Metabolic Metamorphosis:

Updates in Hypertension & Diabetes Management

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I have no financial relationships to disclose .

The views expressed in this presentation are my own and do not necessarily represent the views of the Department of Veterans Affairs.

Objectives

1

Compare and contrast

recommendations from the 2017 hypertension guidelines to the 2025 hypertension guidelines

2

Utilize

the 2025 PREVENT risk calculator to determine the need for initiation of pharmacotherapy for stage 1 hypertension

3

Analyze

changes in the 2026 ADA guidelines Type 2 Diabetes management algorithm focusing on the incorporation of medications for comorbid conditions (CVD, CKD, MASLD, etc) independent of A1C goals

4

Evaluate

the updated recommendations regarding use of diabetes technology

Hypertension Updates

What's New?

1. BP treatment threshold
2. BP goals
3. Risk assessment
4. Lifestyle recommendations
5. Additional Screening

Blood Pressure Treatment Threshold

2017

Primary Prevention:
10-y ASCVD risk of <10% WITH SBP ≥140 mmHg OR DBP ≥90 mmHg

10-y ASCVD risk of ≥10% WITH
SBP ≥130 mmHg OR DBP ≥80 mmHg

Secondary Prevention:
Clinical CVD WITH SBP >130 mmHg OR DBP >80 mmHg

2025

Everyone:
AVG SBP ≥140 mmHg OR DBP ≥90 mmHg

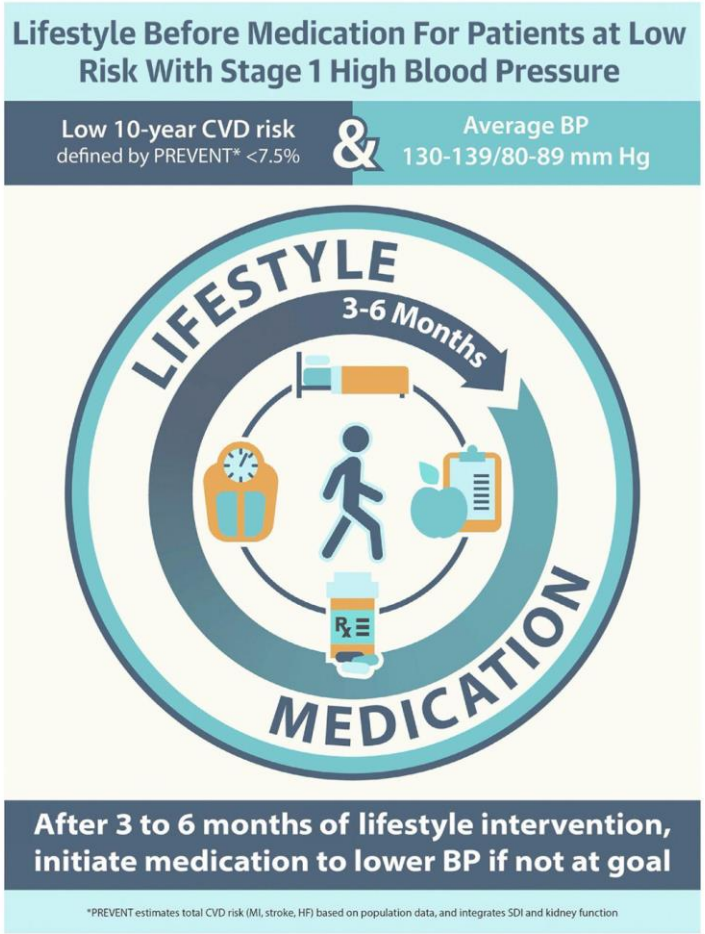
Primary Prevention:
With DM or CKD or 10-y CVD risk of ≥7.5% (using PREVENT)
SBP ≥130 mmHg OR DBP ≥80 mmHg

Secondary Prevention:
SBP ≥130 mmHg OR DBP ≥80 mmHg

Jones DW, et al. 2025
Whelton PK, et al. 2017
Khan SS, Abdalla M, Bello NA, et al. 2025

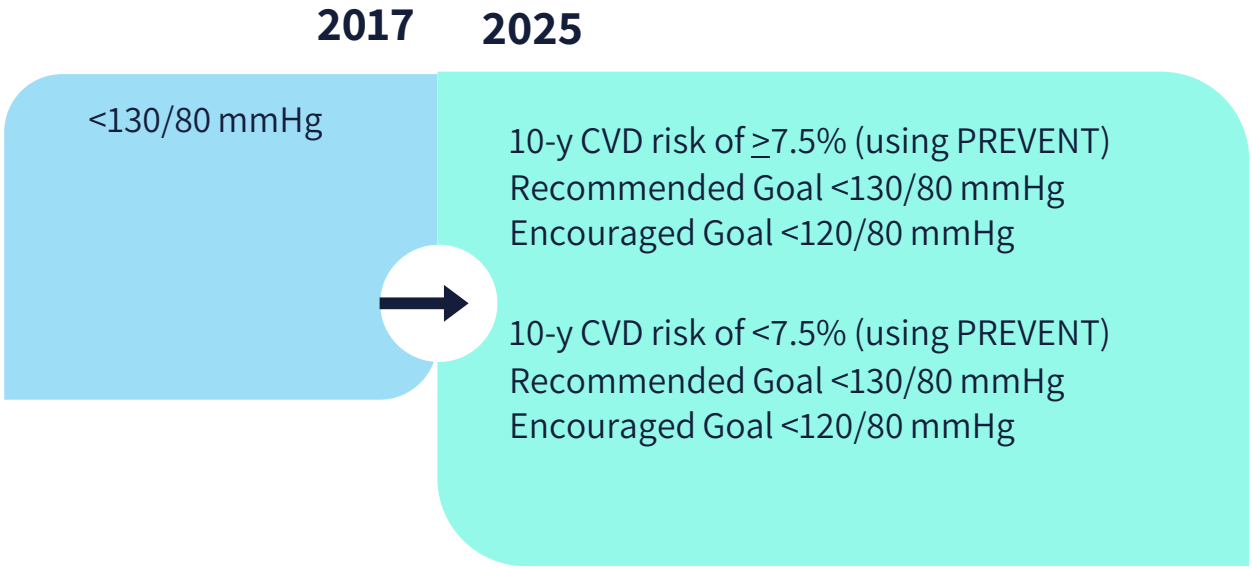
What about a primary prevention patient whose BP is >130/80 mmHg but has a 10-y CVD risk of <7.5% per PREVENT?

CENTRAL ILLUSTRATION: 2025 High Blood Pressure Guideline-at-a-Glance



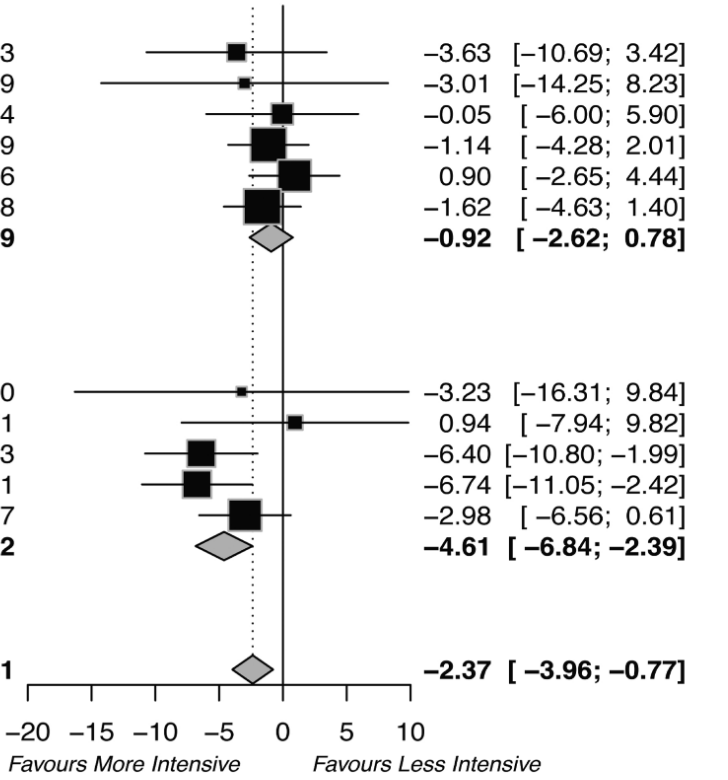
Gulati M, et al. JACC. 2025;86(18):1560-1566.

Blood Pressure Goals



Jones DW, et al. 2025
Whelton PK, et al. 2017

Cardiovascular Death



Study	More Intensive Events	More Intensive Total	Less Intensive Events	Less Intensive Total	Risk Difference (events per 1000 patients) RD	95% Confidence Interval
Less Intensive SBP Target (125-140 mm Hg)						
Cardio–Sis [26]	1	558	3	553	–3.63	[–10.69; 3.42]
SPS3 [25]	36	1501	41	1519	–3.01	[–14.25; 8.23]
VALISH [24]	11	1545	11	1534	–0.05	[–6.00; 5.90]
HOMED–BP [22]	3	1759	5	1759	–1.14	[–4.28; 2.01]
JATOS [23]	9	2212	7	2206	0.90	[–2.65; 4.44]
STEP [27]	18	4243	25	4268	–1.62	[–4.63; 1.40]
Overall	**78**	**11818**	**92**	**11839**	**–0.92**	**[–2.62; 0.78]**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.8471						
Test for effect in subgroup: z = –1.06 (p = 0.2875)						
Intensive SBP Target (<120 mm Hg)						
RESPECT [18]	8	633	10	630	–3.23	[–16.31; 9.84]
ACCORD BP [20]	60	2362	58	2371	0.94	[–7.94; 9.82]
SPRINT [21]	41	4678	71	4683	–6.40	[–10.80; –1.99]
ESPRIT [19]	59	5624	97	5631	–6.74	[–11.05; –2.42]
BPROAD [17]	60	6414	79	6407	–2.98	[–6.56; 0.61]
Overall	**228**	**19711**	**315**	**19722**	**–4.61**	**[–6.84; –2.39]**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.4192						
Test for effect in subgroup: z = –4.06 (p < 0.0001)						
Overall	**306**	**31529**	**407**	**31561**	**–2.37**	**[–3.96; –0.77]**

Heterogeneity: I^2 = 20.6%, τ^2 < 0.0001, p = 0.2471
Test for overall effect: z = –2.91 (p = 0.0036)

Verdecchia P, Angeli F, Reboldi G. 2025

Risk Assessment

2017
ASCVD Risk Estimator PLUS

AKA Pooled Cohort Equation (PCE) or ASCVD Risk Calculator

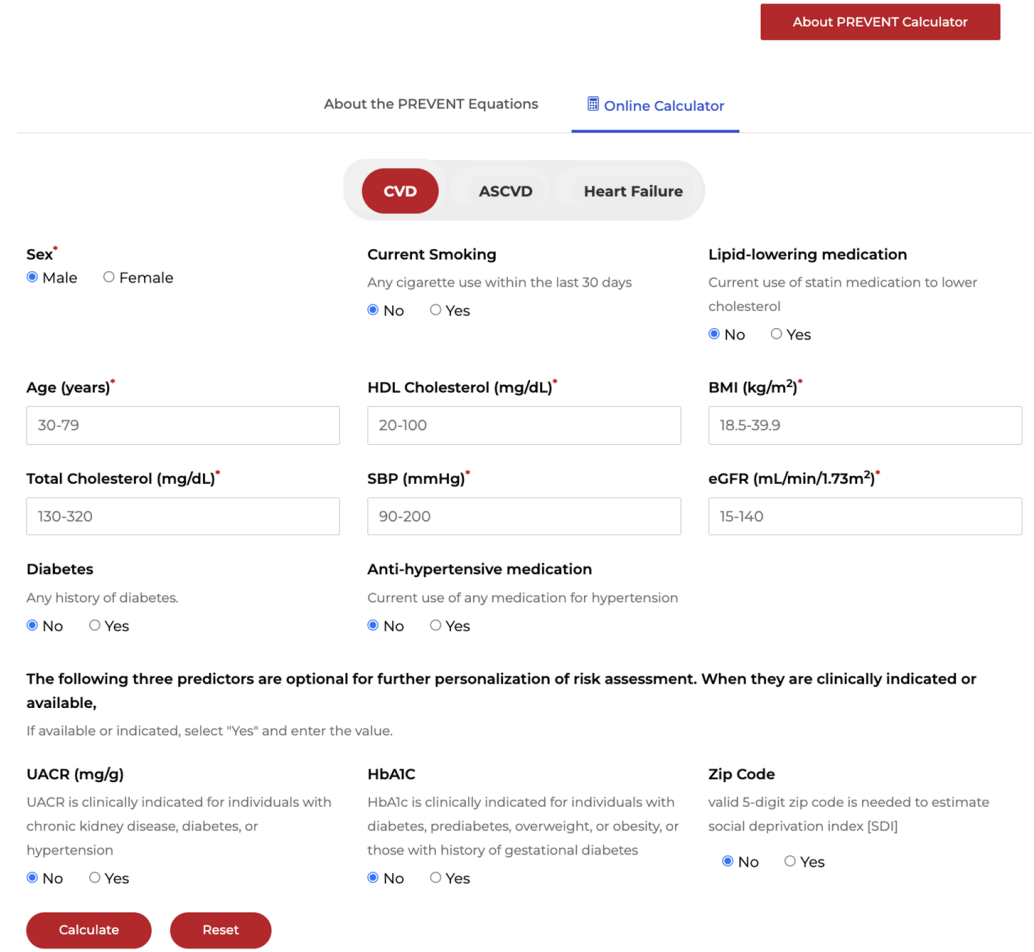
2025
PREVENT

Predicting **R**isk of cardiovascular disease **EVENTS**

American Heart Association®

What's Different?

The American Heart Association PREVENT™ Online Calculator



The American Heart Association PREVENT™ Online Calculator

About PREVENT Calculator

About the PREVENT Equations | Online Calculator

CVD | ASCVD | Heart Failure

Sex*
Male | Female

Current Smoking
Any cigarette use within the last 30 days
No | Yes

Lipid-lowering medication
Current use of statin medication to lower cholesterol
No | Yes

Age (years)*
30-79

HDL Cholesterol (mg/dL)*
20-100

BMI (kg/m^2)*
18.5-39.9

Total Cholesterol (mg/dL)*
130-320

SBP (mmHg)*
90-200

eGFR (mL/min/1.73m^2)*
15-140

Diabetes
Any history of diabetes.
No | Yes

Anti-hypertensive medication
Current use of any medication for hypertension
No | Yes

The following three predictors are optional for further personalization of risk assessment. When they are clinically indicated or available,

If available or indicated, select "Yes" and enter the value.

UACR (mg/g)
UACR is clinically indicated for individuals with chronic kidney disease, diabetes, or hypertension
No | Yes

HbA1C
HbA1c is clinically indicated for individuals with diabetes, prediabetes, overweight, or obesity, or those with history of gestational diabetes
No | Yes

Zip Code
valid 5-digit zip code is needed to estimate social deprivation index [SDI]
No | Yes

Calculate | Reset

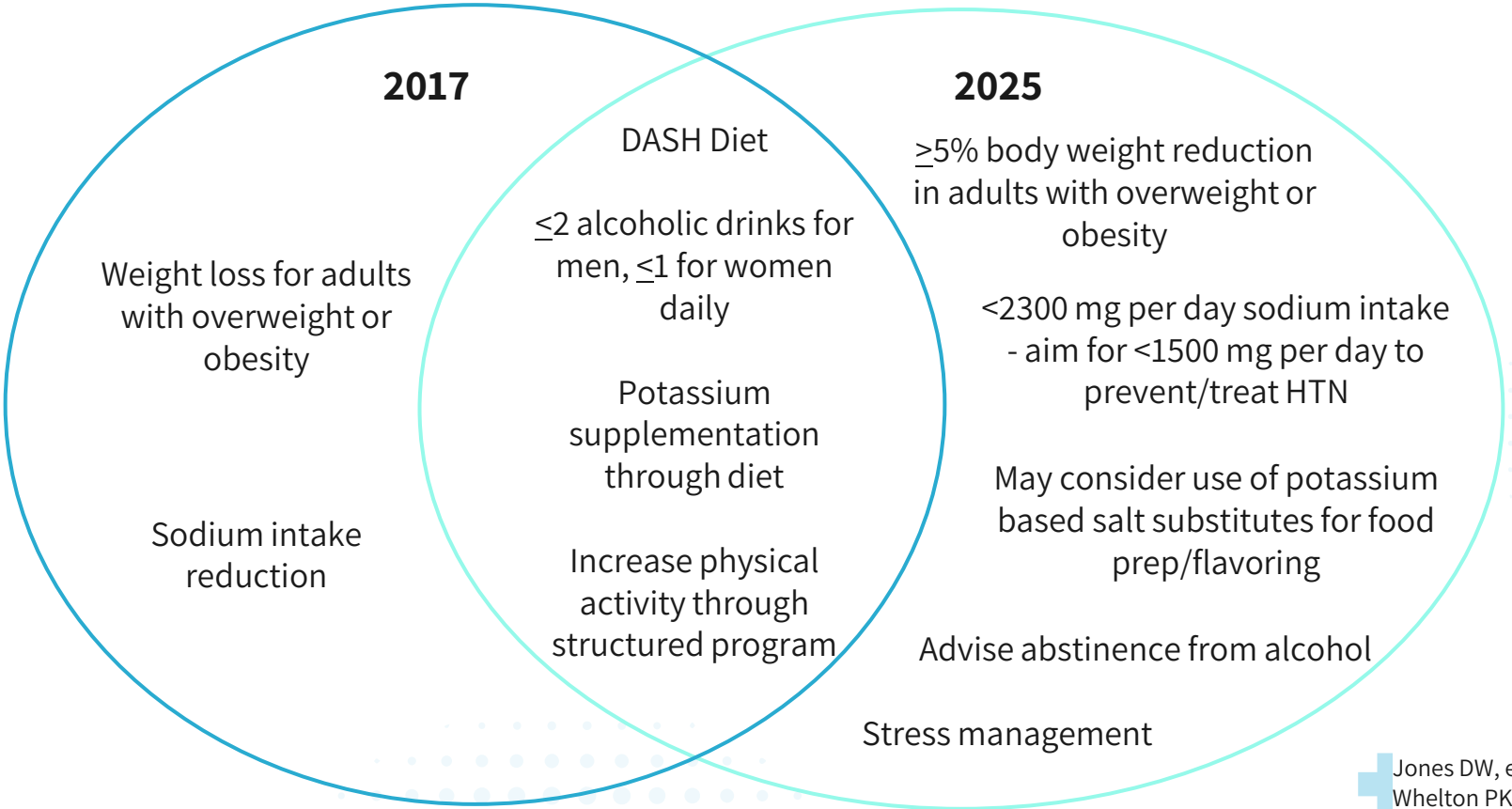
Data	ASCVD Plus	PREVENT	Comments
Age, Sex	✓	✓	• PREVENT: 30-79 yrs • ASCVD Plus: 20-79 yrs ○ Must be 40+ to calc 10-y risk
SBP, HDL, LDL, total cholesterol, Hx DM, Smoking status, statin use, HTN medication	✓	✓	
Race, DBP, Aspirin use	✓	✗	• Race is a social rather than biological construct - replaced by zip code
BMI, eGFR, UACR, A1C, Zip Code	✗	✓	• UACR, A1C, and Zip Code optional

ASCVD plus
10 year and lifetime risk
Only ASCVD

PREVENT
10 year and 30 risk
CVD, ASCVD, HF

Khan SS, Matsushita K, Sang Y, et al. 2024

Lifestyle Recommendations



Jones DW, et al. 2025
Whelton PK, et al. 2017

Additional Screening

Evaluation of secondary causes of HTN in adults with resistant hypertension

OSA
CKD
Primary aldosteronism**
Drug or alcohol induced
Renovascular hypertension

Screening tests:

- Electrolytes (Na+ and K+)
- Plasma aldosterone/renin activity ratio
  - Correct hypokalemia
  - Hold MRA for 4-6 weeks

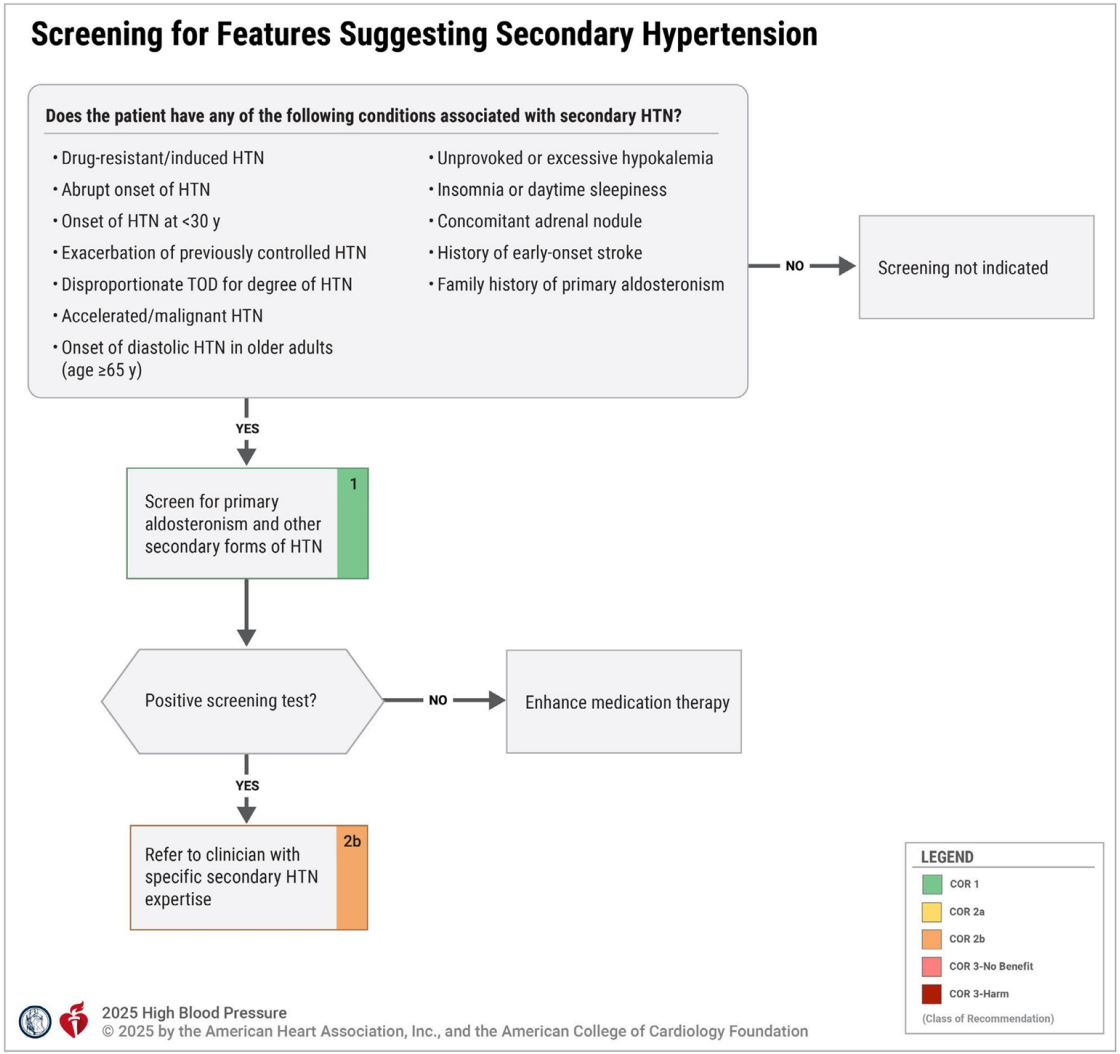
Confirmatory tests:

- Oral sodium loading test (with 24-hr urine aldosterone)
- Or IV saline infusion test with plasma aldosterone at 4 hr of infusion
- Or captopril suppression test (in patient not on ACEi or ARB)
- Adrenal CT scan
- Adrenal vein sampling

**Depending of etiology, treat with MRA or unilateral adrenalectomy

Jones DW, et al. 2025

TOD: Target Organ Damage



Jones DW, et al. 2025

Diabetes Updates

Person-first Language

A means of communication that emphasizes the person and view the disorder, disease, condition or disability as only one part of the whole person

Describe what the person “has” rather than what the person “is”

ADA first formalized use of person-first language in the 2017 *Standards of Care in Diabetes*

- Language should be neutral, non-judgemental, and strength based

Why should you care?

- Reduce feelings of stigma, shame, and bias
- Impact patient self care and mental health

J S, T C S, T D, et al. 2021
Dickinson JK, Guzman SJ, Maryniuk MD, et al. 2017

Jack has been a type 2 diabetic for 10 years. He is non-adherent.
He is failing on oral anti-diabetic agents and with lifestyle modifications. His diabetes is uncontrolled.
Its been getting worse over the past 12 months. His HbA1c is 9.4%

Jack has had type 2 diabetes for 10 years. Sometimes, he doesn't take his tablets because of their side effects. He finds it hard to maintain healthy habits at work.
His HbA1c has increased over the past 12 months, now 9.4%.

J S, T C S, T D, et al. 2021

What's New?

1. Comprehensive Management
2. Pharmacologic Treatment
3. Diabetes Technology
4. Weight Management
5. Perioperative Goals

Comprehensive Management and Pharmacologic Treatment

Recommendation 4.26 - Update

- **GLP-1 RA** with demonstrated benefits in **MASH** can be considered for treatment in adults with **T2DM, MASLD and overweight or obesity**

Recommendation 4.27a - Update

- **GLP-1 RA** with demonstrated benefit is preferred for glycemic management due **beneficial effects on MASH in adults with T2DM and biopsy proven MASH or those at high risk of fibrosis**

Recommendation 9.12 - Revision

- **GLP-1 RA** with demonstrated benefits in **MASH** or a **dual GIP and GLP-1 RA** with potential benefits in **MASH in people with T2DM, MASLD, and overweight or obesity** for glycemic management

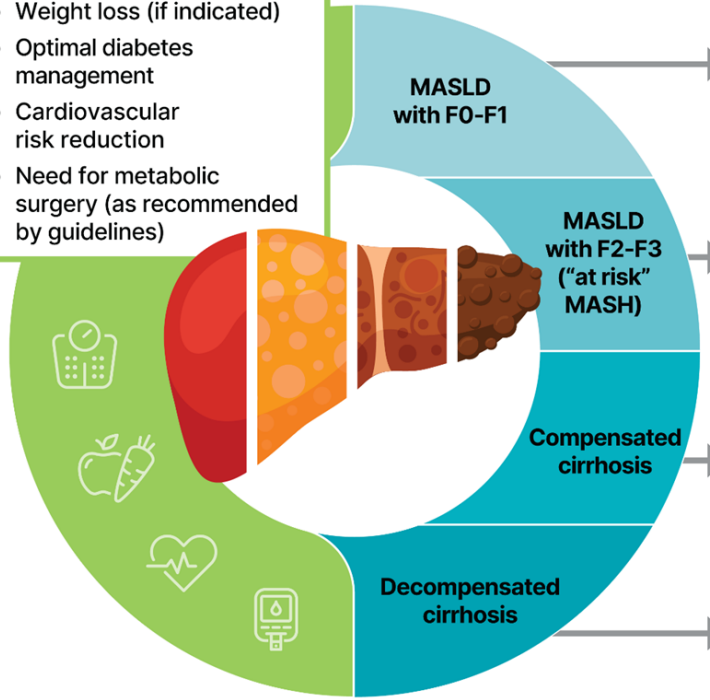
Recommendation 9.13a - Change

- **GLP-1 RA** with beneficial effects on **MASH** is preferred for glycemic management and a **pioglitazone or a dual GIP and GLP-1 RA** with potential beneficial effects on MASH can be **considered for glycemic management in adults with T2DM, biopsy proven MASH, or those at high risk for liver fibrosis**

Metabolic dysfunction–associated steatotic liver disease (MASLD) treatment algorithm

Individualize care, targeting the following:

- Adoption of a healthy lifestyle
- Weight loss (if indicated)
- Optimal diabetes management
- Cardiovascular risk reduction
- Need for metabolic surgery (as recommended by guidelines)



Obesity pharmacotherapy	Diabetes pharmacotherapy	MASH pharmacotherapy
Prefer GLP-1 RA, dual GIP and GLP-1 RA	Prefer GLP-1 RA, dual GIP and GLP-1 RA, pioglitazone, SGLT2i	Not indicated

Obesity pharmacotherapy	Diabetes pharmacotherapy	MASH pharmacotherapy
Prefer GLP-1 RA, dual GIP and GLP-1 RA	Prefer GLP-1 RA, dual GIP and GLP-1 RA, pioglitazone	Resmetirom, GLP-1 RA†

Obesity pharmacotherapy	Diabetes pharmacotherapy	MASH pharmacotherapy
As with F2-F3 with caution*	As with F2-F3 with caution*	ⓘ AVOID

Obesity pharmacotherapy	Diabetes pharmacotherapy	MASH pharmacotherapy
ⓘ AVOID	Only use insulin	ⓘ AVOID

† Only semaglutide among GLP-1 RAs has been approved by the FDA for treatment of MASH.

* Individualized care and close monitoring needed in compensated cirrhosis given limited safety data available.

American Diabetes Association.

Pioglitazone

A Placebo-Controlled Trial of Pioglitazone in Subjects with Nonalcoholic Steatohepatitis (2006)

- 55 patients randomized to diet + pioglitazone 45 mg daily OR diet + placebo
- Results favored pioglitazone over placebo
- ↓AST (by 40% vs. 12%, P=0.04), ↓ ALT (by 58% vs. 34%. P<0.001), ↓ hepatic fat content (by 54% vs 0%, P<0.001, improved histologic findings of steatosis (P=).003)
- BUT reduction in fibrosis did not differ significantly from that in the placebo group (P=0.08)

Improvement of Liver Fibrosis in Patients with MASLD Undergoing Pioglitazone Treatment: An Update (2025)

- Meta Analysis - Pioglitazone shows benefit in treating steatohepatitis, but has not shown to resolve fibrosis
- Resmetirom and GLP-1/GIP receptor agonists are showing better performance than pioglitazone

Phase 3 ESSENCE Trial: Semaglutide in Metabolic -Dysfunction Associated Steatohepatitis (Part 1)

Methods

- Phase 3, multicenter, randomized, double-blind, placebo-controlled trial
- 1197 patients with biopsy-defined MASH and fibrosis stage 2 or 3
- 2:1 ratio to receive once-weekly SQ semaglutide 2.4 mg or placebo for 240 weeks (5 years)

Results

- 800 participants evaluated at week 72 (part 1 interim analysis)

	Placebo	Semaglutide	Difference
Resolution of steatohepatitis without worsening of fibrosis	34.3%	62.9%	28.7 percentage points 95% CI (21.1 - 36.2)P<0.001
Reduction in liver fibrosis without worsening of steatohepatitis	22.4%	36.8%	14.4 percentage points 95% CI (7.5 -21.3) P<0.001

Conclusion

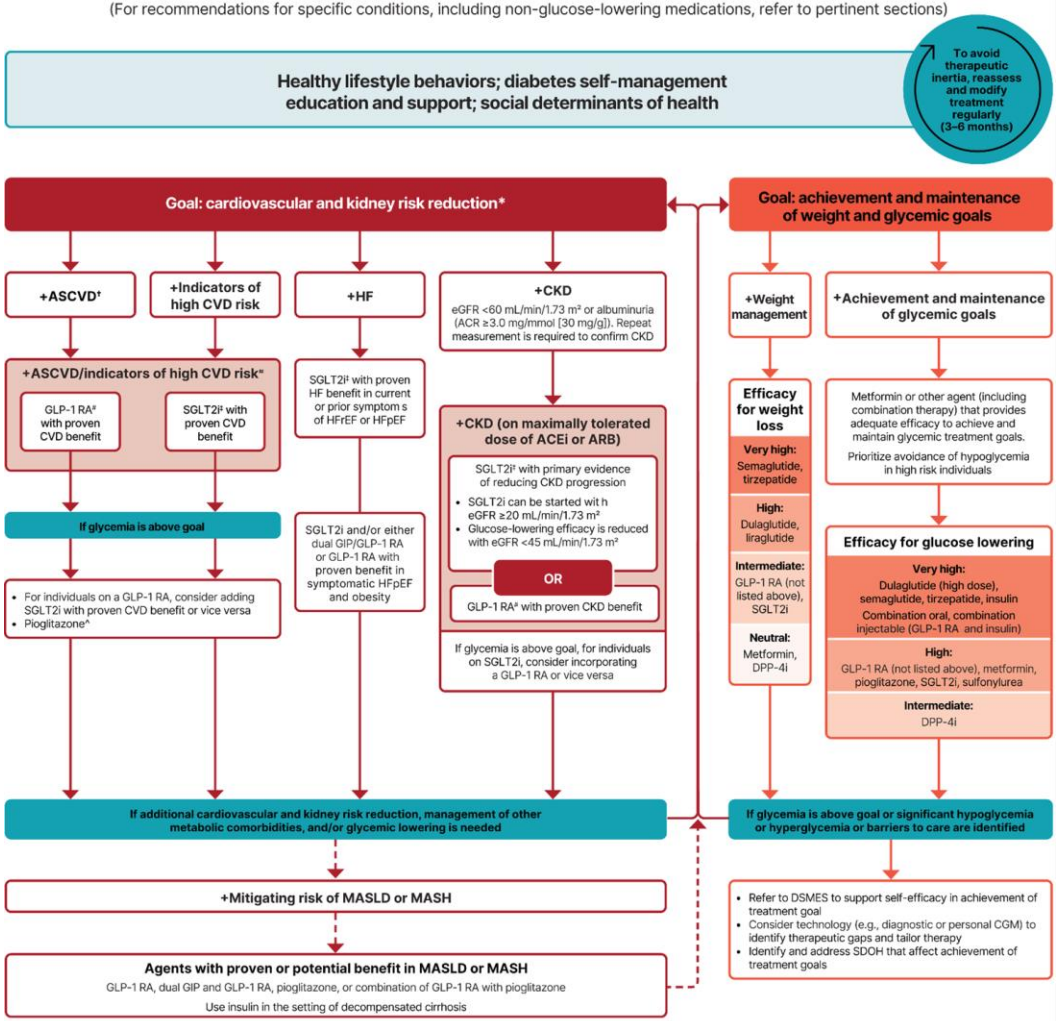
- Overall once weekly SQ semaglutide 2.4 mg improved histologic results in patient with MASH and moderate or advanced liver fibrosis
- August 2025 FDA granted accelerated approval of semaglutide for this indication
- Part 2 is ongoing

Phase 2 SYNERGY NASH Trial: Tirzepatide for Metabolic-Dysfunction Associated Steatohepatitis with Liver Fibrosis

<table>
<tr><td>Methods</td><td>
- Phase 2, dose-finding, multicenter, double-blind, randomized, placebo-controlled trial
- Participants with biopsy-confirmed MASH and stage F2 or F3 (moderate or severe) fibrosis
- Participants were randomly assigned to receive once-weekly subcutaneous tirzepatide (5 mg, 10 mg, or 15 mg) or placebo for 52 weeks.
</td></tr>
<tr><td>Results</td><td>
- 157 participants evaluated at week 52
<table>
<tr><th></th><th>Placebo</th><th>5 mg</th><th>10 mg</th><th>15 mg</th></tr>
<tr><td>% who met the criteria for resolution of MASH w/out worsening of fibrosis</td><td>10%</td><td>44%
95% CI (17-50)</td><td>56%
95% CI (29-62)</td><td>62%
95% CI (37-60)</td></tr>
<tr><td>% who had an improvement of at least one fibrosis stage without worsening of MASH</td><td>30%</td><td>55%
95% CI (5-46)</td><td>51%
95% CI (1-42)</td><td>51%
95% CI (1-42)</td></tr>
</table>
P<0.001 for all three
</td></tr>
<tr><td>Conclusion</td><td>In participants with MASH with moderate to severe fibrosis treatment with tirzepatide was more effective than placebo with respect to resolution of MASH without worsening of fibrosis</td></tr>
</table>

Use of glucose-lowering medications in the management of type 2 diabetes

(For recommendations for specific conditions, including non-glucose-lowering medications, refer to pertinent sections)



American Diabetes Association.

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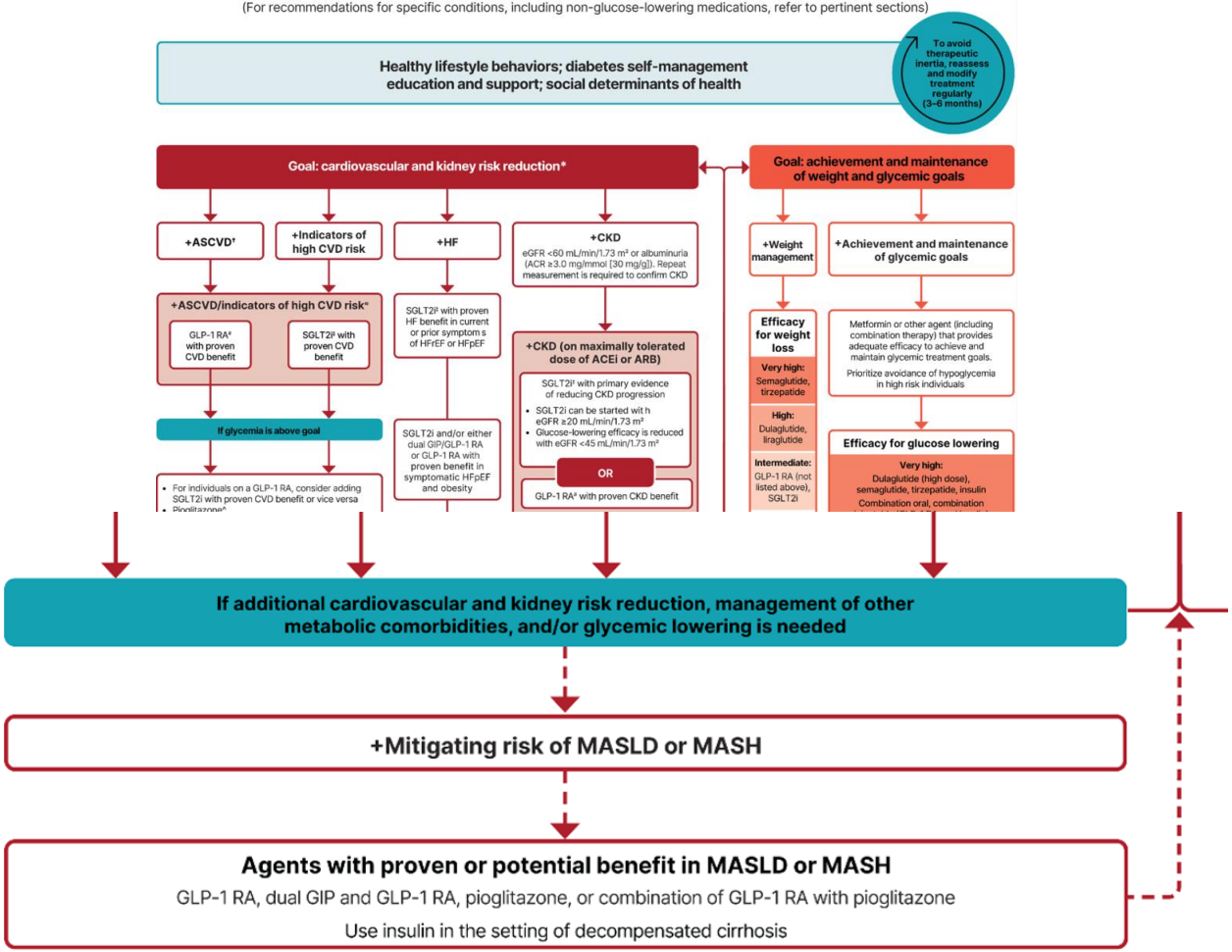


American Diabetes Association.

2024

Obesity Association™

A division of the **American Diabetes Association®**

Obesity

Recommendation 8.5 - Revised

- **Weight loss of 5-7%** of baseline body weight improves glycemia and other intermediate cardiovascular risk factors

Recommendation 8.14 - Modified

- Engaging other care team members to **minimize use of weight promoting medications** whenever clinically appropriate

Recommendation 8.20 - Added

- The individualized **dose and and dose titration for obesity pharmacotherapy** should **balance efficacy, benefits, and tolerability**

Recommendation 8.29 - Added

- Include **GLP-1 RA based therapy and/or metabolic surgery as treatment options** for **obesity** in people with **T1DM**

TIRTLE 1: Tirzepatide in Adults With Type 1 Diabetes: A Phase 2 Randomized Placebo-Controlled Clinical Trial

<table>
<tr><td>Methods</td><td>
- Phase 2, double-blind, placebo-controlled trial
- Adults with type 1 diabetes and BMI >30 kg/m2
- Randomized to once-weekly SQ tirzepatide (2.5 mg x 4 weeks, 5.0 mg x 8 weeks) or placebo
</td></tr>
<tr><td>Results</td><td>
- ~~22 participants evaluated at 12 weeks~~
<table>
<tr><th></th><th>Placebo</th><th>Tirzepatide</th><th>Difference</th></tr>
<tr><td>Mean change in weight</td><td>-0.7 kg</td><td>−10.3 kg</td><td>−8.7 kg (95% CI −12.0 to −5.5 kg; P < 0.0001)</td></tr>
<tr><td>Reduction in total daily insulin dose</td><td>−0.3 u/day</td><td>−24.2 u/day</td><td>−35.1% (95% CI −46.5 to −21.3%; P = 0.0002)</td></tr>
</table>
</td></tr>
<tr><td>Conclusion</td><td>In adults with type 1 diabetes and obesity, tirzepatide was superior to placebo for weight loss over 12 weeks.</td></tr>
</table>

Diabetes Technology

Recommendation 7.8a - New

- Should be **no requirement of C-peptide level, presence of islet autoantibodies or duration of insulin treatment** before initiation of **CSII or AID****

Recommendation 7.15

- Use of **CGM is now recommended at diabetes onset and anytime thereafter** for children, adolescents, and adults with diabetes who are **on insulin therapy, non-insulin therapies that can cause hypoglycemia, and on any diabetes treatment where CGM helps management**

Recommendation 7.25b

- **AID systems** can be considered in people with **T2DM on basal insulin who are not meeting their individualized glycemic goals**

****CSII**: Continuous Subcutaneous Insulin Infusion
AID: Automated Insulin Delivery

Table 7.3 Continuous glucose monitoring devices

Type of device	Brand*	Availability	Alarms
rtCGM	Libre 2 Plus and Libre 3 Plus	Prescription	Yes
	Dexcom G6 and G7	Prescription	Yes
	Eversense 365	Prescription	Yes
	Guardian 4	Prescription	Yes
	Simplera	Prescription	Yes
OTC-CGM	Dexcom Stelo	OTC	No
	Abbott Lingo	OTC	No
Professional CGM	Abbott FreeStyle Libre Pro	In office	No
	Dexcom G6 Pro	In office	No

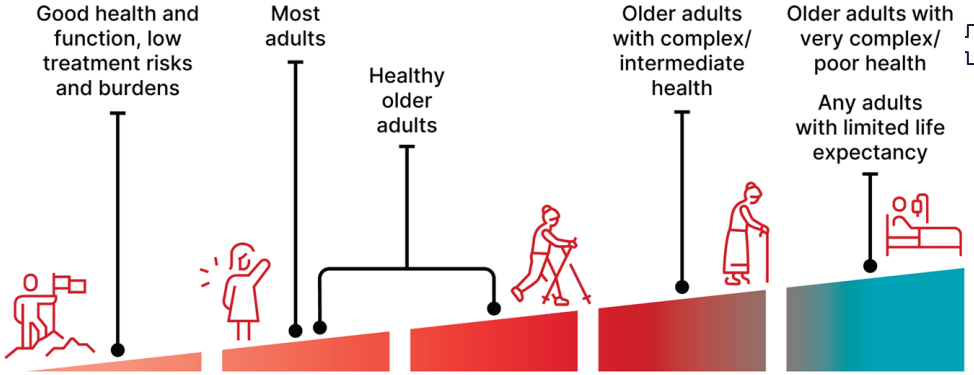
CGM, continuous glucose monitoring; isCGM, intermittently scanned CGM; OTC, over the counter; rtCGM, real-time CGM.

*Generic names not available.

Table 7.4—Continuous glucose monitoring device interfering substances

Medication	Systems affected	Effect
Acetaminophen		
>4 g/day	Dexcom G6, Dexcom G7	Higher sensor readings than actual glucose
Any dose	Medtronic Guardian 4	Higher sensor readings than actual glucose
Ascorbic acid (vitamin C), >500 mg/day	FreeStyle Libre 2, FreeStyle Libre 3	Higher sensor readings than actual glucose
Ascorbic acid (vitamin C), >1,000 mg/day	FreeStyle Libre 2 Plus, FreeStyle Libre 3 Plus	Higher sensor readings than actual glucose
Hydroxyurea	Dexcom G6, Dexcom G7, Medtronic Guardian 4	Higher sensor readings than actual glucose
Mannitol (intravenously or as peritoneal dialysis solution)	Senseonics Eversense365	Higher sensor readings than actual glucose
Sorbitol (intravenously or as peritoneal dialysis solution)	Senseonics Eversense365	Higher sensor readings than actual glucose

Glycemic Goals



A1C goals	<6.5%	<7.0%	<7.5%	<8.0%	No A1C goal
CGM goals TIR:	—	>70%	—	>50%	—
• TBR <70	—	<4%	—	<1%	<1%
• TBR <54	—	<1%	—	<1%	<1%
• TAR >180	—	<25%	—	<50%	Avoid symptomatic hyperglycemia
• TAR >250	—	<5%	—	<10%	

Modifying Factors

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

American Diabetes Association.

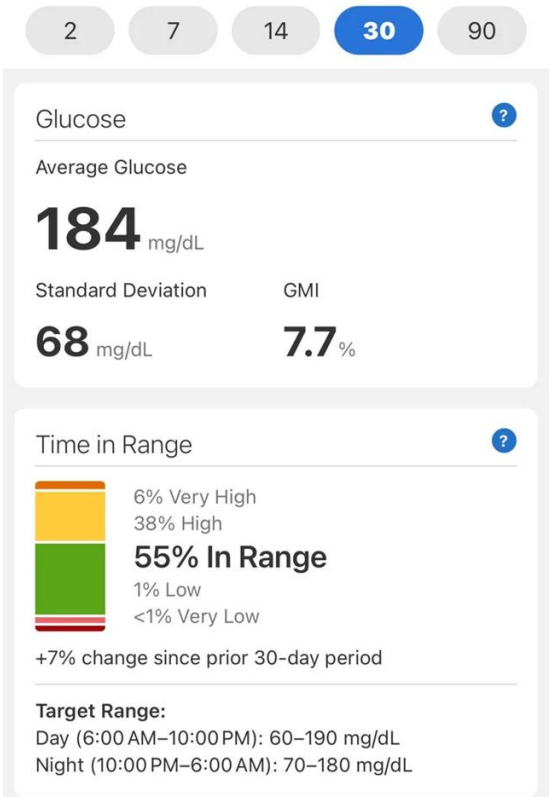
Perioperative Goals

Recommendation 16.14 - New

- To improve postoperative outcomes, suggests an **A1C goal <8% within 3 months** of elective surgery . **Alternatively a 14-day glucose management indicator goal of <8% or time in range >50% can also be used**

Recommendation 16.15 - New

- Advises a blood glucose range of 100-180 mg/dL during the perioperative period



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Questions?