



RCHC Clinical Guidelines Type 2 Diabetes; Adults

Screening for diabetes in asymptomatic adults¹

Population:

- Aged ≥ 45 years;
- Aged < 45 years who are overweight ($BMI \geq 25\text{kg/m}^2$) and have an additional risk factor: physical inactivity, first degree relative with diabetes, high-risk race/ethnicity (e.g. AA, Latino, Native American, Asian American, Pacific Islander), HDL level < 35 mg/dl and/or any triglyceride level > 250 mg/dl, women with polycystic ovary syndrome, $A1C \geq 5.7\%$, IGT or IFG on previous testing, other clinical conditions associated with insulin resistance (acanthosis nigricans, $BMI \geq 40$), history of CVD, hypertension;
- Reclassify women with gestational diabetes after 6 weeks postpartum and prior to planning future pregnancies²

Screening interval: if normal results, repeat testing at one to three-year intervals

Screening tests:

- HbA1C is preferred method - reflects long-term blood glucose concentration, not affected by acute changes in glucose levels due to stress or illness and does not require fasting.
 - May not be accurate with hemoglobinopathies, significant anemia or prior to 3 months postpartum
- Fasting plasma glucose
- Glucose tolerance test – fasting glucose, followed by measurement of blood glucose concentration two hours after 75-g oral glucose load

Diagnosis³

Diagnostic criteria for diabetes – positive findings should be confirmed by repeat testing using the same test on a different day

Test	Normal	IFG or IGT*	Type 2 Diabetes
Hemoglobin A1C level, %	< 5.7	5.7-6.4	≥ 6.5
Fasting plasma glucose mg/dL (mmol/L)	< 100 (< 5.6)	100-125 (5.6-6.9)	≥ 126 (≥ 7.0)
OGTT results mg/dL (mmol/L) 2-hours p 75-g oral glucose load	< 140 (< 7.8)	140-199 (7.8-11.0)	≥ 200 (≥ 11.1)
A random plasma glucose ≥ 200 mg/dL (11.1 mmol/L) in patients with classic symptoms of hyperglycemia or hyperglycemic crisis is also diagnostic for type 2 diabetes			

*Impaired fasting glucose (IFG)/ Impaired glucose tolerance (IGT) - behavioral interventions indicated; may delay or avoid progression to type 2 diabetes



Initial Evaluation

Rule out diabetic ketoacidosis (DKA) if symptomatic

Complete medical evaluation to classify diabetes, detect complications (e.g. neuropathy), and identify other risks for cardiovascular disease (e.g. hypertension); include:

- Height, weight, BP, funduscopic exam, thyroid, skin, cardiac, neurologic, and vascular exams
- Mental health assessment
- Assess social context using PRAPARE tool.

Laboratory

- Urine dipstick: glucose, protein, ketones
- HgA1C if no results within past 2-3 months
- Within past year: Fasting lipid profile, liver function tests, urine albumin excretion with spot urine albumin-to-creatinine ratio, serum creatinine and estimated GFR. TSH if dyslipidemia or women >50 years.

Treatment Goals

Shared decision-making with individualize goals based on duration of diabetes, age/life expectancy, known CVD or advanced microvascular complications, extensive comorbidity, hypoglycemia unawareness, patient resources and support system.

- More stringent control with patients who have short duration of diabetes, long life expectancy and no significant CVD
- Less tight control for aged and those at high risk for hypoglycemia
- HbA1c < 7%; ≥ 65 years or clinical factors < 8%
 - Most oral medications lower HgA1C about 1-2% (at most); over time most patients will need insulin to achieve goals
- Self-monitoring Blood Glucose (SMBG) targets:
 - AM SMBG 70-130 mg/dL; ≥65 yrs or clinical factors 100-160 mg/dL
 - before meals 70-130 mg/dL
 - 1-2 hours after beginning of meals (postprandial) <180 mg/dL
 - bedtime 100-150 mg/dL
- Avoid hypoglycemia: defined as <54 mg/dL; alert value ≤70 mg /dL
- Blood pressure: SBP <139 mmHg , DBP < 89 mmHg
- Lipids: LDL cholesterol ≤ 99mg/dL, TG<150, HDL>50
- BMI: goal < 25 kg/m²

Pharmacological Management - see Appendix A for RCHC medication titration algorithm

HgA1C <2% above goal

- Initiate metformin as first-line choice
 - Titrate q. 1-2 weeks aiming for AM SMBG target
 - Contraindicates: eGFR <30, heart failure class 3-4 or LFTs greater than three times upper limit of normal
- Maintain therapy when reach goal



- If not at goal on metformin monotherapy after 3 months, initiate combination/dual therapy using sulfonylureas.
 - Titrate every two weeks until at target
 - Contraindication: severe hypoglycemia, defined as resulting or likely to result in seizures, loss of consciousness or needing help from others; sulfa allergy
- Use alternate second-line oral agent if indicated: thiazolidinedione, meglitinide, α -glucosidase inhibitor, dipeptidyl peptidase-4 (DPP-4), sodium-glucose cotransporter-2 (SGLT-2) inhibitor, or GLP-1 receptor agonist if risk of severe hypoglycemia
 - When selecting agent, consider factors such as comorbidities, patient preferences, adherence, BMI (impact on weight), potential side effects, and cost. (see Appendix B)
- Each new class of noninsulin agents added to initial therapy lowers A1C approximately 1%.
- If A1C remains above goal after three months, reevaluate:
 - If >1% above goal on dual therapy, add basal long acting insulin 10 units SQ at bedtime to metformin, discontinuing alternate agents.
 - Increase 2 units q. 2 days until at target
 - If risk of severe hypoglycemia or <1% above goal on dual therapy, add a third oral agent considering patient and disease-specific factors.

HgA1C > 2% above goal or FBS >300 mg/dL

- Initiate basal insulin 10U SQ at hs or 0.1-0.2 U/kg/day SQ hs
 - Long acting insulin – Basalgar (PHC formulary), Lantus, Levemir
 - Intermediate - NPH
- Monitor blood glucose before breakfast and up to 2-4 times/day a few times per week
- Hypoglycemia - determine & address cause or if unclear, decrease dose by 4 units or 10-20% and prescribe glucagon
- Adjust insulin 10-15% or 2-4 units once or twice weekly to reach FBG target
- Target daytime highs with prandial and short-acting insulin
 - Regular – Novolog, Humalog
 - Monitor blood glucose before breakfast and before meals 2-4 times/day

Treat co-morbidities to reduce the risk for cardiovascular events

- Hypertension – see HTN guidelines*
- Aspirin therapy for 40-75 years of age**
- Angiotensin-converting enzyme inhibitors (ACEs) and angiotensin receptor antagonists (ARBs) for 18-75 years**
- Dyslipidemia - statins (HMG-CoA reductase inhibitors) for 18-75 years**

*RCHC Management of Adult Hypertension 6/27/2016

**PHASE Algorithm 2012

Contraception for women of reproductive age (see Appendix C)

- Non-hormonal long acting reversible contraception or sterilization preferred.
- Women desiring pregnancy should be in good control (HgA1C <6.5%) prior to conception.² Follow guidelines from California Diabetes and Pregnancy Program (CDAPP)



Immunization – flu vaccine annually, pneumococcal polysaccharide vaccine (revaccinate after 65 years if more than 5 years), hepatitis B

Screening/Referrals

Retinal screening with dilated comprehensive exam by ophthalmologist or optometrist- monitor every 1-2 years

- More frequently for patients with background retinopathy or severe disease

Foot screening – inspection, pulses and annual monofilament test; if abnormal referral to podiatry foot care program

Dental care – comprehensive periodontal exam

Regular screening for depression and referral for mental health services if indicated.

Medical nutrition therapy (MNT) with registered dietitian

- MNT delivered by a registered dietitian is associated with A1C decreases of 0.3–1% for people with type 2 diabetes 0.5–2%.

Self-management Education and Support

Assess and provide individualized education at the initial visit and annually. Adjust the plan when new complicating factors arise and/or transitions in care occur.

- Employ health coaching and motivational techniques
- Link patient with navigators, community health workers and other resources as needed
- Use one-to-one and group instruction of patient or patient & family
- Utilized community resources as needed
- Address following topics at initial diagnosis and review annually:
 - Glucose targets, relationship between glucose levels, CHO intake and physical activity,
 - Self-monitoring blood glucose (2-4 times/day)
 - Test 3 or more times/day if taking multiple injections, ill or changing therapies
 - Keep logs including factors that affect blood glucose levels: exercise, meal timing and amount, missed medication doses, injection sites, insulin status
 - Hypoglycemia: prevention, signs, use of keto sticks
 - Glucagon kit - instruct patient and caregivers/family on use
 - Glucose 15-20 gm preferred treatment for conscious ≤ 70 gm/dL
 - Foot care
 - Infections and sick day management
 - Safe disposal of needles & syringes
 - Physical activity - 30 minutes per day or 150 minutes a week of moderate-intensity aerobic
 - add resistance training twice a week
 - interrupt prolonged sitting every 30 minutes with short bouts of physical activity
 - balance and flexibility training in older adults
 - Weight management
 - BMI >25 decrease calories by 500-1000/day to sustain weight loss of 5-7%
 - Pharmacotherapy may be indicated for BMI categories >27



- Metabolic surgery may be indicated for BMI categories > 30
- Nutritional guidelines - no advantage to any particular diet (Mediterranean, DASH and plant-based diets acceptable):
 - Eat small, frequent meals throughout the day to maintain blood glucose levels
 - Eat 1-2 servings of carbohydrate before and after physical activity
 - Carbohydrates limited to 45-65% of daily calories, with intake from whole grains, vegetables, fruits, legumes and dairy products; emphasis on foods high in soluble fiber and low glycemic index
 - 20-35 grams fiber daily
 - Reduce saturated fats, trans fat and cholesterol intakes; increase monounsaturated fats, increase intake of foods rich in long-chain ω -3 fatty acids: fish, nuts, and seeds
 - Adequate water intake
 - Avoid sugar sweetened beverages and other foods with added sugar
 - Include 20-35 grams a day of soluble fiber from plant sources
 - Dietary sodium limited to < 2,300 mg/day
 - Patients with nephropathy should avoid excessive protein
- Alcohol consumption \leq 1 drink/day for women; \leq 2 drinks for men; exercise caution as alcohol consumption may increase risk of hypoglycemia
- Tobacco cessation – counseling & pharmacotherapy indicated

Ongoing Evaluation & Monitoring

Quarterly evaluation for patients at goal with stable glycemic control including:

- Medication reconciliation
 - Assess cognitive function
 - BP every visit
 - Ask about symptomatic and asymptomatic hypoglycemia at each encounter
 - Monitor for complications – e.g. peripheral neuropathy
 - HgA1C at least two times a year
 - Assess urinary micro albumin once a year with spot urinary albumin-to-creatinine ratio (UACR)
 - Estimated glomerular filtration rate (eGFR) once a year (all type 2 and type 1 diabetes duration \geq 5 years)
 - If eGFR < 60 mL/min/1.73 m² evaluate and manage potential complications of chronic kidney disease (CKD)
 - With long term use of metformin, vitamin B12 level
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- For patients not at goal, increase visit frequency and titrate medications. Endocrinology consultation should be obtained as needed.



References

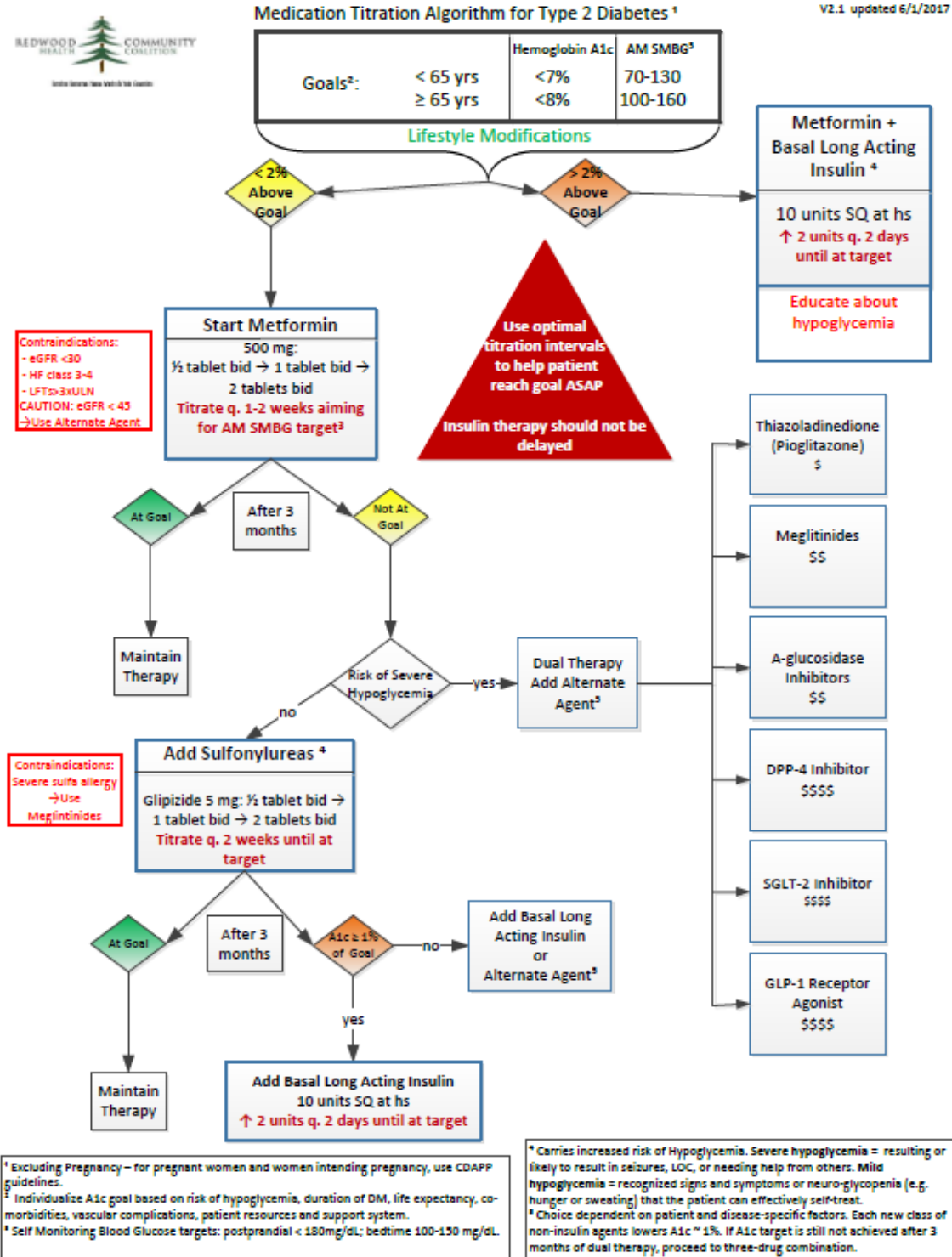
¹American Diabetes Association (ADA). Standards of Medical Care in Diabetes – 2017. Diabetes Care. 2017 Jan; Vol 40 (Supplement 1).

²California Diabetes and Pregnancy Program; 2015 CDAPP Sweet Success Guidelines for Care <http://www.cdappssweetsuccess.org/Professionals/CDAPPSweetSuccessGuidelinesforCare.aspx>

³Siu, A. Screening for Abnormal Blood Glucose and Type 2 Diabetes Mellitus: U.S. Preventive Services Task Force Recommendation Statement. Annals of Internal Medicine. 2015; 163:861-868.

Appendix A

Medication Titration Algorithm for type 2 diabetes



Appendix B

Comparative Efficacy, Adverse Effects, and Costs for Add-on Oral Therapies to Metformin

Comparative Efficacy vs. Other Combinations With Metformin (Quality of Evidence)	Comparative Harms vs. Other Combinations With Metformin/Class Adverse Effects and FDA Warnings	Agents	Fair Price for a 60-d Supply, \$*	Adverse Effects
SUs				
SU + metformin favored for weight vs. TZD + metformin (moderate)	Higher risk for hypoglycemia than with metformin combinations with TZD, DPP-4 inhibitor, or SGLT-2 inhibitor	Glipizide, 5 mg	9	Diarrhea, gas, jitteriness, dizziness, uncontrollable shaking, red or itchy skin, rash, hives, and blisters
		Glimepiride, 4 mg	14	Dizziness and nausea
		Glyburide (DiaBeta, Sanofi-Aventis), 5 mg	111	Nausea and upper abdominal fullness
		Glyburide (Glynase, Pfizer), 6 mg	226	Nausea and upper abdominal fullness
TZDs				
TZD + metformin favored for short-term CVD mortality (rosiglitazone only) (low) and HbA _{1c} vs. DPP-4 inhibitor + metformin (moderate)	TZDs increase risk for congestive heart failure May also be associated with increased risk for fracture or bladder cancer	Pioglitazone, 30 mg	24	Headache; muscle, arm, or leg pain; sore throat; and gas
		Rosiglitazone (Avandia, GlaxoSmithKline), 2 mg	178	Headache, runny nose and other cold symptoms, sore throat, and back pain
DPP-4 inhibitors				
DPP-4 inhibitor + metformin favored for long-term all-cause mortality, long-term CVD mortality, and CVD morbidity vs. SU + metformin (low) DPP-4 inhibitor + metformin favored for short-term CVD morbidity vs. pioglitazone + metformin (low) DPP-4 inhibitor + metformin favored for weight vs. SU + metformin (high) or TZD + metformin (moderate)	FDA warns that sitagliptin, saxagliptin, linagliptin, and alogliptin may be associated with potentially severe and disabling joint pain	Alogliptin, 25 mg	335	Headache, stuffy or runny nose, sore throat, and joint pain
		Linagliptin (Tradjenta, Boehringer Ingelheim), 5 mg	734	Headache and joint pain
		Saxagliptin (Onglyza, AstraZeneca), 5 mg	752	Sore throat, headache, and joint pain
		Sitagliptin (Januvia, Merck), 100 mg	746	Stuffed or runny nose, sore throat, headache, diarrhea, nausea, and joint pain
SGLT-2 inhibitors				
SGLT-2 inhibitor + metformin favored for CVD mortality (low), HbA _{1c} (moderate), weight (high), systolic blood pressure (high), and heart rate (moderate) vs. SU + metformin SGLT-2 inhibitor + metformin favored for weight and systolic blood pressure (moderate) vs. DPP-4 inhibitor + metformin	Higher risk for genital mycotic infection than metformin alone or metformin combinations with SU or DPP-4 inhibitor FDA warns that canagliflozin may be associated with increased risk for bone fracture and risk for decreased bone mineral density	Canagliflozin (Invokana, Janssen), 300 mg	808	Excessive urination, including at night; increased thirst; constipation; and dry mouth
		Dapagliflozin (Farxiga, AstraZeneca), 10 mg	812	Excessive urination, including at night, and increased thirst
		Empagliflozin (Jardiance, Boehringer Ingelheim), 25 mg	812	Excessive urination, including at night, and increased thirst

CVD = cardiovascular disease; DPP-4 = dipeptidyl peptidase-4; FDA = U.S. Food and Drug Administration; HbA_{1c} = hemoglobin A_{1c}; SGLT-2 = sodium-glucose cotransporter-2; SU = sulfonylurea; TZD = thiazolidinedione.

* Data obtained from <https://healthcarebluebook.com>.

Source: Qaseem et al



Appendix C

U.S. Medical Eligibility Criteria for Contraceptive Use, 2016

Severity of Diabetes Mellitus	Combined hormonal (pill, patch, ring)	Progestin-only pill	Injection DMPA ^a	Implant (Implanon)	LNG IUD ^b (Mirena)	Copper T (ParaGard)
Non-vascular disease (oral or insulin)	2	2	2	2	2	1
Nephropathy/retinopathy/neuropathy/ other vascular disease with diabetes OR diabetes of >20 years duration	Initiation- 3					
	Continuation- 4	2	3	2	2	1
	Continuation- 4					

1- No restrictions for the use of this method.

2- Advantages generally outweigh theoretical or proven risks.

3- Theoretical or proven risks usually outweigh advantage.

4- Unacceptable health risk (method not to be used)

^a depot medroxyprogesterone acetate

^b levonorgestrel-releasing intrauterine system

Source: CDC; U.S. Medical Eligibility Criteria for Contraceptive Use; updated July 2016,

https://www.cdc.gov/reproductivehealth/contraception/pdf/summary-chart-us-medical-eligibility-criteria_508tagged.pdf