Type 2 Diabetes Guidelines and Comprehensive Treatment Plans

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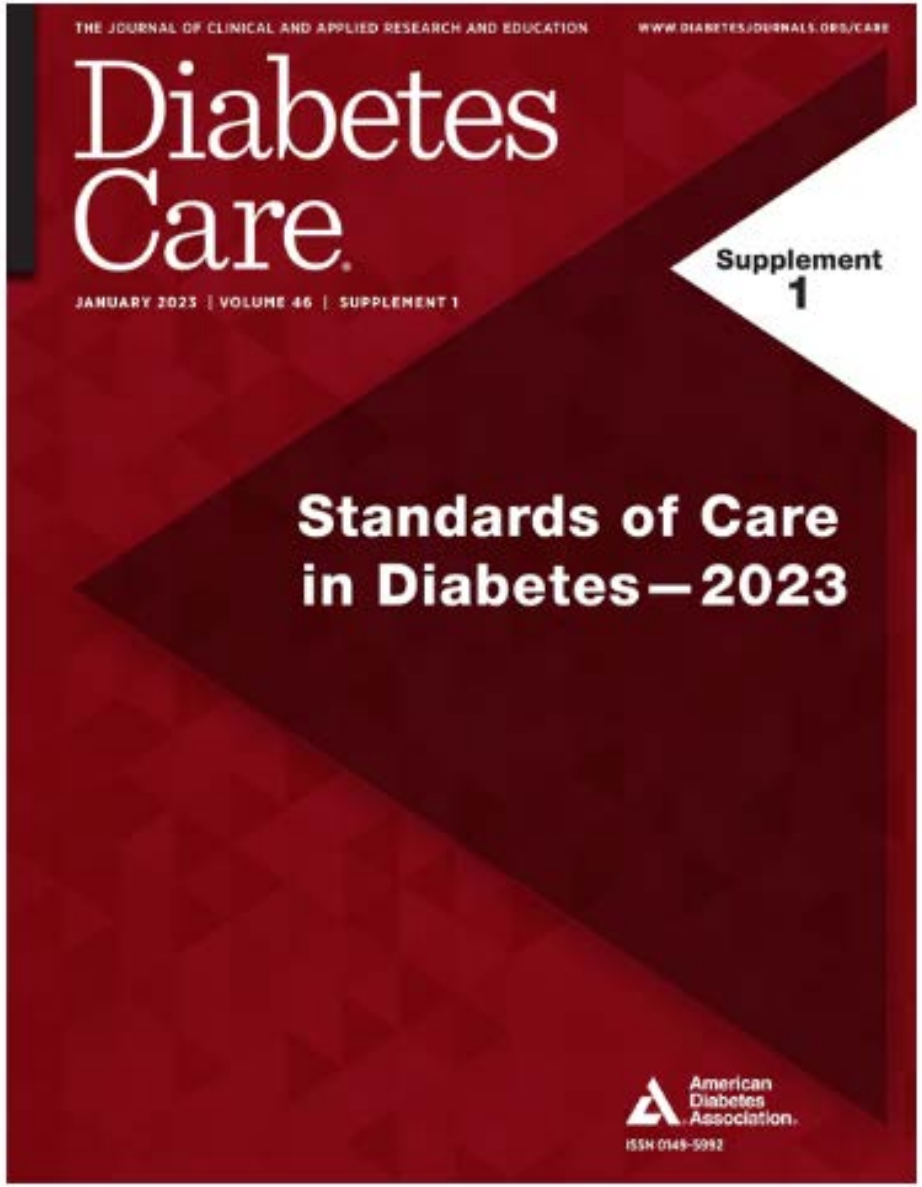
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Prevention or Delay of Type 2 Diabetes and Associated Comorbidities

- **Person-Centered Care Goals -** care goals can include

- weight loss or prevention of weight gain,
- minimizing the progression of hyperglycemia, and
- attention to cardiovascular risk and associated comorbidities. B

- Pharmacotherapy may be considered to support person-centered care goals for people at high risk of developing diabetes. B

Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes

- Social determinants of health should be included in guiding design and delivery of diabetes self-management education and support (DSMES).

Time-restricted eating and Intermittent fasting

- Intermittent fasting is an umbrella term which includes three main forms of restricted eating:

- Alternate-day fasting (energy restriction of 500–600 calories on alternate days)
- 5:2 diet (energy restriction of 500–600 calories on consecutive or nonconsecutive days) with usual intake the other five, and
- Time-restricted eating (daily calorie restriction based on window of time of 8–15 h).

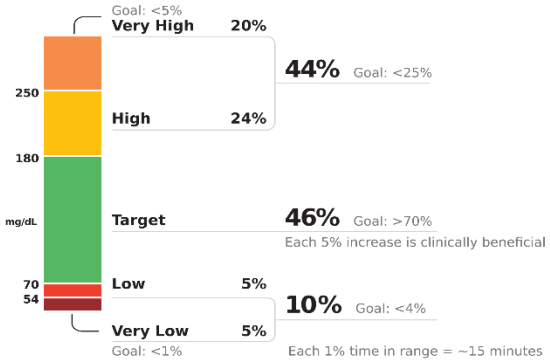
- Each produces mild to moderate weight loss (3–8% loss from baseline) over short durations (8–12 weeks) with no significant differences in weight loss when compared with continuous calorie restriction
- Similar findings when extended up to 52 weeks.

AGP

AGP Report: Continuous Glucose Monitoring

Time in Ranges

Goals for Type 1 and Type 2 Diabetes



Test Patient DOB: Jan 1, 1970

14 Days: August 8–August 21, 2021

Time CGM Active: 100%

Glucose Metrics

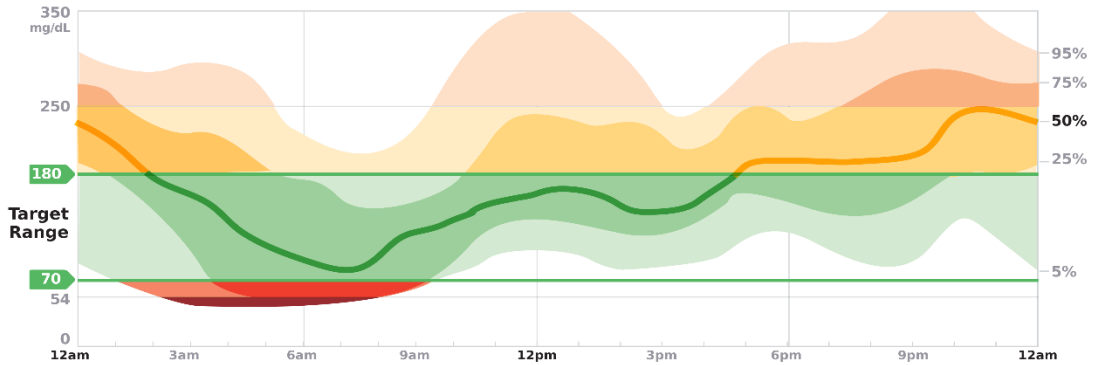
Average Glucose ..... **175 mg/dL**
Goal: <154 mg/dL

Glucose Management Indicator (GMI) **7.5%**
Goal: <7%

Glucose Variability **45.5%**
Defined as percent coefficient of variation
Goal: ≤36%

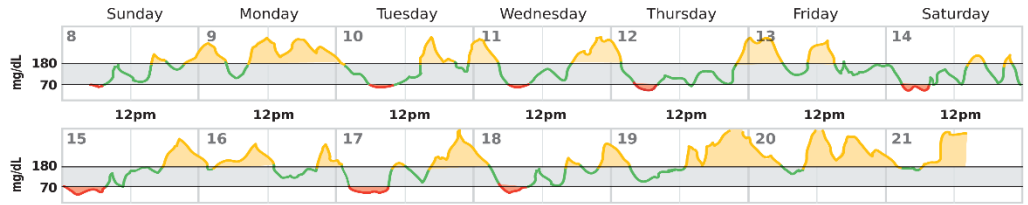
Ambulatory Glucose Profile (AGP)

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



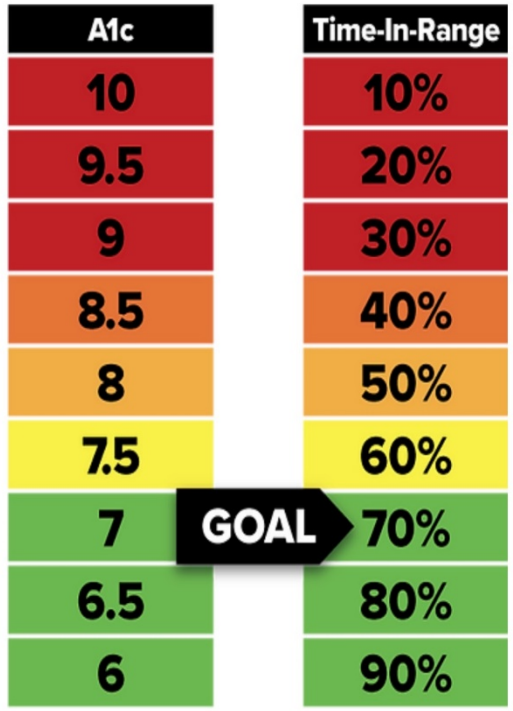
Daily Glucose Profiles

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



Glycemic Goals

- If using ambulatory glucose profile/glucose management indicator to assess glycemia, a parallel goal for many nonpregnant adults is time in range of >70% with time below range <4% and time <54 mg/dL <1%.B
- For those with frailty or at high risk of hypoglycemia, a target of >50% time in range with <1% time below range is recommended.B



WELL-AHEAD

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Diabetes Technology

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

Table 7.4—Continuous glucose monitoring devices interfering substances

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

Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes

- Obesity is a chronic disease.
- Larger, sustained weight losses (>10%) usually confer greater benefits, including disease-modifying effects and possible remission of type 2 diabetes, and may improve long-term cardiovascular outcomes and mortality. B

Pharmacologic Approaches to Glycemic Treatment

USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

Goal: Cardiorenal Risk Reduction in High-Risk Patients with Type 2 Diabetes (in addition to comprehensive CV risk management)*

+ASCVD†

Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, any revascularization procedure). Variably included: conditions such as transient ischemic attack, unstable angina, amputation, symptomatic or asymptomatic coronary artery disease.

+Indicators of high risk

While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria)

+ASCVD/Indicators of High Risk

GLP-1 RA# with proven CVD benefit **EITHER/ OR** SGLT2i§ with proven CVD benefit

If A1C above target

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit or vice versa
- TZD^

+HF

Current or prior symptoms of HF with documented HFrEF or HFpEF

+HF

SGLT2i§ with proven HF benefit in this population

+CKD

eGFR <60 mL/min per 1.73 m² OR albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). These measurements may vary over time; thus, a repeat measure is required to document CKD.

+CKD (on maximally tolerated dose of ACEi/ARB)

PREFERABLY

SGLT2i§ with primary evidence of reducing CKD progression

Use SGLT2i in people with an eGFR ≥20 mL/min per 1.73 m²; once initiated should be continued until initiation of dialysis or transplantation

OR

GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated

If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA or vice versa

If additional cardiorenal risk reduction or glycemic lowering needed

Goal: Achievement and Maintenance of Glycemic and Weight Management Goals

Glycemic Management: Choose approaches that provide the efficacy to achieve goals:

Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals

Consider avoidance of hypoglycemia a priority in high-risk individuals

In general, higher efficacy approaches have greater likelihood of achieving glycemic goals

Efficacy for glucose lowering

Very High:
Dulaglutide (high dose), Semaglutide, Tirzepatide

Insulin

Combination Oral, Combination Injectable (GLP-1 RA/Insulin)

High:
GLP-1 RA (not listed above), Metformin, SGLT2i, Sulfonylurea, TZD

Intermediate:
DPP-4i

Achievement and Maintenance of Weight Management Goals:

Set individualized weight management goals

General lifestyle advice: medical nutrition therapy/eating patterns/ physical activity

Intensive evidence-based structured weight management program

Consider medication for weight loss

Consider metabolic surgery

When choosing glucose-lowering therapies:

Consider regimen with high-to-very-high dual glucose and weight efficacy

Efficacy for weight loss

Very High:
Semaglutide, Tirzepatide

High:
Dulaglutide, Liraglutide

Intermediate:
GLP-1 RA (not listed above), SGLT2i

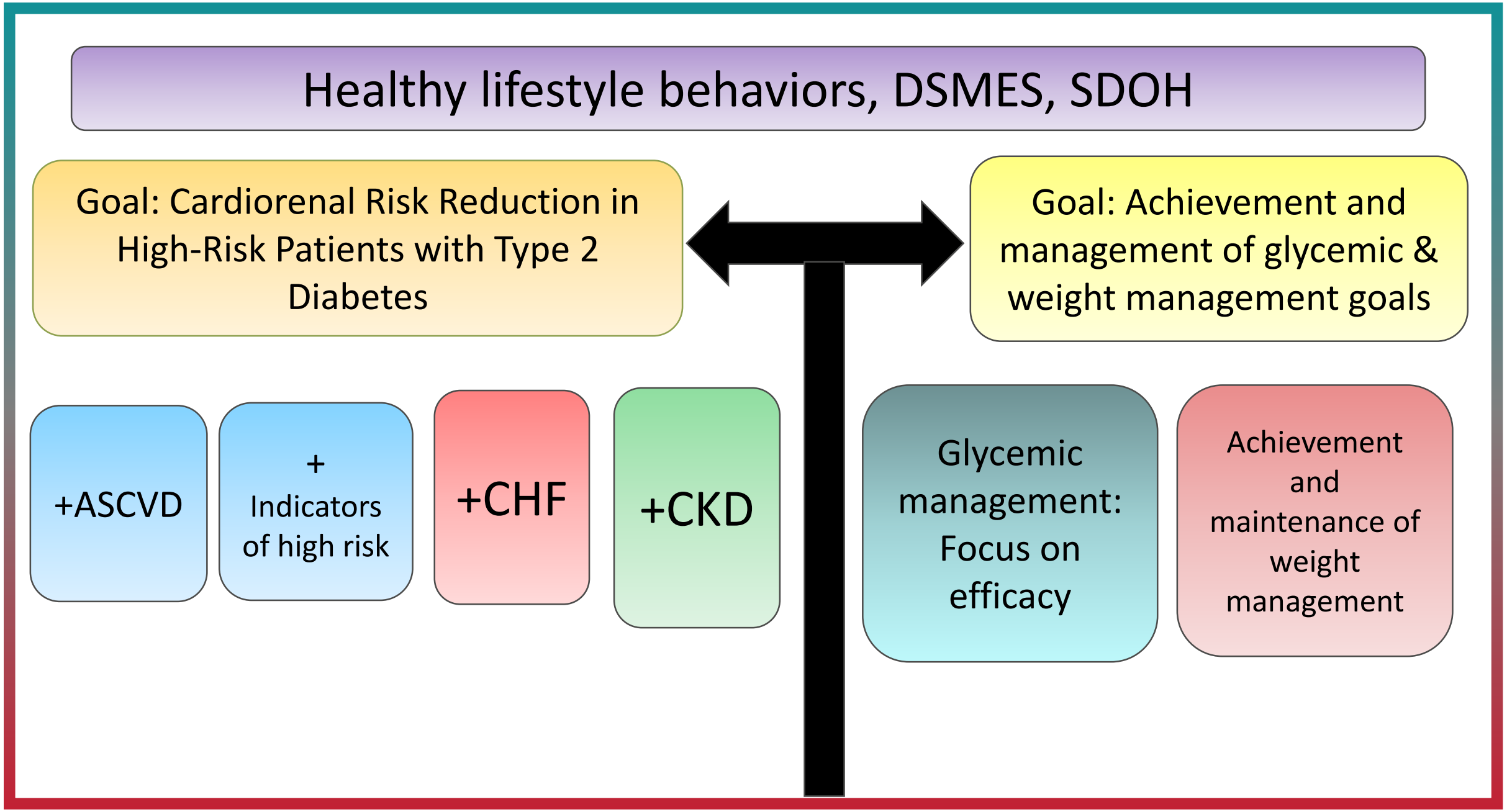
Neutral:
DPP-4i, Metformin

If A1C above target

Identify barriers to goals:

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

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


Healthy lifestyle behaviors, DSMES, SDOH
Goal: Cardiorenal Risk Reduction in High-Risk Patients with Type 2 Diabetes
Goal: Achievement and management of glycemic & weight management goals
+ASCVD
+ Indicators of high risk
+CHF
+CKD
Glycemic management: Focus on efficacy
Achievement and maintenance of weight management

+ASCVD

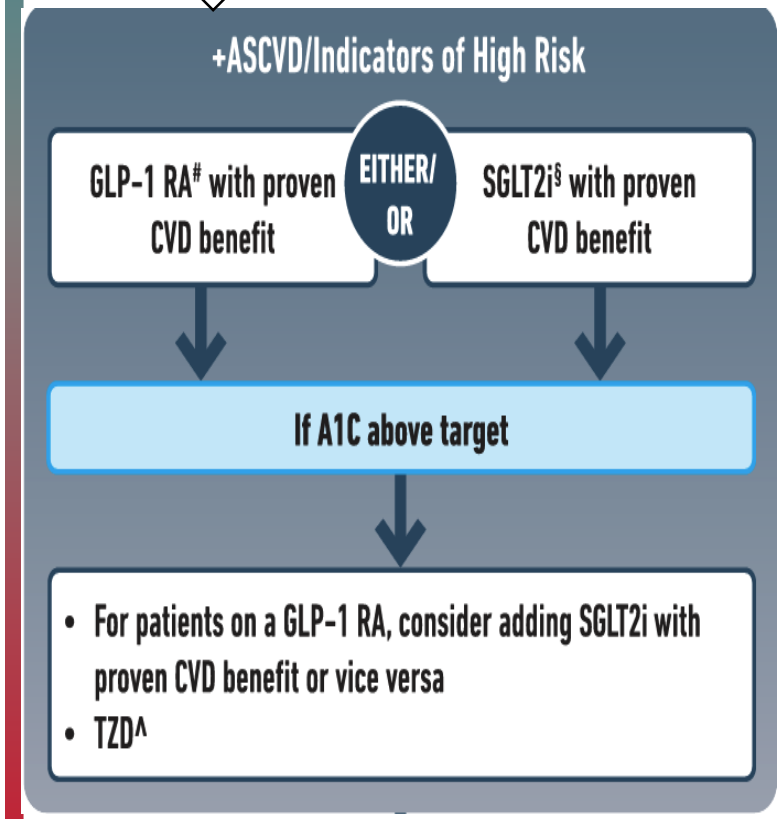
\+
Indicators of high risk

+CHF

+CKD

Glycemic management: Focus on efficacy

Achievement and maintenance of weight management



SGLT2i

Use SGLT2i in people with an eGFR ≥ 20 mL/min

----------OR----------

GLP-1 RA if SGLT2i is not tolerated or C/I

+ASCVD

+ Indicators of high risk

+CHF

+CKD

Glycemic management: Focus on efficacy

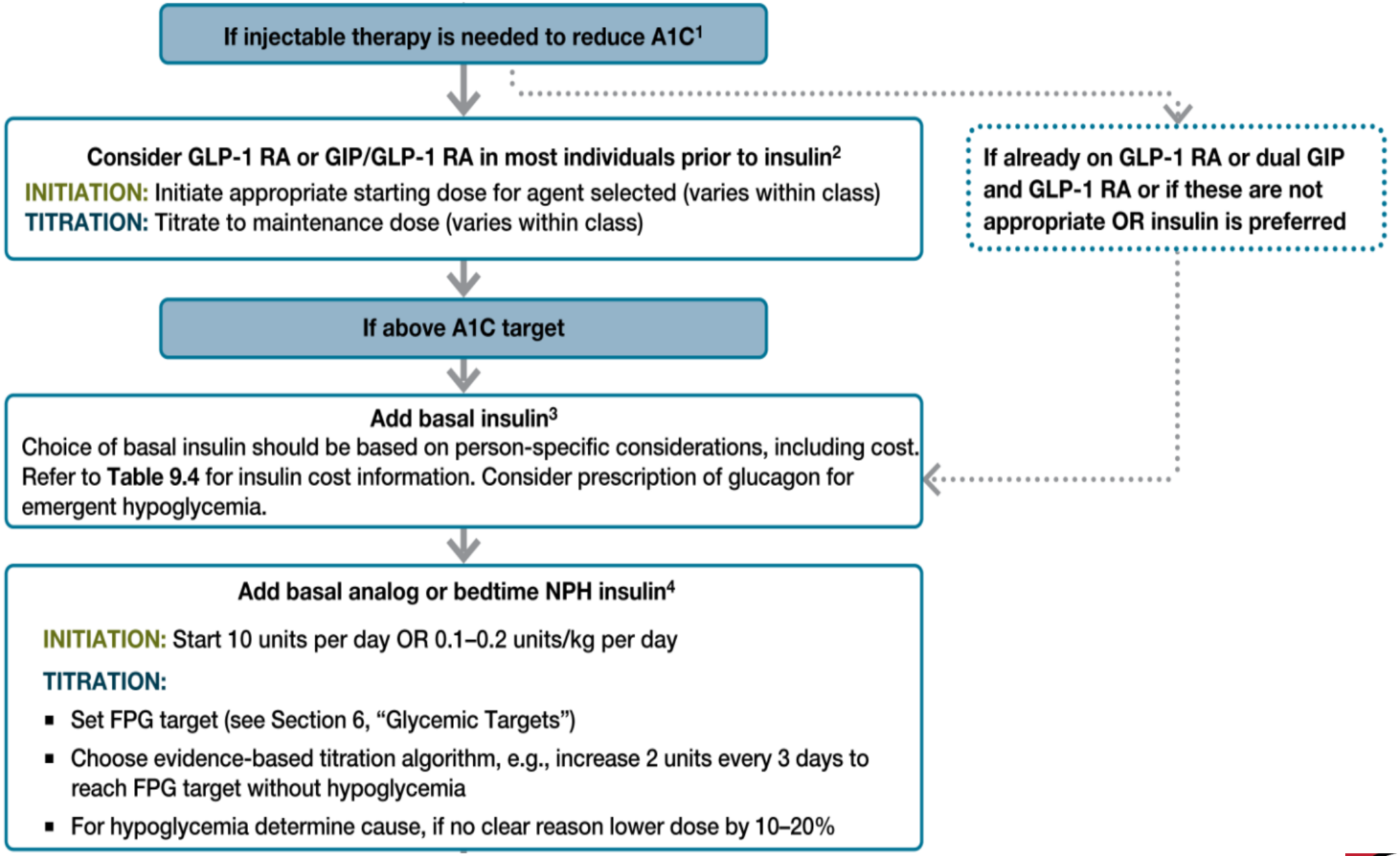
Very High
Dulaglutide, Semaglutide, Tirzepatide,
Insulin, Combination injectable (GLP-1 RA/Insulin)
High
GLP-1 (Not listed above), MTF, SGLT-2i, SU, TZD
Intermediate
DPP-4i

Achievement and maintenance of weight management

Very High
Semglutide, Tirzepatide
High
Dulaglutide, Liraglutide
Intermediate
SGLT2i, GLP-1 RA (not listed above)
Neutral
DPP-4i, Metformin

SGLT-2i

- Use of sodium–glucose cotransporter 2 inhibitor is recommended in individuals with type 2 diabetes and established heart failure with either preserved or reduced ejection fraction to improve symptoms, physical limitations, and quality of life. A


If injectable therapy is needed to reduce A1C[1]
Consider GLP-1 RA or GIP/GLP-1 RA in most individuals prior to insulin[2]
INITIATION: Initiate appropriate starting dose for agent selected (varies within class)
TITRATION: Titrate to maintenance dose (varies within class)
If already on GLP-1 RA or dual GIP and GLP-1 RA or if these are not appropriate OR insulin is preferred
If above A1C target
Add basal insulin[3]
Choice of basal insulin should be based on person-specific considerations, including cost. Refer to Table 9.4 for insulin cost information. Consider prescription of glucagon for emergent hypoglycemia.
Add basal analog or bedtime NPH insulin[4]
INITIATION: Start 10 units per day OR 0.1–0.2 units/kg per day
TITRATION:
Set FPG target (see Section 6, "Glycemic Targets")
Choose evidence-based titration algorithm, e.g., increase 2 units every 3 days to reach FPG target without hypoglycemia
For hypoglycemia determine cause, if no clear reason lower dose by 10–20%

Assess adequacy of basal insulin dose

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

- If above A1C target and not already on a GLP-1 RA or dual GIP and GLP-1 RA, consider these classes, either in free combination or fixed-ratio combination, with insulin.
- If A1C remains above target:

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

TITRATION:

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

If above A1C target

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 units 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 premixed 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

- Consider a GLP-1 receptor agonist prior to prandial insulin

Overbasalization with insulin therapy

- Clinical signals that may prompt evaluation of overbasalization include

- basal dose more than ~0.5 units/kg/day,
- high bedtime–morning or postpreprandial glucose differential,
- hypoglycemia (aware or unaware), and
- high glycemic variability.

- For people on GLP-1RA and basal insulin combination, consider use of a fixed-ratio combination product.
- Two different once-daily, fixed dual combination products containing basal insulin plus a GLP-1 RA are available: insulin glargine plus lixisenatide (iGlarLixi) and insulin degludec plus liraglutide (IDegLira).

Chronic Kidney Disease and Risk Management

- T2D + CKD use SGLT-2i to
  1. Reduce chronic kidney disease progression and cardiovascular events
  2. Used in patients with GFR≥20 mL/min/1.73 m^2 and urinary albumin ≥200 mg/g creatinine.

- SGLT-2i might also be effective in people with eGFR ≥20 mL/min/1.73 m^2 urinary albumin of normal to ≥200 mg/g creatinine

Finerenone

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

Cardiovascular Disease and Risk Management

Hypertension

- SBP ≥130 mmHg or DBP ≥80 mmHg x 2 on ≥2 occasions

- BP≥180/110 mmHg + CAD at a single visit

BP Goals

- DM + HTN with BP persistently ≥130/80 mmHg= need treatment

- The on-treatment BP goal is <130/80 mmHg, if safe

Hyperlipidemia

- Pt with DM aged 40-75 years at higher CV risk →use high intensity statin to
  - 1. ↓ LDL by >50% and
  - 2. target LDL of <70
- If note at goal, add ezetimibe or a PCSK9 inhibitor to maximum tolerated statin

- Pt with DM aged 40-75 years with CAD →use high intensity statin to
  - 1. ↓ LDL by >50% and
  - 2. target LDL of <55
- If not at goal, add ezetimibe or a PCSK9 inhibitor to maximum tolerated statin

WELL-AHEAD

Project ECHO

Statins and Bempedoic Acid

- After 6 months, the reduction in the mean LDL cholesterol level was greater with bempedoic acid than with placebo by 29.2 mg per deciliter; the observed difference in the percent reductions was 21.1 percentage points in favor of bempedoic acid.

- Among statin-intolerant patients, treatment with bempedoic acid was associated with a lower risk of major adverse cardiovascular events.

Nissen et al. N Engl J Med. 2023 Mar 4. doi: 10.1056/NEJMoa2215024. Epub ahead of print. PMID: 36876740.

Thank you