Diabetes

Ambulatory Care Pathway

Mount Sinai Health Partners

Care Standardization at Mount Sinai

Mount Sinai Ambulatory Care Pathways are one component of our care standardization initiatives within the Mount Sinai Health System. Evidence-based standardized care helps achieve:

- Better health outcomes
- Consistency in processes and decision making
- Improved quality of care and patient safety
- Reduced costs and ED utilization
- More accurate clinical documentation

With these outcomes and goals in mind, Mount Sinai Health Partners has developed, in consultation with clinical experts across the Health System, a series of care pathways, quick reference guides, and CME events to help primary care providers manage diabetes, heart failure, hypertension, COPD, CKD, and PAD according to the latest professional guidelines.

This Diabetes Ambulatory Care Pathway is a detailed guide to managing patients with type 2 diabetes mellitus*, with or without common comorbidities. We cover:

- Screening and diagnosis
- Lifestyle interventions
- Pharmacologic therapy
- Complications and common combordities
- When to refer to specialty care
- Care coordination and team-based care

To access all of our Ambulatory Care Pathways, patient resources, and more resources to help you manage chronic conditions visit our Chronic Condition Management Hub.

* Unless otherwise specified, understand “diabetes” to refer to type 2 diabetes mellitus throughout this document

January 2024 Updates

This version of the Mount Sinai Diabetes Ambulatory Care Pathway includes a number of new and expanded sections, as well as updates to previous guidance to reflect the latest evidence-based standards.

New

- Diet, Nutrition, and Physical Activity (preventive)
- Medications that can affect blood sugar
- Medication summary table
- Finerenone for patients with comorbid diabetes and CKD
- Obesity management
- Liver disease

Expanded

- Prediabetes
- Glucose monitoring
- Hypoglycemia treatment and patient education
- GLP-1 RA therapy

Updated

- Immunization recommendations
- Treatment algorithm
- Medication dosing guidelines
- Guidelines for managing comorbidities

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Overview

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Over 37 million people in the United States live with diabetes (about 11% of the population), with 90-95% of this group living with type 2 diabetes. This number includes an estimated 8.5 million people who are not yet diagnosed.[1] Another 96 million adults have prediabetes (38% of the population) and research suggests 1 in 3 people will develop diabetes in their lifetime. Diabetes is the most expensive chronic condition in the country with a total annual cost of $327 billion.[2]

Initial visits and follow-up visits should include a comprehensive medical evaluation, including interval medical history, assessment of medication taking behavior and intolerance/side effects, physical examination, laboratory evaluation as appropriate to assess attainment of A1C and metabolic targets, and assessment of risk for complications, diabetes self-management behaviors, nutrition, psychosocial health, and the need for referrals, immunizations, or other routine health maintenance screening.

Key steps in the management of diabetes:

- Confirm the diagnosis
- Evaluate for complications of diabetes and potential comorbid conditions
- Review previous treatment and risk factor control in patients with established diabetes
- Ongoing management should be guided by the assessment of diabetes complications and shared decision-making to set therapeutic goals

Team-Based Care

Managing and empowering patients living with diabetes is a team sport.[3] A wide variety of team members can be involved in the diagnosis, lifestyle changes, medication management and disease management. Below are potential team members and options to integrate specialty care, primary care, and advanced practice providers.

To learn more about team-based care services available through the Mount Sinai Health System, review the appendix.

Care component	Possible team members
Diagnosis and severity classification	• Endocrinologist • PCP • Advanced Practice Provider (APP)
Initial treatment (lifestyle, medications, nutrition)	• Endocrinologist • PCP • APP • Clinical Pharmacist
Maintenance treatment (medication adjustment and adherence, nutrition)	• Endocrinologist • PCP • APP • Clinical Pharmacist
Self-management (weight monitoring, symptom response, motivational interviewing)	• Endocrinologist • PCP • Clinical Pharmacist • Care Management (RN) • Certified Diabetes Educators (CDE) • Wellness Coach
Coordination of specialty treatment, testing, and care	• Care Management (SW, RN)
Behavioral health screening, referrals, and care	• PCP • APP • Pharmacy • LCSW
Ambulatory care management/Skilled Home Care	• Care Managers (RN, SW) • Home Health Aide • Community Paramedicine
Telemonitoring/home care services	• Endocrinologist • Clinical Pharmacist • Care Management (RN) • Home Health Aide

Palliative Care	• Endocrinologist • Geriatrics or palliative care specialist • PCP • APP • Pharmacist • Care Management (RN)

Screening & Diagnosis[4]

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HbA1c, fasting plasma glucose (FPG), **or** an oral glucose tolerance test (OGTT) can be used to diagnose prediabetes or type 2 diabetes. The American Diabetes Association (ADA) 2022 Standards of Care guidelines outline the below criteria for diagnosing prediabetes and diabetes.[5]

	Prediabetes	Type 2 Diabetesae
HbA1c	5.7% – 6.4%	> 6.4%
Fasting plasma glucose (FPG)	100 – 125 mg/dl	> 125 mg/dl
2-hour plasma glucose (PG) during oral glucose tolerance test (OGTT)	140 mg/dl – 199 mg/dl	> 199 mg/dl

Any one of these three tests can be used for diagnostic screening.

Additionally, patients with classic symptoms of hyperglycemia or hyperglycemic crisis can be diagnosed with type 2 diabetes if they have a random plasma glucose of at least 200 mg/dL.

Prediabetes[6]

Prediabetes is a risk factor for progression to diabetes and cardiovascular disease, and interventions at this stage are a significant opportunity to improve health outcomes.[7] Engage patients in a discussion about their prediabetes and its implication for the future.

Lifestyle interventions are the recommended first-line treatment at this stage, including a **7% reduction in body weight**. Obesity management can delay the progression from prediabetes to type 2 diabetes.[8] See the lifestyle section for more details.

Metformin may be used to treat prediabetes, particularly for patients < 60 years old, a prior history of gestational diabetes, and/or a BMI > 35.

- Monitor B12 levels in metformin-treated individuals, as long-term use may be associated with deficiency, especially in those with anemia or peripheral neuropathy[9,10]

For all patients who meet the criteria for prediabetes:

- Screen for cardiovasular disease, as prediabetes is associated with increased cardiovascular risk

- Perform annual follow-up testing to monitor progression to diabetes

Diet, Nutrition, and Physical Activity

Prevention is key in delaying the progression from prediabetes to diabetes. Lifestyle interventions should be the first line of treatment for all patients with diabetes. We recommend a combination of nutrition counseling, physical activity, and behavioral therapy. Referring patients to a nutritionist/dietician can be very helpful.

Overweight patients who moderately reduce their body weight (5-10%) can improve glycemic control and reduce the need for glucose-lowering medications. Further weight loss may incur greater benefits.[11]

It is important to use person-centered and non-judgmental language when discussing weight management.

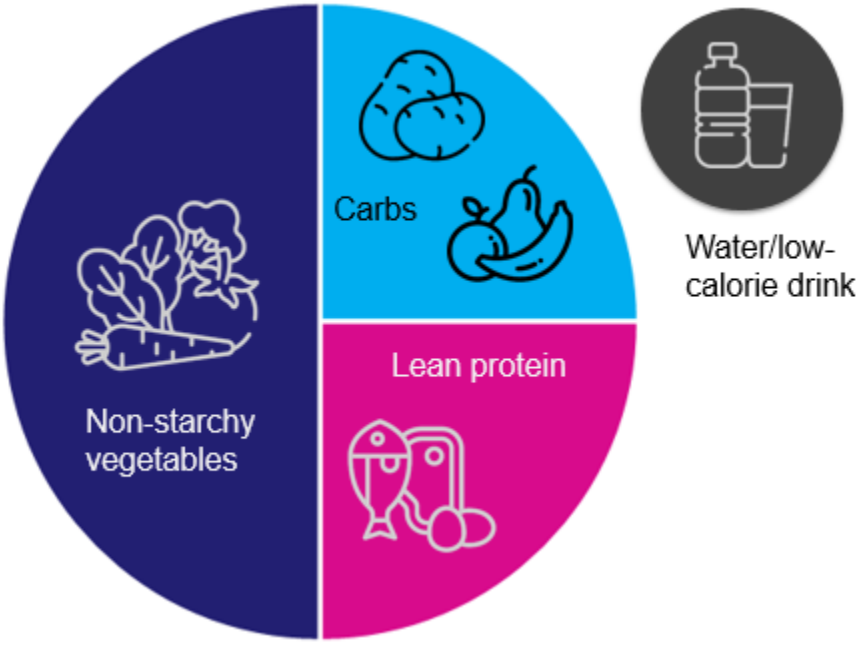
To learn more about obesity management, watch this presentation from Dr. Elisa Bocchieri-Bustros at our September 2023 Town Hall Gathering.

Diet & Nutrition

Reducing daily calorie intake by 500-1000 calories can help achieve stable weight loss of 1-2 pounds per week over the course of 6-12 months. For many patients, calorie reduction by 500-750 is more realistic and achieveable. Equally important is eating balanced, healthy meals. When clinically necessary, very-low-calorie diets (800-1000kcal) may be prescribed for weight management but should only be short term and under close provider supervision and monitoring, with comprehensive, long-term strategies for weight management incorporated into the plan.[12]

Initially developed for hypertension management, the DASH diet may improve insulin resitance, hyperlipidemia, and weight loss, in addition to promoting blood pressure control.[13]

The Diabetes Plate Method from the ADA is an easy way to create healthy meals that can help manage blood sugar.[14]



Fill half the plate with non-startchy vegetables, one quarter with lean protein, and the remaining quarter with carbs.

Physical Activity

Counsel patients to spend at least 150 minutes per week exercising (such as a brisk walk). They should aim to do, at a minimum:

- 700 calorie per week expenditure
- Minimum 3 sessions per week
- Minimum 10 mins per session
- Maximum 75 min per week of weight training towards 150 minute weekly target

Find patient education handouts and materials on our Condition Management Hub

Monitoring and Follow Up

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HgbA1c measures average blood sugar over the prior 3 months and is used as the main clinical indicator of disease control. It also has strong predictive value for diabetes complications.

Conduct a HgbA1c test:

- Every **6 months** for patients with stable glycemic control who are meeting treatment goals
- Every **3 months** for patients whose therapy has recently changed and/or those who are not meeting glycemic goals

The ADA, European Association for the Study of Diabetes (EASD), and the International Diabetes Federation (IDF) encourage care providers to discuss blood surgar with patients in terms of estimated average glucose (eAG) instead of A1C. Because eAG is measured in the same units as their daily blood sugar readings, the relationship between these two measurements is much more intuitive.[15]

The following table translates A1C into eAG. You can also use the online ADA eAG calculator.

Estimated Average Glucose (eAG)[16]

A1C	eAG	
%	mg/dL	mmol/L
5	97	5.4
6	126	7.0
7	154	8.6
8	183	10.2
9	212	11.8
10	240	13.4
11	269	14.9
12	298	16.5

A1C Limitations

HgbA1c measures average blood sugar over a 3 month period and therefore does not capture glucose variability. Other forms of blood glucose monitoring should be used to supplement A1C results in patients with hypoglycemia or wide variations in blood sugars.

The HgbA1c test also has known limitations in patients with certain conditions that affect red blood cell turnover and lifespan such as advanced chronic kidney disease and end stage renal disease, anemia, hemoglobinopathies, chronic alcohol use, splenomegaly, asplenia, and pregnancy.[17]

HgbA1c Goals

Most adults should strive for an A1C below 7% but goals <6.5% or <8% are appropriate for some patients.[18]

HgbA1c <6.5%	May be used selectively for patients at lower risk of hypoglycemia or other adverse effects of more intensive treatment.
HgbA1c <7%	This is the general target for most adults. This threshold has been proven to reduce development of microvascular complications (retinopathy, neuropathy and CKD) and, to a lesser extent, macrovascular complication (non-fatal MI, stroke, CV death) in patients with diabetes. Corresponds to pre-prandial plasma glucoses between 80-130 mg/dl and postprandial (1-2 hrs.) plasma glucose <180 mg/dl.
HgbA1c <8%	Patients at increased risk of severe hypoglycemia, limited life expectancy, well established complications, or other compelling reasons for less stringent control.

Blood Glucose Monitoring

Blood Glucose Monitoring (BGM)

Patients can measure their blood glucose at home as part of a broader educational/behavioral intervention surrounding diet counseling, healthy eating, and physical activity.

The focus should be on preprandial blood glucose measurement, but measurements taken 1-2 hours after meals can be helpful when HgbA1c remains above the goal in spite of pre-prandial results within the target range.

Note: peritoneal dialysis may cause interference with accuracy of blood glucose readings and providers should take this into consideration with these patients.

Continuous Glucose Monitoring (CGM)

A continuous glucose monitor (CGM) is a medical device that measures blood glucose in real time, providing the information through a mobile app, wearable device, insulin pump, or a stand-alone receiver that displays the data.

CGM is used to help patients to gain a better understanding of their blood glucose levels without the need to manually check repeatedly, and provides key information for providers to understand the trends of their patients' blood glucose levels. It measures interstitial glucose levels and estimates blood glucose levels.

Personal CGMs provide un-blinded data to patients than can be used to adjust treatment (e.g. Dexcom G6). Professional CGMs provide blinded data that can be retrospectively reviewed by provider and patient (e.g. Freestyle Libre Pro).

Patients who may be candidates for CGM:

- Taking medications that cause hypoglycemia with hypoglycemia unawareness
- Treated with insulin therapy
- Having frequent and/or nocturnal hypoglycemia or other excessive glucose variability
- Physical activity & exercise is variable/intense
- Willing and able to use CGM on a nearly daily basis and receive ongoing device education
- Unable to meet glycemic goals

Insurance coverage and the cost to the patient remain major considerations. CMS now covers CGM services for all patients with diabetes who are treated with insulin or who have a documented history of problematic hypoglycemia.

Interpretation of results

- Downloadable glucose reports show time in range, time above range, and time below range
- Glucose levels that are in-range 70% of the time correlate with HgbA1c <7%
- For patients with frailty or at high risk of hypoglycemia, blood glucose should be in range >50% of the time and below range <1% of the time

Hypoglycemia[19]

Hypoglycemia affects almost 2/3 of people living with diabetes.

- Severe hypoglycemia is associated with 3x greater risk of 5-year mortality
- Can lead to medication non-adherence, disruption of life and work, weight gain, costly emergency department visits and hospitalizations, increased morbidity and mortality
- Repeated episodes leads to Impaired Hypoglycemia Awareness (IHA), hypoglycemia-associated autonomic failure, and distress in patients, their families, and caregivers

Counseling Patients/Caregivers on Treating Hypoglycemia

- If the patient is conscious and glucose is <70 mg/dl, give 15-30 grams of glucose or other carbohydrate
    - Repeat in 15 minutes if hypoglycemia persists, followed by a snack once level returns to desired range
- If patient is unconscious, administer glucagon

All patients at risk of more pronounced hypoglycemia should be prescribed glucagon, preferably in a form that does not require re-constitution (ready for immediate administration).[20]

- Counsel family members, roommates, and friends on how to use and administer glucagon

Avalilable glucagon preparations

- Glucagon emergency kit, with powder and diluent
- Nasal glucagon*
- Glucagon (stable liquid)*: autoinjector, prefilled syringe
- Dasiglucagon*: autoinjector, prefilled syringe

*ready for immediate administration

Screening and Management Targets

The table below summarizes key screening and management targets.[21, 22, 23]

Screening/ Management Component	Goal	Frequency	Possible interventions and next steps
HgbA1c	A1C <7.0%	Every 6 months if meeting goal Every 3 months if not meeting goal	• Lifestyle modification • Medication adjustment • Referral to CDE • Care Management/ Behavioral Health/ Diabetes Alliance referral(s), as indicated • Refer to endocrinology if HgbA1c difficult to control and remains >9%
Blood pressure	BP <130/80*	Every visit	• Lifestyle modification • Home BP monitoring • Referral to RPM • If no CKD, use ACE/ARB, diuretic, or CCB • If CKD or microalbuminuria present, use ACE/ARB • If resistant hypertension or progressive kidney disease, refer to nephrology • Considerations for older and/or frail patients • Review the Mount Sinai Ambulatory Care Pathway
Lipid management	LDL <100 mg/dL For patients at **increased risk for CVD**, reduce LDL ≥50% of baseline and target LDL <70 mg/dL	Annually	• Lifestyle modification • Moderate or high intensity statin therapy for all patients age 40-75 • PCSK-9 inhibitor as appropriate

	For patients with **established CVD**, reduce LDL ≥50% of baseline and target LDL <55mg/dL		
CVD	Use ASCVD Risk Calculator to assess HF Risk (valid for patients 40-79)[24] Antiplatelet therapy for primary/secondary prevention	Annually	• Shared decision-making whether to start ASA 75-162 mg daily for primary prevention for patients 50-75 years old with **increased CVD risk** • ASA 75-162 mg daily for **established ASCVD** • SGLT-2i or GLP-1 RA if **multiple risk factors or known ASCVD and/or CKD** • SGLT-2i if **heart failure** present
Kidney disease	eGFR >100 UACR <30 mg/g C	Annually (Consider semiannually if EGFR <60 or UACR >30 mg/g of C)	• ACE/ARB if eGFR <60 or UACR >30 • Addition of SGLT-2i for diabetic kidney disease if eGFR >20 • Intensify diabetic medications to optimize glycemic control • Dietary intake of ~0.8 g protein/kg weight per day • Consider nephrology referral

Retinopathy screening†	Absence of retinopathy or macular edema	Every 2 years if no evidence of retinopathy	• Annual evaluation by ophthalmologist if retinopathy or macular edema present
Foot care and neuropathy screening	No ulcerations or fungal infections, 2+ pedal pulses, normal sensory response with monofilament	Annually	• Referral to podiatrist for management of any abnormalities • Refer for Ankle Branchial Index (ABI) if Peripheral Arterial Disease (PAD) suspected

Pharmacologic Therapy

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Pharmacologic treatment should be patient centered, taking into account cardiovascular and renal comorbidities, efficacy, hypoglycemia risk, body weight, cost, side effects, patient preferences, and treatment goals.

Medication selection and considerations

A SGLT-2 inhibitor and/or GLP-1 receptor (GLP-1 RA) should be part of the treatment regimen for patients who meet any of the following criteria, regardless of A1C:

- Established cardiovascular disease
- High cardiovascular risk
- Kidney disease
- Heart failure

† Retinopathy screening can be performed in PCP office with a retinal camera, optometry clinic, or ophthalmology clinic

Consider introducting insulin early if any of the following are present:

- Evidence of ongoing catabolism (weight loss)
- Symptoms of hyperglycemia
- A1C >10% or blood glucose levels ≥300 mg/dL

GLP-1 RAs are preferred to insulin when possible. When insulin is used, consider combination therapy with a GLP-1 receptor agonist for greater efficacy, durability of treatment effect, weight management, and hypoglycemia prevention.

- Evaluate for hypoglycemia and glycemic variability if basal dose is more than 0.5 units/kg/day

Medication Class	Compounds	Trade names	Available dosages	Starting dose*	Maximum daily dose
Biguanides	Metformin	Glucophage Riomet	500 mg (IR)	500 mg qd	2,000 mg
			850 mg (IR)		2,550 mg
			1,000 mg (IR)		2,000 mg
		Fortamet Glucophage XR Glumetza Riomet ER	500 mg (ER)	500 mg qd	2,000 mg
			750 mg (ER)		1,500 mg
			1,000 mg (ER)		2,000mg
Sulfonylureas (2nd generation)	Glimepiride	Amaryl	1 mg, 2 mg, 4 mg	1 mg qd	8 mg
	Glipizide	Glucotrol	5 mg, 10 mg (IR)	5 mg qd	40 mg (IR)
		Glucotrol XL	2.5 mg, 5 mg, 10 mg (XL)	2.5 mg qd	20 mg (XL)
	Glyburide	Glynase PresTabs	1.5 mg, 3 mg, 6 mg**	1.5 mg qd	12 mg**
Thiazolidinediones	Pioglitazone	Actos	15 mg, 30 mg, 45 mg	15 mg qd	45 mg
Meglitinides (glinides)	Nateglinide	Starlix	60 mg, 120 mg	60 mg tid ac	360 mg
	Repaglinide	Prandin	0.5 mg, 1.0 mg, 2 mg	0.5 mg tid ac	16mg
DPP-4 inhibitors	Alogliptin	Nesina	6.25 mg, 12.5 mg, 25 mg	25 mg qd	25 mg
	Saxagliptin	Onglyza	2.5 mg, 5 mg	5 mg qd	5 mg

	Linagliptin	Tradjenta	5 mg	5 mg qd	5 mg
	Sitagliptin	Januvia	25 mg, 50 mg, 100 mg	100 mg qd	100 mg
SGLT2 inhibitors	Ertugliflozin	Steglatro	5 mg, 15 mg	5 mg qd	15 mg
	Dapagliflozin	Farxiga	5 mg, 10 mg	5 mg qd	10 mg
	Empagliflozin	Jardiance	10 mg, 25 mg	10 mg qd	25 mg
	Canagliflozin	Invokana	100 mg, 300 mg	100 mg qd	300 mg
	Bexagliflozin	Brenzavvy	20 mg	20 mg qd	20 mg
GLP-1 RAs	Exenatide (ER)	Bydureon Bcise	2 mg powder for suspension or pen	2 mg qweek	2 mg†
	Exenatide	Byetta	5 mcg, 10 mcg pen	5 mcg bid	20 mcg
	Dulaglutide	Trulicity	0.75mg, 1.5 mg, 3.0 mg, 4.5 mg,	0.75 mg qweek	1.5 mg†
	Semaglutide	Ozempic	0.25 mg. 0.5 mg, 1 mg, 2 mg pens	0.25 mg qweek	2 mg†
		Rybelsus	3 mg, 7 mg, 14 mg (tablet)	3 mg qday	14 mg
	Liraglutide	Victoza	0.6 mg, 1.2 mg, 1.8 mg	0.6 mg qweek	1.8 mg
GIP and GLP-1 RA	Tirzepatide	Mounjaro	2.5 mg/0.5 mL; 5 mg/0.5 mL; 7.5 mg/0.5 mL; 10 mg/0.5 mL; 12.5 mg/0.5 mL;15 mg/0.5 mL	2.5 mg qweek	15 mg†

*No renal/hepatic impairment ** Micronized † Administered once weekly

Efficacy		Hypo-glycemia	Weight impact	Cardiovascular Effects		Renal Effects		Additional Considerations
				MACE	Heart Failure	Progression of DKD	Dosing Considerations	
Biguanides	High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Neutral	Contraindicated with eGFR <30 mL/min/1.73m^2	Gastrointestinal side effects common (diarrhea, nausea) Potential for B12 deficiency Low cost
Sulfonylureas (2nd generation)	High	Yes	Gain	Neutral	Neutral	Neutral	**Glyburide** is not recommended in CKD **Glipizide and glimepiride**: initiate conservatively to avoid hypoglycemia	FDA Special Warning on increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)

Thiazolidinediones	High	No	Gain	***Potential benefit*** pioglitazone	Increased risk	Neutral	No dose adjustment required Generally not recommender in renal impairment due to potential for fluid retention	FDA Black Box: Congestive heart failure Fluid retention (edema, heart failure) Benefit in NASH Risk of bone fractures Bladder cancer
DPP-4 inhibitors	Inter-mediate	No	Neutral	Neutral	***Potential risk*** saxagliptin	Neutral	Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment No dose adjustment required for linagliptin	Potential risk of acute pancreatitis Joint pain Bullous pemphigoid

SGLT2 inhibitors	Inter-mediate to High	No	Loss (intermediate)	***Benefit*** empagliflozin† canagliflozin	***Benefit*** empagliflozin† canagliflozin dapagliflozin‡ ertrugliflzoin	***Benefit*** Empagliflozin canagliflozin dapagliflozin	Renal dose adjustment required (canagliflozin, dapagliflozin, empagliflozin) In patients with CKD, use in people with eGFR >20 mL/min/1.73 m2. Continue until initiation of dialysis or transplant	DKA risk (all agents, rare in T2DM) Genitourinary infections Risk of volume depletion, hypotension Risk of Fournier's gangrene
GLP-1 RAs	High to very high	No	Loss (intermediate to very high)	***Neutral*** exenatide once weekly	Neutral	***Benefit*** *(driven by albuminuria outcomes)* dulaglutide liraglutide semaglutide (SQ)	Renal dose adjustment required (exenatide) Caution when initiating or increasing dose due to potential risk of acute kidney injury in patient with renal impairment reporting severe adverse GI reactions	FDA Black Box: Risk of thyroid C-cell tumors (semaglutide, liraglutide, dulaglutide, exenatide extended release) and Multiple Endocrine Neoplasia Syndrome (MEN) Type 2 Gastrointestinal side effects common (nausea, vomiting, diarrhea) Acute pacreatitis risk

GIP and GLP-1 RA	Very high	No	Loss (very high)	Under investigation	Under investigation	Under investigation	No dose adjustment Caution when initiating or increasing dose due to potential risk of acute kidney injury in patient with renal impairment reporting severe adverse GI reactions	FDA Black Box: Risk of thyroid C-cell tumors (semaglutide, liraglutide, dulaglutide, exenatide extended release) and Multiple Endocrine Neoplasia Syndrome (MEN) Type 2 Gastrointestinal side effects common (nausea, vomiting, diarrhea) Acute pacreatitis risk
Insulin	High to very high	Yes	Gain	Neutral	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) versus analogs

Medications that can affect blood sugar[25]

The medications listed below have the potential to impact glycemic control and/or cause diabetes. The impact of the medications can be difficult to predict; therefore we recommend increased monitoring with Hba1c, plasma glucose, or self-monitored blood glucose monitoring, especially upon initiation of these medications.

Medication	Agents	Mechanism/Impact
Systemic glucocorticoids	Prednisone, cortisone, dexamethasone, fludrocortisone, triamcinolone	Dose dependent mild increase in fasting glucose levels, greater increase in postprandial glucose
HIV antiretrovirals: Protease inhibitors, NRTIs (lesser extent)	Ritonavir, atazanavir, darunavir, fosamprenavir, indinavir, lopinavir, tipranavir	Increased fasting glucose caused by insulin resistance without compensatory increase in insulin release
Anti-infective	Pentamidine	Unclear, thought to be direct drug induced dysfunction in pancreatic beta cells
Antipsychotics	Chlorpromazine, clozapine, olanzapine	Unclear, thought to be related to insulin resistance secondary to increased adipose tissue
Immune checkpoint inhibitors	PD-1 inhibitors: Nivolumab, pembrolizumab, cemiplimab, dostarlimab, and retifanlimab	Rapid beta cell destruction May lead to onset of type 1 diabetes, requires long term insulin therapy. May present with DKA. **Monitor glucose with each dose and watch for symptoms of hyperglycemia.**
	PD-L1inhibitors: atezolizumab, avelumab, and durvalumab	
	CTLA-4 inhibitors: Ipilimumab and tremelimumab	
Androgen deprivation therapy, typically used in patients with	Leuprolide (Lupron, Eligard), Goserelin (Zoladex), Triptorelin	Decreased insulin sensitivity

metastatic prostate cancer	(Trelstar), Leuprolide mesylate (Camcevi)	
Immunosuppressants	Cyclosporine, sirolimus, tacrolimus	Decreased insulin secretion promoted by calcineurin
Statins	Atorvastatin (Lipitor) Fluvastatin (Lescol) Lovastatin (Altoprev) Pitavastatin (Livalo, Zypitamag) Pravastatin (Pravachol) Rosuvastatin (Crestor, Ezallor) Simvastatin (Zocor)	While there is potential for statins to increase blood glucose, statin use is still recommended in patients with diabetes given the benefit of cardiovascular risk reduction outweighs the risk of worsening glycemic control in patients with type 2 diabetes. More common with higher dosages, atorvastatin and rosuvastatin

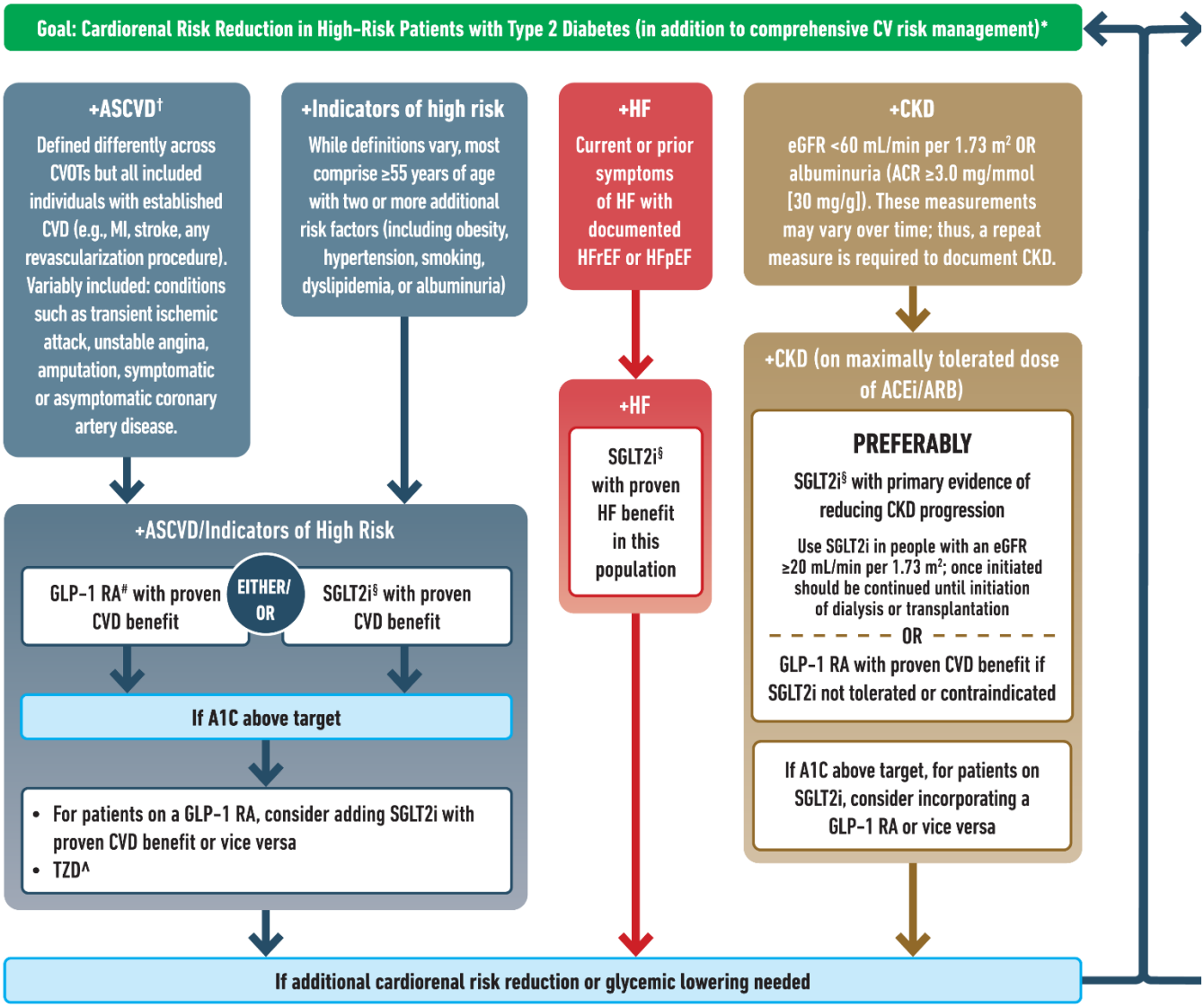
Treatment Algorithm

Use the ADA treatment algorithm on the following pages to guide your pharmacologic decision making.

Note: Due to space constraints and readability concerns, this algorithm spans 2 pages. The section regarding glycemic and weight management goals appear to the right of the section on cardiorenal risk reduction in the original version.

Click here to view the original, full-size version.

To avoid therapeutic inertia reassess and modify treatment regularly (3-6 months)



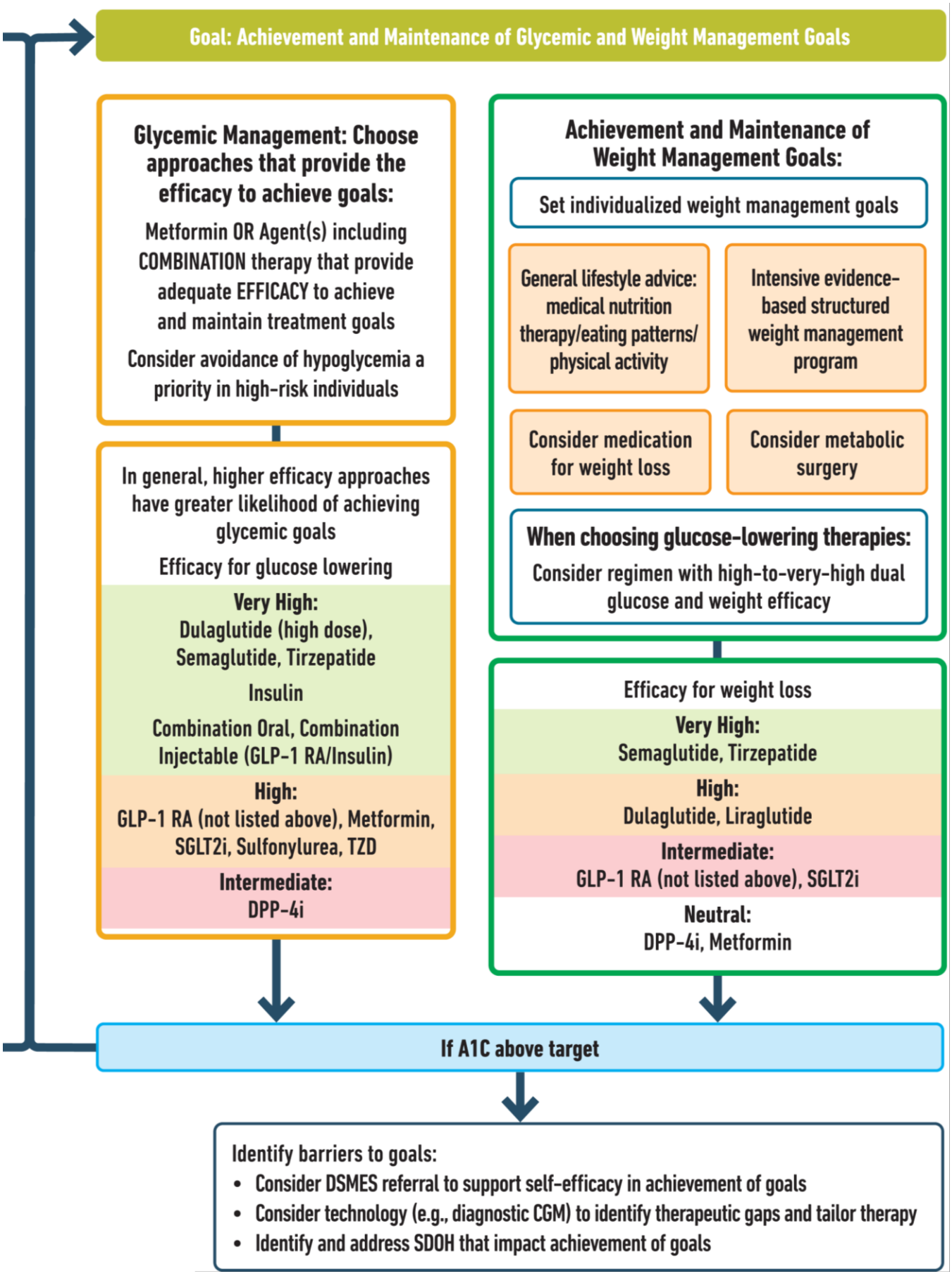
*In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of packground use of metformin

† 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 reducation 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 demonstate 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, stoke, and renal endpoints in individuals with T2D with established/high risk of CVD.


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

Medication Classes

There are a variety of medications available to manage diabetes, and prescribers should consider factors such as cost, dosing regimen, patient preferences, and treatment goals when choosing and adjusting pharmacologic therapy.

Medication Summary Table

The below table summarizes key points from the major medications used to treat diabetes. Please refer to individual medication sections for additional indications for use, contraindications, and other considerations.

Medication class	Common medications	Preferred use cases	Expected reduction in HgbA1c	Combination therapy considerations
Sulfonylureas	glimepiride glipizide glipizide glyburide	Severe hyperglycemia; metformin and injectable insulin are not options	1-2%	Typically not used with insulin
SGLT2-i	empagliflozin canagliflozin dapagliflozin	History of diabetic kidney disease with eGFR of ≥ 20 AND/OR Heart failure or high CVD risk	0.5-0.7%	Can be used in combination with other glycemic therapies
GLP-1 RA	liraglutide semaglutide dulaglutide	Heart failure or high CVD risk CKD	0.9% - 2.3%	Can add insulin to GLP-1 RA but start with GLP-1 RA Do not use in combination with DPP-4i

DPP-4i	sitagliptin linagliptin saxagliptin alogliptin	Adjunct when glycemic goals are not met with other therapies	0.4-0.9%	Do not use in combination with GLP-1 RA
Insulin	insulin degludec insulin glargine insulin detemir insulin lispro insulin aspart insulin regular	Severe or persistent hyperglycemia	Varies by dosing	Basal or multiple daily dose regimens can be combined with a GLP-1RA to achieve better control Sulfonylureas and DPP-4i are typically stopped insulin injections are started

Sulfonylureas[26, 27]

Mechanism of action

Sulfonylureas interact with receptors on pancreatic B-cells to potentiate the release of insulin at all glucose concentrations and modestly increase tissue sensitivity to insulin.

Considerations for Use

- Expected to reduce HgbA1c by 1-2%
- If a sulfonylurea is required, glimepiride is preferred in patients with heart disease who cannot tolerate a SGLT-2I or GLP-1 RA
- Glipizide is the preferred sulfonylurea in patients with chronic kidney disease
- Second generation sulfonylureas do not appear to increase CV risk
- Patient is unable to take metformin, especially if cost is a barrier
- Patients with severe hyperglycemia who refuse or cannot afford injectable therapy

- Typically used in combination with other medications in patients who are not meeting goal on metformin alone

Contraindications

- Hypersensitivity to another medication in this class
- Typically not used in combination with insulin
- Concerns regarding cross reactivity in patients with allergy to sulfonamide antibiotics appear to be unfounded
- Type I diabetes

Adverse effects

- Hypoglycemia, particularly with long acting agents and underlying kidney disease
- Weight gain

Dosing

- Shorter acting agents (glipizide and glimepiride) are generally preferred
- Higher doses of sulfonylureas (glimepiride 4-8mg daily, glipizide 10mg twice a day) can be helpful in patients with severe hyperglycemia (Hgba1c <10, without ketones or weight loss) who prefer not to use injections

Sodium Glucose Cotransporter-2 Inhibitors (SGLT-2i)[28,29]

Mechanism of action

SGLT-2 inhibitors reduce glucose reabsorption in the proximal tubule, promoting glycosuria and an osmotic diuresis to lower blood glucose levels.

Indications for use

- Expected to reduce HgbA1c by 0.5-0.7%
- Consider a SGLT-2i with known CV benefit (empagliflozin, dapagliflozin, canagliflozin) for patients with heart failure, CKD stages 1-4 (eGFR of ≥ 20) , or those at higher risk for cardiovascular disease, independent of metformin use

- Can be a second or third line agent if glycemic goals are not met with existing therapies

Contraindications

- Type 1 diabetes
- CKD with eGFR <20

Cautions

- Recurrent genitourinary tract infections
- Low bone density
- Recurrent falls
- Foot ulceration
- Prior amputations

Adverse effects

- Hypovolemia, hypotension, and/or dehydration
- DKA, including euglycemic DKA
- Recurrent bacterial urinary tract infections and fungal vulvovaginitis
- Possible increased risk of amputations

Dosing

- Close monitoring and dose adjustments may be needed in presence of severe liver disease
- Glycemic benefit is reduced in patients with more severe kidney disease and may necessitate dose adjustment

Glucagon-like peptide-1 Receptor Agonists GLP-1 RA)[30, 31, 32, 33]

Mechanism of action

GLP-1 RAs enhance glucose-dependent insulin secretion, slow gastric emptying, reduce postprandial glucagon secretion, and increase satiety, thus leading to a reduction in food intake.

Expected effect

- Reduces HgbA1c by 0.9% - 2.3%

Indications for use

- Type 2 diabetes
- A GLP-1 RA with known CV benefit (liraglutide, semaglutide, dulaglutide) should be considered for patients who are at higher risk of, or have known cardiovascular disease, heart failure, or CKD
- GLP-1 RAs are preferred to insulin when glycemic goals are not met with oral therapy and the expected impact on HbA1C reduction will bring the patient close to goal and there are no co-morbidities that prioritize another class of agent (such as HF, DKD).

Contraindications

- Personal or family history of medullary thyroid cancer and/or multiple endocrine neoplasia (MEN) 2A or 2B
- Should not be used in combination with DPP-4 inhibitors

Cautions

- History of acute pancreatitis
- Gastroparesis and inflammatory bowel disease

Adverse effects

- GI side effects, including nausea, vomiting, and diarrhea, may result in AKI due to volume loss
- Injection site reactions

Dosing

- Titrate dose every 4 weeks to mitigate GI side effects
- With exception of oral semaglutide, other agents are injected subcutaneously, ranging from twice daily to once a week
- Long acting agents appear to lower fasting glucose and HgbA1c, while shorter acting agents have greater impact on post-prandial blood glucose

- Can be safely used with insulin but may require insulin dose reduction to avoid hypoglycemia

Other considerations

- Antibodies to the GLP-1 RAs occur infrequently but generally do not impact efficacy
- Prior to procedures/surgery requiring anesthesia, GLP-1 RAs should be held for risk of aspiration.[34] MSHS guidelines advise holding for at least 2 dosing intervals (e.g. semaglutide and terzepatide should be held for a minimum of 15 days).

Dipeptidyl-peptidase- 4 Inhibitors (DPP-4i)[35, 36, 37]

Mechanism of action

Inhibit DPP-4 enzyme that inactivates bioactive peptides, including GLP-1 and gastrointestinal peptide (GIP), with a modest glucose lowering effect.

Indications for use

- Expected to reduce HgbA1c by 0.4-0.9%
- As an additional agent when glycemic goals are not met with metformin and/or other agents

Contraindications

- Should not be used in conjunction with a GLP-1 RA
- Avoid in patients with a history of pancreatitis

Adverse effects

- Headache, nasopharyngitis, URI, are commonly reported effects
- Increased risk of hospitalizations related to heart failure with saxagliptin and alogliptin, with a neutral effect on HF and ASCVD with other agents in class
- Potential risk of acute pancreatitis

Dosing

- Doses should be adjusted in patients with comorbid CKD, with exception of linagliptin

Insulin (injection)[38, 39]

Considers for Use

- Severe hyperglycemia (A1C >10%, blood glucose >300), particularly with evidence of catabolism (weight loss)
- Persistent hyperglycemia despite oral therapy
- Latent autoimmune diabetes in adults (LADA)
- Pancreatic insufficiency

Adverse Effects

- Hypogylcemia
- Weight gain
- Lipohypertrophy

Dosing

- Initial treatment is with NPH or long acting analogues
    - Longer-acting agents (U100 glargine or detemir) have a modest advantage in reducing symptomatic and nocturnal hypoglycemic episodes, albeit at increased cost
- Starting basal doses are 0.1-0.2 units/kg/day
- Clinicians should be aware of and evaluate for overbasalization when:
    - Basal dose greater than ~0.5 units/kg
    - High bedtime–morning or postpreprandial glucose differential (e.g., bedtime–morning glucose differential ≥50 mg/dL)
    - Hypoglycemia (aware or unaware)
    - High glycemic variability in glucose readings

- Prandial insulin can be added to basal insulin if necessary, initially given with the largest meal, and then added prior to other meals
    - **Consider a GLP-1 RA prior to prandial insulin to minimize hypoglycemia and weight gain**
    - Prandial insulin can bebe started at 10-33% of daily basal insulin, given with the largest meal
- Human insulin (NPH, Regular, 70/30 NPH/Regular) is appropriate for many patients and can reduce treatment costs. Because of the pharmacokinetic profile of these insulins with a peak effect, additional education around onset of action and strategies to avoid hypoglycemia should be given to patients.

Other considerations

- Recurrent severe hypoglycemia requires therapy adjustments
- Basal or multiple daily dose regimens can be combined with a GLP-1RA to achieve better control
- Metformin, thiazolidinediones, and SGLT-2i are generally continued when combination injectable therapy is started, while sulfonylureas and DPP-4i are typically stopped
- Both syringes and insulin pens are able to effectively administer insulin
    - Pens may be helpful for patients with problems with dexterity and vision
- Educate patients regarding correct injection technique, including subcutaneous delivery (not IM) to appropriate sites, periodic site rotation to avoid lipohypertophy, and care to avoid infections at injections sites

Cost Considerations

Patients living with diabetes may face high costs managing their health. Expenses typically include:

- Copays from diabetes care visits
- Specialty referrals, such as ophthalmology and podiatry
- Multiple prescription medications

- Supplies (pen needles, syringes, blood glucose testing supples, other durable medical equipment)

Comorbid cardiovascular disease, dyslipidemia, hypertension, and obesity may further increase the total cost of care.

Prescriptions will have varying out-of-pocket costs depending on insurance plan and formulary coverage, but can also vary based on the time of year if they have a deductible or are in a coverage gap (e.g. Medicare donut hole). The inability to afford medications can lead to medication rationing or simply not being able to fill the prescription, ultimately leading to worsening glycemic control.

It is therefore essential to consider cost when developing a diabetes treatment plan and prescribing medications. **At each visit be sure to discuss with the patient their ability to afford and obtain their prescriptions.**

Alternative medications, referrals to a social worker, and referrals to specialized programs such as the Mount Sinai Medication Access Program can all be made to help address potential issues (see Pharmacy Referrals section for additional details).

Managing Complications and Common Comorbidities

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Complications

Diabetic Foot Care[40]

Risk factors for diabetes-related foot ulcers and amputations include:

- Poor glycemic control
- Neuropathy with loss of protective sensation
- Cigarette smoking
- Foot deformities

- Pre-ulcerative corns and callouses
- Peripheral arterial disease (PAD)
- Prior foot ulcer or amputation
- Visual impairment
- Chronic kidney disease (especially dialysis dependence)

Annual Physical Examination

- Includes inspection to assess for skin integrity, deformities, vascular perfusion including pedal pulses, and neuropathy/loss of protective reflexes
- Order an ankle-brachial index (ABI) for all patients with signs or symptoms of PAD
- Educate all patients living with diabetes, but particularly those at increased risk, about general foot care and proper footwear

Treatment

- Patients with neuropathy, increased plantar pressure, or deformities may be treated with well fitted walking and athletic shoes, including extra wide/deep or custom molded footwear
- Next steps if ulcer or PAD are present:
    - At least one of the following should also be performed, as available: skin perfusion pressure (≥40 mmHg), toe pressure (≥30 mmHg), transcutaneous oxygen pressure (TcP02 ≥25 mmHg)
    - An **urgent vascular referral** is indicated for patients with a diabetic foot ulcer with ABI <50 mm Hg, toe pressure <30 mm Hg, or TcP02 <25 mmHg
- Patients with neuropathy and acute onset of a red, warm, and/or swollen foot or ankle should be rapidly assessed for Charcot joint and, if present, promptly treated
- Infected wounds are typically polymicrobial, with staphylococci and streptococci being the most common pathogens
    - Most infections respond to antibiotics directed against these pathogens, though more chronic, severe, and/or previously treated infections may require broader spectrum antibiotics

    - Referral to a podiatrist, orthopedist, or vascular surgeon may be warranted

- Hyperbaric oxygen therapy (HBOT) has not been proven effective in treating diabetic foot infections

Diabetic Neuropathy[41]

Most cases of diabetic neuropathy can be diagnosed in the primary care office and do not require a referral.

- Small fiber damage occurs earlier and leads to pain and dysesthesias
- Injury to large fibers leads to numbness and loss of protective sensation (LOPS)
- If acute onset of a red, warm, and/or swollen foot or ankle, rapidly assess and treat Charcot joint if present

Screening

- Annual assessment for distal symmetric polyneuropathy should include:
    - A careful history
    - Assessment of either temperature or pinprick sensation (small-fiber function)
    - Assessment of vibration sensation using a 128-Hz tuning fork (large-fiber function)
- All patients living with diabetes should also have annual 10g monofilament testing to identify feet at risk for ulceration and amputation

Additional Tests for Small & Large Fiber Function

Type of Nerve Injured	Potential Test	Recommended Screening
Small Fiber	Pinprick, temperature sensation	Pinprick
Large Fiber	Lower-extremity reflexes, vibration perception, 10g monofilament	10g monofilament
Protective Sensation	10g monofilament	10g monofilament

Autonomic neuropathy can also affect the cardiovascular system and is associated with poorer prognosis. Screen for autonomic neuropathy annually:

- Ask about positional dizziness and syncope
- Evaluate for orthostatic hypotension and resting tachycardia

Treatment

- Glycemic control may prevent peripheral and autonomic neuropathy and progression
- Gabapentin, pregabalin, and duloxetine; may also consider tricyclic antidepressants, carbamazepine, venlafaxine, and capsaicin
- Refer to neurologist or pain specialist for refractory pain

Diabetic Retinopathy[42]

- Diabetic retinopathy and macular edema may be asymptomatic, thus screening is required
- Intensive treatment to achieve near normalization of glucose can prevent or delay progression of retinopathy
- Aspirin is not contraindicated in diabetic retinopathy, as the risk of bleeding is not increased

Screening

- Dilated retinal exam by an ophthalmologist or optometrist, or retinal photography reviewed by an ophthalmologist
- If retinopathy is present at the time of diabetes diagnosis, annual exam required
- Women should be screening prior to a planned pregnancy or in the first trimester

Treatment

- **Refer to an ophthalmologist** for any level of diabetic macular edema, moderate or worse nonproliferative diabetic retinopathy (a precursor of proliferative diabetic retinopathy), or any proliferative diabetic retinopathy

- Intravitreous injections of anti-vascular endothelial growth factor (ranizibumab, bevacizumad, aflibercept) are indicated for diabetic macular edema and/or moderate to proliferative retinopathy, which is not inferior to laser photocoagulation
    - Associated with less peripheral visual loss, fewer vitrectomies and additional surgeries for complications
- Injections are also indicated for central macular edema accruing beneath the fovea, in order to preserve reading

- Pan-retinal laser photocoagulation therapy is indicated for high risk proliferative retinopathy and some cases of severe non-proliferative retinopathy

Comorbidities

Hypertension and Blood Pressure Management[43]

- For patients with elevated BP >120/80, lifestyle modification is recommended
- For patients with confirmed hypertension, lifestyle modification and medication therapy should be used to target a general goal blood pressure <130/80
- Blood pressure targets should be further tailored to individual patient's circumstances including CV risk, age, and risk for hypotension
- Home blood pressure monitoring is recommended

Treatment

- Lifestyle modification
    - Dietary Approaches to Stop Hypertension (DASH) diet, low salt (<2,300 mg/d), increased fruits and vegetables, low fat, and limited alcohol intake
    - Increased physical activity, ideally achieving moderate levels of exercise (such as a brisk walk) for 150 minutes per week[44]
- Treatment with antihypertensive medications with proven efficacy in diabetes (ACE/ARB, thiazide diuretics, and calcium channel blockers)
    - ACE inhibitors or ARBs are the recommended first line treatment for hypertension in patients with diabetes and CAD

- ACE/ARB at maximally tolerated dose are preferred treatment if urine albumin ≥30 mg/g creatinine

Refer to the Mount Sinai Ambulatory Care Hypertension Pathway for detailed guidance on managing hypertensions in patients with and without diabetes.

Atherosclerotic Vascular Disease (ASCVD) and Heart Failure (HF)[45]

Screening

The ASCVD Risk Calculator from the American College of Cardiology estimates the 10-year risk of a first ASCVD event, and to what extent recommended interventions may help mitigate risk. **We recommend you use this tool annually.**

Testing is indicated if patient presents with typical/atypical chest pain, any signs or symptoms of other vascular disease, or an abnormal ECG

- Initial testing should include exercise testing with/without echocardiography
- Pharmacologic stress echo or nuclear imaging is indicated for those who are unable to exercise or have significant resting ECG abnormalities

Routine screening for ASCVD with CT calcium scores/CT angiography in asymptomatic high risk patients is **not recommended.**

Antiplatelet Therapy

Aspirin therapy (ASA) (75–162 mg/day) may be considered for patients with diabetes **and** known ASCVD (prior MI/stroke) **or** increased cardiovascular risk, after a **comprehensive discussion** with the patient on the benefits versus the comparable increased risk of bleeding. Clopidogrel may be used in patients with known ASA allergy.

In patients with known or multiple risk factors for ASCVD and/or CKD, a **SGLT-2i** should be part of the medication regimen. For patients who are unable to take or fail SGLT-2i, consider a GLP-1 RA.

Heart Failure (HF)

In patients with hear failure (with or without diabetes), a SGLT-2i may be used to reduce risk of worsening heart failure and mortality, and improve symptoms, physical limitations, and quality of life.

Medication contraindications

- DPP-4s (saxagliptin, alogliptin) are associated with an increased risk hospitalization for HF and are not recommended in HF patients
- Thiazolidinediones are also contraindicated in patients with heart failure
- Metformin should be avoided in unstable or hospitalized individuals with heart failure

Chronic Kidney Disease (CKD)[46]

Twenty to forty percent of patients with diabetes have comorbid CKD, as defined by increased urinary albumin excretion, reduced glomerular filtration rate, or other evidence of kidney damage. CKD may be present at the time of diagnosis of T2DM. https://mshp.mountsinai.org/web/mshp/ckd-in-primary-care

Glomerular filtration rate (GFR) is the best overall index of kidney function. The National Kidney Foundation's eGFR calculator uses the 2021 CKD-EPI Creatinine Equation.

Urine albumin/microalbumin to creatinine ratio (uACR) measures albuminuria. Albuminuria increases the risk of mortality, CVD, and CKD prorgression at any GFR.

Note: False positive results can occur with exercise within 24 hours of testing, fever, hyperglycemia, heart failure, severe hypertension, and menstruation. Consider retesting if suspected under these factors.

Surveillance

Serum creatinine, eGFR, potassium, and urinary albumin secretion should be monitored at least annually.

- Test patients with uACR >30 mg/g creatinine and/or eGFR <60 **twice yearly**
- If eGFR <60, medication doses should be adjusted accordingly and nephrotoxins avoided

- ACE/ARBs can cause modest increases (<30%) in serum creatinine in absence of volume depletion or AKI
- KidneyIntelX™ is an option for risk assessment of kidney disease progression (Disclosure) 47
    - A quantitative electrochemiluminescence immunoassay combined with clinical data that uses an advanced machine learning algorithm to generate a patient-specific score for assessing the five-year risk of progressive decline in kidney function in patients with existing DKD (diabetic kidney disease)
    - Categorizes patients as low, intermediate or high risk of progressive DKD
    - For patients with T2DM and DKD stages 1-3b
    - KidneyIntelX.dkd was granted Breakthrough Device designation by the US Food and Drug Administration (FDA) in June 2023.

Interventions

Dietary changes and/or medications may be used to manage CKD progression.

Nutrition

- Reduce protein intake: no more than 0.8 g per kg body weight per day to delay progression for patients with non-dialysis dependent CKD
    - Higher protein intake in patients with end-stage renal disease (ESRD)
- Sodium restriction: <2,300 mg/d
- Potassium restriction if hyperkalemic

Glycemic Targets

Intensive treatment to achieve near normal glycemic control slows the development and progression of CKD in patients with comborbid diabetes.

Medication Considerations

- Metformin should not be started if GFR <45
    - Discontinue if GFR <30 or prior to/at time of administration of iodinated contrast for GFR 30-60

- SGLT2i is recommended for patients with abnormal kidney function and eGFR ≥20 mL/min/1.73 m^2 **and/or** patients with elevated uACR
    - If an SGLT2i is not an option, you may consider a GLP-1 RA for additional cardiovascular risk reduction
- In patients with **hypertension** in addition to diabetes and established CKD (uACR ≥ 300 mg/g creatinine and/or eGFR < 60 mL/min/1.73 m^2), titrate ACEi or ARB to maximum tolerated dose as a first-line agent to reduce the risk of progression of CKD to ESRD
    - In trials of patients with diabetes, hypertension, and lower levels of albuminuria (uACR 30-299 mg/g creatinine), ACEi or ARB at maximum tolerated doses reduced progression to severely increased albuminuria (≥300 mg/g creatinine), slowed CKD progression, and reduced cardiovascular events, but did not reduce progression to ESRD
    - Outcome trials have not been performed to determine whether ACEi or ARB treatment have renoprotective effects in patients with diabetes who are normotensive with or without albuminuria
- **Finerenone** may be added as an adjunctive agent for patients with persistently elevated urinary albumin excretion (uACR ≥30 mg/g) to improve cardiovascular outcomes and reduce risk of CKD progression[48]
    - Patients who are treated with both an ACEi/ARB and an SGLT2i are appropriate candidates for finerenone treatment
    - Finerenone may be added to an ACEi/ARB alone for patients who do not tolerate or are not candidates for an SGLT2i
    - Patients must also meet the following criteria: eGFR >25 mL/min/1.73 m^2 and normal serum potassium levels

Obesity Management

- Lifestyle changes should be paired with a structured nutrition plan, behavioral therapy, and physical activity program
    - Refer to the Lifestyle section of this guide for more guidance
    - Intensive behavioral interventions should include ≥16 sessions during the initial 6 months

- Maintaining ≥5% weight loss is recommended for most patients with T2DM who are above a healthy weight

- Consider initiating glucagon-like peptide 1 receptor agonist (GLP-1 RA)

- Review, minimize, or provide alternatives for concomitant medications that promote weight gain, including those used in the treatment of diabetes, whenever possible

- Refer to obesity medicine specialist or bariatric surgery to consider other weight loss treatments if patient is not a candidate for GLP-1 RA or does not achieve weight loss goals with GLP-1 RA.

Liver Disease

Screen and risk stratify patients for nonalcoholic fatty liver disease (NAFLD) with clinically significant fibrosis (defined as moderate fibrosis to cirrhosis) using a calculated fibrosis-4 index (derived from age, ALT, AST, and platelets), even if they have normal liver enzymes.

- Consider fibroscan if patients have elevated liver enzymes and/or high suspicion of NAFLD

For patients with biopsy-proven **nonalcoholic steatohepatitis** (NASH) or those at high risk for **NAFLD** with clinically significant **liver fibrosis** using noninvasive tests:

- Pioglitazone or GLP-1 RAs are the preferred agents for the treatment of hyperglycemia

Metabolic Surgery

Consider metabolic surgery in appropriate candidates as an option to treat NASH and to improve cardiovascular outcomes.

- Use caution in adults with T2DM with compensated cirrhosis from NAFLD
- Not recommended for patients with decompensated cirrhosis

Lipid Management[49]

Lifestyle modifications should include increased physical activity, Mediterranean style or DASH diet, reduced saturated and trans fat consumption, increased n-3 fatty acids, viscous fiber, plant stanols/sterols, and weight loss (if overweight).

Statins have been proven to reduce ASCVD events when used for both primary and secondary prevention in patients with diabetes and is a standard quality reporting measurement metric.

Prevention of Complications

ASCVD Considerations

Patients 20-39 years	
No ASCVD	Consider statin therapy
Patients 40-75 years	
No ASCVD	Initiate moderate-intensity statin therapy
>20% ASCVD 10-year risk	Initiate high-intensity statin therapy to reduce LDL cholesterol by ≥50% of baseline and to target an LDL cholesterol goal of <70 mg/dL
Multiple ASCVD risk factors and LDL cholesterol ≥70 mg/dL	Consider adding ezetimibe or PCSK9 inhibitor to maximum tolerated statin therapy
Patients >75 years	
Already on statin therapy	Reasonable to continue statin
Higher CV risk	Consider moderate-intensity statin therapy after discussion of potential benefits and risks

Secondary Prevention

Initiate high-intensity statin therapy to target an LDL cholesterol reduction of ≥50% from baseline and an LDL cholesterol goal of <55 mg/dL.

Addition of ezetimibe or a PCSK9 inhibitor with proven benefit in this high risk population is recommended if this goal is not achieved on maximum tolerated statin therapy.

Immunizations[50]

Influenza	Annual vaccination recommended for all patients with diabetes ≥6 months old
COVID-19	Patients with diabetes are at higher risk for COVID-19 complications and should be kept up to date on COVID-19 boosters
Pneumococcal Pneumonia	Patients with diabetes are at higher risk of pneuomonia and vaccination schedule will depend on previous pneumococcal vaccination historyhistory Use the PneomoRecs VaxAdvisor mobile app to quickly and easily determine your specific patient's vaccination schedule
RSV	Recommended for patients ≥ 60
Hepatitis B[51]	Administer a 2- or 3-dose series of hepatitis B vaccine, depending on the vaccine, to unvaccinated adults with diabetes ages 18 through 59 years. Consider administering a 3-dose series of hepatitis B vaccine to unvaccinated adults with diabetes ≥60 years of age.

Special Populations

Pregnancy[52]

Preconception counseling should address:

- Importance of achieving glucose levels as close to normal as is safely possible, ideally A1C <6.5% (48 mmol/mol), to reduce the risk of congenital anomalies, preeclampsia, macrosomia, preterm birth, and other complications
- Risk of development and/or progression of diabetic retinopathy

Engage pregnant patients with a multidisciplinary care team of an endocrinologist, maternal-fetal medicine specialist, registered dietitian nutritionist, and diabetes care and education specialist, when available.

Screen for diabetic retinopathy prior to a planned pregnancy or in the 1st trimester.[53]

- If evidence of diabetic retinopathy is present, monitor the patient every trimester and for 1 year postpartum, as indicated by the degree of retinopathy.

Prescribe low-dose aspirin 100–150 mg/day starting at 12 to 16 weeks of gestation to lower the risk of preeclampsia. 162mg/day may be acceptable (81 mg tablets currently available).

Older Adults[54]

- Common comorbidities may impact outcomes more than glycemic control in older patients
- Optimize nutrition (including protein intake) and regular exercise (aerobic and resistance)
- Tailor treatment plans as needed for individual patients if the standards of care are cost prohibitive or unmanageably complex; risk/benefit and goals of care will dictate the treatment plan for older adults
- Screen for and take into account common geriatric syndromes, like polypharmacy, cognitive impairment, and depression which may impair treatment adherence[55]
- HgbA1c < 7.5% is a reasonable goal for **older, highly functional patients** with limited comorbidities. However, HgbA1c <8.5% is acceptable for those with more **extensive comorbidities and/or functional/cognitive impairment**.

Dementia

Diabetes increases the risk of dementia, and recurrent, severe hypoglycemia is associated with cognitive impairment.

Screen patients annually after age 65 using a validated tool (Minicog, MOCa, MMSE), with appropriate work up and treatment if results are abnormal.

Hypoglycemia

Older adults, particularly those with cognitive impairment and/or receiving insulin therapy, are at increased risk for hypoglycemia.

- Frequency of monitoring, glycemic targets, and medications should be adjusted accordingly

Treatment considerations

- Avoid insulin secreatogogues, such as sulfonylureas due to potential for hypoglycemia. If a sulfonylurea is required, shorter acting agents like glimepiride and glipizide are preferred to longer acting agents like glyburide.

- GLP-1 RAs are administered by injection (except for oral semaglutide) which may be difficult for impaired seniors to use
- SGLT-2i may be more likely to cause volume depletion in the elderly
- The use of basal insulin once daily is easier to manage than multiple dose regime

Referral Indications

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Endocrinology

- Patients with A1C > 9, despite 6 months of adherent therapy
- Recurrent hypoglycemia
- Continuous subcutaneous insulin infusion (insulin pump) therapy
- Pregnant or planning pregnancy

Cardiology

- For treatment of concomitant cardiac disease (CAD, HF) and orthostatic hypotension
- Optimize treatment of lipid disorders

Nephrology

- To clarify the cause of CKD and assistance managing related complications
- All stage 4 CKD (eGFR <30)
- KidneyIntelX^{TM} intermediate or high risk score

KidneyIntelX^{TM} is a diagnostic blood test that predicts risk of progressive decline in kidney function in patients with T2DM and existing diabetic kidney disease at stages 1-3 (eGFR 30-59 or UACR ≥ 30).

E-consults

Consider an eConsult when

- You have a clear, focused clinical question that does not require a physical exam **and**
- The patient is not established with a physician in that specialty

Benefits of eConsults

- Access to specialty advice
    - Decreased wait time for face-to-face visits with specialists due to reduction of unnecessary referrals (and, in some cases, expedited scheduling if urgency identified during eConsult)

- Decrease high-cost utilization
    - Fewer In-person visits with specialists

- Patient-centered care empowers primary care team and reduces burden for patients

Appendix

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MSHS Disease Management Services

Certified Diabetes Education Disease Management Team

Certified Diabetes Educators (CDEs) practice at the top of their license. They can help manage patients living with diabetes and associated comorbidities, such as heart failure. CDEs are embedded in primary and specialty care.

Patients receive customized education and strategies to achieve an optimal quality of life. CDE engagement includes:[56]

- Assessing and educating patients and caregivers on their health conditions
- Cohesive collaboration with the medical team to integrate evidenced-based care into patient's plan of care, ongoing monitoring, real time support and follow up by the medical team
- Seamless communication amongst the medical team, and Specialty care consultations for high risk patients
- Oversight and training by a medical director, and outcomes evaluation (HgbA1C, BP, weight loss, BMI etc.)

Clinical Pharmacy

Pharmacists are a key part of the care team for chronic disease management including diabetes, heart failure, and COPD.[57] They are **credentialed providers that can prescribe and adjust medications** through the Collaborative Drug Therapy Management Model.[58] Pharmacists are embedded in primary and specialty care, as well as the Condition Management Program.

Referral Indications

- Uncontrolled chronic diseases, such as hypertension, diabetes, heart failure, asthma, COPD
- Hospital discharge

- High utilization
- Polypharmacy and medication reconciliation
- Medication adherence barriers/challenges

Mount Sinai Medication Access Program (MAP)

The Medication Access Program (MAP) is a telehealth service that offers personalized, one-on-one support to address medication needs. The dedicated and knowledgeable team provides education, counseling, medication home delivery, and financial assistance for eligible patients.

Care Management at MSHS

Mount Sinai Health Partners Care Management social workers and nurses partner with patients, family caregivers, and providers to identify and address known risk factors that can impact patients' health.

The medical complexity inherent in many patients with diabetes requires the involvement of multiple clinicians across many care settings.[59] Interdisciplinary, team-based care may be the most effective approach to complex diabetes care.

Care Management intervention includes:

- A comprehensive assessment of the patient's understanding of and ability to manage their illness, including a psychosocial assessment
- Development of a comprehensive care plan to set goals to optimize health and quality of life
- Follow-up communication with referring provider

Referral Criteria

May include those with:

- Multiple no-shows
- Unexplained non-adherence to medications, testing, or treatment
- Demonstrated difficulty managing symptoms and/or disease processes (including those newly diagnosed)
- Frequent admissions or ED visits that may be preventable with additional support
- Complex family dynamics that deplete the provider

- Difficulty accessing needed community-based care
- A high “worry score” — patients you as the provider are most worried about from visit to visit

Note: *MSHP Care Management Priorities patients in MSSP and Healthfirst contracts and those patients with Medicaid.*

How to refer to Care Management and/or Home Health

- Use the MSHP Care Management Referral in Epic (order #391414)
- Email mshpcmreferral@mountsinai.org
- Call 212-241-7228

Providers who refer patients can expect:

- Prompt and efficient processing of your referral
- Communication about referral processing and assignment through the Epic Inbasket
- Follow up from clinical staff within one week of assignment

Home Health Program (Skilled Home Services)

- Home Health referrals should be handled through the designated Home Health nurse coordinator, and a member of the care management team through the Care Management referral information above. The Home Health nurse coordinator will assess the patient’s needs and determine appropriateness of Home Health.
- **Telephonic education and reinforcement** can be also be delivered by the Nurse Clinical Coordinator. (The home health RN will not provide patient interventions, they will refer to nurse care coordinator if needed.)
- Nursing interventions can include various educational components including recognition of high risk symptoms with an action plan, dietary guidelines, medication management, and monitoring of blood glucose, weight, and blood pressure.

Behavioral Health[60]

Individuals with chronic conditions are 2-5 times more likely to have anxiety and depressive disorders compared with the general population.[61] All patients should be screened annually for depression using the PHQ-2/9 and referred to psychiatric services as appropriate.

Patients with chronic medical illness and a comorbid psychiatric diagnosis have poorer quality of life, increased functional disability, and increased mortality. Depression, however, is highly treatable. Screening and intervention are therefore essential aspects of care.

The Mount Sinai Health Partners Behavioral Health Hub has a variety of multimedia resources to help you learn about and manage behavioral health needs in primary care.

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