Options for Treating Prediabetes and Diabetes: Get Your Patient to Goal

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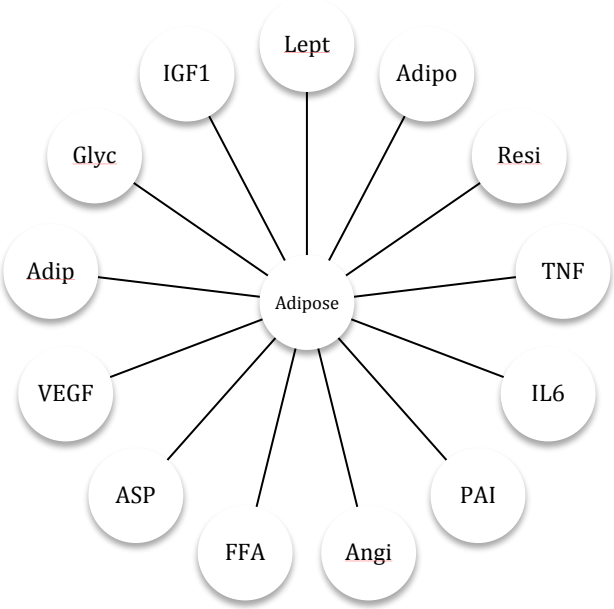
Objectives
- Differentiate types of diabetes and prediabetes
- Describe various treatment options for managing diabetes and prediabetes
- Describe various treatment options for managing diabetes and prediabetes

CDC Diabetes Statistics Report 2017[1]
- Diabetes 30.3 million (9.4%)
- Diabetes: 25% in age 65+
- Highest in Asians, non-Hispanic blacks, and Hispanics
- Children: in 2012: 17,900 w T1DM, 5,300 w T2DM
- Prediabetes: 84.1 million (33.9%)
- Prediabetes: 48% in age 65+

Screening for Prediabetes & Diabetes[2]
- Overweight/obese who have 1+ risk factors
    - 1st degree relative with DM
    - High-risk ethnic group
    - Hx CVD, HTN, HDL < 35, Triglyceride > 250
    - PCOS
    - Sedentary lifestyle
    - Other: Acanthosis nigricans
    - If normal: test at least every 3 years or more often
- GDM lifelong testing every 3 years

Secreted by Adipose Tissue[3]



Lept = Leptin	Signals to brain about body fat stores, regulates appetite and energy expenditure
Adipo = Adiponectin	Plays role in protection in patho of T2DM and CVD
Resi = Resistin	May contribute to insulin resistance
TNF = TNF-α	Affects insulin signaling may cause insulin resistance in obesity
IL6 = Interleukin-6	Pro-inflammatory, plays role in lipid and glucose metabolism, and weight regulation
PAI = Plasminogen activator inhibitor 1	Inhibitor of fibrinolytic system by inhibition of activation of plasminogen
Angi = Angiotensinogen	Precursor of angiotensin II, regulator of BP and electrolyte homeostasis
FFA = Free fatty acids	Oxidized in tissues to produce local energy, substrate for triglyceride and structural molecular synthesis, involved in development of insulin resistance
ASP = acylation stimulating protein	Influences rate of triacylglycerol synthesis in adipose tissue
VEGF = vascular endothelial growth factor	Stimulates angiogenesis
Adip = Adipsin	Potential relation between complement pathway and adipose tissue metabolism
Glyc=Glycerol	Structural component of major classes of biological lipids and gluconeogenic precursor
IGF1= insulin-like growth factor 1	Stimulates proliferation of wide variety of cells and mediates many cells and many of the effects of growth hormone

Diagnosis of Prediabetes/Diabetes[2]

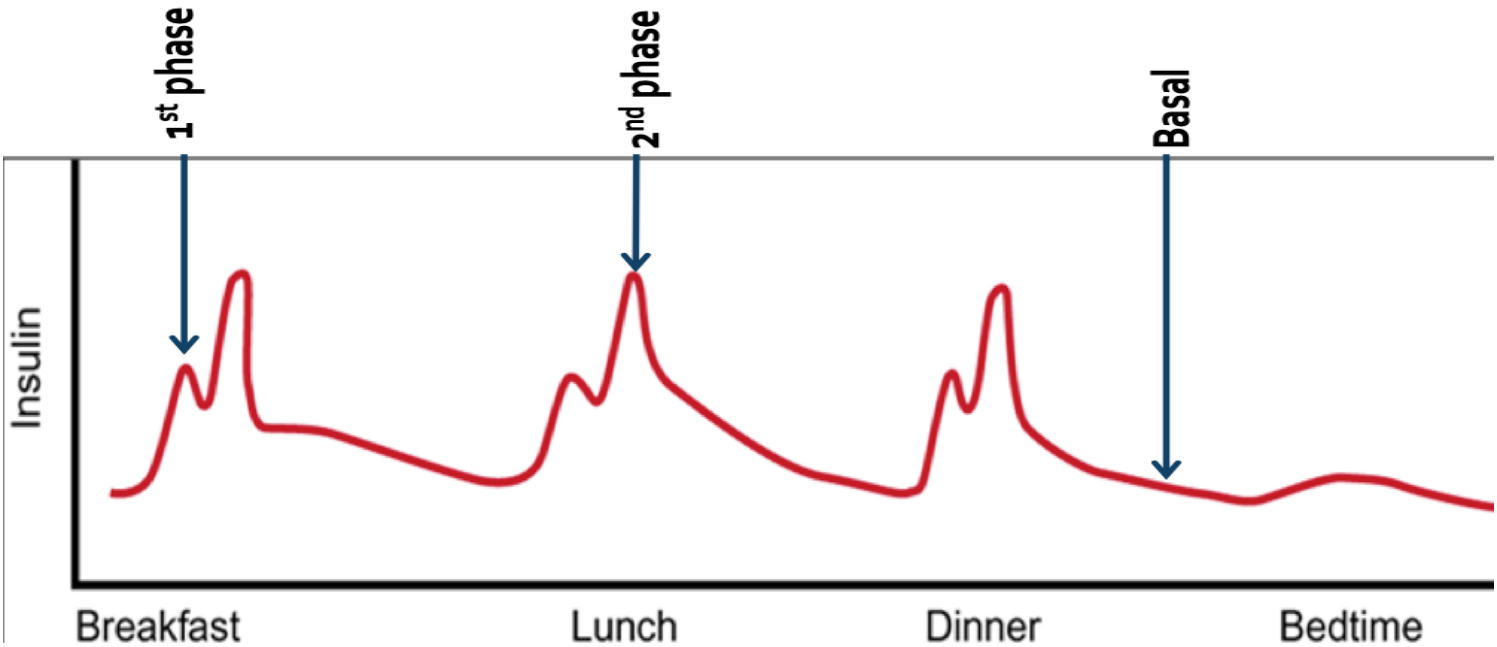
	Normal	Prediabetes	Diabetes
Fasting	< 100	100-125	126±
2 h PG	<140	140-199	200±
HbA1c	<5.7	5.7-6.4	6.5±

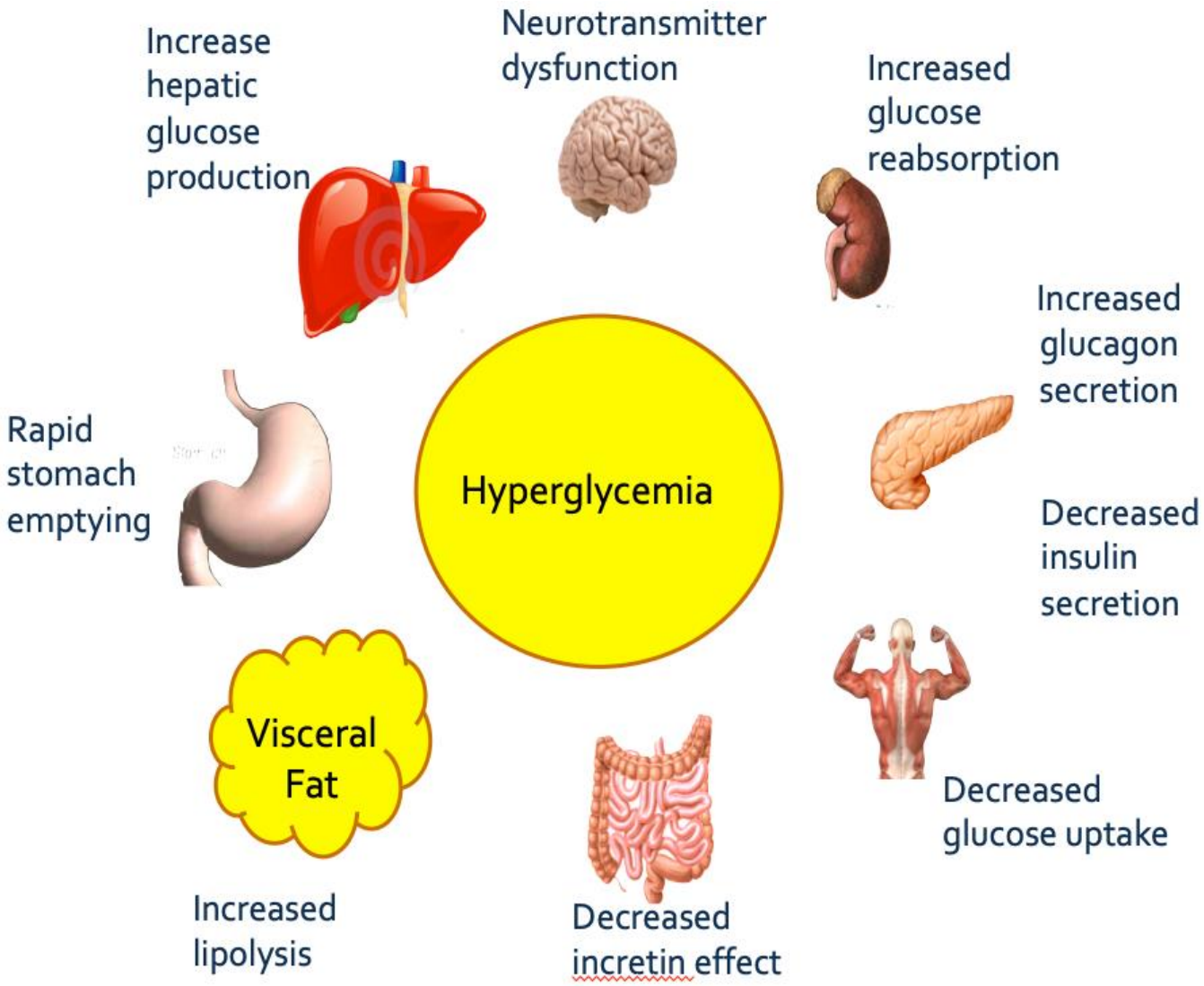
In absence of unequivocal hyperglycemia, dx requires 2 abnormal tests from 1 or 2 separate test sample(s)

Estimated Average Glucose = AG $_{mg/dL}$ = 28.7 x A1c – 46.7[4]

Causes of Inaccurate HbA1c [2]

- Hemoglobin variants
- Sickle cell disease
- Pregnancy 2nd or 3rd trimester, Postpartum
- Glucos-6 phosphate dehydrogenase deficiency
- HIV
- Hemodialysis
- Recent blood loss, Blood transfusion
- Erythropoietin therapy


1st phase
2nd phase
Basal
Insulin
Breakfast
Lunch
Dinner
Bedtime


Increase hepatic glucose production
Neurotransmitter dysfunction
Increased glucose reabsorption
Increased glucagon secretion
Rapid stomach emptying
Hyperglycemia
Decreased insulin secretion
Visceral Fat
Decreased glucose uptake
Increased lipolysis
Decreased incretin effect

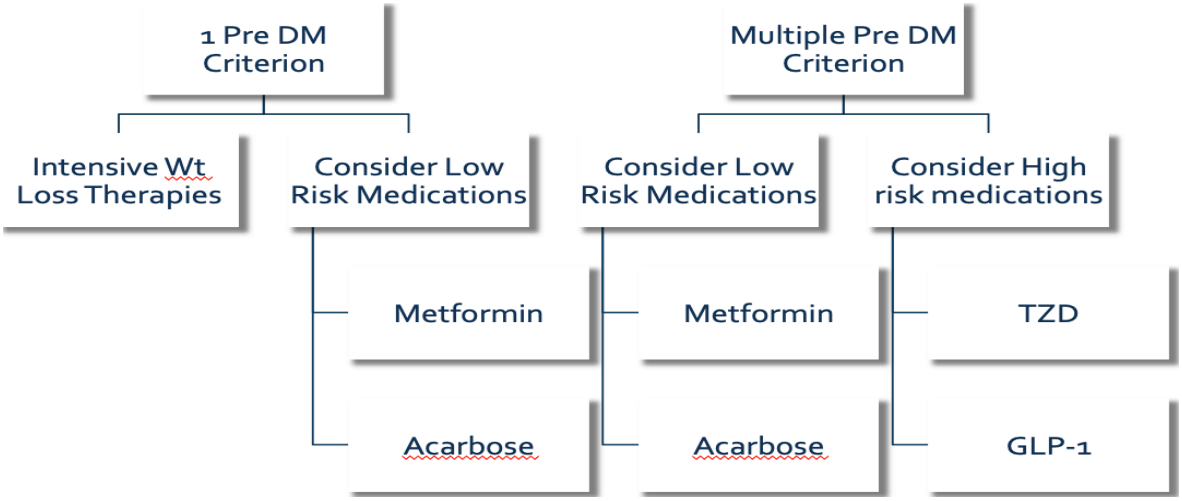
Prediabetes[5]

- Impaired Fasting Glucose
  - Normal insulin sensitivity in skeletal muscle
  - Impaired 1st phase insulin
  - Decreased liver glucose uptake
  - Impaired suppression of endogenous glucose production

- Impaired Glucose Tolerance
  - Severe skeletal muscle insulin resistance
  - Impaired 2nd phase insulin
  - The 1-hour PP BG is strongest predictor of T2DM
  - If IFG and 1 hr PP > 155 had 4 fold increased risk of T2DM

Treatment of Prediabetes[2,6]

- Intensive Lifestyle Therapy
  - Weight loss ~7%
  - Nutrition: mostly plant based polyunsaturated/monounsaturaterd fat, avoid trans and saturated fat
  - Exercise: moderate intensity 150 min week + strength training
  - Moderate alcohol consumption
  - Sleep 7 hours per night
  - No tobacco products
- Dyslipidemia management
- Hypertension management
- Consider Diabetes Medications:

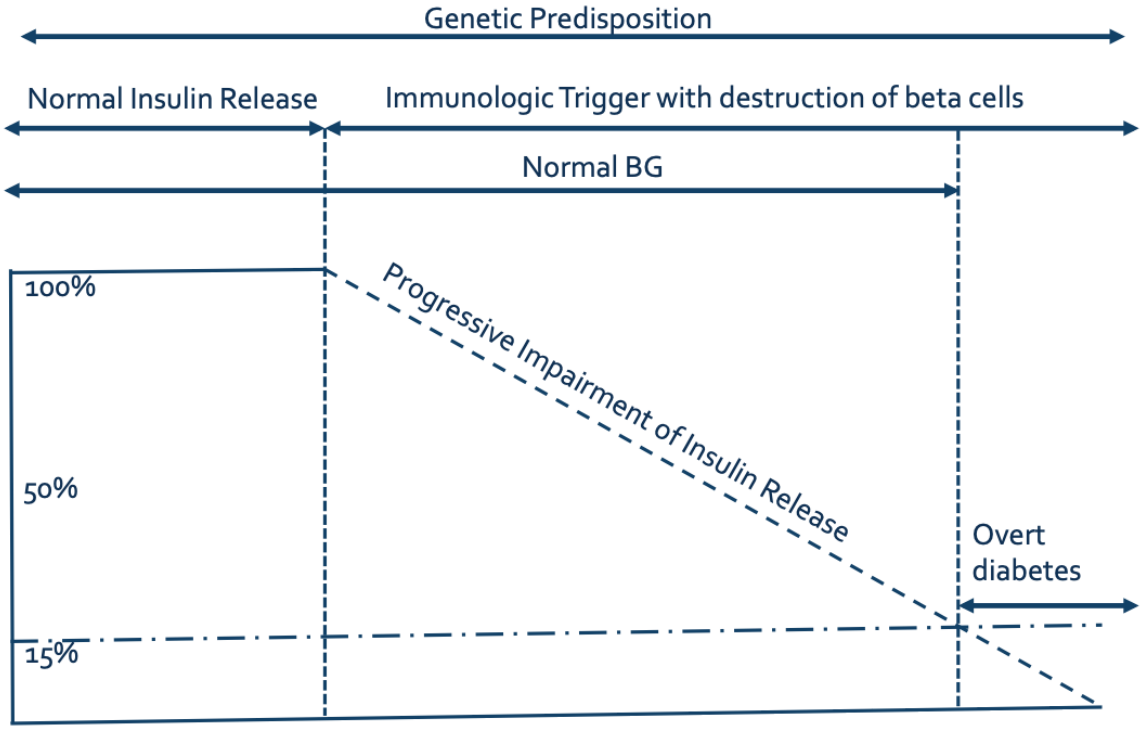


Classifications of Diabetes Mellitus [2]

- Type 1 DM autoimmune B-cell destruction
- Type 2 DM progressive insulin resistance / B-cell failure
- Gestational DM diagnosed 2nd or 3rd trimester
- Specific types due to other causes
  - Monogenic diabetes syndromes: neonatal, MODY
  - Medications: steroids
  - Cystic fibrosis
  - Pancreatitis

Type 1 Diabetes[2]

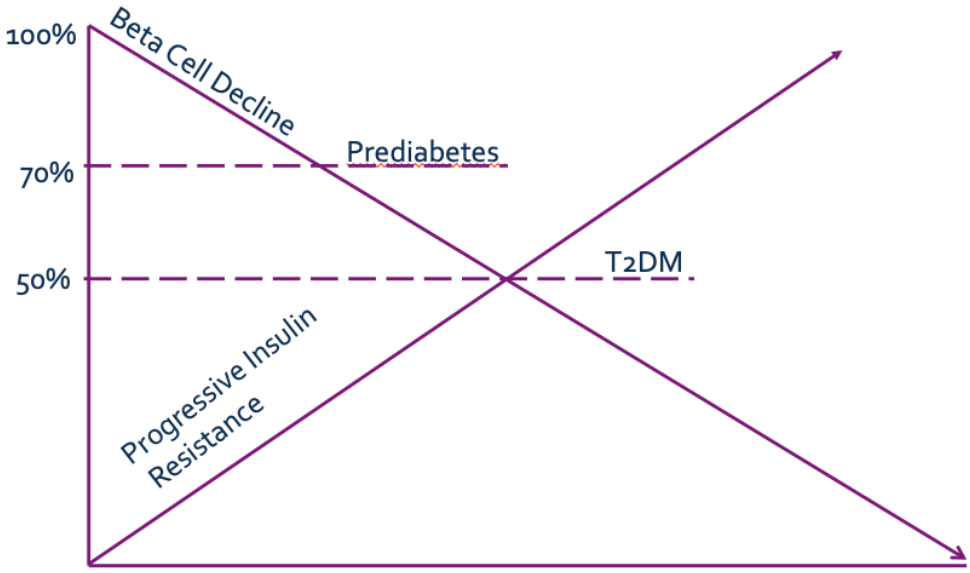
	Stage 1	Stage 2	Stage 3
Characteristics	Autoimmunity Normoglycemia Presymptomatic	Autoimmunity Normoglycemia Presymptomatic	Hyperglycemia Symptomatic
Diagnostic Criteria	Multiple autoantibodies No IGT or IFG	Multiple autoantibodies Dysglycemia IFG and/or IGT	Clinical symptoms Diabetes by standard criteria



Type 1 Diabetes

- Antibodies:
  - GAD65
  - Insulin
  - Tyrosine phosphatases IA-2, IA-2B, and ZnT8
- HLA associations
  - DQA and DQB
- Prone to other autoimmune disorders
  - Hashimoto thyroiditis
  - Graves disease
  - Addison disease
  - Celiac disease
  - Vitiligo
  - Autoimmune hepatitis
  - Myasthenia gravis
  - Pernicious anemia

Type 2 Diabetes



Treatment of Diabetes[2]

- Uses person-centered and strength-based language
  - Active listening
  - Elicit patient preferences and beliefs
  - Assesses literacy, numeracy, barriers
- Multidisciplinary team

Patient Centered Approach

- Assess key patient characteristics
- Consider factors that impact care
- Shared decision making
- Agree on management plan
- Implement management plan
- Ongoing monitoring / adjust plan as needed

Initial Diabetes Evaluation

- DM hx including hx of DM education
- Family hx
- Hx of DM complications and medical
- Lifestyle assessment
- Current medication/vaccines
- Psychosocial assessment

Physical exam

- Ht, wt, BMI, growth & development in children
- BP, orthostatic BP if indicated
- Fundoscopic exam by eye specialist
- Thyroid palpation
- Skin exam (acanthosis, injection sites)
- Foot exam

Lab evaluation
- A1c
- Lipid profile
- Liver function
- Spot urinary albumin-to-creatinine ratio
- Serum creatinine and eGFR
- TSH if autoimmune T1DM
- Vitamin B12 if on metformin
- Serum K+ if on ACEI, ARB, or diuretics

Chronic Kidney Disease Stages

Stage	eGFR
No clinical evidence	≥ 60
1	> 90
2	60-89
3	30-59
4	15-29
5	<15

Refer to nephrologist if uncertain about etiology, difficulty in managing complications of CKD including anemia, secondary hyperparathyroidism, metabolic bone disease, resistant hypertension, electrolyte disturbances, eGFR < 30

Diabetic Retinopathy
- Initial exam
  - Type 1 after 5 years duration
  - Type 2 at time of dx
- Retinal photography with remote reading by an ophthalmologist or optometrist can be screening tool until comprehensive eye exam can be done
- Pregnant or planning pregnancy: eye exsm before or in 1st trimester
- Optimize blood glucose, blood pressure, and lipids

Treatment of Diabetic Retinopathy
- If any DR, refer to a specialist experienced with management of DR
- Treatment
  - Laser photocoagulation
  - Intravitreous injections of antivascular endothelial growth factor ranibizumab
  - Intravitreous injections of antivascular endothelial growth factor

Goal setting
- A1c / Blood glucose / BP / lipid goals
- Self management goals

A1c / Blood Glucose Goals

	Less Stringent	More stringent
Hypoglycemia risk	High risk	Low risk
Disease duration	Long duration	Short duration
Life expectancy	Short	Long

Comorbidities	Severe	None
Vascular disease	Severe	None
Patient preference	Wants less burden	Highly motivated
Resources/support	Limited	Readily available

ADA General Recommendations for A1c, Glucose, BP and Lipids

Health status	**Rationale**	**A1c goal**	**FBS/ac**	**Bedtime BG**	**BP**	**Lipids**
Healthy, few complications, good cognition	Long life	<7.5%	90-130	90-150	<140/90	Statin if possible
Intermed, multiple complications, impaired cognition	Less life exp, high hypo risk	<8%	90-150	100-180	<140/90	Statin if possible
Very complex limited life, severe cognitive impairment	Benefit of tight control uncertain	<8.5%	100-180	110-200	<150/90	Consider benefit of statin?

Nutrition

- No such thing as a "diabetic diet"
- No recommendations for macronutrients
- Mostly plant based, healthy fats, high fiber, low sugar
- Limit alcohol, sodium, sugar sweetened beverages
- Individualized meal planning with registered dietitian
- Promote healthy eating pattern to achieve weight, BP, lipid goals

Dyslipidemia Management

- Intensive lifestyle
- Assess ASCVD Risk: American College of Cardiology/American Heart Association ASCVD risk calculator
- http://tools.acc.org/ASCVD-Risk-Estimator-Plus
- Does not account for duration of diabetes or presence of diabetes complications
- Risk factors: DM, HTN, Fam Hx, low HDL-C, smoking, CKD 3-4

	HIGH RISK DM but no other major risk and/or age <40	VERY HIGH RISK DM + major ASCVD risk	EXTREME RISK DM plus dx CVD
	Desirable	Desirable	Desirable
LDL-C	<100	<70	<55
Non HDL-C	<130	<100	<80
TG	<150	<150	<150
Apo B	<90	<80	<70

Lipid Management

No statin	Moderate statin	High statin
Pregnancy	< age 40 with ASCVD risk factors	All ages with ASCVD or 10 yr CVD risk > 20%
< 40 no ASCVD risk fx	Age >40 without ASCVD	Consider in those with multiple ASCVD risk fx
If don't tolerate statin dose, try alternate statin, decrease dose or frequency If not at goal with statin: Intensify statin, add ezetimibe, PCSK9i, colesevelam or niacin If triglycerides over 500: add fibrate, Rx-grade omega-3 fatty acids, niacin		

Statin Therapy

High intensity statin ↓ ≥ 50%	Moderate intensity ↓ ≥ 30-50%
Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Pitavastatin 2-4 mg

Blood Pressure

- Measure at each visit
- Measured by a trained professional
- Seated position, feet on floor, arm supported at level of the heart after 5 minutes of rest
- Cuff size appropriate
- Elevated values confirmed on another day

Blood Pressure Goals

- If DM + HTN and ASCVD or 10-year risk > 15% may choose target of <130/80 if can safely do so
- Lower risk individuals < 140/90

HTN TX: Initial BP < 160/100

- Start with 1 agent + intensive lifestyle
- No albuminuria: ACEI or ARB or β-blocker or CCB or thiazide diuretic
- Albuminuria: ACEI or ARB
- Not meeting target: add different drug class from ACEI/ARB, β-blocker, CCB, thiazide diuretic (don't combine ACEI and ARB).
- If not meeting goal with above agents consider adding mineralocorticoid receptor antagonist, α-blocker, central agents, vasodilator, aldosterone antagonist or refer to specialist

HTN TX: Initial BP < 160/100

- No albuminuria: Start with 2 agents: ACEI/ARB or β-blocker, or CCB, or thiazide diuretic
- Albuminuria: ACEI or ARB **AND** β-blocker, or CCB or thiazide diuretic
- Not meeting target: add different drug class from ACEI/ARB, β-blocker, CCB, thiazide diuretic (don't combine ACEI and ARB).
- If not meeting goal with above agents consider adding mineralocorticoid receptor antagonist, α-blocker, central agents, vasodilator, or aldosterone antagonist or refer to specialist

References

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