Diabetes Type 2 Protocol

Diagnosis

- A1c
  - Prediabetes 5.7-6.4%
  - DM ≥ 6.5%
- 2 hr GTT, 75G load
  - Prediabetes: 140-199 mg/dL
  - DM ≥ 200 mg/dL
- Fasting glucose
  - Prediabetes 100-125 mg/dL
  - DM ≥ 126 mg/dL
- Random glucose with classic symptoms
  - DM ≥ 200 mg/dL

Labs

- A1C
- Lipids
- LFTs
- Spot urinary albumin-to-creatinine ratio
- Serum Creatinine and eGFR
- Vitamin B12 if taking metformin > 5 yrs
- CBC with platelets
- Serum K+ (if on ACE/ARB or diuretic)
- Ca, Vit D, phosphorus for appropriate people with diabetes

Repeat labs annually (A1C more frequently)

Treatment of PreDM

May consider if:

- Age 25-59 years
- Women w/ h/o GDM
- Fasting glucose ≥ 110 mg/dL or A1C ≥ 6.0

Lifestyle interventions +/- Metformin

Vaccines

- All routine vaccines plus pneumococcal vaccine

A1C Goal†

Pt health	A1C goal
Good health, low Rx risk	< 6.5%
Most adults	< 7-7.5%
Older, complex history	<8.0
Older adults with very complex/poor health or limited life expectancy	No A1C goal

†Based on ADA; AACE recommends ≤ 6.5 for most or 7-8% if high risk for adverse complications or limited life expectancy

DKA and HHS

Consider hyperglycemic crises in all patients with polyuria, polyuria, weight loss, n/v, dehydration, and changes in cognitive state:

- DKA (must meet all 3 criteria):
  - Glucose ≥ 200 mg/dL or prior history of diabetes
  - β-hydroxybutyrate ≥ 3.0 mmol/L or urine ketone strip 2+ or more
  - pH < 7.3 and/or bicarb < 18 mmol/L
- HHS (must meet all criteria):
  - Glucose ≥ 600 mg/dL
  - Effective osmolality > 300 mOsm/kg or total osmolality > 320 mOsm/kg
  - pH ≥ 7.3 and bicarb > 18 mmol/L
  - β-hydroxybutyrate < 3.0 mmol/L or urine ketone strip < 2+

Treating Hypoglycemia

- Glucose preferred if <70 mg/dL but any fast acting carbohydrate can be used
- Glucagon for all those taking insulin
- Consider de-intensifying regimen or switching Rx

MASLD

- 70% of diabetics have MASLD
- Screen with FIB-4 score (calculation based on age, AST, ALT, and platelets)
  - Low < 1.3 ----> Routine monitoring q 1-2 yrs
  - Intermediate 1.3-2.67 ---> Elastography (Fibroscan - u/s based test) or alternatively ELF blood test
    - if Liver Stiffness Measurement ≥ 8.0 kPa on Fibroscan (or ELF ≥ 9.8) – refer to specialist; otherwise continue to monitor q1-2yrs
  - High > 2.67 ---> Refer to hepatology (for advanced fibrosis or possible liver biopsy)

A1C Limitations/Alternatives

A1C influenced by RBC pathology:

- Anemia:
  - Anemia due to low iron/b12/folic acid: falsely elevates A1C due to prolonged RBC lifespan
  - Hemolytic anemia falsely lowers A1C due to shoter RBC lifespan
- Blood transfusions - may lower A1C (based on donor's blood sugar

Alternative measures:

- Fructosamine (estimates average glucose over 2-3wks)
- Glycated albumin
- CGM (goal: TIR >70%, TBR <4%, <1% of time glucose <54

Screen CVD

- Screening for asymptomatic CVD not routinely recommended
  - No stress or echo on asymptomatic patients
- Ankle-Brachial Index (ABI) recommended if
  - Symptoms of claudication
  - May consider if diabetes ≥ 10 yrs
  - If PAD diagnosis would change management and:
    - ≥ 65 yrs
    - Microvascular diagnosis
    - Foot complications
    - End stage organ damage

ADA Weight Management

BMI Category	Treatment	Info
BMI ≥ 25 (*23.0-24.9)	Lifestyle	Goal 5-10% weight loss
BMI ≥ 27 (*25.0-27.4)	Lifestyle + Rx	• GLP-1 or • SGLT-2
BMI ≥ 30 (* ≥ 27.5)	Consider Sx	• Gastric bypass • Sleeve

* For Asian Americans

Drug Class	Example Drugs	*Expected A1C Reduction (%)
Biguanides	Metformin (Glucophage)	1.0–1.3
SGLT2 Inhibitors	Empagliflozin (Jardiance), Dapagliflozin (Farxiga)	0.5–0.9
GLP-1 RAs	Semaglutide (Ozempic), Dulaglutide (Trulicity)	0.8-2.0
GLP-1 RA/GIP	Tirzepatide (Mounjaro)	1->2.5%
DPP-4 Inhibitors	Sitagliptin (Januvia), Linagliptin (Tradjenta)	0.5–0.9
Sulfonylureas	Glipizide, Glyburide	0.4-1.2
TZDs	Pioglitazone (Actos)	0.5–1.4
Meglitinides	Repaglinide (Prandin)	0.5–1.0
Alpha-glucosidase Inhibitors	Acarbose (Precose)	0.5–0.8

References: ADA 2026 Guidelines; 2023 AACE Guideliens

* Powers AC, D'Alessio D. Goodman & Gilman's Pharmacology. 12th ed. 2011; ADA 2025 Guidelines

New Drug Classes

SGLT2-i

- Proven CV benfit: canagliflozin (Invokana), dapagliflozin (Farxiga), empagliflozin (Jardiance)
- MOA: lower glucose by blocking glucose reabsorption in the kidneys --> Glucose excretion
- Key proven benefits:
  - Reduces MACE
  - Renal protection: significantly lowers progression of kidney disease (including in nondiabetics)
  - Reduces heart failure progression (including in nondiabetics)
  - Reduces all-cause mortality
  - Modest weight loss
- Side effects: Risk of urinary infx, dehydration, electrolyte imbalance, amputation risk
- Contraindicated:
  - eGFR <30 (dapa/empa may be used at lower eGFRs in heart failure or for renal protection)
  - DKA
  - Volume depletion
  - Hypersensitivity

GLP-1 Agonists

- Proven CV benefit: liraglutide (Victoza), semaglutide (Ozempic, Wegovy), dulaglutide (Trulicity)
- MOA: Mimics GLP-1 hormone:
  - Increases insulin secretion
  - Reduces glucagon
  - Slows gastric emptying
  - Increases satiety
- Key proven benefits:
  - Significant weight loss
  - Reduces MACE
  - Reduces CVA risk
  - Reduces all-cause mortality
  - Reduces progression of CKD
- Contraindications:
  - Personal or fhx of medullary thyroid cancer or MEN 2
  - Severe GI distress
  - Caution if h/o pancreatitis
  - Hypersensitivity

GLP-1/GIP

- Example: tirzepatide (Mounjaro or Zepbound)
- MOA: Activates GLP-1 and GIP receptors, offering additional blood sugar control and weight loss
  - GIP activation
    - Increases insulin secretion and sensitivity
    - Reduces appetite
    - Promotes fat metabolism
- Superior to GLP-1 for weight loss, glucose control
- Likely CV protection (long-term studies ongoing)
- Likely improved insulin sensitivity compared to GLP-1
- Contraindications: same as GLP-1

The Rx Guidelines

Start with Lifestyle Changes + Metformin

AACE Guidelines - Complications Centric

ASCVD --> GLP-1 or SGLT2i --> SGLT2i or GLP-1

Heart faiure --> SGLT2i --> GLP-1

Stroke/TIA --> GLP-1 or Pioglitazone --> Pioglitazone or GLP-1

CKD --> SGLT2i or GLP-1 --> GLP-1 or SGLT2i

In all cases use Metformin if appropriate

ACP Recommendations

1. Add an SGLT-2 or GLP-1 to metformin and lifestyle modifications in adults with type 2 diabetes and inadequate glycemic control
2. ACP recommends against adding a DPP-4i to metformin and lifestyle modifications in adults with type 2 diabetes and inadequate glycemic control to reduce morbidity and all-cause mortality

AACE Guidelines - Glucose Centric

Overweight or Obese --> GLP-1 or GIP/GLP-1 or SGLT2i

Hypoglycemic risk --> GLP-1 or GIP/GLP-1 or SGLT2i

Cost --> SU or TZD

Severe hyperglycemia --> Basal + Prandial Insulin or GLP-1 vs GIP/GLP-1

In all cases use Metformin if appropriate

Early Combo Therapy

- Early combination therapy reduces long-term treatment failure and preserves beta-cell function
- Consider when:
  - A1C ≥ 1.5% above target
  - Combination should include Metformin unless contraindicated

Whento Start Insulin

- If AlC ≥ 10% or significant hyperglycemia with symptoms
- Failure to meet goals w/ oral agents
- Start with basal, add prandial if needed
- Consider newer weekly insulin
- Preferred to combine insulin with GLP-1 or GLP/GIP
- Glucagon recommended for all patients on insulin

Step	Insulin Type	Starting Dose	Adjustment	Target
1. Basal	Long-acting (e.g., glargine, detemir)	10 units/day or 0.1–0.2 units/kg body weight	Adjust by 2–4 units every 3–4 days based on fasting glucose Fasting glucose: 80–130 mg/dL	Fasting glucose: 80–130 mg/dL
2. Prandial	Rapid-acting (e.g., lispro, aspart)	4–6 units or 10% of total basal insulin before meals	Adjust based on pre-meal glucose levels and carbohydrate intake	Pre-meal glucose: 80–130 mg/dL
3. Basal-Bolus Regimen	Combination of basal + prandial insulins	Basal: 0.2–0.3 units/kg/day Bolus: 4–6 units or 10% of basal insulin before meals	Adjust both insulin doses based on blood glucose patterns	Fasting: 80–130 mg/dL Postprandial: <180 mg/dL
4. Fixed-Dose Regimen	Premixed insulin (e.g., 70/30, 75/25)	Two doses daily as alternative to basal-prandial	Adjust based on fasting and post-meal glucose levels	Fasting glucose: 80–130 mg/dL Postprandial: <180 mg/dL

Additional Notes:

- Once-weekly basal insulins (icodec or Awiqli) are coming options that simplify dosing.
- U-300 glargine (Toujeo) and U-500 regular insulin provide alternative concentrated options for patients requiring higher doses
- Inhaled insulin (Affreza) is rapid-acting insulin option for prandial control that is needle-free, avoid in lung disease, monitor FEV1

HTN Management

- Goal < 130/80 for most
- ACE/ARB if albuminuria or CAD but otherwise may choose any first line agent (ACE/ARB, CCB, Diuretic)
- Start 2 meds if ≥150/90 (ADA) or ≥140/90 (ACC/AHA)
- If not at goal with 3 first line meds, add MRA & refer

Statins/Cholesterol

- Consider if age 20-39 years plus additional ASCVD risk factors
- Moderate-intensity statin if 40-75 yrs w/ diabetes (regardless of LDL)
- For diabetes + ASCVD or high CV risk (10 yr risk score ≥ 20%)
  - High-Intensity statin: either Atorvastatin (40-80mg) or Rosuvastatin (20-40mg)
  - Aim to lower LDL to < 70 mg/dL
  - May use non-statins if not at goal or not tolerated: Ezetimibe, PCSK9i, siRNA, Bempedoic acid
- Secondary prevention after ASCVD
  - Reduce LDL by ≥ 50% and < 55 mg/dL
    - Use ezetimibe or PCSK9i if needed
    - Consider PCSK9i, bempedoic acid, or siRNA (inclisiran) if statin intolerant

References: ADA 2026 Guidelines; AACE 2023 Type 2 Diabetes Guidelines, ACP 2024 Type 2 Diabetes Guidelines