

台灣血脂衛教協會

「2019-慢性腎臟病新舊防治法研討會」

109年01月11日(星期六)，高雄場 高醫

# 我們有機會阻止腎功能的惡化嗎？ Can we stop CKD from progression? – What's old and what's new?

## 黃尚志

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國家衛生研究院 成人健康研究所 兼任研究員



## 2019 Symposium: New Paradigms for CKD Prevention – From Old's to New's

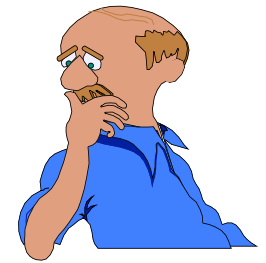
109/01/11 Sat. 13:30-17:00

【高雄】高醫\_自由(啓川)大樓六樓第2講堂 / 高雄市三民區自由一路100號

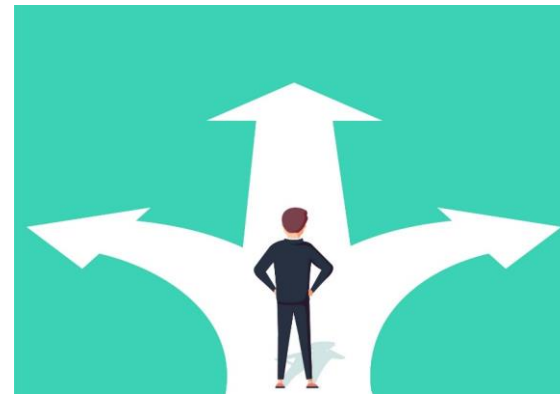
開始時間	結束時間	Topic	Speaker	Moderator
13:30	00:05 13:35	Opening	吳造中 理事長 台大醫院 內科部心臟科教授	
13:35	00:40 14:15	<ul style="list-style-type: none"> <li>● 以病人臨床醫療之藥物治療為主軸</li> <li>● 病人對象有DM、DKD、CKD、(CVD)</li> <li>● 參加的醫師包括CV、Endocrine、Nephrology、及其他</li> <li>● 主辦的是血脂學(協)會理事長CV大老</li> <li>● 講求的是What's New?</li> <li>● 我是非EBM/Guideline man</li> <li>● → 不好講！是個挑戰！</li> </ul>		吳造中 理事長 台大醫院 內科部心臟科教授
14:15	00:40 14:55			
14:55	00:15 15:10			
15:10	00:40 15:50			洪士元 部長 義大醫院 內科部部長
15:50	00:40 16:30	A special form of activated charcoal	義大醫院 內科部部長	
16:30	00:30 17:00	Panel discussion	All speakers and moderators	黃尚志 理事長 高雄醫學大學醫院 腎臟內科教授
17:00	00:05 17:05	Closing		

# Disease Treatment and Management

## -- Viewpoint from a senior physician

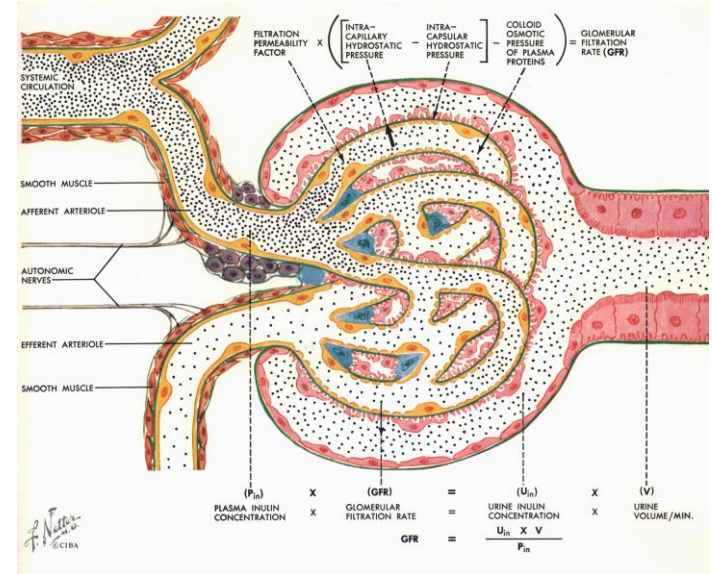


- Cure the disease, Eradicate the causative factors
- Control the disease activity , Slow the progression
- Prevent/Manage the complications
- Prevent the development of disease
- Prolong survival, Ensure quality of life
- Promote ACP 、 Palliative care 、 Hospice
- Outcome measures
  - Hard outcomes
  - Composite outcomes
  - Surrogate markers



# Can we **Stop** CKD from progression?

- Stop
  - **CKD** progression or
  - **Renal Function** deterioration or
  - **GFR** decline
- What is renal function?
- GFR 狹義腎功能
- Does other renal markers help? (Uacr or Upcr)
- Is it possible to **stop** GFR decline in CKD?
- Or just **slow (retard)** GFR decline in CKD?



Glomerular Filtration Rate, GFR  
單位時間內(分鐘)腎動脈內血漿由腎絲球過濾出之過濾液總量(每分鐘毫升)

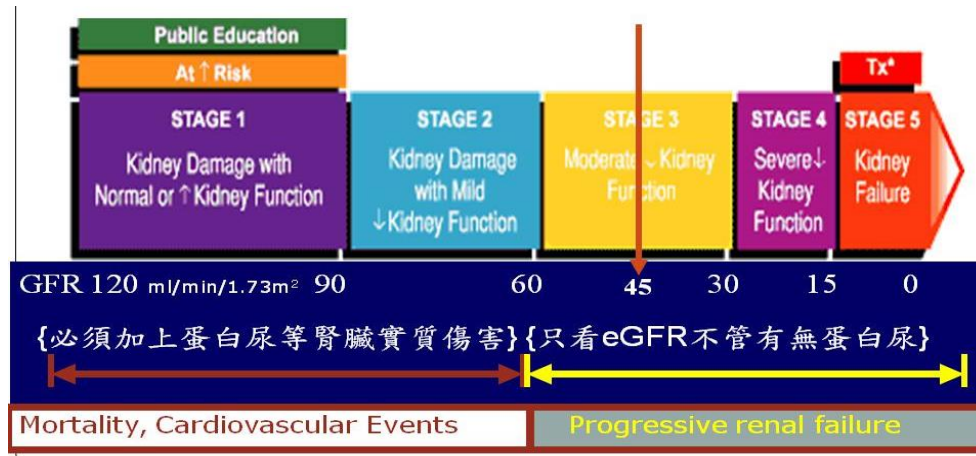
Uacr : Urine albumin to creatinine ratio (mg/g creatinine)

Upcr : Urine total protein to creatinine ratio (mg/g creatinine)

# Can we slow GFR decline in CKD?

## 慢性腎臟病 (CKD)的定義

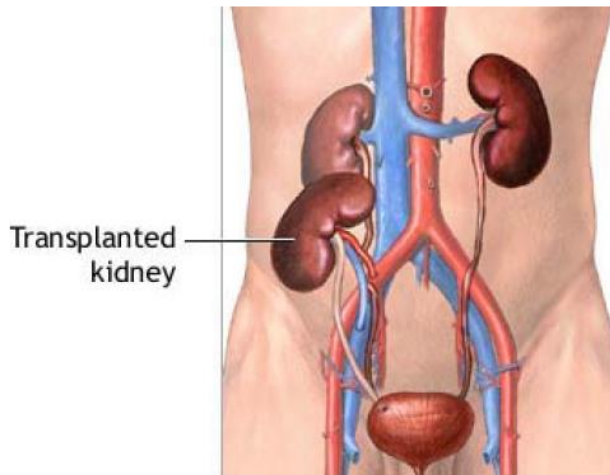
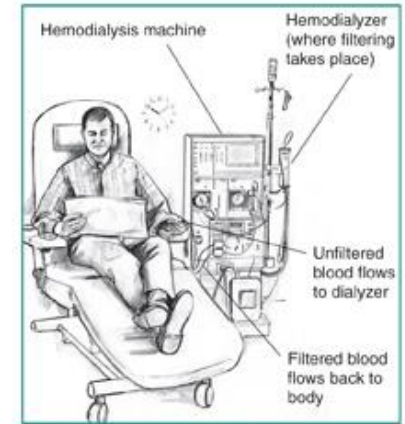
- 2002美國國家腎臟基金會的定義
  - 腎絲球濾過率: >60 ml/min + 腎臟實質傷害
    - 微蛋白尿、血尿、影像學證據、病理學證據
  - 腎絲球濾過率: <60 ml/min
  - 大於三個月
- 腎絲球濾過率的測定 (運用公式計算)
  - MDRD (CKD-EPI)



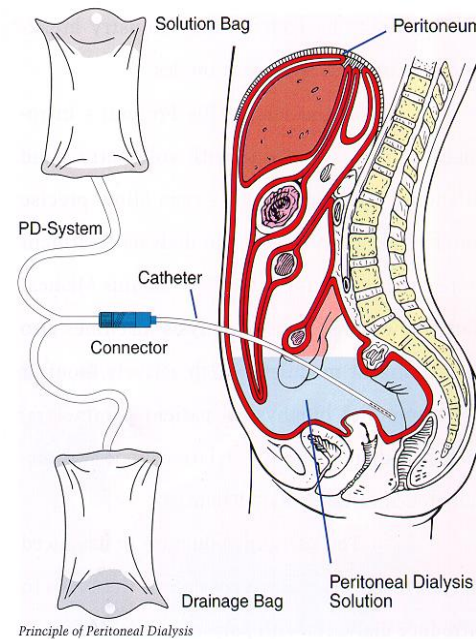
- To Slow GFR decline (CKD Progression)
  - What? (What kind of disease?)
  - Who? (Man or Woman, Young or Old Age, New or Old)
  - When? (At which period of disease course, CKD G1-G5, A1-A3)
  - Why? (Through what mechanisms)
  - How? (Treatment Regimens or Medications or Care plan)

# 腎臟替代療法 Renal Replacement Therapy, RRT

- 透析 Dialysis(洗腎)
  - 血液透析 HD (洗血液)
  - 腹膜透析 PD (洗肚子)
- 腎臟移植 Renal Transplantation(換腎)
  - 屍腎移植(換往生者的)
  - 活體腎移植(換親人的)



斯斯有兩種



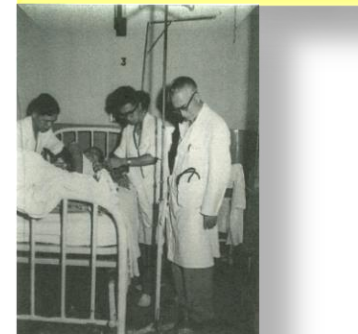
# 台灣透析醫療發展里程碑

- 1963: 血液透析
- 1964: 腹膜透析
- 1968: 腎臟移植
- 1983: 中華民國腎臟醫學會成立
- 1984: 連續性攜帶式腹膜透析(CAPD)
- 1987: 台灣地區透析院所實地訪查評量
- 1995: 全民健康保險
- 1996: 透析軟體
- 2001: 透析總額預算
- 2003: 健康局與TSN慢性腎臟疾病防治(CKD)
- 2004: 健保局透析品質監測(季報告)
- 2005: 台灣地區透析醫療品質監測與新制透析評量



1963年8月 日本建倍式血液透析者

1963 The First HD case



1964

The  
First  
PD  
case

1968 The first renal  
transplantation case



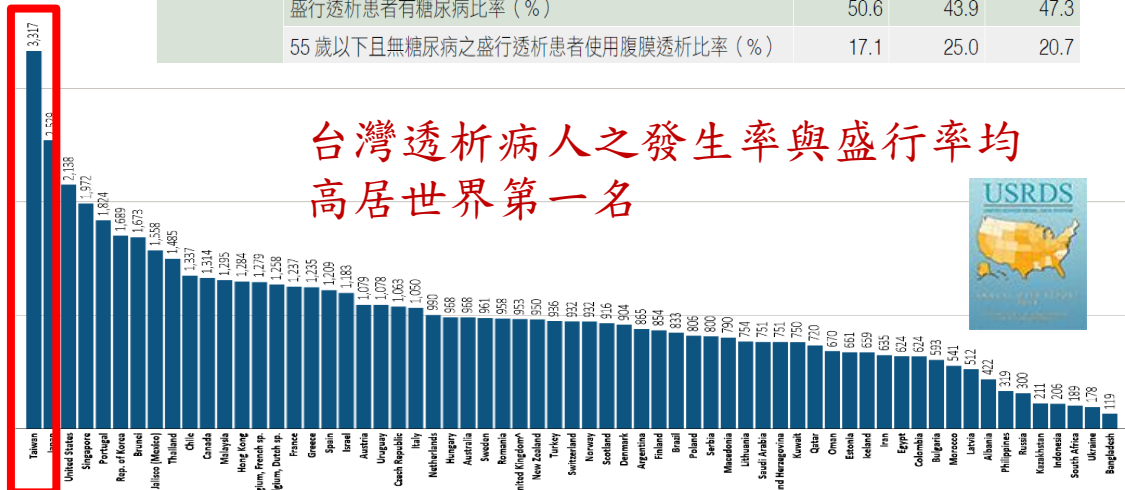
表 1

2016 年台灣透析現況

	男性	女性	總計
透析發生數	6,363	5,233	11,596
使用血液透析人數	5,735	4,667	10,402
使用腹膜透析人數	628	566	1,194
透析前參與 Pre-ESRD 照護計畫人數	3,860	3,191	7,051
透析前參與 Pre-ESRD 計畫比率 (%)	60.7	61.0	60.8
透析前一年參與 Pre-ESRD 計畫人數	1,008	779	1,787
透析前一年參與 Pre-ESRD 計畫比率 (%)	15.8	14.9	15.4
透析發生率 (每百萬人)	543	443	493
年齡標準化透析發生率 (每百萬人)	374	268	322
新發透析患者合併有糖尿病人數	2,976	2,364	5,340
新發透析患者合併有糖尿病比率 (%)	45.2	46.8	46.1
新發透析患者合併有糖尿病於透析前一年參與 Pre-ESRD 計畫人數	575	433	1,008
新發透析患者合併有糖尿病於透析前一年參與 Pre-ESRD 計畫比率 (%)	19.3	18.3	18.9
55 歲以下且無糖尿病之新發透析患者使用腹膜透析比率 (%)	25.2	39.0	30.9
透析盛行數	40,844	39,004	79,848
透析盛行率 (每百萬人)	3,485	3,300	3,392
年齡標準化透析盛行率 (每百萬人)	2,436	2,064	2,255
盛行透析患者有糖尿病比率 (%)	50.6	43.9	47.3
55 歲以下且無糖尿病之盛行透析患者使用腹膜透析比率 (%)	17.1	25.0	20.7

發生

盛行



台灣透析病人之發生率與盛行率均高居世界第一名



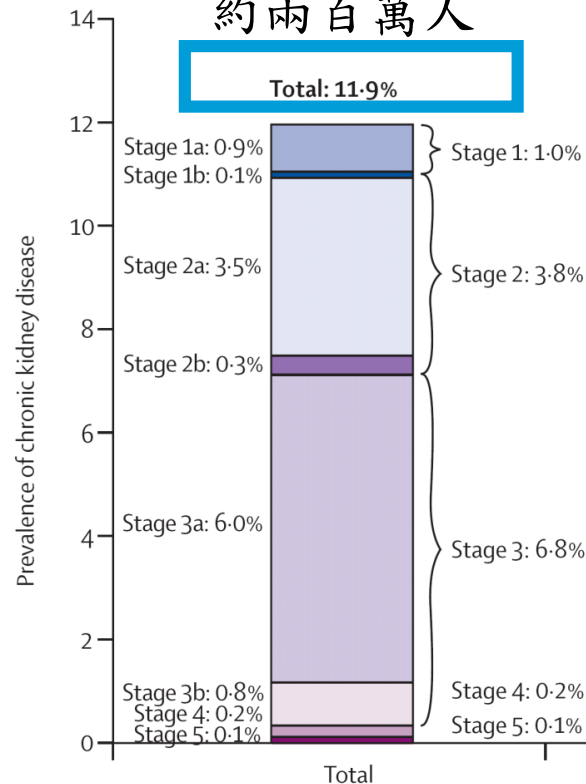
2015 接受治療透析病人之盛行率

# Hard outcomes in Renal Medicine – Death, ESRD on RRT

The culprits 罪魁禍首  
萬惡的罪魁 – 藏鏡人

CKD

約兩百萬人



2: National prevalence of chronic kidney disease in adults in



# 健保年度預算與透析支出

自由時報 2019-09-02 9萬人洗腎創新高...年花健保近450億 腎病醫療費513億 蟬聯10大疾病首位

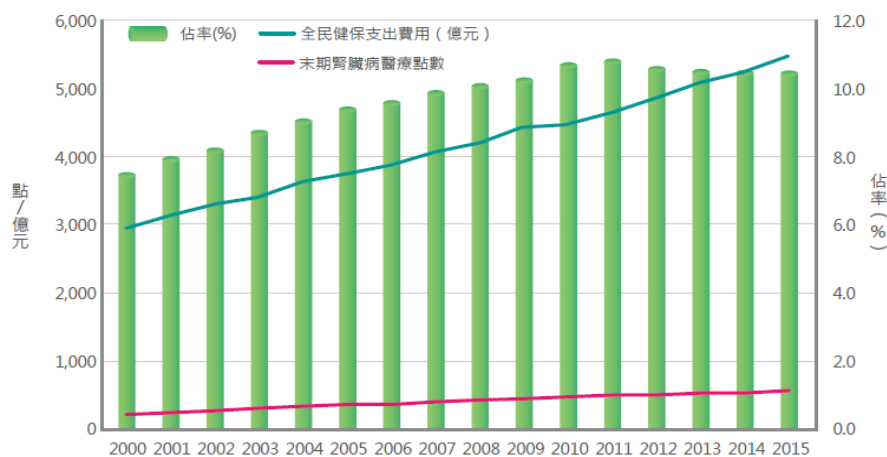
健保支出腎病最花錢！衛福部健保署統計，慢性腎臟病再度蟬聯去年(107年, 2018)使用醫療費用最多的十大疾病首位，共計36.4四萬人就醫，花費約513.78億元，占健保總額近7%，為所有單一疾病花費之首，且洗腎達到9萬人，一年花費449.46億，包含血液透析8.2萬人、腹膜透析6490人，平均每名洗腎患者年花健保近50萬元。

除了慢性腎臟病，其次花費健保最多是糖尿病291.68億、齒齦炎及牙周疾病171.02億、齲齒167.09億、高血壓139.2億元。

## 透析總額每年成長率

Year	Dialysis budget Growth rate, %
2003	10.0
2004	8.0
2005	7.8
2006	6.68
2007	2.886
2008	2.886
2009	2.886
2010	2.0
2011	0
2012	0+1
2013	1+1
2014	3.7
2015	3.7
2016	3.8
2017	4.0
2018	3.5
2019	3.1
2020	3.25

圖 95 全民健保支出與末期腎臟病患者總醫療點數之歷年趨勢

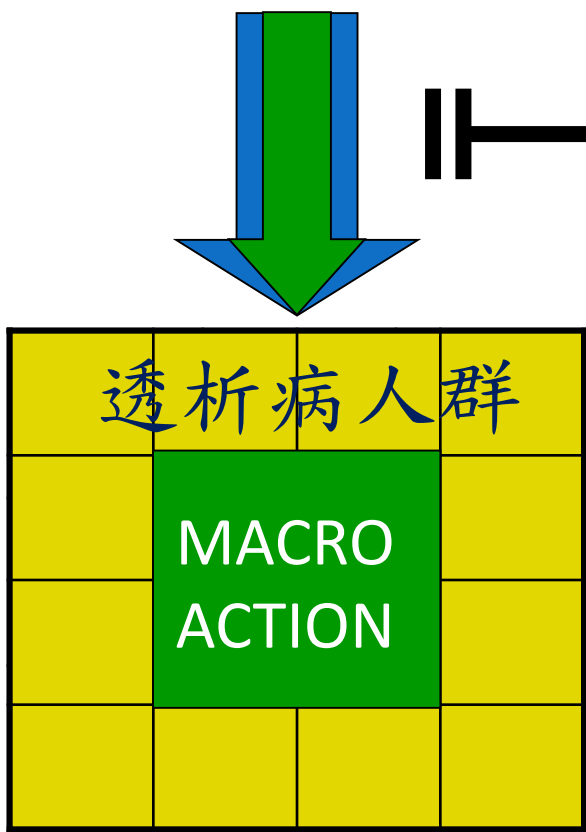


公衛健康----  
排名，名聲  
面子問題

醫療財務----  
支出，負擔  
裡子問題

減少末期腎臟病患人數的基本策略

## 減少進入透析流量



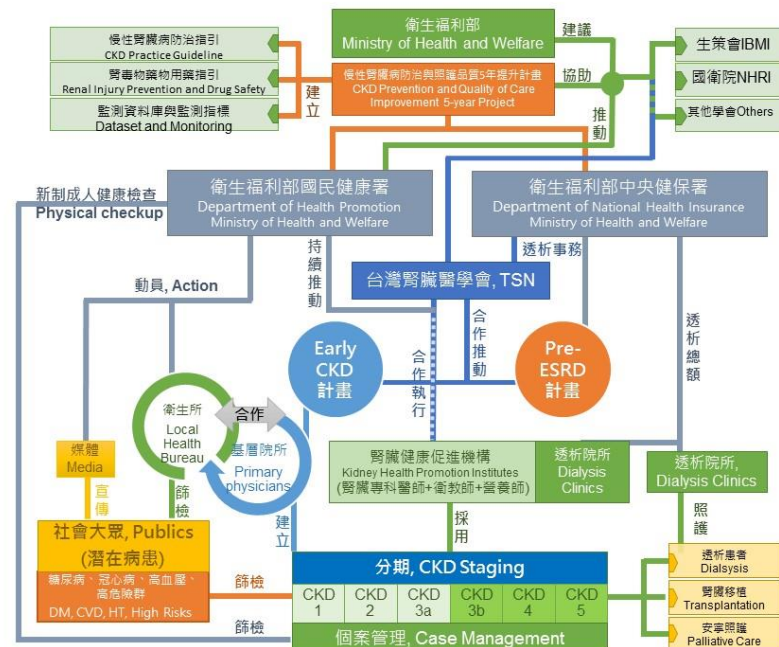
疏導退出透析流量

1. 找出造成CKD/ESRD的危險因子
2. **CKD的防治行動**
  - 1) 全民運動
  - 2) 民眾教育
  - 3) 篩檢危險群
3. **治療腎臟疾病**
  - 1) 醫師教育
  - 2) 衛教體系
  - 3) 治療準則
4. **阻緩腎功能惡化速度**
5. 嚴格管控開始透析之條件
6. 處理慢性病患急性發作的問題
7. **做好Pre-ESRD之照護計畫**
8. 防治急性腎傷害AKI
9. **特殊ESRD病患是否進入透析**: 極老、失能、多重器官衰竭ESRD病人....

鼓勵腎臟移植  
透析終止與退出透析

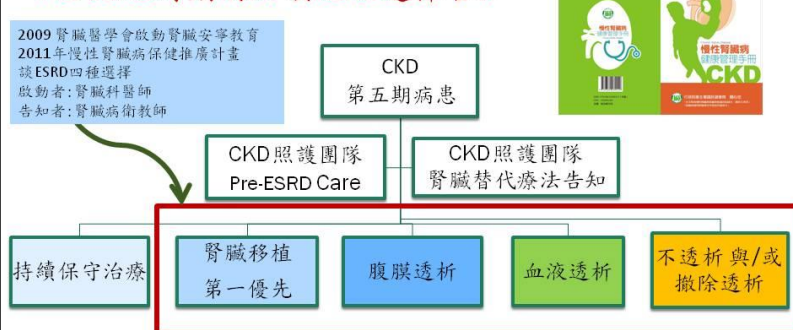
# 台灣CKD防治計畫的推展 Macro-Action Plans

- 2001 TSN於衛生署慢性病委員會提議
- 2002國民健康局開始投入先導計畫
- 2003腎臟醫學會成立CKD防治委員會
- 2003健康局與腎臟醫學會合作腎臟保健推廣機構計畫
- 2007健保局Pre-ESRD整體照護計畫
- 2011健保局初期慢性腎臟病醫療給付改善方案計畫
- 2009腎臟醫學會年會開始安排安寧療護教育課程
- 2111慢性腎臟病保健推廣計畫談ESRD四種選擇
- 2014~腎病年報、臨床診療指引



台灣腎臟病防治計畫佈陣圖 2003~

## Pre-ESRD時期的四項ESRD選擇告知



## 醫療自主照護計畫 Advance Care Plan



# 台灣CKD 整體照護研究有效性證據

## Summarized results of Early CKD and Pre-ESRD Program

- 降低病患死亡率
- 較佳的生活品質
- 較少的醫療費用
- 較好的照護品質
- 較慢的惡化速度

Chronic kidney disease care program improves quality of pre-end-stage renal disease care and reduces medical costs

SHU-YI WEI,<sup>1</sup> YONG-YUAN CHANG,<sup>2</sup> LIH-WEN MAU,<sup>3</sup> MING-YEN LIN,<sup>4</sup> HERNG-CHIA CHIU,<sup>5</sup> JER-CHIA TSAI,<sup>4,5</sup> CHIH-JEN HUANG,<sup>6,7</sup> HUNG-CHUN CHEN<sup>4,5</sup> and SHANG-JYH HWU<sup>1</sup> *Nephrology* 15 (2010) 108-115

*Nephrology* 2010;15:108-115

**NDT 2009;24:3426-3433**

*Nephrology*. 2014;19:699-707

NDT 2013.28:671-682

*Am J Medicine*. 2015;128:68-76

NDT 2017;32(7):1184-1194

- 改善Pre-ESRD病人的血壓良好率，改善第五期病人血比容良好率
- 每年 eGFR ml/min/1.73m<sup>2</sup>/yr 改變
  - 蛋白尿 (-2.93), Stage 3b (-1.19), Stage 4 (-1.67), Stage 5 (-0.86)
- 降低心臟、中風、周邊血管併發症的發生
- 降低透析與死亡的發生
- 較頻繁的檢驗，較佳的透析準備
- 降低死亡風險並節省醫療費用
- 提升病患遵從性

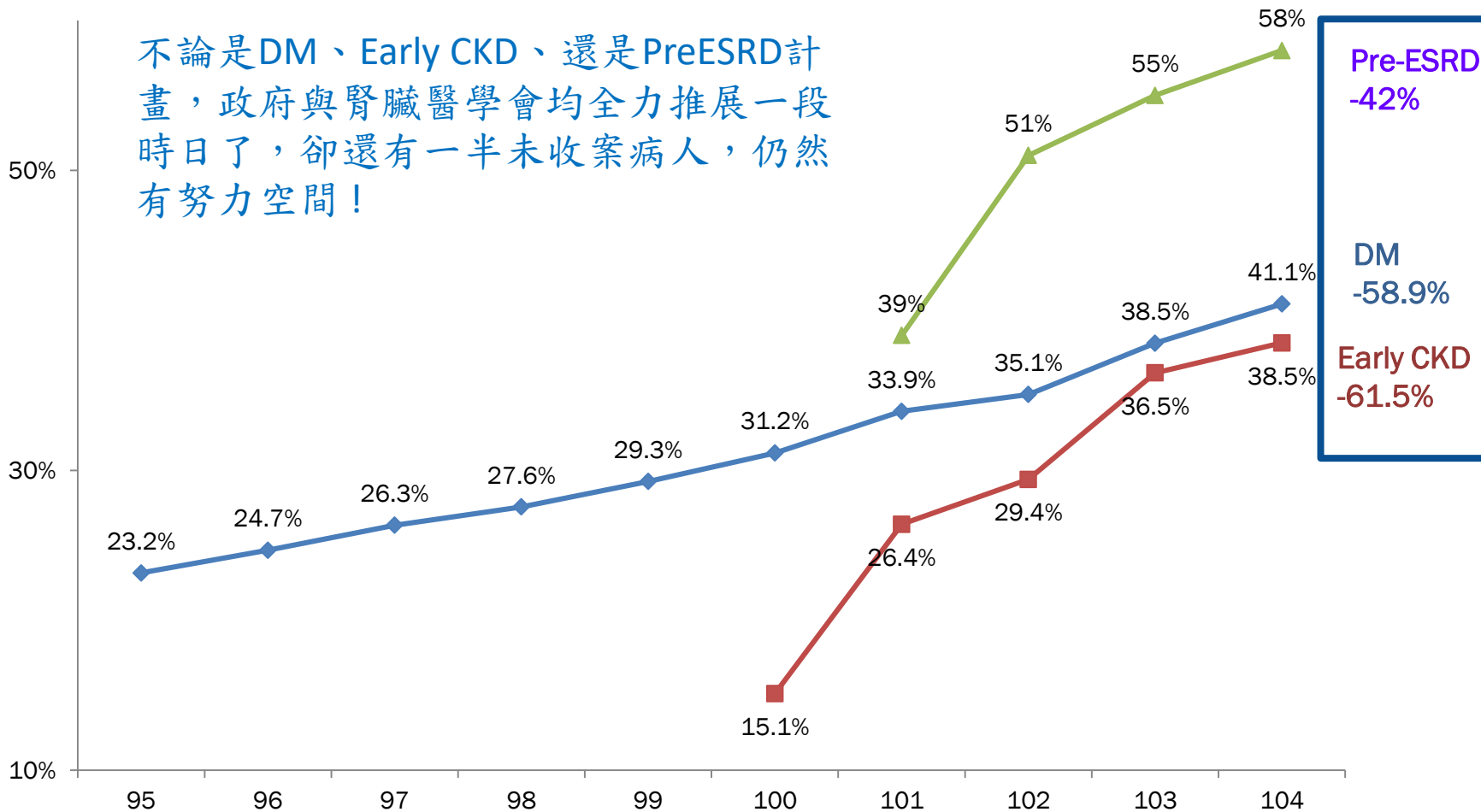
**Better Quality, Less Cost**

Pre-ESRD 計畫全國資料呢?

全民健康保險末期腎臟病前期(Pre-ESRD)之病人照護與衛教計畫執行成效評估. 黃尚志等 MOHW103-NH-1001  
PLOS ONE, 2018; NDT, 2017

# DM, Early CKD, and Pre-ESRD program 等 論質計酬 整合性照護計畫之涵蓋率(未涵蓋率)

不論是DM、Early CKD、還是PreESRD計畫，政府與腎臟醫學會均全力推展一段時日了，卻還有一半未收案病人，仍然有努力空間！

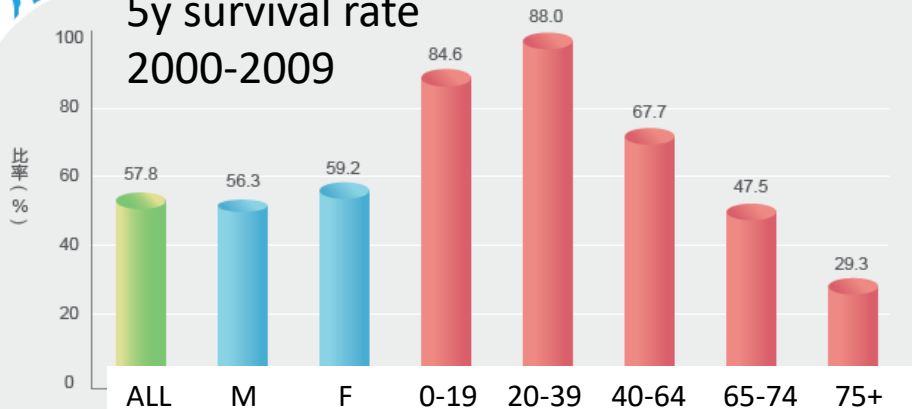


# Survival rate for chronic dialysis patients in Taiwan, 2000~2009

	一年 (95% 信賴區間)	二年 (95% 信賴區間)	三年 (95% 信賴區間)	五年 (95% 信賴區間)	十年 (95% 信賴區間)
RRT Mode	1y	2y	3y	5y	10y
Hemodialysis	92.3 (92.0-92.6)	80.9 (80.5-81.4)	71.6 (71.1-72.1)	56.6 (56.0-57.1)	31.9 (31.4-32.4)
Peritoneal D	94.3 (93.4-95.1)	83.5 (82.1-84.8)	75.0 (73.3-76.5)	61.9 (60.0-63.6)	42.7 (40.9-44.6)
Renal Tx	97.2 (96.5-97.8)	95.5 (94.6-96.3)	93.8 (92.7-94.7)	90.0 (88.7-91.2)	80.0 (78.1-81.7)
Average	92.8 (92.5-93.0)	82.0 (81.6-82.4)	73.2 (72.7-73.7)	58.9 (58.4-59.4)	35.3 (34.8-35.7)

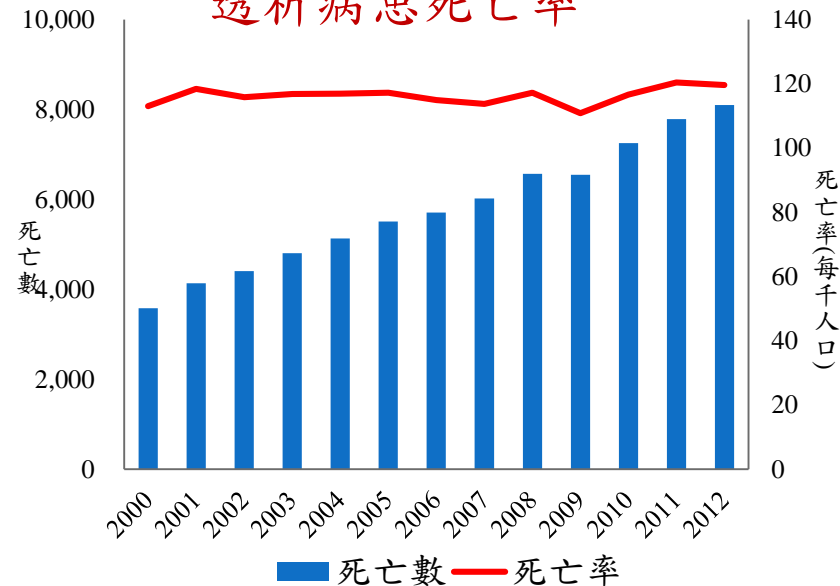
圖 33 2000-2009 年台灣透析患者五年存活率 (%) (依性別及年齡別)

## 5y survival rate 2000-2009

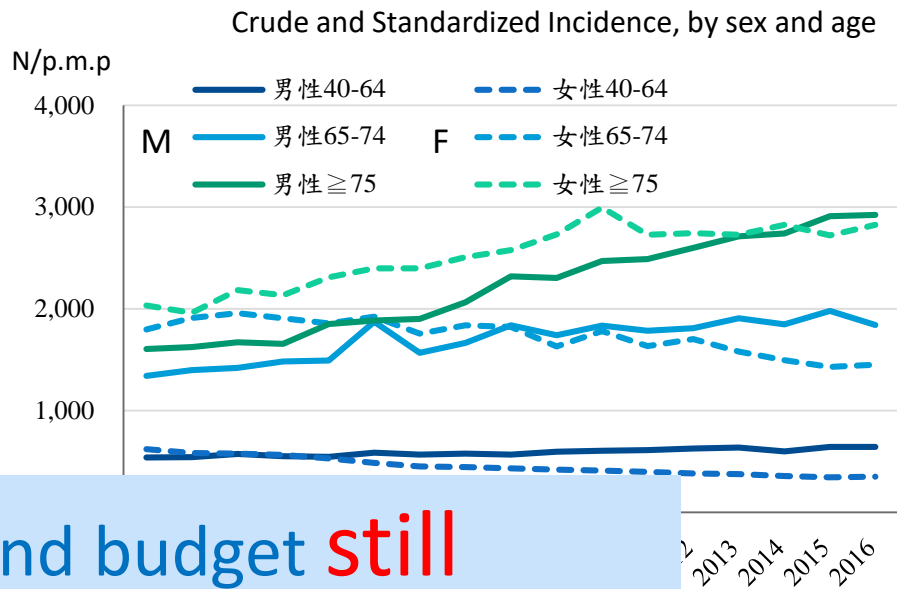
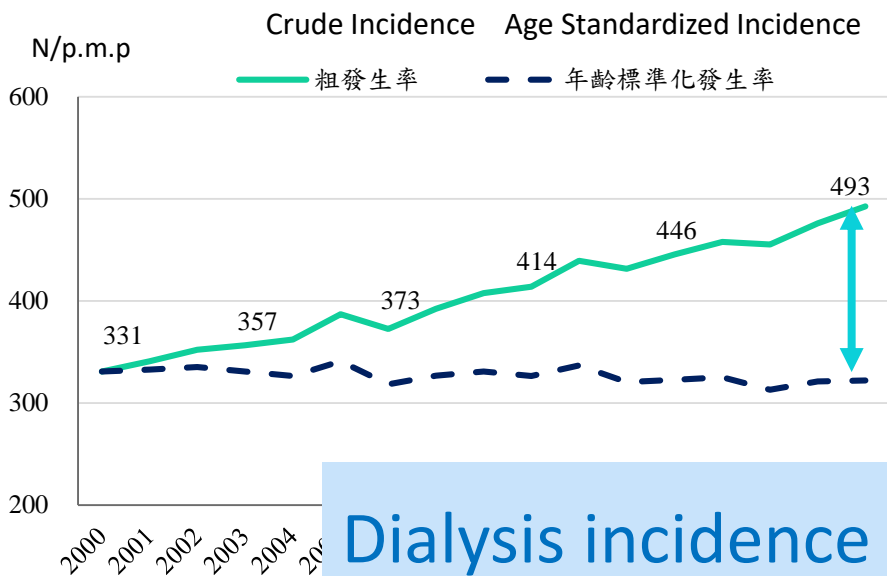


Chronic dialysis: undertaking dialysis for at least 3 months

## 透析病患死亡率



# 2016 末期腎臟病透析發生率與病人總醫療點數



Dialysis incidence and budget **still** progressively increasing.

圖 98 末期腎臟病患者總醫療點數 (依就診模式別)

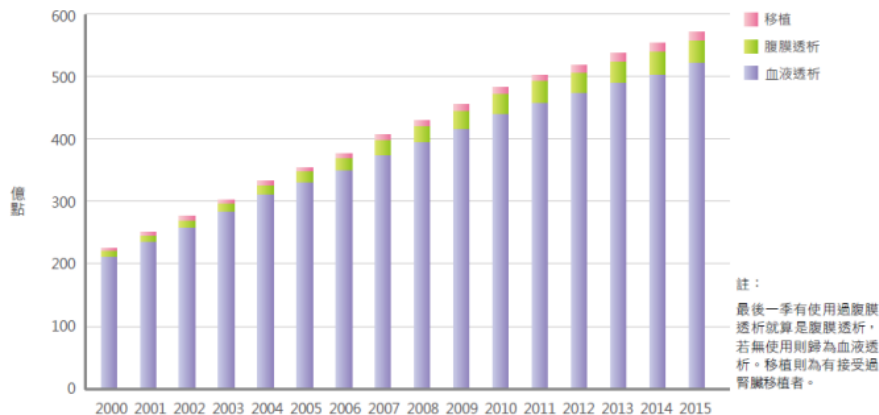
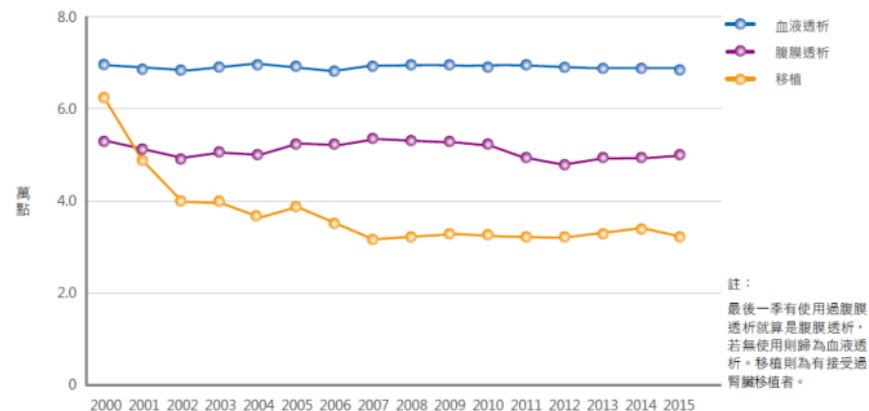


圖 106 末期腎臟病患者月平均醫療點數 (依就診模式別)



Total medical expenses per month in points of all ESRD patients on RRT, by mode of Dialysis and Non-dialysis

Stable in monthly medical expense per patient, but increase of % non-dialysis costs and decrease in % dialysis costs

Increase of the medical costs of hospitalization

圖 108 末期腎臟病患者月平均醫療點數 (依就診項目別)

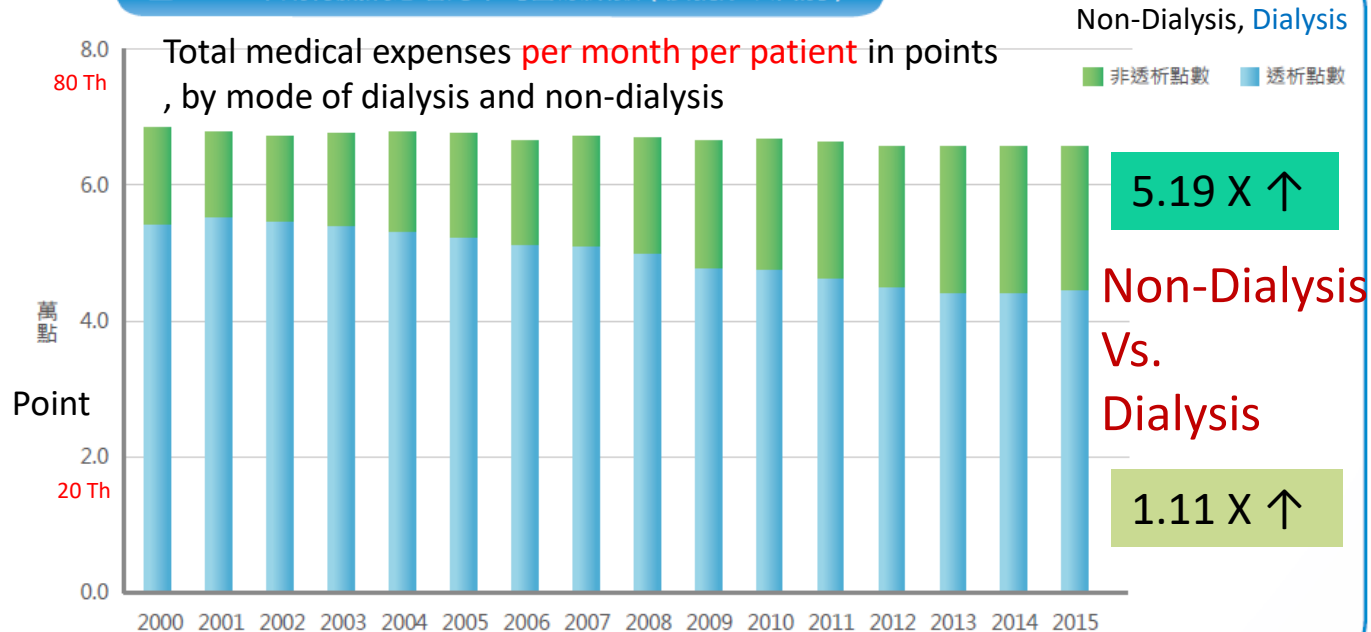
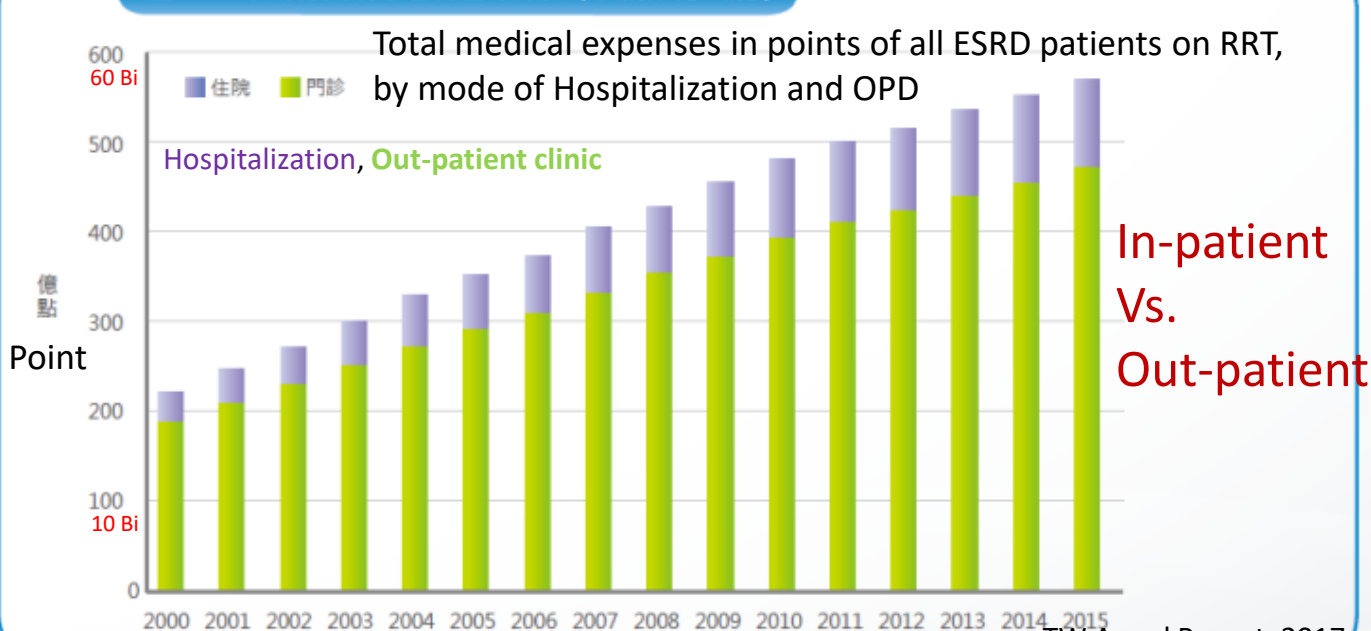


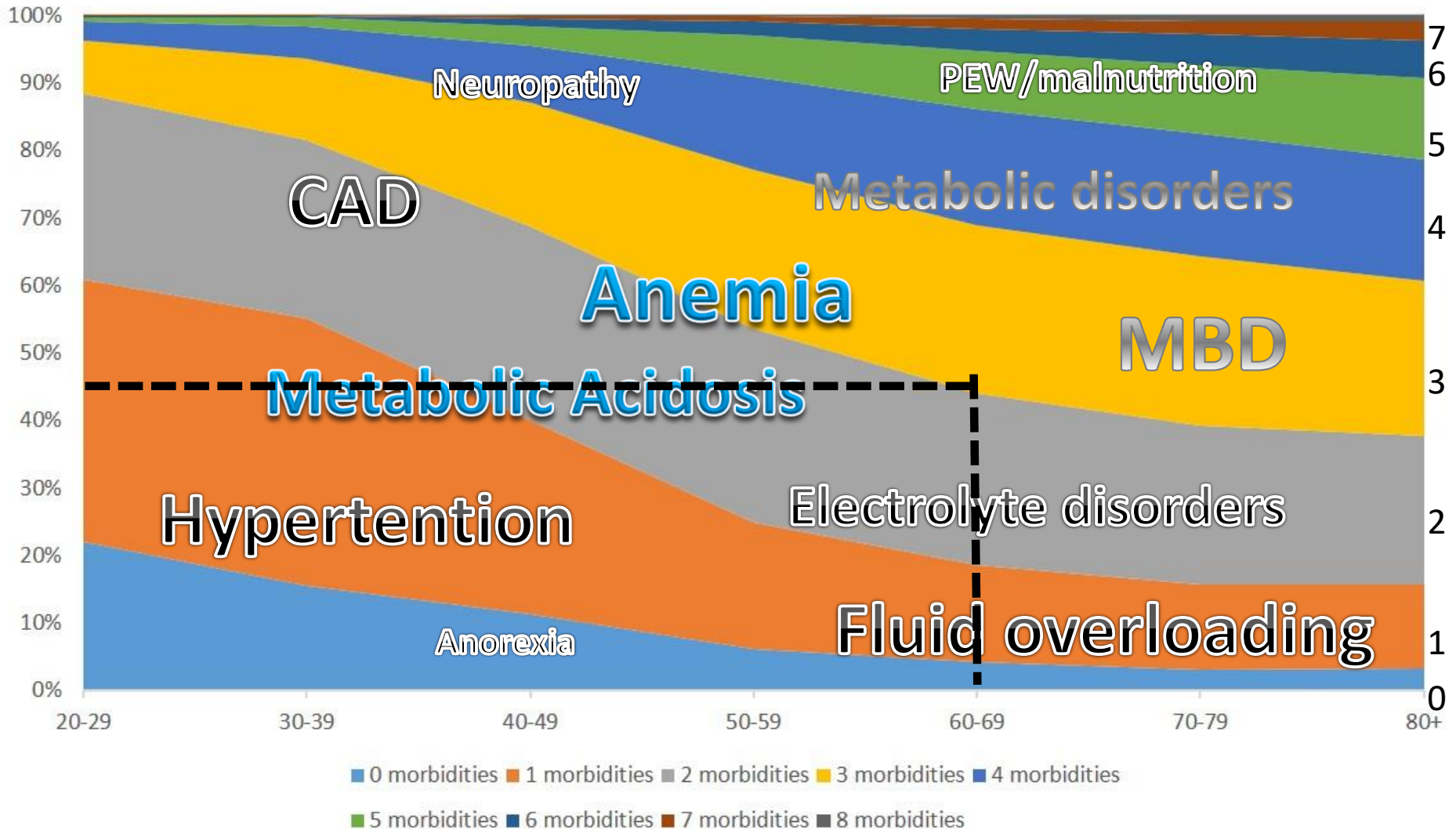
圖 96 末期腎臟病患者總醫療點數 (依就診方式別)



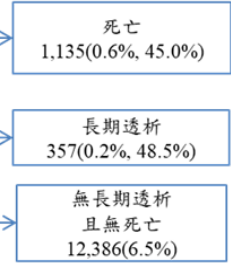
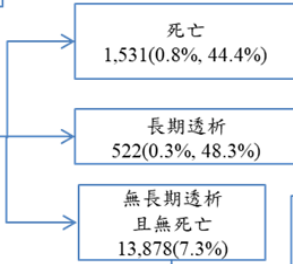
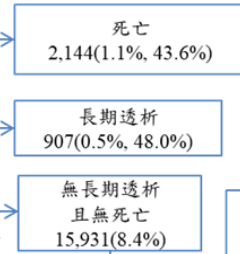
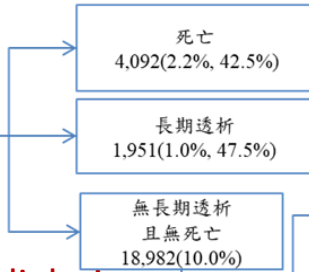
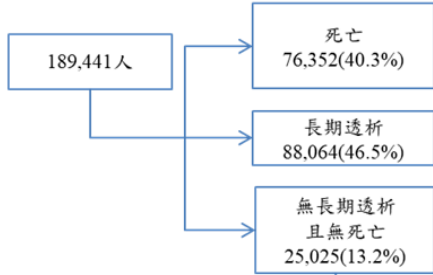


# CKD - a complex, multi-cause disease with high comorbidities and diverse complications

1997-2008 Taiwan incident dialysis population

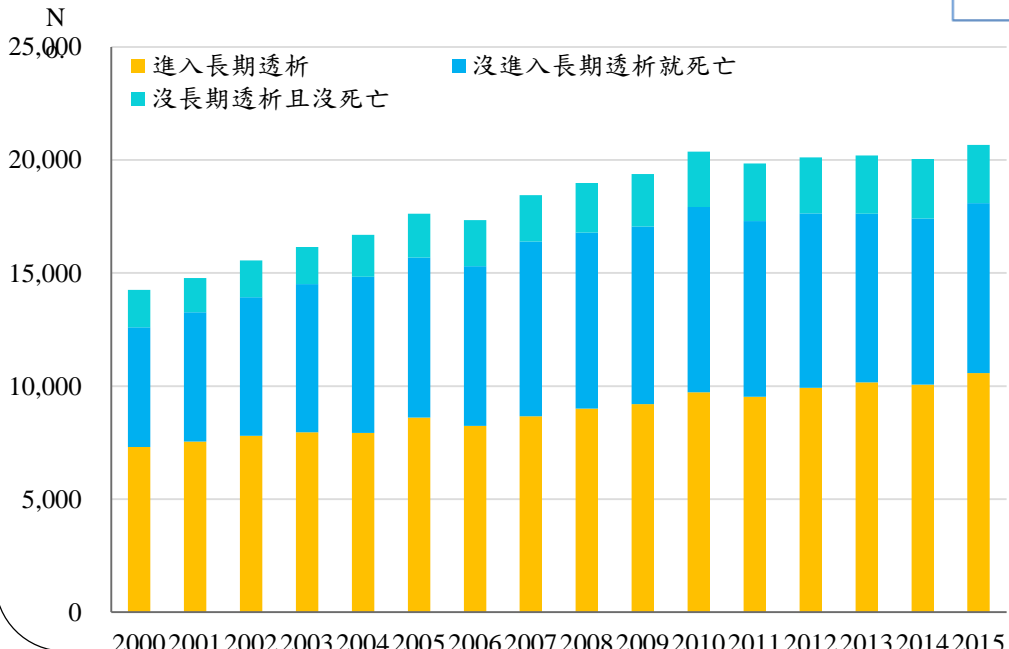


# After 5 year follow-up for patients with first-ever dialysis, 2000-2010



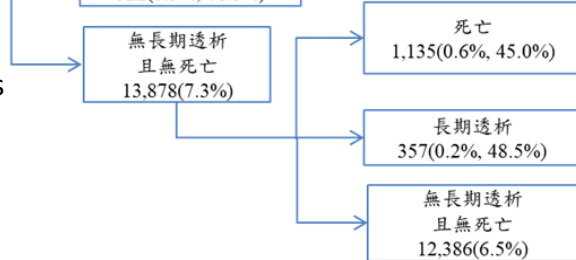
45.0% patients died  
 48.5% patients entering long-term dialysis  
 6.5% patients → Recovery? CKD?

## Outcomes in patients with first-ever dialysis, 2000-2015



Survival without dialysis  
 Died before entering long term dialysis

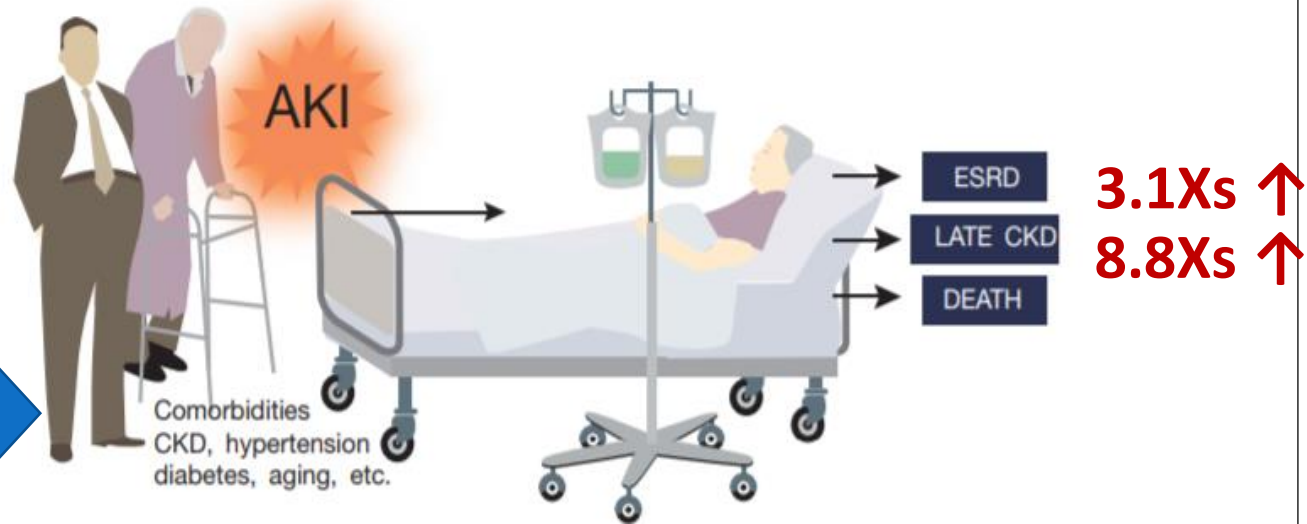
Enter Long term dialysis



# 急性腎傷害: 慢性腎臟病的前哨站

Etiology:

1. Surgery
2. Nephrotoxic drugs
3. Poisonous plants & animals
4. Others,  
DM, CAD, CHF, LC in systemic D's;  
Infection, Sepsis in elderly patients



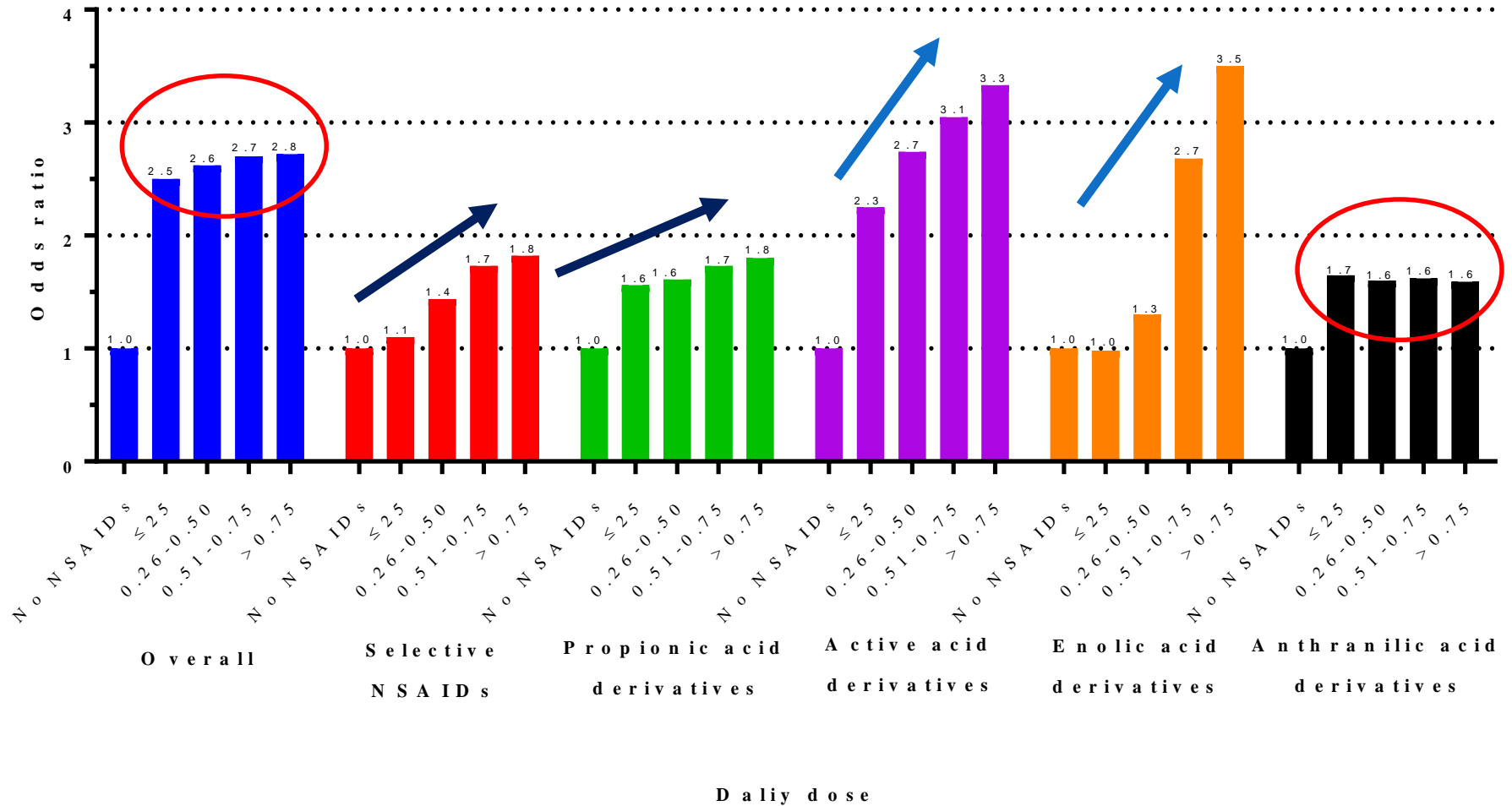
這些病人大部分不是在腎臟專科醫師手中照顧，但是我們沒有參與他們疾病的前半，卻在無能為力地在後半收拾透析的殘局。



Change the Education and Training Policy of TSN

- ❑ Educate Nephrologists and other Specialties about AKI
- ❑ Collaborate and communicate with different sub-specialties of different medical societies in caring AKI, Post-AKI, and multi-comorbidities CKD/Non-CKD patients
- ❑ Promote critical care nephrology to Nephrologists

# Risks of dialysis associated with short-term exposure of NSAIDs, which might further deteriorate the renal function

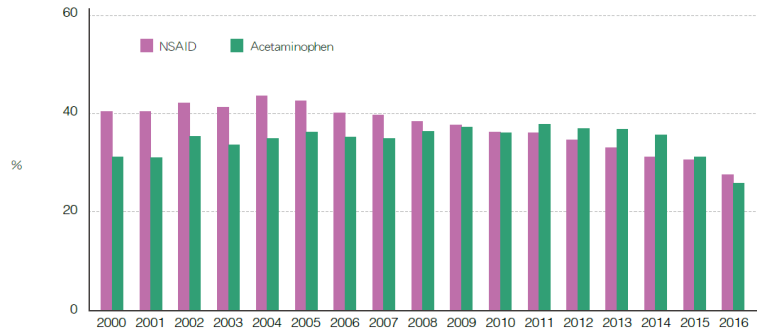


# Use of Analgesics one year before Dialysis

Use more than 1m



圖 64 20 歲以上透析患者於透析前一年使用各止痛藥物比率 (%) (依藥物別)

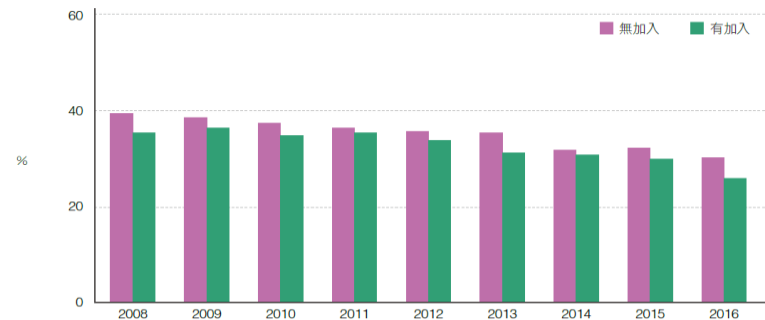


註：該年度累計使用超過一個月（30 天）才算有使用。

## NSAIDs vs. Acetaminophen



圖 70 20 歲以上透析患者於透析前一年使用止痛藥物 (NSAID) 比率 (%) (依有無加入 Pre-ESRD 計畫)



註：該年度累計使用超過一個月（30 天）才算有使用。

NSAIDs : No vs. Yes (PreESRD Project)



圖 67 20 歲以上透析患者於透析前一年使用止痛藥物 (NSAID) 比率 (%) (依年齡別)

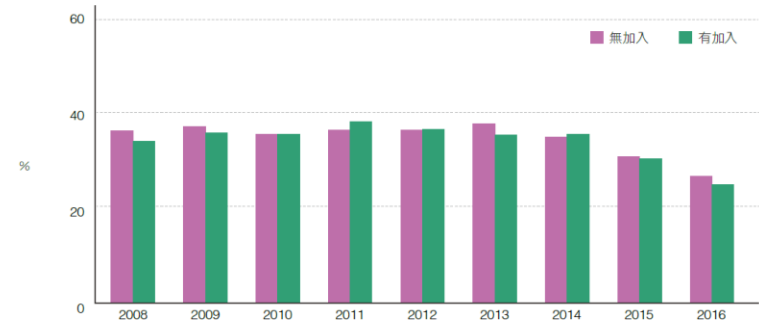


註：該年度累計使用超過一個月（30 天）才算有使用。

## Age 20-64 vs. Age over 65



圖 71 20 歲以上透析患者於透析前一年使用止痛藥物 (Acetaminophen) 比率 (%) (依有無加入 Pre-ESRD 計畫)



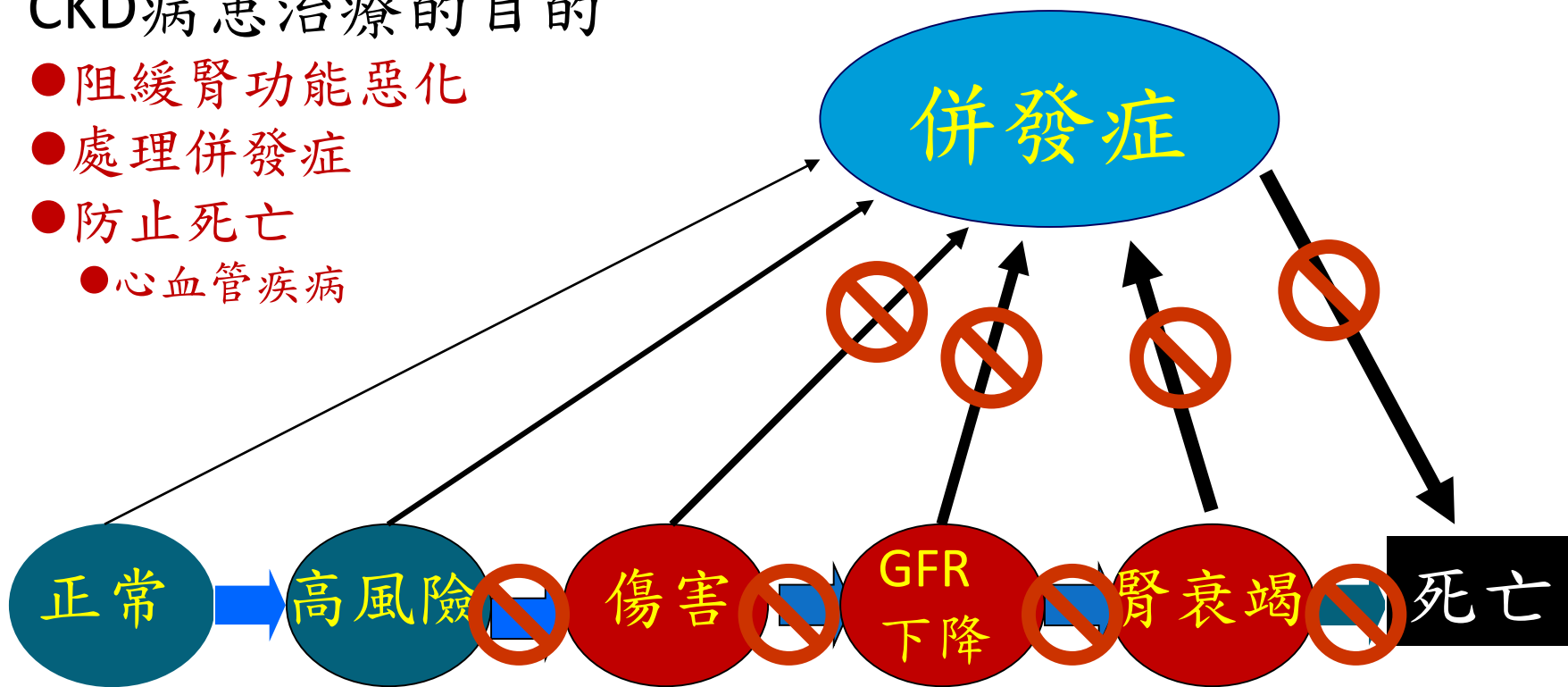
註：該年度累計使用超過一個月（30 天）才算有使用。

Acetaminophen : No vs. Yes (PreESRD Project)

# CKD自然病程與治療策略

## CKD病患治療的目的

- 阻緩腎功能惡化
- 處理併發症
- 防止死亡
  - 心血管疾病



CKD危險  
因子篩檢

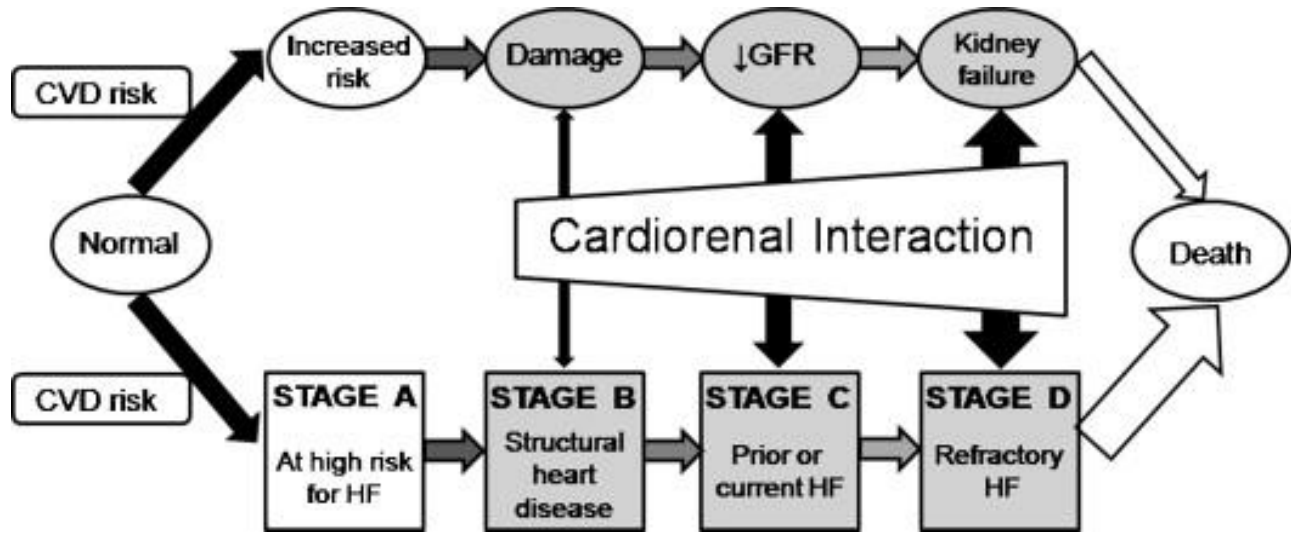
減少CKD  
危險因子，  
篩檢CKD

診斷與治療，  
治療合併症，  
阻緩腎病惡化

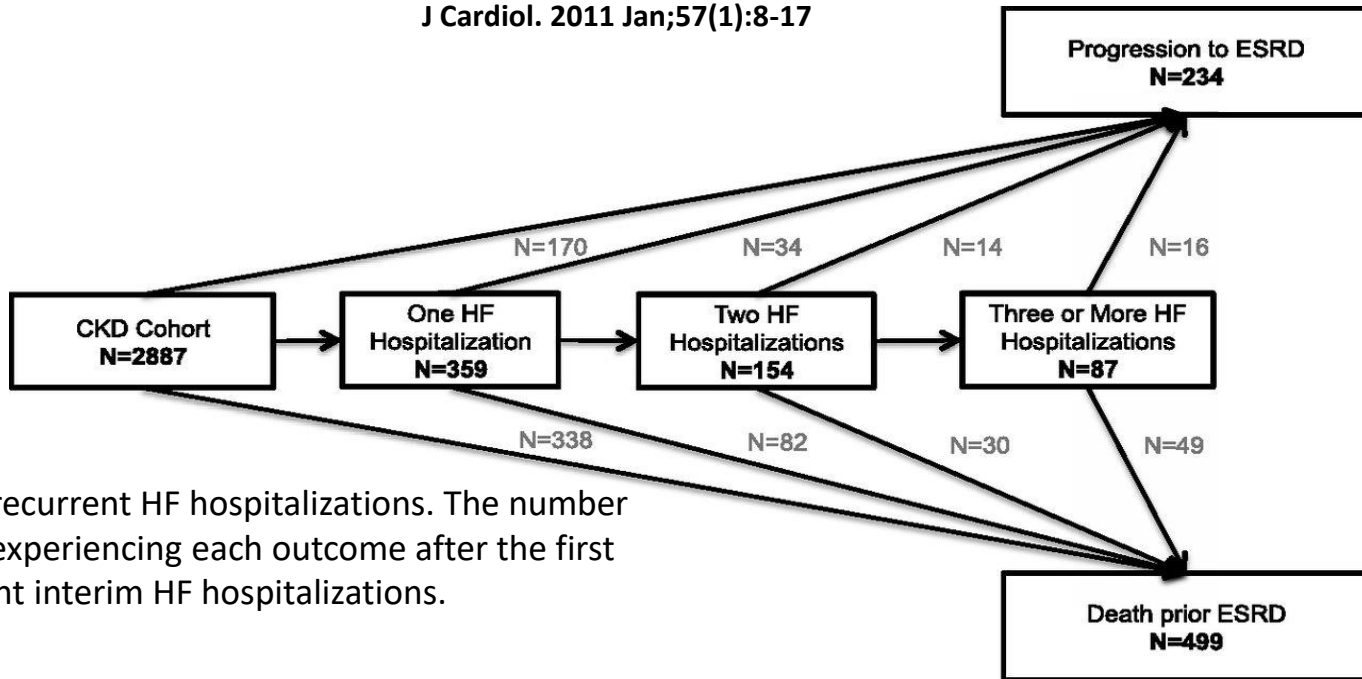
評估惡化速度  
治療併發症，  
準備替代療法

進行腎臟  
替代療法

心腎交互作用  
心腎症候群

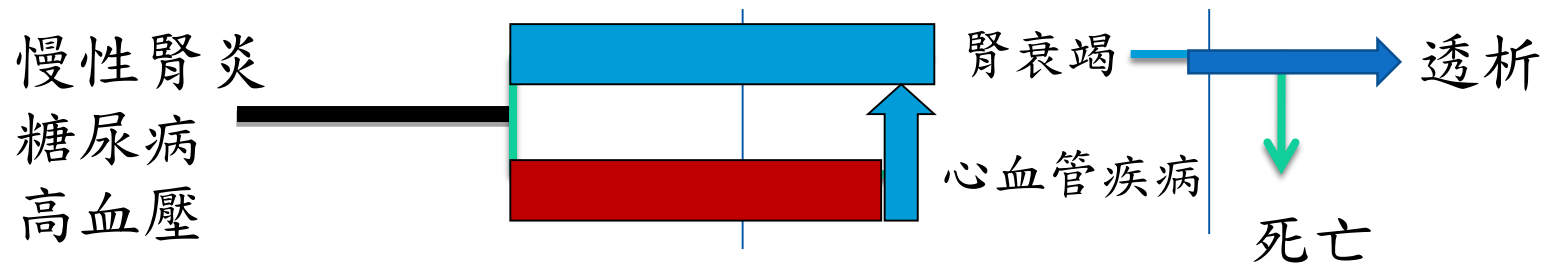


J Cardiol. 2011 Jan;57(1):8-17



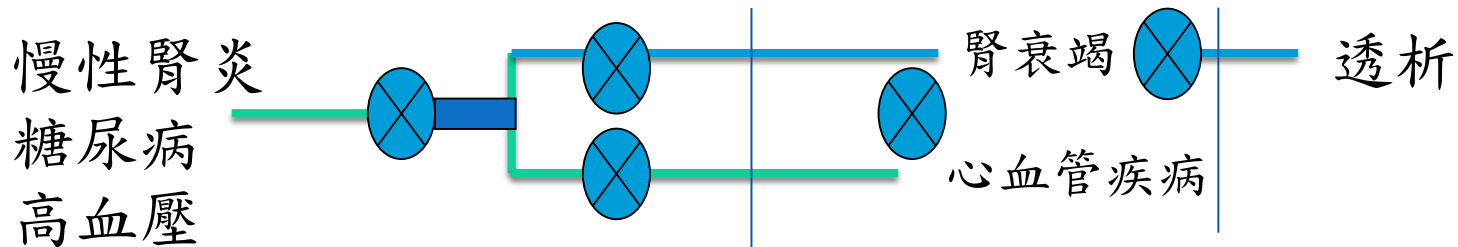
Number of recurrent HF hospitalizations. The number of patients experiencing each outcome after the first and recurrent interim HF hospitalizations.

# 慢性疾病的自然過程與競爭死亡



Live to ESRD (& let dialysis) or to Die (& died on CVD)

## 可介入之阻斷時機

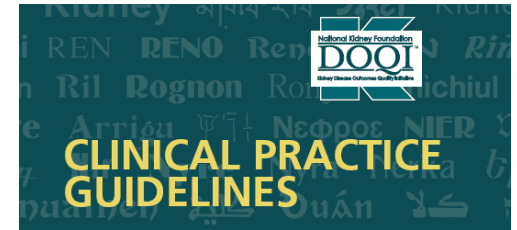




# Outlines of CKD Management (Old principles)

- Slow the rate of progression (Deterioration of eGFR )
  - Treatment of hypertension
  - Reduction of proteinuria
  - Glycemic control
  - Dietary management
- Prevent complications and early death (Management of associated disorders)
  - Cardiovascular disease
  - Dyslipidemia
  - Mineral and bone disorders
  - Anemia
  - Electrolyte and Acid-Base disturbances

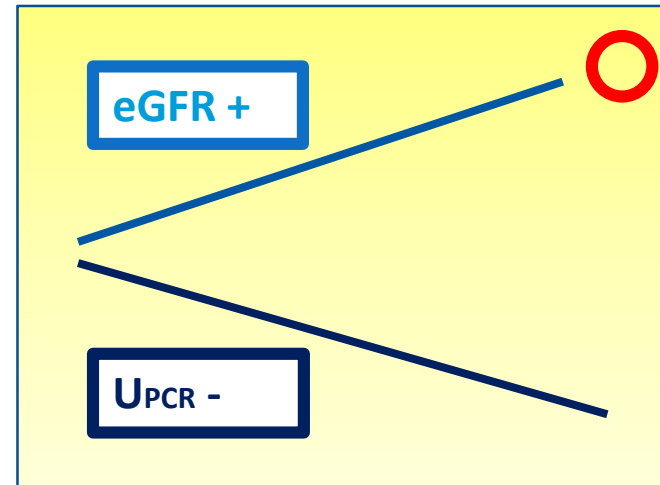
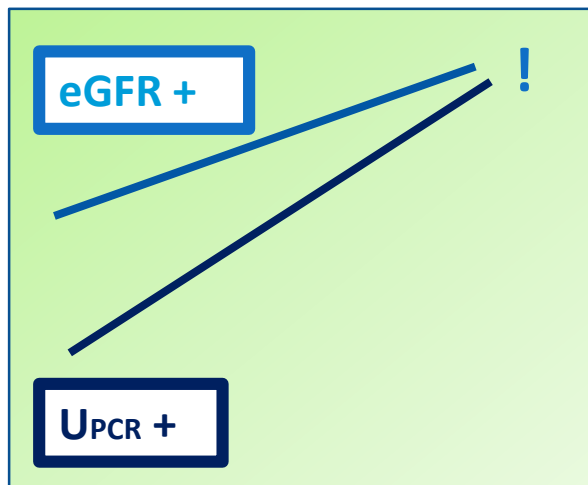
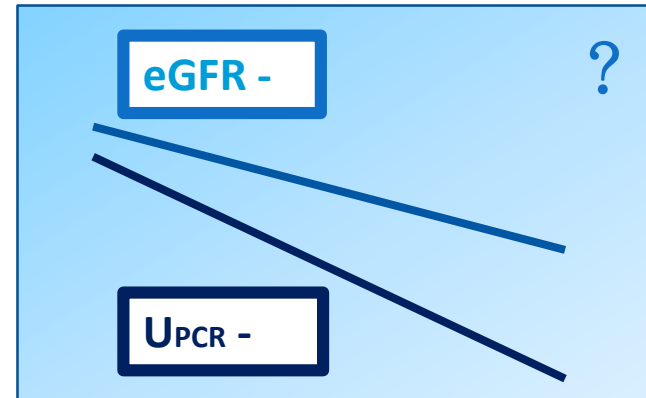
# How to Treat Chronic Kidney Disease---A summary



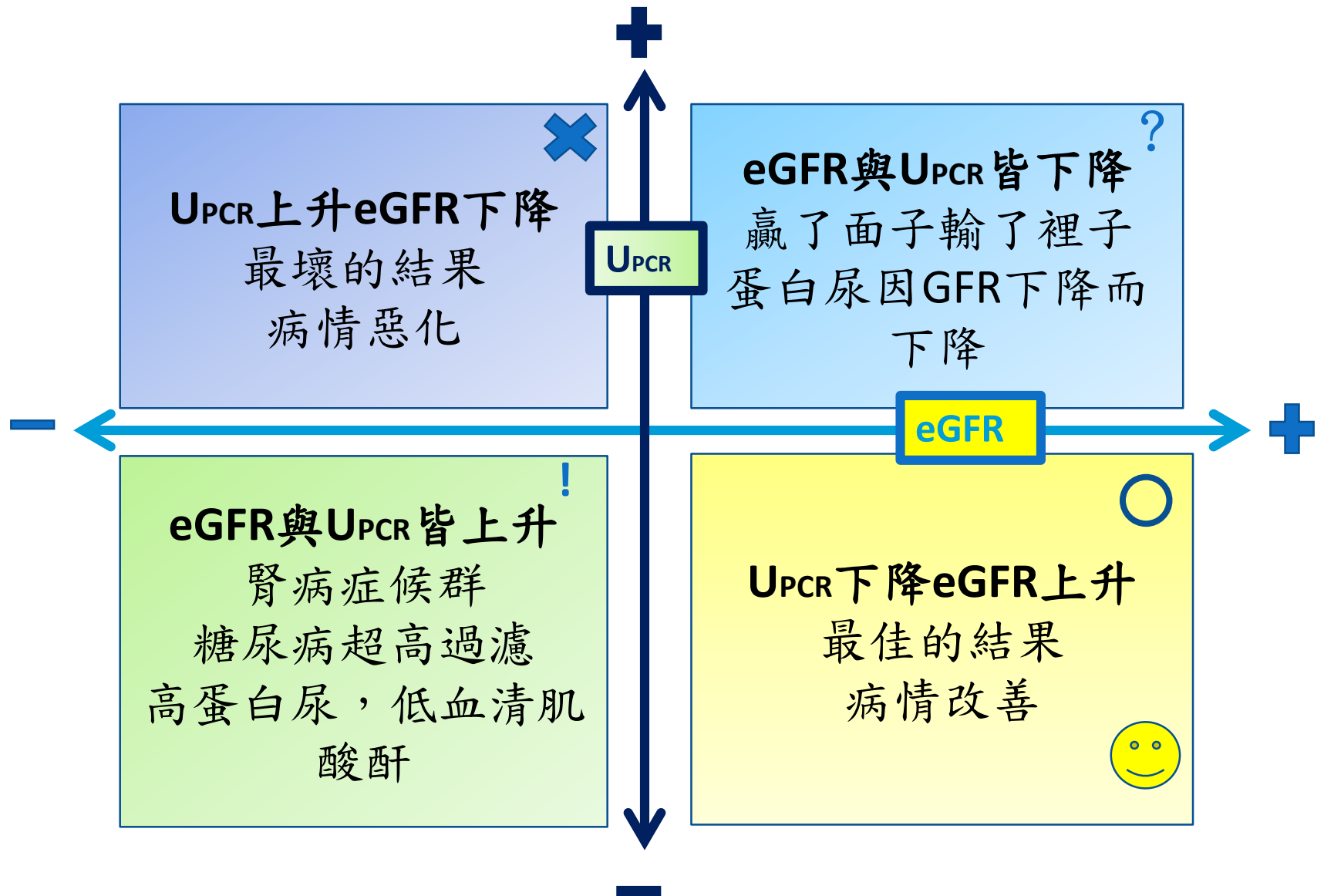
- Treat the underlying glomerular or tubulointerstitial nephritis
- **Maintain blood pressure less than 130/80 mmHg**
  - Use an ACE Inhibitor or ARB, more than one drug is usually required and a diuretic should be part of the regimen
- Continue best possible glycemic control in individuals with diabetes (HbA1c < 7%)
- Refer to dietician for a reduced protein diet
- Consult a Nephrologist early
  - Team with the nephrologist for care if GFR < 30 mL/min/1.73 m<sup>2</sup>
- Monitor hemoglobin and phosphorous with treatment as needed (ESA, Phosphate binders)
- **Treat cardiovascular risk, especially quit smoking and hypercholesterolemia**

# Major Indicators for Treatment

## eGFR的變化 vs. UPCR的變化



# eGFR的變化 vs. UPCR變化意義



ml/min

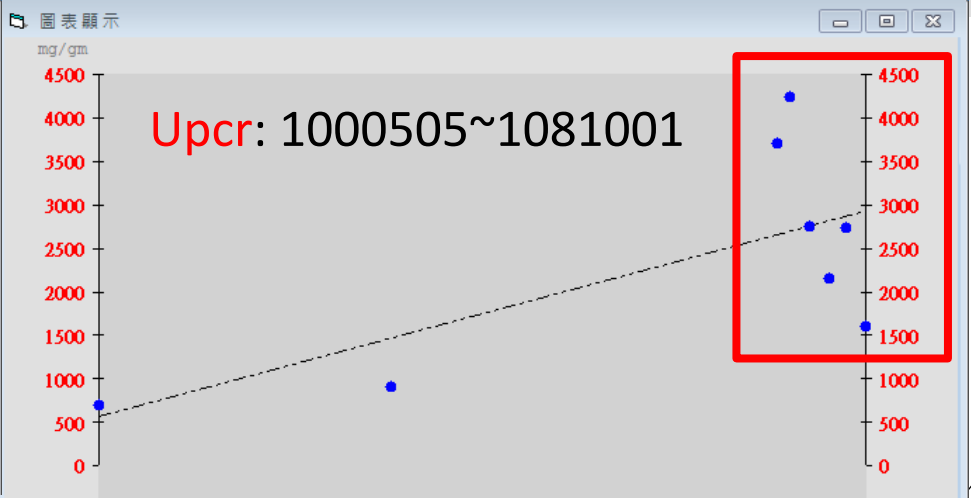
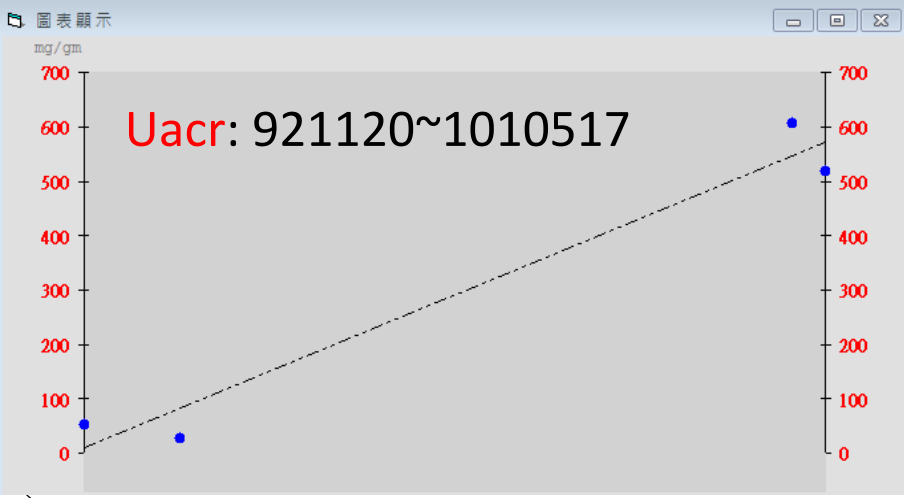
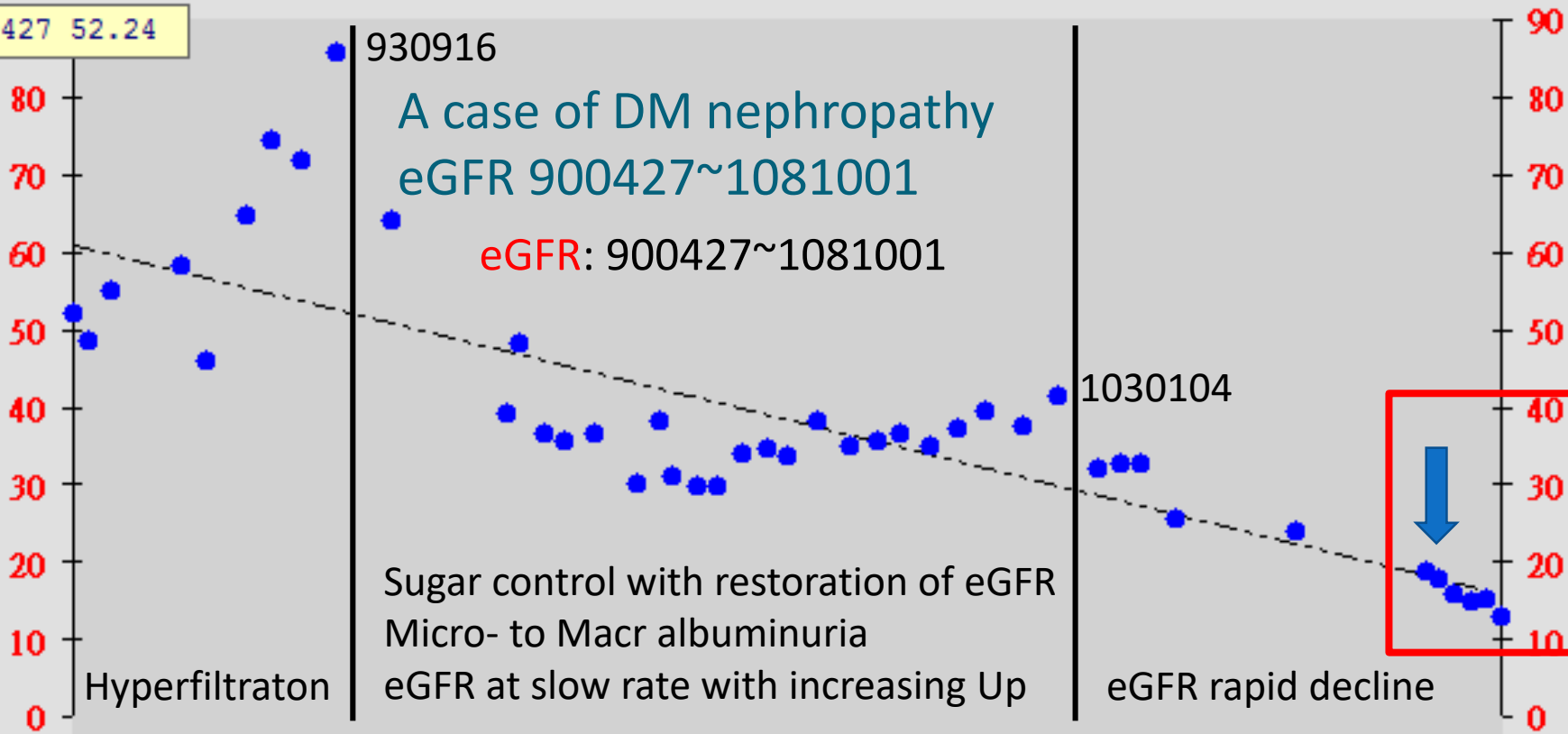
【GFR 變化率】

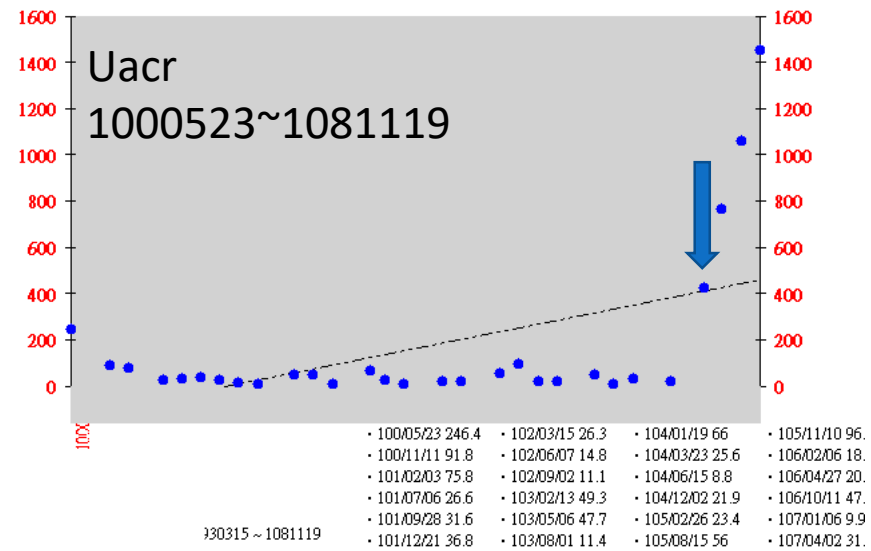
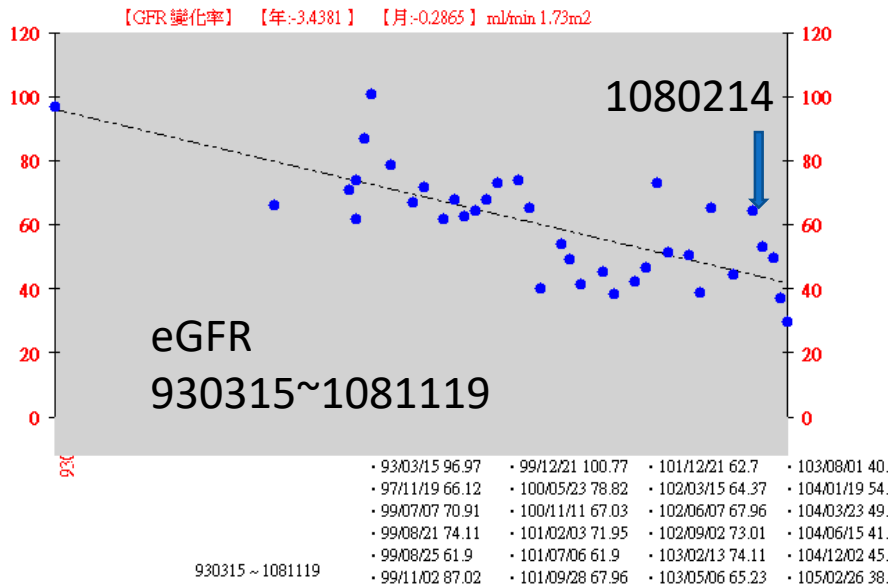
【年:-2.443】

【月:-0.2036】

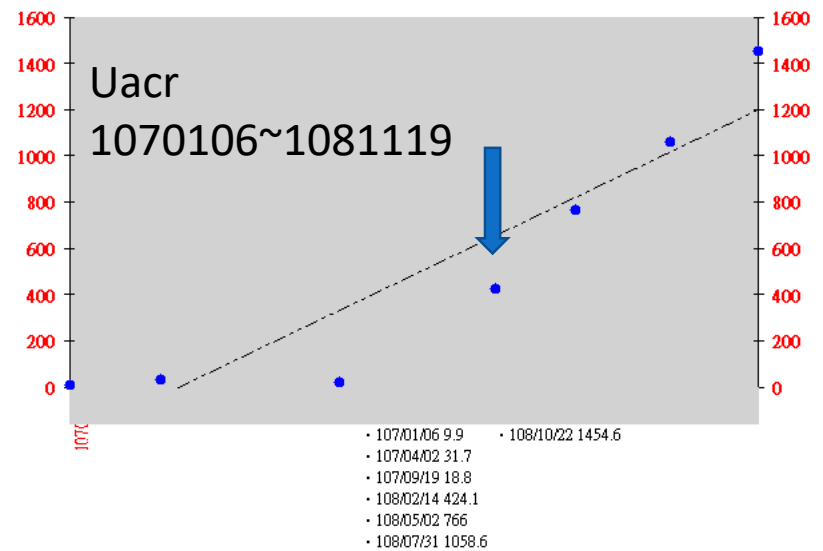
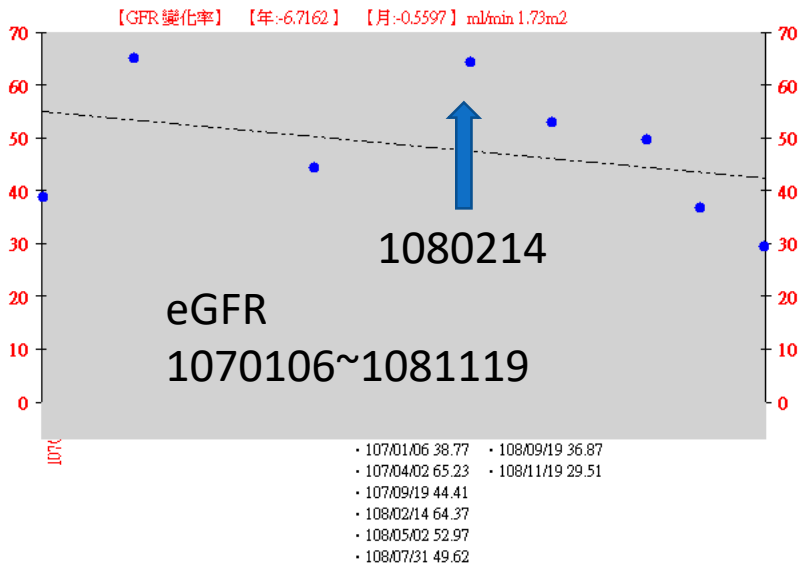
ml/min 1.73m2

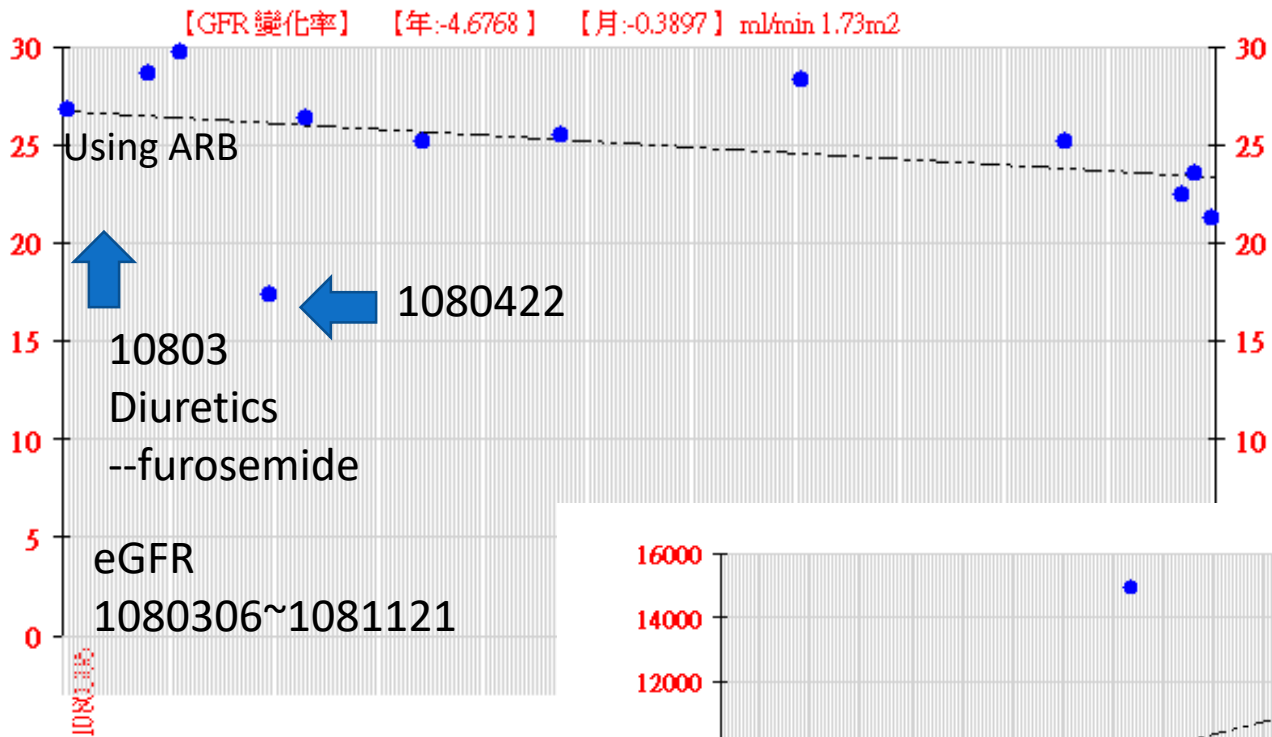
900427 52.24





### A 68 y/o female case of DM nephropathy

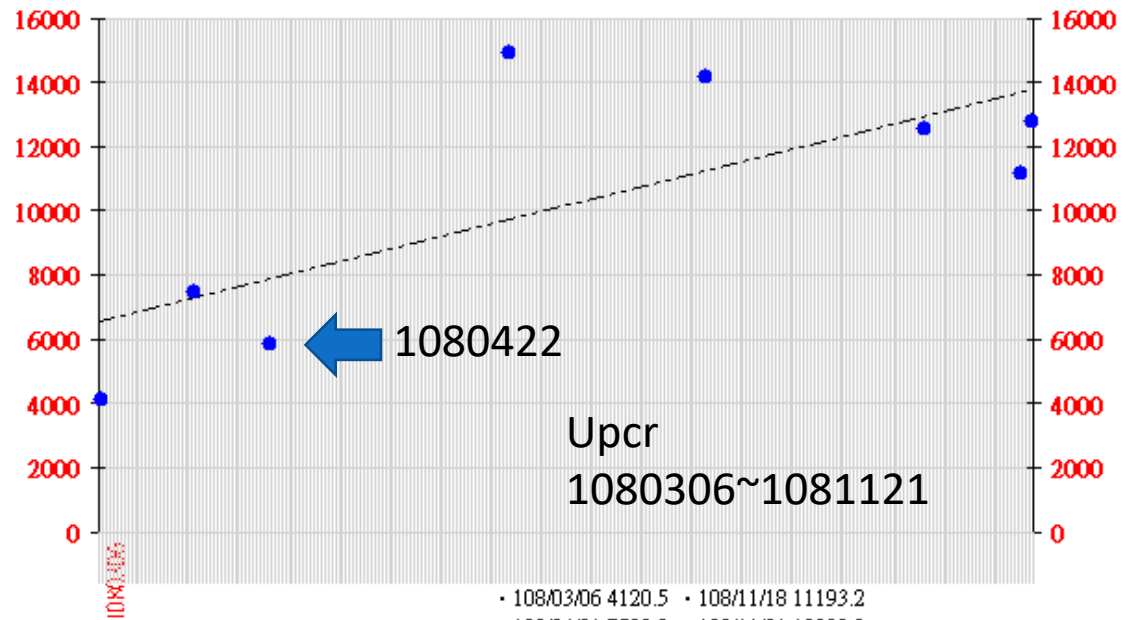




A 82 years old male patient of DM, CAD (3-vessel), CHF, DKD with Reduced eGFR and Heavy proteinuria

Diuretics furosemide induced Marked decrease of eGFR, but eGFR returned to baseline after stop of furosemide.

Edema (++)  
Occasional dyspnea



- 108/03/06 4120.5
- 108/04/01 7500.9
- 108/04/22 5865.8
- 108/06/28 14920.4
- 108/08/22 14176.9
- 108/10/22 12563.3
- 108/11/18 11193.2
- 108/11/21 12800.2

# 控糖保腎還是救心？

「越調」元曲「憑闌人  
寄征衣」<姚燧>

- 欲寄君衣君不還，不  
寄君衣君又寒。

寄與不寄間，妾身千  
萬難。

- Puzzling
- Bewildering
- Confusing
- Perplexing

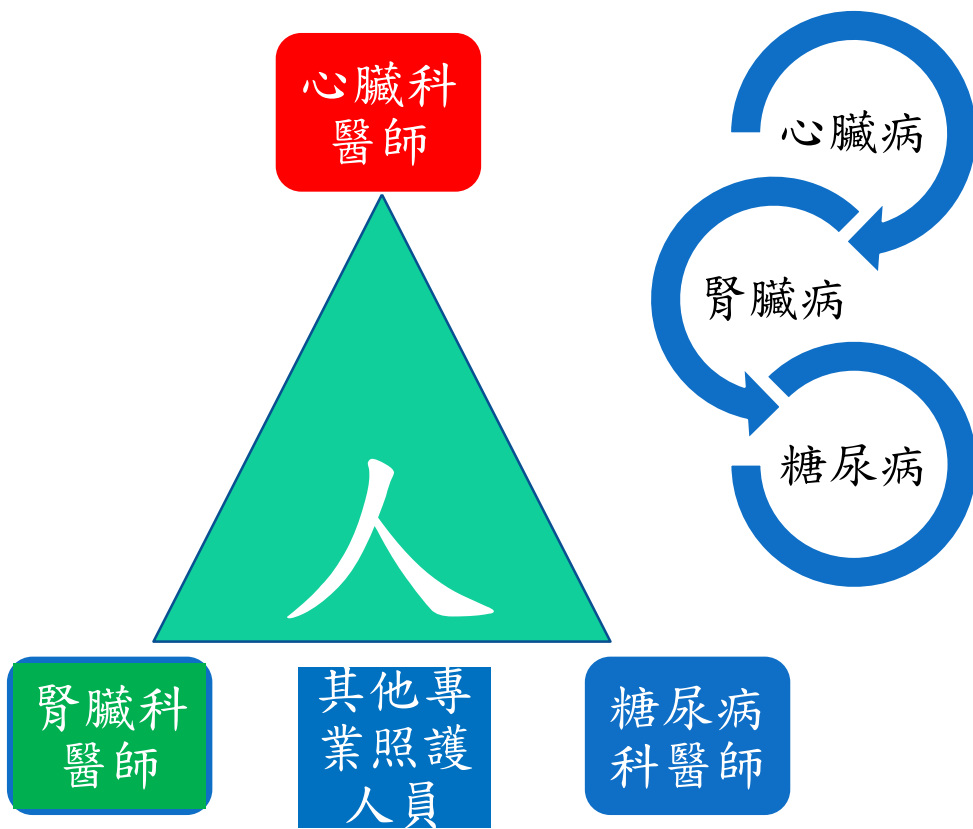
- 達賴六世倉央嘉措  
世間安得雙全法  
不負如來不負卿

## 改變的契機

- 跨次專科的合作
- 跨專科跨領域的照  
護平台
- 新的治療藥物



# 105年NHRI整合性計畫—心臟-腎臟-糖尿-神經整合性照護計畫之臨床品質與成本效益研究



進行各項併發症必要之評估、治療、衛教照護，營養師參與並調整飲食計畫

## 新的照護平台

# What's New in slow (retard) renal function deterioration?

ACEI

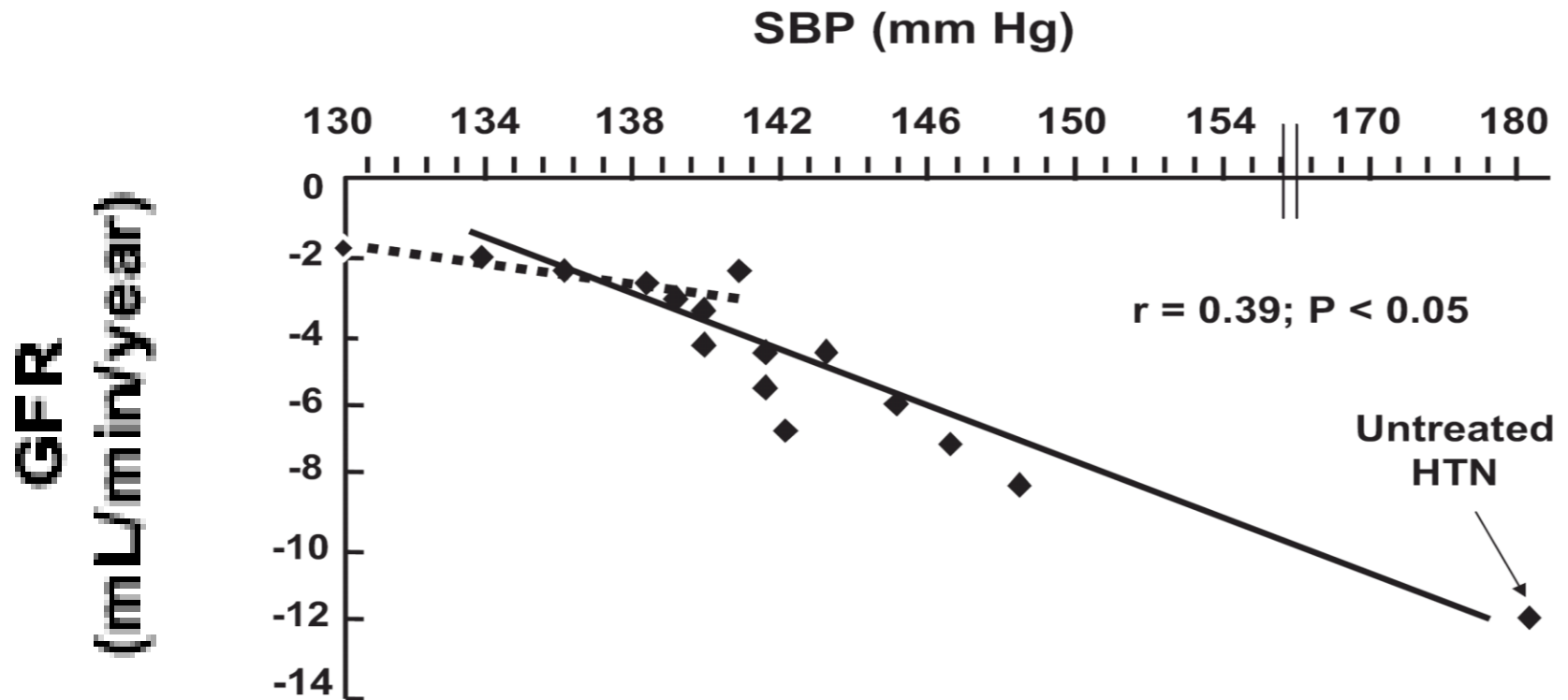
ARB

Ketoanalogues

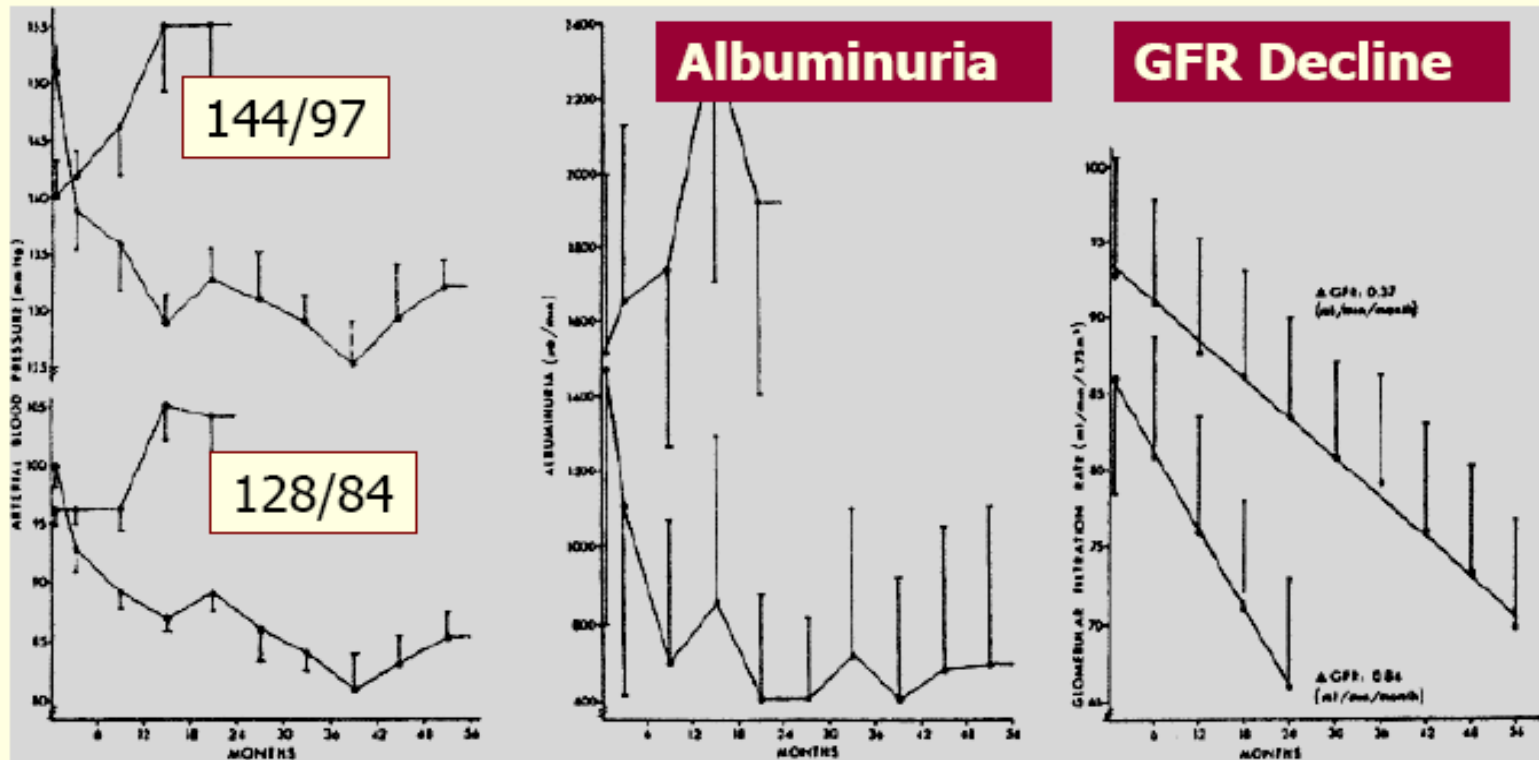
SGLT2 Inhibitors

Activated Charcoal

# Blood pressure level and rate of GFR decline in controlled trials of Diabetic KD.



# Early Aggressive Antihypertensive Treatment in Diabetic Nephropathy (n=10)

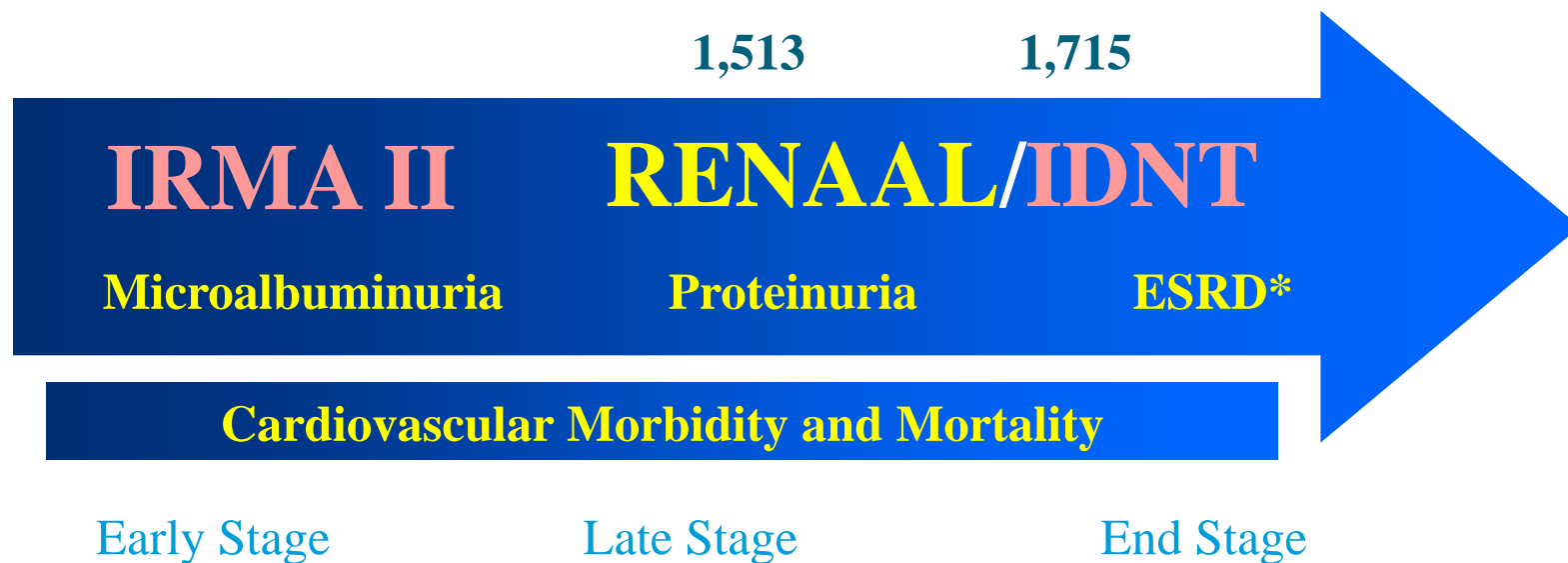


metoprolol, hydralazine, and furosemide or thiazide

Parving HH... [Lancet 1:1175-1179, 1983](#)

1993 Lewis Trial. Captopril effective in reducing proteinuria and retard GFR decline

# ARB: Landmark Nephrology Trials in Type 2 DM



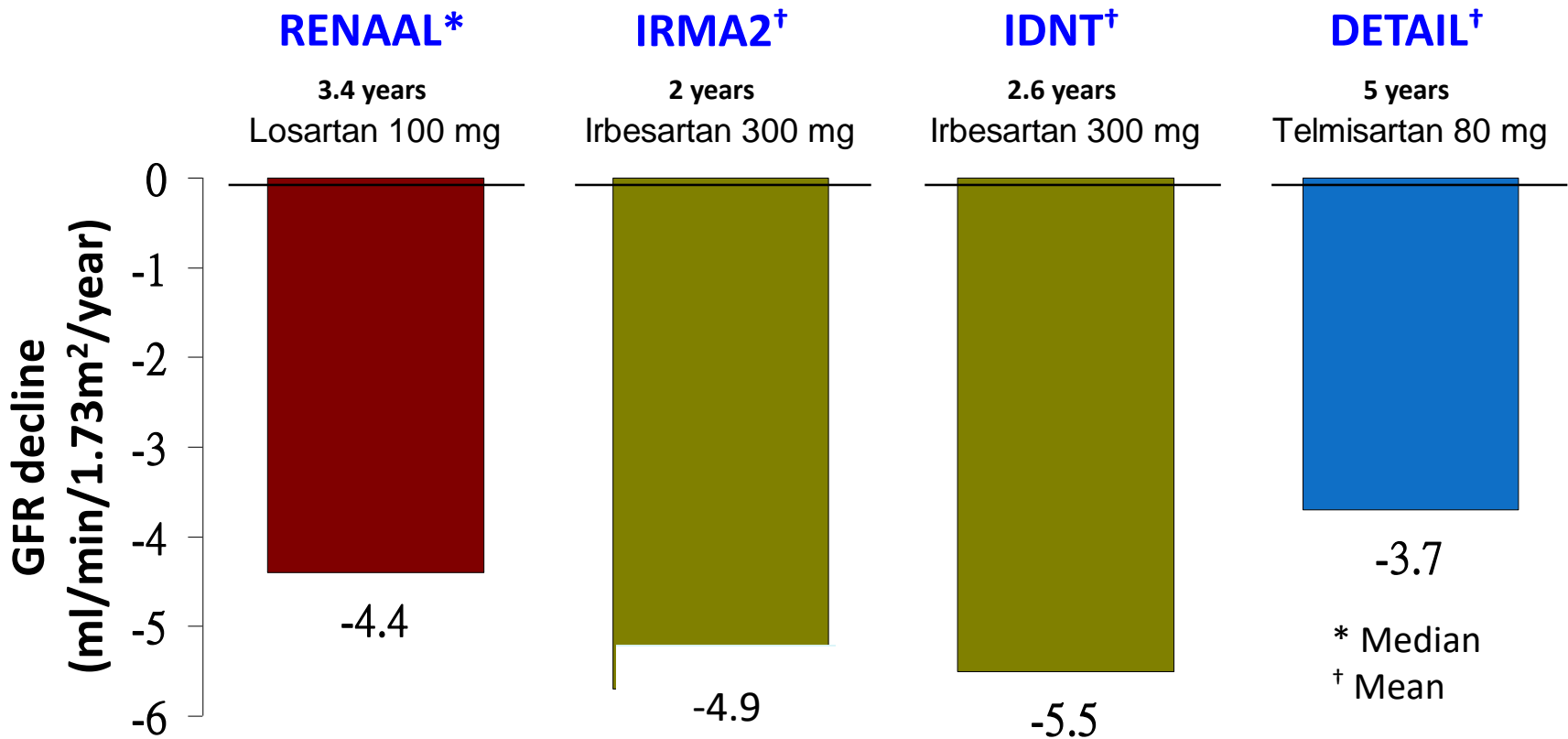
## Diabetic Kidney Disease

Parving H-H, et al. *N Engl J Med* 2001;345:870-878.

Lewis EJ et al. *N Engl J Med* 2001;345:851-860.

Brenner BM et al *New Engl J Med* 2001;345(12):861-869.

# Renoprotective effects of ARBs: GFR decline in DETAIL, IRMA 2, IDNT and RENAAL



Currently attainable rates of decrease in glomerular filtration rate remain at 2 to 8 mL/min/y depending on the underlying disease.

# ACEI/ARB 類降血壓藥的特殊角色

- 蛋白尿對腎臟病人的預後有極大影響，同時是腎臟遭到傷害的結果，也可能是進一步惡化的原因。
- ACEI/ARB 此類藥物同時可以在降血壓的同時，降低腎絲球內的壓力進而降低蛋白尿，被認為是可以延緩腎功能惡化的利器。

此類藥物同時可以減輕心臟負擔，對於治療心衰竭和降低心血管併發症和死亡率亦有實證上的效果。

# 實證研究通常排除腎臟功能較差病人

- 但是以往的研究都是局限於腎臟功能正常或輕微損傷的病人，對於腎臟功能較差 (慢性腎臟病第4、5期，即腎絲球過濾率  $< 30 \text{ ml/min}$ ) 的病人，因為可能臨床狀況比較不穩定，所以都是敬而遠之，排除在外。
- 因此當病患已進入慢性腎臟病第4、5期，是不是要續用或加上ACEI/ARB 此類降血壓藥就是腎臟科醫師很掙扎的問題了。

## 續用

高血鉀風險  
腎功能進行式↓  
提早透析/洗腎?

## 停用

↑血壓  
↑心血管風險  
↑蛋白尿  
? 腎功能↓



CKD 4、5期  
ACEI/ARB用或不用?



# Efficacy and Safety of **Benazepril** for **Advanced Chronic Renal Insufficiency**

Fan Fan Hou, M.D., Ph.D., Xun Zhang, M.D., Guo Hua Zhang, M.D., Ph.D.,  
Di Xie, M.D., Ping Yan Chen, M.D., Wei Ru Zhang, M.D., Ph.D.,  
Jian Ping Jiang, M.D., Min Liang, M.D., Ph.D., Guo Bao Wang, M.D.,  
Zheng Rong Liu, M.D., and Ren Wen Geng, M.D.



The **NEW ENGLAND**  
**JOURNAL of MEDICINE**

N Engl J Med 2006;354:131-40.

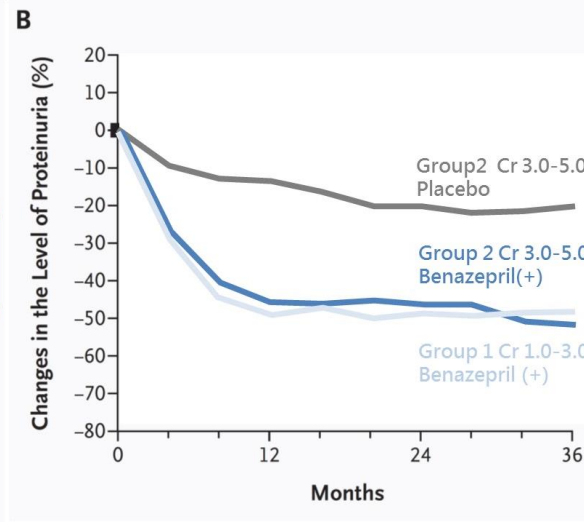
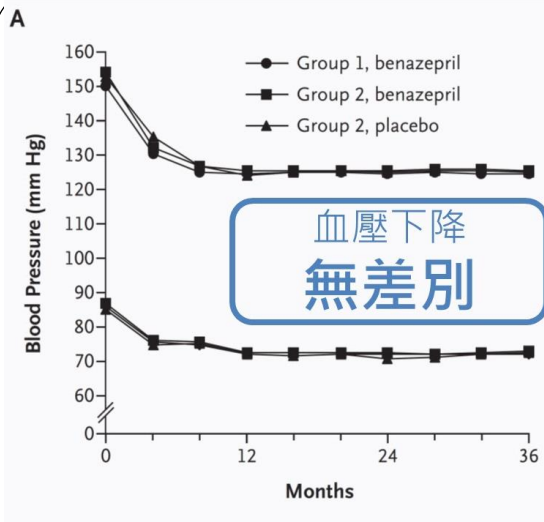
**422個病人**

**隨機雙盲研究**

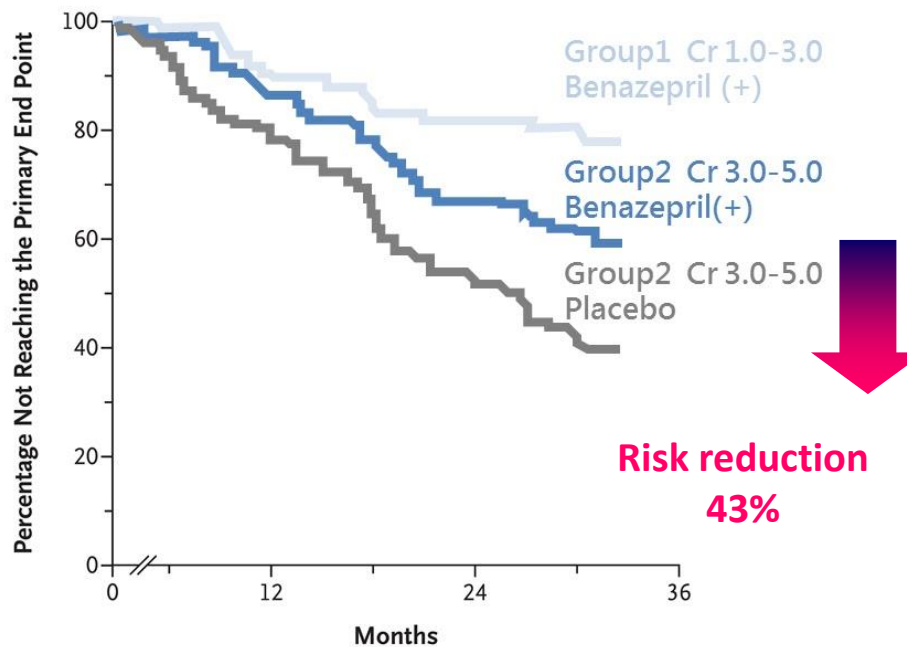
**Cr 3.0-5.0 mg/dl**

**非糖尿病**

**ACEI vs 安慰劑**



蛋白尿的減少: 有使用 ACEI(Benazepril) 的 Cr 1.0 -3.0 mg/dl 和 Cr 3.0-5.0 mg/dl 的蛋白尿下降的幅度差不多, 而 Cr 3.0 -5.0 mg/dl 只使用安慰劑的下降幅度最少。



ESRD、Doubling Scr、Death: Cr 3.0 -5.0 mg/dl 只使用安慰劑的最差, Cr 3.0 -5.0 mg/dl 使用 ACEI(Benazepril) 的次之, Cr 1.0-3.0 mg/dl 使用 ACEI(Benazepril) 的最好。

**No. at Risk**

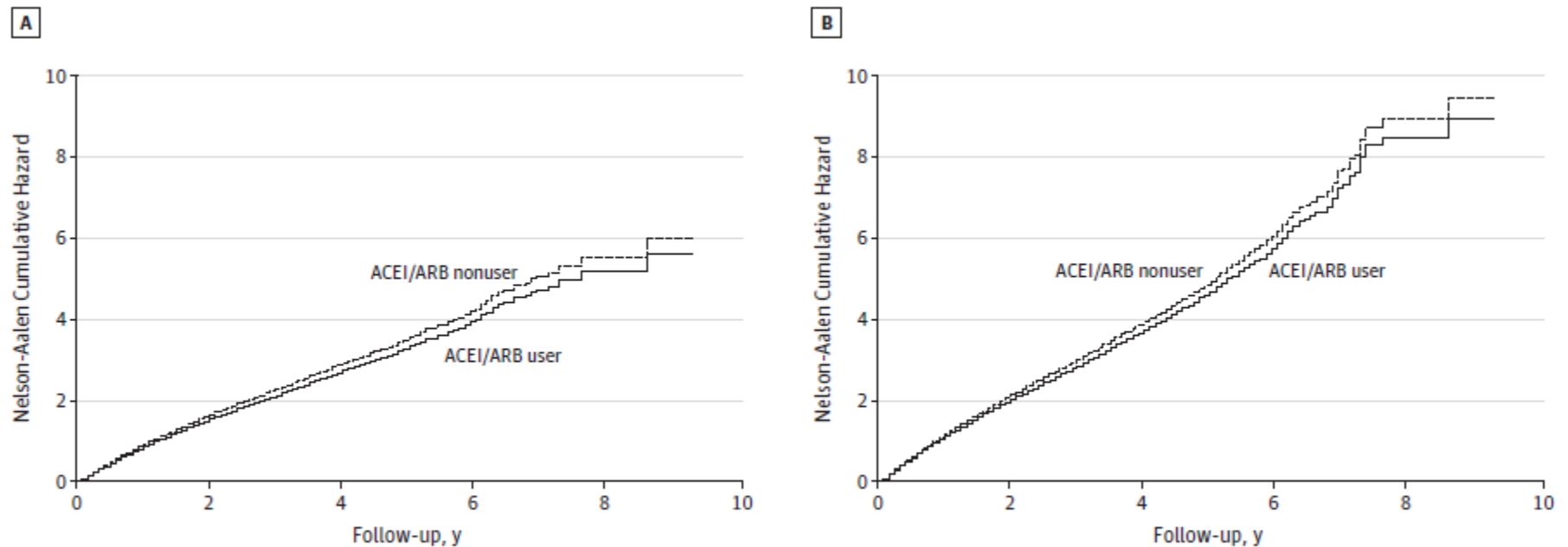
Group 1, benazepril	102	96	84	40
Group 2, benazepril	107	96	73	32
Group 2, placebo	108	88	59	22

# Renoprotective Effect of Renin-Angiotensin-Aldosterone System Blockade in Patients With Predialysis Advanced Chronic Kidney Disease, Hypertension, and Anemia

Ta-Wei Hsu, MD; Jia-Sin Liu, MS; Szu-Chun Hung, MD; Ko-Lin Kuo, MD; Yu-Kang Chang, PhD; Yu-Chi Chen, PhD; Chih-Cheng Hsu, MD, DrPH; Der-Cherng Tarng, MD, PhD

*JAMA Intern Med.* 2014;174(3):347-354.

Figure 2. Cumulative Hazards of Study Outcomes Among Patients With Predialysis Stage 5 Chronic Kidney Disease



A, Long-term dialysis. B, Composite outcome of long-term dialysis or death. We used the Nelson-Aalen method<sup>12</sup> to calculate the cumulative hazards of both outcomes in users and nonusers of angiotensin-converting enzyme inhibitors

(ACEIs) and/or angiotensin II receptor blockers (ARBs). A multivariate analysis was adjusted for all variables listed in Table 1.  $P < .001$ , users vs nonusers.

# Multicentre randomized controlled trial of ACEI/ARB withdrawal in advanced renal disease: the STOP-ACEi trial

Sunil Bhandari<sup>1,2</sup>, Natalie Ives<sup>3</sup>, Elizabeth A. Brettell<sup>3</sup>, Marie Valente<sup>3</sup>, Paul Cockwell<sup>4</sup>, Peter S. Topham<sup>5</sup>, John G. Cleland<sup>6</sup>, Arif Khwaja<sup>7</sup> and Meguid El Nahas<sup>7</sup>

<sup>1</sup>Department of Renal Medicine, Hull and East Yorkshire Hospitals NHS Trust, Kingston upon Hull, UK, <sup>2</sup>Hull York Medical School, East Yorkshire, UK, <sup>3</sup>Birmingham Clinical Trials Unit, University of Birmingham, Birmingham, UK, <sup>4</sup>Department of Renal Medicine, Queen Elizabeth Hospital, Birmingham, UK, <sup>5</sup>Department of Renal Medicine, Leicester General Hospital, Leicester, UK, <sup>6</sup>National Heart & Lung Institute, Imperial College London, London, UK and <sup>7</sup>Sheffield Kidney Institute, Sheffield, UK

Correspondence and offprint requests to: Sunil Bhandari; E-mail: sunil.bhandari@hey.nhs.uk



## 410個病人

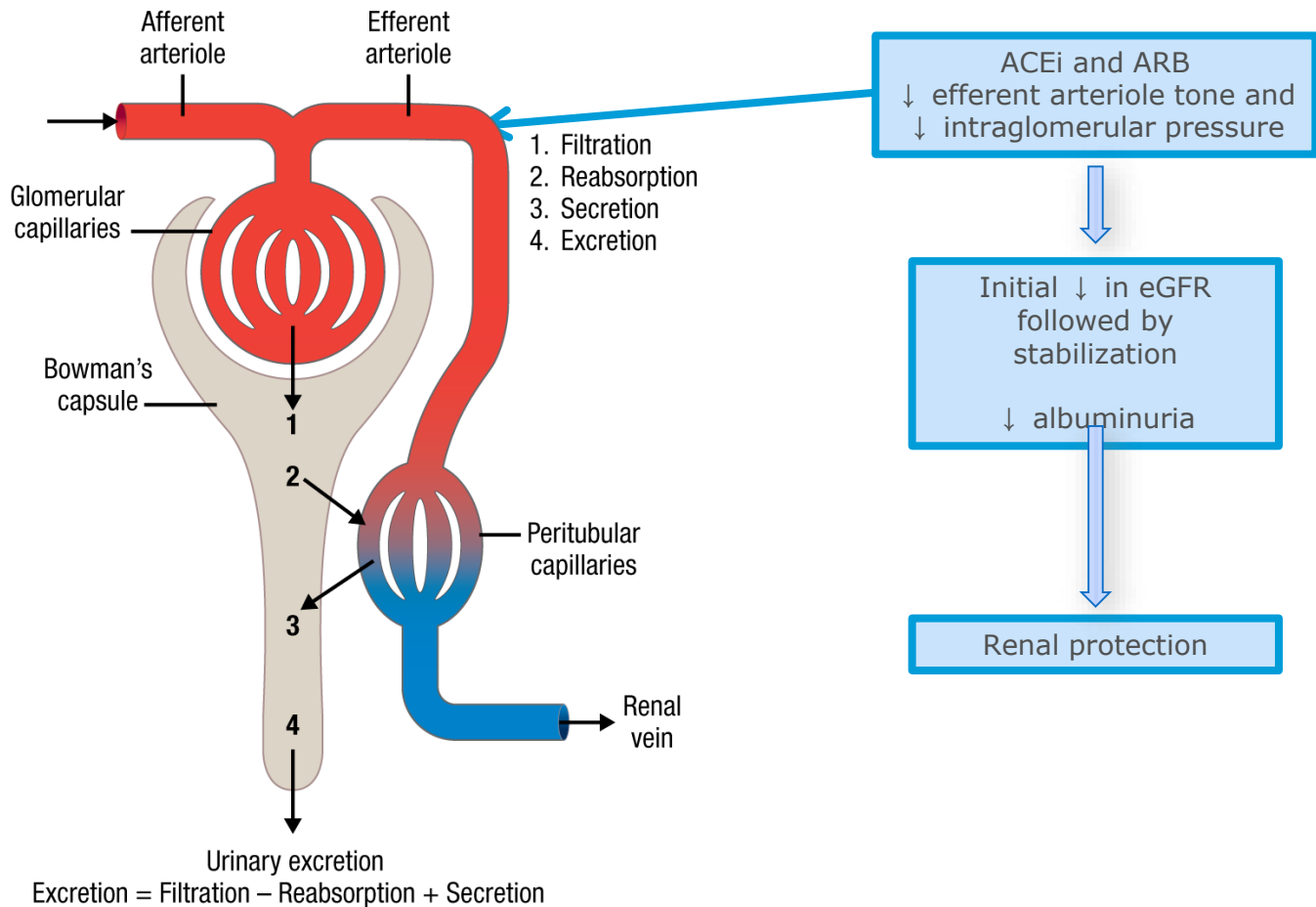
## 多機構 非雙盲 隨機分組

## CKD 4-5期

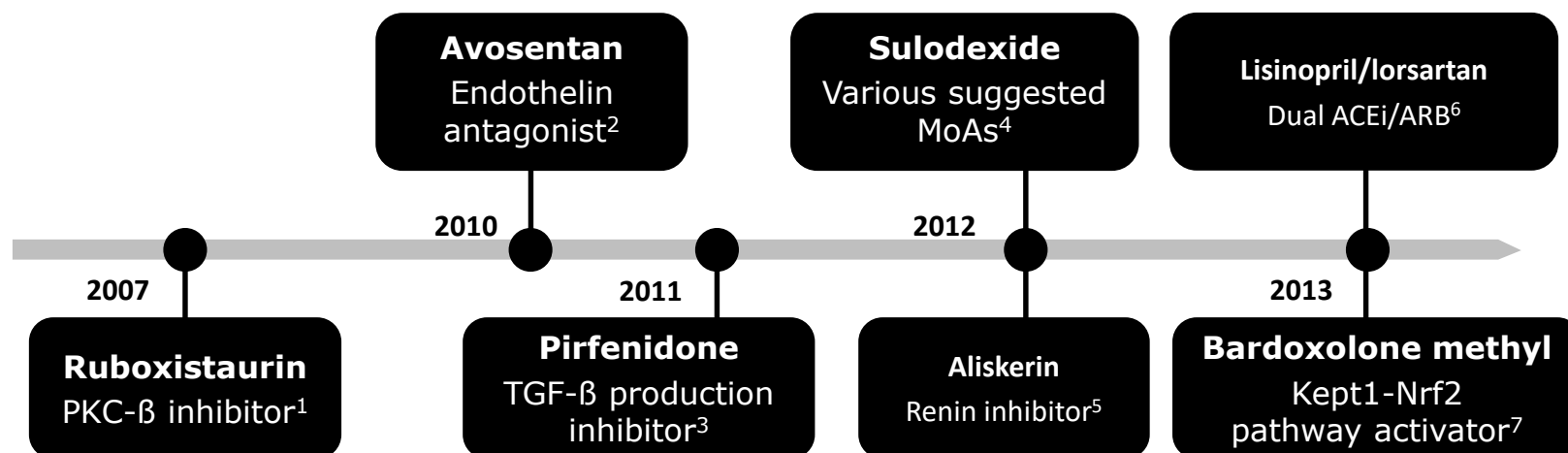
## 停掉原使用ACEI/ARB

- 慢性腎臟病第4、5期的病人，若是以糖尿病病人來說，目前並沒有臨床證據可以證明ACEI/ARB可以延緩腎功能惡化。
- 而非糖尿病的病人目前則是仍有爭議，中國大陸的研究認為ACEI(以Benazepril試驗)，在高度篩選掉不適合的病人後，仍可安全有效的使用，降低蛋白尿且延緩腎功能惡化。(注意ARB並沒有實證)
- 但近期英國團隊的研究發現，ACEI/ARB原本已普遍用於早期的慢性腎臟病病人，在進入慢性腎臟病4-5期的病人，ACEI/ARB可能沒有好處，反而有害。
- 前驅的52個病人觀察型的研究證實這個觀點，進行中的4百多人的多中心、隨機分組的STOP-ACEi研究可以進一步證實，提供另一方面證據。

# ACEi/ARB Reduce Intraglomerular Pressure: Mechanism for Renal Protection



# Since RENAAL and IDNT, New Therapeutic Strategies for Patients With T2DM and CKD Have Failed



1. Tuttle KR, et al. *Clin J Am Soc Nephrol.* 2007;2(4):631-636.  
2. Mann JFE, et al. *J Am Soc Nephrol.* 2010;21(3):527-535.  
3. Sharma K, et al. *J Am Soc Nephrol.* 2011;22(6):1144-1151.  
4. Packham DK, et al. *J Am Soc Nephrol.* 2012;23(1):123-130.

5. Parving HH, et al. *N Engl J Med.* 2012;367(23):2204-2213.  
6. Fried LF, et al. *N Engl J Med.* 2013;369(20):1892-1903.  
7. de Zeeuw D, et al. *N Engl J Med.* 2013;369(26):2492-2503.

# New evidence on Ketosteril

繼MDRD試驗後最大的RCT研究，發表于JASN

CLINICAL RESEARCH

[www.jasn.org](http://www.jasn.org)

## Ketoanalogue-Supplemented Vegetarian Very Low-Protein Diet and CKD Progression

Liliana Garneata,<sup>\*†</sup> Alexandra Stancu,<sup>†</sup> Diana Dragomir,<sup>†</sup> Gabriel Stefan,<sup>\*†</sup> and Gabriel Mircescu<sup>\*†</sup>

<sup>\*</sup>Department of Nephrology and Internal Medicine, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; and <sup>†</sup>Department of Nephrology, "Dr. Carol Davila" Teaching Hospital of Nephrology, Bucharest, Romania



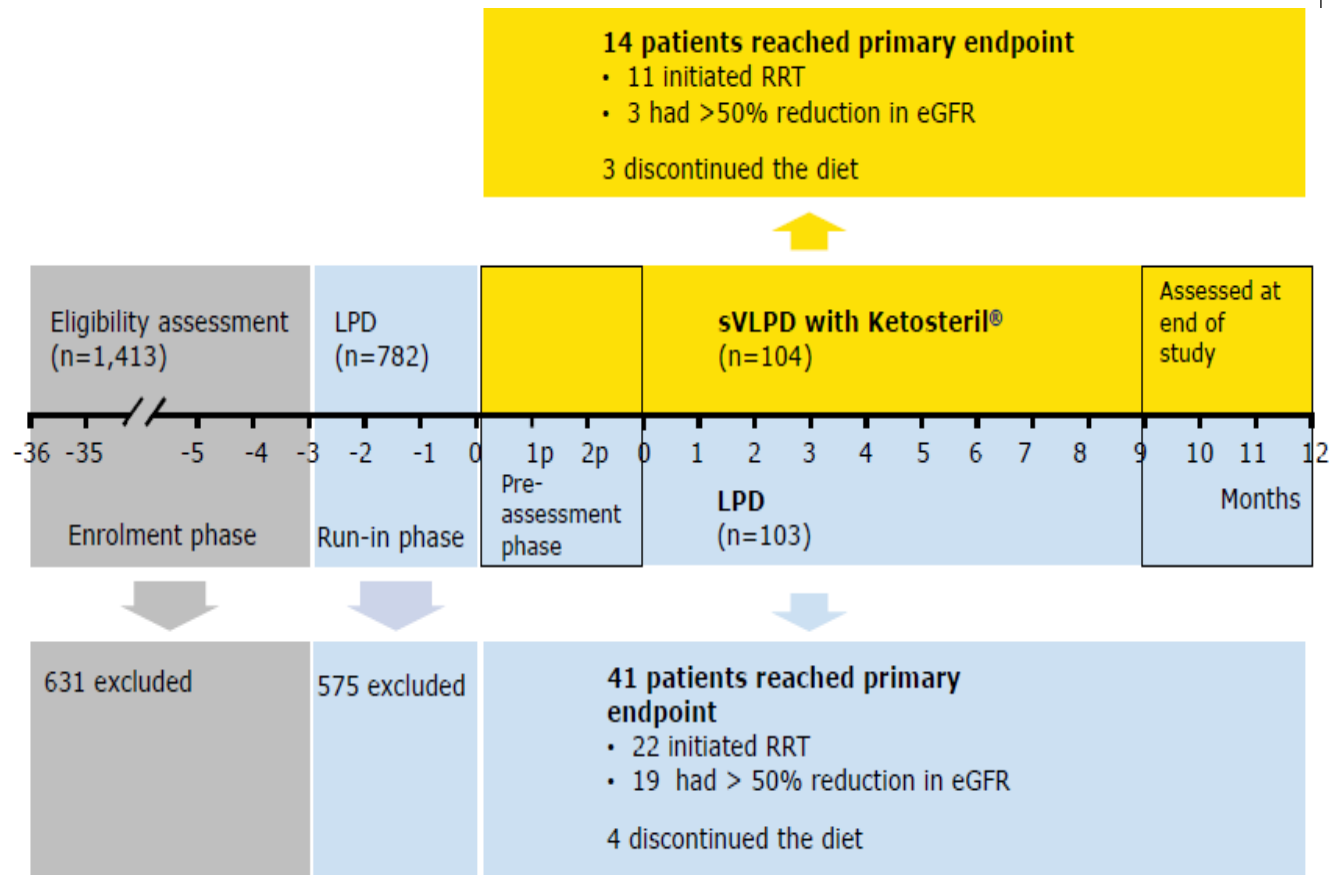
## Ketoanalogue-Supplemented Vegetarian Very Low-Protein Diet and CKD Progression

Liliana Garneata,<sup>\*†</sup> Alexandra Stancu,<sup>†</sup> Diana Dragomir,<sup>†</sup> Gabriel Stefan,<sup>\*†</sup> and Gabriel Mircescu<sup>\*†</sup>

- Nondiabetic
- Stable eGFR < 30 ml/min/1.73 m<sup>2</sup>
- Proteinuria < 1 g/g urinary creatinine
- Good nutritional status
- Good diet compliance

**Primary endpoint:**

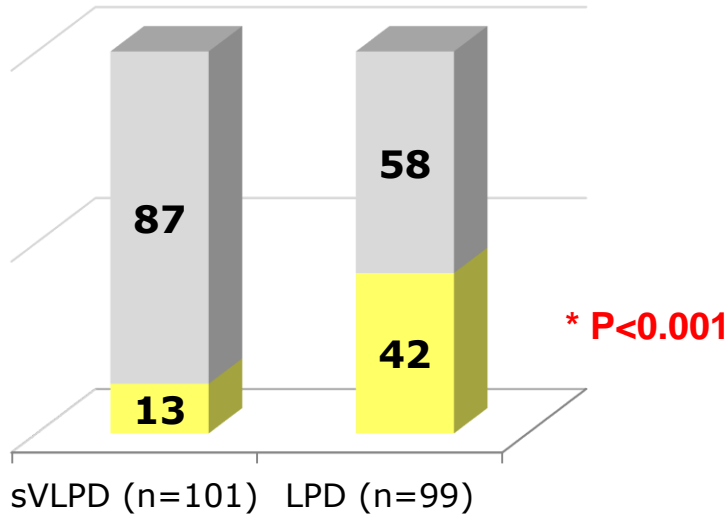
1. Renal replacement therapy initiation
2. > 50% reduction of baseline eGFR



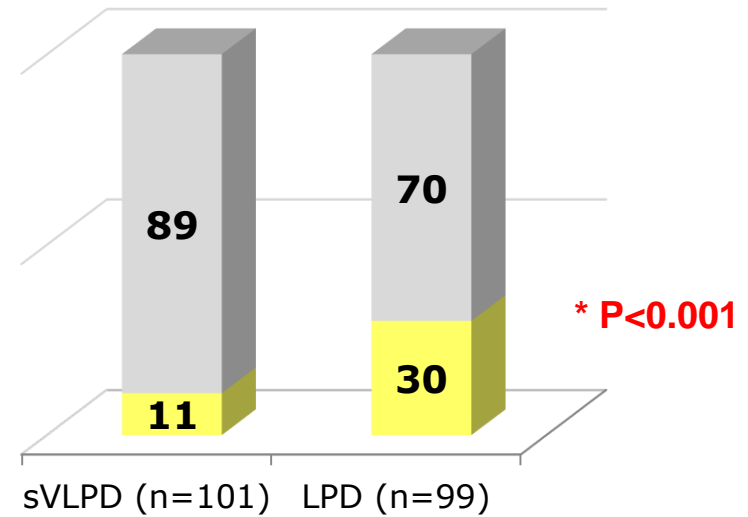


# Efficacy: Progression of CKD

進入ESRD或 eGFR下降50%的患者 ( % )

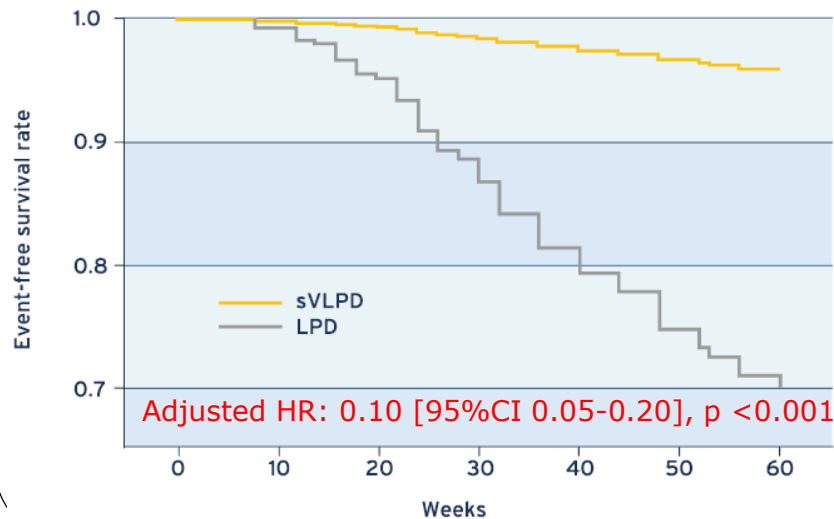


Renal replacement therapy initiation

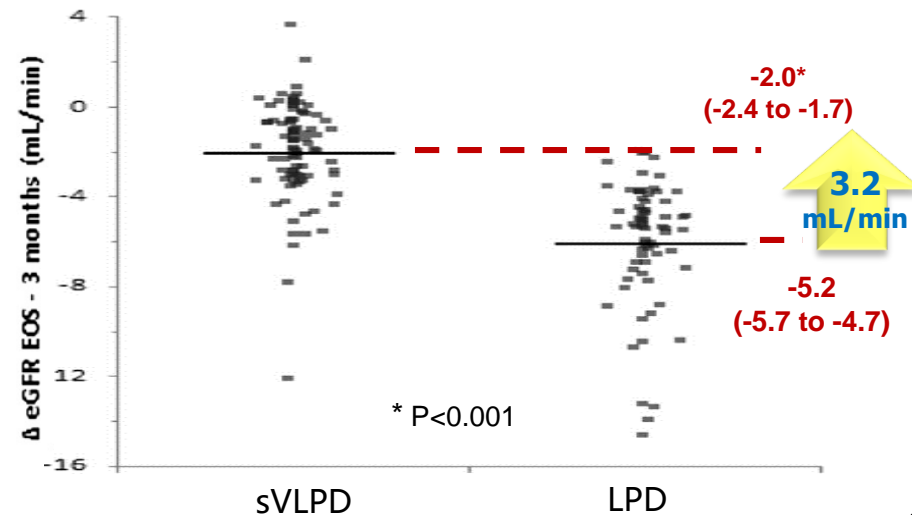


Ketosteril不僅能延緩患者開始洗腎時間，還可有效提高CKD患者存活率

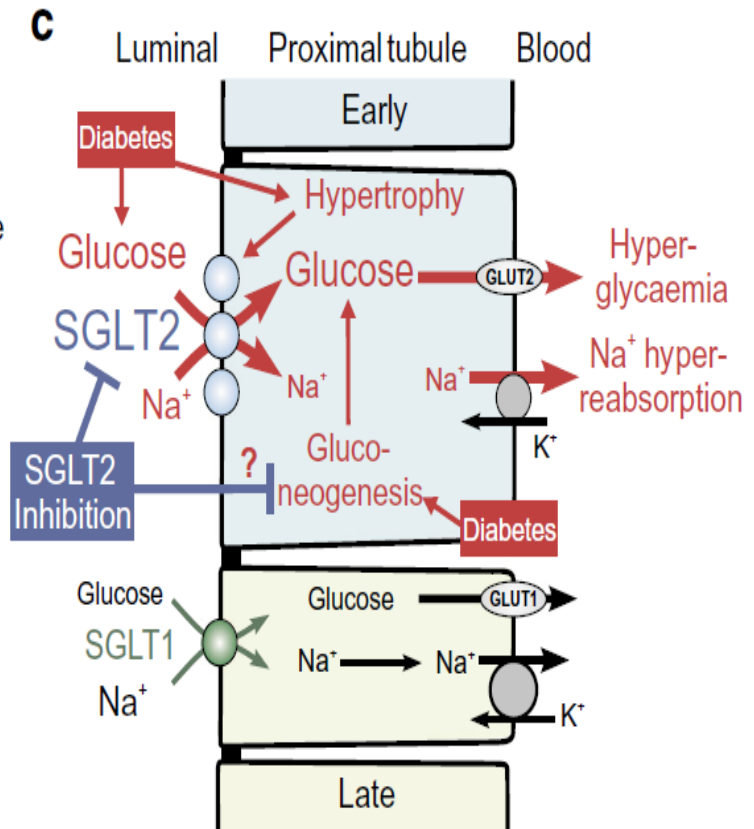
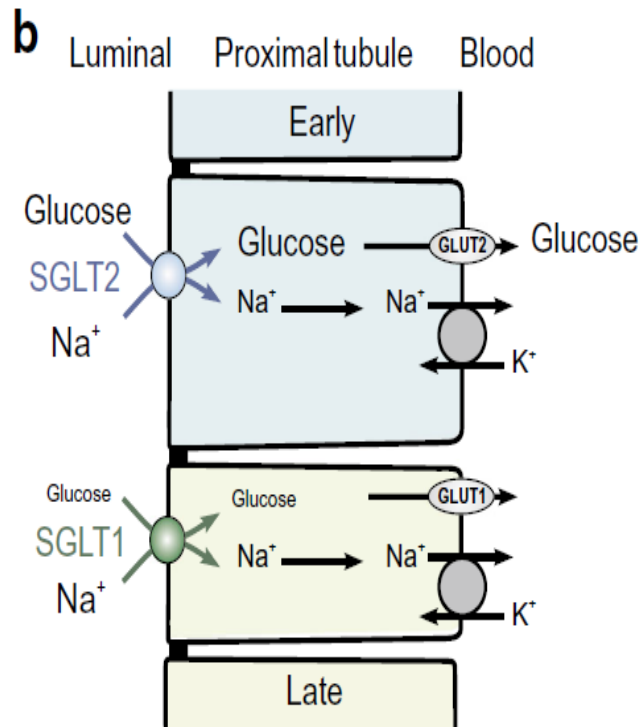
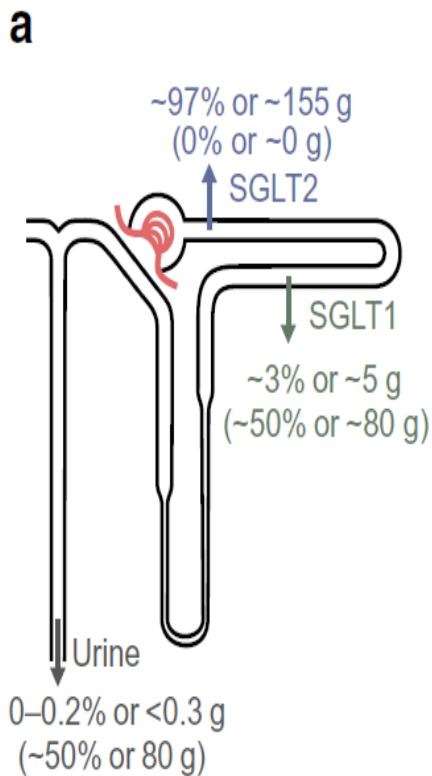
Time to the composite endpoint



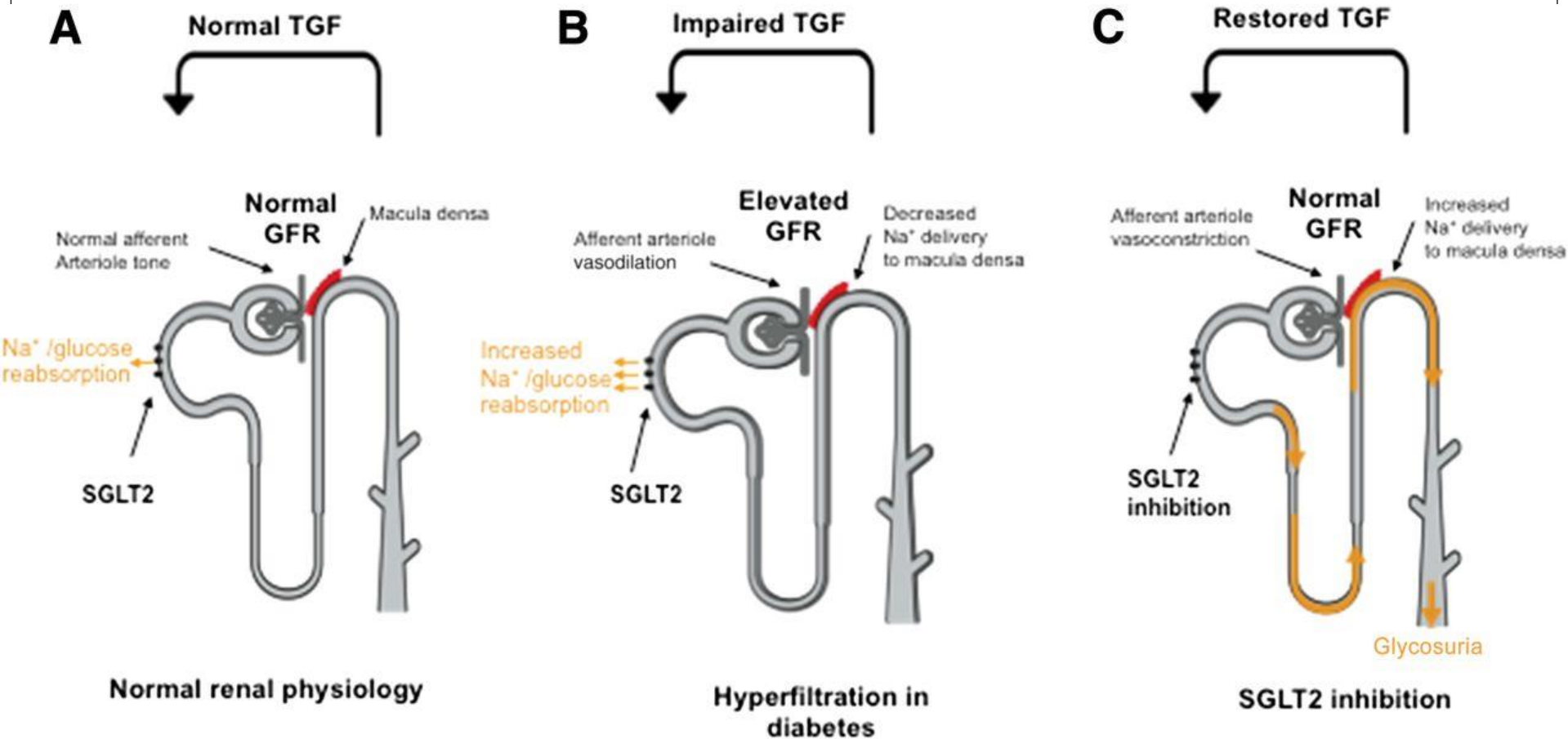
eGFR change



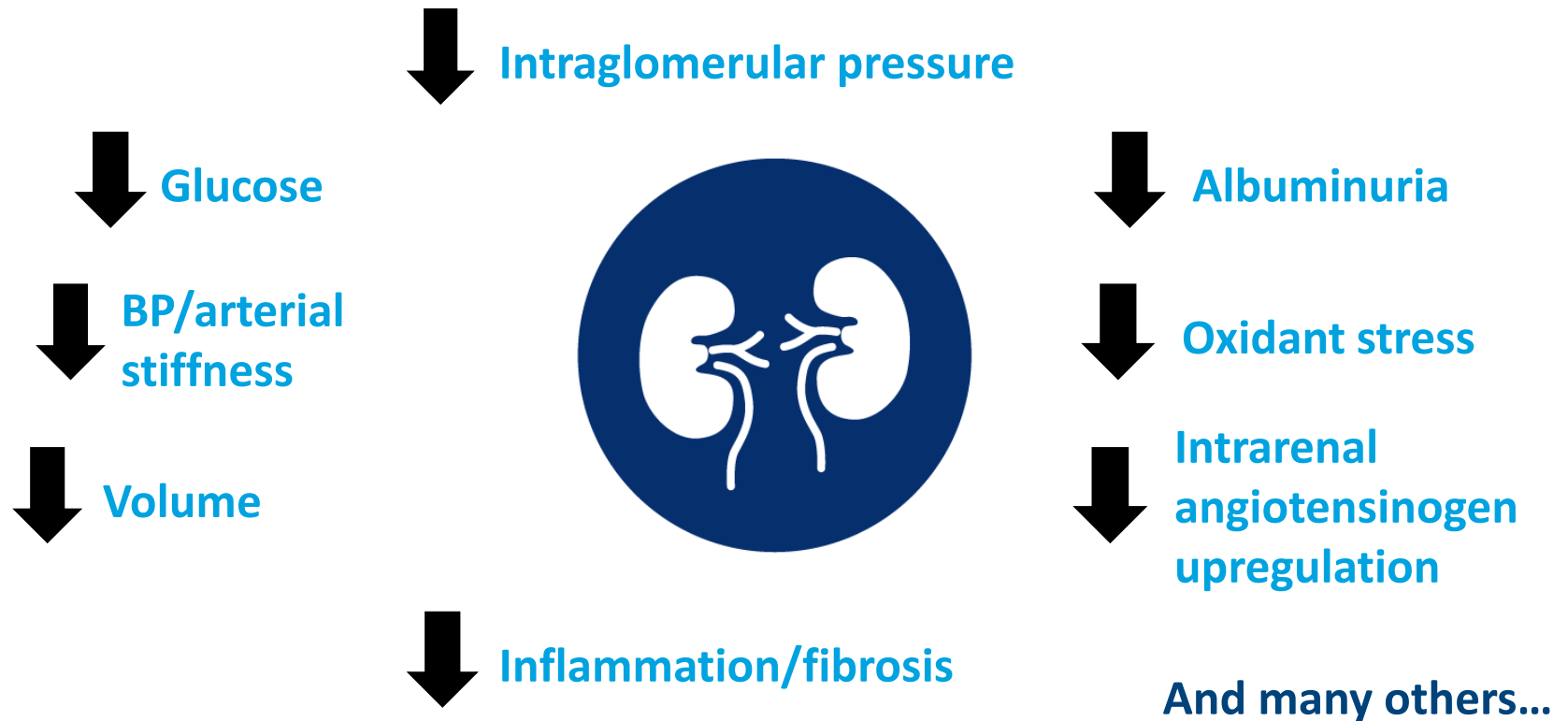
# SGLT<sub>2</sub>-mediated Glucose Reabsorption in the Kidney



# Tubuloglomerular feedback system in normal physiology (A), diabetes (B), and diabetes after treatment with SGLT2 inhibition (C)

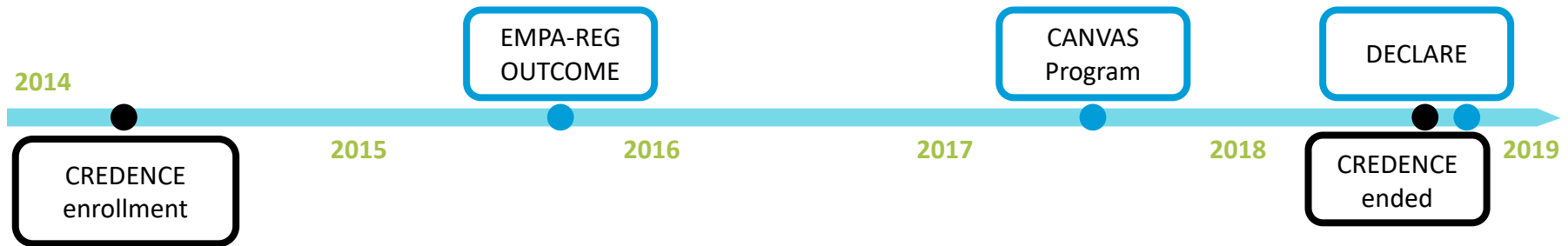


# Cardiovascular and Renal Effects of SGLT2 Inhibition



# Timeline of Major SGLT2 Inhibitor Trials

- CREDENCE began before any CV outcomes trials had reported



- Renal effects were not the primary focus of the CV outcomes trials

## SGLT-2抑制劑的心腎好處

# Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes



The NEW ENGLAND  
JOURNAL of MEDICINE

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D.,  
David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D.,  
Michaela Mattheus, Dipl. Biomath., Theresa Devins, Dr.P.H.,  
Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Uli C. Broedl, M.D.,  
and Silvio E. Inzucchi, M.D., for the EMPA-REG OUTCOME Investigators

n engl j med 373;22 November 26, 2015

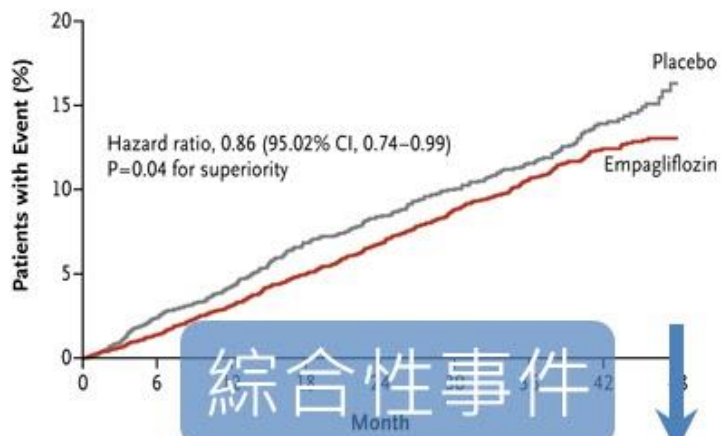
## EMPA-REG OUTCOME

隨機 雙盲 多國 多中心

→ 降血糖藥 Empagliflozin

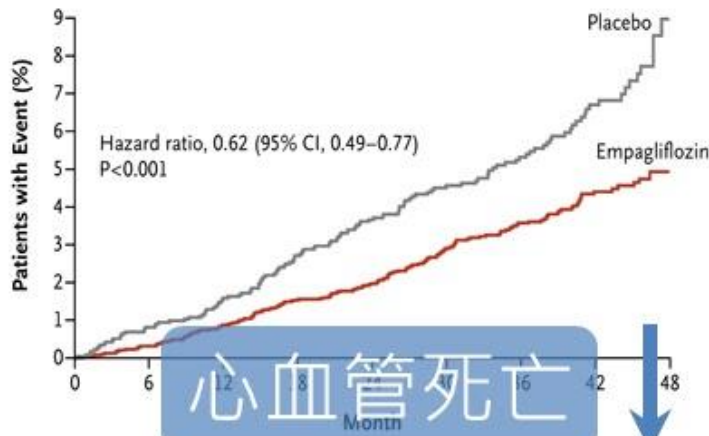
VS 心血管風險、死亡率

### A Primary Outcome



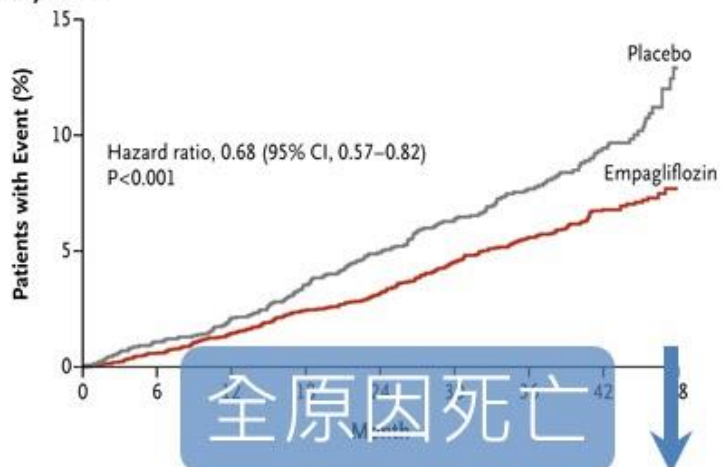
No. at Risk	0	6	12	18	24	30	36	42	48
Empagliflozin	4687	4580	4455	4328	3851	2821	2359	1534	370
Placebo	2333	2256	2194	2112	1875	1380	1161	741	166

### B Death from Cardiovascular Causes



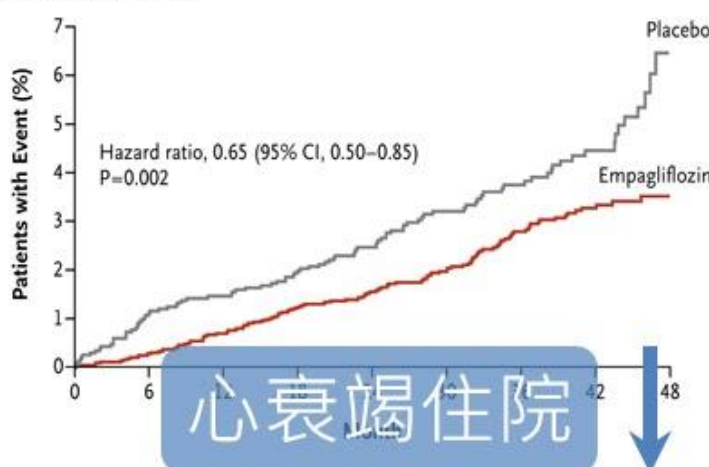
No. at Risk	0	6	12	18	24	30	36	42	48
Empagliflozin	4687	4651	4608	4556	4128	3079	2617	1722	414
Placebo	2333	2303	2280	2243	2012	1503	1281	825	177

### C Death from Any Cause



No. at Risk	0	6	12	18	24	30	36	42	48
Empagliflozin	4687	4651	4608	4556	4128	3079	2617	1722	414
Placebo	2333	2303	2280	2243	2012	1503	1281	825	177

### D Hospitalization for Heart Failure



No. at Risk	0	6	12	18	24	30	36	42	48
Empagliflozin	4687	4614	4523	4427	3988	2950	2487	1634	395
Placebo	2333	2271	2226	2173	1932	1424	1202	775	168

# Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy

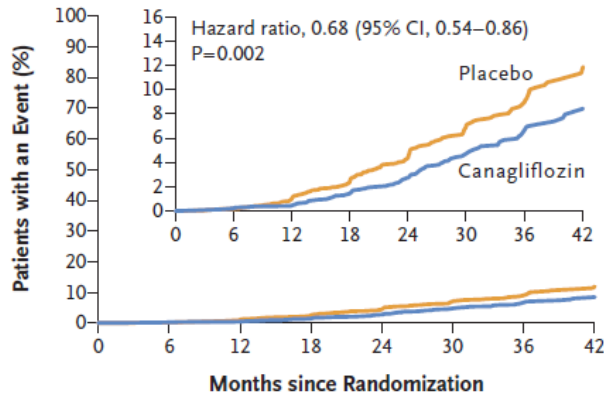
This article was published on April 14, 2019, at NEJM.org.

## A Primary

Patients with an Event (%)

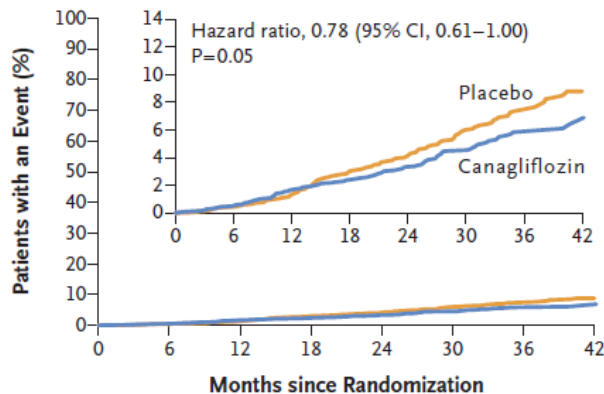
No. at Risk  
Placebo  
Canagliflozin

## C End-Stage Kidney Disease



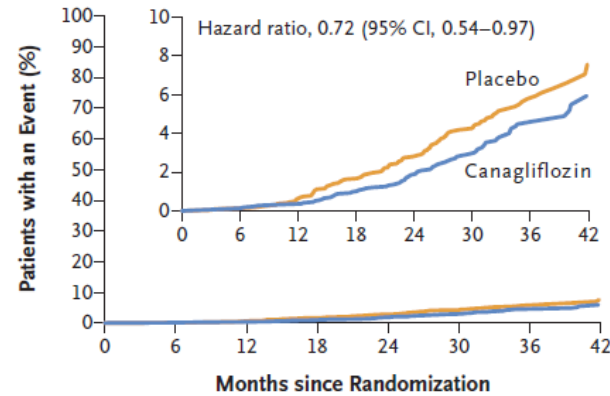
No. at Risk	0	6	12	18	24	30	36	42
Placebo	2199	2182	2141	2063	1752	1152	641	178
Canagliflozin	2202	2182	2146	2091	1798	1217	654	199

## E Death from Cardiovascular Cause



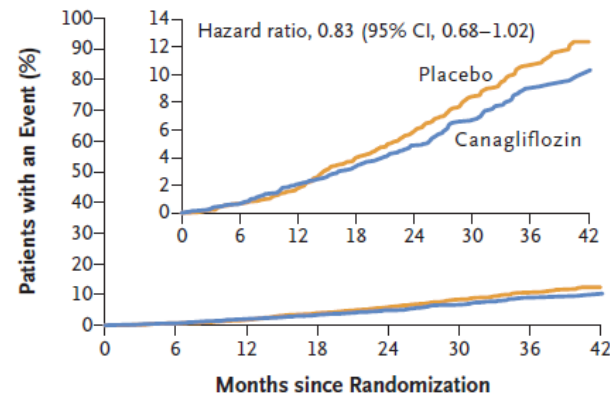
No. at Risk	0	6	12	18	24	30	36	42
Placebo	2199	2185	2160	2106	1818	1220	688	189
Canagliflozin	2202	2187	2155	2120	1835	1263	687	212

## D Dialysis, Kidney Transplantation, or Renal Death



No. at Risk	0	6	12	18	24	30	36	42
Placebo	2199	2183	2147	2077	1776	1178	653	180
Canagliflozin	2202	2184	2148	2100	1811	1236	661	199

## F Death from Any Cause

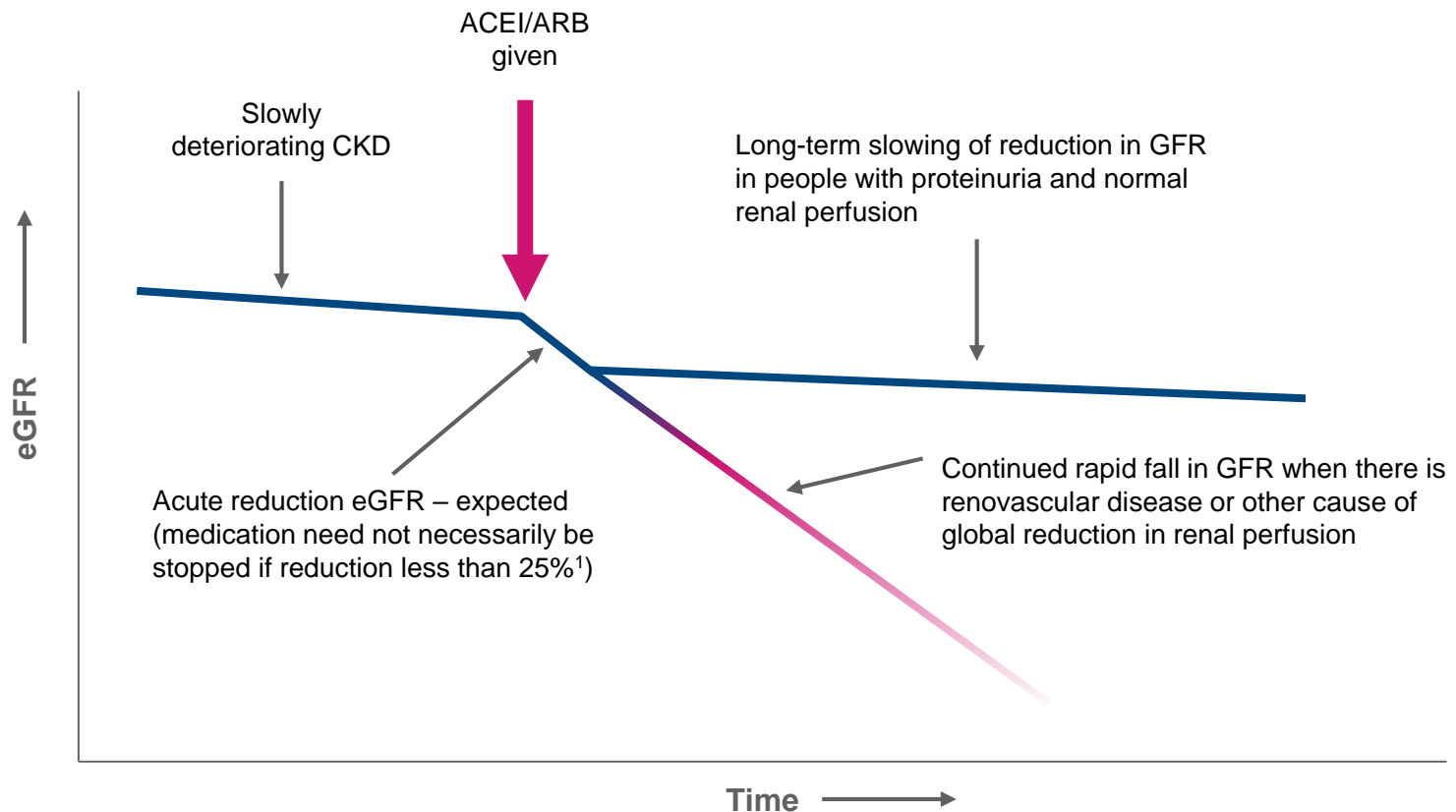


No. at Risk	0	6	12	18	24	30	36	42
Placebo	2199	2185	2160	2106	1818	1220	688	189
Canagliflozin	2202	2187	2155	2120	1835	1263	687	212

81) Placebo  
Canagliflozin  
36 42  
621 170  
646 196



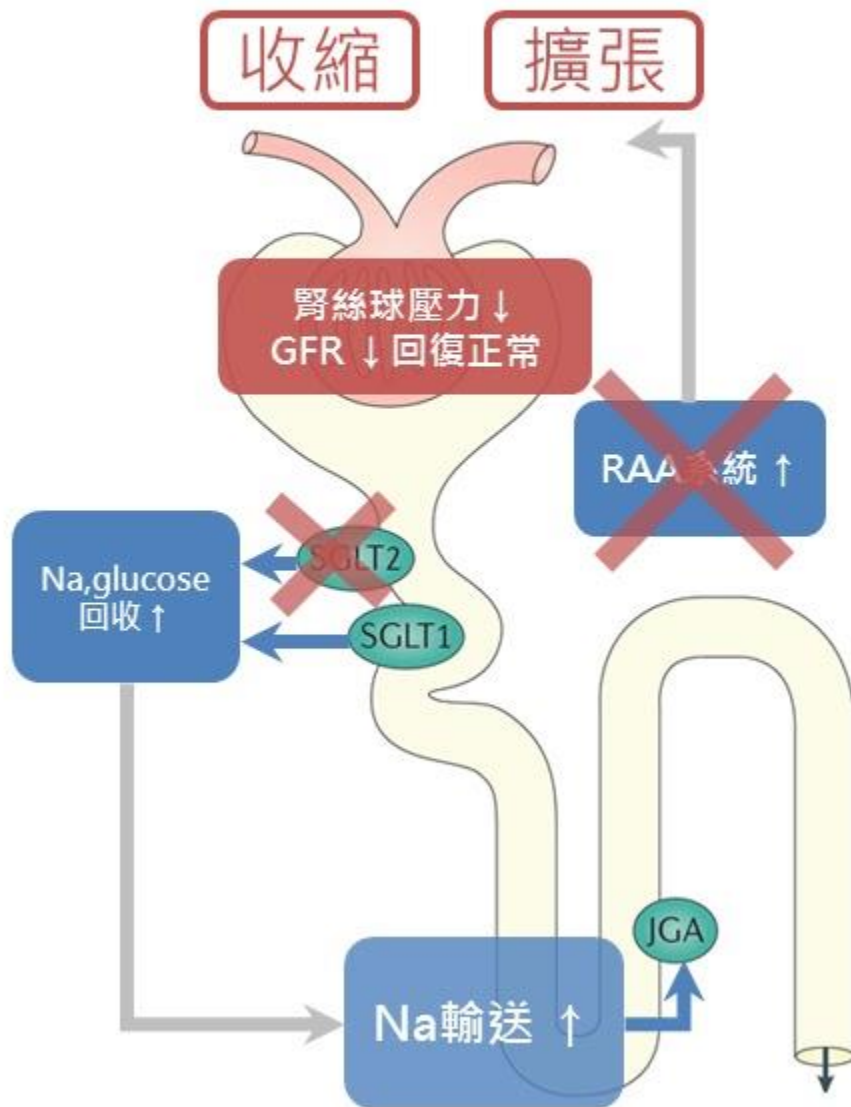
# ACE inhibitors or ARBs may reduce the rate of GFR decline



## Reference:

NICE clinical guideline 182. Chronic kidney disease early identification and management of chronic kidney disease in adults in primary and secondary care. July 2014.

# SGLT2 + ACEI/ARB



# 結論

- 雖然台灣ESRD發生率與盛行率仍持續上升，但是若去除老化因素，整體發生率是持平的，中年人與青年人的發生率更是下降的。
- CKD病人的整體照護，展現良好的成效，應該加強收治。
- 跨專科跨領域的整合性醫療照護，以及新發展的ACEI/ARB 與SGLT2 inhibitors 提供治療與照護的新契機，尤其在DM早期的治療。
- DM晚期已發生CVD、DKD時的治療原則，應因人因狀況而異。
- **控糖保腎救心，仍是一個持續進展的重要議題**

謝 謝 聆 聽

Thank You 

Kaohsiung Medical University Hospital

