2023年美國糖尿病學會標準化醫療照護指引解讀

May 20, 2023 9:10~10:40

衛生福利部彰化醫院2樓大講堂

彰基 內分泌新陳代謝科

林世鐸

The Contents of ADA Standards of Care in Diabetes—2023

1. Improving Care and Promoting Health in Populations
2. Classification and Diagnosis of Diabetes
3. **Prevention or Delay of T2D** and Associated Comorbidities
4. Comprehensive Medical Evaluation and **Assessment of Comorbidities**
5. **Facilitating Positive Health Behaviors** and Well-being to Improve Health Outcomes
6. **Glycemic Targets**
7. **Diabetes Technology**
8. **Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes**
9. **Pharmacologic Approaches to Glycemic Treatment**
10. **CVD and Risk Management**
11. **CKD and Risk Management**
12. Retinopathy, Neuropathy, and Foot Care
13. Older Adults
14. Children and Adolescents
15. Management of Diabetes in Pregnancy
16. Diabetes Care in the Hospital
17. Diabetes and Advocacy

Table 2.3—Criteria for screening for diabetes or prediabetes in asymptomatic adults

1. Testing should be considered in adults with overweight or obesity (BMI ≥25 kg/m^2 or ≥23 kg/m^2 in Asian American individuals) who have one or more of the following risk factors:
   - First-degree relative with diabetes
   - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - History of CVD
   - Hypertension (≥130/80 mmHg or on therapy for hypertension)
   - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   - Individuals with polycystic ovary syndrome
   - Physical inactivity
   - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
2. People with prediabetes (A1C ≥5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.
3. People who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other people, testing should begin at age 35 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.
6. People with HIV

無症狀要考慮篩檢的條件:

過重(或肥胖) +
- 一等親家族史
- 心血管疾病史
- 高血壓
- 血脂異常(低HDL高TG)
- PCOS
- 缺乏運動
- 胰島素阻抗證據

篩檢頻率
PreDM，每年一次
GDM，終身至少每3年一次
35歲以上就開始篩檢
結果正常，至少3年一次

More intensive preventive approaches should be considered in individuals who are at particularly high risk of progression to diabetes, including individuals with BMI ≥35 kg/m^2, those at higher glucose levels (FPG 110–125 mg/dL, 2-h OGTT 173–199 mg/dL, A1C ≥6.0%), and individuals with a history of GDM. A

BMI ≥35

Hx of GDM

A1C ≥6.0

FPG 110–125

OGTT 2hr 173–199

Pharmacotherapy (e.g., for weight management, minimizing the progression of hyperglycemia, cardiovascular risk reduction) may be considered to support person-centered care goals. B

Life style changes	Metformin	Pioglitazone
• Reduced-calorie diet • 150 min/week moderate-intensity physical activity • ≥7% weight loss	• Age 25-59 years with BMI > 35; Previous GDM; FBS > 110; HbA1C > 6% (based on DPP)	• Lower the risk of stroke MI and progression to DM
• Government-recognized behavioral counseling programs • Technology-assisted programs	• Long term use ? • Vitamin B12 deficiency	• Side effect ?

Prevention of Vascular Disease and Mortality

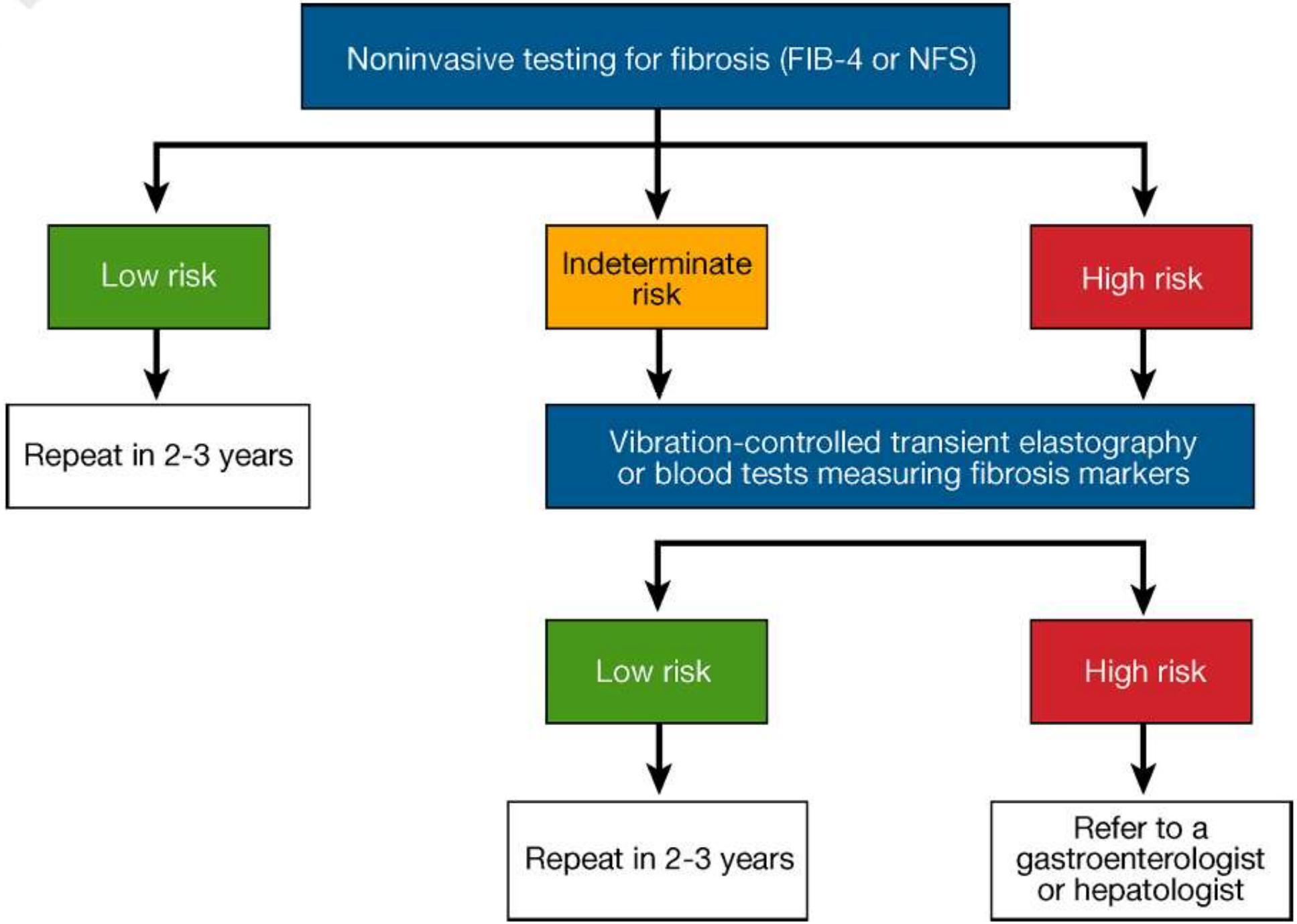
- Prediabetes is associated with heightened CV risk; therefore, screening for and treatment of modifiable risk factors for CVD are suggested. B
- In people with a history of stroke and evidence of insulin resistance and prediabetes, **pioglitazone** may be considered to lower the risk of stroke or MI. However, this benefit needs to be balanced with the increased risk of weight gain, edema, and fracture. A
- Lower doses may mitigate the risk of adverse effects. C
- Statin therapy may increase the risk of T2D in people at high risk of developing type 2 diabetes. In such individuals, **glucose status** should be **monitored regularly** and diabetes prevention approaches reinforced. It is **not recommended** that statins be discontinued. B

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PAST MEDICAL AND FAMILY HISTORY	**Diabetes history**			
	▪ Characteristics at onset (e.g., age, symptoms)	✓		
	▪ Review of previous treatment plans and response	✓		
	▪ Assess frequency/cause/severity of past hospitalizations	✓		
	Family history			
	▪ Family history of diabetes in a first-degree relative	✓		
	▪ Family history of autoimmune disorder	✓		
	Personal history of complications and common comorbidities			
	▪ Common comorbidities (e.g., obesity, OS , NAFLD)	✓		
	▪ High blood pressure or abnormal lipids	✓		✓
	▪ Macrovascular and microvascular complications	✓		✓
	▪ Hypoglycemia: awareness/frequency/causes/timing of episodes	✓	✓	✓
	▪ Presence of hemoglobinopathies or anemias	✓		✓
	▪ Last dental visit	✓		✓
	▪ Last dilated eye exam			✓
	▪ Visits to specialists			✓
	Interval history			
	▪ Changes in medical/family history since last visit		✓	✓

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
BEHAVIORAL FACTORS	▪ Eating patterns and weight history	✓	✓	✓
	▪ Assess familiarity with carbohydrate counting (e.g., type 1 diabetes, type 2 diabetes treated with MDI)	✓		✓
	▪ Physical activity and sleep behaviors	✓	✓	✓
	▪ Tobacco, alcohol, and substance use	✓		✓
MEDICATIONS AND VACCINATIONS	▪ Current medication plan	✓	✓	✓
	▪ Medication-taking behavior	✓	✓	✓
	▪ Medication intolerance or side effects	✓	✓	✓
	▪ Complementary and alternative medicine use	✓	✓	✓
	▪ Vaccination history and needs	✓		✓
TECHNOLOGY USE	▪ Assess use of health apps, online education, patient portals, etc.	✓		✓
	▪ Glucose monitoring (meter/CGM): results and data use	✓	✓	✓
	▪ Review insulin pump settings and use, connected pen and glucose data	✓	✓	✓
SOCIAL LIFE ASSESSMENT	**Social network**			
	▪ Identify existing social supports	✓		✓
	▪ Identify surrogate decision maker, advanced care plan	✓		✓
	▪ Identify social determinants of health (e.g., food security, housing stability & homelessness, transportation access, financial security, community safety)	✓		✓

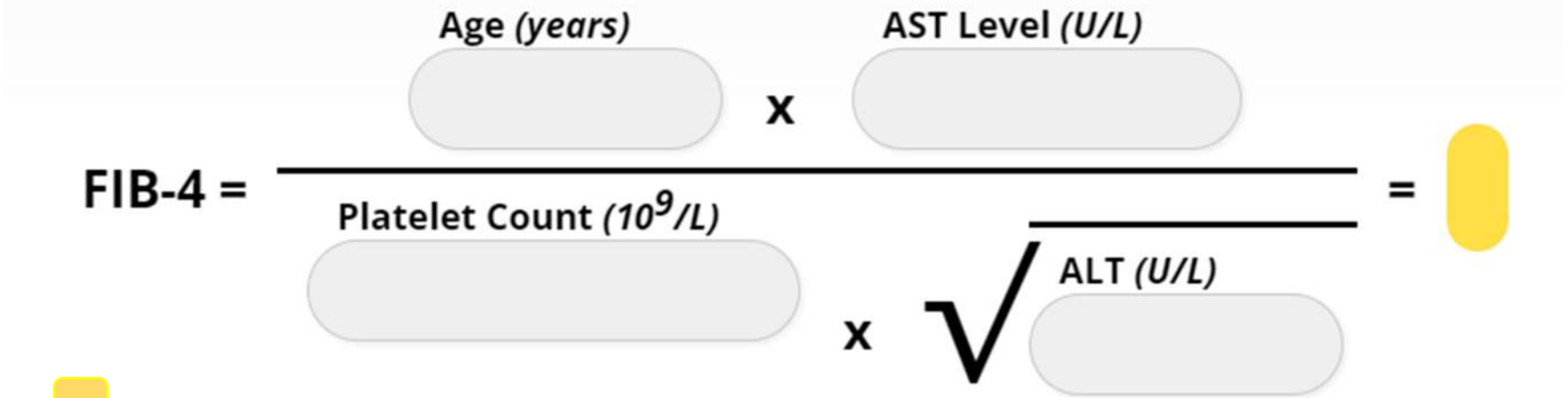
		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PHYSICAL EXAMINATION	▪ Height, weight, and BMI; growth/pubertal development in children and adolescents	✓	✓	✓
	▪ Blood pressure determination	✓	✓	✓
	▪ Orthostatic blood pressure measures (when indicated)	✓		
	▪ Fundoscopic examination (refer to eye specialist)	✓		✓
	▪ Thyroid palpation	✓		✓
	▪ Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)	✓	✓	✓
	▪ Comprehensive foot examination			
	• Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, toenails)**	✓		✓
	• Screen for PAD (pedal pulses—refer for ABI if diminished)	✓		✓
	• Determination of temperature, vibration or pinprick sensation, and 10-g monofilament exam	✓		✓
	▪ Screen for depression, anxiety, and disordered eating	✓		✓
	▪ Consider assessment for cognitive performance*	✓		✓
	▪ Consider assessment for functional performance*	✓		✓

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
LABORATORY EVALUATION	▪ A1C, if the results are not available within the past 3 months	✓	✓	✓
	▪ If not performed/available within the past year	✓		✓
	• Lipid profile, including total, LDL, and HDL cholesterol and triglycerides[#]	✓		✓^
	• Liver function tests[#]	✓		✓
	• Spot urinary albumin-to-creatinine ratio	✓		✓
	• Serum creatinine and estimated glomerular filtration rate[+]	✓		✓
	• Thyroid-stimulating hormone in people with type 1 diabetes[#]	✓		✓
	• Vitamin B12 if on metformin	✓		✓
	• Serum potassium levels in people with diabetes on ACE inhibitors, ARBs, or diuretics[+]	✓		✓


Noninvasive testing for fibrosis (FIB-4 or NFS)
Low risk
Indeterminate risk
High risk
Repeat in 2-3 years
Vibration-controlled transient elastography or blood tests measuring fibrosis markers
Low risk
High risk
Repeat in 2-3 years
Refer to a gastroenterologist or hepatologist

Fibrosis-4 (FIB-4) Calculator

Hepatology 2006;43:1317-1325.



<1.45 NPV 90% for advanced fibrosis

>3.25 PPV of 65% & 97% specificity for advanced fibrosis

Weight Loss | **Pioglitazone** | **GLP1RA** | **SGLT2i**

5S

Sitting
減少久坐

Stepping
增加步行

Sleep
保好睡眠

Sweating
中強運動

Strengthening
阻力運動

每坐30分鐘就起身慢走、伸展

每天多走500步可以減少2-9%的心血管疾病其全因死亡率

每天快走5-6分鐘可以增加4年預期壽命

睡6-8小時最適中

熬夜會讓血糖控制變差

失眠、睡眠呼吸中止症、不寧腿症候群會影響睡眠品質，對血糖有不好的影響

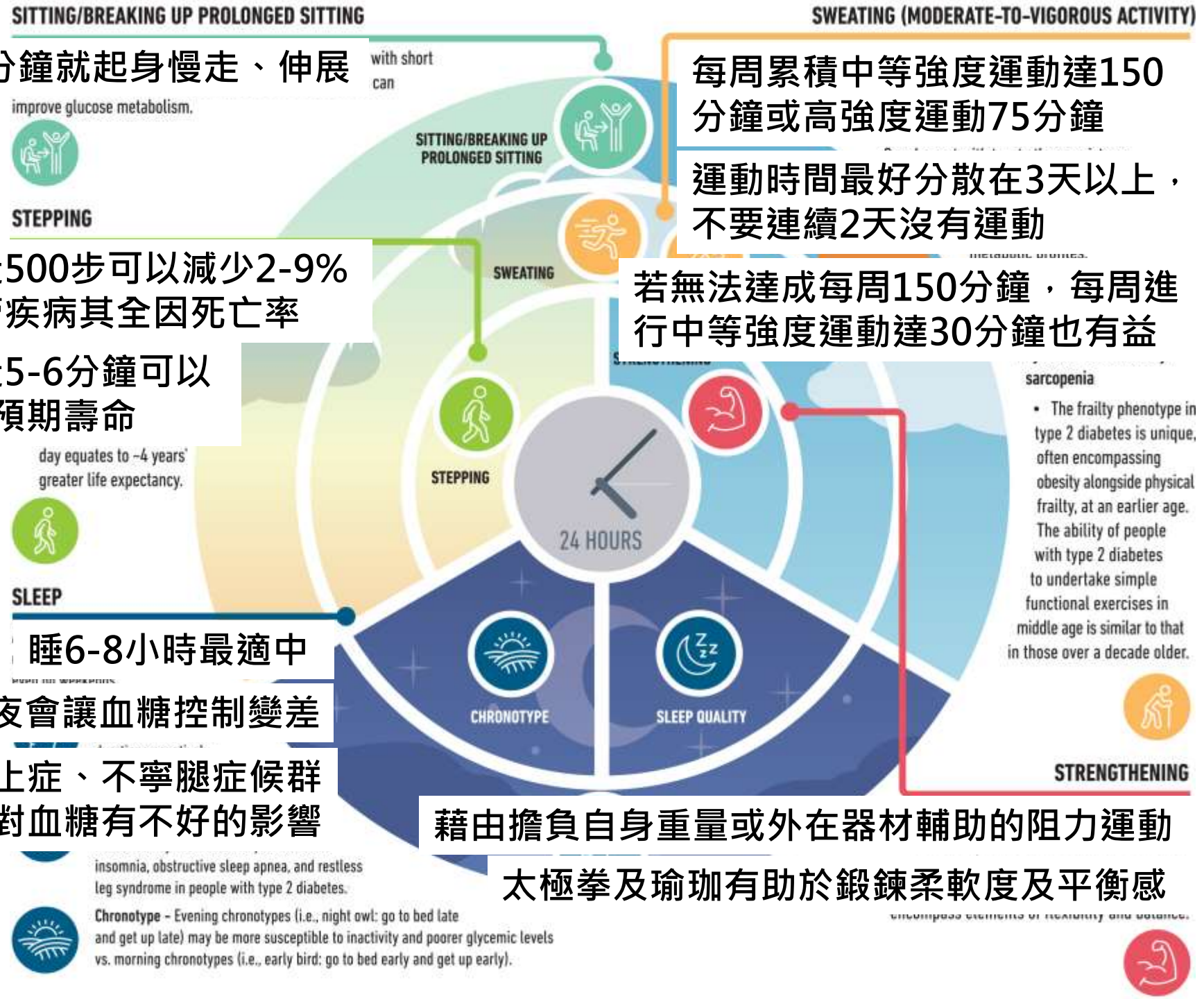
每周累積中等強度運動達150分鐘或高強度運動75分鐘

運動時間最好分散在3天以上，不要連續2天沒有運動

若無法達成每周150分鐘，每周進行中等強度運動達30分鐘也有益

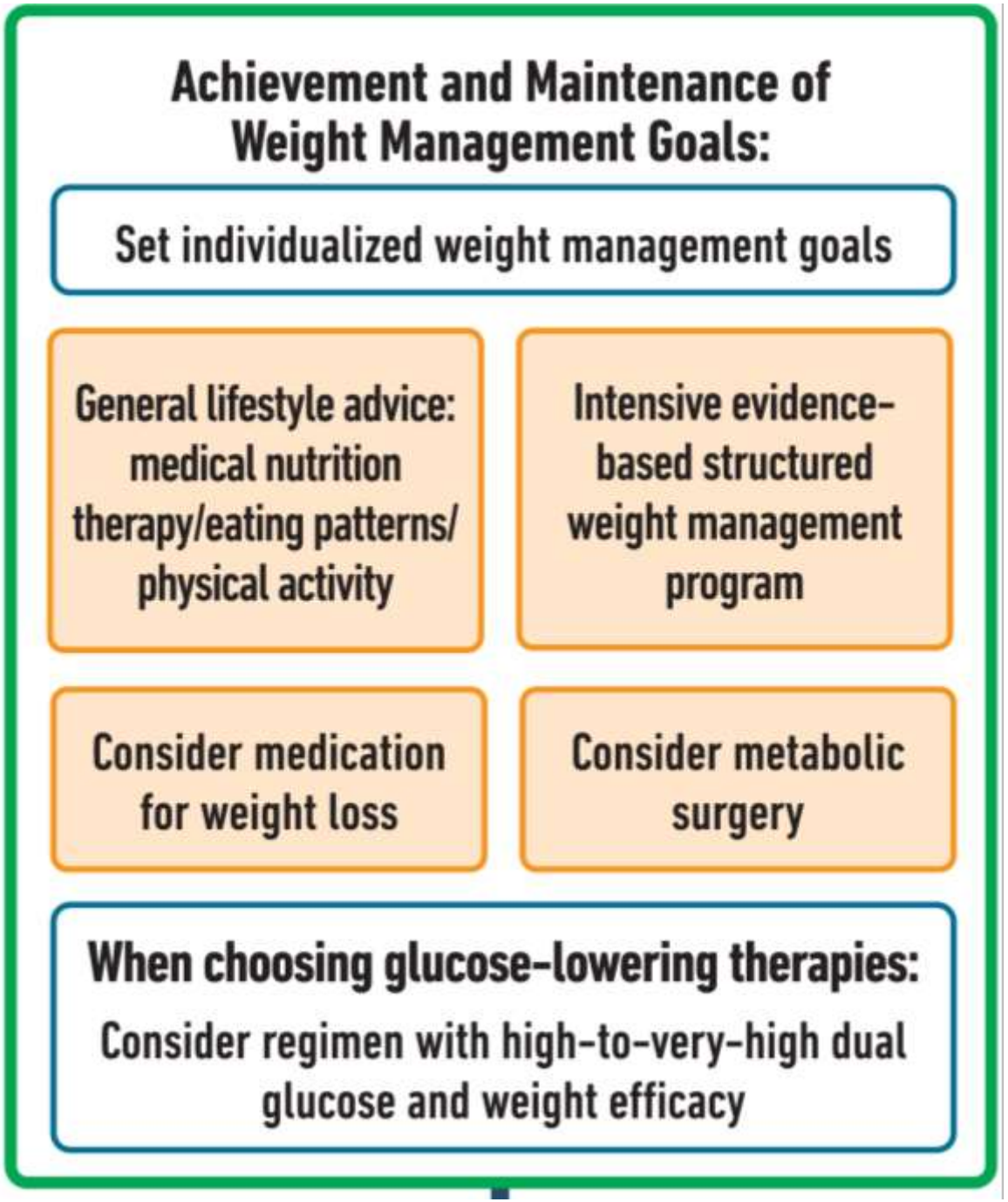
藉由擔負自身重量或外在器材輔助的阻力運動

太極拳及瑜珈有助於鍛鍊柔軟度及平衡感



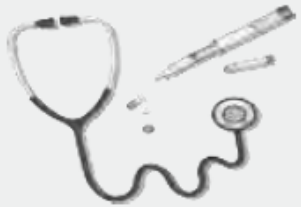
Weight reduction (of baseline)	Effect	Evidence
▽ 3-7% (5%)	improves glycemia & other intermediate cardiovascular risk factors	A
▽ > 10%	disease-modifying effects and possible remission of type 2 diabetes, and may improve long-term cardiovascular outcomes and mortality	B

Achieve a 500–750 kcal/day energy deficit for significant weight loss
→ 1kgw / 2wks



	BMI category		
Treatment	25-26.9 (23-24.9)	27-29.9 (25-27.4)	≥30 (≥27.5)
Nutrition, exercise, behavior counseling	V	V	V
Medication		V	V
Surgery			V

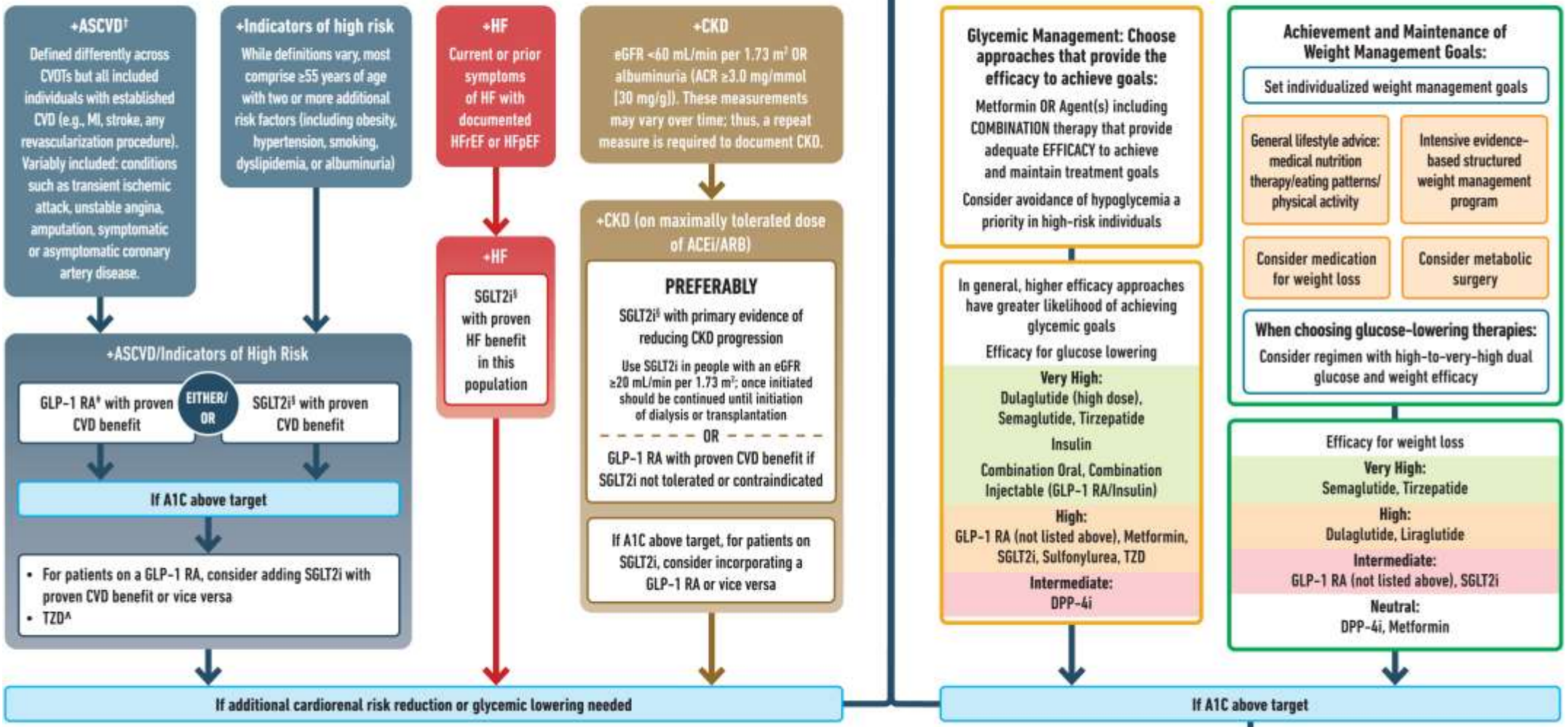
減重手術之健保給付規範 (2020年五月更新)



1. BMI大於37.5 kg/m^2，或BMI大於32.5 kg/m^{2}且合併有高危險併發症。高危險併發症如高血壓、睡眠呼吸中止症、第二型糖尿病（糖化血色素經內科治療後仍大於7.5%）。
2. 減重門診治療（或門診相關佐證）滿半年，經運動及飲食控制半年以上。
3. 年齡在20至65歲之間。
4. 無其他內分泌疾病引起之病態性肥胖。
5. 無酗酒、嗑藥及其他精神疾病。
6. 精神狀態健全，經由精神科專科醫師會診認定無異常。

目標: 降低具有高風險的第2型糖尿病個案之心腎風險

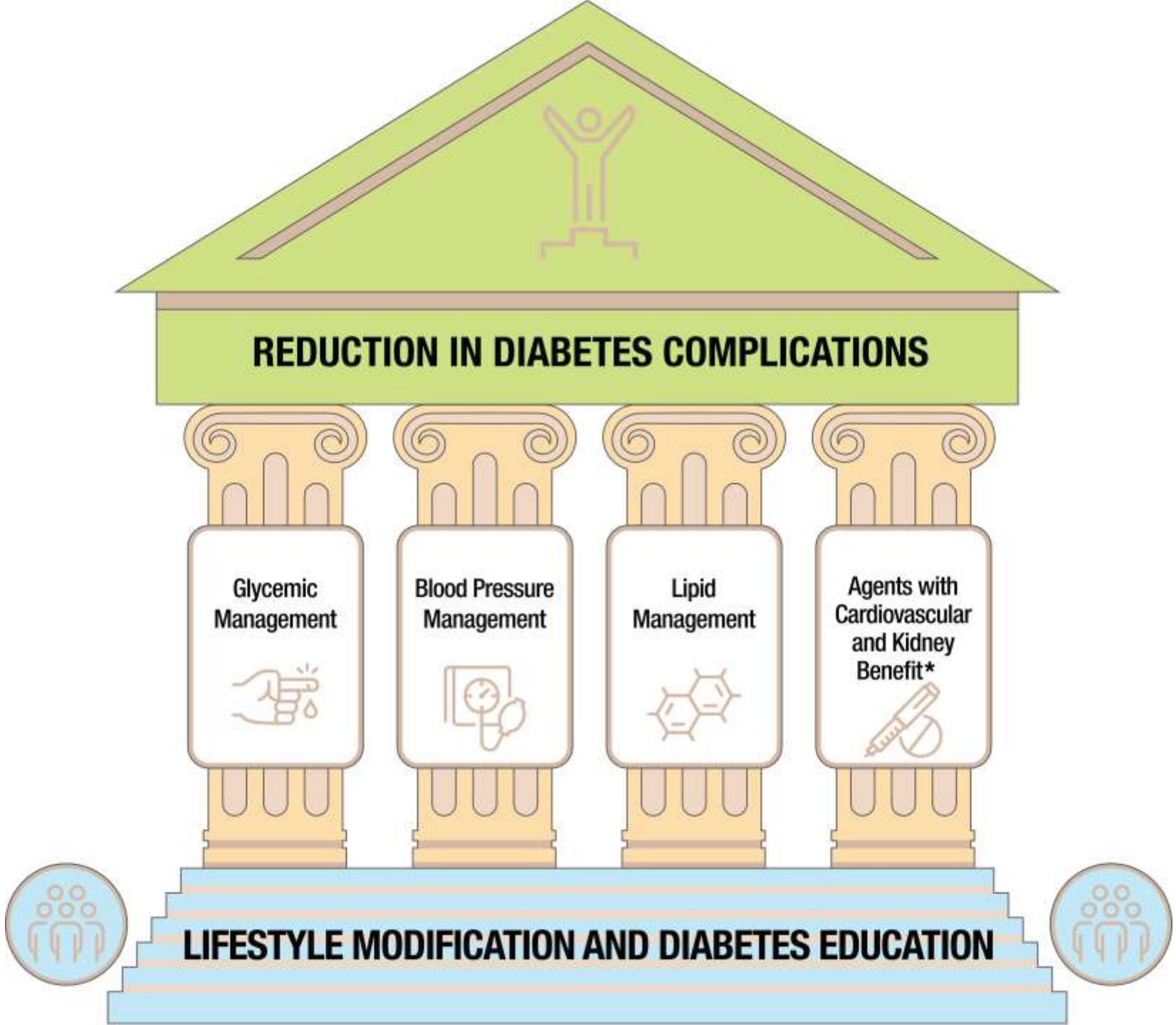
目標: 達成及維持血糖與體重的控制目標



* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

	Efficacy[1]	Hypoglycemia	Weight change[2]	CV effects		Renal effects	
				Effect on MACE	HF	Progression of DKD	Dosing/use considerations*
Metformin	High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Neutral	• Contraindicated with eGFR <30 mL/min per 1.73 m^2
SGLT2 inhibitors	Intermediate to high	No	Loss (intermediate)	Benefit: canagliflozin, empagliflozin	Benefit: canagliflozin, dapagliflozin, empagliflozin, ertugliflozin	Benefit: canagliflozin, dapagliflozin, empagliflozin	• See labels for renal dose considerations of individual agents • Glucose-lowering effect is lower for SGLT2 inhibitors at lower eGFR
GLP-1 RAs	High to very high	No	Loss (intermediate to very high)	Benefit: dulaglutide, liraglutide, semaglutide (SQ) Neutral: exenatide once weekly, lixisenatide	Neutral	Benefit for renal endpoints in CVOTs, driven by albuminuria outcomes: dulaglutide, liraglutide, semaglutide (SQ)	• See labels for renal dose considerations of individual agents • No dose adjustment for dulaglutide, liraglutide, semaglutide • Monitor renal function when initiating or escalating doses in patients with renal impairment reporting severe adverse GI reactions

		Efficacy[1]	Hypoglycemia	Weight change[2]	CV effects		Renal effects	
					Effect on MACE	HF	Progression of DKD	Dosing/use considerations*
GIP and GLP-1 RA		Very high	No	Loss (very high)	Under investigation	Under investigation	Under investigation	• See label for renal dose considerations • No dose adjustment • Monitor renal function when initiating or escalating doses in patients with renal impairment reporting severe adverse GI reactions
DPP-4 inhibitors		Intermediate	No	Neutral	Neutral	Neutral (potential risk, saxagliptin)	Neutral	• Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment • No dose adjustment required for linagliptin
Thiazolidinediones		High	No	Gain	Potential benefit: pioglitazone	Increased risk	Neutral	• No dose adjustment required • Generally not recommended in renal impairment due to potential for fluid retention
Sulfonylureas (2nd generation)		High	Yes	Gain	Neutral	Neutral	Neutral	• Glyburide: generally not recommended in chronic kidney disease • Glipizide and glimepiride: initiate conservatively to avoid hypoglycemia
Insulin	**Human**	High to very high	Yes	Gain	Neutral	Neutral	Neutral	• Lower insulin doses required with a decrease in eGFR; titrate per clinical response
	Analogs							


REDUCTION IN DIABETES COMPLICATIONS
Glycemic Management
Blood Pressure Management
Lipid Management
Agents with Cardiovascular and Kidney Benefit*
LIFESTYLE MODIFICATION AND DIABETES EDUCATION

Diagnosis & Treatment goal

- Hypertension is defined as **a SBP ≥130 mmHg or a DBP ≥80 mmHg based on an average of ≥2 measurements obtained on ≥2 occasions**. A Individuals with blood pressure ≥180/110 mmHg and cardiovascular disease could be diagnosed with hypertension at a single visit. E
- People with diabetes and hypertension **qualify for antihypertensive drug therapy when the blood pressure is persistently elevated ≥130/80 mmHg**. The on-treatment target blood pressure goal is <130/80 mmHg, if it can be safely attained. B

Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes

DASH

Initial BP ≥130/80 and <160/100 mmHg

Initial BP ≥160/100 mmHg

Start one agent

Lifestyle management

Start two agents

Albuminuria or CAD*

Albuminuria or CAD*

No

Yes

No

Yes

Start one drug:
- ACEi or ARB
- CCB***
- Diuretic**

Start
- ACEi or ARB

Start drug from 2 of 3 options:
- ACEi or ARB
- CCB***
- Diuretic**

Start:
- ACEi or ARB

and
- CCB*** or Diuretic**

Assess BP Control and Adverse Effects

Treatment tolerated and target achieved

Not meeting target

Adverse effects

Continue therapy

Add agent from complementary drug class:
- ACEi or ARB
- CCB***

Consider change to alternative medication:
- ACEi or ARB
- CCB***

***Dihydropyridine CCB

**Thiazide-like diuretic; long-acting agents, such as chlorthalidone & indapamide, are preferred

Treatment Strategies—Resistant Hypertension

- Individuals with hypertension who are not meeting blood pressure targets on three classes of antihypertensive medications (including a diuretic) should be considered for mineralocorticoid receptor antagonist therapy. A

Statin Treatment—Primary Prevention

- For people with diabetes **aged 40–75 years without atherosclerotic cardiovascular disease**, use **moderate-intensity statin therapy** in addition to lifestyle therapy. A
- For people with diabetes **aged 40–75 at higher cardiovascular risk**, including those with one or more atherosclerotic cardiovascular disease risk factors, it is recommended to use **high-intensity statin therapy to reduce LDL cholesterol by ≥50% of baseline and to target an LDL cholesterol goal of <70 mg/dL**. B

Statin Treatment—Primary Prevention

- For people with diabetes **aged 40–75 years at higher cardiovascular risk**, especially those with multiple atherosclerotic cardiovascular disease risk factors and an LDL cholesterol ≥70 mg/dL, it may be reasonable to **add ezetimibe or a PCSK9 inhibitor** to maximum tolerated statin therapy. C
- In adults with **diabetes aged >75 years already on statin therapy**, it is reasonable to **continue statin treatment**. C
- In adults with **diabetes aged >75 years**, it may be reasonable **to initiate moderate-intensity statin therapy** after discussion of potential benefits and risks. B
- Statin therapy is contraindicated in pregnancy. B

Lipid management-statin for primary prevention

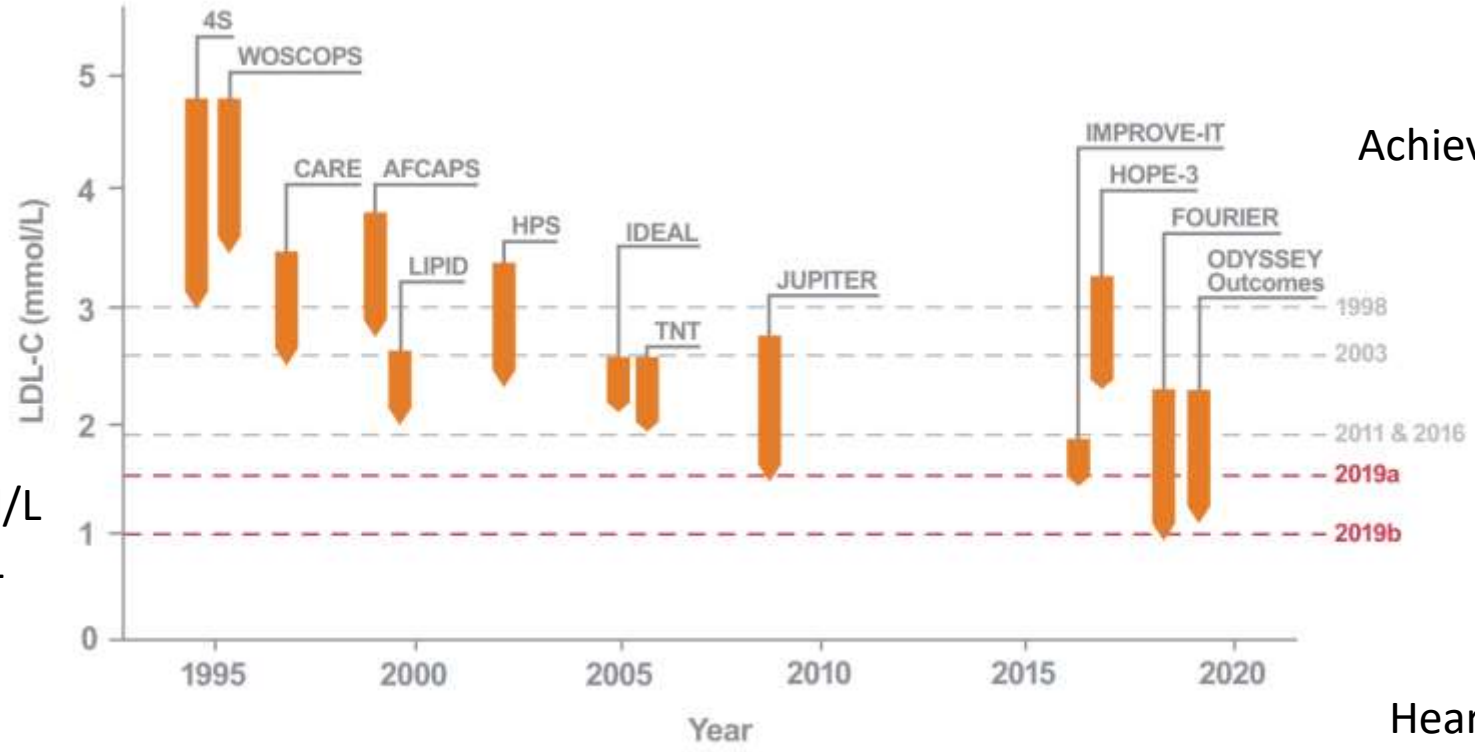
Age	CV risk factors	Statin use	Comments
20-39	+	Reasonable to initiate statin	
40-75	Nil	Moderate intensity statin	LDL-C goal < 100 mg/dL
40-75	1 or more	High internsity statin	Reduce LDL-C by > 50% from baseline and LDL-C < 70
>75	Nil	Reasonable to initiate moderate intensity statin	After discussion of potential benefits and risks
>75	+	Continue statin therapy	For those already on statin

Statin Treatment—Secondary Prevention

- For people of all ages with diabetes and atherosclerotic cardiovascular disease, high intensity statin therapy should be added to lifestyle therapy. A
- For people with diabetes and atherosclerotic cardiovascular disease, treatment with **high intensity statin** therapy is recommended to target an **LDL cholesterol reduction of ≥50% from baseline** and **an LDL cholesterol goal of <55 mg/dL**. Addition of ezetimibe or a PCSK9 inhibitor with proven benefit in this population is recommended if this goal is not achieved on maximum tolerated statin therapy. B
- For individuals who do not tolerate the intended intensity, the maximum tolerated statin dose should be used. E

Statin Treatment—Secondary Prevention

- People with diabetes + ASCVD: high intensity statin + lifestyle therapy
- Goal: **LDL-C ▽ ≥50% from baseline** and **LDL-C <55 mg/dL**. If not achieving goal → add on ezetimibe / PCSK9 inhibitor

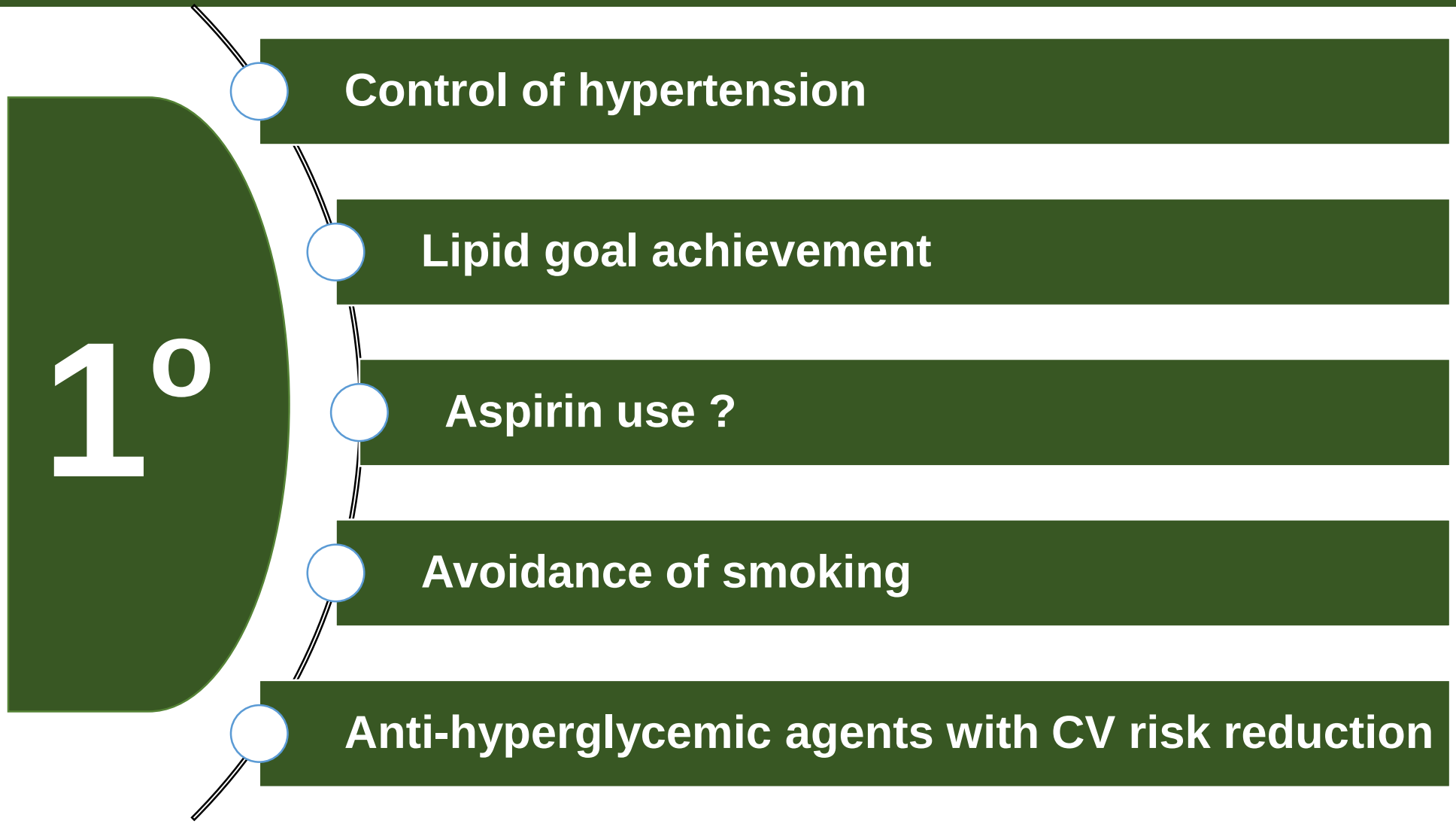


Achievable LDL-C levels

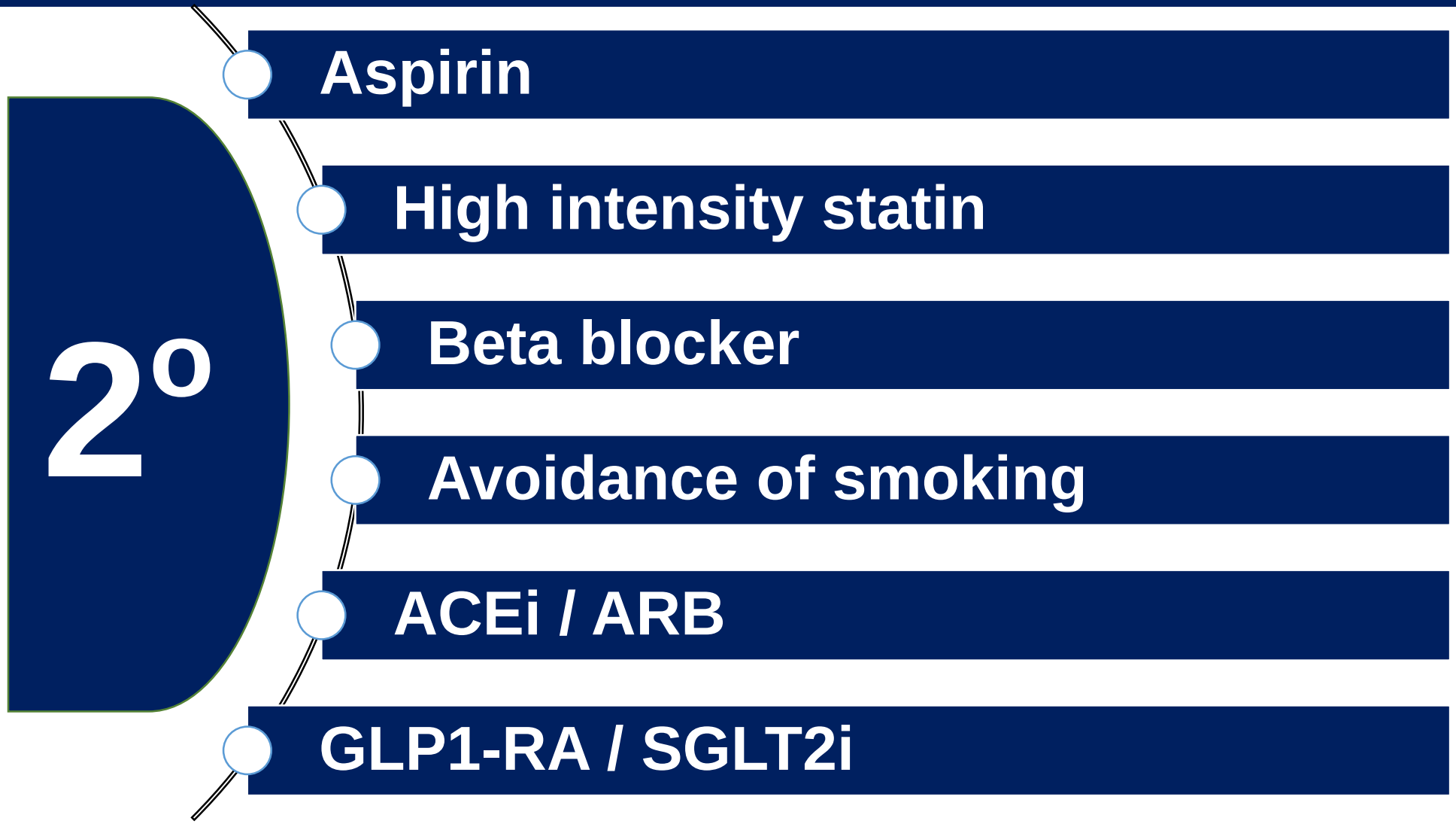
LDL-C 1 mmol/L =38.67 mg/dL

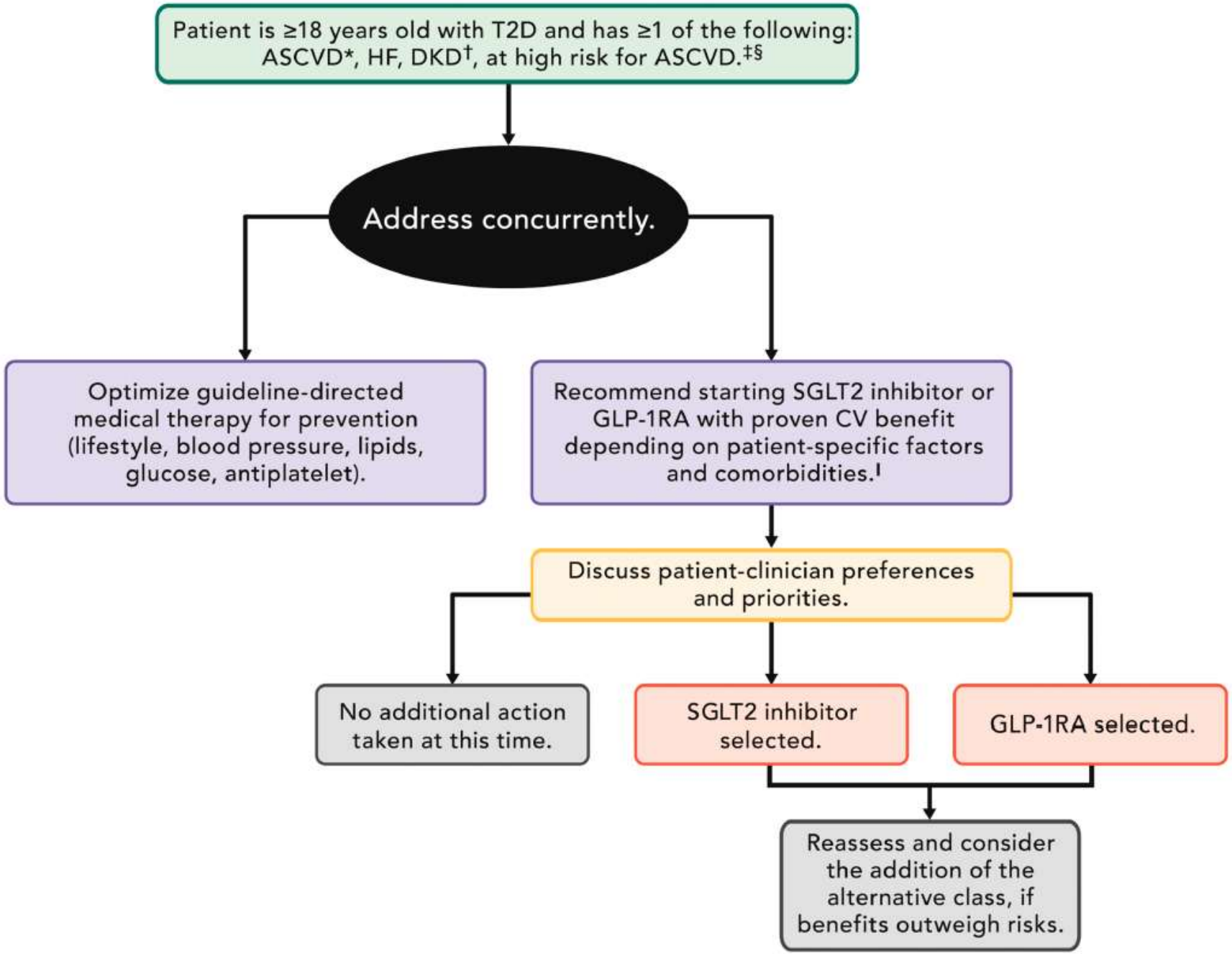
Heart 2021;107:1369–1375

Reduce cardiovascular risk - Primary prevention



Reduce cardiovascular risk - Secondary prevention




Patient is ≥18 years old with T2D and has ≥1 of the following: ASCVD*, HF, DKD†, at high risk for ASCVD.‡§
Address concurrently.
Optimize guideline-directed medical therapy for prevention (lifestyle, blood pressure, lipids, glucose, antiplatelet).
Recommend starting SGLT2 inhibitor or GLP-1RA with proven CV benefit depending on patient-specific factors and comorbidities.‖
Discuss patient-clinician preferences and priorities.
No additional action taken at this time.
SGLT2 inhibitor selected.
GLP-1RA selected.
Reassess and consider the addition of the alternative class, if benefits outweigh risks.

Cardiovascular Disease—Treatment (continued)

For people with type 2 diabetes and chronic kidney disease with albuminuria treated with maximum tolerated doses of ACE inhibitor or angiotensin receptor blocker, addition of **finerenone** is recommended to improve cardiovascular outcomes and reduce the risk of chronic kidney disease progression. A

CKD screening and diagnosis for people living with diabetes

Who and when to screen?

T1D Yearly starting 5 years after diagnosis

T2D Yearly starting at diagnosis

How to screen?

Spot urine ACR

and

eGFR

What to do with a positive result?

Repeat and confirm:
- Evaluate possible temporary or spurious causes
- Consider using cystatin C and creatinine to more precisely estimate GFR
- Only persistent abnormalities define CKD

Initiate evidence-based treatments

What defines CKD diagnosis?

Persistent urine ACR ≥30 mg/g

and/or

Persistent eGFR <60 mL/min/1.73 m^2

and/or

Other evidence of kidney damage

Diabetes Care. 2022 Oct 3;dci220027.

Chronic Kidney Disease—Treatment

- Patients should be **referred for evaluation by a nephrologist**

  if continuously increasing ACR ± continuously decreasing eGFR

  and

  if the eGFR is <30 mL/min/1.73 m2. A

Chronic Kidney Disease—Treatment

- For people with T2D and diabetic kidney disease, use of a SGLT2i is recommended to reduce chronic kidney disease progression and cardiovascular events in patients with an estimated glomerular filtration rate ≥20 mL/min/1.73 m2 and urinary albumin ≥200 mg/g creatinine. A
- For people with T2D and diabetic kidney disease, use of a SGLT2i is recommended to reduce chronic kidney disease progression and cardiovascular events in patients with an estimated glomerular filtration rate ≥20 mL/min/1.73 m2 and urinary albumin ranging from normal to 200 mg/g creatinine. B
- In people with T2D and diabetic kidney disease, consider use of SGLT2i (if estimated glomerular filtration rate is ≥20 mL/min/1.73 m2), a GLP1RA, or a nonsteroidal mineralocorticoid receptor antagonist (if estimated glomerular filtration rate is ≥25 mL/min/1.73 m2) additionally for cardiovascular risk reduction . A

Chronic Kidney Disease—Treatment

ACE inhibitor /ARB

Recommended in moderately increased albuminuria (UACR 30-299 mg/g Cr)
Strongly recommended in severely increased albuminuria (UACR >300 mg/g Cr) ± eGFR <60

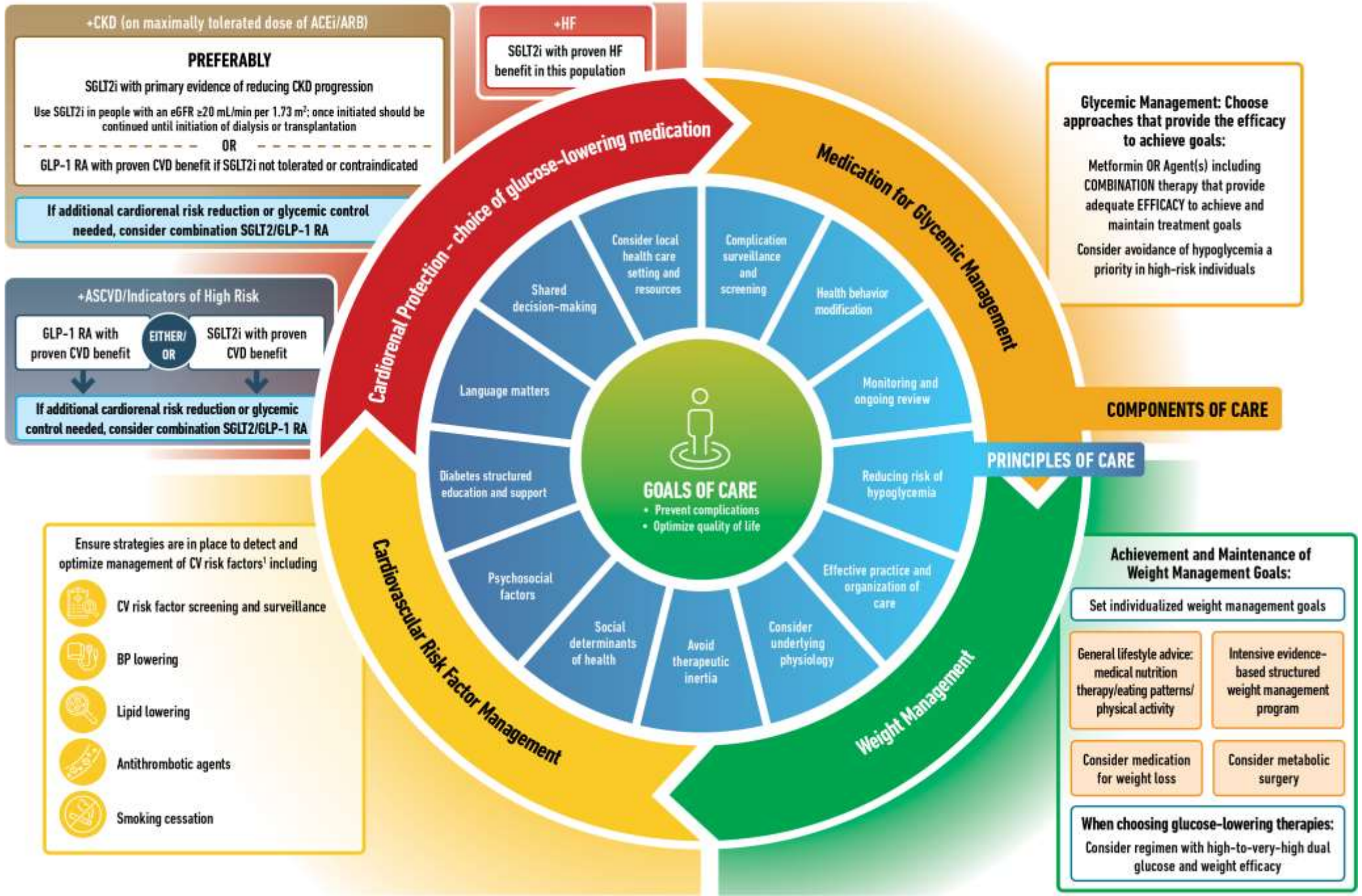
SGLT2 inhibitor

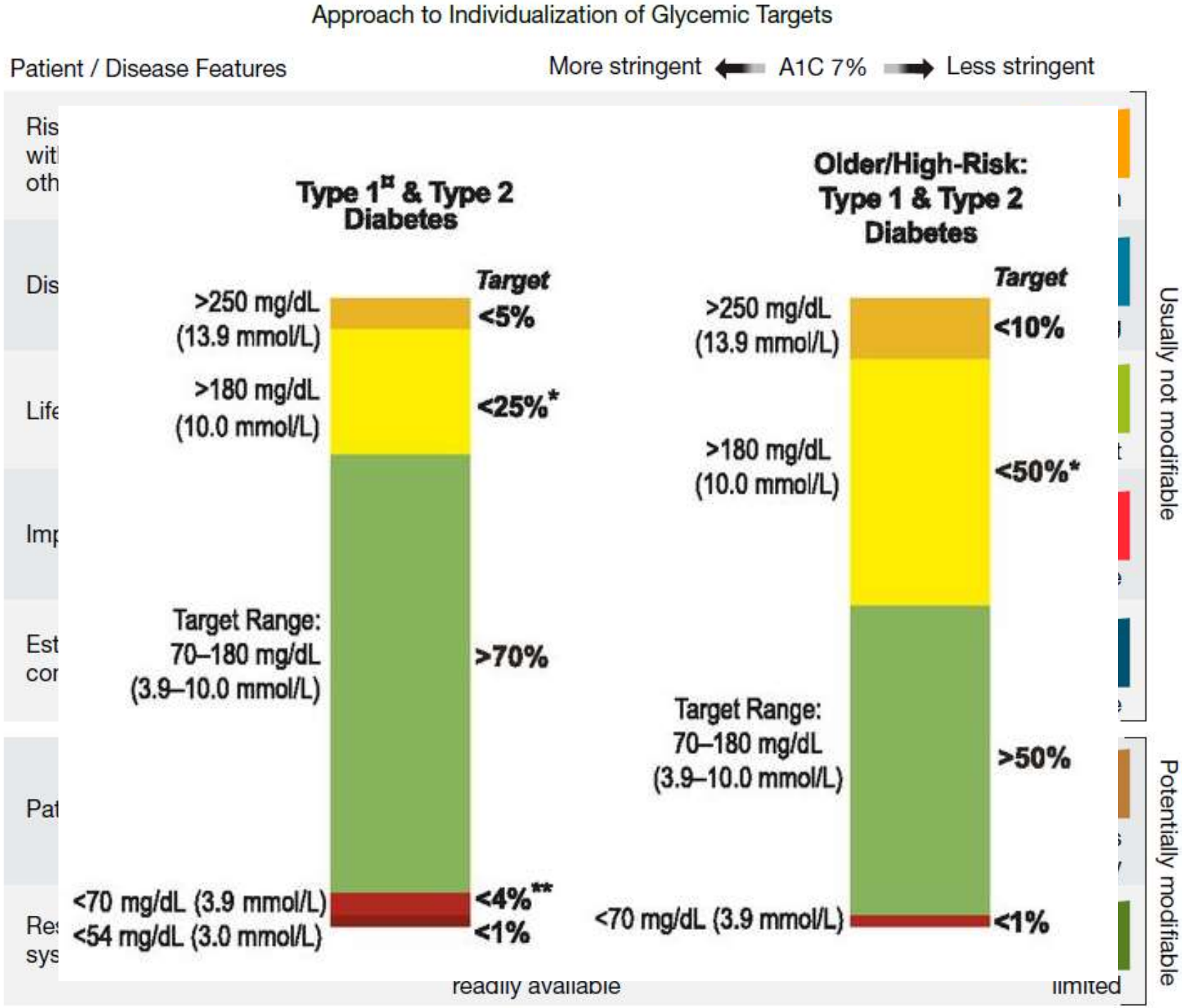
In all patients with DKD, recommended to reduce CKD progression and CV events in patients with an eGFR > 20 and UACR > 200

Finerenone

Used if eGFR > 25 and K <5
10 mg / 20 mg once daily and Monitor eGFR and K

HOLISTIC PERSON-CENTERED APPROACH TO T2DM MANAGEMENT




Approach to Individualization of Glycemic Targets
Patient / Disease Features
More stringent
A1C 7%
Less stringent
Type 1¤ & Type 2 Diabetes
Target
>250 mg/dL (13.9 mmol/L)
<5%
>180 mg/dL (10.0 mmol/L)
<25%*
Target Range: 70–180 mg/dL (3.9–10.0 mmol/L)
>70%
<70 mg/dL (3.9 mmol/L)
<4%**
<54 mg/dL (3.0 mmol/L)
<1%
Older/High-Risk: Type 1 & Type 2 Diabetes
Target
>250 mg/dL (13.9 mmol/L)
<10%
>180 mg/dL (10.0 mmol/L)
<50%*
Target Range: 70–180 mg/dL (3.9–10.0 mmol/L)
>50%
<70 mg/dL (3.9 mmol/L)
<1%
Usually not modifiable
Potentially modifiable
readily available
limited

Real-time CGM (rt-CGM); intermittent scanned CGM (isCGM)

- rt-CGM **A** or isCGM **C** should be offered for diabetes management in adults with diabetes **on basal insulin** who are capable of using the devices safely (either by themselves or with a caregiver).
- The choice of device should be made based on the individual's circumstances, preferences, and needs.

Real-time CGM (rt-CGM); intermittent scanned CGM (isCGM)

- In people with diabetes on **MDI** or **CSII**, rt-CGM devices should be used as close to daily as possible for maximal benefit. **A**
- isCGM devices should be scanned frequently, at a minimum once every 8 h. **A**
- People with diabetes should have uninterrupted access to their supplies to minimize gaps in continuous glucose monitoring. **A**

Real-time CGM (rt-CGM); intermittent scanned CGM (isCGM)

- Continuous glucose monitoring device users should be educated on potential interfering substances and other factors that may affect accuracy. **C**

Table 7.4—Continuous glucose monitoring devices interfering substances

Medication	Systems affected	Effect
Acetaminophen		
>4 g/day	Dexcom G6	Higher sensor readings than actual glucose
Any dose	Medtronic Guardian	Higher sensor readings than actual glucose
Alcohol	Medtronic Guardian	Sensor readings may be higher than actual glucose
Ascorbic acid (vitamin C), >500 mg/day	FreeStyle Libre	Higher sensor readings than actual glucose
Hydroxyurea	Dexcom G6, Medtronic Guardian	Higher sensor readings than actual glucose
Mannitol	Senseonics Eversense	Sensor bias within therapeutic concentration ranges
Tetracycline	Senseonics Eversense	Sensor bias within therapeutic concentration ranges

Real-time CGM (rt-CGM); intermittent scanned CGM (isCGM)

- For people with type 1 diabetes using CGM, frequency of sensor use was an important predictor of A1C lowering for all age-groups
- The frequency of scanning with isCGM devices was also correlated with improved outcomes

新糖尿病用藥及胰島素新知

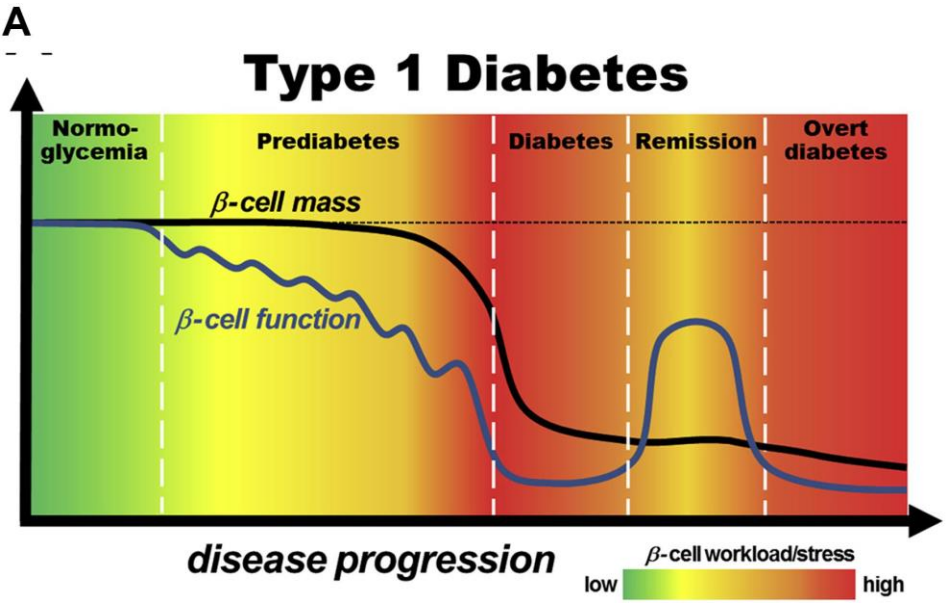
2023/0520 1050-1220

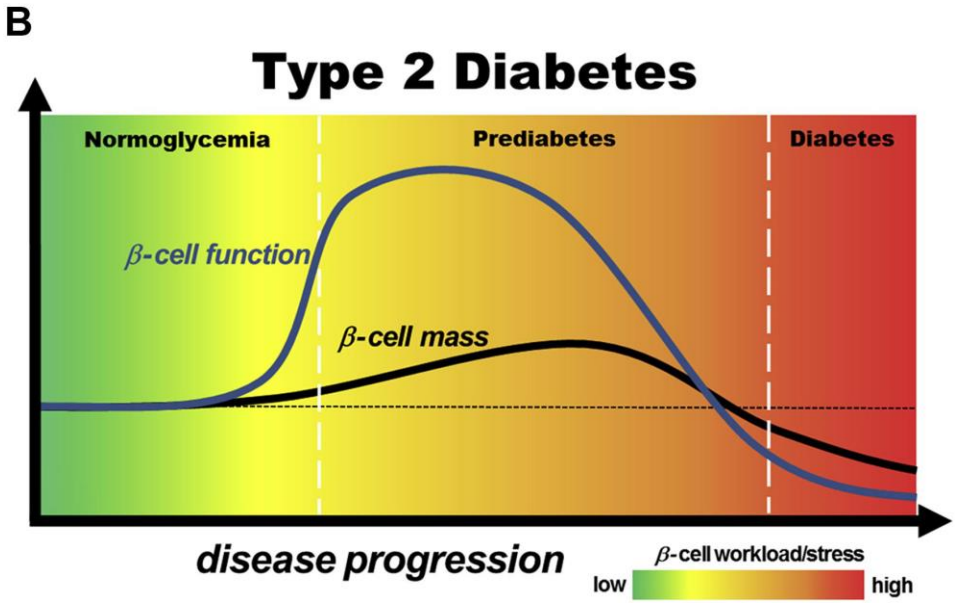
衛福部立彰化醫院

Outline

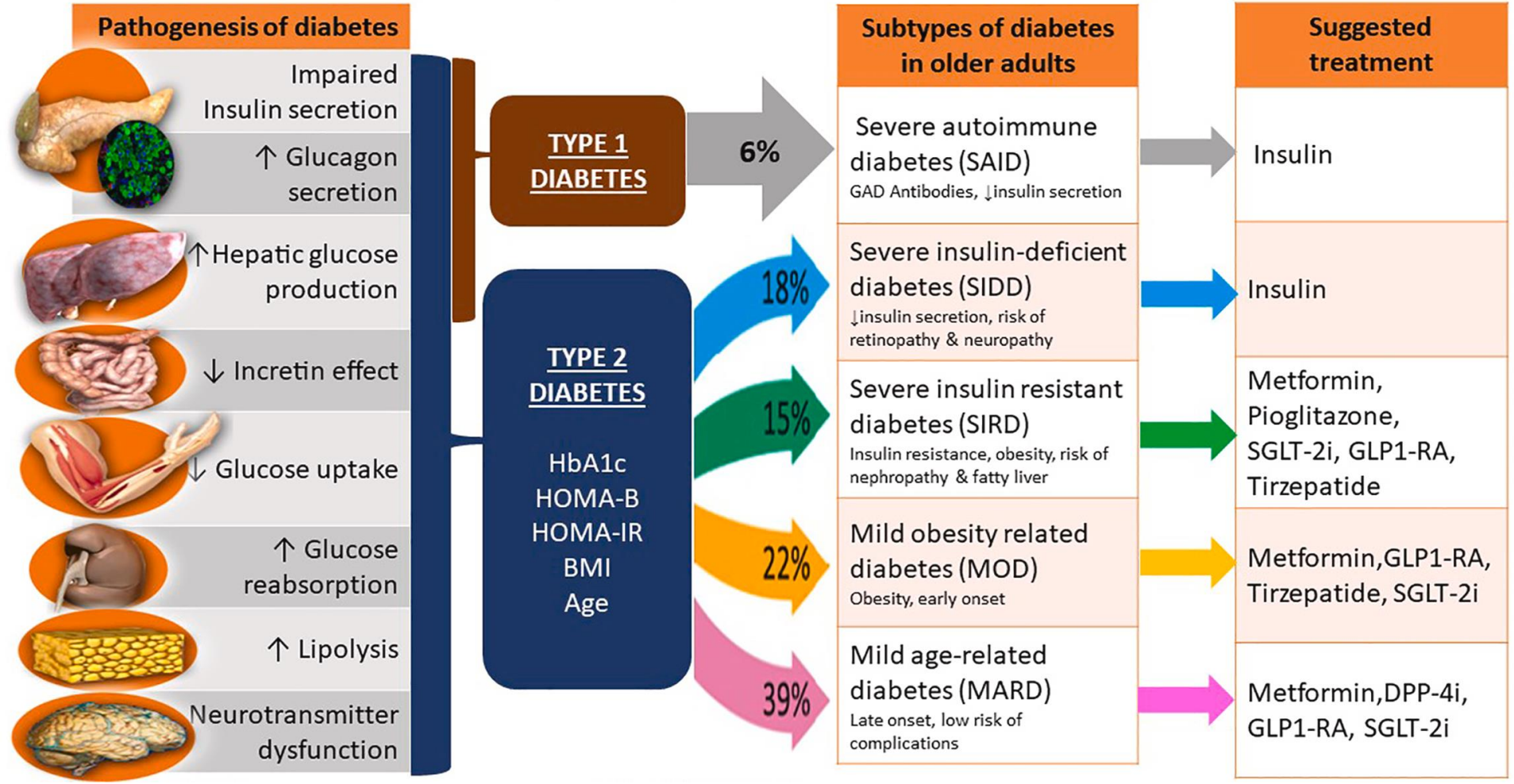
- Drugs development in diabetes
- Oral antidiabetic drugs (OAD)
- Injectable antidiabetic drugs (IAD)
- Summary

Models of the contribution of pancreatic β-cell mass and function to pathogenesis of T1DM (A) and T2DM (B).



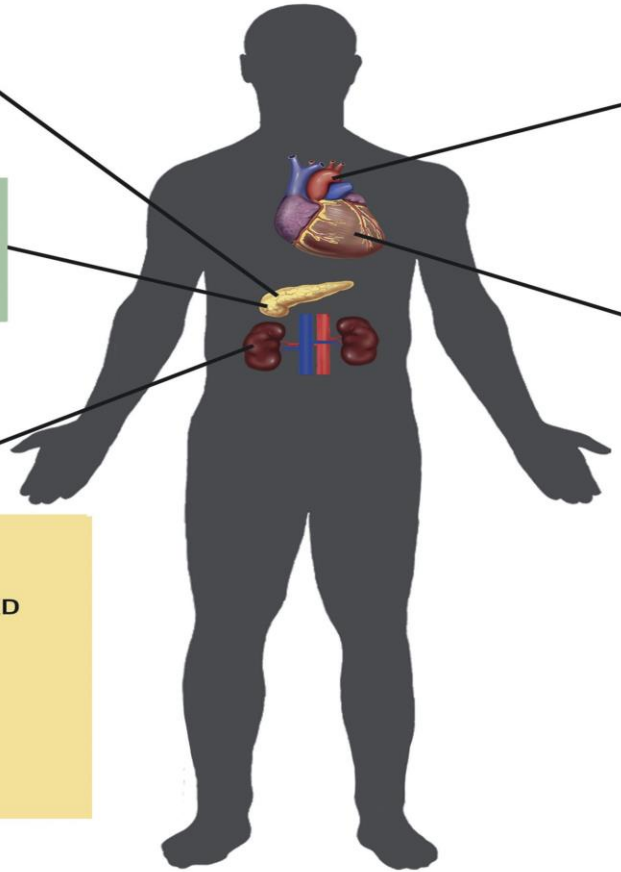


Mol. Metab. 2017, 6, 943–957.



Endocrinology and Metabolism Clinics, 2023-06-01, 卷 52, 期 2, 頁面 355-375

CENTRAL ILLUSTRATION: Cardiovascular Risk Reduction in Type 2 Diabetes Mellitus Guidelines and Consensus Recommendations



ADA

2022 Standards of medical care in diabetes

AACE/ACE

2020 Consensus statement on comprehensive T2DM management algorithm

ESC/EASD

2019 Guidelines on diabetes, pre-diabetes, and CVD

ACC/AHA

- 2018 Guideline on the management of blood cholesterol
- 2019 Guideline on the primary prevention of CVD
- 2020 Expert consensus decision pathway on novel therapies for CV risk reduction in patients with T2DM

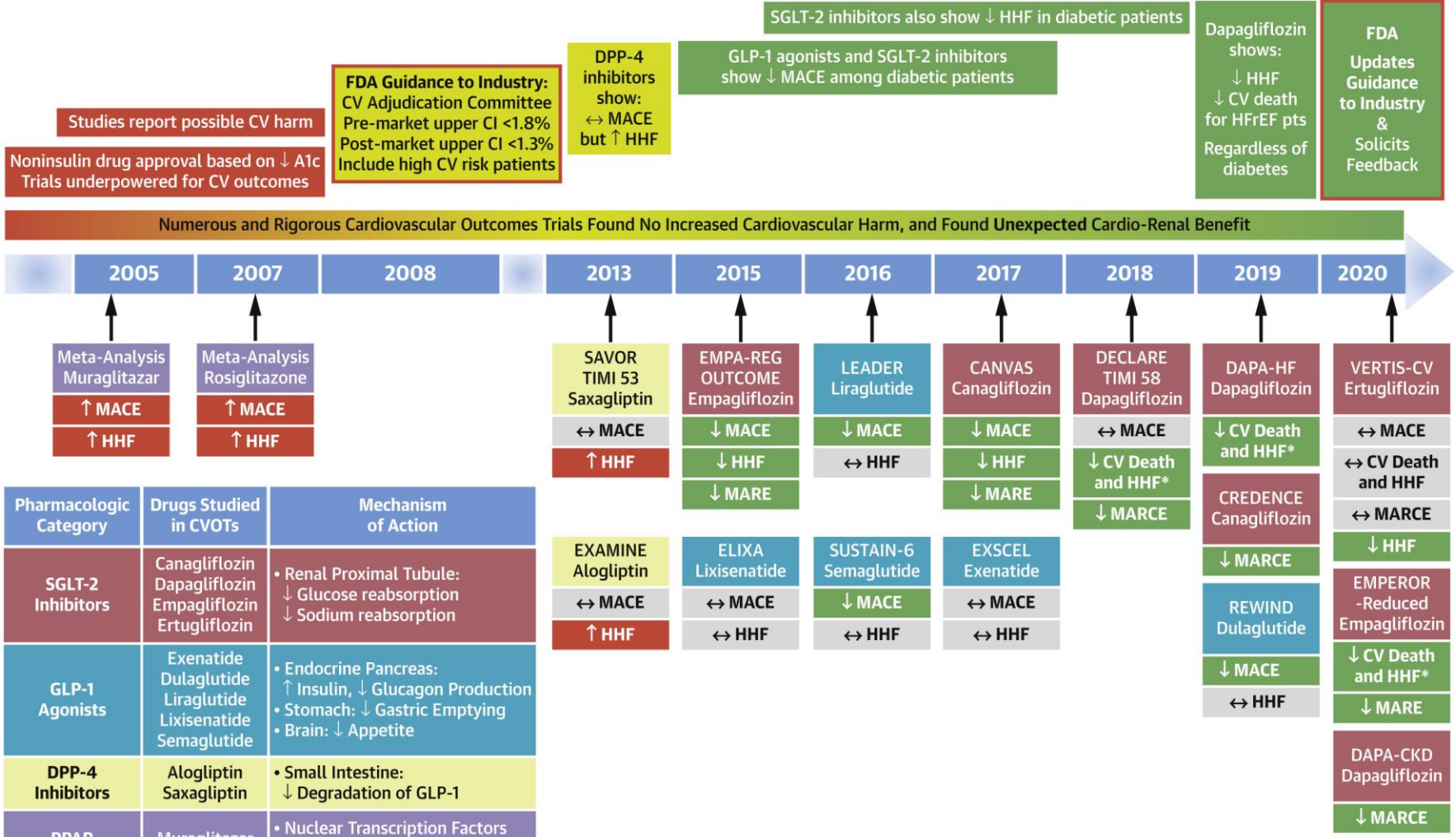
KDIGO

- 2013 Clinical practice guideline for lipid management in CKD
- 2020 Clinical practice guideline for diabetes management in CKD
- 2021 Clinical practice guideline for management of blood pressure in CKD

USPSTF

- 2016 Aspirin use to prevent CVD and colorectal cancer
- 2016 Statin use for the primary prevention of CVD in adults
- 2021 Screening for abnormal blood glucose and T2DM

Kelsey MD, et al. J Am Coll Cardiol. 2022;79(18):1849–1857.

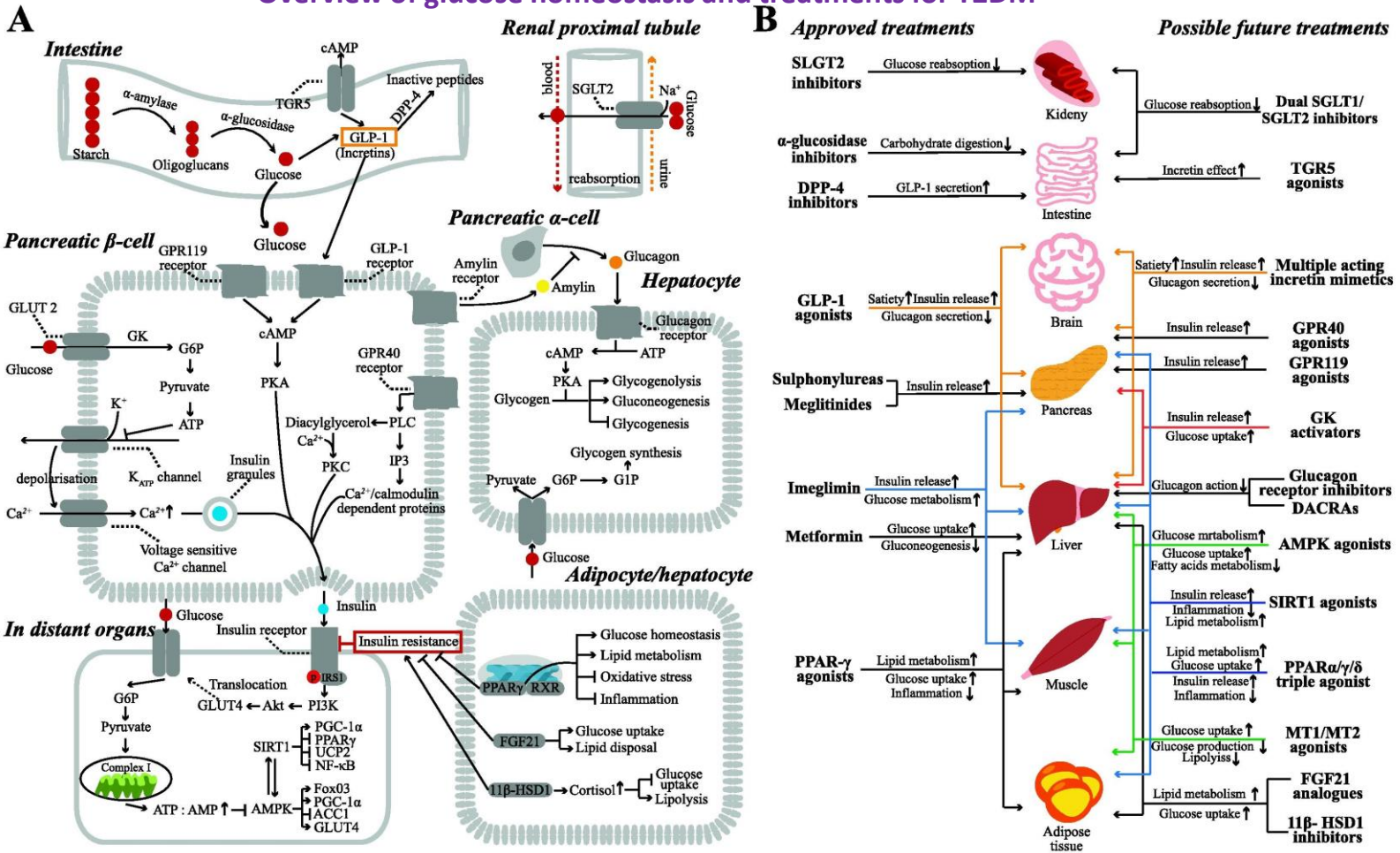


Enrico G. Ferro et al. *J Am Coll Cardiol* 2020; 76:2522-2526.

藥物分類
Antidiabetic Drug Groups

- **Oral Antidiabetic Drugs (OAD)**
  - Sulfonylureas (SU)
  - Meglitinides (SU-like)
  - Biguanides
  - Thiazolidinediones (TZD)
  - Alpha-glucosidase inhibitors (AGI)
  - Dipeptidylpeptidase-4 inhibitors (DPP4 inhibitors)
  - Sodium-glucose co-transporter 2 inhibitor (SGLT-2 inhibitor)
  - Oral Semaglutide (GLP-1)
- **Injectable Antidiabetic Drugs (IAD)**
  - Insulin
  - Non-Insulin Injectables
  - Glucagon-like peptide 1 receptor (GLP-1) agonists
  - Amylin analogues

Overview of glucose homeostasis and treatments for T2DM



Drug Discovery Today Volume 27, Issue 10, October 2022,

Outline

- Drugs development in diabetes
- **Oral antidiabetic drugs (OAD)**
- Injectable antidiabetic drugs (IAD)
- Summary

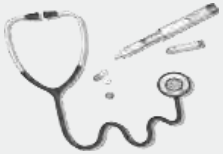
Teaching Note: Topics to include are name of drug, purpose and action, accurate dose, timing of administration, and storage requirements. If hypoglycemia is a risk, include definition, risk factors, recognition/symptoms, glucose monitoring, and treatment options.

Drug Class Generic Name	Approximate % A1c Lowering	Risk of Hypoglycemia	Side Effects/Cautions Patient Teaching
Biguanide Metformin Glucophage Immediate or extended release	1–2	Minimal to none	GI side effects. Vitamin B12 deficiency. Best tolerated when taken with food. Caution with renal insufficiency, hepatic disease, or heart failure. Hold if NPO or renal compromise likely.
Sulfonylurea Glyburide Glipizide Glimepiride	1–2	Yes	Caution in sulfa allergy. Hold if NPO. May cause weight gain. Decreased efficacy over time.
Metiglinide Nateglinide Repaglinide	0.75–1.5	Yes	Hold if NPO or meal is skipped. May cause weight gain. Decreased efficacy over time.
Thiazolidinedione Pioglitazone Rosiglitazone	0.75–1.5	Minimal to none	Not for use in preexisting edema, heart failure, or hepatic failure. Weight gain is expected. Requires initial and periodic liver function tests. May increase risk of fracture. Not approved for use in pregnancy.
DPP-4 inhibitor Sitagliptin Saxagliptin	0.5–1	Minimal to none	Daily at any time of day with or without food. No expected weight gain, may be slight weight loss. Dose adjusted in renal failure.
SGLT-2 blocker Canagliflozin Dapagliflozin	0.7–1	Minimal to none	UTI and genital yeast infections more common. Polyuria. Not for use with severe renal impairment, eGFR less than 30 mL/min/1.73 m^2, or ESRD. May ↑LDL.

NPO = nothing by mouth; eGFR = estimated glomerular filtration rate; GI = gastrointestinal; UTI = urinary tract infections; ESRD = end-stage renal disease; LDL = low-density lipoprotein.

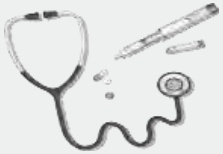
Note. Table recreated with information from Riddle & Yuen (2014) and Inzucchi et al. (2015).

口服抗糖尿病藥物臨床建議



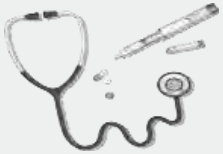
臨床建議	證據等級	臨床建議強度	華人資料
第2型糖尿病患者，若無contraindication，建議以metformin作為首選藥物。	中	中等建議	
當患者有肝、腎或心臟功能不全時，不建議使用metformin， 以減少乳酸中毒的可能性。腎絲球體過濾率(eGFR)小於30 ml/min/1.73m2時，禁用metformin；腎絲球體過濾率 (eGFR)介於30~45 ml/min/1.73m2時，metformin應減量 使用。80歲以上的第2型糖尿病患者，若以前未曾使用過 metformin，不建議以metformin治療。	低	中等建議	有
使用thiazolidinedione，可能會出現體液滯留、水腫和體重增加的現象，也可能會增加鬱血性心臟衰竭的風險。	高	中等建議	

口服抗糖尿病藥物臨床建議



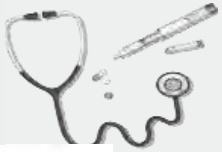
臨床建議	證據等級	臨床建議強度	華人資料
患者肝功能不全（血清轉胺酶，ALT，超過正常值上限的2.5 倍），或心臟衰竭的嚴重度符合紐約心臟學會（New York Heart Association，NYHA）功能分類第III級和第IV級時。 不建議使用thiazolidinedione。	中	強烈建議	
鈉葡萄糖協同轉運蛋白2抑制劑可減少糖尿病腎臟病惡化與 因心臟衰竭住院的風險。	高	強烈建議	
及早合併使用較低劑量的多種口服抗糖尿病藥物，比起使用 高劑量的單一口服抗糖尿病藥物，更能有效控制血糖，且較 不會增加藥物的副作用。	中	強烈建議	

口服糖尿病藥(I)



種類	治療的建議與考量
雙胍類 Metformin	• 所有促胰島素分泌劑在降低血糖的效果上，大致相似。病患合併肝、腎、心臟功能不全，低血 氧時，不建議使用。 • 腎絲球體過濾率（eGFR）小於 30 ml/min/1.73m2時，禁止使用；腎絲球體過濾率（eGFR）介於 30~45 ml/min/1.73m2時，應減量使用。 • 80歲以上的第2型糖尿病患者，若以前 未曾使用過metformin，不建議以 metformin治療。 • 不會增加體重，單獨使用時，較少發生 低血糖。 • 可能有腸胃道的副作用。

Metformin具有長期安全性及心血管保護



UKPDS 34 試驗 (Metformin)

初診斷第 2 型過重的糖尿病患者

糖尿病相關試驗終點事件

死亡率

腦中風

觀察性研究的統合分析 (Meta-analysis)

共815639人

死亡率

-26%

(相較於對照組)

回朔性世代追蹤研究

第 2 型糖尿病合併腎功能不全患者

主要不良心血管事件

(心肌梗塞住院、出血或缺血性腦中風、短暫性腦缺血發作、心血管死亡)

-20%

(相較於sulfonylurea)

回朔性世代追蹤研究

急性冠心症的糖尿病患者

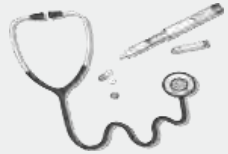
再發性心血管事件

-67%

(相較於non-metformin)

UKPDS 34 Lancet 1998; 352: 854–65; JAMA. 2019;322(12):1167-1177;
Circulation. 2019;140:1004–1014;
Komaru Y, et al. J Diabetes Complications. 2019;doi:10.1016/j.jdiacomp.2019.107511.

Metformin的治療建議與考量



雙胍類 (Biguanide)

Metformin

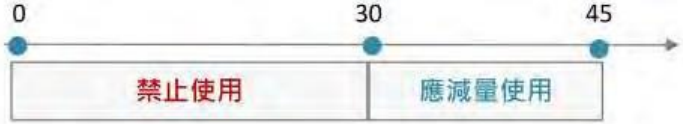
- 病患合併**肝**、**腎**、**心臟功能不全**
- **低血氧**時

不建議使用

- 不會增加**體重**
- 單獨使用時，較少發生**低血糖**

- **腎功能不全**之劑量調整建議

腎絲球體過濾 (eGFR)
mL/min/1.73m²

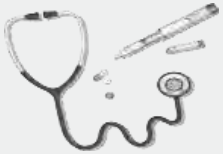


- **80歲**以上之第 2 型糖尿病患者，若**未**曾使用過 **metformin**

不建議使用

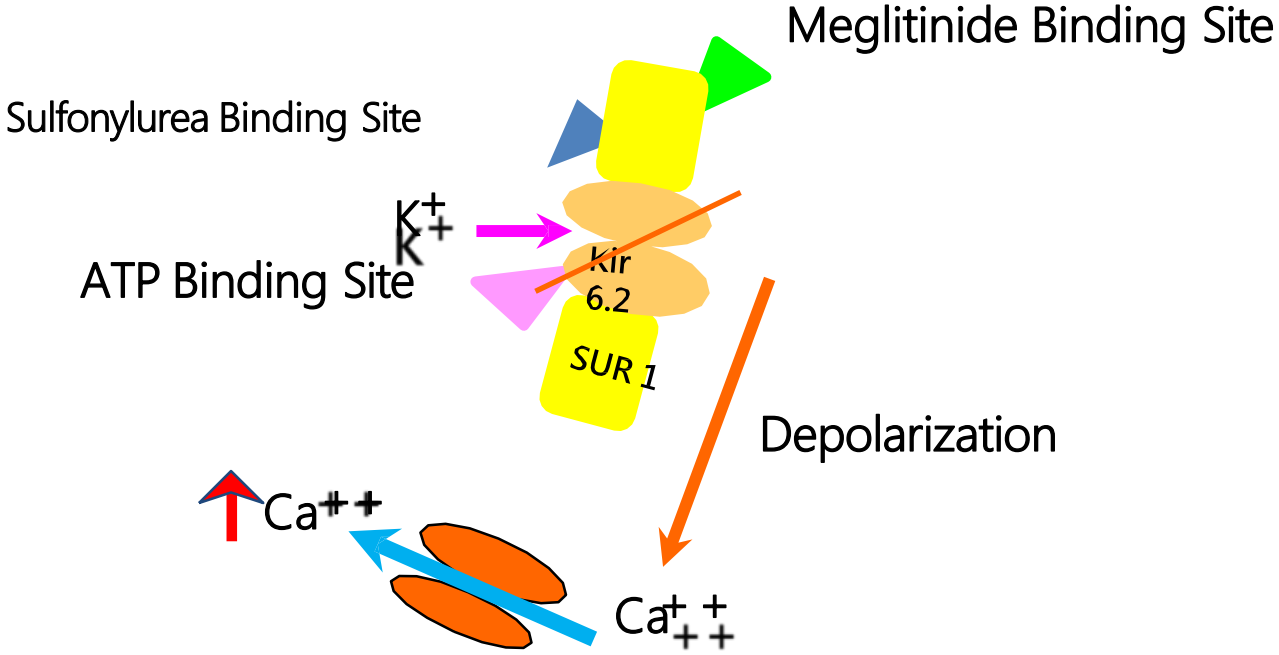
- 可能有**腸胃道**的副作用

口服糖尿病藥(II)

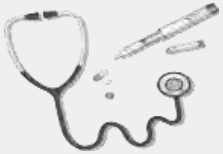


種類	治療的建議與考量
促胰島素分泌劑 磺醯脲類 Gliclazide Glimepiride Glipizide Glibenclamide 非磺醯脲類 Repaglinide Nateglinide Mitiglinide	• 所有促胰島素分泌劑在降低血糖的效果上，大致相似。 • 促胰島素分泌劑都可能引起低血糖或體重增加。 • 對於低血糖風險較高的族群(例如:老年患者， 肝、腎功能不全，或血糖波動較大的患者)， 考慮使用較短效的促胰島素分泌劑(例如:非磺 醯脲類)。 • 非磺醯脲類(Repaglinide、Nateglinide和Mitiglinide)主要用於降低餐後血糖波動。

促胰島素分泌劑在胰島β細胞的作用



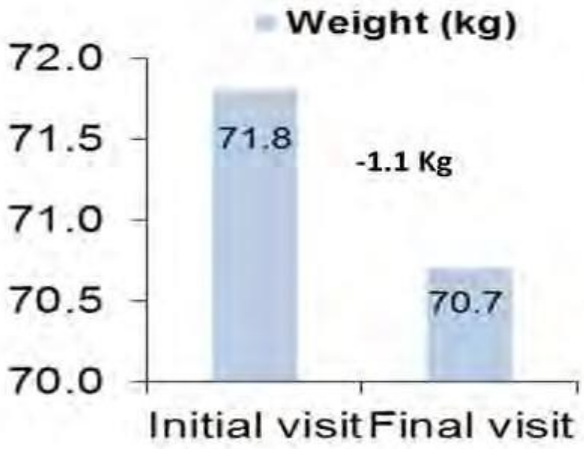
口服糖尿病藥(III)

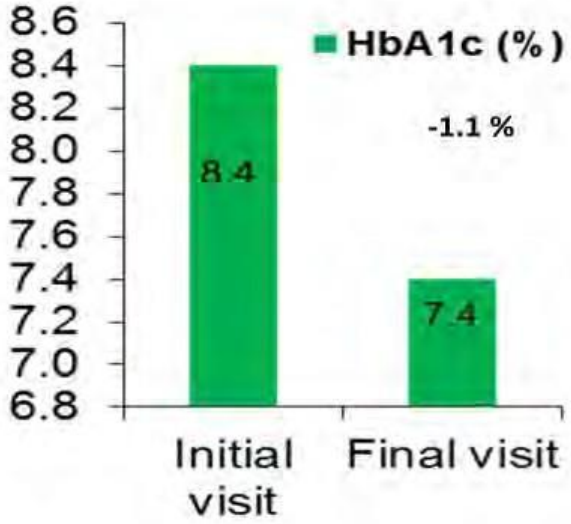


種類	治療的建議與考量
阿爾發葡萄糖苷酶抑制劑 Acarbose Miglitol	• 可降低餐後血糖波動。 • 可能有腸胃道的副作用。 • 不會增加體重，單獨使用時不會發生低血糖。 • 發生低血糖時，建議使用單醣(例如:葡萄糖) 來治療。

Glucobay在亞洲的研究顯示有降體重效果

- Observational study in **China**, **Middle-East, Indonesia, Morocco, Pakistan, Philippines, Poland and Taiwan**
- **14,574 patients** with type 2 diabetes (74.1% previously treated with glucose-lowering agent); Final visit = **11.3 weeks** (mean)





P<0.0001

Li C et al. *Diabetes Res Clin Pract* 2011;92:57-64

AGI降低餐後血糖波動

阿爾發葡萄糖苷酶抑制劑 (AGI)

Miglitol、Acarbose

- 可降低**餐後血糖波動**
- 可能有**腸胃道副作用**
- 不會增加**體重**
- 單獨使用，不會發生**低血糖**

低血糖時

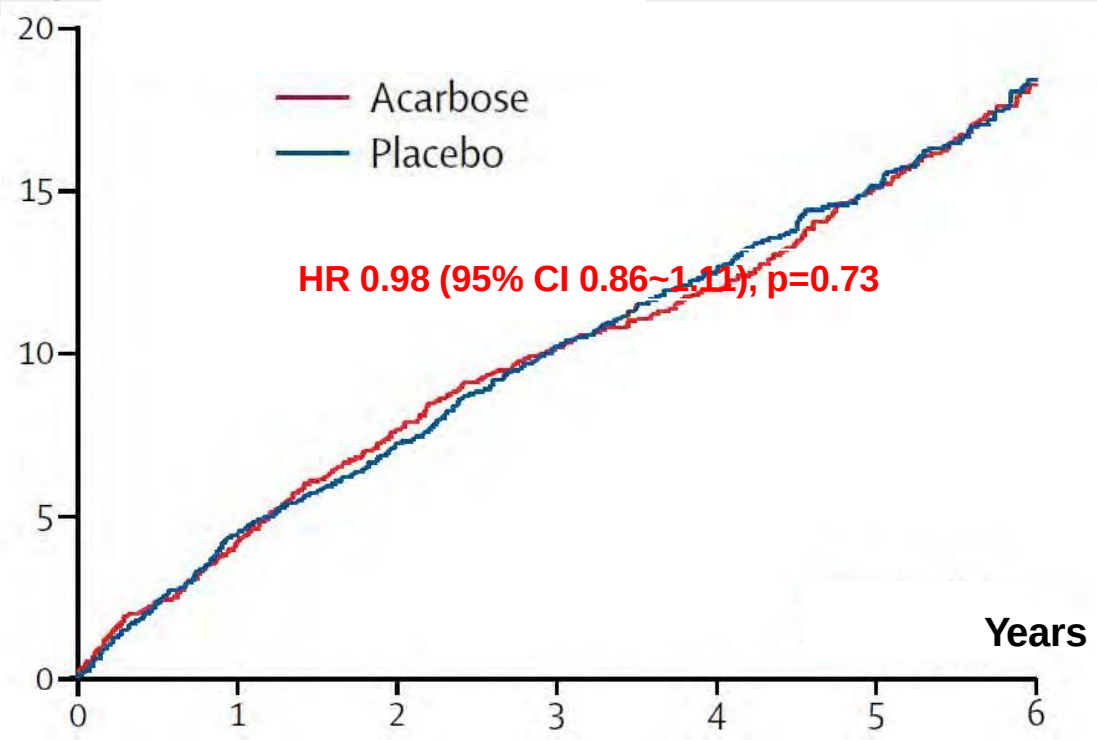
- 建議使用單醣 (葡萄糖)治療

Acarbose Cardiovascular Evaluation (ACE)

Holman RR, et al. Am Heart J. 2014; 168: 23-9.

Acarbose Cardiovascular Evaluation (ACE)

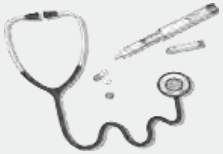
Five-point MACE



Holman RR, et al. Lancet Diabetes Endocrinol. 2017.

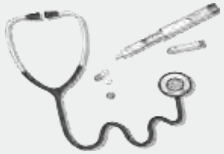
AGI與心血管疾病預後

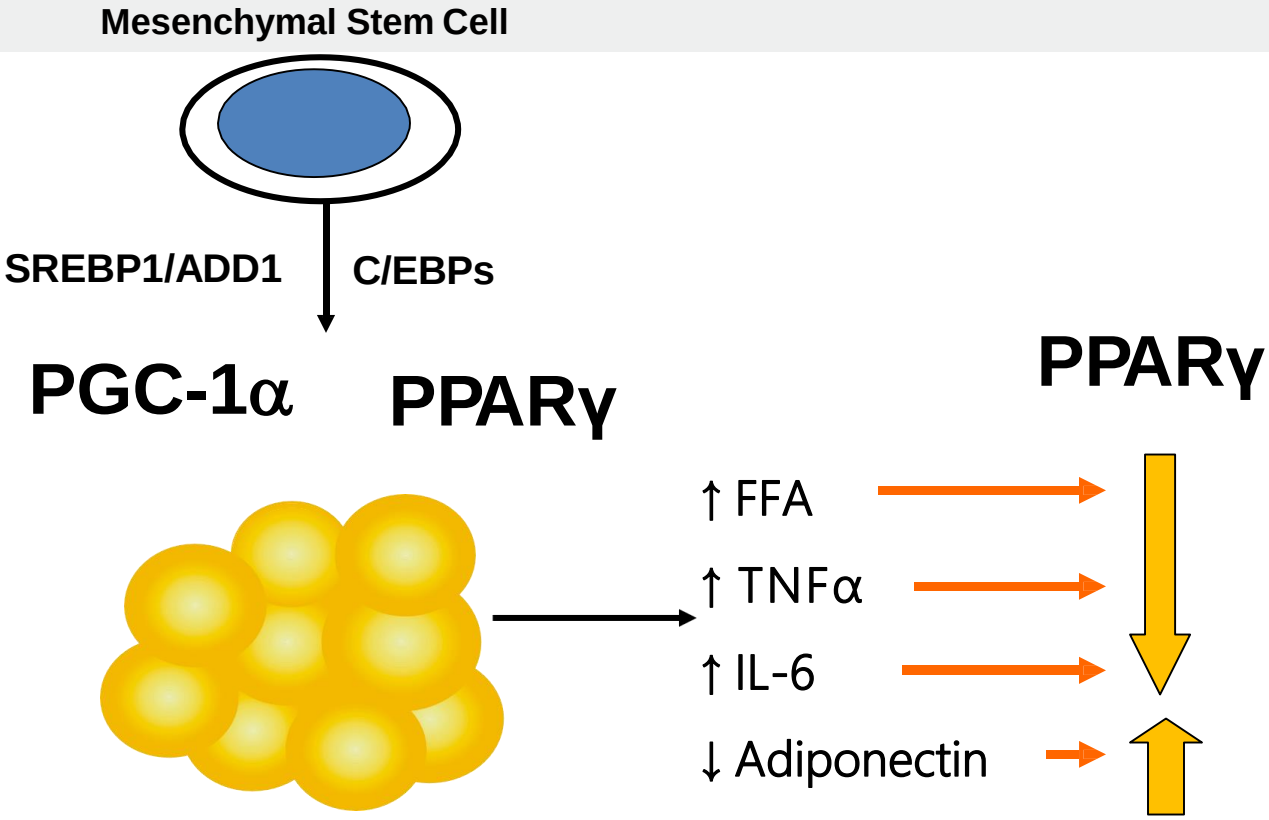
口服糖尿病藥(IV)



種類	治療的建議與考量
Thiazolidinedione Pioglitazone	• 患者肝功能不全（血清轉胺酶，ALT，超過 正常值上限的2.5倍），或紐約心臟學會（New York Heart Association，NYHA）功能分類第III級和第IV級心臟衰竭時。不建 議使用 。 • 約需6-12週才達到最大療效。 • 可能會出現體液滯留、水腫和體重增加的現象。 • 若與胰島素合併使用，可能會增加水腫和鬱 血性心衰竭的風險。

PPARγ在脂肪細胞的作用





Pioglitazone的治療建議與考量

Thiazolidinedione (TZD)

Pioglitazone

- 肝功能不全*
- 嚴重心臟衰竭**

不建議使用

*血清轉胺酶 (ALT) 超過正常值上限的 2.5 倍

**NYHA (New York Heart Association, 紐約心臟學會) 功能分類第 III 級和第 IV 級

可能的副作用：

- 體液滯留
- 水腫
- 體重增加

Max.

Pioglitazone

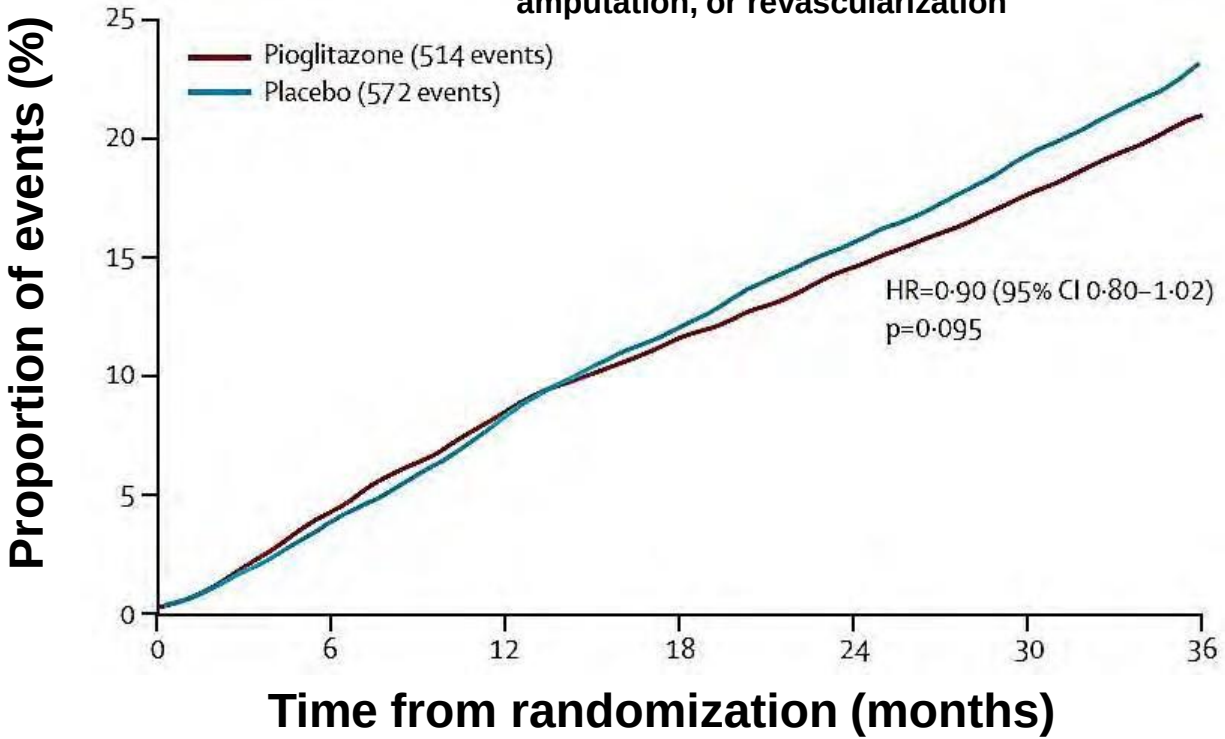
- 約需 **6-12** 週才達到**最大療效**

若與胰島素合併使用，可能會增加的風險：

- 水腫
- **鬱血性心衰竭**

Proactive Study: Kaplan-Meier Curve of Time to Primary End Points

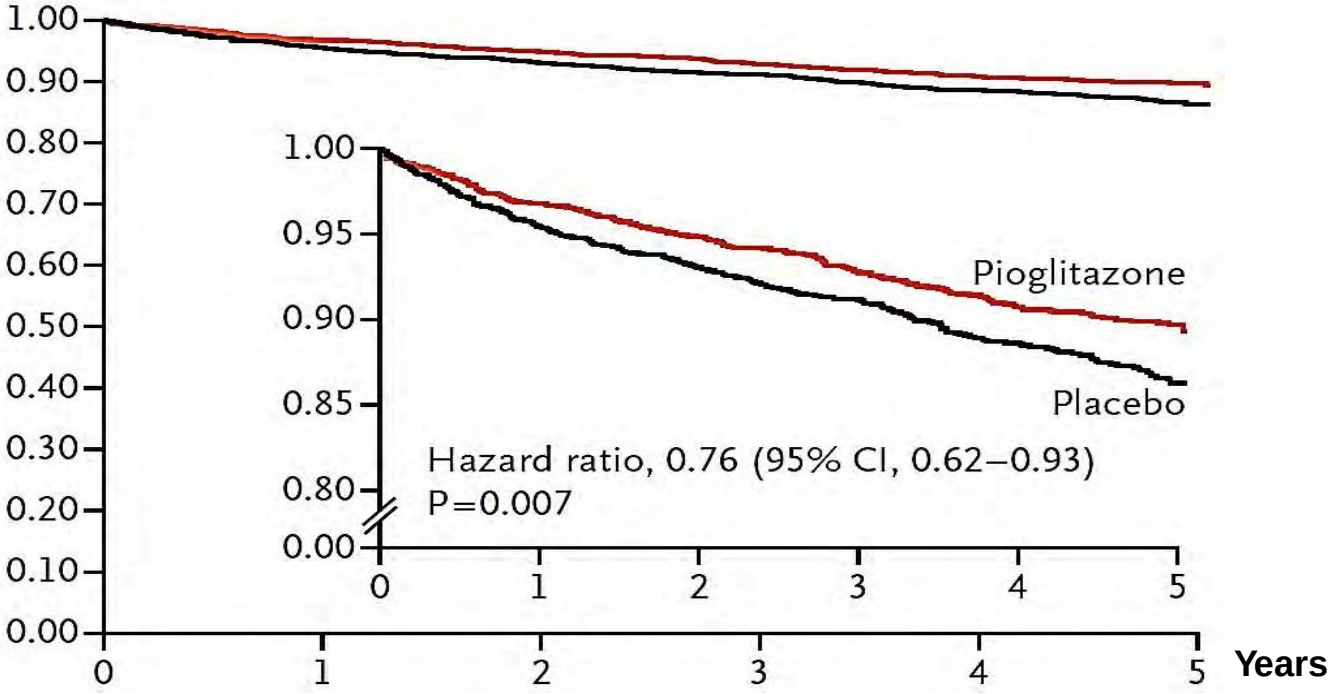
Death from any cause, non-fatal MI, stroke, ACS, leg amputation, or revascularization



Dormandy JA, et al. Lancet. 2005; 366: 1279-89.

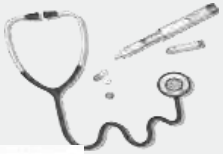
Insulin Resistance Intervention after Stroke

Event-free survival (Primary outcome: any stroke or MI)



Kernan WN, et al. N Engl J Med. 2016; 374: 1321-31

Pioglitazone與心血管疾病預後



PROACTIVE 試驗 (Pioglitazone)

第 2 型糖尿病合併心血管疾病的患者

次要試驗終點風險
（死亡率、非致死性心肌梗塞、腦中風）

-16%

(相較於對照組)

IRIS 試驗 (Pioglitazone)

缺血性腦中風或暫時性腦缺血發作的患者併有高胰島素阻抗性(HOMA-IR>3)

主要試驗終點風險
（致死或非致死性腦中風、心肌梗塞）

-24%

(相較於對照組)

TOSCA.IT 試驗 (Pioglitazone vs. sulfonylurea)

第2型糖尿病，metformin控制不佳的患者

無法減少主要不良心血管事件
(死亡率、非致死性心肌梗塞、非致死性腦中風、 緊急冠狀動脈再通)

(相較於sulfonylurea組)

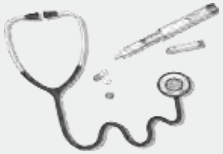
在TOSCA.IT試驗中高胰島素阻抗次族群中主要不良心血管事件
(死亡率、非致死性心肌梗塞、非致死性腦中風、 緊急冠狀動脈再通)

-52%

(相較於sulfonylurea組)

Lancet Diabetes Endocrinol. 2017 Nov;5(11):887-897.
J Clin Endocrinol Metab 104: 3296–3302, 2019
N Engl J Med 2016; 374:1321-1331

口服糖尿病藥(V)



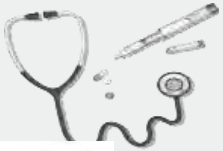
種類	治療的建議與考量
二肽基酶-4抑制劑 Alogliptin Linagliptin Saxagliptin Sitagliptin Vildagliptin	• 可能產生輕微感染如鼻咽炎及產生急性胰臟炎 等副作用。 • 不會增加體重，單獨使用時，較少發生低血糖。 • 除了linagliptin外，均需根據腎功能減少劑量。

DPP4 Inhibitors的藥理性質比較

Parameter	Sitagliptin	Vildagliptin	Saxagliptin	Alogliptin	Linagliptin
Therapeutic dose	100 mg QD	50 mg BID	5 mg QD	25 mg QD	5 mg QD
In vitro DPP-4 inhibition (nmol/L)	IC_{50}: 19	IC_{50}: 62	IC_{50}: 50	IC_{50}: 24	IC_{50}: 1
	Inhibition percentage over 24 hours				
Effect on plasma DPP-4 activity (multiple oral doses)	≥ 80% at ≥100 mg qd	≥ 80% at 50 mg bid	≥ 70% at 5 mg qd	≥ 80% at 25 mg bid	≥ 80% at 5 mg qd
	Increasing fold				
Effect on active GLP-1 levels	~2x at ≥100 mg qd	~3x at 50 mg bid	1.5-3x at ≥2.5 mg qd	2-3x at ≥25 mg (single oral dose)	4x at ≥5 mg (single oral dose)

Drugs 2011; 71 (11): 1441-1467

DPP4 inhibitors的CVOT摘要

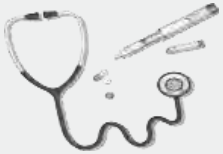


	SAVOR	EXAMINE	TECOS	CAMELINA
medication	Saxagliptin	Alogliptin	Sitagliptin	Linagliptin
Patients	16,496	5,380	14,671	6,979
Follow-up (yr)	2.1	1.5	3.0	2.2
CVD history	78.5%	100%	74%	57%
CKD history	15.6%	29.1%	9.4%	62.3%
MACE	1.00 (0.89-1.12)	0.96 (≤1.16)	0.98 (0.88-1.09)	1.02 (0.89-1.17)
HHF	1.27 (1.07-1.51)*	1.07 (0.79-1.46)	1.00 (0.83-1.20)	0.90 (0.74-1.08)

*significant

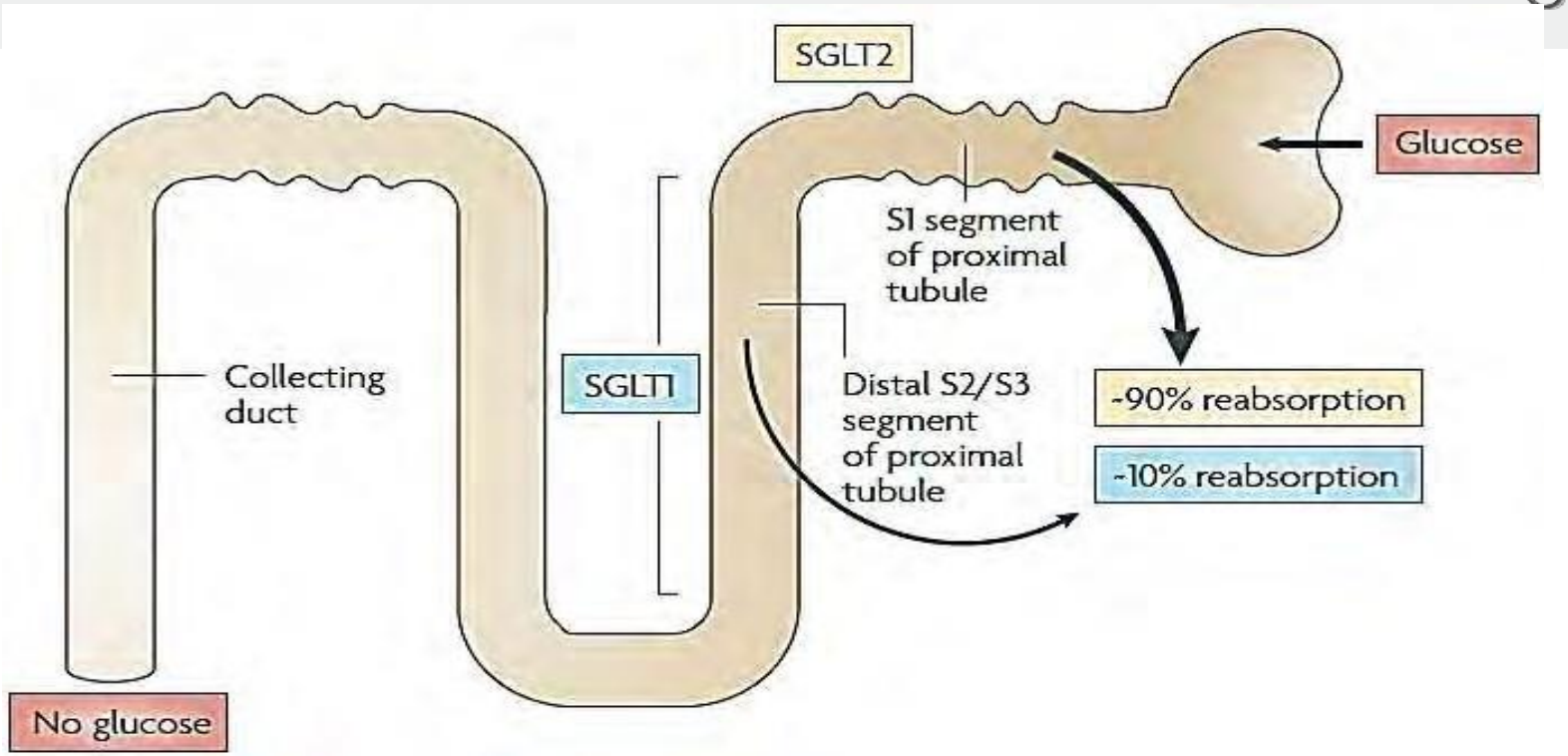
1. N Engl J Med. 2013 Oct 3;369(14):1317-26. 2. Lancet. 2015 May 23;385(9982):2067-76. 3. N Engl J Med. 2015 Jul 16;373(3):232-42. 4. JAMA. 2018 Nov 9. doi: 10.1001/jama.2018.18269. 5. JACC Heart Fail. 2018 Jan;6(1):8-17.

口服糖尿病藥(VI)



種類	治療的建議與考量
鈉葡萄糖協同轉運蛋白2抑制劑(SGLT2i) Canagliflozin Dapagliflozin Empagliflozin Ertugliflozin	• 較少發生低血糖，使用後通常可降低體重與 血壓。 • 會增加泌尿道與生殖器感染的風險。 • 可減少糖尿病腎臟病惡化與因心臟衰竭住院 的風險。

Renal Glucose Handling in Non-DM Subjects



Chao EC, Henry RR. Nat Rev Drug Discov. 2010; 9: 551-9.

SGLT2 inhibitors的藥理性質比較

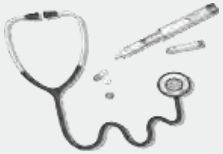
	Empagliflozin	Dapagliflozin	Canagliflozin	Ertugliflozin
Therapeutic dose (mg/day) **Starting dose**	10-25 10	5-10 5	100-300 100	5-15 5
Administration	QD With or without food	QD With or without food	QD Before the first meal of the day	QD With or without food
Peak plasma concentration (hours post-dose)	1.5	Within 2	1–2	1
Absorption (mean oral bioavailability)	≥ 60%	~ 78%	~ 65%	100%
Metabolism	Primarily glucuronidation, No active metabolite			
Elimination (half-life, hours)	Hepatic:renal 44:56 [12.4]	Hepatic:renal 22:78 [12.9]	Hepatic:renal 67:33 [13.1]*	Hepatic : renal 49.8:50.2 [16.6]
Selectivity over SGLT1	1:5000	> 1:1400	> 1:160[1]	1:2200[2,3]
Glucose excretion with higher dose (g/day)	78 (25 mg dose)	~ 70 (5 or 10mg dose)	87 (100mg dose)	75.12 (15 mgdose)[4]

SGLT, sodium glucose cotransporter; **QD,** once daily.; *For the 300 mg dose.

http://www.ema.europa.eu/.

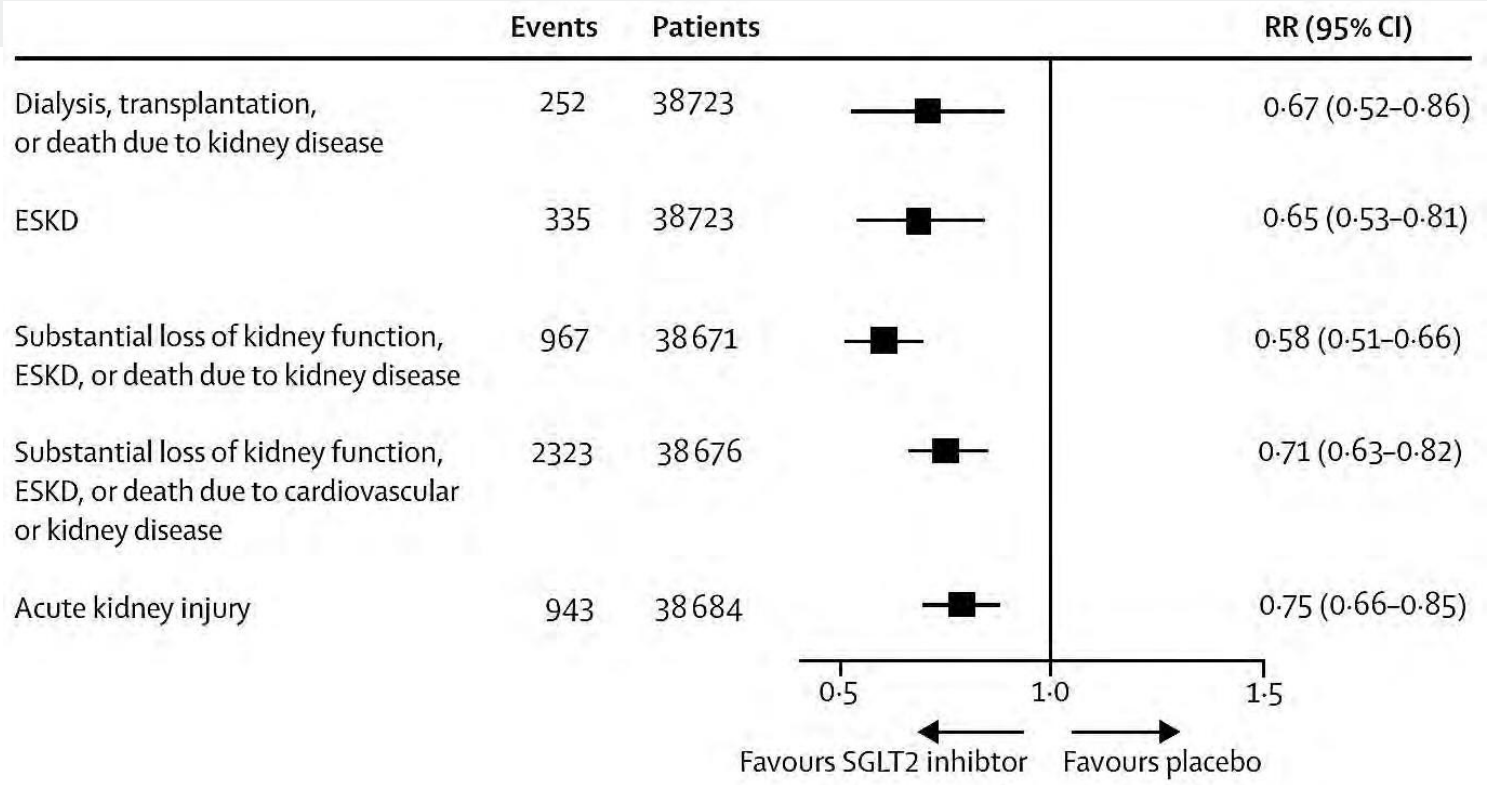
1. Sha S, et al. Diab Obes Metab. 2015; 17:188–197; 2. Mudaliar S et al. Diabetes Care. 2015;38:2344–2353; 3. Mascitti V et al. J Med Chem. 2011;54:2952–2960; 4. Sahasrabudhe V, et al. J Clin Pharmacol. 2017;57(11):1432–1443.

SGLT2i的CVOT摘要



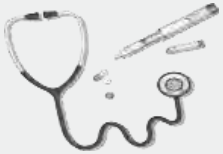
Trial	EMPA-REG[1]	CANVAS[2]	DECLARE[3]	VERTIS-CV[4]
Medication	Empaglifozin	Canagliflozin	Dapagliflozin	Ertugliflozin
No. of patients	7,020	10,142	17,160	8,246
History of CVD, %	100	66	40.6	100
Follow-up years (median)	3.1	2.4	4.2	3.5
Primary MACE Outcome, %	**-14***	**-14***	-7	-3
CV Death, %	**-38***	-13	-2	-8
Nonfatal MI, %	-13	-15	-11	+4
Nonfatal Stroke, %	24	-10	1	0
Primary HHF or CV death Outcome, %	–	–	**-17***	-12
All-Cause Mortality, %	**-32***	-13	-7	-7
Hospitalization for HF, %	**-35***	**-33***	**-27***	**-30***

Effects of SGLT-2 Inhibitors on DKD

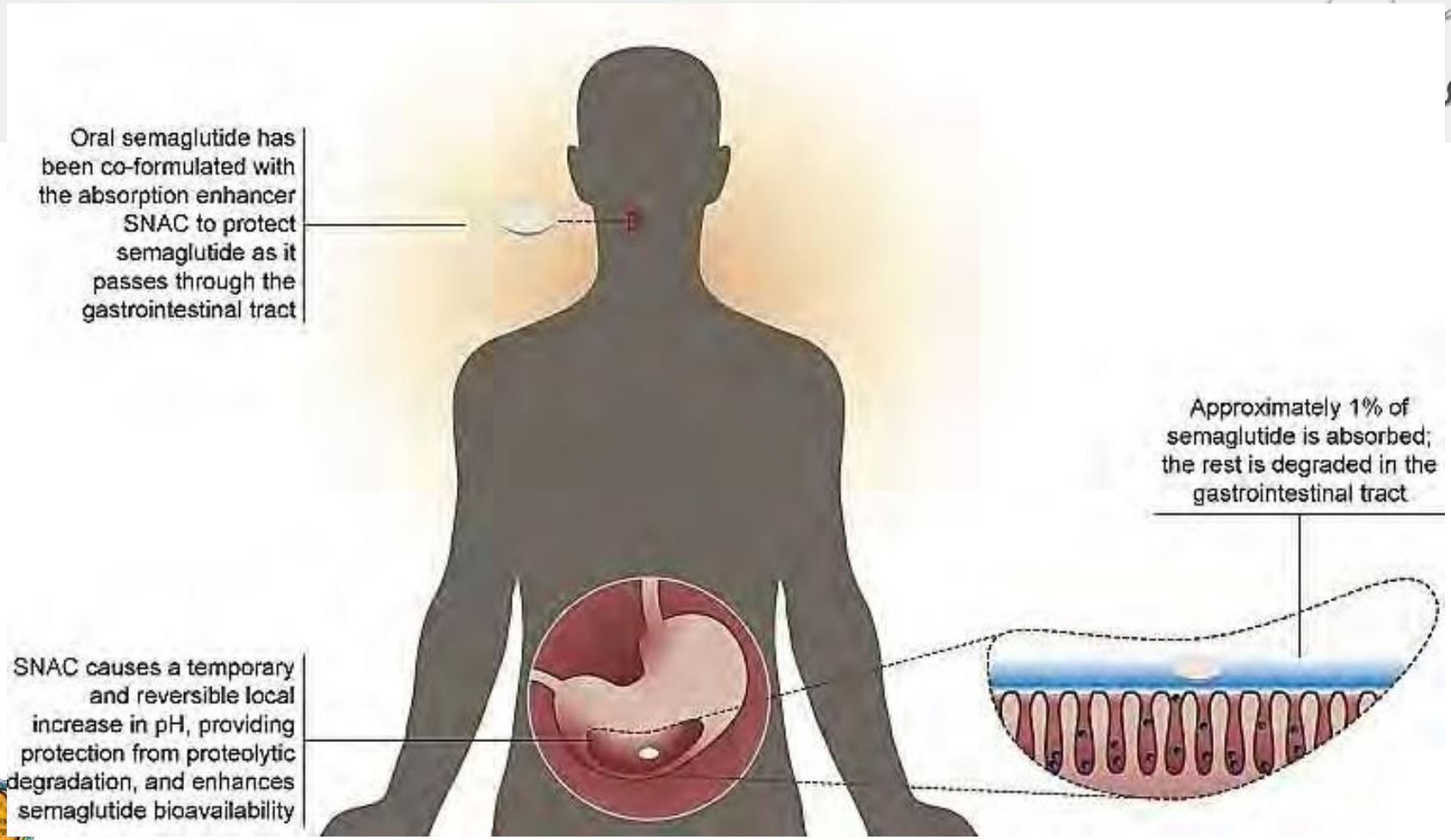


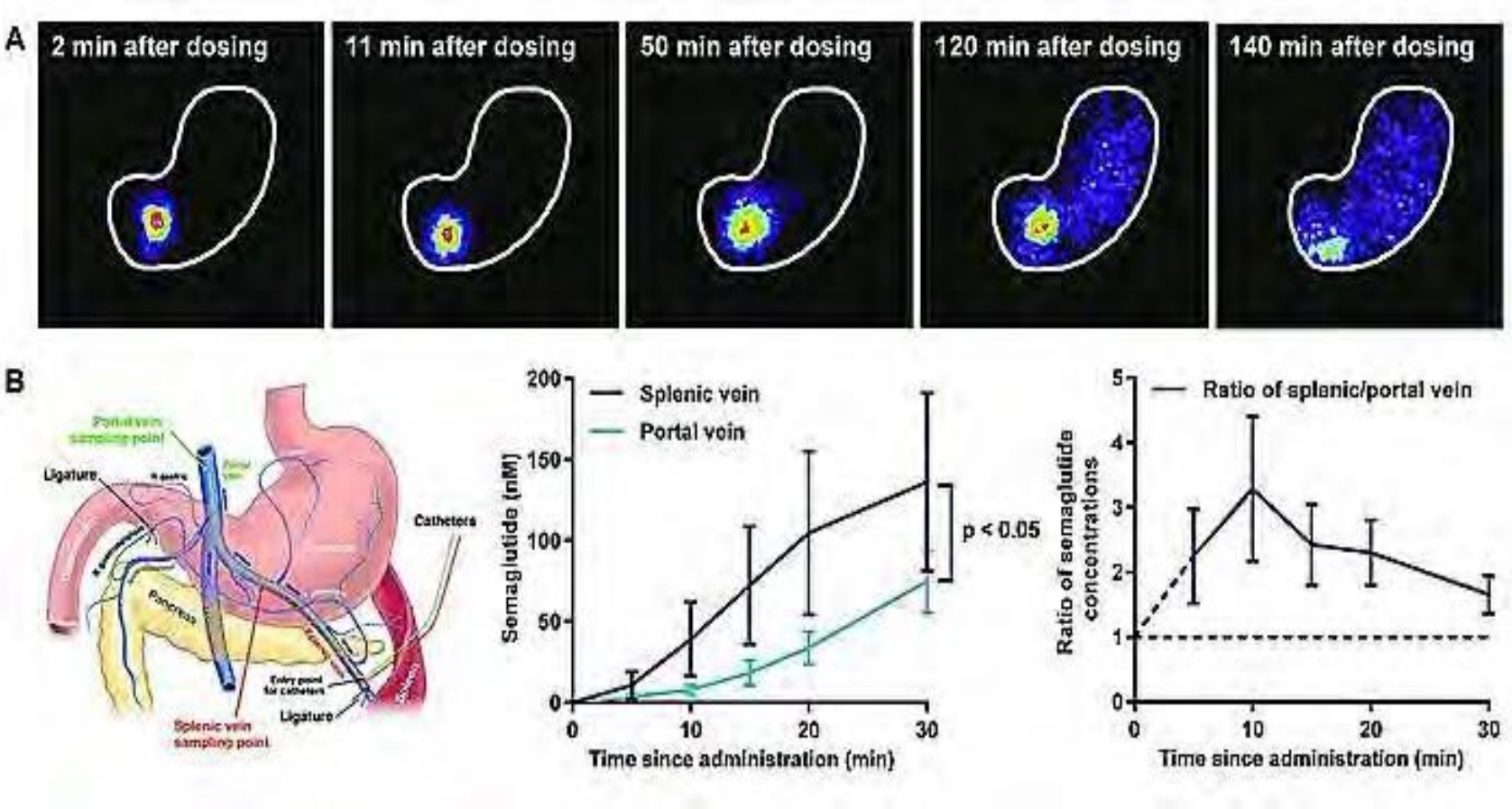
Neuen BL, et al. Lancet Diabetes Endocrinol. 2019.

口服糖尿病藥(VII)

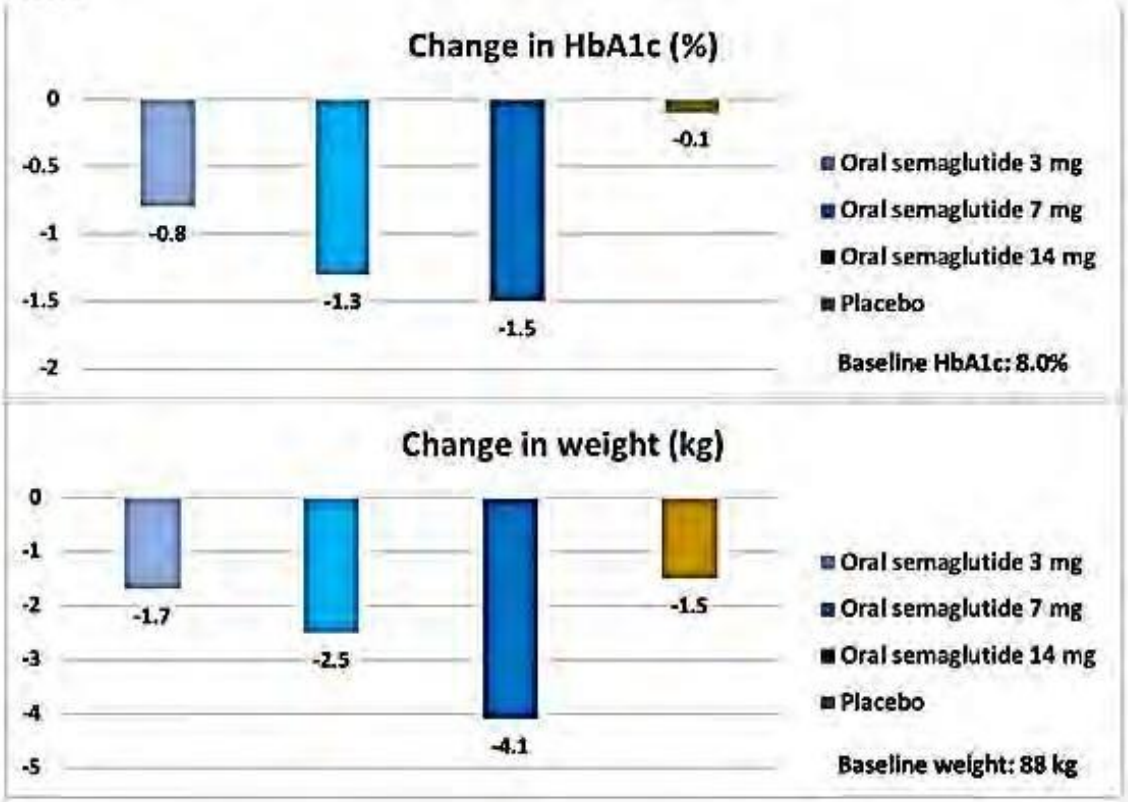


種類	治療的建議與考量
口服類升糖素肽-1受體促效劑 Rybelsus®(semaglutide)	• 有腸胃道的副作用。 • 顯著降低體重。 • 可減少糖尿病心因性死亡及總死亡的風險。


Oral semaglutide has been co-formulated with the absorption enhancer SNAC to protect semaglutide as it passes through the gastrointestinal tract
Approximately 1% of semaglutide is absorbed; the rest is degraded in the gastrointestinal tract
SNAC causes a temporary and reversible local increase in pH, providing protection from proteolytic degradation, and enhances semaglutide bioavailability


A
2 min after dosing
11 min after dosing
50 min after dosing
120 min after dosing
140 min after dosing
B
Ligature
Catheters
Pancreas
Splenic vein sampling point
Ligature
Splenic vein
Portal vein
Somaglutide (nM)
Time since administration (min)
p < 0.05
Ratio of splenic/portal vein
Ratio of somaglutide concentrations
Time since administration (min)

PIONEER 1: Daily oral semaglutide versus placebo in people with type 2 diabetes treated with diet and exercise alone

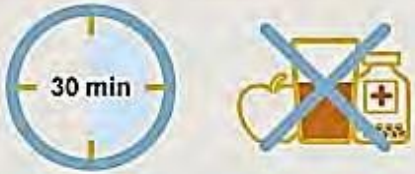


Take when you wake

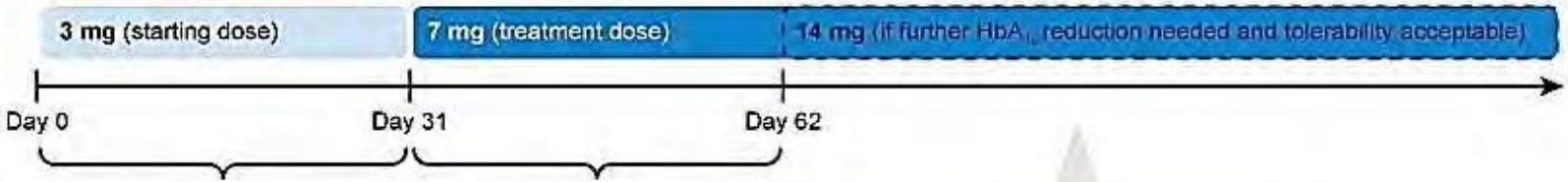
Wake up and take your semaglutide tablet straight away with up to half a glass of water (approximately 120 mL/4 fl oz)

Then wait

Wait at least **30 minutes** before eating, drinking anything else or taking any other oral medication



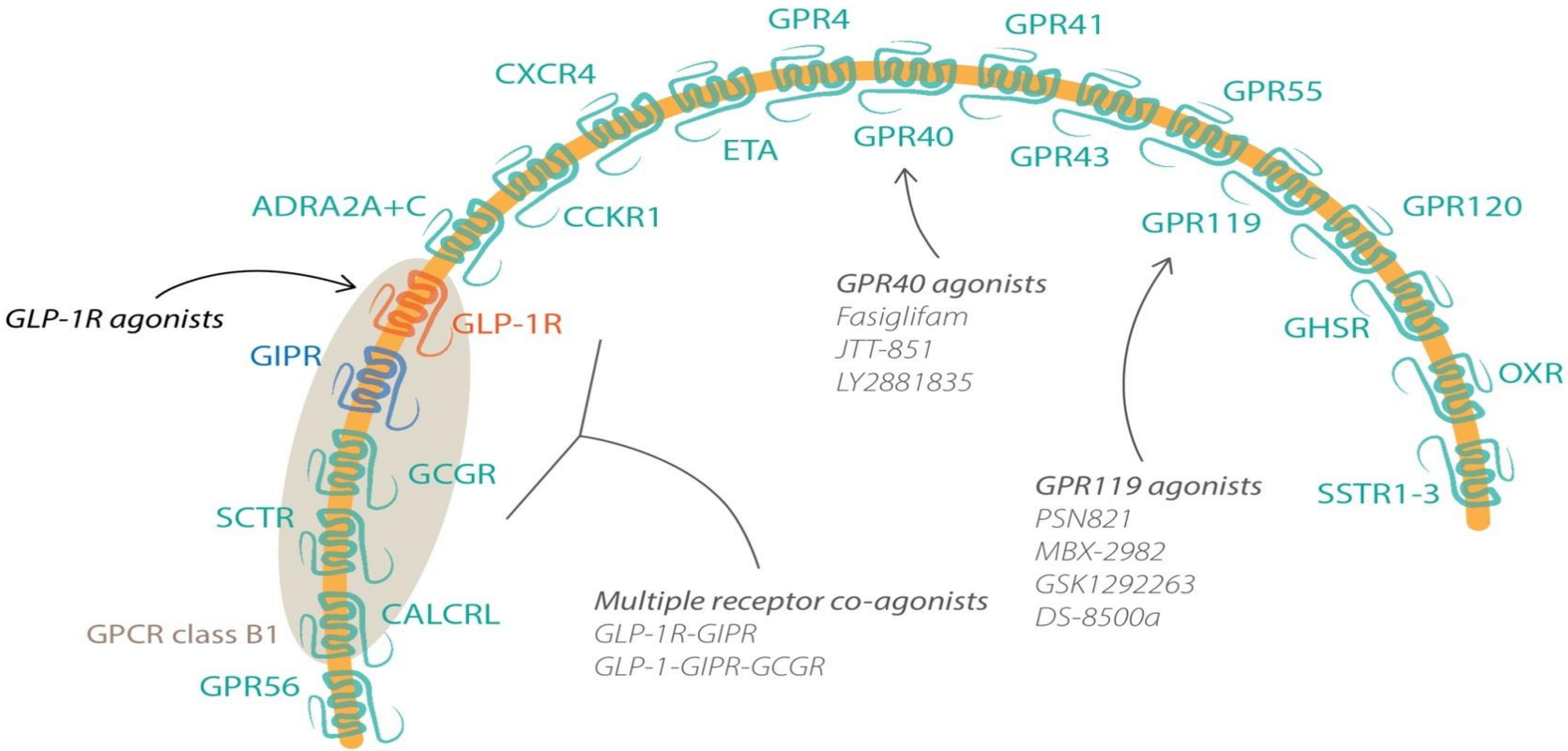
Dosing schedule



Mitigation of GI side effects

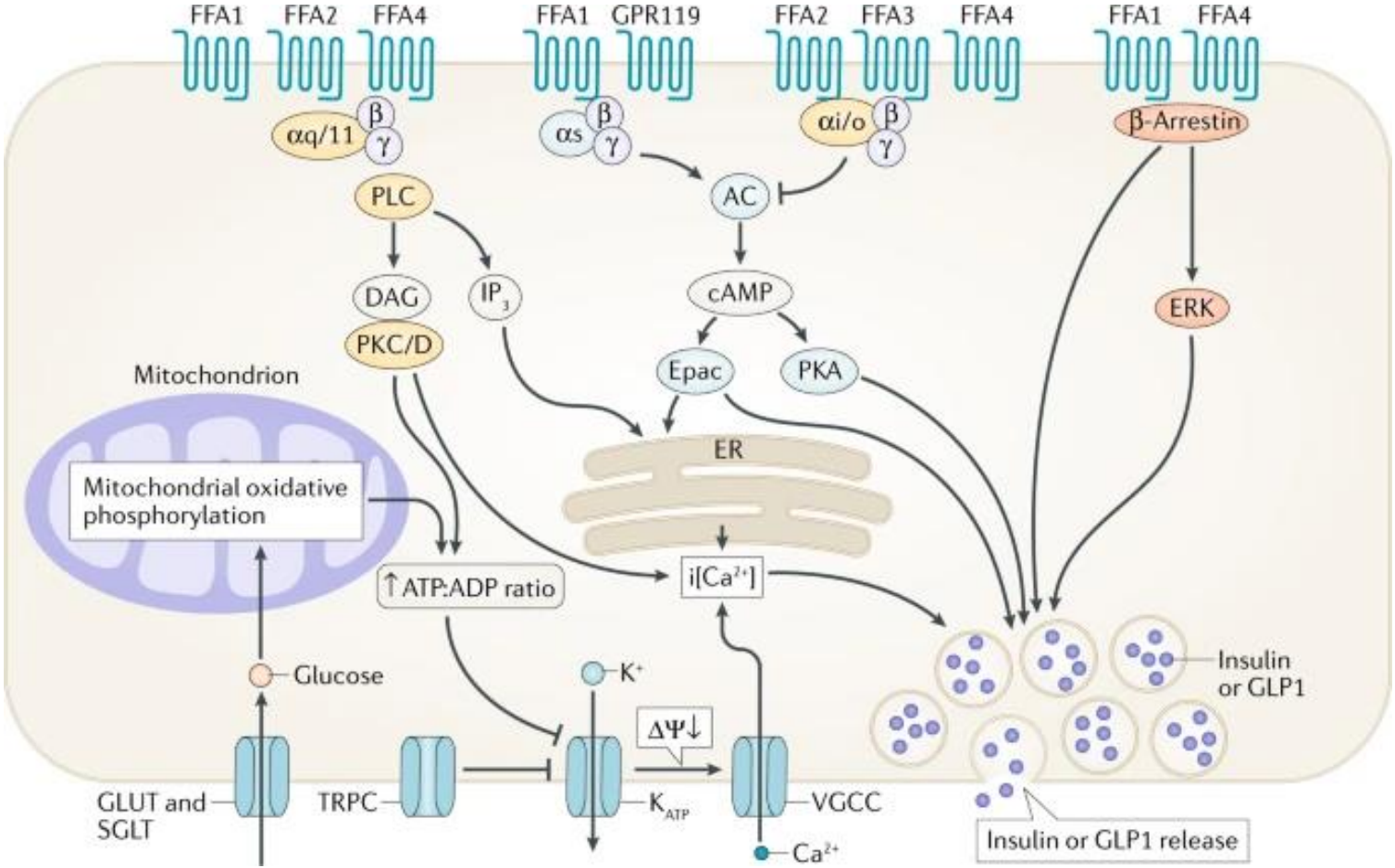
1. **Discuss potential for GI side effects** and rationale for dose escalation; explain that any nausea and other symptoms are likely to be non-severe and last for a few weeks (but can recur when the dose is increased)
2. **Suggest mitigating measures** in the case of GI symptoms, e.g. meal size reduction, natural supplements
3. **Consider adjusting the dose** of oral semaglutide or metformin, or temporarily withholding treatment until symptoms resolve, in the case of severe or persistent GI effects

G protein-coupled receptors on the human beta cell

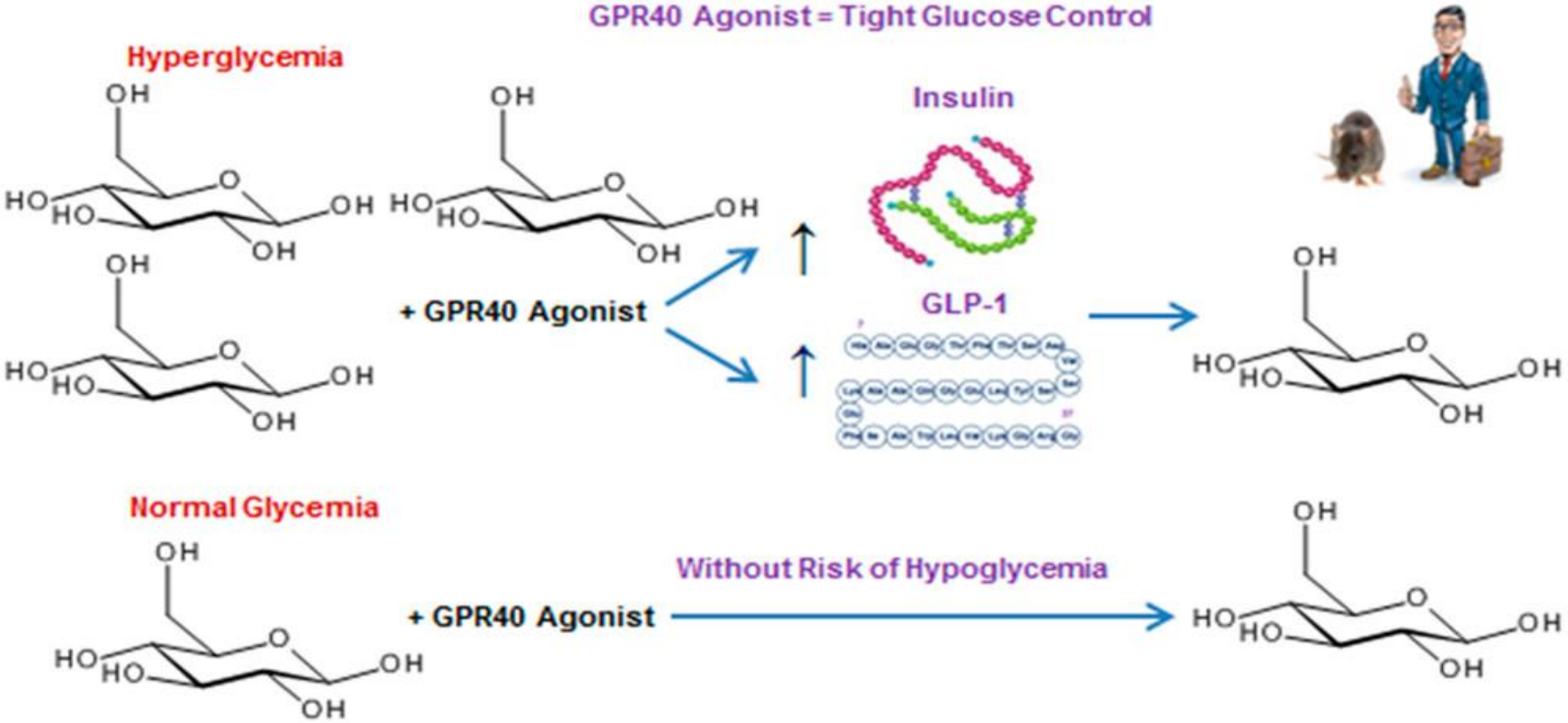


Peptides. 2022 May;151:170749

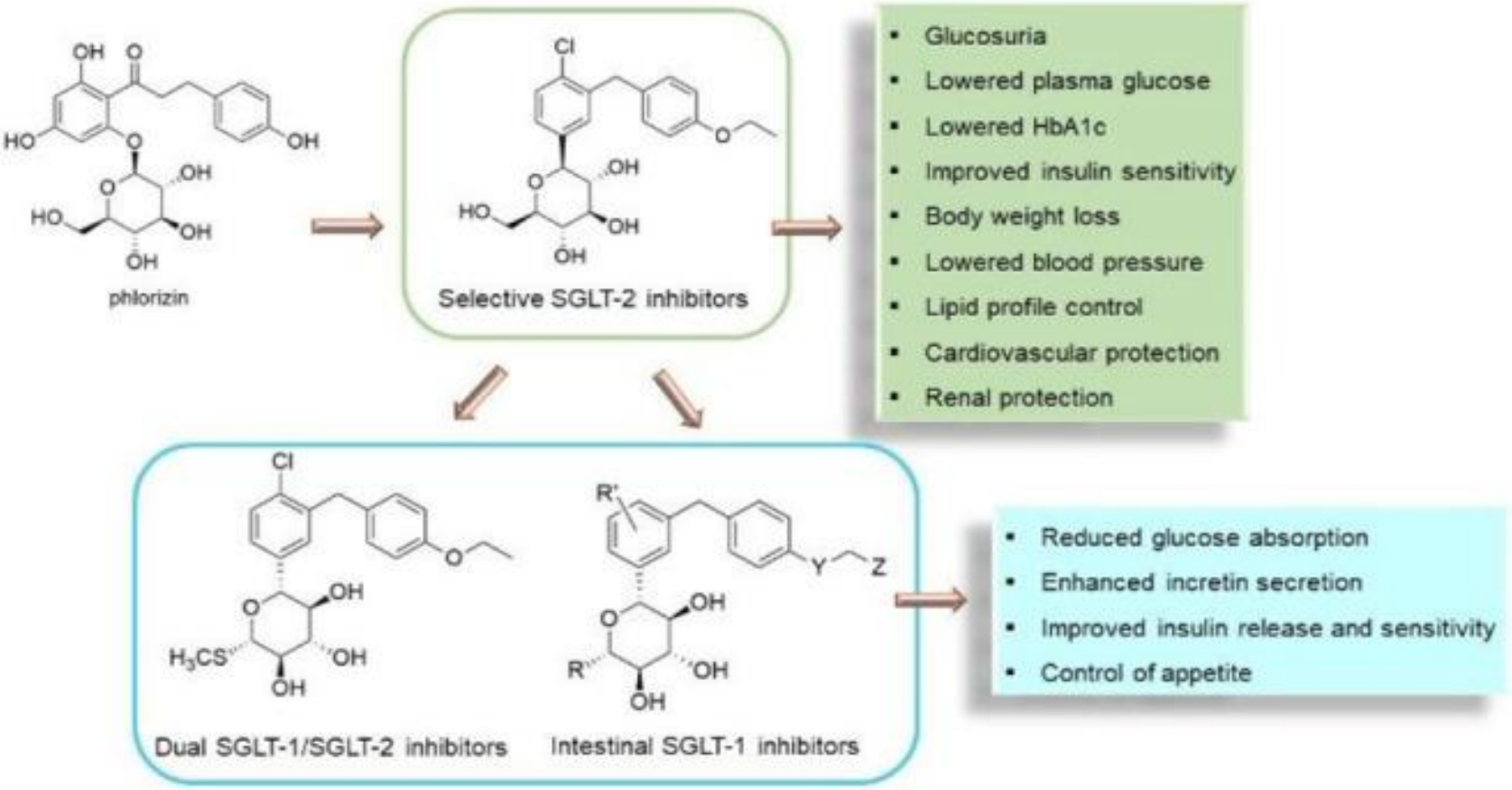
Lipid metabolite-specific GPCR signalling in the control of hormone secretion.



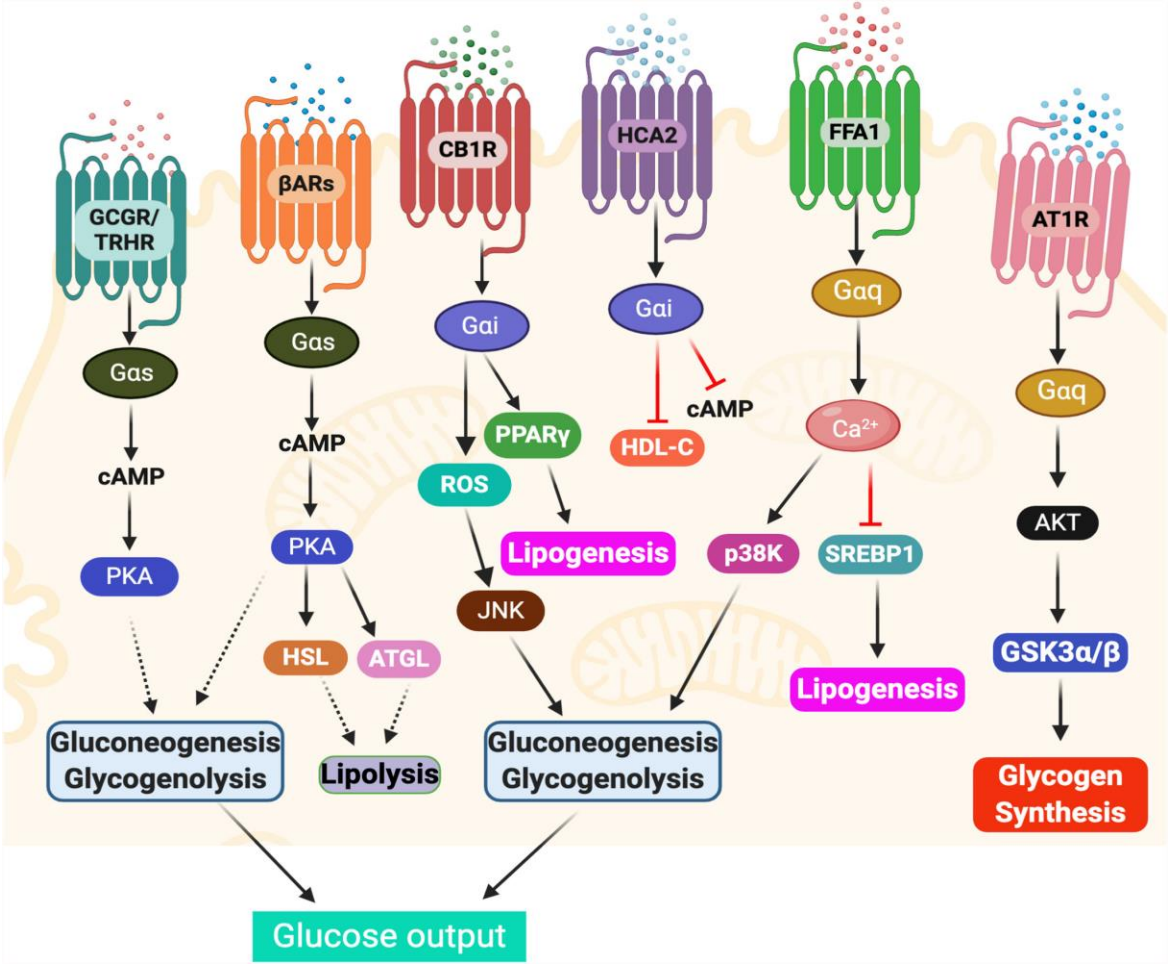
Nature Reviews Endocrinology volume 17, pages162–175 (2021)



J. Med. Chem. 2016, 59, 24, 10891–10916



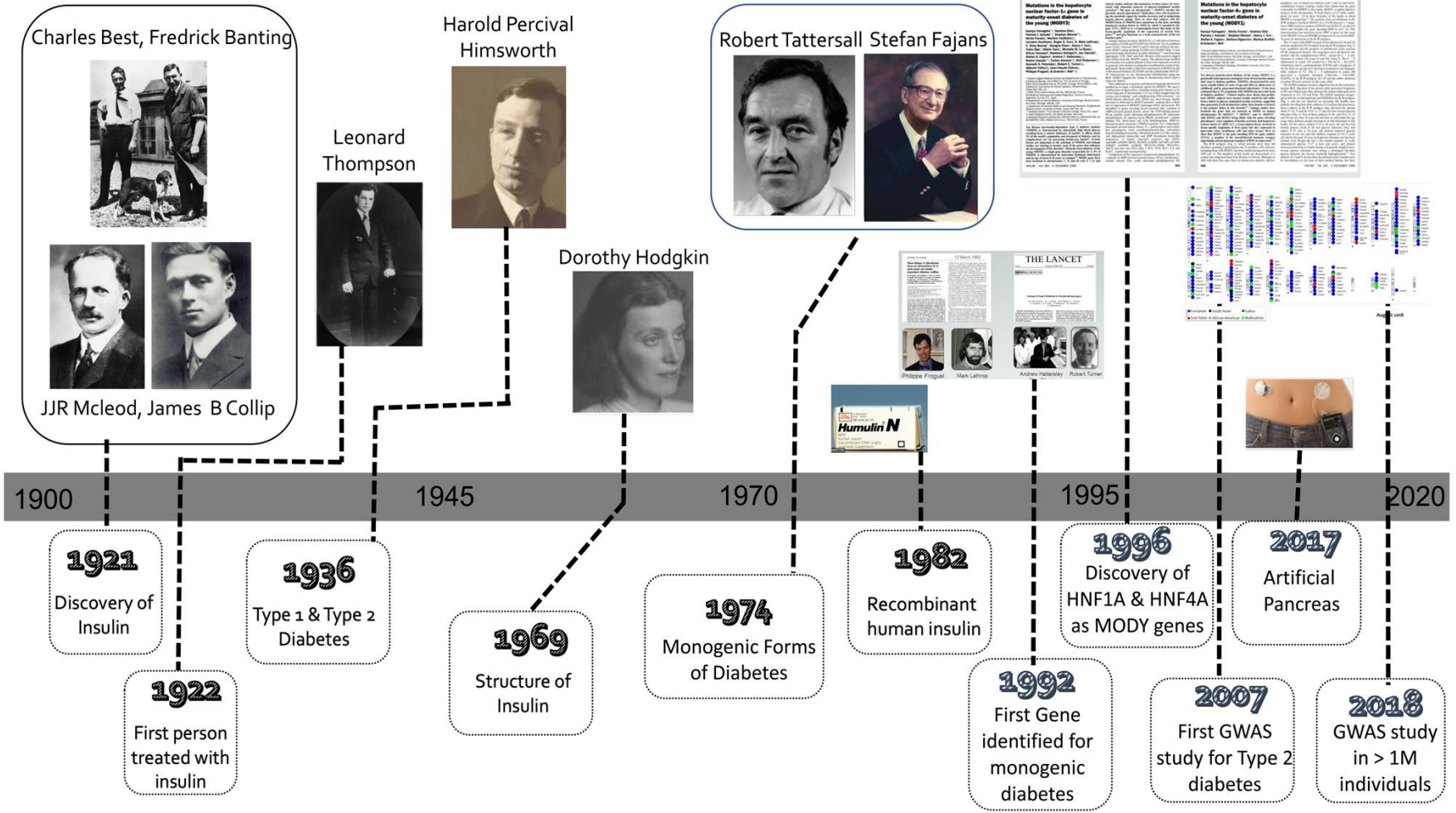
J Med Chem. 2022 Aug 25; 65(16): 10848–10881



The FEBS Journal, Volume: 288, Issue: 8, Pages: 2622-2644, First published: 07 March 2021, DOI: (10.1111/febs.15800)

Outline

- Drugs development in diabetes
- Oral antidiabetic drugs (OAD)
- **Injectable antidiabetic drugs (IAD)**
- Summary

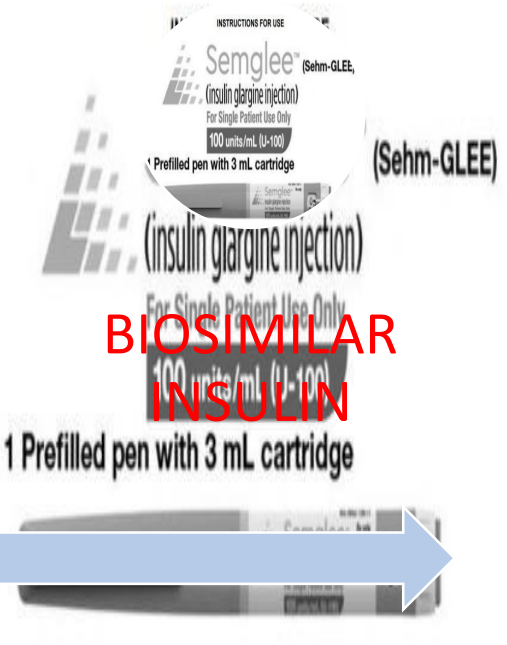


Timeline indicating key genetic discoveries in the context of our understanding of the hormone insulin and its use therapeutically.

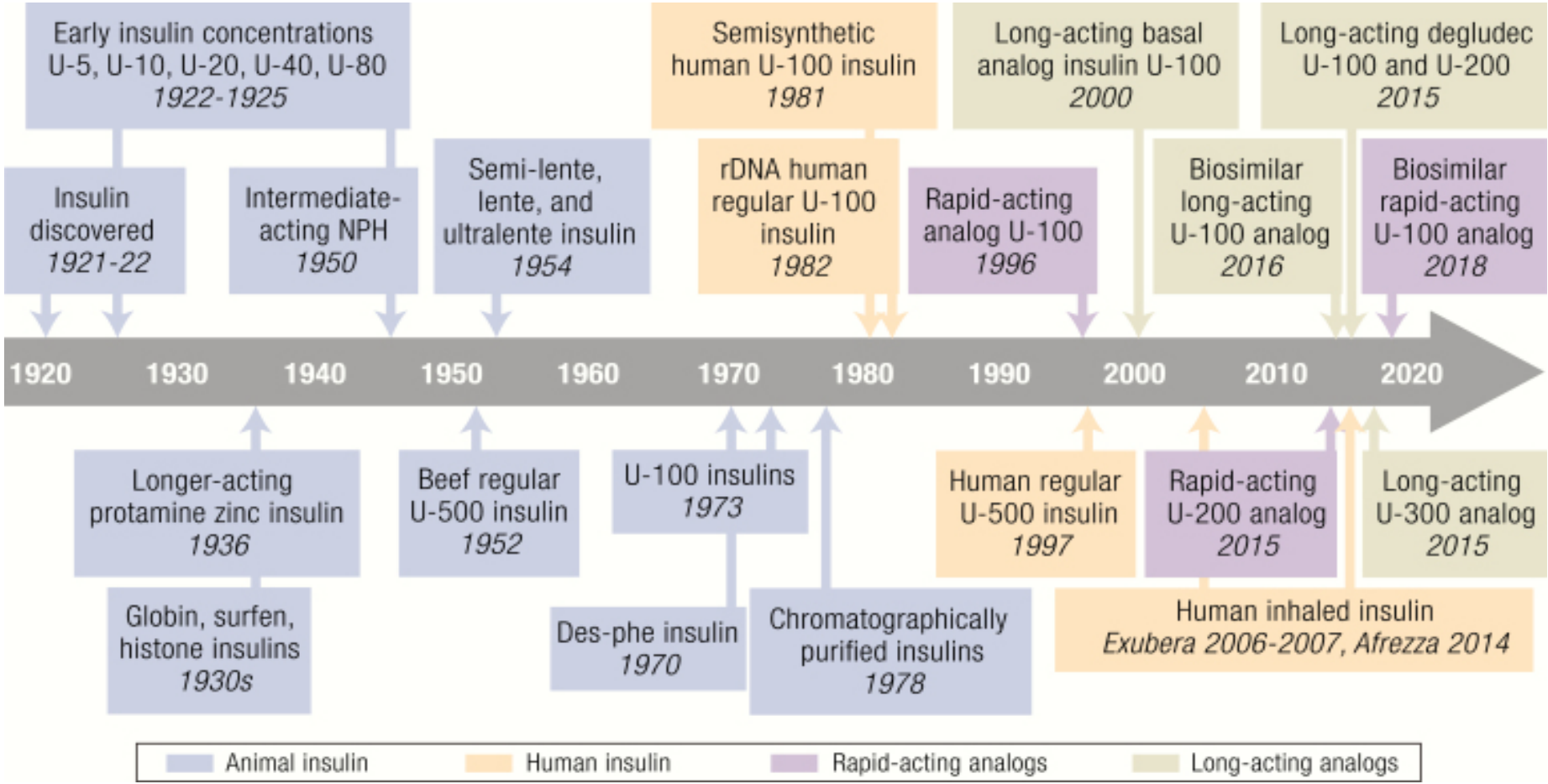
100 Years of Insulin

1941 INSULIN AMENDMENT

GENETICALLY-MODIFIED INSULIN



BIOSIMILAR INSULIN



Endocr Rev. 2020 Oct; 41(5): 733–755.

Teaching Note: Topics to include are name of insulin, accurate dose measurement, timing of administration, onset, peak, and duration, injection sites, and storage requirements. Ask patient to demonstrate preparing and injecting insulin. Hypoglycemia is a risk for all patients taking insulin; include definition, risk factors, carrying medical ID, recognition/symptoms, glucose monitoring, and treatment options.

Products Available	Onset	Peak	Duration	General Use
Rapid-Acting Insulin Analogs				
Aspart (Novolog) Glulisine (Apidra) Lispro (Humalog) Available in vial and pen form	15 min	1–2 hours	4–6 hours	Used as a bolus or mealtime dose, may be administered just prior, during, or immediately after a meal. Drugs of choice for prandial or mealtime insulin.
Short-Acting				
Regular insulin (Humulin R, Novolin R) Available in vial	30–45 minutes	2–4 hours	6–8 hours	Can be administered as bolus or mealtime insulin, but should be administered 30 to 45 minutes prior to the meal.
Intermediate-Acting				
NPH insulin (Humulin N, Novolin N)	1–2 hours	6–12 hours	12–24 hours	Requires twice-daily administration.
Long-Acting Insulin Analogs				
Detemir (Levemir) Glargine (Lantus) Available in vial and pen form	1–2 hours	No peak	12–24 hours	Basal or background insulin of choice; peakless; generally given once daily, every 24 hours.
Premixed Insulin				
70% insulin aspart protamine + 30% insulin aspart (NovoLog Mix 70/30); 75% insulin lispro protamine + 25% insulin lispro (Humalog Mix 75/25) Available in pen form	15–30 min	1–6 hours	Up to 24 hours	Combining protamine with aspart or lispro, allows for slow, continuous release and serves as the basal component of the combination.
70% NPH + 30% regular (Humulin 70/30, Novolin 70/30) 50/50 preparations are also available	30–45 minutes	2–12 hours	Up to 24 hours	This combination is the least expensive of the mixed insulins, however, is less desirable given the delayed onset of regular insulin and difficulties with meal timing
Concentrated Insulin U500	30–40	2–4	6–10	Taken 30 minutes before meals. Contains 500 units/mL. Rather than the standard 100 units/mL.

Note. Table recreated with information from Olson et al. (2014) and Inzucchi et al. (2015).

胰島素的劑量與治療計劃(1)

(一) 初次使用劑量及注射計劃乃取決於多項因素如

1. 糖尿病類型?
2. 臨床判斷具胰島素缺乏或/和胰島素阻抗?
3. 患者用餐時間?
4. 餐食量與成份?
5. 體能活動量 (時段、時間及程度)?
6. 生活作息、睡覺習慣...等。
7. 若病患為長者，需考慮由照護者或同住親友協助注射。

(二) 與患者一起設定個人餐前、餐後、睡前、睡覺等時間點可達成的血糖目標值。

胰島素的劑量與治療計劃(2)

(三) 之後再依自我血糖監測(SMBG)值調整生活習慣，及注射必要的胰島素劑量，避免低血糖發作，以求達到最佳血糖控制及健康的體適能。

(四) 胰島素的需求量（第1型糖尿患者或BMI介於24到27）為0.5~1.0單位/公斤/天。於胰島素阻抗、生病、重大壓力狀況時所需量可能要增加，甚至加倍。但於糖尿病蜜月(honeymoon)期患者，胰島素需減量（約0.2~0.6單位/公斤/天）。

胰島素的劑量與治療計劃(3)

(五) 正常人胰臟分泌胰島素約為0.5~1單位/小時，在胰島素與多種反向調節賀爾蒙的交互作用下，肝糖製造左右了我們身體所需的血糖值，用餐時胰島素會即時分泌，讓血糖的波動於60~90分內回到正常值。

(六) 基礎-餐時(basal-bolus)注射法: 配合胰島素的多樣化，更接近生理胰島素分泌的模式，採一天多次注射（搭配速、長效胰島素）。

胰島素的劑量與治療計劃(4)

(七) 懷孕期的胰島素注射

1. 已知糖尿病後懷孕患者，在第2及第3孕期，胰島素需要量逐漸增加（約為0.9~1.2單位/公斤/天），甚至比起懷孕前加倍胰島素需求量。因為胎盤製造反向調節賀爾蒙。
2. 使用一天3~4次basal-bolus或胰島素幫浦的積極血糖控制。
3. 併有肥胖之懷孕婦女因胰島素阻抗，起始胰島素劑量可高達0.8~1.0單位／公斤／天。

胰島素的劑量與治療計劃(5)

(七) 懷孕期的胰島素注射 (續)

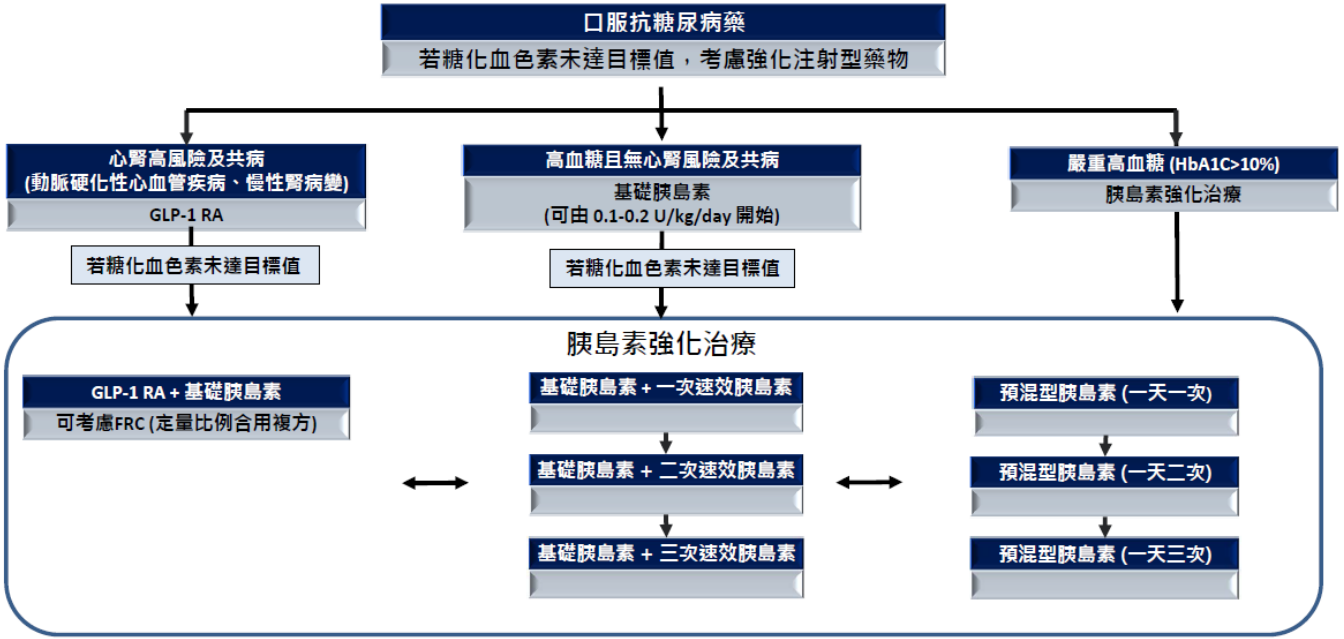
4. 除了RI及NPH, 現在很多insulin analogue 可用於懷孕及哺乳婦女。

- **Insulin lispro, Insulin Aspart 是較有研究證據可使用的**
- **Insulin Detemir 及 Insulin Glargine**
  - **Insulin detemir 現今被FDA核准使用在懷孕婦女 (Category B)**
  - **Insulin Glargine 在文獻中被認為是安全的[1]，仿單中註明如臨床上需要，Lantus 可使用於懷孕婦女**
- **Insulin Degludec目前並無Tresiba用於懷孕女性中的資料說明藥物相關的重大先天缺陷或流產風險**
- **Insulin Glulisine 無證據使用在懷孕婦女**

1. Insulin Glargine Safety in Pregnancy Diabetes Care 2010 Jan; 33(1): 29-33

第 2 型糖尿病人注射型藥物的治療流程圖

(2020)



修改自2020年美國糖尿病醫學會糖尿病照護建議

胰島素使用的注意事項 -副作用

- 過敏: 可能發生但非常罕見
- 脂肪代謝障礙，包含了脂肪萎縮 (lipodystrophy, atrophy)及脂肪增生 (lipohypertrophy)
  1. 脂肪萎縮: 脂肪組織因免疫反應導致凹陷，自從用recombinant DNA人類胰島素後已大大的減少
  2. 脂肪增生:避免最好的方法就是輪替注射部位。

Insulin delivery routes

Delivery	Advantages	Limitations	Representative
Subcutaneous	Widely used; Approved for insurance coverage	Painful administration; Possible bleeding, bruising, lipohypertrophy, lipoatrophy	Insulin syringes; Insulin pen; Insulin jet injectors; Insulin pump
Pulmonary	Large absorption area; Highly vascularized; Low enzymatic activity; Higher transmucosal bioavailability; Rapid and no need for enhancers	Side effect such as cough; Potential lung cancer risk; Clearance by alveolar macrophages	Exubera® Afrezza® Dance 501
Ocular	Fewer immunological reactions; Convenient administration; Fast systemic absorption	Requires enhancer	Gelfoam®

Trends Pharmacol Sci. 2021 Jan; 42(1): 31–44.

Insulin delivery routes

Delivery	Advantages	Limitations	Representative
Nasal	Potential bypass of hepatic first-pass metabolism; Low enzymatic activity	Small surface area; Possible irritation of nasal mucosa; Absorption varies between individuals	Nasulin™
Buccal	Easy removal; Fast-flowing blood supply; Highly acceptable to patients; Direct access to the systemic circulation	Small absorption surface area; Low permeability; Unfavorable taste; Choking hazard; Absorption affected by saliva or drinking	Oral-Lyn™; RapidMist™

Trends Pharmacol Sci. 2021 Jan; 42(1): 31–44.

Insulin delivery routes

Delivery	Advantages	Limitations	Representative
Oral	Highly acceptable to patients; Convenient administration; Reduced peripheral hyperinsulinemia	Low permeability; Enzymatic degradation; Transit time delay; High dosage required	Capsulin™
Transdermal	Easy removal to terminate dosing; Convenient administration; Large surface area	Possible irritation to application sites	Chemical enhancers; Microneedles; Iontophoresis; Electrophoresis; Sonophoresis

Trends Pharmacol Sci. 2021 Jan; 42(1): 31–44.

非注射胰島素 Non-injecting insulin

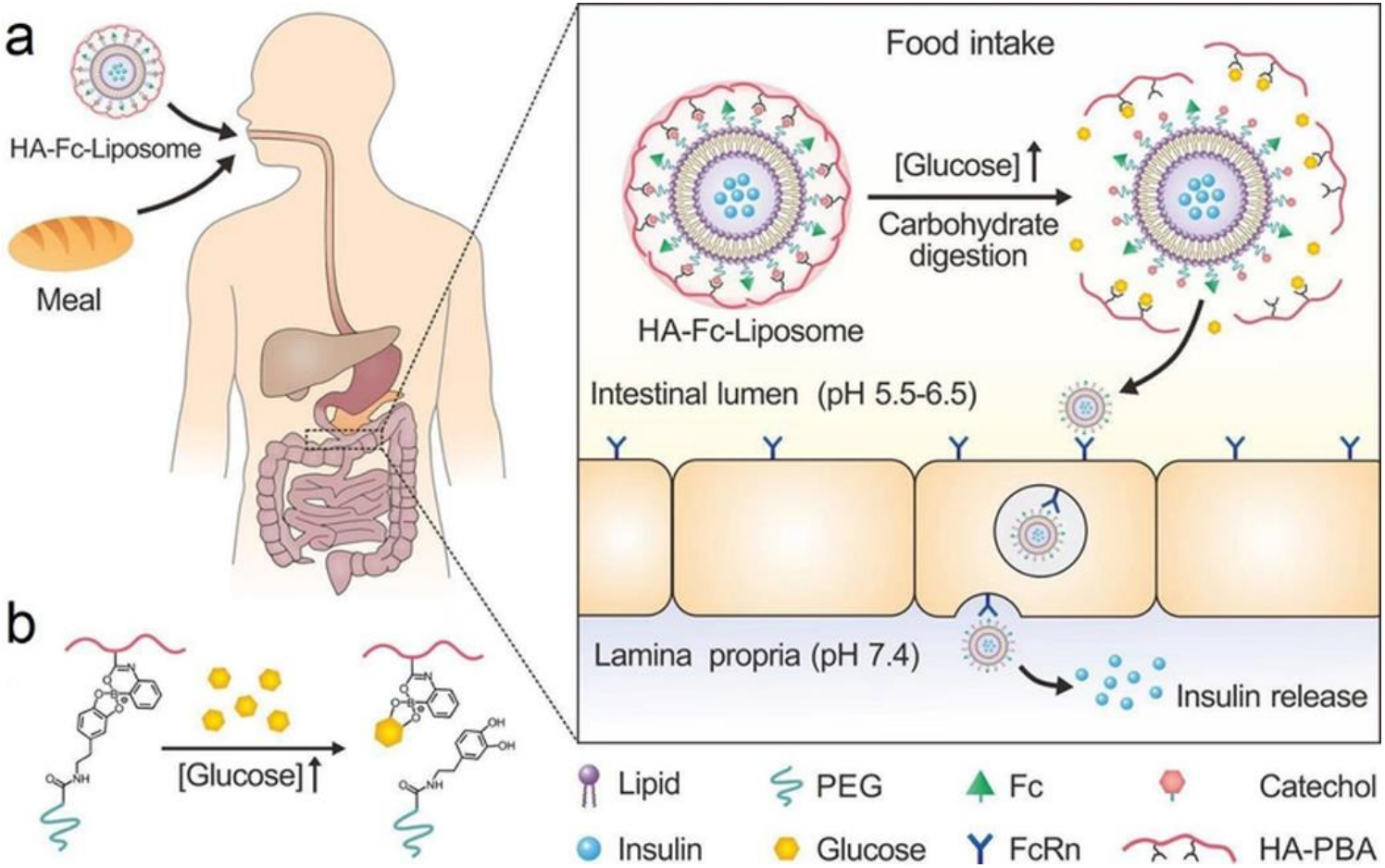
- 吸入式胰島素 Exubera（輝瑞公司，美國紐約州紐約市）於 2006 年獲批上市，但由於銷售不佳很快被製造商撤出市場。胰島素的肺內給藥似乎是一種有吸引力的替代途徑，但由於成本、設備和程序的不便、高指導要求和安全問題而未能普及.
- Afrezza（MannKind，Westlake Village，CA，USA）是 FDA 於 2014 年批准的另一種超速吸入胰島素。這是一種重組人胰島素的乾粉，吸附在富fumaryl diketopiperazine賦形劑上，基於技術圈粒子技術 。當與glargine聯合使用時，它已被證明與每天兩次預混雙倍胰島素一樣有效，體重增加顯著降低，低血糖事件也更少 。
  - 一項包括 Afrezza 試驗中 5,505 名患者的匯總數據分析表明，除了輕度咳嗽的發生率較高和肺功能輕微可逆性下降外，與對照藥相比，肺部安全性 。

Diabetes Metab J. 2021 Sep; 45(5): 629–640.

非注射胰島素 Non-injecting insulin

- 口服胰島素可能需具有生理的門脈與外周胰島素比率.
- 開發口服胰島素的主要挑戰，例如膳食攝入的干擾、高吸收變異性、低生物利用度以及由此產生的商業不可行性，仍然是成功的重大障礙。餐時口服胰島素的第 2 期和第 3 期研究，包括 Tregopil 胰島素（IN-105，通過乙酰鏈與聚乙二醇結合的重組胰島素）和 ORMD-0801（含有胰島素和佐劑的腸溶膠囊，以保護蛋白質並促進腸道吸收）.

Diabetes Metab J. 2021 Sep; 45(5): 629–640.



Adv Mater. 2020 Apr;32(13):e1902004.

Oral Insulin (ORMD-0801)

	QD (at bedtime)				BID			TID
	Placebo	8 mg	16 mg	32 mg	8 mg	16 mg	32 mg	32 mg
N (baseline vs 12 weeks)	51/44	14/13	13/13	62/59	13/12	14/10	62/54	58/52
HbA1c (%) at baseline	9.5±0.5	10.1±0.6	9.6±0.6	9.2±0.5	9.2±0.6	9.4±0.6	9.5±0.5	9.8±0.5
HbA1c (%) at 12 weeks	9.2±0.5	8.8±0.6	9.4±0.6	8.5±0.5	8.1±0.6	8.9±0.6	8.8±0.5	8.9±0.5
Hypoglycemia*	25 events, 1 patient	0	20 events, 1 patient	16 events, 6 patients	16 events, 4 patients	0	4 events, 3 patients	32 events, 6 patients

*All patients experiencing hypoglycemia were concomitantly taking a sulfonylurea.
LSM ± SE are presented for all summary statistics.
Eldor R. Presented at: EASD Virtual Meeting; 2020. Oral presentation OP10; Eldor et al. *Diabetologia.* 2020; 63 (suppl 1): OP10- 60.

Oral Insulin (ORMD-0801)

	QD				BID			TID
	Placebo	8 mg	16 mg	32 mg	8 mg	16 mg	32 mg	32 mg
Body weight (kg)								
N (baseline vs 12 weeks)	51/44	14/13	14/13	62/59	13/12	14/10	62/55	58/52
Baseline	95.7 ± 5.3	109.3 ± 6.5	95.4 ± 6.6	96.3 ± 5.1	100.9 ± 6.4	96.7 ± 6.5	94.0 ± 4.9	97.2 ± 5.1
12 weeks	92.8 ± 5.5	110.3 ± 6.9	97.0 ± 6.9	95.8 ± 5.3	99.7 ± 6.9	92.5 ± 7.3	92.8 ± 5.0	96.6 ± 5.2

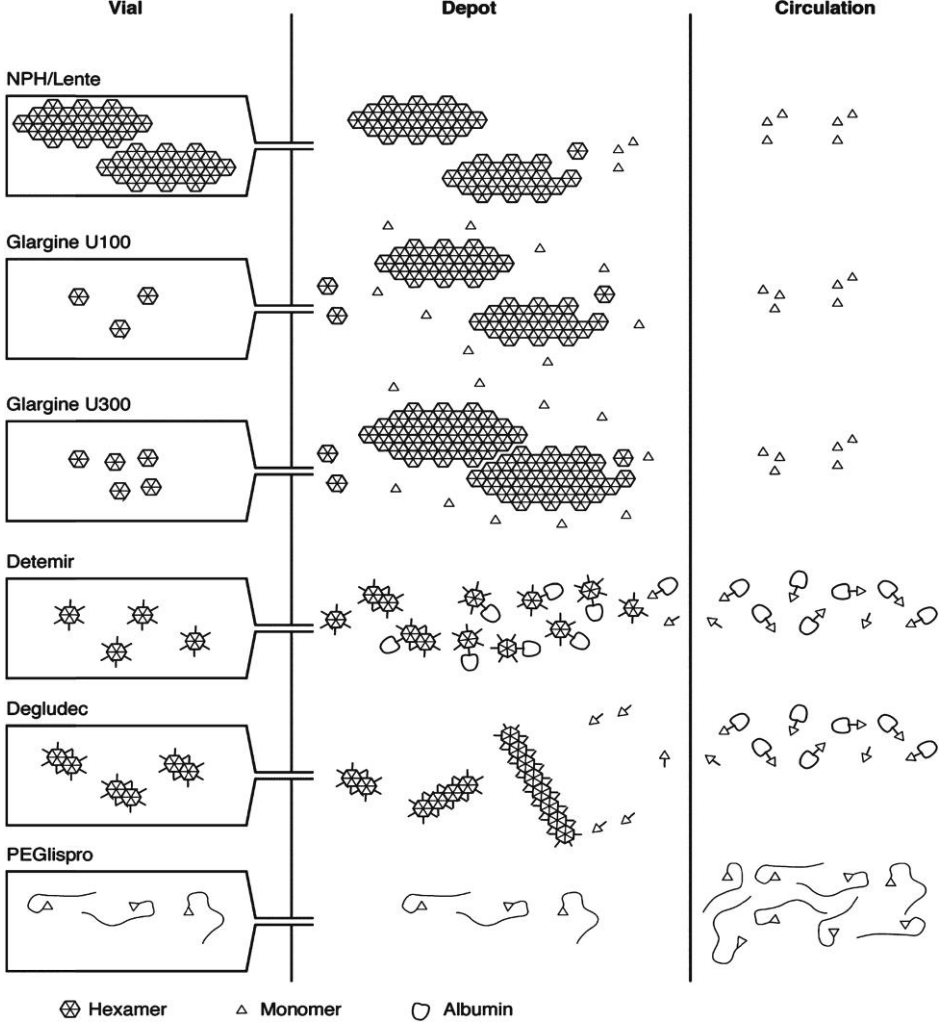
- ORMD-0801 elicited clinically significant HbA1c reductions in patients with poorly-controlled T2DM on standard therapies and with mean HbA1c levels >8%, without increasing hypoglycemia rate or weight
- The 8 mg QD regimen appeared most effective. Further studies to confirm the efficacy of this once daily evening dose are needed

LSM ± SE are presented for all summary statistics.
Eldor et al. *Diabetologia.* 2020; 63 (suppl 1): OP10- 60.

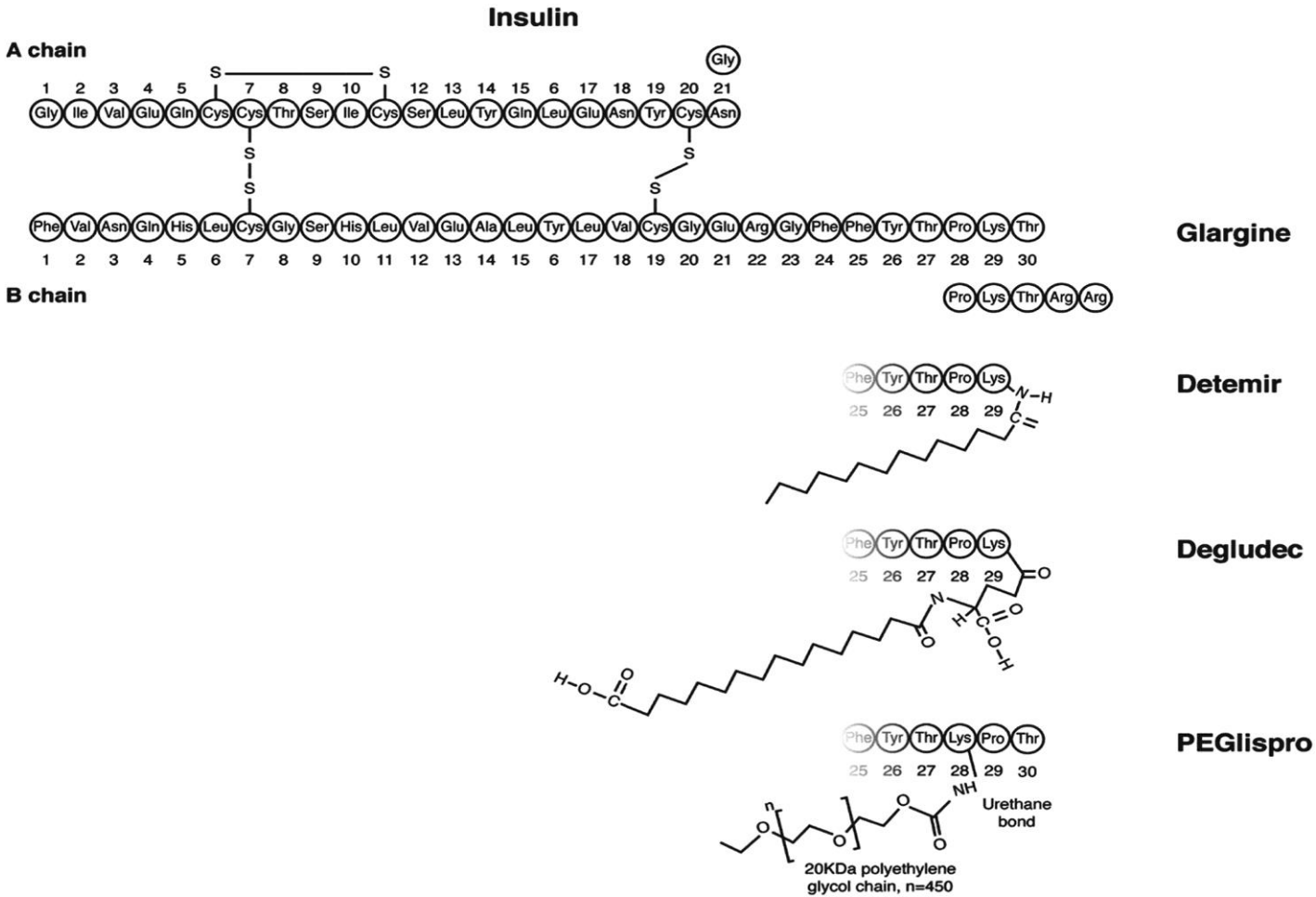
肝臟優先胰島素 Hepatopreferential insulin

- 肝優先胰島素已被建議作為恢復生理性門靜脈與外周胰島素比率並降低低血糖、體重增加和胰島素抵抗風險的替代方法。
- Insulin peglispro是由polyethylene glycol chain共價結合到B28 lysine of insulin lispro的分子，由於其較大的流體動力學尺寸而具有肝優先效應。
- 超過 6,000 名 T1DM 和 T2DM 患者被納入 IMAGINE 3 期臨床試驗計劃，與Glargine和 NPH 相比，Peglispro 顯示出更大的 HbA1c 降低、更小的血糖變異性、減少的夜間低血糖以及體重增加的趨勢.
- 較高的肝脂肪和甘油三酯以及較高頻率的轉氨酶水平升高有關。雖然不是由於嚴重的肝損傷，但製造商決定在 2015 年停止開發 。

Diabetes Metab J. 2021 Sep; 45(5): 629–640.



Diabetes Obesity Metabolism, Volume: 19, Issue: 1, Pages: 3-12, First published: 04 September 2016, DOI: (10.1111/dom.12782)

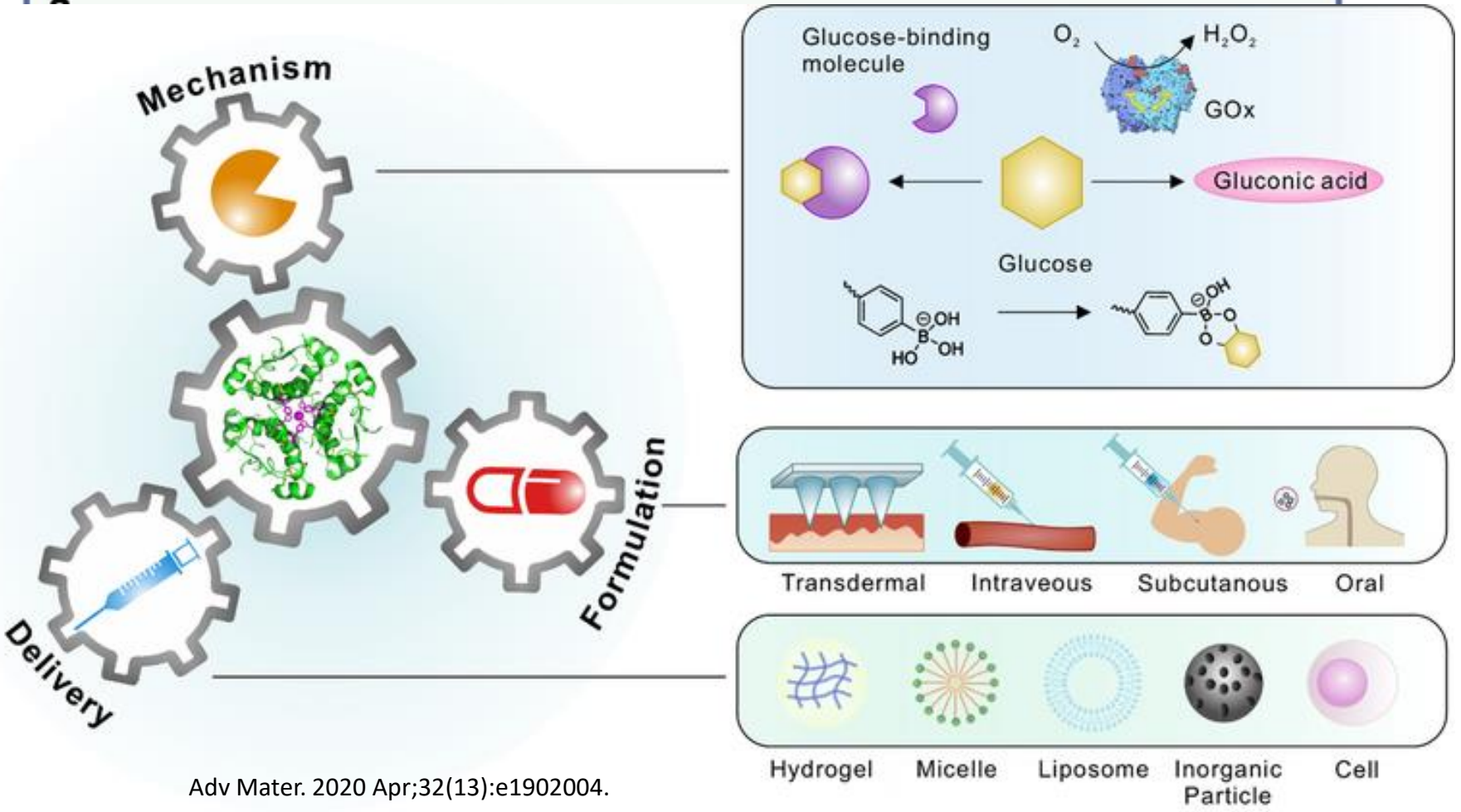


Diabetes Obesity Metabolism, Volume: 19, Issue: 1, Pages: 3-12, First published: 04 September 2016, DOI: (10.1111/dom.12782)

葡萄糖反應性胰島素 Glucose responsive insulin

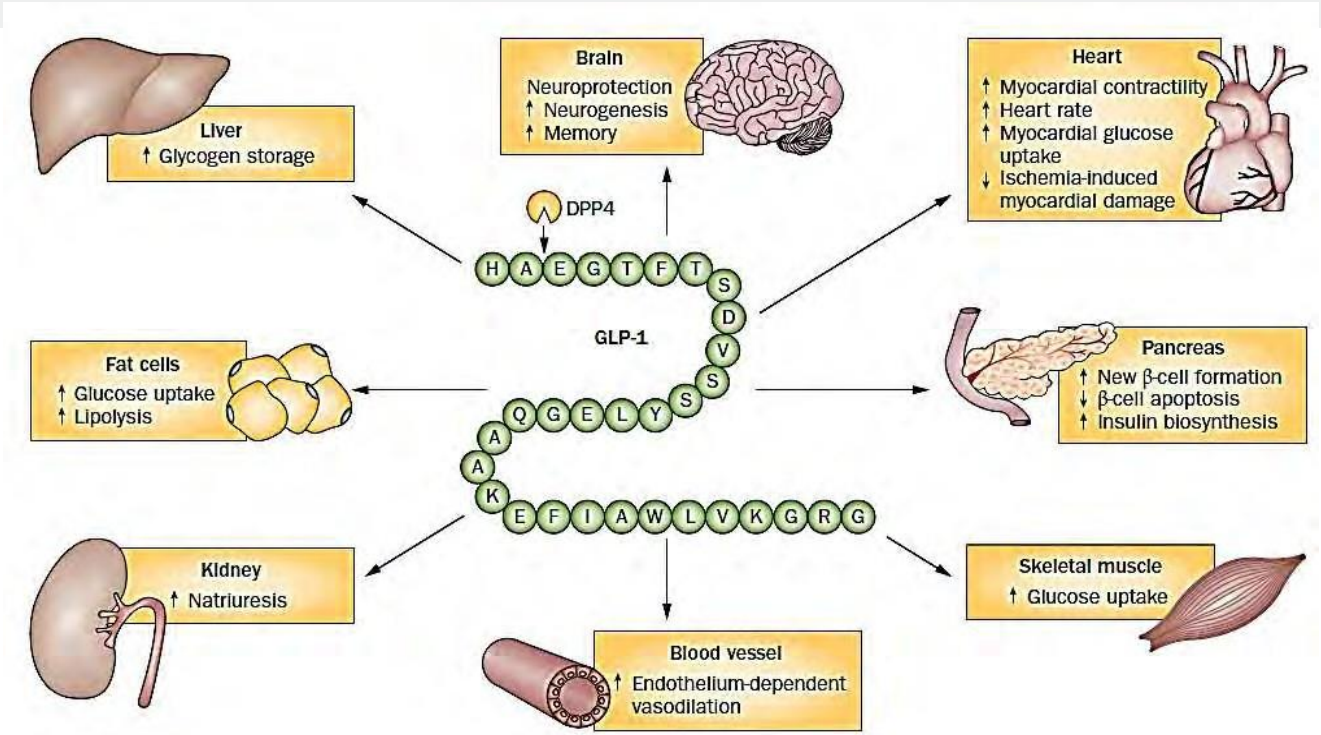
- 僅在高血糖環境中起作用而不會引起低血糖的葡萄糖反應性胰島素 (GRI) 將是胰島素治療的最理想選擇。開發“smart 智能”胰島素需要在配方化學、蛋白質工程、葡萄糖傳感技術和輸送裝置等各個領域取得進展，仍存在許多挑戰.
- GRI 有兩大類：
  - (1) 基於聚合物的系統，包括包含在葡萄糖反應性聚合物基質囊泡或水凝膠中的胰島素，水凝膠由葡萄糖結合蛋白、葡萄糖氧化酶或基於硼酸鹽的化學物質組成.
  - (2) 基於分子的生物共軛系統，將葡萄糖敏感基序（苯硼酸、葡萄糖胺或甘露糖）引入胰島素分子或其製劑中.

Diabetes Metab J. 2021 Sep; 45(5): 629–640.



Adv Mater. 2020 Apr;32(13):e1902004.

Reported Pleiotropic Effects of GLP-1



Meier JJ. Nat Rev Endocrinol. 2012; 8: 728-42.

類升糖素肽-1 受體促效劑的作用

類升糖素肽-1 受體促效劑 (GLP1-RA) 的作用

1. 促進胰島素的釋出
   抑制升糖素的分泌

→ 降低血糖

2. 減緩胃的排空：
   •減少餐後血糖的上升
   •減少飢餓感、增加飽足感

→ 減重效果

短效型 GLP1-RA 製劑

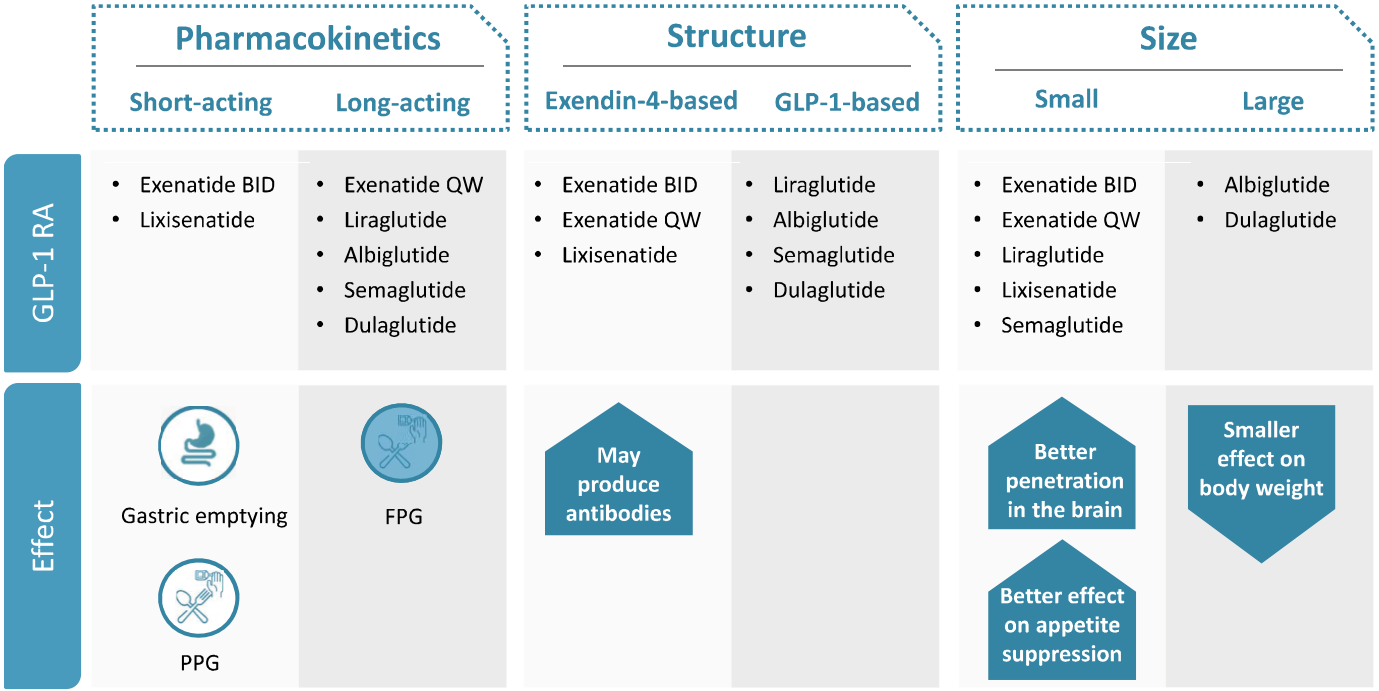
- 如 exenatide，作用時間短，需一日注射二次
- Exenatide: 重度腎功能不全與末期腎病不建議使用

長效型 GLP1-RA 製劑

- Liraglutide, exenatide 的長效懸液注射劑
  Bydureon 及 dulaglutide: 每天或每週注射一次
- 腎功能不全患者：
  - Liraglutide, dulaglutide與semaglutide: 無須調整劑量
  - Bydureon: 重度腎功能不全與末期腎病不建議使用

資料來源： 社團法人中華民國糖尿病學會。2018 糖尿病臨床照護指引。
第2型糖尿病的藥物治療(2020修訂版)

類升糖素肽-1 受體促效劑的比較

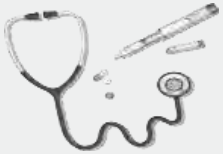


資料來源： 社團法人中華民國糖尿病學會。2018 糖尿病臨床照護指引。
第2型糖尿病的藥物治療(2020修訂版)

GLP-1 RA clinical trials

2022 ADA

American Diabetes Association. Connected for Life



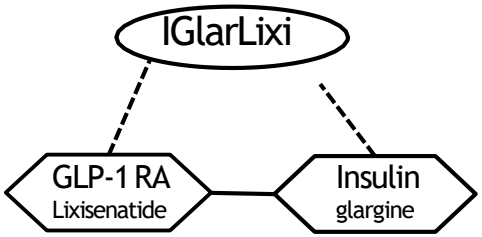
	Lixisenatide	Liraglutide	Semaglutide	Exenatide	Duraglutide	Oral Sema
	ELIXA (199) (n = 6,068)	LEADER (194) (n = 9,340)	SUSTAIN-6 (195)* (n = 3,297)	EXSCEL (200) (n = 14,752)	REWIND (198) (n = 9,901)	PIONEER-6 (196) (n = 3,183)
Primary outcome§	4-point MACE 1.02 (0.89–1.17)	3-point MACE 0.87 (0.78–0.97)	3-point MACE 0.74 (0.58–0.95)	3-point MACE 0.91 (0.83–1.00)	3-point MACE 0.88 (0.79–0.99)	3-point MACE 0.79 (0.57–1.11)
Key secondary outcome§	Expanded MACE 1.02 (0.90–1.11)	Expanded MACE 0.88 (0.81–0.96)	Expanded MACE 0.74 (0.62–0.89)	Individual components of MACE (see below)	Composite microvascular outcome (eye or renal outcome) 0.87 (0.79–0.95)	Expanded MACE or HF hospitalization 0.82 (0.61–1.10)
Cardiovascular death§	0.98 (0.78–1.22)	0.78 (0.66–0.93)	0.98 (0.65–1.48)	0.88 (0.76–1.02)	0.91 (0.78–1.06)	0.49 (0.27–0.92)
MI§	1.03 (0.87–1.22)	0.86 (0.73–1.00)	0.74 (0.51–1.08)	0.97 (0.85–1.10)	0.96 (0.79–1.15)	1.18 (0.73–1.90)
Stroke§	1.12 (0.79–1.58)	0.86 (0.71–1.06)	0.61 (0.38–0.99)	0.85 (0.70–1.03)	0.76 (0.61–0.95)	0.74 (0.35–1.57)
HF hospitalization§	0.96 (0.75–1.23)	0.87 (0.73–1.05)	1.11 (0.77–1.61)	0.94 (0.78–1.13)	0.93 (0.77–1.12)	0.86 (0.48–1.55)
Unstable angina hospitalization§	1.11 (0.47–2.62)	0.98 (0.76–1.26)	0.82 (0.47–1.44)	1.05 (0.94–1.18)	1.14 (0.84–1.54)	1.56 (0.60–4.01)
All-cause mortality§	0.94 (0.78–1.13)	0.85 (0.74–0.97)	1.05 (0.74–1.50)	0.86 (0.77–0.97)	0.90 (0.80–1.01)	0.51 (0.31–0.84)
Worsening nephropathy§‖	—	0.78 (0.67–0.92)	0.64 (0.46–0.88)	—	0.85 (0.77–0.93)	—

糖尿病腎臟疾病患者 GLP-1RA 調整建

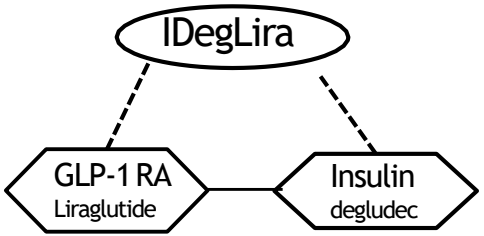
	根據 eGFR 調整劑量	透析患者
Exenatide (and extended release)	• CCr 30-50 mL/min，應謹慎使用 • CCr < 30 mL/min 或 ESRD 的病人禁用 • 腎臟移植的病人應慎用	不建議使用
Lixisenatide	• eGFR ≧ 60: 不須調整劑量 • eGFR 30-59: 建議慎用 • eGFR 15-29: 受限於實證經驗需慎用 • eGFR < 15: 不建議使用	不建議使用
Liraglutide	• 不須調整劑量 • 衛署菌疫輸字第 000914 號說明：於 eGFR 30~60 的安全性有 26 週臨床試驗評估 • 加拿大指引不建議用於 eGFR < 50	受限於實證經驗需慎用
Albiglutide	不須調整劑量	受限於實證經驗需慎用
Dulaglutide	不須調整劑量	受限於實證經驗需慎用
Semaglutide	不須調整劑量	受限於實證經驗需慎用

Basal Insulin/GLP-1 RA定量比例合用 (Fixed-Ratio Combinations)

10 units IGlar + 5 ug Lixisenatide



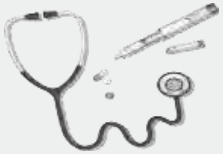
10 units IDeg + 0.36 mg Liraglutide



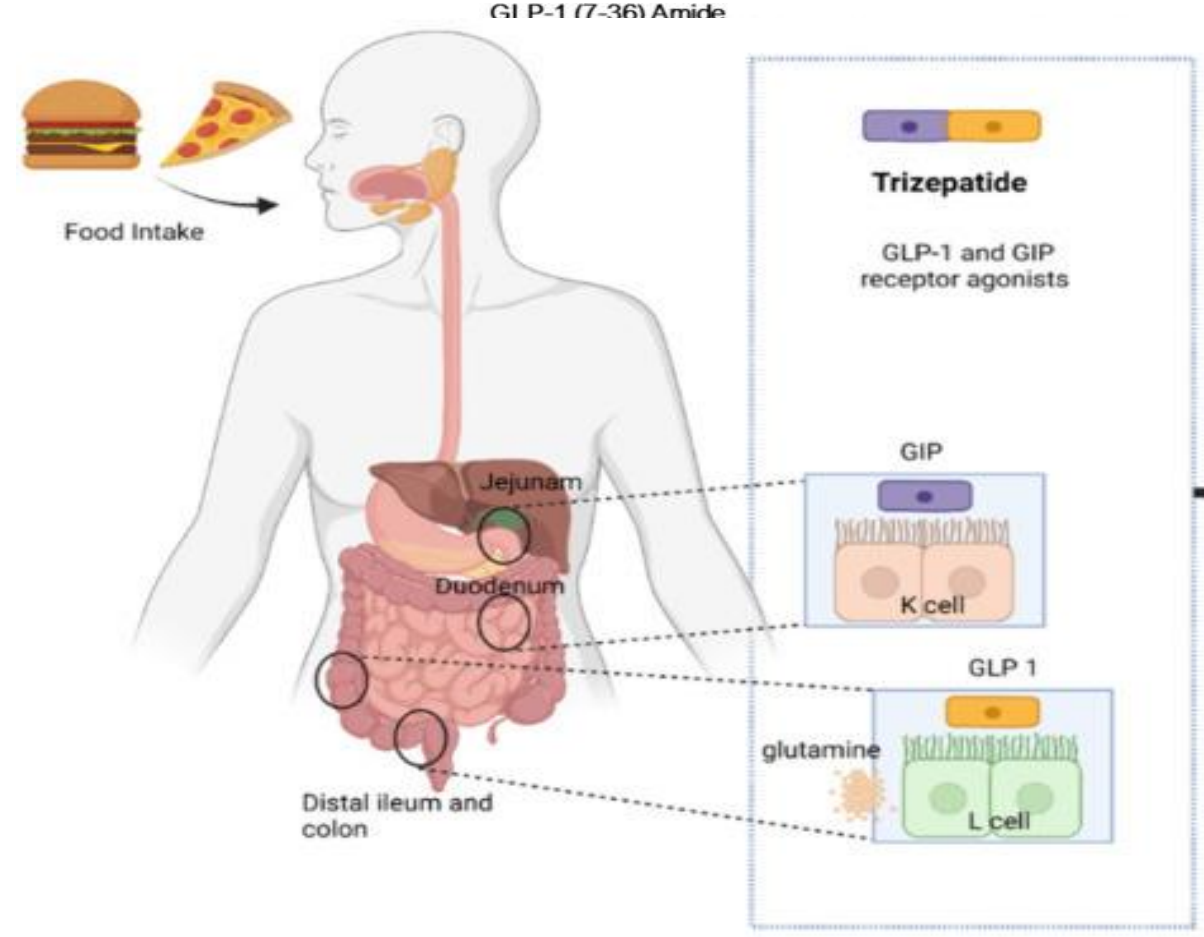
- Single injection
- Combines the FPG-lowering effect of basal insulin with the PPG-lowering effect of GLP-1 RA
- Highly effective HbA1c reduction
- Mitigates the weight gain associated with insulin
- Lower risk of hypoglycemia
- Gradual titration mitigates GI side effects of GLP-1 RA

Diabetes Care. 2016;39:1972-1980; Diabetes Care. 2016;39:2026-2035
Lancet Diabetes Endocrinol. 2014;2:885-893; JAMA. 2016;315:898-907

定例複方 (FRC: Fixed-ratio combination) :GLP-1受體促效劑+ 基礎胰島素



- 目前在台灣本類藥物有insulin glargine/lixisenatide固定比例複方(簡稱iGlarlixi)，每 個劑量單位含有insulin glargine U100 1 unit及lixisenatide 0.5 μg (2:1固定比例)， 每支預填注射筆3 mL溶液內含有insulin glargine*300 units及lixisenatide 150 μg。
- 複方當中的insulin glargine可調控空腹血糖，而lixisenatide可透過調控胰島素與升 糖素以及延緩胃排空來控制餐後血糖。透過固定比例設計，iGlarlixi在施打時可等比 例給予兩種降血糖藥物。劑量調整為根據患者自我量測血糖、並依基礎胰島素為基準調整。
- 起始劑量乃依先前的抗糖尿病治療而定，且lixisenatide的起始建議劑量不得超過10 μg，即iGlarLixi的起始建議劑量不得超過20個劑量單位。先前為口服治療之患者或使用小於20單位的基礎胰島素治療之患者，建議從10劑量單位為起始劑量；之前為使用大於或等於20單位基礎胰島素之患者，建議從20劑量單位為起始劑量。建議於餐前1小時內注射，每日一次。每日都固定在同一餐的餐前進行注射。



Decrese Food Intake

Decrese Appetite

Increase Weight Loss

Increases insuling secretion and Synthesis

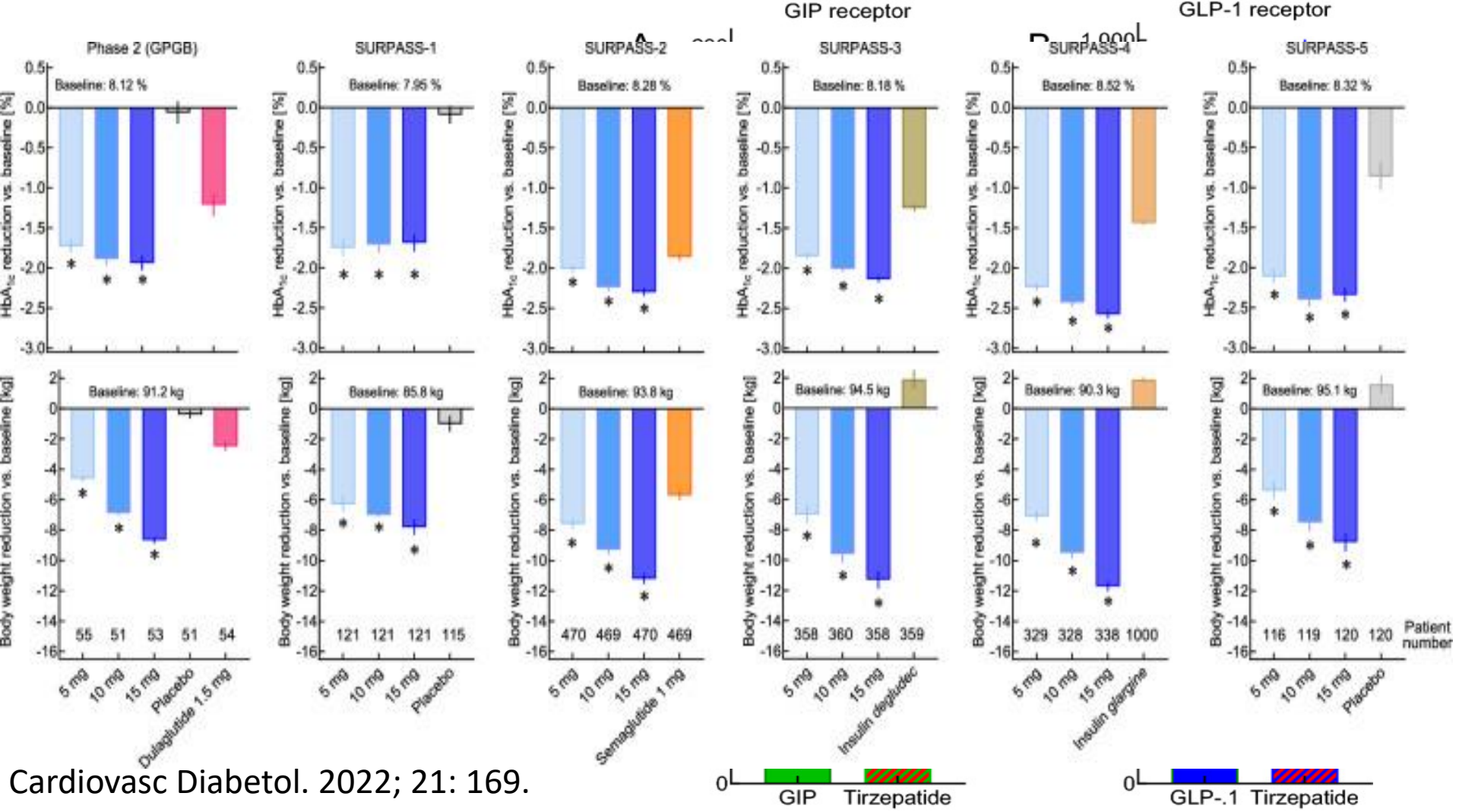
Increase Lipolysis (GLP-1)

Increase Lipogenesis (GIP)

Increase beta cell survival

Increase cardioprotection (GLP-1)

Decrease Bone reabsorption (GIP)



Cardiovasc Diabetol. 2022; 21: 169.

Outline

- Drugs development in diabetes
- Oral antidiabetic drugs (OAD)
- Injectable antidiabetic drugs (IAD)
- **Summary**

糖尿病的治療

第2型糖尿病人高血糖的處理流程圖

健康生活型態的飲食和運動及醫病共享決策

第一線治療: 以病人為中心，臨床考量涵蓋如相關共病及年齡、認知、體重體能、高低血糖風險，治療上通常包括Metformin及生活型態調整

(Metformin: 控糖強，低血糖少，有減少心血管事件的好處)

合併高血糖症狀

- 是 → 建議先以 Insulin 治療
- 否 → 糖化血色素高於個別化目標值1.5%以上
  - 是 → 建議使用兩種抗糖尿病藥
  - 否 → 使用一種抗糖尿病藥

評估是否併有ASCVD[1]，HF[2]或DKD[3]共病或風險
有則優先選擇有器官保護實證之抗糖尿病藥；無且治療未達控制目標時，加上以下不同機轉的抗糖尿病藥

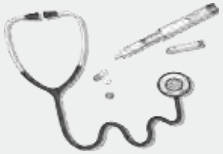
SGLT2i	GLP-1 RA[6]	DPP-4i	TZD	SU/Glinide	AGI	Insulin
心血管：有[4] 心衰竭：有 腎疾病：有[5] 死亡率：有 控制血糖效果：中等 體重：下降 低血糖：低 副作用：高酮酸血症、生殖泌尿道感染、骨折、截肢、脫水	心血管：有[4] 心衰竭：中立 腎疾病：有[7] 死亡率：有 控制血糖效果：強 體重：下降(強) 低血糖：低 副作用：腸胃道	心血管：中立 腎疾病：有[7] 控制血糖效果：中等[8] 體重：無 低血糖：低 副作用：關節痛、皮膚病變、心衰竭[9] 耐受性：佳	心血管：有[10] 控制血糖效果：強 體重：增加 低血糖：低 副作用：水腫、心衰竭、骨折	控制血糖效果：強 體重：增加 低血糖：中 醫療成本：合宜	心血管：中立 控制血糖效果：中等 體重：稍降 低血糖：低 副作用：腸胃道	心血管：中立 心衰竭：中立 腎疾病：中立 控制血糖效果：最強 體重：增加 低血糖：高

未達控制目標

再加上另一種不同機轉的抗糖尿病藥 (SU 和 Glinide 不建議合併，DPP-4i 和 GLP-1 RA 不建議合併)
若仍未達控制目標，建議照會專科或強化注射型藥物治療

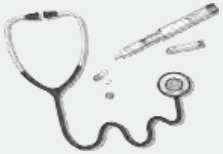
1. ASCVD:動脈硬化心血管疾病
2. HF:心衰竭
3. DKD:糖尿病腎疾病
4. 選擇具有實證能減少心血管事件之藥物
5. 指腎絲球過濾率，透析及腎因性或心因性死亡終點
6. 包含口服及注射GLP-1 RA
7. 指蛋白尿之改善
8. 初診斷即合併metformin+vildagliptin比metformin能更長期控制血糖
9. Saxagliptin 潛在性心衰竭風險
10. 對減少心血管事件有潛在性的好處

使用抗糖尿病藥物注意事項



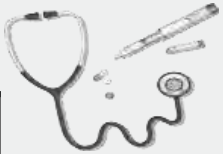
- 不建議合併使用磺醯脲類與非磺醯脲類之促胰島素分泌劑。
- 某些國家(例如：加拿大)不建議合併使用胰島素和thiazolidinedione。
- 嚴重心臟衰竭(紐約心臟學會New York Heart Association，NYHA，功能分類第III級和第IV級)和急性心臟衰竭的患者，不建議使用thiazolidinedione。
- 二肽基酶-4抑制劑和類升糖素肽-1受體促效劑，對18歲以下的患者和孕婦的安 全性和有效性尚未確定，因此目前不建議使用。
- 使用複方的口服抗糖尿病藥物時，需注意複方藥物間彼此的交互作用。
- 類升糖素肽-1受體促效劑單獨使用時，不會發生低血糖；但若和促胰島素分泌劑或胰島素同時使用，則需注意發生低血糖的風險。減少促胰島素分泌劑或胰島素的劑量可能會降低發生低血糖的風險。

使用抗糖尿病藥物建議



- 第2型糖尿病患者，需調整生活型態及飲食控制，若在診斷後3個月內，仍無法達到血糖治療目標時，可考慮使用口服抗糖尿病藥物。
- 使用單一種類的口服抗糖尿病藥物，仍無法達到血糖治療目標時，可加上其他種類的口服抗糖尿病藥物，並考慮藥物動力學特性，希望能在3-12個月內達到血糖控制目標。
- 建議依照患者個別情況，選擇口服抗糖尿病藥物的種類，減少可能發生低血糖的風險。除非有禁忌症或無法忍受藥物的副作用，否則建議以metformin為第2型糖尿病患者口服抗糖尿病藥物的首選。
- 在維持合理血糖控制的情況下，根據患者心腎合併症的風險，選擇具有實證的藥物，應能進一步減少相關慢性併發症的發生。

各類降血糖藥物比較



	降低糖化血色素	降低空腹血糖	降低餐後血糖	低血糖風險	體重
雙胍類	1-2%	+ +	+	低	中性或減輕
促胰島素分泌劑 磺醯脲類	1-2%	+ +	+ +	高	增加
非磺醯脲類	0.5-1.5%	+	+ +	中	增加
胰島素增敏劑	0.5-1.4%	+ +	+	低	增加
阿爾發葡萄糖苷酶 抑制劑	0.5-0.8%	-	+ +	低	中性
二肽基酶-4 抑制劑	0.5-0.8%	+	+ +	低	中性
類升糖素肽-1受體 的促效劑	0.5-1%	+	+ +	低	減輕
胰島素	1.5-3.5%	+ + +	+ + +	高	增加
鈉-葡萄糖共同輸送 器-2抑制劑	0.62-0.85%	+	+	低	減輕

Thank you for Listening!

ADA 2023 - 糖尿病醫療營養治療&
第2型糖尿病人之體重管理

Medical Nutrition Therapy (MNT) &
Weight Management for Type 2 Diabetes

歐陽鍾美 營養師

大綱

- 糖尿病營養治療 (MNT)建議
  - 營養治療的效益
  - 熱量平衡
  - 飲食型態/營養素分配與建議
  - 酒精、鈉
  - 非營養性甜味劑
- 第2型糖尿病人之體重控制
  - 評估建議
  - 飲食、運動和行為治療
  - 藥物治療
  - 代謝手術

Diabetes Care 2023;46(Suppl. 1):S68–S96

糖尿病營養治療目的

1.促進和支持**健康飲食型態**，強調在適當份量下攝取各種**營養素豐富**的食物，以改善整體健康，以及：

- **達到和保持體重目標**
- **獲得個人化的血糖、血壓和血脂目標**
- **延遲或預防糖尿病併發症**

2.依個人及文化喜好、健康識能、計算能力、健康食物的取得、行為改變意願、能力及障礙等因素，提供**個別化營養需求**。

3.為維持用餐的樂趣，**不提供**對食物選擇**批判性**的訊息，同時僅在有足夠**科學證據**下，做限制食物選擇的建議。

4.提供**個別化**實用的衛教工具以**發展健康的飲食型態**，相較聚焦於個人之巨量營養素、微量營養素或單一食物上佳。

營養治療建議 (MNT recommendations)

Table 5.1—Medical nutrition therapy recommendations

		Recommendations
Effectiveness of nutrition therapy (營養治療的效益)	5.10	由營養師提供之個別化MNT可達到治療目標，患者需要理解知識和照顧糖尿病的經驗。
		people with type 1 or type 2 diabetes, prediabetes, and gestational diabetes mellitus. A
	5.11	糖尿病MNT可節省成本，改善臨床結果。 ings B and improved dequately reimbursed by insurance and other payers. E
Energy bala (熱量平衡)	5.12	建議所有體重過重或肥胖病人，體重減輕至少5%以上
Eating patterns and macronutrient distribution (飲食型態/巨量營養素分配)	5.13	沒有理想的營養素比例，飲食計畫應依個別化評估 E
	5.14	各類型飲食型態可管理和預防糖尿病
	5.15	減少醣類攝取證實可改善血糖，應用各類飲食型態可達個人化的需求和喜好。

熱量平衡(Energy Balance)/體重管理

- 糖尿病前期，體重減輕 7－10% 可預防第2型糖尿病進展。體重過重或肥胖的第2型糖尿病患，體重減輕 5% 對血糖、血脂和血壓有幫助。若依病人需求、可及性和安全性下，體重減輕更進步，達減重目標(如減15%)，則臨床好處更大。

- 研究證明各類飲食計畫，其巨量營養素組成不同，糖尿病人可有效且安全用在短期計畫中(1－2 年)達到體重減輕目的。這些結構性低熱量飲食計畫包括代餐、地中海飲食型態和有額外給予支持之低醣飲食計畫。

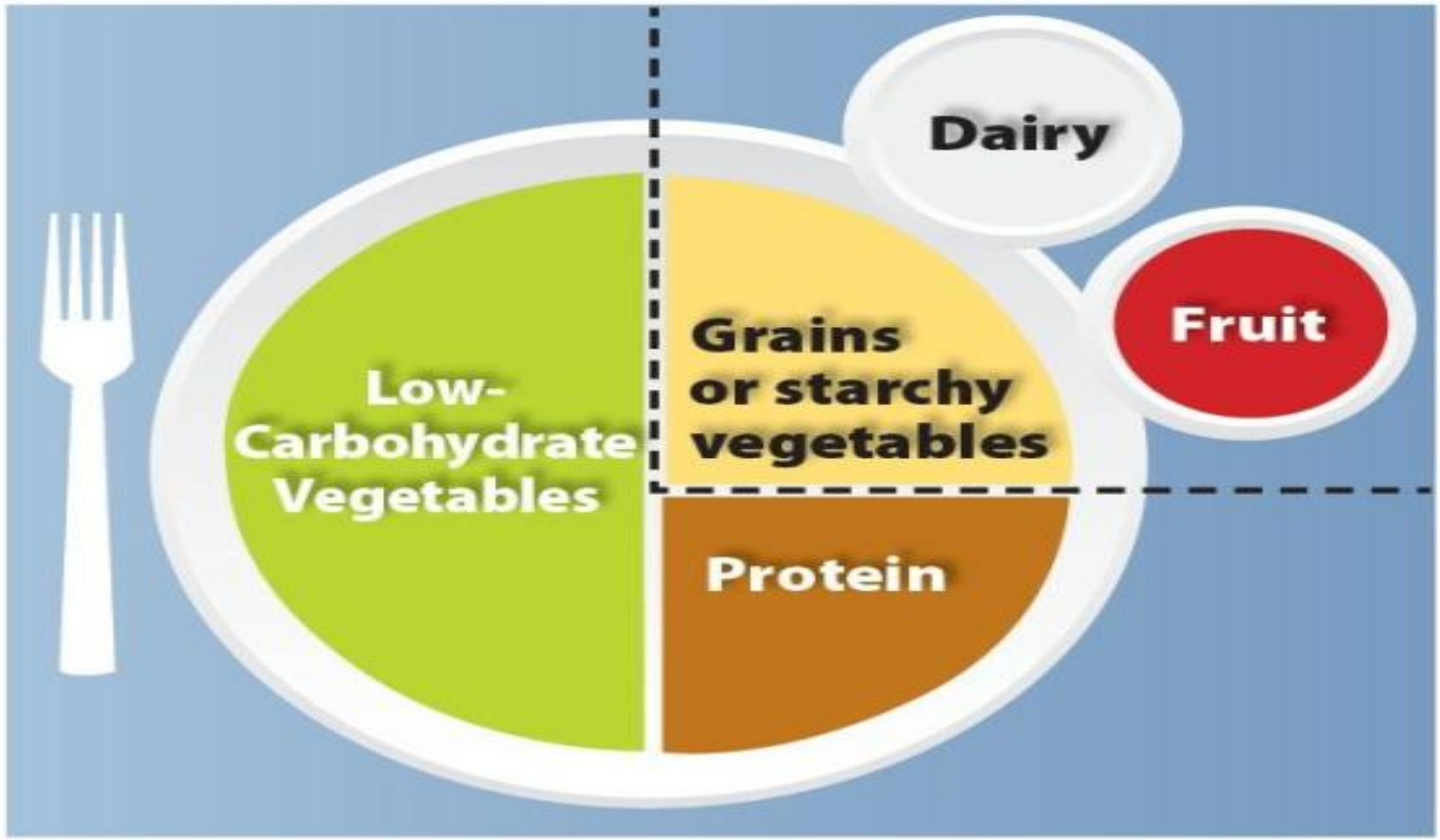
- 沒有單一介入可以持續很好，需要更多數據證實這些飲食計畫適合長期食用且病人可接受。

飲食型態 (Eating Patterns)/飲食計畫 (Meal Planning)

- 飲食型態應強調: (1)健康飲食型態，勝過個人營養素、食物和食物分類。(2)個人喜好 (如傳統、文化、宗教、健康信念、目標和經濟等) (3)代謝目標 (metabolic goals)。
- 健康型態主要因素: (1) 強調非澱粉類蔬菜, (2) 減少添加糖和精緻澱粉, (3)選擇原型食物(whole foods)勝過加工食物

- 個人飲食計畫應聚焦於個人喜好、需要和目標。
- 低醣飲食長期計畫較難維持，所以個人是否有興趣執行很重要。大部分糖尿病人選擇適量醣類(44~46% of TC)。
- 兩種RCT研究有效飲食計畫方法: (1)糖尿病餐盤法(diabetes plate method)較簡單； (2)醣類計算(CHO counting)則是進階技巧，適合需要計算能力佳者。

My Diabetes Plate



營養治療建議 (MNT recommendations)

Carbohydrates (醣類)	5.16	加強營養素密度高之醣類， 1000卡飲食至少含14g纖維質，應減少精緻醣類(B)。
	5.17	以水取代含糖飲料(B)。應減少含糖食物，選擇健康、營養素豐富食物(A)。
	5.18	利用彈性胰島素注射，需衛教醣類、脂肪和蛋白質對血糖的影響，並依個人需求與喜好調整劑量(A)。
	5.19	使用固定胰島素注射者需衛教固定醣類、進食時間和食物份量，以改善血糖和降低低血糖風險 (B)。
Protein (蛋白質)	5.20	第2型糖尿病人消化蛋白質，在血糖沒有增加的情況下，會增加胰島素反應，因此含高蛋白質之醣類食物應避免作為治療或預防低血糖用途 (B)。
Dietary fat (脂肪)	5.21	加強於地中海飲食型態，因含豐富單元不飽和脂肪酸，可改善醣類代謝和降低心血管疾病風險(B)。
	5.22	吃含豐富ω3食物，如肥的魚(EPA & DHA)和堅果、種子(含ALA)，建議用來預防心血管疾病(B)。

醣類 (Carbohydrate)

- 沒有固定醣類比例。
- 升糖指數(GI)和升醣負荷(GL)對空腹血糖和A1C結果不一致。
- 整體而言，降低醣類攝取可改善血糖，可依個人需求和喜好，應用於各類飲食型態中。
- 低醣飲食研究因定義差異大，在解說上是一挑戰。大部分研究對短期(<6個月)效果佳，而長期低醣飲食較難維持。
- 非常低醣飲食(VLCD)不建議用於懷孕、哺乳、小孩、腎臟病人和有飲食異常風險者。

Classification of Reduced-Carbohydrate Diets

Carbohydrate amount	Diet name	Defining features/Comments
≥45% EI; ≥225 g/d	High-carbohydrate	Prevailing dietary pattern in the US; consistent with recent recommendations for people with diabetes and USDA recommendations for general public
26%–44% EI; 131–224 g/d	Moderate-carbohydrate	Moderate reduction of grains, starchy vegetables, added sugar Unlimited legumes, whole fruits Unlimited non-starchy vegetables
10%–25% EI; 51–130 g/d	Low-carbohydrate (低醣飲食)	Substantial reduction of grains, starchy vegetables, added sugar Moderate reduction of legumes, whole fruits Unlimited non-starchy vegetables
<10% EI; ≤50 g/d	Very-low-carbohydrate (非常低醣飲食)	Elimination of grains, starchy vegetables, added sugar Substantial reduction of legumes, whole fruits Unlimited non-starchy vegetables
(非常低醣生酮飲食)	Very-low-carbohydrate ketogenic	As above, with protein intake typically limited to ≤20% of EI Serum BOHB characteristically 0.5–5.0 mmol/L

Calculations based on a 2000-kcal/d diet. BOHB, β-hydroxybutyrate; EI, energy intake; USDA, US Department of Agriculture.

J Clin Invest. 2021;131(1):e142246

醣類 (Carbohydrate)

- 使用胰島素注射者，需瞭解醣類與胰島素之關係，學習**Insulin-to-carb ratios (C/I)**，來幫助血糖控制。
- 若為混合食物，食物中除了醣類，還有**高油脂、高蛋白**，餐後血糖表現則與單獨攝取醣類不同，它們可能提早或延後餐後血糖值，有甚至延後3小時或更長。因此胰島素注射可考慮**分兩次注射**。
- 有效的胰島素既需配合結構性的**血糖監測**或**連續血糖監測**，併依結果調整胰島素。
- 每日**固定胰島素劑量**者需配合每餐**固定時間**和**醣量**攝取。

蛋白質 (Protein)

- **沒有證據**顯示調整每日蛋白質攝取量 (通常1 – 1.5 g/kg/day 或 15 – 20% total calories) 可以改善健康。研究對血糖管理或心血管疾病風險之理想蛋白質攝取量也有沒有定論。
- 蛋白質攝取目標應依目前飲食型態而**個別化**。有些研究發現稍微提高蛋白質攝取量(20 – 30%) 可增加飽足感，對第2型糖尿病管理較成功。
- DKD病人蛋白質攝取量**不建議少於0.8 g/kg**，因這不會改變血糖值、心血管風險或GFR值，但可能增加營養不良風險。
- 第2型糖尿病蛋白質會增加**胰島素對食物醣類反應**，因此應**避免**使用**含蛋白質豐富的醣類食物**(如牛奶)來治療或預防低血糖，因為它可能同時增加胰島素分泌。建議病人使用**單純葡萄糖**治療低血糖。

脂肪 (Fat)

- 沒有固定脂肪比例，強調要**個別化**。
- 油脂種類比總量更重要。要減少飽和脂肪酸的攝取，**地中海飲食型態**油脂種類較佳(MUFA & PUFA)。
- 對於糖尿病人是否要補充ω-3並沒有定論，但對心血管疾病是有好處。**REDUCE-IT**試驗顯示每日補充4公克EPA可降低心血管疾病風險。

營養治療建議 (MNT recommendations)

Micronutrients and herbal supplements (微量營養素/草本植物補充劑)	5.23	沒有明顯證據顯示草本植物或非草本(如維生素、礦物質)補充劑對沒缺乏之糖尿病人有幫助。C and they are not generally recommended for glycemic control. C There may be evidence of harm for certain individuals with β carotene supplementation. B
Alcohol (酒精)	5.24	成人飲酒要適量，即女生不超過1酒精當量，男生不超過2個酒精當量。C
	5.25	Educating people with diabetes about the signs, symptoms, and self-management of delayed hypoglycemia after drinking alcohol, especially when using insulin or insulin secretagogues, is recommended. The importance of glucose monitoring after drinking alcoholic beverages to reduce hypoglycemia risk should be emphasized. B
Sodium (鈉)	5.26	Na 攝取量 < 2,300 毫克/天 B
Nonnutritive sweeteners (非營養性甜味劑)	5.27	可取代含糖食品，減少熱量和醣類攝取，但仍鼓勵以水取代含糖和非營養性甜味劑。B compensatory increase in energy intake from other sources. There is evidence that low- and no-calorie sweetened beverages are a viable alternative to water. B

微量營養素/草本植物補充劑

- 沒有明顯證據顯示草本植物或非草本(如維生素、礦物質)補充劑對糖尿病人有幫助。
- **Metformin**與**B12**缺乏相關，因此建議服用者可定期檢測血中B12值，尤其患有貧血或周邊經炎者

- **缺乏**證據顯示要**規律補充抗氧化劑**，如**維生素E**、**C**和**胡蘿蔔素**，(亦考量其長期服用之安全性)。
- 有研究補充**維生素D**可能對第2型糖尿病特殊族群有潛在好處，但在臨床上仍須更多研究確認。

酒精 (Alcohol)

- **適量飲酒**對血糖控制不會有傷害。
- 飲酒風險包括低血糖(注射胰島素者)、體重增加、和高血糖(飲酒過量者)等
- 糖尿病人須瞭解飲酒可能的風險，以及監測血糖的重要
- 適量飲酒:
  - **12 oz 啤酒、5 oz 釀造酒、1.5 oz蒸餾酒**。

鈉 (Sodium)

- 建議量與一般民眾同，< 2300 mg/d
- 高血壓患者並不建議 < 1500 mg/dL
- 鈉質的限制應考量食物的美味、可取得性、可負擔性和低鹽食物取得之困難。

非營養性甜味劑 (Nonnutritive Sweeteners)

- 非營養性甜味劑對血糖影響小，可減少熱量攝取，證據顯示對**體重控制有幫助**，但不可額外增加食物。

- 非營養性甜味劑飲料可作為短期取代含糖飲料之策略；然而，糖尿病人應**鼓勵喝水**，減少含糖和甜味劑飲料攝取

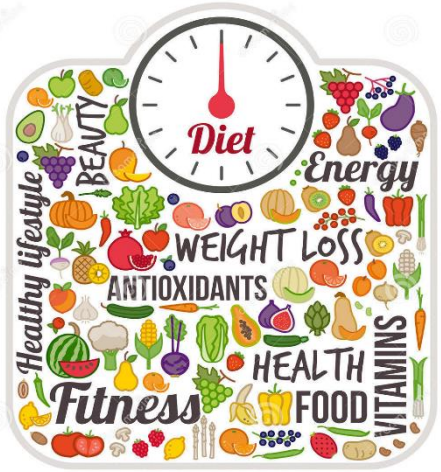
- 研究發現攝取較多的非營養性甜味劑飲料與一般含糖飲料，與**第2型糖尿病發展**相關。

小 結

- **2023 糖尿病營養治療(MNT)建議**
  - **營養治療的效益:** 個別化MNT可達智目標，節省成本。
  - **熱量平衡:** 體重過重或肥胖病人，體重減輕至少**5%**。
  - **飲食型態:** 飲食計畫應依個別化評估
  - **醣類、蛋白質和脂肪:** 糖尿病人消化蛋白質，會增加胰島素反映，因此高蛋白質醣類應避免作為治療或預防低血糖用
  - **微量營養素/草本植物:**證據不足
  - **酒精、鈉:** 適量攝取
  - **非營養性甜味劑:**可減少熱量但鼓勵以水取代含糖飲料。

第2型糖尿病人之體重管理

Weight Management for Type 2 Diabetes



體重管理 - 前言

- 體重管理和減輕體重對第 1 型糖尿病、第2 型糖尿病或糖尿病前期過重或肥胖病人很重要。

- 為支持體重過重或肥胖之糖尿病人或糖尿病前期之減重和改善 A1C、心血管疾病 (CVD) 風險因素和健康狀況，個人化之醫療營養治療和糖尿病自我管理教育和支持(DSMES)，應包括**個人化負熱量平衡**之飲食計畫，且伴隨著**增加身體活動量**。

- 生活型態介入計畫應該**密集**且**頻繁追蹤**以達顯著減輕體重。

大綱

- **2023-ADA 建議** (Recommendation)
- 飲食、身體活動和行為治療

  (Diet, physical activities and behavioral therapy)
- 藥物治療 (pharmacotherapy)
- 代謝手術 (Metabolic surgery)

建議 (Recommendation)

- 8.1 Use person-centered, nonjudgmental language that fosters collaboration between individuals and health care professionals, including person-first language (e.g., “person with obesity” rather than “obese person”). (E)
  - 以病人為中心、用不批判的語言支持病人與醫療人員的合作。包括以病人優先的語言(people-first language) (如稱呼 person with obesity 較obese person 胖子佳)。(E)

- 8.2 Measure height and weight and calculate BMI at annual visits or more frequently. Assess weight trajectory to inform treatment considerations. (E)
  - 每年1次或多次測量身高與體重來計算BMI。評估病人體重變化曲線(軌道)，以作為治療參考。 (E)

建議 (Recommendation)

- 8.3 Based on clinical considerations, such as the presence of comorbid heart failure or significant unexplained weight gain or loss, weight may need to be monitored and evaluated more frequently. (B) If deterioration of medical status is associated with significant weight gain or loss, inpatient evaluation should be considered, especially focused on associations between medication use, food intake, and glycemic status. (E)

- 基於臨床考量,如心臟合併症出現，或明顯無法說明的體重增加或減輕，則須頻繁監測和評量體重。(B) 如果醫療狀況與體重增加或減輕相關，則應考慮住院評量，特別著重於藥物使用、攝食和血糖情況面。 (E)

建議 (Recommendation)

- 8.4 Accommodations should be made to provide privacy during weighing. (E)
  - 測量體重時須在有**隱私**的空間。(E)

- 8.5 Individuals with diabetes and overweight or obesity may benefit from modest or larger magnitudes of eight loss. Relatively small weight loss (approximately 3–7% of baseline weight) improves glycemia and other intermediate cardiovascular risk factors. A Larger, sustained weight losses (>10%) usually confer greater benefits, including disease-modifying effects and possible **remission of type 2 diabetes**, and may improve long-term cardiovascular outcomes and mortality. (B)
  - 肥胖或體重過重之糖尿病人**適度或大幅度減重是有好處**的。相對於小幅度減重(約3~7%)，可改善血糖和心血管風險因子。較大幅度減重(>10%)通常有較大好處，包括減緩疾病影響和第2型糖尿病可能緩解，和可能可改善長期心血管疾病的結果與死亡。

營養、身體活動和行為改變

- 8.6 Nutrition, physical activity, and behavioral therapy to achieve and maintain ≥5% weight loss are recommended for most people with type 2 diabetes and overweight or obesity. Additional weight loss usually results in further improvements in the management of diabetes and cardiovascular risk. (B)
- 體重過重或肥胖之第2型糖尿病人，建議以飲食、運動和行為治療達到**減輕體重 ≥ 5%**。額外體重減輕通常對糖尿病和心血管風險控制更好。(B)

營養、身體活動和行為改變

- 8.7 Such interventions should include a high frequency ofcounseling ($16 sessions in 6 months) and focus on nutrition changes, physical activity, and behavioral strategies to achieve a 500–750 kcal/day nergy deficit. (A)
- 介入計畫應包括高頻率諮商(6個月≥ 16次課程) 和著重於飲食改變、運動和行為策略，以達每天減少500~750卡熱量。(A)

- 8.8 An individual's preferences, motivation, and life circumstances should be considered, along with medical status, when weight loss interventions are recommended. (C)
- 當體重減輕計畫介入時，建議應考量個人喜好、動機，生活環境以及醫療情況。(C)

營養、身體活動和行為改變

- 8.9 Behavioral changes that create an energy deficit, regardless of macronutrient composition, will result in weight loss. Nutrition recommendations should be individualized to the person's preferences and nutritional needs. (A)
- 行為改變可減少熱量攝取使得體重減輕(忽略巨量營養素比例)。飲食建議應病人喜好和營養需求而個別化設計。(A)

- 8.10 Evaluate systemic, structural, and socioeconomic factors that may impact nutrition patterns and food choices, such as food insecurity and hunger, access to healthful food options, cultural circumstances, and social determinants of health. (C)
- 評量系統、結構和社經因素，可能影響飲食型態和食物選擇如食品安全、健康食物取得、文化環境和社會因素等。(C)

營養、身體活動和行為改變

- 8.11 For those who achieve weight loss goals, long-term ($1 year) weight maintenance programs are recommended when available. Such programs should, at minimum, provide monthly contact and support, recommend ongoing monitoring of body weight (weekly or more frequently) and other self-monitoring strategies, and encourage regular physical activity (200–300 min/week). (A)
- 那些體重達到減重目標者,建議參與長期(≥1 年) 體重維持計畫。這些計畫至少每月應提供聯繫和支持，並建議持續監測體重(每周1次以上)、其他監測策略，以及和鼓勵規律運動 (200~300 分鐘/周)。(A)

營養、身體活動和行為改變

- 8.12 Short-term nutrition intervention using structured, very-low-calorie meals (800–1,000 kcal/day) may be prescribed for carefully selected individuals by trained practitioners in medical settings with close monitoring. Long-term, comprehensive weight maintenance strategies and counseling should be integrated to maintain weight loss. (B)
- 在醫療機構經訓練人員小心選擇個案，使用非常低熱量飲食(800~1,000 kcal/day)進行短期飲食介入須密集監控。 長期減重者則需瞭解體重維持策略與諮商應併入計畫中。(B)

- 8.13 There is no clear evidence that nutrition supplements are effective for weight loss. (A)
- 沒有明顯證據說明保健食品可以有效減輕體重。(A)

Treatment options for overweight and obesity in type 2 diabetes

Treatment	BMI: 23~24.9	BMI: 25~27.4	BMI: ≧ 27.5
Diet, physical activities and behavioral counseling	+	+	+
Pharmacotherapy (藥物)		+	+
Metabolic surgery (手術)			+

※ Recommended cutpoints for **Asian American individuals**
Treatment may be indicated for select motivated patients

Look AHEAD Trial

- 雖然Look AHEAD試驗並沒有顯示，第2型糖尿病體重過重或肥胖者，經密集生活介入可降低心血管發生；但它確認了達到和維持長期體重減輕是可行的。**密集生活型態介入組在8年減輕4.7%體重，(其中約50% 受試者在第8年時，減輕和維持體重 ≧ 5%；27% 受試者可減輕和維持≧ 10%的體重。)**

- 分析Look AHEAD和其他大型心血管研究結果發現，第2型糖尿病人體重減輕有很多好處，包括改善mobility, physical and sexual function, 和生活品質。另外，許多心血管結果次項也得到改善，包括體重減輕>10% 和起始點血糖控制適度或不佳患者(>6.8%)。

Look AHEAD: Study design

Look Action for Health in Diabetes

N = 5145
45-74 years with T2DM, BMI ≥25 kg/m² (≥27 kg/m² if taking insulin)

Usual medical care + diabetes support and education for 4 years	Total follow-up 11.5 years	Usual medical care + lifestyle intervention* for 4 years, with maintenance counseling thereafter

Primary endpoint: **CV death, nonfatal MI, nonfatal stroke**

*≥7% mean weight loss with hypocaloric diet ± pharmacologic therapy + ≥175 min/week moderate physical activity
Diet = 1200-1500 kcal/day (<250 lbs) or 1500-1800 kcal/day (≥250 lbs)

Look AHEAD Research Group. *Control Clin Trials*. 2003;24:610-28; *Obesity*. 2006;14:737-52.

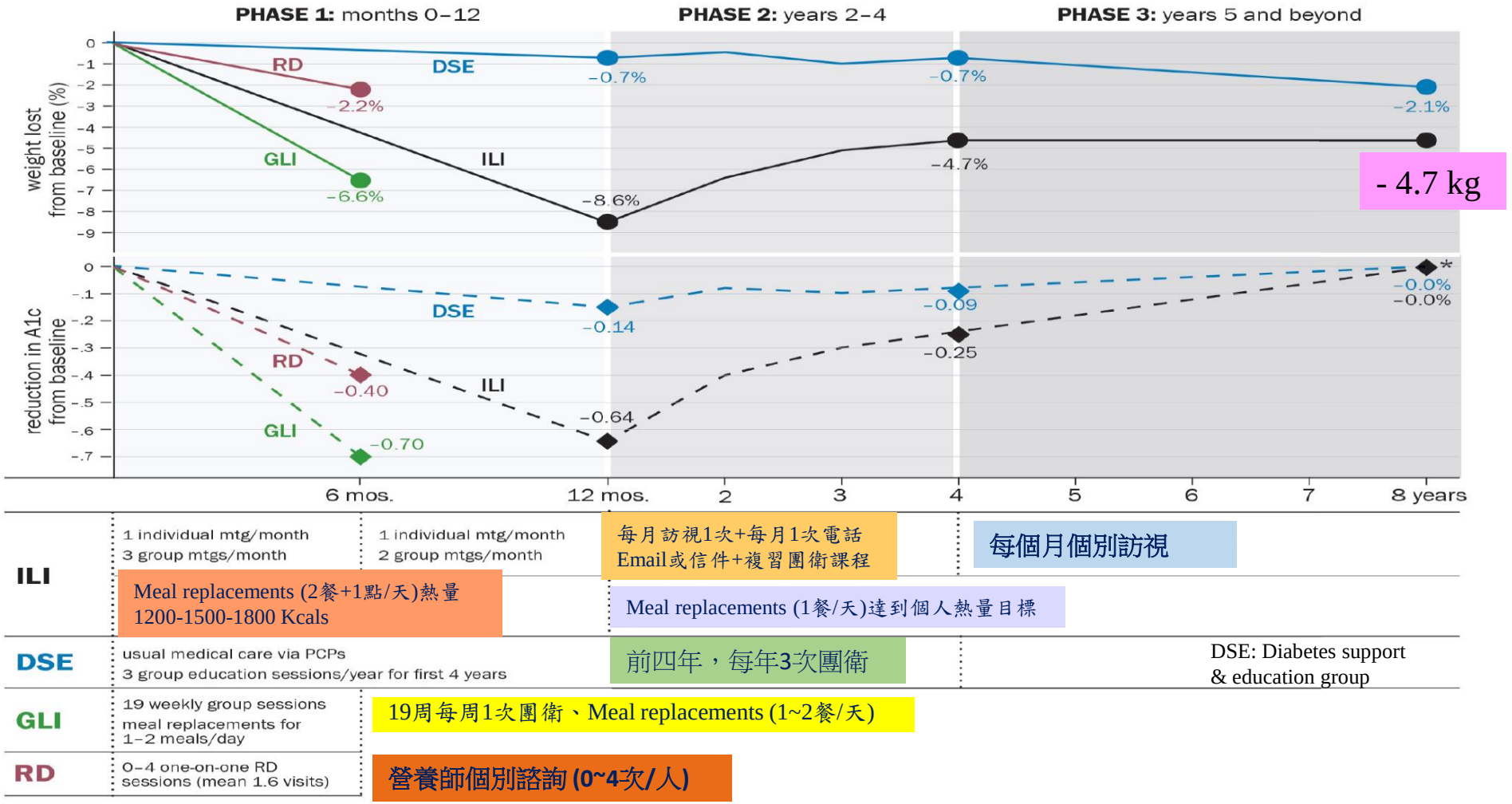


FIGURE 1. Weight loss and A1C reduction over time in the Look AHEAD and IDOLc studies. Six-month weight loss values and A1C values for the ILI and DSE groups were not published as individual data points. Eight-year A1C values are estimated from a published chart (1) because data were not presented in tables elsewhere. mos, months; mtg, meeting; PCP, primary care provider.

Diabetes Spectrum 2017 Aug; 30(3): 166-170

行為介入 (Behavioral Interventions)

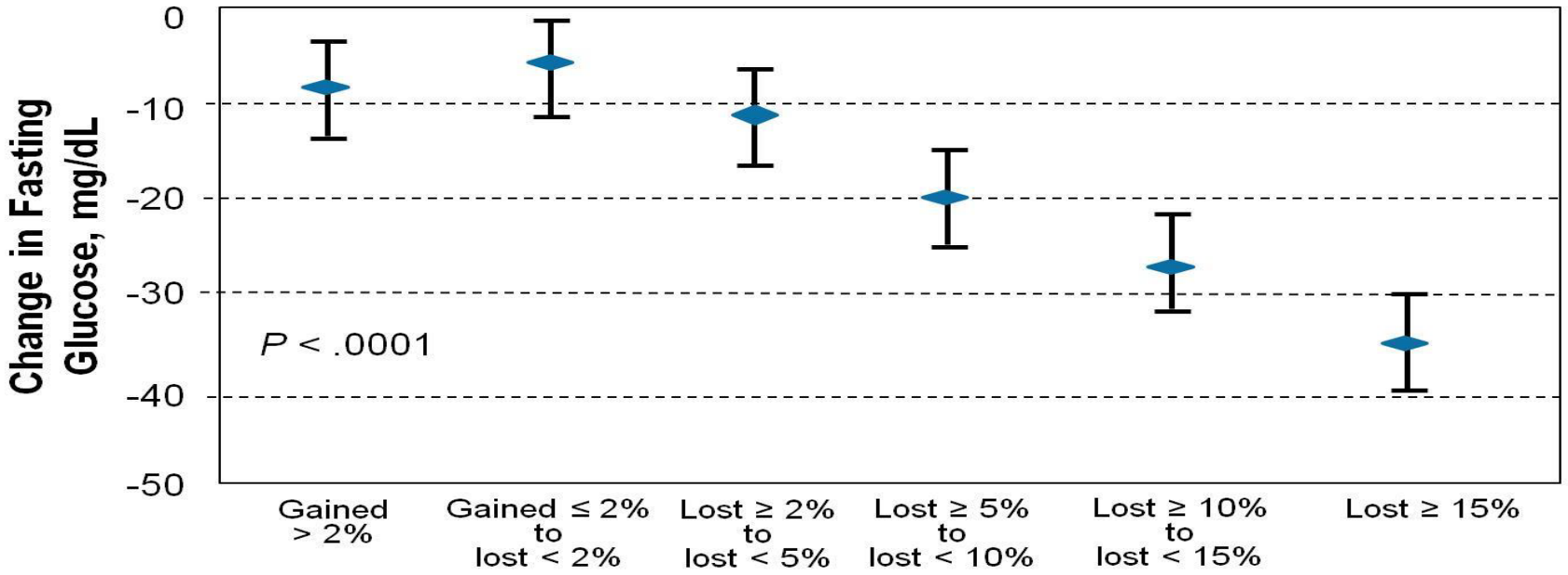
- 在生活型態計畫中，體重有顯著減少者每天減少 500~750卡 (女性每天約 1,200~1,500卡/天，男性約1,500~1,800卡/天)。體重減輕3~5%可看到臨床結果進步。達密集減重輕目標者(>5%, >7%, >15%等)能達更好的健康改善，如果病人動機較強且可安全達成目標。

- 飲食介入與巨量營養素控制目標和食物選擇不同，**只要熱量差距，就可減輕體重**。使用代餐和密集監控是有好處，在 Look AHEAD試驗之密集生活型態介入組(Intensive lifestyle intervention；ILI)，使用部分代餐，它與飲食品質和體重減輕有相關性。食物選擇應基於病人之健康狀況和喜好而訂，包括食物取得因素和文化環境等，都會影響飲食型態。

- ILI應包括前六個月 ≧ 16堂課和著重於飲食改變、運動和行為策略，以達每天減少500~750卡熱量。介入者應提供個別或團體課程，計畫開始時評估個案體重減輕之動機程度、生活環境和執行行為改變之意願，以及醫療狀況。

Look AHEAD: Effect of Amount of Weight Loss on Fasting Glucose

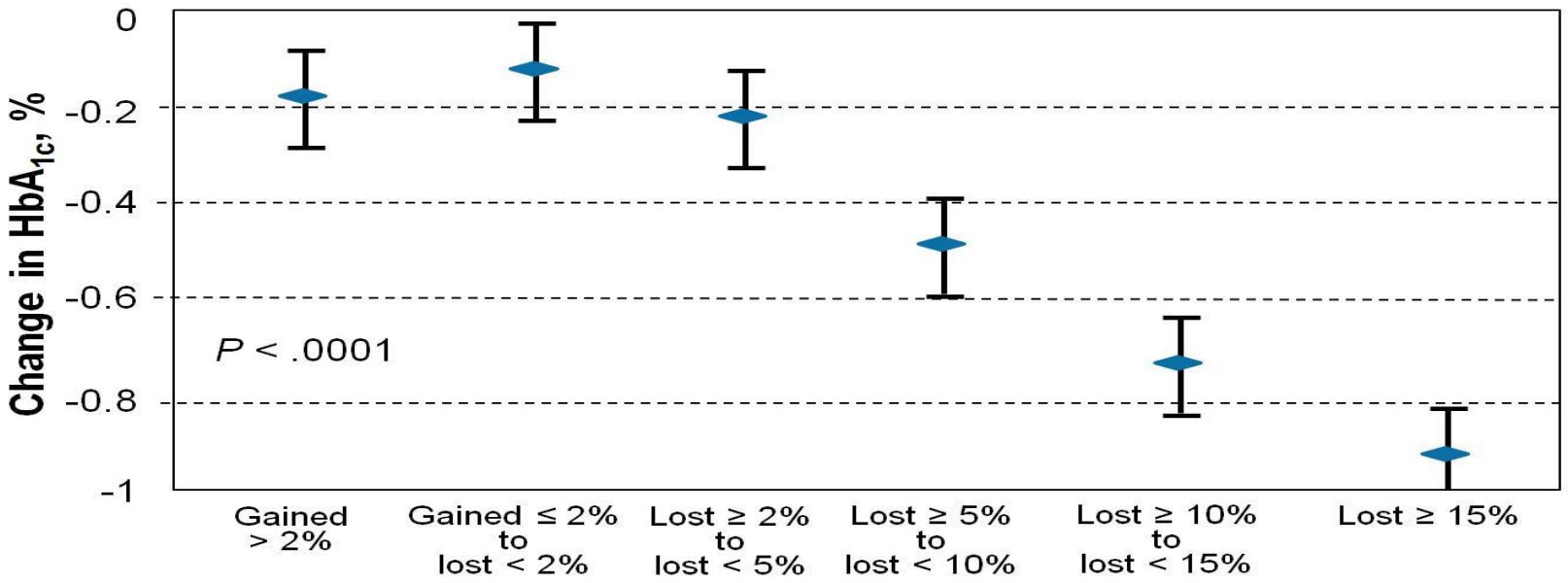
體重減輕對空腹血糖的影響



Wing RR, et al. *Diabetes Care*. 2011;34:1481-1486.[4]

Look AHEAD: Effect of Amount of Weight Loss on HbA_{1c}

體重減輕對糖化血色素(A1C)的影響



Wing RR, et al. *Diabetes Care*. 2011;34:1481-1486.[4]

行為介入 (Behavioral Interventions)

- 體重過重或肥胖之第2型糖尿病人曾經減重過者，應提供長期(≥1年)體重控制計畫，訓練過之介入者至少每月聯繫減重者，著重於體位監控(至少每周1次)和/或其他自我監控策略如飲食、步數等；繼續聚焦於飲食和行為改變，以及高強度運動量(200~300分鐘/周)。有些廣告保證減重效果之課程，大部分缺乏有效證據，許多不符合指引建議，有的甚至執行過程是危險的。

- 在醫療機構進行監控計畫，會審慎選擇病人並提供短期(約3個月)密集飲食介入，如在外科手術前減重和需減較多體重和改善血糖者。 結構性非常低醣飲食(800~1,000 卡/天)結合行為支持和諮商，可利用高蛋白飲食和代餐，以增加減重幅度和血糖改善。
- 體重回復是很平常，此需要提供長期體重維持策略和諮商以維持體重減輕和行為改變。

行為介入 (Behavioral Interventions)

- 儘管有廣泛的市場和宣稱，但**沒有明確的證據**顯示膳食補充劑（如草藥和植物藥、高劑量維生素和礦物質、氨基酸、酶、抗氧化劑等）對肥胖管理或減重有效。幾項大型系統分析研究顯示，大多數評估膳食補充劑減重試驗**品質不佳**且**有偏差風險高**。在已發表的高品質研究顯示，**減重效果差**或**沒效果**。
- 反之，維生素/礦物質（例如鐵、維生素 B12和 D）補充劑可能需要在有記錄證明病人缺乏的情況下進行，然而**蛋白質補充劑**可能可作為減重輔助處方。

- **健康差異**會對那些因種族、社經地位、性別、殘疾或其他因素而系統性地經歷較大健康問題者產生不利影響。很多研究顯示，這些差異可能顯著地影響健康結果，包括增加肥胖、糖尿病和糖尿病相關併發症風險。

藥物治療 (Pharmacotherapy)

- 8.14 When choosing glucose-lowering medications for people with type 2 diabetes and overweight or obesity, consider the medication's effect on weight. (B)
- 過重或肥型之第2型糖尿病人選擇降血糖藥物時，應考慮藥物對體重的影響

- 8.15 Whenever possible, minimize medications for comorbid conditions that are associated with weight gain. (E)
- 盡可能減少與體重增加相關的合併症的藥物治療。

糖尿病藥物對體重的影響

體重增加	不影響體重	體重減少
Insulin	Alpha-glucosidase inhibitors	GLP-1 agonists
Meglitinides	Bromocriptine	Metformin
Sulfonylureas	Colesevelam	Pramlintide
Thiazolidinediones	DPP-4 inhibitors	SGLT2 inhibitors

GLP-1 agonists: glucagon-like peptide-1 agonists, DPP-4 inhibitors: dipeptidyl peptidase-4 inhibitors, SGLT2 inhibitors: sodium-glucose co-transporter 2 inhibitors

藥物治療 (Pharmacotherapy)

- 8.16 Obesity pharmacotherapy is effective as an adjunct to nutrition, physical activity, and behavioral counseling for selected people with type 2 diabetes and BMI ≥27 kg/m^2. Potential benefits and risks must be considered. (A)
- 對於特定的 2 型糖尿病病人和 BMI ≥ 27 kg/m^2 ，肥胖藥物療法作為營養、身體活動和行為諮詢的輔助手段是有效的。必須考慮潛在的利益和風險。

藥物治療 (Pharmacotherapy)

- 8.17 If obesity pharmacotherapy is effective (typically defined as ≥ 5% weight loss after 3 months' use), further weight loss is likely with continued use. When early response is insufficient (typically <5% weight loss after 3 months' use) or if there are significant safety or tolerability issues, consider discontinuation of the medication and evaluate alternative medications or treatment approaches. (A)

- 如果肥胖藥物治療有效（通常定義為: 使用 3 個月後體重減輕≥ 5%），則繼續使用可能可以進一步減輕體重。當早期反應不夠時（通常使用 3 個月後體重減輕 <5%）或存在明顯的安全性或耐受性問題，考慮**停藥**並評估替代藥物或治療方法。(A)

代謝手術 (Metabolic Surgery)

- 8.18 Metabolic surgery should be a recommended option to treat type 2 diabetes in screened surgical candidates with BMI ≥ 40 kg/m^2 (BMI ≥ 37.5 kg/m^2 in Asian American individuals) and in adults with BMI 35.0– 39.9 kg/m^2 (32.5–37.4 kg/m^2 in Asian American individuals) who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with nonsurgical methods. (A)
- 對於經篩選的 BMI ≥ 40 kg/m^2（亞裔美國人 BMI ≥ 37.5 kg/m^2）和 BMI 為 35.0-39.9 kg/m^2（亞裔32.5-37.4 kg/m^2）的成人，使用非手術方法無法實現持久的體重減輕和改善合併症（包括高血糖症）的改善，代謝手術應該是治療 2 型糖尿病建議的選擇。

代謝手術 (Metabolic Surgery)

- 8.19 Metabolic surgery may be considered as an option to treat type 2 diabetes in adults with BMI 30.0–34.9 kg/m^2 (27.5–32.4 kg/m^2 in Asian American individuals) who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with nonsurgical methods.(A)
- 對於 BMI 為 30.0-34.9 kg/m^2（亞裔美國人為 27.5-32.4 kg/m^2）且非手術方法未實現持久體重減輕和改善合併症（包括高血糖症）的成年人，代謝手術可被視為治療 2 型糖尿病的一種選擇。

代謝手術 (Metabolic Surgery)

- 8.20 Metabolic surgery should be performed in high-volume centers with multidisciplinary teams knowledgeable about and experienced in managing obesity, diabetes, and gastrointestinal surgery. (E)
- 代謝手術應在有醫療團隊的大型中心進行，此團隊在管理肥胖、糖尿病和胃腸道手術方面的知識且經驗豐富。

- 8.21 People being considered for metabolic surgery should be evaluated for comorbid psychological conditions and social and situational circumstances that have the potential to interfere with surgery outcomes. (B)
- 考慮進行代謝手術的人，應評量共病心理狀況以及社會和情境狀況可能影響手術的結果。

代謝手術 (Metabolic Surgery)

- 8.22 People who undergo metabolic surgery should receive long-term medical and behavioral support and routine micronutrient, nutritional, and metabolic status monitoring. B
- 接受代謝手術的人應該接受長期的醫療和行為支持，以及常規的微量營養素、營養和代謝狀態監測。

代謝手術 (Metabolic Surgery)

- 8.23 If **postbariatric hypoglycemia** is suspected, clinical evaluation should exclude other potential disorders contributing to hypoglycemia, and management includes education, medical nutrition therapy with a dietitian experienced in postbariatric hypoglycemia, and medication treatment, as needed. (A) **Continuous glucose monitoring** should be considered as an important adjunct to improve safety by alerting individuals to hypoglycemia, especially for those with severe hypoglycemia or hypoglycemia unawareness. (E)
- 如果可能會有手術減肥後的低血糖，臨床評量應排除導致低血糖的潛在問題，管理包括教育、由對減肥後低血糖有經驗的營養師進行醫療營養治療(MNT)，以及藥物治療。**連續血糖監測**應被視為通過提醒個體注意低血糖來提高安全性的重要輔助方法，尤其是對於那些嚴重低血糖或未意識到低血糖的人。

代謝手術 (Metabolic Surgery)

- 8.24 People who undergo metabolic surgery should routinely be evaluated to assess the need for ongoing mental health services to help with the adjustment to medical and psychosocial changes after surgery. (C)
- 接受代謝手術的人應定期接受評量，以評估是否需要持續的心理健康服務，以幫助適應手術後的醫療和社會心理變化。

總結

- 建議以飲食、運動和行為治療達到減輕體重 ≥ 5%。
- 介入計畫應包括高頻率諮商(6個月≥ 16次課程) 和著重於飲食改變、運動和行為策略，以達每天減少500~750卡熱量。
- 應考量個人喜好、動機，生活環境以及醫療情況。
- 長期(≥1 年) 體重維持計畫，建議持續監測體重(每周1次以上)、其他監測策略，以及和鼓勵規律運動 (200~300 分鐘/周)。
- 使用非常低熱量飲食(800~1,000 kcal/day)之短期飲食介入須密集監控。
- 沒有明顯證據說明保健食品可以有效減輕體。

總結

- 過重或肥型之第2型糖尿病人選擇降血糖藥物時，應考慮藥物對體重的影響，盡可能減少與體重增加相關的合併症的藥物治療。
- BMI ≥ 27 kg/m^2 ，**肥胖藥物治療**可作為營養、身體活動和行為諮詢的輔助手段是有效的。
- 如果肥胖藥物治療(3個月)有效，則繼續。若使用 3 個月後體重減輕 <5%，可能要考慮**停藥**並評估替代方案。
- 對於 BMI ≥ 30.0 kg/m^2（亞裔≥ 27.5 kg/m^2 ）且非手術方法未實現持久體重減輕和改善合併症的成年人，**代謝手術**可被視為治療 2 型糖尿病的一種選擇。
- 接受代謝手術的人應該接受長期的醫療和行為支持，以及常規的微量營養素、營養和代謝狀態監測。

感謝您的聆聽

健康識能－創意衛教篇

根秀欽

教育部部定講師

【講字第106998號】

ken.lucy826@msa.hinet.net

0922880882

學 歷

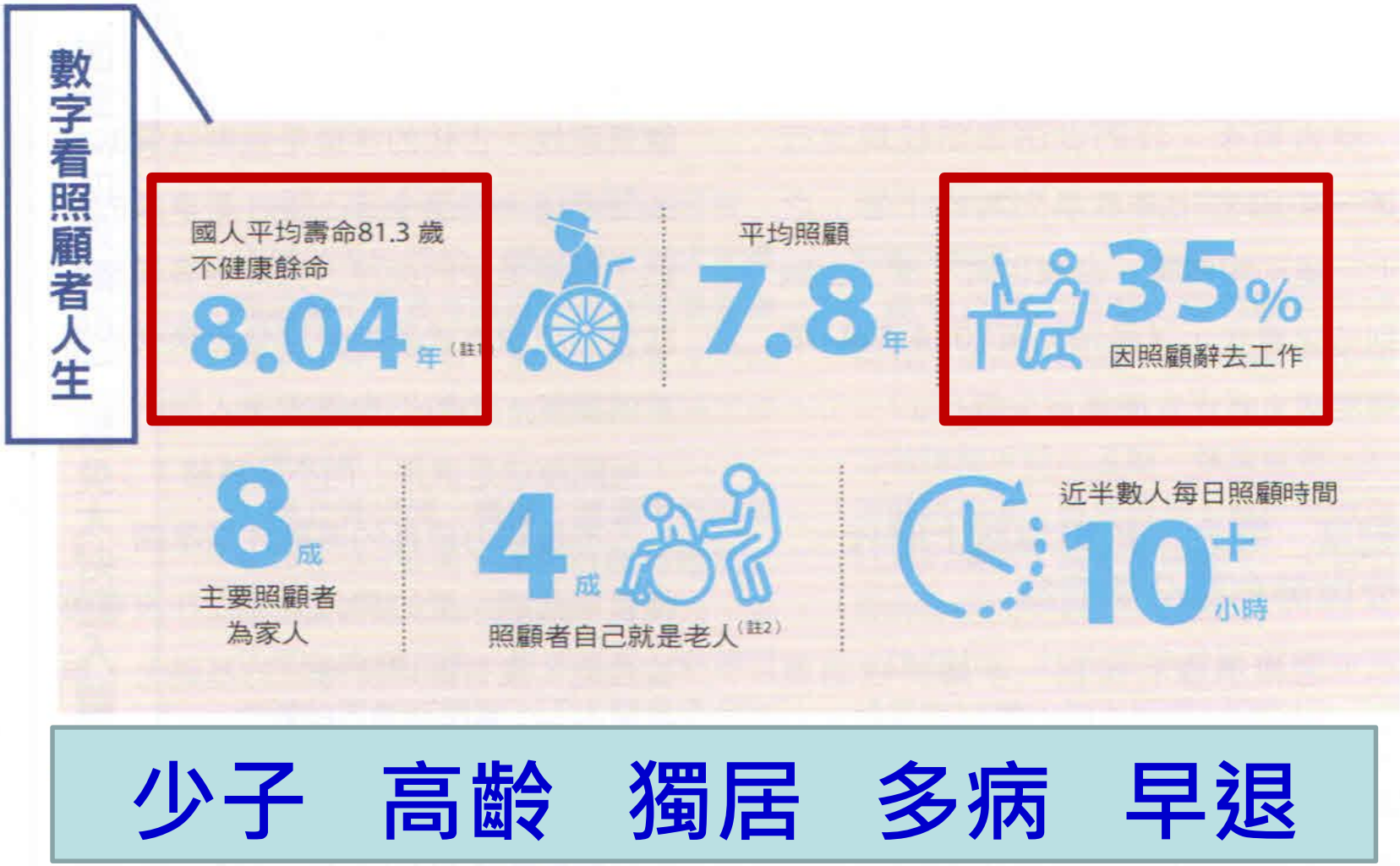
- 苗栗縣南庄鄉東河國小（60-65年）
- 苗栗縣頭份鎮大成國中（66-68年）
- 台北市私立稻江護校（69-71年）
- 國立台北護理學院護理學士（88-92年）
- 國立屏東科技大學社工二十學分班（93-94年）
- 國立屏東教育大學幼兒教育碩士（96-98年）
- 高雄師範大學性別教育研究所博士班備取3（101年）

經 歷

- 台北（林口、高雄）長庚紀念醫院　護士
- 新北市淡水區馬偕醫院安寧病房　護理組長
- 衛生福利部桃園醫院安寧病房　護理師
- 新北市三芝區雙連安養中心　副護理長
- 屏東基督教醫院社區醫學部　居服督導
- 寶建醫療社團法人附設春風護理之家　副主任
- 美和科技大學暨大仁科技大學護理系　兼任講師
- 高雄市政府衛生局暨屏東縣政府衛生局　外聘講師
- 記者會暨活動主持人- 社區金點獎、不老騎士、世界無菸日

高齢化挑戦篇

2022年出生率0.89 未來最多要照顧6個長輩



少子　高齡　獨居　多病　早退

投入醫療照護的初衷是?

服務是創造感動的機會

形象 = 個人、機構、專業

創意衛教篇

什麼是健康識能？

健康識能是利用很多不同技能來獲取、理解、表達及使用資訊，以方便就自己的健康做出正確決定。你的健康識能越高，就越能管控自己的健康及善用醫療資源。

健康識能是獲得健康知識並體認價值後，**採取有效措施和行為的能力**；進而能從社會醫療環境獲得最好醫療照護，採取有效健康促進、疾病預防、及善用社會醫療資源，**落實自我健康照護管理**。

對於健康充分了解並有效實施各種方式去保障及加強健康是每一個國民的基本能力，這種**「獲取並了解健康狀況、和掌握所有健康有關的知識，持續去經營管理健康的知識，並且實踐促進健康的行為的能力」，就是「健康識能（Health Literacy）」**。健康識能好，簡單講，就是智慧管理健康，醫療機構能幫助醫療人員和病患以至於家人和社區健康識能的提升，就是智慧醫院。

林老先生因自身罹患多種慢性疾病，必須按時服用超過8種以上的藥物，由於每種藥的服用頻率不同，常常一不注意就錯過用藥時間；**「按時服藥」對他來講是個傷腦筋的麻煩事**。但現在醫院主動在藥袋上以放大的公雞、太陽、月亮與床鋪等圖案，標明早、中、晚與睡前服用等資訊，一目了然，實在太便利了，醫院更將藥品拍照建檔，只要用手機掃描QR Code，就有藥師親自針對該項藥物的用藥說明，林老先生再也不怕吃錯藥。

有醫學中心引進擬人化機器人，協助就醫及衛教服務，來院就醫民眾與機器人互動簡單完成就診流程，或了解用藥及各項健康諮詢，有些醫院透過機器人在候診區帶動運動，別小看機器人威力，**這種訊息單一、生動有趣的帶領，往往提升病人學習意願，且因為重複學習，進而增加病人採行正確健康行為。**台中榮民總醫院糖尿病門診專區前，每天都有就醫民眾來跟機器人學機器舞，讓醫院實踐健康促進的服務目的。

根據世界衛生組織（WHO）的定義：

健康促進（Health promotion）

促使人們 **提高與改善** 健康狀態的過程。

在美國一般採用狹義的定義，即指

幫助人們改變其生活習慣

以達到理想健康狀態的一門科學與藝術。

建立新的習慣取代舊的習慣

一次一個就好

先做個小小的改變

創意是需要團隊合作的

團隊合作 是指一群人為相同目標而組成團隊合力工作的概念。

最弱的決定整個團隊的績效

行銷學 (Marketing)

要先 *認同* 行銷的產品




創意衛教三大基礎核心要素

- **認知（態度）- 健康識能（Health Literacy）**

  理性分析 - 趨勢、現況、專業、數據、政策、方法等

- **情意（情緒）- 醫病共享決策（SDM）**

  感性分享 - 情緒、故事、自我經驗、家人影響等

- **行為（動機）- 巧推理論（Nudge Theory）**

  知性落實 - 娛樂性、多元性、幽默性、方便性等

創意衛教原則

重點在「衛教」，創意是協助轉化，依不同的對象、在特定的時間點、以適當的方式，提供對方能夠吸收且能確實實踐的內容，完成既定的目的。

創意思維的定義

- 創意思維是指，運用思考得出新而有用的理念，**用以解決問題**，或是達到某些有價值的目的。
- 創意思考與邏輯思考不同，它沒有一套嚴謹的方法準則。
- 創意的關鍵在於思考新的可能性，包括新發明、新理念、和解決問題的新方法。
- **創意是一種習慣，而最佳的創意是從良好的工作習慣中產生**。

2017 年諾貝爾經濟學獎得主 Richard H. Thaler **輕推理論**（Nudge Theory），著名例子是西班牙實行器官捐贈選擇退出制度，**所有公民都會自動註冊成器官捐贈者，除非他們選擇另行說明才能退出**，這項制度是西班牙在器官捐贈方面處於世界領先地位原因之一。

創意思考要三生

1. 生命「創造力」

   壯遊擴展生命寬度

2. 生活「創意力」

   隨時觀察激發想像

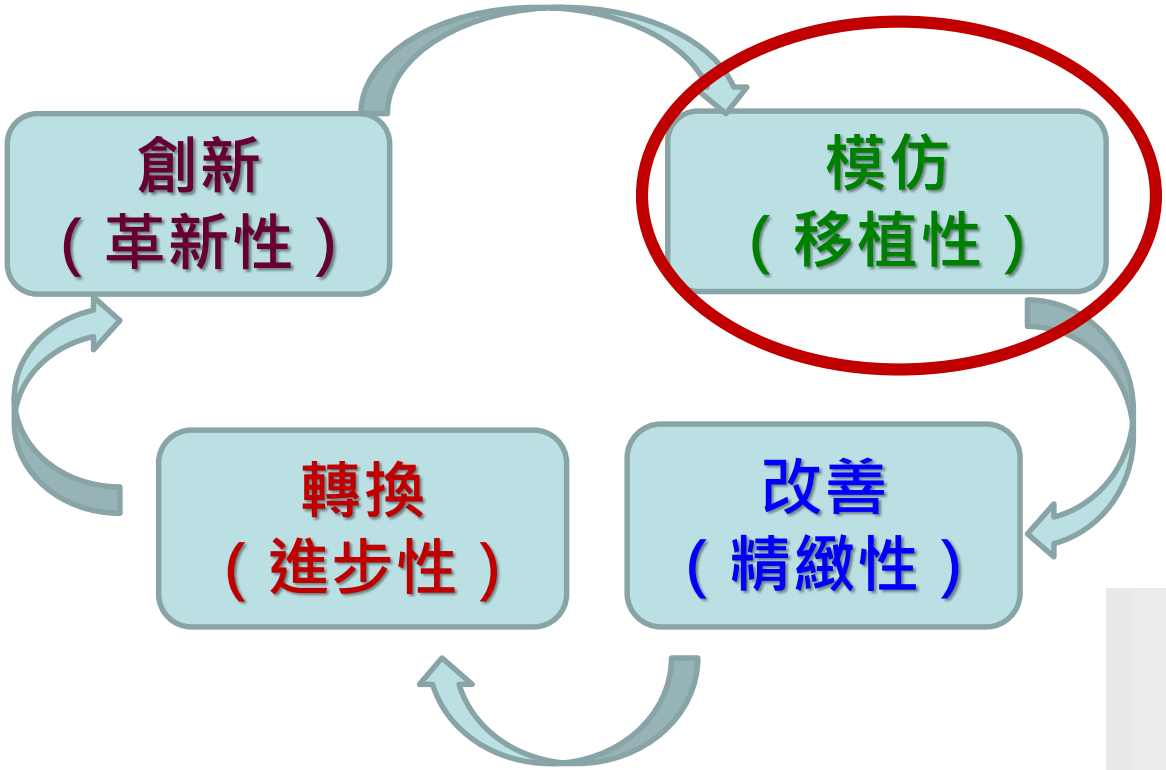
3. 生涯「創新力」

   學習興趣要跨領域

創意思維的訓練理念

- 創意思維技巧
  - 鼓勵**以不同角度去思考和探索問題**，不受常規所限，發展創造力及培養勇於創新的精神。
  - 可**按學習者的特性和需要**，延伸內容，彈性處理，提供支持性的環境，以開放性的提問技巧及靈活的策略，**激發學習者的創造潛能**。
  - 根據不同特性的問題，採用不同創意思考法。

創意從何開始？



創意思考哪裡找？

天時

- 從過去經驗找靈感
- 從現在問題找機會
- 從未來想像新創意

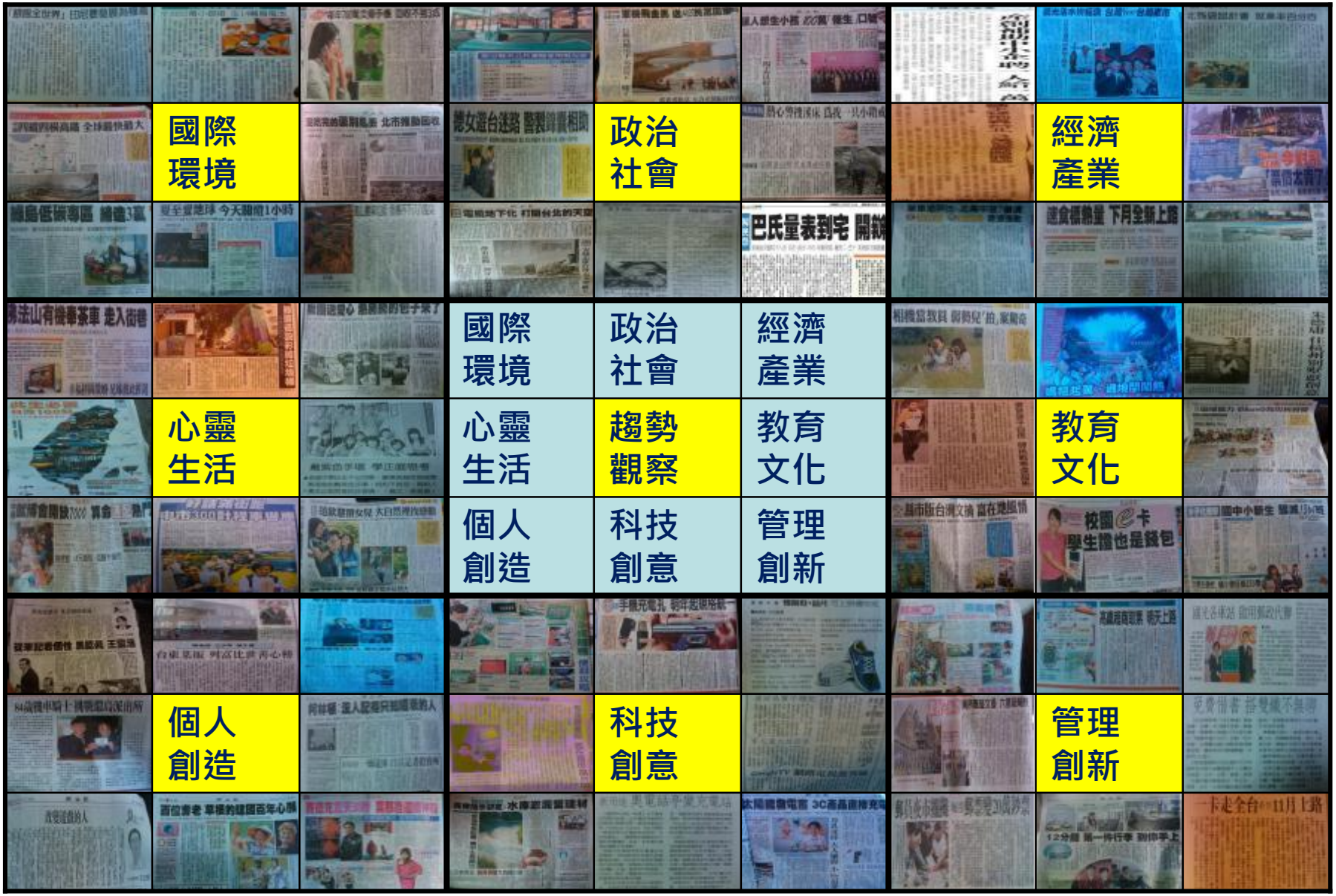
地利

- 身邊需求看到機會
- 報章雜誌趨勢創意
- 跨界旅行刺激靈感

人和

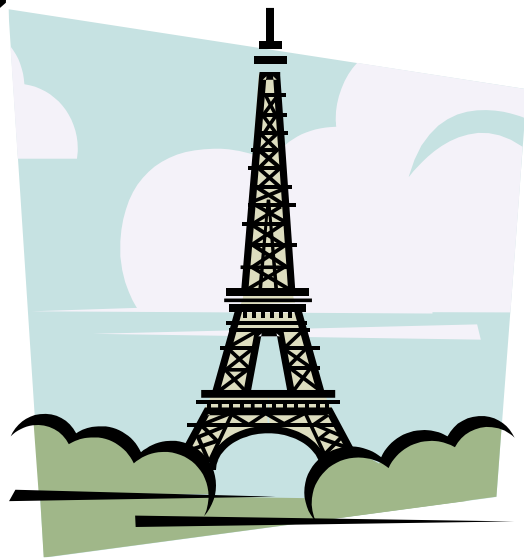
- 朋友對談激發創意
- 大師專家分享實務
- 異業學習啟發創新

瞭解趨勢變化 養成資料蒐集與觀察習慣



從生活中學習，充實自己

- 多觀察
- 多閱讀
- 多遊歷
- 多分享
- 多互動



創意行銷貼心小叮嚀

- 創意的關鍵在於概念的轉換。
- 洞察事物之間的關係可增強創意。
- **新的意念並非一定是好的。**
- 創新的意念不單是新的還必須有用。
- **創意是一種習慣可落實在生活環境中。**

練習. 練習. 再練習

1. 自信的態度
2. 吸引人的自我介紹
3. 真誠溫暖的語句
4. 說故事的原則
5. 方言的運用

創造「說」與「聽」之間的良性互動

會說話很重要嗎？

聲音表情 =

音調 +

速度 +

感情 +

用字遣詞

禮物運動

「我們每一天都可以得到禮物，也可以當個送禮物的人。」**一句問候、一句讚美、一句關心的話語都可以是禮物**，在簡單的語言之間，送禮物的動作已經完成了。面對挫折、挑戰與困境，只需換個心境，以積極思路去思考如何解決問題，不要陷入問題本身，**逆境也將會是一份禮物**。

不要想「改變」任何他人。

你可以「幫忙」，但不是「改變」。

「幫忙」是，幫可以幫的忙，

幫了之後就離開。並且放下。

不要用你的「幫忙」想去改變別人，

那是控制，也可能是一種對人的支配。

幫你能幫的，放下你不能幫的...