서울아산병원 Asan Medical Center 당뇨병센터 Asan Diabetes Center

2025년 서울아산병원
당뇨병 개원의 연수강좌

임상에서 바로 쓰는 당뇨병 치료 실전 노하우

일시: 2025년 **6월 29일**(일) **08:30~13:10** 장소: **ONLINE**

온라인 시청

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PROGRAM

08:30 – 08:35	개회사	서울아산병원 당뇨병센터 소장 **고은희**
Session 1	**당뇨병 치료의 핵심**	좌장: 서울아산병원 내분비내과 **고은희**
08:35 – 08:55	**2025 당뇨병 진료 지침: 무엇이 바뀌었나?**	서울아산병원 내분비내과 **정창희**
08:55 – 09:15	**경구혈당강하제, 효과적인 처방 노하우**	서울아산병원 내분비내과 **조윤경**
09:15 – 09:35	**다양한 당뇨병 주사 치료제: 이것만은 기억하자!**	건국대학교병원 내분비내과 **최종한**
09:35 – 10:00	Q&A	
10:00 – 10:10	Break	
Session 2	**당뇨병 치료제의 부작용 대처법**	좌장: 서울아산병원 내분비내과 **이우제**
10:10 – 10:30	**SGLT2 억제제, 잘 쓰려면 꼭 알아야 할 포인트**	한림대학교 동탄성심병원 내분비내과 **이지우**
10:30 – 10:50	**GLP-1 수용체작용제, 효과와 부작용 사이에서 균형잡기**	중앙대학교 광명병원 내분비내과 **김휘승**
10:50 – 11:05	**연속혈당측정 장치: 처방부터 부착까지**	서울아산병원 당뇨병센터 **신윤정**
11:05 – 11:30	Q&A	
11:30 – 11:40	Break	
Session 3	**당뇨병 동반 질환 제대로 관리하기**	좌장: 서울아산병원 내분비내과 **김민선**
11:40 – 12:00	**지방간, 놓치면 손해! 조기 진단과 치료 업데이트**	서울아산병원 소화기내과 **최원묵**
12:00 – 12:20	**당뇨병 만성콩팥병 관리의 모든 것**	서울아산병원 내분비내과 **민세희**
12:20 – 12:40	**당뇨병 환자의 뇌 건강, 어떻게 지킬까?**	서울아산병원 신경과 **임재성**
12:40 – 13:05	Q&A	
13:05 – 13:10	폐회사	서울아산병원 당뇨병센터 소장 **고은희**

* 목 차

Session 1 당뇨병 치료의 핵심

Session 2 당뇨병 치료제의 부작용 대처법

Session 3 당뇨병 동반 질환 제대로 관리하기

서울아산병원 당뇨병센터
Asan Medical Center Asan Diabetes Center

01
Session

당뇨병 치료의 핵심

2025 당뇨병 진료 지침: 무엇이 바뀌었나?

서울아산병원 내분비내과 **정창희**

경구혈당강하제, 효과적인 처방 노하우

서울아산병원 내분비내과 **조윤경**

다양한 당뇨병 주사 치료제: 이것만은 기억하자!

건국대학교병원 내분비내과 **최종한**

01
Session

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최근 다양한 기관의 가이드라인을 살펴보면, 2형 당뇨병 치료의 핵심이 심장 및 신장 위험 감소(Cadio-Renal Risk Reduction)에 맞춰져 있음을 알 수 있습니다. 특히 미국에서는 강력한 체중 감소 효과를 가진 항당뇨병 약물들이 등장하면서, 2형 당뇨병의 진행과 밀접한 관련이 있는 '비만' 관리의 중요성이 더욱 부각되고 있습니다. 우리나라의 대한당뇨병학회 진료 지침 역시 전반적인 방향은 미국 당뇨병학회의 지침과 유사하여 큰 차이는 없었으나, 최근 2025년 진료 지침에서는 다음과 같은 큰 변화가 있습니다.

1) 혈당 강하, 췌도부전 치료, 심장혈관신장 위험인자 조절 세가지 축으로 제시
2) 혈당 조절과 췌도부전 치료에 대한 강조 (동반질환에 대한 지나친 강조 자제)
3) 근거 중심의 지침 (정부주도 의료보험 시스템 하에서 발생하는 약제 급여심사기준에 의해, 처방 지침이 왜곡되는 현상 주의)
4) 메트포민 1차 약제로서의 권고 삭제, 환자 개별화된 약제 선택 강조

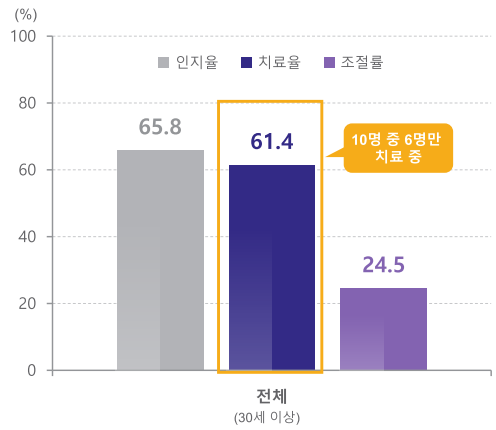
이번 강의에서는 미국과 한국의 최신 2형 당뇨병 진료 지침을 간략히 살펴보고, 실제 환자 진료 시 주의해야 할 핵심 포인트들을 중심으로 설명 드리고자 합니다.

2025 당뇨병 진료 지침: 무엇이 바뀌었나?

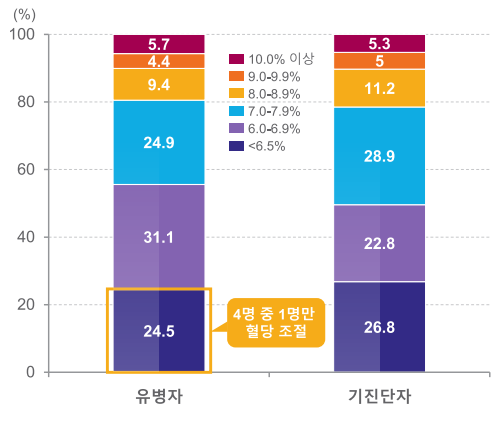
서울아산병원 내분비내과
정 창 희

Target Achievement Rate in Korea

당뇨병 관리 수준*†



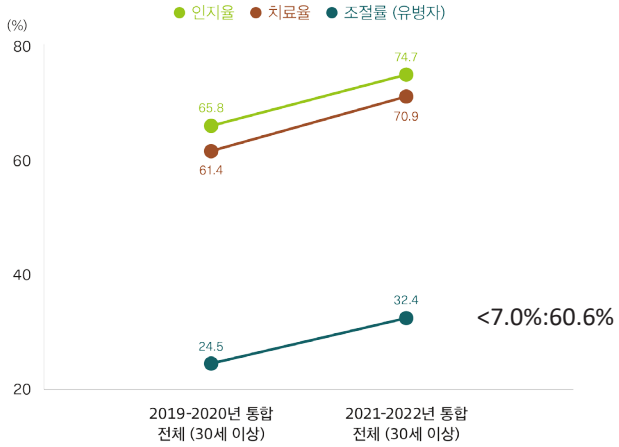
혈당 조절 상태*



*2019-2020년 통합
†당뇨병 인지율: 당뇨병 유병자(당화혈색소 기준) 중 의사로부터 당뇨병 진단을 받은 분율.당뇨병 치료율: 당뇨병 유병자(당화혈색소 기준) 중 현재 당뇨병 약제로 치료 중인 분율. 당뇨병 조절률: 당뇨병 유병자(당화혈색소 기준) 중 당화혈색소가 6.5% 미만인 분율.
Korean Diabetes Association. Diabetes fact sheet in Korea 2022.

당뇨병 관리 수준

2019-2020년에 비해 2021-2022년 조사에서 당뇨병 인지율, 치료율, 조절률이 모두 증가하였음.



당뇨병 유병자: 공복혈당이 126 mg/dL 이상이거나 의사로부터 당뇨병을 진단받았거나 당뇨병약제로 치료 중이거나 당화혈색소가 6.5% 이상인 경우
당뇨병 인지율: 당뇨병 유병자 (당화혈색소 기준) 중 의사로부터 당뇨병 진단을 받은 분율
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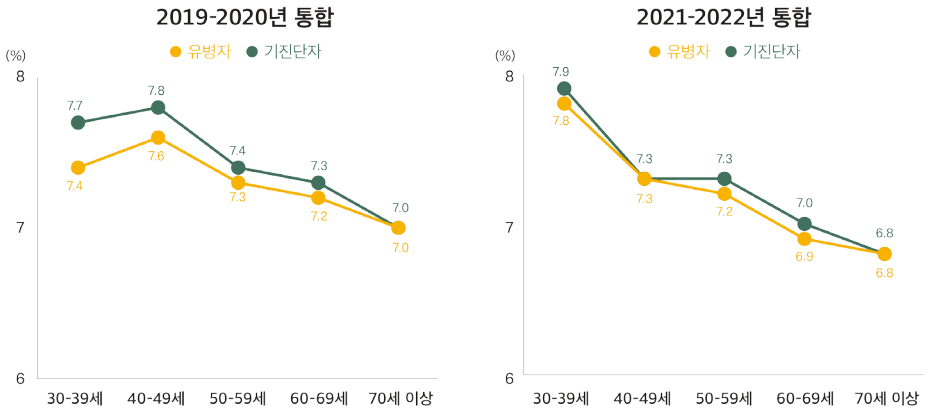
당뇨병 조절률: 당뇨병 유병자 (당화혈색소 기준) 중 당화혈색소가 6.5% 미만인 분율

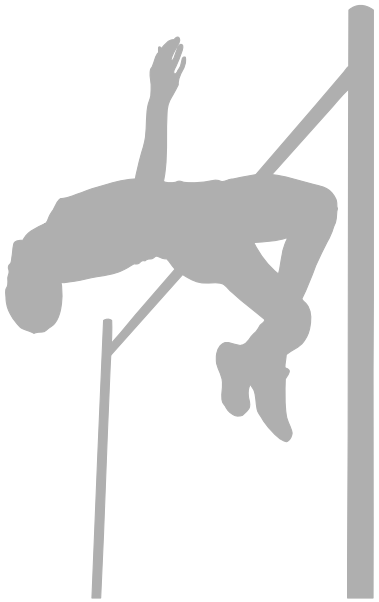
연령대별 평균 당화혈색소

연령대별 평균 당화혈색소는 30-40대에서 다른 연령대에 비해 더 높음.
40대 이후 평균 당화혈색소가 2021-2022년도 향상되었으나 30대에서는 이전에 비해 더 높은 수치를 보임.



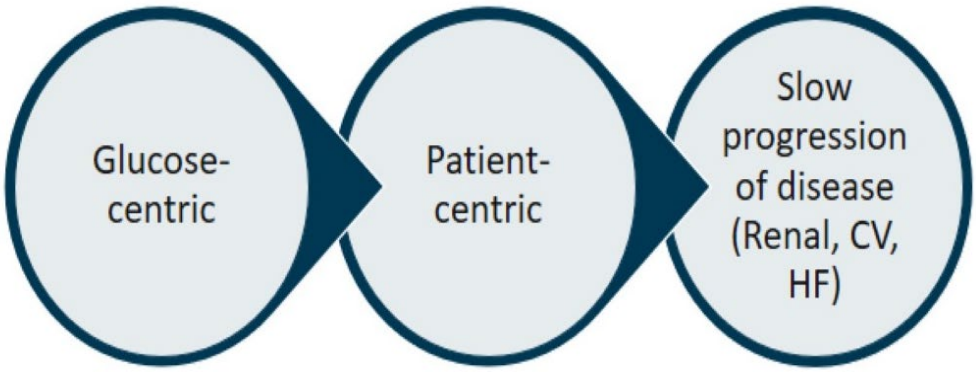
Challenges in the Treatment of T2DM

- Progressive disease[1]
- Numerous pathophysiological dysfunctions[2]
- Effective treatment requires multiple drugs used in combination to correct multiple pathophysiological defects[2]
- Lack of Cardiovascular Benefit of conventional treatments



[1]Diabetes 2009;58:773-795
[2]Diabetes Care 2001;24:89-94

Paradigm Shift in T2DM Management



Paradigm Shift in T2DM Management

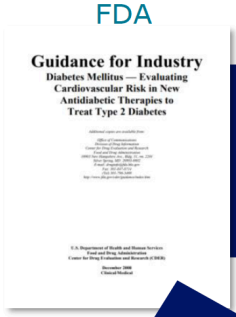
- T2DM 치료 가이드라인은 2018년을 기점으로 동반질환 및 합병증 등, 환자 중심의 접근 방식으로 발전

2017	2018	2020	2022	2023, 2024
American Diabetes Association	American Diabetes Association. EASD	American Diabetes Association	American Diabetes Association	American Diabetes Association
First line therapy:	**First line therapy:**	**First line therapy:**	**First line therapy:**	**First line therapy:**
Metformin and comprehensive lifestyle management	Metformin and comprehensive lifestyle management	Metformin and comprehensive lifestyle management	Depends on co-morbidities, patient-centered factors, etc	Not mentioned
Monotherapy unless A1c ≥ 9% Step-wise therapy Patient-& disease-specific factors	Established ASCVD, HF or CKD	Indicators of high risk of eASCVD, ASCVD, HF or CKD Independent of A1c (Consider)	Indicators of high risk of eASCVD, ASCVD, HF or CKD Independent of A1c or Metformin (Recommend)	Goal: Cardiorenal risk reduction in high-risk patients with T2DM Indicators of high risk of eASCVD, ASCVD, HF or CKD Independent of A1c or Metformin

1. Diabetes Care 2016;40(Suppl) S64-S74 2. Melanie J Davies et al., Diabetologia. 2018 Dec;61(12):2461-2498 3. Diabetes Care 2020;43(Suppl. 1):S98-S110 4. Diabetes Care 2022;45(Suppl. 1):S125-S143 5. Diabetes Care 2023;46(Suppl. 1):S140-S157 6. Diabetes Care 2024;47(Suppl. 1):S158-S178

Cardiovascular outcome trials (CVOTs)

2008
FDA


Guidance for Industry
Diabetes Mellitus — Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes

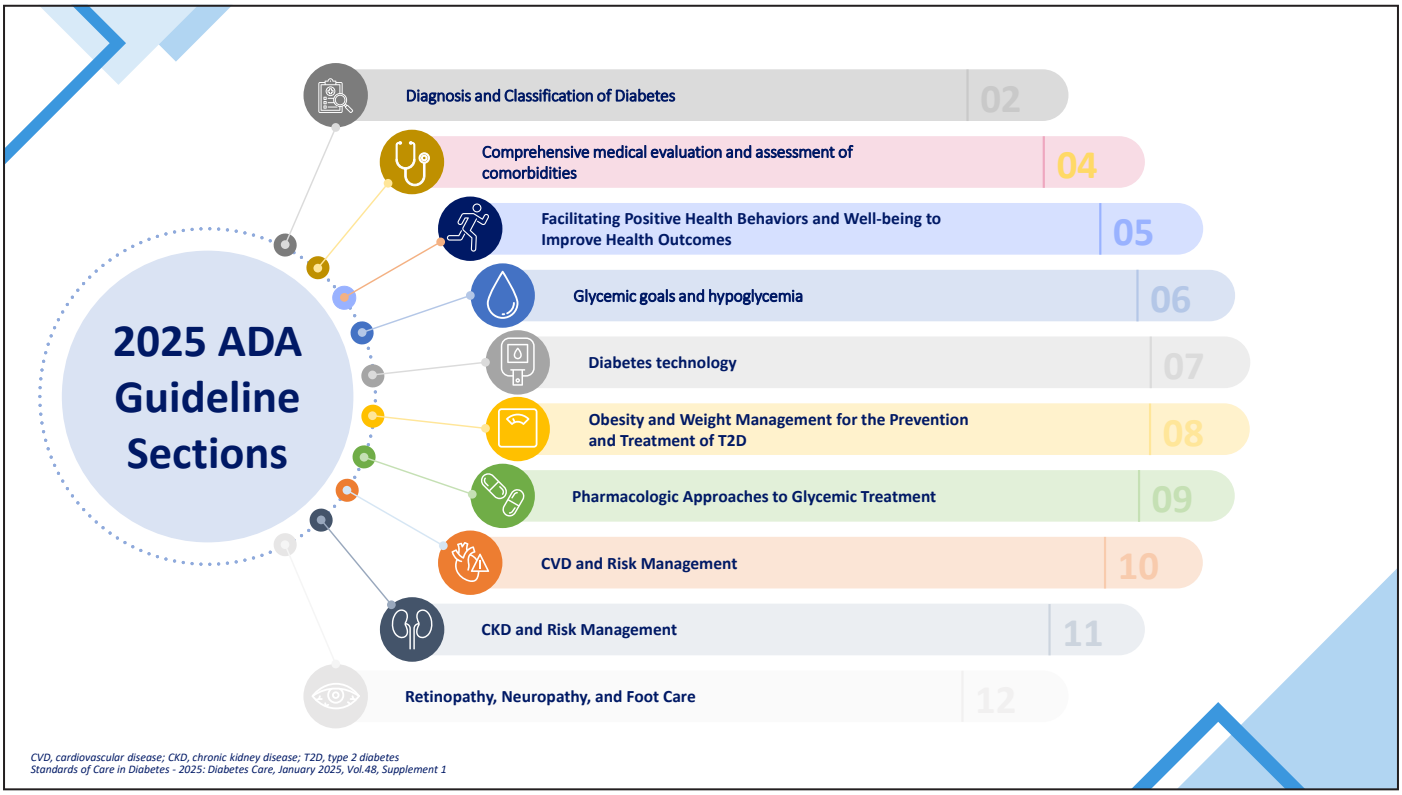
CVOTs for all new drugs:
- DPP-4i
- GLP-1RA
- SGLT2i
- Insulin

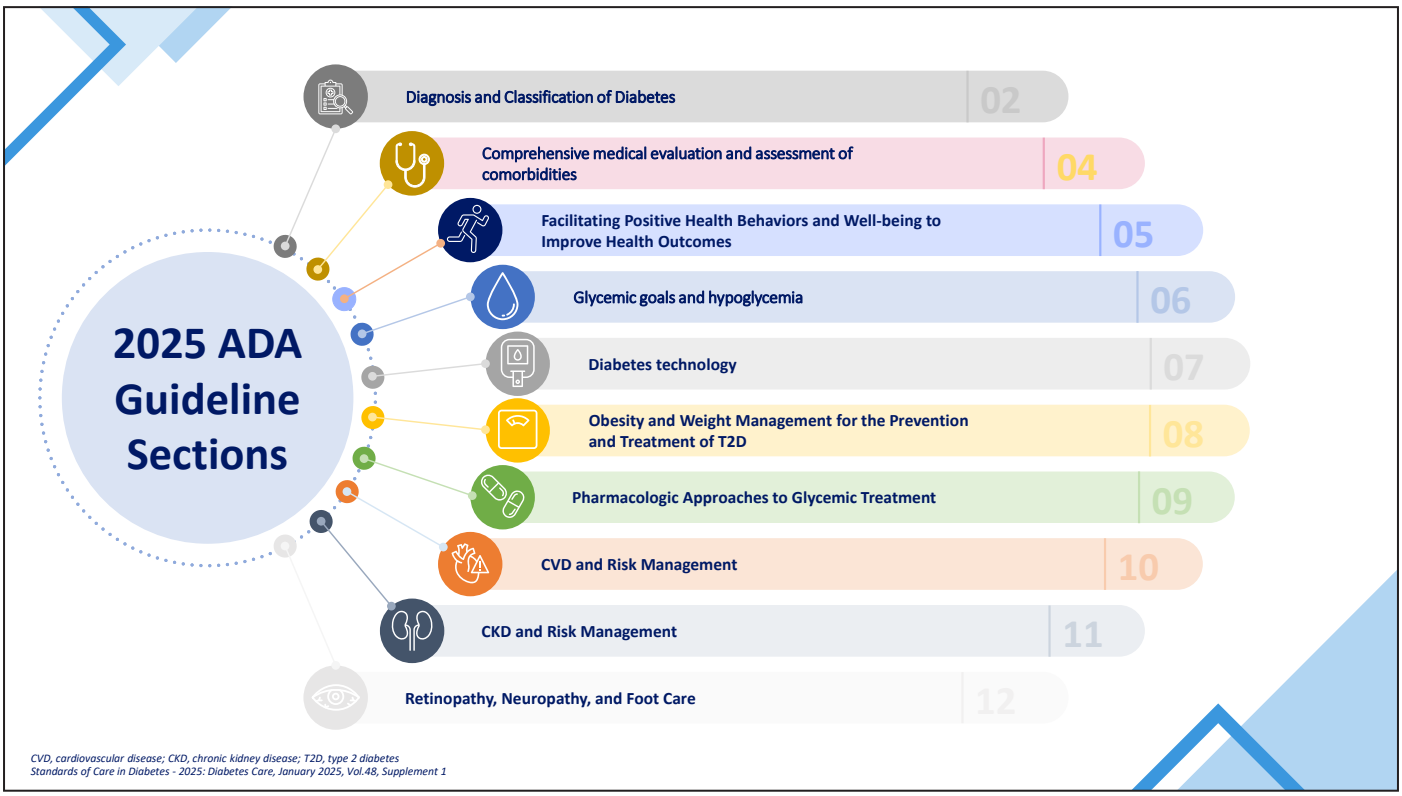
"Recommendations:
To establish the safety of a new antidiabetic therapy to treat type 2 diabetes, sponsors should demonstrate that the therapy will not results in an unacceptable increase in cardiovascular risk"

2015-2020
ADA/EASD, AACE/ACE, ACC/AHA.

NEW GUIDELINES

AACE, American Association of Clinical Endocrinologists; ACC, American College of Cardiology; ACE, American College of Endocrinology; AHA, American Heart Association; CV, cardiovascular; CVOT, cardiovascular outcomes trial; DPP-4i, dipeptidyl peptidase-4 inhibitor; EASD, European Association for the Study of Diabetes; FDA, U.S. Food and Drug Administration; GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT2i, sodium-glucose co-transporter 2 inhibitor.


2025 ADA Guideline Sections
Diagnosis and Classification of Diabetes 02
Comprehensive medical evaluation and assessment of comorbidities 04
Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes 05
Glycemic goals and hypoglycemia 06
Diabetes technology 07
Obesity and Weight Management for the Prevention and Treatment of T2D 08
Pharmacologic Approaches to Glycemic Treatment 09
CVD and Risk Management 10
CKD and Risk Management 11
Retinopathy, Neuropathy, and Foot Care 12
CVD, cardiovascular disease; CKD, chronic kidney disease; T2D, type 2 diabetes
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1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Chapter 04

MASLD and MASH Screening

Recommendations		
4.22a	Screen adults with T2D or with prediabetes, particularly those with obesity or other cardiometabolic risk factors or established cardiovascular disease, for their risk of having or developing cirrhosis related to MASH using a **calculated FIB-4, even if they have normal liver enzymes.**	B
4.22b	Adults with diabetes or prediabetes with **persistently elevated plasma aminotransferase levels for >6 months and low FIB-4 should be evaluated for other causes of liver disease.**	B
4.23	Adults with T2D or prediabetes with a **FIB-4 ≥1.3** should have additional risk stratification by **liver stiffness measurement** with transient elastography, or, if unavailable, the ELF test.	B
4.24	Refer adults T2D or prediabetes at higher risk for **significant liver fibrosis** (i.e., as indicated by FIB-4, liver stiffness measurement, or ELF) to a **gastroenterologist or hepatologist** for further evaluation and management.	B

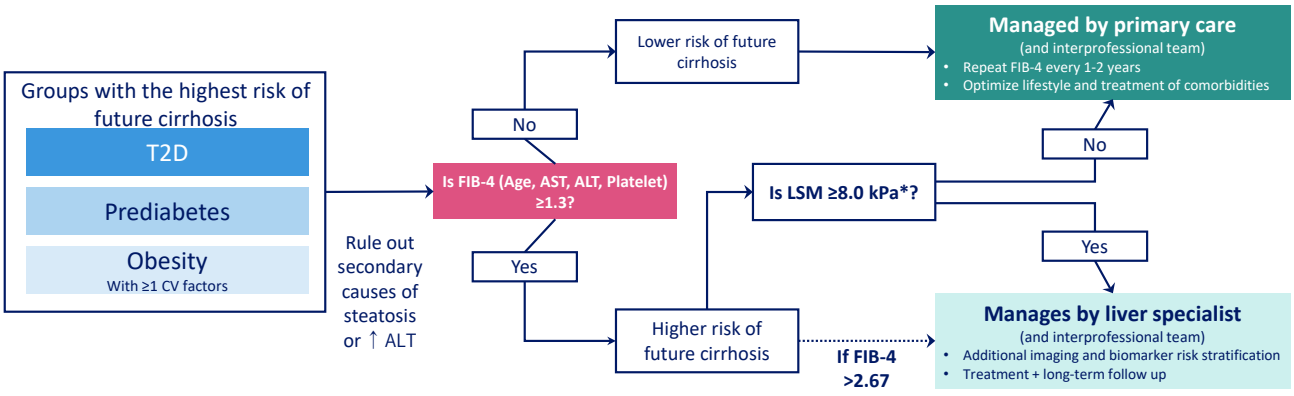
Refer to diagnostic algorithm for risk-stratification and prevention of cirrhosis in individuals with MASLD

ELF, enhanced liver fibrosis; Fib-4, fibrosis-4; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; T2D, type 2 diabetes.
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1

Chapter 04

Diagnostic algorithm for risk stratification in individuals with MASLD

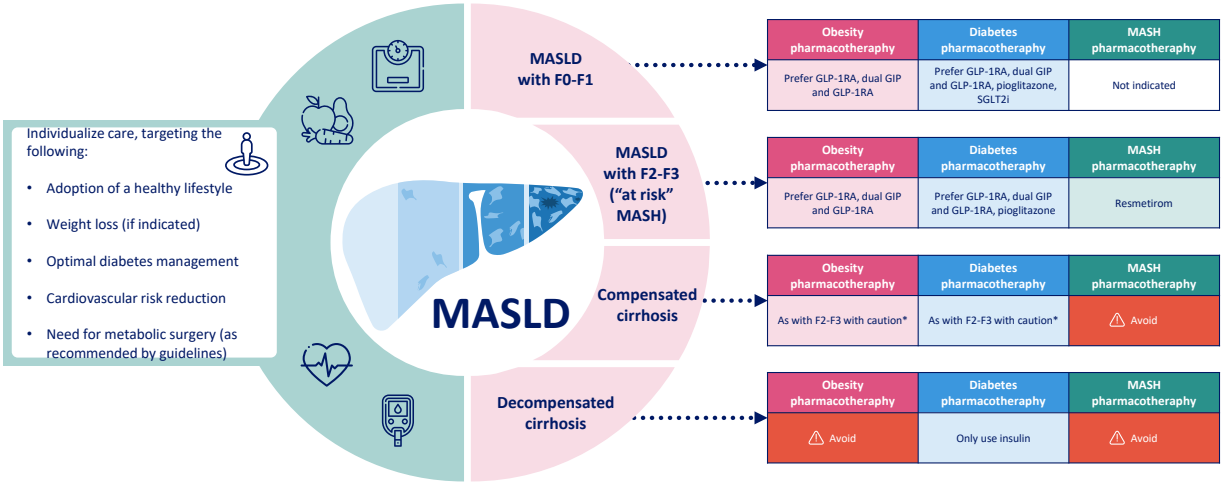
Diagnostic Algorithm for the Prevention of cirrhosis in people with MASLD



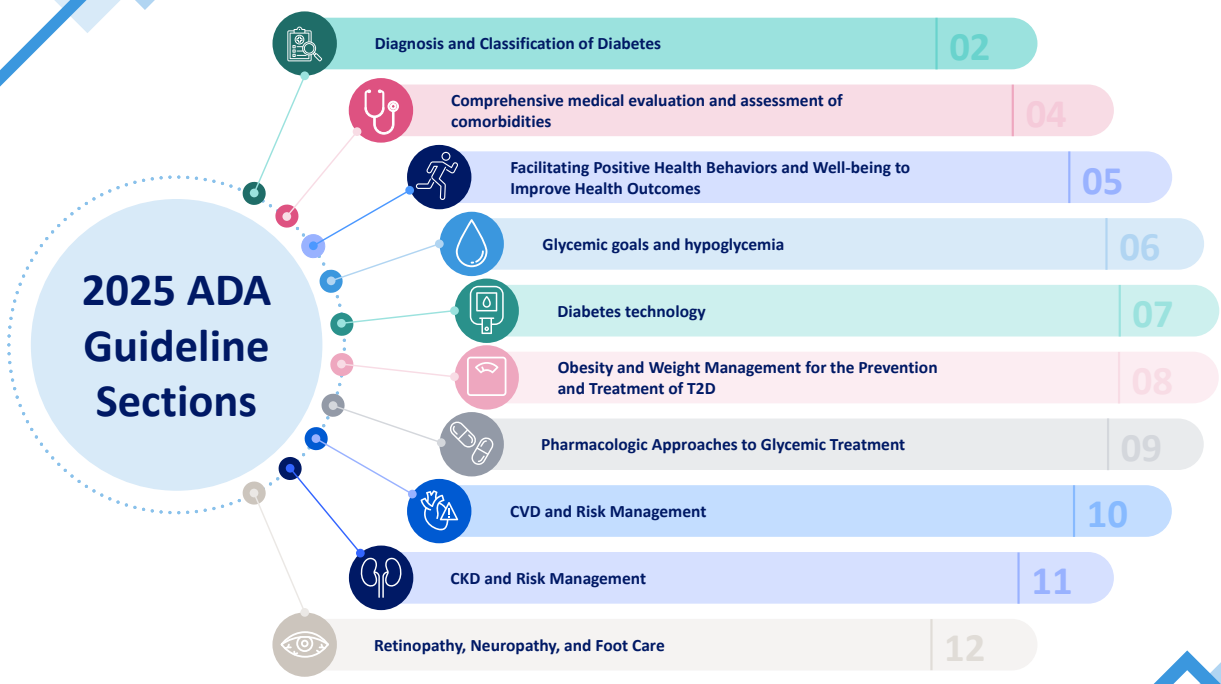
*CV, cardiovascular; ELF, enhanced liver fibrosis test; FIB-4, fibrosis-4 index; LSM, liver stiffness measurement, as measured by vibration-controlled transient elastography; MASLD, metabolic dysfunction-associated steatotic liver disease; T2D, type 2 diabetes.*In the absence of LSM, consider ELF a diagnostic alternative. If ELF ≥9.8, an individual is at high risk of metabolic dysfunction–associated steatohepatitis with advanced liver fibrosis (≥F3–F4) and should be referred to a liver specialist. Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1,* ***Figure 4.2***

Chapter 04

Treatment algorithm in individuals with MASLD



*Individualised care and close monitoring needed in compensated cirrhosis given limited safety data available.
F0-F1, no to minimal fibrosis; F2-F3, moderate fibrosis; F4, cirrhosis; GIP, glucose-dependent insulinotropic polypeptide; GLP-1RA, glucagon-like peptide-1 receptor agonist; MASH, metabolic dysfunction–associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; SGLT2i, sodium–glucose cotransporter-2 inhibitor. Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1. ***Figure 4.3***

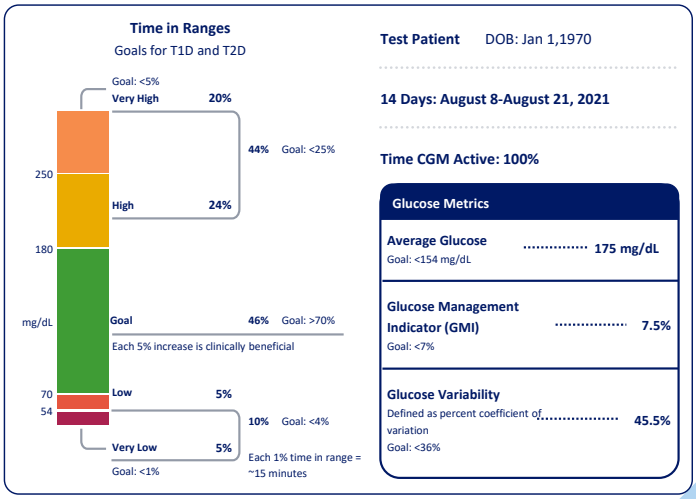


CVD, cardiovascular disease; CKD, chronic kidney disease; T2D, type 2 diabetes
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1

Glucose assessment by continuous glucose monitoring

Recommendations		
6.3a	An HbA_{1c} goal of <7% (<53 mmol/ mol) is appropriate for many nonpregnant adults without severe hypoglycemia or frequent hypoglycemia affecting health or quality of life.	A
6.3b	A goal time in range of >70% in people using CGM is appropriate for many nonpregnant adults.	B
6.3c	A goal percent time <70 mg/dL (<3.9 mmol/L) of <4% (or <1% for older adults) and a goal percent time <54 mg/dL (<3.0 mmol/L) of <1% are recommended in people using CGM to prevent hypoglycemia. Deintensify or modify therapy if these goals are not met.	B

Fig 6.1. AGP report: Continuous Glucose Monitoring



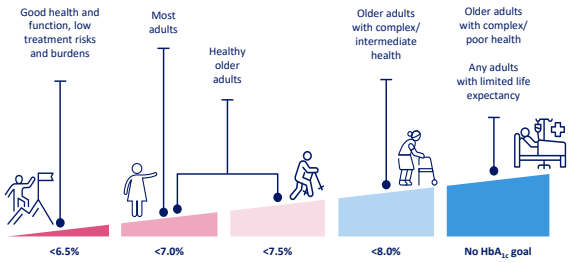
AGP, ambulatory glucose profile; CGM, continuous glucose monitoring; DOB, date of birth; HbA_{1c}, glycated hemoglobin; T1D, type 1 diabetes; T2D, type 2 diabetes; TIR, time in range
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1

Glycemic goals

Recommendations		
6.4	Based on health care professional judgment and the preference of the person with diabetes, **achievement of lower HbA_{1c} levels than the goal of 7% (53 mmol/mol) may be acceptable and even beneficial** if it can be achieved safely without significant hypoglycemia or other adverse effects of treatment.	B
6.5	**Less stringent glycemic goals** may be appropriate for individuals with limited life expectancy or where the harms of treatment are greater than the benefits.	B
6.8	Reassess glycemic goals based on the individualized criteria shown in Fig. 6.2.	E
6.9	Set a glycemic goal during consultations to improve outcomes.	A

Figure 6.2

Individualized HbA_{1c} goals for nonpregnant adults.



Favor more stringent goal	Favor less stringent goal
Short diabetes duration	Long diabetes duration
Low hypoglycemia risk	High hypoglycemia risk
Low treatment risks and burdens	High treatment risks and burdens
Pharmacotherapy with cardiovascular, kidney, weight, or other benefits	Pharmacotherapy without nonglycemic benefits
No cardiovascular complications	Established cardiovascular complications
Few or minor comorbidities	Severe, life-limiting comorbidities

HbA_{1c}, glycated hemoglobin
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1

Novo Nordisk®

2025 ADA Guideline Sections

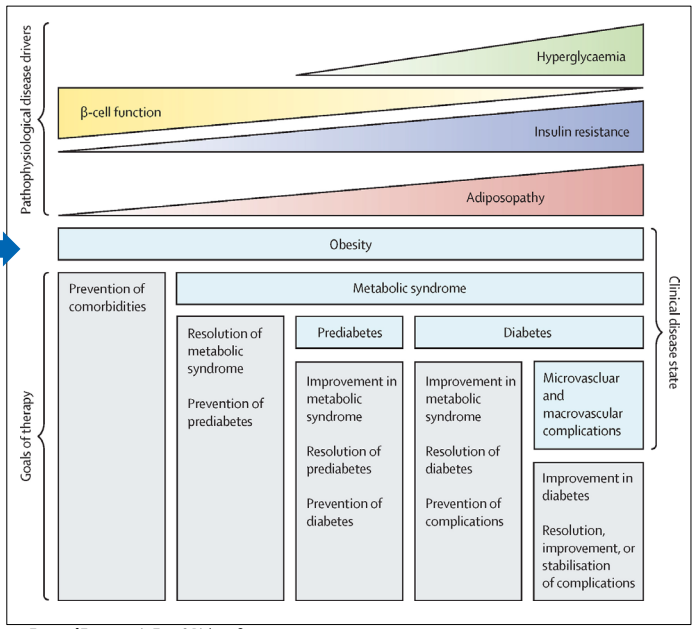
- Diagnosis and Classification of Diabetes — 02
- Comprehensive medical evaluation and assessment of comorbidities — 04
- Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes — 05
- Glycemic goals and hypoglycemia — 06
- Diabetes technology — 07
- Obesity and Weight Management for the Prevention and Treatment of T2D — 08
- Pharmacologic Approaches to Glycemic Treatment — 09
- CVD and Risk Management — 10
- CKD and Risk Management — 11
- Retinopathy, Neuropathy, and Foot Care — 12

CVD, cardiovascular disease; CKD, chronic kidney disease; T2D, type 2 diabetes
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1

Benefits of weight loss across the disease continuum

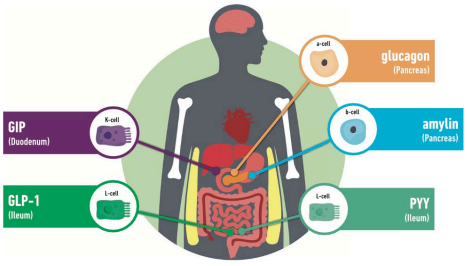
>15% TBWL

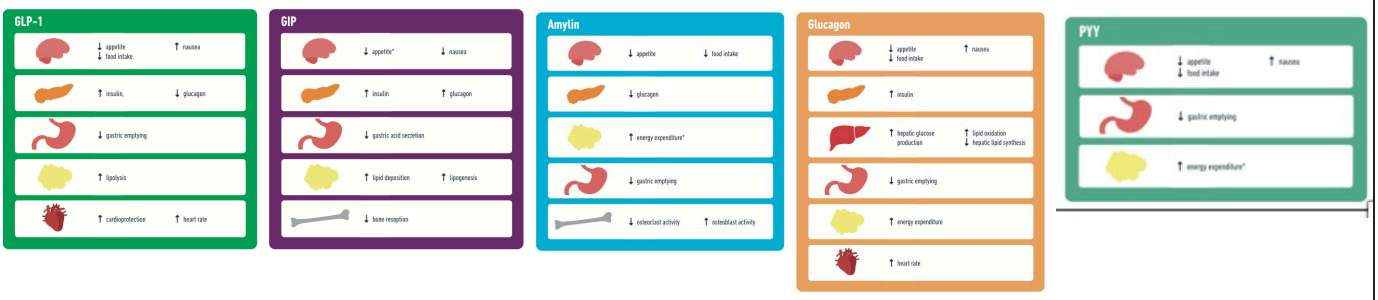
- **Weight loss disrupts the disease continuum.**



1. Presented by Ildiko Lingvay at ADA 2022 –Weighing the evidence -Should Obesity Be the Primary Target of Treatment in Type 2 Diabetes?
2. Ildiko Lingvay et al. Lancet 2022. Jan.399;394–405

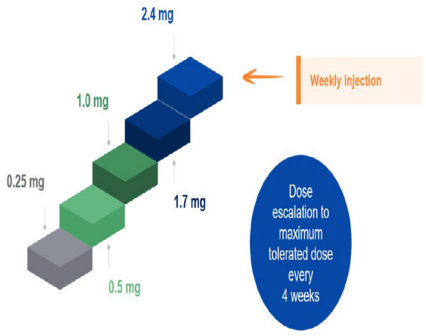
Novel nutrient-stimulated hormone (NUSH)-based therapies for obesity treatment

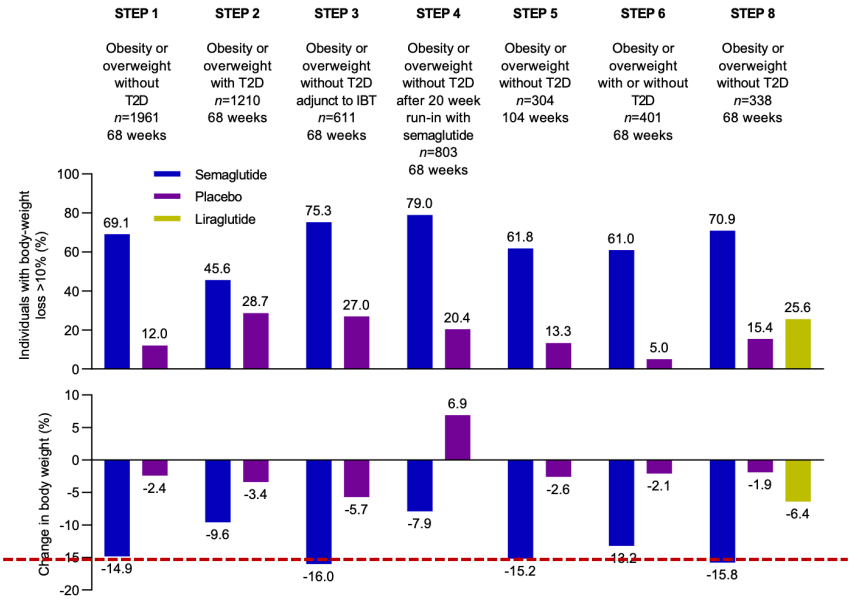




Int J Obesity 2024, Epub ahead of print

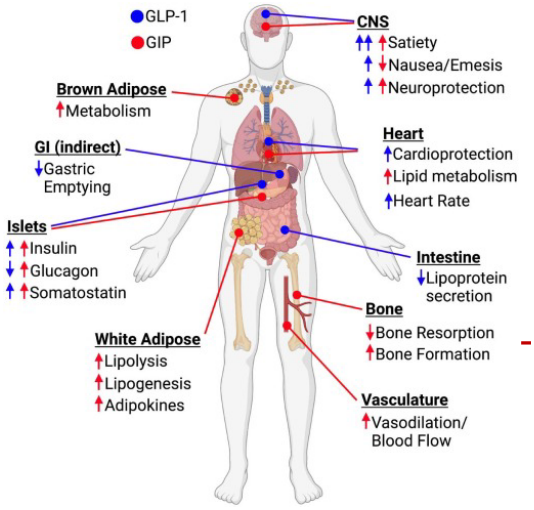
Semaglutide: Weight Loss in the STEP Trials

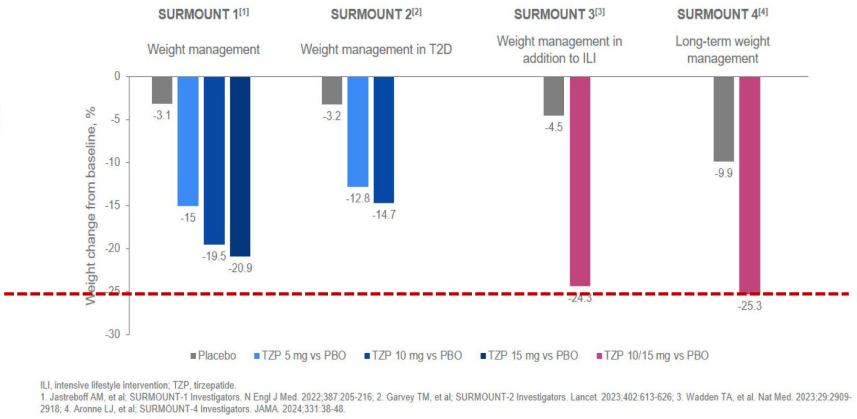




Diabetologia 2023;66:1846

Tirzepatide: Weight Loss in the SURMOUNT Trials

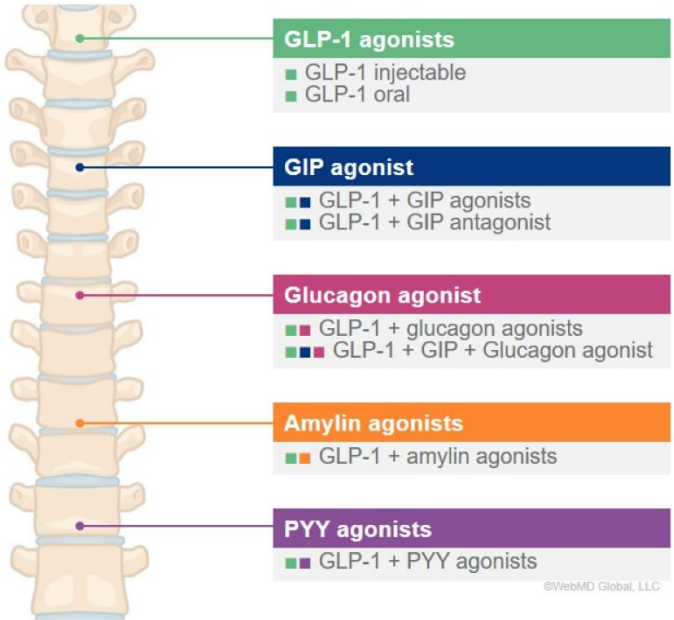




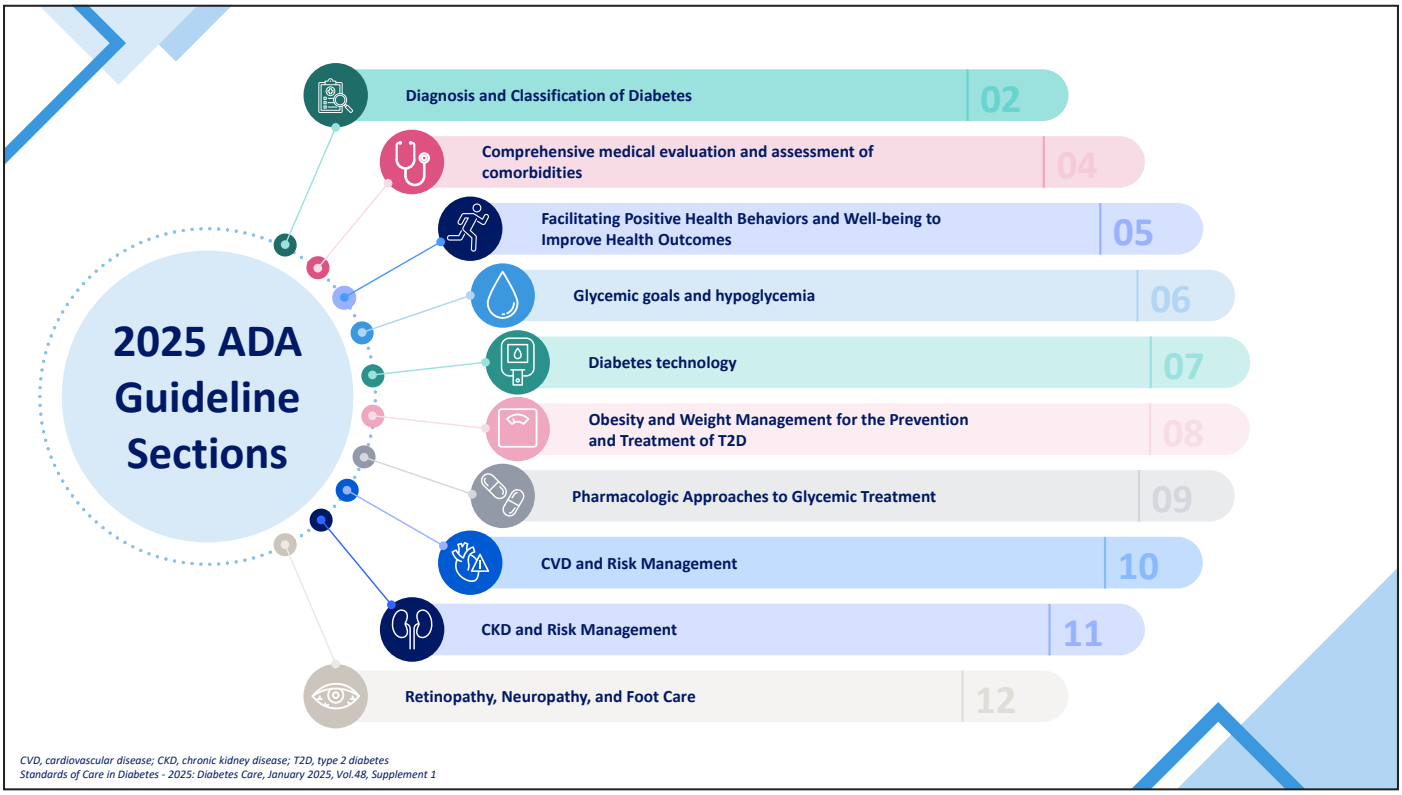
ILI, intensive lifestyle intervention; TZP, tirzepatide.
1. Jastreboff AM, et al; SURMOUNT-1 Investigators. N Engl J Med. 2022;387:205-216; 2. Garvey TM, et al; SURMOUNT-2 Investigators. Lancet. 2023;402:613-626; 3. Wadden TA, et al. Nat Med. 2023;29:2909-2918; 4. Aronne LJ, et al; SURMOUNT-4 Investigators. JAMA. 2024;331:38-48.

Cell Metab 2023;35:1519-1529

GLP-1 Backbone for NUSH in Development



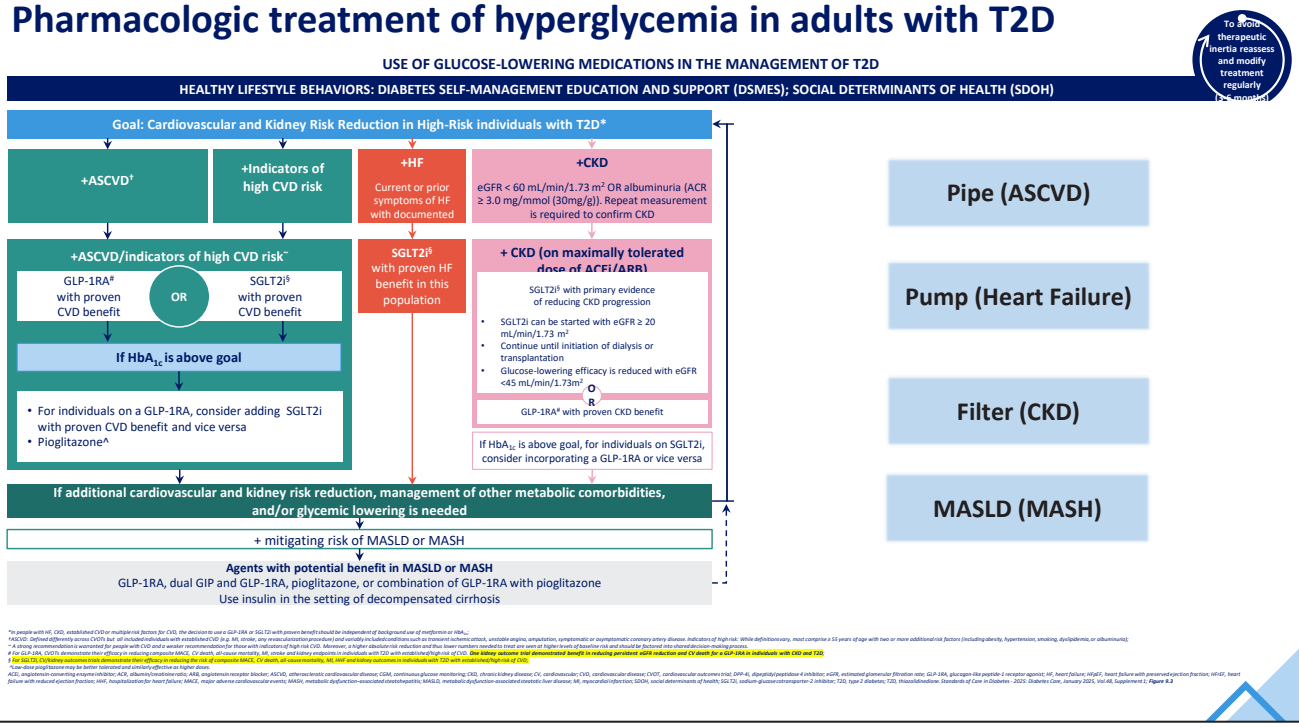
Int J Obesity 2024, Epub ahead of print



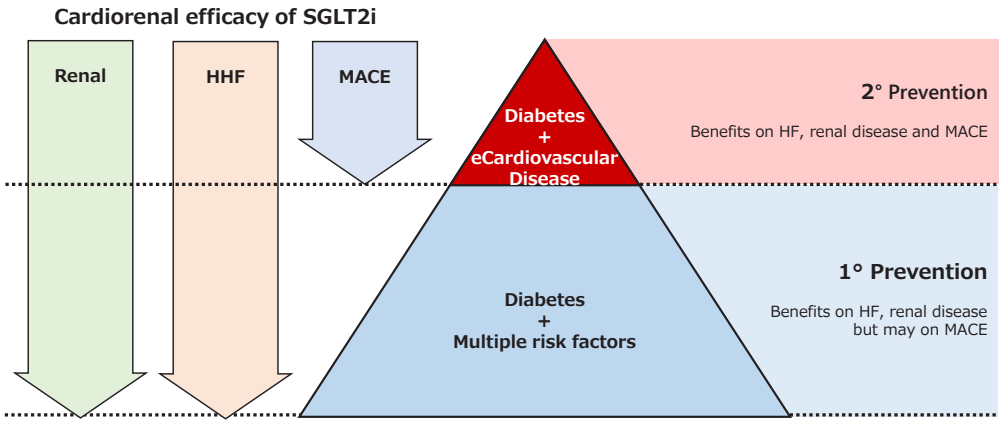
CVD, cardiovascular disease; CKD, chronic kidney disease; T2D, type 2 diabetes
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1

Chapter 09

Pharmacologic treatment of hyperglycemia in adults with T2D



Pump, pipes, and filter: do SGLT2 inhibitors cover it all?



Lancet. 2019;393(10166):3-5.

Chapter 09

Achievement and maintenance of weight and glycemic management goals in those without established ASCVD, CKD or HF

Goal: Achievement and Maintenance of Weight and Glycemic Goals

+ Weight management

Efficacy for weight loss

Very High:
Semaglutide, Tirzepatide

High:
Dulaglutide, Liraglutide

Intermediate:
GLP-1RA (not listed above), SGLT-2i

Neutral:
Metformin, DPP-4i

+ Achievement and maintenance of glycemic goals

Metformin or other agent (including combination therapy) that provides adequate EFFICACY to achieve and maintain glycemic treatment goals

Prioritize avoidance of hypoglycemia in high-risk individuals

Efficacy for glucose lowering

Very High:
Dulaglutide (high dose), semaglutide, tirzepatide, insulin
Combination oral, combination injectable (GLP-1RA and insulin)

High:
GLP-1RA (not listed above), metformin, pioglitazone, SGLT2i, sulfonylurea

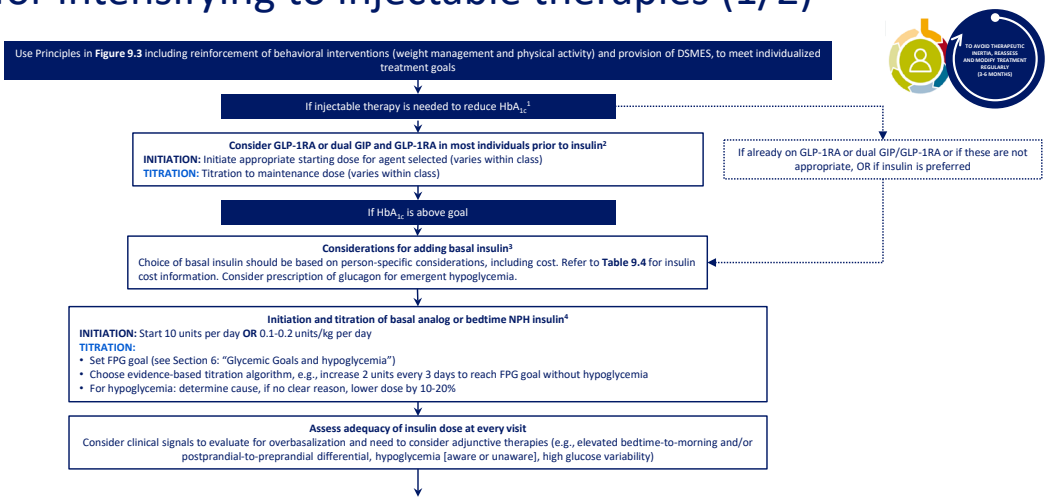
Intermediate:
DPP-4i

If HbA_{1c} is above goal or significant hypoglycemia or hyperglycemia or barriers to care are identified

- Refer to DSMES to support self-efficacy in achievement of treatment goals
- Consider technology (e.g. diagnostic or personal CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact achievement of treatment goals

ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; CKD, chronic kidney disease; DPP4i, Dipeptidyl peptidase-4 inhibitor; HbA1c, glycated hemoglobin; HF, heart failure; GLP-1RAs, glucagon-like peptide-1 receptor agonists; SGLT2i, sodium–glucose cotransporter-2 inhibitors; T2D, type 2 diabetes; TZD, thiazolidinedione. Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1; ***Figure 9.3***

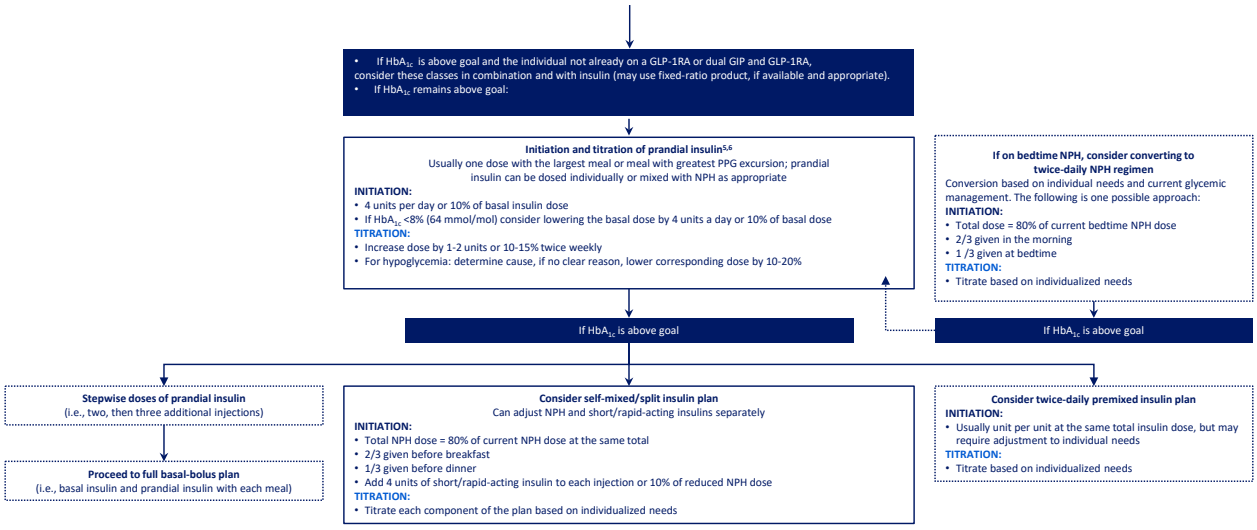
Algorithm for intensifying to injectable therapies (1/2)



1. Consider insulin as the first injectable if symptoms of hyperglycemia are present, when HbA_{1c} levels (>10% [86 mmol/mol]) or blood glucose levels (≥300 mg/dL [≥16.7 mmol/L]) are very high, or a diagnosis of T1D is a possibility.
2. When selecting GLP-1RA, consider: individual preference, HbA_{1c} lowering, weight-lowering effect, or frequency of injection. If CVD, consider GLP-1RA with proven CVD benefit. Oral or injectable GLP-1RA are appropriate.
3. For people on GLP-1RA and basal insulin combination, consider use of a fixed-ratio combination product (iDegLira or iGlarLixi).
4. Consider switching from evening NPH to a basal analog if the patient develops hypoglycemia and/or frequently forgets to administer NPH in the evening and would be better managed with an AM dose of a long-acting basal insulin.
CVD, cardiovascular disease; DSMES, diabetes self-management education and support; FPG, fasting plasma glucose; GIP, glucose-dependent insulinotropic polypeptide; GLP-1RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, glycated hemoglobin; NPH, Neutral Protamine Hagedorn; T1D, type 1 diabetes
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1; ***Figure 9.4***

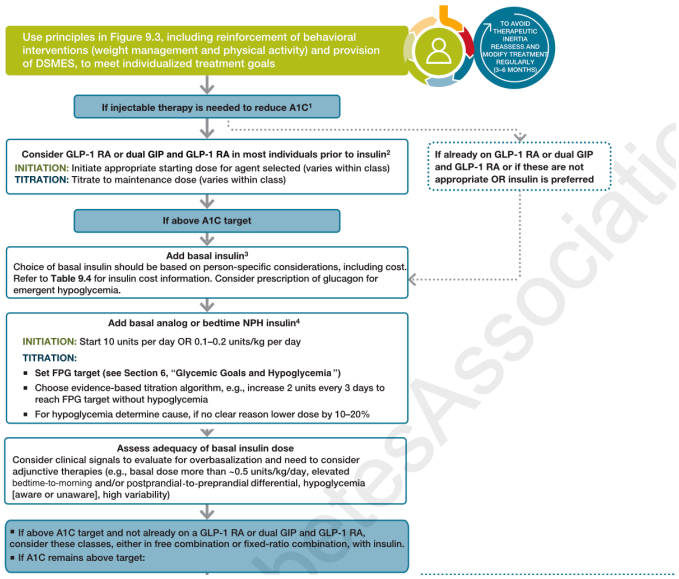
Chapter 09

Algorithm for intensifying to injectable therapies (2/2)



5. Prandial insulin options include injectable rapid- and ultra-rapid-acting analog insulins, injectable short-acting human insulin, or inhaled human insulin.
6. If adding prandial insulin to NPH, consider initiation of a self-mixed or premixed insulin plan to decrease the number of injections required.
HbA_{1c}, glycated hemoglobin; FPG, fasting plasma glucose; GLP-1RA, glucagon-like peptide-1 receptor agonist; GIP, glucose-dependent insulinotropic polypeptide; NPH, Neutral Protamine Hagedorn; PPG, postprandial glucose
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1; ***Figure 9.4***

Injectables



대부분 GLP-1 RA 먼저 고려

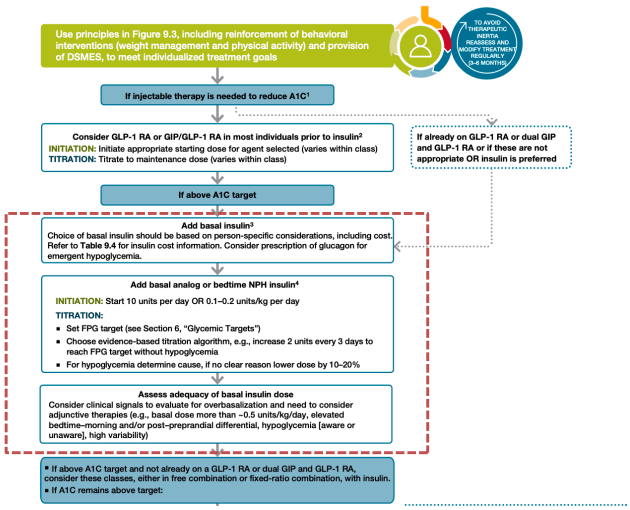
Basal Insulin add-on

Basal Insulin 먼저 사용하고 있었다면 GLP-1 RA add-on or FRC change

Diabetes Care 2024;47:S158-S178

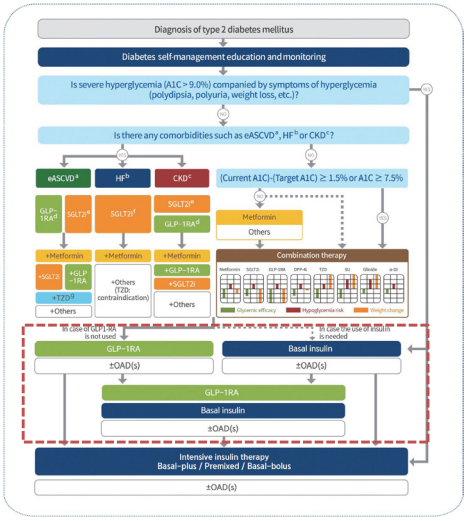
Options after Basal Insulin Failure

2024 ADA Guideline

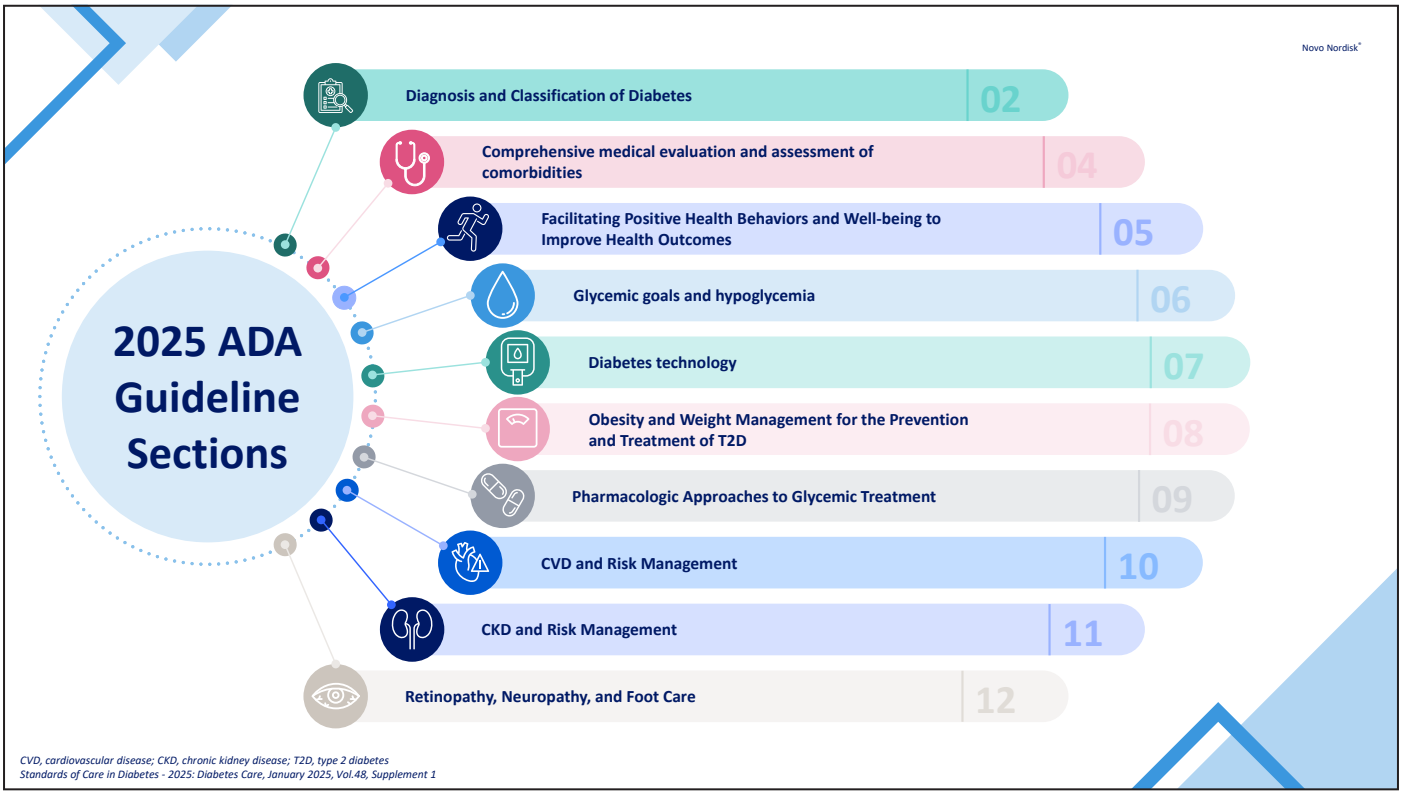


Diabetes Care 2024;47:S158-S178

2023 KDA Guideline



Diabetes & Metabolism Journal 2023;47:575-594.



CVD, cardiovascular disease; CKD, chronic kidney disease; T2D, type 2 diabetes
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1

Chapter 11

Screening and Treatment

Recommendations		
11.1b	In people with established CKD, urinary albumin (e.g., spot UACR) and eGFR should be monitored 1–4 times per year depending on the stage of the kidney disease.	B
11.2	Optimize glucose management to reduce the risk or slow the progression of CKD.	A
11.3	Optimize blood pressure management (aim for <130/80 mmHg) and reduce blood pressure variability to reduce the risk or slow the progression of CKD and reduce cardiovascular risk	A
11.4a	In nonpregnant people with diabetes and hypertension, either an ACEi or an ARB is recommended for those with moderately increased albuminuria (UACR 30–299 mg/g creatinine) **(B)** and is strongly recommended for those with severely increased albuminuria (UACR ≥300 mg/g creatinine) and/or eGFR <60 mL/min/1.73 m^2 to maximally tolerated dose to prevent the progression of kidney disease and reduce cardiovascular events. **(A)**	B/A
11.4c	An ACEi or an ARB is not recommended for the primary prevention of CKD in people with diabetes who have normal blood pressure, normal UACR.	A
11.4d	Continue renin angiotensin system blockade for mild to moderate increases in serum creatinine (≤30%) in the absence of signs of extracellular fluid volume depletion.	A

ACEi, angiotensin converting enzyme inhibitor; ARBs, angiotensin receptor blockers; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; UACR, urinary albumin creatinine ratio
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1

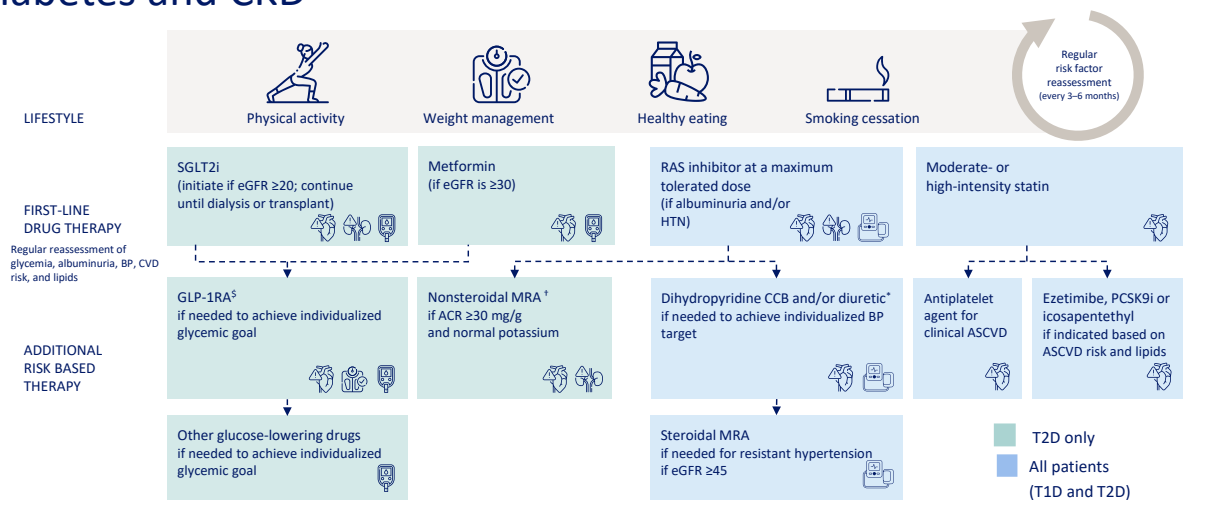
Treatment

Recommendations		
11.5a	For people with T2D and CKD, use of a SGLT2i **is recommended to reduce CKD progression and cardiovascular events** in individuals with eGFR ≥20 mL/min/ 1.73 m^2.	A
11.5b	**To reduce cardiovascular risk and kidney disease progression in people with T2D and CKD, a GLP-1RA with demonstrated benefit in this population is recommended.**	A
11.5c	To reduce cardiovascular events and CKD progression in people with CKD and albuminuria, **a nonsteroidal MRA that has been shown to be effective in clinical trials is recommended (if eGFR is ≥25 mL/min/1.73 m^2).** Potassium levels should be monitored.	A
11.6	Aim to reduce urinary albumin by ≥30% in people with CKD and albuminuria ≥300 mg/g to slow CKD progression.	B

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GLP-1RAs, glucagon-like peptide-1 receptor agonists; SGLT2is, sodium-glucose cotransporter-2 inhibitors; T2D, type 2 diabetes
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1

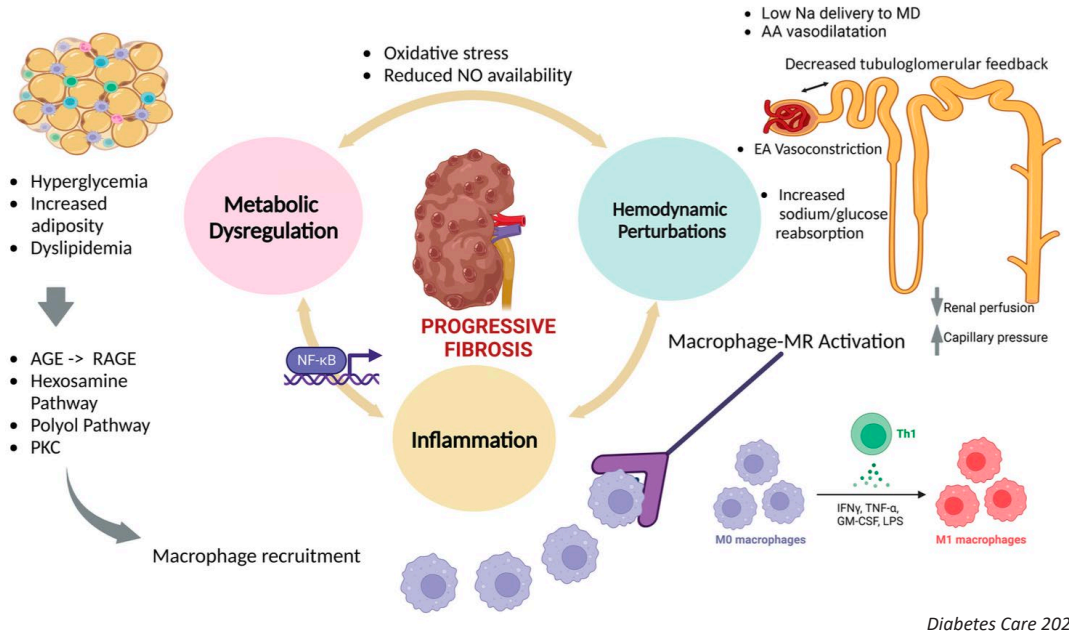
Novo Nordisk*

Holistic approach for improving outcomes in patients with diabetes and CKD



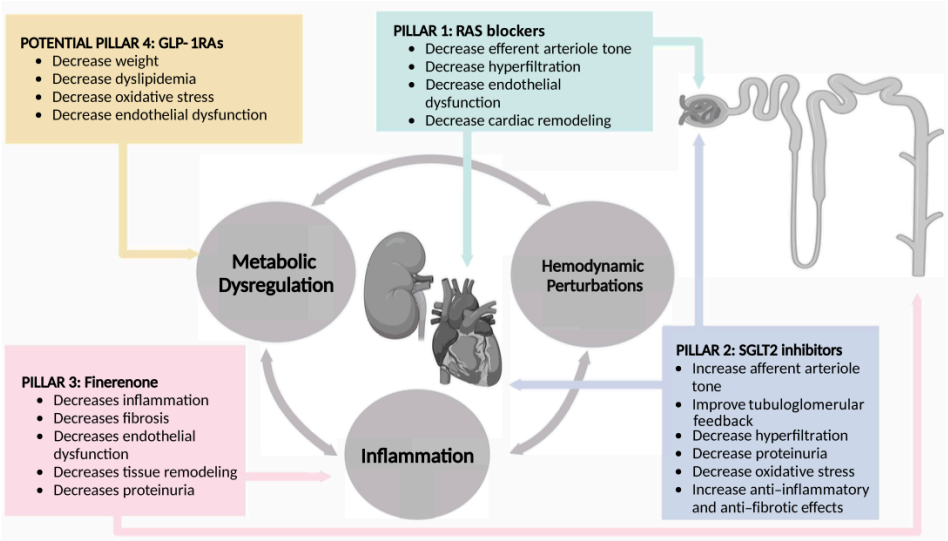
§ Semaglutide can be used as another first-line agent for people with CKD; † Finerenone is currently the only ns-MRA with proven clinical kidney and cardiovascular benefits. * ACEi or ARB (at maximal tolerated doses) should be first-line therapy for hypertension when albuminuria is present. Otherwise, dihydropyridine calcium channel blocker or diuretic can also be considered; all three classes are often needed to attain BP targets.*
ACR, albumin-to-creatinine ratio; ASCVD, atherosclerotic cardiovascular disease; BP, blood-pressure; CCB, calcium channel blocker; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; GLP-1RA, GLP-1 receptor agonist; HTN, hypertension; ns-MRA, nonsteroidal mineralocorticoid receptor antagonist; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; RAS, renin-angiotensin system; SGLT2i, sodium–glucose cotransporter-2 inhibitor; T1D, type 1 diabetes; T2D, type 2 diabetes
Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48, Supplement 1; ***Figure 11.2***

Diabetic Nephropathy



Diabetes Care 2023;46(9):1574–1586

4 Pillars for Diabetic Nephropathy

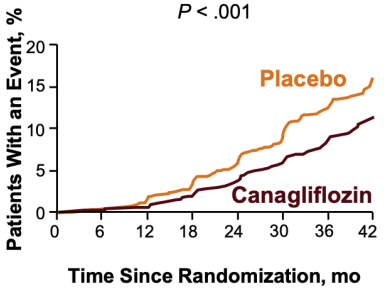


Diabetes Care 2023;46(9):1574–1586

SGLT2i and CKD

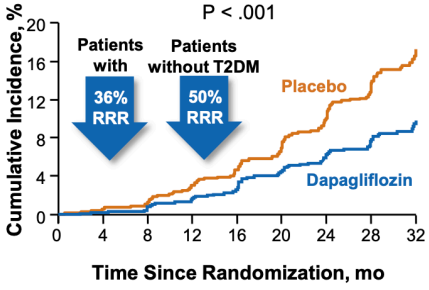
CREDENCE[1,a]

HR = 0.66 (95% CI, 0.53-0.81); *P* < .001



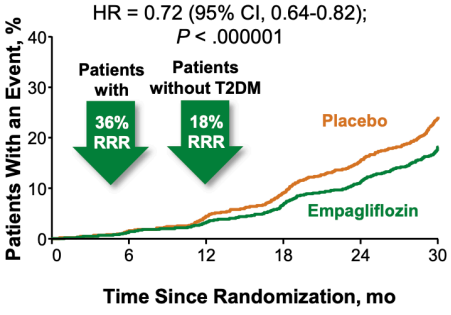
DAPA-CKD[2,b]

HR = 0.56 (95% CI, 0.45-0.68); P < .001



EMPA-KIDNEY[3,c]

HR = 0.72 (95% CI, 0.64-0.82); *P* < .000001

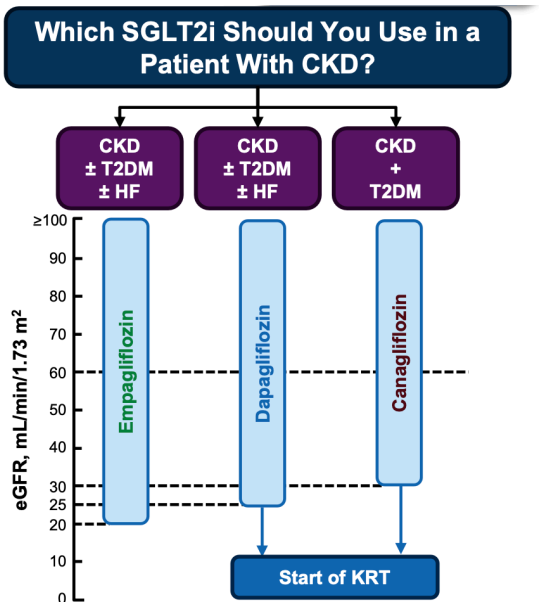


- KDIGO prioritizes SGLT2 inhibitors with documented kidney or cardiovascular benefits in CKD[4]
- Only dapagliflozin and empagliflozin are indicated for CKD in the European Union and United States[5,6]

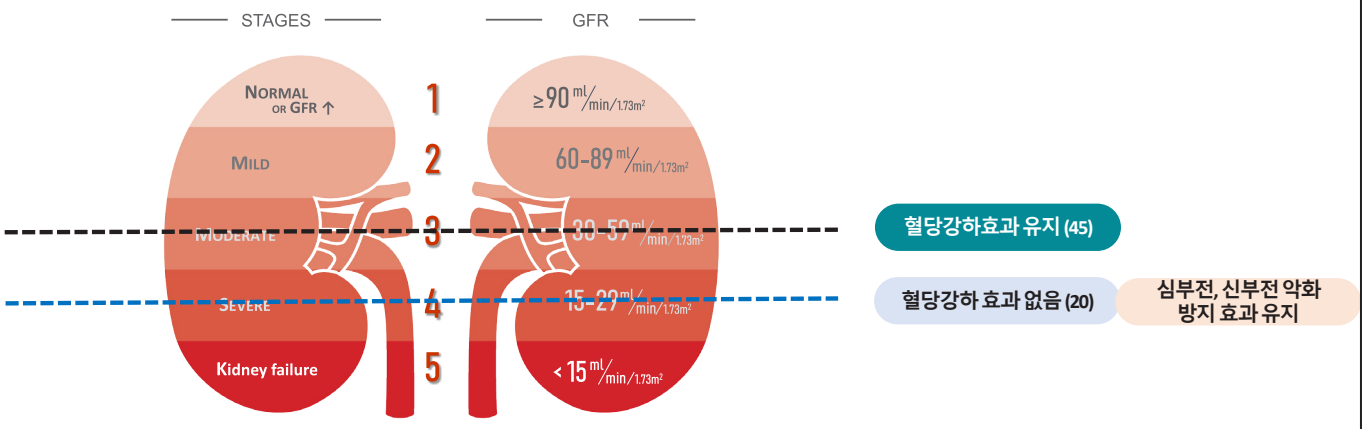
[a] Kidney-specific composite outcome of ESKD, doubling of serum creatinine level, or renal death. [b] Kidney-specific composite outcome of a sustained decline in eGFR of ≥50%, ESKD, or death from renal causes. [c] Kidney disease progression defined as ESKD, sustained decrease in eGFR t0 <10 mL/min/1.73 m^2, sustained ≥40% decrease in eGFR from baselines, or death from renal causes.

1. Heerspink HJL et al. *N Engl J Med.* 2020;383:1436-1446. 2. Perkovic V et al. *N Engl J Med.* 2019;380:2295-2306. 3. The EMPA-KIDNEY Collaborative Group et al. *N Engl J Med.* 2023;388:117-127. 4. KDIGO Diabetes Work Group. *Kidney Int.* 2022;102(5S):s1-s127. 5. https://www.accessdata.fda.gov/scripts/cder/daf/. 6. https://www.ema.europa.eu/en/medicines.

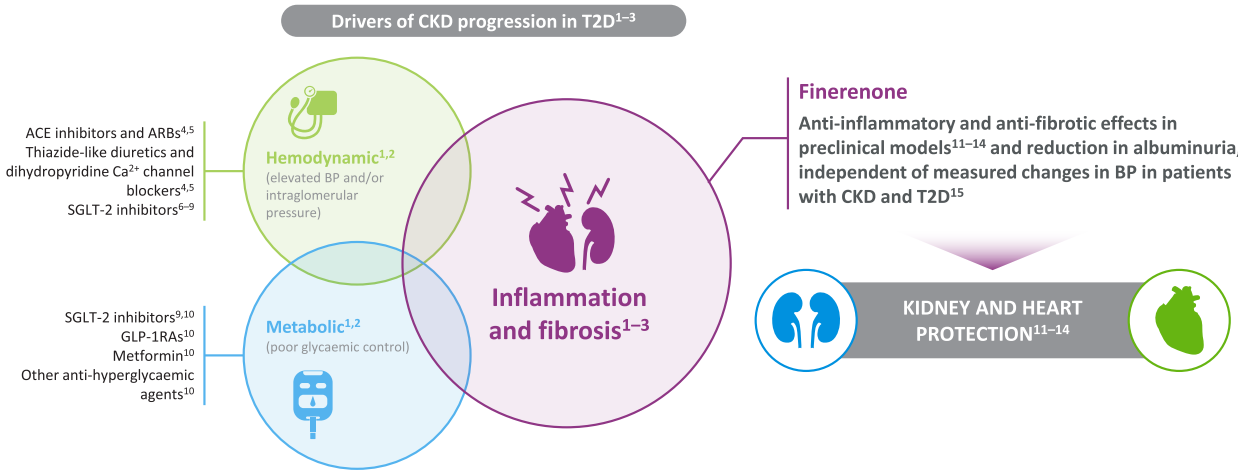
SGLT2i and CKD



SGLT2i and eGFR

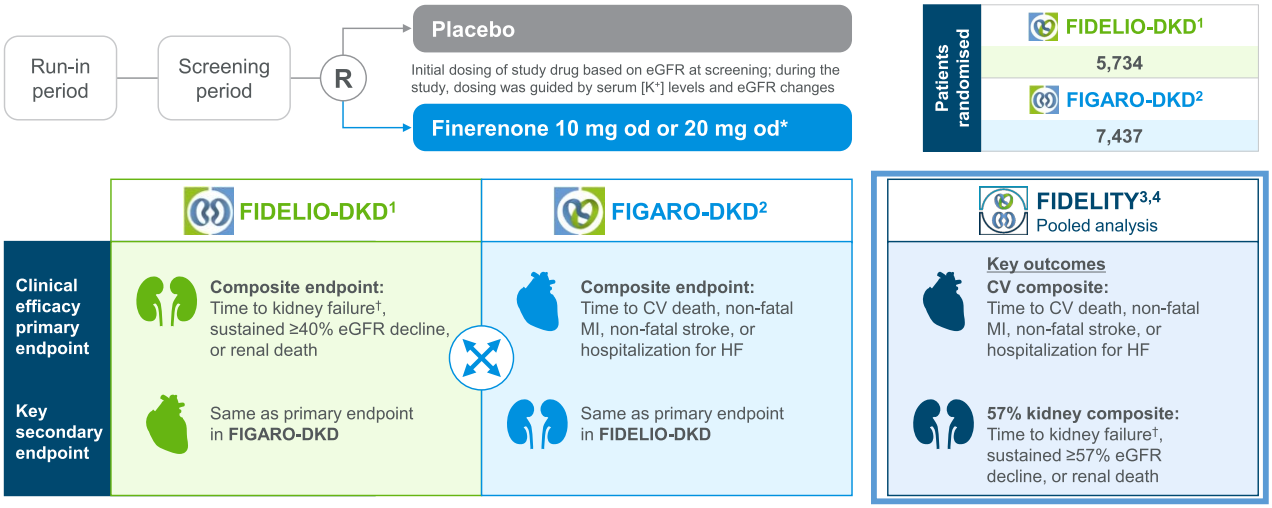


Finerenone (non-steroidal MRA)

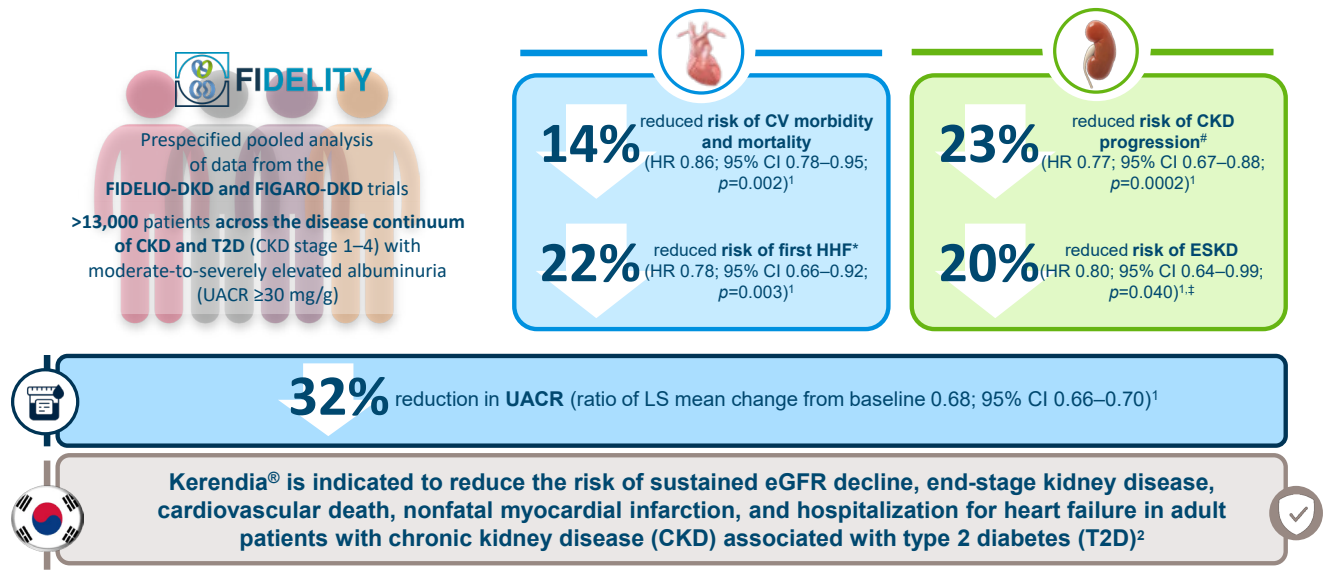


Finerenone (non-steroidal MRA)

FIDELIO-DKD, FIGARO-DKD, and FIDELITY: Study designs and their main outcomes



Finerenone (non-steroidal MRA)

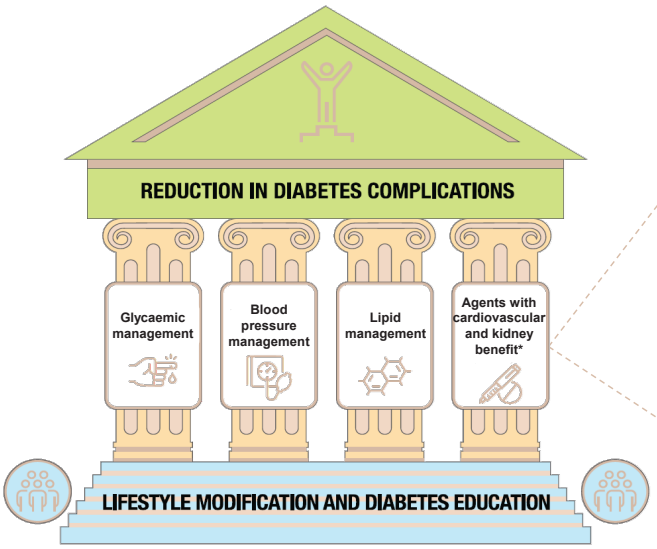


*First HHF defined as first event after randomisation; #ESKD or an eGFR <15 ml/min/1.73 m²; events were classified as renal death if: (1) the patient died; (2) KRT had not been initiated despite being clinically indicated; and (3) there was no other likely cause of death; ‡analysis for *p*-value not prespecified. HHF, hospitalisation for heart failure; KRT, kidney replacement therapy; LS, least-squares

1. Agarwal R, *et al. Eur Heart J* 2022;43:474–484; 2. 케렌디아®정 국내허가사항 (식품의약품안전처 https://nedrug.mfds.go.kr/searchDrug)

42

2024 ADA Recommendation on non-steroidal MRA



Recommended agents with cardiovascular and kidney benefits include[2]:

SGLT-2is

In patients with an eGFR ≥20 mL/min/1.73 m² and UACR ≥200 mg/g (LoE: A)

In patients with an eGFR ≥20 ml/min/1.73 m² and UACR ranging from normal to 200 mg/g (LoE: B)

Finerenone (nonsteroidal MRA)

In patients with CKD and albuminuria who are at increased risk for CV events or CKD progression (if eGFR ≥25 mL/min/1.73 m²)

43 43

*Risk reduction interventions to be applied as individually appropriate
1. American Diabetes Association. *Diabetes Care* 2024;47(Suppl 1):S179–S218;
2. American Diabetes Association. *Diabetes Care* 2024;47(Suppl 1):S219–S230

American Diabetes Association.

국내 Finerenone 급여 개시

요양 보험 급여 기준

케렌디아®정 요양 급여 적용 기준[1]

제2형 당뇨가 있는 만성 신장병 성인 환자로서, ACE 억제제 또는 Angiotensin II 수용체 차단제를 최대허용(내약) 용량으로 4주 이상 안정적으로 투여 중에도 불구하고 다음 조건을 모두 만족하는 경우 표준요법(ACE 억제제 또는 Angiotensin II 수용체 차단제)과 병용하여 투여함. 다만, 지속적인 증상을 보이는 만성 심부전 환자(NYHA class II~IV)는 제외함.

- 다음 -

1) uACR >300 mg/g 또는 요 시험지봉 검사(urine dipstick test) 양성(1+ 이상)
2) 25≤ eGFR <75 mL/min/1.73m² 인 경우

투여 중단: eGFR이 15 mL/min/1.73m² 미만으로 감소하는 경우 투여 중단하여야 함.

• 케렌디아®정 10 mg 보험 약가: 1,670원[1,3] • 케렌디아®정 20 mg 보험 약가: 1,670원[1,3]

해당 보험약가는 요양 급여 기준을 만족하는 경우, 보험상한금액에 따라 산정된 가격을 표시한 것으로, 개별 환자에 따라 실제 부담금액은 달라질 수 있음.

상병코드[2]

N18 만성 신장병

이외 가능 상병코드[2]

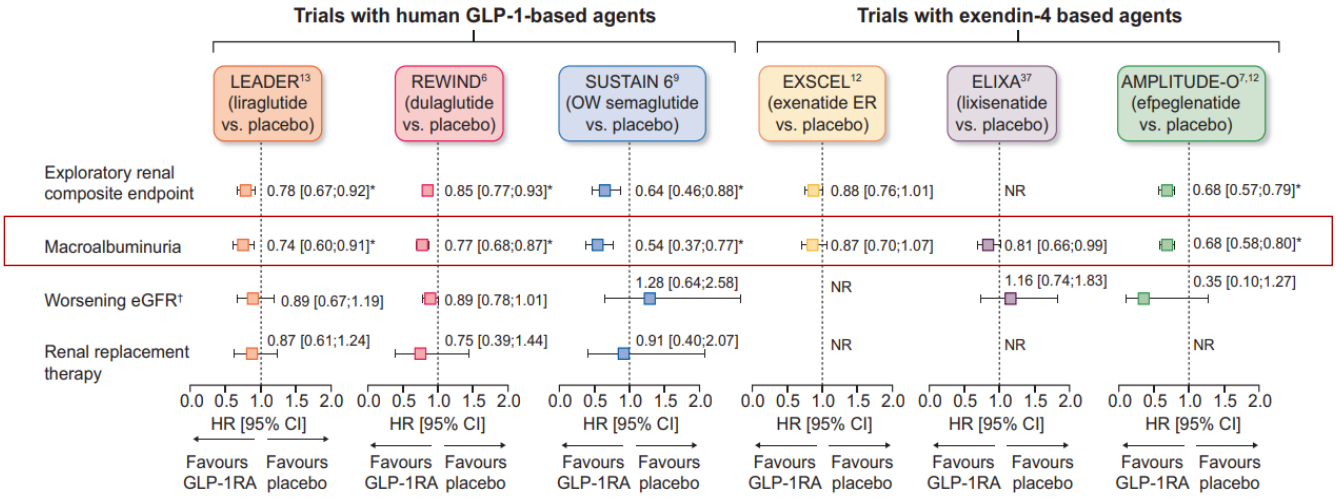
N182 만성 신장병 (2기)
N183 만성 신장병 (3기)
N184 만성 신장병 (4기)

E112 신장 합병증을 동반한 제2형 당뇨병

E112를 제외한 N18,N182,N183,N184의 경우 제2형 당뇨병 관련 상병코드 E11/E13/E14 기사용 또는 추가 필요

1.보건복지부 고시 제2024-20호 요양급여의 적용기준 및 방법에 관한 세부사항 일부개정 (2024.01.31)
2.한국표준질병사인분류(KCD), https://www.koicd.kr/kcd/kcd.do?degree=08 accessed in Jan 2024
3.보건복지부 고시 제2024-11호 약제 급여 목록 및 급여 상한금액표 일부개정 (2024.01.26)

Results of exploratory kidney analyses from GLP-1RA CV outcome trials



Nephrol Dial Transplant 2023: 38 :2041-2051

Prognosis of CKD by eGFR and albuminuria categories

GLP-1RA CVOTs

L = LEADER
R = REWIND
E = EXSCEL
A = AMPLITUDE-O
S = SUSTAIN

eGFR categories(ml/min/1.73㎡), description and rage				Albuminuria categories Description and rage		
				A1	**A2**	**A3**
				Normal to Mildly increased	Moderately Increased	Severerely increased
				<30 mg/g <3 mg/mmol	30 – 299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
	G1	Normar or high	≥ 90			
	G2	Mildly decreased	60-89	L R E A	S	
	G3a	Mildly to Moderately Decreased	45-59			
	G3b	Moderately to severely decreased	30–44			FLOW
	G4	Severely decreased	15–29			
	G5	Kidney failure	< 15			

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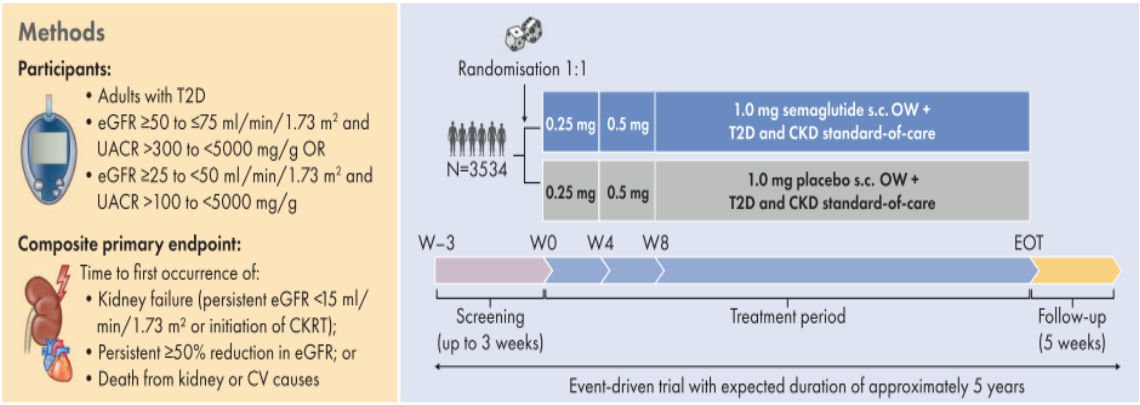
Flow trial: the first kidney disease outcomes trial in T2DM

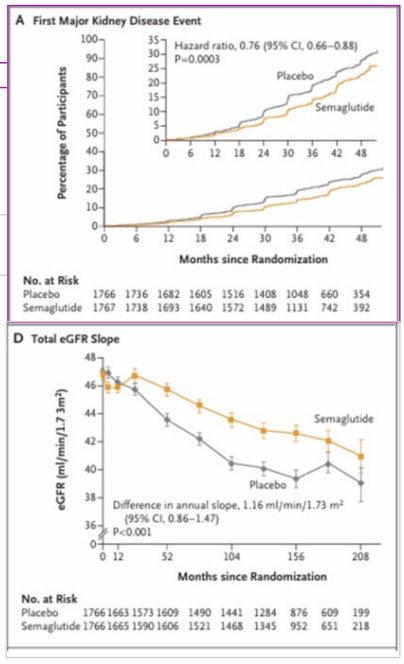


Nephrol Dial Transplant 2023: 38 :2041-2051

Flow trial: the first kidney disease outcomes trial in T2DM

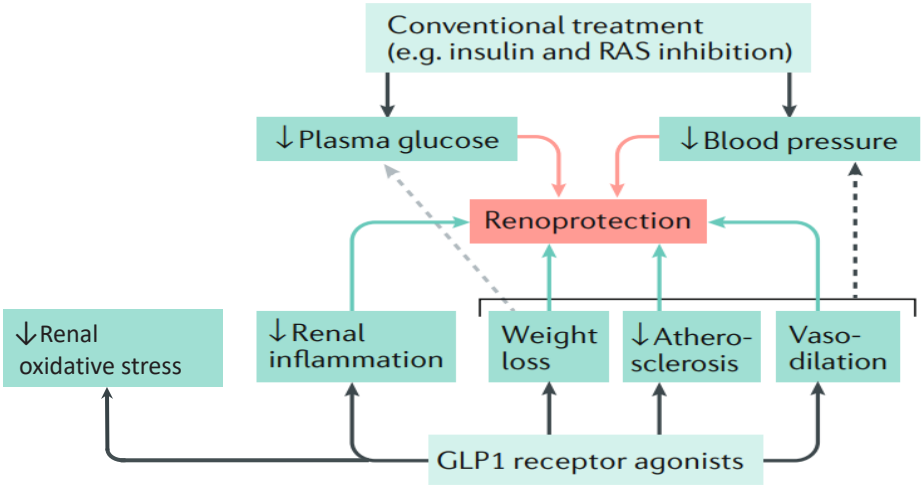
Table 2. Efficacy and Safety Outcomes.*

Outcome	Semaglutide (N=1767)	Placebo (N=1766)	Hazard Ratio (95% CI)	Estimated Difference (95% CI)	P Value
Primary outcome: major kidney disease events — no. (%)†	331 (18.7)	410 (23.2)	0.76 (0.66 to 0.88)	**24% Risk reduction**	0.0003
Components of primary outcome — no. (%)					
Persistent ≥50% reduction from baseline in eGFR	165 (9.3)	213 (12.1)	0.73 (0.59 to 0.89)	—	—
Persistent eGFR <15 ml/min/1.73 m²	92 (5.2)	110 (6.2)	0.80 (0.61 to 1.06)	—	—
Initiation of kidney-replacement therapy	87 (4.9)	100 (5.7)	0.84 (0.63 to 1.12)	—	—
Death from kidney-related causes	5 (0.3)	5 (0.3)	0.97 (0.27 to 3.49)	—	—
Death from cardiovascular causes	123 (7.0)	169 (9.6)	0.71 (0.56 to 0.89)	—	—
Composite of kidney-specific components of the primary outcome	218 (12.3)	260 (14.7)	0.79 (0.66 to 0.94)	—	—
Confirmatory secondary outcomes					
Mean annual rate of change in eGFR — ml/min/1.73 m²	−2.19	−3.36	—	1.16 (0.86 to 1.47)	<0.001
Major cardiovascular events — no. (%)	212 (12.0)	254 (14.4)	0.82 (0.68 to 0.98)	—	0.029
Death from cardiovascular causes	123 (7.0)	169 (9.6)	0.71 (0.56 to 0.89)	—	—
Nonfatal myocardial infarction	52 (2.9)	64 (3.6)	0.80 (0.55 to 1.15)	—	—
Nonfatal stroke	63 (3.6)	51 (2.9)	1.22 (0.84 to 1.77)	—	—
Death from any cause — no. (%)	227 (12.8)	279 (15.8)	0.80 (0.67 to 0.95)	—	0.01
Supportive secondary outcomes					
Ratio of urinary albumin-to-creatinine ratio at week 104 to urinary albumin-to-creatinine ratio at baseline	0.60	0.88	0.68 (0.62 to 0.75)‡	—	—
Mean change in body weight from baseline to week 104 — kg	−5.55	−1.45	—	−4.10 (−4.56 to −3.65)	—
Mean change in glycated hemoglobin level from baseline to week 104 — percentage points	−0.87	−0.06	—	−0.81 (−0.90 to −0.72)	—
Mean change in systolic blood pressure from baseline to week 104 — mm Hg	−3.79	−1.55	—	−2.23 (−3.33 to −1.13)	—
Mean change in diastolic blood pressure from baseline to week 104 — mm Hg	−0.23	−1.01	—	0.78 (0.16 to 1.41)	—
Mean change in eGFR from baseline to week 12 — ml/min/1.73 m²	−1.07	−1.05	—	−0.03 (−0.56 to 0.51)	—
Mean annual rate of change in eGFR from week 12 to end of trial — ml/min/1.73 m²	−2.36	−3.30	—	0.94 (0.62 to 1.26)	—
Mean change in eGFR by the cystatin C equation from baseline to week 104 — ml/min/1.73 m²	−2.01	−5.41	—	3.39 (2.63 to 4.15)	—



N Engl J Med 2024;391:109-121

Proposed mechanisms of GLP1RA's reno-protective effect



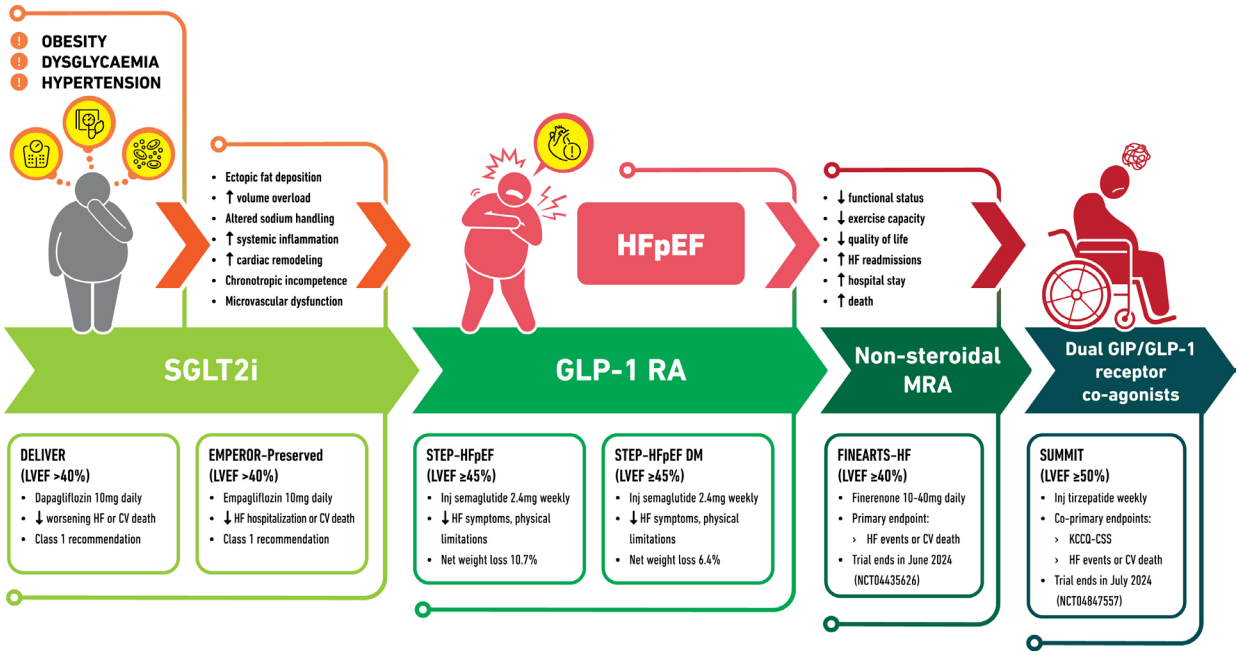
Nat Rev Nephrol. 2018:14:659

SGLT2 Inhibitor CVOTs: Cardiovascular Outcomes

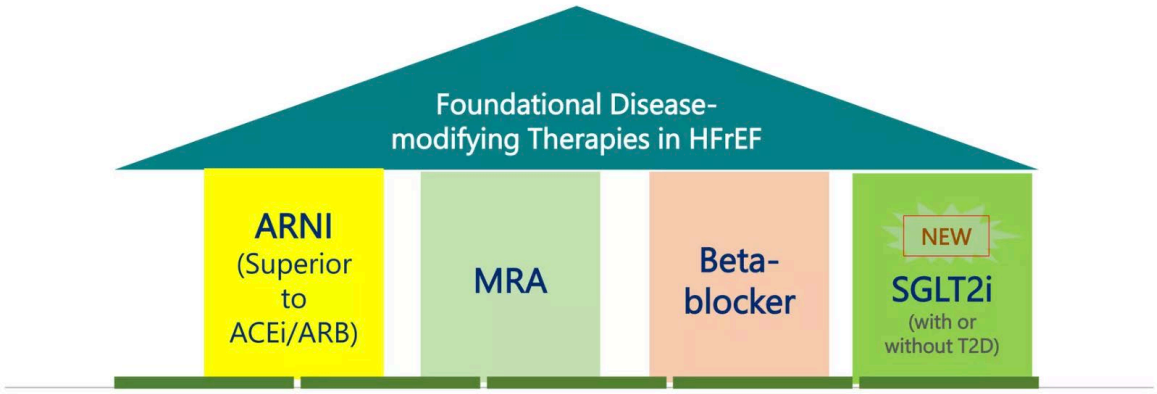
	MACE HR (95% CI)	CV death HR (95% CI)	HHF HR (95% CI)
EMPA-REG OUTCOME[1]	**0.86** (0.74–0.99)	**0.62** (0.49–0.77)	**0.65** (0.50–0.85)
CANVAS Program[2]	**0.86** (0.75–0.97)	**0.87** (0.72–1.06)	**0.67** (0.52–0.87)
DECLARE-TIMI 58[3]	**0.93** (0.84–1.03)	**0.98** (0.82–1.17)	**0.73** (0.61–0.88)
VERTIS CV[4]	**0.97**† (0.85–1.11)	**0.92**‡ (0.77–1.11)	**0.70** (0.54–0.90)

1. Zinman B et al. N Engl J Med. 2015;373:2117–2128. 2. Neal B et al. N Engl J Med. 2017;377:6. 3. Wiviott SD et al. N Engl J Med. 2019;380:347–357. 4. Cannon CP et al. N Engl J Med. 2020;383:1425-1435.

Therapy for HFpEF:
A step forward brings new hope for people with obesity and diabetes



Fundamental 4 Pillars for HFrEF Therapy



HFrEF, HFpEF 환자에서 Empagliflozin 10 mg급여 인정

1. 당뇨병 동반 유무와 관계 없이

-아 래-
○ 좌심실 수축기능이 저하된 만성 심부전 환자(NYHA class II~IV)중, 좌심실 박출률(LVEF: Left Ventricular Ejection Fraction)이 **40% 이하**인 환자로서 표준치료(RASi, Sabutril/Valsatan, Aldosterone antagonist)를 안정적인 용량(stable dose)으로 투 여 중인 경우

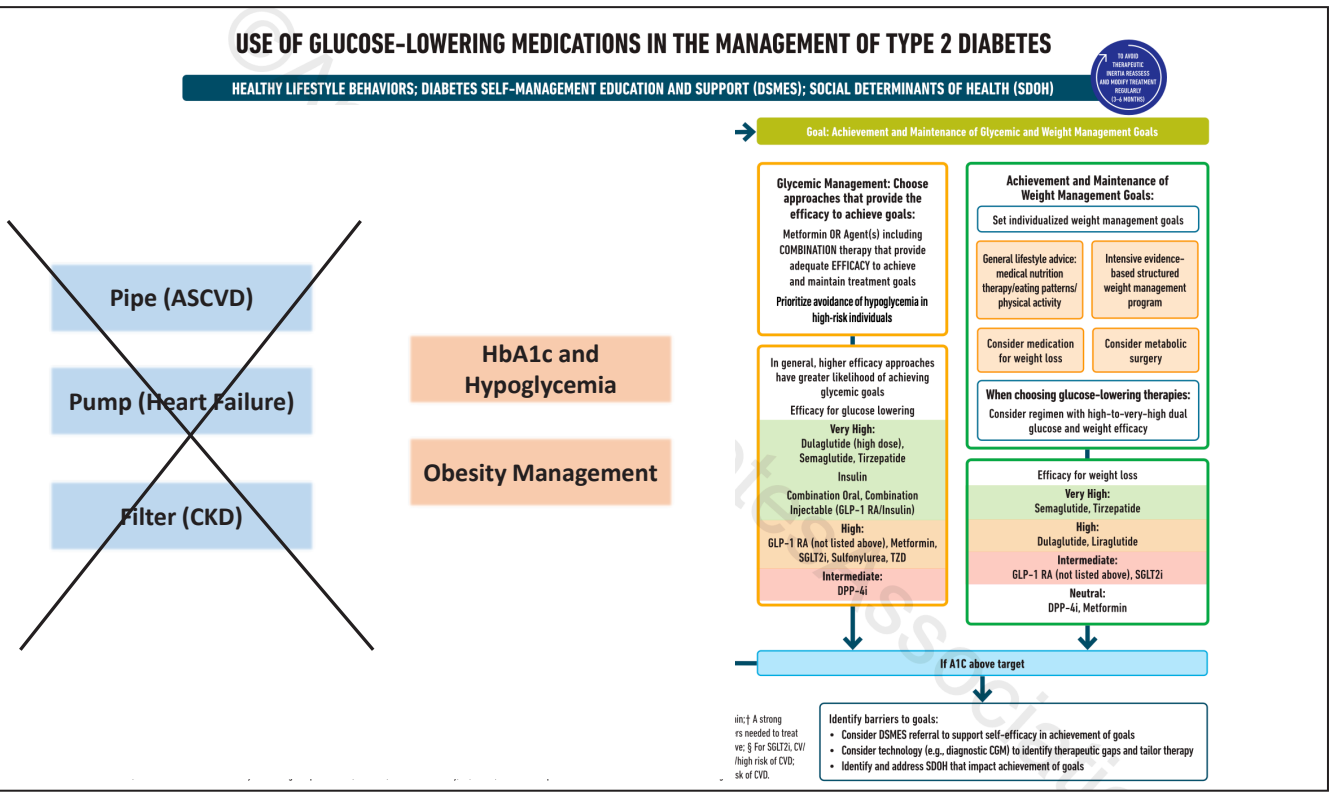
○ 심부전의 증상 및 징후가 있으면서 좌심실 박출률(LVEF: Left Ventricular Ejection Fraction)이 40% **초과**한 환자로서 다음 중 하나를 만족하는 경우

- 다 음 -

가) 좌심실 이완기능 이상/좌심실 충만압의 증가(NT-proBNP≥125pg/mL 또는 BNP≥35pg/mL)에 부합하는 심장 구조 또는 기능 이상의 객관적인 증거가 있는 경우

나) 12개월 이내 심부전 악화로 응급실을 방문하였거나 입원한 경우

2. **제2형 당뇨병에 투여 시 [일반원칙] 당뇨병용제 "세부사항" 범위 내에서 요양급여를 인정함.**



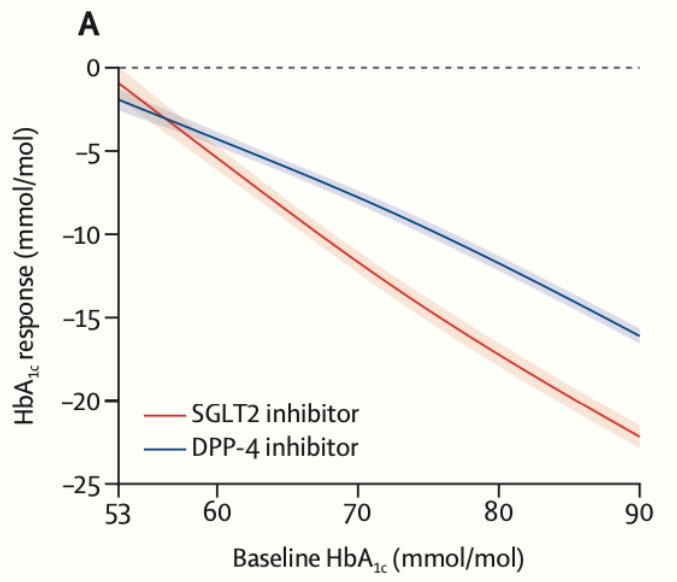
Efficacy, Risk of Hypoglycemia and Weight Change

	Efficacy[1]	Hypoglycemia	Weight change[2]
Metformin	High	No	Neutral (potential for modest loss)
SGLT2 inhibitors	Intermediate to high	No	Loss (intermediate)
GLP-1 RAs	High to very high	No	Loss (intermediate to very high)
Dual GIP and GLP-1 RA	Very high	No	Loss (very high)

		Efficacy[1]	Hypoglycemia	Weight change[2]
DPP-4 inhibitors		Intermediate	No	Neutral
Thiazolidinediones		High	No	Gain
Sulfonylureas (2nd generation)		High	Yes	Gain
Insulin	Human	High to very high	Yes	Gain
	Analogs			

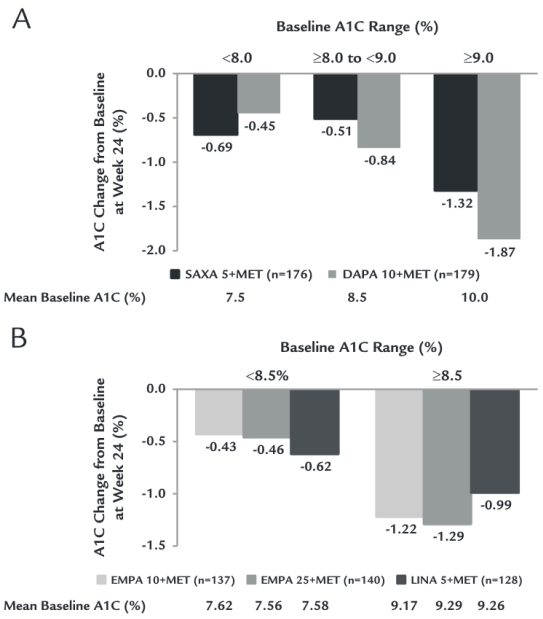
Diabetes Care 2024;47:S158-S178

DPP4i vs. SGLT2i; Patient Baseline Characteristics Are Crucial



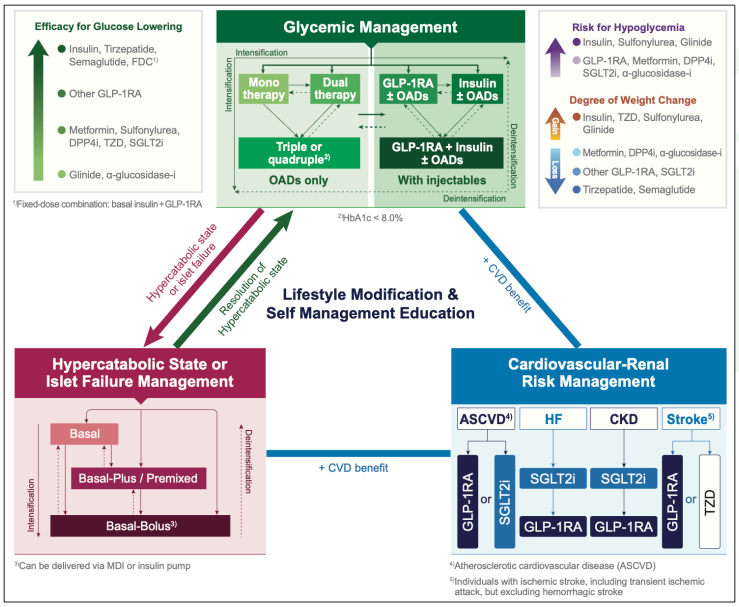
Lancet Digit Health 2022;4:e873-83

DPP4i vs. SGLT2i;
Patient Baseline Characteristics Are Crucial



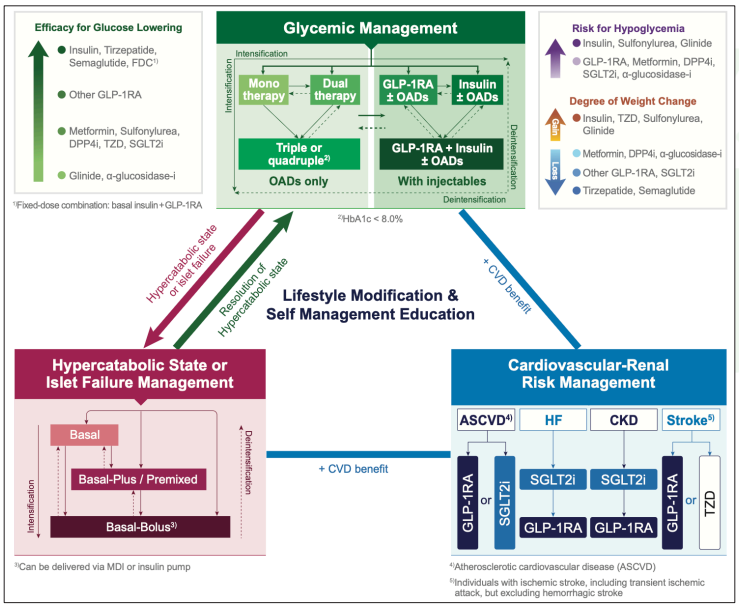
Clin Ther. 2017;39:2438-2447

2형당뇨병 약물치료 알고리듬



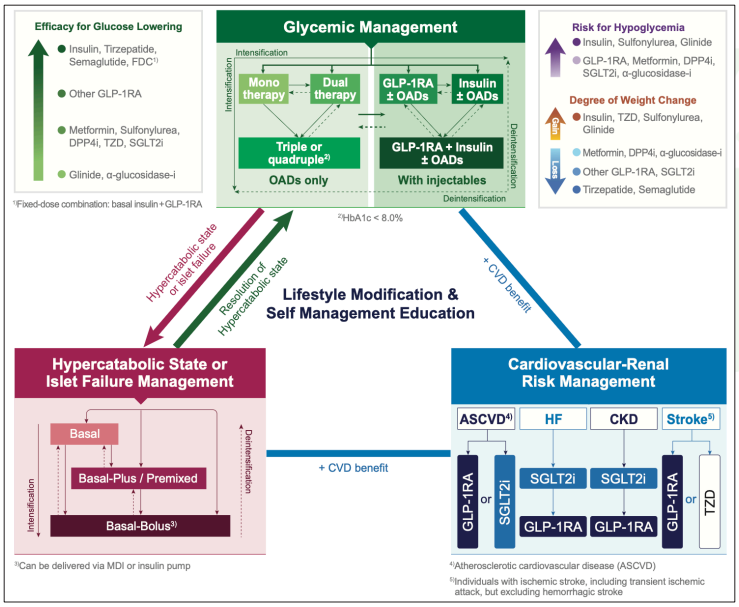
- 혈당 강하, 췌도부전 치료, 심장혈관신장 위험 인자 조절 세가지 축으로 제시
- 혈당 조절과 췌도부전 치료에 대한 강조 (동반 질환에 대한 지나친 강조 자제)
- 근거 중심의 지침 (정부주도 의료보험 시스템 하에서 발생하는 약제 급여심사기준에 의해, 처방 지침이 왜곡되는 현상 주의)
- 생활습관 관리, 자기관리 및 교육의 중요성 다시 강조
- 약제특성 비교 제시 (혈당강하, 저혈당, 체중)
- 메트포민 1차약제로서의 권고 삭제, 환자 개별화된 약제 선택 강조

2형당뇨병 약물치료 알고리듬



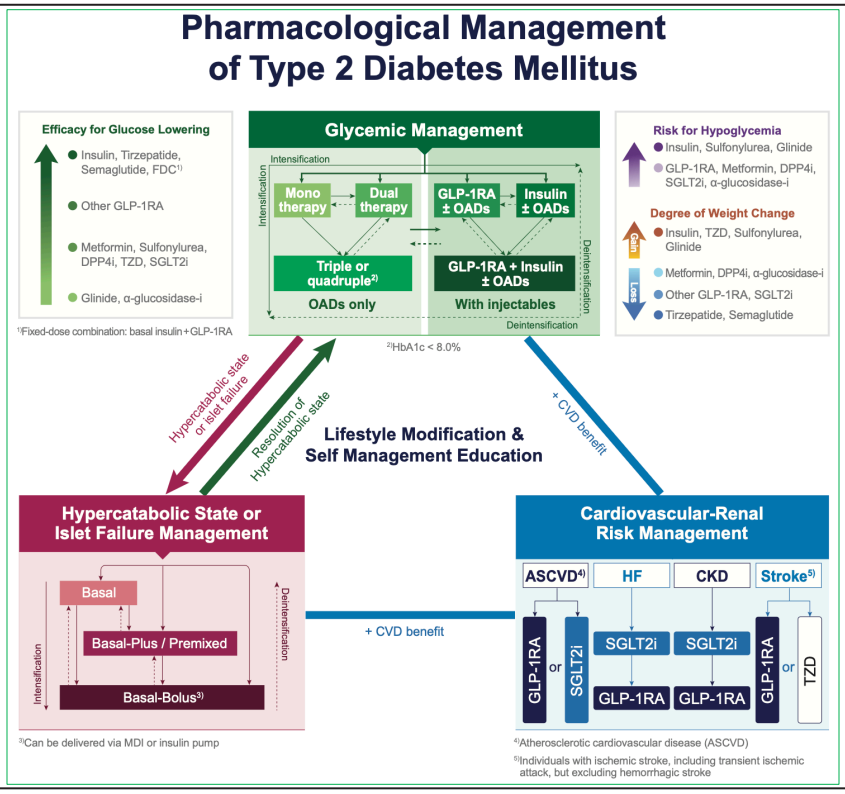
- **약제 선택에 있어서 한국 임상 현장 및 환자의 의학적 이득 고려**
  - 약물의 증가와 함께 감량에 대한 고려 제시
  - 처음 치료 시작 시 환자의 의학적 특성에 따라, (당화혈색소 무관하게) 경구약 2제, GLP-1RA, 인슐린을 바로 선택할 수 있도록 제시
  - 초기 적극적 병용요법 강조
  - 경구약 4제 사용 근거 제시
  - GLP-1RA와 (SU, metformi 이외) 다양한 경구약제 사용 제시
  - GLP-1RA와 다양한 인슐린 제형 (premixed insulin) 사용 제시

2형당뇨병 약물치료 알고리듬

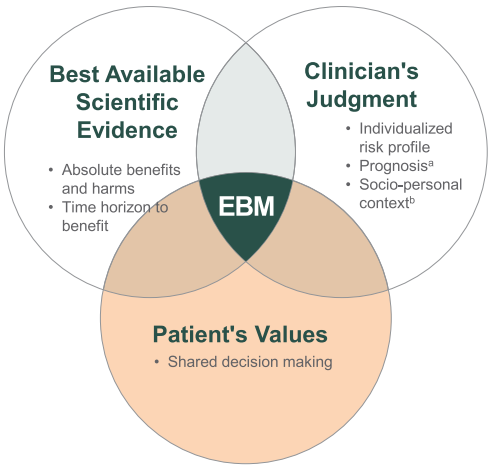


- **췌도부전 (중증당뇨병) 치료 강조**
  - 과이화증상이 있거나, 췌도부전이 있을 시 적극적인 인슐린 치료 강조

- **동반질환 위험인자 관리**
  - 약제 선택 시 혈당조절을 우선적으로 고려하고, 동반질환은 추가적으로 고려해야 할 인자로 제시
  - 동반질환을 cardiovascular-renal risk로 구체화함
  - 국내 유병률이 높은 '뇌경색'을 따로 분류하고 정확한 약제 지침 제시



Core Components Consisted with Evidence-Based Medicine



EBM

- 전문의는 이용 가능한 최선의 근거를 평가 및 이해
- 임상적 판단을 통해 개별 환자의 치료에 적용
- 환자의 삶과 가치를 고려

메트포민 1차약제 권고가 환자의 가치에 따른 최선의 치료 선택을 제한하고 있는가?

Yes !

[a]Estimated on the basis of age, comorbidities, and functional status. [b]Includes an individual's lifestyle, social support, financial circumstances, and workload capacity.
EBM, evidence-based medicine.
Reference 1. Makam AN and Nguyen OK. An Evidence-Based Medicine Approach to Antihyperglycemic Therapy in Diabetes Mellitus to Overcome Overtreatment. *Circulation*. 2017;135(2):180-195

2형당뇨병 약물치료 권고

Clinician's Judgment & Patient's Values

권고 2. 약물 선택 시 동반질환(심부전, 죽상경화심혈관질환, 만성신장질환)에 대한 이득, 혈당강하 효과, 체중에 대한 효과, 저혈당 위험도, 부작용, 비용 등의 약물의 특성과 치료수용성과 관련된 환자의 특성을 고려한다. [전문가의견, 일반적권고]

2형당뇨병 약물치료 권고

권고 2. 약물 선택 시 동반질환(심부전, 죽상경화심혈관질환, 만성신장질환)에 대한 이득, 혈당강하 효과, 체중에 대한 효과, 저혈당 위험도, 부작용, 비용 등의 약물의 특성과 치료수용성과 관련된 환자의 특성을 고려한다. [전문가의견, 일반적권고]

다만 메트포민은 오랜 임상경험을 통해 **혈당강하 효과와 안전성이 입증**된 약물이다. 또한 **저렴한 약가**와 현재의 **국민건강보험 보험급여 기준**을 고려할 때, **1) 다른 계열 약물을 우선적으로 고려할 만한 동반질환이 없고, 2) 메트포민에 금기나 부작용 우려가 없으며, 3) 환자가 사용을 꺼리지 않는 경우**, 여전히 **초치료 약물로 우선 고려할 수 있다**.

대한당뇨병학회 : 당뇨병환자의 혈압조절 목표

2023 KDA

- 심혈관질환이나 심혈관질환 위험인자를 동반하지 않은 당뇨병환자에게서 혈압조절 목표는 140/ 90 mm Hg 미만이다. [무작위대조연구, 일반적권고]
- 심혈관질환이 있거나 표적장기손상 (알부민뇨, 만성신장질환, 망막병증, 좌심실비대) 또는 심혈관질환 위험인자를 동반한 당뇨병환자에게서 혈압조절 목표는 130/80 mm Hg 미만이다. [무작위대조연구, 일반적권고]

2025 KDA

- 당뇨병환자에게서 혈압조절 목표는 130/80 mm Hg 미만이다. [무작위대조연구, 일반적권고]

Take Home Message

1. 2025 ADA guideline: Complication oriented guideline
2. 2025 KDA guideline:

- 약제 선택 시 혈당조절을 우선적으로 고려하고, 동반질환은 추가적으로 고려해야 할 인자로 제시
- 인슐린 사용 시 HbA1c의 기준을 없애고 과이화증상의 동반 유무를 중요시 하게 고려함.
- 1차 치료제로 Metformin을 무조건으로 선택하기 보다는, 다른 여러 요소를 고려하여 다른 약제를 1차 치료제로 선택할 수 있게끔 권고 사항을 변경함
- 4제 요법에 대한 가이드를 제시함
- 당뇨병 환자의 혈압 조절 목표를 130/80 미만으로 단순화함


경청해 주셔서 감사합니다.

01
Session

당뇨병 치료의 핵심

경구혈당강하제, 효과적인 처방 노하우

서울아산병원 내분비내과 **조윤경**

2형 당뇨병은 병인이 이질적이며 다양한 임상 양상을 보이는 질환으로, 효과적인 혈당 조절을 위해서는 환자의 나이, 체중, 신기능, 동반질환 등을 고려한 맞춤형 약제 선택이 필수적이다. 특히 최근에는 여러 작용기전을 가진 경구혈당강하제가 이용 가능해짐에 따라, 초기 치료에서의 약제 선택 뿐 아니라 2제, 3제, 나아가 4제 병용요법까지 보다 전략적인 접근이 요구된다.

최신 주사제인 GLP-1 수용체 작용제 및 SGLT2 억제제는 별도 강의에서 다루어질 예정이므로, 본 강의에서는 비교적 전통적인 경구혈당강하제를 임상 현장에서 효과적이고 안전하게 활용하기 위한 처방 노하우를 공유하는 데에 강의의 초점을 두었다. 이에 Metformin, sulfonylurea, thiazolidinedione (TZD), 및 DPP-4 억제제를 중심으로 각 약제의 주요 작용 기전과 부작용, 신기능 저하 등 특정 상황에서의 사용 시 주의사항을 중심으로 살펴보고자 한다. 또한 최근의 임상 연구 결과를 바탕으로 약제별 특징과 효과를 논의하고, 실제 처방 사례를 통해 실질적인 처방 전략을 제시할 예정이다.

2025년 서울아산병원 당뇨병 센터 개원의 연수강좌

경구혈당강하제, 효과적인 처방 노하우

서울아산병원 내분비내과

조 윤 경

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Tips for prescribing oral antidiabetic agents

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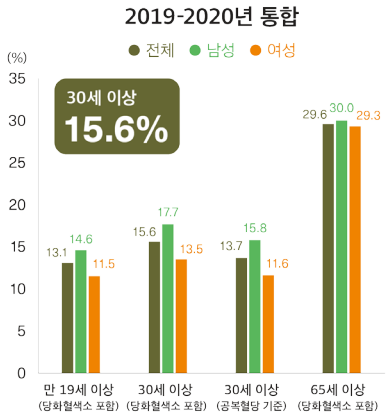
Tips for prescribing oral antidiabetic agents

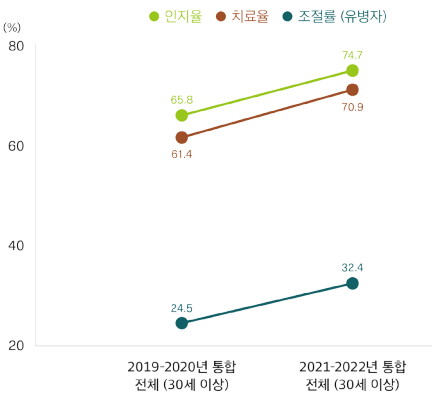
당뇨병 현황 (1)

Diabetes Fact Sheet in Korea 2024

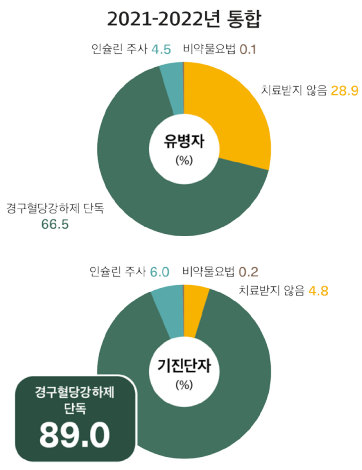
당뇨병 유병률



당뇨병 관리 수준



혈당 관리 방법

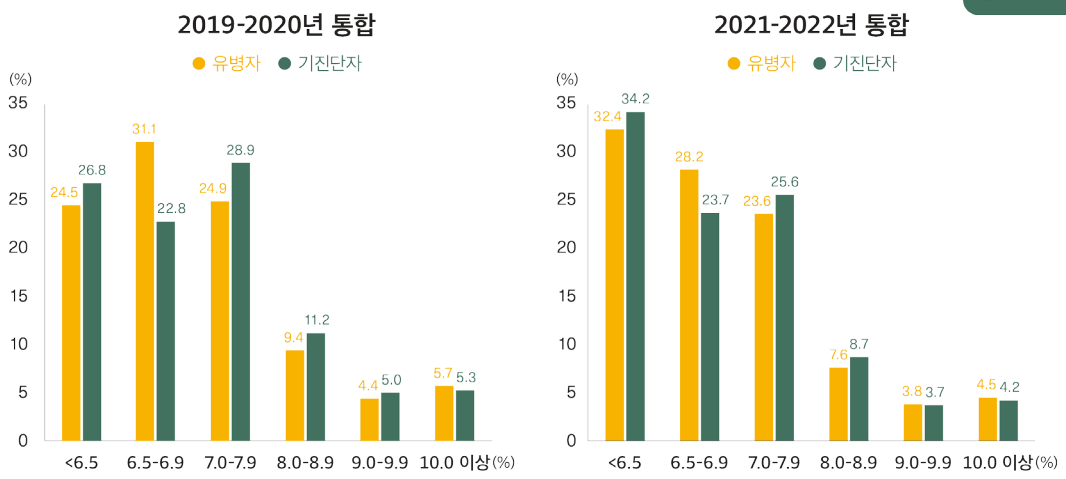


당뇨병 현황 (2)

Diabetes Fact Sheet in Korea 2024

혈당 조절 상태

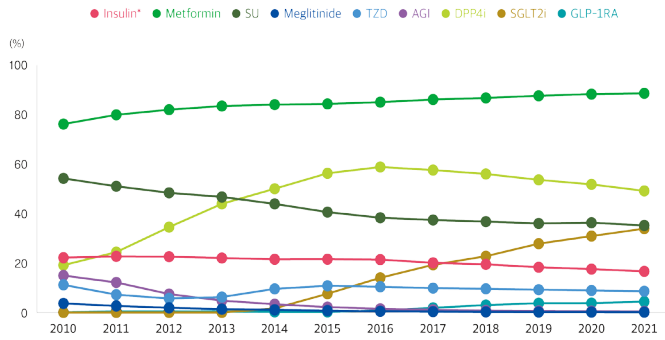
<6.5%, 기진단자
34.2%



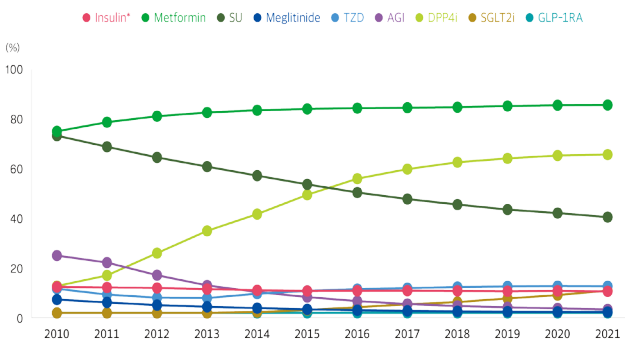
당뇨병 현황 (3)

Diabetes Fact Sheet in Korea 2024

처방 패턴 (청년)



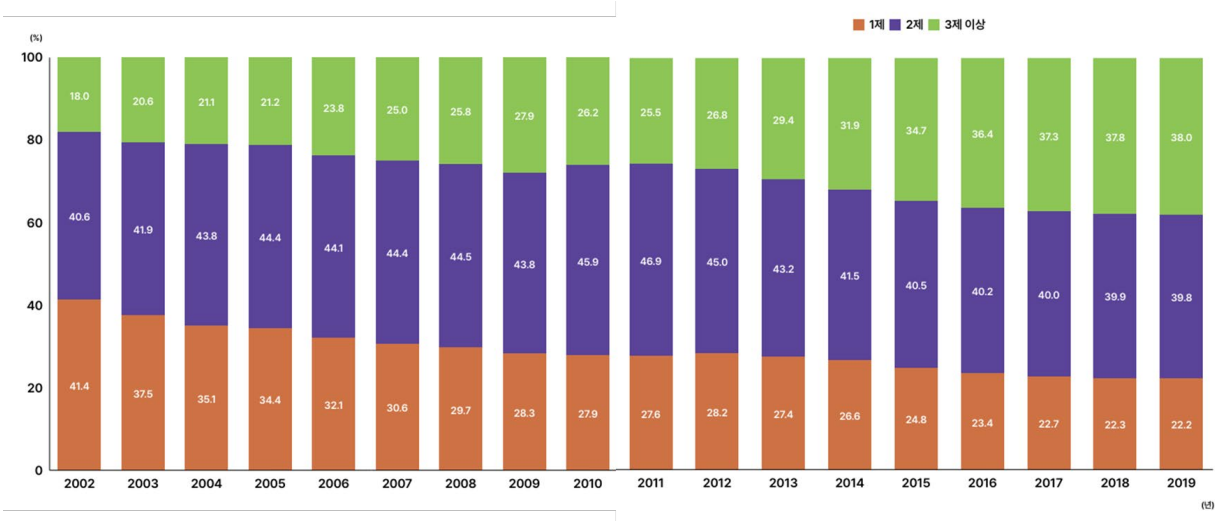
처방 패턴 (노인)



당뇨병 현황 (4)

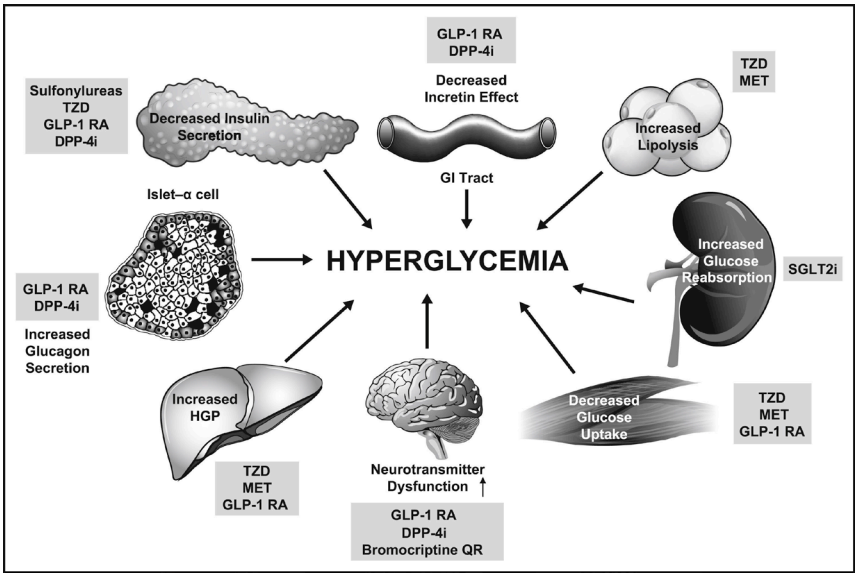
Diabetes Fact Sheet in Korea 2022

처방 패턴 (병용 요법)



당뇨병 약제 (경구약)

2형 당뇨병의 병인에 기반한 당뇨병 약제



01 Metformin

02 Sulfonylurea

03 TZD

04 DPP4 inhibitor

05 SGLT2 inhibitor

06 Alpha glucosidase inhibitor

Am J Cardiol. 2017 Jul 1;120(1S):S4-S16

당뇨병 약제 (경구약)

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대한당뇨병학회, 새 진료지침 발표...75년 만에 메트포르민 권고 지위 변경

당뇨병 환자 혈압 목표치 **130/80mmHg**로 하향 조정

2025-05-02
김영신 medicalkorea1@daum.net

+ 100% -

대한당뇨병학회가 지난 4월 30일 기자간담회에서 '2025 당뇨병 진료지침' 개정안을 공개했다.
그동안 제2형 당뇨병 환자의 1차 약제로 권고해온 메트포르민을 우선 사용 약제에서 제외한다.
이는 1950년대부터 75년간 당뇨병 치료의 기본으로 여겨졌던 메트포르민이 1차 치료제 자리에서 물러나는 중요한 변화다.

◆ "환자 특성 고려한 선택권 확대"

이번 진료지침 개정의 핵심은 메트포르민 1차 약제 권고 철회다.
대한당뇨병학회 이병완(세브란스병원 내분비내과 교수) 진료지침이사는 "메타분석 시행 결과 메트포르민이 타 약제 대비 우월하다는 증거를 찾지 못했다. 한국 당뇨병 환자 특성을 반영한 결정"이라고 설명했다.

◆ 약물치료 초기부터 병용요법 적극 권고

이번 지침에서는 '약물 치료 시 메트포르민을 우선 사용하고 금기나 부작용이 없는 한 유지한다'는 항목을 삭제하고, 대신 환자 특성에 따른 맞춤형 처방과 초기 병용요법을 권장했다.

새 지침은 약물치료 초기부터 당화혈색소 목표와 현재 수준을 고려해 병용요법을 적극적으로 고려하도록 권고했다.
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개정 진료지침 알고리듬은 3가지 핵심 원칙(▲고혈당 증상을 동반한 심한 고혈당이나 췌도부전 환자에게는 인슐린 치료 ▲환자 특성에 맞는 다양한 약물 선택 및 조기 병용요법 ▲동반질환에 따른 맞춤형 치료)을 제시했다.

보험인정기준

고시 제2025-51호 [일반원칙] 당뇨병용제 (2025-04-01)

◆ 단독요법

다음의 하나에 해당하는 경우 **Metformin 단독투여**를 인정하고,
Metformin 투여 금기 환자 또는 부작용으로 Metformin을 투여할 수 없는 경우에는
Sulfonylurea계 약제의 단독 투여를 인정하며, 이 경우 투여소견을 첨부하여야 함.

- 다 음 -

가) 헤모글로빈A1C(HbA1C) ≥6.5%

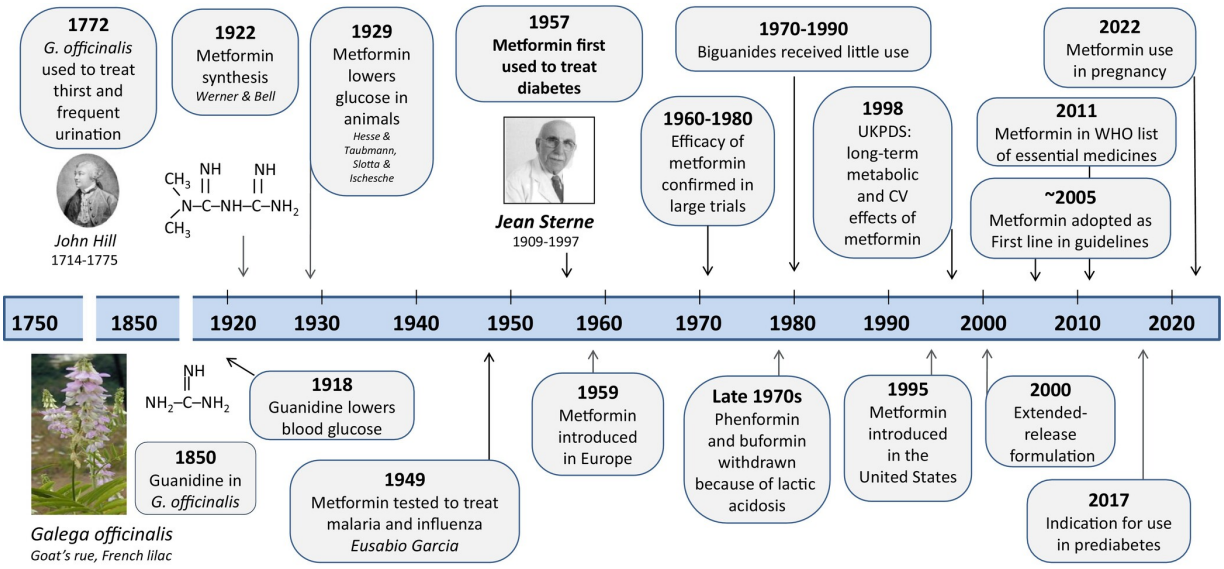
나) 공복혈장혈당 ≥ 126mg/dl

다) 당뇨의 전형적인 증상과 임의혈장혈당 ≥ 200mg/dl

라) 75g 경구당부하검사 후 2시간 혈장혈당 ≥ 200mg/dl

Metformin - History

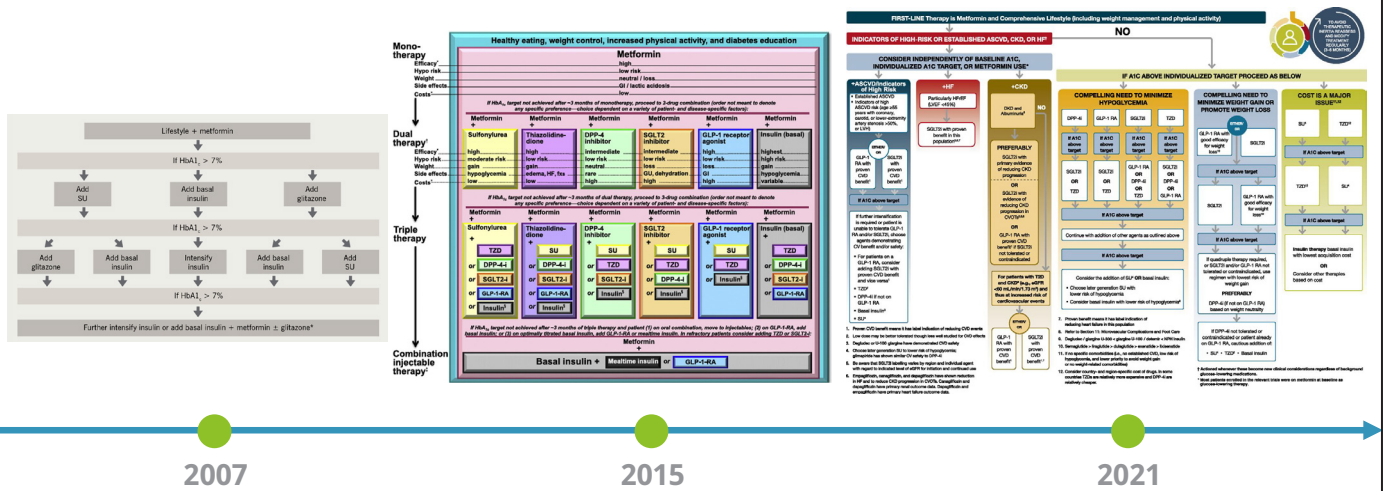
Timeline of the history of metformin



Diabetes Obes Metab. 2024 Aug:26 Suppl 3:3-19

Metformin in ADA Guidelines

Therapeutic positions of Metformin



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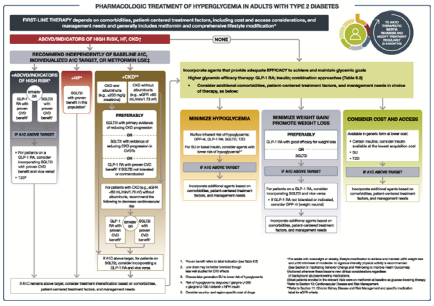


2022

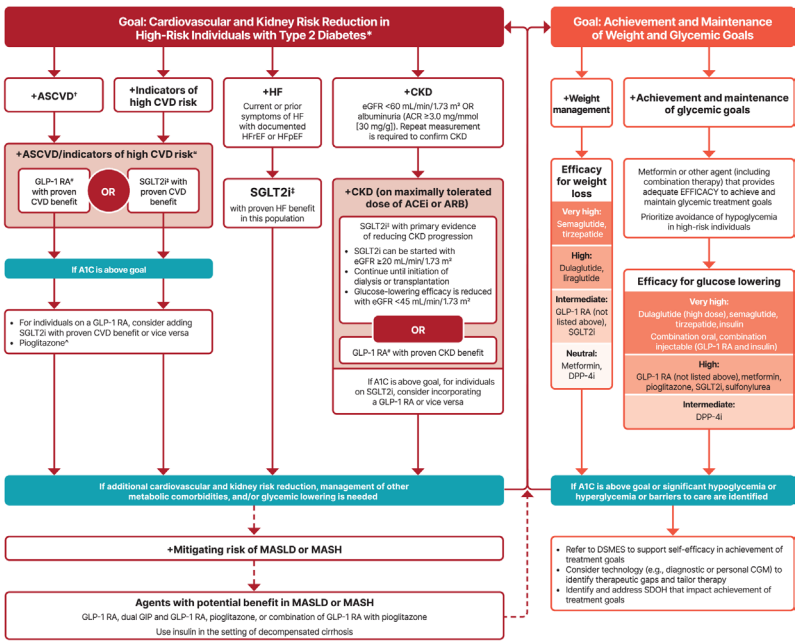
Recommendations

9.4a First-line therapy depends on comorbidities, patient-centered treatment factors, and management needs and generally includes metformin and comprehensive lifestyle modification. **A**

9.4b Other medications (glucagon-like peptide 1 [GLP-1] receptor agonists, sodium–glucose cotransporter 2 [SGLT2] inhibitors), with or without metformin based on glycemic needs, are appropriate initial therapy for individuals with type 2 diabetes with or at high risk for atherosclerotic cardiovascular disease (ASCVD), HF, and/or chronic kidney disease (CKD).

2025 ADA Guidelines

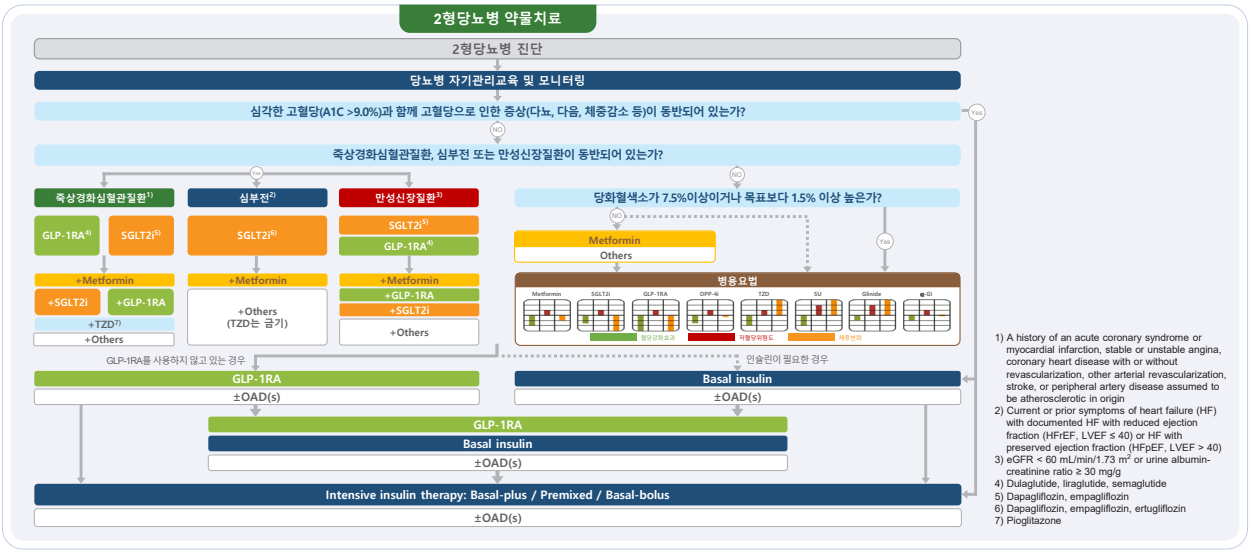
Diabetes-related complications and end-organ effects & weight and glucose management goals



2023 KDA Guidelines

Diabetes-related complications and end-organ effects & glucose management goals (based on characteristics of OADs)

그림 11.1 2형당뇨병 약물치료 알고리듬



α-GI, alpha-glucosidase inhibitors; **DPP-4i,** dipeptidyl peptidase-4 inhibitor; **GLP-1RA,** glucagon-like peptide-1 receptor agonist; **SGLT2i,** sodium-glucose cotransporter 2 inhibitors; **OAD,** oral antidiabetic drug; **SU,** sulfonylurea; **TZD,** thiazolidinedione

2025 KDA Guidelines

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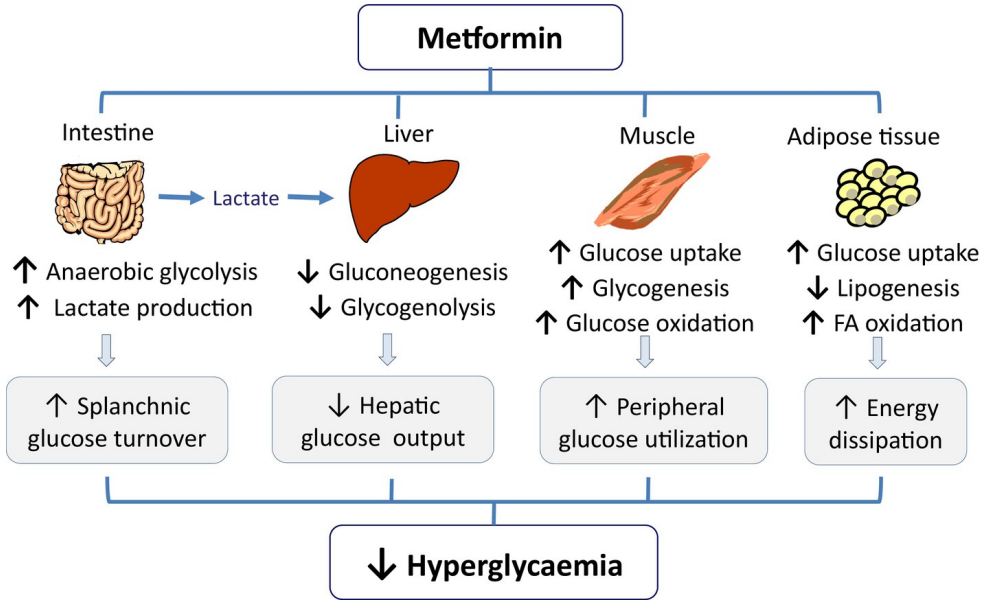
Metformin

Key tissues contributing to the glucose-lowering effect of metformin

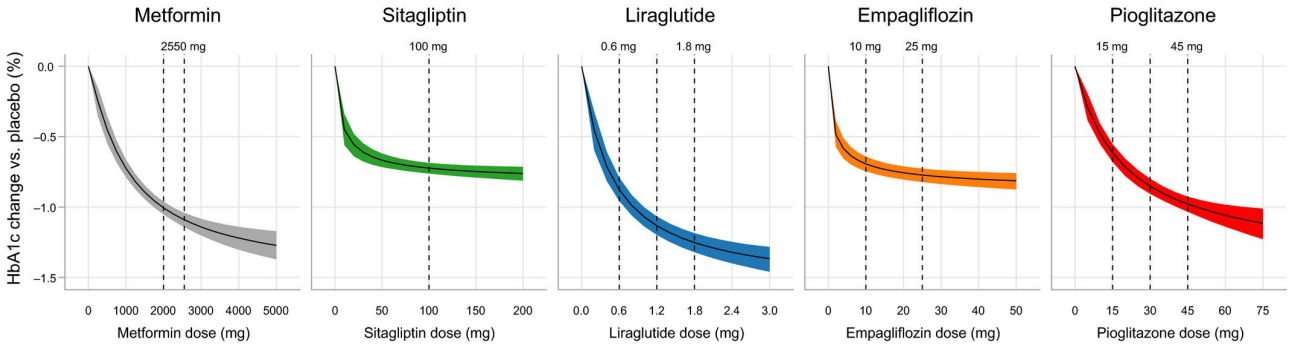


Diabetes Obes Metab. 2024 Aug:26 Suppl 3:3-19

Metformin - Potency

Potent glucose lowering effect

A Model-Based Meta-Analysis of 24 Antihyperglycemic Drugs for Type 2 Diabetes: Comparison of Treatment Effects at Therapeutic Doses

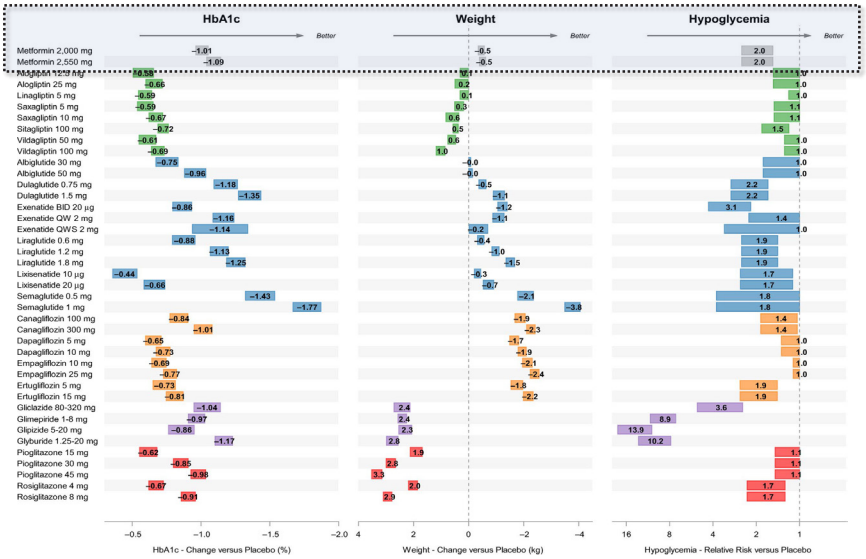


Clin Pharmacol Ther. 2019 May;105(5):1213-1223.

Metformin - Potency

Potent glucose lowering effect

Treatment estimates and 95% credible intervals (bars) vs. placebo for a drug-naive population with a baseline HbA1c of 8.0%, a baseline weight of 90 kg, after 26 weeks of treatment.

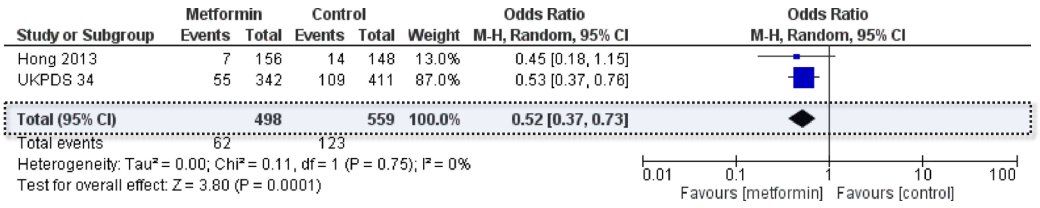


Clin Pharmacol Ther. 2019 May;105(5):1213-1223.

Metformin – Cardiovascular protection

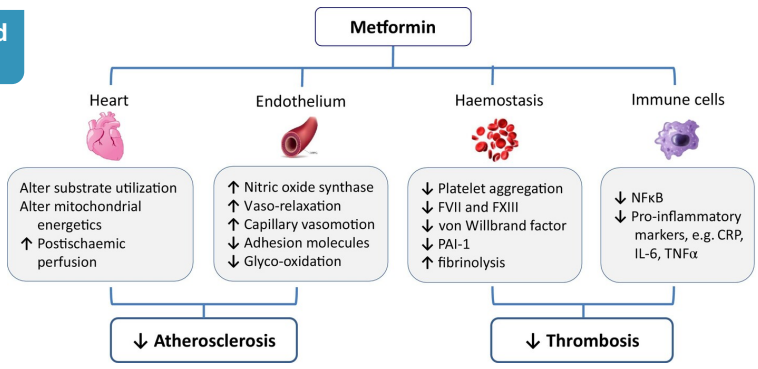
Clinical outcomes and Underlying mechanisms

Risk of 3-point MACE with metformin (vs. other active comparators)



Nutr Metab Cardiovasc Dis. 2021 Mar 10;31(3):699-704

Reduced atherosclerosis and improved thrombolysis



Clin Pharmacol Ther. 2019 May;105(5):1213-1223.

Metformin – 신기능에 따른 약물 조절

eGFR (mL/min/1.73m²)	CKD1-2 ≥ 60	CKD3a 59-45	CKD3b 44-30	CKD4 29-15	ESKD < 15
Metformin			최대용량 1000 mg/일 이하, 새로 시작하지 않음	금기	
Meglitinides					
Repaglinide					주의
Mitiglinide					주의
Nateglinide					금기
DPP-4 inhibitors					
Sitagliptin	100 mg		50 mg	25 mg	
Vildagliptin	100 mg[1]	50 mg			
Saxagliptin	5 mg[2]		2.5 mg		
Linagliptin	5 mg				
Gemigliptin	50 mg				
Teneligliptin	20 mg				
Alogliptin	25 mg[1]	12.5 mg		6.25 mg	
Evogliptin	5 mg				
Anagliptin	200 mg			100 mg	자료 없음
SGLT2 inhibitors					
Dapagliflozin	10 mg		심부전 및 신장이득(≥ 25)[3]		새로 시작하지 않음
Empagliflozin	10 mg/25 mg		심부전 및 신장이득(≥ 20)[3][4]		새로 시작하지 않음
Ertugliflozin	5 mg	자료 없음			
Ipragliflozin	50 mg	자료 없음			
Enavogliflozin	0.3 mg	자료 없음			
Sulfonylureas					
Gliclazide			주의		
Glimepiride			주의		
Glipizide			주의		
Alpha-glucosidase inhibitors					
Acarbose				금기	
Voglibose				자료 없음	
Thiazolidinediones					
Pioglitazone					
Lobeglitazone					
GLP-1 receptor agonists					
Liraglutide					자료 없음
Dulaglutide					

용량 조절 불필요

[1]eGFR ≥ 50 mL/min/1.73 m² 용량 조절 불필요.
[2]eGFR > 45 mL/min/1.73 m² 용량 조절 불필요.
[3]이 사구체여과율 범위에서는 혈당강하효과는 제한적임.
[4]1일 10 mg 용량 사용.

CKD, chronic kidney disease
ESKD, end-stage kindney disease.

대한당뇨병학회 진료지침 2023

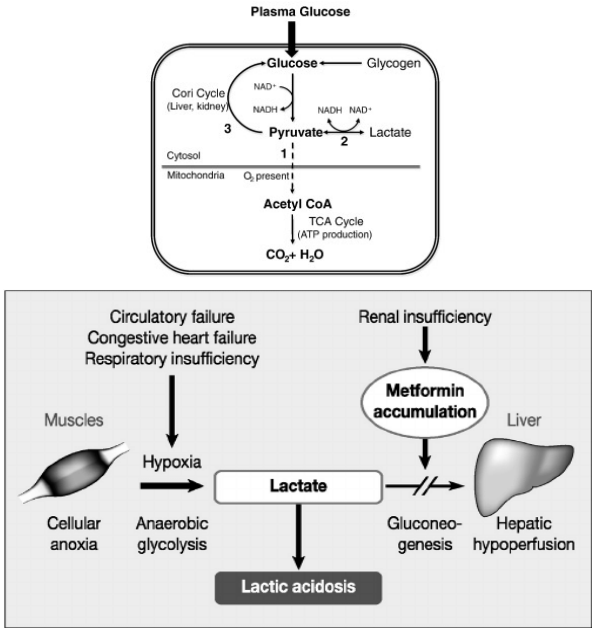
Metformin – 요오드조영제 사용 시 주의사항

CKD stage		1	2	3a	3b	4b	5b
eGFR (mL/min/1.73m²)		≥ 90	89-60	59-45	44-30	29-15	< 15
요오드 조영제	정맥 투여 시	중단 필요 없음		요오드조영제 사용 당일부터 48시간까지 중단하고, 신장기능 평가 후 재개		금기	
	동맥 투여 시	요오드조영제 사용 당일부터 48시간까지 중단하고, 신장기능 평가 후 재개					

CKD, chronic kidney disease.

대한당뇨병학회 진료지침 2023

Metformin-associated lactic acidosis (MALA)



Risk Factors for MALA

- **Renal impairment (eGFR <60, especially <30 mL/min/1.73m²)**
- **Acute kidney injury**
- Hepatic dysfunction (impaired lactate clearance)
- Conditions increasing lactate production (sepsis, CHF, hypoxia, poor perfusion)
- Advanced age
- High plasma metformin levels (>5 µg/mL)
- Increased metformin absorption (e.g., bariatric surgery)
- Continued metformin use during acute illness
- Alcohol use, shock, severe dehydration

Metabolism. 2016 Feb;65(2):20-9. doi: 10.1016/j.metabol.2015
Rev Med Suisse. 2013 Aug 28;9(395):1527-33.

Metformin – Profiles and Tips

Therapeutic profiles of Metformin

Drug Class	Glucose-lowering Efficacy	Hypo-glycemia Risk	Weight Effect	CV Effects	Renal Effects	CKD Progression	MASH Effect	Key Clinical Considerations
Metformin (oral)	**High**	None	Neutral (possible weight loss)	**Potential CV benefit**	Neutral	Neutral	Neutral	**Contraindicated if eGFR <30 mL/min;** risk of B12 deficiency; **GI side effects**

- Start with low dose (500mg) with food to minimize GI side effect
- If GI intolerance develops, try extended-release formulations
- Discontinue in acute illness

- Don’t forget to lower doses or discontinue in case of renal dysfunction

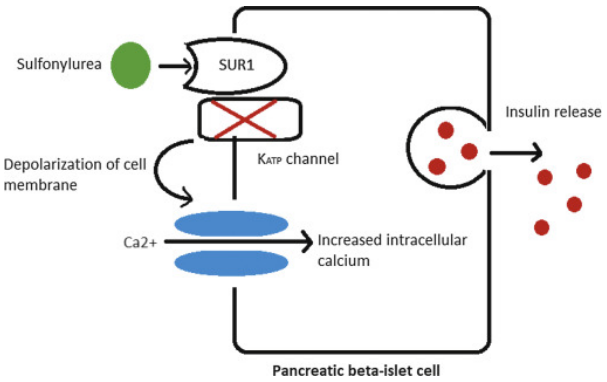
American Diabetes Association. Diabetes Care 2025;48(Suppl 1):S181–S206

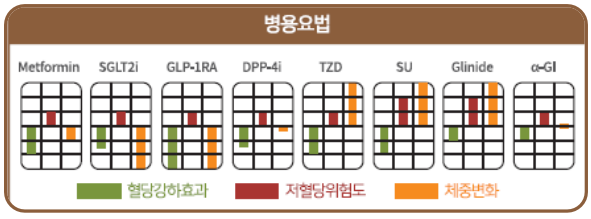
CONTENTS

Tips for prescribing oral antidiabetic agents

Sulfonylurea

Mechanism of action and Potency





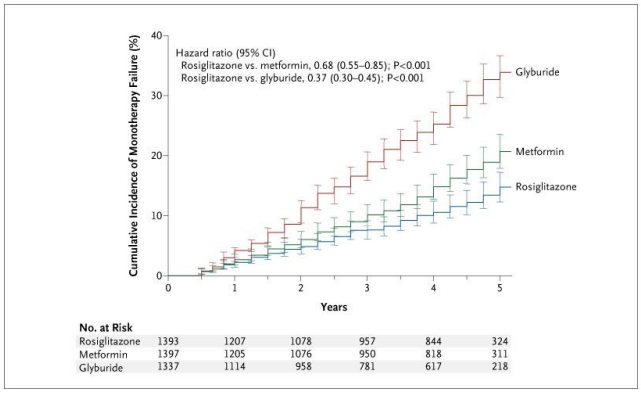
당화혈색소 감소 효과 (단독)	
Metformin	**1.0-2.0%**
SGLT2i	0.5-1.0%
GLP-1 RA	0.8-1.5%
DPP-4i	0.5-1.0%
SU	**1.0-2.0%**
TZD	0.5-1.4%
AGI	0.5-1.0%
Meglitinide	0.5-1.5%

Pharmacology & Therapeutics, 2000
2023 대한당뇨병학회 진료지침

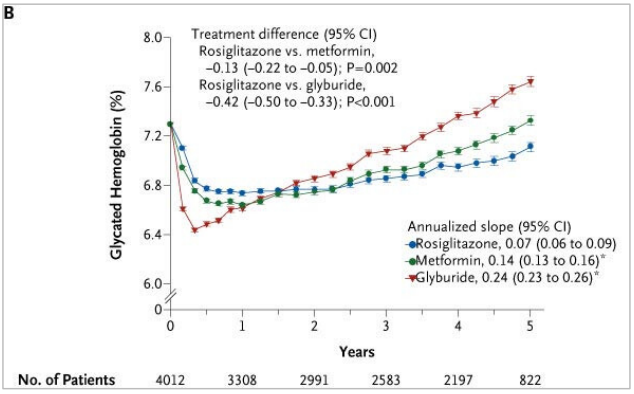
Sulfonylurea - Durability

A Diabetes Outcome Progression Trial (ADOPT)

Cumulative Incidence of Monotherapy Failure at 5 Years



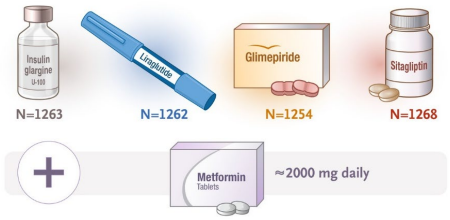
Glycated Hemoglobin

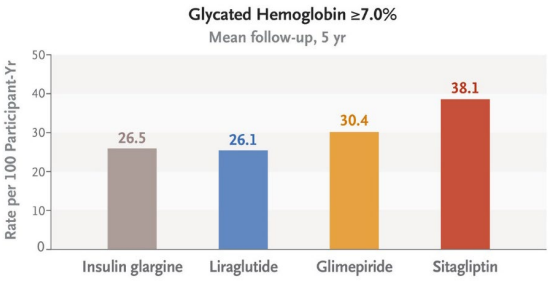


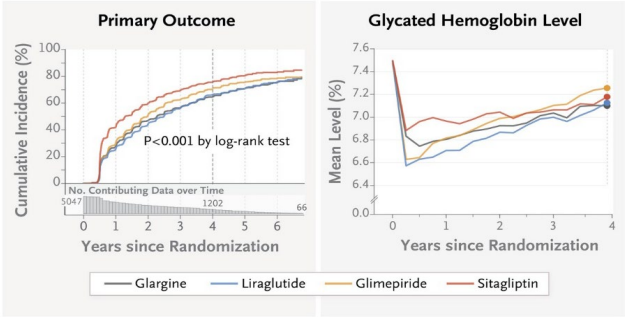
N Engl J Med. 2006 Dec 7;355(23):2427-43.

Sulfonylurea – Efficacy and Durability

The Glycemia Reduction Approaches in Type 2 Diabetes: A Comparative Effectiveness (GRADE) Study







*The primary metabolic outcome was a glycated hemoglobin level, measured quarterly, of 7.0% or higher that was subsequently confirmed, and the secondary metabolic outcome was a confirmed glycated hemoglobin level greater than 7.5%.

N Engl J Med. 2022 Sep 22;387(12):1063-1074

Sulfonylurea – Safety

The Glycemia Reduction Approaches in Type 2 Diabetes: A Comparative Effectiveness (GRADE) Study

Adverse Event	Glargine (N=1263)		Glimepiride (N=1254)		Liraglutide (N=1262)		Sitagliptin (N=1268)		Pairwise Treatment Comparisons
	no. of participants (%)	*event rate (95% CI)*	*no. of participants (%)*	*event rate (95% CI)*	*no. of participants (%)*	*event rate (95% CI)*	*no. of participants (%)*	*event rate (95% CI)*	
Death	42 (3.3)	0.65 (0.47–0.87)	43 (3.4)	0.67 (0.48–0.90)	27 (2.1)	0.42 (0.27–0.60)	41 (3.2)	0.63 (0.45–0.86)	None are significant
Severe hypoglycemia	16 (1.3)	0.32 (0.19–0.49)	28 (2.2)	0.61 (0.43–0.84)	12 (1.0)	0.21 (0.11–0.35)	9 (0.7)	0.16 (0.08–0.29)	
Any adverse event	468 (37.1)	15.3 (14.3–16.3)	480 (38.3)	16.0 (15.0–17.0)	427 (33.8)	13.7 (12.8–14.7)	452 (35.7)	14.9 (13.9–15.8)	
Weight gain	166 (13.1)	3.0 (2.6–3.5)	152 (12.1)	2.8 (2.3–3.2)	77 (6.1)	1.3 (1.1–1.7)	115 (9.1)	2.0 (1.7–2.4)	
Gastrointestinal symptoms	451 (35.7)	16.5 (15.0–18.0)	422 (33.7)	15.1 (13.7–16.6)	551 (43.7)	22.9 (21.0–24.9)	435 (34.3)	15.1 (13.7–16.6)	

I Glargine G Glimepiride L Liraglutide S Sitagliptin

····· P≤0.05 --- P≤0.01 — P≤0.001 No statistical difference

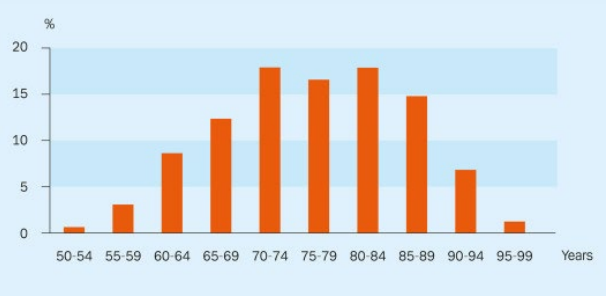
N Engl J Med. 2022 Sep 22;387(12):1063-1074

Sulfonylurea – Hypoglycemia

Severe hypoglycaemia during treatment with sulphonylureas in patients with type 2 diabetes in the Capital Region of Denmark

Real-life data on SU use, and prevalence of severe hypoglycaemia & precipitating factors

Age distribution



Putative reasons

Unchanged SU dose despite of decreased food intake	56 (35)
Excessive use of other medications	17 (11)
Alcohol intoxication	9 (6)
Concomitant infection	11 (7)
Dehydration	27 (17)
Combined infection, decreased food intake and unchanged SU dose	36 (22)
No obvious reason	32 (20)

*Number (%)

Diabetes Res Clin Pract. 2015 Nov;110(2):202-7.

Sulfonylurea – Profiles and Tips

Therapeutic profiles of sulfonylurea

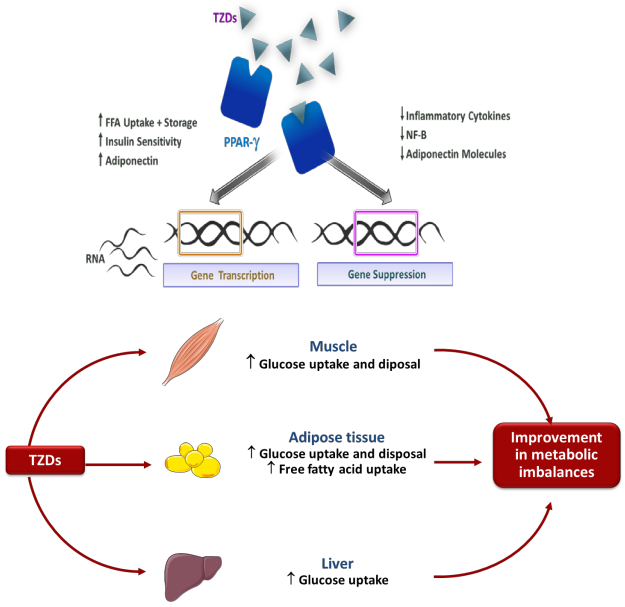
Drug Class	Glucose-lowering Efficacy	Hypo-glycemia Risk	Weight Effect	CV Effects	Renal Effects	CKD Progression	MASH Effect	Key Clinical Considerations
Sulfonyl-ureas	High	**Yes**	**Weight gain**	Neutral	Neutral	Neutral	Un-known	**Hypoglycemia risk** (especially with renal impairment);

- Highly effective in lowering glucose at first
- Use the lowest effective dose
- Reduce dose in CKD, and avoid in patients with history of severe hypoglycemia

American Diabetes Association. Diabetes Care 2025;48(Suppl 1):S181–S206

TZD

Mechanism of action and Potency

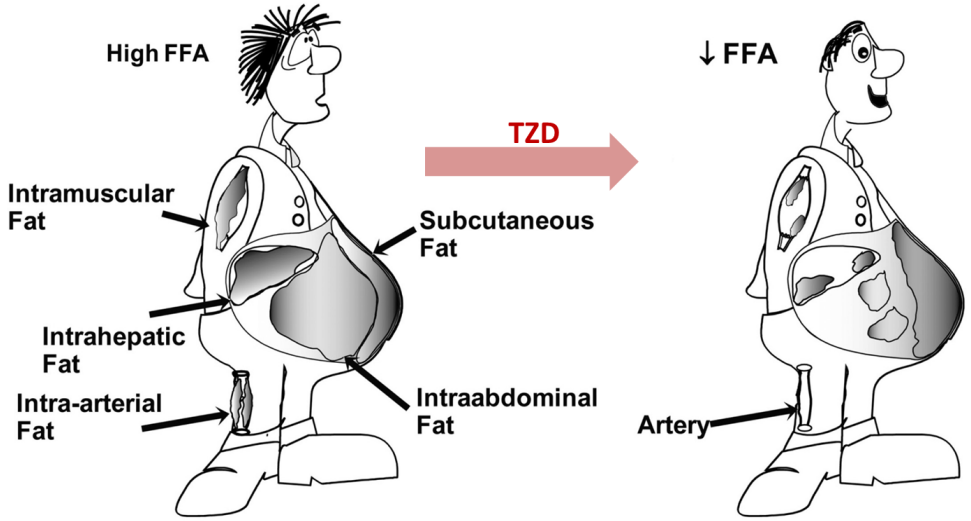


당화혈색소 감소 효과 (단독)	
Metformin	**1.0-2.0%**
SGLT2i	0.5-1.0%
GLP-1 RA	0.8-1.5%
DPP-4i	0.5-1.0%
SU	**1.0-2.0%**
TZD	**0.5-1.4%**
AGI	0.5-1.0%
Meglitinide	0.5-1.5%

Trends Endocrinol Metab. 1999;10:9-13

TZD

Mechanism of action and Potency



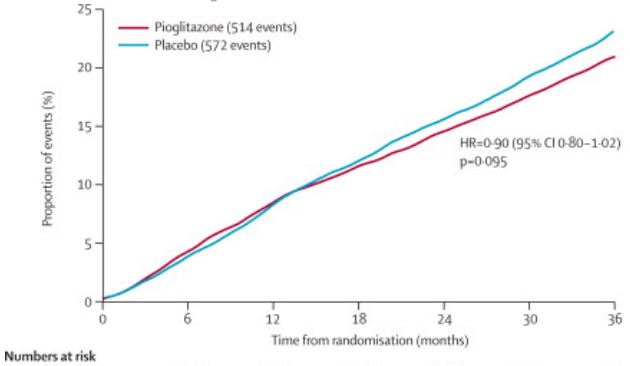
Vasc Health Risk Manag 2010;6:671-90

TZD – Cardiovascular outcome trial

Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlled trial

Primary endpoint

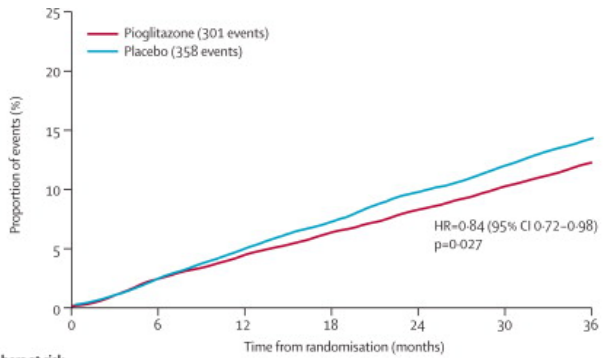
*Death from any cause, non-fatal myocardial infarction (including silent myocardial infarction), stroke, acute coronary syndrome, leg amputation, coronary revascularisation, or revascularisation of the leg.



Numbers at risk							
Pioglitazone	2488	2373	2302	2218	2146	348
Placebo	2530	2413	2317	2215	2122	345

Secondary endpoint

*Death from any cause, non-fatal myocardial infarction (excluding silent myocardial infarction), or stroke.



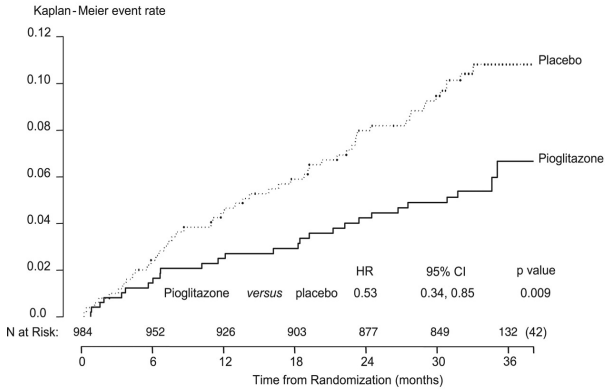
Numbers at risk							
Pioglitazone	2536	2487	2435	2381	2336	396
Placebo	2566	2504	2442	2371	2315	390

Vasc Health Risk Manag 2010;6:671-90

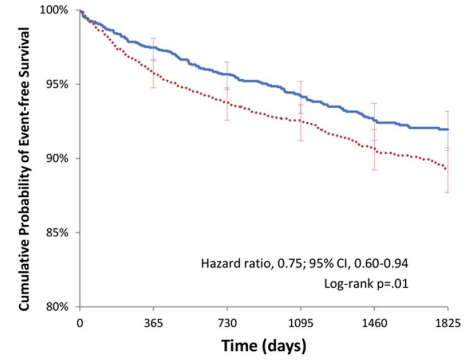
TZD and Stroke prevention

PROactive (PROspective pioglitAzone Clinical Trial In macroVascular Events 04)
IRIS trial (Insulin Resistance Intervention after Stroke)

Stroke in DM patients with previous stroke



Stroke in insulin resistant patients with previous stroke



No. at Risk:

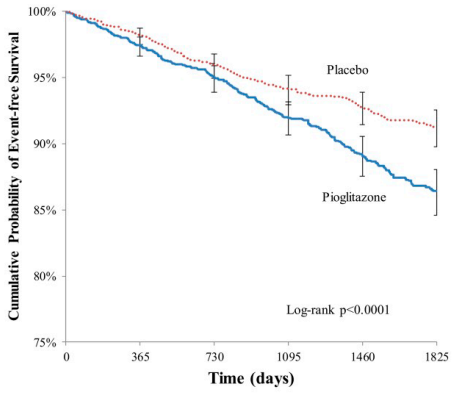
Pioglitazone	1939	1804	1712	1509	1214	536
Placebo	1937	1780	1698	1495	1199	505

Circulation. 2018 Jan 30;137(5):455-463.

TZD and Fracture risk

Time to first fracture

5-year risk of first fracture, 13.6% vs 8.8%
Risk difference (RD), 4.9%
HR, 1.53; 95% CI, 1.24 to 1.89

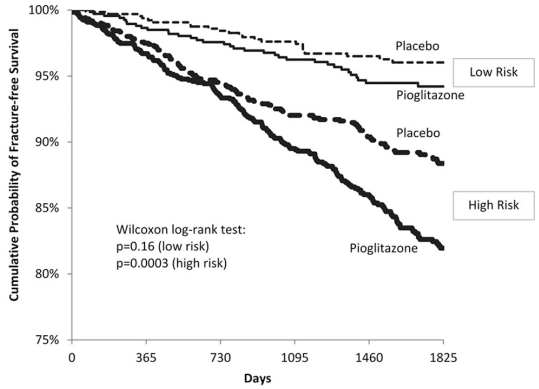


No. at Risk:

Pioglitazone	1939	1798	1694	1469	1164	494
Placebo	1937	1809	1717	1499	1208	511

Risk Scoring

Age
Race-ethnicity
Sex
BMI
Disability
Medications



No. at risk:

Low risk stratum:

Pioglitazone	680	648	618	544	442	203
Placebo	667	630	612	552	447	193

High risk stratum:

Pioglitazone	1214	1110	1041	895	700	281
Placebo	1227	1137	1063	907	724	302

J Clin Endocrinol Metab. 2016 Dec 9;102(3):914–922
Stroke. 2019 Jan;50(1):95-100

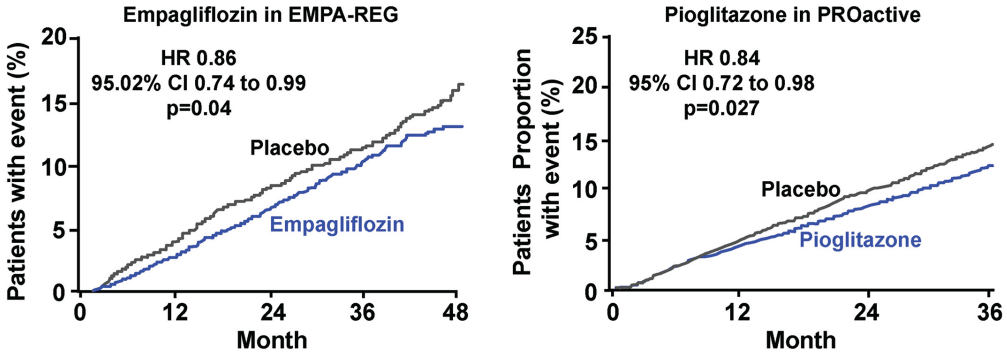
TZD: optimum agent with SGLT2 inhibitor?

Revitalization of pioglitazone: the optimum agent to be combined with a sodium-glucose co-transporter-2 inhibitor

R. A. DeFronzo[1], R. Chilton[2], L. Norton[1], G. Clarke[3], R. E. J. Ryder[4] & M. Abdul-Ghani[1]

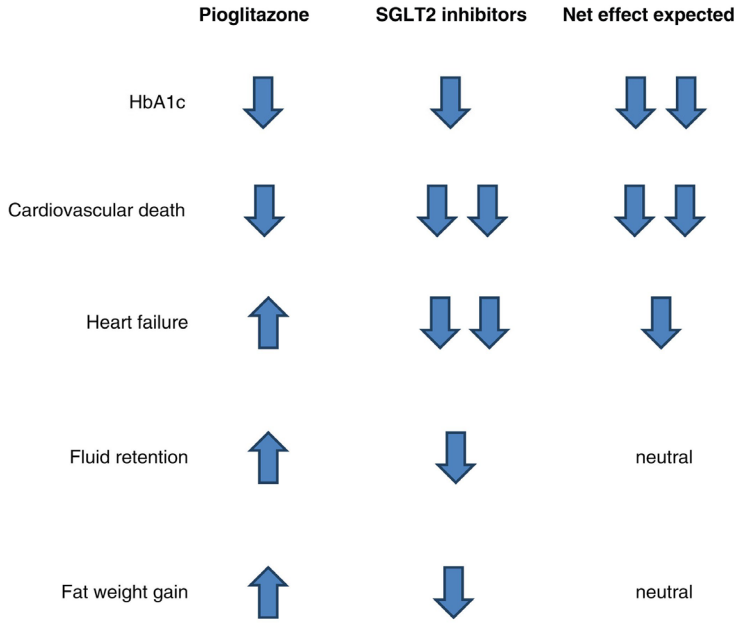
Effect on 3-point MACE

*Three-point major adverse cardiac events include cardiovascular death, stroke, myocardial infarction.



Diabetes Obes Metab. 2016 May;18(5):454-62

TZD: optimum agent with SGLT2 inhibitor?



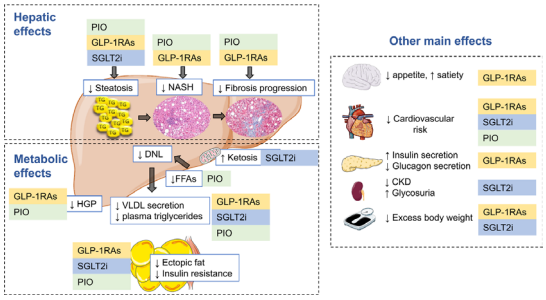
Diabetes Obes Metab. 2016 May;18(5):454-62

TZD and Fatty liver disease

TABLE 2 RCTs Reporting Histological Outcomes in People With NASH Treated With Pioglitazone

Study	*n*	Pioglitazone Dose, mg/day	Patients With Type 2 Diabetes, %	Duration, weeks	Patients With NASH Resolution, %*	People With Fibrosis Improvement, %*
Belfort et al. (29)	55	45	42	24	Not reported†	13
Aithal et al. (30)	74	30	0	50	Not reported†	9
Sanyal et al. (32)	247	30	0	96	26‡	13
Cusi et al. (31)	101	45	51	72	32‡	14
Bril et al. (34)	105	45 + vitamin E	100	72	31‡	22
Huang et al. (33)	90	30	23	24	16	1

*Resolution of NASH and fibrosis improvement are rounded, placebo-subtracted data. †Histological data are not reported as NASH resolution; improved necroinflammation (Belfort et al. [29]): 47%; improved hepatocellular injury (Aithal et al. [30]): 22%. ‡Significant vs. placebo.



Diabetes Spectr. 2024 Winter;37(1):48-58.

◆ **대한간학회 진료지침 (2021)**

1. **Pioglitazone**은 당뇨병 동반 여부와 무관하게 간 조직검사로 진단된 비알코올 지방간염에서 지방간염을 개선시키는 효과가 있지만, 장기 치료 시 안전성에 우려가 있어 이득위험비를 고려해 사용해 볼 수 있다. (B1)

2. **Metformin**은 당뇨병이 있는 비알코올 지방간질환 환자에서 당뇨병의 1차 치료제로 우선 사용될 수 있다. (B1)

TZD – Profiles and Tips

Therapeutic profiles of TZD

Drug Class	Glucose-lowering Efficacy	Hypo-glycemia Risk	Weight Effect	CV Effects	Renal Effects	CKD Progression	MASH Effect	Key Clinical Considerations
Pioglitazone (oral)	**High**	None	**Weight gain**	**Possible CV benefit (but increased HF risk)**	Neutral	Neutral	**Potential benefit**	Risk of HF, fluid retention, edema **Risk of fractures** Avoid in bladder cancer

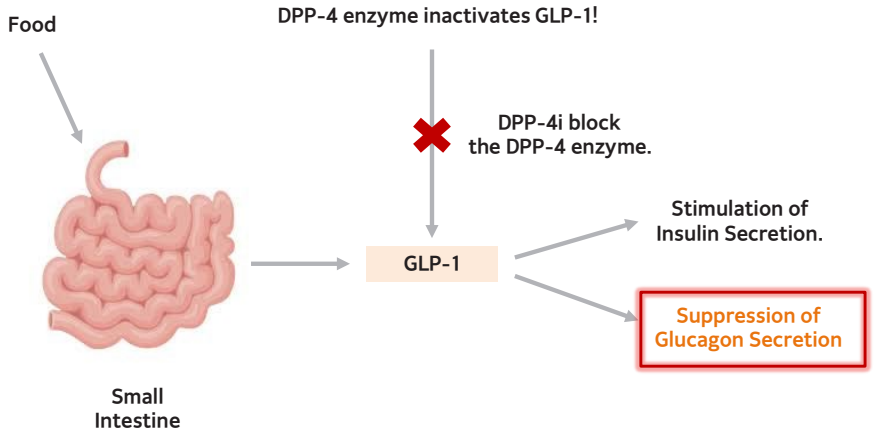
- **Effective, durable** and potential benefit in CV risk and **MASH**
- Don't forget side effect and contraindications – edema/HF, fracture and bladder cancer

American Diabetes Association. Diabetes Care 2025;48(Suppl 1):S181–S206

DPP4 inhibitors

Mechanism of action

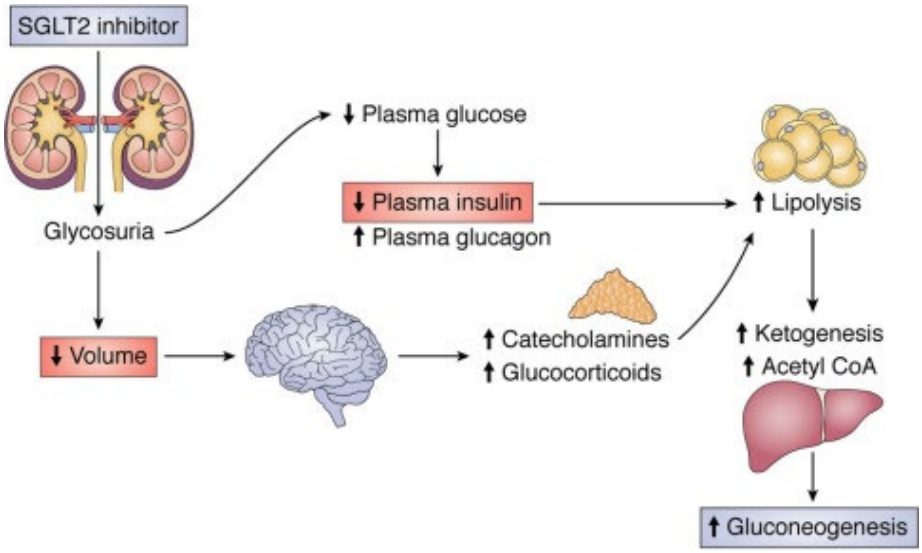
*DPP-4 inhibition leads to **post-prandial** GLP-1 plasma concentrations that mediates the glucose-dependent inhibition of **glucagon secretion***



Front Endocrinol (Lausanne). 2019 Jun 19;10:389

DPP4 inhibitors & SGLT2 inhibitors

Mechanism of action



J Biol Chem. 2020 Oct 16;295(42):14379-14390

DPP4 inhibitors & SGLT2 inhibitors

Complementary effect

Mediating pathways	DPP-4i	SGLT-2i
Glucose-dependent insulin secretion	V	
Glucose-dependent decrease in glucagon secretion	**V**	
Increased glucagon secretion		**V**
Increased glucosuria		V
Increased β-cell sensitivity/function	V	V
Decreased glucotoxicity		V
Inhibit degradation of incretin hormones (GLP-1, GIP)	V	
Anti-inflammatory effects	V	
Physiologic effects	**DPP-4i**	**SGLT-2i**
HbA1c reduction	V	V
FPG reduction	V	V
Weight loss		V
Blood pressure reduction		V

Postgrad Med. 2017;129(4):409-420.

DPP4 inhibitors & SGLT2 inhibitors

Efficacy and safety

SGLT-2i as add-on to DPP-4i

DPP-4i as add-on to SGLT-2i

	SGLT2 inhibitor + DPP-4 inhibitor vs DPP-4 inhibitor				SGLT2 inhibitor + DPP-4 inhibitor vs SGLT2 inhibitor			
Efficacy outcomes	n	N	WMD (95% CI)	I^2 (%)	n	N	WMD (95% CI)	I^2 (%)
HbA1c (%)	8	2522	−0.71 (−0.80, −0.61)[b]	8.4	7	2648	−0.31 (−0.38, −0.24)[b]	3.4
FPG (mg/dL)	8	2511	−25.62 (−39.38, −11.86)[b]	96.9	7	2627	−8.94 (−11.93, −5.95)[b]	35.8
PPG (mg/dL)	1	301	−44.00 (−53.70, −34.30)[b]	–	1	298	−9.00 (−18.65, 0.65)	–

	SGLT2 inhibitor + DPP-4 inhibitor vs DPP-4 inhibitor				SGLT2 inhibitor + DPP-4 inhibitor vs SGLT2 inhibitor			
Safety outcomes	n	E/N	RR (95% CI)	I^2 (%)	n	E/N	RR (95% CI)	I^2 (%)
Overall adverse events	8	1628/2616	0.98 (0.90, 1.06)	44.5	7	1844/2764	1.01 (0.96, 1.07)	9.9
Serious adverse events	8	116/2616	0.84 (0.55, 1.30)	15.7	7	126/2764	0.85 (0.60, 1.21)	0.0
Hypoglycaemia	8	55/2616	1.07 (0.62, 1.85)	0.0	7	55/2764	0.82 (0.46, 1.46)	0.0
Severe hypoglycaemia	8	3/2616	1.19 (0.15, 9.63)	0.0	7	1/2764	0.33 (0.01, 8.10)	–
Drug-related adverse events	5	172/1490	1.21 (0.89, 1.64)	0.0	5	382/2091	0.91 (0.75, 1.10)	0.0
Adverse events leading to discontinuation	8	67/2616	1.23 (0.66, 2.28)	18.6	7	88/2764	0.86 (0.55, 1.34)	0.0

* As dual add-on or subsequent add-on.
CI, Confidence Interval; WMD, Weighted Mean Difference. bResults with statistical differences between comparisons.

Diabetes Obes Metab. 2018;20(8):1972-1976

DPP4-inhibitor – 신기능에 따른 약물 조절

eGFR (mL/min/1.73m²)	CKD1-2 ≥ 60	CKD3a 59-45	CKD3b 44-30	CKD4 29-15	ESKD < 15
Metformin			최대용량 1000 mg/일 이하, 새로 시작하지 않음	금기	
Meglitinides					
Repaglinide					주의
Mitiglinide					주의
Nateglinide					금기
DPP-4 inhibitors					
Sitagliptin	100 mg		50 mg	25 mg	
Vildagliptin	100 mg[1]		50 mg		
Saxagliptin	5 mg[2]		2.5 mg		
Linagliptin	5 mg				
Gemigliptin	50 mg				
Teneligliptin	20 mg				
Alogliptin	25 mg[1]		12.5 mg	6.25 mg	
Evogliptin	5 mg				
Anagliptin	200 mg			100 mg	자료 없음
SGLT2 inhibitors					
Dapagliflozin	10 mg		심부전 및 신장이득(≥ 25)[3]		새로 시작하지 않음
Empagliflozin	10 mg/25 mg		심부전 및 신장이득(≥ 20)[3,4]		새로 시작하지 않음
Ertugliflozin	5 mg	자료 없음			
Ipragliflozin	50 mg	자료 없음			
Enavogliflozin	0.3 mg	자료 없음			
Sulfonylureas					
Gliclazide			주의		
Glimepiride			주의		
Glipizide			주의		
Alpha-glucosidase inhibitors					
Acarbose				금기	
Voglibose				자료 없음	
Thiazolidinediones					
Pioglitazone					
Lobeglitazone					
GLP-1 receptor agonists					
Liraglutide					자료 없음
Dulaglutide					

용량 조절 불필요

[1]eGFR ≥ 50 mL/min/1.73 m² 용량 조절 불필요.
[2]eGFR > 45 mL/min/1.73 m² 용량 조절 불필요.
[3]이 사구체여과율 범위에서는 혈당강하효과는 제한적임.
[4]1일 10 mg 용량 사용.

CKD, chronic kidney disease
ESKD, end-stage kindney disease.

대한당뇨병학회 진료지침 2023

DPP4-inhibitor – 신기능에 따른 약물 조절

Outcomes for Inappropriate Renal Dose Adjustment of DPP-4 inhibitors (Korea)

A retrospective observational cohort study of 82,332 patients aged 30 to 75 years with T2DM and CKD being treated with DPP-4 inhibitors from January 1, 2012, through December 31, 2014, using the Korean National Health Information Database

TABLE 2. Risk of Death, Emergency Department Visits, and Severe Hypoglycemia in Patients With Type 2 Diabetes and Chronic Kidney Disease (Stage 3 or 4) by Cox Proportional Hazards Regression Analysis[a]

Variable	Patients (No.)	Events (No.)	Duration (person-days)	Rate (No. [95% CI] of events per 1000 person-days)	Model 1 Hazard ratio (95% CI)	Model 1 *P* value	Model 2 Hazard ratio (95% CI)	Model 2 *P* value	Model 3 Hazard ratio (95% CI)	Model 3 *P* value
Severe hypoglycemia										
Appropriate dosing group	60,773	805	78,644.02	10.24 (9.55-10.97)	1 (Reference)		1 (Reference)		1 (Reference)	
Inappropriate dosing group	21,559	372	29,662.12	12.54 (11.33-13.88)	1.199 (1.061-1.357)	.004	1.194 (1.056-1.351)	.004	1.192 (1.054-1.349)	.005
Emergency department visits										
Appropriate dosing group	60,773	4845	75,095.49	64.52 (62.73-66.36)	1 (Reference)		1 (Reference)		1 (Reference)	
Inappropriate dosing group	21,559	1885	28,310.03	66.58 (63.65-69.66)	1.076 (1.02-1.135)	.007	1.072 (1.017-1.131)	.01	1.074 (1.018-1.133)	.009
Death										
Appropriate dosing group	60,773	1134	80,202.27	14.14 (13.34-14.99)	1 (Reference)		1 (Reference)		1 (Reference)	
Inappropriate dosing group	21,559	529	30,514.98	17.34 (15.92-18.88)	1.149 (1.036-1.275)	.008	1.142 (1.03-1.267)	.01	1.115 (1.005-1.237)	.04

[a]Model 1 is adjusted for age, sex, and history of emergency department visits or severe hypoglycemia events. Model 2 is adjusted for age, sex, smoking and alcohol drinking status, systolic blood pressure, total cholesterol level, and history of emergency department visits or severe hypoglycemia events. Model 3 is adjusted for age, sex, smoking and alcohol drinking status, systolic blood pressure, total cholesterol level, other antidiabetic drug treatment, and history of emergency department visits or severe hypoglycemia events.

Mayo Clin Proc. 2020 Jan;95(1):101-112

DPP-4 inhibitors – Profiles and Tips

Therapeutic profiles of sulfonylurea

Drug Class	Glucose-lowering Efficacy	Hypo-glycemia Risk	Weight Effect	CV Effects	Renal Effects	CKD Progression	MASH Effect	Key Clinical Considerations
DPP-4 inhibitors (oral)	Moderate	None	Neutral	Neutral (potential HF risk with saxagliptin)	Neutral	Neutral	Neutral	Risk of joint pain; rare pancreatitis; dose adjust in renal impairment

- Effective in lowering postprandial glucose with **great safety**
- Don’t forget to **adjust dose** in renal impairment

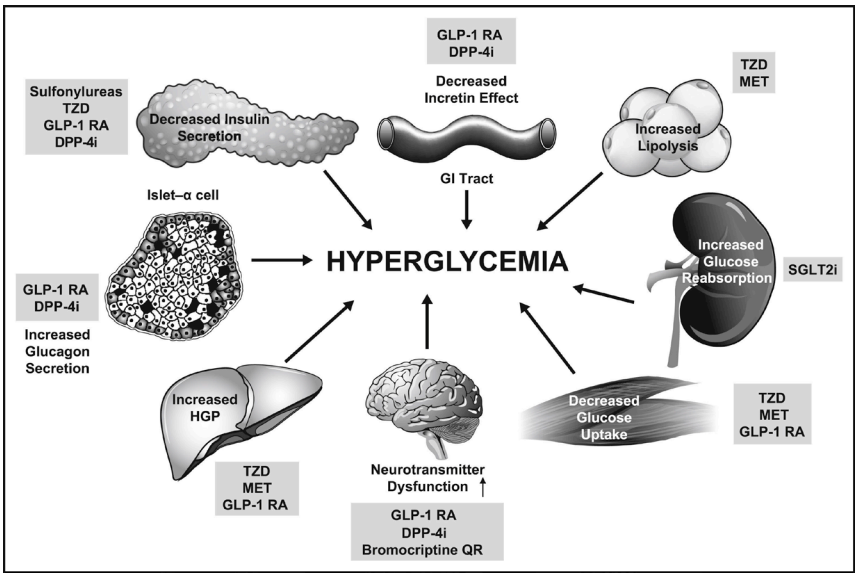
American Diabetes Association. Diabetes Care 2025;48(Suppl 1):S181–S206

CONTENTS

Tips for prescribing oral antidiabetic agents

4제 요법의 기반 – 다양해진 당뇨병 약제 (경구약)

2형 당뇨병의 병인에 기반한 당뇨병 약제



01 Metformin

02 Sulfonylurea

03 TZD

04 DPP4 inhibitor

05 SGLT2 inhibitor

06 Alpha glucosidase inhibitor

Am J Cardiol. 2017 Jul 1;120(1S):S4-S16

보험인정기준

고시 제2025-51호 [일반원칙] 당뇨병용제 (2025-04-01)

◆ **병용요법 (2제요법)**

구분		MET	SU	Glinide	AGI	TZD	DPP-4i	SGLT-2i				
								DAPA	IPRA	EMPA	ERTU	ENAVO
MET			인정	인정	인정	인정	인정	인정	인정	인정	인정	인정
SU		인정		x	인정	인정	인정	인정	인정	인정	인정	x
Glinide		인정	x		인정	인정	인정	x	x	x	x	x
AGI		인정	인정	인정		x	x	x	x	x	x	x
TZD		인정	인정	인정	x		인정	x	x	x	x	x
DPP-4I		인정	인정	x	x	인정		x	x	x	x	x
SGLT-2I	DAPA	인정	인정	x	x	x	x					
	IPRA	인정	인정	x	x	x	x					
	EMPA	인정	인정	x	x	x	x					
	ERTU	인정	인정	x	x	x	x					
	ENAVO	인정	x	x	x	x	x					

◆ **병용요법 (3제요법)**

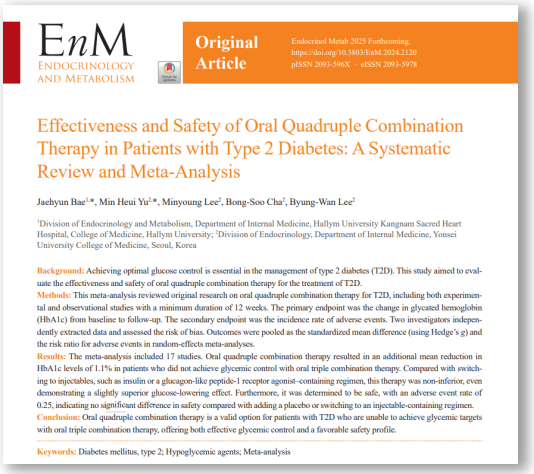
2제 요법에서 인정되지 않는 약제의 조합이 포함되어서는 아니되나, 다음의 3제요법은 인정함.

(1) metformin + SGLT-2 inhibitor + DPP-IV inhibitor

(2) metformin + SGLT-2 inhibitor(ertugliflozin, enavogliflozin 제외) + Thiazolidinedione

Evidence on Oral Quadruple Combination therapy

Systematic Review and Meta-analysis (2025)



EnM Endocrinology and Metabolism — Original Article

Endocrinol Metab 2025 Forthcoming
https://doi.org/10.3803/EnM.2024.2120
pISSN 2093-596X · eISSN 2093-5978

Effectiveness and Safety of Oral Quadruple Combination Therapy in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis

Jaehyun Bae[1,*], Min Heui Yu[2,*], Minyoung Lee[2], Bong-Soo Cha[2], Byung-Wan Lee[2]

[1]Division of Endocrinology and Metabolism, Department of Internal Medicine, Hallym University Kangnam Sacred Heart Hospital, College of Medicine, Hallym University; [2]Division of Endocrinology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea

Background: Achieving optimal glucose control is essential in the management of type 2 diabetes (T2D). This study aimed to evaluate the effectiveness and safety of oral quadruple combination therapy for the treatment of T2D.

Methods: This meta-analysis reviewed original research on oral quadruple combination therapy for T2D, including both experimental and observational studies with a minimum duration of 12 weeks. The primary endpoint was the change in glycated hemoglobin (HbA1c) from baseline to follow-up. The secondary endpoint was the incidence rate of adverse events. Two investigators independently extracted data and assessed the risk of bias. Outcomes were pooled as the standardized mean difference (using Hedge's *g*) and the risk ratio for adverse events in random-effects meta-analyses.

Results: The meta-analysis included 17 studies. Oral quadruple combination therapy resulted in an additional mean reduction in HbA1c levels of 1.1% in patients who did not achieve glycemic control with oral triple combination therapy. Compared with switching to injectables, such as insulin or a glucagon-like peptide-1 receptor agonist–containing regimen, this therapy was non-inferior, even demonstrating a slightly superior glucose-lowering effect. Furthermore, it was determined to be safe, with an adverse event rate of 0.25, indicating no significant difference in safety compared with adding a placebo or switching to an injectable-containing regimen.

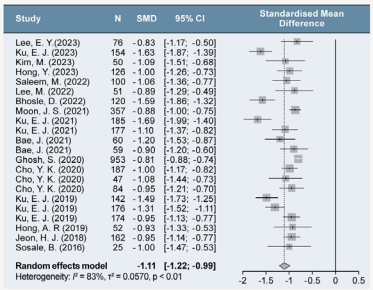
Conclusion: Oral quadruple combination therapy is a valid option for patients with T2D who are unable to achieve glycemic targets with oral triple combination therapy, offering both effective glycemic control and a favorable safety profile.

Keywords: Diabetes mellitus, type 2; Hypoglycemic agents; Meta-analysis

Uncontrolled type 2 diabetes mellitus under oral triple combination therapy

Oral quadruple combination therapy

Further HbA1c reduction of 1.11%



Study	N	SMD	95% CI
Lee, E. Y.(2023)	76	-0.83	[-1.17; -0.50]
Ku, E. J. (2023)	154	-1.63	[-1.87; -1.39]
Kim, M. (2023)	50	-1.09	[-1.51; -0.68]
Hong, Y. (2023)	126	-1.00	[-1.26; -0.73]
Saleem, M. (2022)	100	-1.06	[-1.36; -0.77]
Lee, M. (2022)	51	-0.89	[-1.29; -0.49]
Bhosle, D. (2022)	120	-1.59	[-1.86; -1.32]
Moon, J. S. (2021)	357	-0.88	[-1.00; -0.75]
Ku, E. J. (2021)	185	-1.69	[-1.99; -1.40]
Ku, E. J. (2021)	177	-1.10	[-1.37; -0.82]
Bae, J. (2021)	60	-1.20	[-1.53; -0.87]
Bae, J. (2021)	59	-0.90	[-1.20; -0.60]
Ghosh, S. (2020)	953	-0.81	[-0.88; -0.74]
Cho, Y. K. (2020)	187	-1.00	[-1.17; -0.82]
Cho, Y. K. (2020)	47	-1.08	[-1.44; -0.73]
Cho, Y. K. (2020)	84	-0.95	[-1.21; -0.70]
Ku, E. J. (2019)	142	-1.49	[-1.73; -1.25]
Ku, E. J. (2019)	176	-1.31	[-1.52; -1.11]
Ku, E. J. (2019)	174	-0.95	[-1.13; -0.77]
Hong, A. R (2019)	52	-0.93	[-1.33; -0.53]
Jeon, H. J. (2018)	162	-0.95	[-1.14; -0.77]
Sosale, B. (2016)	25	-1.00	[-1.47; -0.53]
Random effects model		**-1.11**	**[-1.22; -0.99]**

Heterogeneity: I^2 = 83%, τ^2 = 0.0570, p < 0.01

Standardised Mean Difference: -2 -1.5 -1 -0.5 0 0.5

Comparable efficacy to injectable regimens

Comparison with regimens including GLP-1RA

Study	N	SMD	95% CI
Lee, E. Y.(2023)	76	-0.26	[-0.50; -0.02]
Kim, M. (2023)	50	0.00	[-0.40; 0.40]
Random effects model		**-0.18**	**[-0.41; 0.05]**

Heterogeneity: I^2 = 16%, τ^2 = 0.0055, p < 0.27

Standardised Mean Difference: -2 -1.5 -1 -0.5 0 0.5

Comparison with regimens including basal insulin

Study	N	SMD	95% CI
Ku, E. J. (2023)	154	-0.42	[-0.65; -0.20]
Ku, E. J. (2019)	142	-0.26	[-0.50; -0.02]
Random effects model		**-0.35**	**[-0.51; -0.018]**

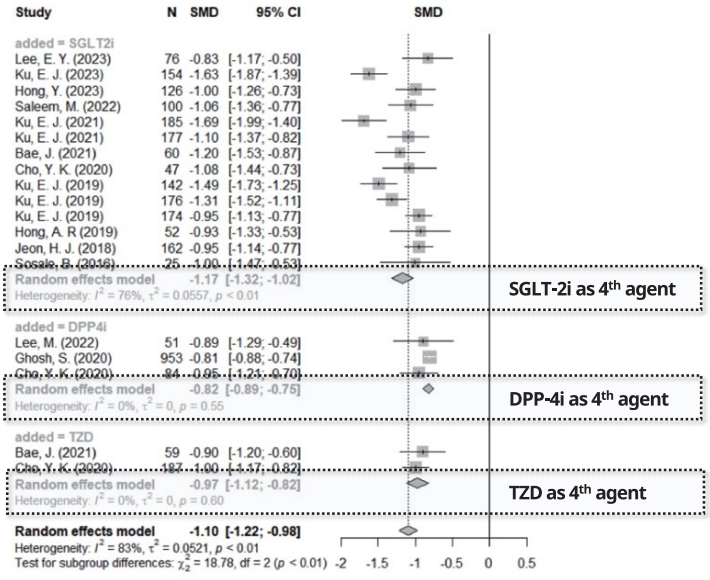
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.34

Standardised Mean Difference: -2 -1.5 -1 -0.5 0 0.5

Endocrinology and Metabolism 2025;40(2):258-267

Evidence on Oral Quadruple Combination therapy

Systematic Review and Meta-analysis (2025)



Study	N	SMD	95% CI
added = SGLT2i			
Lee, E. Y. (2023)	76	-0.83	[-1.17; -0.50]
Ku, E. J. (2023)	154	-1.63	[-1.87; -1.39]
Hong, Y. (2023)	126	-1.00	[-1.26; -0.73]
Saleem, M. (2022)	100	-1.06	[-1.36; -0.77]
Ku, E. J. (2021)	185	-1.69	[-1.99; -1.40]
Ku, E. J. (2021)	177	-1.10	[-1.37; -0.82]
Bae, J. (2021)	60	-1.20	[-1.53; -0.87]
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Ku, E. J. (2019)	142	-1.49	[-1.73; -1.25]
Ku, E. J. (2019)	176	-1.31	[-1.52; -1.11]
Ku, E. J. (2019)	174	-0.95	[-1.13; -0.77]
Hong, A. R (2019)	52	-0.93	[-1.33; -0.53]
Jeon, H. J. (2018)	162	-0.95	[-1.14; -0.77]
Sosale, B. (2016)	25	-1.00	[-1.47; -0.53]
Random effects model		-1.17	[-1.32; -1.02]
Heterogeneity: I^2 = 76%, τ^2 = 0.0557, p < 0.01			
added = DPP4i			
Lee, M. (2022)	51	-0.89	[-1.29; -0.49]
Ghosh, S. (2020)	953	-0.81	[-0.88; -0.74]
Cho, Y. K. (2020)	84	-0.95	[-1.21; -0.70]
Random effects model		-0.82	[-0.89; -0.75]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.55			
added = TZD			
Bae, J. (2021)	59	-0.90	[-1.20; -0.60]
Cho, Y. K. (2020)	187	-1.00	[-1.17; -0.82]
Random effects model		-0.97	[-1.12; -0.82]
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.60			
Random effects model		**-1.10**	**[-1.22; -0.98]**

Heterogeneity: I^2 = 83%, τ^2 = 0.0521, p < 0.01
Test for subgroup differences: χ^2_2 = 18.78, df = 2 (p < 0.01)

SMD: -2 -1.5 -1 -0.5 0 0.5

SGLT-2i as 4th agent

DPP-4i as 4th agent

TZD as 4th agent

SGLT2 inhibitors showed the most potent effect when added as the fourth OAD, followed by TZD and DPP4 inhibitors (p<0.01) .

Endocrinology and Metabolism 2025;40(2):258-267

CONTENTS

Tips for prescribing oral antidiabetic agents

경청해 주셔서 감사합니다

01
Session

당뇨병 치료의 핵심

다양한 당뇨병 주사 치료제: 이것만은 기억하자!

건국대학교병원 내분비내과 **최종한**

환자와 의사 모두에게 당뇨병 주사제 치료는 어려운 숙제와 같다. 더군다나 최근에는 다양한 계열의 새로운 당뇨병 경구약물이 사용 가능해지면서 주사제 사용의 필요성이 더욱 감소하고 있다. 그러나 당뇨병 유병률의 증가와 고령화로 인하여 당뇨병 주사제 치료는 당뇨병 환자에게 다양한 상황에서 평생 한 번은 필요한 치료인 경우가 더 많아지고 있다. 하지만 많은 의사와 환자에게 당뇨병 주사제는 여전히 무섭고 어렵고 '말기 당뇨병 환자'에게나 사용하는 수단이라는 인식이 있다. 적절한 시점에 주사제를 도입하고 효과적으로 활용하는 것은 단순한 혈당 조절이 아니라 고혈당으로 인한 베타세포 손상을 막아 많은 환자에서 다시 경구약으로 변경하는 탈강화(deintensification) 치료를 가능하게 할 수 있다. 뿐만 아니라 심혈관 및 신장보호, 체중관리 측면에서도 매우 중요한 전략이다. 이번 강의에서는 GLP-1수용체작용제와 인슐린의 당뇨병 주사제를 임상현장에서 활용할 때 꼭 기억해야 할 다음과 같은 주제들에 대해 다루려고 한다.

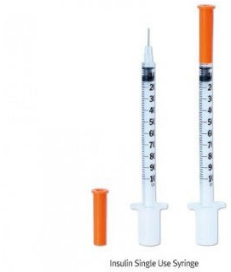
- 당뇨병 주사치료제의 적절한 시작시점
- 당뇨병 주사치료제 사용의 장애물 제거하기
- GLP-1수용체작용제의 장점과 활용하기
- 기저인슐린 치료 시작하기
- 복잡한 다회인슐린요법 맛보기

다양한 당뇨병 주사 치료제: 이것만은 기억하자!

건국대학교병원 내분비내과
최 종 한

Contents

당뇨병 주사 치료제 = 인슐린



당뇨병 주사 치료제 = 인슐린 + GLP-1RA

인슐린펌프: 센서강화인슐린펌프 (SAP), 자동인슐린주입(AID)

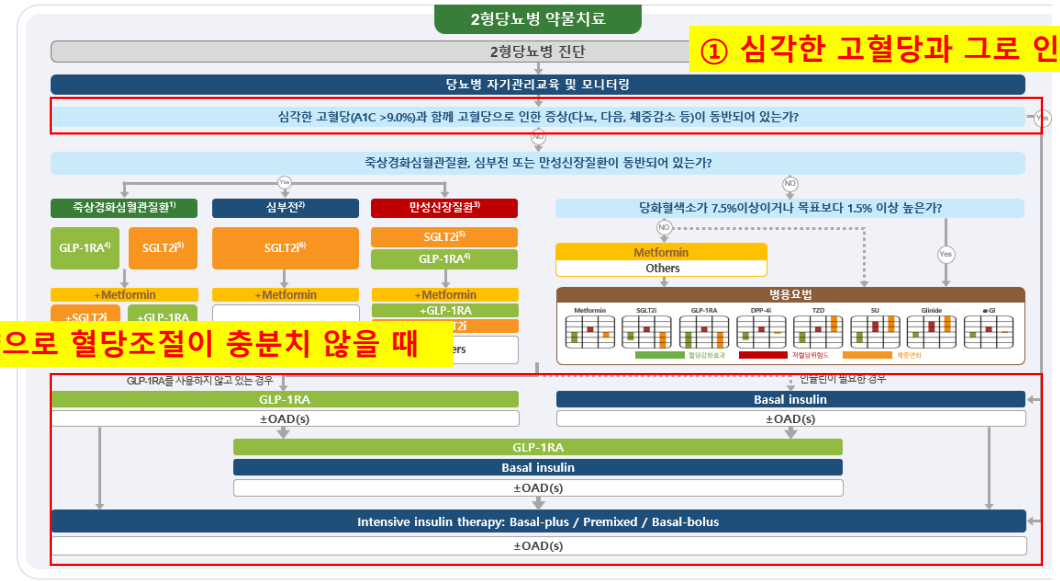
GLP-1RA

인슐린

인슐린+GLP-1RA
→ 고정비율복합제 (Fixed-ratio combination, FRC)

2023
당뇨병 진료지침 제8판
Clinical Practice Guidelines for Diabetes (KDA)

당뇨병 주사 치료제는 언제 시작하나요?

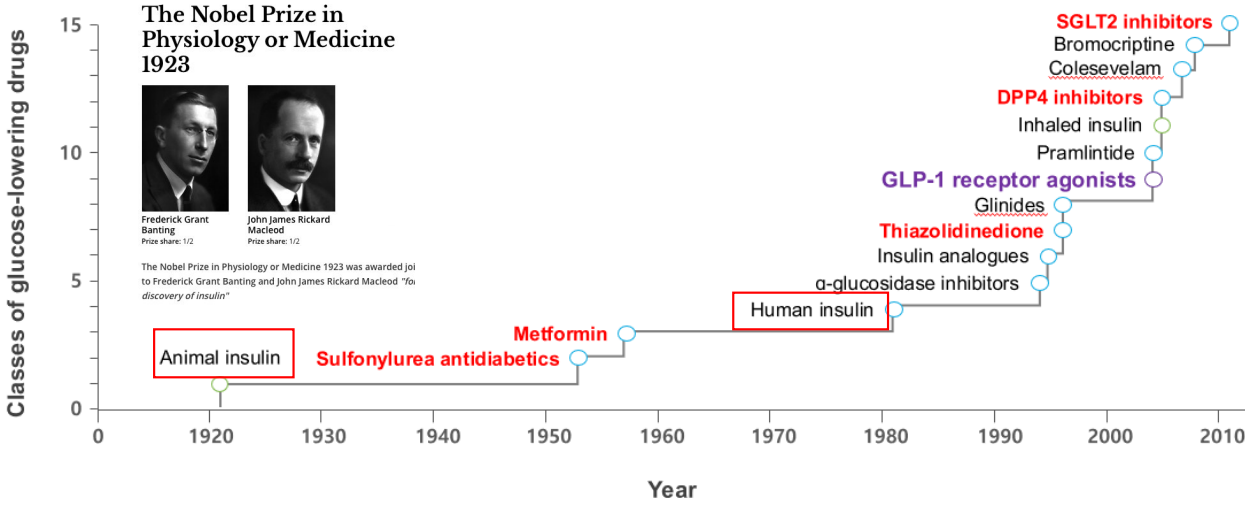


① 심각한 고혈당과 그로 인한 증상

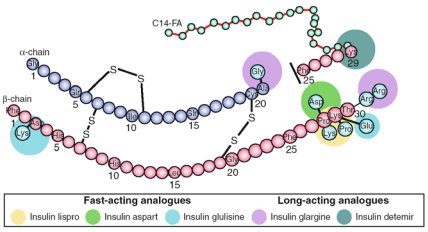
② 경구약으로 혈당조절이 충분치 않을 때

인슐린, 가장 오래된 치료제지만 여전히 당뇨병 치료제의 끝판왕?

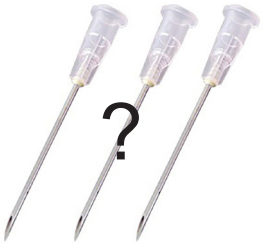
History of Diabetes Medications



인슐린 사용의 어려움, 주사제라는 장벽?



흡입제



주1회 기저인슐린

주사제라서 두렵다면 그러면 삭센다나 위고비 열풍은?

Severe Therapeutic inertia in Use of Insulin in Korea

	People with type 2 diabetes*	Years	Mean HbA_{1c} (95% centiles)	Percentage of people treated with insulin, among those diagnosed	Mean bodyweight, kg (95% centiles)
US National Health and Nutrition Examination Survey	1441	2009–14	7·4% (5·2–12·2)	22·2%	89·5 (53·7–148·2)
US National Institutes of Health Global Health Centers of Excellence surveys from South Africa	1842	2012	9·1% (5·4–14·6)	NA	83·0 (51·0–125·0)
US National Institutes of Health Global Health Centers of Excellence surveys from India	1605	2015	8·7% (5·5–13·4)	NA	67·9 (43·0–98·2)
South Africa National Health and Nutrition Examination Survey	747	2012	7·7% (5·4–12·8)	4·4%	78·0 (44·0–116·6)
UK National Health Service National Diabetes Audit	16 585	2016–17	7·3% (5·1–12·1)	12·5%	80·3 (48·1–133·0)
Indian Jaipur Diabetes Registry	8699	2014	9·0% (6·3–14·8)	9·1%	60·4 (30·6–101·2)
Swedish National Diabetes Register	17 827	2016	8·4% (6·1–10·1)	11·7%	75·6 (48·5–102·7)
Danish Adult Diabetes Registry	11 205	2014–15	7·7% (5·4–12·7)	15·8%	70·9 (33·9–123·5)
Turkish Nationwide survey of Glycemic and Other Metabolic Parameters of Patients with Diabetes Mellitus	4672	2017	7·5% (5·3–12·4)	9·6%	84·7 (52·2–117·2)
China Health and Nutrition Study	1422	1999–2015	7·8% (5·2–12·7)	18·3%	65·5 (45·2–90·0)
DiabCare study of the Philippines	770	2008	8·0% (5·6–13·2)	25·0%	58·5 (36·2–85·9)
Japan National Health and Nutrition Survey	1434	2016	7·2% (5·0–11·8)	7·0%	59·5 (32·2–90·4)
Korea National Health and Nutrition Examination Survey	1341	2010–12	8·2% (5·7–13·5)	3·0%	66·0 (38·5–93·7)
Joint Asia Diabetes Evaluation Registry	28 111	2007–12	7·7% (5·4–12·7)	21·0%	76·8 (58·4–90·0)

References for each cohort dataset are provided in the appendix. NA=not available. *Previous diagnosis, treatment, or laboratory results.

Use of insulin in Korea: 3%

Lancet Diabetes Endocrinol 2019;7:25-33

Clinical study of therapeutic inertia in Korea

Delay of insulin initiation in patients with type 2 diabetes mellitus inadequately controlled with oral hypoglycemic agents (analysis of patient- and physician-related factors): A prospective observational DIPP-FACTOR study in Korea

Sin Gon Kim[1], Nam Hoon Kim[1], Bon Jeong Ku[2], Ho Sang Shon[3], Doo Man Kim[4], Tae Sun Park[5], Yong-Seong Kim[6], In Joo Kim[7], Dong Seop Choi[1]*

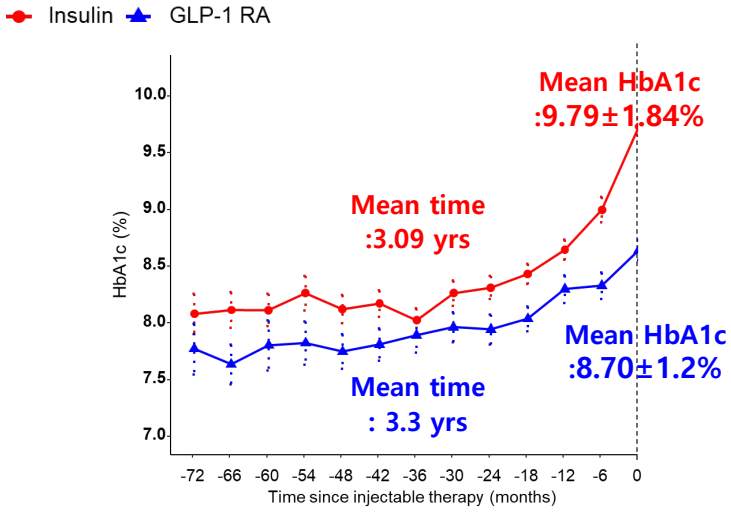
Table 1 | Baseline and demographic characteristics

	Insulin-initiated group (n = 386)
Patient characteristics	
Age (years)	56.0 ± 12.0
BMI (kg/m^2)	25.3 ± 4.3
HbA1c (%)	9.7 ± 1.5
FPG (mg/dL)	203.9 ± 75.8
Duration of diabetes (years)	8.5 ± 6.9
Microvascular complications, n (%)	144 (37.3)
Macrovascular complications, n (%)	73 (18.9)

- A prospective, observational disease registry study (69 centers in Korea, **2009-2012**)
- To assess the time to **initiation of insulin therapy**
- investigate both patient- and physician-related factors associated with delaying insulin therapy in Korean patients with type 2 diabetes
- Type 2 diabetes patients (n=1959) who had received two or more OADs within the past 5 years, had an A1C ≥8%

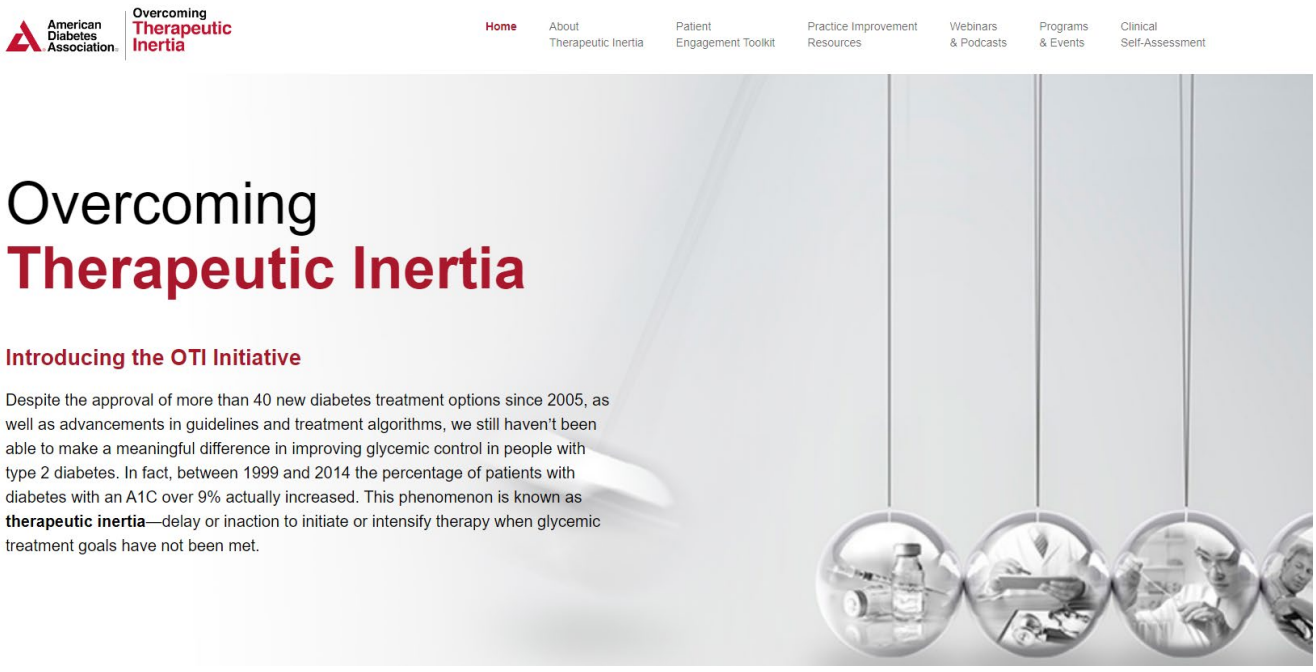
J Diabetes Investig 2017; 8: 346–353

Clinical study of therapeutic inertia in Korea



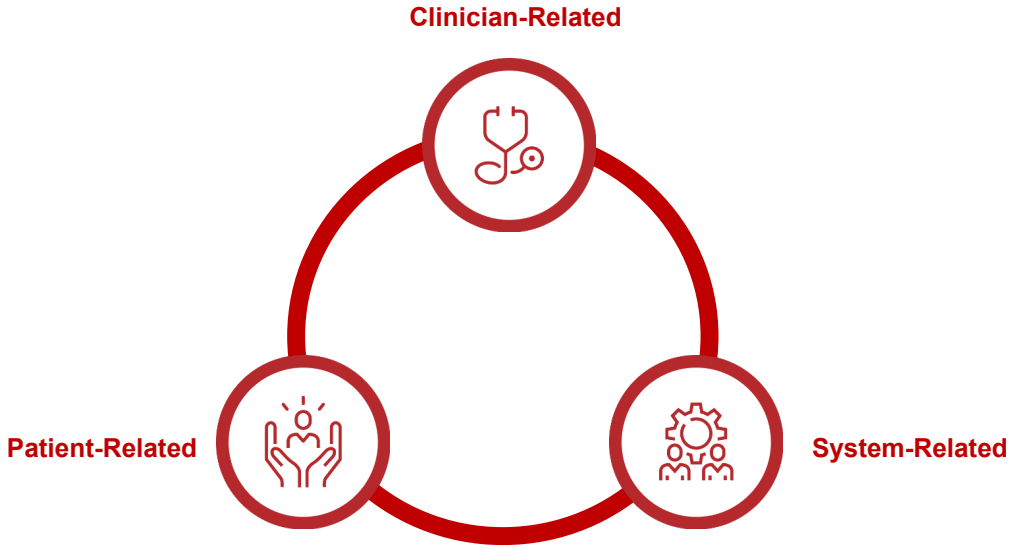
- A retrospective, observational study (10 centers in Korea, **2015-2021**)
- To assess the time to **initiation of injectable therapy**

Endocrinol Metab 2025 Forthcoming. Posted online 2025



https://www.therapeuticinertia.diabetes.org/

Therapeutic inertia happens in all aspects of diabetes treatment



인슐린 치료를 꺼리는 이유

- **환자요인**
  - 주사의 통증, 두려움
  - 번거로움, 주변의 시선
  - **당뇨병의 마지막 단계라는 인식**
  - 저혈당 위험 등의 부작용 우려

- **의사 및 의료체계 관련 요인**
  - 약물에 대한 이해부족: **보관 및 주사법, 용량 조절 등**
  - 교육 시간 및 수가 부족: **저혈당을 포함한 심한 부작용 발생 시 소송 등의 우려**

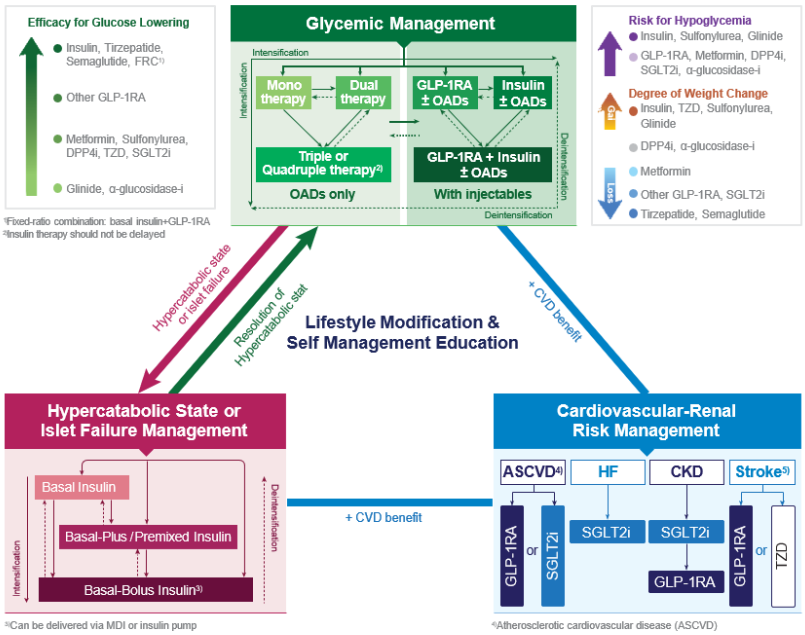
만성질환 당뇨병, 벼랑 끝에서 평생 주사를 맞아야 한다는 두려움

2025 당뇨병진료지침 제9판, 대한당뇨병학회

Pharmacological Management of Type 2 Diabetes Mellitus

당뇨병 진료지침
Clinical Practice Guidelines for Diabetes
2025 제9판

Hypercatabolic State or Islet Failure → Insulin Management

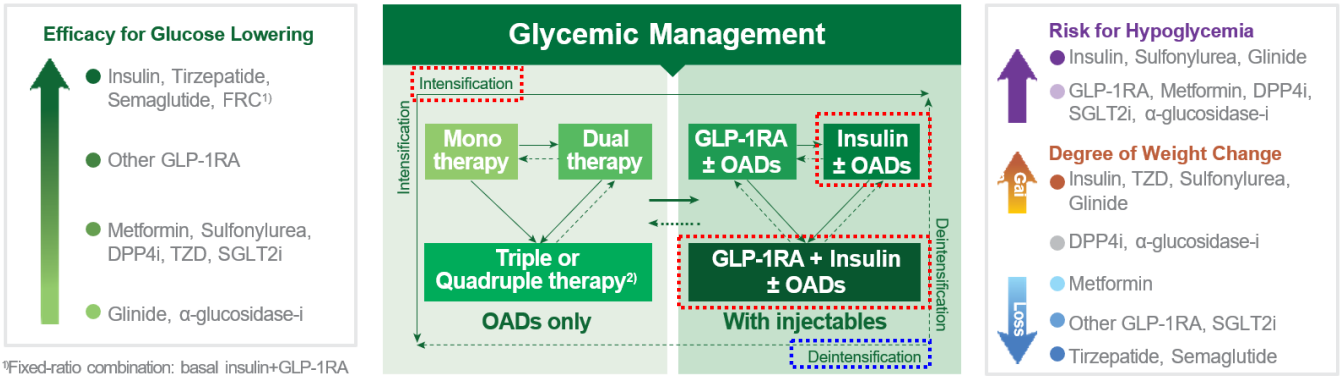


1)Fixed-ratio combination: basal insulin+GLP-1RA
2)Insulin therapy should not be delayed
3)Can be delivered via MDI or insulin pump
4)Atherosclerotic cardiovascular disease (ASCVD)
5)Individuals with ischemic stroke, including transient ischemic attack, but excluding hemorrhagic stroke

대한당뇨병학회, 당뇨병진료지침 제9판, 2025, 공개전 미확정 자료입니다. 추후 대한당뇨병학회 공식홈페이지를 통해 확정된 자료를 확인하시기 바랍니다.

Insulin Use in Glycemic Management

혈당조절 목표달성을 위해 적절한 시기에 언제든 인슐린 치료를 시작하는 것이 필요



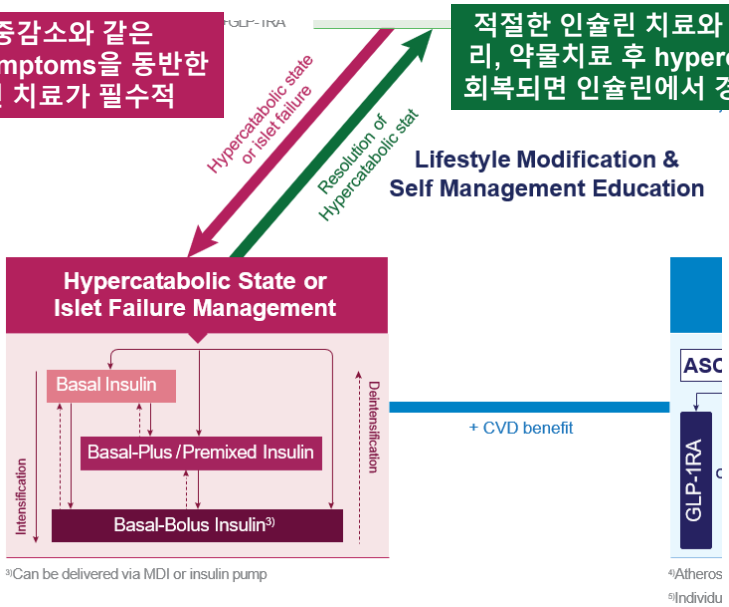
1)Fixed-ratio combination: basal insulin+GLP-1RA
2)Insulin therapy should not be delayed

적절한 생활관리와 약물치료를 통해 인슐린 치료를 중단할 수도 있음

Insulin Use in Hypercatabolic State

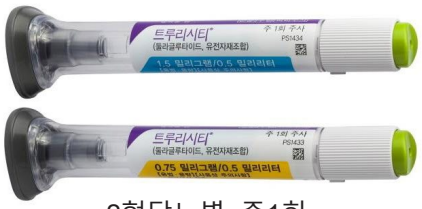
다음, 다뇨, 체중감소와 같은 hypercatabolic symptoms을 동반한 경우 빠른 인슐린 치료가 필수적

적절한 인슐린 치료와 생활습관 및 자기관리, 약물치료 후 hypercatabolic state에서 회복되면 인슐린에서 경구약으로 변경 가능



3)Can be delivered via MDI or insulin pump
4)Atheros
5)Individu

GLP-1수용체작용제 또는 유사약물



2형당뇨병, 주1회

비만, 일1회

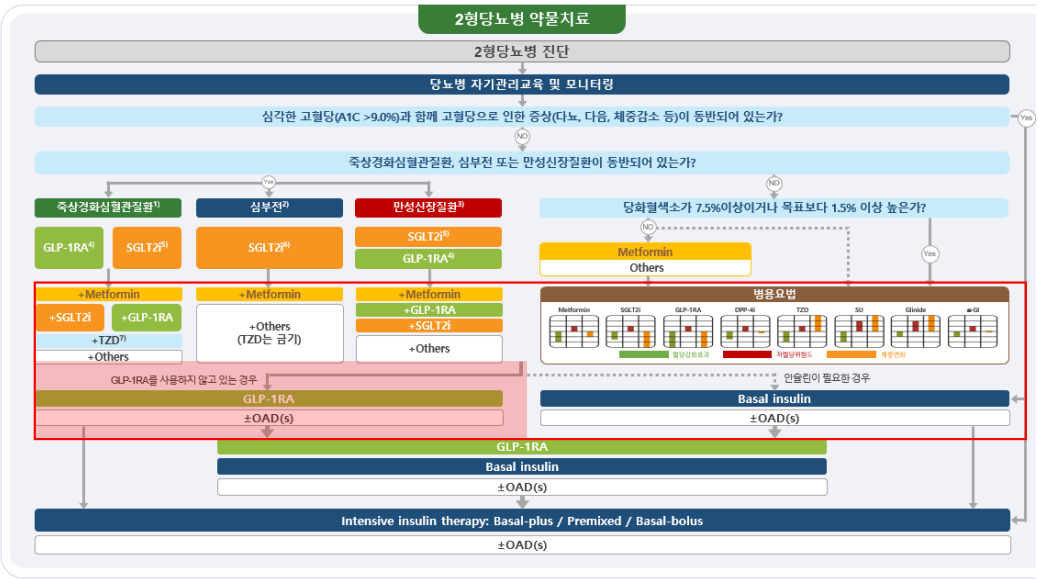
비만, 주1회

2026년 출시예정 (GLP-1/GIP 이중작용제)
2형당뇨병, 비만, 주1회

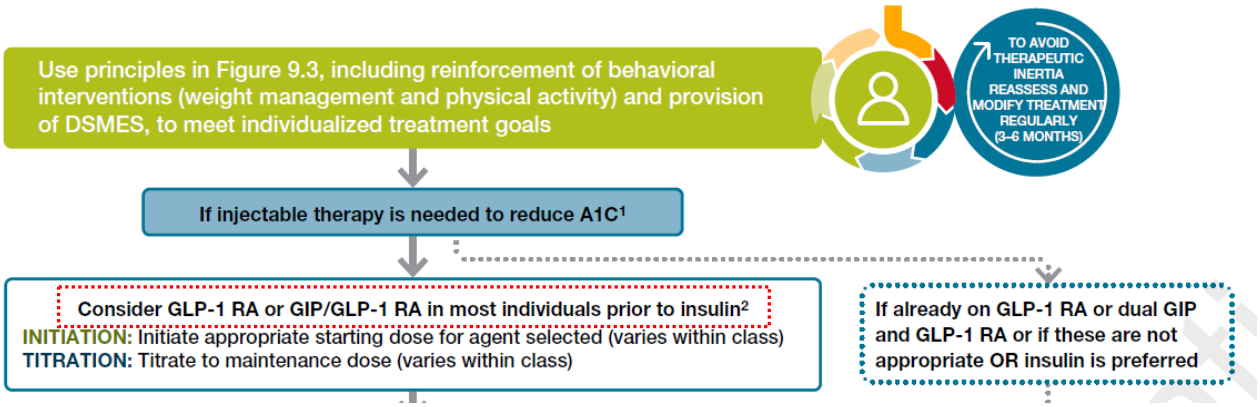
2023
당뇨병 진료지침 제8판
Clinical Practice Guidelines for Diabetes (KDA)

경구약으로 혈당조절이 충분하지 않을 때

주로 GLP-1RA을 인슐린보다 먼저

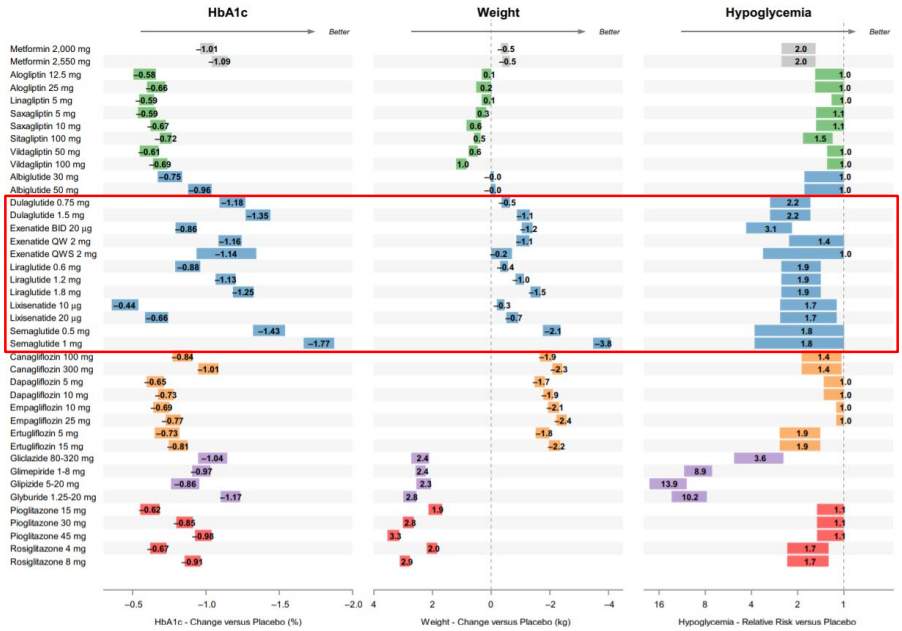


GLP-1RA, consider 1st choice of injectable therapy prior to insulin



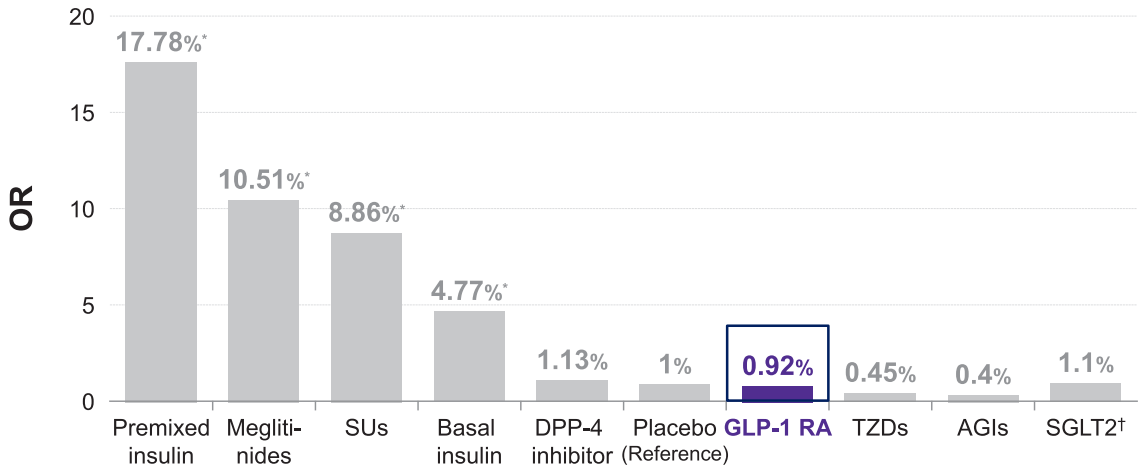
Diabetes Care 2024;48 (Supplement_1)

GLP-1RA의 장점(1): 강력한 혈당강하효과



Clin Pharm Ther 2019; 105 (5)

GLP-1RA의 장점(2): 매우 낮은 저혈당 위험

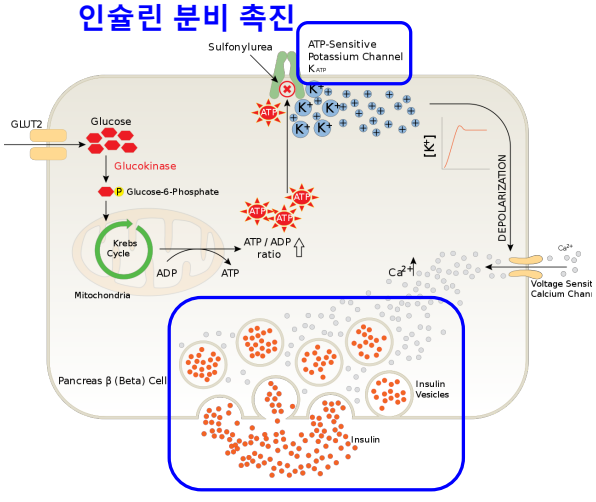


Liu SC, et al. Diabetes Obes Metab. 2012;14:810-820; Fujita Y, et al. J Diabetes Investig. 2014;5:2650275.

23

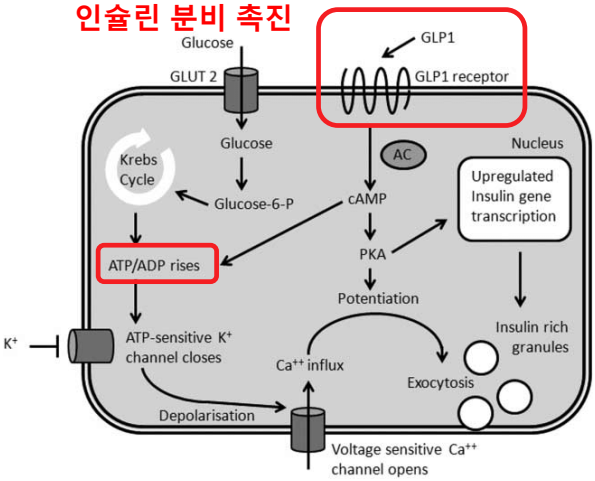
GLP-1RA의 장점(2): 매우 낮은 저혈당 위험

혈당과 무관하게 인슐린 분비 촉진



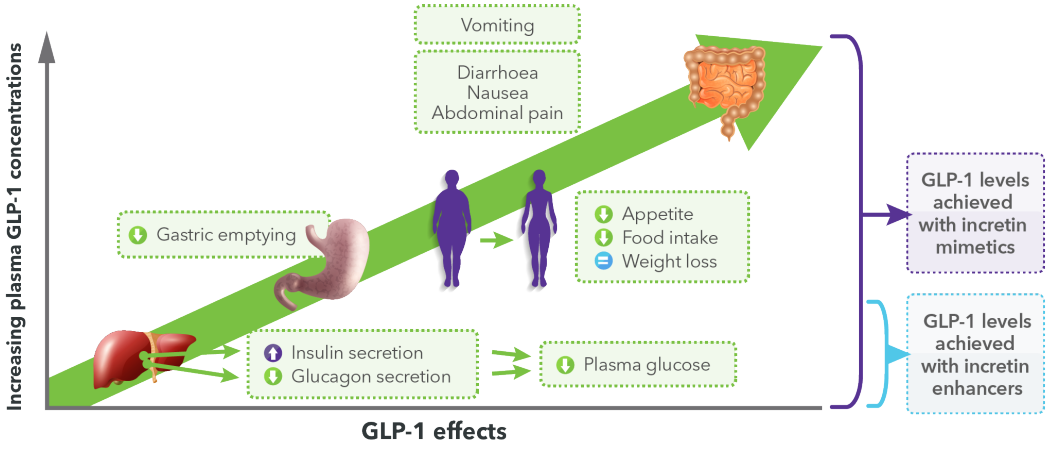
Sulfonylurea / Glinide

혈당에 의존적으로 인슐린 분비 촉진



GLP-1RA

GLP-1RA 장점(3): 용량-의존적 체중 감소 효과



GLP-1유사체 (고용량, 비만)

GLP-1유사체 (저용량, 당뇨병)

DPP-4억제제 (당뇨병)

Madsbad, Lancet 2009; 373: 438-439

GLP-1RA 장점(4): 심혈관-신장이득

	REWIND	LEADER	SUSTAIN-6
Patients, n	9,901	9,340	3,297
Drug	Dulaglutide	Liraglutide	Semaglutide SC
Dose	1.5 mg/week	1.8 mg or max tolerated dose /day	0.5 mg or 1 mg/week
Duration of follow up (years)	5.4	3.8	2.1
Baseline A1C (%)	7.2	8.7	8.7
Duration of diabetes (years)	9.5	12.8	13.9
Baseline statin (%)	66.0	72.0	73.0
Baseline ASCVD/HF (%)	31.0	81.0	72.0
Baseline HF (%)	9.0	18.0	24.0
Primary outcome	0.88 (0.79–0.99)	0.87 (0.78–0.97)	0.74 (0.58–0.95)
CV death	0.91 (0.78–1.06)	0.78 (0.66–0.93)	0.98 (0.65–1.48)
All-cause mortality	0.90 (0.80–1.01)	0.85 (0.74–0.97)	1.05 (0.74–1.50)
HF hospitalization)	0.93 (0.77–1.12)	0.87 (0.73–1.05)	0.86 (0.48–1.55)
Renal composite outcome	0.85 (0.77–0.93)	0.78 (0.67–0.92)	0.64 (0.46–0.88)

2025 당뇨병진료지침 9판, 대한당뇨병학회

GLP-1RA 장점 및 단점

장점	단점

▪ 매우 우수한 혈당강하효과 (1.0~2.5% 감소)
▪ 매우 낮은 저혈당 위험
▪ 우수한 체중감량 효과
▪ 심혈관(죽상경화심혈관질환, 뇌졸중) 위험 및 신장질환 위험 감소, 지방간위험 감소 효과
▪ 다양한 용법: **주1회 주사**, 월 1회 사용 제제도 개발 중
▪ **인슐린 치료 전 주사제 치료의 심리적 장벽을 낮춰줌**
	▪ **고가의 비용**
	  ▪ 당뇨병치료제는 급여가능: 약제 조합에는 제한
	  ▪ 비만치료제는 비급여, 실비보험도 불가
	▪ **오심, 구토, 설사, 변비 등의 위장관 부작용**
	▪ **췌장염**, 담석 및 담낭-담도염 위험 증가 가능성
	▪ **갑상선 수질암**, MEN2 병력 또는 가족력 있는 경우 금기

증례1

- 56세 여자, 158 cm, 71 kg, BMI 28.4 kg/m^2
- 2형당뇨병, 2009년부터 약물치료 시작
- Mild NPDR, mild DSPN, U-ACR 413 mg/g, eGFR 64 ml/min/1.73m^2
- Metformin 1700mg, sitagliptin 100mg, empagliflozin 25mg
- HbA1c 8.1%, c-peptide 4.21 ng/ml

➔ **GLP-1RA vs 기저인슐린 vs 경구 4제 ?**

증례1

- Metformin 1700mg, sitagliptin 100mg, empagliflozin 25mg
- HbA1c 8.1%, c-peptide 4.21 ng/ml

➔ Metformin 1700mg, **dulaglutide 0.75 ➔ 1.5mg**, glimepiride 2mg

HbA1c 6.4%, **간헐적인 저혈당, 체중 증가 (+4kg)**

➔ Metformin 1700mg, dulaglutide 1.5mg, **empagliflozin 10mg (100:100)**

HbA1c 6.1%, **저혈당 없음, 체중 감소 (-5kg)**

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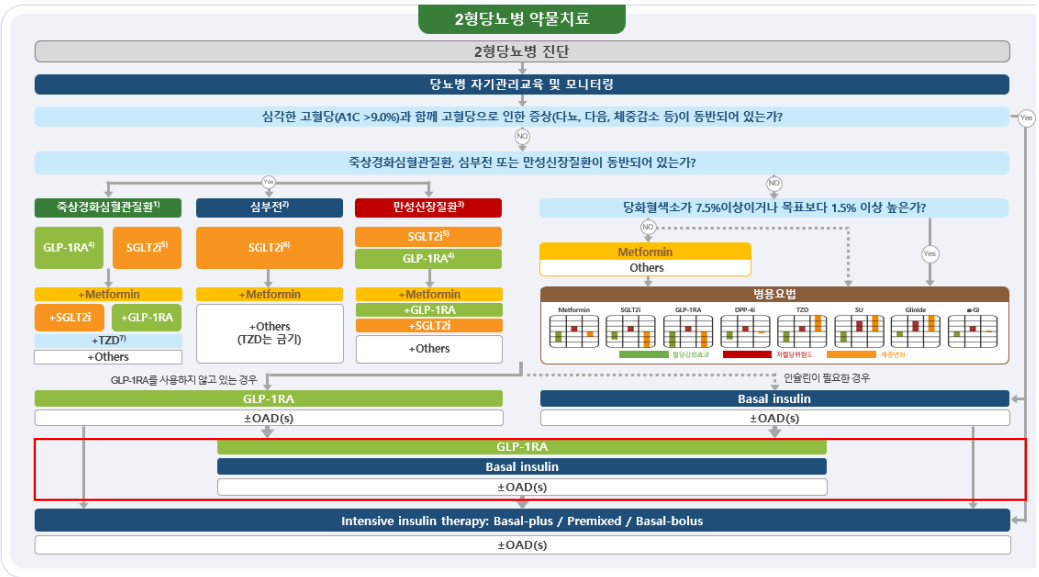
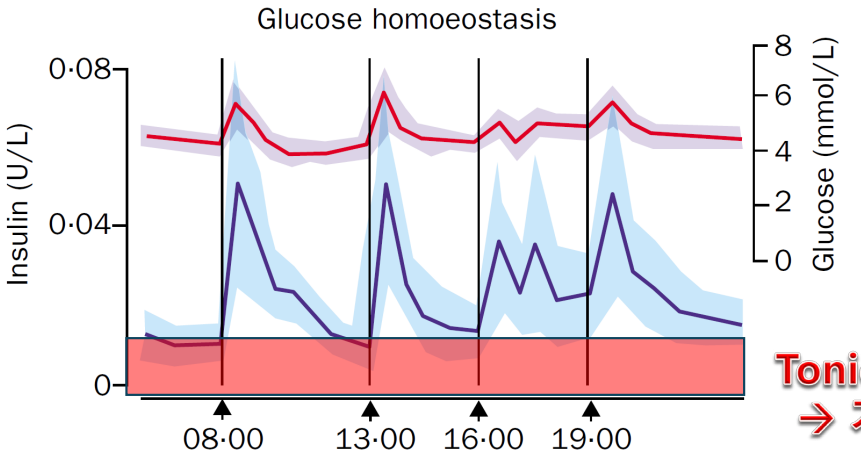
GLP-1RA 또는 경구약을 사용하다가

기저인슐린 사용하기

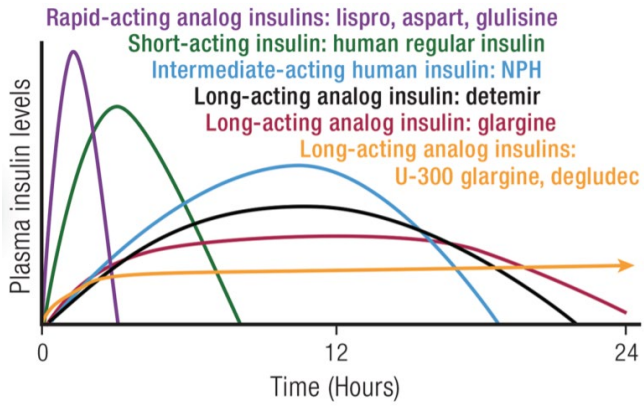


생리적 인슐린 분비와 기저인슐린



Tonic secretion
→ 기저인슐린

기저인슐린 종류



기저인슐린

Intermediate-acting insulin
- NPH (Humulin N®)

Long-acting insulin
- Determir (Levemir®)
- Glargine U-100 (Lantus®)

Ultralong-acting insulin
- Glargine U-300 (Toujeo®)
- Degludec (Tresiba®)

기저인슐린의 시작과 용량조절

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시작 용량
10 단위/day 또는 0.1– 0.2 단위/kg/day
▶고혈당 정도를 고려하여 결정

용량 조절
10 –15% 또는 2–4 단위를 주 1–2회 조절
▶목표 공복혈당을 기준으로 증감

목표혈당은 대개 아침공복혈당,
또는 최장시간 공복혈당

저혈당 발생
우선 원인을 찾는 것이 중요
▶4 단위 또는 10 –20% 감량

- 주사시간은 기저인슐린 종류에 따라 조금씩 차이가 있으나 하루 중 환자가 가장 일정하게 잘 맞을 수 있는 시간과 인슐린 종류를 선택
- 시작 용량, 용량 증-감량 간격 등은 정답이 없음
- 기존 약물 중 일부나 전부를 빼거나, 혈당이 너무 높은 경우에는 더 높은 용량으로 시작할 수 있음
- 환자의 나이, 판단능력, 저혈당 감수성, 보호자의 조력 가능성 등을 다양하게 고려해서 판단해야

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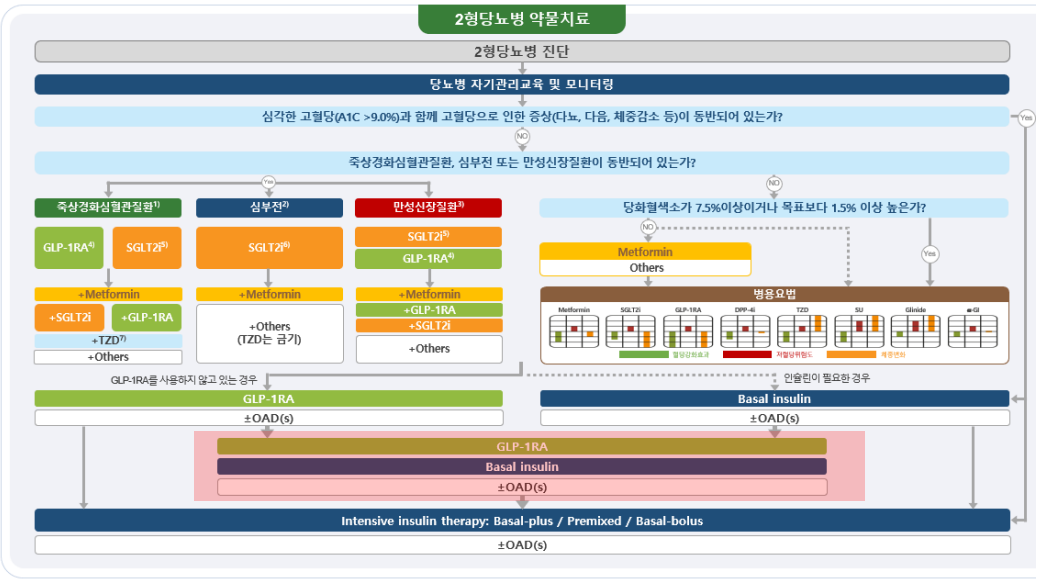
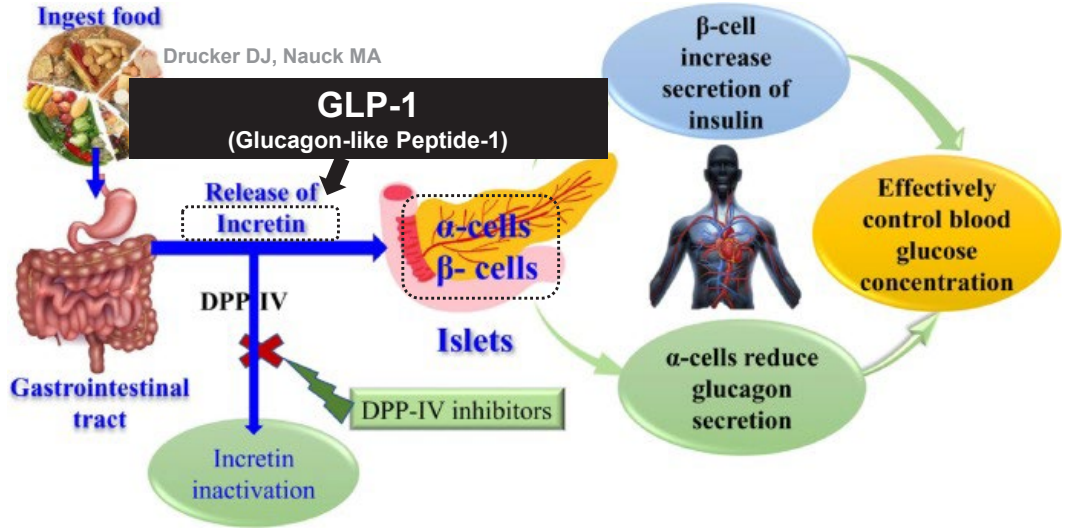
인슐린 다회요법이 걱정된다면, 그 전에?

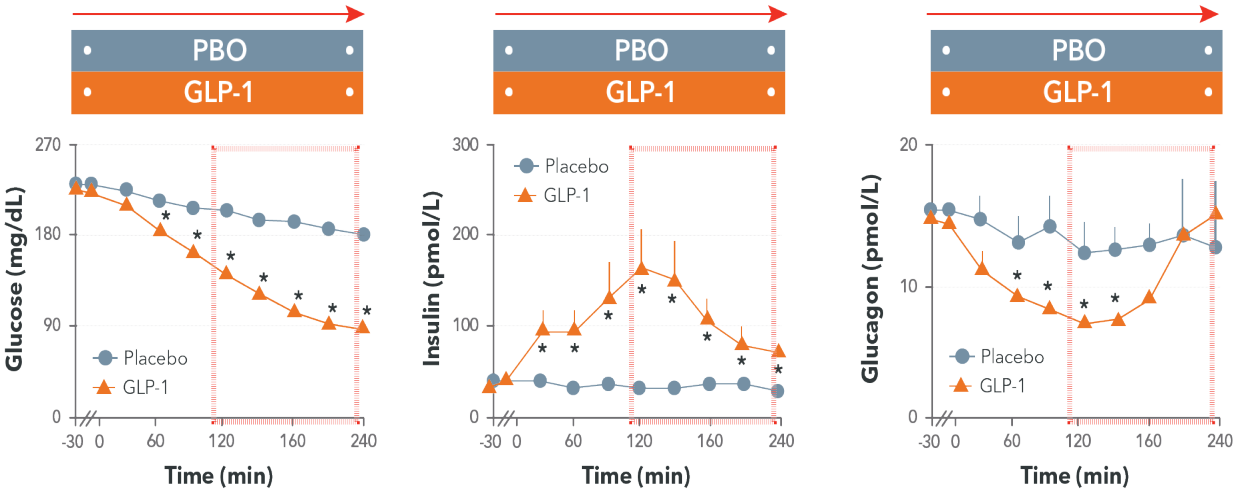


GLP-1RA: Strong Incretin Hormone



Kublaoui et al. Pediat Endocrol 4th Ed 2014

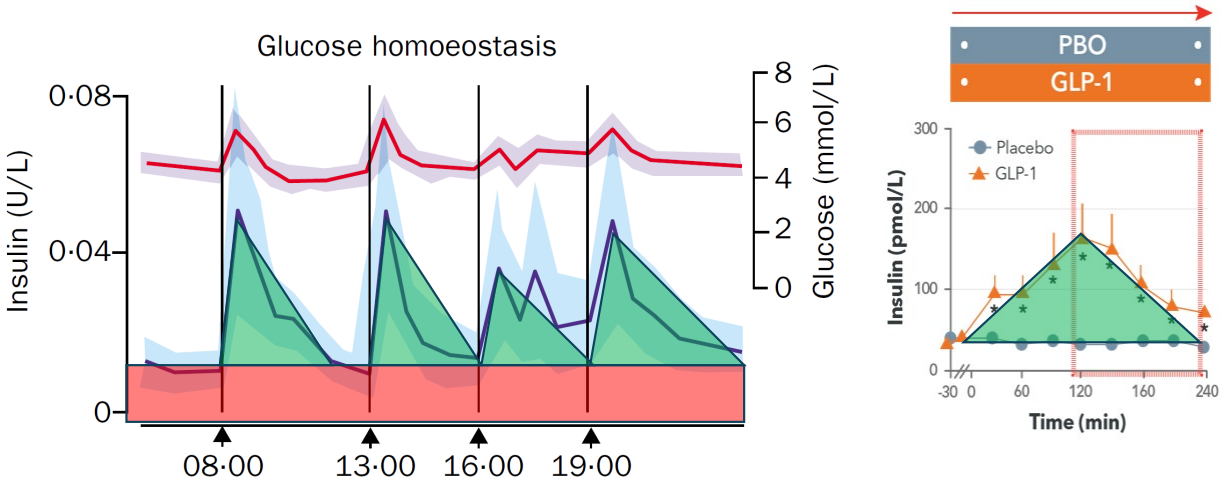
GLP-1 Effects Are Glucose-Dependent in Type 2 Diabetes



N = 10; Mean (SE); *P<0.05

Nauck MA, et al. Diabetologia 1993;36:741-744

GLP-1RA의 식후인슐린 분비효과?



Fixed ratio combination of basal insulin with GLP-1RA

이름	상품명	사진 및 용량/펜	가격(원)/펜	용법
Insulin Glargine /Lixisenatide	솔리쿠아 (Soliqua) Glargine 100 IU/mL /Lixisenatide 50 ug/mL	 300 IU/150 µg/3 mL	39,468	식사 전 1시간 이내에 투여 1일 1회
	솔리쿠아 (Soliqua) Glargine 100 IU/mL /Lixisenatide 33 ug/mL	 300 IU/100 µg/3 mL	39,498	
Insulin degludec /liraglutide	줄토피 플렉스터치주 (Xultophy FlexTouch)	 300 IU/10.8 mg/3 mL	39,487	하루 중 어느 때나 투여 (가급적이면 매일 같은 시간) 1일 1회

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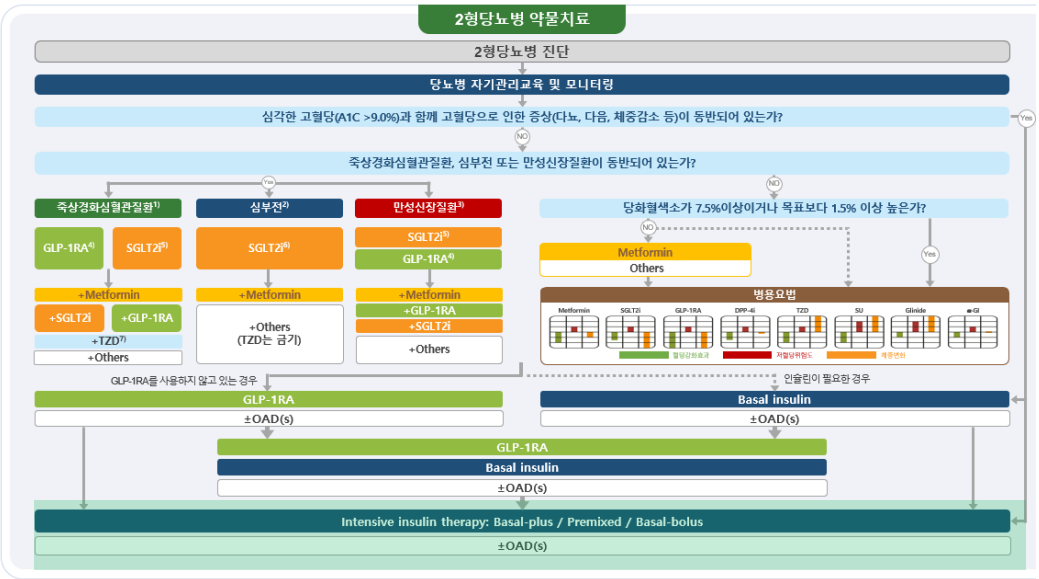
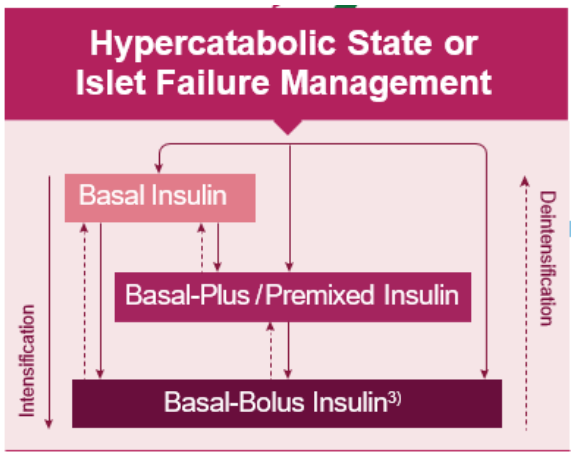
복잡한 인슐린 용법 ➔ 식전인슐린 사용하기



Insulin Use in Islet Failure



3)Can be delivered via MDI or insulin pump

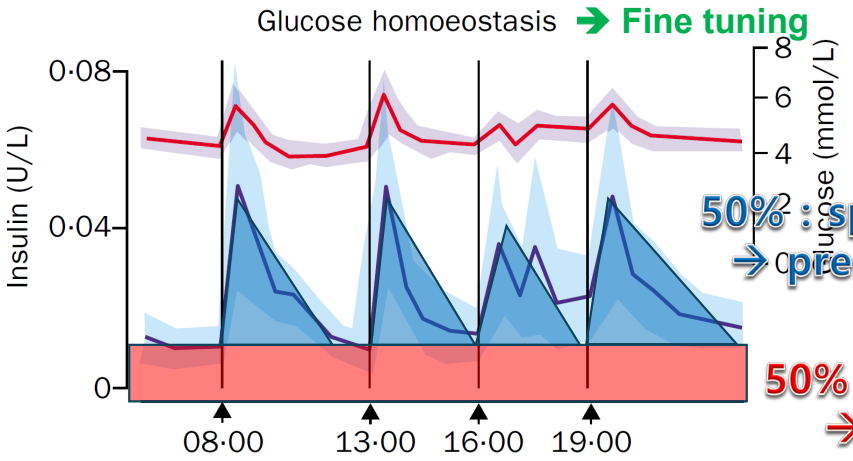
췌도부전여부 또는 정도 평가
➔ 혈당, insulin, c-peptide 등 참고(절대적인 것은 아님), 연속혈당측정기를 활용해볼 수도

식사, 운동, 혈당측정(연속혈당측정 포함), 인슐린 용량 및 주사 시간 등에 대한 전문적인 교육이 필요

전문적인 교육이 가능한 센터로 전원도 고려

대한당뇨병학회, 당뇨병진료지침 제9판, 2025, 공개전 미확정 자료입니다. 추후 대한당뇨병학회 공식홈페이지를 통해 확정된 자료를 확인하시기 바랍니다.

생리적 인슐린 분비와 이상적인 인슐린 용법

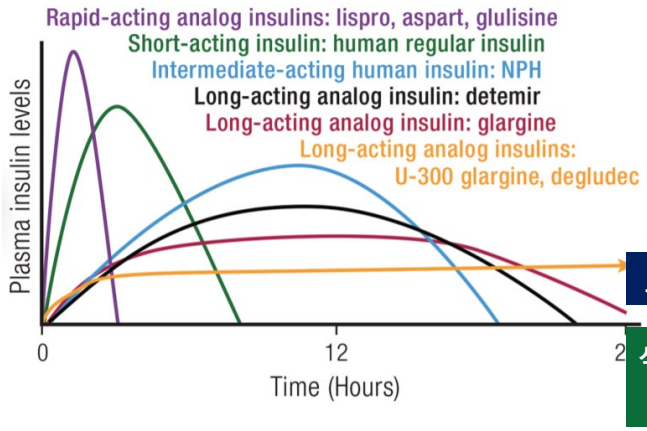


50% : spike
→ premeal (prandial) insulin

50% : tonic secretion
→ basal insulin

→ Multiple daily injection (MDI) = multiple subcutaneous insulin injection (MSII)

식전인슐린 종류와 조절하기



Premeal (prandial) insulin

Rapid-acting insulin
- Lispro (Humalog®, Lyumjev®))
- Aspart (Novorapid®, Fiasp®)
- Glulisine (Apidra®)

Short-acting insulin
- Human regular insulin (Humulin R®, RI)

보통 매 식전 30분~식사직전, 2~4단위 투여로 시작

식사패턴, 운동시간, 혈당조절 목표 등 다양한 요인에 따라 인슐린 주사용량, 시간을 개별화

혼합형 인슐린

상품명	중간형	속효성
Humalog mix 25 kwik pen®	75% NPL	25% Lispro
Humalog mix 50 kwik pen®	50% NPL	50% Lispro
Humulin mix 70/30 kwik pen®	70% NPH	30% RI
Novomix 30 flex pen®	70% NPA	30% Aspart
Novomix 50 flex pen®	50% NPA	50% Aspart
Ryzodeg flex pen®	70% Degludec	30% Aspart

- **50:50 mix insulin**
  - ✓ 아침 : 점심 : 저녁 식전 = 1 : 1 : 1
- **70:30 or 75:25 mix insulin**
  - ✓ 아침 식전 : 저녁 식전 = 2 : 1

인슐린 치료 시 연속혈당측정기 활용하기

- **CONTINUOUS GLUCOSE MONITORS**

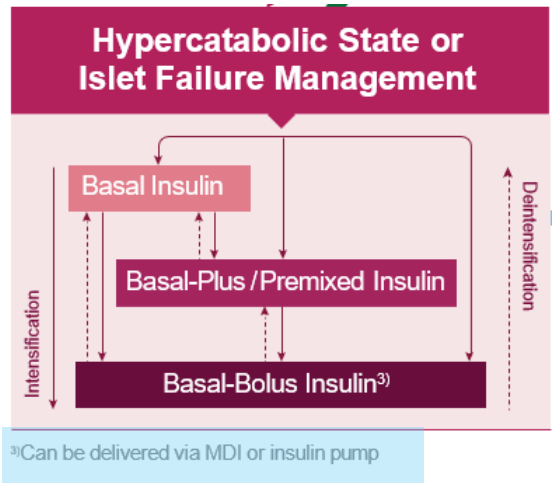
2024 ADA	2025 ADA
7.14 Real-time CGM (rtCGM) **A** or intermittently scanned CGM (isCGM) **B** should be offered for diabetes management in **adults** with diabetes on **multiple daily injections (MDI) or CSII** who are capable of using the devices safely (either by themselves or with a caregiver). The choice of device should be made based on the individual's circumstances, preferences, and needs.	**7.15** Recommend real-time CGM (rtCGM) **A** or intermittently scanned CGM (isCGM) for diabetes management to **youth C** and **adults B** with diabetes on **any type of insulin therapy**. The choice of CGM device should be made based on the individual's circumstances, preferences, and needs.
7.15 rtCGM **A** or isCGM **B** 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.	
7.16 rtCGM **A** or isCGM **E** should be offered for diabetes management in **youth with type 1 diabetes on MDI or CSII** 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.	
7.17 rtCGM or isCGM should be offered for diabetes management in **youth with type 2 diabetes on MDI or CSII** 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. **E**	

인슐린 치료 시 연속혈당측정기 활용하기

2023 KDA	2025 KDA
4. 모든 1형당뇨병 성인은 혈당을 조절하고 저혈당위험을 낮추기 위해 실시간연속혈당측정장치를 상시적으로 사용한다. [무작위대조연구, 일반적권고]	
4. 인슐린주사요법을 하는 2형당뇨병 성인은 혈당조절을 위해 실시간연속혈당측정장치를 상시적으로 사용할 수 있다. [무작위대조연구, 제한적권고]	4. 다회인슐린주사나 인슐린펌프를 사용하는 2형당뇨병 성인은 혈당조절을 위해 실시간연속혈당측정장치를 상시적으로 사용한다. [무작위대조연구, 일반적권고]
	5. 기저인슐린 치료를 하는 2형당뇨병 성인은 혈당조절을 위해 실시간연속혈당측정장치를 상시적으로 사용할 수 있다. [무작위대조연구, 제한적권고]

➔ 1형당뇨병, 임신부에서 요양비 청구 및 처방전에 대한 수가청구 가능

Insulin Use in Islet Failure



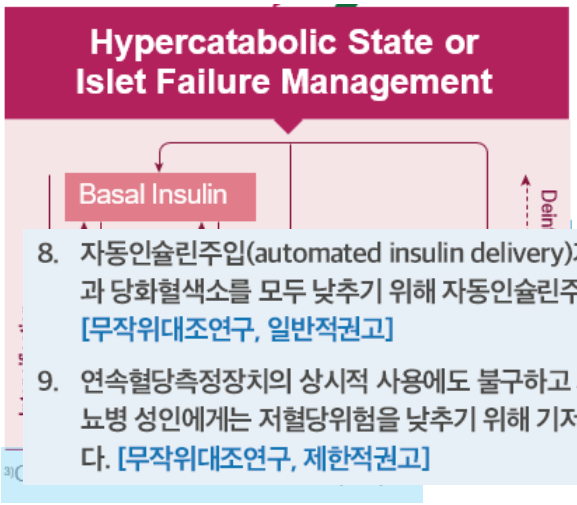
Insulin Pumps and Automated Insulin Delivery (AID) Systems

7.26. **AID systems should be the preferred insulin delivery method** to improve glycemic outcomes and reduce hypoglycemia and disparities in youth and adults with **type 1 diabetes A and other types of insulin-deficient diabetes E** who are capable of using the device (either by themselves or with a caregiver).

7.27 **Insulin pump therapy, preferably with CGM**, should be offered for diabetes management to youth and adults on **MDI with type 2 diabetes** who can use the device safely (either by themselves or with a caregiver).

대한당뇨병학회, 당뇨병진료지침 제9판, 2025, 공개전 미확정 자료입니다. 추후 대한당뇨병학회 공식홈페이지를 통해 확정된 자료를 확인하시기 바랍니다.
Diabetes Care 2025;48 (Supplement_1)

Insulin Use in Islet Failure



당뇨병 진료지침 Clinical Practice Guidelines for Diabetes 2025 제9판

8. 자동인슐린주입(automated insulin delivery)기기를 안전하게 사용할 수 있는 모든 1형당뇨병 성인은 저혈당위험과 당화혈색소를 모두 낮추기 위해 자동인슐린주입기기를 사용한다. [무작위대조연구, 일반적권고]
9. 연속혈당측정장치의 상시적 사용에도 불구하고 저혈당위험이 높으나, 자동인슐린주입기기를 사용할 수 없는 1형당뇨병 성인에게는 저혈당위험을 낮추기 위해 기저인슐린주입중단알고리듬을 내장한 센서강화 인슐린펌프를 사용한다. [무작위대조연구, 제한적권고]

대한당뇨병학회, 당뇨병진료지침 제9판, 2025, 공개전 미확정 자료입니다. 추후 대한당뇨병학회 공식홈페이지를 통해 확정된 자료를 확인하시기 바랍니다.

증례2

- 64세 남자, 168 cm, 61 kg, BMI 21.6 kg/m^2
- 2형당뇨병, 2004년부터 약물치료 시작
- Severe NPDR, DSPN, U-ACR 965 mg/g, eGFR 38 ml/min/1.73m^2
- Metformin 500mg, dulaglutide 1.5mg, insulin degludec 30 iu
- HbA1c 9.1%, c-peptide 2.98 ng/ml

➔ **인슐린 다회요법 vs 혼합형인슐린 vs 인슐린펌프?**

증례2

- Metformin 500mg, dulaglutide 1.5mg, insulin degludec 30 iu
- HbA1c 9.1%, c-peptide 2.98 ng/ml

➔ **연속혈당측정기 부착하고 2주 후 내원하시도록**

GMI 7.2%, 3개월 후 HbA1c 7.6%

요약

- **주사제 치료의 필요성에 대해 이해시키기**
  - 1형당뇨병을 포함한 췌도부전: 인슐린 치료의 불가피성, 보다 적극적인 치료가 가능하도록
  - 그 외의 경우: 시의적절한 인슐린 치료는 당뇨병 말기 치료가 아니라는 것을 이해시키기
- **GLP-1RA의 적절한 활용**
  - 편리한 용법과 낮은 저혈당 위험, 환자의 주사제에 대한 거부감 완화
- **인슐린 치료의 시작 및 교육**
  - 기저인슐린부터: 적은 용량(보통 10단위)으로 시작, 개별화된 공복혈당 조절 목표로
  - 연속혈당측정기의 활용: 숨겨진 저혈당과 혈당스파이크
  - 복잡한 인슐린 용법: 식전인슐린과 혼합형인슐린의 활용, 연속혈당측정을 활용한 펌프(SAP, AID)

    ➔ 전문적이고 장시간의 교육이 필요, 어려운 경우에는 가능한 병원으로 의뢰 고려

02 Session 당뇨병 치료제의 부작용 대처법

SGLT2 억제제, 잘 쓰려면 꼭 알아야 할 포인트

한림대학교 동탄성심병원 내분비내과 **이지우**

GLP-1 수용체작용제, 효과와 부작용 사이에서 균형잡기

중앙대학교 광명병원 내분비내과 **김휘승**

연속혈당측정 장치: 처방부터 부착까지

서울아산병원 당뇨병센터 **신윤정**

02
Session

당뇨병 치료제의 부작용 대처법

SGLT2 억제제, 잘 쓰려면 꼭 알아야 할 포인트

한림대학교 동탄성심병원 내분비내과 **이지우**

SGLT2 억제제는 제2형 당뇨병 치료에서 혈당 강하뿐 아니라 심혈관 및 신장 보호 효과까지 입증되며, 최근 국내외 가이드라인에서 1차 치료 약제로 주목받고 있다. 본 강의는 실질적 진료 현장에서 SGLT2 억제제를 안전하고 효과적으로 사용하기 위한 핵심 포인트를 다룬다.

강의에서는 먼저 SGLT2 억제제의 작용 기전과 현재 사용 가능한 주요 약제를 요약하고, 다양한 병용 요법에서의 활용 가능성을 제시한다. 이어서 실제 외래 진료에서 자주 마주치는 부작용 증례들을 중심으로 생식기 감염, 당뇨병케토산증(DKA), 탈수 및 저혈압, 근감소증을 포함한 과도한 체중 감소 등 상황별 대응 전략을 구체적으로 설명한다. 각 증례에서는 발생 기전과 예방법, 약제 지속 또는 중단 여부 결정에 필요한 임상 판단 기준도 함께 제시된다.

또한, SGLT2 억제제를 안전하게 사용하기 위한 5가지 체크리스트(위생교육, DKA 리스크 평가, 위생 교육, 탈수 예방, 급성질환 시 중단 원칙)를 정리하고, 이상적인 처방 대상(심혈관질환, 심부전, 신기능 저하 환자군)을 소개함으로써, 실제 진료에서의 적용 전략을 제시한다.

본 강의는 단순한 약물 정보 전달을 넘어, 증례 기반 교육을 통해 개원가에서 환자 안전을 확보하면서도 최신 가이드라인에 기반한 치료 전략을 구현하는 데 실질적인 도움이 될 것이다.

2025년 서울아산병원 당뇨병 센터 개원의 연수강좌

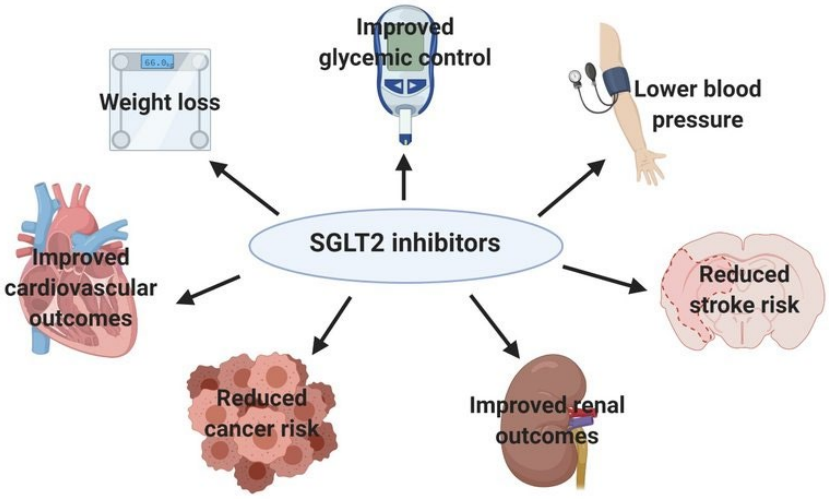
SGLT2 억제제
잘 쓰려면 꼭 알아야 할 포인트

한림대학교 동탄성심병원 내분비내과
이 지 우

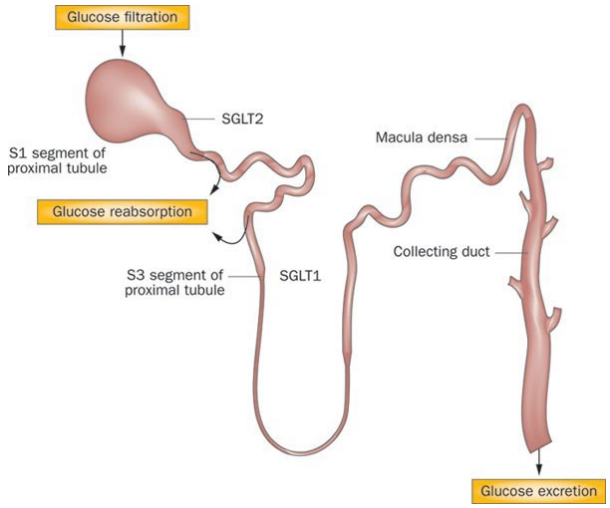
목차

- SGLT2 억제제의 역할과 기전
- 실제 진료에서 흔한 부작용 증례
- 안전하게 잘 쓰고, 누구에게 쓸지 판단하는 전략
- Take-home message

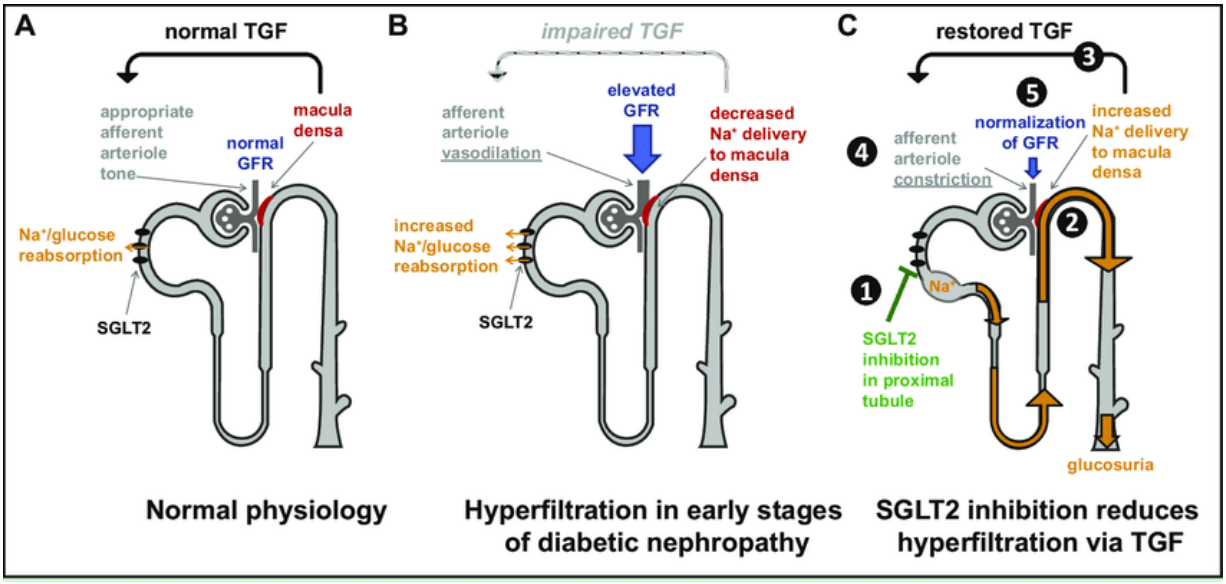
SGLT2 억제제, 왜 주목받는가?



SGLT2 inhibitor



SGLT2 inhibitor



Cardiovascular outcome trials in DM

Study	SAVOR[1]	EXAMINE[2]	TECOS[3]	CAROLINA[4]	CAROLINA[5]
DPP4-i	saxagliptin	alogliptin	sitagliptin	linagliptin	linagliptin
Comparator	NEUTRAL	NEUTRAL	NEUTRAL	NEUTRAL	NEUTRAL
N					
Results	2013	2013	2015	2018	2019

Study	EMPA-REG[6]	CANVAS(& -R)[7]	(CREDENCE)[8]	DECLARE[9]	VERTIS CV[10]
SGLT2-i	empagliflozin	canagliflozin	canagliflozin	dapagliflozin	ertugliflozin
Comparator	+	+	+	+	NEUTRAL
N					
Results	2015	2017	2019	2018	2019

Study	ELIXA[11]	LEADER[12]	SUSTAIN-6[13]	EXSCEL[14]	REWIND[15]	HARMONY[16]
GLP1-RA	lixisenatide	liraglutide	semaglutide	exenatide LR	dulaglutide	albiglutide
Comparator	NEUTRAL	+	+	NEUTRAL	+	+
N						
Results	2015	2016	2016	2018	2019	2018

FDA, Food and Drug Administration; DPP4-i;, dipeptidyl peptidase-4 inhibitor; SGLT2-i, sodium glucose cotransporter 2-inhibitor; GLP 1-RA, glucagon like peptide 1-receptor agonist.

1. Scirica BM, et al. N Engl J Med. 2013;369(14):1317-26. 2. White WB, et al. N Engl J Med. 2013;369(14):1327-35. 3. Green JB, et al. N Engl J Med. 2015;373(3):232-42. 4. Rosenstock J, et al. JAMA. 2019;321(1):69-79. 5. CAROLINA trial 6. Zinman B, et al. N Engl J Med. 2015;373(22):2117-28. 7. Neal B, et al. N Engl J Med. 2017;377(7):644-657. 8. Perkovic V, et al. N Engl J Med. 2019;380(24):2295-2306. 9. Wiviott SD, et al. N Engl J Med. 2019;380(4):347-357. 10. VERTIS CV trial 11. Pfeffer MA, et al. N Engl J Med. 2015;373(23):2247-57. 12. Marso SP, et al. N Engl J Med. 2016;375(4):311-22. 13. Marso SP, et al. N Engl J Med. 2016;375(19):1834-1844. 14. Holman RR, et al. N Engl J Med. 2017;377(13):1228-1239. 15. Gerstein HC, et al. Lancet. 2019. pii: S0140-6736(19)31149-3. 16. Hernandez AF, et al. Lancet. 2018;392(10157):1519-1529.
Exenatide ER, Semaglutide, Albiglutide and Canagliflozin are not approved in Korea

Renal Composite kidney outcome

Reduced risk	EMPA-REG OUTCOME[1,2] (empagliflozin)	CANVAS Program[3,4] (canagliflozin)	DECLARE-TIMI 58[5] (dapagliflozin)	VERTIS CV[6] (ertugliflozin)	CREDENCE[7*] (canagliflozin)
3P-MACE†	↓ *p*=0.04	↓ *p*=0.02	*p*=0.17	*p*=0.001 for non-inferiority	↓ *p*=0.01
CV death or HHF‡	↓ *p*<0.001§	↓ *p*=0.002§	↓ *p*=0.005**	*p*=0.11	↓ *p*<0.001
Composite kidney outcome‡	↓ *p*<0.001‡§	*p*=NR‡¶	*p*=NR‡¶	*p*=NR‡¶	↓ *p*=0.001‡†
CV death‡	↓ *p*<0.001§	*p*=NR¶	*p*=NR¶	*p*=NR¶	↓ *p*=0.05
HHF‡	↓ *p*=0.002§	↓ *p*=0.002§	*p*=NR¶	*p*=NR¶	↓ *p*<0.001

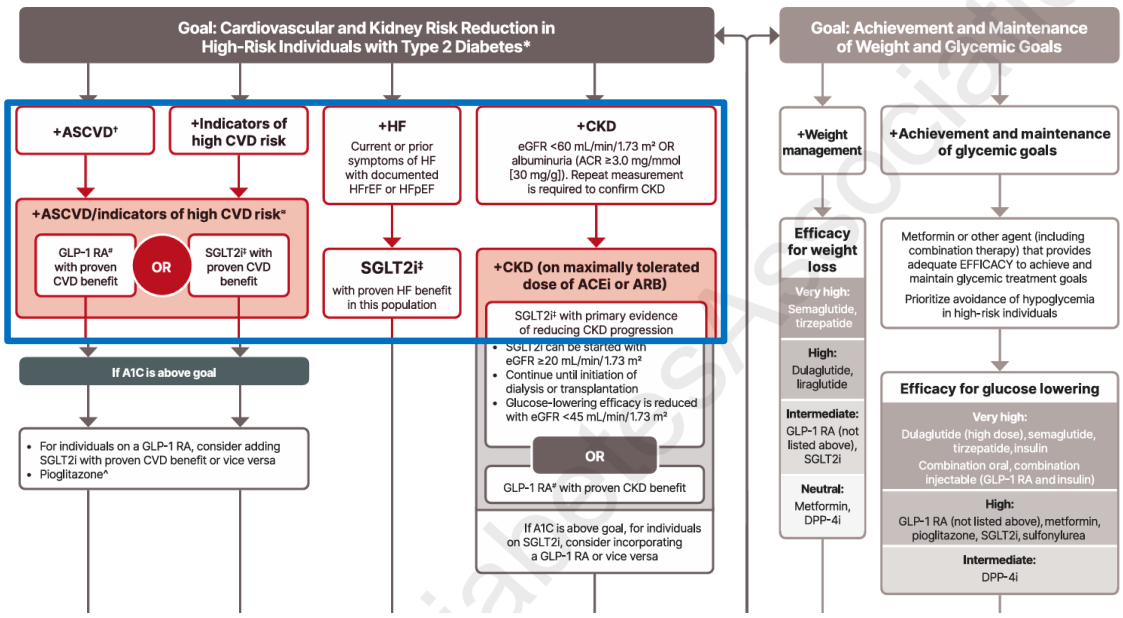
Highlights indicate that the upper bound limit of the confidence interval for the active versus placebo comparison is below unity (<1.00)

Comparison of studies should be interpreted with caution due to differences in study design, populations and methodology

*CREDENCE was a kidney outcomes trial in patients with T2D and albuminuric chronic kidney disease; †Primary endpoint was 3P-MACE in EMPA-REG OUTCOME and CANVAS Program (co-primary endpoint in DECLARE-TIMI 58), *p*-values are for superiority, except for 3P-MACE in VERTIS CV, which is for non-inferiority; ‡Secondary endpoints as defined in the study protocols; §Nominal *p*-value; ¶*p*-value not reported in publication; **Co-primary endpoint in DECLARE-TIMI 58; ††Primary endpoint in CREDENCE

See slide notes for definitions of kidney outcomes, abbreviations and references

2025 ADA guideline



2023 대한당뇨병학회 진료지침

SGLT2 inhibitor

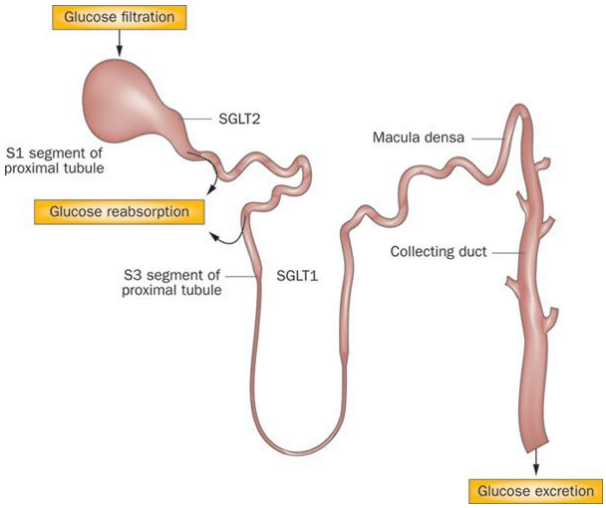
종류	작용기전	HbA1c 감소	저혈당 위험	체중 변화	주요 부작용	주요 금기 및 주의사항
SGLT-2 inhibitor	• 신장에서 포도당 배설 증가	0.5-1.0%	없음	감소	체중감소, 생식기 감염	금기 – 투석중인 환자 주의 – 중증 간장애

- ✓ Empagliflozin 10mg, 25mg
- ✓ Dapagliflozin 10mg
- ✓ Enavogliflozin 0.3mg

증례 1

- 이름 :김o o
- 나이 /성별: 45/F
- 신장 /체중/BMI: 172cm/80kg/27
- 반복적 질염 병력
- Lab: HbA1c 7.6%
- Metformin + Dapagliflozin 투약
- 2 주 후 질염으로 재내원

생식기 감염



생식기 감염

Table 2: Incidence rate of urogenital infections.

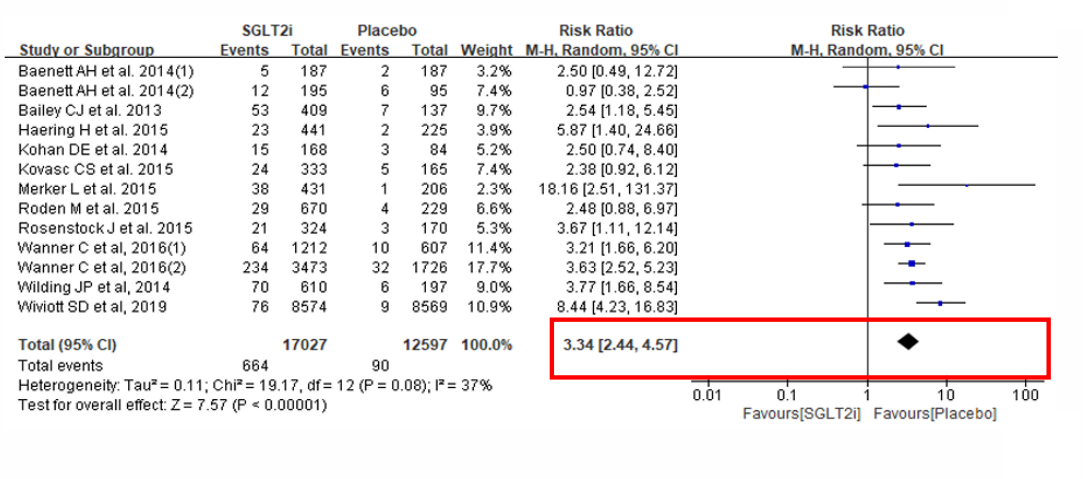
Infections	No. of infected	Incidence rate (per 100 Persons)
Urogenital infections	58/300	19.3
Males	35/193	18
Females	23/107	21
Bacterial infection	47/300	15.6
	Males 25/193	12.95
	Female 22/107	20.56
Fungal infection	11/300	3.6
	Males 10/193	0.051
	Females 1/107	0.009

Benoy A et al. Int J Adv Med. 2025 Jan;12(1):50-56

Reasons for discontinuation of the SGLT2 inhibitors

	Total (n = 97)	<3 Months (n = 22)	3 to 12 Months (n = 43)	12 to 24 Months (n = 32)
Frequent urination	19 (19.6%)	4 (18.2%)	7 (16.2%)	8 (22.8%)
Genital infection	11 (11.3%)	2 (9.1%)	3 (9.3%)	6 (17.1%)
Renal dysfunction	8 (8.2%)	2 (9.1%)	5 (11.6%)	1 (2.9%)
Urinary tract infection	7 (7.2%)	0 (0%)	5 (11.6%)	2 (5.7%)
Fatigue	4 (4.1%)	2 (9.1%)	2 (4.7%)	0 (0%)
Digestive symptoms	4 (4.1%)	0 (0%)	3 (7.0%)	1 (2.9%)
Body weight loss	5 (5.2%)	2 (9.1%)	2 (4.7%)	1 (2.9%)
Diabetic ketoacidosis	3 (3.1%)	0 (0%)	2 (4.7%)	1 (2.9%)
Drug allergy	3 (3.1%)	1 (4.5%)	2 (4.7%)	0 (0%)
Unknown	23 (23.7%)	8 (36.4%)	7 (16.3%)	8 (22.9%)
Improved glycemic control	10 (10.6%)	1 (4.5%)	5 (11.6%)	4 (17.1%)

생식기 감염



Diabetes & Metabolism Journal 2020;44(4):489-497

회음 괴저 (Fournier gangrene)

ORIGINAL RESEARCH

Annals of Internal Medicine

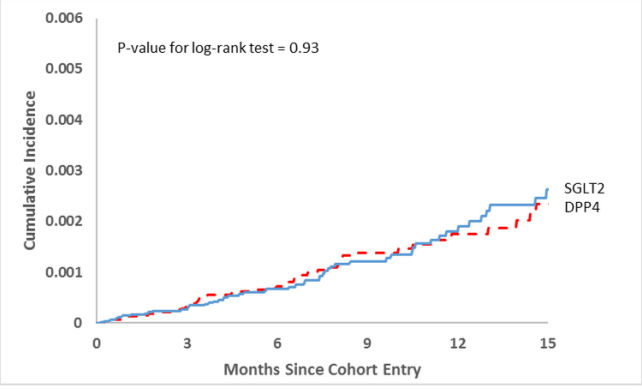
Fournier Gangrene Associated With Sodium-Glucose Cotransporter-2 Inhibitors
A Review of Spontaneous Postmarketing Cases

- 드물지만 환자가 사망할 수도 있는 심각한 합병증
- 조기에 진단하고, 광범위 항생제를 빠르게 사용하는 것이 중요
- 음낭과 항문 주위에 압통과 발적이 발생할 경우 회음 괴저의 가능성도 고려

생식기 감염

- 특히 진균 감염(주로 칸디다 종 감염)의 위험 증가와 관련
- 약 3-5배 정도 위험이 증가
- 과거에 생식기 진균 감염 병력이 있는 환자
  - ✓ 회음부 위생에 대한 교육이 필요
- 경미한 감염 or 치료에 잘 반응하는 환자: SGLT2억제제 유지 가능
  - ✓ 증상시 초기 치료가 중요

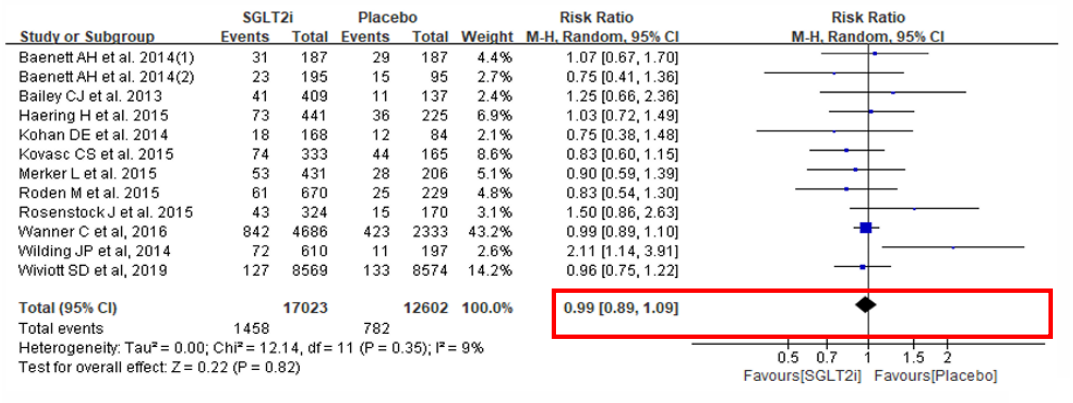
요로감염



At risk (months), n	0	3	6	9	12	15
DPP4	61,876	44,268	30,983	20,951	13,675	8,679
SGLT2	61,876	45,804	32,513	22,800	15,280	9,405

Ann Intern Med. 2019 Jul 30;171(4):248–256

요로감염



Diabetes & Metabolism Journal 2020;44(4):489-497

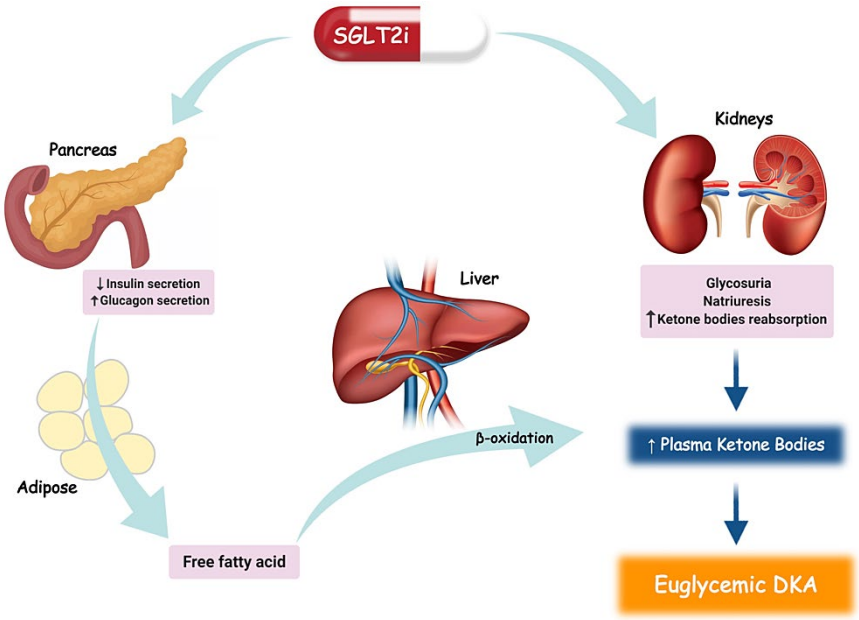
요로감염

- SLGT2 억제제가 요로 감염 증가와 관련이 있다는 확실한 근거는 부족
- 급성 신우신염 또는 요독증 치료 중에는 SGLT2억제제를 일시적으로 중단할 것을 권고

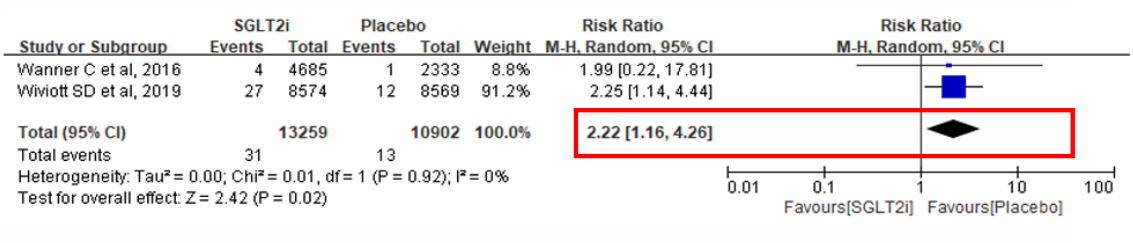
증례2

- 이름 :이o o
- 나이 /성별: 50/M
- Metformin + empagliflozin + linagliptin
- 다이어트 후 식사량 급감, 감기 후 내원
- Lab: HbA1c 7.2%, FPG 150, 혈중 케톤 3.5
- 복통, 구역, 구토 동반

당뇨병케토산증



당뇨병케토산증



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당뇨병케토산증

- SGLT2억제제와 관련된 당뇨병케토산증은 고혈당을 동반하지 않는 정상혈당당뇨병케토산증(euglycemic diabetic ketoacidosis)도 많아 진단 어려움
- 음식 섭취가 어려운 상황, 과도한 음주, 급성 질환, 외상, 수술

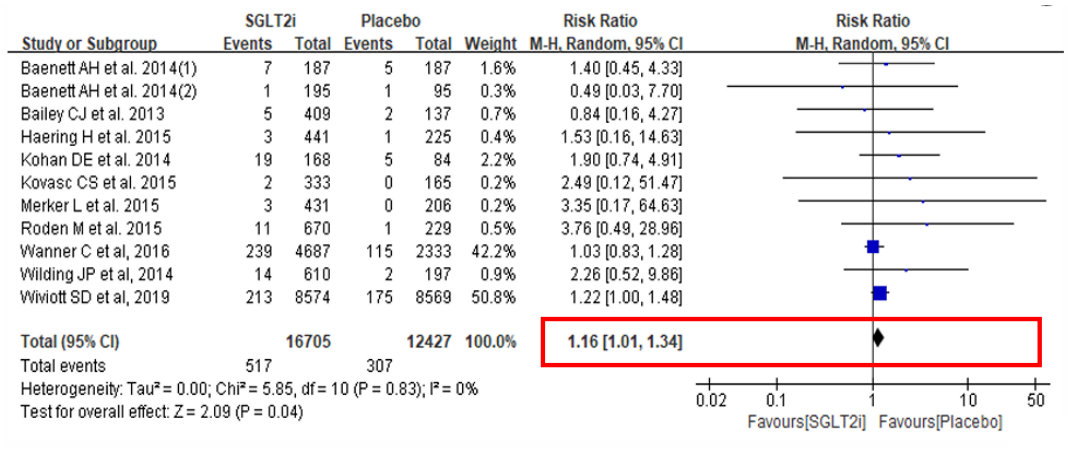
→ 케토산증 발생 위험이 증가할 수 있으므로, SGLT2억제제 일시적으로 중단

- 식사 못할 땐 복용 중단(Sick-day rule) 반드시 설명

증례3

- 이름 :박o o
- 나이 /성별: 78/F
- 고혈압으로 Olmesartan+ Hydrochlorothiazide
- Metformin 복용 중 혈당 조절 안되어 Dapagliflozin 추가
- 일주일 후 어지럼증으로 내원
- 기립성 저혈압 확인

탈수, 저혈압



Study or Subgroup	SGLT2i Events	SGLT2i Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Baenett AH et al. 2014(1)	7	187	5	187	1.6%	1.40 [0.45, 4.33]
Baenett AH et al. 2014(2)	1	195	1	95	0.3%	0.49 [0.03, 7.70]
Bailey CJ et al. 2013	5	409	2	137	0.7%	0.84 [0.16, 4.27]
Haering H et al. 2015	3	441	1	225	0.4%	1.53 [0.16, 14.63]
Kohan DE et al. 2014	19	168	5	84	2.2%	1.90 [0.74, 4.91]
Kovasc CS et al. 2015	2	333	0	165	0.2%	2.49 [0.12, 51.47]
Merker L et al. 2015	3	431	0	206	0.2%	3.35 [0.17, 64.63]
Roden M et al. 2015	11	670	1	229	0.5%	3.76 [0.49, 28.96]
Wanner C et al, 2016	239	4687	115	2333	42.2%	1.03 [0.83, 1.28]
Wilding JP et al, 2014	14	610	2	197	0.9%	2.26 [0.52, 9.86]
Wiviott SD et al, 2019	213	8574	175	8569	50.8%	1.22 [1.00, 1.48]
Total (95% CI)		**16705**		**12427**	**100.0%**	**1.16 [1.01, 1.34]**
Total events	517		307			

Heterogeneity: Tau² = 0.00; Chi² = 5.85, df = 10 (P = 0.83); I² = 0%
Test for overall effect: Z = 2.09 (P = 0.04)

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탈수, 저혈압

Table 4. Summary of Overall Safety and Selected Adverse Events (AEs) According to Age: Safety Population

Parameter	<75			≥75		
	Non-canagliflozin, n = 3,107	Canagliflozin 100 mg, n = 2,929	Canagliflozin 300 mg, n = 2,913	Non-canagliflozin, n = 155	Canagliflozin 100 mg, n = 163	Canagliflozin 300 mg, n = 172
Any AE	2,048 (65.9)	1,965 (67.1)	1,997 (68.6)	112 (72.3)	118 (72.4)	136 (79.1)
AE leading to discontinuation	109 (3.5)	113 (3.9)	163 (5.6)	12 (7.7)	16 (9.8)	10 (5.8)
AE related to study drug[a]	553 (17.8)	716 (24.4)	850 (29.2)	32 (20.6)	49 (30.1)	62 (36.0)
Serious AE	235 (7.6)	211 (7.2)	228 (7.8)	36 (23.2)	28 (17.2)	21 (12.2)
Death	14 (0.5)	10 (0.3)	13 (0.4)	4 (2.6)	2 (1.2)	0
Selected AE						
Urinary tract infection	131 (4.2)	158 (5.4)	163 (5.6)	10 (6.5)	13 (8.0)	12 (7.0)
Genital mycotic infection						
Men[b,c]	20 (1.1)	98 (5.8)	130 (7.9)	0	6 (5.8)	10 (8.5)
Women[d,e]	29 (2.3)	153 (12.4)	154 (12.2)	1 (1.7)	8 (13.3)	7 (12.7)
Osmotic diuresis–related AE[f]	55 (1.8)	203 (6.9)	202 (6.9)	7 (4.5)	7 (4.3)	17 (9.9)
Volume depletion–related AE[g]	45 (1.4)	63 (2.2)	90 (3.1)	4 (2.6)	8 (4.9)	15 (8.7)
Hypoglycemia episode						
Not taking insulin, sulfonylurea, or meglitinide, n	1,592	1,386	1,390	45	47	42
Documented hypoglycemia[h]	192 (12.1)	73 (5.3)	68 (4.9)	7 (15.6)	2 (4.3)	2 (4.8)
Severe hypoglycemia	14 (0.9)	6 (0.4)	4 (0.3)	1 (2.2)	0	1 (2.4)
Taking insulin, sulfonylurea, or meglitinide, n	1,515	1,543	1,523	110	116	130
Documented hypoglycemia[h]	492 (32.5)	617 (40.0)	646 (42.4)	43 (39.1)	61 (52.6)	55 (42.3)
Severe hypoglycemia	31 (2.0)	34 (2.2)	39 (2.6)	6 (5.5)	4 (3.4)	5 (3.8)

Am Geriatr Soc 2016;64(3):543-52.

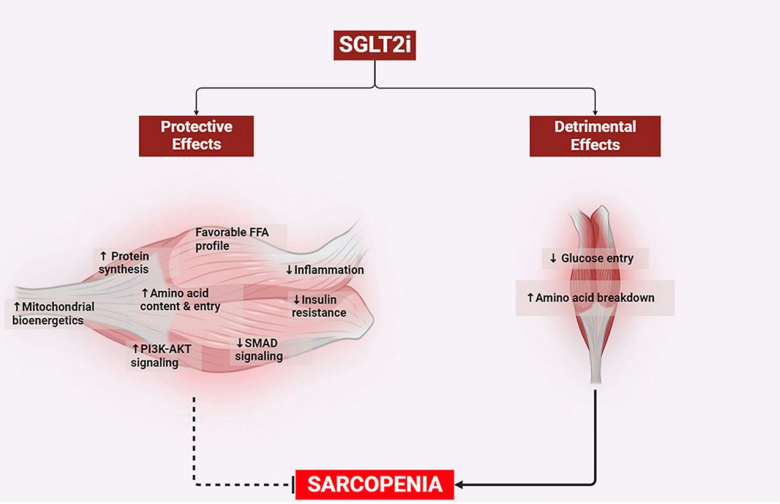
탈수, 저혈압

- SGLT2 억제제는 이뇨 효과가 있어 탈수 및 저혈압 가능성
- 시작 전 체중, 혈압, Cr 확인
- 고령자에선 저용량부터 시작
- 특히 이뇨제를 복용 중인 환자에서는 사용에 주의 필요

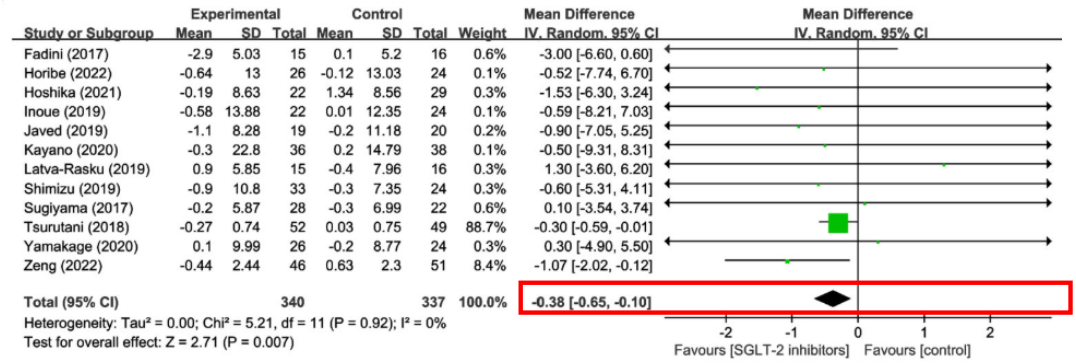
증례 4

- 이름 :최o o
- 나이 /성별: 65/M
- HTN, eGFR 60
- Metformin + Dapagliflozin 병용 3개월 째
- 피로, 기력저하, 체중 6kg 감소

과도한 체중 감소, 근감소증



과도한 체중 감소, 근감소증



Front Endocrinol (Lausanne) 2023;14: 1203666.

과도한 체중 감소, 근감소증

- SLGT2 억제제: 약 2-3 kg 정도의 체중감소
- 마른 고령 당뇨병 환자에서의 사용은 주의가 필요
- 노인에서 근감소증이 있거나 BMI가 낮은 환자라면 SGLT2억제제 복용에 조심
- SGLT2억제제 처방 시 근육량을 유지할 수 있는 운동요법을 권하고, 체중 변화를 잘 감시하는 것이 필요

SGLT2 억제제를 안전하게 쓰는 체크리스트

- 생식기 감염 예방
- 당뇨병케토산증 예방
- 급성질환 시 복용 중단
- 탈수 예방
- 노인 주의

Take-home message

- 심혈관 질환이 있거나 신장 질환이 있는 환자에겐 1순위 약제
- 혈당만 보지 말고, '동반 질환'까지 고려한 전략적 처방이 중요
- 의료진이 SGLT2억제제를 처방할 때 부작용에 주의를 기울여 사용
- 사전에 복용 교육하고 모니터링 중요

감사합니다

02
Session

당뇨병 치료제의 부작용 대처법

GLP-1 수용체작용제, 효과와 부작용 사이에서 균형잡기

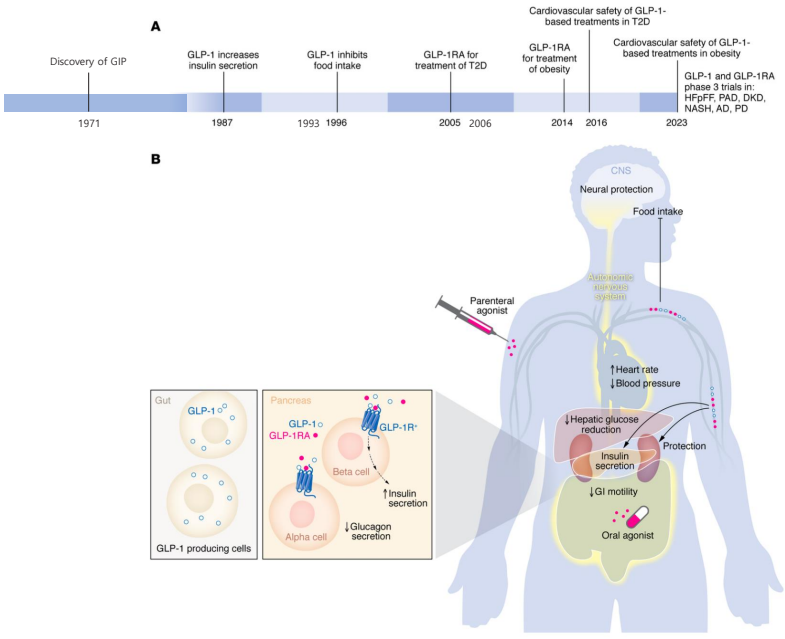
중앙대학교 광명병원 내분비내과 **김휘승**

GLP-1 수용체 작용제는 2형 당뇨병 치료제 중에서도 체중 감소와 심혈관 보호 효과를 동시에 기대할 수 있는 약제로, 최근 1차 및 2차 의료현장에서 그 활용도가 크게 증가하고 있습니다. 특히 세마글루타이드나 둘라글루타이드 등 장시간 작용제의 등장과 함께 비만에 대한 적응증, 심혈관 사건 위험 감소 등 새로운 근거가 축적되고 있어, 단순한 혈당 조절을 넘어 만성질환 관리의 핵심 축으로 주목받고 있습니다. 하지만 그 임상적 유용성에도 불구하고, GLP-1 RAs는 특유의 위장관 부작용, 드물지만 중대한 부작용(위마비, 췌장염 등), 비용 부담 등의 한계도 존재하여, 무분별한 사용보다는 적절한 환자 선별과 부작용 예방 전략이 필수적입니다. 본 강의에서는 최신 근거를 바탕으로 GLP-1 수용체 작용제의 효과와 한계를 균형 있게 조망하고, 실제 진료에서 균형 잡힌 접근을 위한 처방 전략과 주의사항을 공유하고자 합니다.

GLP-1 수용체작용제, 효과와 부작용 사이에서 균형잡기

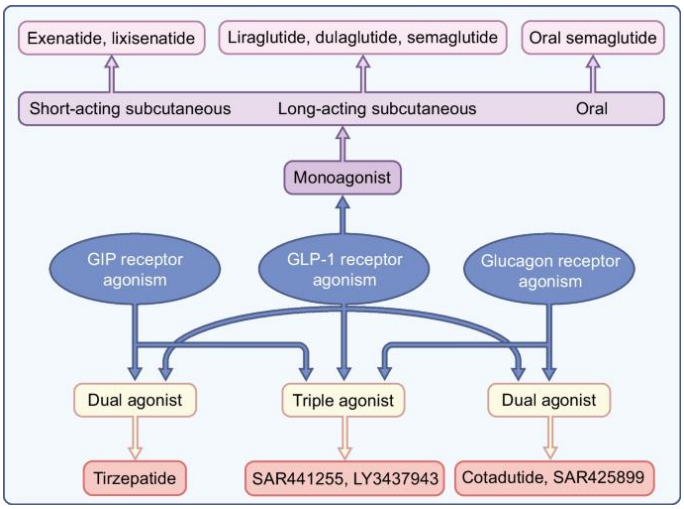
중앙대학교 광명병원 내분비내과
김 휘 승

Nutrient-stimulated hormone



J Clin Invest. 2024;134(2):e175634

NuSH-based pharmacology

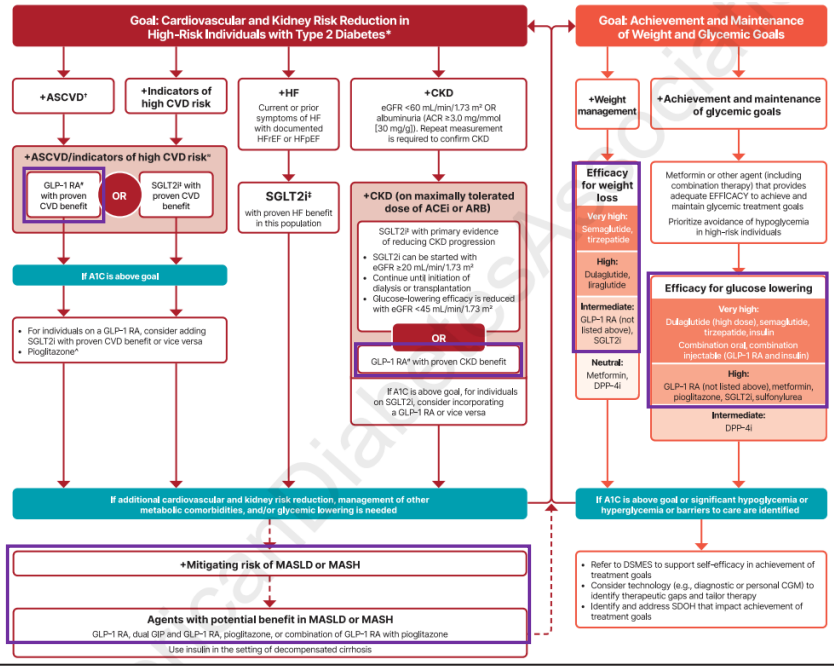


Retatrutide

Diabetologia 66, 1796–1808 (2023).

2025 ADA guidelines

: Use of Glucose-Lowering Medications in the Management of Type 2 Diabetes



2025 ADA guidelines

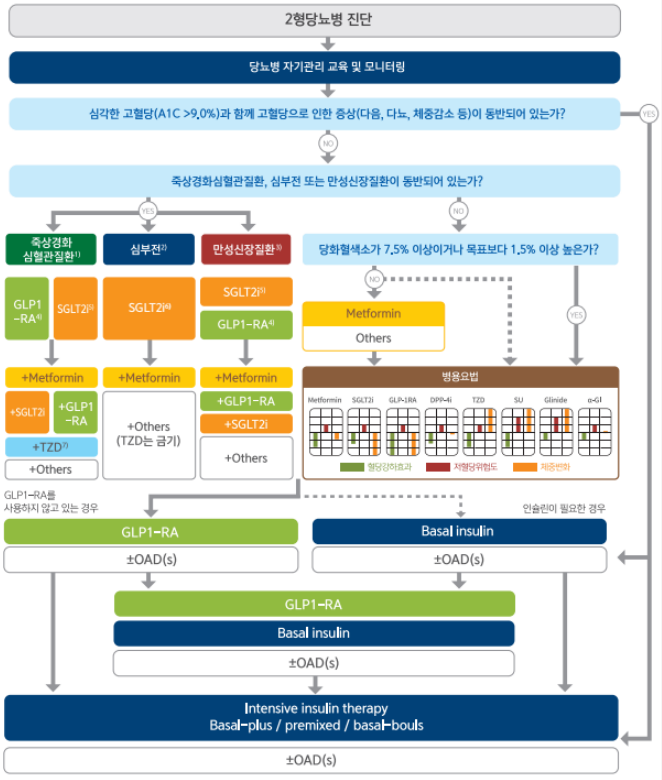
: Features of medications for lowering glucose in type 2 diabetes

Medication (route of administration)	Glucose-lowering efficacy[1]	Hypoglycemia risk	Weight effects[2]	CV effects		Kidney effects		MASH effects	Clinical considerations and adverse effects
				Effect on MACE	Effect on HF	Progression of CKD	Dosing/use considerations*		
GLP-1 RAs (SQ; semaglutide also available in oral formulation)	High to very high	No	Loss (intermediate to very high)	Benefit: dulaglutide, liraglutide, semaglutide (SQ) Neutral: exenatide once weekly, lixisenatide	Neutral	Benefit for renal end points in CVOTs, driven by albuminuria outcomes: dulaglutide, liraglutide, semaglutide (SQ) Demonstrated benefit for progression of CKD for semaglutide (SQ)	• See labels of individual agents for dosage considerations for kidney function • No dose adjustment for dulaglutide, liraglutide, or semaglutide • Monitor kidney function when initiating or escalating doses in individuals with kidney impairment reporting severe adverse GI reactions	Potential benefit	• Thyroid C-cell tumors identified in rodents; human relevance not determined. • Ileus: risk level is not well established; provide guidance on discontinuation prior to surgical procedures. • Pancreatitis: acute pancreatitis has been reported, but causality has not been established. Do not initiate if at high risk for pancreatitis, and discontinue if pancreatitis is suspected. • Biliary disease: evaluate for gallbladder disease if cholelithiasis or cholecystitis is suspected; avoid use in at-risk individuals. • Diabetic retinopathy: close monitoring of retinopathy in those at high risk (older individuals and those with longer duration of T2D [≥10 years]). • Impact on drug absorption: orally administered drug absorption may be impaired during dose titration (including of oral contraceptives). • GI side effects: counsel on potential for GI side effects; provide guidance on dietary modifications to mitigate GI side effects (reduction in meal size, mindful eating practices [e.g. stop eating once full], decreasing intake of high-fat or spicy food); consider slower dose titration for those experiencing GI challenges. Not recommended for individuals with gastroparesis.
GLP-1 receptor agonists Exenatide Liraglutide Dulaglutide Semaglutide	- 포도당의존 인슐린 분비 증가; 식후 글루카곤 분비 감소; 위배출 억제 - 식후혈당 개선 - 식사와 관계없이 피하주사 (일 1-2회 또는 주 1회)	감소	없음	0.8-1.5%	• 주의: 췌장염, 급성신장손상, 중증 간장애, 신장장애, 중증 위마비를 포함한 중증 위장관질환(권장되지 않음), 당뇨병성 망막증, 급성담낭질환 • 금기: 갑상선수질암 또는 MEN2[3]의 과거력 또는 가족력				

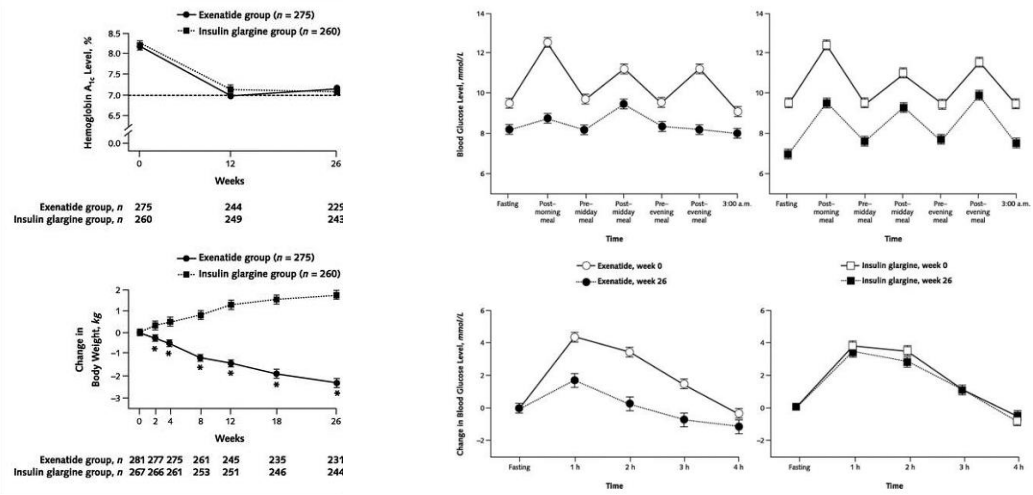
2023 KDA guidelines

2025 KDA guidelines

- Metformin의 일차약제 권고 내용 삭제
- 심각한 고혈당 (A1c >9.0%) 기준이 삭제되고 고혈당으로 인한 증상 대신 '이화작용 증상'



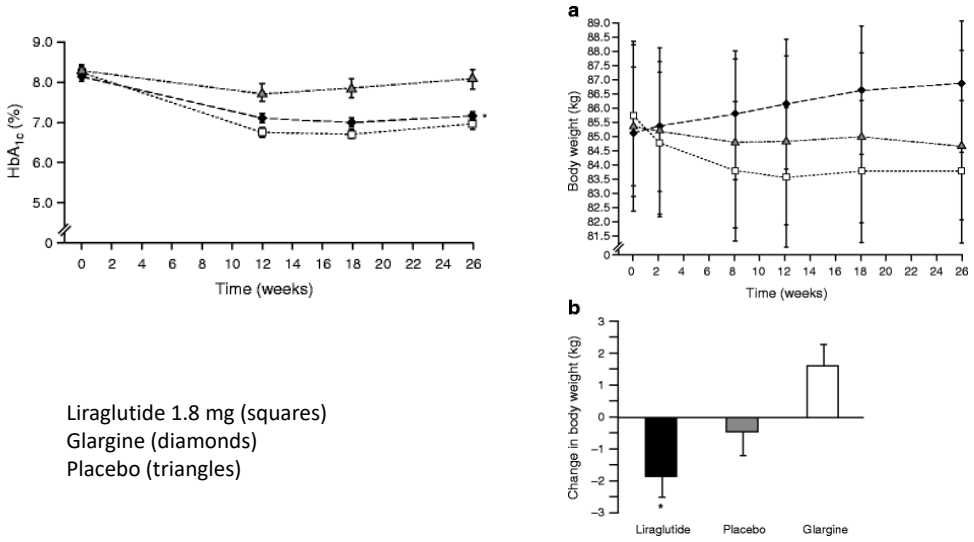
Exenatide



Exenatide, 10 µg twice daily, or insulin glargine, 1 daily dose titrated to maintain fasting blood glucose levels of less than 5.6 mmol/L (<100 mg/dL).

Ann Intern Med. 2005 Oct 18;143(8):559-69.

Liraglutide

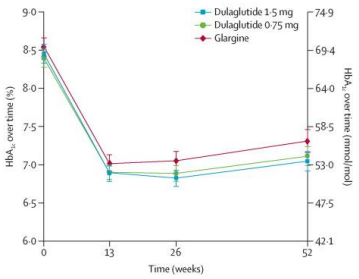


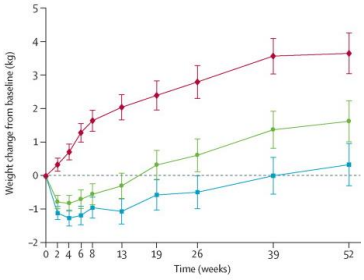
Liraglutide 1.8 mg (squares)
Glargine (diamonds)
Placebo (triangles)

Diabetologia. 2009 Oct;52(10):2046-55.

Dulaglutide

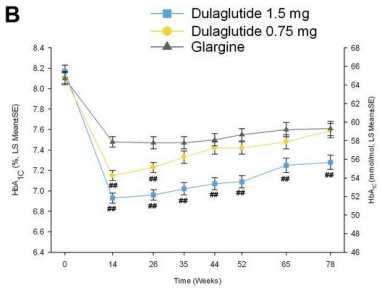
AWARD-4
: combination with
prandial insulin lispro

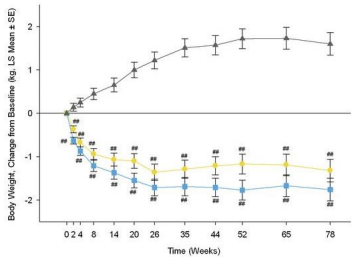




Lancet. 2015 May 23;385(9982):2057-66.

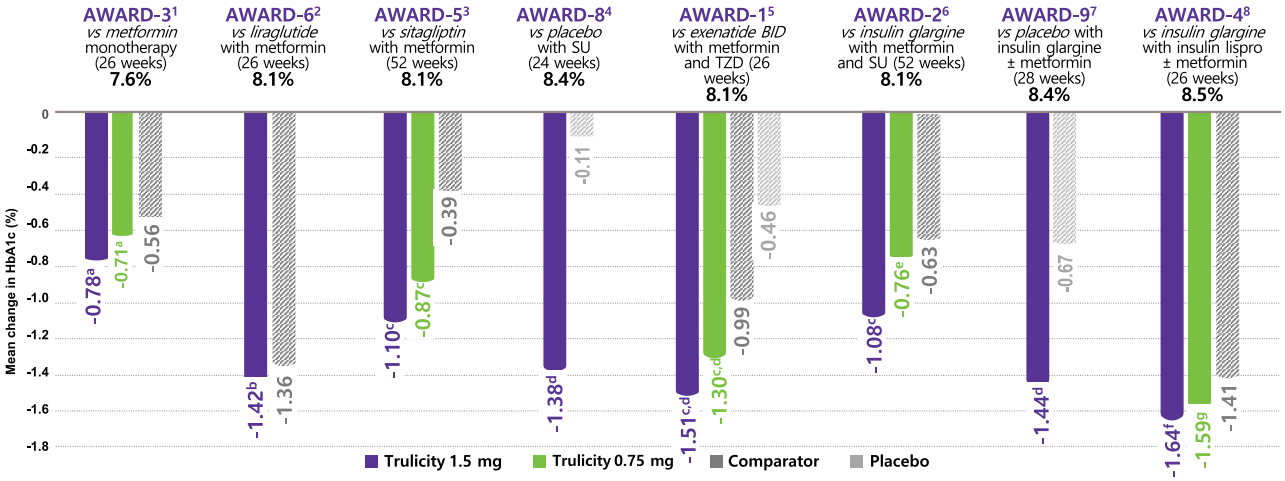
AWARD-2
: add-on to
metformin + SU





Diabetes Care. 2015 Dec;38(12):2241-9.

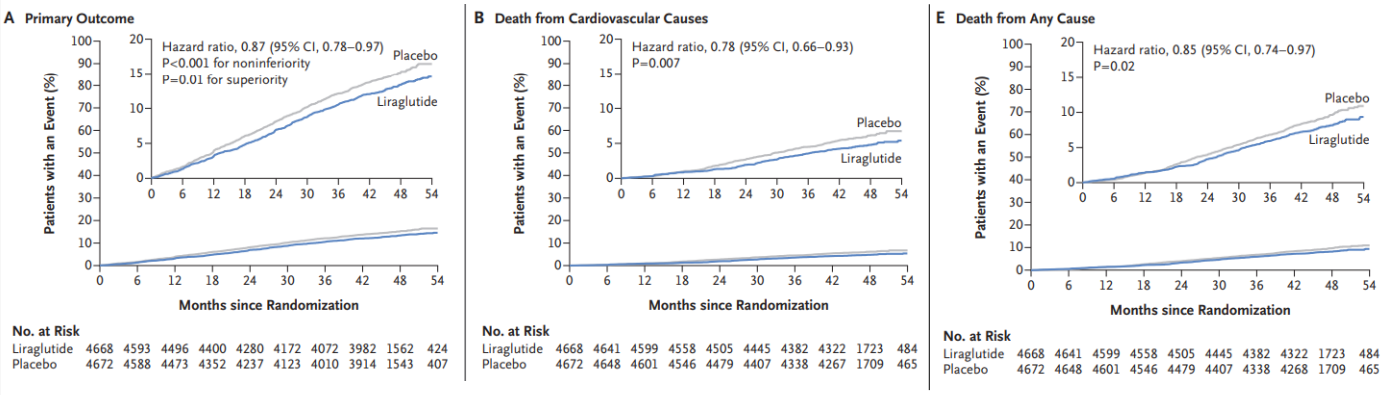
Dulaglutide (AWARD program)



[a]$p<0.025$ superiority vs comparator; [b]$p<0.0001$ noninferiority vs comparator; [c]$p<0.001$ superiority vs comparator; [d]$p<0.001$ superiority vs placebo; [e]$p<0.001$ noninferiority vs comparator; [f]$p=0.005$ superiority vs comparator; [g]$p=0.015$ superiority vs comparator.

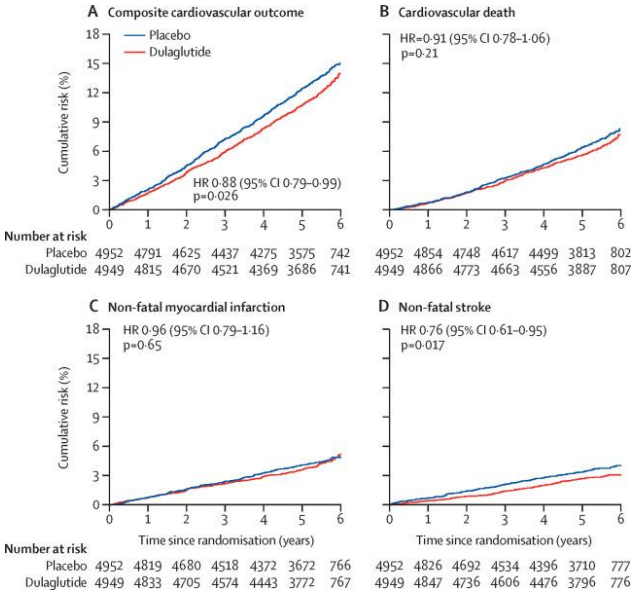
1. Umpierrez G, et al. Diabetes Care 2014;37:2168-76. 2. Dungan KM, et al. Lancet 2014;384:1349-57. 3. Nauck M, et al. Diabetes Care 2014;37:2149-58. 4. Dungan KM, et al. Diabetes Obes Metab 2016;18:475-82.
5. Wysham C, et al. Diabetes Care 2014;37:2159-67. 6. Giorgino F, et al. Diabetes Care 2015;38:2241-9. 7. Pozzilli P, et al. Diabetes Obes Metab 2017;19:1024-31. 8. Blonde L, et al. Lancet 2015;385:2057-66.

Liraglutide and Cardiovascular Outcomes (LEADER)



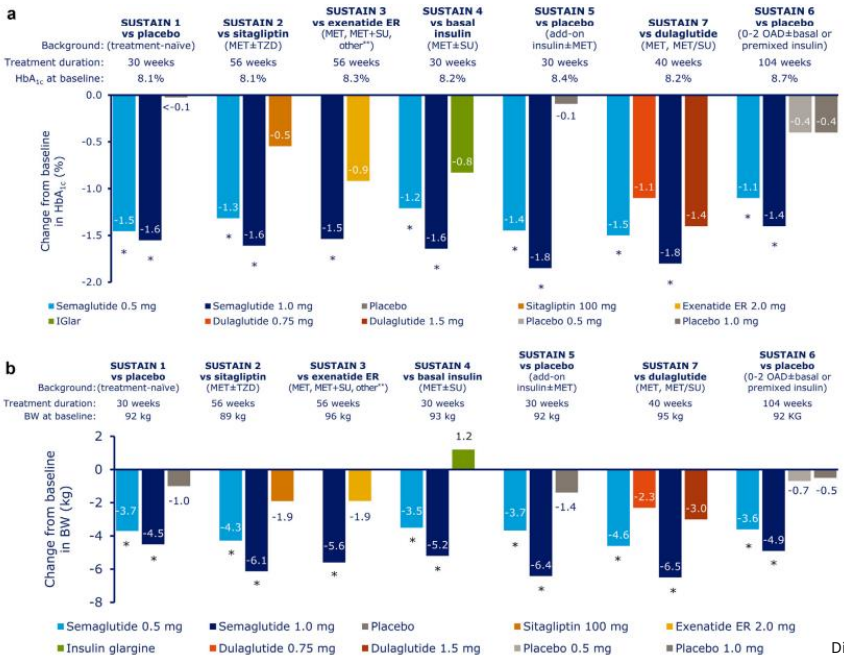
N Engl J Med. 2016 Jul 28;375(4):311-22.

Dulaglutide and Cardiovascular Outcomes (REWIND)



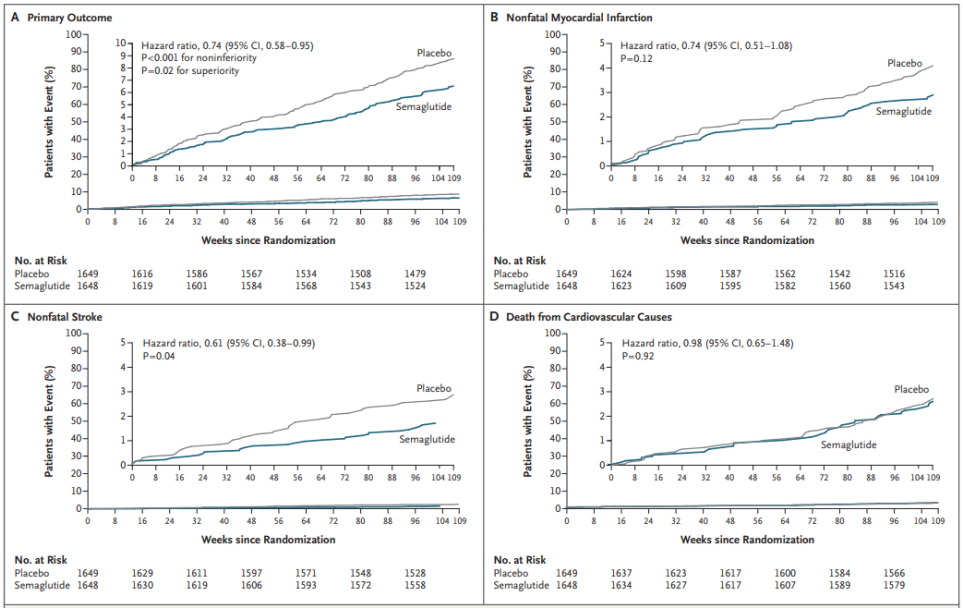
Lancet. 2019 Jul 13;394(10193):121-130.

Semaglutide (SUSTAIN program)



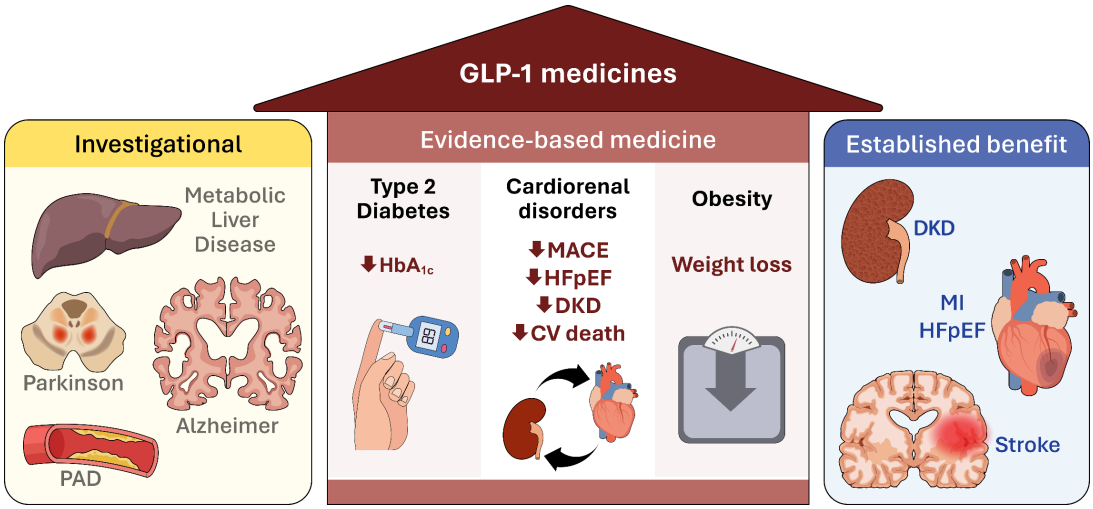
Diabetes Metab. 2019 Oct;45(5):409-418.

Semaglutide and Cardiovascular Outcomes(SUSTAIN-6)



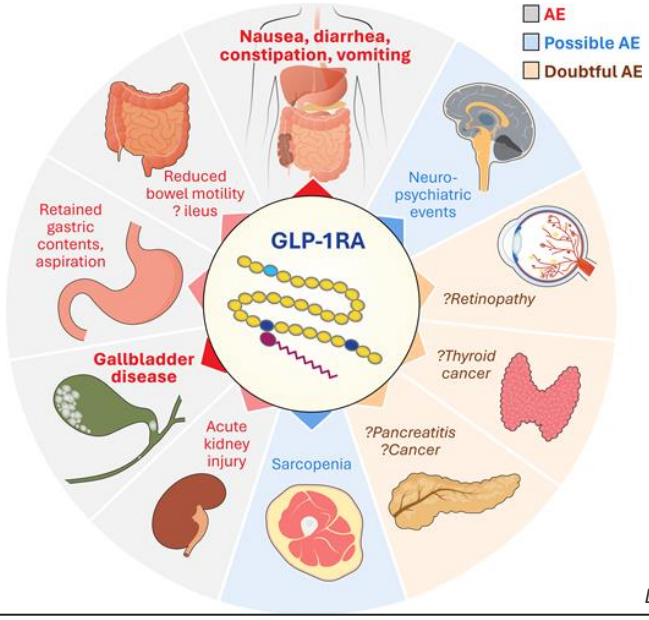
N Engl J Med. 2016 Nov 10;375(19):1834-1844.

Established and emerging evidence supporting use of GLP-1 medicines



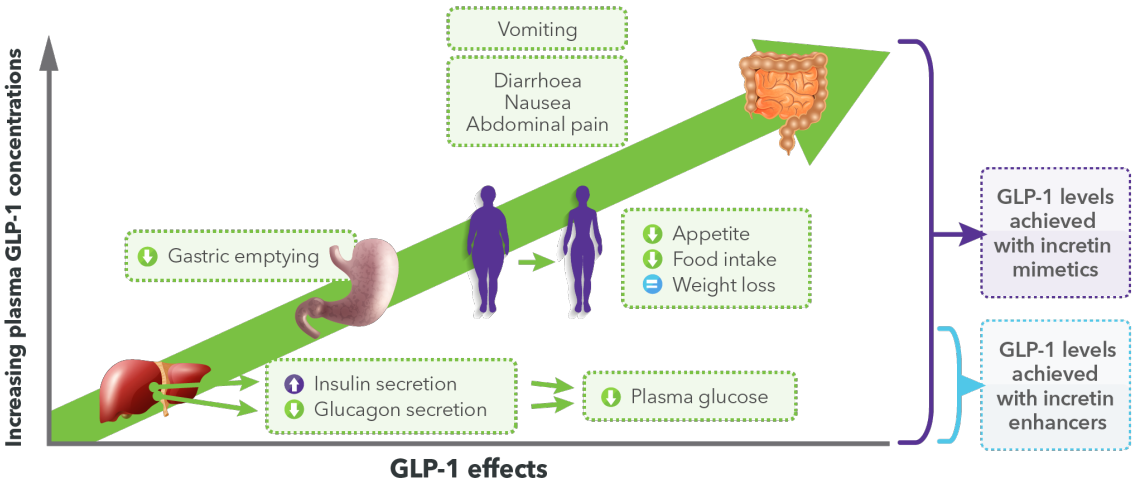
Diabetes Care 2024;47(11):1873–1888

Established and putative adverse events associated with GLP-1 medicines



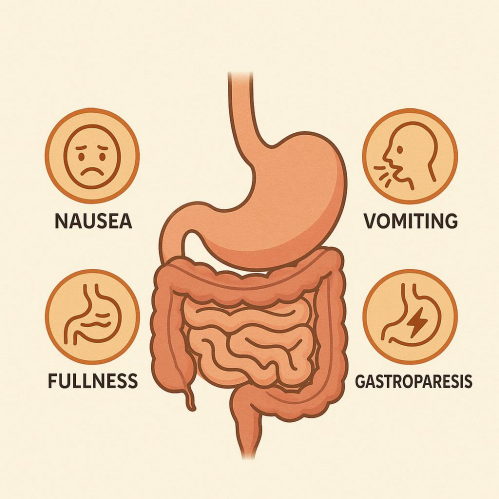
Diabetes Care 2024;47(11):1873–1888

Dose–response relationships for the effects of GLP-1



Trends Mol Med 2008;14:161-68.

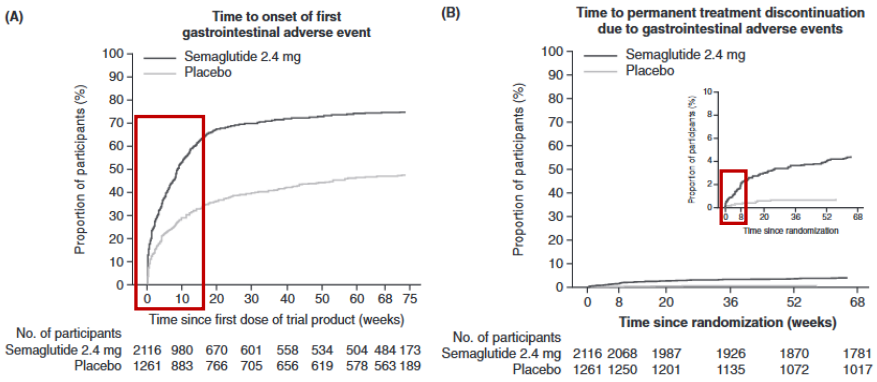
Typical GI side effects of GLP-1RAs



- ✓ Dose-dependent
- ✓ Mild-to-moderate in severity
- ✓ Transient
- ✓ Mostly occur during initiation and up-titration

Gastrointestinal tolerability of once-weekly semaglutide 2.4 mg in adults with overweight or obesity, and the relationship between gastrointestinal adverse events and weight loss

STEP 1-3 (pooled)	Semaglutide (n=2,116)	Placebo (n=1,261)
GI AE	72.9	47.1
Serious GI AE	1.3	0.4
Severity: mild	65.7	40.6
Severity: moderate	32.7	14.3
Severity: severe	4.1	0.9
Permanent discontinuation	4.3	0.7
Temporary interruption	5.9	1.4
Dose reduction	8.0	0.5



Diabetes Obes Metab. 2022 Jan;24(1):94-105.

Gastrointestinal tolerability of once-weekly semaglutide 2.4 mg in adults with overweight or obesity, and the relationship between gastrointestinal adverse events and weight loss

Incidence of most common GI AEs

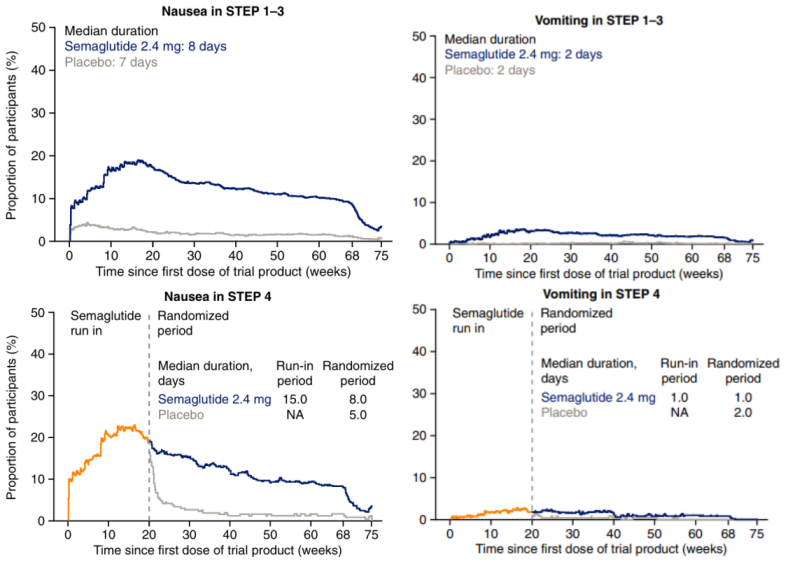
STEP 1-3 (pooled)	Semaglutide (n=2,116)	Placebo (n=1,261)
Nausea	43.9	16.1
Diarrhea	29.7	15.9
Vomiting	24.5	6.3
Constipation	24.2	11.1

Incidence of other GI AEs reported in ≥5% of participants

STEP 1-3 (pooled)	Semaglutide (n=2,116)	Placebo (n=1,261)
Dyspepsia	9.0	3.2
Abdominal pain	8.8	4.3
Abdominal pain upper	7.9	4.2
Abdominal distension	7.5	5.1
Eructation	7.4	0.4
Flatulence	5.9	4.2
GERD	5.4	2.5

Diabetes Obes Metab. 2022 Jan;24(1):94-105.

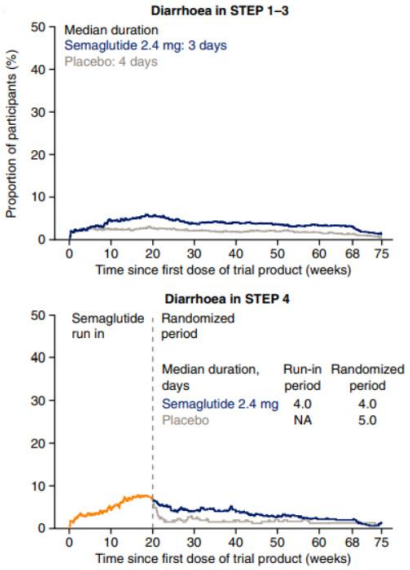
Nausea / Vomiting



- Provided that 30 min have passed since the last GLP-1 RA dose
- Eat foods able to ease the symptoms of nausea
- Avoid strong smells
- Consider anti-emetics, prokinetics (domperidone)

Diabetes Obes Metab. 2022 Jan;24(1):94-105.

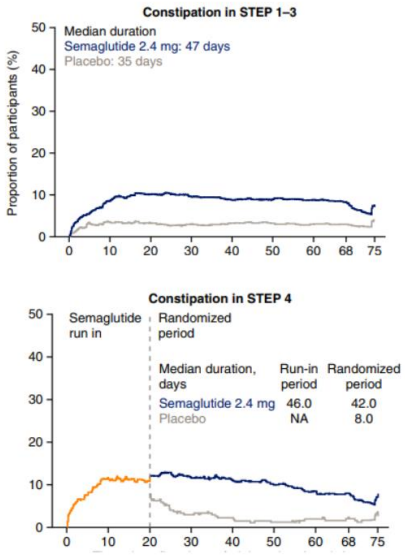
Diarrhea



- Avoiding trigger foods (high-fiber foods, raw fruits and vegetables, spicy or greasy foods, caffeine, and alcohol)
- Small, frequent meals
- Dose reduction or discontinuation of metformin
- Anti-motility drugs(loperamide), protectants (dioctahedral smectite), probiotics etc

Diabetes Obes Metab. 2022 Jan;24(1):94-105.

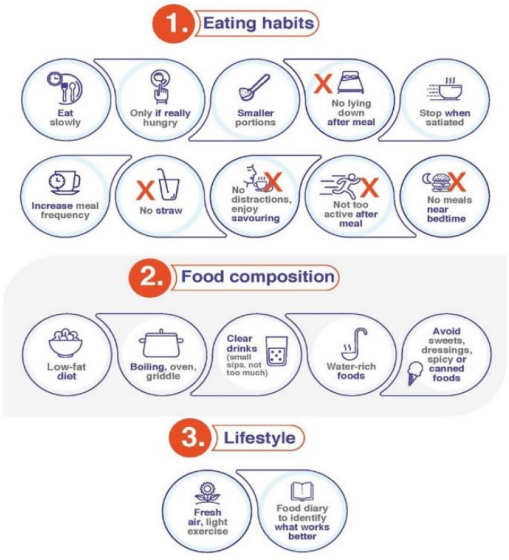
Constipation



- Increase fluid & fiber intake
- Increase physical activity
- A 15–30 minute walk after meals
- Maintain regular bowel habits
- Short-term use of stool softeners (docusate sodium etc)

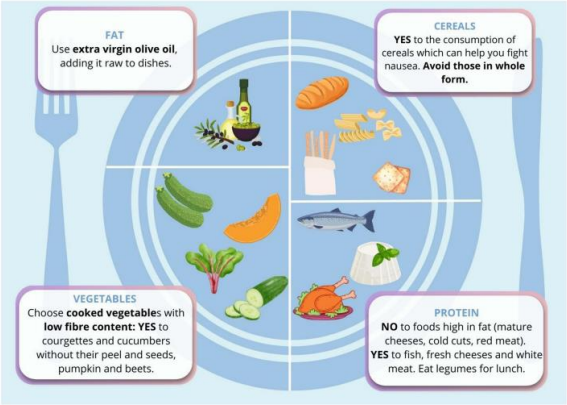
Diabetes Obes Metab. 2022 Jan;24(1):94-105.

Clinical Recommendations to Manage Gastrointestinal Adverse Events in Patients Treated with GLP-1 Receptor Agonists: A Multidisciplinary Expert Consensus



J Clin Med. 2022 Dec 24;12(1):145.

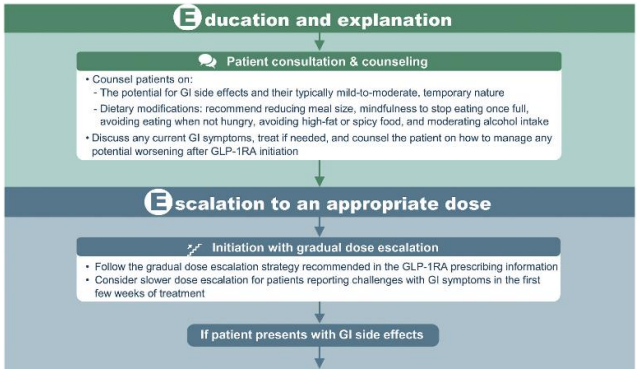
Dietary Recommendations for the Management of Gastrointestinal Symptoms in Patients Treated with GLP-1 Receptor Agonist

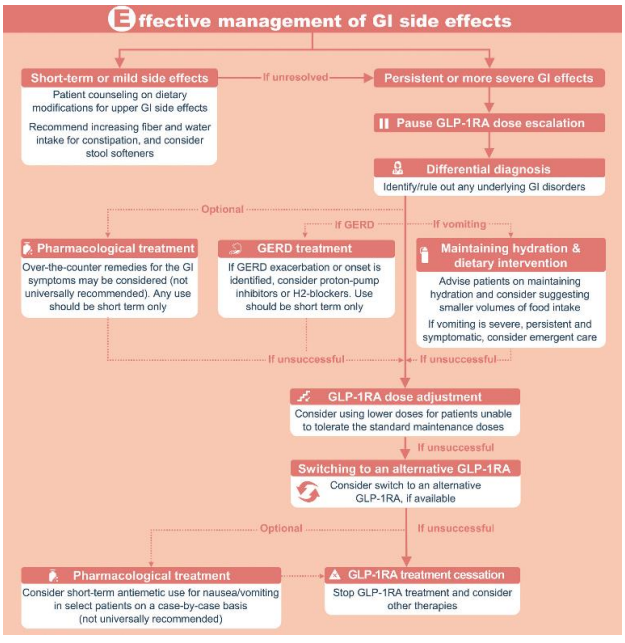


- Eat small, frequent meals, and eat slowly.
- Use simple cooking methods such as steaming, baking, and boiling, avoiding frying and sautéing.
- Avoid complex or heavily seasoned dishes, spicy foods, and alcoholic drinks.
- Avoid consuming liquid foods like soups, and broths during the evening meal, as they may slow down digestion and increase symptoms.
- Stay hydrated by drinking water in small sips, avoiding excessive intake during meals.
- Avoid lying down or vigorous activity after meals.
- Avoid wearing tight clothes or belts.

Diabetes Metab Syndr Obes. 2024 Dec 19:17:4817-4824.

Managing the gastrointestinal side effects of GLP-1 receptor agonists in obesity: recommendations for clinical practice



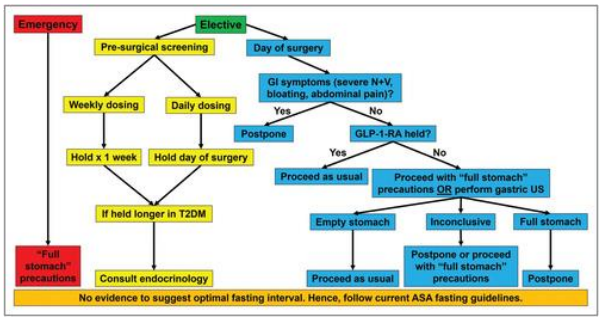


Postgrad Med. 2022 Jan;134(1):14-19.

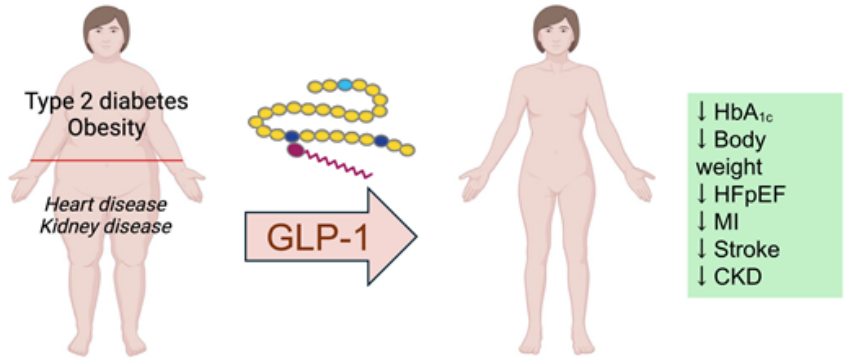
Other possible adverse effects of semaglutide

- Acute gallbladder disease
- Acute pancreatitis
- Gastroparesis and bowel obstruction
  - Retained gastric contents and risk of pulmonary aspiration for endoscopy or general anesthesia
- Diabetic retinopathy progression and Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)

Recommendations from American Society of Anesthesiologists



Curr Opin Anaesthesiol. 2024 Jun 1;37(3):323-333.



CKD, chronic kidney disease; GLP-1, glucagon-like peptide 1; HFpEF, heart failure with preserved ejection fraction; MI, myocardial infarction.

Diabetes Care 2024;47(11):1873–1888

경청해주셔서 감사합니다.

02
Session

당뇨병 치료제의 부작용 대처법

연속혈당측정 장치: 처방부터 부착까지

서울아산병원 당뇨병센터 **신윤정**

연속 혈당 모니터링(CGM)은 혈당 변동을 실시간으로 파악할 수 있는 기술로, 기존 혈당 측정 방식과 달리 24시간 연속 모니터링이 가능하며 저혈당 및 고혈당 경고 기능을 제공한다. 이를 통해 혈당 조절을 최적화하고 인슐린 투여량 결정에 도움을 주며, 생활 습관과 혈당의 관계를 분석할 수 있다.

CGM이 필요한 환자는 1형 당뇨병 환자, 저혈당 무감지증 환자, 혈당 조절이 어려운 2형 당뇨병 환자 및 임신 당뇨병 환자 등이 포함되며, 일부 대상자는 의료 보험 및 의료 급여 지원을 받을 수 있다.

CGM은 다양한 기기가 출시되고 활용되고 있으며 각각 정확도, 사용 기간, 비용 및 혈당 공유 등 차이가 있다.

실제 CGM 적용을 위해 사전에 확인이 필요한 부분, 센서의 선택, 처방전의 작성과 발행, 센서 부착 시 주의사항에 대해 정리해보고 CGM을 효과적으로 활용해보도록 하자.

2025년 서울아산병원 당뇨병 센터 개원의 연수강좌

연속 혈당 측정기: 처방부터 부착까지

서울아산병원 당뇨병센터 당뇨교육실
당뇨병 교육 전담 간호사 신 윤 정

목차

연속 혈당 모니터링의 개요

혈당 관리의 새로운 패러다임

연속 혈당 모니터링은 실시간으로 포도당 수치를 모니터링하는 기술

기존 방식과의 차이점

- 24시간 연속 모니터링 가능
- 혈당 변동 패턴 파악 용이
- 저혈당/고혈당 조기 경고
- 비침습적 측정으로 편의성 증가
- 인슐린 투여량 결정 지원
- 생활 습관과 혈당 관계 분석 가능
- 식사 메뉴에 따른 혈당 변화 파악 가능

연속 혈당 측정기의 적용 대상과 처방 과정

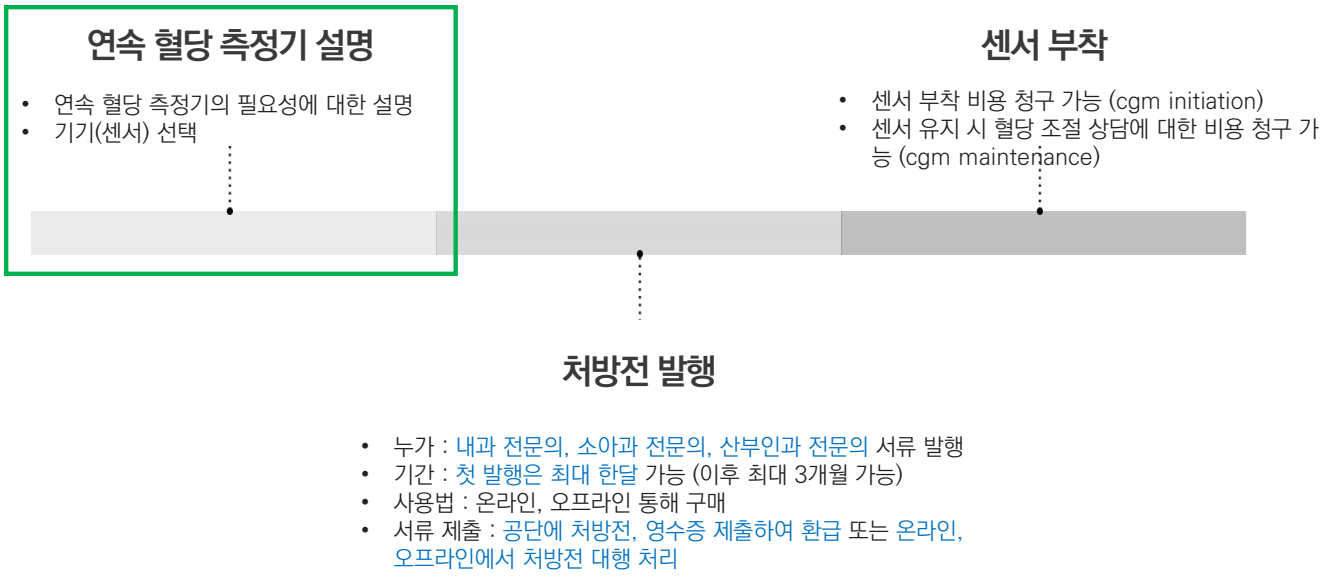
연속 혈당 측정기 활용이 필요한 환자군

- 1형당뇨병
- 저혈당 무감지증
- 혈당 조절이 어려운 2형당뇨병, 다회 인슐린 주사 요법의 2형당뇨병
- 임신 당뇨병
- 당뇨병 첫 진단 시 식단, 생활 습관 개선이 필요한 환자

지원을 받을 수 있는 환자군

- 1형당뇨병
- 임신 당뇨병

연속 혈당 측정기의 처방부터 부착까지



연속 혈당 측정기의 설명

진료 및 평가 (미리 확인이 필요한 부분)

☐ 스마트폰 사용자 인가
☐ 혜택 받을 수 있는 1형당뇨병 대상자인가 (의료 급여 환자는 전액 지원)
☐ 환자의 이해도 및 수용 능력 확인
☐ 고령 환자의 경우 가족, 주변 환경의 지원을 받을 수 있는가
☐ 혈당 관리의 필요성에 대해 인지하고 있고 관심이 있는가

연속 혈당 측정기 선택 시 고려사항

환자 생활 패턴

- 직업 특성
- 운동 습관
- 식사 패턴
- 스트레스 수준

정확도

- 센서 정확도
- 보정 필요성
- 데이터의 안정성
- 오류 발생

사용 편의성

- 착용감
- 샤워, 운동 가능
- 생활 방수 (30분 이상 제한)
- 알람 기능
- 테이프 알러지 문제

데이터 분석 기능

- 혈당 수치 확인의 용이성
- 보고서 정리
- 의료진 공유

기기(센서)의 선택

[연속 혈당 측정기의 종류와 일반적인 특징]

센서 종류	센서 유지 기간	보정 여부	정확도 (MARD,%)	본인 부담금 (2025년 5월 기준)	보호자 공유 기능	주의
프리스타일 리브레2	14일(월 2개)	불필요	9.2	약 7만원/월	웹으로 가능 www.libreview.com	•비타민 C(500mg 이상) 복용 – 일시적 높은 혈당 •아스피린 650mg 이상 복용 – 낮은 혈당
덱스콤 G7	10일(월 3개)	불필요 (필요시 가능)	8.2	약 9만원/월	있음 Dexcom follow	•Acetaminophen(타이레놀): 6시간 이내 1g이상 투여 시 혈당 높게 측정됨 •Hydroxyurea: 투여 시 혈당 높게 측정됨
가디언4	7일(월 4개)	불필요 (필요시 가능)	8.5	약 11만원/월	웹으로 가능 http://carelink.minimed.eu	–
바로잰 핏 (케어센스에어)	15일(월 2개)	불필요 (필요시 가능)	9.0	약 5.1만원/월	바로잰 care (케어센스 365)	•비타민 C(500mg 이상) 복용 – 일시적 높은 혈당

사용자 입장에서 기기 별 특징

	이점	불편한 점	초기 추천 환자
리브레2	• 1개의 앱에서 혈당 확인과 혈당 정리 • 센서 부착 용이 (시그널 넘버 입력 없음)	• 부착 상태나 휴대폰에 따라 신호 손실 잦음 • 다른 센서에 비해 크기가 큼 • 확인하지 않은 혈당 수치 확인이 어려움 – 웹에서 가능	→ 경제적인 측면 고려 → 센서 부착이 어려운 환자 → 일반적으로 많이 쓰는 기기
덱스콤 G7	• 높은 정확도 • 혈당 공유가 가능 • 혈당 확인 용이 (지나간 혈당에 대해서도)	• 가입이 어려움 – 실제 사용하는 메일 주소 필요 • 센서 부착 시 시그널 넘버 입력이 필요 • 살을 눌러 버튼 누르기	→ 혈당 정보 공유가 필요한 환자 → 높은 정확도를 원하는 환자 → 센서 부착 등 가까운 곳에서 도움이 가능한 환자
바로잰핏	• 가입이 간편함 – 카카오/구글/네이버 • 혈당 공유가 가능 • 혈당 확인 용이 (지나간 혈당에 대해서도) • 합리적 가격	• 센서 부착 시 시그널 넘버 입력이 필요 • 첫 24-48시간 정도 혈당이 지나치게 낮게 측정 • 센서 버튼 눌러야 시작	→ 혈당 정보 공유가 필요한 환자 → 경제적인 부분이 중요한 환자 → 24-48시간의 혈당 오차를 이해하는 환자 → 센서 부착 등 가까운 곳에서 도움이 가능한 환자

연속 혈당 측정기의 처방부터 부착까지

연속혈당측정장치 설명

- 연속혈당측정장치의 필요성에 대한 설명
- 기기(센서) 선택

센서 부착

- 센서 부착 비용 청구 가능 (cgm initiation)
- 센서 유지 시 혈당 조절 상담에 대한 비용 청구 가능 (cgm maintenance)

처방전 발행

- 누가 : 내과 전문의, 소아과 전문의, 산부인과 전문의 서류 발행
- 기간 : 첫 발행은 최대 한달 가능 (이후 최대 3개월 가능)
- 사용법 : 온라인, 오프라인 통해 구매 후 공단에 제출
- 서류 제출 : 공단에 처방전, 영수증 제출하여 환급 또는 온라인, 오프라인에서 처방전 대행 처리

연속 혈당 측정기의 적용 대상과 처방 과정

의료 보험 대상자 및 절차

☐ 누가 : 내과 전문의, 소아과 전문의, 산부인과 전문의
☐ 대상자 : 1형당뇨병 (E10), 임신 당뇨병 중 인슐린 쓰는 환자(O244)
☐ 처방전 종류 : “보험급여” 소모성 재료 처방전 (전극용), 당뇨병 관리기기 처방전 (송신기용)
☐ 서류 제출 : 의료기상 또는 약국에서 바로 처리 또는 처방전과 영수증을 공단에 제출하고 환급
☐ 지원 금액 : 10,000원/일 지원 (실 구입 금액의 70%, 한달 최대 약 21만원까지 가능)
☐ 주의 사항 : 리더기는 지원 대상 아님
※ 19세 미만은 11,000원/일 지원

연속 혈당 측정기의 적용 대상과 처방 과정

의료 급여 대상자 및 절차

☐ 누가 : 내과 전문의, 소아과 전문의, 산부인과 전문의
☐ 대상자 : 1형당뇨병 (E10), 임신 당뇨병 중 인슐린 쓰는 환자(O244)
☐ 처방전 종류 : “의료급여” 소모성 재료 처방전 (전극용), 당뇨병 관리기기 처방전 (송신기용)
☐ 서류 제출 : 처방전과 영수증을 **주민센터**에 제출하고 환급
☐ 지원 금액 : 10,000원/일 지원 (실 구입 금액의 70%, 한달 최대 약 21만원까지 가능)
☐ 주의 사항 : 리더기는 지원 대상 아님
※ 19세 미만은 11,000원/일 지원

연속 혈당 측정기의 적용 대상과 처방 과정

Case 1: 처음 1형당뇨병으로 등록하고 연속혈당측정기 시작하는 의료 보험 환자

- 건강보험 당뇨병환자 등록신청서 작성
- 이전 2형당뇨병으로 등록되어 있는 환자
  : 2형 → 1형당뇨병으로 전환 되었다는 진단서 또는 소견서 필요
- 보험급여) 당뇨병환자 소모성 재료 처방전(연속혈당측정용 전극)
- 첫 발행은 최대 한달 가능
  : 센서에 따라 일수 작성, 리브레 14일, 28일 / 덱스콤 G7 10일, 20일, 30일 / 바로잰핏 15일, 30일

Case 1: 처음 1형당뇨병으로 등록하고 연속혈당측정기 시작하는 의료 보험 환자

■ 요양비의 보험급여 기준 및 방법 [별지 제2호의3서식]

당뇨병환자 소모성재료 처방전(연속혈당측정용 전극)

※ 요양기관이 임의하여 요양급여와 요양비를 중복하여 급여를 받거나 국외 체류기간 중 구입한 경우 지급된 요양비는 환수될 수 있습니다.
※ 건강보험 당뇨병환자 등록 여부를 확인하시기 바라며, 최초 발행시 당뇨병환자 등록 신청서와 동시에 발행할 수 있습니다.
※ 그 밖의 유의사항 및 작성방법은 뒤쪽을 참고하여 주시기 바랍니다. (앞 쪽)

① ☐재발급

② 수진자		주민(외국인)등록번호	
		전화번호 (자택) (휴대전화)	

진료 과목	내분비내과	상병명	상세불명의 합병증을 동반한 1형 당뇨병	상병코드	E108

처방전 확인사항

③ 구분	④ 확인사항
☑1형 당뇨병	☐연속혈당측정 시작일 ( ) ~ 종료일 ( ) 기간 동안 착용일수 ( ) 일 또는 착용비율 ( ) %
☐임신 중 당뇨병 -분만예정일( )	☐당 평균값 ( )mg/dl ☐변동계수 ( )% 혹은 표준편차 ( )mg/dl ☐당화혈색소 검사내역 : 시행일 ( ), 검사수치 ( ) %

※ 임신 중 당뇨환자는 인슐린 투여자에 한하여 처방 가능합니다. 또한, 임신할 때마다 최초 처방 시 분만예정일을 반드시 기재해야하며, 분만예정일로부터 15일까지 요양비가 지원됩니다.

처방 및 지시사항

⑤ 총 처방기간	(30) 일	※ 총 처방기간은 100일(최초처방은 30일) 이내로 처방이 가능합니다.
처방전 사용기간	교부일로부터 처방기간까지	※ 사용기간 내에 구입 · 제출하여야 합니다.

2025년 05월 19일

요양기관명(기호) : 서울아산병원 (11100800)

← 보험급여 처방전

← 1형당뇨병 체크
첫 발행 시 '확인사항'은 공란 가능

← 첫 발행은 최대 한달 가능
센서에 따라 일수 작성,
리브레 14일, 28일
덱스콤 G7 10일, 20일, 30일
바로잰핏 15일, 30일

연속 혈당 측정기의 적용 대상과 처방 과정

Case 2: 연속 혈당 측정기를 유지 중인 1형당뇨병 환자, 의료 보험 환자

- 보험 급여) 당뇨병환자 소모성재료 처방전(연속혈당측정용 전극)
- 확인사항 (AGP 보고서 & 당화혈색소 기재 필요)

센서	센서 사용 앱	AGP 보고서 확인 앱
리브레	FreeStyle LibreLink –... Abbott Diabetes Care	https://www.libreview.com/
Dexcom G7	Dexcom G7 연속혈당측정기	Dexcom Clarity 의료
바로잰핏	바로잰 Fit 의료	바로잰 Care 건강 및 피트니스

- 최대 3개월 가능

  : 리브레 98일 / 덱스콤 G7 100일 / 바로잰핏 90일

Case 2: 연속 혈당 측정기를 유지 중인 1형당뇨병 환자, 의료 보험 환자

■ 요양비의 보험급여 기준 및 방법 [별지 제2호의3서식]

당뇨병환자 소모성재료 처방전(연속혈당측정용 전극용)

※ 요양기관에 입원하여 요양급여와 요양비를 중복하여 급여를 받거나 국외 체류기간 중 구입한 경우 지급된 요양비는 환수될 수 있습니다.
※ 건강보험 당뇨병환자 등록 여부를 확인하시기 바라며, 최초 발행시 당뇨병환자 등록 신청서와 동시에 발행할 수 있습니다.
※ 그 밖의 유의사항 및 작성방법은 뒤쪽을 참고하여 주시기 바랍니다. (앞 쪽)

① ☐ 재발급

② 수진자		주민(외국인)등록번호	
		전화번호	
진료 과목	내분비내과	상병명	상세불명의 합병증을 동반한 1형 당뇨병
상병코드	E108		

처방전 확인사항

구분	③ 확인사항
제1형 당뇨병	☑ 연속혈당측정 시작일 (2024.09.08) ~ 종료일 (2024.10.07) 기간 동안 착용일수 ( ) 일 또는 착용비율 (74) % ☑ 당 평균값 (143) mg/dl ☑ 변동계수 (30.1) % 혹은 표준편차 (43) mg/dl ☑ 당화혈색소 검사내역 : 시행일 (20240910), 검사수치 (6.0) %

처방 및 지시사항

④ 총 처방기간	(98) 일	※ 총 처방기간은 100일(최초처방은 30일) 이내로 처방이 가능합니다.
처방전 사용기간	교부일로부터 처방기간까지	※ 사용기간 내에 구입 · 제출하여야 합니다.

2024년 10월 08일

요양기관명(기호) : 서울아산병원 (11100800)

희

← AGP 보고서 중
연속혈당측정 시작일~종료일, 당 평균값, 변동계수

← 당화혈색소 검사 내역

← 최대 3개월 가능
리브레 98일
덱스콤 G7 100일
바로잰핏 90일

연속 혈당 측정기의 적용 대상과 처방 과정

Case 3: 임신 당뇨병 환자 중 인슐린을 쓰는 환자

- 당뇨병환자 소모성재료 처방전(연속혈당측정용 전극)
- 확인사항 (AGP 보고서 & 당화혈색소 기재 필요)

센서	센서 사용 앱	AGP 보고서 확인 앱
리브레	FreeStyle LibreLink –... Abbott Diabetes Care	https://www.libreview.com/
Dexcom G7	Dexcom G7 연속혈당측정기	Dexcom Clarity 의료
바로잰 핏	바로잰 Fit 의료	바로잰 Care 건강 및 피트니스

- 첫 발행은 최대 한달 가능, 이후 최대 3개월 가능
- **중요 : 분만 예정일 기재 필수, 분만 예정일로부터 15일까지 지원**

Case 3: 임신 당뇨병 환자 중 인슐린을 쓰는 환자

■ 요양비의 보험급여 기준 및 방법 [별지 제2호의3서식]

당뇨병환자 소모성재료 처방전(연속혈당측정용 전극)

※ 요양기관에 입원하여 요양급여와 요양비를 중복하여 급여를 받거나 국외 체류기간 중 구입한 경우 지급된 요양비는 환수될 수 있습니다.
※ 건강보험 당뇨병환자 등록 여부를 확인하시기 바라며, 최초 발행시 당뇨병환자 등록 신청서와 동시에 발행할 수 있습니다.
※ 그 밖의 유의사항 및 작성방법은 뒤쪽을 참고하여 주시기 바랍니다. (앞 쪽)

① ☐ 재발급

② 수진자		주민(외국인)등록번호	
		전화번호	(자택) (휴대전

진료 과목	내분비내과	상병명	임신중 생긴 당뇨병	상병코드	O244

처방전 확인사항

③ 구분	④ 확인사항
☐ 1형 당뇨병	☐ 연속혈당측정 시작일 ( ) ~ 종료일 ( ) 기간 동안 착용일수 ( ) 일 또는 착용비율 ( ) %
☑ 임신 중 당뇨병 -분만예정일(20250723)	☐ 당 평균값 ( )mg/dl ☐ 변동계수 ( )% 혹은 표준편차 ( )mg/dl ☐ 당화혈색소 검사내역 : 시행일 ( ), 검사수치 ( ) %

※ 임신 중 당뇨환자는 인슐린 투여자에 한하여 처방 가능합니다. 또한, 임신할 때마다 최초 처방 시 분만예정일을 반드시 기재 해야하며, 분만예정일로부터 15일까지 요양비가 지원됩니다.

처방 및 지시사항

⑤ 총 처방기간	(28) 일	※ 총 처방기간은 100일(최초처방은 30일) 이내로 처방이 가능합니다.
처방전 사용기간	교부일로부터 처방기간까지	※ 사용기간 내에 구입 · 제출하여야 합니다.

2025년 02월 10일

요양기관명(기호) : 서울아산병원 (11100800)

■ 요양비의 보험급여 기준 및 방법 [별지 제2호의3서식]

당뇨병환자 소모성재료 처방전(연속혈당측정용 전극)

※ 요양기관에 입원하여 요양급여와 요양비를 중복하여 급여를 받거나 국외 체류기간 중 구입한 경우 지급된 요양비는 환수될 수 있습니다.
※ 건강보험 당뇨병환자 등록 여부를 확인하시기 바라며, 최초 발행시 당뇨병환자 등록 신청서와 동시에 발행할 수 있습니다.
※ 그 밖의 유의사항 및 작성방법은 뒤쪽을 참고하여 주시기 바랍니다. (앞 쪽)

① ☐ 재발급

② 수진자		주민(외국인)등록번호	
		전화번호	(자택) (휴대전화)

진료 과목	내분비내과	상병명	임신중 생긴 당뇨병	상병코드	O244

처방전 확인사항

③ 구분	④ 확인사항
☐ 1형 당뇨병	☑ 연속혈당측정 시작일 (2025.03.25) ~ 종료일 (2025.04.07) 기간 동안 착용일수 ( ) 일 또는 착용비율 (99) %
☑ 임신 중 당뇨병 -분만예정일(20250723)	☑ 당 평균값 (105)mg/dl ☑ 변동계수 (23.4)% 혹은 표준편차 ( )mg/dl ☑ 당화혈색소 검사내역 : 시행일 (2025.01.06), 검사수치 (5.7) %

※ 임신 중 당뇨환자는 인슐린 투여자에 한하여 처방 가능합니다. 또한, 임신할 때마다 최초 처방 시 분만예정일을 반드시 기재 해야하며, 분만예정일로부터 15일까지 요양비가 지원됩니다.

처방 및 지시사항

⑤ 총 처방기간	(42) 일	※ 총 처방기간은 100일(최초처방은 30일) 이내로 처방이 가능합니다.
처방전 사용기간	교부일로부터 처방기간까지	※ 사용기간 내에 구입 · 제출하여야 합니다.

2025년 03월 10일

요양기관명(기호) : 서울아산병원 (11100800)

담당의사

전문과목(

연속 혈당 측정기의 처방부터 부착까지

연속혈당측정장치 설명

- 연속혈당측정장치의 필요성에 대한 설명
- 기기(센서) 선택

센서 부착

- 센서 부착 비용 청구 가능 (cgm initiation)
- 센서 유지 시 혈당 조절 상담에 대한 비용 청구 가능 (cgm maintenance)

처방전 발행

- 누가 : 내과 전문의, 소아과 전문의, 산부인과 전문의 서류 발행
- 기간 : 첫 발행은 최대 한달 가능 (이후 최대 3개월 가능)
- 사용법 : 온라인, 오프라인 통해 구매
- 서류 제출 : 공단에 처방전, 영수증 제출하여 환급 또는 온라인, 오프라인에서 처방전 대행 처리

연속 혈당 측정기 센서 부착

센서 부착에 대한 비용 청구

- 센서 부착 비용 청구 가능 (cgm initiation)
- 센서 유지 시 혈당 조절 상담에 대한 비용 청구 가능 (cgm maintenance)

센서 부착 위치

- 상완 뒷 부분 – 지방층이 많은 곳
- 움직임이 덜한 곳
- 수면 시 덜 눌리는 위치의 상완

센서 삽입 및 고정

- 센서 부착 후 멈춤 (10–30초) : 누르면서 멈추지 않기
- 접착 패치 부착
- 센서 연결 확인 (리브레 : 스캔, 바로잰핏 : 버튼 누르고 연결 확인, 덱스콤 : 연결 확인)

센서별 부착 방법 – QR 코드로 확인하세요 !!

리브레	바로잰 fit	케어센스 에어	덱스콤

연속 혈당 측정기 사용 시 주의 사항

부착 시 주의 사항	부착 위치
▪ 소독 후 소독액이 마른 상태에서 센서 부착 ▪ 센서 부착 후 멈춤 시 누르면서 멈추지 않기 – '붙잡고 있는다'	▪ 상완 뒷 부분, 수면 중 눌리는 부분은 피하기 – 저혈당 알람 또는 센서 연결 끊김
부착 부위	**운동 및 일상 생활**
▪ 부착 부위 정기적 관찰 ▪ 센서에 따라 다른 부착제 사용 ▪ 피부 트러블 시 즉시 제거	▪ 수영 전 방수 확인 (30분 이상 물속 안됨) ▪ 센서 부착 부위 충격 주의 ▪ 땀 많을 시 추가 고정 및 유연성 있는 적용

감사합니다

03 Session 당뇨병 동반 질환 제대로 관리하기

지방간, 놓치면 손해! 조기 진단과 치료 업데이트

서울아산병원 소화기내과 **최원묵**

당뇨병 만성콩팥병 관리의 모든 것

서울아산병원 내분비내과 **민세희**

당뇨병 환자의 뇌 건강, 어떻게 지킬까?

서울아산병원 신경과 **임재성**

03
Session

당뇨병 동반 질환 제대로 관리하기

지방간, 놓치면 손해! 조기 진단과 치료 업데이트

서울아산병원 소화기내과 **최원묵**

대사이상지방간질환(Metabolic dysfunction-associated steatotic liver disease, MASLD)은 기존의 비알코올성 지방간질환(NAFLD)을 대체하는 새로운 개념으로, 단순한 음주력 유무가 아닌 대사 이상(예: 제2형 당뇨병, 비만, 고혈압, 이상지질혈증 등)을 기반으로 정의되는 간질환이다. MASLD는 질환의 병태생리와 임상적 연관성을 보다 명확히 반영하는 명칭으로, 최근 국제 학계에서 빠르게 받아들여지고 있다. 특히 **서구화된 식습관, 좌식 생활, 대사이상질환의 유병 증가**에 따라 MASLD의 발생률은 전 세계적으로 급속히 증가하고 있으며, 한국을 포함한 아시아 지역에서도 유사한 추세를 보인다. MASLD는 일반 인구에서의 유병률도 상당하지만, **특히 제2형 당뇨병 환자에서는 MASLD의 유병률이 약 2배 이상 높으며,** 이들에서의 MASLD는 간질환뿐 아니라 심혈관질환 및 악성종양 등 여러 전신적 합병증의 위험을 높이는 것으로 알려져 있다. MASLD의 장기 예후에 있어서 가장 중요한 인자는 **간섬유화의 정도이며,** 간경변증과 간세포암뿐 아니라 **심혈관계 질환 및 암**이 주요 사망 원인으로 보고되고 있다. 이에 따라 당뇨병 환자에서 MASLD에 대한 적극적인 선별검사(screening)가 필요하며, **복부 초음파, FIB-4 index, FibroScan**과 같은 **비침습적 평가 도구**를 활용하여 고위험군을 분류하고, 필요시 간조직검사까지 고려하는 단계적 접근이 권장된다.

MASLD의 치료 전략에서 가장 핵심이 되는 것은 **생활습관 개선**이다. 특히 **체중의 7~10% 감량**을 달성할 경우 지방간염의 소실과 섬유화의 역전 가능성이 보고되고 있으며, 이는 모든 MASLD 환자에서 기본이 되는 치료 원칙이다. 이와 더불어, **제2형 당뇨병이 동반된 MASLD 환자**에서는 혈당 조절과 간기능 개선을 동시에 기대할 수 있는 GLP-1 수용체 작용제와 SGLT-2 억제제의 사용이 점차 임상 현장에서 확대되고 있다. 특히 최근 발표된 여러 무작위 임상시험 결과에서 이들 약물은 체중 감소뿐 아니라 **간효소 정상화, 간지방 감소, 조직학적 호전**까지 입증된 바 있다. 반면, **당뇨병이 없는 MASLD 환자**에서는 **고용량 비타민 E**가 간조직 개선에 일부 효과를 보이며 제한적으로 사용되고 있다.

MASLD는 이제 단순한 간질환의 범주를 넘어, **대사질환 및 만성질환 관리의 핵심 요소**로 인식되고 있다. 본 강의에서는 실제 임상에서 마주치는 다양한 증례를 바탕으로 MASLD의 진단과 감별, 단계적 평가 전략, 그리고 최신 치료 지견을 통합적으로 정리하여 제시하고자 한다. 이를 통해 당뇨병 환자에서 MASLD를 보다 체계적이고 효과적으로 관리하기 위한 실질적인 접근법을 공유하고자 한다.

2025년 서울아산병원 당뇨병 센터 개원의 연수강좌

당뇨병 환자에서의 대사이상지방간질환: 이렇게 진단하고 관리하자

서울아산병원 소화기내과

최 원 묵

1. Introduction
2. Prognosis of MASLD
3. Diagnosis of MASLD
4. Treatment of MASLD
5. Summary

서울아산병원 Asan Medical Center

Introduction

서울아산병원 Asan Medical Center

Case 1

Age	54 years
Gender	Male
Weight	83.5 kg
Height	175 cm
BMI	27.3 kg/m^2

Brief History

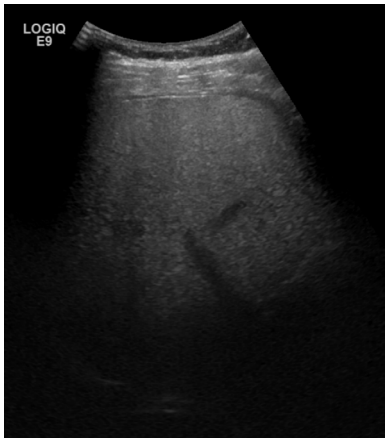
- **Duration of T2DM**: since 2014
- **Current Medications**
  - Glimepiride/Metformin 2/500 mg 1T BID
- **Past Medical History**
  - DM/HTN/Dyslipidemia (+/-/-)
  - Alcohol: 주 4회, 소주 1병/회
- **Laboratory Findings**
  - AST/ALT 82/121 IU/L, GGT 211 IU/L
  - HbA1c 8.5%

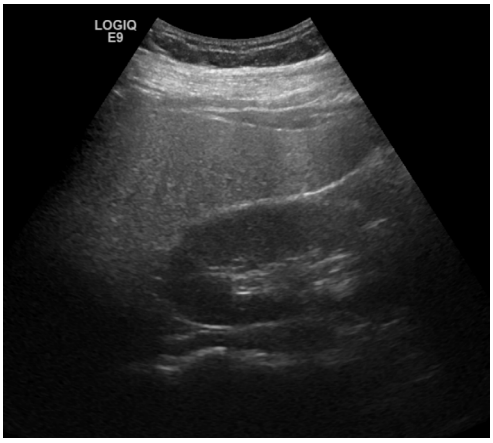
서울아산병원 Asan Medical Center

Case 1

Age	54 years
Gender	Male
Weight	83.5 kg
Height	175 cm
BMI	27.3 kg/m^2

Abdomen USG

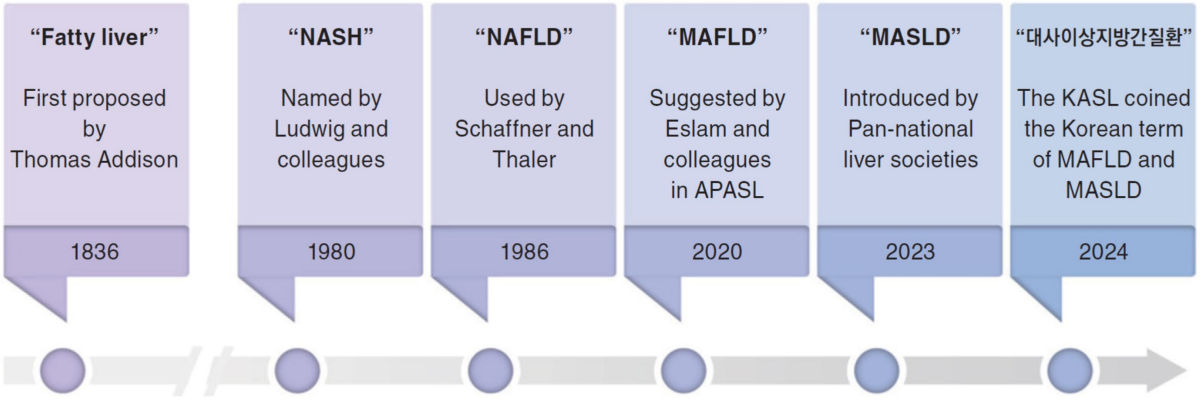




이 환자분은 대사이상지방간질환으로 진단할 수 있을까요?

서울아산병원 Asan Medical Center

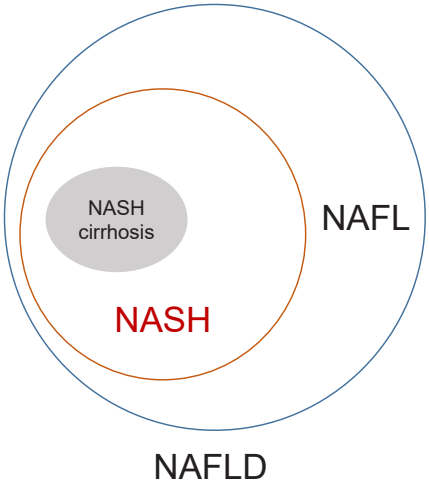
지방간질환의 변천사 및 명명법



서울아산병원 Asan Medical Center

Clin Mol Hepatol. 2025

NAFLD and related definitions



- **NAFLD:** the entire spectrum of fatty liver disease without significant alcohol consumption
- **NAFL:** Presence of ≥5% hepatic steatosis without evidence of hepatocellular injury or fibrosis
- **NASH:** Presence of ≥5% hepatic steatosis + inflammation and hepatocyte injury (ballooning) with or without fibrosis
- Causes of secondary hepatic steatosis
: Alcohol, hepatitis C, Wilson's disease, starvation, parenteral nutrition, medications (amiodarone, methotrexate, tamoxifen, steroids, valproate,…)

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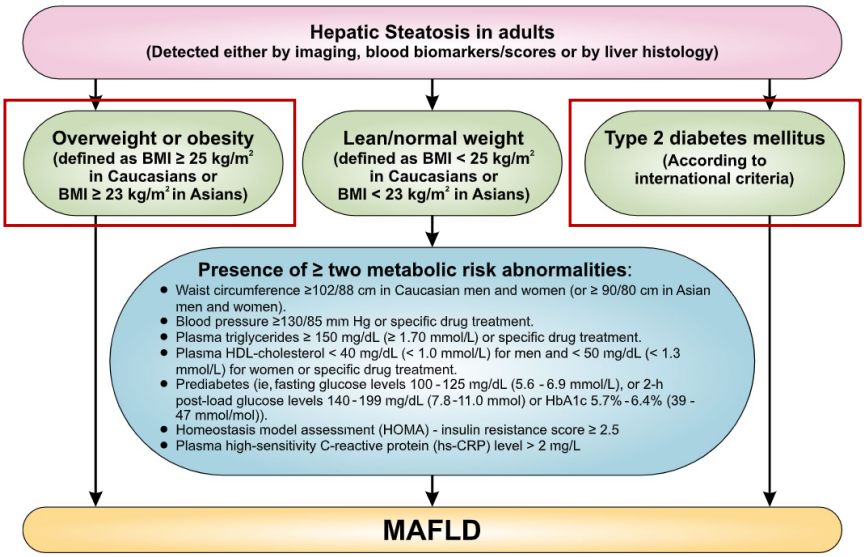
Hepatology. 2018

Metabolic associated fatty liver disease



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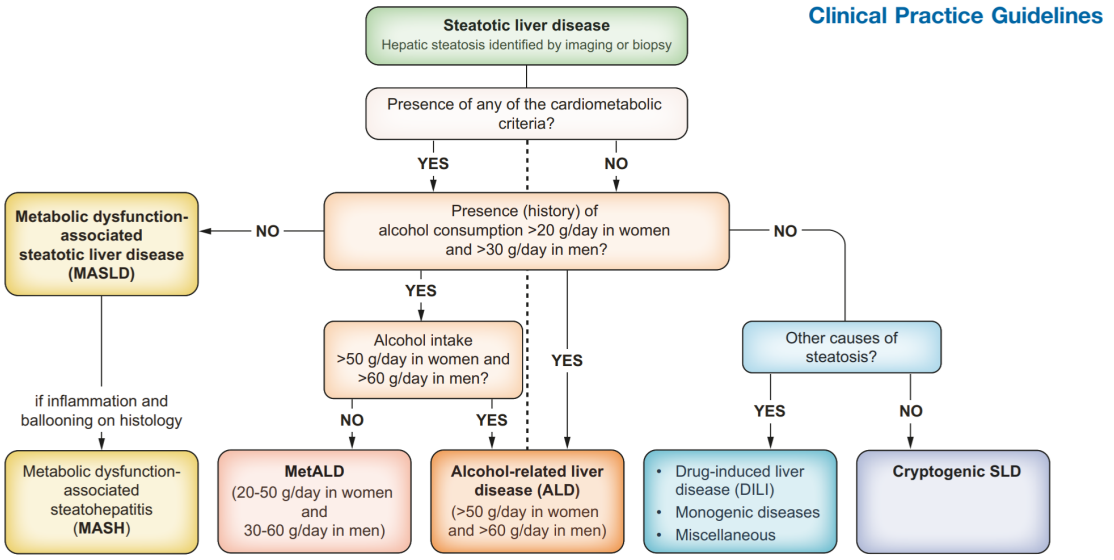
Liver Int. 2020

Metabolic dysfunction-associated steatotic liver disease (MASLD)



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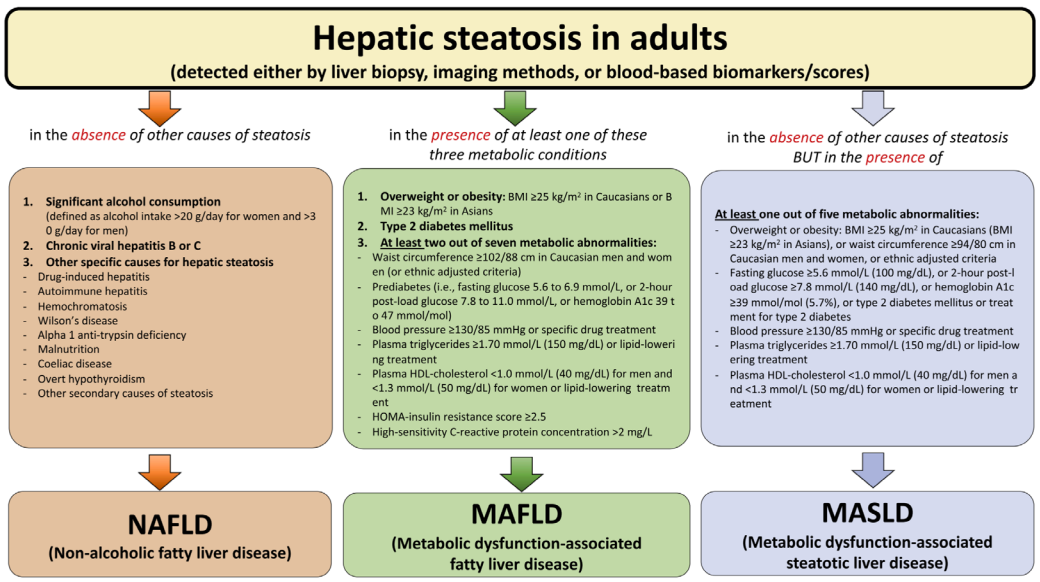
J Hepatol. 2024

Comparison between diagnostic criteria



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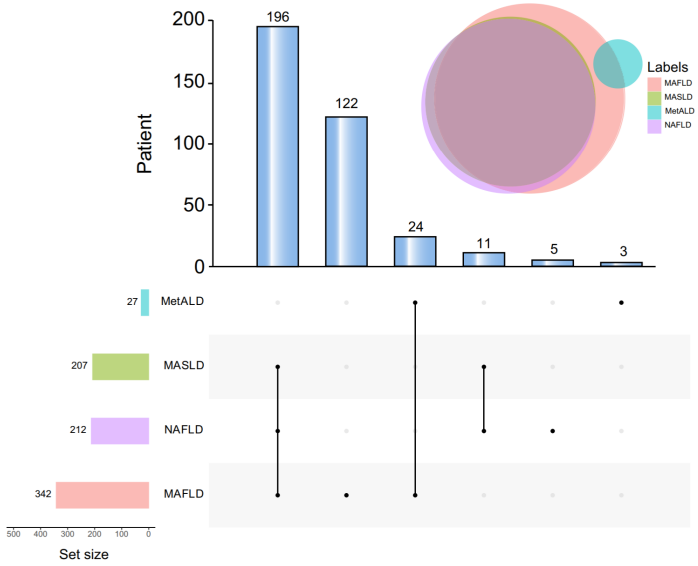
Diabetes Metab. 2024

Comparing intersections of MASLD/MAFLD/NAFLD



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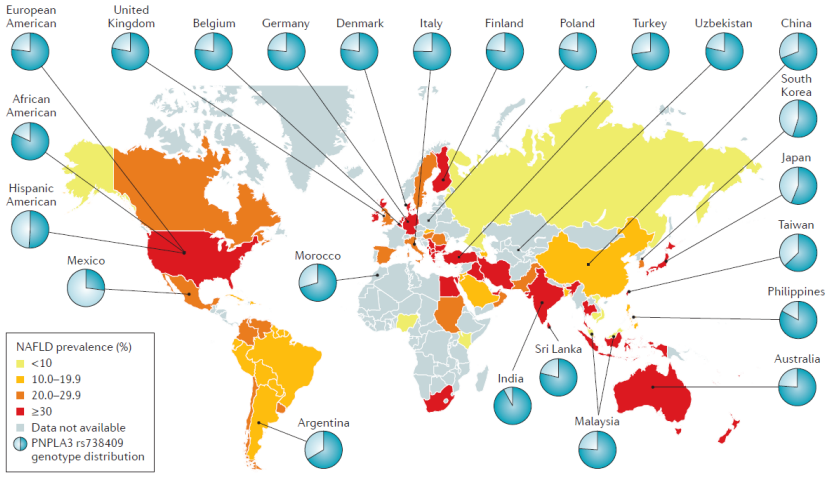
J Hepatol. 2024

Worldwide prevalence of NAFLD



- The prevalence of NAFLD is constantly increasing (15% in 2005 to 25% in 2010).
- The prevalence of NASH in the general population ranges between **1.5% and 6.45%**.

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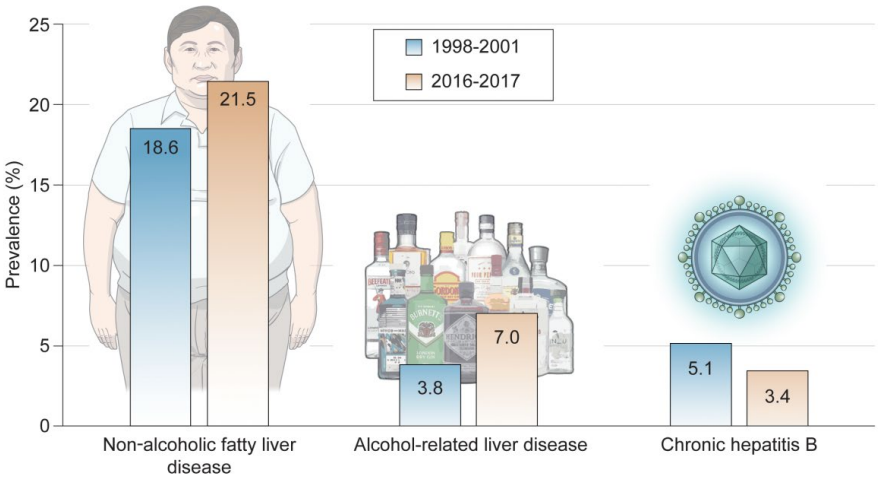
Nat Rev Gastroenterol Hepatol. 2018

NAFLD in Korea



- The prevalence of NAFLD increased from 18.6% to 21.5% between 1998–2001 and 2016–2017.

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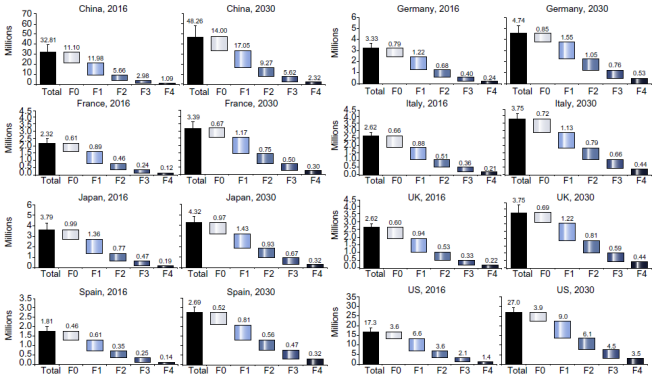
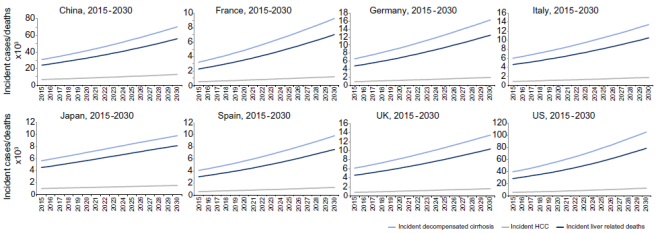
Clin Mol Hepatol. 2020

Increasing disease burden of NAFLD

NASH population



Outcome (cirrhosis, HCC, liver-related death)



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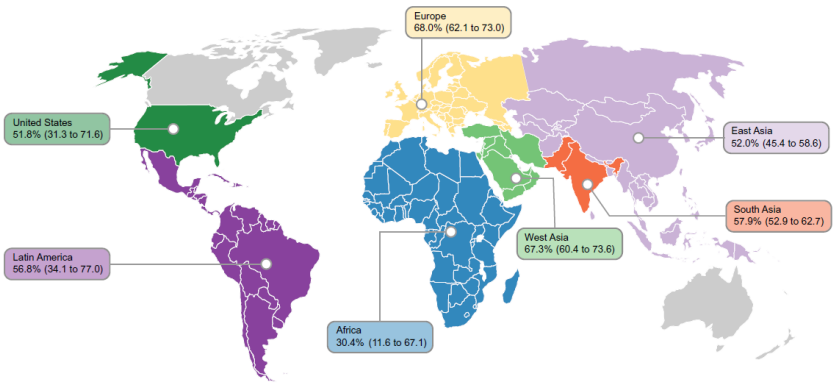
J Hepatol. 2018

Global prevalence of NAFLD in T2DM



Global prevalence of NAFLD among T2DM patients 55.5%
(95% confidence interval: 47.3-63.7)

- NAFLD prevalence in T2DM is more than 2-fold higher than in the general population.
- The global prevalence of NASH in T2DM is 37.3%.

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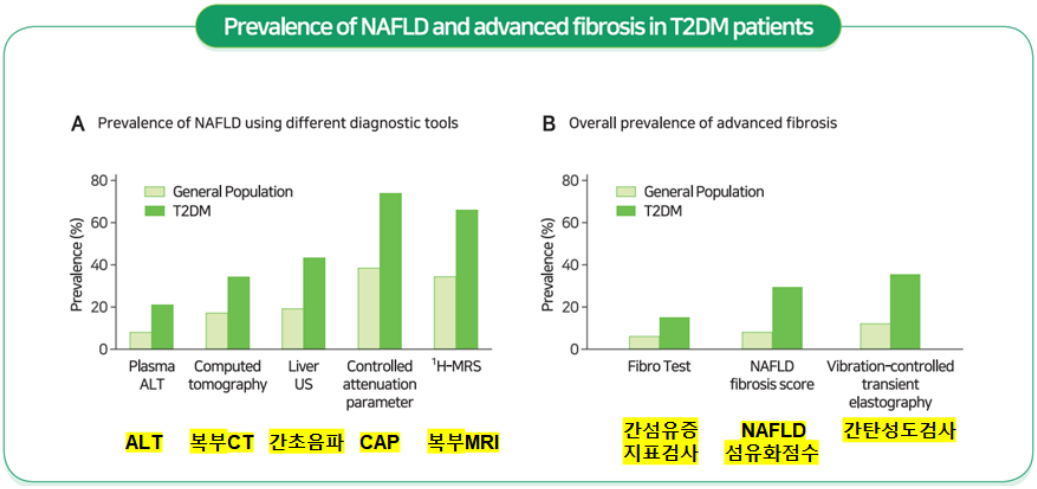
J Hepatol. 2019

Prevalence of Liver Disease in T2DM patients



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Diabetes Care. 2017

Case 1

Age	54 years
Gender	Male
Weight	83.5 kg
Height	175 cm
BMI	27.3 kg/m^2

Brief History

- **Past Medical History**
  - DM/HTN/Dyslipidemia (+/-/-)
  - Alcohol: 주 4회, 소주 1병/회
- **Laboratory Findings**
  - AST/ALT 82/121 IU/L, GGT 211 IU/L
  - HbA1c 8.5%

- **약 28g/day의 음주량을 동반한 상태로 MetALD로 진단이 가능함. NAFLD는 아니며, MAFLD에는 해당함.**

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Prognosis of MASLD

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Case 2

Age	65 years
Gender	Male
Weight	76 kg
Height	170 cm
BMI	26.3 kg/m^2

Brief History

- 2년 전 당뇨병을 진단 받고 당뇨약 복용 중으로 검진 목적으로 시행한 검사 상 간수치 상승 소견 보여 내원함.
- **Past Medical History**
  - DM/HTN/Dyslipidemia (+/+/+)
  - Alcohol: none
- **Laboratory Findings**
  - AST/ALT 132/242 IU/L, GGT 120 IU/L
  - ANA Speckled 1:80, IgG 1785 mg/dL
  - USG: moderate degree fatty liver
  - Fibroscan: LSM 9.8 kPa, CAP 321 dB/m

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Case 2

Age	65 years
Gender	Male
Weight	76 kg
Height	170 cm
BMI	26.3 kg/m^2

Liver biopsy

DIAGNOSIS :
A) Liver, US guided core needle biopsy:
- Mild fatty change with ballooning degeneration
- Moderate portal inflammation
- Septal and perisinusoidal fibrosis,

consistent with steatohepatitis, grade 2, stage 3

이 환자의 예후에 가장 중요한 요소는?

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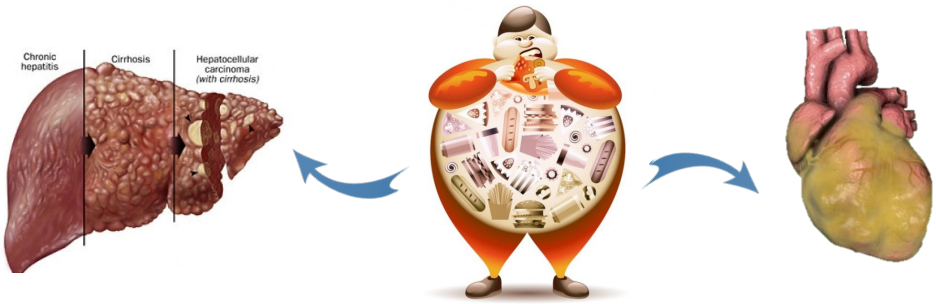
Natural history of NAFLD



Liver diseases
- NASH
- LC
- HCC

Cardiovascular and metabolic disease
- DM, HTN, DL
- CVD

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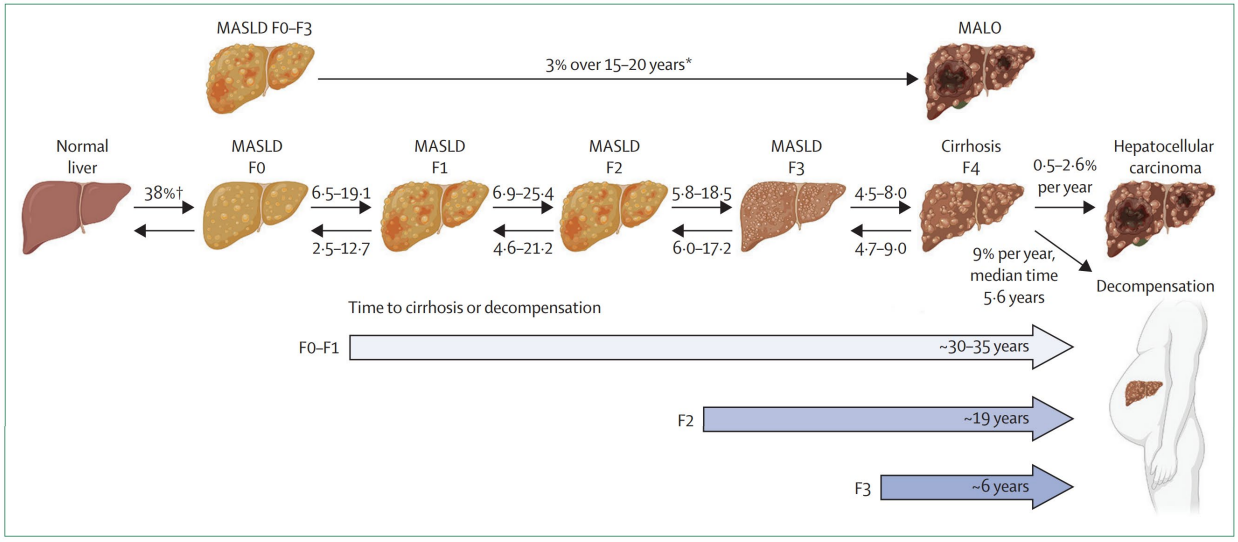
Cell Biol Toxicol. 2017

Natural history of NAFLD/MASLD



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Lancet Gastroneterol Hepatol. 2024

Outcome of NAFLD in meta-analysis

Incidence and IRR for progression of NAFLD and NASH

Population	Outcome	Incidence Rate Per 1,000 Person-Years*	Number of Studies	95% CI	I^2 (%)	Follow-up (Years)
NAFLD	CVD-specific mortality	4.79	6	(3.43-6.7)	91.17	12.96
NAFLD	HCC	0.44	3	(0.29-0.66)	0.00	5.82
NAFLD	Liver-specific mortality	0.77	7	(0.33-1.77)	91.84	13.17
NAFLD	Overall mortality	15.44	7	(11.73-20.34)	97.17	13.17
NASH	Advanced fibrosis	67.95	3	(46.84-98.56)	9.80	4.05
NASH	HCC	5.29	1	(0.75-37.56)	NA	4.50
NASH	Liver-specific mortality	11.77	3	(7.1-19.53)	0.00	8.08
NASH	Overall mortality	25.56	2	(6.29-103.8)	73.85	6.17
		IRR*				
NAFLD	Liver-specific mortality	1.94	5	(1.28-2.92)	26.78	13.38
NAFLD	Overall mortality	1.05	5	(0.7-1.56)	97.99	13.38
NASH	Liver-specific mortality	64.6	3	(35.43-117.8)	0.00	8.08
NASH	Overall mortality	2.56	2	(0.63-10.39)	73.76	6.17

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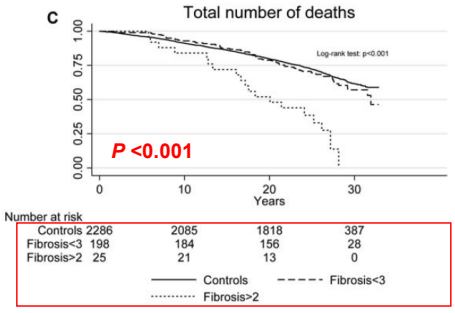
Hepatology. 2016

Most important predictor for mortality in NAFLD

Case: 229 patients with biopsy-proven NAFLD
Controls: the National Registry of Population
Mean follow-up: 26.4 (range 6-33) years

Cause of Death	Number of Patients (n = 96)
Cardiovascular disease	41 (43%)
Non-gastrointestinal malignancy	18 (19%)
Hepatocellular carcinoma	5 (5%)
Infection	5 (5%)
Gastrointestinal malignancy	4 (4%)
Cirrhosis	4 (4%)
Endocrine	3 (3%)*
Respiratory	3 (3%)
Other	7 (7%)
Missing	6 (6%)



- **Fibrosis stage** was the most useful marker to predict future mortality in patients with NAFLD

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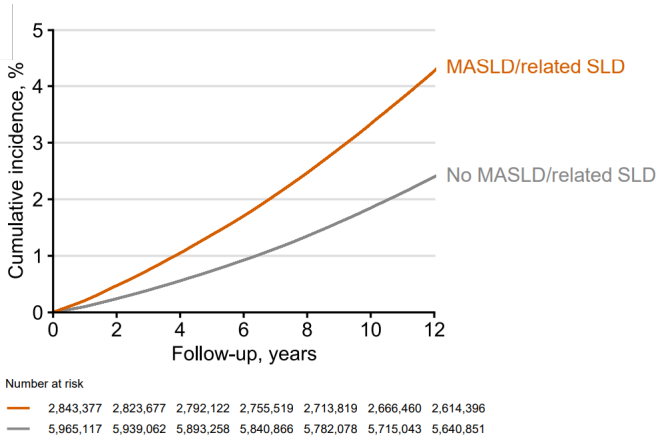
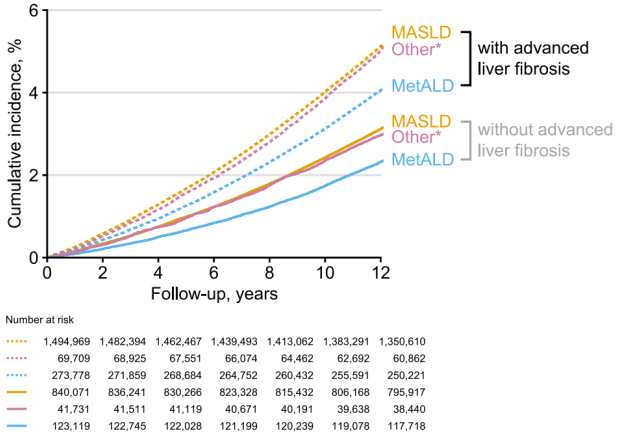
Hepatology. 2015

MASLD and risk of cardiovascular disease

- Nationwide study in Korea (n = 9,775,066)





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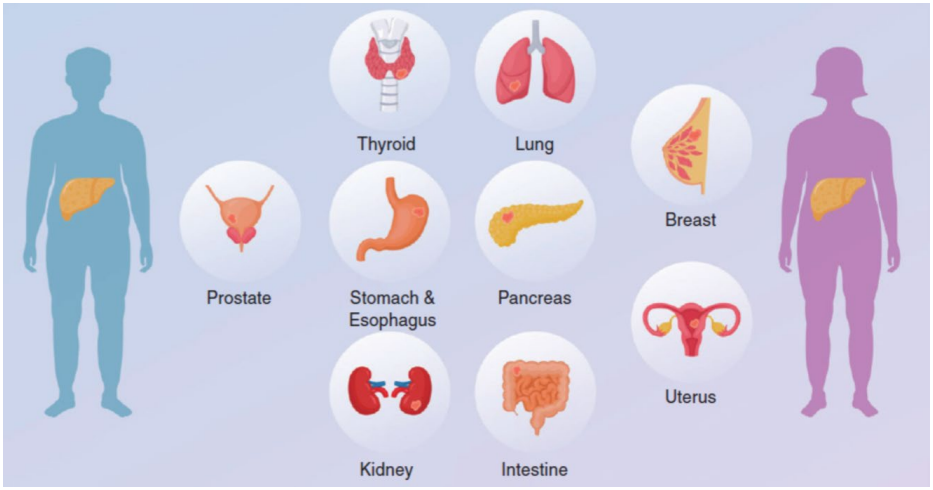
Gut. 2023

MASLD and extrahepatic malignancy risk

- Risk factors: Obesity, type 2 diabetes



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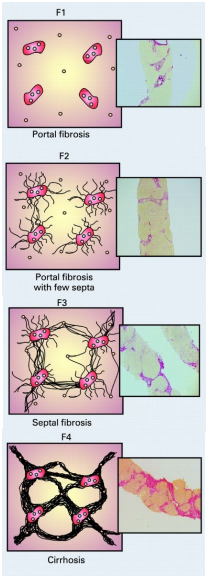
Clin Mol Hepatol. 2025

Fibrosis progression rate of NAFLD

		Final fibrosis stage					Total stages of fibrosis progressed	Person-years of follow-up evaluation	FPR (95% CI)	Time taken to progress by 1 stage (95% CI)
NAFLD (11 studies)										
		0	1	2	3	4				
Baseline fibrosis stage	0 (131)	79	28	13	7	4	+91	968	0.13 (0.07–0.18)	7.7 (5.5–14.8)
	1 (119)	26	44	32	15	2	+43	628.4	0.10 (0.04–0.16)	10.0 (6.2–25.0)
	2 (61)	9	17	14	13	8	−6	331.8	NA	-
	3 (34)	2	5	10	7	10	−16	153.4	NA	-
	4 (21)	0	0	1	6	14	−8	63.8	NA	-
	Overall (366)						+104	2145.4	NA	-
	Stage 0 plus stage 1 fibrosis (250)						+134	1596.4	0.12 (0.07–0.16)	8.3 (6.2–14.3)
NAFL (6 studies)										
		0	1	2	3	4				
Baseline fibrosis stage	0 (81)	52	16	8	4	1	+48	751.3	0.07 (0.02–0.11)	14.3 (9.1–50.0)
	1 (39)	6	13	14	6	0	+20	112.6	0.15 (-0.09 to 40)	NA
	2 (13)	2	3	5	2	1	−3	40.7	NA	-
	3 (0)	0	0	0	0	0	0	0	NA	-
	4 (0)	0	0	0	0	0	0	0	NA	-
	Overall (133)						+75	904.6	NA	-
	Stage 0 plus stage 1 fibrosis (120)						+68	863.9	0.09 (0.04–0.14)	11.1 (7.1–25.0)
NASH (7 studies)										
		0	1	2	3	4				
Baseline fibrosis stage	0 (21)	10	7	2	1	1	+18	115.5	0.14 (0.07–0.21)	7.1 (4.8–14.3)
	1 (49)	9	25	9	5	1	+13	396.6	0.08 (-0.01 to 0.17)	NA
	2 (25)	3	10	4	4	4	−4	222.3	NA	
	3 (16)	0	4	4	2	6	−6	95.8	NA	
	4 (5)	0	0	0	1	4	−1	12.6	NA	
	Overall (116)						+20	842.8	NA	
	Stage 0 plus stage 1 fibrosis (70)						+31	512.1	0.10 (0.03–0.17)	10.0 (5.9–33.3)



- Patients with NAFL progresses **one stage of fibrosis every 14 years.**
- Patients with NASH progresses **one stage of fibrosis every 7 years.**

서울아산병원 Asan Medical Center

Clin Gastroenterol Hepatol. 2015

Case 2

Age	65 years
Gender	Male
Weight	76 kg
Height	170 cm
BMI	26.3 kg/m^2

Liver biopsy

DIAGNOSIS :
A) Liver, US guided core needle biopsy:
- Mild fatty change with ballooning degeneration
- Moderate portal inflammation
- Septal and perisinusoidal fibrosis,

consistent with steatohepatitis, grade 2, stage 3

- 이 환자에서 가장 중요한 예후 인자는 간섬유화의 정도이며, 대사이상지방간염 관리를 안할 시 약 7년 뒤에는 간경변증으로 진행 가능함을 설명

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Diagnosis of MASLD

서울아산병원 Asan Medical Center

Case 3

Age	66 years
Gender	Female
Weight	62kg
Height	158 cm
BMI	24.8 kg/m^2

Brief History

- 3년 전 당뇨병을 진단 받고 당뇨약 복용 중으로 간수치 상승 소견 보여 내원함
- **Past Medical History**
  - DM/HTN/Dyslipidemia (+/+/+)
  - Alcohol: none
- **Laboratory Findings**
  - AST/ALT 95/211 IU/L, GGT 234 IU/L,
  - Platelet count 131×10^3/μL
  - Hepatic steatosis index 46.6 (>36)
  - FIB-4 index 3.29

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Diagnosis of NAFLD

- **지속적 간효소수치 상승이 있거나, 당뇨병이 있는 경우 비알코올 지방간질환 선별검사를 시행한다. (A1)**
- **대사증후군, 비만, 비알코올 지방간질환 발생 위험인자가 있는 경우 선별검사**를 시행할 수 있다. (B1)
- 선별검사를 위해 **복부초음파 검사를 일차적으로 시행**할 수 있다. (B1)
- 비알코올 지방간염 또는 진행된 간섬유화 등 고위험군이 의심되는 경우에 간 조직검사를 시행할 수 있다. (B1)
- 다른 간질환의 배제가 필요한 경우에 간 조직검사를 시행할 수 있다. (B1)

→ 간조직검사의 제한점: 1) 표본오차, 2) intra and inter-observer variability, 3) 침습적임

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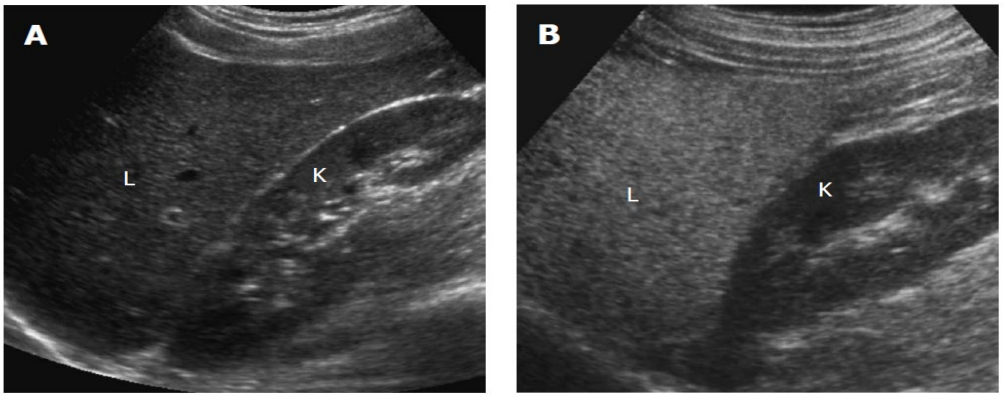
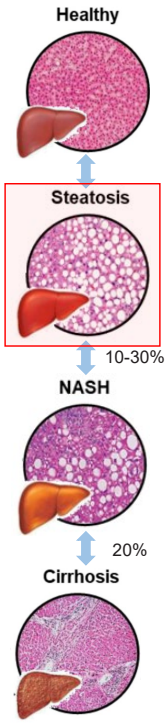
대한간학회 비알코올 지방간질환 진료 가이드라인. 2021.

Imaging tests for NAFL: 1) Ultrasound

L : Liver parenchyma / K : Kidney cortex
A : Normal / B : Hepatic steatosis





- Sensitivity: 60 – 94%, Specificity: 84 – 95%
- Sensitivity >90% when >20% hepatic steatosis

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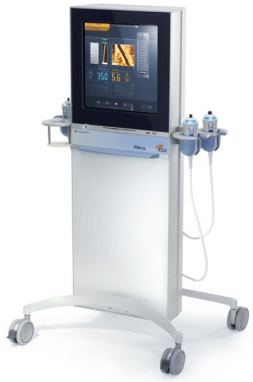
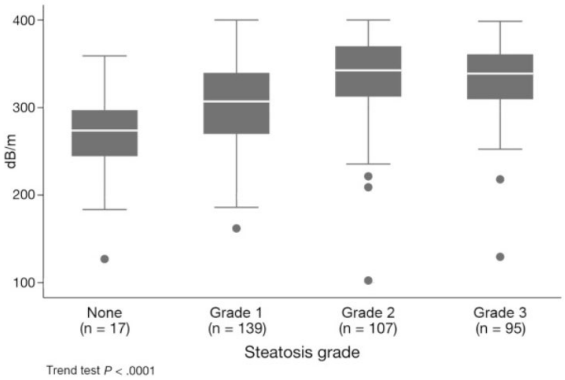
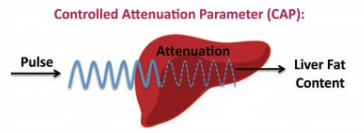
World J Gastroenterol. 2019

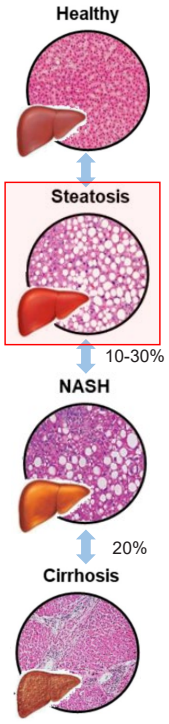
Imaging tests for NAFL: 2) Fibroscan (CAP)







- S1(5-33%): 299> CAP value ≥250 dB/m
- S2(34-66%): 327> CAP value ≥299 dB/m
- S3(>66% steatosis of hepatocytes): CAP value ≥ 327 dB/m



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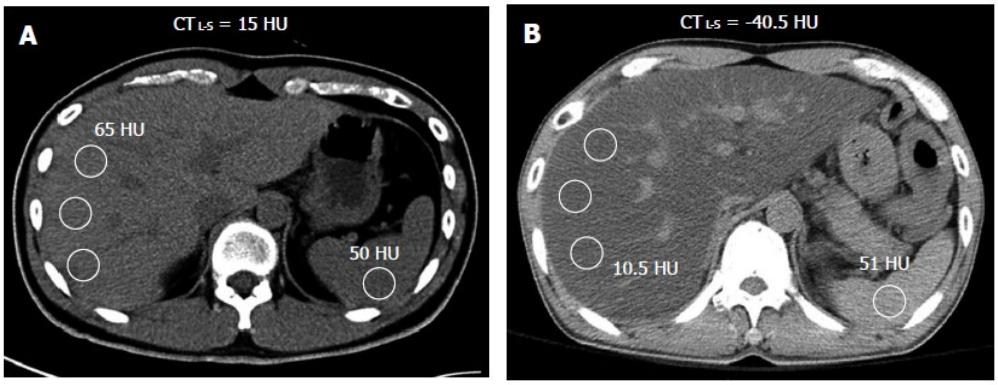
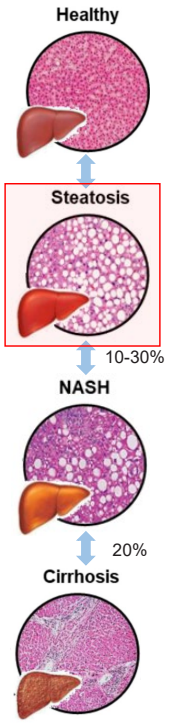
Liver Int. 2014

Imaging tests for NAFL: 3) CT



A : Normal / B : Hepatic steatosis

- Unenhanced CT scans are usually preferred.
- Moderate-to-severe hepatic steatosis when hepatic-splenic attenuation ratio is <0.8.



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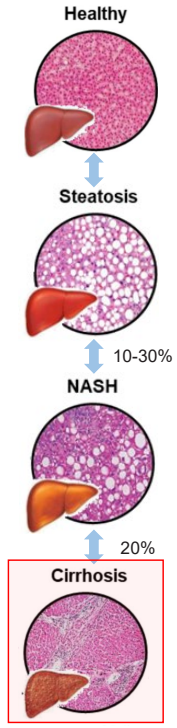
World J Gastroenterol. 2019

Non-invasive tests for fibrosis: Blood marker

Table 2 | Biomarkers and prediction scores of liver fibrosis in NAFLD

Score	Components	Class I or II biomarkers	F2		F3	
			Sensitivity	Specificity	Sensitivity	Specificity
Specific for NAFLD						
NAFLD fibrosis score[82]	Age, hyperglycaemia, BMI, platelet, albumin, AST/ALT ratio (dual cut-offs)	II	–	–	0.77	0.96
BARD score[111]	BMI, AST/ALT ratio, diabetes	II	–	–	0.62	0.66
FibroMeter NAFLD[112]	Glucose, AST, ferritin, platelet, ALT, body weight, age	II	0.79	0.96	–	–
Not specific for NAFLD						
AST/ALT ratio[113]	AST, ALT	II	–	–	0.21	0.90
APRI[114]	AST, platelets (dual cut-offs)	II	–	–	0.65	0.97
ELF[115]	Hyaluronic acid, TIMP1, PIIINP (dual cut-offs)	I	0.80	0.67	0.80	0.90
FIB-4[116]	Age, AST, platelet, ALT (dual cut-offs)	II	–	–	0.74	0.98
FibroTest[117]	Total bilirubin, GGT, α_2-macroglobulin, ApoA1, haptoglobin (dual cut-offs)	I and II	0.71	0.98	0.88	0.99



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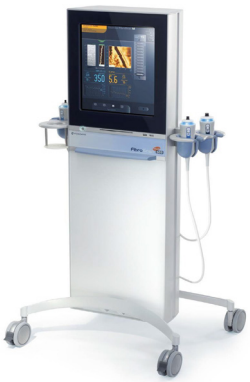
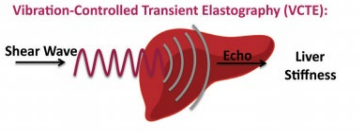
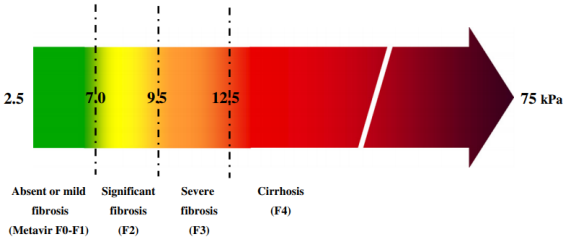
Nat Rev Gastroenterol Hepatol. 2018

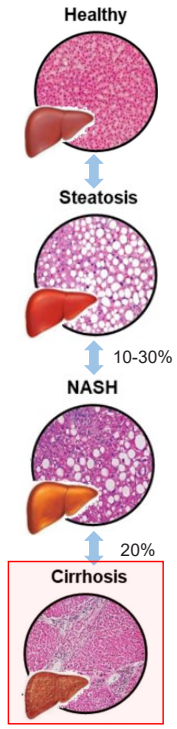
Non-invasive tests for fibrosis: Fibroscan







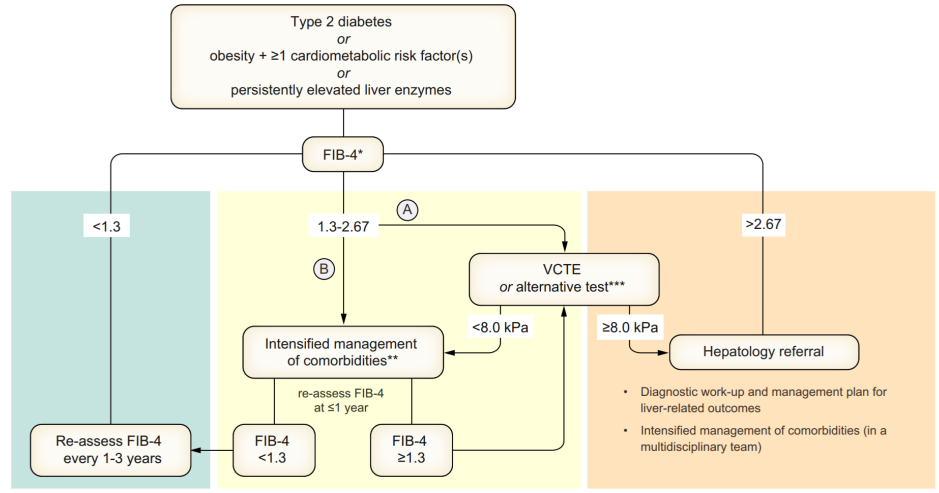
- High AUROC
  - LC : 0.87-0.98
  - Significant fibrosis 0.75-0.93
- Limitations: Ascites, obesity
  - XL probe (2.5MHz); Lower value than M probe



서울아산병원 Asan Medical Center

J Hepatol. 2008

Proposed strategy for identifying high-risk patients



* FIB-4 thresholds valid for age ≤65 years (for age >65 years: lower FIB-4 cut-off is 2.0)
** *e.g.* lifestyle intervention, treatment of comorbidities (*e.g.* GLP1RA), bariatric procedures
*** *e.g.* MRE, SWE, ELF, with adapted thresholds
Ⓐ and Ⓑ are options, depending on medical history, clinical context and local resources

서울아산병원 Asan Medical Center

J Hepatol. 2024

Case 3

Age	66 years
Gender	Female
Weight	62kg
Height	158 cm
BMI	24.8 kg/m^2

Liver biopsy

DIAGNOSIS :
A) Liver, US guided core needle biopsy:
- Moderate fatty change with ballooning degeneration
- Severe portal inflammation
- Septal fibrosis

consistent with steatohepatitis, grade 3, stage 3

- 당뇨병이 있는 환자에서는 **복부초음파를 이용하여 대사이상지방간질환에 대한 선별검사를 권고**하며, **FIB-4 index, Fibroscan** 검사를 통해 중등도 혹은 고위험군이라면 상급병원으로 refer를 고려

서울아산병원 Asan Medical Center

Treatment of MASLD

서울아산병원 Asan Medical Center

Case 4

Age	45 years
Gender	Female
Weight	70kg
Height	158 cm
BMI	28.0 kg/m^2

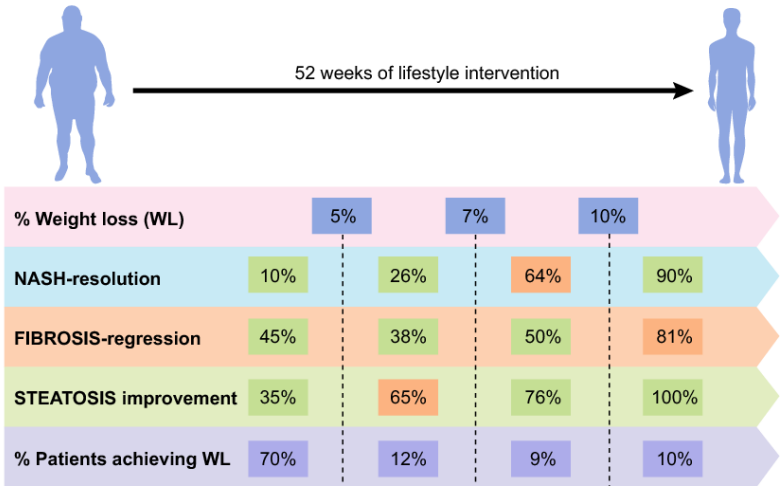
Brief History

- 이전 건강하던 분으로 건강검진 시 혈당 상승 및 간수치 상승 소견 보여 내원함.
- **Past Medical History**
  - DM/HTN/Dyslipidemia (-/-/-)
  - Alcohol: none
- **Laboratory Findings**
  - AST/ALT 74/121 IU/L, GGT 184 IU/L
  - Baseline HbA1c 6.4%
  - Fibroscan LSM 9.8 kPa, CAP 321 dB/m

서울아산병원 Asan Medical Center

Lifestyle modification

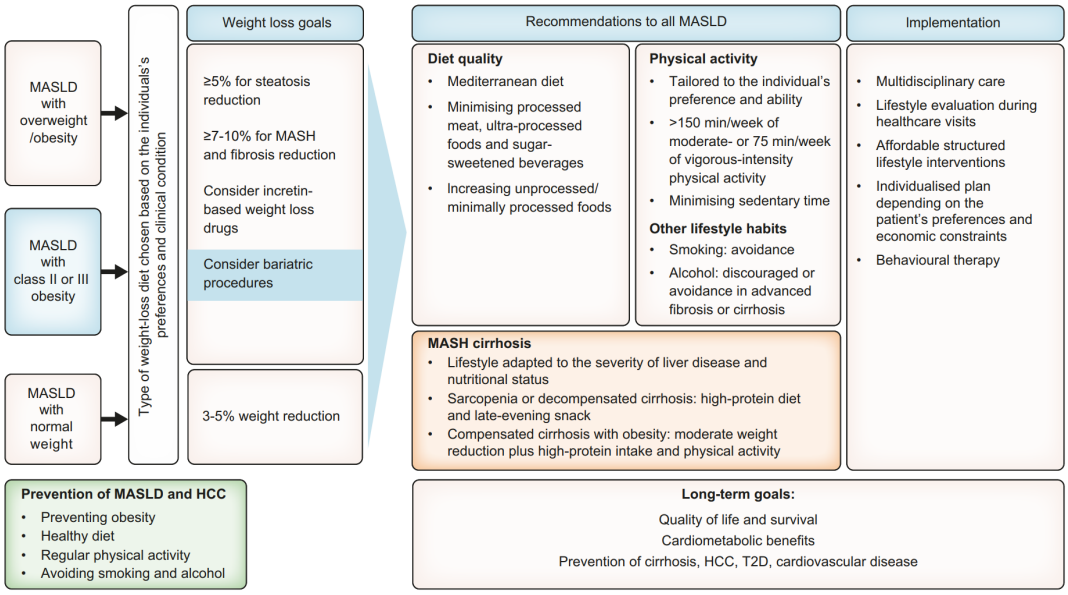
Prospective study, 293 patients with histologically proven NASH



서울아산병원 Asan Medical Center

Gastroenterology. 2015

Lifestyle management algorithm for MASLD



서울아산병원 Asan Medical Center

J Hepatol. 2024

Case 4

Age	45 years
Gender	Female
Weight	70kg
Height	158 cm
BMI	28.0 kg/m^2

Disease Course

- 6개월 간 5kg 체중 감량에 성공함
- Laboratory Findings (6개월 뒤)
  - AST/ALT 25/34 IU/L, GGT 45 IU/L
  - HbA1c 5.9%

- 당뇨병 여부에 관계 없이 대사이상지방간질환 환자에서 7-10% 정도의 체중 감량을 포함한 생활습관 개선을 권고

서울아산병원 Asan Medical Center

Case 5

Age	39 years
Gender	Female
Weight	86.5 kg
Height	155.8 cm
BMI	35.6 kg/m^2

Brief History

- 최근 6개월 동안 6kg 정도 체중 증가가 있었으며 검진 시에 간수치 상승으로 내원함.
- Past Medical History
  - DM/HTN/Dyslipidemia (-/+/+)
  - Alcohol: none
- Laboratory Findings
  - AST/ALT 111/157 IU/L
  - Fasting glucose 90 mg/dL
  - USG: Moderate fatty liver
  - Fibroscan LSM 11.9 kPa, CAP 271 dB/m

서울아산병원 Asan Medical Center

Treatment recommendations beyond lifestyle intervention

Vitamin E

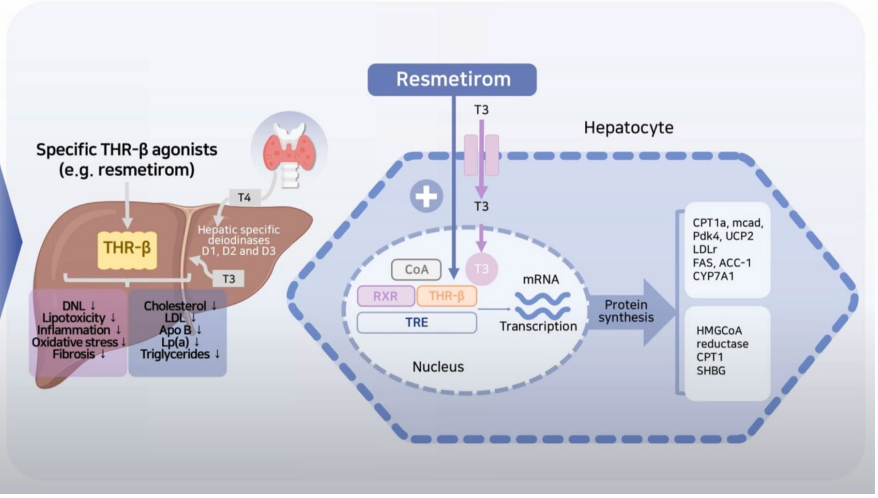
Pioglitazone

Resmetirom(국내 승인전)

Selective Thyroid Hormone Receptor (THR)-β agonist

Resmetirom

간경변증이 없고
F2/F3의 간섬유화가 있는
대사이상지방 간염



서울아산병원 Asan Medical Center

Clin Mol Hepatol. 2025

Drug treatment: Hepatotonics (UDCA, Legalon, DDB…)

성분명	주요제품	약가(원)	하루약가	구분	적응증
UDCA + DDB[PEG]	리비디	258	774원	전문	지속적으로 SGPT가 상승되어 있는 만성지속성 간염
Adenine, Antitoxic liver, DDB, Carnitine, Cyanocobalamin, Pyridoxine, Riboflavin	고덱스 (셀트리온)	376	1504 ~2256원	전문	트란스아미나제(SGPT)가 상승된 간질환
DDB + Garlic oil	펜넬 (파마킹)	330	990 ~1980원	전문	트란스아미나제가 상승된 급·만성 간염
UDCA	우루사 (대웅)	90 180 273	270 540 546	일반 전문 전문	간기능의 개선/ 담즙성 개선
Carduus marianus	레가론 (부광)	241	723	일반	독성간질환, 간세포보호, 만성간염, 간경변의 보조치료

DDB: Diphenyl dimethyl bicarboxylate

서울아산병원 Asan Medical Center

Hepatology. 2018

Drug treatment: Hepatotonics (UDCA, Legalon, DDB…)

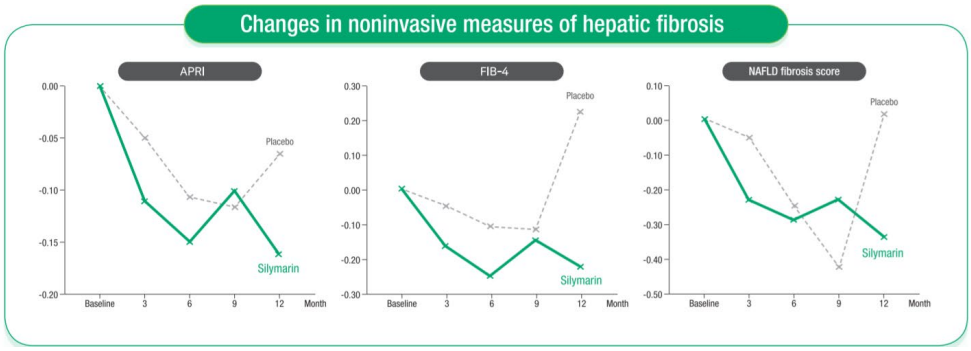
Clinical Gastroenterology and Hepatology 2017;15:1940–1949

A Randomized Trial of Silymarin for the Treatment of Nonalcoholic Steatohepatitis

Chan Wah Kheong,* Nik Raihan Nik Mustapha,‡ and Sanjiv Mahadeva*

*Gastroenterology and Hepatology Unit, Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; ‡Department of Pathology, Hospital Sultanah Bahiyah, Alor Setar, Malaysia

A significantly higher percentage of subjects in the **silymarin group had 30% improvement in liver stiffness measurement** compared with the placebo group (24.2% vs 2.3%; P =.002).



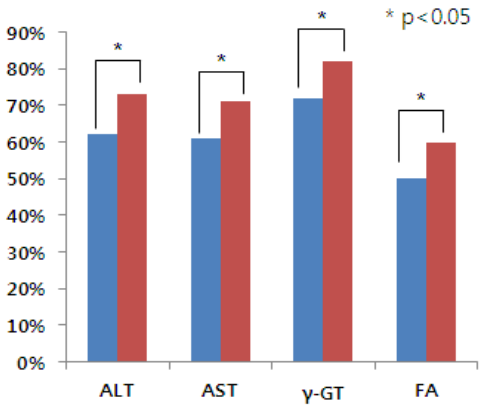
서울아산병원 Asan Medical Center

Clin Gastroenterol Hepatol. 2017

Drug treatment: Hepatotonics (UDCA, Legalon, DDB…)

■ 대상: **간질환 환자 60명**

■ 투여방법: UDCA 450mg (n=30), **UDCA + silymarin 400mg (n=30)**, **3 months**



레가론과 UDCA를 병용 투여시,
UDCA 단독 투여에 비해 **전반적인 간 수치 개선 효과** 향상

서울아산병원 Asan Medical Center

Clin Ter. 2002

Drug treatment: Hepatotonics (UDCA, Legalon, DDB…)

Legalon® vs DDB

	Legalon (Silymarin)	DDB (dimethyl diphenyl bicarboxylate)
ALT(Alanine Aminotransferase)	✓	✓
AST(Aspartate Aminotransferase)	✓	?
Albumin	✓	?
Total bilirubin	✓	?
Prothrombin time	✓	?
Liver Histological Improvement	✓	?
Survival Rate Increasing	✓	?

CONCISE COMMUNICATION

DDB Treatment of Patients With Chronic Hepatitis

We report 13 patients (10 with chronic hepatitis C, 1 with chronic hepatitis B, 2 with nonalcoholic steatohepatitis) with persistently elevated alanine aminotransferase (ALT) levels who were treated with dimethyl-4,4′-dimethoxy-5,6,5′,6-dimethylenedioxybiphenyl-2,2′ dicarboxylate (DDB). ALT rapidly normalized in 12/13 patients and remained normal during treatment. Unlike ALT levels, aspartate aminotransferase, gamma-glutamyl transferase and glutamate dehydrogenase levels were not affected. Furthermore, there was no beneficial effect on the histological grade and stage of liver disease. In vitro experiments with hepatocytes resulted in a significant decrease of hepatocellular ALT levels in the DDB treated cells, suggesting, that DDB affects the synthesis and/or degradation of ALT in liver cells. In conclusion, the normalization of ALT during DDB treatment does not indicate therapeutic efficacy. In view of the wide use of DDB in patients with chronic liver diseases who participate in clinical studies DDB use should be excluded. (HEPATOLOGY 2004;39:1732–1733.)

서울아산병원 Asan Medical Center

Hepatology. 2004

Drug treatment: Hepatotonics 처방의 실제

세부 인정 기준 및 방법

1. 허가사항 범위 내에서 필요·적절히 사용시 요양급여를 인정함.
2. 허가사항 중 간질환에 사용시는 아래와 같은 기준으로 투여 시 요양급여를 인정하며, 동 인정기준 이외에 투여하는 경우에는 약값 전액을 환자가 부담토록 함.

-아 래-

(1) 대상환자

- **투여개시 : AST(Aspartate Transaminase) 또는 ALT(Alanine Transaminase) 수치가 60U/L이상인 경우**
  또는 AST 또는 ALT 수치가 40~60U/L인 경우는 3개월 이상 40U/L이상으로 지속되는 경우
- **투여 중 : AST 또는 ALT 수치가 40U/L 미만이라 할지라도 환자의 상태나 의사의 소견에 따라 지속투여 인정**
  ☞ 간암, 간경변 환자가 간염을 동반한 경우에도 동일한 기준 적용

(2) 투여방법

- **이담제를 포함하여 경구제 2종 이내 인정**
- **"국민건강보험 요양급여의 기준에 관한 규칙 [별표1] 요양급여의 적용기준 및 방법 제3호 나목. 주사"의 조건에 적합한 경우에 한하여 비경구제 1종과 경구제 1종 인정**

(3) 항바이러스제(Lamivudine, Clevudine, Telbivudine, Entecavir, Adefovir, Tenofovir disoproxil, Tenofovir alafenamide, Besifovir, Asunaprevir, Daclatasvir, Sofosbuvir, Ledipasvir+ Sofosbuvir, Elbasvir+Grazoprevir, Ombitasvir+Paritaprevir +Ritonavir, Dasabuvir 경구제, 인터페론제제, 페그인터페론제제)와 병용투여시 1종은 약값 전액을 환자가 부담토록 함.

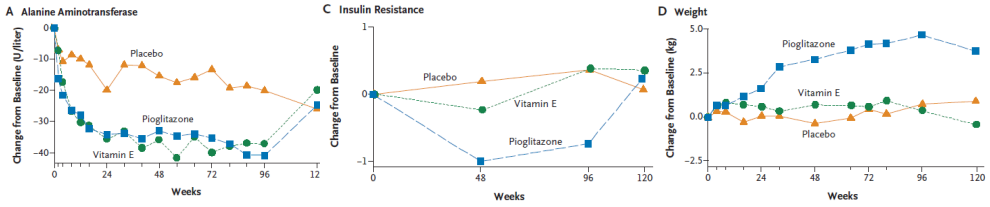
주요 상병코드			
K70	알코올성 간염	K71	독성 간질환
K73	달리 분류되지 않은 만성 간염	K74	간의 섬유증 및 경화증
K75	기타 염증성 간질환	B18	만성바이러스간염

서울아산병원 Asan Medical Center

Drug treatment: Vitamin E

Biopsy-proven NASH patients without diabetes enrolled between 2005 and 2007
Pioglitazone (n=80), Vitamin E (n=84), placebo (n=83) for 96 weeks
Primary outcome: improvement in histologic findings

Variable	Placebo	Vitamin E	Pioglitazone	P Value*	
				Vitamin E vs. Placebo	Pioglitazone vs. Placebo
Primary outcome†					
No. of subjects randomly assigned	83	84	80		
Subjects with improvement (%)	19	43	34	0.001	0.04



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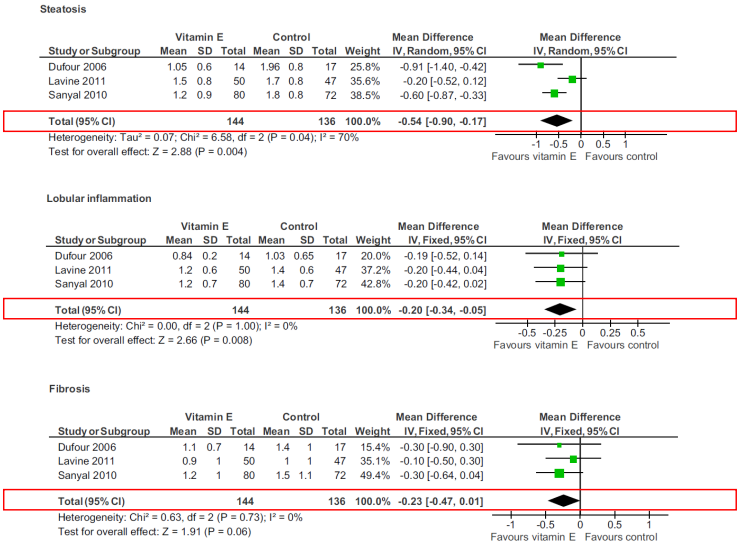
N Engl J Med. 2010

Drug treatment: Vitamin E



서울아산병원 Asan Medical Center

Nutrition. 2015

Case 5

Age	39 years
Gender	Female
Weight	85.6 kg
Height	155.8 cm
BMI	35.3 kg/m^2

서울아산병원 Asan Medical Center

Disease Course

- 고용량 vitamin E 800 IU/day 복용 시작.
- Laboratory Findings (1년 뒤)
  - AST/ALT 29/16 IU/L
  - USG: Moderate fatty liver
  - Fibroscan LSM 7.9 kPa, CAP 264 dB/m

- 당뇨가 없는 대사이상지방간염 환자에서는 **고용량 비타민 E (800 IU/day) 치료를 고려**해 볼 수 있음

Case 6

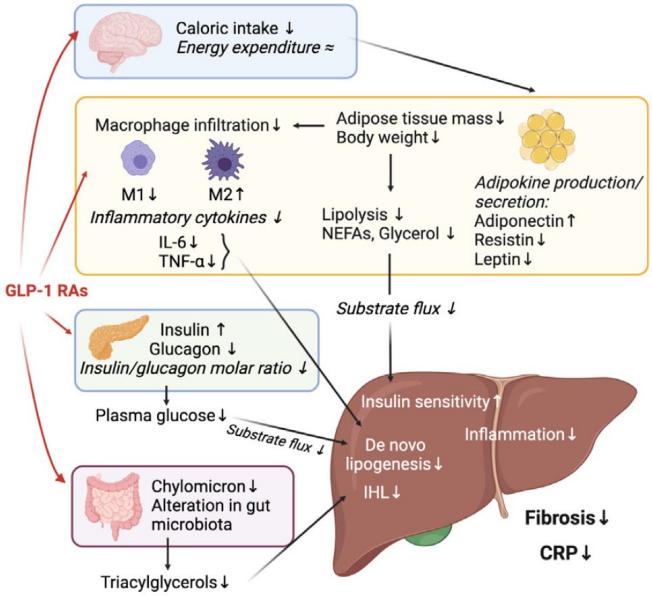
Age	41 years
Gender	Female
Weight	82.5 kg
Height	162.8 cm
BMI	31.1 kg/m^2

서울아산병원 Asan Medical Center

Brief History

- 1년 전 당뇨 진단 후 metformin 복용 중인 상태로 간수치 상승 주소로 내원함.
- Past Medical History
  - DM/HTN/Dyslipidemia (+/-/+)
  - Alcohol: none
- Laboratory Findings
  - AST/ALT 56/132 IU/L
  - HbA1c 7.1%
  - USG: Moderate fatty liver
  - Fibroscan LSM 9.6 kPa, CAP 311 dB/m

Drug treatment: GLP-1 receptor agonists



서울아산병원 Asan Medical Center

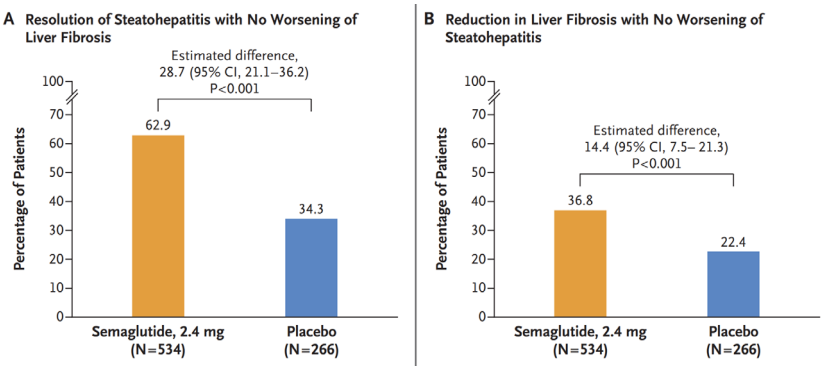
Trends Endocrinol Metab. 2022

Drug treatment: Semaglutide for MASH with liver fibrosis

Phase 3: Semaglutide SC once weekly (GLP-1 receptor agonists)

Indication: biopsy-proven NASH and F2-3 (55.4–56.8% with DM)

Higher rates of histologic resolution of steatohepatitis, fibrosis (at 72 weeks)



Side effects: nausea (36.2%), diarrhea (26.9%), constipation (22.2%), vomiting (18.6%)

서울아산병원 Asan Medical Center

N Engl J Med. 2025

Drug treatment: Survodutide for MASH with liver fibrosis

PARTICIPANTS

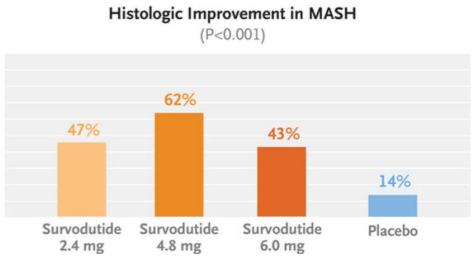
WHO	293 adults
	18–80 years of age
	Women: 53%; Men: 47%
CLINICAL STATUS	Biopsy-confirmed MASH
	Fibrosis stage F1 through F3

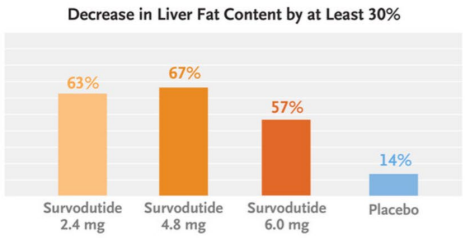
TRIAL DESIGN

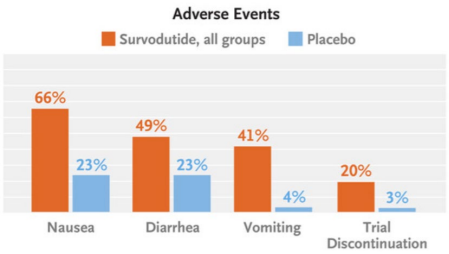
- PHASE 2
- DOUBLE-BLIND
- RANDOMIZED
- PLACEBO-CONTROLLED
- DOSE-FINDING
- LOCATION: 155 SITES IN 25 COUNTRIES

Phase 2: Survodutide SC once weekly

(GLP-1 and glucagon receptor dual agonists)





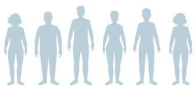


서울아산병원 Asan Medical Center

N Eng J Med. 2024

Drug treatment: Tirzepatide for MASH with liver fibrosis

PARTICIPANTS



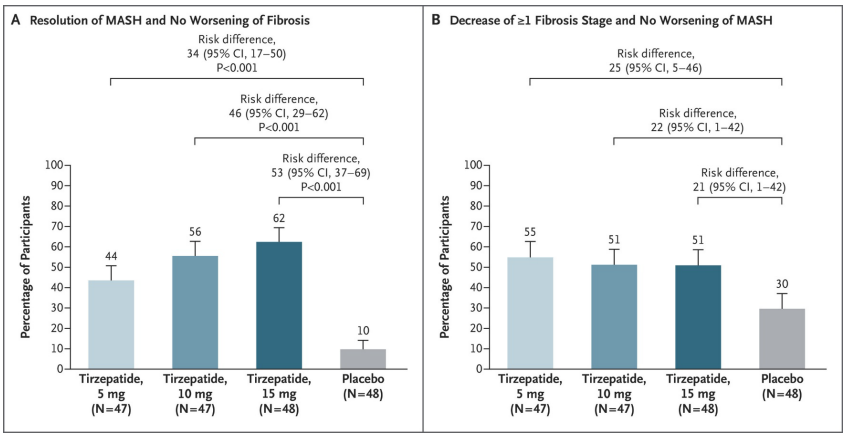
WHO	190 participants
	18 to 80 years of age
	Women: 57%; Men: 43%
CLINICAL STATUS	Biopsy-confirmed MASH
	Stage 2 or 3 fibrosis
	BMI, 27 to 50
	With or without type 2 diabetes mellitus

TRIAL DESIGN

- PHASE 2
- MULTICENTER
- DOUBLE-BLIND
- RANDOMIZED
- PLACEBO-CONTROLLED
- LOCATION: 10 COUNTRIES

Phase 2: Tirzepatide SC once weekly

(GLP-1 receptor and GIP dual agonists)

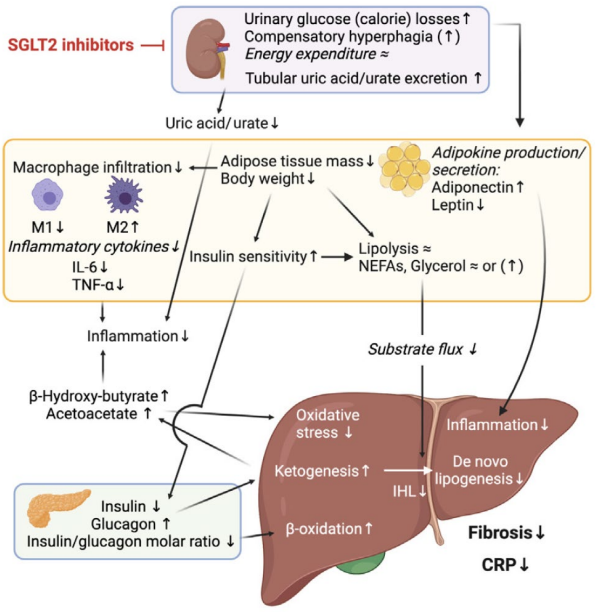


Common S/E: Nausea (~40%), Diarrhea (~30%), Constipation (~20%)

서울아산병원 Asan Medical Center

N Eng J Med. 2024

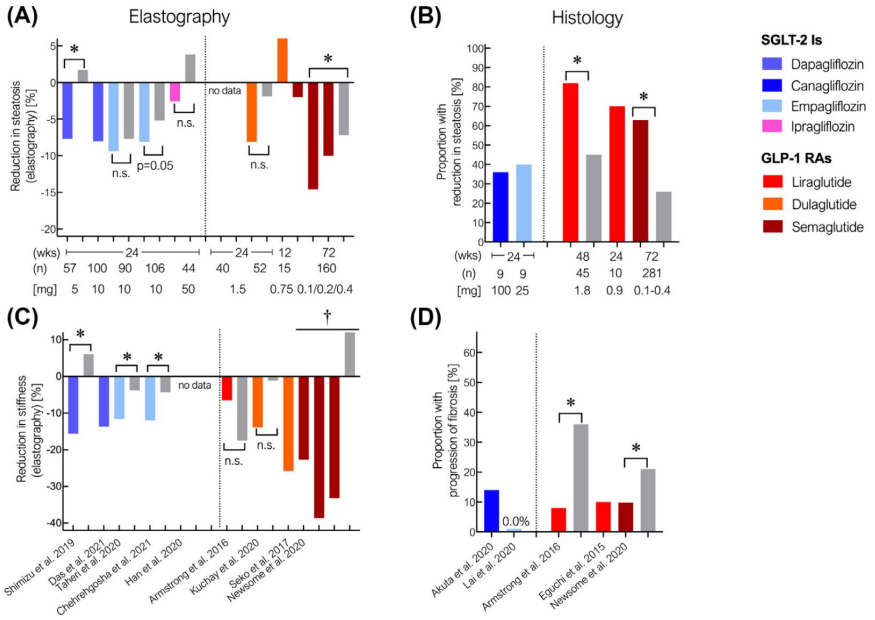
Drug treatment: SGLT-2 inhibitors



서울아산병원 Asan Medical Center

Trends Endocrinol Metab. 2022;33(6):424-442.

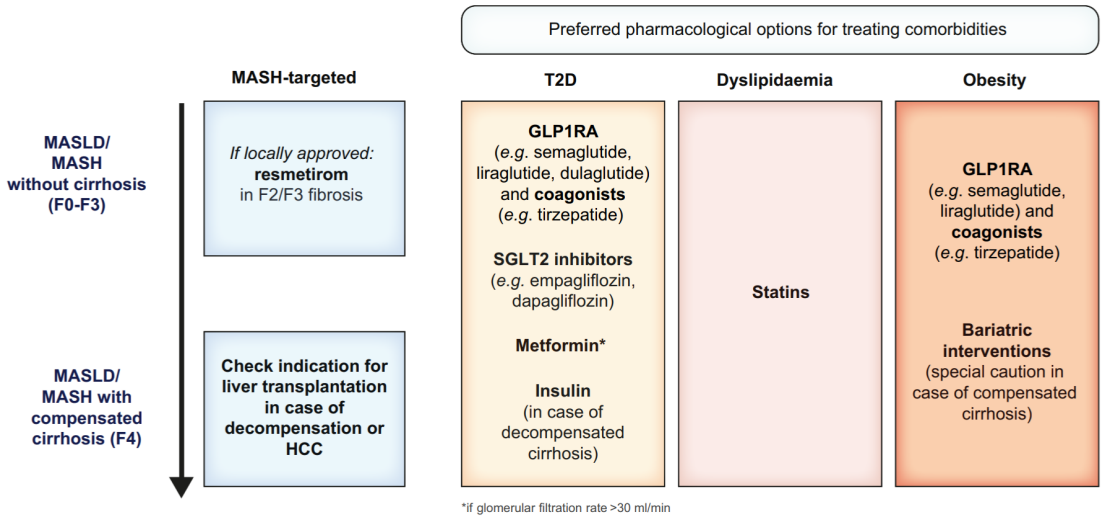
Drug treatment: SGLT-2 inhibitors



서울아산병원 Asan Medical Center

Trends Endocrinol Metab. 2022;33(6):424-442.

Treatment recommendations beyond lifestyle intervention



서울아산병원 Asan Medical Center

J Hepatol. 2024

Case 6

Age	41 years
Gender	Female
Weight	73.5 kg
Height	162.8 cm
BMI	27.7 kg/m^2

Disease course

- Saxenda (liraglutide) 비급여 투약 시작. 6개월 뒤 체중 9kg 감소.
- Laboratory Findings (6개월 뒤)
  - AST/ALT 25/32 IU/L
  - HbA1c 6.4%
  - Fibroscan LSM 7.9 kPa, CAP 261 dB/m

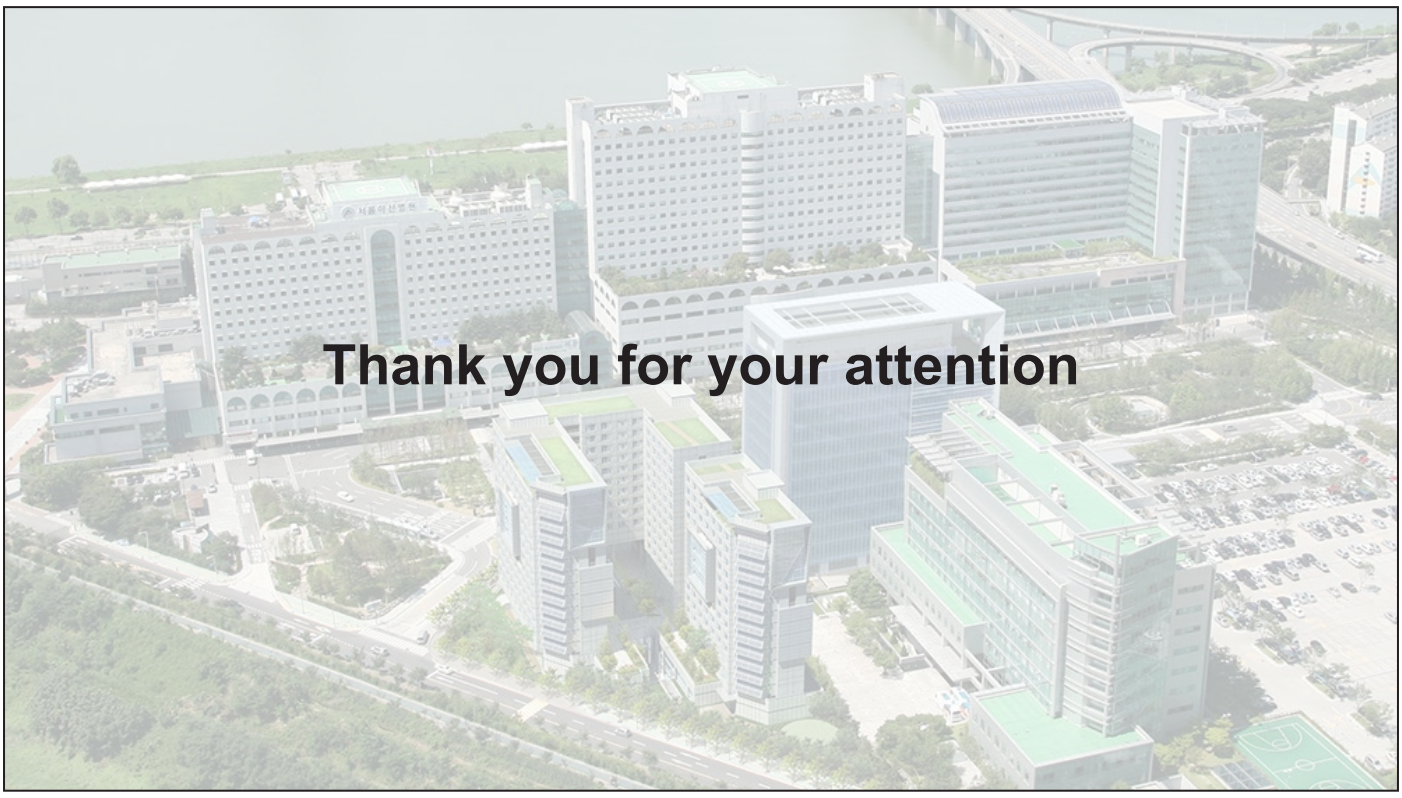
- 당뇨가 있는 대사이상지방간염 환자에서는 GLP-1 receptor agonist나 SGLT-2 inhibitor 치료를 우선적으로 고려

서울아산병원 Asan Medical Center

Take home messages

- **대사이상지방간질환**의 유병률은 점차 증가 중이며, 당뇨병이 있는 환자에서의 유병률은 일반 인구 대비 2배이고 진행성 섬유화와 연관되어 있다.
- 대사이상지방간질환의 주요 사망 원인은 **심혈관계질환, 악성종양** 등이며 **간섬유화**의 정도가 예후에 가장 중요한 요소이다.
- 당뇨병 환자에서는 대사이상지방간질환에 대한 선별검사를 시행해야 하며, **복부 초음파 검사** 혹은 간단한 혈액 마커(**FIB-4 index**)를 활용해 볼 수 있다.
- 7-10%의 **체중감량**을 포함한 생활습관 교정과 더불어 당뇨병을 동반한 대사이상지방간질환 환자에서는 **GLP-1 수용체작용제, 혹은 SGLT-2 억제제의 사용을 우선 고려**해 볼 수 있다.

서울아산병원 Asan Medical Center



03
Session

당뇨병 동반 질환 제대로 관리하기

당뇨병 만성콩팥병 관리의 모든 것

서울아산병원 내분비내과 **민세희**

당뇨병과 만성콩팥병은 모두 환자와 의료진에게 있어 예후와 삶의 질에 중대한 영향을 미치는 질환이다. 특히 당뇨병성 신장병(DKD)은 말기신부전으로의 진행 위험뿐 아니라 심혈관계 질환 발생과도 밀접히 연관되어 있어 적극적인 관리가 필요하다. 최근에는 기존의 RAS 차단제(ACEi/ARB) 외에도, SGLT2 억제제와 비스테로이드성 MRA(finerenone) 등의 새로운 치료 옵션이 등장하면서, 당뇨병성 신장병에 대한 전략적 접근이 가능해지고 있다. 이러한 치료제들은 단순한 혈당 조절을 넘어 신장기능 보존, 단백뇨 감소, 심혈관 보호에 이르는 다면적 효과를 통해 환자의 장기 예후 개선에 기여한다. 이번 강의에서는 당뇨병성 신장병의 진단부터 병태생리, 최신 치료 지침, 그리고 임상에서의 실질적 적용에 이르기까지 꼭 알아야 할 핵심 내용을 사례 중심으로 정리하고자 한다.

2025년 서울아산병원 당뇨병 센터 개원의 연수강좌

당뇨병 만성콩팥병 관리의 모든 것

서울아산병원 내분비내과
민 세 희

- 당뇨병 신장병증 진단
- 당뇨병 신장병증 치료
- 새로운 당뇨병 신장병증의 치료

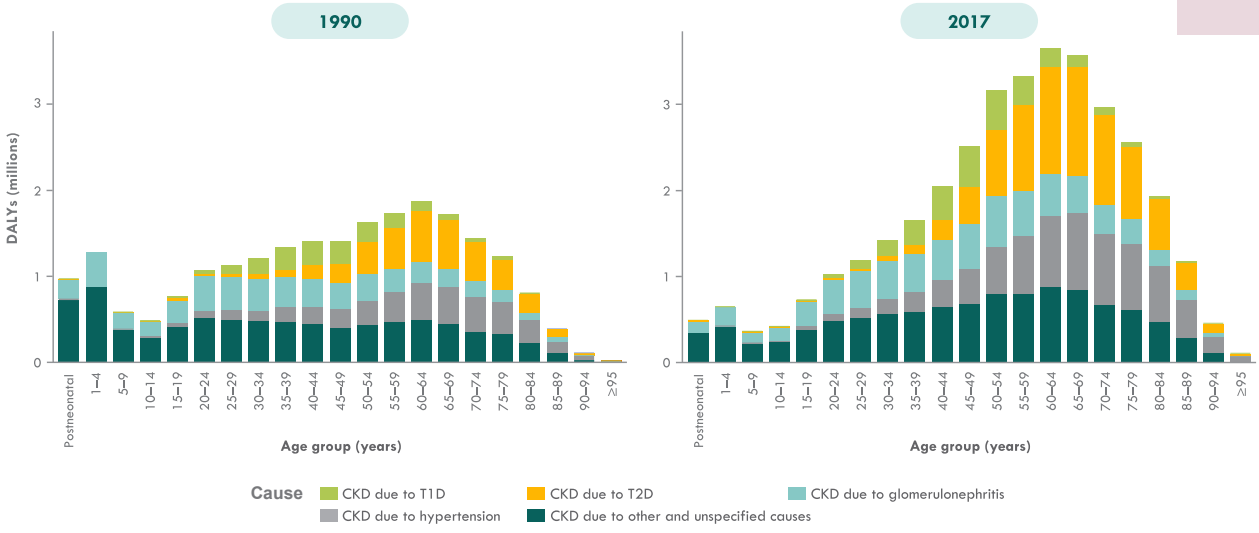
56/M

- 10년전 당뇨병 진단
- 8년전 고혈압 진단

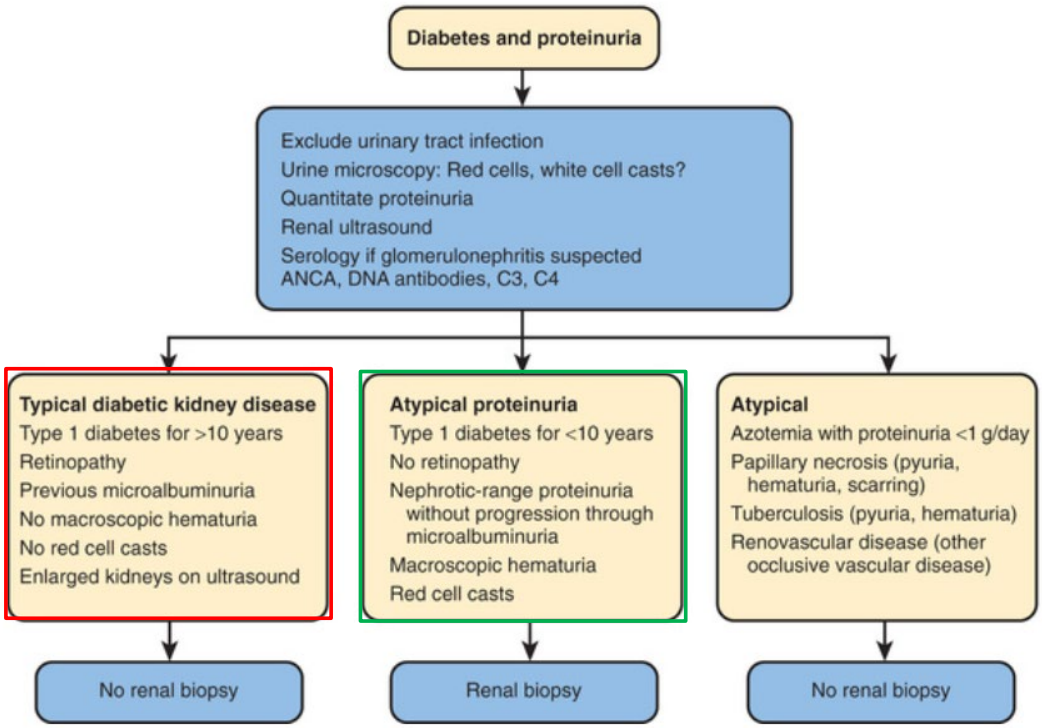
- 거품뇨가 많이 나온다.

- HbA1c 7.5%
- Metformin 1000 mg BID, Linagliptin 5 mg QD
- BUN/Cr: 21/1.3 mg/dL, eGFR 54 mL/min/1.73 m^2
- U/A: SG 1.015 pH 5.5 Alb(+++) OB(-) WBC(-)
- Urine Albumin/creatinine ratio: 2,150 mg/g

만성 콩팥병의 원인



Data from 195 countries
CKD, chronic kidney disease; DALY, disability-adjusted life-year; T1D, type 1 diabetes; T2D, type 2 diabetes
GBD Chronic Kidney Disease Collaboration. Lancet 2020;395:709.



Comprehensive Clinical Nephrology, 7th Edition

- China
- 1993-2003
- Diabetic patients with over proteinuria but no severe renal failure for kidney biopsy
- N = 110

Clinical manifestations	DN ($n = 60$)	NDRD ($n = 50$)
Haematuria	10 (16.7%)	34 (68.0%)†
Nephrotic syndrome	25 (41.7%)	13 (26.0%)†
Renal insufficiency	21 (35.0%)	5 (10.0%)†
Hypertension	46 (76.7%)	25 (50.0%)†
Hyperlipidaemia	39 (65.0%)	38 (76.0%)
Hyperuricaemia	13 (21.7%)	14 (28.0%)
Cardiovascular disease	32 (53.3%)	17 (34.0%)*
Diabetic retinopathy	46 (76.7%)	5 (10.0%)†

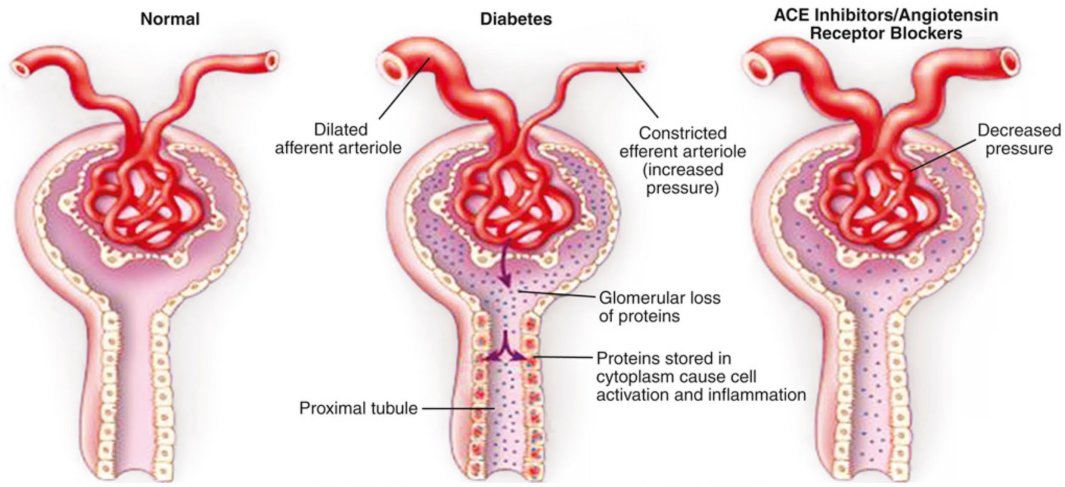
*$P < 0.05$, †$P < 0.01$ versus DN.

Nephrol Dial Transplant (2008) 23: 1940–1945

Pathological types	Case	Percentage (%)
IgA nephropathy	17	34.0
Membranous nephropathy	11	22.0
Mesangial proliferative GN[a]	7	14.0
HBV-associated GN	4	8.0
Minor glomerular abnormalities	3	6.0
Minimal change disease	2	4.0
Hypertensive nephrosclerosis	2	4.0
FSGS	2	4.0
Crescentic GN	1	2.0
Lupus glomerulonephritis	1	2.0

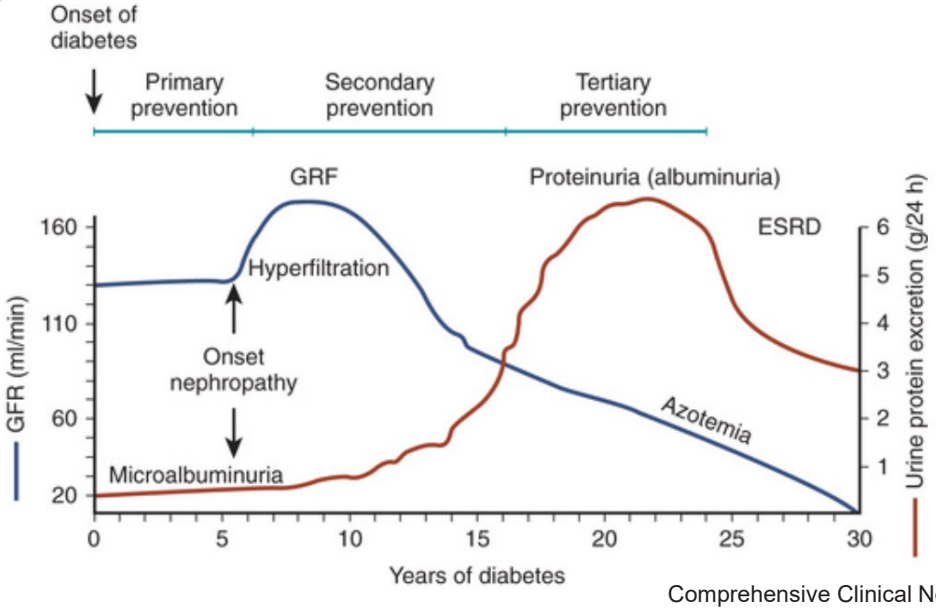
Nephrol Dial Transplant (2008) 23: 1940–1945

Hemodynamic Changes in Diabetes



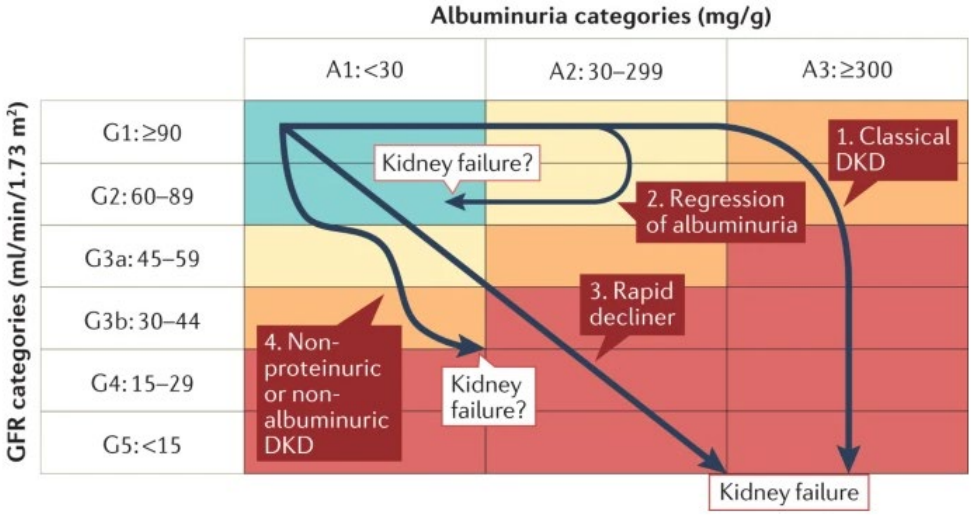
Comprehensive Clinical Nephrology, 7th Edition

Natural course of diabetic kidney disease (DKD)



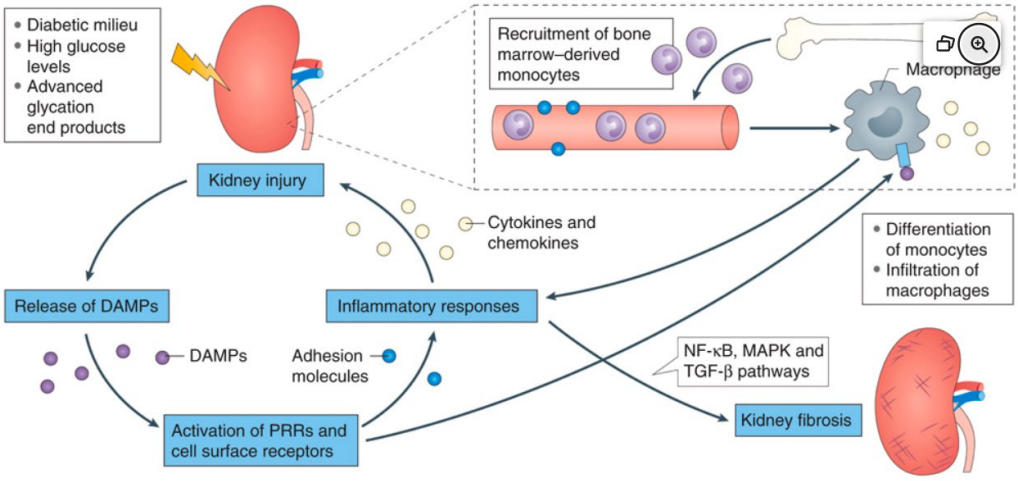
Comprehensive Clinical Nephrology, 7th Edition

Trajectories of kidney function in DKD



10

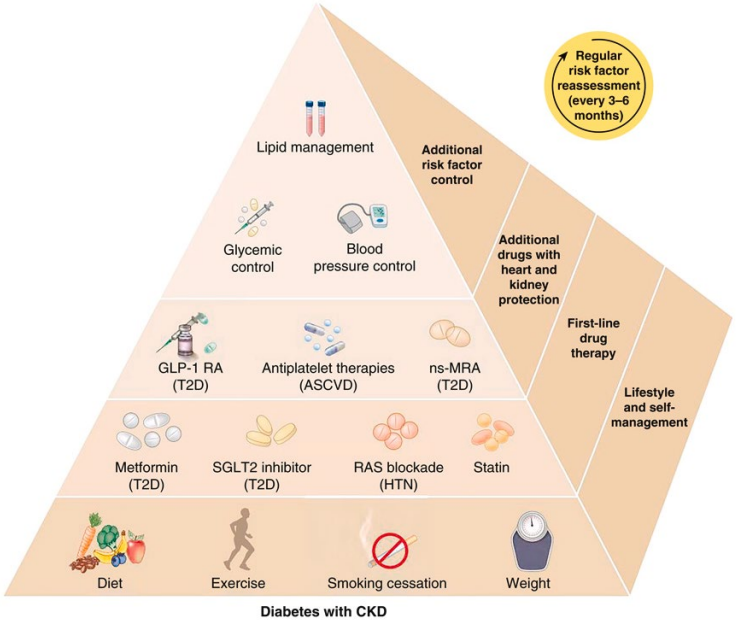
Pathophysiology of diabetic kidney disease (DKD)



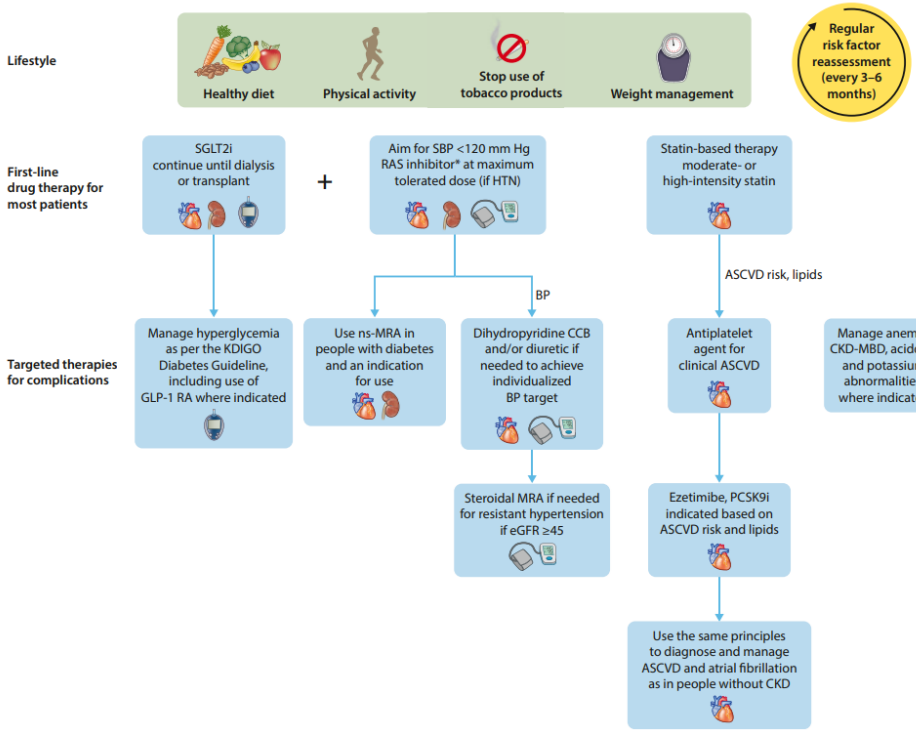
Comprehensive Clinical Nephrology, 7th Edition

Management of diabetic kidney disease

KDIGO guideline



Kidney Int. 2022;102:990–999.



Kidney International, 2024, 684-701

60/M

- DM (20YA Dx)
- HTN (10YA Dx)
- DM retinopathy (+)

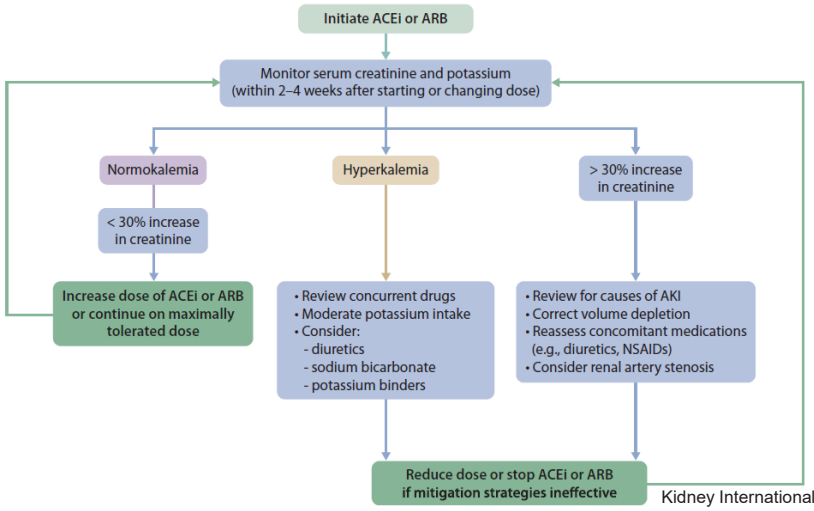
- Smoking/alcohol (+/+)
- Exercise: 1hr/1wk

- BP135/85 mmHg
- BUN/Cr: 28/1.9 mg/dL, eGFR 40 mL/min/1.73 m^2

- U/A: SG 1.010 pH 5.5 Alb(+++) OB(-) WBC(-),
- Urine albumin/creatinine ratio: 2,850 mg/g

ACE inhibitor/ARB

Recommendation 1.2.1: We recommend that treatment with an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) be initiated in patients with diabetes, hypertension, and albuminuria, and that these medications be titrated to the highest approved dose that is tolerated *(1B)*.



Kidney International (2022) 102 (Suppl 5S), S1–S127 S21

ACE inhibitor/ARB

- Continue ACEi or ARB
  → If serum creatinine increases ≤30% within 4 weeks after initiation or dose escalation, treatment can be continued.
- Manage hyperkalemia without stopping the drug
  → Do not discontinue ACEi or ARB immediately; instead, use strategies to lower serum potassium levels.
- Avoid dual RAS blockade
  → Use only one agent at a time.
  → Combining an ACEi with an ARB, or with a direct renin inhibitor, is potentially harmful.

Kidney International (2022) 102 (Suppl 5S), S1–S127 S21

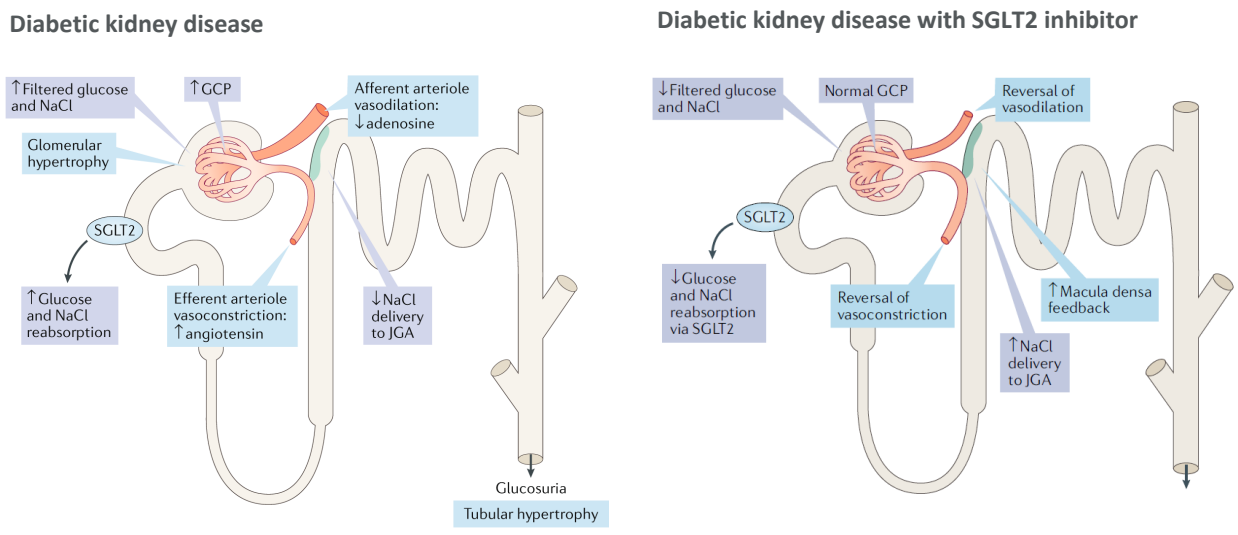
SGLT2 inhibitor

Recommendation 1.3.1: We recommend treating patients with type 2 diabetes (T2D), CKD, and an eGFR ≥20 ml/min per 1.73 m^2 with an SGLT2i *(1A)*.

- For kidney and cardiovascular protection
- Once an SGLT2i is initiated, it is reasonable to continue an SGLT2i even if the eGFR falls below 20 ml/min per 1.73 m2, unless it is not tolerated or kidney replacement therapy is initiated.
- It is reasonable to withhold SGLT2i during times of prolonged fasting, surgery, or critical medical illness (when patients may be at greater risk for ketosis).
- A reversible decrease in the eGFR with commencement of SGLT2i treatment may occur and is generally not an indication to discontinue therapy.

Kidney International (2022) 102 (Suppl 5S), S1–S127 S21

Effect of DM and SGLT2i on tubuloglomerular feedback



DCT, distal convoluted tubule; GCP, glomerular capillary pressure; PCT, proximal convoluted tubule.

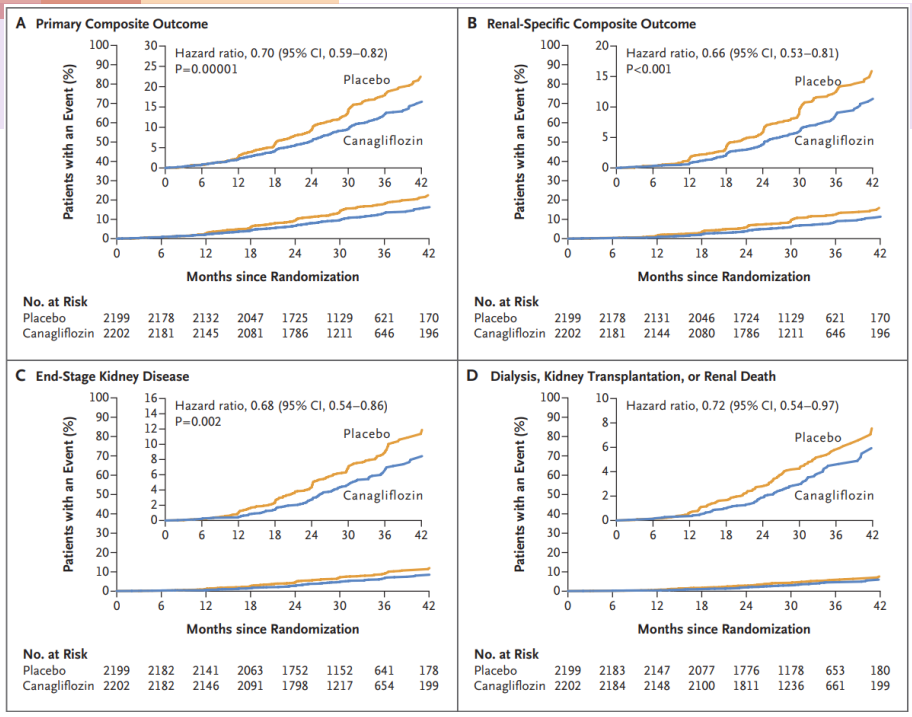
DeFronzo, R.A., Reeves, W.B. & Awad, A.S. Pathophysiology of diabetic kidney disease: impact of SGLT2 inhibitors. *Nat Rev Nephrol* **17**, 319–334 (2021). https://doi.org/10.1038/s41581-021-00393-8

CREDENCE trial

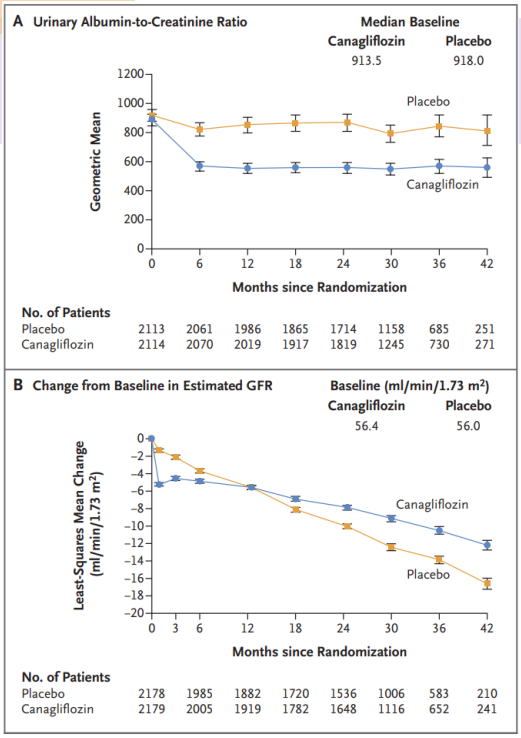
- Double-blind, randomized trial
- 4401 patients with T2DM and albuminuric CKD
- eGFR 30~<90 ml/min/1.73m2 & albuminuria (>300~5000)
- RAAS blocker
- Canagliflozin 100mg or placebo

- Primary outcome
  - A composite of ESRD (dialysis, Tx, eGFR<15 ml/min/1.73m2)
  - A doubling of the serum Cr level
  - Death from renal or CV causes

N Engl J Med 2019;380:2295-306.



N Engl J Med 2019;380:2295-306.



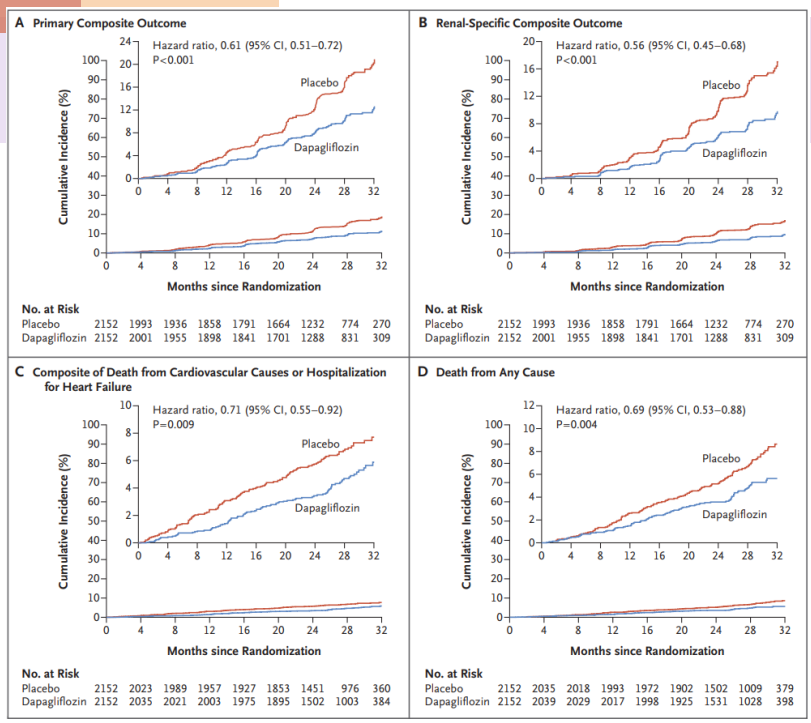
N Engl J Med 2019;380:2295-306.

DAPA-CKD

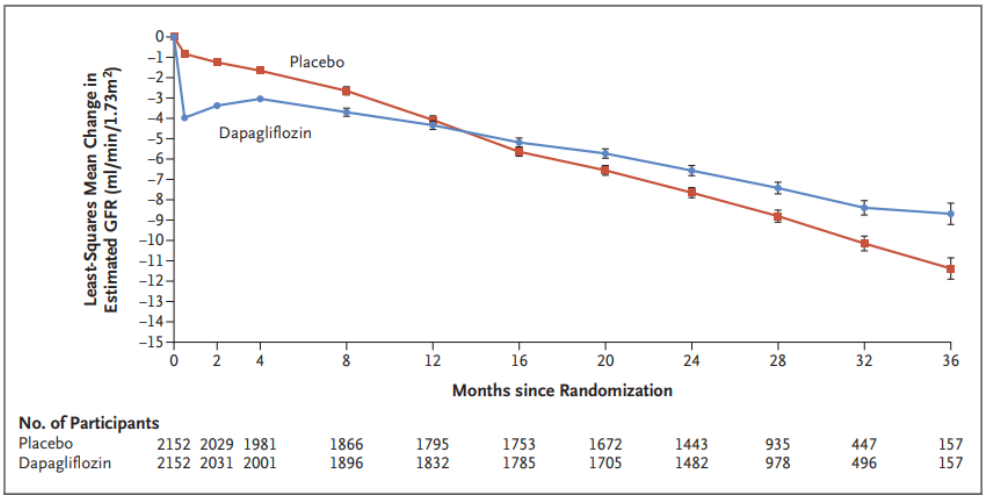
- 4304 patients regardless of the presence or absence of diabetes
- eGFR 25-75 ml/min/1.73m2 & urine albumin/creatinine ratio 200-5000 mg/g
- Dapagliflozin 10mg or placebo

- Primary outcome
  - A composite of a sustained decline in the eGFR at least 50%
  - ESRD
  - Death from renal or CV causes

N Engl J Med 2020;383:1436-46.



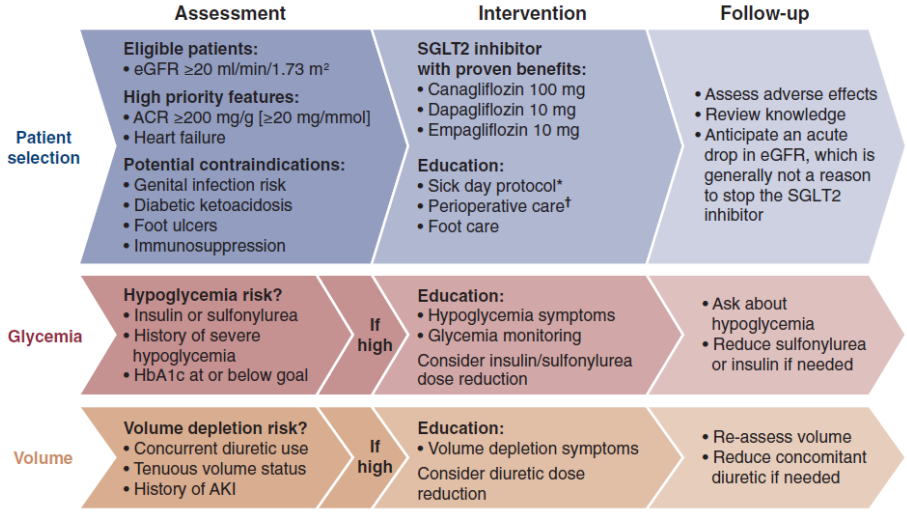
N Engl J Med 2020;383:1436-46.



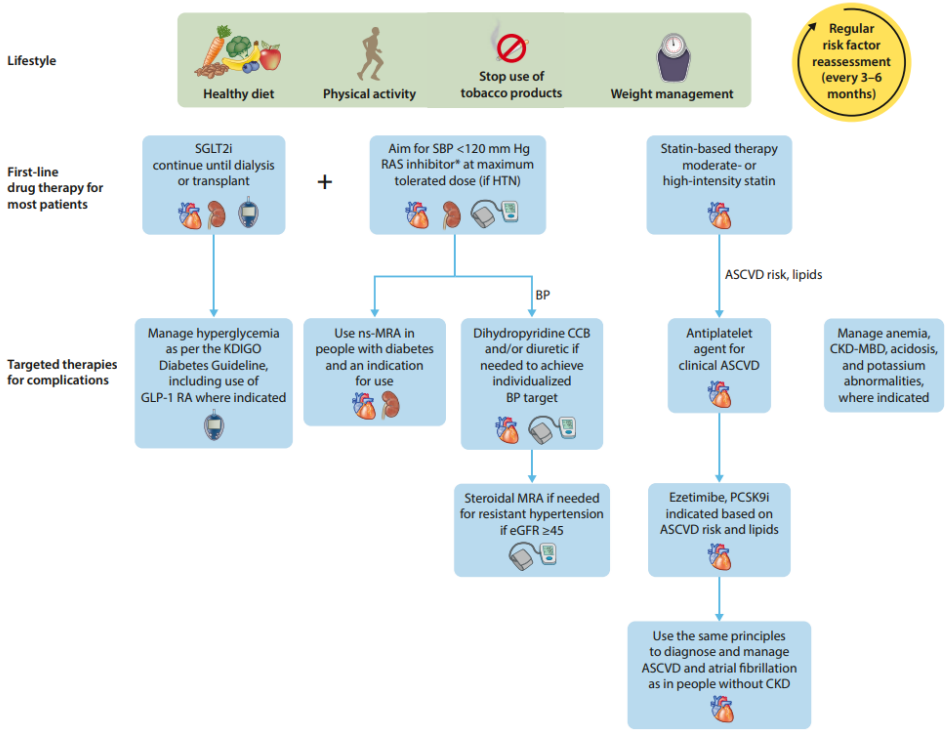
N Engl J Med 2020;383:1436-46.

SGLT2 inhibitor

Practical provider guide to initiating SGLT2 inhibitors in patients with type 2 diabetes and CKD



Kidney International (2022) 102 (Suppl 5S), S1–S127 S21



Kidney Int. 2022;102:990–999.

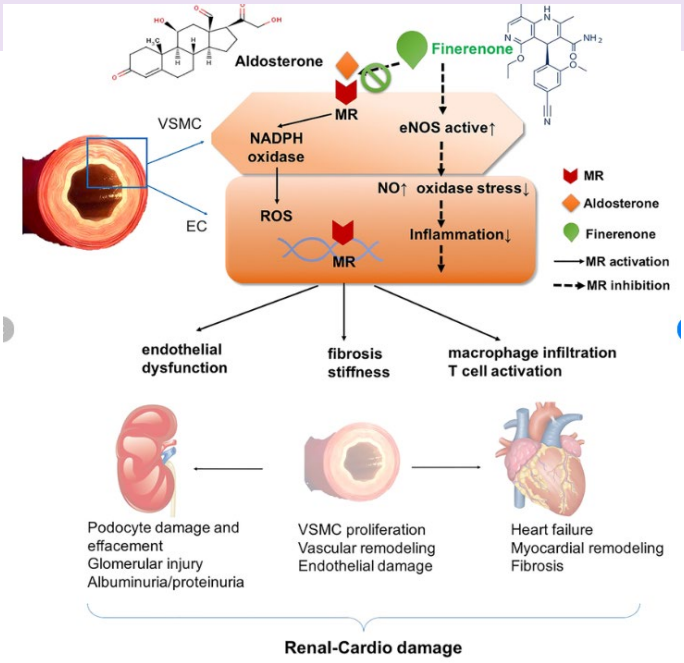
Mineralocorticoid Receptor Antagonists

Recommendation 1.4.1: We suggest a nonsteroidal mineralocorticoid receptor antagonist with proven kidney or cardiovascular benefit for patients with T2D, an eGFR ≥25 ml/min per 1.73 m^2, normal serum potassium concentration, and albuminuria (≥30 mg/g [≥3 mg/mmol]) despite maximum tolerated dose of RAS inhibitor (RASi) *(2A)*.

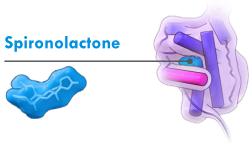
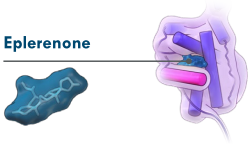
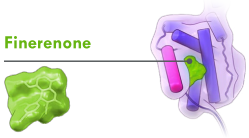
- A nonsteroidal MRA can be added to a RASi and an SGLT2i for treatment of T2D and CKD.
- A steroidal MRA should be used for treatment of heart failure, hyperaldosteronism, or refractory hypertension, but may cause hyperkalemia or a reversible decline in glomerular filtration, particularly among patients with a low GFR.

Kidney International (2022) 102 (Suppl 5S), S1–S127 S21

MR overactivation: targeting systemic impact with non-steroidal mineralocorticoid receptor antagonists



Differential MR binding of steroidal MRAs vs finerenone

	Steroidal MR antagonists		Finerenone
	Spironolactone 	Eplerenone 	Finerenone 
Structural properties	Flat (steroidal)	Flat (steroidal)	Bulky (nonsteroidal)[1,5]
Potency to MR	High[4,10]	Low[1,4,10]	High[1,2,10]
Selectivity to MR	Low[4,10]	Moderate[4,10]	High[1,2,10]
CNS penetration	Yes	Yes	No, based on preclinical data[3]
Sexual side effects	Yes (gynecomastia)[4]	Less than spironolactone[4]	No signal, based on phase II data[7-9]
Hyperkalemia	Yes[4]	Yes[4]	Moderately increased*[,7-9]
Tissue distribution	Kidney > heart (at least 6-fold)[6,10]	Kidney > heart (~3-fold)[6,10]	Balanced kidney : heart (1:1)[6,10]

Based on preclinical data and ARTS phase II programme

Bärfacker L, et al. Discovery of BAY 94-8862: a nonsteroidal antagonist of the mineralocorticoid receptor for the treatment of cardiorenal diseases. *ChemMedChem*. 2012;7:1385–403

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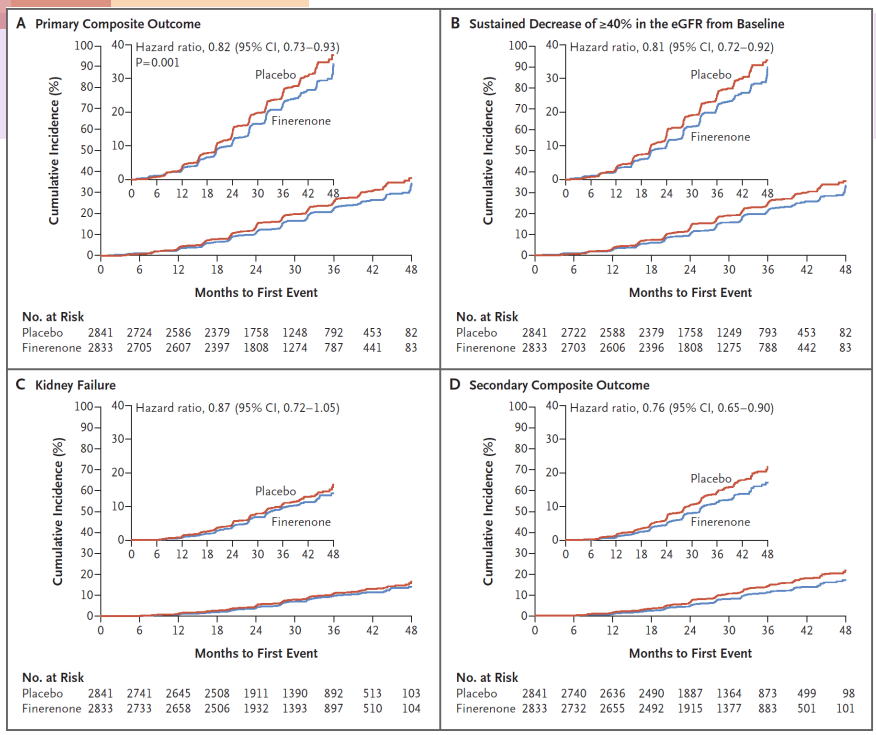
FIDELIO-DKD

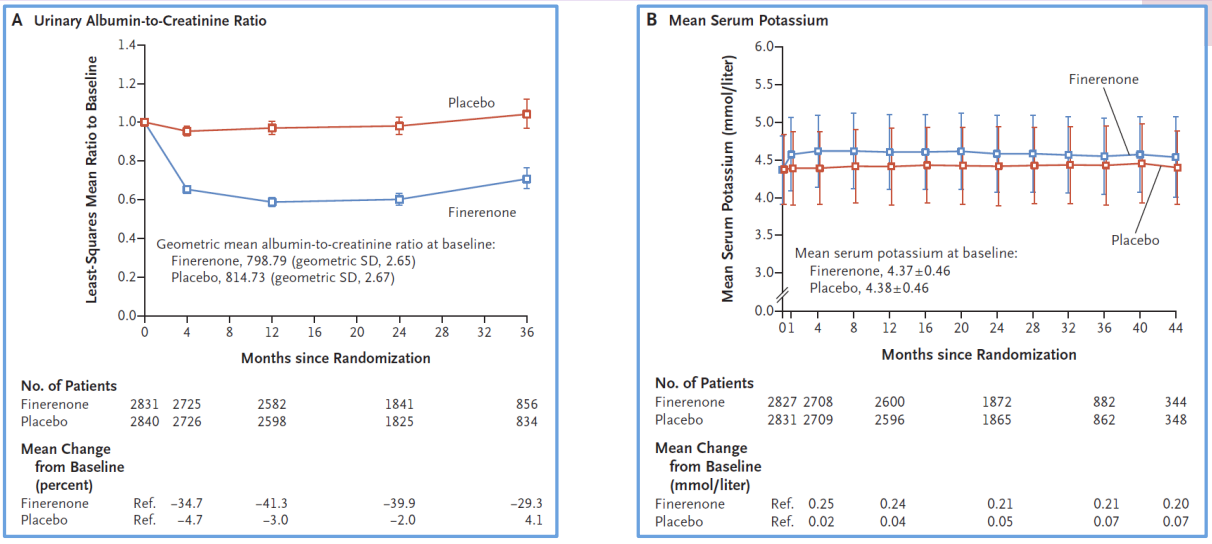
- Randomized double-blind trial
- 5734 patients with CKD and T2DM
- 1:1 to receive finerenone or placebo
- Urine Alb/Cr ratio 30-<300/ eGFR 25-<60/ diabeteic retinopathy
- Urine Alb/Cr ratio 300-5000/ eGFR 25-<75

- Primary composite outcome
  - Kidney failure
  - A sustained decrease of at least 40% in the eGFR from baseline
  - Death from renal causes
- Secondary composite outcome
  - Death from CV causes
  - Nonfatal myocardial infarction
  - Nonfatal stroke
  - Hospitalization for heart failure

N Engl J Med 2020;383:2219-29.



N Engl J Med 2020;383:2219-29.



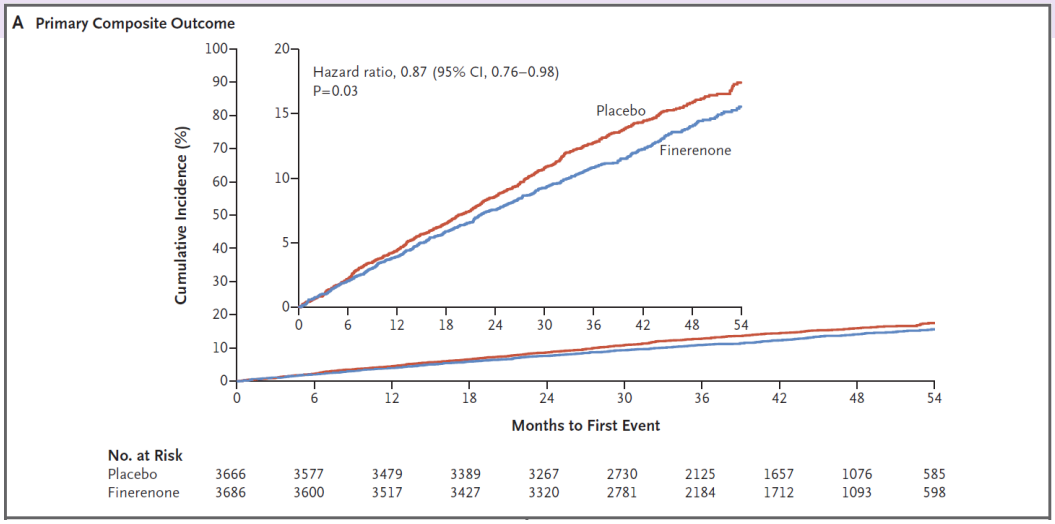
N Engl J Med 2020;383:2219-29.

FIGARO-DKD

- Randomized, double-blind study
- CKD and type 2 DM
- Finerenone or placebo
- Urine albumin/Cr ratio 30~<300 and eGFR 25-90 ml/min/1.73m2 or
- Urine albumin/Cr ratio 300-5000 and eGFR ≥ 60 ml/min/1.73m2
- RAAS blocker

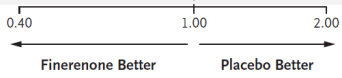
- Primary outcome
  - A composite of death from CV causes, nonfatal MI, nonfatal stroke or hospitalization for heart failure
- Secondary outcome
  - A composite of kidney failure, a sustained decrease from baseline of at least 40% in the eGFR or death from renal causes

N Engl J Med 2021;385:2252-63.



N Engl J Med 2021;385:2252-63.

Outcome	Finerenone (N=3686)	Placebo (N=3666)	Finerenone (N=3686)	Placebo (N=3666)	Hazard Ratio (95% CI)	P Value
	no. of patients with event (%)		*no. of patients with event per 100 patient-yr*			
Primary composite outcome	458 (12.4)	519 (14.2)	3.87	4.45	0.87 (0.76–0.98)	0.03
Death from cardiovascular causes	194 (5.3)	214 (5.8)	1.56	1.74	0.90 (0.74–1.09)	—
Nonfatal myocardial infarction	103 (2.8)	102 (2.8)	0.85	0.85	0.99 (0.76–1.31)	—
Nonfatal stroke	108 (2.9)	111 (3.0)	0.89	0.92	0.97 (0.74–1.26)	—
Hospitalization for heart failure	117 (3.2)	163 (4.4)	0.96	1.36	0.71 (0.56–0.90)	—
Kidney composite outcome with ≥40% decrease in eGFR	350 (9.5)	395 (10.8)	3.15	3.58	0.87 (0.76–1.01)	—
Kidney failure	46 (1.2)	62 (1.7)	0.40	0.54	0.72 (0.49–1.05)	—
End-stage kidney disease	32 (0.9)	49 (1.3)	0.26	0.40	0.64 (0.41–0.995)	—
Sustained decrease in eGFR of <15 ml/min/1.73 m²	28 (0.8)	38 (1.0)	0.24	0.33	0.71 (0.43–1.16)	—
Sustained ≥40% decrease in eGFR from baseline	338 (9.2)	385 (10.5)	3.04	3.49	0.87 (0.75–1.00)	—
Death from renal causes	0	2 (0.1)	—	—	—	—
Hospitalization for any cause	1573 (42.7)	1605 (43.8)	16.9	17.5	0.97 (0.90–1.04)	—
Death from any cause	333 (9.0)	370 (10.1)	2.68	3.01	0.89 (0.77–1.04)	—
Kidney composite outcome with ≥57% decrease in eGFR	108 (2.9)	139 (3.8)	0.95	1.23	0.77 (0.60–0.99)	—
Sustained ≥57% decrease in eGFR from baseline	90 (2.4)	116 (3.2)	0.79	1.02	0.76 (0.58–1.00)	—



N Engl J Med 2021;385:2252-63.

Finerenone is recommended to slow CKD progression and reduce CV events in patients with CKD and T2D

	AACE 2022[1]	KDIGO 2024[2]	ADA 2024[3]	ESH 2023[4]
ACEi/ ARB	**Recommended** for persons with albuminuria (T1D or T2D) **to reduce risk of DKD or CKD in DM progression**	Recommend starting RASi (ACEi or ARB) for people with CKD and **moderately-to-severely increased** albuminuria (G1–G4, A2 and A3) **with diabetes** (1B)	Strongly recommended in patients with **UACR ≥300 mg/g** and/or **eGFR <60 mL/min/1.73 m²*(LOE A)** Recommended in patients with **UACR 30–299 mg/g* (LOE B)**	**Antihypertensive treatment** in **T2D** is recommended for **macrovascular and microvascular protection** **Recommended** for patients with **CKD** and **UACR >30 mg/g**, titrated to **maximum tolerated dose**
nsMRA	Recommended for persons with T2D, an **eGFR ≥25 mL/min/1.73 m²,** normal serum [K⁺], and albuminuria (**UACR ≥30 mg/g**) despite a maximum tolerated dose of a RASi IA	Suggest **Nonsteroidal mineralocorticoid receptor** antagonist with proven kidney or cardiovascular benefit for adults with T2D, an **eGFR >25 ml/min** per 1.73 m², normal serum potassium concentration, and **albuminuria (>30 mg/g [>3 mg/mmol])** despite maximum tolerated dose of RAS inhibitor (RASi) 2A	Recommended for patients with CKD and albuminuria who are at **increased risk for CV events or CKD progression** (if **eGFR ≥25 mL/min/1.73 m²**) to reduce CKD progression and CV events. Potassium levels should be monitored. A	Finerenone is recommended for patients with **CKD** and **albuminuria** associated with **T2D** if eGFR ≥25 ml/min/1.73 m² and serum [K⁺] <5.0 mmol/l – the drug has a BP lowering effect IA
SGLT-2i	Recommended as foundational therapy for persons with T2D and CKD with **eGFR ≥20 mL/min/1.73m² to reduce progression of CKD and risk of CV disease**	Recommend treating patients with T2D, CKD, and an eGFR ≥20 ml/min/1.73 m²(1A)	Recommended for patients with an **eGFR ≥20 mL/min/1.73 m²** and **UACR ≥200 mg/g** to reduce risk of CKD progression and CV events# (LoE: A) Recommended for patients with an **eGFR ≥20 mL/min/1.73 m²** and **UACR ranging from normal to 200 mg/g** to reduce CKD progression and CV events# (LoE: B)	Recommended to reduce **cardiac** and **kidney events** in **T2D** – they have a BP lowering effect Recommended for patients with **diabetic** and non-diabetic **nephropathies CKD** if eGFR is at least 20 or 25 ml/min/1.73 m² *
GLP-1RA	Recommended for persons with T2D and DKD or CKD in diabetes with **eGFR ≥15 mL/min/1.73 m²** for **glycaemic control** and to **reduce risk of ASCVD and progression of albuminuria**	In adults with T2D and CKD who have not achieved individualized glycemic targets **despite use of metformin and SGLT2** inhibitor treatment, or who are unable to use those medications, **we recommend a long-acting GLP-1 RA** (1B)	Should be **considered** for **additional CV risk reduction‡**	–

*In non-pregnant patients with diabetes and hypertension; #for patients with T2D and CKD; ‡in patients with T2D and diabetic kidney disease, with eGFR ≥25 mL/min/1.73 m²

1. Blonde L, *et al. Endocr Pract* 2022; 28:923–1049; 2. KDIGO. *Kidney Int* 2024;105(Suppl 4S):S117–S314; 3. American Diabetes Association. *Diabetes Care* 2024;47(Suppl 1):S219–S230; 4. Mancia G, *et al. J Hypertens 2023:* Dec 1;41(12):1874-2071

Finerenone 요양 급여 적용 기준

제2형 당뇨가 있는 **만성 신장병 성인 환자**로서,
ACE 억제제 또는 Angiotensin II 수용체 차단제를 최대허용(내약) 용량으로
4주 이상 안정적으로 투여 중에도 불구하고 다음 조건을 모두 만족하는 경우
표준요법(ACE 억제제 또는 Angiotensin II 수용체 차단제)과 병용하여 투여함.
다만, 지속적인 증상을 보이는 만성 심부전 환자(NYHA class II~IV)는 제외함.

- 다 음 -

1) **uACR >300 mg/g 또는 요 시험지봉 검사(urine dipstick test) 양성(1+ 이상)**
2) **25≤ eGFR <75 mL/min/1.73m²인 경우**

투여 중단: eGFR이 15 mL/min/1.73m² 미만으로 감소하는 경우 투여 중단하여야 함.

상병코드: 당뇨병용제와 같이 처방 시 N18 코드를 추가합니다.[2]

E11 (2형 당뇨병 관련 상병코드) + **N18** (만성 신장병)

N182 만성신장병(2기)
N183 만성신장병(3기)
N184 만성신장병(4기)
N189 상세불명의 만성 신장병

해당 보험약가는 요양 급여 기준을 만족하는 경우, 보험상한금액에 따라 산정된 가격을 표시한 것으로, 개별 환자에 따라 실제 부담금액은 달라질 수 있습니다.

ACE, angiotensin-converting enzyme; eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association; uACR, urine albumin-creatinine ratio

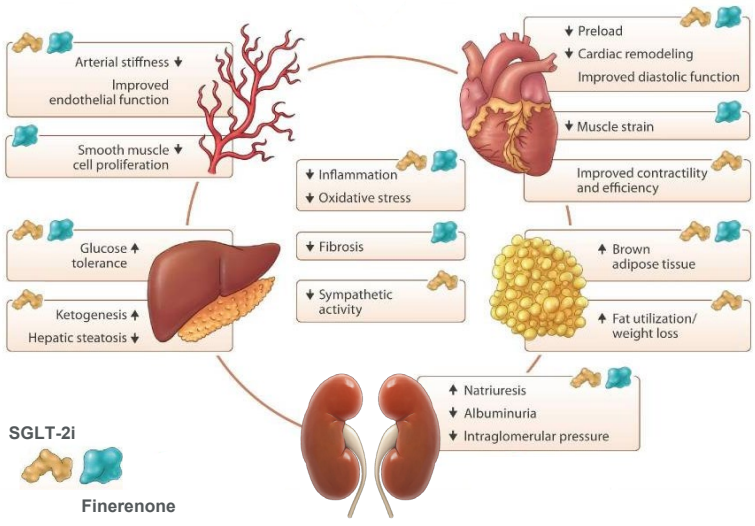
References 1.「요양급여의 적용기준 및 방법에 관한 세부사항」 일부개정 (보건복지부 고시 제2024-20호(2024.01.31)). 2. 한국표준질병사인분류(KCD), https://www. koicd.kr/kcd/kcd.do?degree=08 accessed on Jan 2024. 3. 약제급여목록및급여상한금액표일부개정(보건복지부 고시 제2024-11호(2024.01.26)).

The complementary MoA of Finerenone and SGLT-2is have the potential for additive beneficial effects

Finerenone: Inhibits MR overactivation, which may contribute to CKD progression (driven by metabolic factors, haemodynamic factors, inflammation and fibrosis)

SGLT-2i: Kidney haemodynamic effect that induces glucosuria and natriuresis, resulting in a reduction in intraglomerular hypertension

Complementary MoA → potential for additive beneficial effect in CKD + T2D and CVD



CVD, cardiovascular disease; MoA, mechanism of action; MR, mineralocorticoid receptor
This figure is reproduced from Green, et al. 2022, under the terms of the Creative Commons Attribution-NonCommercial License (https://creativecommons.org/licenses/by-nc/4.0/)
Green JB, et al. *Nephrol Dial Transplant* 2023;38(4):894–903.

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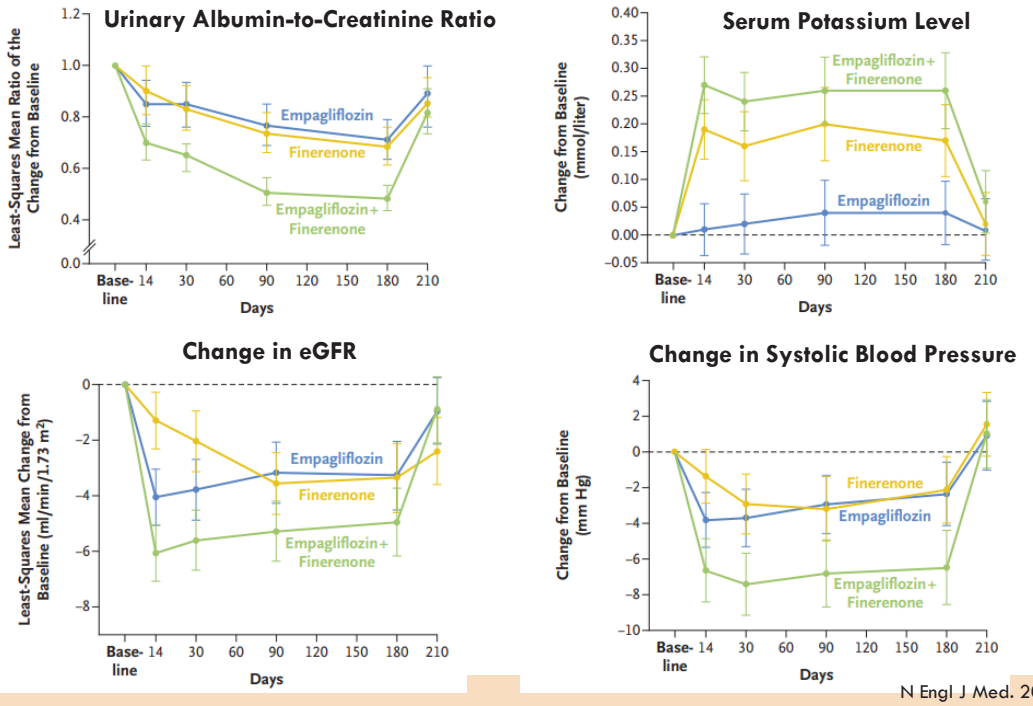
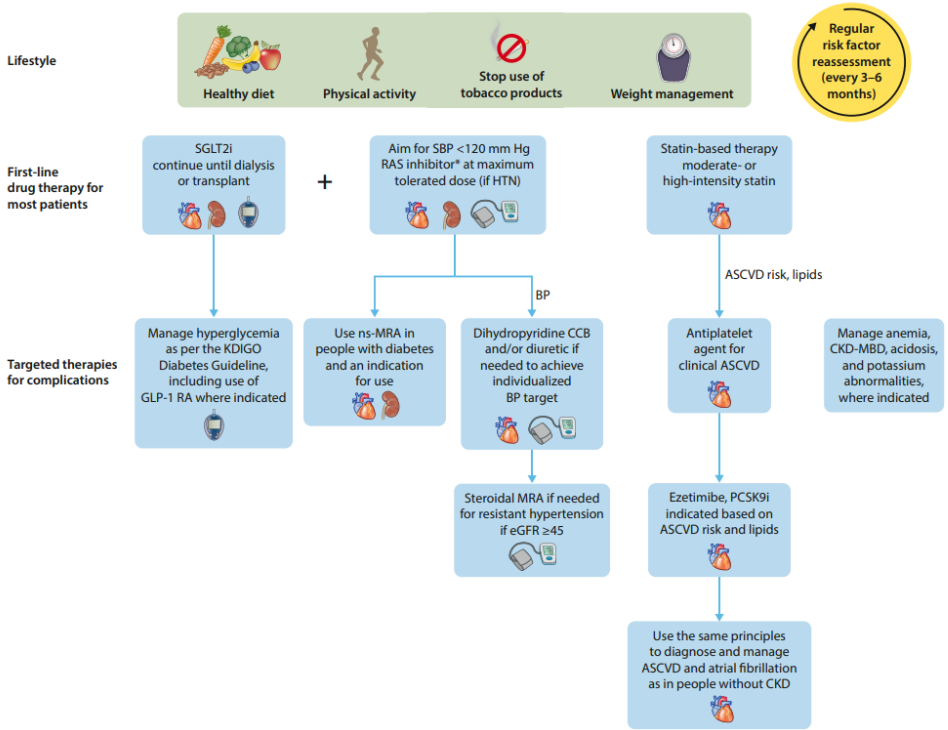
Finerenone with Empagliflozin in CKD and T2DM



N Engl J Med. 2025 Jun 5.



Kidney Int. 2022;102:990–999.

Risks of progression to kidney failure, HF and death can be dramatically reduced with new therapeutics

Anticipated event-free survival* with optimal kidney therapeutics in people with diabetes and CKD[1,3]

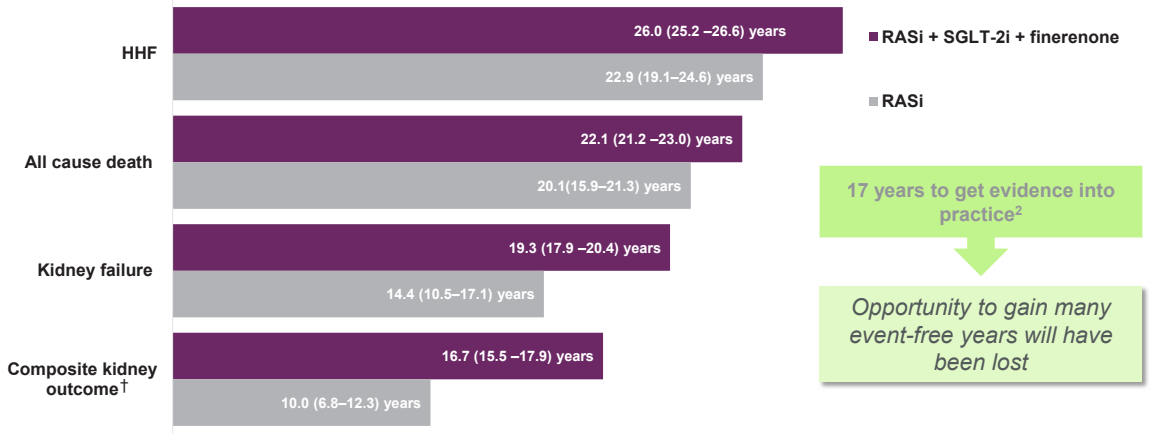


Figure adapted from Luyckx VA, et al. Am J Nephrol 2024;55(3):298–315.

*Estimated event-free survival for various outcomes if indicated therapies were initiated at age 50 years in subjects with diabetes and CKD (eGFR <60 mL/min/1.73[2]
†Composite kidney outcome = doubling of serum creatinine, kidney failure, and death from kidney failure.
Data derived from Heerspink H, et al (2024)[3]
1. Luyckx VA, et al. *Am J Nephrol.* 2024;55(3):298–315; 2. Rubin R. *JAMA.* 2023;329(16):1333–1336; 3. Heerspink H, et al. *Diabetes Obes Metab.* 2023;25(11):3327–3336.

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GLP1 receptor agonists

Recommendation 4.2.1: In patients with T2D and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i treatment, or who are unable to use those medications, we recommend a long-acting GLP-1 RA *(1B)*.

- To minimize gastrointestinal side effects, start with a low dose of GLP-1 RA, and titrate up slowly
- GLP-1 RA should not be used in combination with dipeptidyl peptidase-4 (DPP-4) inhibitors.
- The risk of hypoglycemia is generally low with GLP-1 RA when used alone, but risk is increased when GLP-1 RA is used concomitantly with other medications such as sulfonylureas or insulin. The doses of sulfonylurea and/or insulin may need to be reduced.
- GLP-1 RA may be preferentially used in patients with obesity, T2D, and CKD to promote intentional weight loss.

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GLP1 receptor agonists

GLP-1 RA	Dose	CKD adjustment
Dulaglutide	0.75 mg and 1.5 mg once weekly	No dosage adjustment Use with eGFR >15 ml/min per 1.73 m^2
Exenatide	10 µg twice daily	Use with CrCl >30 ml/min
Exenatide extended-release	2 mg once weekly	Use with eGFR >45 ml/min per 1.73 m^2
Liraglutide	1.2 mg and 1.8 mg once daily	No dosage adjustment Limited data for severe CKD
Lixisenatide	10 µg and 20 µg once daily	No dosage adjustment Limited data for severe CKD Not recommended with eGFR <15 ml/min per 1.73 m^2
Semaglutide (injection)	0.5 mg and 1 mg once weekly	No dosage adjustment Limited data for severe CKD
Semaglutide (oral)	3 mg, 7 mg, or 14 mg daily	No dosage adjustment Limited data for severe CKD

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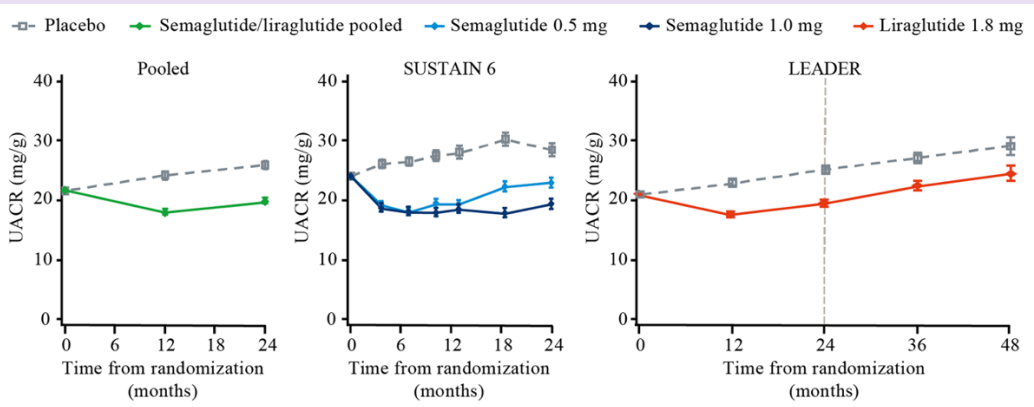
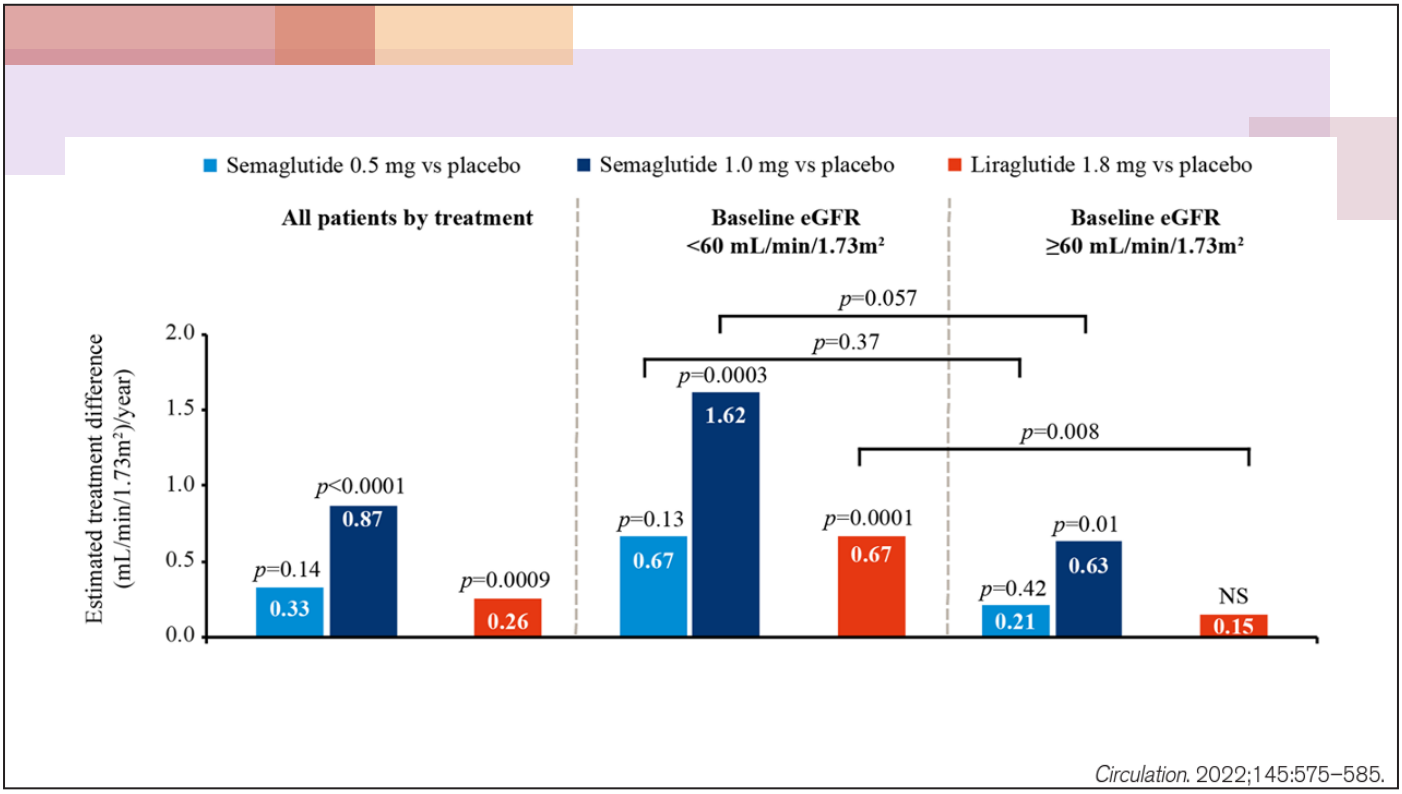
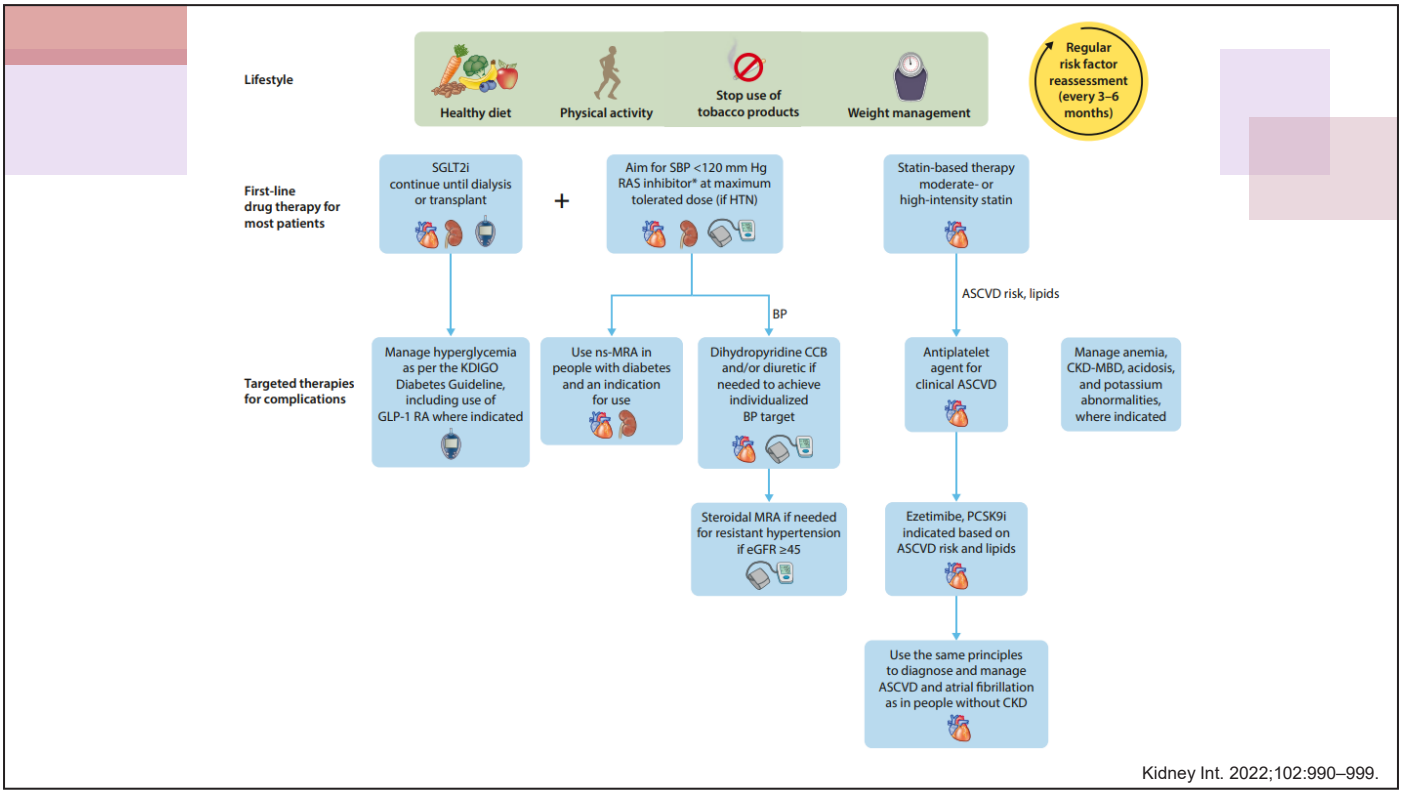


Overall pooled trial population	Estimated treatment ratio at 2 years (treatment vs placebo) [95% CI]; *p* value*		
	SUSTAIN 6		LEADER
	Semaglutide 0.5 mg	Semaglutide 1.0 mg	Liraglutide 1.8 mg
0.76 [0.73, 0.80]; $p<0.001$	0.80 [0.72, 0.90]; $p<0.001$	0.67 [0.60, 0.76]; $p<0.001$	0.77 [0.73, 0.82]; $p<0.001$
	Estimated treatment ratio at 2 years (by-treatment comparisons) [95% CI]; *p* value		
Liraglutide 1.8 mg vs semaglutide 0.5 mg	0.96 [0.85, 1.09]; $p=0.53$	Liraglutide 1.8 mg vs semaglutide 1.0 mg	1.15 [1.02, 1.31]; $p=0.024$

Circulation. 2022;145:575–585.



Circulation. 2022;145:575–585.



Kidney Int. 2022;102:990–999.

Nutrition intake

Recommendation 3.1.2: We suggest that sodium intake be <2 g of sodium per day (or <90 mmol of sodium per day, or <5 g of sodium chloride per day) in patients with diabetes and CKD *(2C)*.

https://m.health.chosun.com/article/article.html?contid=2016031002577

Nutrition intake

Recommendation 3.1.1: We suggest maintaining a protein intake of 0.8 g protein/kg (weight)/d for those with diabetes and CKD not treated with dialysis *(2C)*.

- Patients treated with hemodialysis, and particularly peritoneal dialysis, should consume between 1.0 and 1.2 g protein/kg (weight)/d.

Recommendation 1.5.1: We recommend advising patients with diabetes and CKD who use tobacco to quit using tobacco products *(1D)*.

Recommendation 3.2.1: We recommend that patients with diabetes and CKD be advised to undertake moderate-intensity physical activity for a cumulative duration of at least 150 minutes per week, or to a level compatible with their cardiovascular and physical tolerance *(1D)*.

03
Session

당뇨병 동반 질환 제대로 관리하기

당뇨병 환자의 뇌 건강, 어떻게 지킬까?

서울아산병원 신경과 **임재성**

Cognitive impairment represents a frequent yet under-recognized complication of diabetes mellitus, particularly affecting older adults. Diabetes significantly increases the risk of all-cause dementia (RR 1.73), Alzheimer's disease (RR 1.53), and vascular dementia (RR 2.27), with cognitive changes emerging during prediabetic stages and progressing gradually over years. Central insulin resistance emerges as a key pathogenic pathway, involving dysregulated insulin signaling in critical brain regions and promoting advanced glycation end-product formation and neuroinflammation. Glycemic variability correlates more strongly with cognitive decline than average glycemic control alone. Routine cognitive screening is recommended for diabetes patients aged 65 and older using validated assessment tools. Pharmacological interventions show promise, with GLP-1 receptor agonists demonstrating consistent neuroprotective effects, while SGLT-2 inhibitors show emerging cognitive benefits and metformin's role remains controversial. Lifestyle interventions prove highly effective: structured exercise programs (≥3 times weekly, ≥40 minutes, ≥24 weeks) and MIND diet adherence significantly improve cognitive outcomes. For patients with established cognitive impairment, diabetes management requires individualized glycemic targets while rigorously avoiding hypoglycemia, emphasizing treatment simplification and multidisciplinary care coordination. This evidence-based approach provides clinicians with practical frameworks for integrating cognitive health assessment and protection into routine diabetes care.

2025년 서울아산병원 당뇨병 센터 개원의 연수강좌

당뇨병 환자의 뇌 건강, 어떻게 지킬까?

서울아산병원 신경과
임 재 성

Synopsis

- Understand the epidemiology and pathophysiology of diabetes-related cognitive impairment
- Implement appropriate cognitive screening protocols in diabetes patients
- Apply evidence-based protective strategies in clinical practice
- Modify diabetes management for patients with cognitive impairment

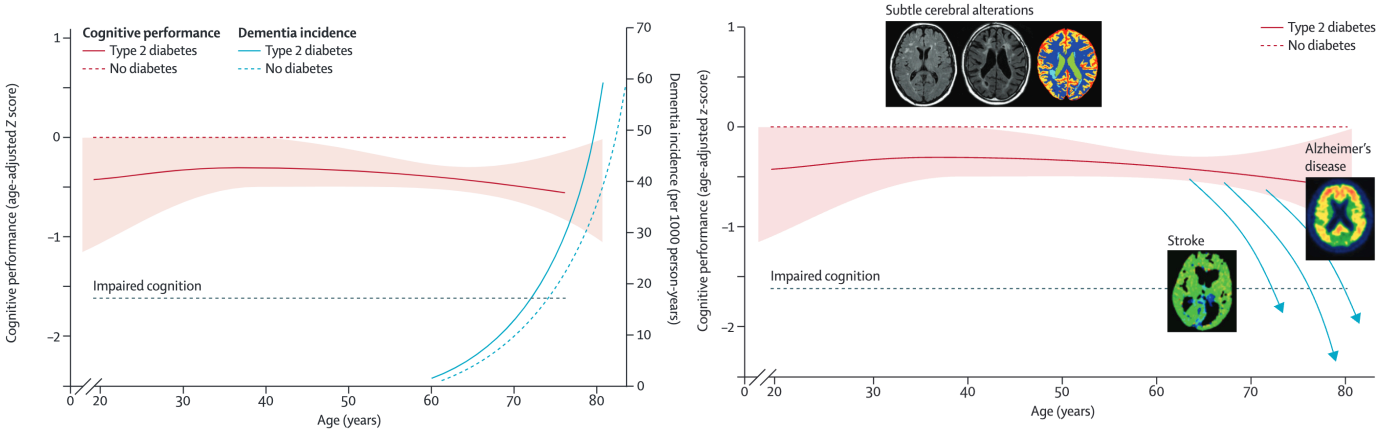
Epidemiology and pathophysiology of diabetes-related cognitive impairment

Stages of cognitive dysfunction related to diabetes mellitus

Diabetes-associated cognitive decrements
- Slow progression, stable course

MCI, dementia
- Over 65 years of age
- Year-by-year cognitive decline

Not a continuum



GJ Biessels, Nat Rev Endocrinol 2018;14(10):591-604

Diabetes Mellitus and Risk of Alzheimer Disease and Decline in Cognitive Function

Diabetes mellitus may be associated withan increased risk of developing AD and may affect cognitive systems differentially

Table 1. Characteristics of the 824 Participants, According to the Presence or Absence of Diabetes Mellitus*

Characteristic	Diabetes Mellitus	
	Present (n = 127)	Absent (n = 697)
Age at baseline, y	74.4 (6.1)	75.2 (7.1)
Male sex, No. (%)	57 (44.9)	200 (28.7)
Education, y	18.0 (3.3)	18.1 (3.4)
MMSE score at baseline	28.3 (1.7)	28.5 (1.7)

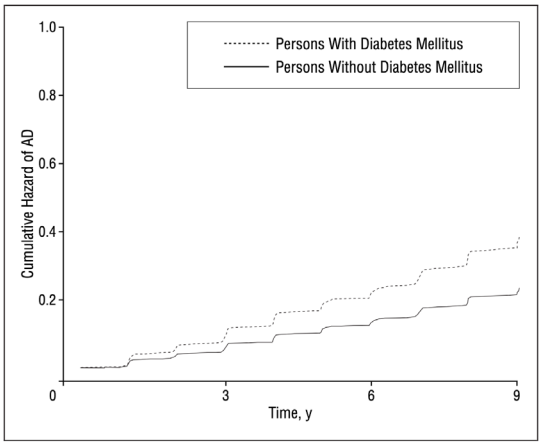


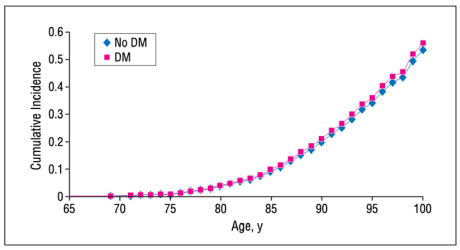
Figure 1. Cumulative hazard of Alzheimer disease (AD) among persons with diabetes mellitus compared with those without diabetes mellitus.

Z Arvanitakis, et al . Arch Neurol. 2004;61:661-666

Diabetes Mellitus and Risk of Developing Alzheimer Disease

Results From the Framingham Study

Cumulative incidence of AD in entire sample
: comparison of groups with and without DM, adjusted for age and sex



Cumulative incidence of AD in low-risk group
: comparison of persons with and without DM, adjusted for age and sex

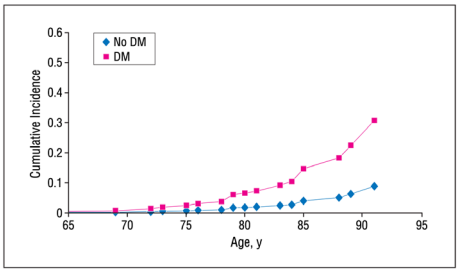


Table 2. Multivariable Cox Proportional Hazards Models Examining the Relation Between Diabetes and the Risk of All-Cause Dementia, Alzheimer Disease, and Vascular Dementia Using Standard and Time-Dependent Cox Models

Variables Adjusted for in Multivariable Analysis	All-Cause Dementia		Alzheimer Disease		Vascular Dementia	
	Cases/N	HR (95% CI)	Cases/N	HR (95% CI)	Cases/N	HR (95% CI)
All cases						
Age, sex	319/2210	1.19 (0.79-1.78)	237/2210	1.07 (0.65-1.75)	32/2210	1.81 (0.63-5.23)
Multivariable*	233/1594	1.20 (0.74-1.96)	176/1594	1.15 (0.65-2.05)	23/1594	0.81 (0.18-3.70)
Age <75 y, multivariable*	122/1183	1.99 (1.04-3.7) (P = .04)	82/1183	1.21 (0.99-4.96)	17/1183	1.21 (0.23-6.37)
Time-dependent, multivariable*	233/1594	1.14 (0.61-2.11)	176/1594	1.35 (0.68-2.70)	23/1594	1.60 (0.34-7.62)
Subjects with APOE ε4 information						
Age y, sex	186/1290	1.18 (0.64-2.18)	140/1290	1.02 (0.48-2.19)	18/1290	3.54 (1.01-12.44) (P = .049)
Multivariable*	142/1009	1.40 (0.70-2.81)	107/1009	1.44 (0.66-3.18)	13/1009	1.24 (0.15-10.11)
Multivariable* + APOE ε4	142/1009	1.20 (0.60-2.40)	107/1009	1.14 (0.52-2.51)	13/1009	1.24 (0.15-10.11)
Age <75 y, multivariable*	86/853	22.20 (0.94-5.18)	58/853	2.39 (0.84-6.81)	12/853	1.74 (0.21-14.55)
Time-dependent, multivariable* + APOE ε4	142/1009	1.58 (0.78-3.20)	107/1009	1.88 (0.84-4.19)	13/1009	2.93 (0.54-15.75)
Subjects with plasma homocysteine in lower 3 quartiles and without APOE ε4						
Age, sex	65/684	2.48 (1.10-5.60) (P = .03)	44/684	2.91 (1.10-7.71) (P = .03)	9/684	1.80 (0.21-15.27)
Multivariable*	58/607	2.39 (0.96-5.91)	39/607	2.98 (1.06-8.39) (P = .04)	7/607	
Time-dependent, multivariable*	58/607	1.88 (0.93-3.80)	39/607	2.24 (0.97-5.21)		
Subjects <75 y with plasma homocysteine in lower 3 quartiles and without APOE ε4						
Age, sex	37/591	3.37 (1.30-8.73) (P = .01)	21/591	3.94 (1.15-13.54) (P = .03)	8/591	2.28 (0.27-19.28)
Multivariable*	32/517	3.54 (1.17-10.770 (P = .03)	18/517	4.77 (1.28-17.72) (P = .02)	6/517	
Time-dependent, multivariable*	32/517	2.13 (0.85-5.30)	18/517	2.46 (0.73-8.21)		

Abbreviations: APOE, apolipoprotein E; CI, confidence interval; HR, hazard ratio.
*Adjusted for age, sex, education, plasma homocysteine, systolic blood pressure, body mass index, current smoking, alcohol use, prevalent stroke, and cardiovascular disease.

Diabetes mellitus did not increase the risk of incident AD in the Framingham cohort overall; however, DM may be a risk factor for AD in the absence of other known major AD risk factors.

A Akomolafe, et al. Arch Neurol. 2006;63:1551-1555

Risk of Cognitive Impairment

Table 3. Random Effects Models Examining the Relation of Diabetes Mellitus to Baseline Level of and to Annual Rate of Change in Cognitive Function*

Cognitive System	Model Terms	Estimate	SE	*P* Value
Global cognitive function	Time	−0.03	0.01	<.001
	Diabetes mellitus	−0.16	0.04	<.001
	Diabetes mellitus × time	−0.02	0.01	.06
Episodic memory	Time	−0.03	0.01	.001
	Diabetes mellitus	−0.16	0.05	.003
	Diabetes mellitus × time	−0.02	0.02	.26
Semantic memory	Time	−0.05	0.01	<.001
	Diabetes mellitus	−0.14	0.06	.01
	Diabetes mellitus × time	−0.01	0.01	.43
Working memory	Time	−0.03	0.01	<.001
	Diabetes mellitus	−0.18	0.06	.001
	Diabetes mellitus × time	−0.01	0.01	.30
Visuospatial ability	Time	−0.02	0.01	<.001
	Diabetes mellitus	−0.21	0.06	.001
	Diabetes mellitus × time	−0.02	0.01	.08
Perceptual speed	Time	−0.08	0.01	<.001
	Diabetes mellitus	−0.08	0.07	.28
	Diabetes mellitus × time	−0.03	0.02	.02

*Analyses were adjusted for the effects of age, sex, educational level, and time interactions with age, sex, and educational level.

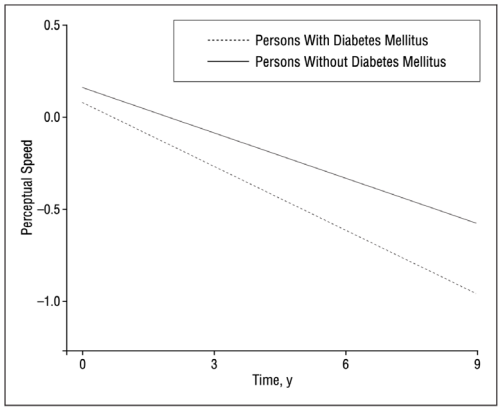


Figure 2. Predicted 9-year paths of change in perceptual speed in typical participants with and without diabetes mellitus.

Z Arvanitakis, et al . Arch Neurol. 2004;61:661-666

Risk of Dementia

Table 2—*Estimated mean differences (95% CI)*

	Unadjusted	Adjusted for NART-IQ
Abstract reasoning	−0.20 (−0.48 to 0.08)	−0.01 (−0.26 to 0.23)
Memory	−0.21 (−0.32 to −0.08)†	−0.15 (−0.28 to −0.03)†
Working memory	−0.20 (−0.42 to 0.01)	−0.07 (−0.27 to 0.13)
Immediate memory and learning rate	−0.24 (−0.41 to −0.06)*	−0.18 (−0.35 to −0.003)†
Forgetting rate	0.04 (−0.18 to 0.26)	0.04 (−0.18 to 0.26)
Incidental memory	−0.49 (−0.73 to −0.17)*	−0.42 (−0.71 to −0.14)*
Information processing speed	−0.26 (−0.48 to −0.03)†	−0.13 (−0.33 to 0.08)
Attention and executive functions	−0.23 (−0.42 to −0.04)†	−0.12 (−0.29 to 0.05)
Visuoconstruction	−0.23 (−0.52 to 0.05)	−0.10 (−0.37 to 0.17)
Language comprehension	−0.35 (−0.65 to −0.04)†	−0.19 (−0.49 to 0.11)

*$P < 0.01$; †$P < 0.05$.

C Ruis, et al. Diabetes Care 2009;32:1261-1265

Outcome measure	Reference	Quality rating	Results (95% CI)
Any dementia*	Schnaider Beeri[26]	7	OR 2·8 (1·4–5·7)
	Curb[19]	5	RR 1·1 (0·7–1·8)
	Whitmer[29]	5	HR 1·5 (1·2–1·8)
Alzheimer's disease	Yamada[24]†	7	OR 4·4 (p<0·01)
	Curb[19]‡	5	RR 1·0 (0·5-2·0)
Vascular dementia	Yamada[24]†	7	OR 1·3 (p=0·06)
	Curb[19]§	5	RR 1·5 (0·8–2·8)

Risk of dementia in people with diabetes relative to those without diabetes. Results were adjusted for age, sex, and education, and in one study,[26] also for vascular risk factors. Diagnostic criteria for dementia: *DSM III[40] or DSM IV;[41] †DSM IV; ‡NINCDS-ADRDA;[42] §California criteria.[47] OR=odds ratio; HR=hazard ratio; RR=relative risk.

***Table 3*: Risk of incident dementia in patients with diabetes mellitus—studies with midlife diabetes assessment**

GJ Biessels, Lancet Neurol 2006; 5: 64–74

Epidemiological Studies

"Increased risk of all-cause dementia & AD in patients with diabetes"

Diabetes-associated cognitive decrements
- Subtle changes in cognitive dysfunction
- Develop during the prediabetics stages
- Evolve very slowly over the course of many years (up to faster than that of normal cognitive aging)

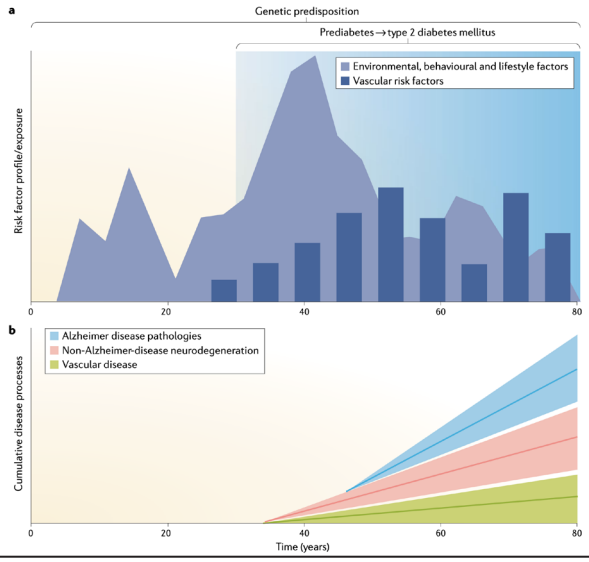
MCI
- HR 1.5 (95% CI 1.0-2.2), 1.6 (95% CI 1.2-2.2) for amnestic MCI
- HR 1.2 (95% CI 0.9-1.8), 1.4 (95% CI 0.8-2.2) for nonamnestic MCI
- Prognosis is worse in patients with diabetes than in patients without diabetes
  - RR of conversion to dementia 1.7 (95% CI 1.1-2.4) compared with patients with MCI+DM

Dementia
- RR for all types of dementia 1.73 (95% CI 1.65-1.82)
- RR for AD 1.53 (95% CI 1.42-1.63)
- RR for VaD 2.27 (95% CI 1.94-2.66)

- HR 1.16 (95% CI 1.15-1.18) for dementia in newly diagnosed diabetes
- Elevated plasma glucose conc. (without diabetes) -> increased risk of dementia

Epidemiological Studies

Diabetes increases the risk of a **clinical diagnosis of AD**
Biomarker and neuropathological studies – burden of AD pathologies is not increased in pts with diabetes
>> Majority of individuals with diabetes,
the clinical phenotype of cognitive dysfunction/dementia is due to **multiple pathologies**



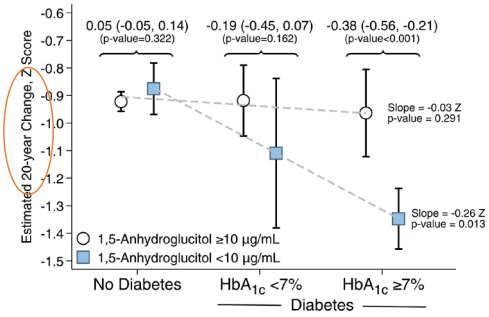
- AD pathologies are still the most common cause of dementia in pts with T2DM
- 40% of T2DM pts. -> Intermediate to severe AD pathology at the time of death

GJ Biessels, Nat Rev Endocrinol 2018;14(10):591-604

Risk Factors for Cognitive Impairment

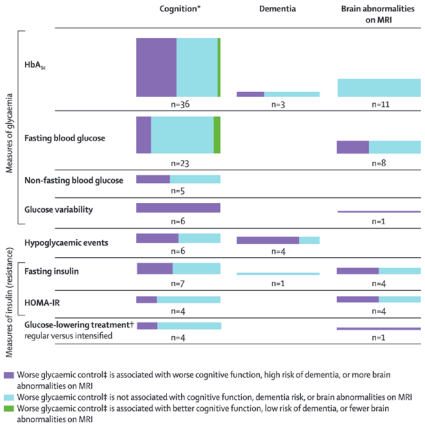
Increased HbA1c
- Linked with diabetes-associated cognitive decrements
- Weak relationship - nonlinearity
  - Both low & high HbA1c: related to increased dementia risk

Fluctuations or peaks in glucose levels

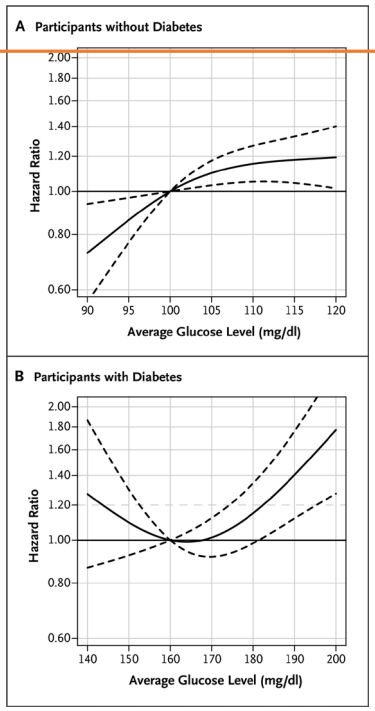


1,5-anhydroglucitol (1,5-AG) level,
<10 ug/mL are associated with glucose peaks
"1,5-AG ≥ 10 + DM" -> similar decline in cognitive function compared with those with "1,5-AG ≥ 10 – DM"

AM Rawlings, et al. Diabetes Care 2017;40:879-886.



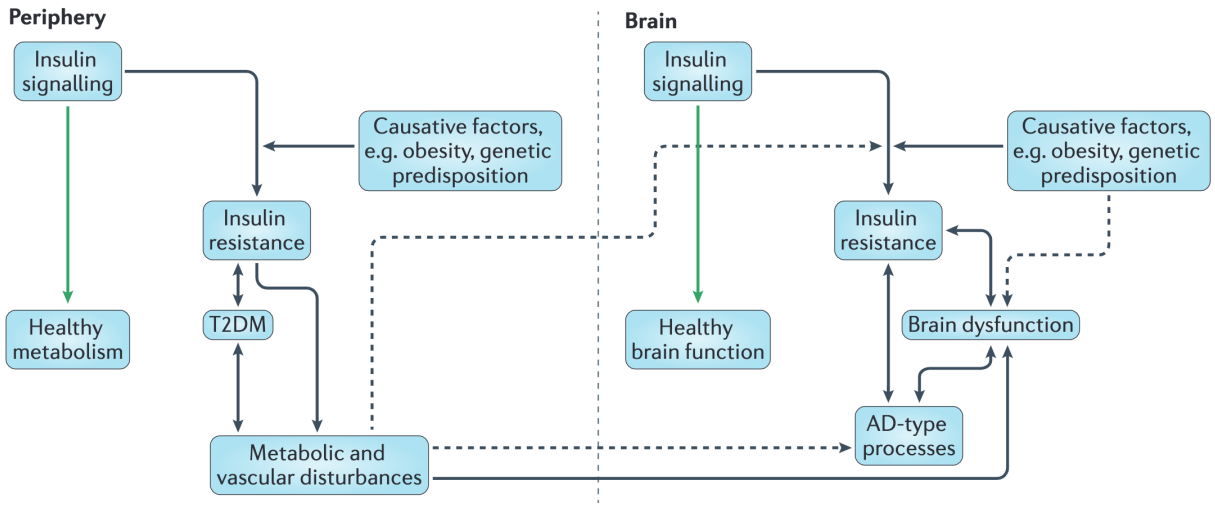
S Geijselaers, et al. Lancet Diabetes Endocrinol 2015;3:75-89.



PK Crane, et al. N Eng J Med 2013;369(6):540-8.

Pathophysiology

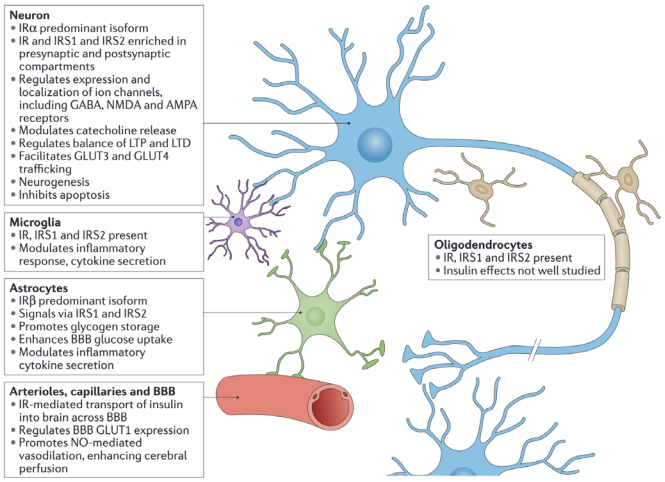
"Complex relationships" between insulin signaling in the brain and elsewhere in the body in health and disease



GJ Biessels, Nat Rev Neurosci 2015;16(11):660-671.

Pathophysiology

Insulin effects in major cell types of the brain



Box 2 | **Brain insulin resistance in ADRDs**

- Increasing age is associated with decreasing cortical insulin concentration and receptor binding in older adults without dementia
- Brain tissue from those with Alzheimer disease (AD) shows major abnormalities in insulin signalling, including
  - Decreased insulin, insulin receptor and insulin receptor substrate 1 (IRS1) mRNA and/or protein expression levels
  - Decreased activation of insulin pathway molecules (for example, IRS1 and AKT) with *ex vivo* stimulation
  - Increased basal phosphorylation levels of multiple insulin–IRS1–AKT pathway molecules
  - Positive correlation between phosphorylated IRS1 and other pathway molecules and AD pathology
- Intranasal insulin administration improves cognitive functioning in humans with AD or mild cognitive impairment and improves measures of insulin signalling, amyloid-β and cognitive behaviours in AD model mice
- Brain insulin resistance might be a feature of other neurodegenerative diseases
  - Insulin receptor expression is decreased and AKT signalling is abnormal in the substantia nigra in Parkinson disease
  - Abnormal phosphorylated IRS1 expression is observed in tauopathies but is not seen in synucleinopathies or TDP-43 proteinopathies

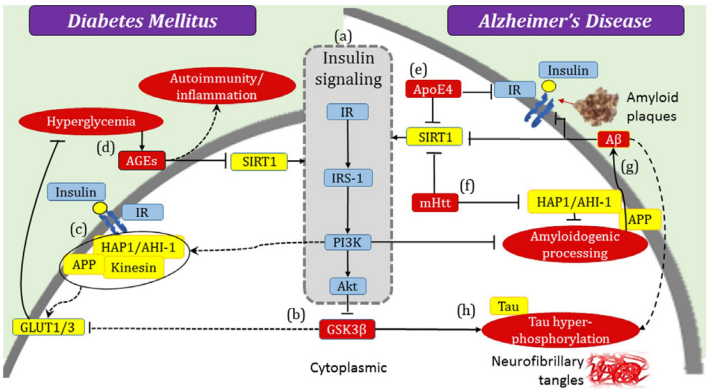
IR density↑ – olfactory bulb, hypothalamus, hippocampus, cerebral cortex, striatum, cerebellum

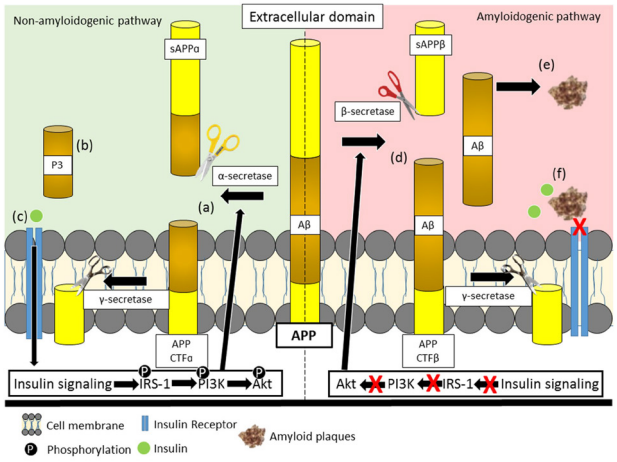
SE Arnold, et al. Nat Rev Neurol 2018;14:168-181.

Pathophysiology

Alzheimer's Disease and Diabetes: Insulin Signaling as the Bridge Linking Two Pathologies

Amyloid plaques degrade IRs and competes with insulin in IR activation -> inhibition of insulin signaling

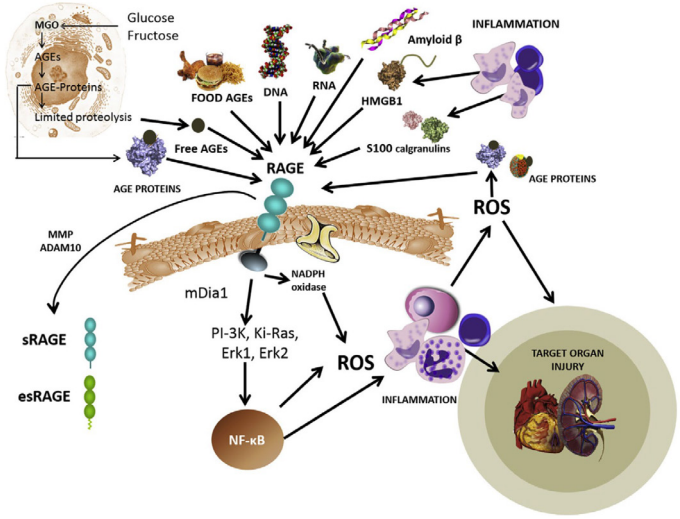




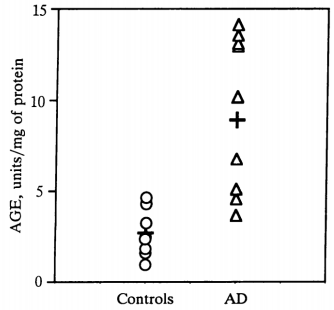
J Shieh, et al. Molecular Neurobiology (2020) 57:1966–1977

Pathophysiology

Advanced Glycation End Products



The Receptor for Advanced Glycation End Products (RAGE) Is a Key Pathway for Inflammatory Complications in Aging and Chronic Disease



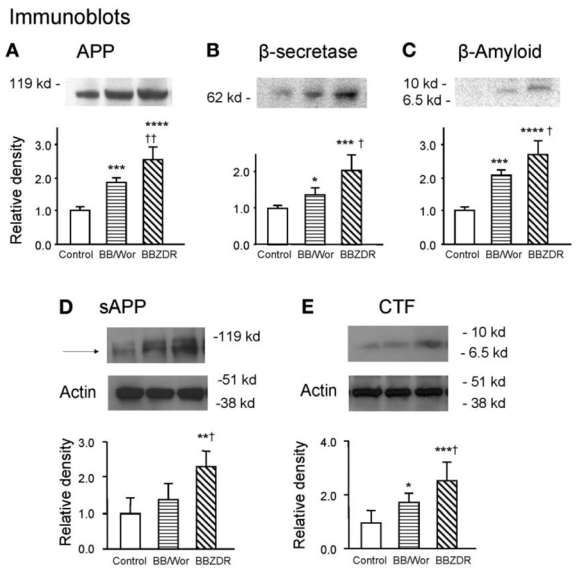
Plaques extracted from AD brains show a 3-fold increase in AGE content compared to age-matched healthy individuals

MP Vitek, et al. PNAS 1994;91:4766-4770

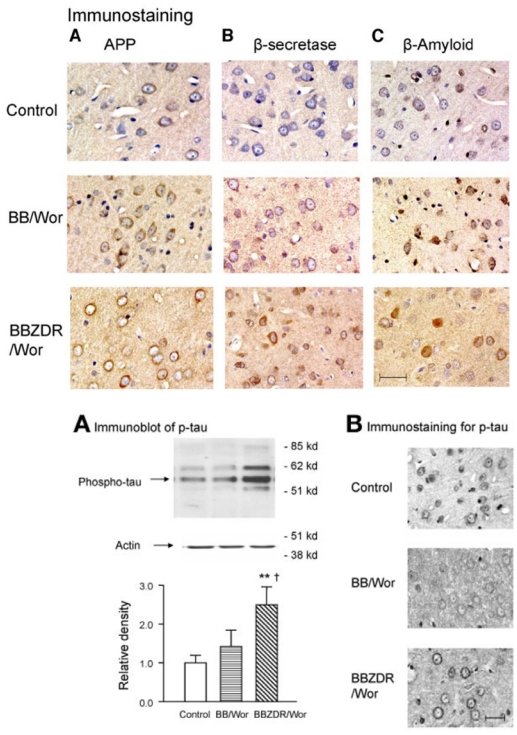
Glycation (AGE formation)
- ↑APP expression, ↑Aβ levels
- ↑Phosphorylation of tau prot.
- Colocalize with nNOS, caspase-3 (neurodegeneration markers)

J Chaudhuri, et al. Cell Metabolism 2018;28(3):337-352.

Alzheimer-Like Changes in Rat Models of Spontaneous Diabetes



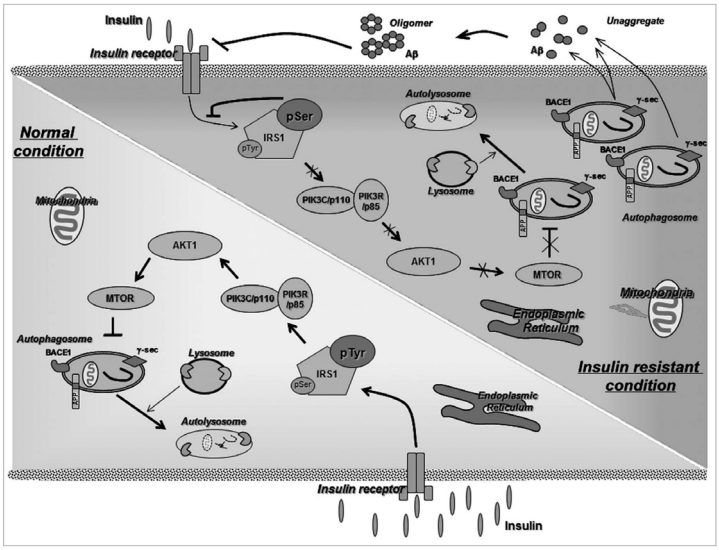
Immunoblotting of APP (A),β-secretase (B), and β-amyloid (C) from frontal cortices in control and type 1 and type 2 diabetic rats



Z Li, et al. Diabetes 2007;56:1817-1824.

Pathophysiology

Altered insulin signal transduction & autophagy
~ correlated with ↑activities of β-secretase1 & γ-secretase &
↑ soluble amyloid-beta in the brains of rats and mice



Insulin resistance-induced autophagosome accumulation resulted in alteration of APP processing through enrichment of secretase proteins in autophagosomes
- Alter APP processing through autophagy activation

SM Son, et al. Autophagy 2012;8(12):1842-1844.

Pathophysiology: Central Insulin Resistance

Brain insulin resistance
-> Promoting amyloid-beta generation & hyperphosphorylation of tau

Altered insulin signal transduction & autophagy
~ Correlated with ↑activities of β-secretase1 & γ-secretase &
↑ soluble amyloid-beta in the brains of rats and mice

Stimulating hippocampal insulin receptors by direct administration of insulin into the hippocampus
-> ↑Learning ability in normal mice
-> Less effect in diabetic mice

Tx that improved insulin availability and/or sensitivity
-> ↓ Levels of amyloid-β and tau hyperphosphorylation in the brain (AD mouse model)

>> Complex role of brain insulin resistance
-> Promoting AD pathology
-> Promising therapeutic target to slow the progression of cognitive decline in humans

Implement appropriate cognitive screening protocols in diabetes patients

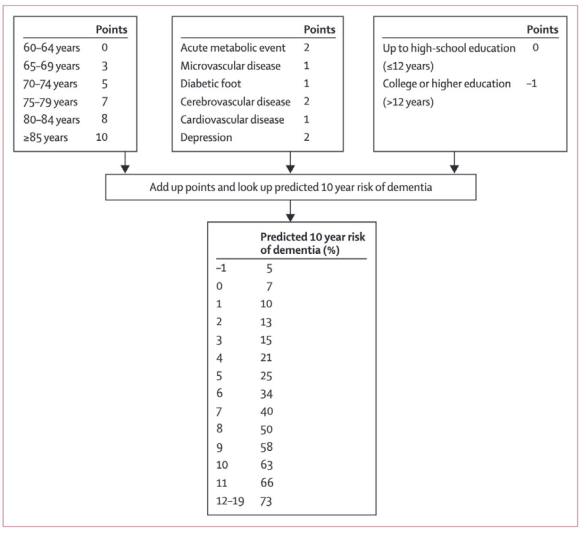
Risk Stratification

	β coefficient†	Hazard ratio (95% CI)	Risk score
Age (years)			
60–64	0	1·00	0
65–69	0·73‡	2·08 (1·85–2·33)	3
70–74	1·28‡	3·61 (3·23–4·03)	5
75–79	1·87‡	6·51 (5·82–7·27)	7
80–84	2·39‡	10·94 (9·68–12·36)	8
>85	2·73‡	15·41 (13·12–18·09)	10
Education			
High school or less (≤12 years)	0	1·00	0
College or higher (>12 years)	−0·14‡	0·87 (0·82–0·92)	−1
Microvascular disease§			
Yes	0·28‡	1·33 (1·19–1·48)	1
No	0	1·00	0
Diabetic foot§			
Yes	0·40‡	1·50 (1·30–1·72)	1
No	0	1·00	0
Cerebrovascular disease§			
Yes	0·50‡	1·65 (1·50–1·82)	2
No	0	1·00	0
Cardiovascular disease§			
Yes	0·19‡	1·21 (1·13–1·29)	1
No	0	1·00	0
Acute metabolic event¶			
Yes	0·45‡	1·58 (1·37–1·81)	2
No	0	1·00	0
Depression¶			
Yes	0·46‡	1·58 (1·48–1·69)	2
No	0	1·00	0

*2449 patients form the total cohort (n=29 661) were not included in the model because of missing data for education or ethnic origin. †Calculated with the Cox proportional hazards model. ‡p<0·0001. §Based on medical history, 1979–97. ¶Based on medical history, 1996–97.

Table 2: **Final multivariable model of the diabetes-specific dementia risk score in 27 512 patients***

Risk score for prediction of 10 year dementia risk in individuals with type 2 diabetes: a cohort study



LG Exalto, et al. Lancet Diabetes Endocrinol 2013;1:183-90.

Risk Stratification

Research Article

The Diabetic Cognitive Impairment Score for Early Screening of Cognitive Impairment in Type 2 Diabetes Patients

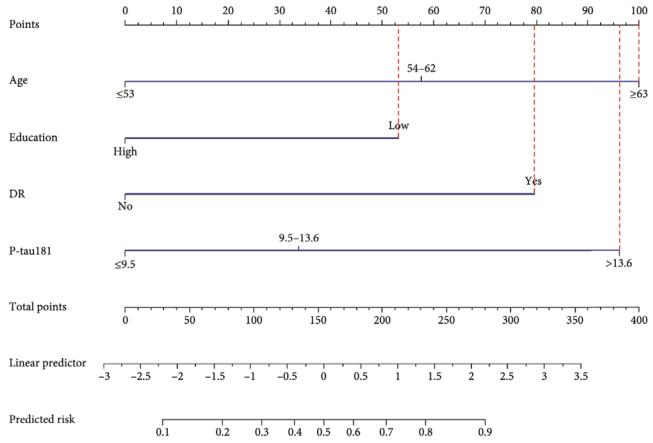
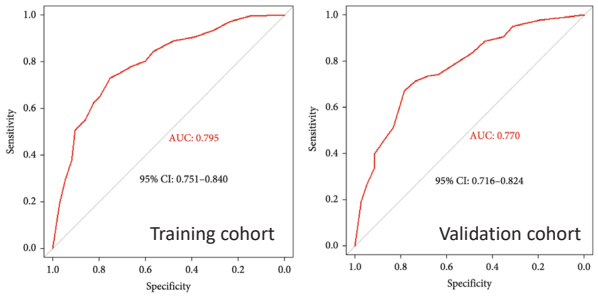


TABLE 3: Nomogram-based preoperative score: Four-variable model.

Variable	Category	Points
Age (years)	≤ 53	0
	54–62	39
	≥ 63	62
Education	High	0
	Low	53
DR	No	0
	Yes	80
P-Tau181 (pg/mL)	≤ 9.5	0
	9.6–13.6	34
	> 13.6	96

Note: Possible score ranges from 0 to 291.
Abbreviation: DR, diabetic retinopathy.



Zhang S, et al. J. Diabetes Res. 2025;2025(1):8029913.

Cognitive Screening

Table 1. Examples of assessment tools and procedures[12-21]*

Assessment domain	Examples of assessment tools and procedures	Comments
Gait, balance, and mobility	IDOP 3-steps package[21]	Easily adapted to guideline resource; contains information on assessing gait speed and balance ability
ADL and IADL	Barthel ADL and IADL	Universally used; minimal training required
Cognition	MiniCog or Montreal Cognitive Assessment Tool	Easy to use; good evidence as screening tools for cognitive impairment
Mood level	Geriatric Depression Score	Widespread use; little training required
Frailty measures	Clinical Frailty Scale or CHSA 9-point Scale	Can be used as a quick assessment for features of frailty
Hypoglycaemia risk	A comprehensive history to identify risk factors *(see Chapter 20-3: Hypoglycaemia)*	Requires a positive commitment to consider risk factors by the clinician
Self-care abilities	SCI-R	A 13-15 item self-completed questionnaire suitable for type 1 and type 2 diabetes
Nutritional assessment	MNA-SF tool or MUST Tool	Well validated tools in widespread use; minimal training required
Pain	Pain thermometer[22] M-RVBPI[23]	For people with diabetes who have moderate to severe cognitive/communication disorder; easy to use but full validity has not yet been established[22]

International Dementia Federation 2023 Guideline

Cognitive Screening

Summary of recommendations on cognitive dysfunction in diabetes from recent guidelines

Managing older people with type 2 diabetes: International Diabetes Federation (IDF) global guideline, 2013 [8]

Assessment of older people with diabetes should be a multidimensional and multidisciplinary process designed to collect information on medical, psychosocial and functional capabilities and how these may limit activities. Use of cognitive screening tests (e.g. MiniCog or MoCA) can be considered for annual assessment. As a minimum, the consultation should include enquiring about functional capacity and cognitive and mental health

Set more lenient treatment targets, particularly for glycaemic control, in patients with cognitive impairment

Diabetes and dementia in older people: a best clinical practice statement by a multidisciplinary national (UK) expert working group, 2014 [31]

Routinely employ a brief cognitive screening test as part of the annual review process

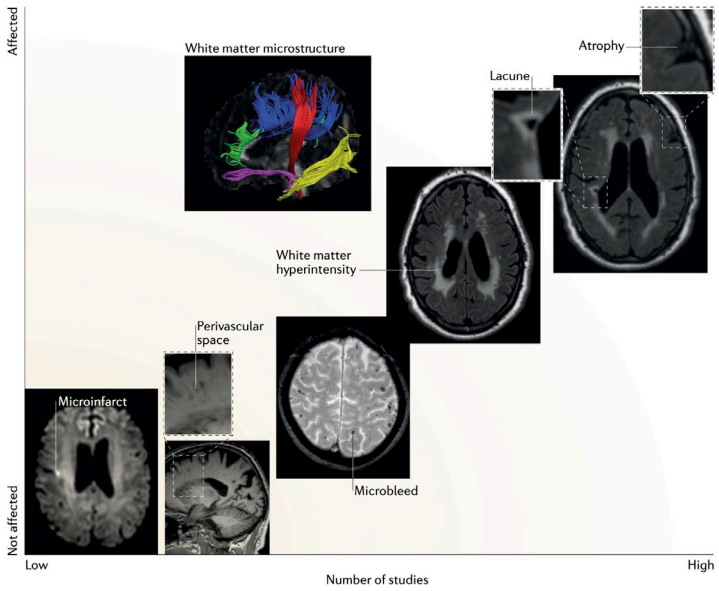
Manage cognitive deficit: ensure self-management deficits are addressed in context of cognitive impairment in partnership with carers

Eliminate diabetes symptoms and/or minimise therapy risk in people with cognitive impairment:

- Avoid overly intensive management
- Use therapies that reduce risk of hypoglycaemia
- Focus education and support on carers as well as patient

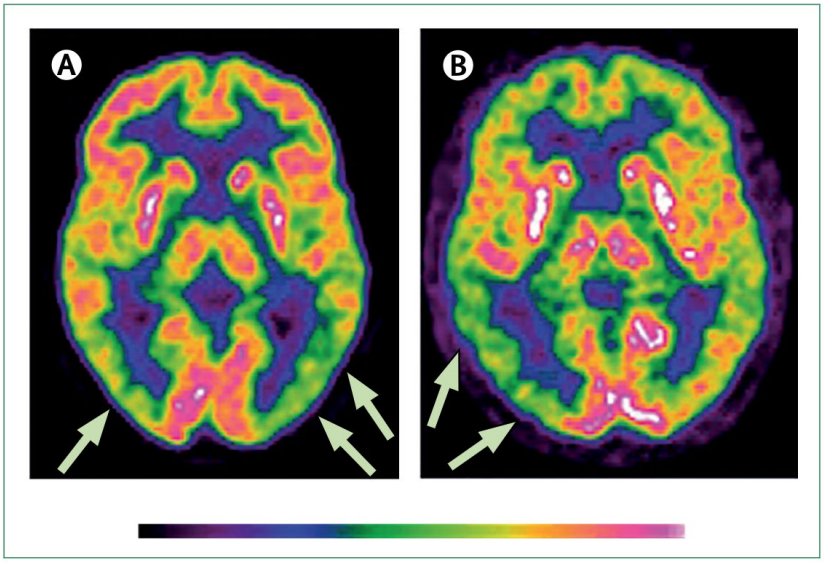
Biessels GJ, et al. Diabetologia. 2020;63(1):3–9.

Biomarkers



GJ Biessels, Nat Rev Endocrinol 2018;14(10):591-604

Biomarkers

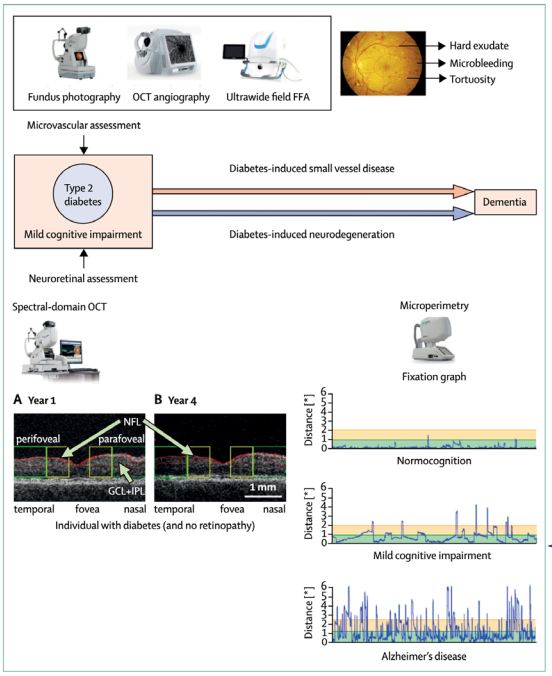


Fluorodeoxyglucose PET in Alzheimer's disease and type 2 diabetes

GJ Biessels, et al. Lancet Neurol 2020;19:699-710

Biomarkers

To identify markers for vascular and neurodegenerative changes underlying cognitive dysfunction



Measuring retinal sensitivity and gze fixation
: progressive impairment of gaze fixation occurring with cognitive decline

GJ Biessels, et al. Lancet Neurol 2020;19:699-710

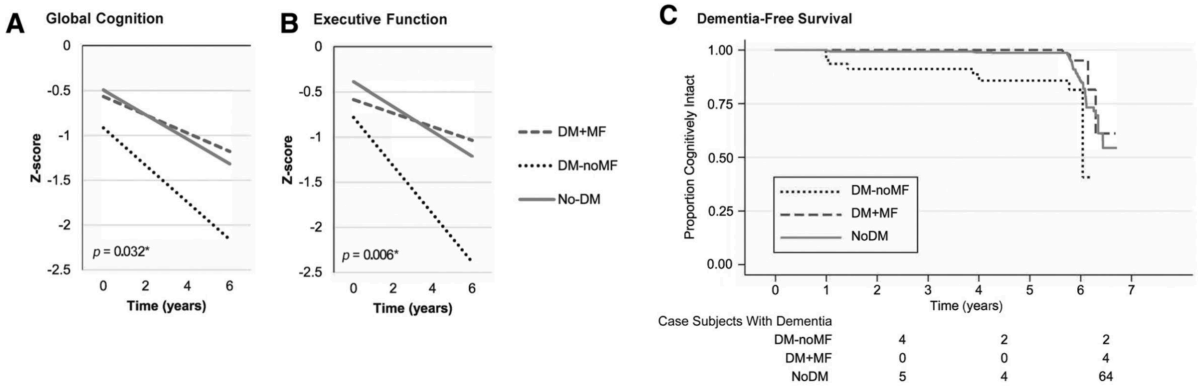
Apply evidence-based protective strategies in clinical practice

Metformin

Metformin Use Is Associated With Slowed Cognitive Decline and Reduced Incident Dementia in Older Adults With Type 2 Diabetes: The Sydney Memory and Ageing Study

Diabetes Care 2020;43:2691–2701 | https://doi.org/10.2337/dc20-0892

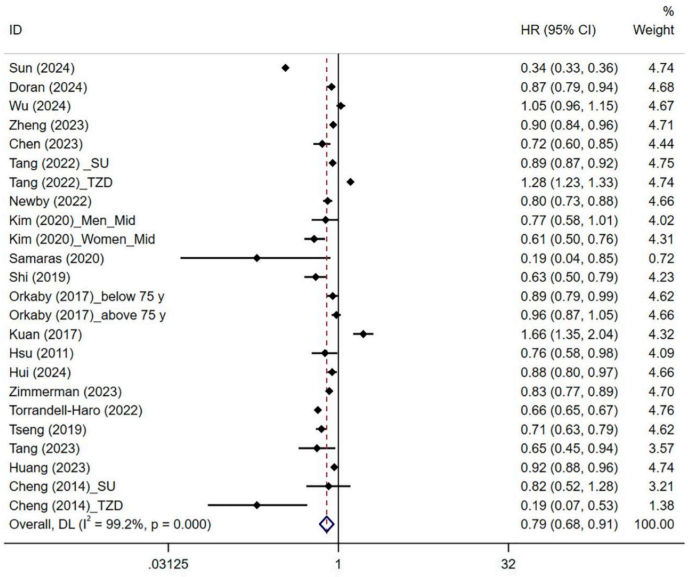
- DM+MF had significantly slower global cognition and executive function decline compared with DM-noMF.
- Incident dementia was significantly higher in DM-noMF compared with DM1MF (odds ratio 5.29 [95% CI 1.17–23.88]; P = 0.05).



Samaras K, et al. Diabetes Care. 2020;43:2691–2701.

Metformin

In comparison with non-users and SU users, metformin users manifested a connection with a decreased risk of dementia.



Tang C, et al. Diabetes, Obes Metab. 2025;27:1992–2001.

Metformin

For specific dementia types, metformin correlates with lower non-Alzheimer's dementia risk (HR = 0.58, 95% CI = 0.57–0.59, p < 0.001), but not for AD (HR = 0.96, 95% CI = 0.71–1.31, p = 0.816) or VD (HR = 1.10, 95% CI = 0.77–1.56, p = 0.610) (P interaction <0.001).

TABLE 2 Subgroup meta-analysis of included studies.

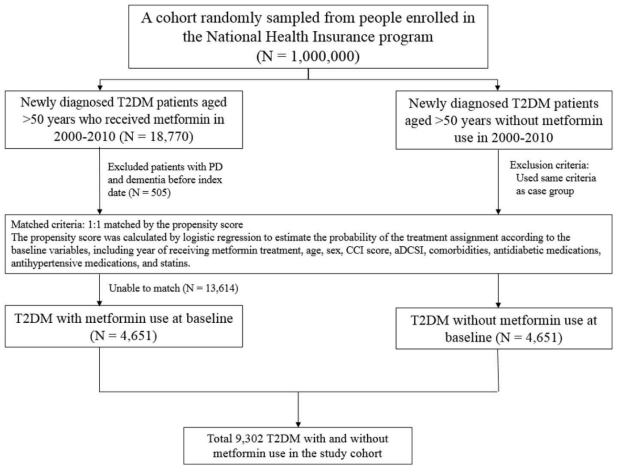
Variables	Comparisons, *n*	HR (95% CI)	*p* value	I^2, %	P for interaction
Overall	24	0.79 (0.68, 0.91)	< 0.001	99.2	
Study design					0.212
Prospective cohort	3	0.98 (0.69, 1.40)	0.925	99.1	
Retrospective cohort	21	0.77 (0.67, 0.89)	< 0.001	98.7	
Contrast types					0.258
Metformin user versus non-user	17	0.76 (0.65, 0.91)	0.002	98.9	
Metformin versus TZD	2	0.53 (0.08, 3.41)	0.503	92.7	
Metformin versus SU	5	0.88 (0.85, 0.90)	<0.001	9.7	
Geographic regions					0.365
The West	13	0.85 (0.72, 1.00)	0.044	99.2	
Asia	11	0.71 (0.50, 1.01)	0.055	99.2	
Sex					0.328
Male	4	0.86 (0.79, 0.93)	<0.001	11.0	
Female	4	0.79 (0.67, 0.91)	0.002	77.1	
Types of dementia					< 0.001
AD	8	0.96 (0.71, 1.31)	0.816	98.4	
VD	7	1.10 (0.77, 1.56)	0.610	98.1	
Non-Alzheimer's dementia	1	0.58 (0.57, 0.59)	<0.001		
Type 2 diabetes status					0.035
Newly diagnosed type 2 diabetes	5	1.01 (0.81, 1.27)	0.900	91.1	
Type 2 diabetes	19	0.75 (0.64, 0.89)	< 0.001	99.3	
HbA1c level					0.469
<7%	5	0.95 (0.77, 1.17)	0.629	98.1	
≥7%	5	0.95 (0.77, 1.17)	0.645	94.8	

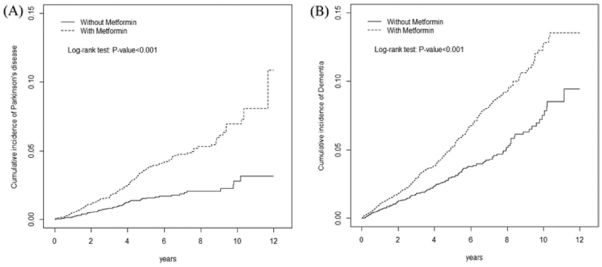
AD, Alzheimer disease; HbA1c, glycated haemoglobin A1c; HR, hazard ratio; SU, sulfonylureas; TZD, thiazolidinedione; VD, Vascular dementia.

Tang C, et al. Diabetes, Obes Metab. 2025;27:1992–2001.

Metformin

Long-term metformin exposure in patients with T2DM may lead to the development of NDs including dementia and PD.





Incidence and subhazard ratios of Parkinson's disease and dementia according to medication status based on the competing-risk regression.

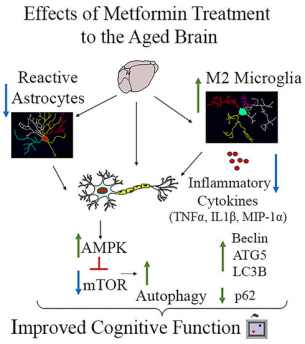
Variables	Metformin	
	No (*N* = 4651)	Yes (*N* = 4651)
Parkinson's disease		
cSHR (95% CI)	1 (Reference)	2.08 (1.57, 2.76)***
aSHR[a] (95% CI)	1 (Reference)	2.00 (1.50, 2.66)***
Dementia		
cSHR (95% CI)	1 (Reference)	1.50 (1.24, 1.83)***
aSHR[a] (95% CI)	1 (Reference)	1.51 (1.24, 1.84)***

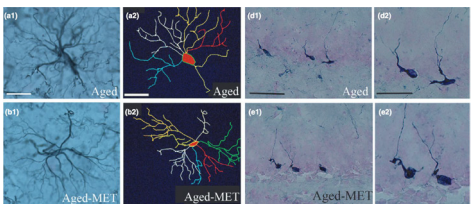
Abbreviations: cHR, crude hazard ratio; aHR, adjusted hazard ratio; cSHR, crude subhazard ratio; aSHR, adjusted subhazard ratio; CI, confidence interval.
*** $P < 0.001$.

Kuan Y-C, et al. Prog Neuro-Psychopharmacol Biol Psychiatry. 2017;79:77–83.

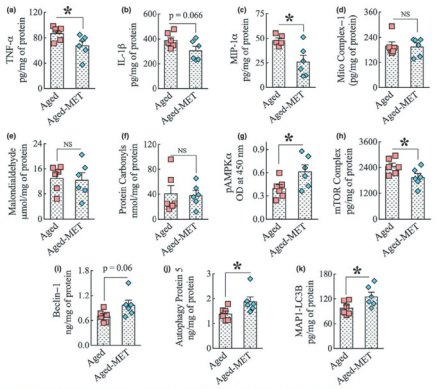
Metformin

Improves cognitive function with alleviation of microglial activation and enhancement of autophagy in the hippocampus



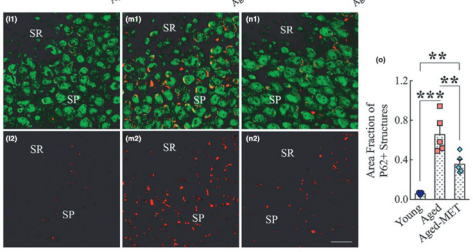


Ten weeks of MET treatment to 18-month-old mice reduced astrocyte hypertrophy but had no effects on neurogenesis or synapses in the hippocampus.



The bar charts a-c show a reduced concentration of proinflammatory markers TNF-α (a), IL-1β (b), and MIP-1α (c) in the hippocampus of the MET-treated aged mice compared to untreated aged mice.

The bar charts i-k show MET treatment enhanced the levels of autophagy-related proteins beclin-1 (i), autophagy protein 5 (j), and microtubule-associated protein 1 light chain 3 beta (MAP1-LC3B; k) in the hippocampus.



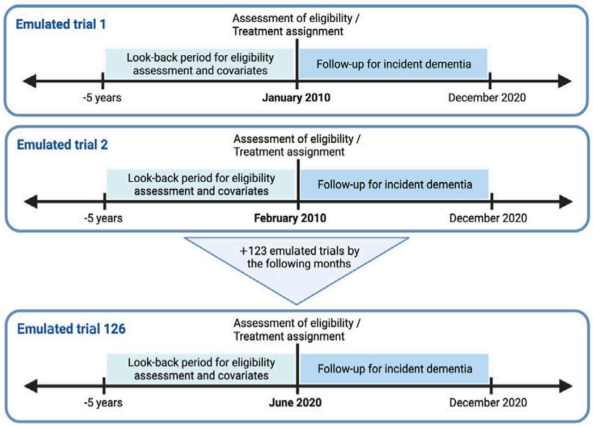
The bar chart (o) compares the area fraction of p62+ structures in the CA3 subfield of the hippocampus across three groups.

자가포식(autophagy) 관련 단백질(beclin-1, ATG5, MAP1-LC3B) 증가 및 p62+ 구조 감소(자가포식 활성 증가)

Kodali M, et al. Aging Cell. 2021;20:e13277.

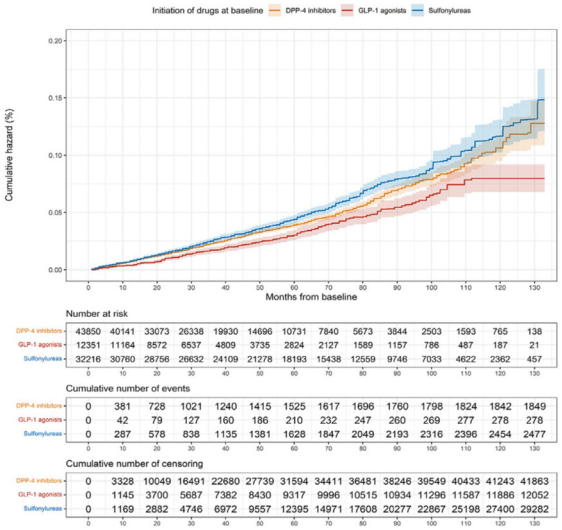
GLP-1 Receptor Agonists

- Sequential trial emulation from 1st January 2010 to 30th June 2020 using data from Swedish national registers
- Aged 65 or older, had T2DM & initiated GLP-1 agonists, DPP-4 inhibitors, or sulfonylureas
- Followed for up to 10 years to assess the risk of dementia
- Assignment to treatment of GLP-1 agonists, DPP-4 inhibitors, or sulfonylureas at baseline and remaining on the assigned drug without taking the other two drugs during follow-up.



- Baseline is defined as the month in which all eligibility criteria are met
- Participants could meet the eligibility criteria in multiple months and be included multiple times
- Fixed 5-year look-back period was used to assess disease histories for each trial

GLP-1 agonists were associated with a lower risk of dementia compared to sulfonylureas and DPP-4 inhibitors in older individuals with T2DM.

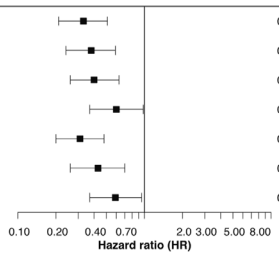


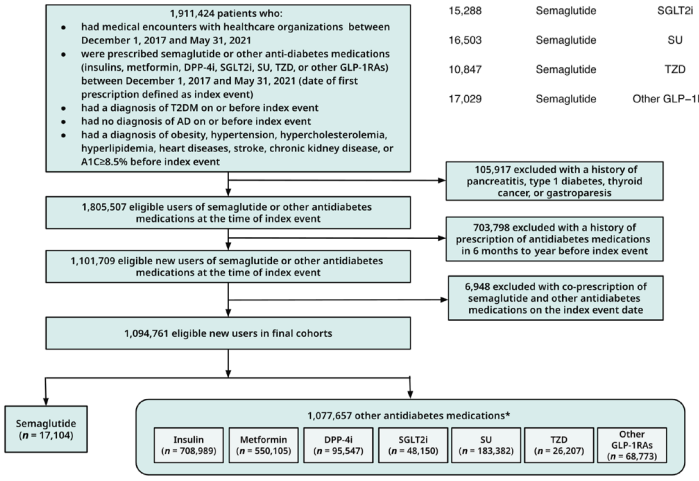
Tang B, et al. eClinicalMedicine. 2024;73:102689.

GLP-1 Receptor Agonists: Semaglutide

Risk of first–time diagnosis of Alzheimer's disease in patients with type 2 diabetes (comparison between matched semaglutide vs other antidiabetes medications groups)

Size/Group	Exposure group	Comparison group	Exposure Group Cases (overall risk)	Comparison Group Cases (overall risk)	HR (95% CI)
17,087	Semaglutide	Insulin	27 (0.16%)	73 (0.43%)	0.33 (0.21 to 0.51)
17,080	Semaglutide	Metformin	27 (0.16%)	68 (0.40%)	0.38 (0.24 to 0.59)
15,878	Semaglutide	DPP–4i	27 (0.17%)	62 (0.39%)	0.40 (0.26 to 0.63)
15,288	Semaglutide	SGLT2i	26 (0.17%)	40 (0.26%)	0.60 (0.37 to 0.98)
16,503	Semaglutide	SU	27 (0.16%)	80 (0.49%)	0.31 (0.20 to 0.48)
10,847	Semaglutide	TZD	24 (0.22%)	51 (0.47%)	0.43 (0.26 to 0.70)
17,029	Semaglutide	Other GLP–1RAs	27 (0.16%)	44 (0.26%)	0.59 (0.37 to 0.95)

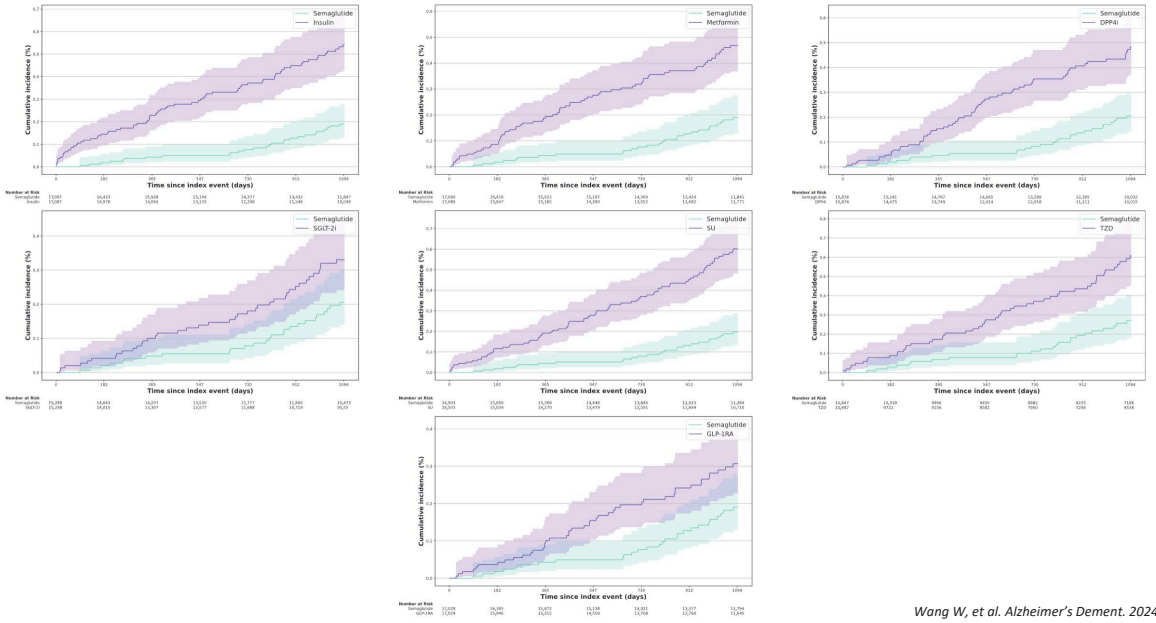




Wang W, et al. Alzheimer's Dement. 2024;20:8661–8672.

GLP-1 Receptor Agonists

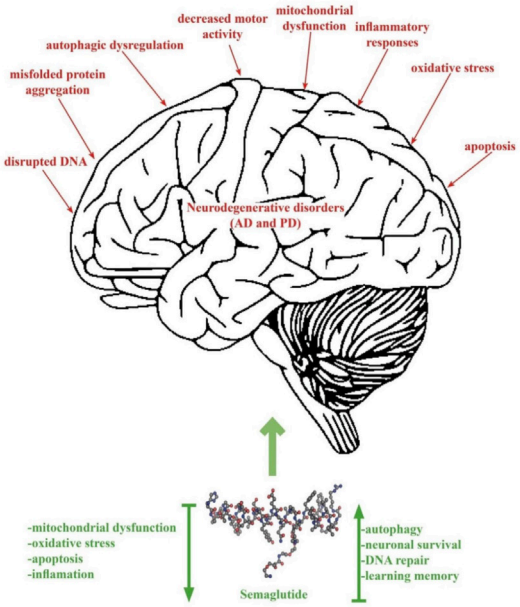
Cumulative AD incidences for the seven comparisons between propensity-score-matched semaglutide vs. other antidiabetic medication groups



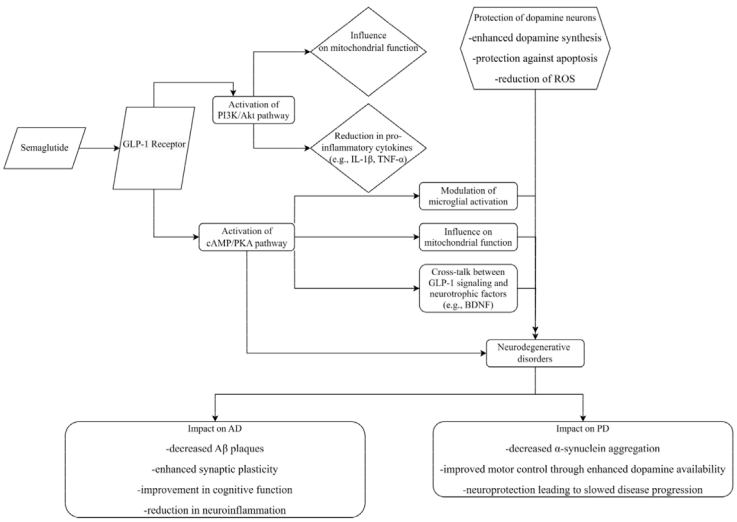
Wang W, et al. Alzheimer's Dement. 2024;20:8661–8672.

GLP-1 Receptor Agonists

The pathogenesis of AD and PD and the effects of SEM



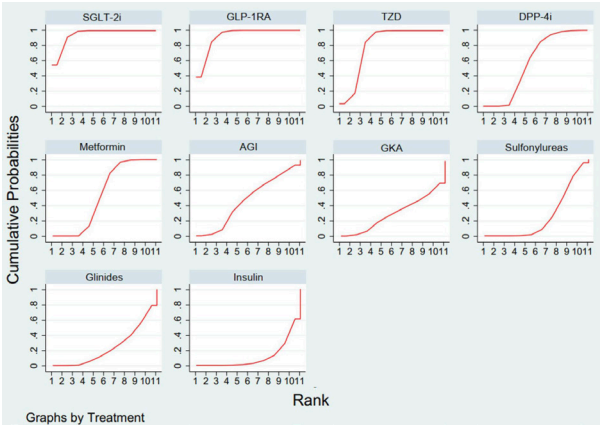
Mechanism of action of SEM and its impact on dopamine in AD and PD



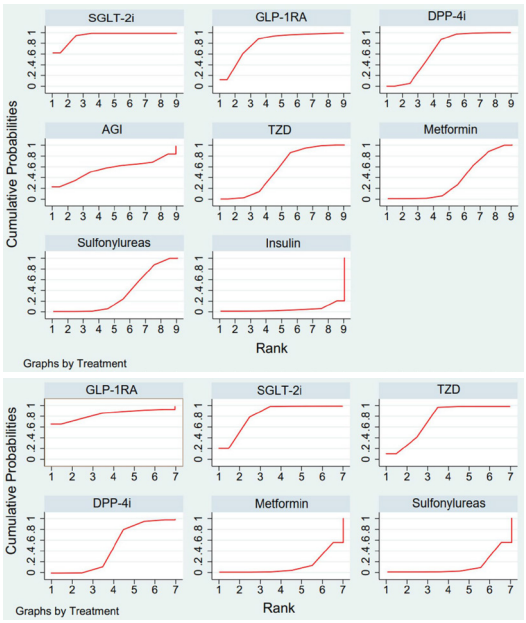
Meca AD, et al. Curr Issues Mol Biol. 2024;46:5929–5949.

SGLT-2 Inhibitors

Network meta-analysis of a total of 41 observational studies (3,307,483 participants) and 23 RCTs (155,443 participants)



SUCRA evaluations of the network meta-analysis for observational studies (anti-diabetic agents and the risks of dementia)

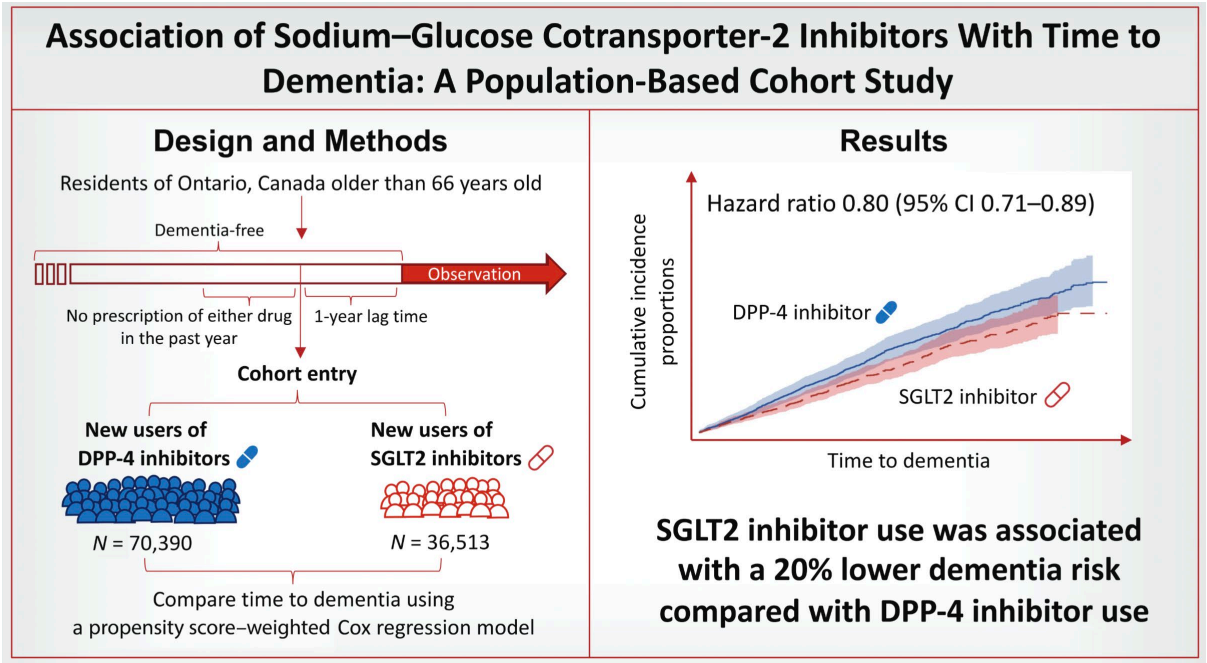


AD

VaD

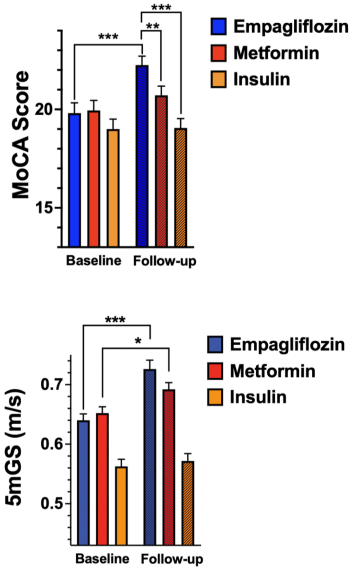
Li Z, et al. Alzheimer's Res Ther. 2024;16:272.

SGLT-2 Inhibitors vs. DPP-4 inhibitors



Wu C-Y, et al. Diabetes Care. 2022;46:297–304.

SGLT-2 Inhibitors: Empagliflozin



Significant beneficial effects of the SGLT2 inhibitor empagliflozin on cognitive and physical impairment in frail older adults with diabetes and HFpEF.

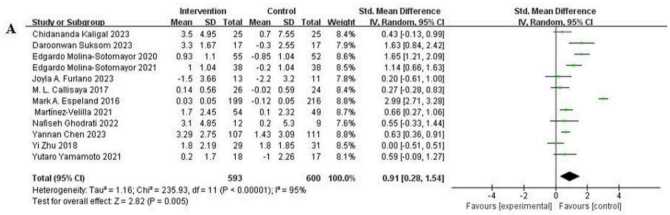
Table 2—Logistic regression analysis in the entire patient sample using the improvement in the MoCA score as the dependent variable

	Regression coefficient	SE	Odds ratio	95% CI Lower	95% CI Upper	*P*
Age	0.020	0.032	1.021	0.958	1.087	0.526
BMI	0.084	0.122	1.088	0.857	1.381	0.490
Heart rate	0.002	0.023	1.002	0.958	1.047	0.933
Glycemia	−0.004	0.005	0.996	0.986	1.006	0.411
Hypertension	−0.308	0.391	0.735	0.341	1.581	0.430
Hyperlipidemia	0.619	0.393	1.857	0.859	4.012	0.115
Chronic obstructive pulmonary disease	0.297	0.392	1.345	0.624	2.900	0.449
Chronic kidney disease	−0.214	0.380	0.807	0.383	1.699	0.573
Empagliflozin	1.284	0.426	3.609	1.566	8.321	**0.003**

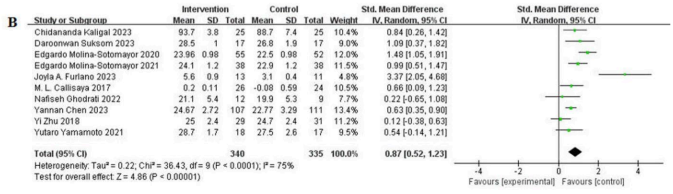
Mone P, et al. Diabetes Care. 2022;45:1247–1251.

Exercise

Change of cognition throughout intervention duration



Post-intervention cognitive scores



복합운동을 주 3회 이상, 24주 이상, 한 번에 40분 넘게 실시할 때 인지 기능 개선 효과가 가장 큼

Table 6. The moderating effect test of exercise intervention on cognitive function in people living with diabetes.

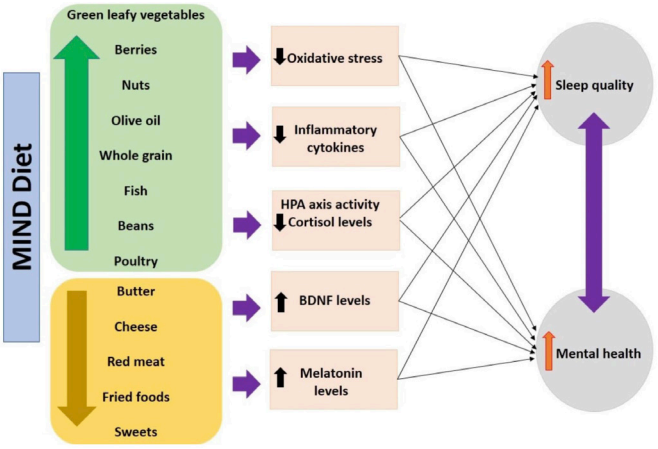
Regulated variable	Homogeneity-testing X^2	Homogeneity-testing P	Homogeneity-testing I^2/%	Category	SMD	95%CI	Two-tail test Z	Two-tail test P	Documents quantity	Sample size
Means of intervention	235.93	< 0.00001	95	Aerobic exercise	1.07	(0.81, 1.33)	8.09	< 0.00001	4	277
				Resistance exercise	0.43	(−0.09, 0.94)	1.61	0.11	2	59
				Multi-component exercise	1.86	(1.65, 2.07)	17.68	< 0.00001	4	589
				Mind-body exercise	0.59	(0.35, 0.84)	4.76	< 0.00001	2	268
Frequency of intervention	236.27	< 0.00001	95	≤3 times/week	0.77	(0.60, 0.94)	8.81	< 0.00001	8	590
				>3 times/week	1.89	(1.68, 2.09)	17.89	< 0.00001	4	603
Intervention cycle	227.81	< 0.00001	96	≤12 weeks	0.47	(0.15, 0.79)	2.29	0.004	4	165
				>12 & ≤24 weeks	0.83	(0.64, 1.02)	8.59	< 0.00001	5	475
				>24	2.64	(2.38, 2.90)	19.95	< 0.00001	2	450
Intervention time	235.93	< 0.00001	95	≤40 min/times	0.44	(0.16, 0.73)	3.05	0.002	3	198
				>40 min/times	1.42	(1.27, 1.56)	18.90	< 0.00001	9	995

Sun Z, et al. PLOS ONE. 2024;19(6):e0304795.

MIND Diet

The effect of MIND diet on sleep status, mental health, and serum level of BDNF in overweight/obese diabetic women with insomnia: a randomized controlled trial

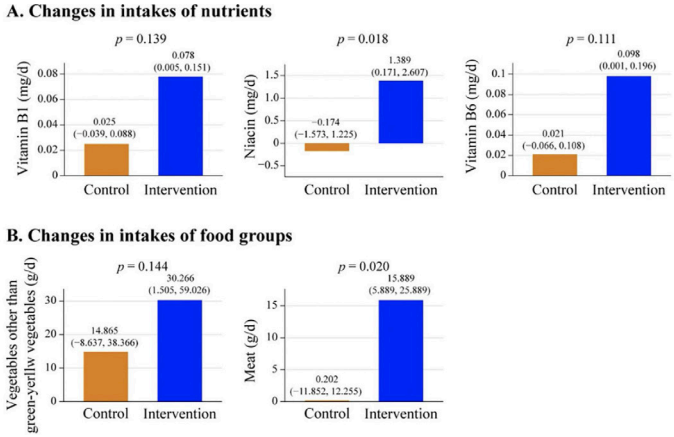
Variables	MIND diet group ($n=22$) Mean (SD)	Control group ($n=22$) Mean (SD)	Mean difference (95% CI)	*P*-value	Difference in outcome measures between MIND diet and control groups [a]	
					β (95% CI)	P-value
BDNF (pg/ml)						
Baseline	1.16 (0.12)	1.18 (0.11)	0.01 (− 0.06, 0.08)	0.003**	0.37 (0.13, 0.61)	0.004[‡]
End of trial	1.67 (0.46)	1.33 (0.27)		0.004[†]		
P-value	< 0.001*	0.009*				
Cortisol (nmol/L)						
Baseline	560.90 (169.83)	593.41 (216.52)	32.51 (− 85.88, 150.91)	0.251**	− 81.58 (− 141.14, − 22.01)	0.009[‡]
End of trial	416.82 (125.60)	498.45 (128.77)		0.022[†]		
P-value	< 0.001*	0.009*				

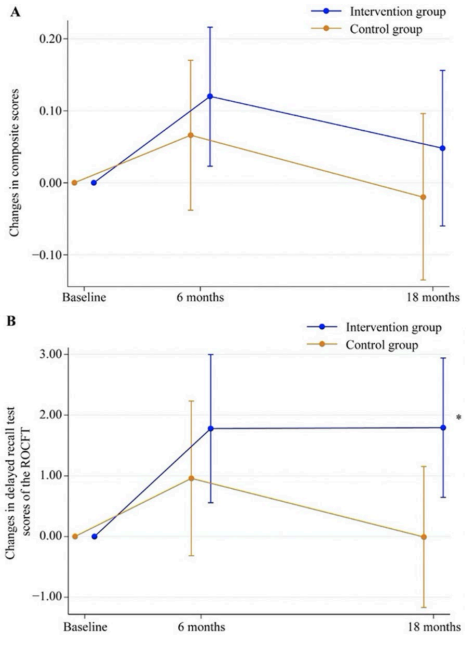


Golmohammadi M, et al. Sci. Rep. 2025;15(1):8237.

Multidomain Intervention Trial

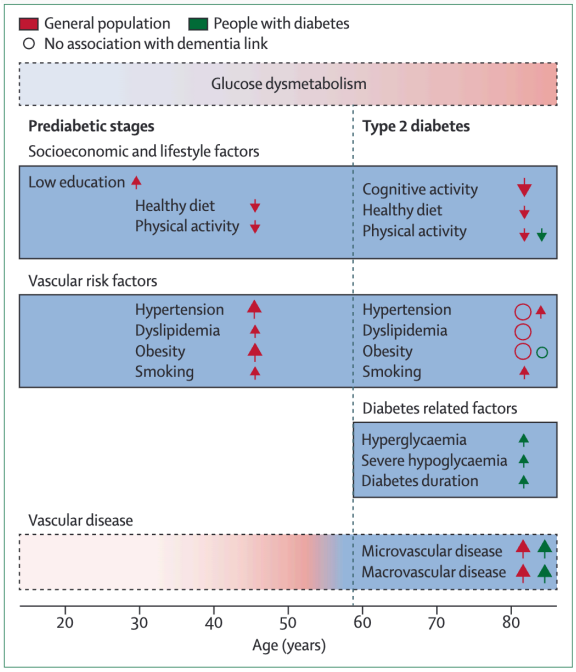
- DESIGN: 18-month, multi-centered, RCT
- SETTING: 12 hospitals in Japan
- PARTICIPANTS: Outpatients with type 2 diabetes aged 70–85 years with cognitive impairment
- 361 participants were screened, and 154 were randomly assigned to
- either the intervention group (n = 81) or the control group (n = 73). Finally, 110 participants completed the trial.





Sugimoto T, et al. J Prev Alzheimer's Dis. 2024;11(6):1604–14.

Multidomain Intervention Trial



Biessels GJ, et al. Lancet Diabetes Endocrinol. 2014;2(3):246–55.

Modify diabetes management for patients with cognitive impairment

Optimizing Glycemic Control

Maintaining individualized targets while rigorously avoiding severe hypoglycemia

While chronic hyperglycemia causes long-term damage, severe low blood sugar can lead to immediate and acute symptoms, potentially culminating in seizures or coma

Table 13.1—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

Characteristics and health status of person with diabetes	Rationale	Reasonable A1C goal*	Fasting or preprandial glucose	Bedtime glucose	Blood pressure	Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.0–7.5% (<53–58 mmol/mol)	80–130 mg/dL (4.4–7.2 mmol/L)	80–180 mg/dL (4.4–10.0 mmol/L)	<130/80 mmHg	Statin, unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses† or two or more instrumental ADL impairments or mild to moderate cognitive impairment)	Variable life expectancy. Individualize goals, considering: • Severity of comorbidities • Cognitive and functional limitations • Frailty • Risk-to-benefit ratio of diabetes medications • Individual preference	<8.0% (<64 mmol/mol)	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)	<130/80 mmHg	Statin, unless contraindicated or not tolerated
Very complex/poor health (LTC or end-stage chronic illnesses‡ or moderate to severe cognitive impairment or two or more ADL impairments)	Limited remaining life expectancy makes benefit minimal	Avoid reliance on A1C; glucose control decisions should be based on avoiding hypoglycemia and symptomatic hyperglycemia	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<140/90 mmHg	Consider likelihood of benefit with statin

Committee ADA PP, ElSayed NA, Aleppo G, et al. Older Adults: Standards of Care in Diabetes—2024. Diabetes Care. 2023;47:S244–S257.

Simplification

Table 13.2—Considerations for treatment plan simplification and deintensification/deprescribing in older adults with diabetes

Characteristics and health status of person with diabetes	Reasonable A1C/ treatment goal	Rationale/considerations	When may medication plan simplification be required?	When may treatment deintensification/ deprescribing be required?
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	<7.0–7.5% (<53–58 mmol/mol)	• Individuals can generally perform complex tasks to maintain good glycemic management when health is stable • During acute illness, individuals may be more at risk for administration or dosing errors that can result in hypoglycemia, falls, fractures, etc.	• If severe or recurrent hypoglycemia occurs in individuals on insulin therapy (regardless of A1C) • If wide glucose excursions are observed • If cognitive or functional decline occurs following acute illness	• If severe or recurrent hypoglycemia occurs in individuals on noninsulin therapies with high risk of hypoglycemia (regardless of A1C) • If wide glucose excursions are observed • In the presence of polypharmacy
Complex/intermediate (multiple coexisting chronic illnesses or two or more instrumental ADL impairments or mild to moderate cognitive impairment)	<8.0% (<64 mmol/mol)	• Comorbidities may affect self-management abilities and capacity to avoid hypoglycemia • Long-acting medication formulations may decrease pill burden and complexity of medication plan	• If severe or recurrent hypoglycemia occurs in individuals on insulin therapy (even if A1C is appropriate) • If unable to manage complexity of an insulin plan • If there is a significant change in social circumstances, such as loss of caregiver, change in living situation, or financial difficulties	• If severe or recurrent hypoglycemia occurs in individuals on noninsulin therapies with high risk of hypoglycemia (even if A1C is appropriate) • If wide glucose excursions are observed • In the presence of polypharmacy
Very complex/poor health (LTC or end-stage chronic illnesses or moderate to severe cognitive impairment or two or more ADL impairments)	Avoid reliance on A1C and avoid hypoglycemia and symptomatic hyperglycemia	• No benefits of tight glycemic management in this population • Hypoglycemia should be avoided • Most important outcomes are maintenance of cognitive and functional status	• If on an insulin plan and the individual would like to decrease the number of injections and finger-stick blood glucose monitoring events each day • If the individual has an inconsistent eating pattern	• If on noninsulin agents with a high hypoglycemia risk in the context of cognitive dysfunction, depression, anorexia, or inconsistent eating pattern • If taking any medications without clear benefits

Committee ADA PP, ElSayed NA, Aleppo G, et al. Older Adults: Standards of Care in Diabetes—2024. Diabetes Care. 2023;47:S244–S257.

Conclusions

- Screen routinely: Annual cognitive assessment for diabetes patients ≥65 years
- Optimize control: Target appropriate HbA1c based on cognitive status
- Prevent hypoglycemia: Especially critical in cognitively impaired patients
- Promote lifestyle: Exercise and MIND diet principles
- Individualize care: Simplify regimens for impaired patients
- Monitor closely: Regular reassessment and adjustment

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Thank you for your attention.

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