بنام خدا

وبینار " درمان های نوین دیابت نوع ۲ "

پنجشنبه ۱۶ بهمن ۱۳۹۹

دبیر برنامه "آقای دکتر فرزاد نجفی پور"

ساعت	عنوان	سخنران	رشته تخصصی – رتبه علمی
۱۱-۱۰	آخرین گایدلاین ADA در درمان هیپرگلیسمی دیابت نوع ۲		
۱۲-۱۱	درمان های دارویی دیابت بر اساس اینکرتین	دکتر فرزاد نجفی پور	دانشیار، فوق تخصص غدد و متابولیسم
۱۳-۱۲	مهار کننده سدیم گلوکوز ترانسپورتر ۲	دکتر وحیده صدرا	استادیار، فوق تخصص غدد و متابولیسم
۱۳-۳۰/۱۳	Case report و پرسش و پاسخ		

Diabetes Care

Volume 44, Supplement 1, January 2021
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6- Glycemic Targets: Standards of Medical Care in Diabetes -2021

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9- Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes - 2021

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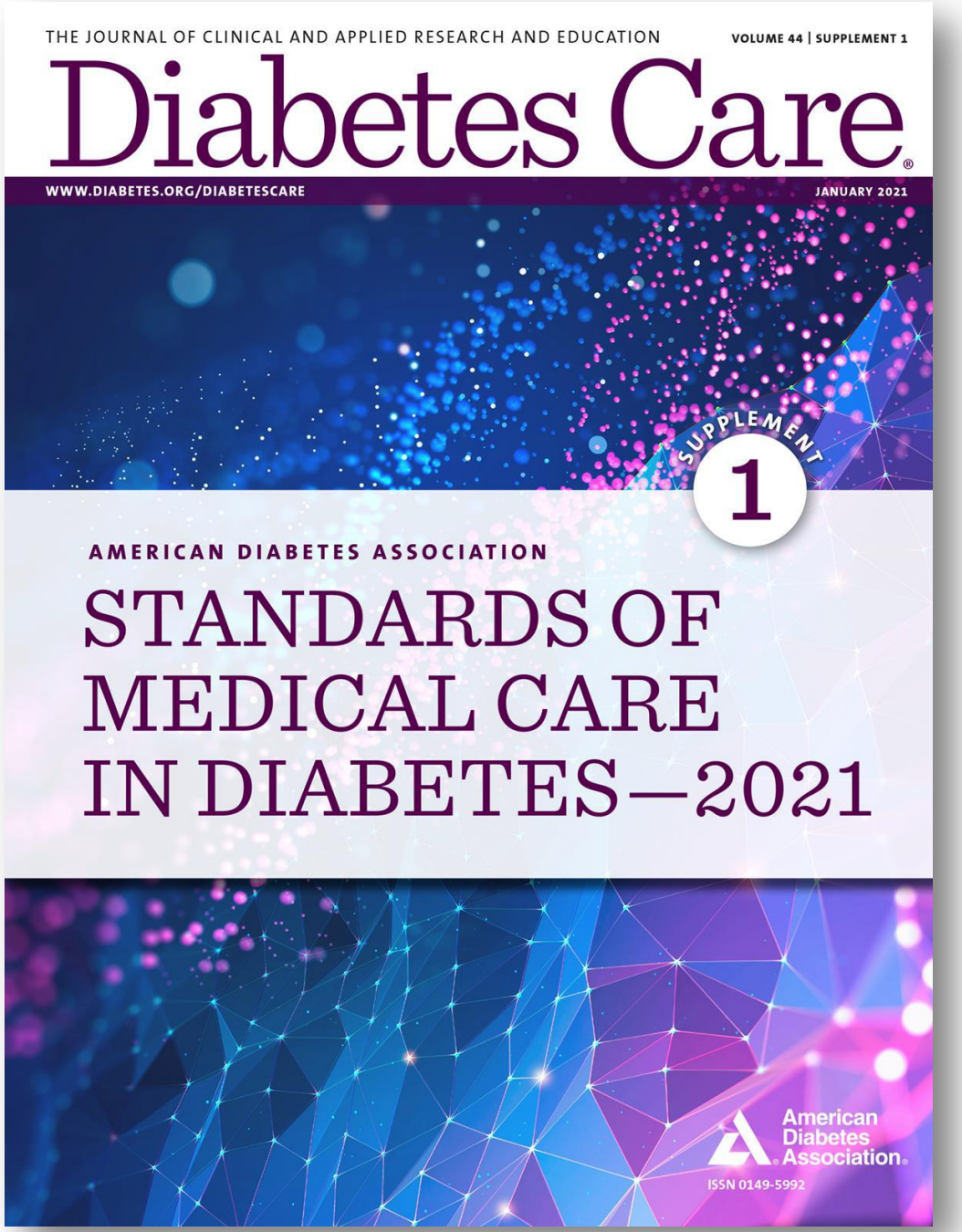

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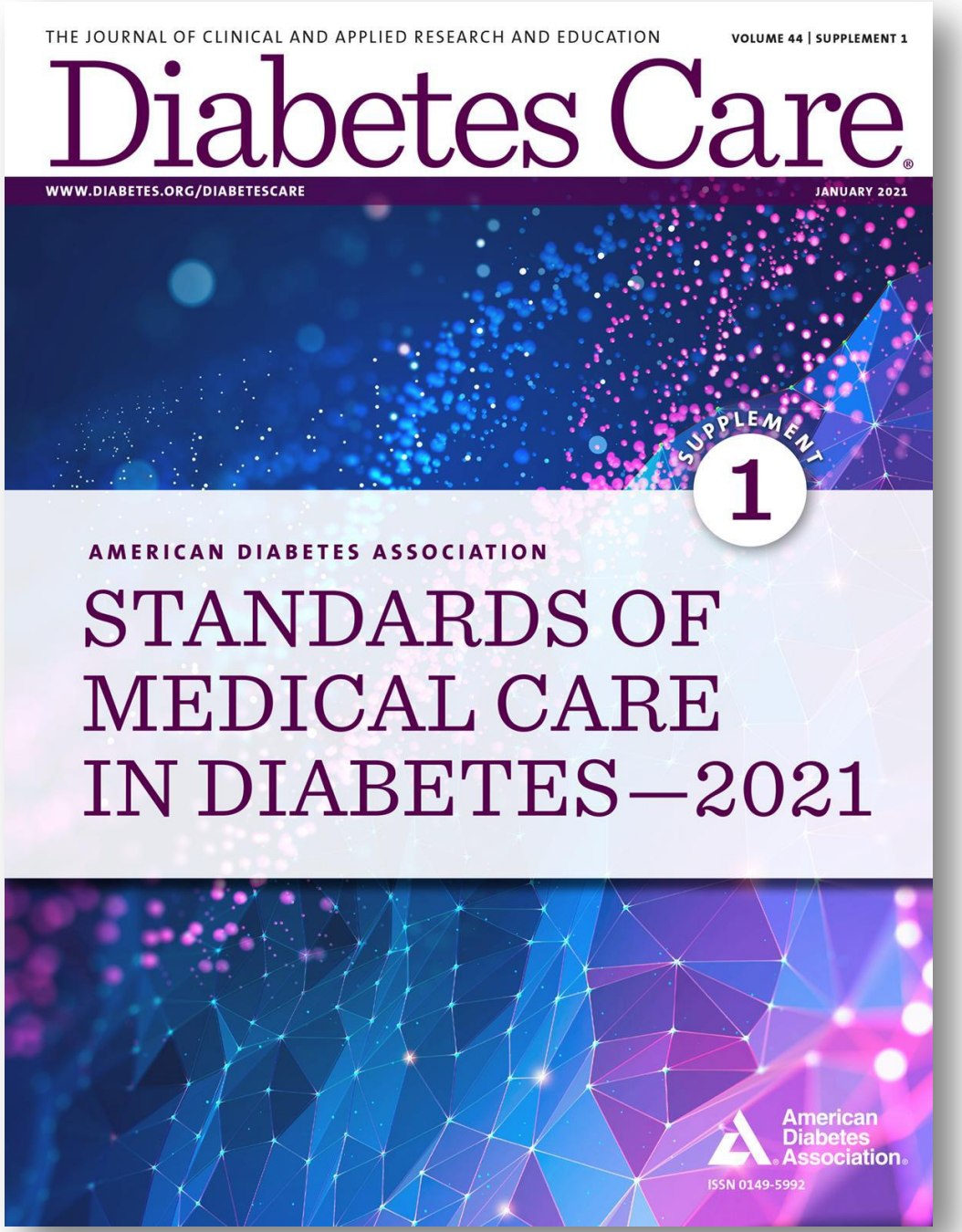


Glycemic Assessment

Recommendations

- Assess glycemic status (A1C or other glycemic measurement) *at least* **two times a year** in patients who are meeting treatment goals (and who have stable glycemic control).

- Assess glycemic status at least **quarterly**, and **as needed**, in patients whose therapy has recently changed and/or who are not meeting glycemic goals.


A1C

Correlation Between SMBG and A1C

estimated Average Glucose (eAG)

A1C (%)	eAG mg/dL
5	97 (76–120)
6	126 (100–152)
7	**154** (123–185)
8	183 (147–217)
9	212 (170–249)
10	240 (193–282)
11	269 (217–314)
12	**298** (240–347)

Data in parentheses are 95% CI. A calculator for converting A1C results into eAG, in either mg/dL or mmol/L, is available at professional.diabetes.org/eAG

These estimates are based on ADAG data of ~2,700 glucose measurements over 3 months per A1C measurement in 507 adults with type 1, type 2, or no diabetes. The correlation between A1C and average glucose was 0.92.

Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ; A1c-Derived Average Glucose Study Group. *Translating the A1C assay into estimated average glucose values. Diabetes Care 2008;31:1473–1478*

Assessment of Glycemic Control

Glucose Assessment by Continuous Glucose Monitoring

CGM

1. Abbott

2. Abbott Laboratories has the longest history of these four companies and was founded in 1888. They are a widely recognized name in industries such as diagnostics, medical devices, nutrition and branded/generic pharmaceuticals. Their CGM was approved by the FDA in 2008. Abbott does not specialize in CGMs or diabetes-related products. However, Abbott's FreeStyle Libre is a major trendsetter. The FreeStyle Libre 2 was released in 2020.

1. Dexcom

2. Dexcom was founded in 1999 and in 2006 was the second company to have its CGM approved by the FDA. Dexcom is headquartered in San Diego, CA and specializes in developing and creating continuous glucose monitoring systems. Dexcom has partnerships with insulin pump manufacturers Insulet Corporation, which offer the Omnipod DASH® Insulin Management System and Tandem Diabetes Care, which offer the Tandem® t:slim X2® Insulin Pump. For those of you who use an insulin pump, this makes for easy connections to your pumps. US MED offers the Dexcom G6 continuous glucose monitor.

1. Eversense

2. The newest CGM brand is Eversense which is created by Senseonics. Their 90-day implantable CGM was approved by the FDA in 2018. Their 180-day Eversense XL was approved for use in Europe in 2017. Like Dexcom, Eversense specializes in diabetes management systems.
3. Update: September 2020
4. On March 26, 2020 Eversense halted sales to new customers and is currently only servicing existing customers.

1. Medtronic

2. Medtronic was founded in 1949 and was the first company to gain FDA approval for CGM devices in 2001. Though not focused specifically on diabetes care, Medtronic's Guardian Sensors are widely used.

All four types of CGM deliver the same basic functions: continuously monitoring blood glucose levels without the need for fingersticks.


140
DexcomG5

Glucose Assessment by Continuous Glucose Monitoring

Recommendations

- Standardized, single-page glucose reports from continuous glucose monitoring (**CGM**) devices with visual cues, such as the ambulatory glucose profile (**AGP**), should be considered as a standard printout for all CGM devices.

- Time in range (**TIR**) is associated with the risk of microvascular complications, should be an acceptable end point for clinical trials moving forward, and can be used for assessment of glycemic control. Additionally, **time below target** (<70 and <54 mg/dL) and **time above target** (>180 mg/dL) are useful parameters for reevaluation of the treatment regimen.

Standardized Continuous Glucose Monitoring (CGM) metrics for clinical care

1. Number of days CGM device is worn (recommend **14** days)

2. Percentage of time CGM device is active (recommend **70%** of data from **14** days)

3. Mean glucose

4. Glucose management indicator

Glucose Management Indicator (GMI) (%) = 3/31+ 0.02392 × [mean glucose in mg/dl) = estimated A1C (eA1C)

5. Glycemic variability (%CV) target **≤36%**

Some studies suggest that lower %CV targets (<33%) provide additional protection against hypoglycemia for those receiving insulin or sulfonylureas

6. Time Above Range (TAR): % of readings and time >250 mg/dL	Level 2 hyperglycemia
7. Time Above Range (TAR): % of readings and time 181–250 mg/dL	Level 1 hyperglycemia
8. Time In Range (T IR): % of readings and time 70–180 mg/dL	In range
9. Time Below Range (TBR): % of readings and time 54–69 mg/dL	Level 1 hypoglycemia
10. Time Below Range (TBR): % of readings and time <54 mg/dL	Level 2 hypoglycemia

AGP Report

Key points included in standard ambulatory glucose profile (AGP) report

Name .....

MRN .....

GLUCOSE STATISTICS AND TARGETS

14 days

..... **% Sensor Time**

Glucose Ranges	**Targets** [% of Readings (Time/Day)]
Target Range 70-180 mg/dL	Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)

Each 5% increase in time in range (70 - 180 mg/dL) is clinically beneficial.

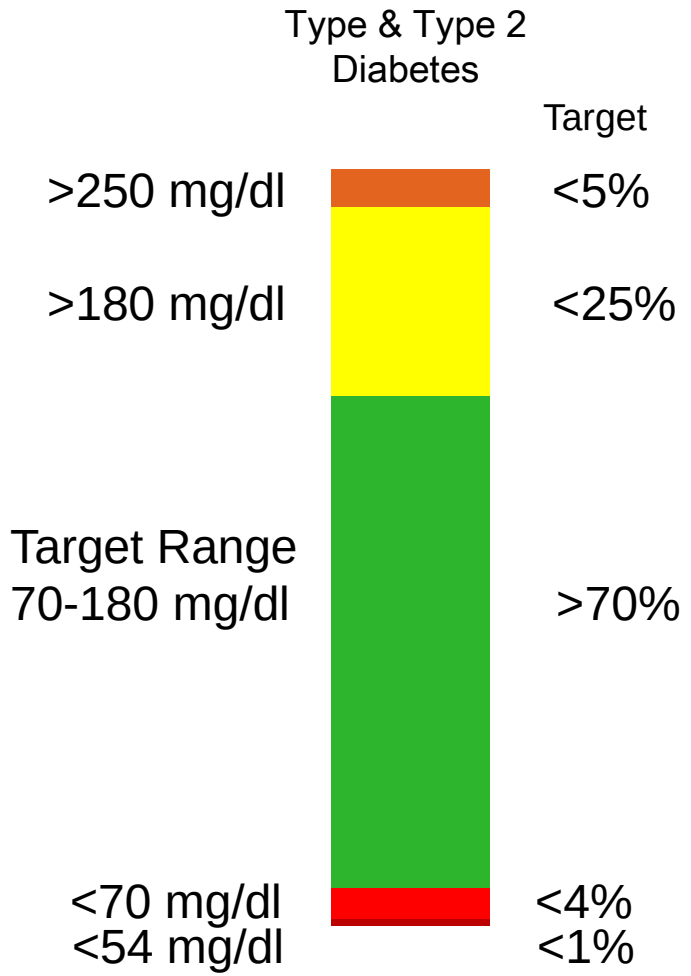
Average Glucose .....

Glucose Management Indicator (GMI) .....

Glucose Variability .....

Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES



AGP Report

Name N..... E.....

MRN ZD 1312985

Sample Report

GLUCOSE STATISTICS AND TARGETS

14 days
78% % Sensor Time

Glucose Ranges	Targets [% of Readings (Time/Day)]	
Target Range 70-180 mg/dL	42% (10h 4min)	Greater than 70% (16h 48min)
Below 70 mg/dL	10% (2h 24min)	Less than 4% (58min)
Below 54 mg/dL	2% (29min)	Less than 1% (14min)
Above 180 mg/dL	34% (8h 10min)	Less than 25% (6h)
Above 250 mg/dL	12% (2h 53min)	Less than 5% (1h 12min)

Each 5% increase in time in range (70 - 180 mg/dL) is clinically beneficial.

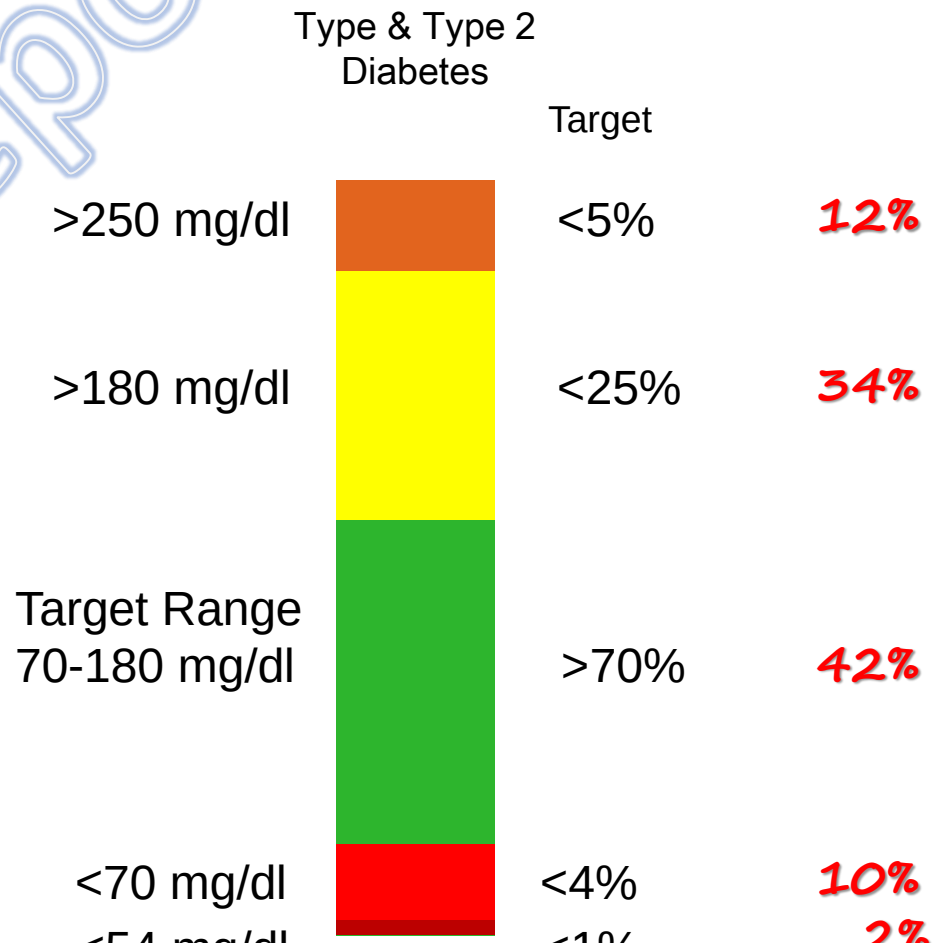
Average Glucose 196 mg/dl

Glucose Management Indicator (GMI) 8%

Glucose Variability 42%

Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES



AGP Report

Name

MRN

GLUCOSE STATISTICS

26 Feb 2019–10 Mar 2019	**13 days**
% Time CGM is Active	**99.9%**
Average Glucose	**173 mg/dL**
Glucose Management Indicator (GMI)	**7.6%**
Glucose Variability	**49.5%**

Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES

Very High (>250 mg/dL) **20%** (4h 48m)

High **23%** (5h 31m)

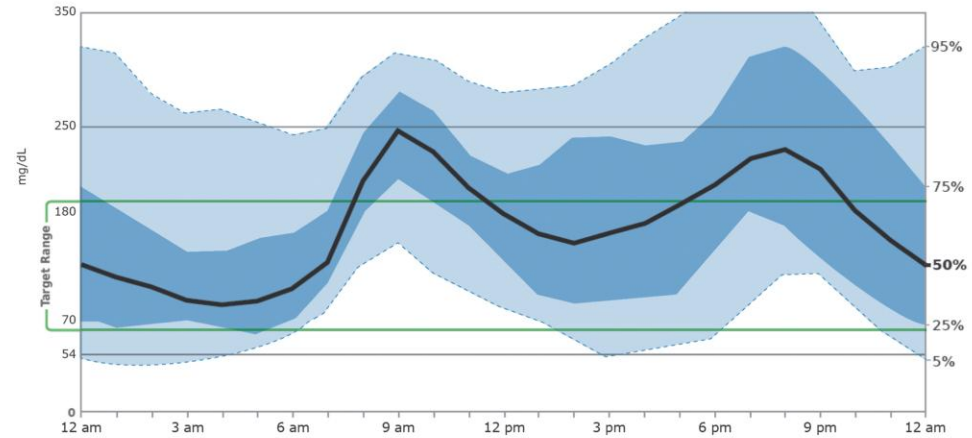
Target Range (70–180 mg/dL) **47%** (11h 17m)

Low **4%** (58m)

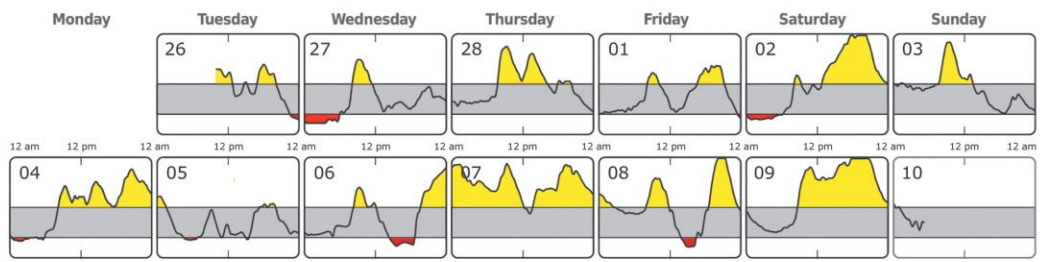
Very Low (<54 mg/dL) **6%** (1h 26m)

AMBULATORY GLUCOSE PROFILE (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.



DAILY GLUCOSE PROFILES



Each daily profile represents a midnight-to-midnight period.

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captūrAGP®

AGP Report

Name

MRN

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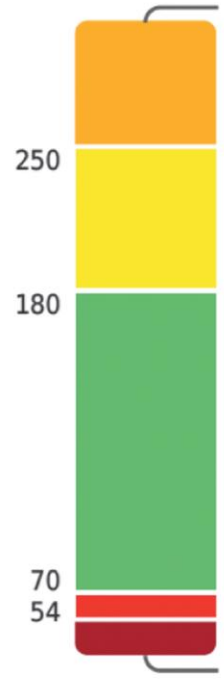

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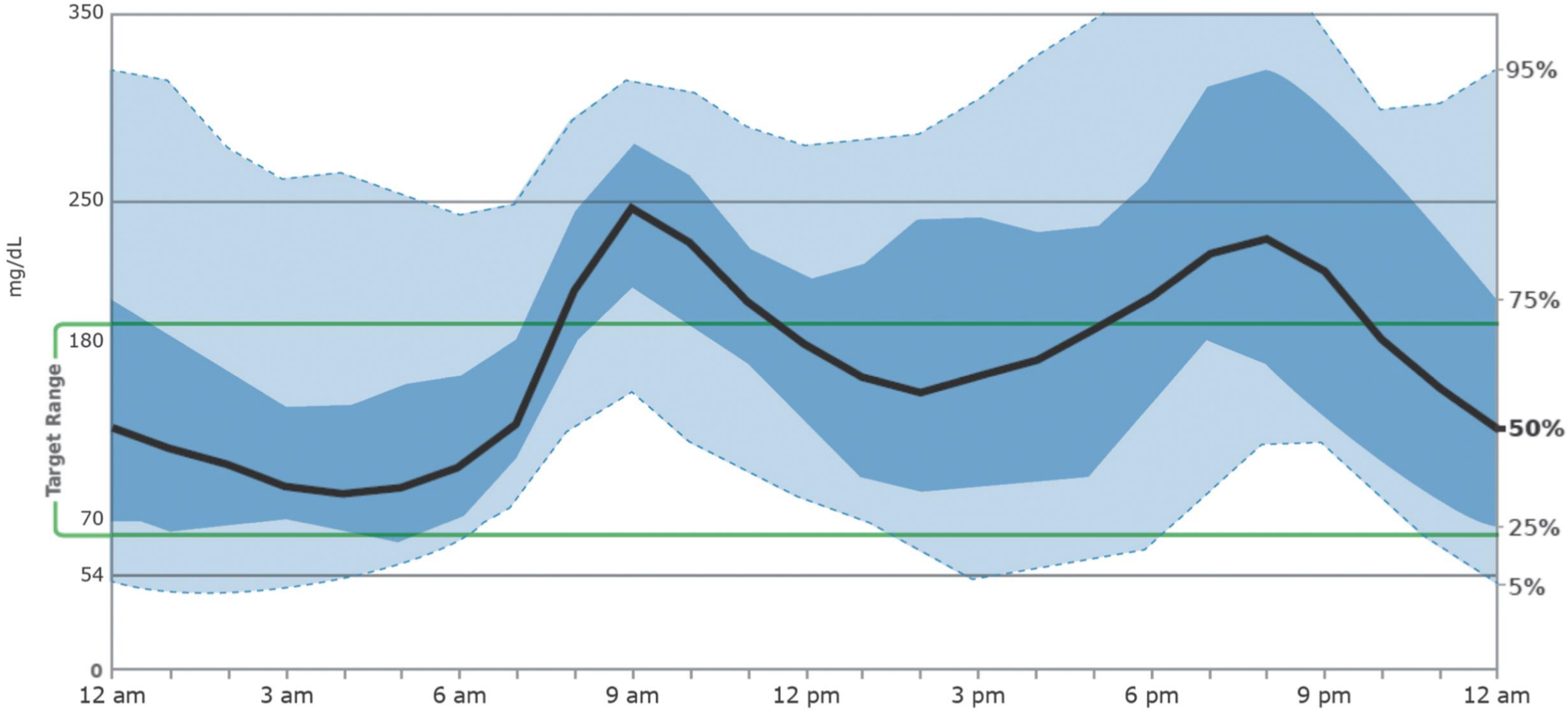
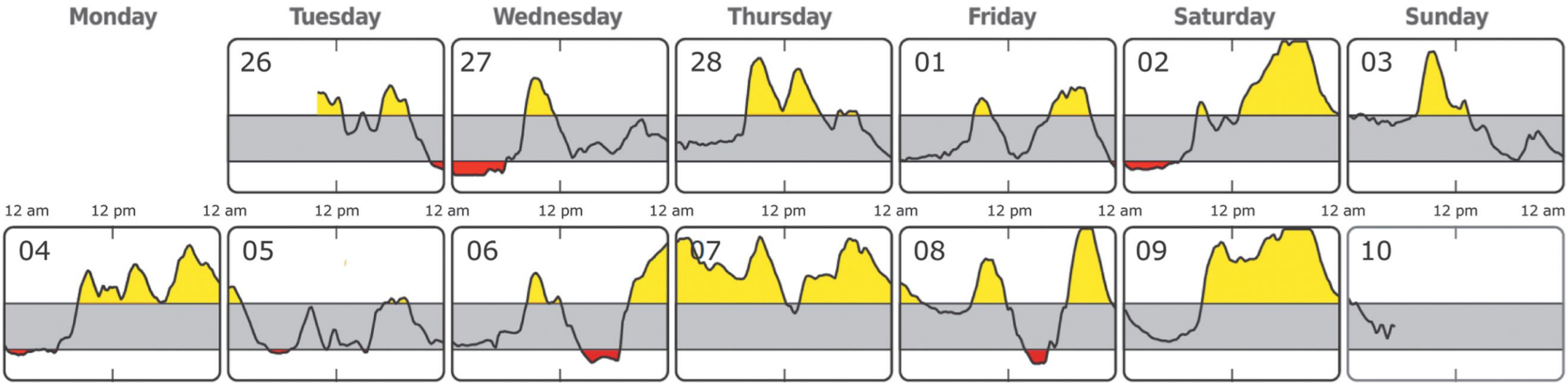


DAILY GLUCOSE PROFILES



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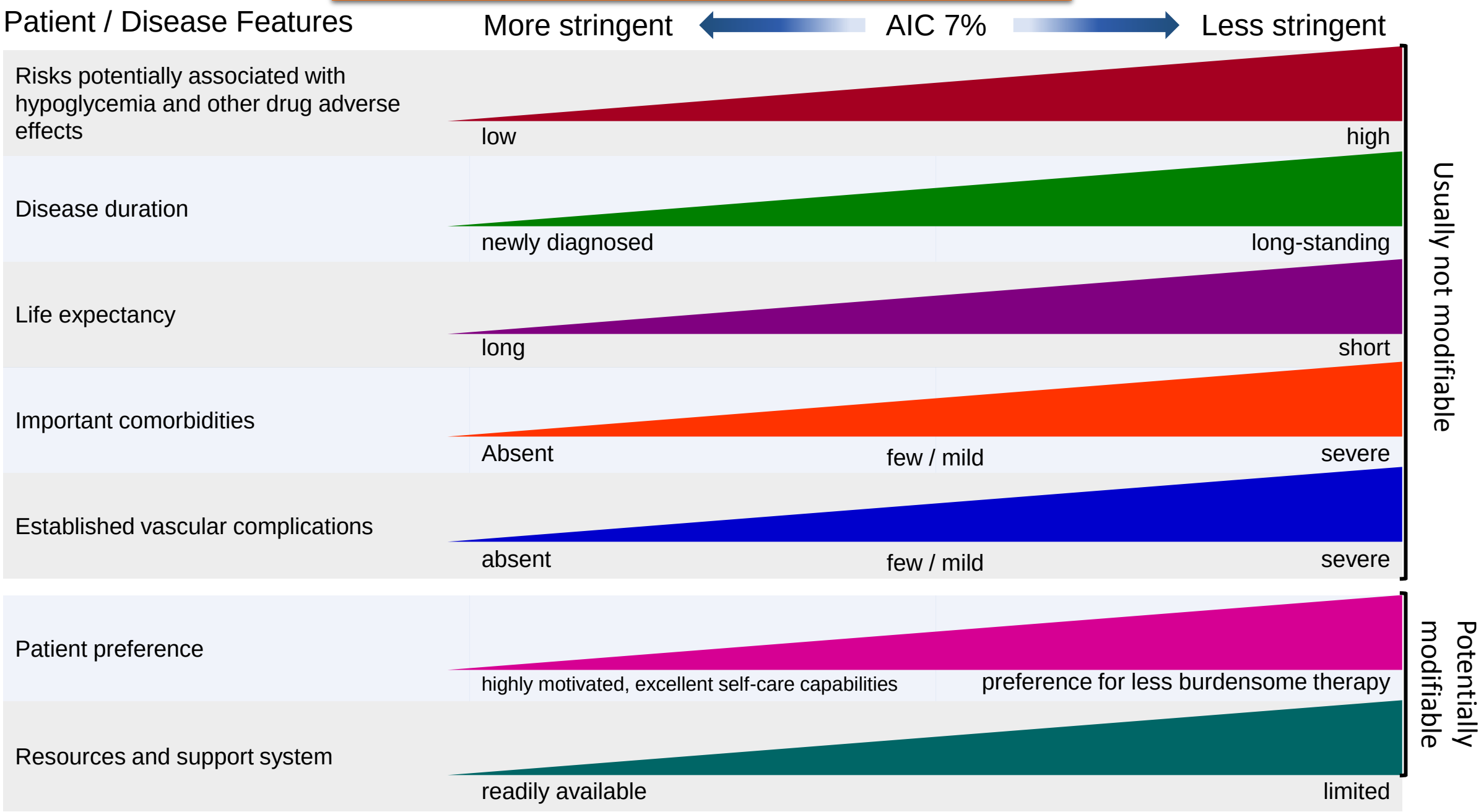
Recommendations

- An **A1C goal** for many nonpregnant adults of **<7%** without significant hypoglycemia is appropriate
- If using **ambulatory glucose profile/glucose management indicator** to assess glycemia, a parallel goal is a **time in range of >70%** with **time below range <4%**
- On the basis of provider judgment and patient preference, achievement of **lower A1C levels than the goal of 7%** may be acceptable, and even beneficial, if it can be achieved safely without significant hypoglycemia or other adverse effects of treatment
- **Less stringent A1C goals** (**such as <8%**) may be appropriate for patients with limited life expectancy, or where the harms of treatment are greater than the benefits
- Reassess glycemic targets over time based on the criteria in **Fig in next slide** and in older adults

Approach to Individualization of Glycemic Targets



Summary of glycemic recommendations for many nonpregnant adults with diabetes

A1C	**<7.0%** More or less stringent glycemic goals may be appropriate for individual patients. CGM may be used to assess glycemic target. Goals should be **individualized** based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations
Preprandial capillary plasma glucose	**80–130 mg/dL** More or less stringent glycemic goals may be appropriate for individual patients. CGM may be used to assess glycemic target. Goals should be **individualized** based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations
Peak postprandial capillary plasma glucose Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.	**<180 mg/dL** More or less stringent glycemic goals may be appropriate for individual patients. CGM may be used to assess glycemic target. Goals should be **individualized** based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations

Glycemic Goals

Hypoglycemia

Classification of Hypoglycemia	
	Glycemic Criteria/Description
Level 1	**Glucose <70 mg/dL and ≥54 mg/dL**
Level 2	**Glucose <54 mg/dL**
Level 3	**A severe event characterized by altered mental and/or physical status requiring assistance for treatment of hypoglycemia**

Hypoglycemia
Recommendations

افت قند خون
توصیه ها

- وقوع و خطر حملات بعدی افت قند خون باید در هر بار که اتفاق می افتد مورد توجه قرار گیرد و در صورت نیاز **علت یابی** لازم صورت گیرد.

- شربت تهیه شده با پودر **گلوکز خوراکی** یا قرص گلوکز یا اسپری آن (تقریباً ۱۵–۲۰ گرم) درمان ترجیحی برای افراد هوشیار با گلوکز خون <۷۰ میلی گرم در دسی لیتر است، ولی می شود هر نوع کربوهیدرات حاوی گلوکز استفاده کرد. پانزده دقیقه پس از درمان، اگر اندازه گیری قند خون با گلوکومتر SMBG نشان دهد که افت قند خون ادامه دارد، درمان باید تکرار شود. هنگامی که الگوی SMBG یا گلوکز رو به افزایش گذاشت، فرد باید از یک وعده غذایی یا میان وعده استفاده کند تا از بروز مجدد افت قند خون جلوگیری کند.

- **گلوکاگون** باید برای همه افراد در معرض خطر کاهش قند خون در سطح ۲ یا ۳ نسخه شود تا در صورت نیاز، در دسترس باشد. مراقبان، پرسنل مدرسه یا اعضای خانواده این افراد باید بدانند که گلوکاگون کجاست و چه موقع و چگونه آن را تزریق کنند. تزریق گلوکاگون فقط به متخصصان مراقبت های بهداشتی محدود نمی شود (هرکس در دور وبر بیمار است باید قادر و مجاز به تزریق باشد)

- وجود وضعیت **عدم آگاهی از کاهش قند خون** Hypoglycemia unawareness یا یک یا چند دوره از کاهش سطح قند خون در سطح ۳ ایجاب میکند آموزش اجتناب از افت قند خون داده شود و برنامه درمانی دوباره مورد بازبینی قرار گیرد.

- به بیماران تحت درمان با انسولین که وضعیت عدم آگاهی از کاهش قند خون Hypoglycemia unawareness دارند، یک واقعه افت قند خون سطح ۳ تجربه کرده اند یا با الگویی از افت قند خون سطح ۲ غیرقابل توجیه مواجه هستند، باید توصیه شود که **اهداف قند خون خود را بالا ببرند** تا حداقل به مدت چند هفته از کاهش قند خون به شدت جلوگیری کنند، تا عدم آگاهی از افت قند خون تا حدی معکوس شود و از خطر حملات آینده کاسته شود.

- در صورت دیده شدن **افت قوای شناختی** یا بروز تدریجی آن حساسیت و هوشیاری پزشک، بیمار و مراقبان در خصوص احتمال حملات هیپوگلیسمی باید بیشتر شود و ارزیابی های مستمر قوای شناختی پیشنهاد می شود.

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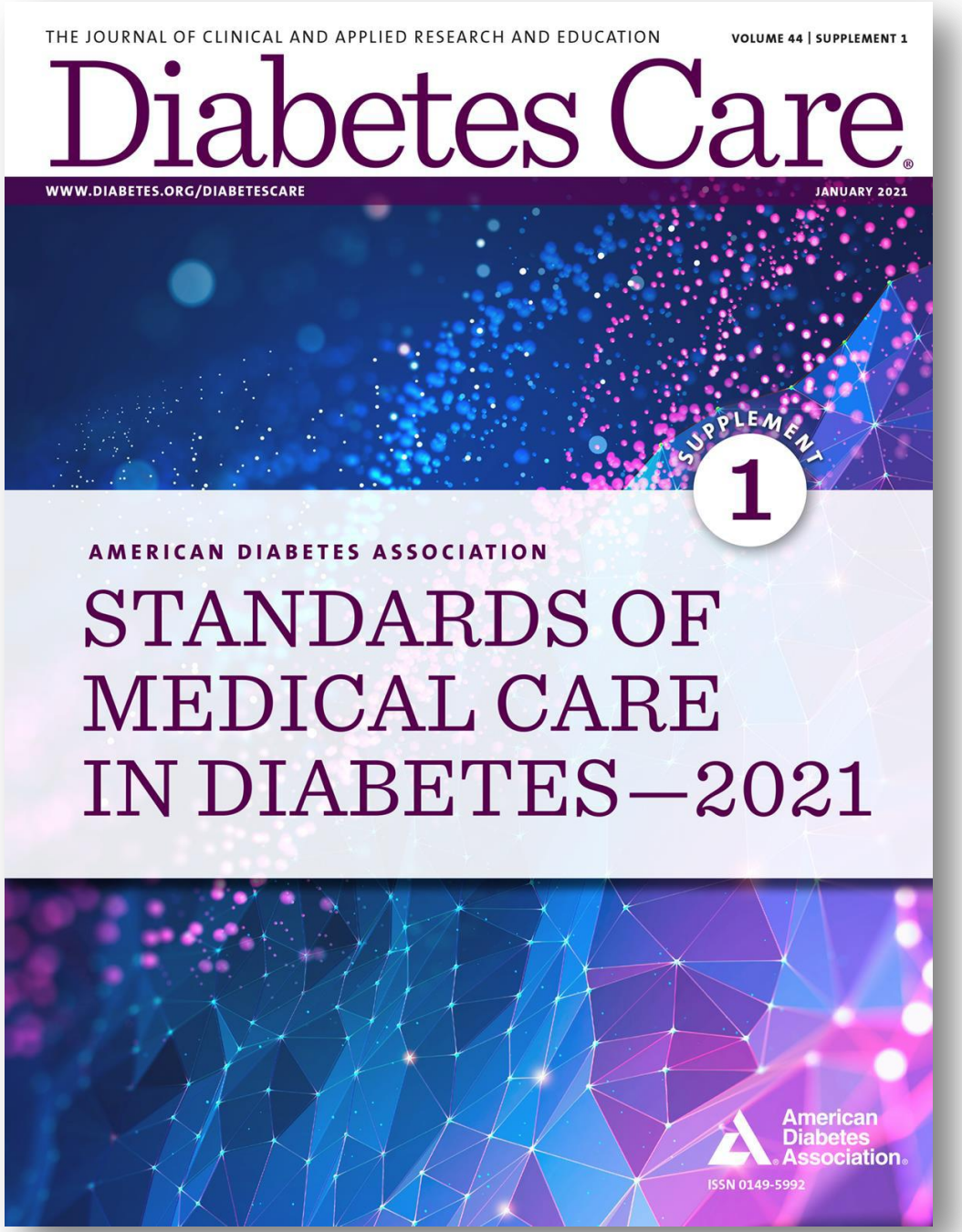


Drug-specific and patient factors to consider when selecting antihyperglycemic treatment in adults with type 2 diabetes	Efficacy	Hypoglycemia	Weight Change	CV Effects		Cost	Oral/SQ	Renal effects		Additional Considerations
				ASCVD	HF			Progression of CKD	Dosing/use Considerations*	
Metformin	High	No	Neutral (Potential for modest loss)	Potential benefit	Neutral	Low	Oral	Neutral	• Contraindicated with eGFR <30	• Gastrointestinal side effects common (diarrhea, nausea) • Potential for B12 deficiency
SGLT 2 Inhibitors	Intermediate	No	Loss	Benefit empagliflozin†, canagliflozin	Benefit empagliflozin†, canagliflozin, dapagliflosin‡	High	Oral	Benefit: canagliflozin‡, empagliflozin, dapaglifloisin	• Renal dose adjustment required (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin)	• Should be discontinued before any scheduled surgery to avoid potential risk for DKA • DKA risk (all agents, rare in T2DM) • Risk of bone fracture (canagliflozin) • Genitourinary infections • Risk of volume depletion, hypotension • ↑LDL • Risk of Fournier's gangrene
GLP 1 Ras	High	No	Loss	Neutral lixisenatide Benefit liraglutide†> Semaglutide> dulaglutide > exenatide	Neutral	High	SQ; oral (semaglutid)	Benefit on renal end points in CVOTs, driven by albuminuria outcomes: Liraglutide, semaglutide, dulaglutide	• exenatide, lixisenatide avoid for eGFR <30mL/min/1.73 m2 • No dose adjustment for dulaglutide, liraglutide, semaglutide • Caution when initiating or increasing dose due to potential risk of nausea, vomiting, or diarrhea, or dehydration. Monitor renal function in patients reporting severe adverse GI reactions when initiating or increasing dose of therapy.	• **FDA Black Box:** Risk of thyroid C-Cell tumors; human relevance not determind **(liraglutide, albiglutide, dulaglutide, exenatide extended release, semaglutide)** • GI side effects common (nausea, vomiting, and diarrhea) • Injection site reactions • Pancreatitis reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected.
PPP 4 Inhibitors	Intermediate	No	Neutral	Neutral	Potential risk sxagliptin	High	Oral	Neutral	• Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin; can be used in renal impairment • No dose adjustment required for linagliptin	• Pancreatitis reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected. • Joint pain
Thiozolidondions	High	No	Gain	Potential benefit Pioglitazone	Neutral	Low	Oral	Neutral	• No dose adjustment required • Generally not recommended in renal impairment due to potential for fluid retention	• **FDA Black Box:** Congestive heart failure **[pioglitazone, rosiglitazone]** • Fluid retention (edema; heart failure) • Benefit in NASH • Risk of bone fractures • Bladder cancer (pioglitazone) • ↑LDL cholesterol (rosiglitazone)
Sulfonylureas Second Generations	High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	• Glyburide: not recommended • Gilpizide and glimepiride: initiate conservatively to avoid hypoglycemia	• FDA Special Warning on Increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)
Insulins – Human	Highest	Yes	Gain	Neutral	Neutral	Low; SQ	SQ; inhaled	Neutral	• Lower Insulin doses required with a decrease in eGFR; titrate per clinical response	• Injection site reactions • Higher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analogs
Insulins – Analogs						High	SQ			

FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)

INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF†

CONSIDER INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE*

NO

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)

IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

+ASCVD/Indicators of High Risk

- Established ASCVD
- Indicators of high ASCVD risk (age >55 years with coronary, carotid, or lower-extremity artery stenosis or LVH)

EITHER/ OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1]

If A1C above target

If further intensification required or patient is unable to tolerate GLP-1 RA and/or SGIT2i, choose agents demonstrating CV benefit and/or safety:

- For patients on a GLP-I RA, consider adding SGLT2i with proven CVD benefit and vice versa[1]
- TZD[2]
- Dpp-4i if not on GLP-1 RA
- Basal insulin[3]
- SU[4]

+HF

Particularly HFrEF (LVEF <45%)

SGLT2i with proven benefit in this population[5,6,7]

1.Proven CVD benefit means it has label indication of reducing CVD events
2.Low dose may be better tolerated though less well studied for CVD effects
3.Degludec or U-IOO glargine have demonstrated CVD safety
4.Choose later generation SU to lower risk of hypoglycemia; glimepiride has shown similar CV safety to DPP-4i
5.Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
6.Empagliflozin, canagliflozin, and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin and dapagliflozin have primary renal outcome data. Dapagliflozin and empagliflozin have primary heart failure outcome data
7. Proven benefit means it has label indication of reducing heart failure in this population
8. Refer to Section 11 : Microvascular Complications and Foot Care
9. Degludec / glargine U-300 < glargine U-100 / detemir < NPH insulin
10. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
11. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
12. Consider country- and region-specific cost of drugs. In some countries TZDs are relatively more expensive and DPP-4i are relatively cheaper.

+CKD

DKD and Albuminuria[8]

NO

PREFERABLY SGLT2i with primary evidence of reducing CKD progression

OR

SGLT2i with evidence of reducing CKD progression in CVOT[5,6,8]

OR

GIP-1 RA with proven CVD benefit if SGIT2i not tolerated or contraindicated

For patients with T2D and CKD[5] (e.g., eGFR <60 mL/min/1.73m^2) and thus at increased risk Of cardiovascular events

EITHER/ OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1,7]

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

DPP-4i	GLP-1 RA	SGLT2i	TZD
if HbA_{1c} above target	if HbA_{1c} above target	if HbA_{1c} above target	if HbA_{1c} above target
SGLT2i **OR** TZD	SGLT2i **OR** TZD	GLP-1 RA **OR** DPP-4i **OR** TZD	SGLT2i **OR** DPP-4i **OR** GLP-1 RA

if HbA_{1c} above target

Continue with addition of other agents as outlined above

if HbA_{1c} above target

Consider the addition of SU[4] **OR** basal insulin:

- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia[9]

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

EITHER/ OR

- GLP-1 RA with good efficacy for weight loss[10]
- SGLT2i

if HbA_{1c} above target

SGLT2i	GLP-1 RA with good efficacy for weight loss[10]

if HbA_{1c} above target

If quadruple therapy required or SGLT2i and/or GLP-1 RA not tolerated or contraindicated regimen with lowest risk of weight gain

PREFERABLY

DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:

•SU[4] •TZD[2] •Basal insulin

COST IS A MAJOR ISSUE[11,12]

SU[4]	TZD[12]
if HbA_{1c} above target	
TZD[12]	SU[4]

if HbA_{1c} above target

Insulin therapy basal insulin with lowest acquisition cost

OR

Consider other therapies based on cost

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

*Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.

چرخه تصمیم گیری برای مدیریت هیپرگلیسمی بیمار محور در دیابت نوع ۲

ویژگی های اصلی بیمار را ارزیابی کنید

- شیوه زندگی فعلی
- بیماری ها ی همراه نظیر بیماری قلبی عروقی آترواسکلروتیک (ASCVD)، بیماری مزمن کلیه و نارسایی قلب
- ویژگی های بالینی، به عنوان مثال، سن، HbA1c، وزن
- مسائلی مانند انگیزه و افسردگی
- زمینه فرهنگی و اجتماعی و اقتصادی

فاکتورهای خاصی که انتخاب شیوه درمان را تحت تاثیر قرار میدهد را در نظر بگیرید

- هدف فردی HbA1c
- تاثیر درمان بر وزن و هیپوگلیسمی
- طیف اثرات جانبی دارو
- پیچیدگی رژیم درمانی، یعنی دفعات و روش مصرف
- شیوه درمانی را امتخاب کنید تا بیشترین امکان به دست آوردن پایبندی و پایداری در ادامه درمان را فراهم سازد.
- هزینه و امکان در دسترس بودن دارو را ارزیابی کنید.

طراحی شیوه درمان با لحاظ نظر بیمار و/یا مراقب

- شامل یک بیمار (و خانواده / مراقب یا پرستار) آموزش دیده و آگاه خواهد بود.
- ترجیحات بیمار را دنبال می کند
- مشاوره موثر شامل مصاحبه انگیزشی، تنظیم هدف و تصمیم گیری مشترک خواهد بود.
- بیمار را توانمند می سازد.
- دسترسی به DSMES (آموزش مدیریت بیماری خویشتن در دیابت و پشتیبانی مستمر) را تضمین می کند.

توافقی دو جانبه بر سر برنامه مدیریت درمان با بیمار برقرار کنید

- اهداف این برنامه باید مشخاصا (SMART)
- ویژه Specific
- قابل اندازه گیری Measurable
- قابل دستیابی Achievable
- واقع بینانه Realistic
- زمان بندی شده Time limited باشد.

اجرای مدیریت درمان طراحی شده

- بیمارانی که قادر به دستیابی به اهداف درمان نمی شوند معمولا تا زمانی که پیشرفتی دیده می شود باید حداقل هر ۳ ماه یکبار ویزیت شوند، در ابتدا اغلب مطلوبتر است فواصل ویزیت ها کمتر باشد تا برنامه آموزشی (DSMES) پیاده شود.

نظارت و پشتیبانی مستمر شامل موارد زیر خواهد بود:

- دستیابی به احساس درونی تندرستی
- قابلیت تحمل داروهای مصرفی را ارزیابی کنید
- وضعیت گلیسمی را پایش کنید
- با ارزیابی مواردی نظیر اندازه گیری خانگی قند خون (SMBG)، وزن، شمارش تعداد قدم های پیموده شده، HbA1C، فشار خون، چربی های خون بازخوردهای تشویقی به بیمار بدهید(بیوفیدبک)

مرور دوره ای مجدد رویه درمان تایید آن در صورت صحیح بودن

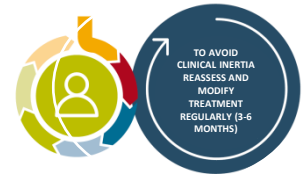
- مرور مجدد برنامه رویه درمان
- قانع کردن بیمار در خصوص تغییرات لازم در رویه درمان
- اطمینان از به اجرا گذاشته شدن تغییرات توافق شده درمانی به صورت زمان بندی شده به منظور جلوگیری از ایجاد بی تفاوتی به روند درمان
- باید به صورت منظم حداقل یک یا دو بار در سال فرآیند چرخه تصمیم گیری بازنگری شده و مجددا انجام گیرد.

اهداف مراقبت

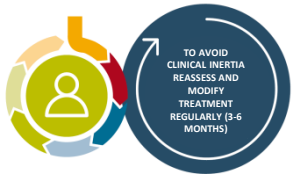
- جلوگیری از عوارض
- بهینه سازی کیفیت زندگی

ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self- Monitored Blood Glucose

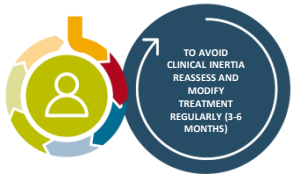

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)


TO AVOID
CLINICAL INERTIA
REASSESS AND
MODIFY
TREATMENT
REGULARLY (3-6
MONTHS)

FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)



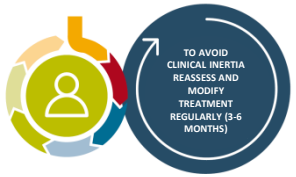
FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)



INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF†

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)



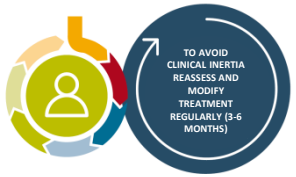
INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF†

CONSIDER INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE*

- +ASCVD/Indicators of High Risk
- +HF
- +CKD

*Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.

FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)



INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF†

NO

CONSIDER INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE*

- +ASCVD/Indicators of High Risk
- +HF
- +CKD

IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

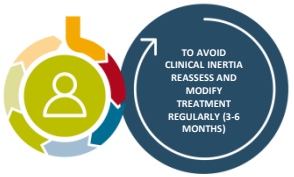
- COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA
- COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS
- COST IS A MAJOR ISSUE[11,12]

FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)

INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF†

NO

CONSIDER INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE*



IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

+ASCVD/Indicators of High Risk

- Established ASCVD
- Indicators of high ASCVD risk (age >55 years with coronary, carotid, or lower-extremity artery stenosis or LVH)

EITHER/OR

GLP-1 RA with proven CVD benefit[1]

SGLT2i with proven CVD benefit[1]

If A1C above target

If further intensification required or patient is unable to tolerate GLP-1 RA and/or SGIT2i, choose agents demonstrating CV benefit and/or safety

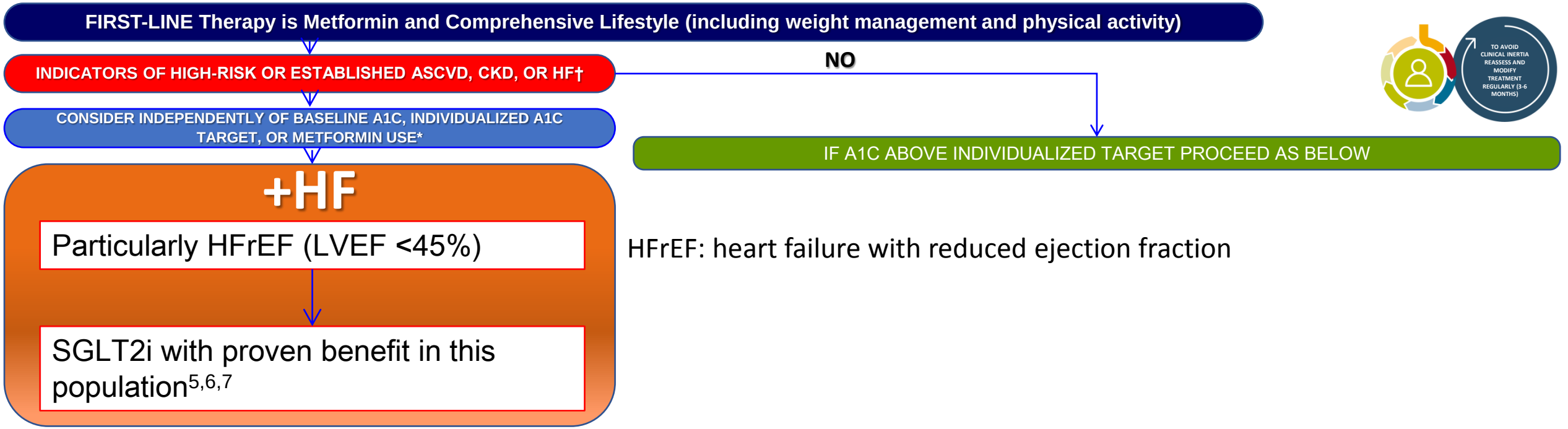
- For patients on a GLP-I RA, consider adding SGLT2i with proven CVD benefit and vice versa[1]
- TZD[2]
- Dpp-4i if not on GLP-1 RA
- Basal insulin[3]
- SU[4]

1.Proven CVD benefit means it has label indication of reducing CVD events

2.Low dose may be better tolerated though less well studied for CVD effects

3.Degludec or U-100 glargine have demonstrated CVD safety

4.Choose later generation SU to lower risk of hypoglycemia; glimepiride has shown similar CV safety to DPP-4i



HFrEF: heart failure with reduced ejection fraction

5.Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use

6.Empagliflozin, canagliflozin, and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin and dapagliflozin have primary renal outcome data. Dapagliflozin and empagliflozin have primary heart failure outcome data

7. Proven benefit means it has label indication of reducing heart failure in this population

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

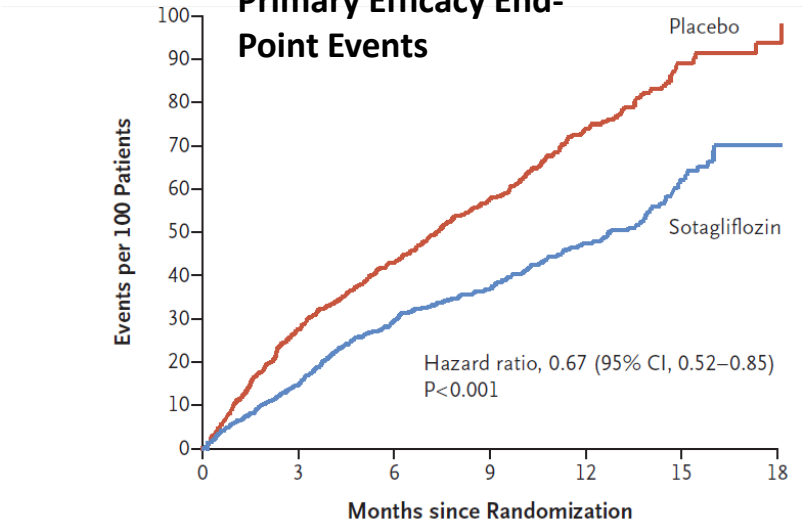
Sotagliflozin in Patients with Diabetes and Recent Worsening Heart Failure

D.L. Bhatt, M. Szarek, P.G. Steg, C.P. Cannon, L.A. Leiter, D.K. McGuire, J.B. Lewis, M.C. Riddle, A.A. Voors, M. Metra, L.H. Lund, M. Komajda, J.M. Testani, C.S. Wilcox, P. Ponikowski, R.D. Lopes, S. Verma, P. Lapuerta, and B. Pitt, for the SOLOIST-WHF Trial Investigators*

CONCLUSIONS

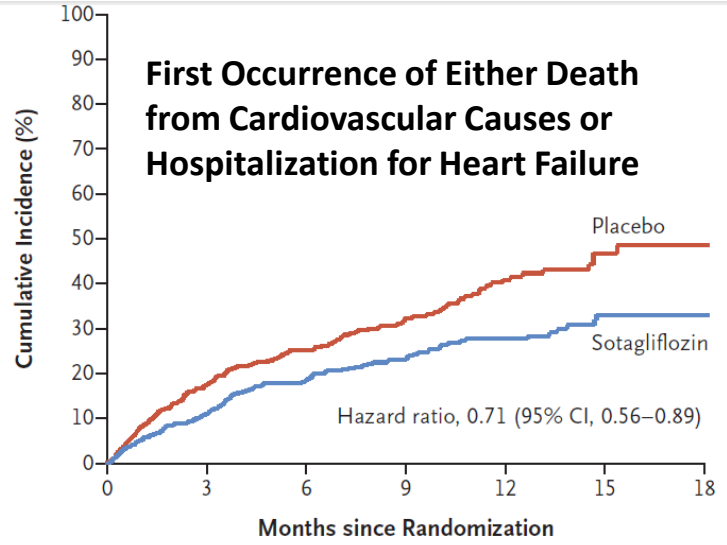
In patients with diabetes and recent worsening heart failure, sotagliflozin therapy, initiated before or shortly after discharge, resulted in a significantly lower total number of deaths from cardiovascular causes and hospitalizations and urgent visits for heart failure than placebo.

Primary Efficacy End-Point Events



No. at Risk							
Placebo	614	524	416	305	195	100	25
Sotagliflozin	608	540	430	310	209	97	29

First Occurrence of Either Death from Cardiovascular Causes or Hospitalization for Heart Failure



No. at Risk							
Placebo	614	461	345	241	144	66	14
Sotagliflozin	608	498	374	266	171	76	25

FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)

INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF†

NO

CONSIDER INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE*

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)

IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

+CKD

DKD and Albuminuria[8]

NO

PREFERABLY SGLT2i with primary evidence of reducing CKD progression

OR

SGLT2i with evidence of reducing CKD progression in CVOT[5,6,]

OR

GIP-1 RA with proven CVD benefit if SGIT2i not tolerated or contraindicated

For patients with T2D and CKD (e.g., eGFR <60 mL/min/1.73m^2) and thus at increased risk Of cardiovascular events

EITHER/OR

GLP-1 RA with proven CVD benefit[1]

SGLT2i with proven CVD benefit[1,7]

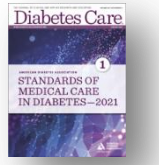
1.Proven CVD benefit means it has label indication of reducing CVD events

5.Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use

6.Empagliflozin, canagliflozin, and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin and dapagliflozin have primary renal outcome data. Dapagliflozin and empagliflozin have primary heart failure outcome data

7. Proven benefit means it has label indication of reducing heart failure in this population

8. Refer to Section 11 :



Microvascular Complications and Foot Care

The NEW ENGLAND JOURNAL of MEDICINE

Sotagliflozin in Diabetes and Chronic Kidney Disease

MULTICENTER, DOUBLE-BLIND, RANDOMIZED, CONTROLLED TRIAL

10,584

Patients with type 2 diabetes mellitus, CKD, and additional cardiovascular risk

	Sotagliflozin	Placebo
		
	N=5292	N=5292
Cardiovascular deaths, hospitalizations, and urgent visits for heart failure	**400 events** 5.6 per 100 patient-yr	**530 events** 7.5 per 100 patient-yr

HR, 0.74; 95% CI, 0.63 to 0.88; P<0.001

Diarrhea, diabetic ketoacidosis, and genital mycotic infections more common with sotagliflozin

Sotagliflozin lowered risk of the composite primary outcome but was associated with adverse events

D.L. Bhatt et al. 10.1056/NEJMoa2030186

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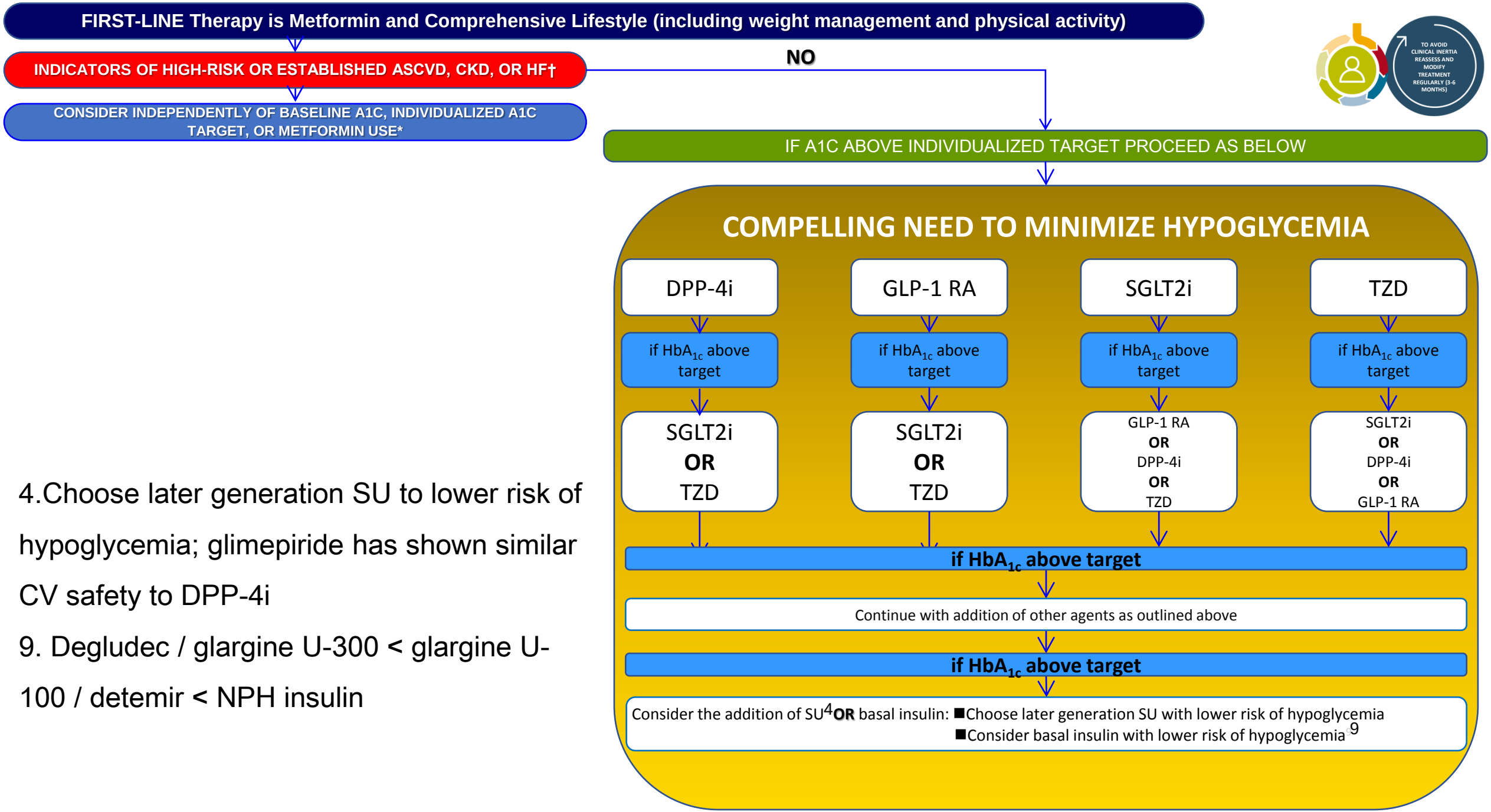
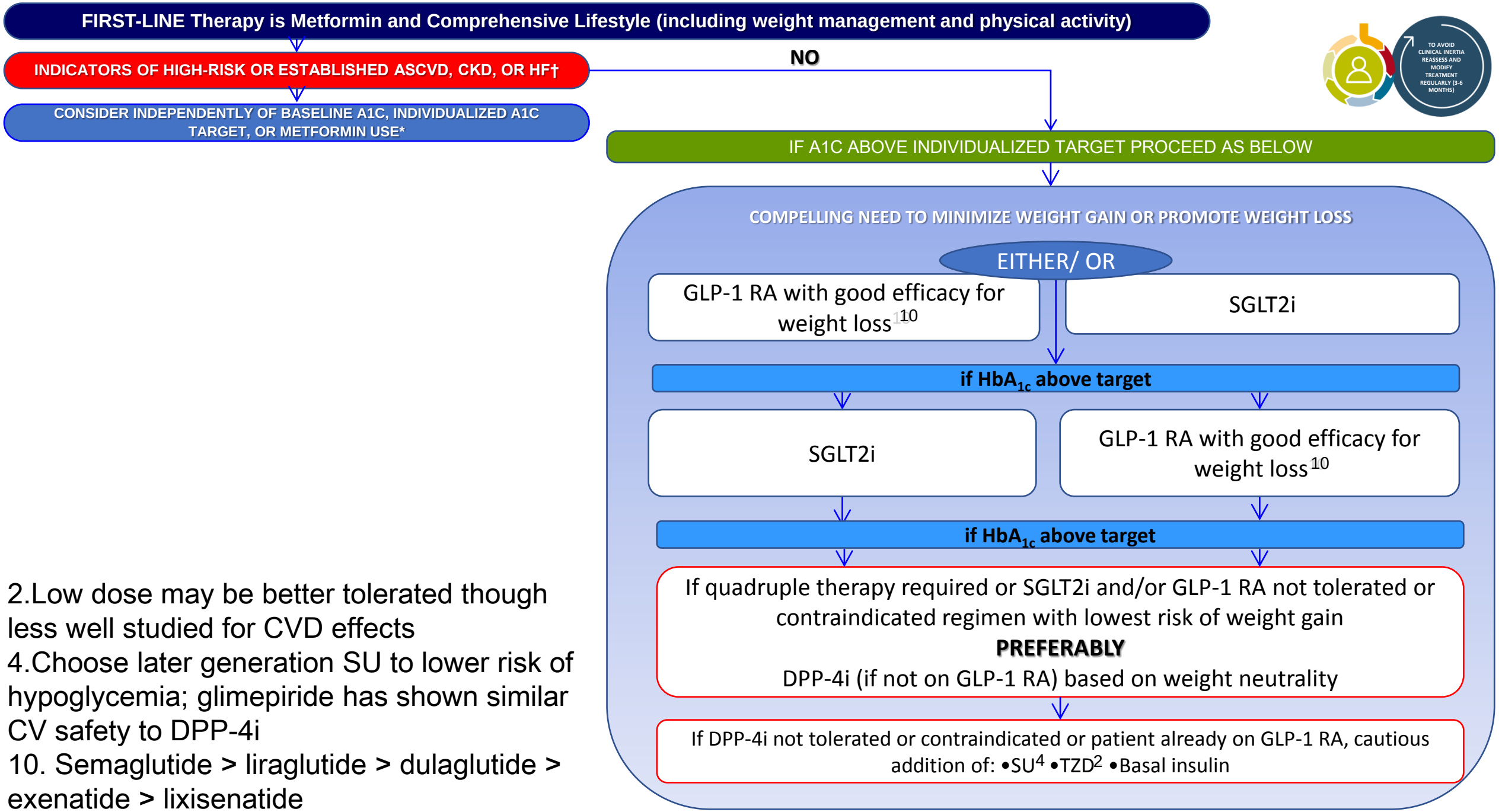


4.Choose later generation SU to lower risk of hypoglycemia; glimepiride has shown similar CV safety to DPP-4i

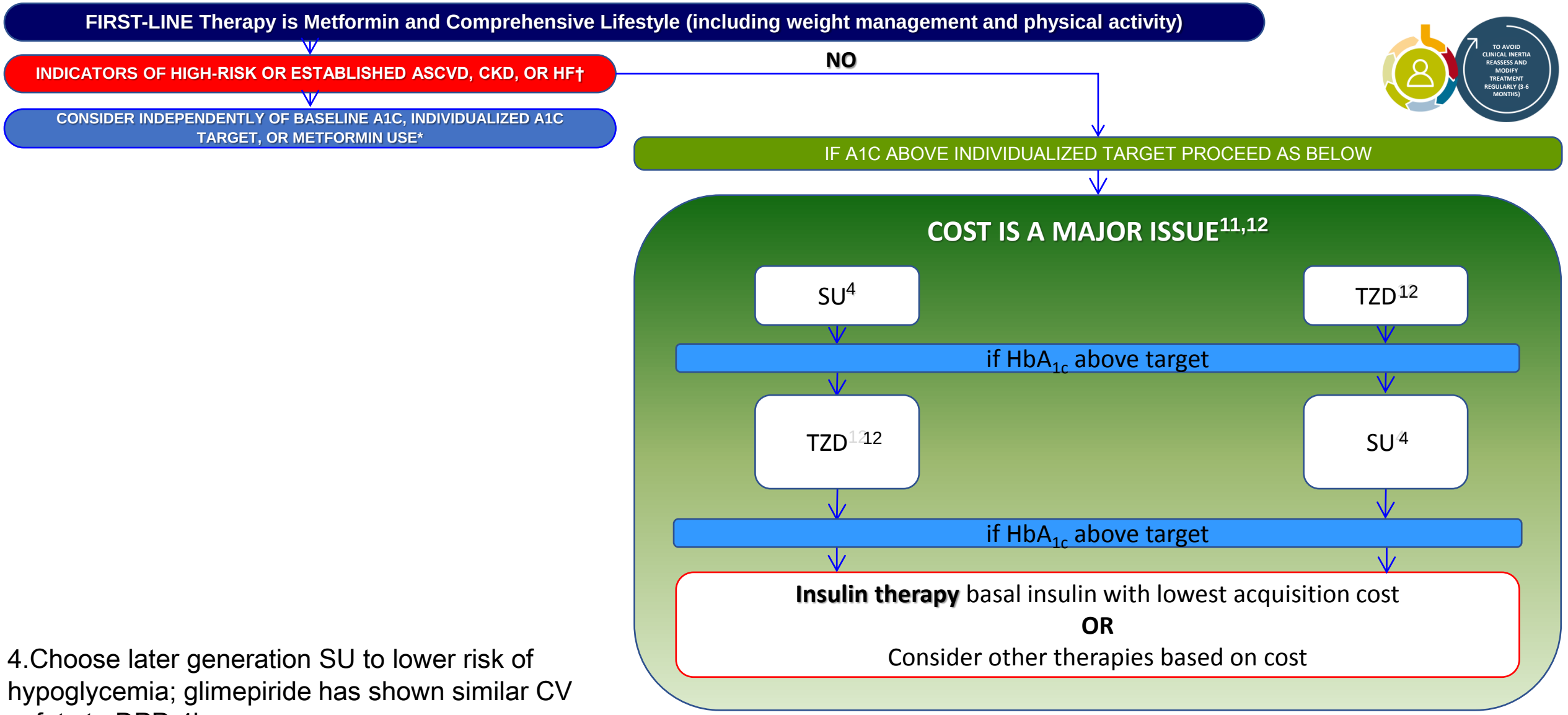
9. Degludec / glargine U-300 < glargine U-100 / detemir < NPH insulin



2.Low dose may be better tolerated though less well studied for CVD effects

4.Choose later generation SU to lower risk of hypoglycemia; glimepiride has shown similar CV safety to DPP-4i

10. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide



4.Choose later generation SU to lower risk of hypoglycemia; glimepiride has shown similar CV safety to DPP-4i

12. Consider country- and region-specific cost of drugs. In some countries TZDs are relatively more expensive and DPP-4i are relatively cheaper.

FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)

INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF†

CONSIDER INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE*

NO

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)

IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

+ASCVD/Indicators of High Risk

- Established ASCVD
- Indicators of high ASCVD risk (age >55 years with coronary, carotid, or lower-extremity artery stenosis or LVH)

EITHER/ OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1]

If A1C above target

If further intensification required or patient is unable to tolerate GLP-1 RA and/or SGIT2i, choose agents demonstrating CV benefit and/or safety:

- For patients on a GLP-I RA, consider adding SGLT2i with proven CVD benefit and vice versa[1]
- TZD[2]
- Dpp-4i if not on GLP-1 RA
- Basal insulin[3]
- SU[4]

+HF

Particularly HFrEF (LVEF <45%)

SGLT2i with proven benefit in this population[5,6,7]

1.Proven CVD benefit means it has label indication of reducing CVD events
2.Low dose may be better tolerated though less well studied for CVD effects
3.Degludec or U-IOO glargine have demonstrated CVD safety
4.Choose later generation SU to lower risk of hypoglycemia; glimepiride has shown similar CV safety to DPP-4i
5.Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
6.Empagliflozin, canagliflozin, and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin and dapagliflozin have primary renal outcome data. Dapagliflozin and empagliflozin have primary heart failure outcome data
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9. Degludec / glargine U-300 < glargine U-100 / detemir < NPH insulin
10. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
11. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
12. Consider country- and region-specific cost of drugs. In some countries TZDs are relatively more expensive and DPP-4i are relatively cheaper.

+CKD

DKD and Albuminuria[8]

NO

PREFERABLY SGLT2i with primary evidence of reducing CKD progression

OR

SGLT2i with evidence of reducing CKD progression in CVOT[5,6,8]

OR

GIP-1 RA with proven CVD benefit if SGIT2i not tolerated or contraindicated

For patients with T2D and CKD[5] (e.g., eGFR <60 mL/min/1.73m^2) and thus at increased risk Of cardiovascular events

EITHER/ OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1,7]

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

DPP-4i	GLP-1 RA	SGLT2i	TZD
if HbA_{1c} above target	if HbA_{1c} above target	if HbA_{1c} above target	if HbA_{1c} above target
SGLT2i **OR** TZD	SGLT2i **OR** TZD	GLP-1 RA **OR** DPP-4i **OR** TZD	SGLT2i **OR** DPP-4i **OR** GLP-1 RA

if HbA_{1c} above target

Continue with addition of other agents as outlined above

if HbA_{1c} above target

Consider the addition of SU[4] **OR** basal insulin:

- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia[9]

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

EITHER/ OR

- GLP-1 RA with good efficacy for weight loss[10]
- SGLT2i

if HbA_{1c} above target

SGLT2i	GLP-1 RA with good efficacy for weight loss[10]

if HbA_{1c} above target

If quadruple therapy required or SGLT2i and/or GLP-1 RA not tolerated or contraindicated regimen with lowest risk of weight gain

PREFERABLY

DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:

•SU[4] •TZD[2] •Basal insulin

COST IS A MAJOR ISSUE[11,12]

SU[4]	TZD[12]
if HbA_{1c} above target	
TZD[12]	SU[4]

if HbA_{1c} above target

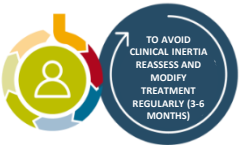
Insulin therapy basal insulin with lowest acquisition cost

OR

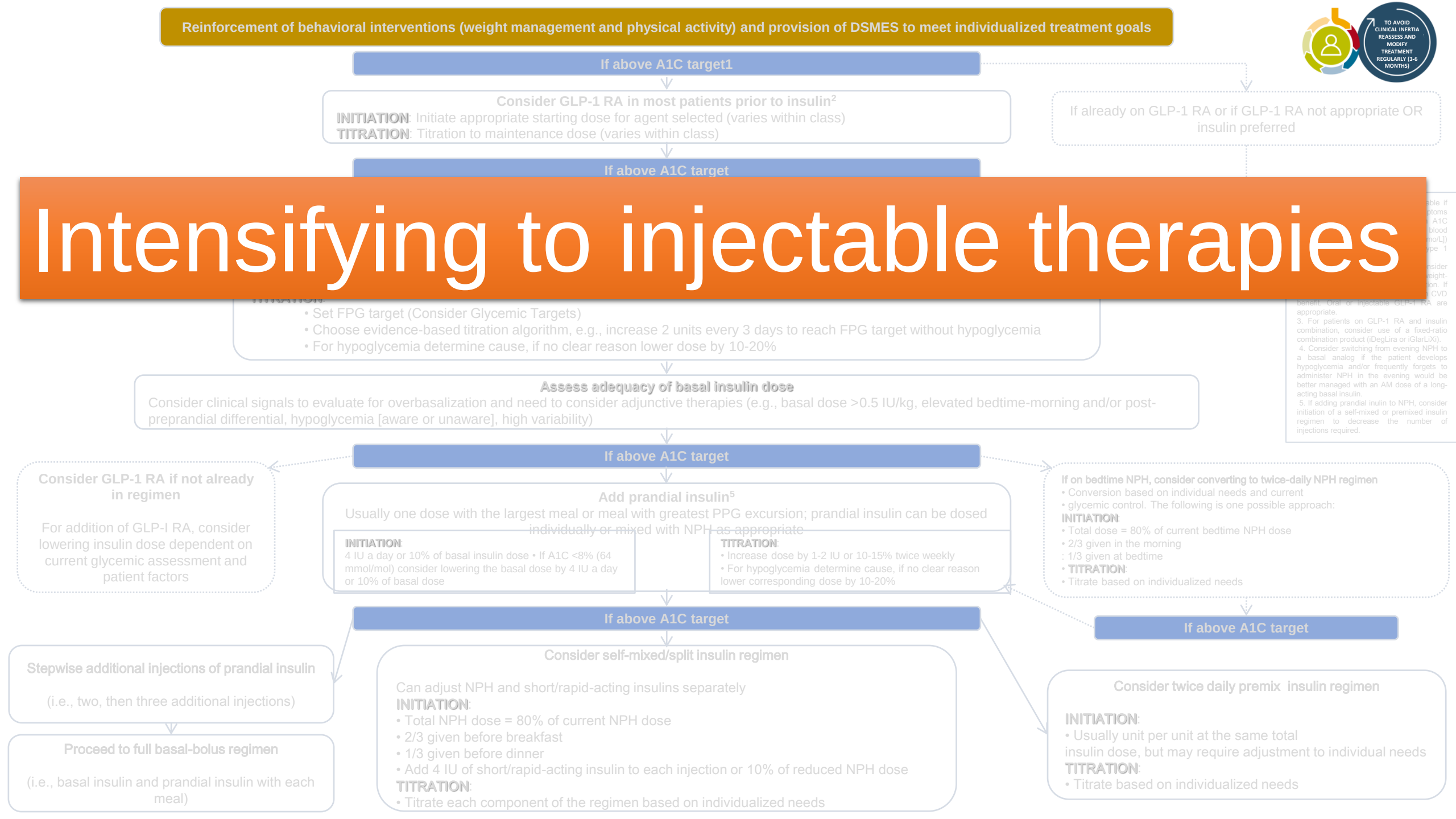
Consider other therapies based on cost

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

*Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.



Intensifying to injectable therapies


Reinforcement of behavioral interventions (weight management and physical activity) and provision of DSMES to meet individualized treatment goals
TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)
If above A1C target1
Consider GLP-1 RA in most patients prior to insulin2
INITIATION: Initiate appropriate starting dose for agent selected (varies within class)
TITRATION: Titration to maintenance dose (varies within class)
If already on GLP-1 RA or if GLP-1 RA not appropriate OR insulin preferred
If above A1C target
Intensifying to injectable therapies
• Set FPG target (Consider Glycemic Targets)
• Choose evidence-based titration algorithm, e.g., increase 2 units every 3 days to reach FPG target without hypoglycemia
• For hypoglycemia determine cause, if no clear reason lower dose by 10-20%
Assess adequacy of basal insulin dose
Consider clinical signals to evaluate for overbasalization and need to consider adjunctive therapies (e.g., basal dose >0.5 IU/kg, elevated bedtime-morning and/or post-preprandial differential, hypoglycemia [aware or unaware], high variability)
If above A1C target
Consider GLP-1 RA if not already in regimen
For addition of GLP-I RA, consider lowering insulin dose dependent on current glycemic assessment and patient factors
Add prandial insulin5
Usually one dose with the largest meal or meal with greatest PPG excursion; prandial insulin can be dosed individually or mixed with NPH as appropriate
INITIATION:
4 IU a day or 10% of basal insulin dose • If A1C <8% (64 mmol/mol) consider lowering the basal dose by 4 IU a day or 10% of basal dose
TITRATION:
• Increase dose by 1-2 IU or 10-15% twice weekly
• For hypoglycemia determine cause, if no clear reason lower corresponding dose by 10-20%
If on bedtime NPH, consider converting to twice-daily NPH regimen
• Conversion based on individual needs and current
• glycemic control. The following is one possible approach:
INITIATION:
• Total dose = 80% of current bedtime NPH dose
• 2/3 given in the morning
: 1/3 given at bedtime
• TITRATION:
• Titrate based on individualized needs
If above A1C target
If above A1C target
Stepwise additional injections of prandial insulin
(i.e., two, then three additional injections)
Proceed to full basal-bolus regimen
(i.e., basal insulin and prandial insulin with each meal)
Consider self-mixed/split insulin regimen
Can adjust NPH and short/rapid-acting insulins separately
INITIATION:
• Total NPH dose = 80% of current NPH dose
• 2/3 given before breakfast
• 1/3 given before dinner
• Add 4 IU of short/rapid-acting insulin to each injection or 10% of reduced NPH dose
TITRATION:
• Titrate each component of the regimen based on individualized needs
Consider twice daily premix insulin regimen
INITIATION:
• Usually unit per unit at the same total insulin dose, but may require adjustment to individual needs
TITRATION:
• Titrate based on individualized needs

چرخه تصمیم گیری برای مدیریت هیپرگلیسمی بیمار محور در دیابت نوع ۲

ویژگی های اصلی بیمار را ارزیابی کنید

- شیوه زندگی فعلی
- بیماری ها ی همراه نظیر بیماری قلبی عروقی آترواسکلروتیک (ASCVD)، بیماری مزمن کلیه و نارسایی قلب
- ویژگی های بالینی، به عنوان مثال، سن، HbA1c، وزن
- مسائلی مانند انگیزه و افسردگی
- زمینه فرهنگی و اجتماعی و اقتصادی

فاکتورهای خاصی که انتخاب شیوه درمان را تحت تاثیر قرار میدهد را در نظر بگیرید

- هدف فردی HbA1c
- تاثیر درمان بر وزن و هیپوگلیسمی
- طیف اثرات جانبی دارو
- پیچیدگی رژیم درمانی، یعنی دفعات و روش مصرف
- شیوه درمانی را امتخاب کنید تا بیشترین امکان به دست آوردن پایبندی و پایداری در ادامه درمان را فراهم سازد.
- هزینه و امکان در دسترس بودن دارو را ارزیابی کنید.

طراحی شیوه درمان با لحاظ نظر بیمار و/یا مراقب

- شامل یک بیمار (و خانواده / مراقب یا پرستار) آموزش دیده و آگاه خواهد بود.
- ترجیحات بیمار را دنبال می کند
- مشاوره موثر شامل مصاحبه انگیزشی، تنظیم هدف و تصمیم گیری مشترک خواهد بود.
- بیمار را توانمند می سازد.
- دسترسی به DSMES (آموزش مدیریت بیماری خویشتن در دیابت و پشتیبانی مستمر) را تضمین می کند.

توافقی دو جانبه بر سر برنامه مدیریت درمان با بیمار برقرار کنید

- اهداف این برنامه باید مشخاصا (SMART)
- ویژه Specific
- قابل اندازه گیری Measurable
- قابل دستیابی Achievable
- واقع بینانه Realistic
- زمان بندی شده Time limited باشد.

اجرای مدیریت درمان طراحی شده

- بیمارانی که قادر به دستیابی به اهداف درمان نمی شوند معمولا تا زمانی که پیشرفتی دیده می شود باید حداقل هر ۳ ماه یکبار ویزیت شوند، در ابتدا اغلب مطلوبتر است فواصل ویزیت ها کمتر باشد تا برنامه آموزشی (DSMES) پیاده شود.

نظارت و پشتیبانی مستمر شامل موارد زیر خواهد بود:

- دستیابی به احساس درونی تندرستی
- قابلیت تحمل داروهای مصرفی را ارزیابی کنید
- وضعیت گلیسمی را پایش کنید
- با ارزیابی مواردی نظیر اندازه گیری خانگی قند خون (SMBG)، وزن، شمارش تعداد قدم های پیموده شده، HbA1C، فشار خون، چربی های خون بازخوردهای تشویقی به بیمار بدهید(بیوفیدبک)

مرور دوره ای مجدد رویه درمان تایید آن در صورت صحیح بودن

- مرور مجدد برنامه رویه درمان
- قانع کردن بیمار در خصوص تغییرات لازم در رویه درمان
- اطمینان از به اجرا گذاشته شدن تغییرات توافق شده درمانی به صورت زمان بندی شده به منظور جلوگیری از ایجاد بی تفاوتی به روند درمان
- باید به صورت منظم حداقل یک یا دو بار در سال فرآیند چرخه تصمیم گیری بازنگری شده و مجددا انجام گیرد.

اهداف مراقبت

- جلوگیری از عوارض
- بهینه سازی کیفیت زندگی

ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self- Monitored Blood Glucose


TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)


TO AVOID
CLINICAL INERTIA
REASSESS AND
MODIFY
TREATMENT
REGULARLY (3-6
MONTHS)

Reinforcement of behavioral interventions (weight management and physical activity) and provision of DSMES to meet individualized treatment goals

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)

If above A1C target1

Consider GLP-1 RA in most patients prior to insulin[2]
INITIATION: Initiate appropriate starting dose for agent selected (varies within class)
TITRATION: Titration to maintenance dose (varies within class)

If already on GLP-1 RA or if GLP-1 RA not appropriate OR insulin preferred

If above A1C target

Add basal insulin[3]
Choice of basal insulin should be based on patient-specific considerations, including cost.

Add basal analog or bedtime NPH insulin
INITIATION: Start 10 IU a day OR 0.1-0.2 IU/kg a day
TITRATION:
- Set FPG target (Consider Glycemic Targets)
- Choose evidence-based titration algorithm, e.g., increase 2 units every 3 days to reach FPG target without hypoglycemia
- For hypoglycemia determine cause, if no clear reason lower dose by 10-20%

Assess adequacy of basal insulin dose
Consider clinical signals to evaluate for overbasalization and need to consider adjunctive therapies (e.g., basal dose >0.5 IU/kg, elevated bedtime-morning and/or post-preprandial differential, hypoglycemia [aware or unaware], high variability)

If above A1C target

Consider GLP-1 RA if not already in regimen

For addition of GLP-I RA, consider lowering insulin dose dependent on current glycemic assessment and patient factors

Add prandial insulin[5]
Usually one dose with the largest meal or meal with greatest PPG excursion; prandial insulin can be dosed individually or mixed with NPH as appropriate

INITIATION:
4 IU a day or 10% of basal insulin dose • If A1C <8% (64 mmol/mol) consider lowering the basal dose by 4 IU a day or 10% of basal dose

TITRATION:
- Increase dose by 1-2 IU or 10-15% twice weekly
- For hypoglycemia determine cause, if no clear reason lower corresponding dose by 10-20%

If on bedtime NPH, consider converting to twice-daily NPH regimen
- Conversion based on individual needs and current
- glycemic control. The following is one possible approach:

INITIATION:
- Total dose = 80% of current bedtime NPH dose
- 2/3 given in the morning
: 1/3 given at bedtime
- TITRATION:
- Titrate based on individualized needs

If above A1C target

If above A1C target

Stepwise additional injections of prandial insulin

(i.e., two, then three additional injections)

Proceed to full basal-bolus regimen

(i.e., basal insulin and prandial insulin with each meal)

Consider self-mixed/split insulin regimen

Can adjust NPH and short/rapid-acting insulins separately
INITIATION:
- Total NPH dose = 80% of current NPH dose
- 2/3 given before breakfast
- 1/3 given before dinner
- Add 4 IU of short/rapid-acting insulin to each injection or 10% of reduced NPH dose

TITRATION:
- Titrate each component of the regimen based on individualized needs

Consider twice daily premix insulin regimen

INITIATION:
- Usually unit per unit at the same total insulin dose, but may require adjustment to individual needs

TITRATION:
- Titrate based on individualized needs

1. Consider insulin as the first injectable if evidence of ongoing catabolism, symptoms of hyperglycemia are present, when A1C levels (>10% (86 mmol/mol) or blood glucose levels (≥300 mg/dL [16.7 mmo/L]) are very high, or a diagnosis of type 1 diabetes is a possibility.
2. When selecting GLP-1 RA consider patient preference, A1C lowering, weight-lowering effect, or frequency of injection. If CVD, consider GLP-1 RA With proven CVD benefit. Oral or injectable GLP-1 RA are appropriate.
3. For patients on GLP-1 RA and 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 would be better managed with an AM dose of a long-acting basal insulin.
5. If adding prandial inulin to NPH, consider initiation of a self-mixed or premixed insulin regimen to decrease the number of injections required.

از حسن توجه و
شرکت شما و
خانواده سپاسگزاریم

Use Principles in Figure 9.1, including reinforcement of behavioral interventions (weight management and physical activity) and provision of DSMES to meet individualized treatment goals

If injectable therapy is needed to reduce A1C[1]

Consider GLP-1 RA in most patients prior to insulin[2]
INITIATION: Initiate appropriate starting dose for agent selected (varies within class)
TITRATION: Titration to maintenance dose (varies within class)

If already on GLP-1 RA or if GLP-1 RA not appropriate OR insulin preferred

If above A1C target

Add basal insulin[3]
Choice of basal insulin should be based on patient-specific considerations, including cost. Refer to **Table 9.3** for insulin cost information.

Add basal analog or bedtime NPH insulin
INITIATION: Start 10 IU a day **OR** 0.1–0.2 IU/kg a day
TITRATION:
- Set FPG target (see Section 6: Glycemic Targets)
- Choose evidence-based titration algorithm, e.g., increase 2 units every 3 days to reach FPG target without hypoglycemia
- For hypoglycemia determine cause, if no clear reason lower dose by 10–20%

Assess adequacy of basal insulin dose
Consider clinical signals to evaluate for overbasalization and need to consider adjunctive therapies (e.g., basal dose >0.5 IU/kg, elevated bedtime-morning and/or post-preprandial differential, hypoglycemia [aware or unaware], high variability)

If above A1C target

Consider GLP-1 RA if not already in regimen
For addition of GLP-1 RA, consider lowering insulin dose dependent on current glycemic assessment and patient factors

Add prandial insulin[5]
Usually one dose with the largest meal or meal with greatest PPG excursion; prandial insulin can be dosed individually or mixed with NPH as appropriate

INITIATION:
- 4 IU a day or 10% of basal insulin dose
- If A1C <8% (64 mmol/mol) consider lowering the basal dose by 4 IU a day or 10% of basal dose

TITRATION:
- Increase dose by 1–2 IU or 10–15% twice weekly
- For hypoglycemia determine cause, if no clear reason lower corresponding dose by 10–20%

If on bedtime NPH, consider converting to twice-daily NPH regimen
Conversion based on individual needs and current glycemic control. The following is one possible approach:

INITIATION:
- Total dose = 80% of current bedtime NPH dose
- 2/3 given in the morning
- 1/3 given at bedtime

TITRATION:
- Titrate based on individualized needs

If above A1C target

If above A1C target

Stepwise additional injections of prandial insulin
(i.e., two, then three additional injections)

Proceed to full basal-bolus regimen
(i.e., basal insulin and prandial insulin with each meal)

Consider self-mixed/split insulin regimen
Can adjust NPH and short/rapid-acting insulins separately

INITIATION:
- Total NPH dose = 80% of current NPH dose
- 2/3 given before breakfast
- 1/3 given before dinner
- Add 4 IU of short/rapid-acting insulin to each injection or 10% of reduced NPH dose

TITRATION:
- Titrate each component of the regimen based on individualized needs

Consider twice daily premix insulin regimen

INITIATION:
- Usually unit per unit at the same total insulin dose, but may require adjustment to individual needs

TITRATION:
- Titrate based on individualized needs

CKD is Classified bassed on:

*Causes (C)

*GFR (G)

*Albuminuria (A)

				Albuminuria categories Description and ranges		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g	30-199 mg/g	≥300mg/g
GFR categories (mL/min/1.73m) Description and range	G1	Normal to high	≥90	1 if CKD	Treat 1	Refer* 2
	G2	Mildly increased	60-89	1 if CKD	Treat 1	Refer* 2
	G3a	Mildly to moderately increased	45-59	Treat 1	Treat 2	Refer 3
	G3b	Severely increased	30-44	Treat 2	Treat 3	Refer 3
	G4	Severely increased	15-29	Refer* 3	Refer* 3	Refer 4+
	G5	Kidney Failure	>15	Refer 4+	Refer 4+	Refer 4+

CKD is Classified bassed on: ***Causes (C)** ***GFR (G)** ***Albuminuria (A)**				**Albuminuria categories** **Description and ranges**		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g	30-199 mg/g	≥300mg/g
GFR categories (mL/min/1.73m) Description and range	G1	Normal to high	≥90	1 visits per year if CKD CKD with normal eGFR and albumin-to-creatinine ratio only in the presence of other markers of kidney damage, such as imaging showing polycystic kidney disease or kidney biopsy abnormalities, with follow-up measurements annually	Treat 1 visits per year requires caution and eGFR and albumin-to-creatinine ratio measurements at least once per year	Refer to nephrology services are recommended (Referring clinicians may wish to discuss with their nephrology service, depending on local arrangements regarding treating or referring) 2 visits per year requires eGFR and albumin-to-creatinine ratio measurements twice per year
	G2	Mildly increased	60-89	1 if CKD	Treat 1	Refer* 2
	G3a	Mildly to moderately increased	45-59	Treat 1 visits per year	Treat 2	Refer 3
	G3b	Severely increased	30-44	Treat 2 visits per year	Treat 3 3 visits per year requires caution and eGFR and albumin-to-creatinine ratio measurements 3 time per year	Refer 3
	G4	Severely increased	15-29	Refer to nephrology services are recommended (Referring clinicians may wish to discuss with their nephrology service, depending on local arrangements regarding treating or referring) 3 visits per year	Refer* 3	Refer to nephrology services are recommended* >4 visits per year requires eGFR and albumin-to-creatinine ratio measurements >4 time per year
	G5	Kidney Failure	>15	Refer 4+	Refer 4+	Refer 4+