慢性腎臟病的高血壓和糖尿病照護

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前言

- 台灣透析發生率從2000年每百萬人口331人，增加至2018年每百萬人口523人，仍居世界第一
- 2020年，治療腎臟疾病的費用為562億元，名列健保支出項目第一；當中有84%都是支付末期腎衰竭患者的洗腎費用，金額達472億元。
- 面對台灣透析發生率與盛行率依然持續上升，而且愈來愈遙遙領先世界各國，我們必須再次強調慢性腎臟病預防的重要性。對於腎功能不佳病患的安全用藥問題，例如長期服用NSAID與Metformin藥物長期使用於末期腎病患者的現象，雖然近年來有逐漸改善，但仍須提醒臨床照護者小心處方
- **有**加入計畫患者使用NSAID比率較無加入計畫患者來得**低**
- 2018年有加入Pre-ESRD計畫的糖尿病透析患者使用**DPP4i**比率較無加入計畫患者來得高，而**無**加入計畫患者使用**Metformin**、Sulfonylurea、Acarbose 及Insulin 比率較有加入計畫患者來得**高**
- 2018年有加入Pre-ESRD計畫的高血壓透析患者使用CCB及Beta blockers 比率都較無加入計畫患者來得高，而**無**加入計畫患者使用**Potassium-sparing diuretics** 比率較有加入計畫患者來得**高**

OUTLINE

1. 慢性腎臟病簡介
2. 糖尿病與慢性腎臟病guideline update
3. 高血壓與慢性腎臟病guideline update

慢性腎臟病簡介

慢性腎臟病定義

CKD 定義（以下任一表現持續三個月以上）	
腎臟受損標記 （一個或更多）	尿液出現白蛋白，其中白蛋白排泄率（AER）≧ 30 mg/24 小時；白蛋白血清肌酸酐比值（ACR）≧ 30 mg/g（≧ 3 mg/mmol）
	尿液出現異常沉積物
	腎小管疾病所造成的電解質及其它異常
	腎臟有組織學異常
	影像學顯示有構造異常
	腎臟移植病史
GFR 降低	GFR<60 ml/min/1.73m^2（GFR 分期的 G3a 期到 G5 期）

2015臺灣慢性腎臟病臨床診療指引

慢性腎臟病的偵測

門診三寶:
抽血、驗尿、
超音波

(一)腎臟損傷可以用直接或間接方法偵測

1.直接證據包括影像學或腎臟切片的組織病理學

影像學檢查包括**超音波、電腦斷層、核磁共振和核子醫學掃描**，可以偵測腎臟的結構異常，例如多囊腎、逆流性腎病變、慢性腎盂腎炎和腎血管疾病。

腎臟切片組織病理可以確定腎絲球疾病，例如免疫球蛋白A 腎病變或局部腎絲球硬化等

2.間接證據可以從**尿液檢查**得知腎臟損傷，當腎絲球發炎或功能異常時，會有血尿或蛋白尿，但尿液異常也可能是有其他泌尿道病因

(二)eGFR:3個月抽血

2015臺灣慢性腎臟病臨床診療指引

慢性腎臟病檢查時機及頻率

(一) 建議所有具危險因子的族群都應接受篩檢：

1. 對於高危險群，篩檢頻率沒有研究可明確定義。美國衛生院轄下國家腎臟病教育計畫The National Kidney Disease Education Program（NKDEP） of the National Institutes of Health（NIH）**建議糖尿病病人每年檢查一次腎功能**。

2. 建議有糖尿病且eGFR ﹤ 60 ml/min/1.73m2 的病人，應檢查**ACR 或PCR** ；如果第一次檢查發現異常，應以清晨第一泡尿液檢體再檢查一次確認。

3. **高血壓**病人在診斷、開始治療時都應檢查腎功能， 之後**每三年追蹤腎功能（NKDEP）**。

4. 有**CKD 家族史的人應每三年檢查腎功能**（NKDEP）。

(二) 使用calcineurin 抑制劑如環孢靈素和鋰鹽（lithium）這類具潛在腎毒性藥物，須定期監測GFR，**長期使用NSAID（非類固醇抗發炎藥物）者，至少一年檢查一次GFR**。

(三) 只有**持續性微觀血尿、沒有蛋白尿，應每年**追蹤血尿、蛋白尿/ 白蛋白尿、GFR及監測血壓。

2015臺灣慢性腎臟病臨床診療指引

Prognosis of CKD and by eGFR and Albuminuria Categories: KDIGO 2012

eGFR categories (mL/min/1.73m²) Description and range				Persistent albuminuria categories Urine ACR (mg/mmol) Description and range		
				A1	**A2**	**A3**
				Normal	Microalbuminuria	Macroalbuminuria
				male < 2.5 female < 3.5	male 2.5 – 25 female 3.5 – 35	male > 25 female > 35
	G1	Normal or high	>90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

low risk if no other markers of kidney disease, no CKD) Moderately increased risk high risk very high risk

慢性腎臟病收案對象

階段	判斷方式	
1	eGFR≧90 腎功能正常但併有微量蛋白尿	初期CKD方案
2	eGFR 60~89.9 輕度慢性腎衰竭	
3a	eGFR 45~59.9 中度慢性腎衰竭	
3b	eGFR 30~44.9 中度慢性腎衰竭	Pre-ESRD計畫
4	eGFR 15~29.9 重度慢性腎衰竭	
5	eGFR ＜15 末期腎臟病變	

EARLY CKD 收案條件

UPCR>150
UACR>30

1. CKD stage 1：腎功能正常但有蛋白尿、血尿等腎臟損傷狀況， 腎絲球過濾率估算值(estimated Glomerular filtration rate, 以下稱 eGFR)≧ 90 ml/min/1.73 m2 ＋尿蛋白與尿液肌酸酐比值**(Urine Protein andCreatinine Ratio，以下稱 UPCR)≧ 150 mg/gm (或糖尿病患者UACR≧ 30 mg/gm)**之各種疾病病患。

2. CKD stage 2：輕度慢性腎衰竭，併有蛋白尿、血尿等 eGFR 60~89.9ml/min/1.73 m2 ＋ **UPCR≧ 150 mg/gm (或糖尿病患者 UACR≧ 30 mg/gm)**之各種疾病病患。

3. CKD stage 3a：中度慢性腎衰竭， eGFR 45~59.9 ml/min/1.73 m2 之各種疾病病患。

EARLY CKD照護原則:

四、慢性腎臟疾病併高血壓之照護原則:

1.**第一線抗高血壓藥物，應使用ACEI或ARB**，除非病人有過敏或其他無法使用之理由。在開始使用ACEI或ARB時，建議定期追蹤腎功能及血鉀。

2.血壓控制之目標為低於**130/80mmHg**。

3.對於有腎血管狹窄之病患，應小心ACEI或ARB可能引起之急性腎衰竭。

五、慢性腎臟疾病併糖尿病之照護原則:

1.**血糖控制之目標，為空腹血糖<160mg/dl及HbA1c＜7.0%。**

2.血糖之控制為多方位治療(multifactorial intervention strategy)之一部分。亦須注意血壓及心血管危險因子之控制，必要時應使用statin及acetylsalicylic acid。

3.**Metformin可以使用於初期慢性腎病(CKD，1-3 stage)且腎功能穩定之糖尿病病患。但在腎功能不穩定，嚴重心衰竭及臨床狀況不佳者，須小心使用。CKD stage 4及stage 5病人不建議使用。**

4.使用Sulfonylurea，其他胰島素刺激或胰島素時，以短效者為佳，且應衛教如何辨識及處理低血糖併發症。

全民健康保險初期慢性腎臟病醫療給付改善方案

PRE ESRD收案條件

UPCR>1000

1、 CKD stage 3b 病患：腎絲球過濾率 (Glomerular Filtration Rate,以下稱 GFR) 30~44.9ml/min/1.73 m^2 之各種疾病病患。

2、 CKD stage 4： GFR 15~29.9 ml/min/1.73 m^2 之各種疾病病患。

3、 CKD stage 5: GFR < 15 ml/min/1.73 m^2 之各種疾病病患。

4、蛋白尿病患： **24 小時尿液總蛋白排出量大於 1,000 mg 或尿蛋白與尿液肌酸酐比值(urine protein and creatinine ratio,以下稱Upcr)> 1,000mg/gm 之明顯蛋白尿病患，不限各 Stage**，主要包含 Stage 1、 2、 3a，即腎絲球過濾率估算值 (estimated Glomerularfiltration rate, 以下稱 eGFR)≧ 45~60 ml/min/1.73 m^2 之蛋白尿患者。

全民健康保險初期慢性腎臟病醫療給付改善方案

2-1、年度照護指標（Stage 3b、4及蛋白尿CKD病患適用）（以最近狀況評估）

A.血壓控制在130/80 mmHg以下	□1.是 □2.否
B.低密度脂蛋白膽固醇控制在100mg/dL以下，三酸甘油脂控制在150mg/dL以下	□1.是 □2.否
C.糖尿病病患HbA1c控制在7.5%以下	□1.是 □2.否 □3.不適用
D.完成護理衛教(完成4次)	□1.是 □2.否
E.完成營養衛教(至少完成2次)	□1.是 □2.否
F.符合Stage 3b、4病患之獎勵條件：收案時eGFR 15-45ml/min/1.73m²/year，給予照護1年後DM病人eGFR下降速率<6 ml/min/1.73m²/year，非DM病人eGFR下降速率<4 ml/min/1.73m²/year	□1.是 □2.否 （請勾選3-1）
G.符合蛋白尿之獎勵條件	□1.是 □2.否 （請勾選3-3）

2-2、年度照護指標（Stage 5 CKD病患適用）（以最近狀況評估）

A.使用EPO	□1.是 □2.否
B.血紅素＞8.5g/dL	□1.是 □2.否
C.血壓控制在130/80 mmHg以下	□1.是 □2.否
D.低密度脂蛋白膽固醇控制在100mg/dL以下，三酸甘油脂控制在150mg/dL以下	□1.是 □2.否
E.糖尿病病患HbA1c控制在7.5%以下	□1.是 □2.否 □3.不適用
F.已作好瘻管或導管	□1.是 □2.否
G.完成護理衛教(完成4次)	□1.是 □2.否
H.完成營養衛教(至少完成2次)	□1.是 □2.否
I.符合Stage 5病患之獎勵條件：收案時eGFR <15ml/min/1.73m²/year，給予照護1年後DM病人eGFR下降速率<6 ml/min/1.73m²/year，非DM病人eGFR下降速率<4 ml/min/1.73m²/year	□1.是 □2.否 （請勾選3-2）

糖尿病與慢性腎臟病
GUIDELINE UPDATE

OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY

SUPPLEMENT TO

kidney INTERNATIONAL

KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Diseas_

www.kidney-international.org

KDIGO executive conclusions

Executive summary of the 2020 KDIGO Diabetes Management in CKD Guideline: evidence-based advances in monitoring and treatment

Check for updates

OPEN

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This is the first Kidney Disease: Improving Global Outcomes (KDIGO) Guideline for Diabetes Management in Chronic Kidney Disease. The guideline comes at a pivotal time, with substantial growth in the public health burden of diabetes and chronic kidney disease (CKD), and with recent development of new therapies applicable to this population.[1,2]

Practice Points are used when

- No systematic review was conducted
- There is insufficient evidence
- Evidence is inconclusive
- The alternative option is illogical

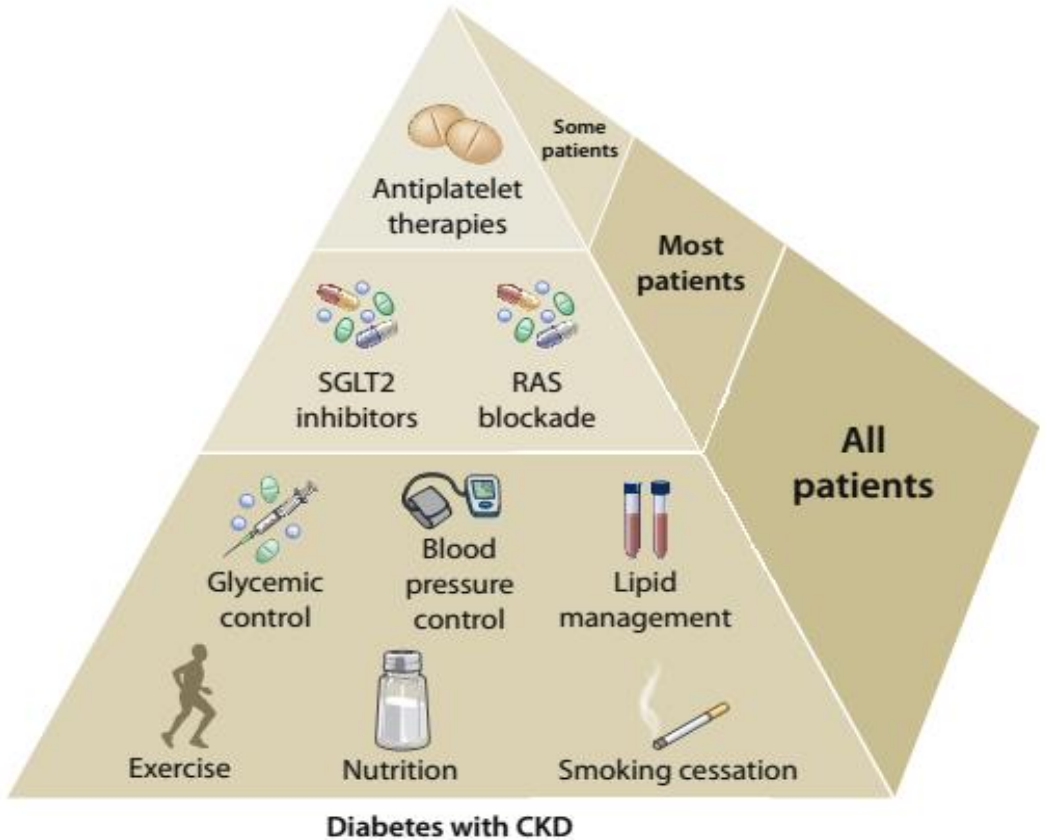
- Guidance is discretionary for the physician
- Consensus statements providing guidance are needed in the absence of evidence. Benefits and harms will not be explicitly discussed
- Guidance does not require an explicit discussion of values and preferences or of resource considerations, although it is implied that these factors were considered
- The guidance may be more useful as a table, figure, or algorithm

Recommendations are provided when

	Implications		
Grade	Patients	Clinicians	Policy
Level 1 "We recommend"	Most people in your situation would want the recommended course of action, and only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be evaluated as a candidate for developing a policy or a performance measure.
Level 2 "We suggest"	The majority of people in your situation would want the recommended course of action, but many would not.	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.

Grade	Quality of evidence	Meaning
A	High	We are confident that the true effect is close to the estimate of the effect.
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C	Low	The true effect may be substantially different from the estimate of the effect.
D	Very low	The estimate of effect is very uncertain, and often it will be far from the true effect.

Chapter 1: Comprehensive care in patients with diabetes and CKD	
• **Practice Point 1.1.1**	Patients with diabetes and CKD should be treated with a comprehensive strategy to reduce risks of kidney disease progression and cardiovascular disease (Figure 2).
• **Recommendation 1.2.1**	We recommend that treatment with an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) be initiated in patients with diabetes, hypertension, and albuminuria, and that these medications be titrated to the highest approved dose that is tolerated (*1B*).
• **Recommendation 1.3.1**	We recommend advising patients with diabetes and CKD who use tobacco to quit using tobacco products (*1D*).



- Patients with diabetes and CKD have multisystem disease that requires treatment from a multidisciplinary team of health care professionals. These patients are at high risk of **CKD progression** and **cardiovascular disease**
- Comprehensive management includes a foundation of **lifestyle intervention** and risk factor management, with additional pharmacotherapy in selected patients

Chapter 1: Comprehensive care in patients with diabetes and CKD	
• Practice Point 1.1.1	Patients with diabetes and CKD should be treated with a comprehensive strategy to reduce risks of kidney disease progression and cardiovascular disease (Figure 2)
• Recommendation 1.2.1	We recommend that treatment with an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) be initiated in patients with diabetes, hypertension, and albuminuria, and that these medications be titrated to the highest approved dose that is tolerated (*1B*).
• Recommendation 1.3.1	We recommend advising patients with diabetes and CKD who use tobacco to quit using tobacco products (*1D*).

- Patients with **T1D or T2D, hypertension**, and **albuminuria**(persistent albumin-creatinine ratio >30 mg/g [3 mg/mmol]) should be treated with a renin–angiotensin system inhibitor (RASi).
- Serum **potassium** and **creatinine** should be monitored. Measures to control potassium should be considered when serum potassium is elevated to continue RASi when possible.
- Patients with **diabetes**, **hypertension**, and **normal albumin excretion** are at lower risk of CKD progression→ evidence **does not** demonstrate clear clinical benefits of RASi for CKD progression, and **other agents** are also appropriate for blood pressure management
- **Aspirin** should generally be used lifelong for **secondary prevention** among those with established **CVD** and may be considered for **primary prevention among high-risk individuals**

• **Recommendation 2.1.1**	We recommend using hemoglobin A1c (HbA1c) to monitor glycemic control in patients with diabetes and CKD (*1C*).
• **Recommendation 2.2.1**	We recommend an individualized HbA1c target ranging from <6.5% to <8.0% in patients with diabetes and CKD not treated with dialysis (Figure 3) (*1C*).

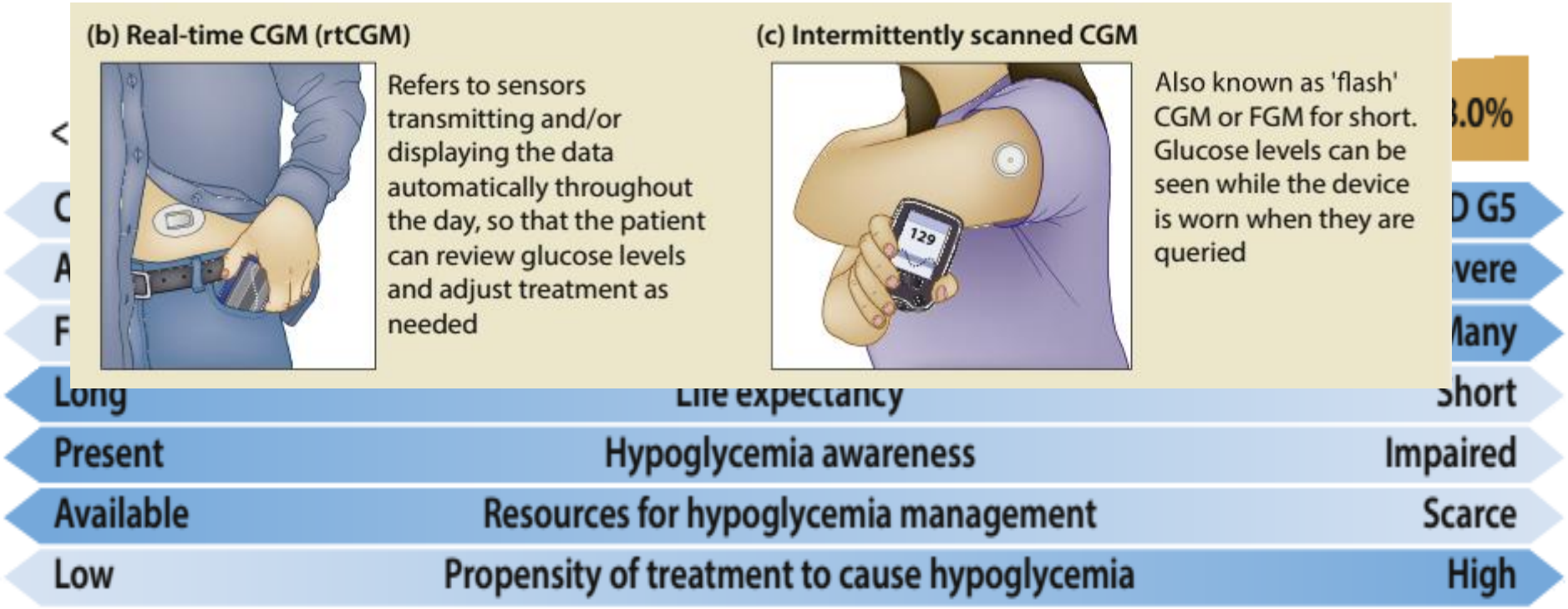


Figure 3| Factors guiding decisions on individual glycated hemoglobin (HbA1c) targets. CKD, chronic kidney disease; G1, estimated glomerular filtration rate (eGFR) >90 ml/min per 1.73 m^2; G5, eGFR <15 ml/min per 1.73 m^2.

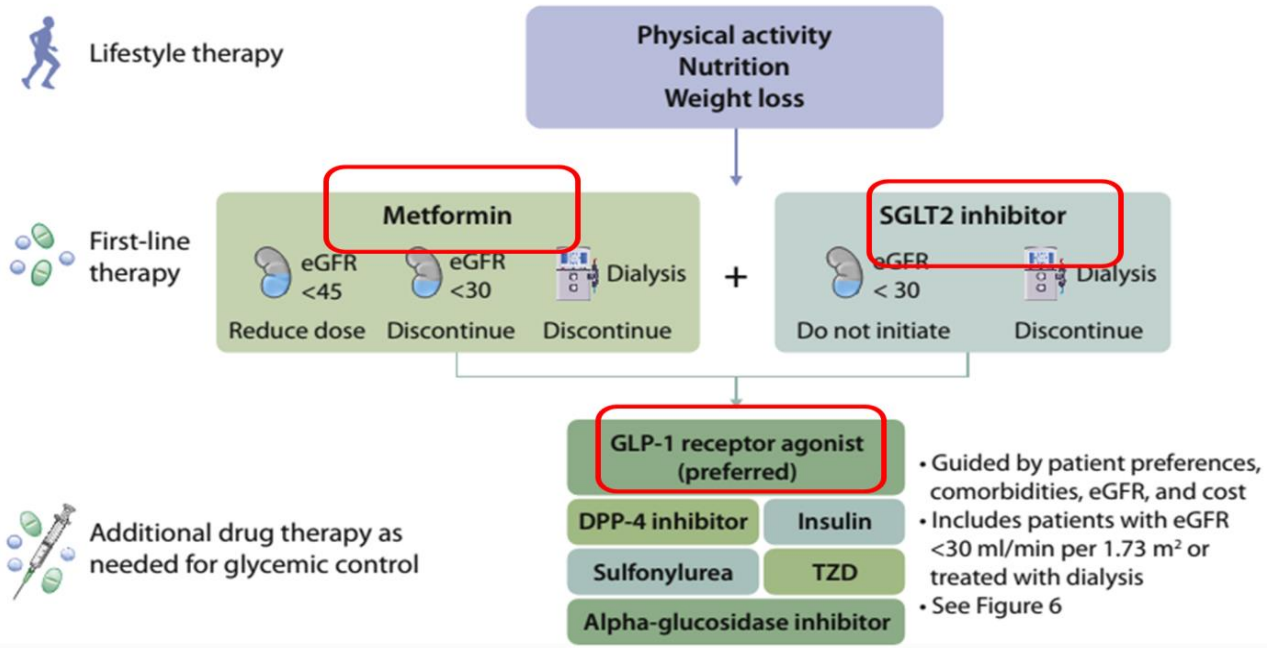
Chapter 3: Lifestyle interventions in patients with diabetes and CKD

• **Practice Point 3.1.1**	Patients with diabetes and CKD should consume an individualized diet high in vegetables, fruits, whole grains, fiber, legumes, plant-based proteins, unsaturated fats, and nuts; and lower in processed meats, refined carbohydrates, and sweetened beverages.
• **Recommendation 3.1.1**	We suggest maintaining a protein intake of 0.8 g protein/kg (weight)/day for those with diabetes and CKD not treated with dialysis (*2C*).
• **Recommendation 3.1.2**	We suggest that sodium intake be <2 g of sodium per day (or <90 mmol of sodium per day, or <5 g of sodium chloride per day) in patients with diabetes and CKD (*2C*).
• **Recommendation 3.2.1**	We recommend that patients with diabetes and CKD be advised to undertake moderate-intensity physical activity for a cumulative duration of at least 150 minutes per week, or to a level compatible with their cardiovascular and physical tolerance (*1D*).

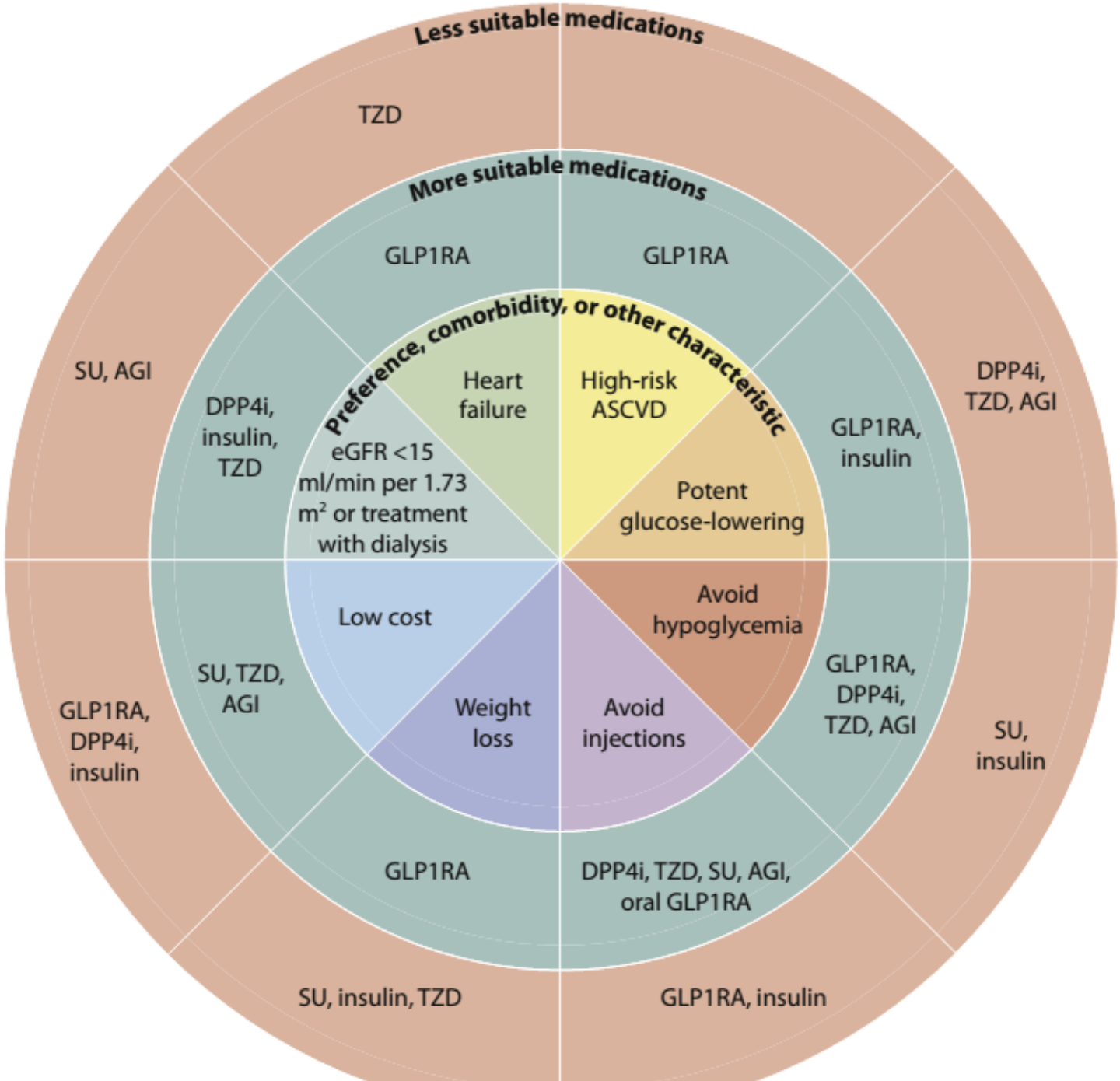
- Dietary prescriptions should be **individualized,** incorporating values, preferences, and resources, and restricting certain foods or nutrients when appropriate (e.g., for treatment of hyperkalemia, when present). Decisions should be based on shared decision-making
- For patients treated with **dialysis**, particularly peritoneal dialysis, an increase in daily dietary **protein intake to 1.0–1.2 g per kg body** weight is advised to offset catabolism and negative nitrogen balance.
- However, evidence review **did not** yield convincing data demonstrating clinical benefits of **weight loss** interventions among people with diabetes and CKD, and interventions targeting caloric intake may cause harm by promoting **malnutrition, particularly in advanced CKD**

Chapter 4: Antihyperglycemic therapies in patients with type 2 diabetes (T2D) and CKD

• **Practice Point 4.1**	Glycemic management for patients with T2D and CKD should include lifestyle therapy, first-line treatment with metformin and a sodium–glucose cotransporter-2 inhibitor (SGLT2i), and additional drug therapy as needed for glycemic control (Figures 4, 5, and 6).
• **Recommendation 4.1.1**	We recommend treating patients with T2D, CKD, and an eGFR ≥30 ml/min per 1.73 m^2 with metformin (*1B*).
• **Recommendation 4.2.1**	We recommend treating patients with T2D, CKD, and an eGFR ≥30 ml/min per 1.73 m^2 with an SGLT2i (*1A*).
• **Recommendation 4.3.1**	In patients with T2D and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i, or who are unable to use those medications, we recommend a long-acting glucagon-like peptide-1 receptor agonist (GLP-1 RA) (*1B*).



			Primary outcome		Kidney outcomes		
Drug	**Trial**	**Kidney-related eligibility criteria**	**Primary outcome**	**Effect on primary outcome**	**Effect on albuminuria or albuminuria-containing composite outcome**	**Effect on GFR loss[a]**	**Adverse effects**
SGLT2 inhibitors							
Empagliflozin	EMPA-REG OUTCOME	eGFR ≥30 ml/min per 1.73 m²	MACE	↓	↓↓	↓↓	Genital mycotic infections, DKA
Canagliflozin	CANVAS trials	eGFR ≥30 ml/min per 1.73 m²	MACE	↓	↓↓	↓↓	Genital mycotic infections, DKA, amputation
	CREDENCE	ACR >300 mg/g [30 mg/mmol] and eGFR 30–90 ml/min per 1.73 m²	Progression of CKD[b]	↓↓	↓↓	↓↓	Genital mycotic infections, DKA
Dapagliflozin	DECLARE-TIMI 58	CrCl ≥60 ml/min	Dual primary outcomes: MACE and the composite of hospitalization for heart failure or CV death[c]	↔/↓	↓	↓↓	Genital mycotic infections, DKA
GLP-1 receptor agonists							
Lixisenatide	ELIXA	eGFR ≥30 ml/min per 1.73 m²	MACE	↔	↓	↔	None notable
Liraglutide	LEADER	eGFR ≥15 ml/min per 1.73 m²	MACE	↓	↓	↔	GI
Semaglutide[d]	SUSTAIN-6	Patients treated with dialysis excluded	MACE	↓	↓↓	NA	GI
	PIONEER 6	eGFR ≥30 ml/min per 1.73 m²	MACE	↔	NA	NA	GI
Exenatide	EXSCEL	eGFR ≥30 ml/min per 1.73 m²	MACE	↔	↔	↔	None notable
Albiglutide	HARMONY	eGFR ≥30 ml/min per 1.73 m²	MACE	↓	↔	NA	Injection site reactions
Dulaglutide	REWIND	eGFR ≥15 ml/min per 1.73 m²	MACE	↓	↓	↓	GI
DPP-4 inhibitors							
Saxagliptin	SAVOR-TIMI 53	eGFR ≥15 ml/min per 1.73 m²	MACE	↔	↓	↔	HF; any hypoglycemic event (minor and major) also more common
Alogliptin	EXAMINE	Patients treated with dialysis excluded	MACE	↔	NA	NA	None notable
Sitagliptin	TECOS	eGFR ≥30 ml/min per 1.73 m²	MACE	↔	NA	NA	None notable
Linagliptin	CARMELINA	eGFR ≥15 ml/min per 1.73 m²	Progression of CKD[b]	↔	↓	↔	None notable


Less suitable medications
More suitable medications
Preference, comorbidity, or other characteristic
TZD
GLP1RA
GLP1RA
SU, AGI
DPP4i, TZD, AGI
DPP4i, insulin, TZD
GLP1RA, insulin
Heart failure
High-risk ASCVD
eGFR <15 ml/min per 1.73 m² or treatment with dialysis
Potent glucose-lowering
Low cost
Avoid hypoglycemia
Weight loss
Avoid injections
SU, TZD, AGI
GLP1RA, DPP4i, TZD, AGI
GLP1RA, DPP4i, insulin
SU, insulin
GLP1RA
DPP4i, TZD, SU, AGI, oral GLP1RA
SU, insulin, TZD
GLP1RA, insulin

Chapter 4: Antihyperglycemic therapies in patients with type 2 diabetes (T2D) and CKD	
• **Practice Point 4.1**	Glycemic management for patients with T2D and CKD should include lifestyle therapy, first-line treatment with metformin and a sodium–glucose cotransporter-2 inhibitor (SGLT2i), and additional drug therapy as needed for glycemic control (Figures 4, 5, and 6).
• **Recommendation 4.1.1**	We recommend treating patients with T2D, CKD, and an eGFR ≥30 ml/min per 1.73 m^2 with metformin (*1B*).
• **Recommendation 4.2.1**	We recommend treating patients with T2D, CKD, and an eGFR ≥30 ml/min per 1.73 m^2 with an SGLT2i (*1A*).
• **Recommendation 4.3.1**	In patients with T2D and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i, or who are unable to use those medications, we recommend a long-acting glucagon-like peptide-1 receptor agonist (GLP-1 RA) (*1B*).

- Metformin dose should be reduced when the eGFR is **less than 45 ml/min per 1.73 m2** (and for some patients with **eGFR 45–59 ml/min per 1.73 m2 who are at high risk of acute kidney injury**); and metformin should be discontinued for patients **with eGFR less than 30ml/min** per 1.73 m2 or kidney failure
- Metformin may cause **vitamin B12 deficiency,** and thusly B12 .Monitoring is advised for patients with long- term use (>4 years)

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- SGLT2:Adverse events included **genital mycotic infections**, **diabetic ketoacidosis,** and in 1 study, a concern for **lower limb amputation**
- SGLT2i cause **modest volume contraction**, **blood pressure reduction**, and **weight loss.**

For patients at risk for hypovolemia (e.g ., due to concomitant diuretic use), providers should consider decreasing dose of a **diuretic**

- The cardiovascular outcome trials included patients with eGFR greater than 15 l/min per 1.73 m2, whereas data with **GLP-1 RA in more advanced CKD are limited**

Chapter 5: Approaches to management of patients with diabetes and CKD

• **Recommendation 5.1.1**	We recommend that a structured self-management educational program be implemented for care of people with diabetes and CKD (Figure 7) (*1C*).
• **Recommendation 5.2.1**	We suggest that policymakers and institutional decision-makers implement team-based, integrated care focused on risk evaluation and patient empowerment to provide comprehensive care in patients with diabetes and CKD (*2B*).

Key objectives are to:

- Improve diabetes-related knowledge, beliefs, and skills
- Improve self-management and self-motivation
- Encourage adoption and maintenance of healthy lifestyles
- Improve vascular risk factors
- Increase engagement with medication, glucose monitoring, and complication screening programs
- Reduce risk to prevent (or better manage) diabetes-related complications
- Improve emotional and mental well-being, treatment satisfaction, and quality of life

Decision Algorithm for Prescribing SGLT2 Inhibitors and GLP-1 Receptor Agonists for Diabetic Kidney Disease

Jiahua Li,[1,2,3] *Oltjon Albajrami*,[2,4] *Min Zhuo*,[1,3,5,6] *Chelsea E. Hawley*,[6,7] *and Julie M. Paik*[1,2,3,6,7]

Abstract

Diabetic kidney disease and its comorbid conditions, including atherosclerotic cardiovascular disease, heart failure, diabetes, and obesity, are interconnected conditions that compound the risk of kidney failure and cardiovascular mortality, and exponentiate health care costs. Sodium glucose cotransporter 2 inhibitor (SGLT2i) and glucagon-like peptide 1 receptor agonist (GLP-1 RA) are novel diabetes medications that prevent cardiovascular events and kidney failure. Clinical trials exploring the cardiovascular and kidney outcomes of SGLT2i and GLP-1 RA have fundamentally shifted the treatment paradigm of diabetes. Clinical guidelines for diabetes management recommend a more holistic approach beyond glycemic control and emphasize heart and kidney protection of SGLT2i and GLP-1 RA. However, the adoption of prescribing SGLT2i and GLP-1 RA for patients with diabetes and high cardiovascular and kidney risk has been slow. In this review, we provide a decision-making tool to help clinicians determine when to consider SGLT2i and GLP-1 RA for heart and kidney protection. First, we discuss a comprehensive risk assessment for patients with diabetic kidney disease. We compare the effectiveness of SGLT2i and GLP-1 RA for different risk categories. Then, we present a decision algorithm using cardiovascular and kidney failure risk stratification and the strength of current evidence for the use of SGLT2i and GLP-1 RA. Lastly, we review the adverse effects of SGLT2i and GLP-1 RA and propose mitigation strategies.

CJASN 15: 1678–1688, 2020. doi: https://doi.org/10.2215/CJN.02690320

Due to the number of contributing authors, the affiliations are listed at the end of this article.

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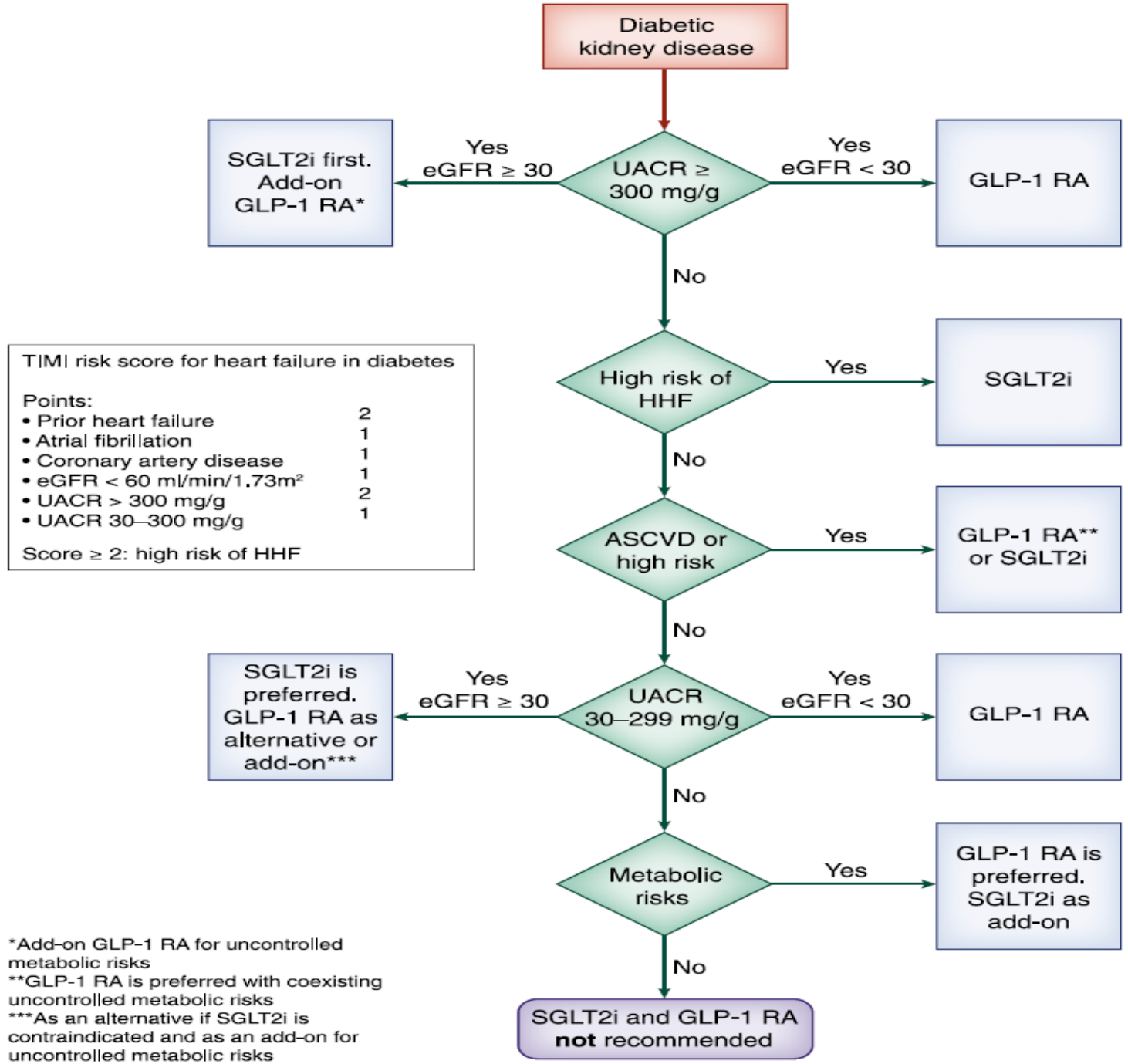

CJASN 15: 1678–1688, November, 2020

eGFR	UACR <30 mg/g	UACR 30–299 mg/g	UACR ≥300 mg/g
>60 ml/min per 1.73 m^2	SGLT2i or GLP-1 RA[a]	SGLT2i is preferred. GLP-1 RA as an alternative if SGLT2i is contraindicated or not tolerated, and as an add-on for uncontrolled metabolic risk[b]	SGLT2i should be initiated. GLP-1 RA as an add-on for uncontrolled metabolic risk[c]
30–60 ml/min per 1.73 m^2	SGLT2i is preferred. GLP-1 RA as an alternative if SGLT2i is contraindicated or not tolerated, and as an add-on for uncontrolled metabolic risk[b]		SGLT2i should be initiated. GLP-1 RA as an add-on for uncontrolled metabolic risk[c]
15–29 ml/min per 1.73 m^2	GLP-1 RA (dulaglutide) is preferred. Initiation of SGLT2i is currently contraindicated[d]		

CJASN 15: 1678–1688, November, 2020

高血壓與慢性腎臟病 GUIDELINE UPDATE

OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY

SUPPLEMENT TO

kidney INTERNATIONAL

Executive summary of the KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease

Check for updates

OPEN

Alfred K. Cheung[1], Tara I. Chang[2], William C. Cushman[3], Susan L. Furth[4,5], Fan Fan Hou[6], Joachim H. Ix[7,8], Gregory A. Knoll[9], Paul Muntner[10], Roberto Pecoits-Filho[11,12], Mark J. Sarnak[13], Sheldon W. Tobe[14,15], Charles R.V. Tomson[16], Lyubov Lytvyn[17,18], Jonathan C. Craig[19,20], David J. Tunnicliffe[20,21], Martin Howell[20,21], Marcello Tonelli[22], Michael Cheung[23], Amy Earley[23] and Johannes F.E. Mann[24]

KIDNEY DISEASE · IMPROVING GLOBAL OUTCOMES

KDIGO

KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease

The original KDIGO Management of Blood Pressure (BP) in Chronic Kidney Disease (CKD) guideline in the CKD population not receiving dialysis was published in 2012. Since then, completion of the Systolic Blood Pressure

Chapter 1: Blood pressure measurement	
• **Recommendation 1.1**	We recommend standardized office BP measurement in preference to routine office BP measurement for the management of high BP in adults (*1B*).
• **Recommendation 1.2**	We suggest that out-of-office BP measurements with ambulatory BP monitoring (ABPM) or home BP monitoring (HBPM) be used to complement standardized office BP readings for the management of high BP *(2B)*.

- Routine office BP refers to measurements obtained without using these preparations and is often called **casual office BP.**
- The BP target cannot be applied if routine BP values are obtained, because large randomized trials that examined target BP, such as SPRINT, employed **standardized BP**
- There is strong evidence that the relationship between routine office BP and standardized office BP is highly variable, for individuals with and without **CKD.**

1 Properly prepare the patient	1 Have the patient relax, sitting in a chair (feet on floor, back supported) for > 5 min 2 The patient should avoid caffeine, exercise, and smoking for at least 30 min before measurement 3 Ensure patient has emptied his/her bladder 4 Neither the patient nor the observer should talk during the rest period or during the measurement 5 Remove all clothing covering the location of cuff placement 6 Measurements made while the patient is sitting or lying on an examining table do not fulfill these criteria
2 Use proper technique for BP measurements	1 Use a BP measurement device that has been validated, and ensure that the device is calibrated periodically 2 Support the patient's arm (e.g., resting on a desk) 3 Position the middle of the cuff on the patient's upper arm at the level of the right atrium (the midpoint of the sternum) 4 Use the correct cuff size such that the bladder encircles 80% of the arm, and note if a larger- or smaller-than-normal cuff size is used 5 Either the stethoscope diaphragm or bell may be used for auscultatory readings
3 Take the proper measurements needed for diagnosis and treatment of elevated BP	1 At the first visit, record BP in both arms. Use the arm that gives the higher reading for subsequent readings 2 Separate repeated measurements by 1–2 min 3 For auscultatory determinations, use a palpated estimate of radial pulse obliteration pressure to estimate SBP. Inflate the cuff 20–30 mm Hg above this level for an auscultatory determination of the BP level 4 For auscultatory readings, deflate the cuff pressure 2 mm Hg per second, and listen for Korotkoff sounds

4 Properly document accurate BP readings	1 Record SBP and DBP. If using the auscultatory technique, record SBP and DBP as onset of the first Korotkoff sound and disappearance of all Korotkoff sounds, respectively, using the nearest even number 2 Note the time of most recent BP medication taken before measurements
5 Average the readings	Use an average of ≥ 2 readings obtained on ≥ 2 occasions to estimate the individual's level of BP
6 Provide BP readings to patient	Provide patients with the SBP/DBP readings verbally and in writing

Chapter 1: Blood pressure measurement

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• **Recommendation 1.2**	We suggest that out-of-office BP measurements with ambulatory BP monitoring (ABPM) or home BP monitoring (HBPM) be used to complement standardized office BP readings for the management of high BP *(2B)*.

- Out-of-office BP measurement: **home BP** , **24 -hour ambulatory BP monitoring(ABPM)** .
- Observational studies show a stronger association of **out - of - office BP measurement** than **office B P measurements** with **cardiovascular** and **kidney** out comes in both the general population and CKD population.

Chapter 2: Lifestyle interventions for lowering blood pressure in patients with CKD not receiving dialysis	
• **Recommendation 2.1.1**	We suggest targeting a sodium intake <2 g of sodium per day (or <90 mmol of sodium per day, or <5 g of sodium chloride per day) in patients with high BP and CKD *(2C)*.
• **Recommendation 2.2.1**	We suggest that patients with high BP and CKD be advised to undertake moderate-intensity physical activity for a cumulative duration of at least 150 minutes per week, or to a level compatible with their cardiovascular and physical tolerance *(2C)*.

- **Dietary Approaches to Stop Hypertension (DASH)** diet, and salt substitutes that are often used in reduced-salt diets. DASH diets employed to lower BP are rich in **potassium,** and salt substitutes usually contain potassium as the primary cation. These approaches may predispose some patients with **CKD** to hyperkalemia.

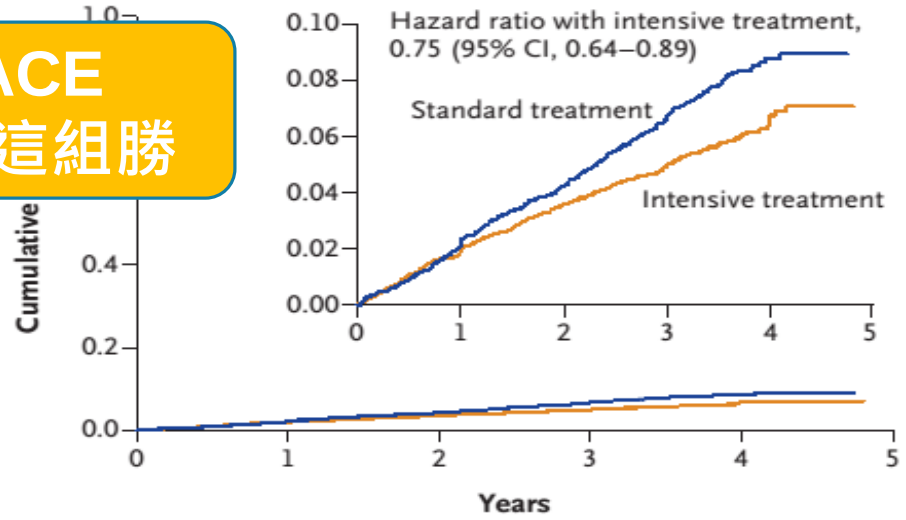
Chapter 3: Blood pressure management in patients with CKD, with or without diabetes, not receiving dialysis

• **Recommendation 3.1.1**	We suggest that adults with high BP and CKD be treated with a target systolic blood pressure (SBP) of <120 mm Hg, when tolerated, using standardized office BP measurement *(2B)*.
• **Recommendation 3.2.1**	We recommend starting renin-angiotensin-system inhibitors (RASi) (angiotensin-converting enzyme inhibitor [ACEi] or angiotensin II receptor blocker [ARB]) for people with high BP, CKD, and severely increased albuminuria (G1–G4, A3) without diabetes *(1B)*.
• **Recommendation 3.2.2**	We suggest starting RASi (ACEi or ARB) for people with high BP, CKD, and moderately increased albuminuria (G1–G4, A2) without diabetes (*2C*).
• **Recommendation 3.2.3**	We recommend starting RASi (ACEi or ARB) for people with high BP, CKD, and moderately-to-severely increased albuminuria (G1–G4, A2 and A3) with diabetes (*1B*).
• **Recommendation 3.3.1**	We recommend avoiding any combination of ACEi, ARB, and direct renin inhibitor (DRI) therapy in patients with CKD, with or without diabetes *(1B)*.

- The recommendation is weak by **GRADE standards (2B)** because it is based on a single, albeit high-quality, randomized trial (**SPRINT**) with a predefined CKD. subgroup showing **cardiovascular** and survival benefits in the study cohort randomized to a SBP goal of <120 mm Hg versus <140 mm Hg.→ Importantly, this recommendation assumes that standardized office BP measurement

MACE <120這組勝

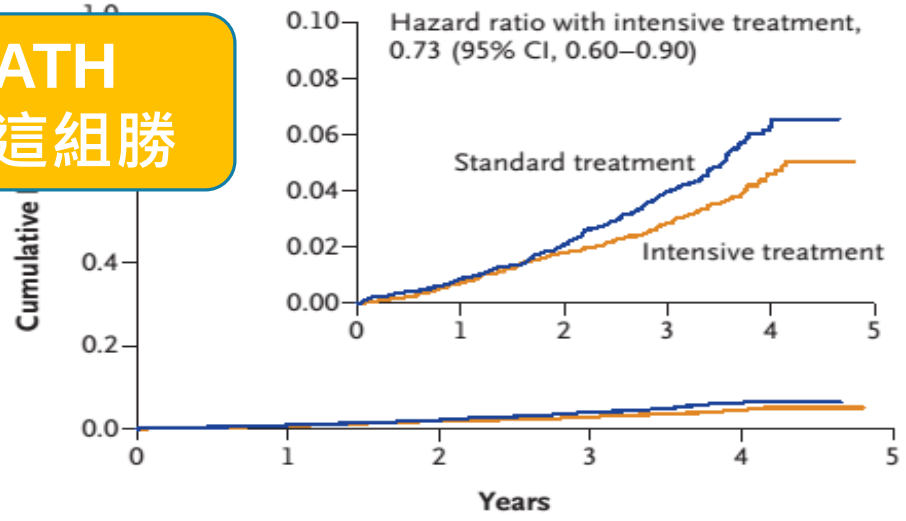
A Primary Outcome



No. at Risk					
Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

DEATH <120這組勝

B Death from Any Cause



No. at Risk					
Standard treatment	4683	4528	4383	2998	789
Intensive treatment	4678	4516	4390	3016	807

The NEW ENGLAND JOURNAL of MEDICINE

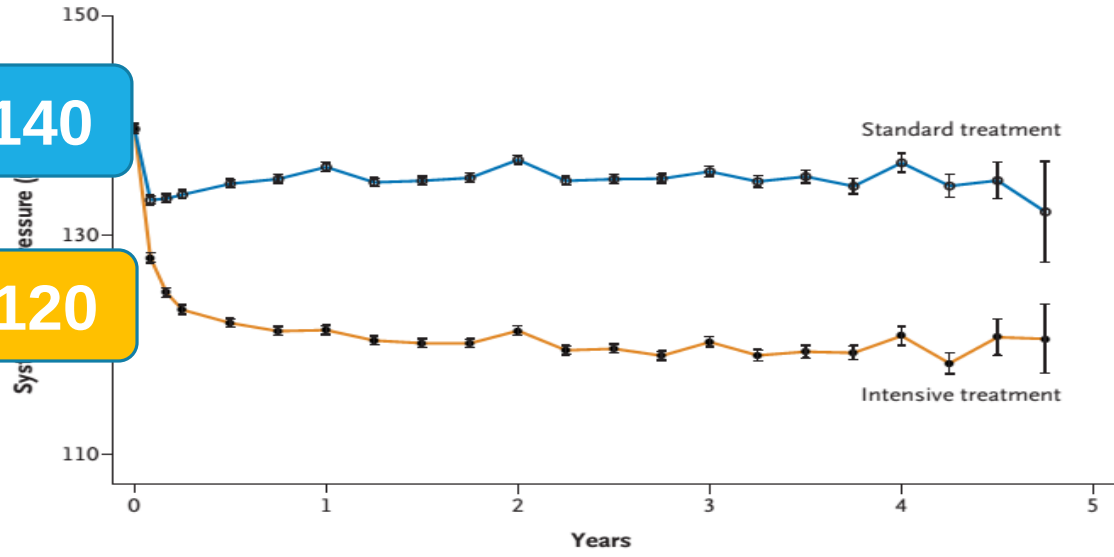
ESTABLISHED IN 1812 NOVEMBER 26, 2015 VOL. 373 NO. 22

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

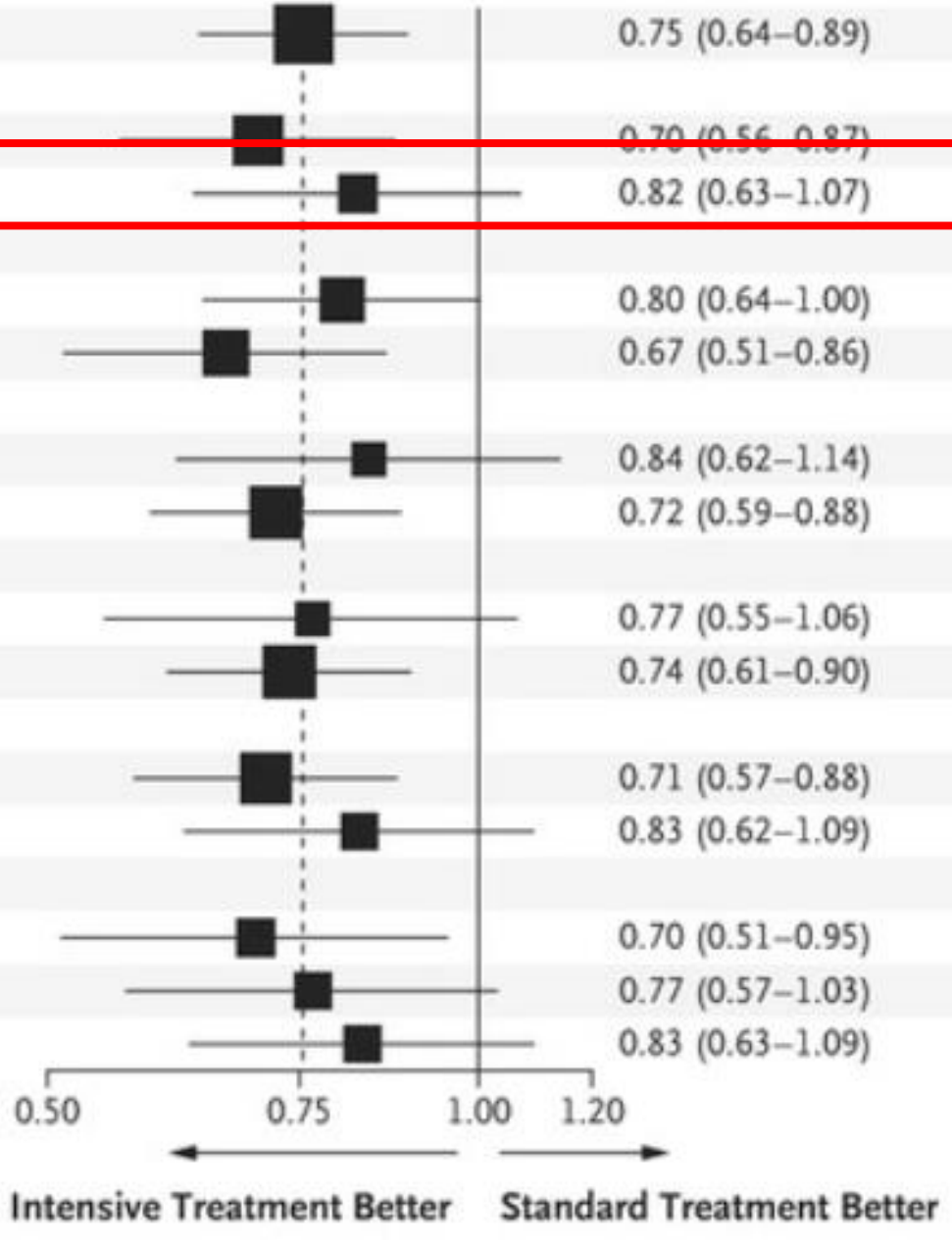
<140

<120



No. with Data										
Standard treatment	4683	4345	4222	4092	3997	3904	3115	1974	1000	274
Intensive treatment	4678	4375	4231	4091	4029	3920	3204	2035	1048	286
Mean No. of Medications										
Standard treatment	1.9	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9
Intensive treatment	2.3	2.7	2.8	2.8	2.8	2.8	2.8	2.8	2.8	3.0

Subgroup	Intensive Treatment	Standard Treatment	Hazard Ratio (95% CI)	P Value for Interaction
	no. of patients with primary outcome/total no. (%)			
Overall	243/4678 (5.2)	319/4683 (6.8)	0.75 (0.64–0.89)	
Previous CKD				0.36
No	135/3348 (4.0)	193/3367 (5.7)	0.70 (0.56–0.87)	
Yes	108/1330 (8.1)	126/1316 (9.6)	0.82 (0.63–1.07)	
Age				0.32
<75 yr	142/3361 (4.2)	175/3364 (5.2)	0.80 (0.64–1.00)	
≥75 yr	101/1317 (7.7)	144/1319 (10.9)	0.67 (0.51–0.86)	
Sex				0.45
Female	77/1684 (4.6)	89/1648 (5.4)	0.84 (0.62–1.14)	
Male	166/2994 (5.5)	230/3035 (7.6)	0.72 (0.59–0.88)	
Race				0.83
Black	62/1454 (4.3)	85/1493 (5.7)	0.77 (0.55–1.06)	
Nonblack	181/3224 (5.6)	234/3190 (7.3)	0.74 (0.61–0.90)	
Previous cardiovascular disease				0.39
No	149/3738 (4.0)	208/3746 (5.6)	0.71 (0.57–0.88)	
Yes	94/940 (10.0)	111/937 (11.8)	0.83 (0.62–1.09)	
Systolic blood pressure				0.77
≤132 mm Hg	71/1583 (4.5)	98/1553 (6.3)	0.70 (0.51–0.95)	
>132 to <145 mm Hg	77/1489 (5.2)	106/1549 (6.8)	0.77 (0.57–1.03)	
≥145 mm Hg	95/1606 (5.9)	115/1581 (7.3)	0.83 (0.63–1.09)	



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Albuminuria category	Diabetes	No diabetes
A1	PP (not graded)	PP (not graded)
A2	1B	2C
A3	1B	1B

UACR>30
必用
ACEi/ARB

Figure 5 | Strength of recommendation for use of RASi in people with high BP and CKD according to diabetes and albuminuric status. 1B, strong recommendation based on moderate quality evidence; 2C, weak recommendation based on low quality evidence; ACR, albumin-creatinine ratio; A1, ACR <30 mg/g (<3 mg/mmol); A2, ACR 30–300 mg/g (3–30 mg/mmol); A3, ACR >300 mg/g (>30 mg/mmol); BP, blood pressure; CKD, chronic kidney disease; PP, practice point; RASi, renin-angiotensin system inhibitors.

Chapter 4: Blood pressure management in kidney transplant recipients (CKD G1T–G5T)

• **Practice Point 4.1**	Treat adult kidney transplant recipients with high BP to a target BP of <130 mm Hg systolic and <80 mm Hg diastolic using standardized office BP measurement (see Recommendation 1.1).
• **Recommendation 4.1**	We recommend that a dihydropyridine calcium channel blocker (CCB) or an ARB be used as the first-line antihypertensive agent in adult kidney transplant recipients (*1C*).

Chapter 5: Blood pressure management in children with CKD

• **Recommendation 5.1**	We suggest that in children with CKD, 24-hour mean arterial pressure (MAP) by ABPM should be lowered to ≤50th percentile for age, sex, and height *(2C)*.

Any Questions


感謝聆聽
好像下課了耶