switch or Add-on



DPP4 inhibitors accounted for the majority (**69.5%**) of the switched agents.



SGLT-2i突破18年未能有藥物降低腎臟硬終點



腎臟硬終點: doubling of serum creatinine, ESKD, or death

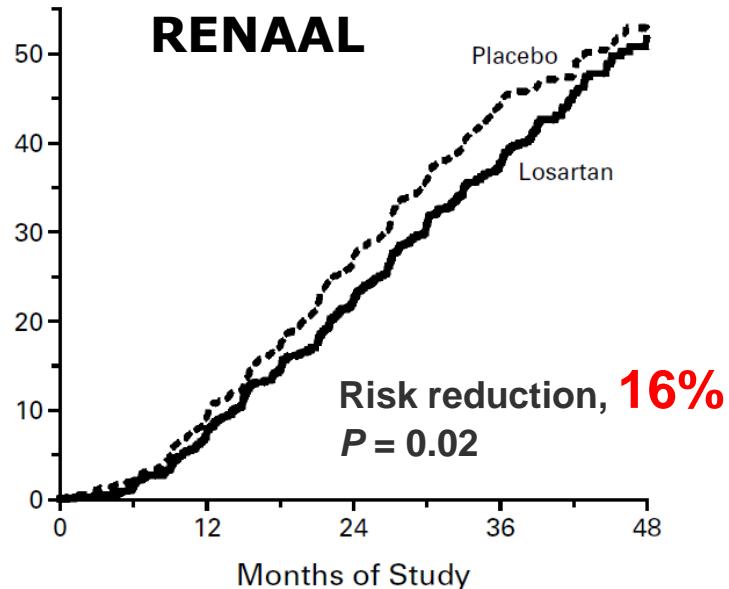
ONTARGET, BEACON demonstrated increased risk of events.

ALTITUDE, Aliskiren Trial in Type 2 Diabetes Using Cardio-Renal Endpoints; ARB, angiotensin receptor blocker; ACE, angiotensin-converting enzyme; BEACON, Bardoxolone Methyl Evaluation in Patients with Chronic Kidney Disease and Type 2 Diabetes Mellitus; IDNT, Irbesartan Diabetic Nephropathy Trial; ONTARGET, Ongoing Telmisartan Along and in Combination with Ramipril Global Endpoint Trial; RENAAL, Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan; SGLT2i, sodium-glucose cotransporter 2 inhibitor; Sun-MACRO, Sulodexide macro-albuminuria; VA NEPHRON-D, Veterans Affairs Nephropathy in Diabetes.

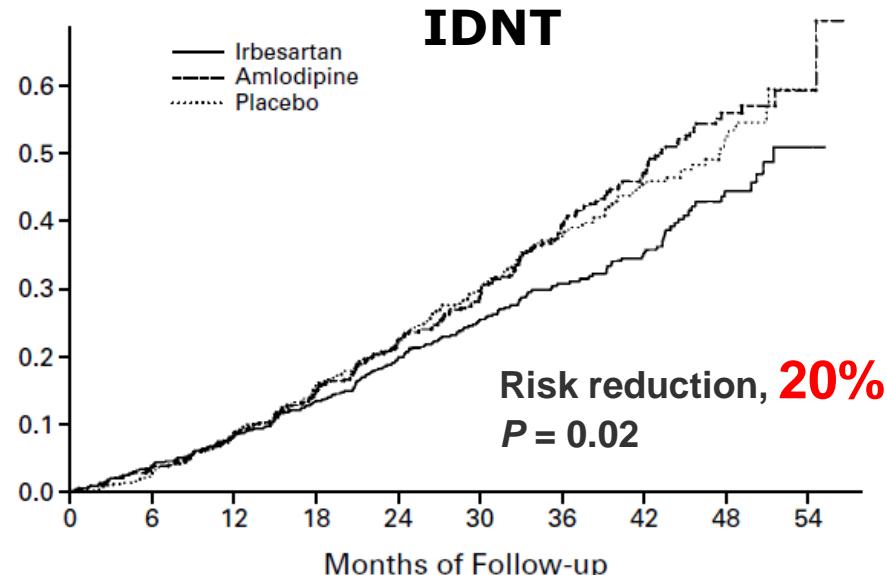
Chan GC, et al. *Nephrol Dial Transplant*. 2016;31:359-368. *Diabetes Metab*. 2019 Apr;45(2):110-121.

ARB在已有腎病變之糖尿病患能降低腎臟硬終點(-16%, -20%)

腎臟硬終點: **doubling of serum creatinine, ESKD, or death**



1513 patients with T2D and nephropathy were randomized to take losartan (50 to 100 mg once daily) vs. placebo with mean follow-up 3.4 years



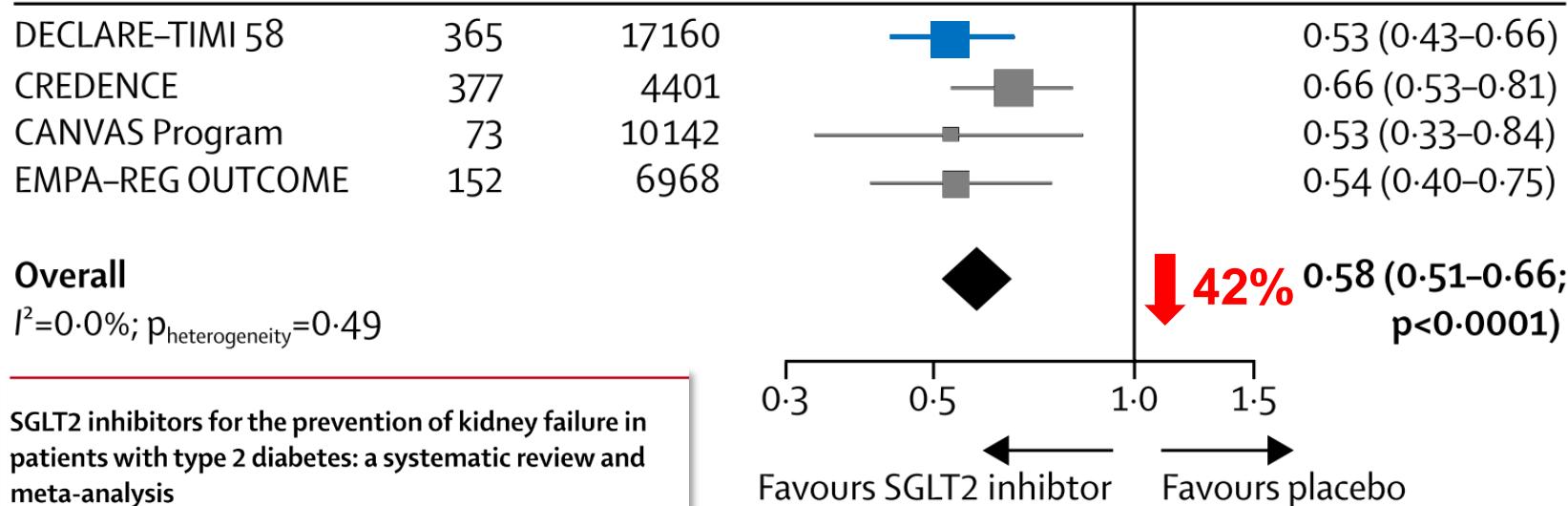
1715 hypertensive patients with nephropathy due to type 2 diabetes to treatment with irbesartan (300 mg daily), amlodipine (10 mg daily), or placebo with mean follow-up 2.6 years



SGLT-2i 統合分析：在>80%已使用ACEI or ARB的糖尿病患， 仍能下降42%腎臟事件風險

	DECLARE-TIMI 58	CREDENCE	CANVAS Program	EMPA-REG
Baseline use of RAS blockade	81.3%	99.9%	80.0%	80.7%

Substantial loss of kidney function, ESKD, or death due to kidney disease



SGLT2 inhibitors for the prevention of kidney failure in patients with type 2 diabetes: a systematic review and meta-analysis

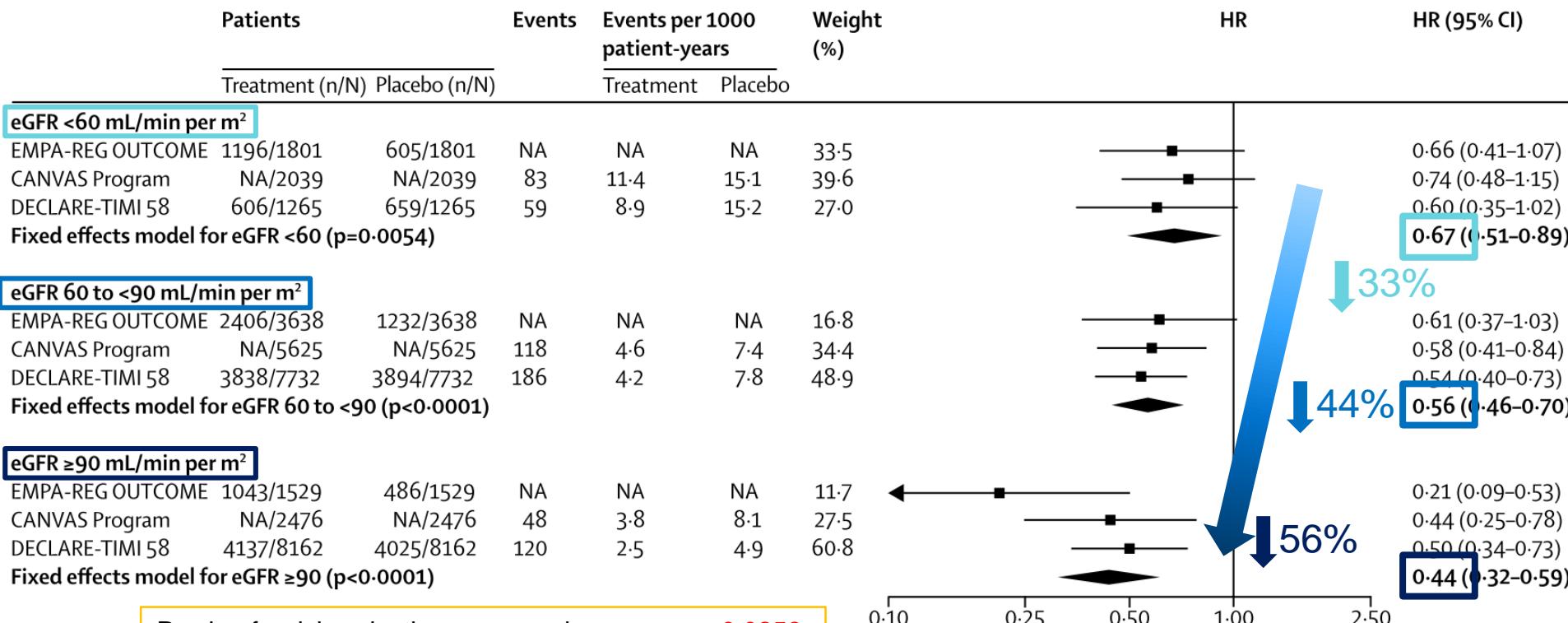
Brendon L Neuen, Tamara Young, Hiddo J Heerspink, Bruce Neal, Vlado Perkovic, Laurent Billot, Kenneth W Mahaffey, David M Charytan, David C Wheeler, Clare Arnott, Severine Bompoint, Adeera Levin, Meg Jardine

Lancet Diabetes Endocrinol. 2019 Nov;7(11):845-854.

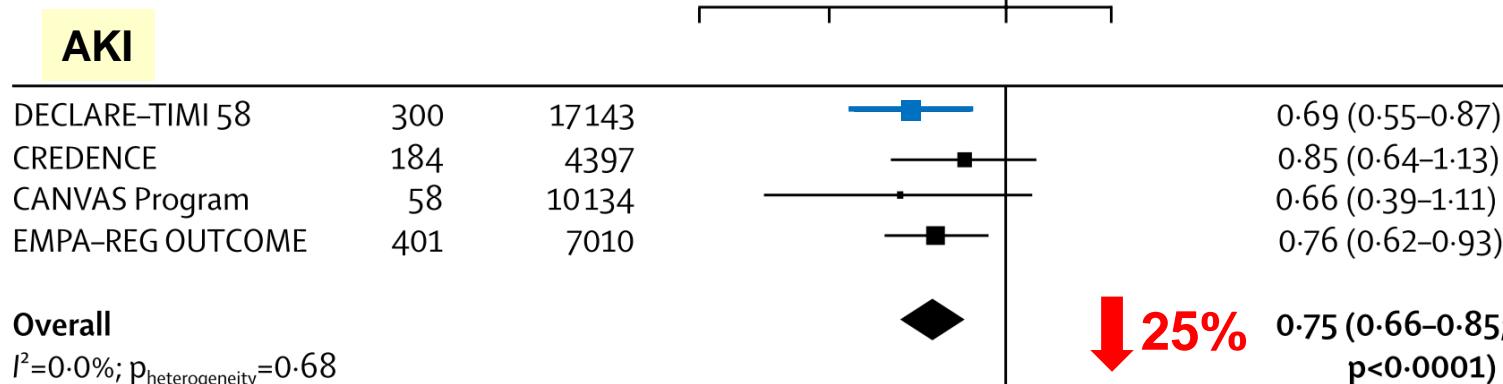
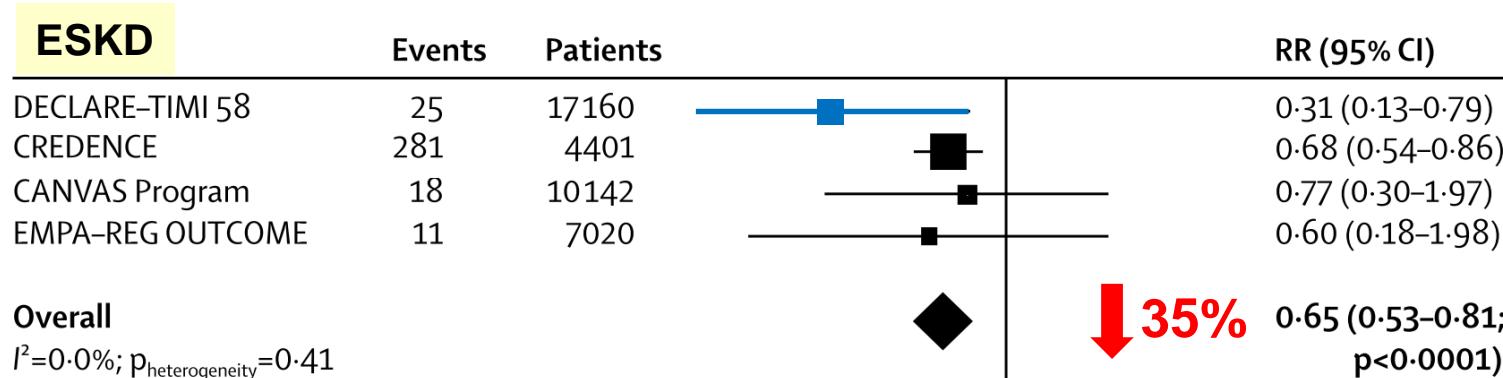
THE LANCET
Diabetes & Endocrinology

SGLT-2i 統合分析：越早使用，腎臟事件風險降低越多

Composite of worsening of renal function, ESRD, or renal death stratified by the eGFR levels

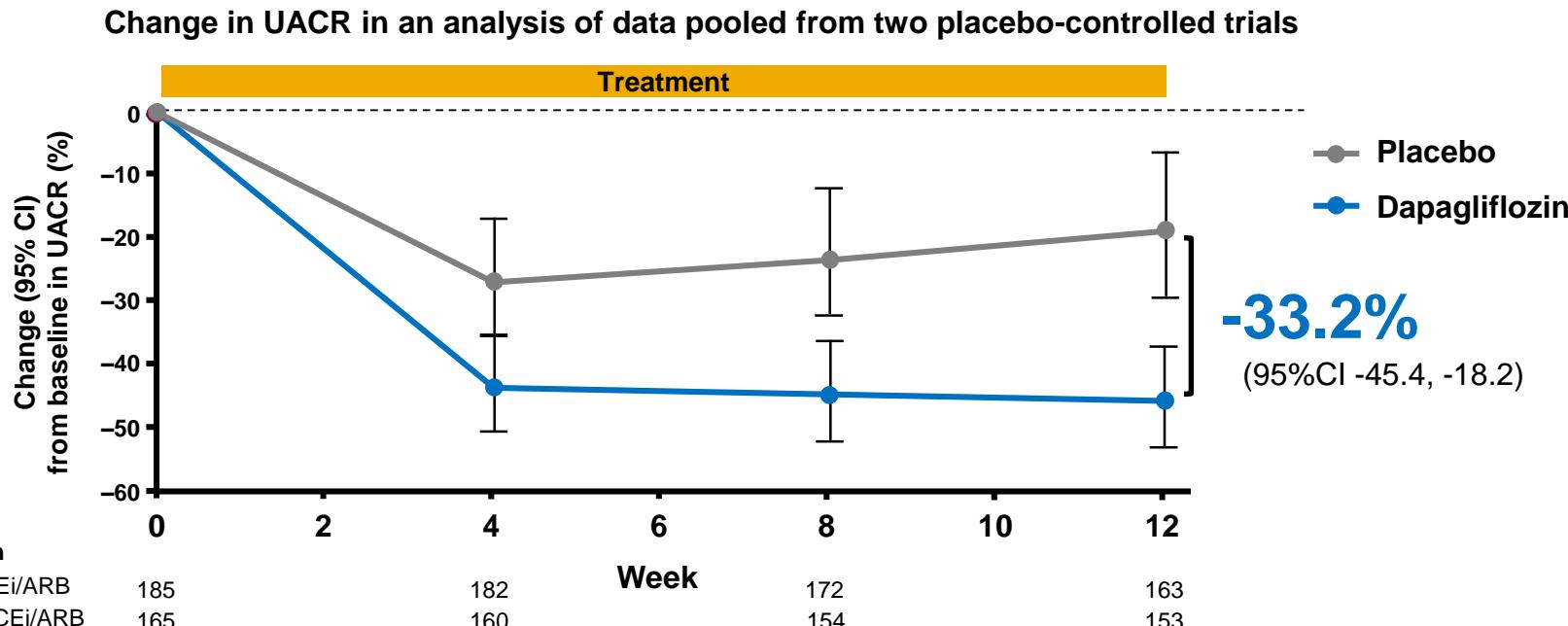


SGLT-2i 統合分析：下降35%ESKD風險、25%AKI風險



已使用ACEI或ARB的T2D病患， Dapagliflozin降低33%蛋白尿

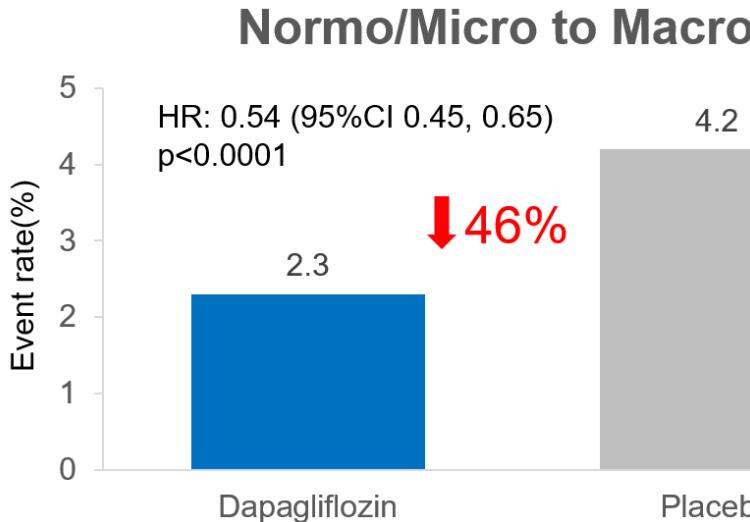
- Dapagliflozin reduces albuminuria in 356 T2DM patients with hypertension receiving ACEI or ARB – without increasing the frequency of renal adverse events



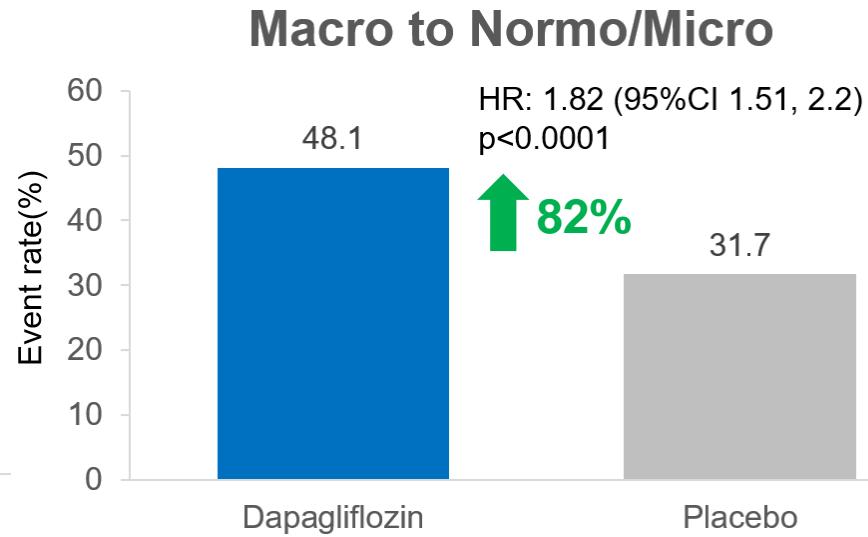
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; UACR, urine albumin:creatinine ratio.

Dapagliflozin 改善或降低蛋白尿惡化風險

蛋白尿惡化風險下降46%

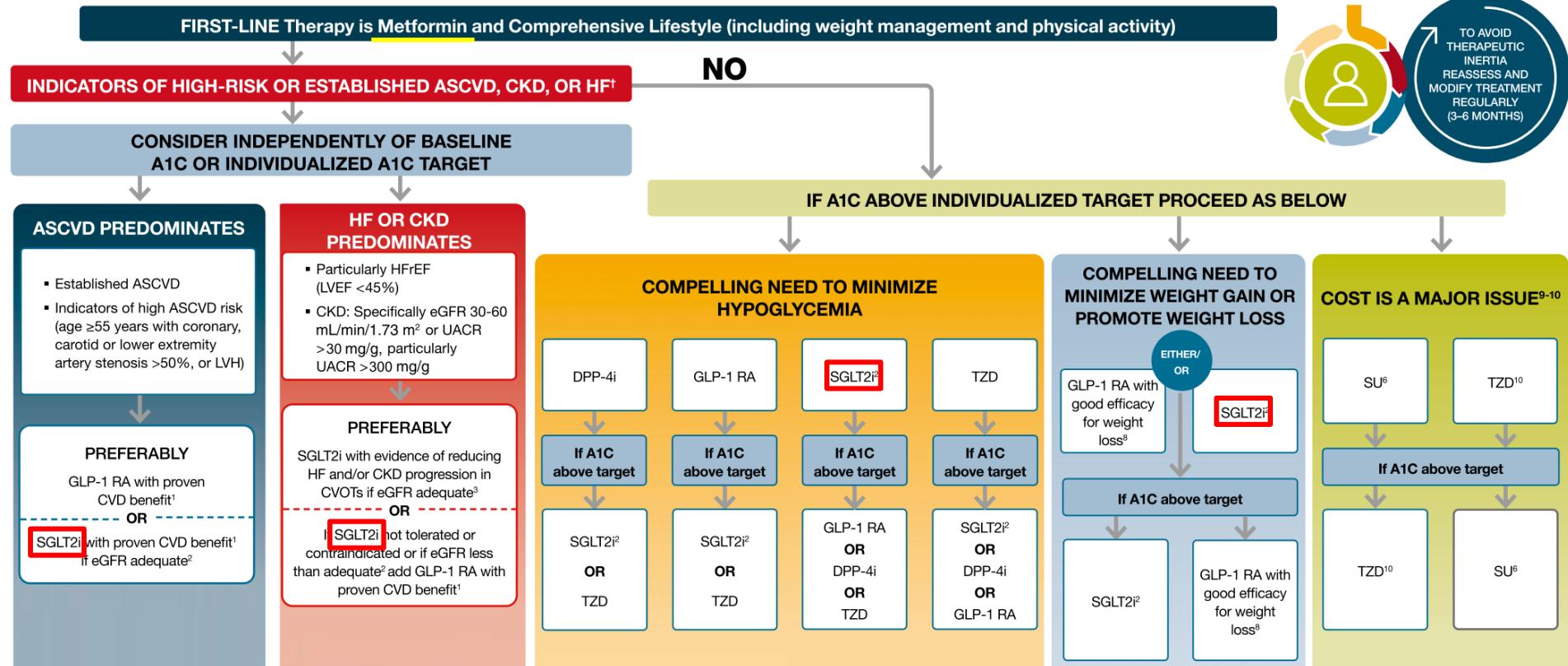


蛋白尿改善機會提升82%

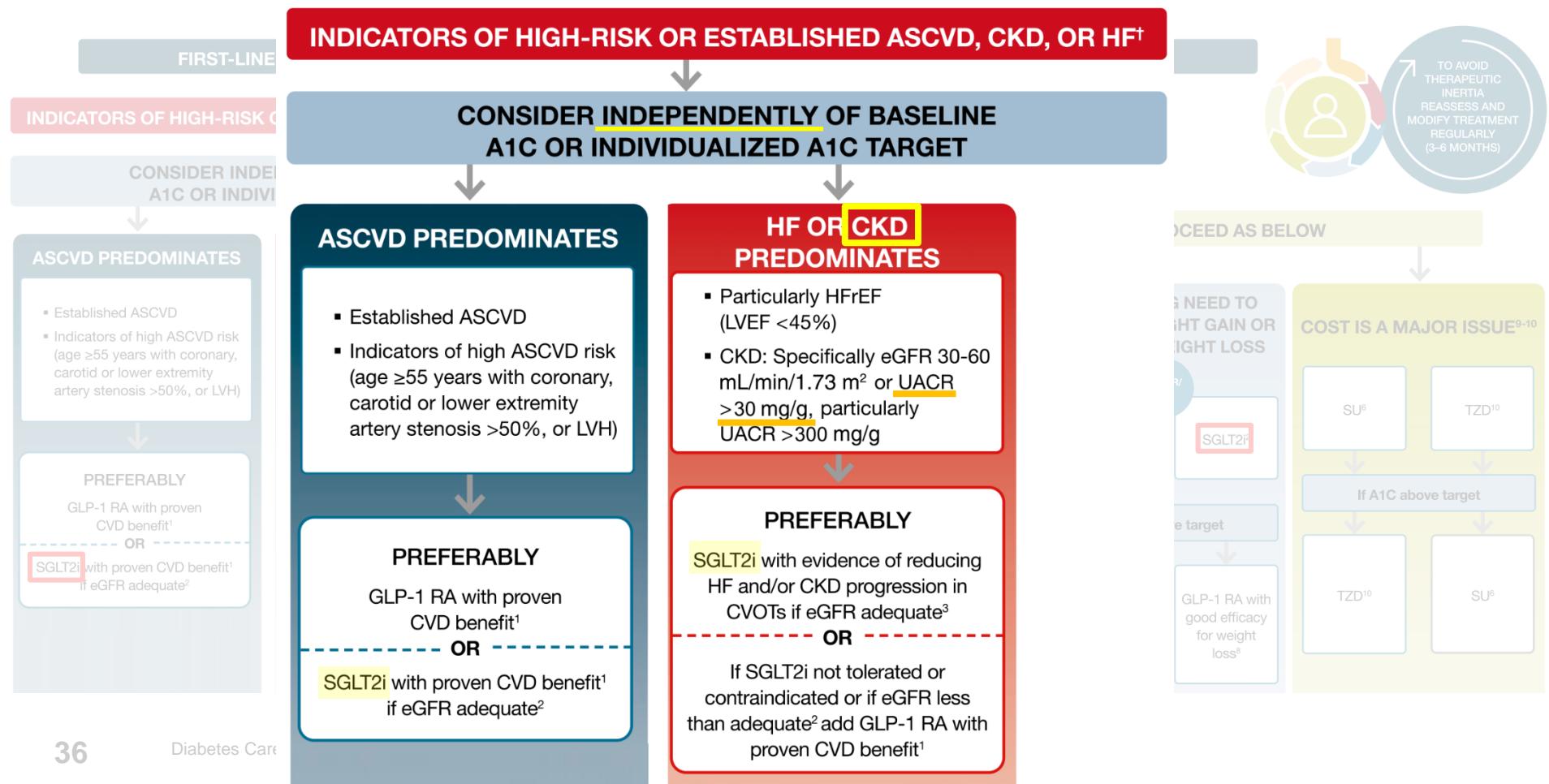


Definitions of Albuminuria Categories	
Macroalbuminuria	UACR ≥300 mg/g
Microalbuminuria	UACR ≥30 to <300 mg/g
Normoalbuminuria	UACR <30 mg/g

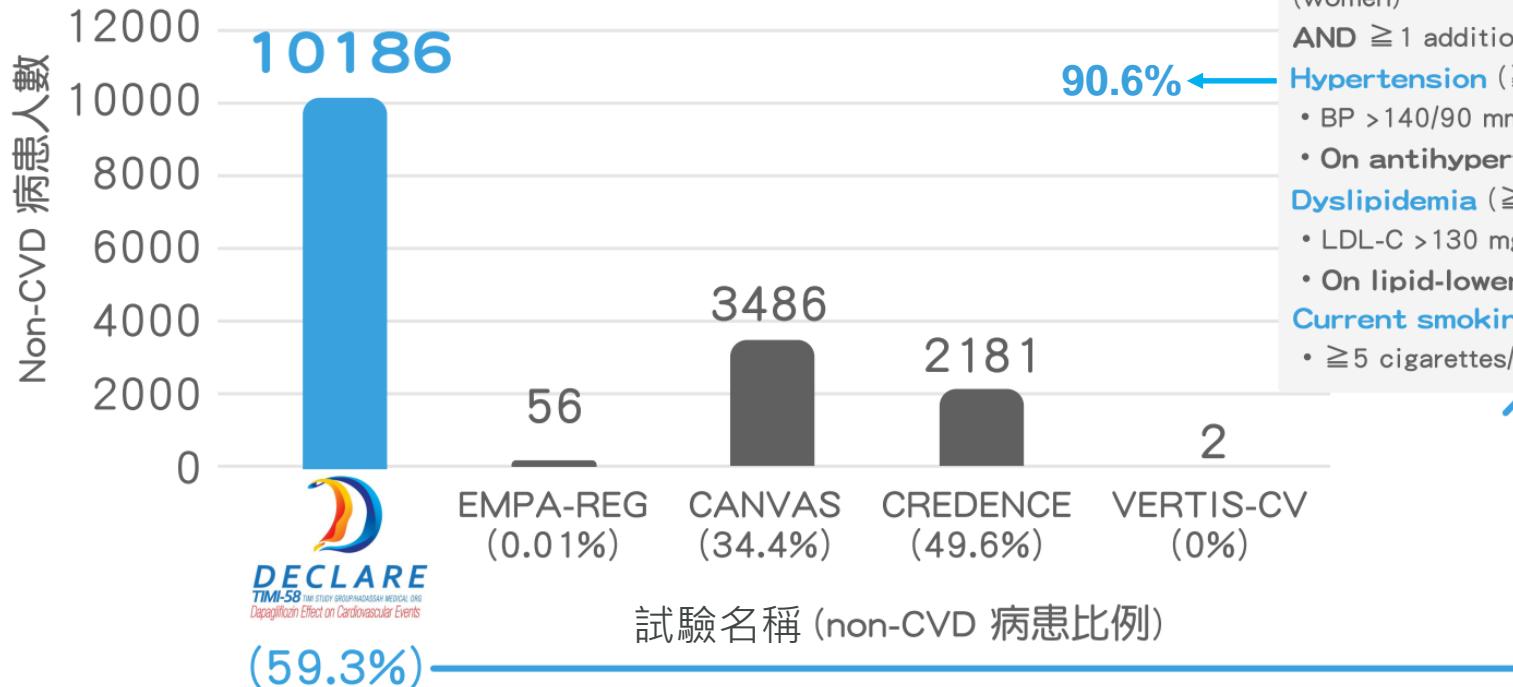
2020年ADA糖尿病治療指引：二線選擇SGLT-2i具多重角色



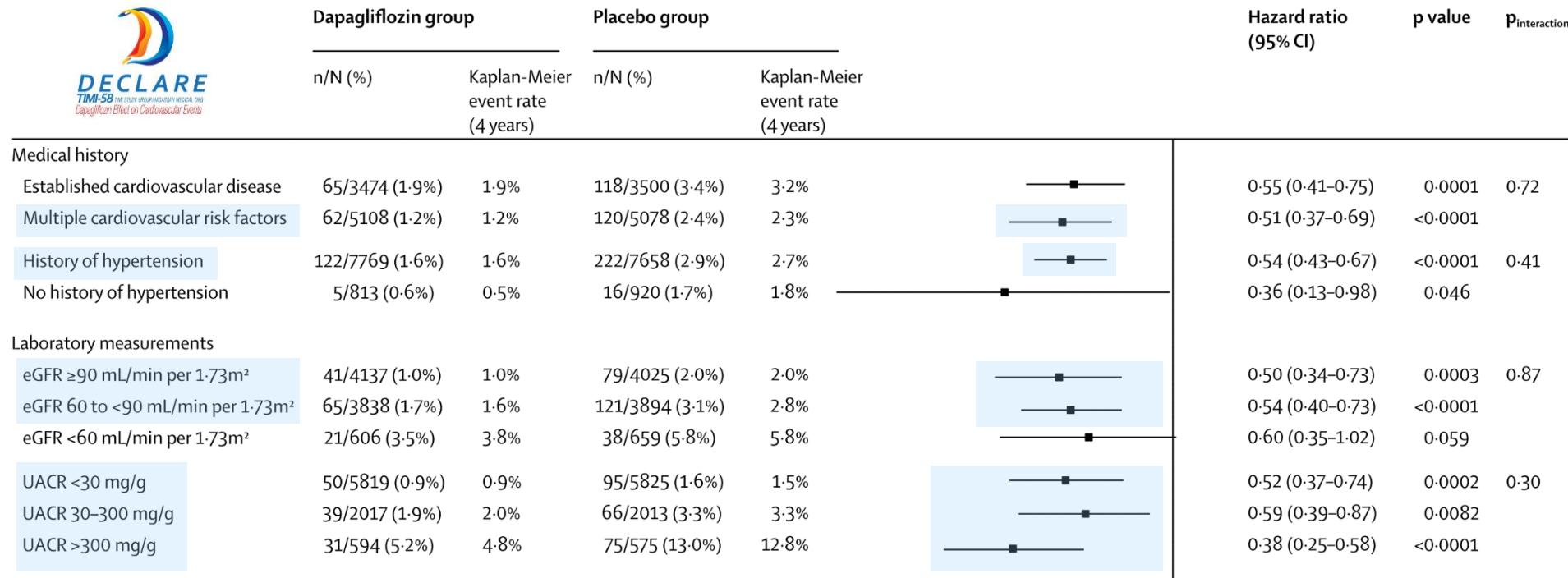
2020年ADA糖尿病治療指引：無論血糖，有蛋白尿病患優先使用SGLT-2i



Dapagliflozin唯一non-CVD糖尿病患萬人實證

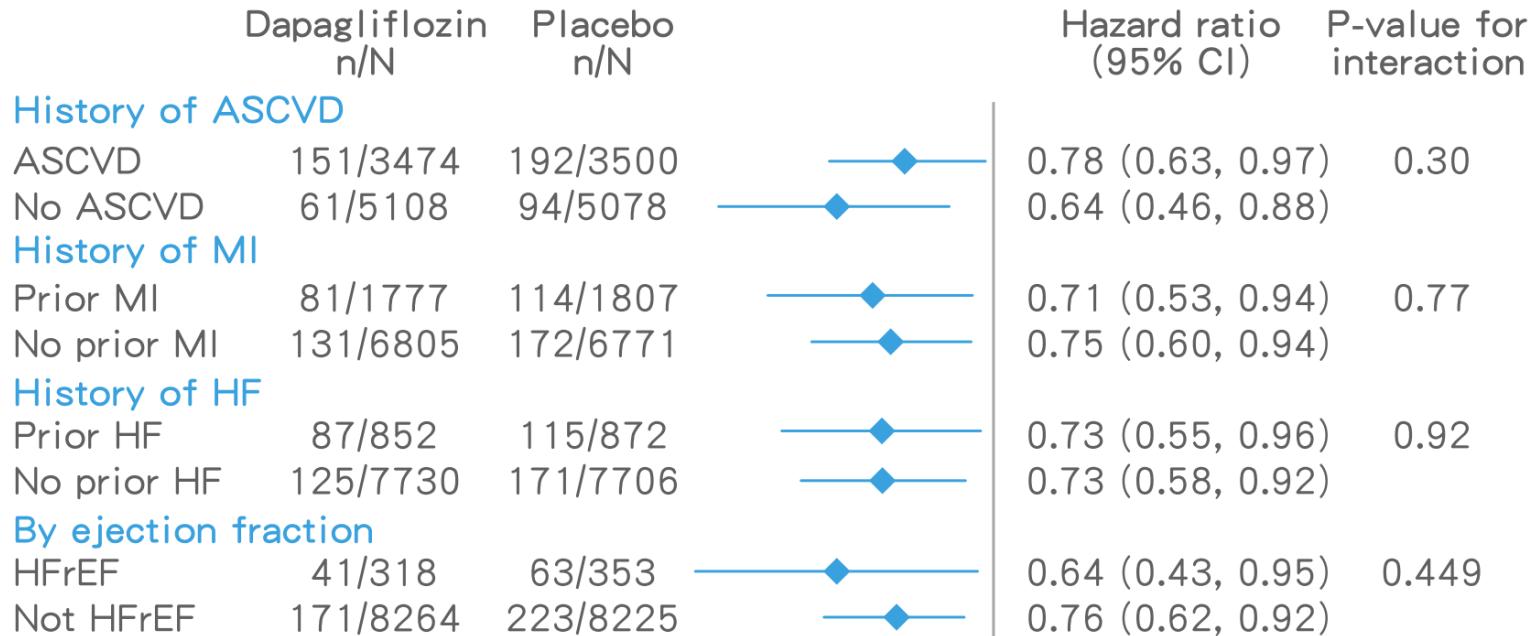


Dapagliflozin在eGFR好、無/微蛋白尿、non-CVD病患 皆一致有較低腎臟事件風險



THE LANCET
Diabetes & Endocrinology

Dapagliflozin在不同T2D病患一致有效預防心衰竭住院

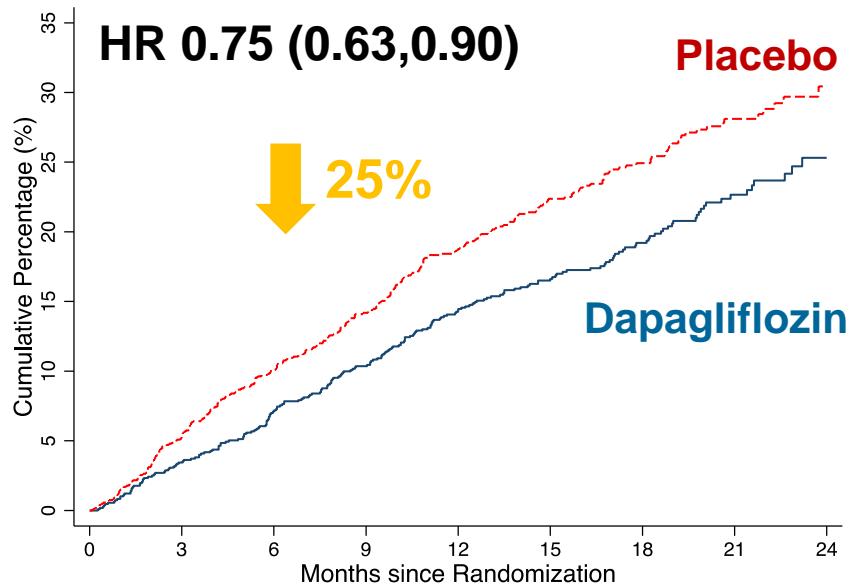


^aDefined as EF <45% or severe/moderate LV systolic dysfunction, with or without hx of HF. ASCVD = atherosclerotic CVD; CV = cardiovascular; CVD = CV disease; HF = heart failure; hHF = hospitalization for heart failure; HFrEF = HF with reduced ejection fraction; MI = myocardial infarction; T2D = type 2 diabetes.

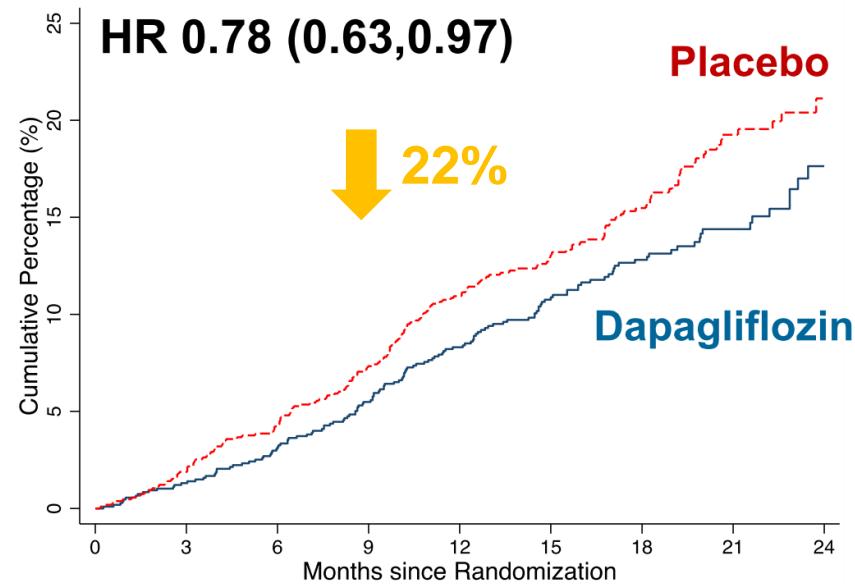
1. Wiviott SD et al. *N Engl J Med*. 2019;380:347-357; 2. Furtado RHM et al. *Circulation*. 2019 May 28;139(22):2516-2527.; 3. Kato ET et al. *Circulation*. 2019 May 28;139(22):2528-2536.

Dapagliflozin降低HF病患心衰竭住院、 心因性死亡、全死因死亡風險

HF hospitalization & CV death



All-cause death



Number at Risk

Dapagliflozin	1075	1037	994	955	876	678	500	259	88
Placebo	1064	1005	949	899	816	630	469	253	89

Number at Risk

Dapagliflozin	1075	1061	1042	1016	952	740	552	295	104
Placebo	1064	1044	1019	986	911	718	535	286	102

2020/4/1 台灣FDA核准Dapagliflozin仿單新增適應症： 針對第二型糖尿病患者可預防心血管事件



福適佳 膜衣錠 5毫克、10毫克 Forxiga Film-coated Tablets 5 mg, 10 mg



本藥須由醫師處方使用
5毫克 衛部藥輸字第026475號
10毫克 衛部藥輸字第026476號



1 適應症

1.1 血糖控制

第二型糖尿病。

1.2 預防心血管事件

用於具第二型糖尿病且已有心血管疾病(CVD)或多重心血管風險因子的成人病人時，Forxiga 可降低心衰竭住院的風險。

CVD MRF

2.2 建議劑量

為降低心衰竭住院的風險，Forxiga 的建議劑量為 10mg 每天 1 次。

News > Medscape Medical News > FDA Approvals

FDA Approves Dapagliflozin (*Farxiga*) for Low-EF Heart Failure

Steve Stiles

DISCLOSURES | May 06, 2020



6 Read Comments



+ ADD TO EMAIL ALERTS

The US Food and Drug Administration (FDA) has come through with the widely anticipated approval of dapagliflozin (*Farxiga*, AstraZeneca) for heart failure and reduced ejection fraction (HF_rEF), adding to the rich array of medications lately available for this indication.

News > Medscape Medical News

Diabetes Drug Slows Kidney Disease: DAPA-CKD Trial Stopped Early

Lucas Franki

March 31, 2020

0 Read Comments



+ ADD TO EMAIL ALERTS



ASN Kidney Week 2020

2020年10月20日 週二 – 2020年10月25日 週日

AstraZeneca has announced that the phase 3 DAPA-CKD trial for dapagliflozin (Farxiga) in patients with chronic kidney disease has been halted early because of overwhelming efficacy of the drug, at the recommendation of an independent data monitoring committee.

News > Medscape Medical News > Conference News > ADA 2020

DAPA-HF: Dapagliflozin Slows T2D Onset in Heart Failure Patients

Mitchel L. Zoler, PhD

June 16, 2020



1

Read Comment



+ ADDED TO EMAIL ALERTS

Dapagliflozin treatment of patients with heart failure but **without diabetes** in the DAPA-HF trial led to a **one-third cut** in the relative incidence of new-onset diabetes over a median follow-up of 18 months in a prespecified analysis from the multicenter trial that included 2,605 heart failure patients without diabetes at baseline.

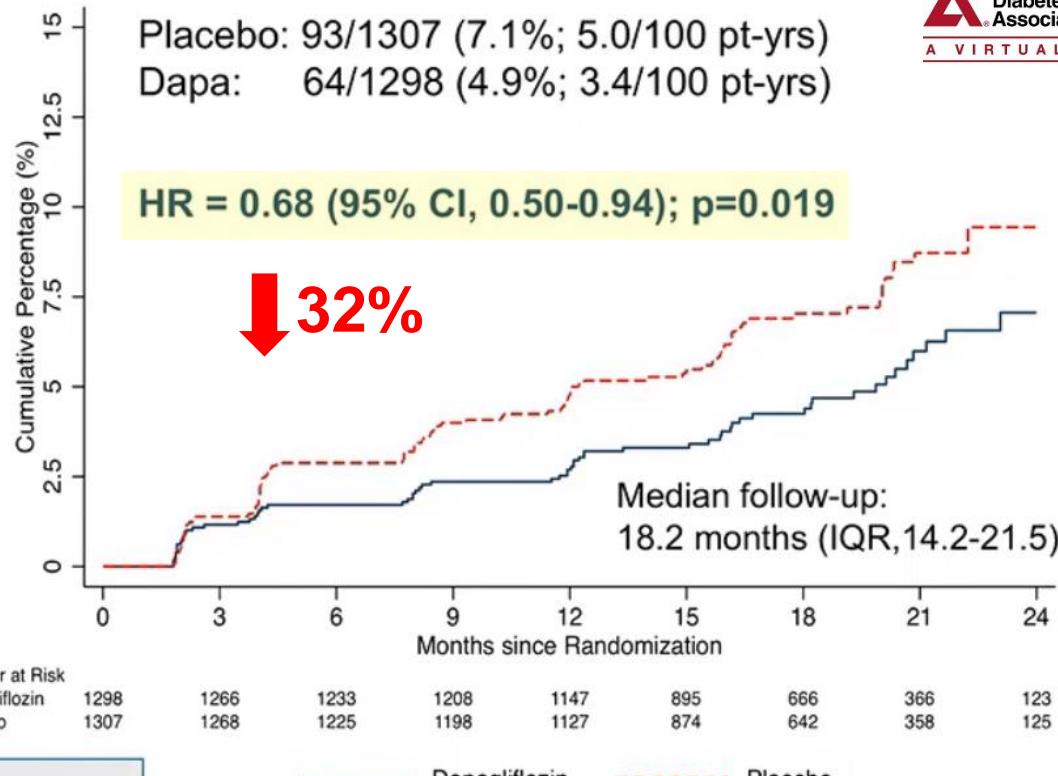


DAPA-HF Dapagliflozin於non-DM病患降低新發糖尿病風險

Results: Incidence of new onset T2D in dapa vs. placebo groups

2605 patients (55%) are no
diabetes in DAPA-HF with
A1c -0.05%

New onset T2D: A1c \geq 6.5%

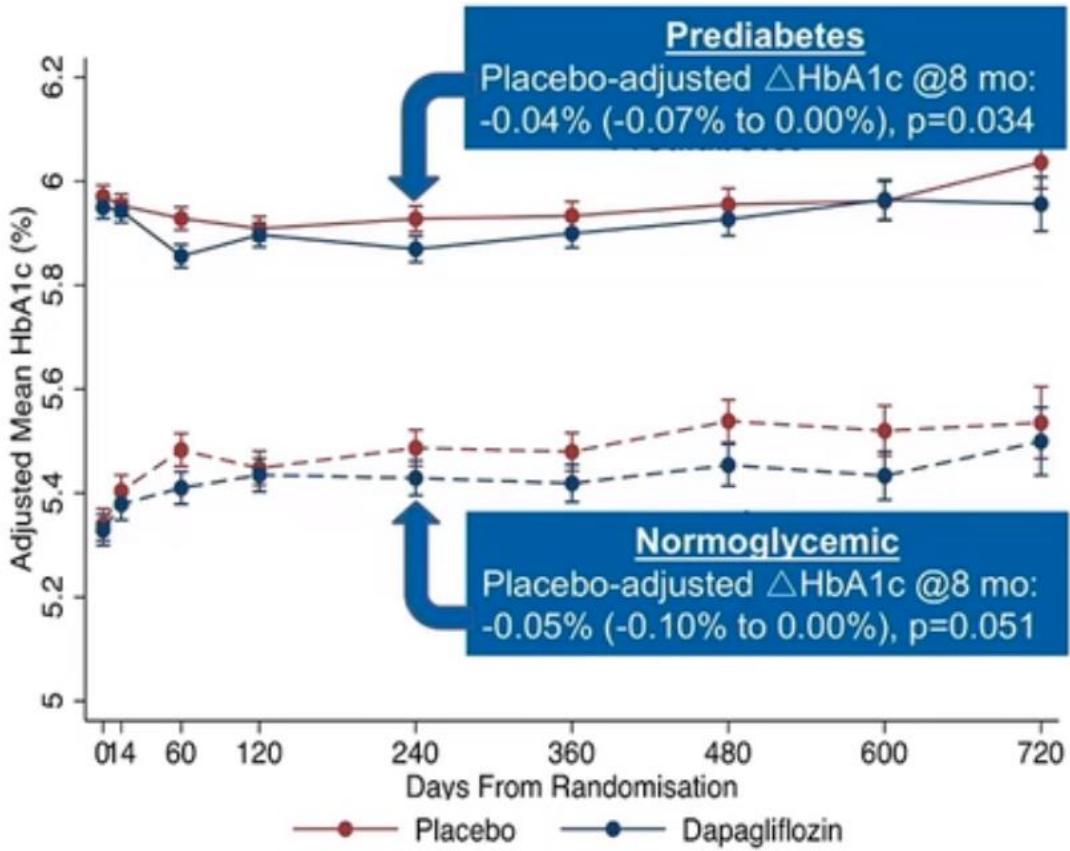




DAPA-HF Dapagliflozin於non-DM病患降低新發糖尿病風險

Results: HbA1c levels over time in dapa vs. placebo groups

- 1750 patients (67%) had pre-diabetes ($\text{HbA } 1\text{c} \geq 5.7\%$)
- 855 patients (33%) with normal HbA1c



結論

- 糖尿病病患，心腎病變已在發生
 - 腎小球高過濾狀態，eGFR正常，但50%腎元已經受損
 - 68%已有左心室功能不全
 - 合併高血壓 or 蛋白尿風險更高
- T2D病患使用**SGLT-2i**能降低心腎併發症風險，ADA、台灣糖尿病學會指引建議使用
- **Dapagliflozin**提供non-CVD糖尿病實證&適應症
 - 優質控糖：降低血糖波動
 - DECLARE 實證於CVD及non-CVD糖尿病患降低心腎風險

