Update management of diabetes mellitus

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Update guideline

- Standard of Care in Diabetes: ADA 2023
- A consensus report by ADA and EASD, Sep 2022
- Thai guideline 2020

Outlines

- Screening and diagnosis
- Lifestyle modification
- Pharmacological management
- Summary

Screening

1. Age ≥ 35 years
2. Hx of GDM (testing at least every 3 years)
3. Hx of prediabetes (A1C >5.7%,IGT,IFG) (testing at least yearly)
4. Overweight or obesity (BMI ≥23 kg/m2) with one or more risk factor*

Diabetes Care Volume 46, Supplement 1, January 2023

Screening

Risk factor*

- First degree relative with diabetes
- History of CVD
- Hypertension
- HDL < 35 mg/dL and/or triglyceride level >250 mg/dL
- Hx PCOS
- Physical inactivity
- Clinical of insulin resistance eg. acanthosis nigrican

Diabetes Care Volume 46, Supplement 1, January 2023

Diagnosis

- FPG ≥ 126 mg/dL . Fasting is defined as no caloric intake for at least 8 h. * or
- 2-h PG ≥ 200 mg/dL during 75 gm-OGTT.*or
- A1C ≥ 6.5% (A1C method that is NGSP certified and standardized to the DCCT assay.)* or
- Random plasma glucose ≥ 200 mg/dL + classic symptoms or hyperglycemia crisis

* Diagnosis requires 2 abnormal test results from the same sample or in 2 separate test samples

Diabetes Care Volume 46, Supplement 1, January 2023

Assessment and treatment plan

Assess risk of diabetes complication	• ASCVD and heart failure history • ASCVD risk factors and 10-yr ASCVD risk assenssment • Staging of CKD • Hypoglycemia risk • Retinopathy and neuropathy
Goal setting	• Set A1C target • Blood pressure target • Diabetes self-management goals
Treatment plan	• Lifestyle management • Pharmacological management (glucose lowering) • Pharmacological management (CVD risk factors and renal)

ASCVD : atherosclerotic cardiovascular disease

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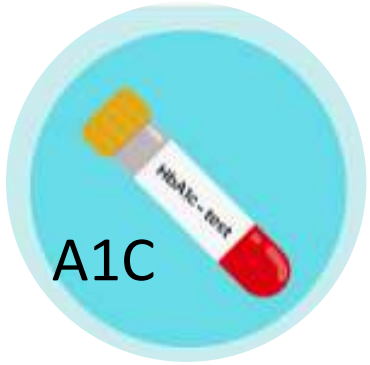

ADA : A1C < 7%
Premeal CPG 80-130 mg/dL
Peak post prandial < 180 mg/dL

KDIGO: target of<6.5% to <8.0% (individulized A1C target)

ADA:

- BP< 130/80 mmHg
- BP< 140/90 mmHg if older adult and multiple comorbidities
- **KDIGO2021**:SBP<120 mmHg

ACEI or ARB : 1 st line treatment

Thai guideline 2017: taget LDL
LDL <100 mg/dL for 1° prevention
LDL < 70 mg/dL for 2° prevention

ADA
Moderate potency statin for 1° prevention
High potency statin for 2 ° prevention

Kidney Int.2022Sep27:S0085-2538(22)00634-2.
Diabetes care 2022;45(suppl.1):S1895-S207
Thai guideline2017

Treatment goals for glycemia and blood pressure in older adults with diabetes

Patient character/ health status	A1C goal	Fasting glucose mg/dL	Bedtime glucose mg/dL	Blood pressure mmHg
Healthy	< 7-7.5 %	80-130	80-180	<130/80
Complex/ intermediate*	< 8 %	90-150	100-180	<130/80
Very complex/ poor health**	A1C base on avoid hypoglycemia and symptomatic hyperglycemia	100-180	110-200	<140/80

*Multiple coexisting chroninc illness or mild to moderate cognitive impairment or ≥ 2 instrument activity daily living impairments

**End stage chronic illness or moderate to severe cognitive impairment or ≥ 2 activity daily living impairment

Diabetes Care Volume 46, Supplement 1, January 2023.

Treatment plan

- Lifestyle management
- Pharmacological management (glucose lowering)
- Pharmacological management (CVD risk factors and renal)

Diabetes Care Volume 46, Supplement 1, January 2023.

Lifestyle modification

	Adiposity-related diabetes	Diabetes with cardiovascular disease	Isolated hyperglycaemia
Primary pathophysiological driver	Insulin resistance	Atherosclerosis, inflammation	β-cell dysfunction
Approximate prevalence*	40–70%	20–40%	10–20%
Primary morbidity	Obesity	Cardiovascular disease	Hyperglycaemia
Foundational diabetes treatment target	Weight-centric	Cardiocentric	Glucocentric
Target	>15% bodyweight loss	Use of proven cardio-protective agents	HbA_{1c} <7%
Examples of foundational diabetes treatment	Anti-obesity agents or intervention, GLP1R agonist, SGLT2 inhibitor, metformin	SGLT2 inhibitor, GLP1R agonist (thiazolidinediones)	Sulfonylurea, insulin, GLP1R agonist
Secondary treatment targets	Glucose, blood pressure, lipids	Weight, glucose, blood pressure, lipids, coagulation	NA

HbA_{1c}=glycated haemoglobin. NA=not applicable. *Prevalence varies by definition and population.

***Table 3*: Proposed primary and secondary treatment goals for type 2 diabetes by prevailing disease phenotype**

Weight-centric approach

Cardiocentric approach

Glucocentric approach

Lancet, The, 2022-01-22, Volume 399, Issue 10322, Pages 394-405

Treatment effectivess of weight loss

% weight loss	Procedure
5-7%	• Self monitor diet • Intensive lifestyle program
8-15%	• Meal replacement • Very low calories diet
9-15%	• Weight-loss medications • GI procedure
20-30 %	• SLEEVE gastrectomy • RYGB

Lifestyle modification

- ≥ 5% weight loss are recommended for most people with type 2 diabetes and overweight or obesity.
- Method of 3-5% weight loss:

  500–750 kcal/day energy deficit or

  colorie restriction : 1,200 –1,500 kcal/day for women

  : 1,500 –1,800 kcal/day for men

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History taking

- Medication
- Hypoglycemia
- Meal: frequency, CHO count
- Simple CHO : sweetener drinks, bakery, Thai dessert

คาร์โบไฮเดรต	18 กรัม	1 ส่วน = 1 คาร์บ
โปรตีน	2 กรัม	
พลังงาน	80 กิโลแคลอรี	

ขนมจีน 1 จับ หรือ $^1/_2$ ถ้วยตวง

ข้าวเหนียว $^1/_2$ ทัพพี หรือ $^1/_4$ ถ้วยตวง

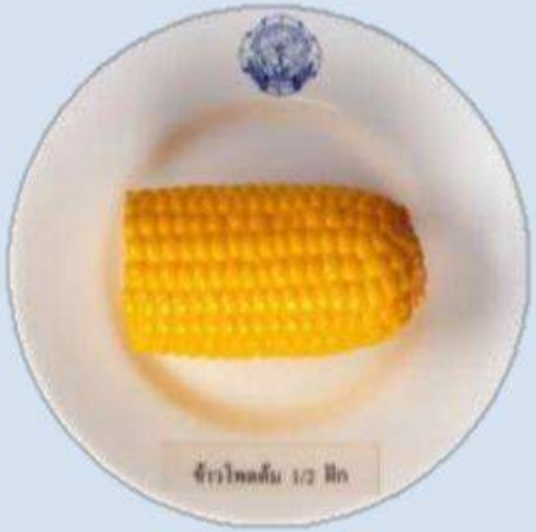
ข้าวขาว 1 ทัพพี หรือ $^1/_3$ ถ้วยตวง

หมวดข้าวแป้งและผลิตภัณฑ์

คาร์โบไฮเดรต	18 กรัม
โปรตีน	2 กรัม
พลังงาน	80 กิโลแคลอรี

1 ส่วน = 1 คาร์บ

ขนมปัง
1 แผ่น



ข้าวโพดต้ม
½ ฝัก

ขนมปังแครกเกอร์
4 – 6 แผ่น

หมวดผัก ก.
(ผักที่ไม่มีแป้ง)

ไม่ดิดพลังงาน อุดมด้วยแร่ธาตุ วิตามิน และใยอาหาร

ผักกาดขาว

แตงกวา

ตำลึง

ผักบุ้งจีน

กะหล่ำปลี

ผักกวางตุ้ง

หมวดผัก ข.
(ผักที่มีแป้ง)

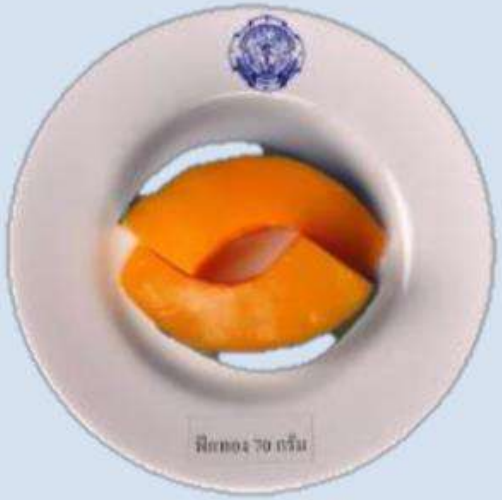
คาร์โบไฮเดรต	5 กรัม
โปรตีน	2 กรัม
พลังงาน	28 กิโลแคลอรี

1 ส่วน = 0.3 คาร์บ

แครอท

ผักคะน้า

บร็อคเคอรี่



ฟักทอง

ผลไม้ วันละ 3-4 ส่วน

Plate model


- มื้ออาหารหลักของฉัน -
นม 1 แก้ว/วัน
ผัก
2 ส่วน/มื้อ
เนื้อสัตว์
1 ส่วน/มื้อ
ผลไม้ 1 ส่วน
ข้าว / แป้ง
1 ส่วน/มื้อ
กินให้ถูกส่วนใน 1 มื้อ
2 : 1 : 1
(ผัก) (ข้าว/แป้ง) (เนื้อสัตว์)

Case scenario

- Goal of treatment
- Diabetes management

Case 1: 60-year-old woman

Underlying diseases: T2DM for 2 years

Physical examination

- V/S: BP 140/90 mmHg, HR 80 bpm, BMI 25 kg/m2
- Acanthosis nigrican at neck
- RS and CVS: unremarkable
- Ext: no pitting edema

Case1 : 60-year-old woman: T2DM for 2 years

Current medication

Metformin2,000mg/day

Physical examination

- V/S: BP120/80 mmHg
- BMI 30 kg/m2

Laboratory

HbA1c=8.5%, FPG=180mg%, LDL=80mg/dL

Cr=0.8mg/dL

Urine microalbumin=20mg/gm.cr

Management ?

Update on Thai DM CPG August 2563

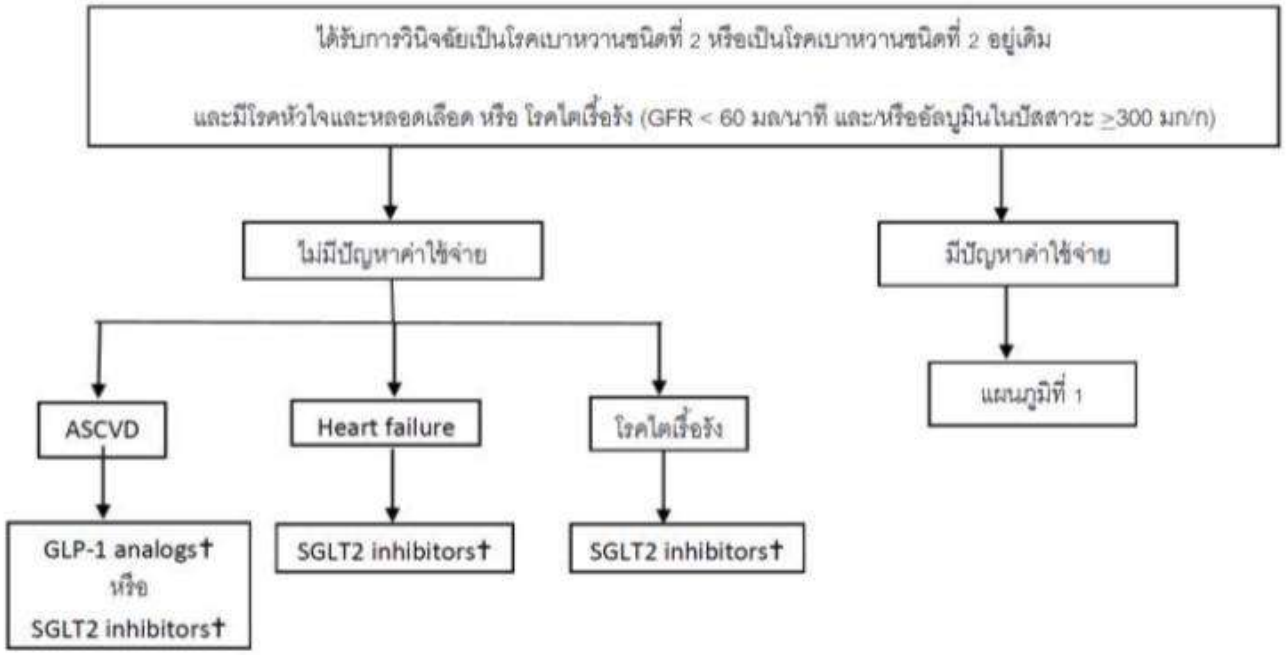
2. การเริ่มต้นให้การรักษาขึ้นอยู่กับ

2.1 ระดับน้ำตาลในเลือด และ A_{1c} (ถ้ามีผลการตรวจ)

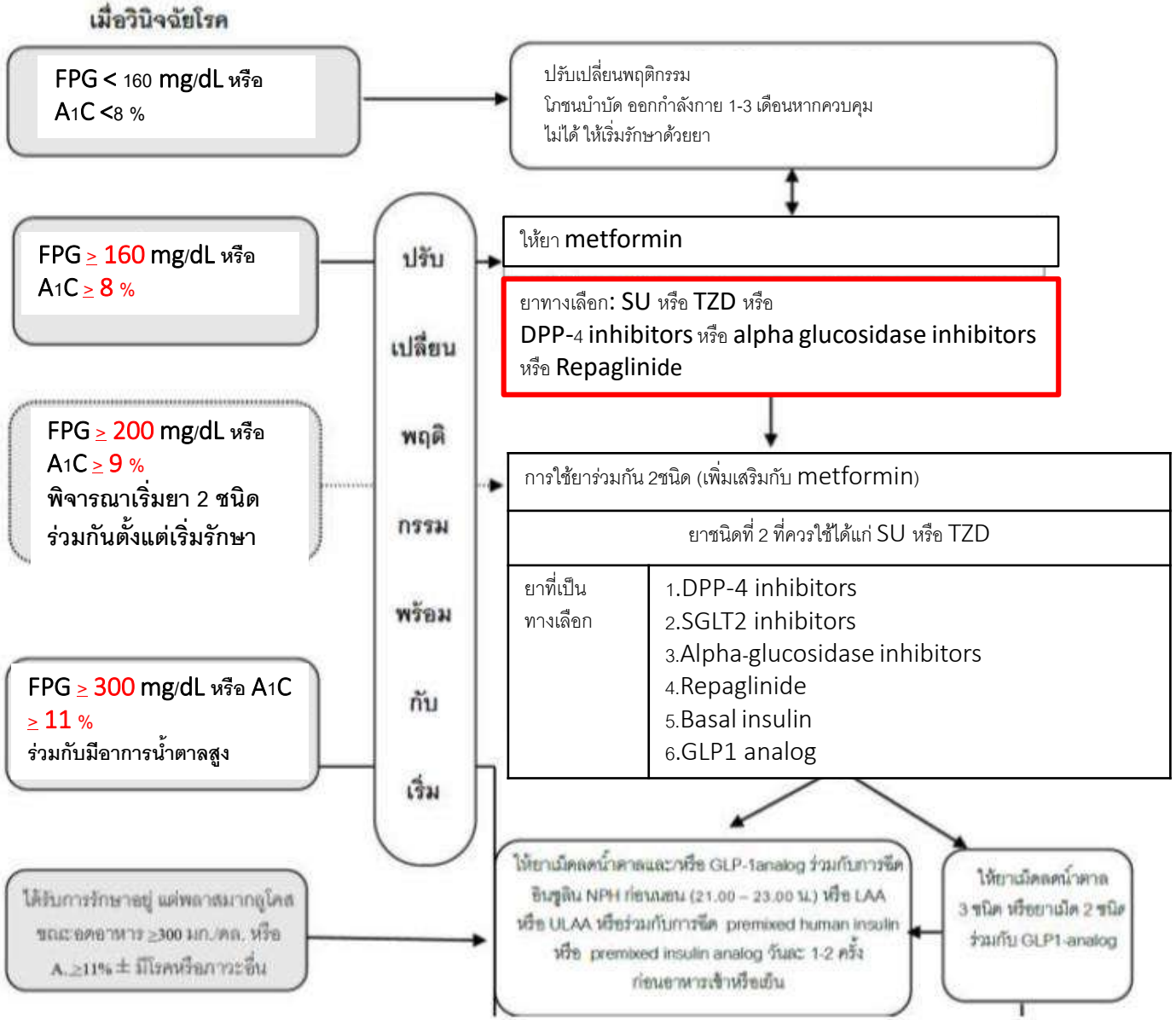
2.2 อาการหรือความรุนแรงของโรค (อาการแสดงของโรคเบาหวานและโรคแทรกซ้อน)

2.3 สภาพร่างกายของผู้ป่วย ได้แก่ โรคอ้วน โรคอื่น ๆ ที่อาจมีร่วมด้วย การทำงานของตับและไต

2.4 โรคร่วมของผู้ป่วย ได้แก่ โรคหัวใจและหลอดเลือด และ/หรือ โรคไตเรื้อรัง (GFR <60 มล/นาที และ/หรืออัลบูมินในปัสสาวะ ≥300 มก/ก)



Update on Thai DM CPG August 2563: Cost concern



Case 1: 60-year-old woman: T2DM for 2 years

Current medication

Metformin2,000 mg/day

Physical examination
- V/S: BP 140/90 mmHg
- BMI 30 kg/m^2

Laboratory

HbA1c 8.5%, FPG 180 mg%, LDL 80 mg/dL
Cr=0.8, Urine microalbumin 20mg/gm.cr

Add glipizide or pioglitazone

Case 2: 60-year-old woman

Underlying diseases: T2DM for 20 years, hypertension, DLD

Physical examination

- V/S: BP 140/90 mmHg, HR 80 bpm, BMI 30 kg/m2
- Acanthosis nigrican at neck
- RS and CVS: unremarkable
- Ext: pitting edema1+

Case 2: 60-year-old woman

Underlying disease
T2DM for 20 years, hypertension, DLD

Physical examination
- V/S: BP140/90 mmHg
- BMI 30 kg/m2

Laboratory

HbA1c 8.5%, FPG 180 mg%, LDL 120 mg/dL

Cr=1.8, eGFR=40 ml/min/1.73m3 (persistent)

Urine microalbumin 2,000 mg/gm.cr

Current medication

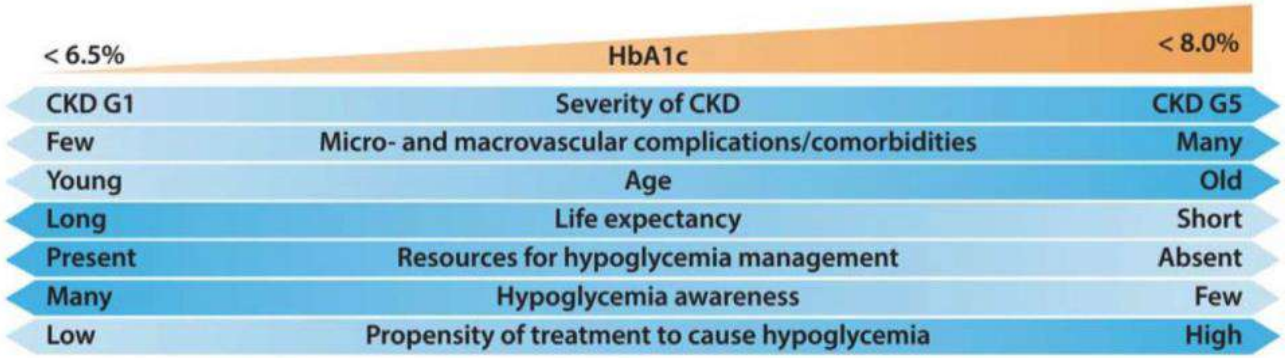
- Metformin 2,000 mg/day
- Glipizide 10 mg/day
- Pioglitazone 30 mg/day
- Sitagliptin 100 mg/day
- Amlodipine 10 mg/day
- Simvastatin 10 mg/day

F 60 yr
:T2DM for20 years, hypertension, DLD

Physical examination
- V/S: BP140/90 mmHg
- BMI 30 kg/m2

Laboratory

HbA1C 8.5% , FPG 180 mg%,
LDL 120 mg/dL
Cr=1.8, eGFR 40 ml/min/1.73m3
Urine microalbumin 2,000 mg/gm.cr



ADA : target of HbA1c <7%

KDIGO : target of <6.5% to<8.0%
(individualized HbA1c target)

Opinion: target of HbA1c 7-8 %

F 60 **yr**
:T2DM for 20 years, hypertension, DLD

Physical examination
- V/S: BP140/90 mmHg
- BMI 30 kg/m2

Laboratory
LDL 120 mg/dL , cholesterol 250 mg/dl,
HDL 40 mg/dl
Cr=1.8, eGFR=40 ml/min/1.73m3
Urine microalbumin 2,000 mg/gm.cr

ACEI or ARB : 1 st line treatment

ADA:
- BP < 140/90 mmHg
  if 10-yr ASCVD risk <15%
- BP <130/80 mmHg
  if 10-yr ASCVD risk >15%

KDIGO 2021: SBP<120 mmHg

Opinion <130/80 mmHg (Thai guideline2017)

Kidney Int. 2022 Sep 27:S0085-2538(22)00634-2.

F 60 yr
:T2DM for 20 years, hypertension, DLD

Physical examination
- V/S: BP140/90 mmHg
- BMI 30 kg/m2

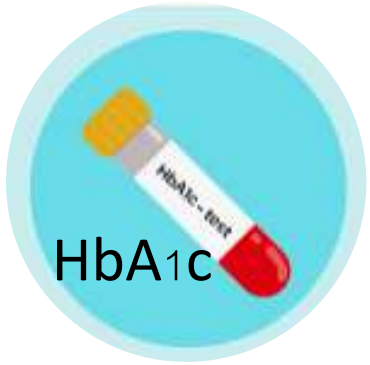
Laboratory
LDL 120 mg/dL , cholesterol 250 mg/dl,
HDL 40 mg/dl
Cr=1.8, eGFR=40 ml/min/1.73m3
Urine microalbumin 2,000 mg/gm.cr

Target : LDL < 100 mg/dl

- Primary prevention: moderate intensity statin
- Secondary prevention: high intensity statin

	High Intensity	Moderate Intensity	Low Intensity
LDL-C lowering†	≥50%	30%–49%	<30%
Statins	**Atorvastatin (40 mg‡) 80 mg** **Rosuvastatin 20 mg (40 mg)**	**Atorvastatin 10 mg** (20 mg) **Rosuvastatin** (5 mg) **10 mg** **Simvastatin 20–40 mg§**	Simvastatin 10 mg
	…	**Pravastatin 40 mg** (80 mg) **Lovastatin 40 mg** (80 mg) Fluvastatin XL 80 mg **Fluvastatin 40 mg BID** Pitavastatin 1–4 mg	**Pravastatin 10–20 mg** **Lovastatin 20 mg** Fluvastatin 20–40 mg

Kidney Int.2022Sep27:S0085-2538(22)00634-2.



ADA : target of HbA1c <7%

KDIGO : target of <6.5% to<8.0
(individualized HbA1c target)

ADA:

- BP < 140/90 mmHg
  if10-yr ASCVD risk< 15%
- BP <130/80 mmHg
  if 10-yr ASCVD risk>15%

KDIGO 2021: SBP<120 mmHg

ACEI or ARB : 1 st line treatment

Thai guideline2017: Target LDL
LDL < 100 mg/dl for 1° prevenntion
LDL < 70 mg/dl for 2° prevention

ADA
1° prevention : moderate potency statin
2° prevention : high potency statin

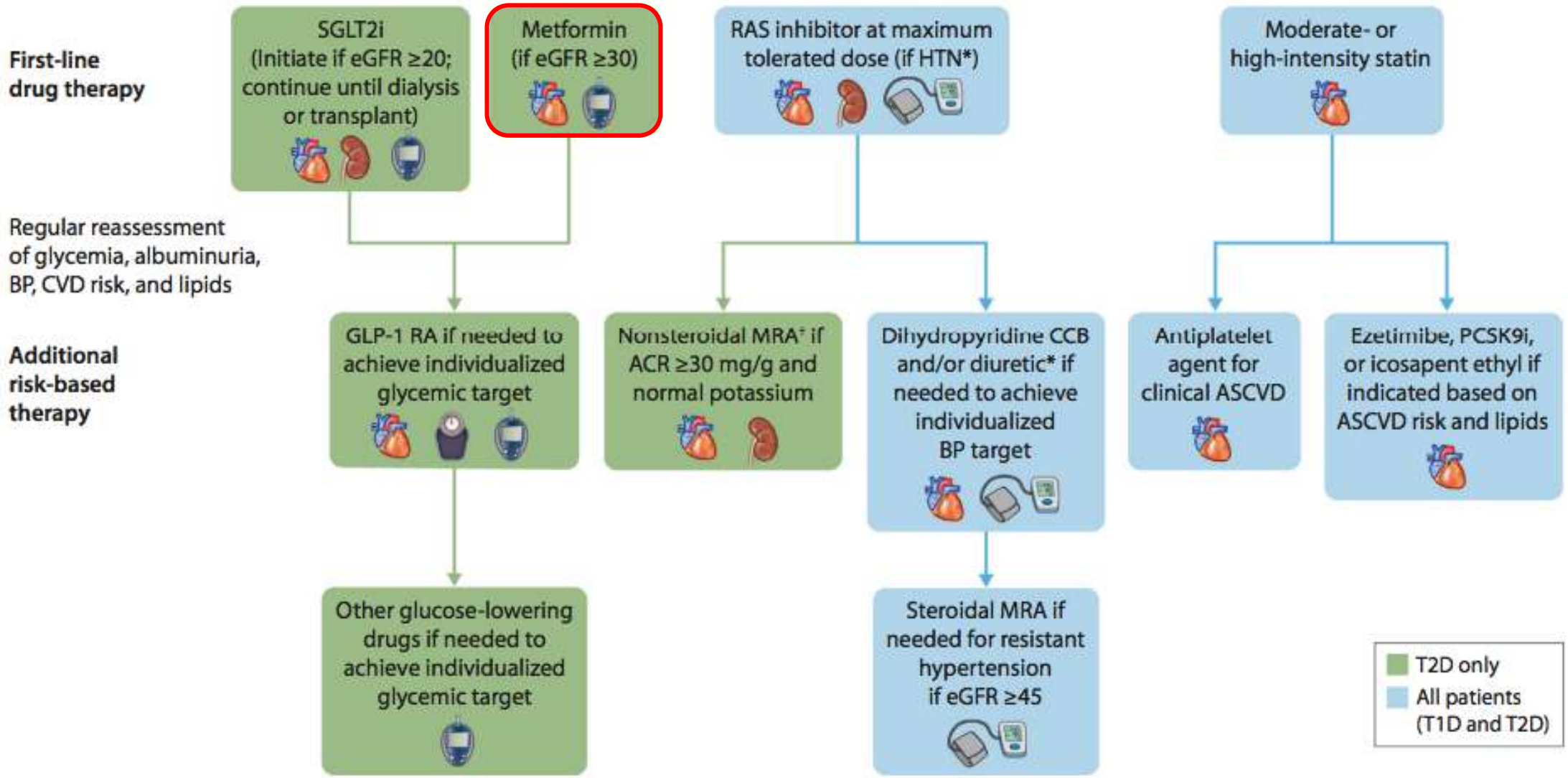
Kidney Int.2022Sep27:S0085-2538(22)00634-2.
Thai guideline2017

Diabetes and CKD management

	ADA 2022	KDIGO 2022
Protein	0.8 gm protein/kg/day	
Sodium	<2,300 mg/d	<2,000 mg/d
Physical activity	Moderate intensity (≥150 min/wk) Vigoruous intensity (≥75min/wk)	Moderate intensity (at least 150 min/wk)
Weight	At least 5% weight loss	Advice weight loss in CKD with obese (eGFR≥ 30) Consider GLP-1agonist for promote weight loss
Alcohol	≤ 1drink in women ≤ 2drinks in men	No recommendation on alcohol intake

Kidney Int.2022Sep27:S0085-2538(22)00634-2.

Diabetes and CKD management



Kidney Int2022. Sep 27:S0085-2538(22)00634-2.

Table 2 | Considerations for selecting glucose-lowering agents in patients with T2D and CKD[2,17]

	Progression of CKD	ASCVD	Heart failure	Glucose-lowering efficacy	Hypoglycemia risk	Weight effects	Cost
Metformin	Neutral	Potential benefit	Potential benefit	High	Low	Neutral	Low
SGLT2 inhibitors	Benefit[a]	Benefit[c]	Benefit	Intermediate	Low	Loss	High
GLP-1 receptor agonists	Benefit[b]	Benefit[c]	Potential benefit	High	Low	Loss	High
DPP-4 inhibitors	Neutral	Neutral	Potential risk[c] (saxagliptin)	Intermediate	Low	Neutral	High
Insulin	Neutral	Neutral	Neutral	Highest	High	Gain	High (analogs) Low (human)
Sulfonylureas	Neutral	Neutral	Neutral	High	High	Gain	Low
Thiazolidinediones	Neutral	Potential benefit (pioglitazone)	Increased risk	High	Low	Gain	Low
α-Glucosidase inhibitors	Neutral	Neutral	Neutral	Intermediate	Low	Neutral	Low

Neutral

Potential benefit or intermediate glucose-lowering efficacy

Benefit (organ protection, high efficacy, low hypoglycemia risk, weight loss, or low cost)

Potential risk or high cost to patient

Increased risk for adverse effects

Kidney Int. 2022 Sep 27:S0085-2538(22)00634-2.

Metformin for T_2DM with CKD

- eGFR 45-59 ml/min/1.73m3 : a reduction should be considerd
- eGFR 30-44 ml/min/1.73m3: max dose 1,000 mg/day
- eGFR <30 ml/min/1.73m3 : contraindication

- Sick day protocol: holding metformin doses during acute illness.

Kidney Int. 2022 Sep 27:S0085-2538(22)00634-2.

SGLT2 inhibitors (SGLT2i)

Benefit	Side effect
Decrease A1C 0.5-0.9 % Low risk hypoglycemia Weight loss 2 kg SBP lowering 2.5-5 mmHg DBP lowering 1-2 mmHg Cardiovascular and renal protection	Volume depletion from polyuria Fungal genital infection (F 10%, M 2-3%) DKA (<0.1%)

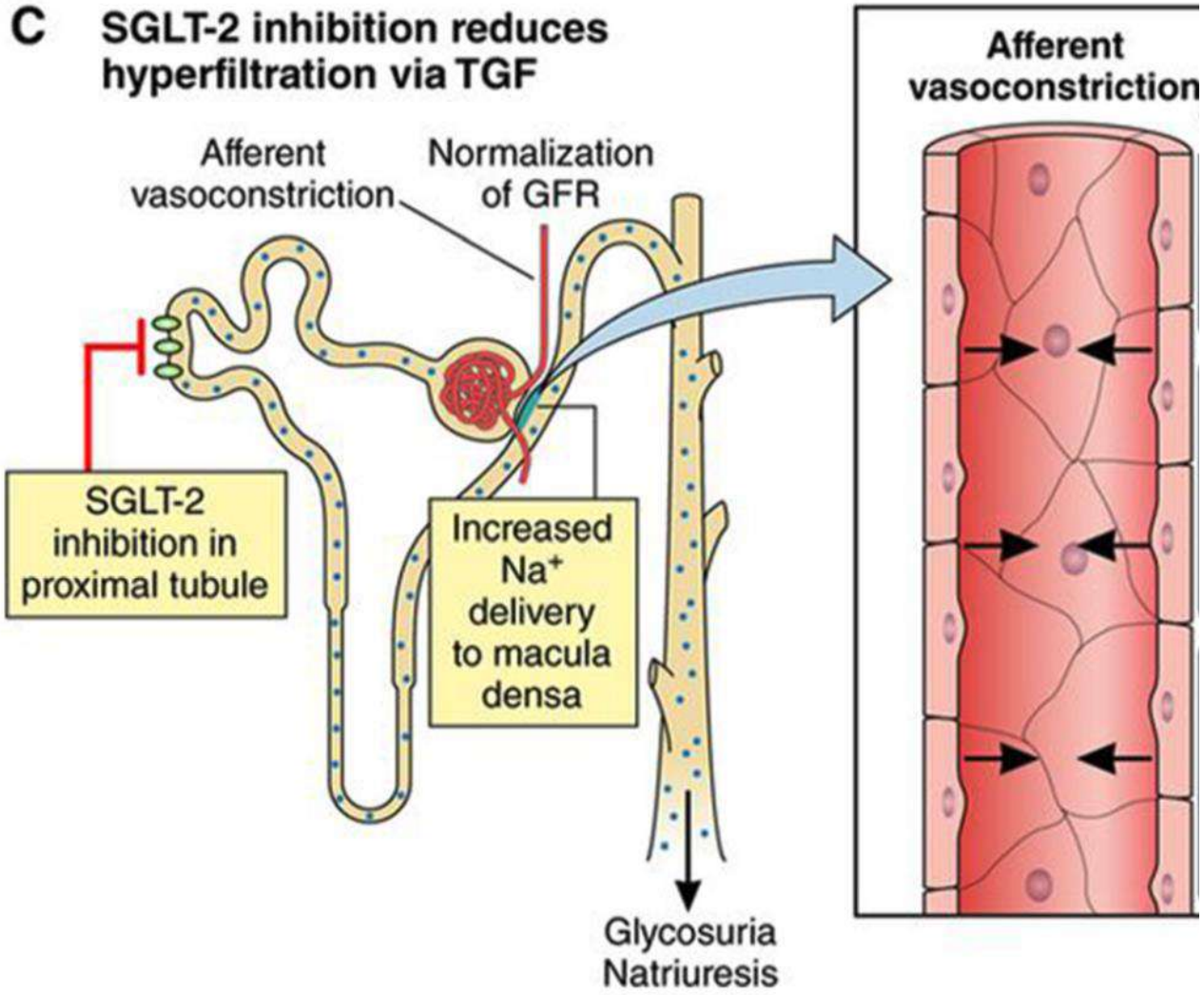
Table 4—Dose adjustments for eGFR <45 mL/min/1.73 m^2 (information presented reflects the package inserts rather than guidance from this consensus report)

	Stage 3b (eGFR 30–44 mL/min/1.73 m^2)	Stage 4 (eGFR 15–29 mL/min/1.73 m^2)	Stage 5 (eGFR <15 mL/min/1.73 m^2)
Canagliflozin	Maximum 100 mg daily	Initiation not recommended; may continue 100 mg daily if tolerated for kidney and CV benefit until dialysis	
Dapagliflozin	10 mg daily†	Initiation not recommended with eGFR <25 mL/min/1.73 m^2; may continue if tolerated for kidney and CV benefit until dialysis	
Empagliflozin	10 mg daily‡	Initiation not recommended with eGFR <20 mL/min/1.73 m^2; may continue if tolerated for kidney and CV benefit until dialysis	

Lancet 2021; 398: 262–76
Kidney Int. 2022 Sep 27:S0085-2538(22)00634-2.

	CREDENCE(N=4401)	DAPA-CKD (N=4094)	EMPA-KIDNEY(N=6609)
Product	Canangliflozin	Dapagliflozin	Empagliflozin
Patient population	CKD+T2DM	CKD+T2DM CKD without T2DM	CKD+T2DM CKD without T2DM
Required eGFR(ml/min/1.73m3) and UACR(mg/d) for enrolment	eGFR ≥30-<90 UACR:>300 - ≤500	eGFR ≥25-<75 UACR:≥200 - ≤5000	eGFR >45-<90 UACR:>200 or eGFR ≥20- <45
Primary endpoint	Composite of ESKD, doubling of serum Cr, renal or CV death	Composite of ≥50% susptanin decline in eGFR, ESKD, renal or CV death	Kidney disease progression (ESKD, susptanin decline in eGFR to < 10 ml/min/1.73m3, renal death or sustain decline of ≥ 40 % in eGFR) or CV death
Outcome	HR 0.7(0.59-0.82), P=0.00001	HR 0.61(0.51-0.72), P < 0.001	HR 0.72(0.64-0.82), P<0.000001

N Engl J Med.2019 Jun13;380(24):2295-2306N Engl J Med. 2020Oct8;383(15):1436-1446.
N Engl J Med.2022Nov 4.doi: 10.1056/NEJMoa2204233.



Tubuloglomerular feedback is mediated by the juxtaglomerular apparatus, which contains the macula densa; a specialised group of cells that detect sodium ion (Na^+) concentration within the tubule, signalling to the glomerulus to regulate the filtration rate and avoid dehydration via a feedback loop.

Improved glomerular haemodynamics

- decreased proximal tubular sodium resorption
- glomerular afferent arteriolar vasoconstriction

(in response to raised adenosine levels, driven by increased membrane Na^+/K^+ ATPase activity)

Outcome:

intraglomerular pressure and reduces the amount of protein filtered through the glomerulus (albuminuria).

Diabetes Ther (2020) 11:2757–2774

GLP-1 receptor agonists

Benefit	Side effect
Decrease A1C 0.9-2.2% Low risk hypoglycemia Weight loss 1.3-8.7 kg BP lowering 2-3 mmHg Cardiovascular and renal protection	GI side effect Nausea25-60% Vomiting 5-15% (risk of cholestasis, pancreatitis)

Liraglutide (once daily)

Dulaglutide(weekly)

Table 4—Dose adjustments for eGFR <45 mL/min/1.73 m^2 (information presented reflects the package inserts rather than guidance from this consensus report)

	Stage 3b (eGFR 30–44 mL/min/1.73 m^2)	Stage 4 (eGFR 15–29 mL/min/1.73 m^2)	Stage 5 (eGFR <15 mL/min/1.73 m^2)
GLP-1 receptor agonists[§]			
Exenatide	Caution initiating or increasing dose; avoid once-weekly formulation	Use not recommended	
Dulaglutide	No dose adjustment required		
Liraglutide	No dose adjustment required		
Lixisenatide	No dose adjustment required		Use not recommended
Semaglutide	No dose adjustment required		

Kidney Int.2022Sep27:S0085-2538(22)00634-2.

Case 1: 60-year-old woman

Dx
1.T2DM with poor control with DN
2.CKD G3b A3
3.HT, DLD, obesity

Underlying disease
T2DM for20 years, hypertension, DLD
- V/S: BP=140/90 mmHg
- BMI 30 kg/m2, pitting edema 1+

Previous lab (last month)

HbA1c 8.5%, FPG 180 mg%, LDL 120 mg/dL

Cr=1.8, eGFR 40 ml/min/1.73m^2 (persistent)

Urine microalbumin2,000 mg/gm.cr

คำแนะนำในการปรับยา

1. ลดขนาด meformin 1,000 mg/day (eGFR 30-44 ml/min/1.73m^2)
2. Glipizide คงขนาดเดิมได้ถ้าไม่มีอาการ hypoglycemia
3. ควร off Pioglizone เนื่องจากเริ่มบวม
4. Sitagliptin ควรลดขนาดยาเป็น 50 mg/day(eGFR 30-44 ml/min/1.73m2)
5. ยาลดความดันควรเพิ่มยากลุ่ม ACEI หรือ ARB (low dose)
   ติดตาม home BP และค่า Cr, K
6. ควรเพิ่มขนาดยา simvastatin 20 mg/day
   หรือปรับเป็น atorvastatin 10-20 mg/day
7. หากต้องเพิ่มยาลดน้ำตาล โดยไม่มีข้อจำกัดเรื่องค่าใช้จ่าย แนะนำ
   SGLT2 inh หรือ
   GLP1 agonist (หากเริ่มยากลุ่มนี้ต้องงดยา DPP4-inh; sitagliptin)

Anti diabetic agent dose adjustment for CKD

Medication	eGFR	Dose
Sulfonylureas(2nd generation)		
Glimepiride	Stage 3b-5	1-8 mg/d
Glipizide	Stage 3b-5	2.5 -20 mg/d
Thiazolidinediones		
Pioglitazone	No dose adjustment	
Alpha-Glucosidase inhibitors		
Acarbose	Stage 3b (30-44)	No dose adjustment
	Stage 4-5	Use not recommend

Kidney Int.2022Sep 27:S0085-2538(22)00634-2.

SGLT2i inhibitors

SGLT2i In Thailand:	(T2DM indication) eGFR (ml/min/1.73m^2)	Dose (mg/day)
Canagliflozin	○ EGFR ≥ 30 with UACR > 300 mg/g ○ eGFR >45	○ 100
	○ eGFR >60	○ 300
Dapagliflozin	○ eGFR ≥ 45	○ 10
Empagliflozin	○ eGFR ≥ 30	○ 10-25
Lusegliflozin	○ eGFR ≥ 60	○ 5

SGLT2i In Thailand:	(Heart failure indication) eGFR (ml/min/1.73m^2)	Dose(mg/day)
Canagliflozin	○ Not approved	
Dapagliflozin	○ eGFR ≥ 25	○ 10
Empagliflozin	○ eGFR ≥ 20	○ 10

SGLT2i In Thailand:	(CKD: Indication) eGFR(ml/min/1.73m^2)	Dose (mg/day)
Canagliflozin	○ EGFR ≥ 30 ○ with UACR > 300 mg/g	○ 100
Dapagliflozin	○ eGFR ≥ 25	○ 10
Empagliflozin	○ eGFR ≥ 30	○ 10

Kidney Int2022. Sep 27:S0085-2538(22)00634-2.

Approved on 24 Feb 2022, https://www.mims.com/thailand/drug/info

DPP4 inhibitors

Medication	eGFR	Dose
Sitagliptin	Stage1-3a (≥45)	100 mg/d
	Stage 3b(30-44)	50 mg/d
	Stage 4-5	25 mg/d
Gemigliptin	No dose adjustment	
Linagliptin	No dose adjustment	
Saxagliptin	Stage1-3a (≥45)	2.5-5 mg/d
	Stage 3b-5	2.5 mg/d

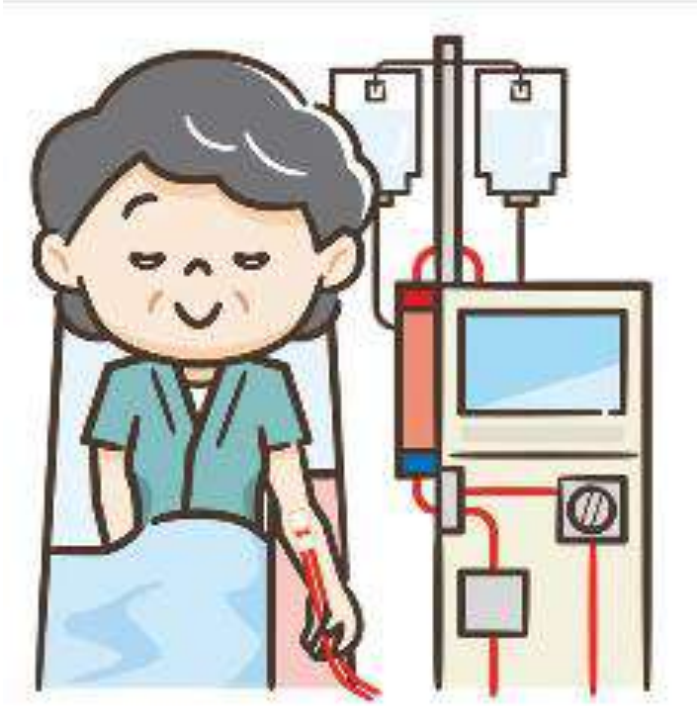
GLP1 agonist

Medication	eGFR	Dose	Thai FDA
Liraglutide	No dose adjustment	0.6-1.8mg sc OD	eGFR >15
Dulaglutide	No dose adjustment	1.5mg sc weekly	eGFR > 15

Kidney Int.2022Sep 27:S0085-2538(22)00634-2.

Case 3:
60-year-old woman

- T2DM for 20 years, hypertension, DLD
- Symptomatic hyperglycemia
- BW 60 kg



Previous Lab

HbA1c=13%, FPG 240 mg%, LDL 80 mg/dL

Cr=1.8 , eGFR 40 ml/min/1.73m2 (persistent)

UACR 2,000 mg/gm

Medication: glipizide 10 mg/day

Add basal insulin[3]

Choice of basal insulin should be based on person-specific considerations, including cost. Refer to **Table 9.4** for insulin cost information. Consider prescription of glucagon for emergent hypoglycemia.

Add basal analog or bedtime NPH insulin[4]

INITIATION: Start 10 units per day OR 0.1–0.2 units/kg per day

TITRATION:

- Set FPG target (see Section 6, "Glycemic Targets")
- Choose evidence-based titration algorithm, e.g., increase 2 units every 3 days to reach FPG target without hypoglycemia
- For hypoglycemia determine cause, if no clear reason lower dose by 10–20%

Assess adequacy of basal insulin dose

Consider clinical signals to evaluate for overbasalization and need to consider adjunctive therapies (e.g., basal dose more than ~0.5 units/kg/day, elevated bedtime–morning and/or post–preprandial differential, hypoglycemia [aware or unaware], high variability)

Neutral Protamine Hagedorn (NPH)

ชนิดยา (ชื่อยา)	เวลาที่เริ่มออกฤทธิ์	เวลาที่มีฤทธิ์สูงสุด	ระยะเวลาการออกฤทธิ์
ฮิวแมนอินซูลินออกฤทธิ์ปานกลาง (Insulin Isophane Suspension, NPH) (Insulatard HM®, Humulin N®, Gensulin N®, Insugen N®, Insuman basal®, Winsulin N®)	2-4 ชั่วโมง	4-8 ชั่วโมง	10-16 ชั่วโมง

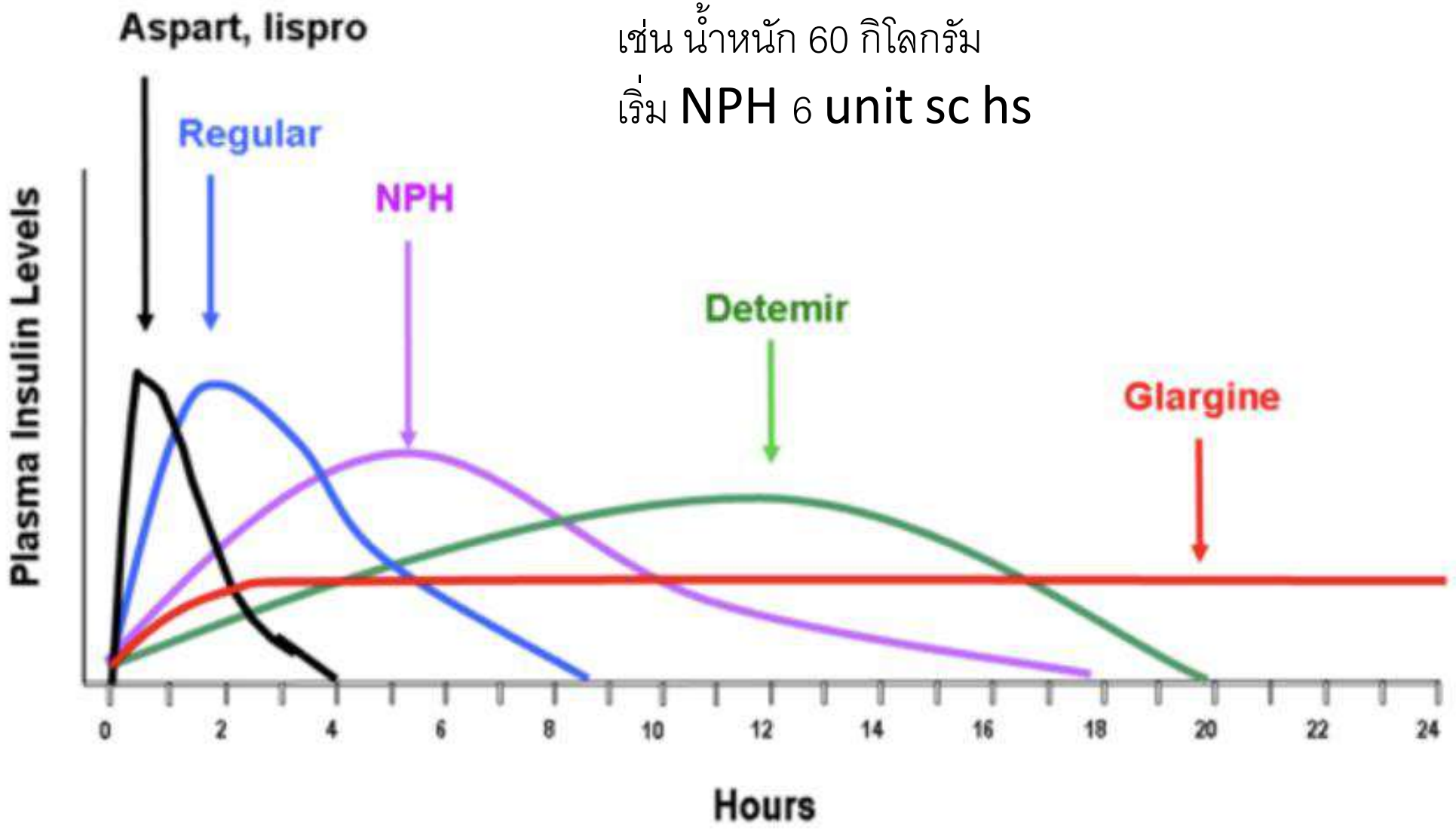
ตารางที่ 2. แสดงยาฉีดอินซูลินชนิดต่างๆ ทีมีในประเทศไทย และเวลาการออกฤทธิ

ชนิดยา (ชื่อยา)	เวลาที่เริ่มออกฤทธิ์	เวลาที่มีฤทธิ์สูงสุด	ระยะเวลาการออกฤทธิ์
อินซูลินอะนาล็อกออกฤทธิ์เร็ว			
- Insulin lispro (Humalog®)	5-15 นาที	1-2 ชั่วโมง	3-4 ชั่วโมง
- Insulin aspart (NovoRapid®)	10-20 นาที	1-2 ชั่วโมง	3-4 ชั่วโมง
- Insulin glulisine (Aprida®)	10-20 นาที	1-2 ชั่วโมง	3-4 ชั่วโมง
อินซูลินอะนาล็อกออกฤทธิ์ยาว			
- Insulin glargine (Lantus®, Basalin®, Glaritus®)	2 ชั่วโมง	ไม่มี	24 ชั่วโมง
- Insulin detemir (Levemir®)	2 ชั่วโมง	ไม่มี	18-24 ชั่วโมง
- Insulin degludec (Tresiba®)	6 ชั่วโมง	ไม่มี	24-36 ชั่วโมง

Start basal insulin 0.1 unit /kg/day

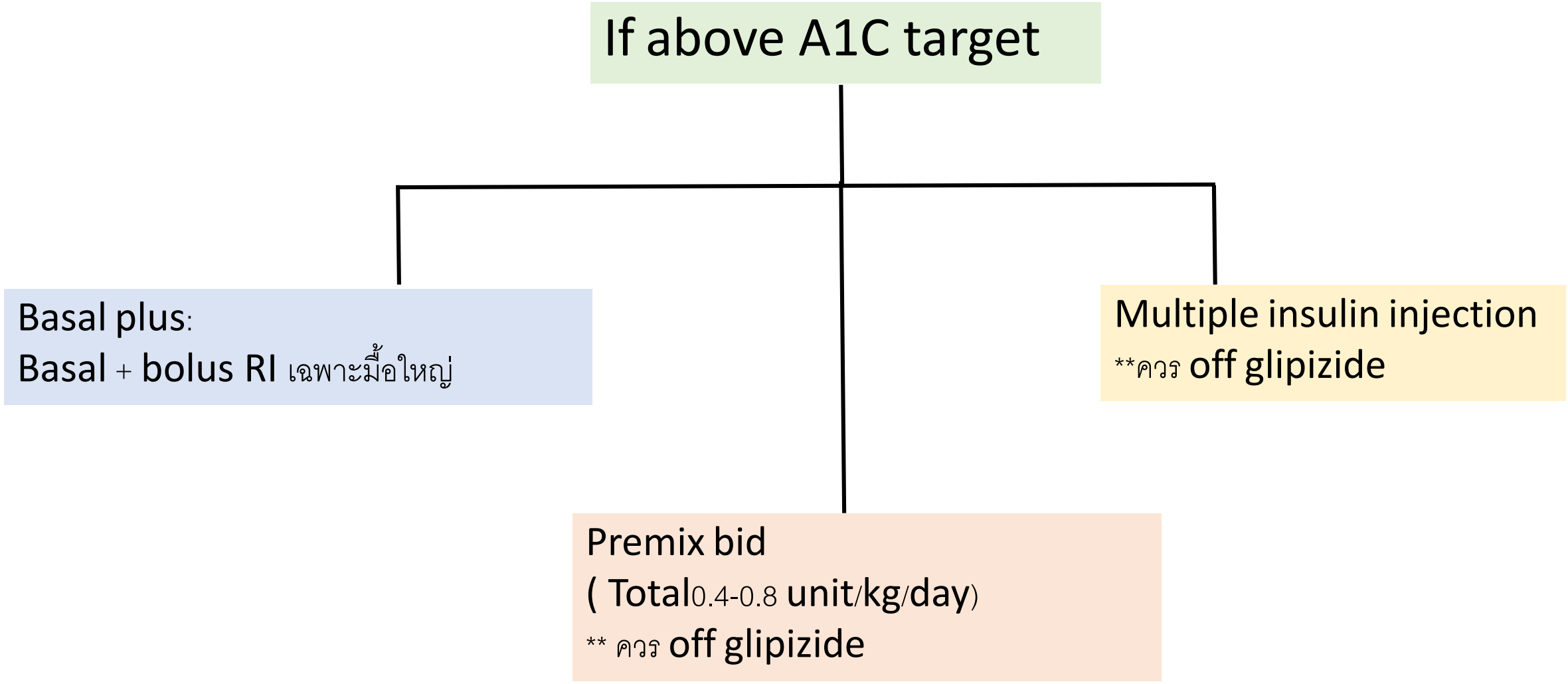
เช่น น้ำหนัก 60 กิโลกรัม

เริ่ม NPH 6 unit sc hs



Case 3: BW 60 kg
60-year-old woman, last A1c=13%, glipizide 10 mg/day

DTX เช้า	**DTX เย็น**	
240	280	NPH 6 unit sc hs
204	275	NPH 6 unit sc hs
184	267	NPH 6 unit sc hs
189	289	NPH 8 unit sc hs
156	300	NPH 8 unit sc hs


If above A1C target
Basal plus:
Basal + bolus RI เฉพาะมื้อใหญ่
Premix bid
(Total0.4-0.8 unit/kg/day)
** ควร off glipizide
Multiple insulin injection
**ควร off glipizide

Case 3: BW 60 kg
60-year-old woman, last A1c=13%, off glipizide
Start premix 0.5 unit/kg/day

DTX เช้า	**DTX** เย็น	
155	200	**Mixtard** 20 **unit sc ac** เช้า **Mixtard** 10 **unit sc ac** เย็น
136	174	ฉีดเท่าเดิม
124	155	ฉีดเท่าเดิม
132	185	ฉีดเท่าเดิม
125	177	**Mixtard** 22 **unit sc ac** เช้า **Mixtard** 10 **unit sc ac** เย็น

Premix insulin (30%RI+70%NPH)

ชนิดยา (ชื่อยา)	เวลาที่เริ่มออกฤทธิ์	เวลาที่มีฤทธิ์สูงสุด	ระยะเวลาการออกฤทธิ์
ฮิวแมนอินซูลินผสมสำเร็จรูป			
- Premixed 30% RI + 70% NPH (Mixtard 30 HM®, Humulin 70/30®, Gensulin M30®, Insugen 30/70®, Insuman combo30®, Winsulin 30/70®)	30-60 นาที	2 และ 8 ชั่วโมง	12-20 ชั่วโมง
- Premixed 50% RI + 50% NPH (Gensulin M50®)	30-60 นาที	2 และ 8 ชั่วโมง	12-20 ชั่วโมง

Novomix: 70% protaminate aspart+30%Aspart

Preparation	Trade name	Timing of Action		
		Onset	Peak	Duration
Pre-mixed insulin				
70%NPH / 30%Regular	Humulin 70/30 Mixtard30	30-60 นาที	Dual	10-16 ชั่วโมง
75% protaminated Lispro / 25% Lispro	Humalog mix 25	15-30 นาที	Dual	10-16 ชั่วโมง
70% Protaminated aspart / 30% aspart	Novomix 30	15-30 นาที	Dual	10-16 ชั่วโมง

Insulin in CKD

Table 4: Insulin preparations: Considerations in hemodialysis patients.

INSULIN PREPARATION	ONSET OF ACTION	PEAK ACTION	EFFECTIVE DURATION
Rapid-acting			
Regular	30–60 min	2–3 hr	8–10 hr
Lispro (Humalog)	5–15 min	30–90 min	4–6 hr
Aspart (NovoLog)	5–15 min	30–90 min	4–6 hr
Long-acting			
Neutral protamine Hagedorn (NPH)	2–4 hr	4–10 hr	12–18 hr
Glargine (Lantus)	2–4 hr	None	20–24 hr
Detemir (Levemir)	3–4 hr	3–14 hr	6–23 (19.9) hr
Premixed			
70/30 human mix	30–60 min	3–12 hr	12–18 hr
70/30 aspart mix	5–15 min	30–90 min	12–18 hr
75/25 lispro mix	5–15 min	30–90 min	12–18 hr

EGFR ($ml/min/1.73m^2$)	**Decrease doses of insulin**
10-50	25%
<10	50%

Arch Clin Nephrol2017.3(1):047-052.

How to start insulin in a patient with CKD

- Total daily dose (TDD) for insulin : 0.1 to 0.3 units/kg (depend on nutritional status or frailty of the patient. (Obese patient : 1.2-1.5 units/kg)

- Regimens: multiple doses of insulin (MDI) or basal bolus regimen > premix

- The rule of thumb to prevent nocturnal hypoglycemia is- "Bedtime glucose should always be higher than before dinner glucose by atle ast 40mg/dl

Arch Clin Nephrol2017.3(1):047-052.

Conclusion

- Lifestyle modification is important management.

- Pharmacological management:risk specific selection:
  - SGLT2 inhibitor(ASCVD, Hx HF, CKD)
  - GLP1 agonist (ASCVD, CKD, weight management goal)

Thank you

For attention