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Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

Diabetes Prevention, Diagnosis, Classification, Prediabetes Comprehensive Evaluation & Assessment of Comorbidities

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Outline

- DM Prevention
- Prediabetes
- Screening
- Diagnosis & Classification
- Comprehensive evaluation & assessment of comorbidities

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Diabetes Prevention/ Prediabetes

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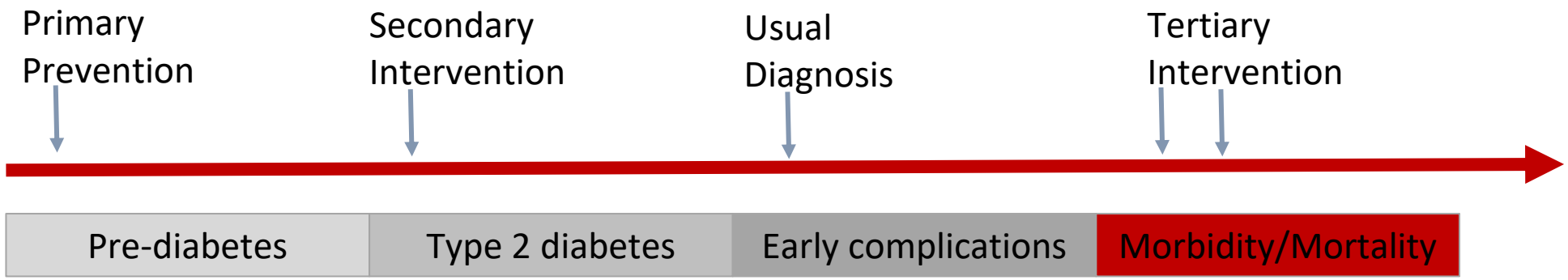
Potential for intervention



Goals of prevention
Preventing or delaying the onset of DM
Preserving beta cell function
Preventing or delaying complications
Reducing costs of care

Lifestyle Modification Trials

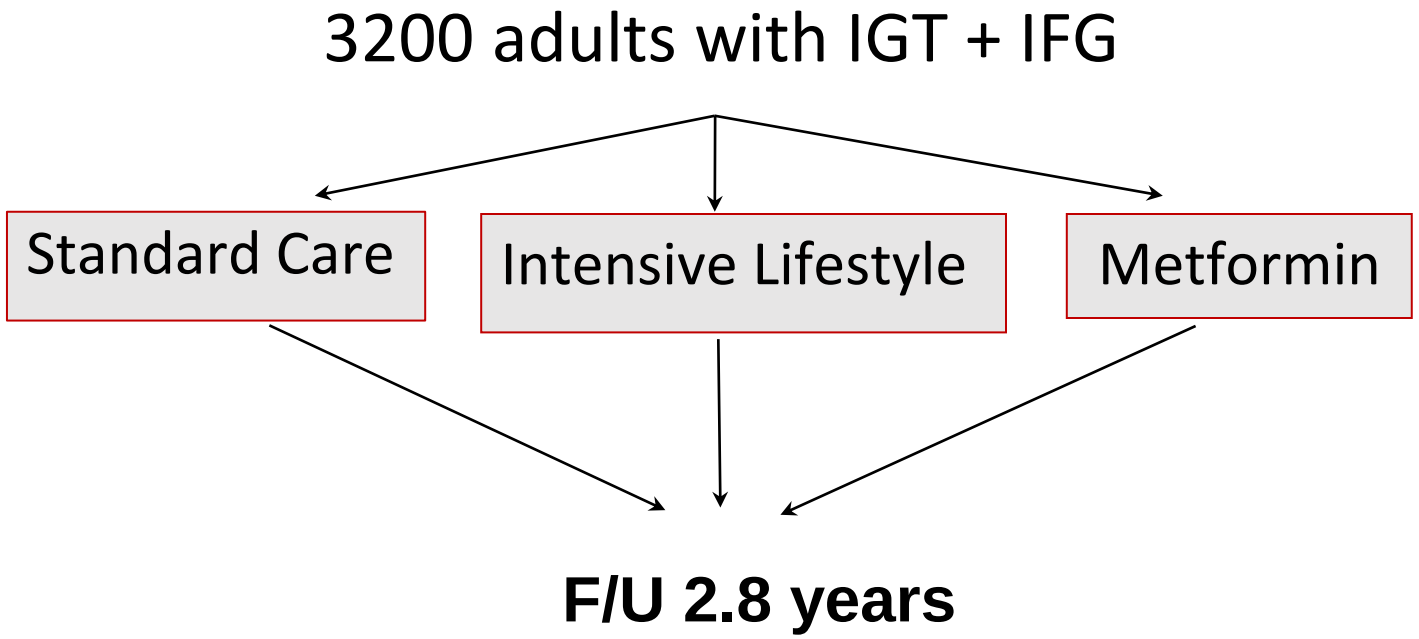
Study	Country	N	Baseline BMI (kg/m^2)	Intervention period (years)	RRR (%)	NNT
Diabetes Prevention Program[1]	USA	3234	34.0	2.8	58	21
Finnish Diabetes Prevention Study[2]	Finland	523	31	4	39	22
Da Qing[3]	China	577	25.8	6	51	30

NNT, number needed to treat; RRR, relative risk reduction; T2D, type 2 diabetes.

**DPP Research Group. N Engl J Med. 2002;346:393-403. Eriksson J, et al. Diabetologia. 1999;42:793-801.
Li G, et al. Lancet. 2008;371:1783-1789. Lindstrom J, et al. Lancet. 2006;368:1673-1679.**

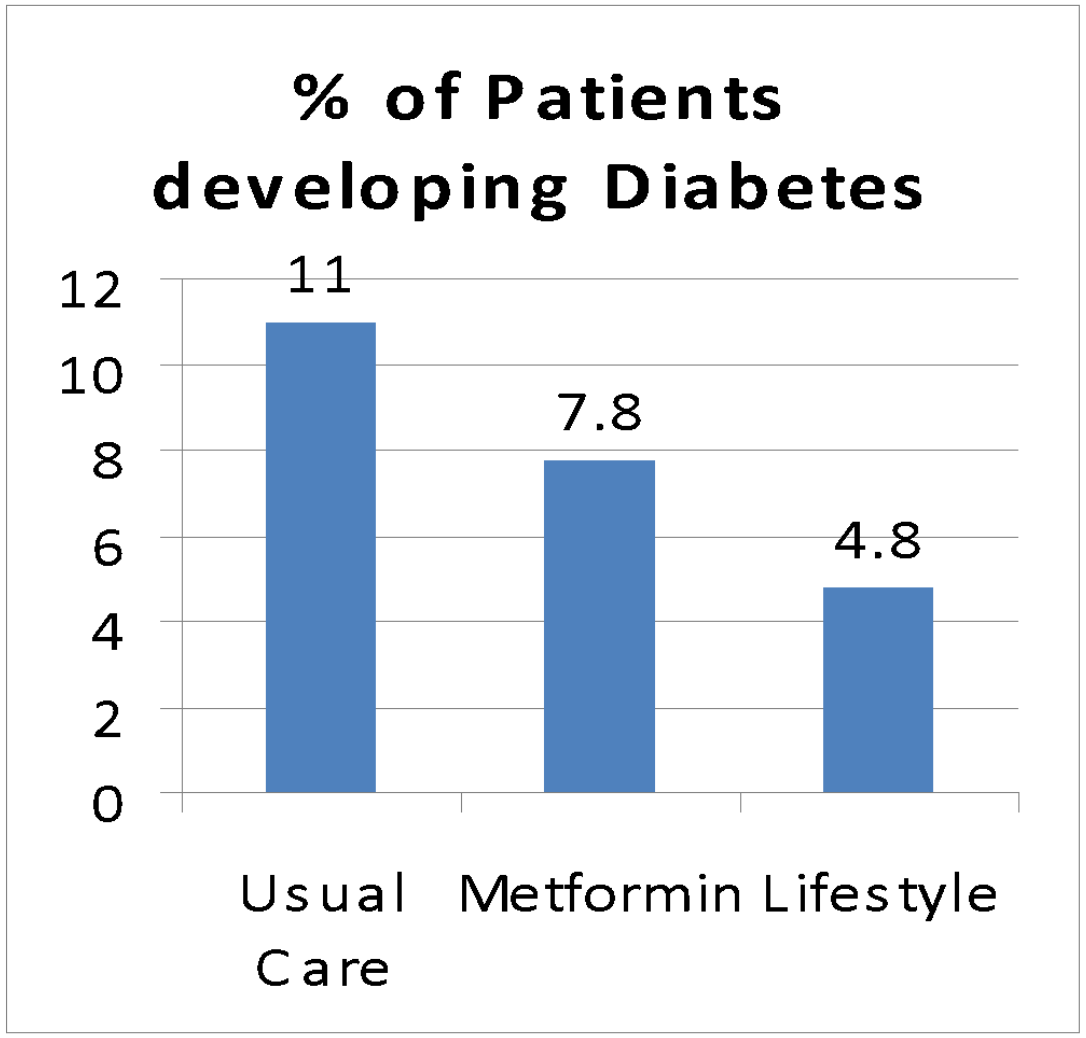
Diabetes Prevention Program

- 7% weight loss, 1-2 lb/week
- 500-1000 calories/day
- Physical activity
  - 700 kcal/week:
  - 150 min mod-intensity PA/week
  - at least 3 day/week
- Individual visits
- 16 core sessions in the first 24 wks
  - Calorie reduction
  - Physical activity
  - Self-monitoring
  - Maintaining healthy lifestyle
  - Psychological, social and motivational challenges



Diabetes Prevention Program Research Group. N Engl J Med. 2002;346(6):393-403.

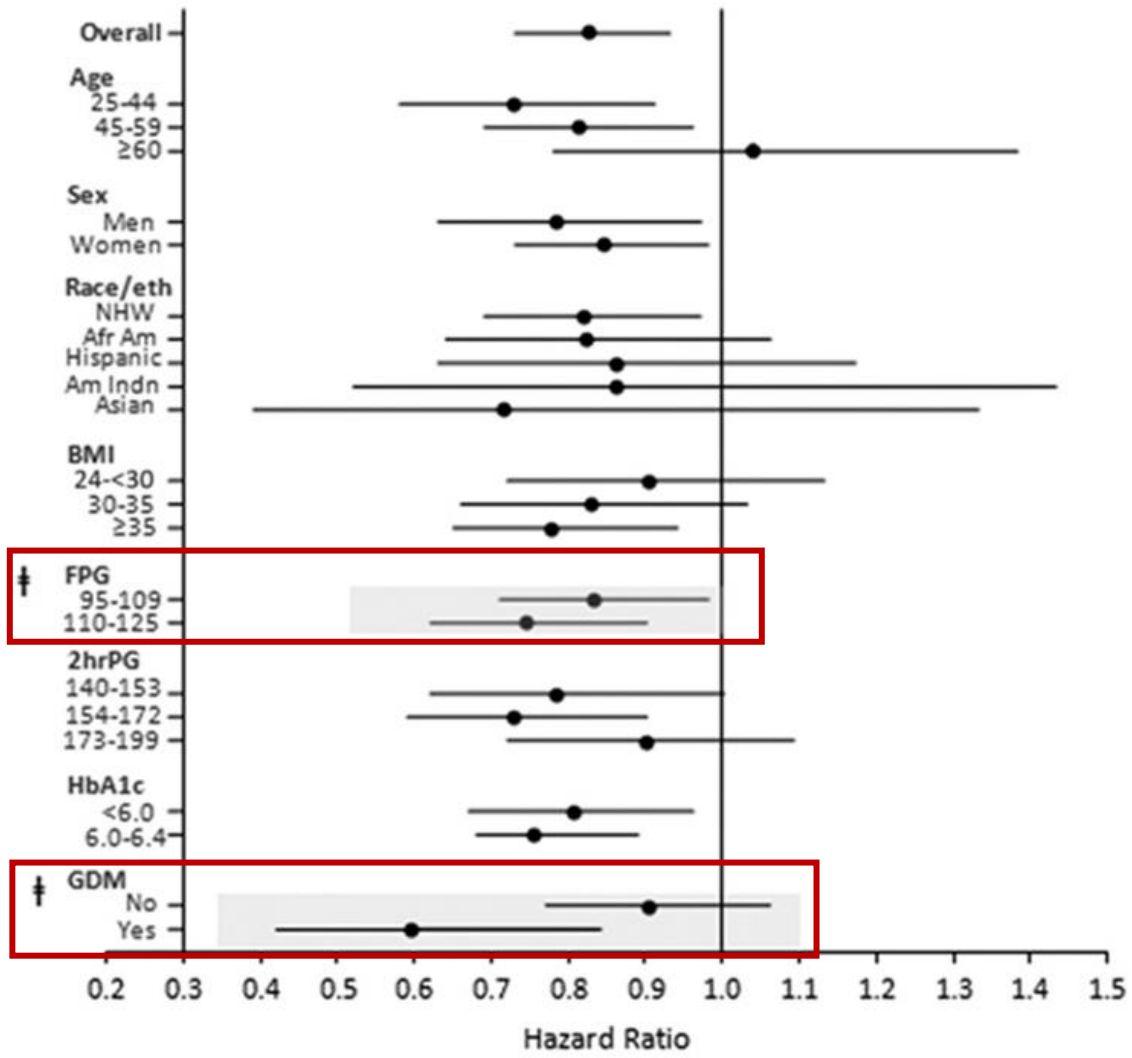
Diabetes Prevention Program



- Study terminated 1 year early
- Outcome correlated with weight loss
- Reduction in DM sustained, though attenuated in lifestyle and metformin groups, at 15 years

N Engl J Med. 2002 Feb 7;346(6):393-403; Lancet Diabetes Endocrinol. 2015 Nov;3(11):866-75.

Effect of Metformin on DPP Subgroups over 15 years

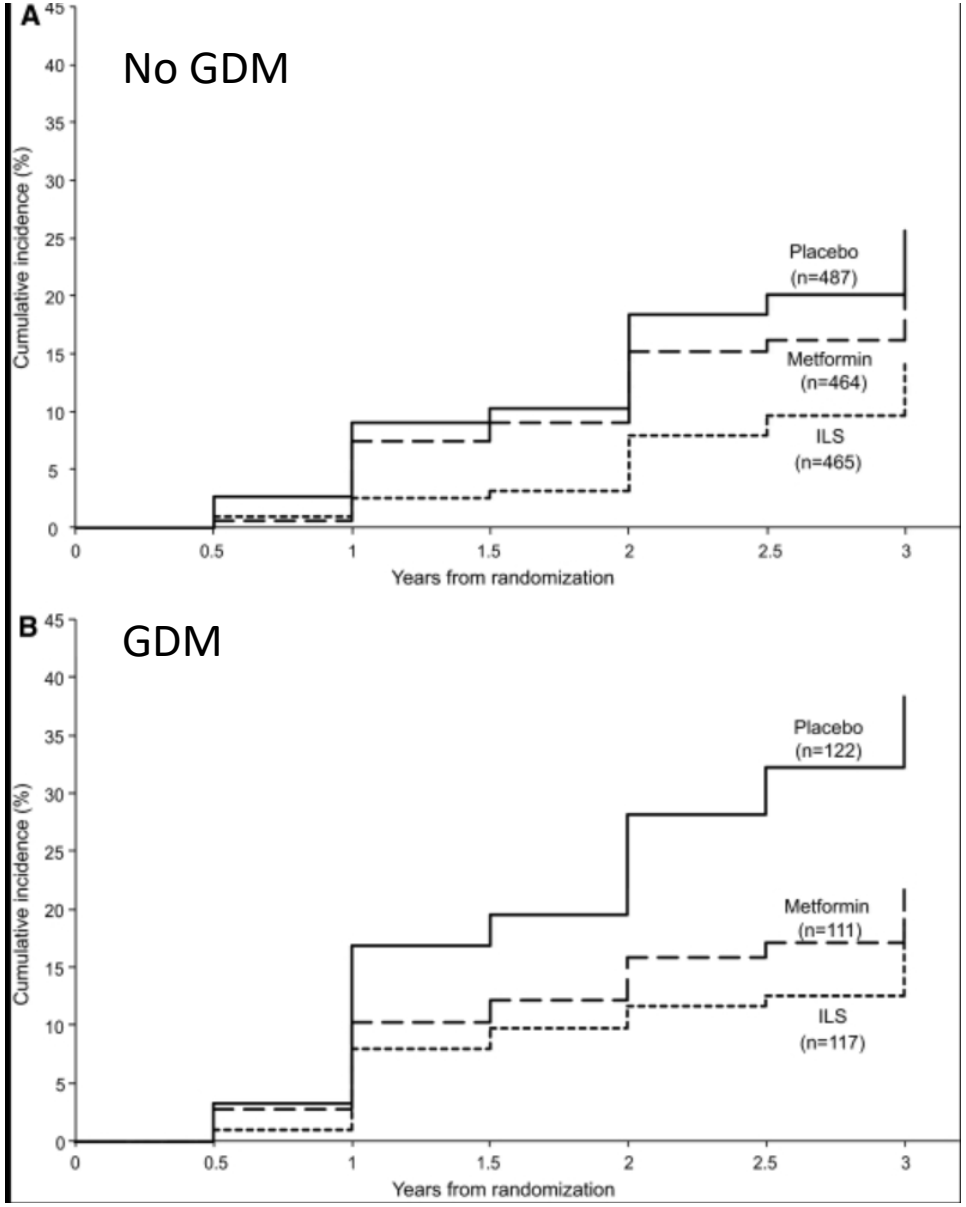


‡FPG-by-treatment interaction $P < 0.001$,
GDM-by-treatment interaction $P = 0.02$.

DPP Research Group. Diabetes Care. 2019 Apr;42(4):601-608.

Benefit of metformin in patients with a history of GDM--DPP

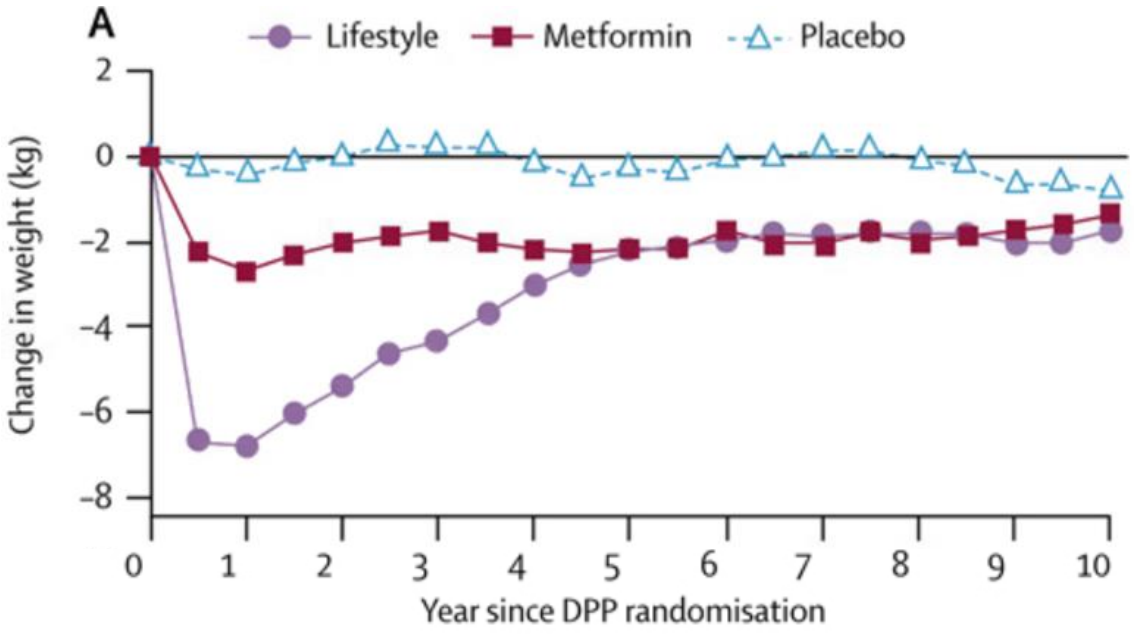
	N	Reduction in DM Incidence	
		Metformin	Intensive Lifestyle
No GDM	1416	14%	49%
GDM	350	50%	50%



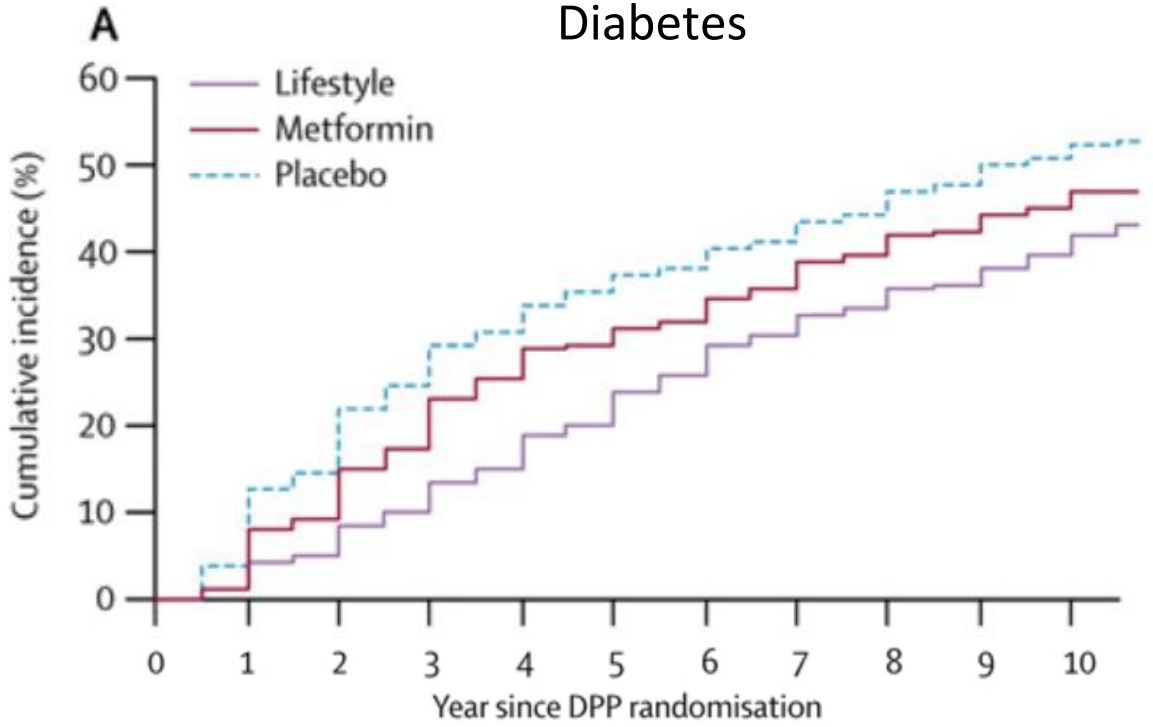
Ratner et al. J Clin Endocrinol Metab. 2008 Dec;93(12):4774-9

Long-term outcomes

Weight



Diabetes



DPP Research Group. Lancet. 2009;374:1677-1686.

ADA Recommendations

Diet

- Individualized macronutrient content based upon current eating patterns, preferences, metabolic goals
  - Mediterranean
  - Low carb
  - Vegetarian
  - DASH
- Emphasis on whole grains, legumes, nuts, fruits, vegetables
- Minimal refined/processed foods

Physical Activity

- Reduced incidence of T2D by 44% even without weight loss
- Regimen may include resistance training
- Break up sedentary time

American Diabetes Association. 3. Prevention or Delay of Type 2 Diabetes: Standards of Medical Care in Diabetes-2023. Diabetes Care. 2023 Jan;46(Suppl 1):S49-S67.

DPP-translation

- DPP and DPPOS
  - Intensive lifestyle change was cost effective
  - Metformin was cost-saving
- Numerous intervention programs
  - CDC National DPP: online resources, certification
  - CMS coverage of CDC certified programs
  - YMCA
  - State-wide initiatives
- Group delivery
- Community or primary care settings

Long-term retention

- Community health workers or coach
- Peer or lay-led support groups
- Individualized MNT
- CDCES
- Technology assisted programs: web, smartphone, telehealth

American Diabetes Association. 3. Prevention or Delay of Type 2 Diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care. 2021 Jan;44(Suppl 1):S34-S39.

Ann Intern Med 2005;142:323-332

Metformin for DM Prevention

- No drug has been FDA approved for DM prevention
- Metformin should especially be considered if
  - Very high risk:
    - IGT + IFG
  - BMI ≥35 kg/m^2
  - <60 years of age
  - Prior GDM
- Follow-up OGTT in 1274 patients ~11 days after stopping metformin demonstrated that 75% of the benefit persisted suggests “true benefit” (?persistence)
- More extensive studies of this type needed using **CGM** to assess AGP transitions

American Diabetes Association. Diabetes Care. 2021 Jan;44(Suppl 1):S34-S39.

DPP Research Group. Diabetes Care. 2003;26(4):977

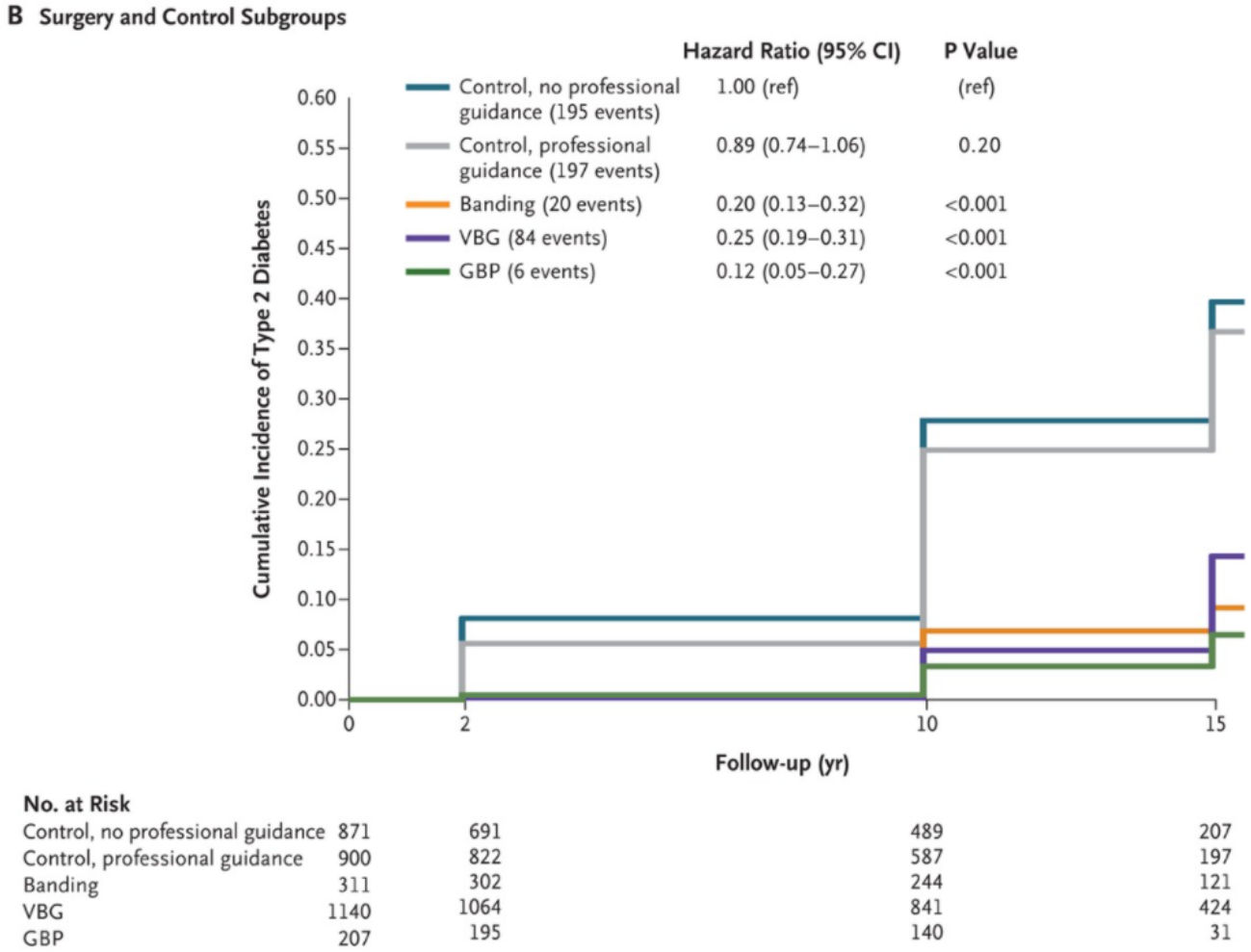
Other medications for DM Prevention

Trial	Intervention	Follow-up (years)	Reduction in Risk of T2D (vs placebo)	Considerations
Antihyperglycemic agents				
DPP[1]	Metformin	2.8	31% (P<0.001)	GI side effects
STOP-NIDDM[2]	Acarbose	3.3	25% (P=0.0015)	GI side effects, taken 3x/day
ACT-NOW[3]	Pioglitazone	2.4	72% (P<0.001)	Weight gain, edema, fracture risk
DREAM[4]	Rosiglitazone	3.0	60% (P<0.0001)	Weight gain, edema, fracture risk, increased LDLc
SCALE[5]	Liraglutide	3	66%	GI side effects

1. DPP Research Group. N Engl J Med. 2002;346:393-403. 2. STOP-NIDDM Trial Research Group. Lancet. 2002;359:2072-2077. 3. Defronzo RA, et al. N Engl J Med. 2011;364:1104-15. 4. DREAM Trial Investigators. Lancet. 2006;368:1096-1105. 5. Le Roux et al. Lancet. 2017 Apr 8;389(10077):1399-1409. 6. Torgerson JS, et al. Diabetes Care. 2004;27:155-161. 7. Garvey WT, et al. Diabetes Care. 2014;37:912-921. 8. Sjostrom L, et al. N Engl J Med. 2004;351:2683-2693. 8.

Bariatric surgery for prevention of diabetes

- Swedish Obese Subjects trial[1]
  - Non-randomized trial initiated in 1987
  - N=4047, 2010 of whom underwent surgery (band, gastroplasty, or bypass)
  - 36% loss to follow-up at 15 years
  - Extent of weight loss is more important than weight-independent effects of GBP on glucose metabolism long-term[2]



1. Carlsson LM, et al. N Engl J Med. 2012;367:695-704.

2. Sjolholm et al. Diabetes Care. 2016;39(4):625-31

Other Considerations

- Prediabetes is not a “disease” in its own right but increases the risk of DM and CVD. Thus there is a need to address other CV risk factors
  - HTN
  - Dyslipidemia
  - Tobacco use
- Co-morbidities of interest in setting of PDM
  - OSA
  - NAFLD/NASH

American Diabetes Association. Diabetes Care. 2023 Jan;46(Suppl 1):S24-S25. Cuthbertson DJ et al. Ann Med. 2021 July; 53(1):1256-1264.

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Screening/Diagnosis

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Who to screen for T2D?

- >35 years old

Or

Overweight or obese adults with 1 or more risk factors:

- High risk ethnicity
- 1st degree relative with DM
- CVD
- GDM or baby > 9 lbs
- HTN
- HDL <35 mg/dl
- TG >250 mg/dl
- PCOS
- Physical inactivity
- Condition associated with insulin resistance (acanthosis nigricans)
- Gestational Diabetes

- *Overweight defined as BMI ≥25 kg/m^2 (≥23 kg/m^2 in Asians)*
- *Repeat screen*
  - *every 3 years if normal*
  - *annually if prediabetes criteria met*

American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2023. Diabetes Care. 2023 Jan;46(Suppl 1):S19-S40.

How Should we Screen?

Method	Normal	Prediabetes	Diabetes
Fasting BG*	<100 mg/dl	100-125 mg/dl	≥126 mg/dl
2 hr OGTT (75 gm)#	<140 mg/dl	140-199 mg/dl	≥200 mg/dl
HbA1c	<5.7%	5.7-6.4%	≥6.5%
Random BG	-	-	Symptoms of DM & random serum BG ≥ 200 mg/dl

*In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate test samples.

Recommendation: Refer people with prediabetes and overweight/obesity to an intensive lifestyle intervention program such as the Diabetes Prevention Program (DPP) and/or to individualized MNT.

American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2023. Diabetes Care. 2023 Jan;46(Suppl 1):S19-S40.

Sensitivity and Specificity of diagnostic tests

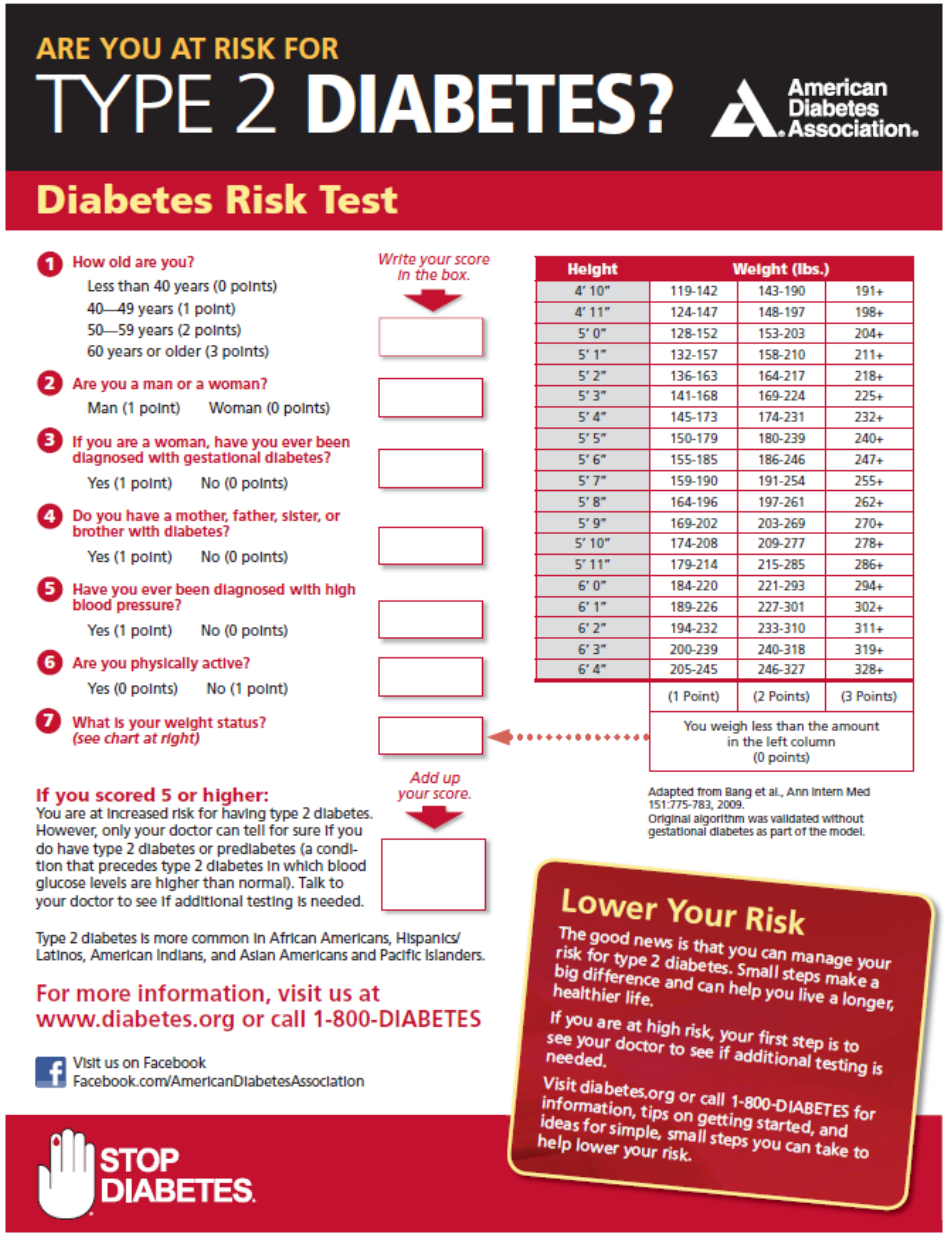
	# Publications	Threshold	Sensitivity	Specificity	Optimal threshold	Sn/Sp at optimal threshold
HbA1c	17	6.5%	50%	97.3%	6.03	Sn 73.9%, Sp 87.2%
Fasting glucose	10	126 mg/dl	59.4%	98.8%	104 mg/dl	Sn 82.3%, Sp 89.4%

Meta-analysis of 37 manuscripts
Vs. gold standard 75-gm OOGTT

Kaur et al. PLoS One. 2020 Nov 20;15(11):e0242415.

Comparison of diagnostic tests

	Pros	Cons
Fasting glucose	Inexpensive	Requires fasting Diurnal variation Affected by duration of fast, exercise, acute stress Within person variability
HbA1c	No need to fast Correlates better than OGTT with retinopathy Good standardization	Difficult to interpret with ↑/↓ RBC turnover or hemoglobinopathies
OGTT	Most sensitive test	Inconvenient Can cause gastrointestinal symptoms Standardized conditions recommended



http://www.diabetes.org/socrisktest

DM Screening: *Special Clinical Circumstances*

	Frequency	Method
Cystic Fibrosis	Annual starting age 10	OGTT (A1c not recommended)
Post-transplant DM	When on stable immunosuppressive regimen, free of infection	OGTT preferred
HIV	Before and 3-6 mo after starting antiretroviral therapy, annual	FBG
Youth: ≥85% body weight + ≥1 risk factors*	Starting after onset of puberty or age 10 years Repeat at every 3 years	

*maternal history of DM or GDM during child's gestation, family history in first degree relative, high risk race/ethnicity, features of insulin resistance or metabolic syndrome

American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2023. Diabetes Care. 2023 Jan;46(Suppl 1):S28-S32.

Gestational Diabetes

	One-step (IADPSG)	Two-step (NIH)	
Method	75-g OGTT at 24-28 weeks	50-g GLT (nonfasting) at 24-28 weeks followed by 100-g OGTT if 1h glucose ≥140 mg/dl (ACOG criteria: 135 mg/dl)	
Criteria	Fasting: ≥92 mg/dl 1h: ≥180 mg/dl 2h: ≥153 md/gl	Diagnosis made if ≥2 of the following are met	
		Carpenter/Coustan Fasting: 95 mg/dl 1h: 180 mg/dl 2h: 155 mg/dl 3h 140 mg/dl	**NDDG** Fasting: 105 mg/dl 1h: 190 mg/dl 2h: 165 mg/dl 3h: 145 mg/dl

IADPSG: International Association of the Diabetes and Pregnancy Study Groups
NIH=National Institutes of Health
OGTT: Oral glucose tolerance test
GLT=glucose load test
ACOG: American College of Obstetricians and Gynecologists
NDDG: National Diabetes Data Group

American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2023. Diabetes Care. 2023 Jan;46(Suppl 1):S32-S35.

Classification of Diabetes

- Type 1 diabetes (T1D): autoimmune β-cell destruction usually leading to absolute insulin deficiency
- Type 2 diabetes (T2D): due to progressive loss of β-cell function frequently in conjunction with insulin resistance
- Other
  - *Monogenic diabetes*
  - *Exocrine pancreas*
  - *Drug-induced*
  - *Secondary*
- Gestational DM (GDM): DM diagnosed in 2nd or 3rd trimester when not clearly present prior to pregnancy

American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2023. Diabetes Care. 2023 Jan;46(Suppl 1):S19-S37.

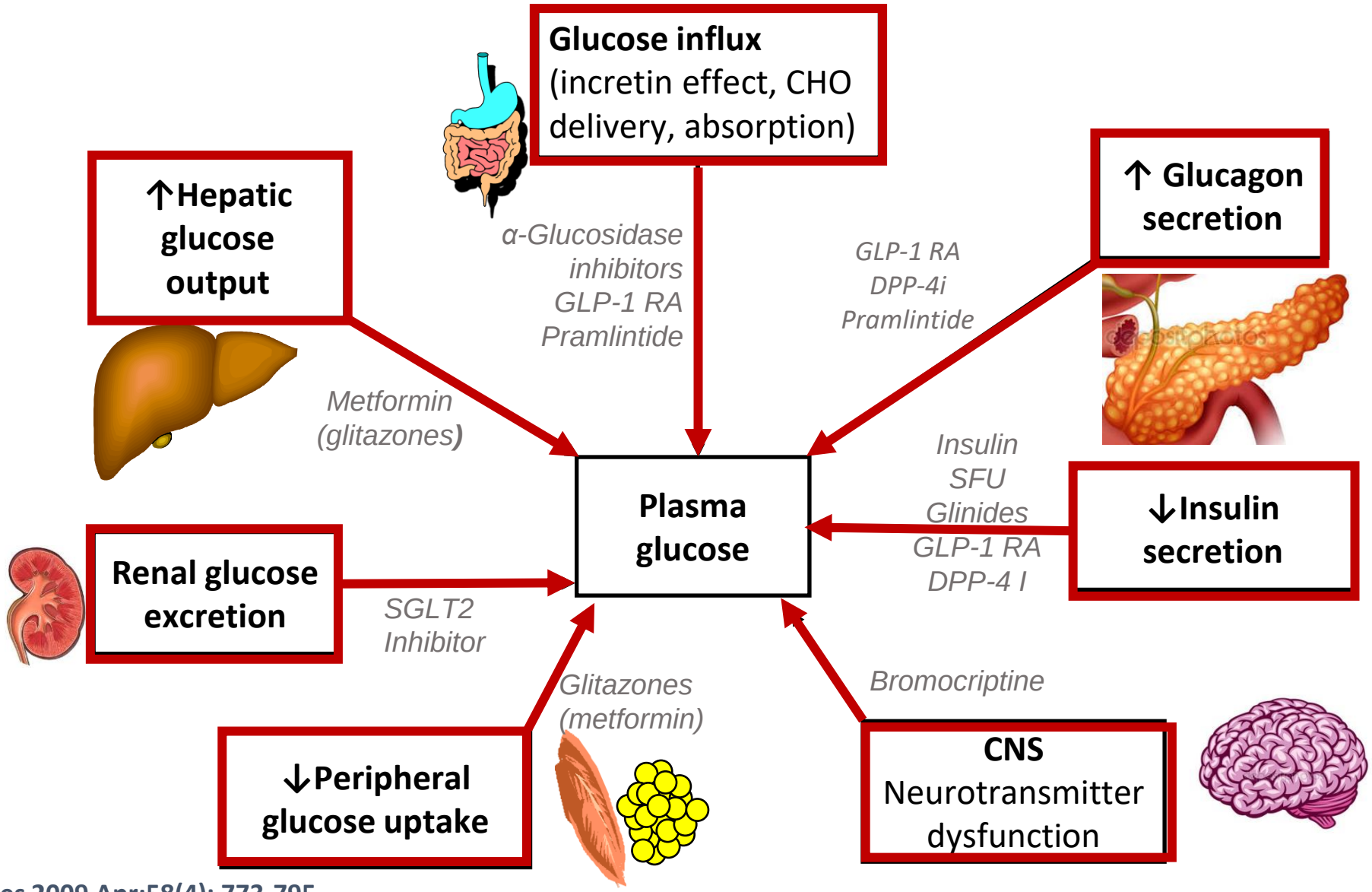
Classification of DM

	T1D	"LADA"	T2D	MODY
Age	Tend to be young	>age 25	Tend to be adult	<age 25
Family history	Occasional	Occasional	Usually	Yes
C-peptide	Low, often undetectable	Varies	Normal or high	normal
Auto-ab	+	+	-	-
Weight	Tend to be lean	Tend to be lean	Usually overweight	Tend to be lean
Metabolic syndrome	No	Varies	Usually	No
Insulin requirement	Yes	Varies, rapid progression	Varies	Varies

Andersen MK. Curr Diab Rep. 2020 Jul 28;20(9):43.

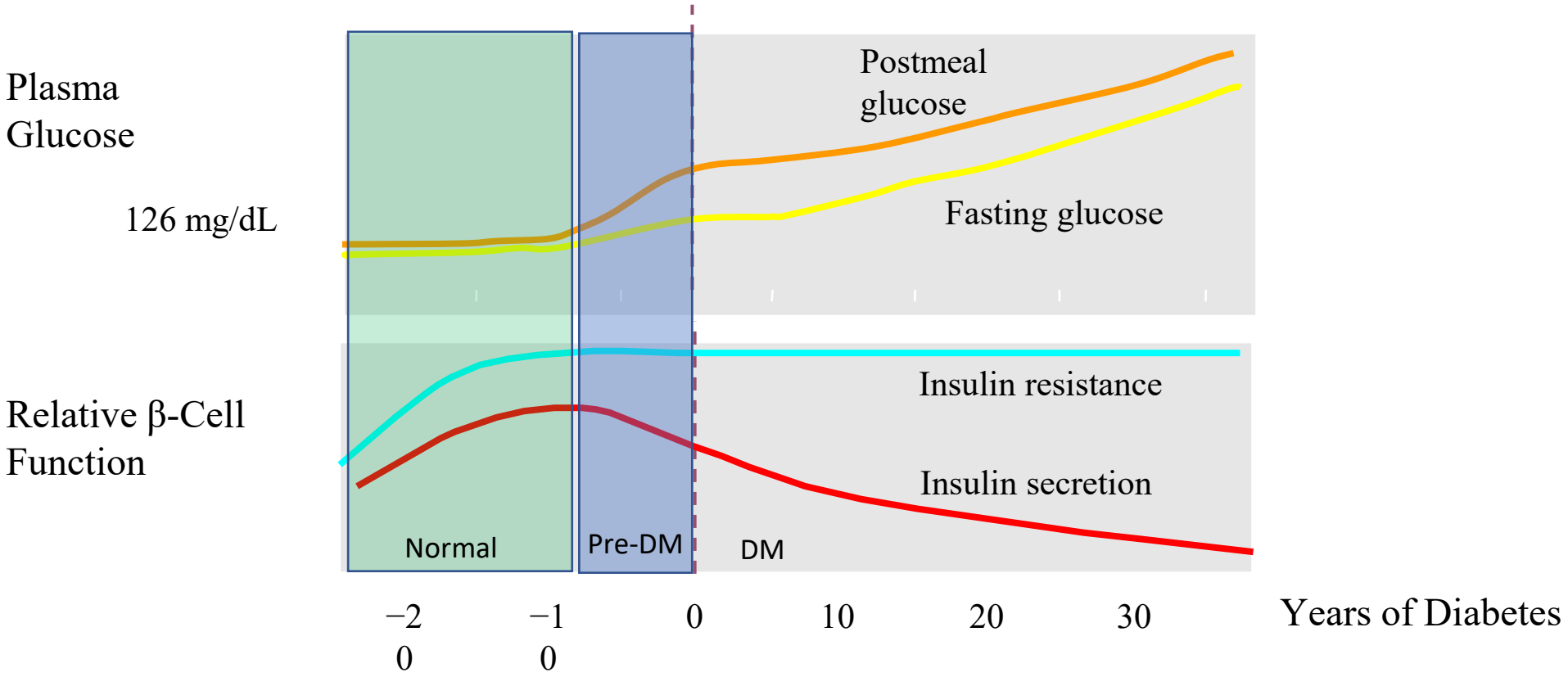
ADA. Diabetes Care. 2023 Jan;46(Suppl 1):S19-S40

T2D: Multiple Pathophysiologic Abnormalities



DeFronzo RA. Diabetes 2009 Apr;58(4): 773-795

Natural History of T2D



- Loss of beta cell function begins before diagnosis and progresses
- Insulin resistance does not change over time

Adapted from International Diabetes Center (IDC). Minneapolis, Minnesota.

Staging of type 1 diabetes

	Stage 1	Stage 2	Stage 3
Autoimmunity	Multiple autoantibodies Presymptomatic	Multiple autoantibodies Presymptomatic	Multiple autoantibodies (AA may become absent) Symptomatic with overt hyperglycemia
Glucose	Normal	IFG and/or IGT or ≥10% increase in A1c	Diabetes by standard criteria; Symptomatic

Routine screening for Type 1 diabetes is not recommended outside of clinical trials.
Consider referring first degree relatives of persons with T1D to clinical trials.

American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2023. Diabetes Care. 2023 Jan;46(Suppl 1):S20-S21.

Definition of LADA

- “LADA” accounts for 2-12% of adult onset diabetes and present as a spectrum of phenotypes from type 1 to type 2 diabetes.
- WHO: slowly evolving immune-mediated diabetes of adults, in the category of hybrid forms of diabetes
- ADA:
  - included under T1D
  - Use of “LADA” valuable to heighten awareness and rapid need for insulin

WHO, Classification of diabetes mellitus 2019. https://www.who.int/publications-detail/classification-of-diabetes-mellitus.

Buzzetti R, et al. Diabetes. 2020 Oct;69(10):2037-2047.

ADA. Diabetes Care. 2023 Jan;46(Suppl 1):S20.

LADA: Diagnostic approach

- A consensus panel recommended GADA testing in all patients with newly diagnosed DM, particularly
  - family history of T1D or autoimmune diseases
  - normal/slightly overweight BMI
  - young age at onset (<60 years)
  - poor metabolic control.
- ADA: Consider testing GADA in adults without traditional risk factors for T2D and/or younger age

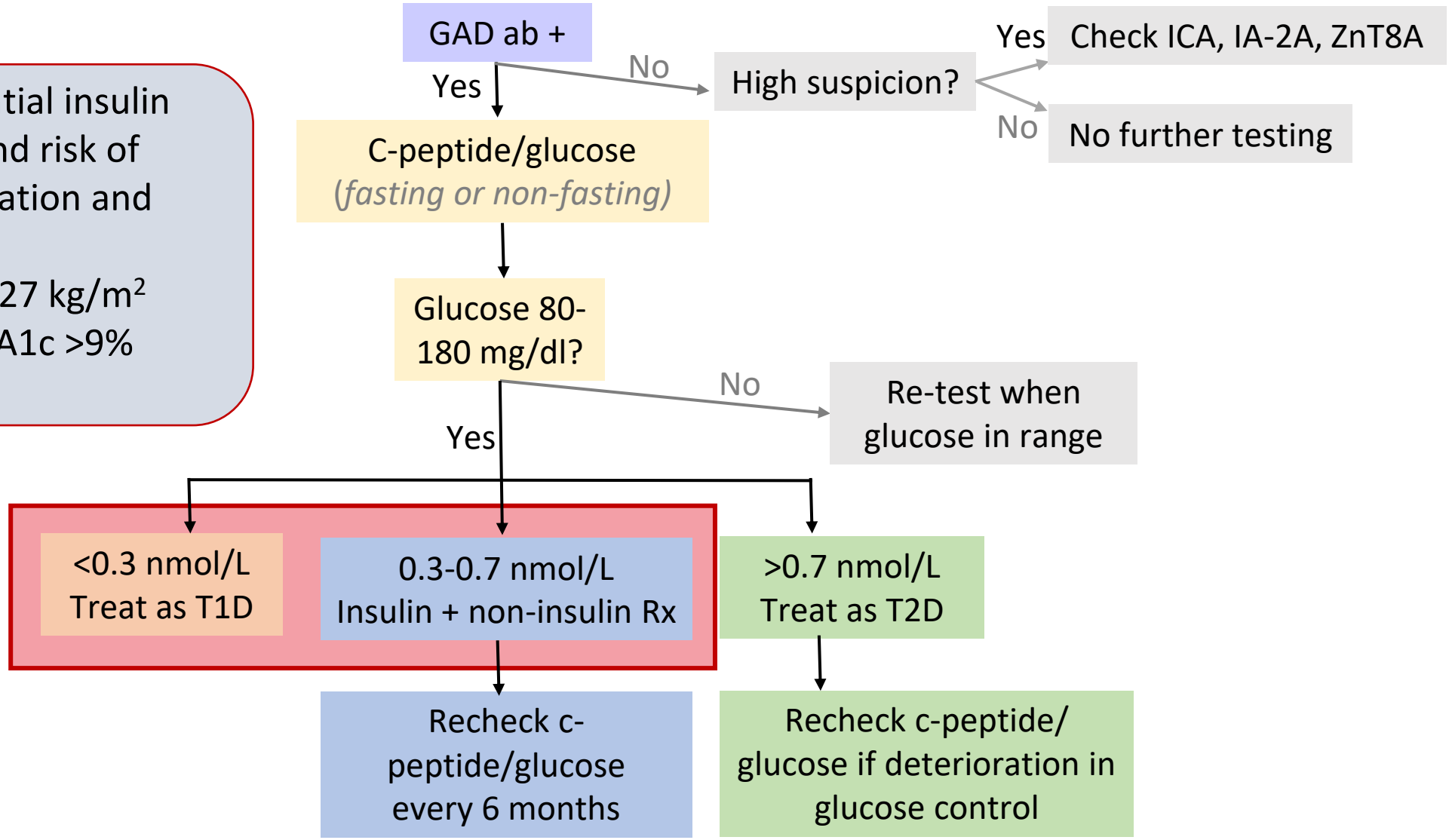
Buzzetti R, et al. Diabetes. 2020 Oct;69(10):2037-2047.

ADA. Diabetes Care. 2023 Jan;46(Suppl 1):S20.

LADA: Therapeutic Approach

- Consider potential insulin requirement and risk of future deterioration and ketoacidosis
- SGLT2i if BMI >27 kg/m^2
- Basal insulin if A1c >9%
- Avoid SU

LADA Algorithm



Buzzetti R, et al. Management of Latent Autoimmune Diabetes in Adults: A Consensus Statement From an International Expert Panel. Diabetes. 2020 Oct;69(10):2037-2047.

Monogenic diabetes

- Most cases of monogenic diabetes remain misdiagnosed
- Includes neonatal diabetes and Maturity onset diabetes of youth (MODY)
- Defects in β-cell function
- Autosomal dominant
- Consider in adults:
  - Dx <25 years of age
  - Normal BMI
  - 1st degree relative with DM
  - Negative auto-ab
  - Normal c-peptide
- Online risk calculator

Chung WK, et al. Precision Medicine in Diabetes: A Consensus Report From the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2020;43(7):1617-1635.

Monogenic diabetes

Common Name	Gene/mechanism	% of MODY	Chromosome	Clinical features
MODY 1	HNF-4α	5	20	Initial response to SFU but progressive May be LGA and neonatal hypoglycemia Risk for complications
MODY 2	Glucokinase gene	30-50	7	Increased threshold for glucose stimulated insulin secretion Mild fasting hyperglycemia
MODY 3	HNF-1α	30-50	12	Low renal threshold for glucosuria, ↑PPG Very sensitive to SFU Risk for complications
MODY 4	Insulin promoter factor (IPF-1)	<1	13	Mean age 35 at diagnosis
MODY 5	HNF-1β	5	17	Pancreatic atrophy Renal abnormalities Hypomagnesemia
MODY 6	NeuroD1	<1	2	Similar to T2D, overweight/obese
MODY 7	Carboxyl ester lipase	<1	9	

Baldacchino et al. Prim Care Diabetes. 2020;14(1):1-11.

Neonatal DM

Common Name	Gene/mechanism	Clinical features
Transient	ZAC/HYAMI imprinting	Dx in first 6 months of life
Permanent	Kir6.2 subunit of the β-cell K_{ATP} channel	Dx in first 6 months of life Very sensitive to SFU

Chung et al. Diabetes Care. 2020 Jul;43(7):1617-1635.

Other genetic disorders

- Other beta cell defects
  - SUR1: hyperinsulinemia in childhood, β-cell dysfunction in adult
  - Point mutation in mitochondrial DNA
  - Others: Proinsulin conversion, mutant insulin
- Defects in insulin action
  - Type A insulin resistance (insulin receptor gene)
  - Leprechaunism
  - Rabson-mendenhall
  - Lipodystrophy
- Defects in mitochondrial DNA
  - Maternally inherited diabetes and deafness: conduction defects, proteinuria, neuropathy
- Wolfram syndrome (DIDMOAD: diabetes insipidus, diabetes mellitus, optic atrophy, deafness): AR, wolframin protein

- Genetic syndromes sometimes associated with DM
  - Down
  - Klinefelter
  - Turner
  - Friedreich ataxia
  - Huntington chorea
  - Laurence-Moon Biedl
  - Myotonic dystrophy
  - Porphyria
  - Prader-Willi

American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2014 Jan;37 Suppl 1:S81-90. doi: 10.2337/dc14-S081. Shi D et al. Obesity Reviews. 2021 July; 22(9): 25-46. https://doi.org/10.1111/obr.13303.

Other disorders associated with diabetes phenotype

- Pancreatogenic (“*Type 3c*”)
  - CF
  - Pancreatitis
  - Pancreatectomy/trauma
  - Hemochromatosis
  - Neoplasia
- Autoimmunity
  - Lipodystrophy
  - Insulin antibodies
  - Insulin receptor antibodies
  - Stiff man syndrome
- Endocrinopathy
  - Cushings syndrome/disease
  - acromegaly
  - Pheochromocytoma
  - Glucagonoma
  - Somatostatinoma
  - Thyrotoxicosis

American Diabetes Association. Diabetes Care. 2014 Jan;37 Suppl 1:S81-90. +

Drug or chemical causes or contributors to DM

- Glucocorticoids
- Check-point inhibitor
- Alpelisib
- Vacor
- Pentamidine
- Nicotinic acid
- Statins
- Diazoxide
- Vasopressors
- B-blocker
- Thiazides
- Dilantin
- Gamma-interferon
- Antiretrovirals (Protease inhibitors, NRTIs)
- Anti-psychotics
- Growth hormone
- Immunosuppressants (cyclosporine, siriolimus, tacrolimus)
- Oral contraceptives (>35 mcg ethinyl estradiol)
- Megestrol acetate

American Diabetes Association. Diabetes Care. 2014 Jan;37 Suppl 1:S81-90. ADA. Diabetes Care. 2023 Jan;46(Suppl 1):S28.

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Comprehensive Medical Evaluation

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	Components of Comprehensive Medical Evaluation	Initial	Follow-up	Annual
PMH/FH	• Diabetes history: duration, prior Rx, hospitalizations	X		
	• Family history: 1st degree relative, AI disease	X		
	• Complications/comorbidities	X		
	• Microvascular/macrovascular	X		
	• Hypoglycemia: awareness, frequency, cause/timing	X	X	X
	• Obesity, OSA, hypertension, hyperlipidemia	X		X
	• Visits to specialists: eye, dental	X	X	X
Lifestyle	• Eating pattern and weight	X	X	X
	• Physical activity and sleep	X	X	X
	• Tobacco, alcohol, substance use	X		X
Medications	• Current regimen, behavior, side effects	X	X	X
	• supplements	X	X	X
	• Vaccinations (incl. COVID, Flu, etc.)	X		X
Technology	• Use of health apps, patient portal	X	X	X
	• Glucose monitor: results and use	X		X
Behavioral and Self-management	• Psychosocial			
	• Screen for depression, anxiety, disordered eating	X		X
	• Identify social support	X		X
	• Consider assessing cognition	X		X
	• DMSE: prior use, assess skills/barriers	X	X	X
	• Pregnancy planning	X	X	X
Exam	• BMI, BP	X	X	X
	• Skin: acanthosis nigricans, injection sites, lipodystrophy	X	X	X
	• Foot: visual, pulses, either temp/vib/pinprick + 10-g MF	X	*	X
Laboratory	• A1c (every 3 months)	X	X	X
	• Annual: Lipids, LFT, UMCR, eGFR, vitamin B12 (metformin use), K+	X	#	X^

*Each visit if neuropathy or prior ulcer/amputation
#more often if medication adjustments
^lipids may be less often if normal, not on therapy

ADA. Diabetes Care 2023 Jan; 46(Supplement 1): S51-S62.

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Assessment of Comorbidities - Obesity

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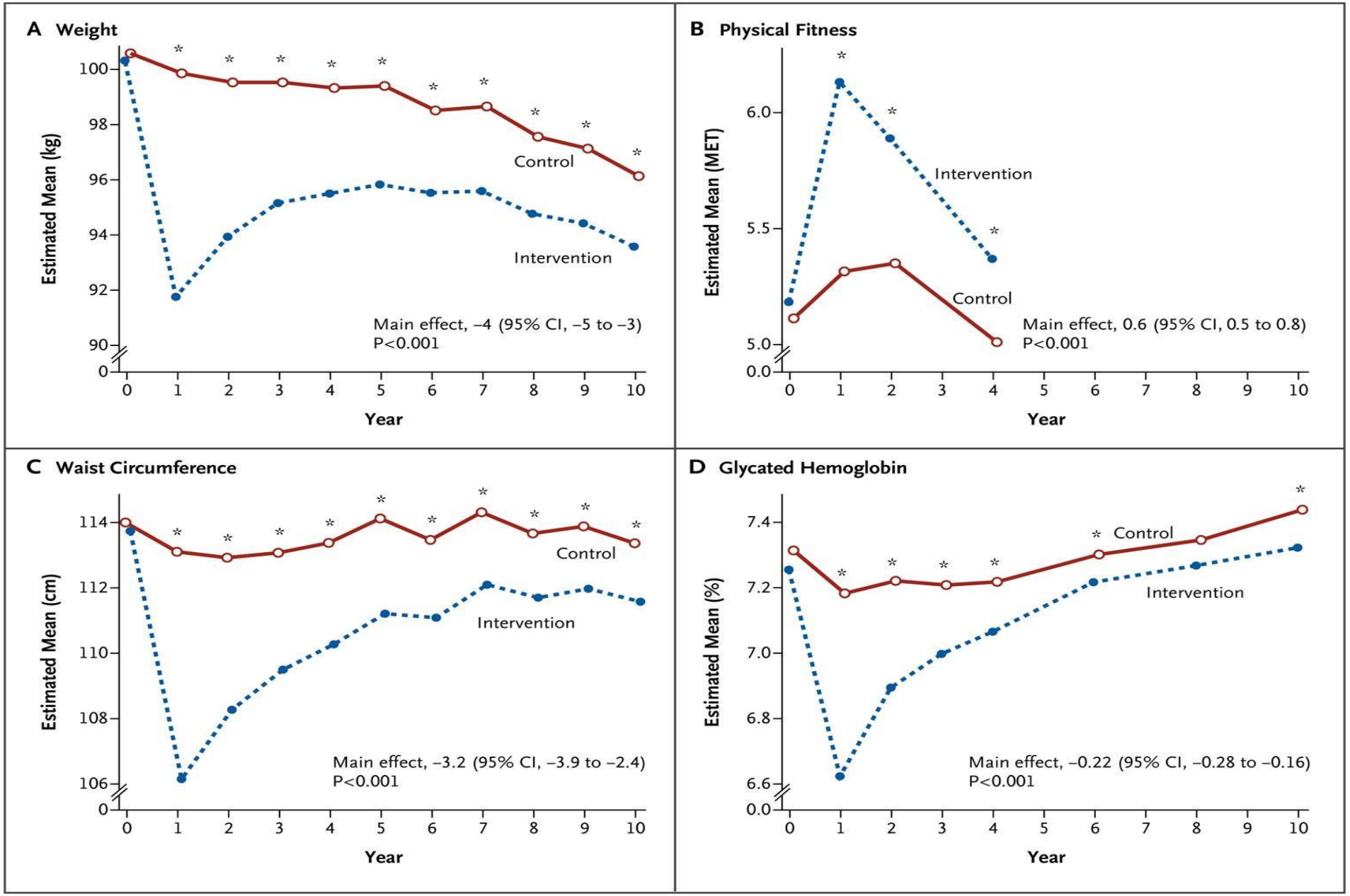
Co-morbid Obesity: LOOK-AHEAD trial

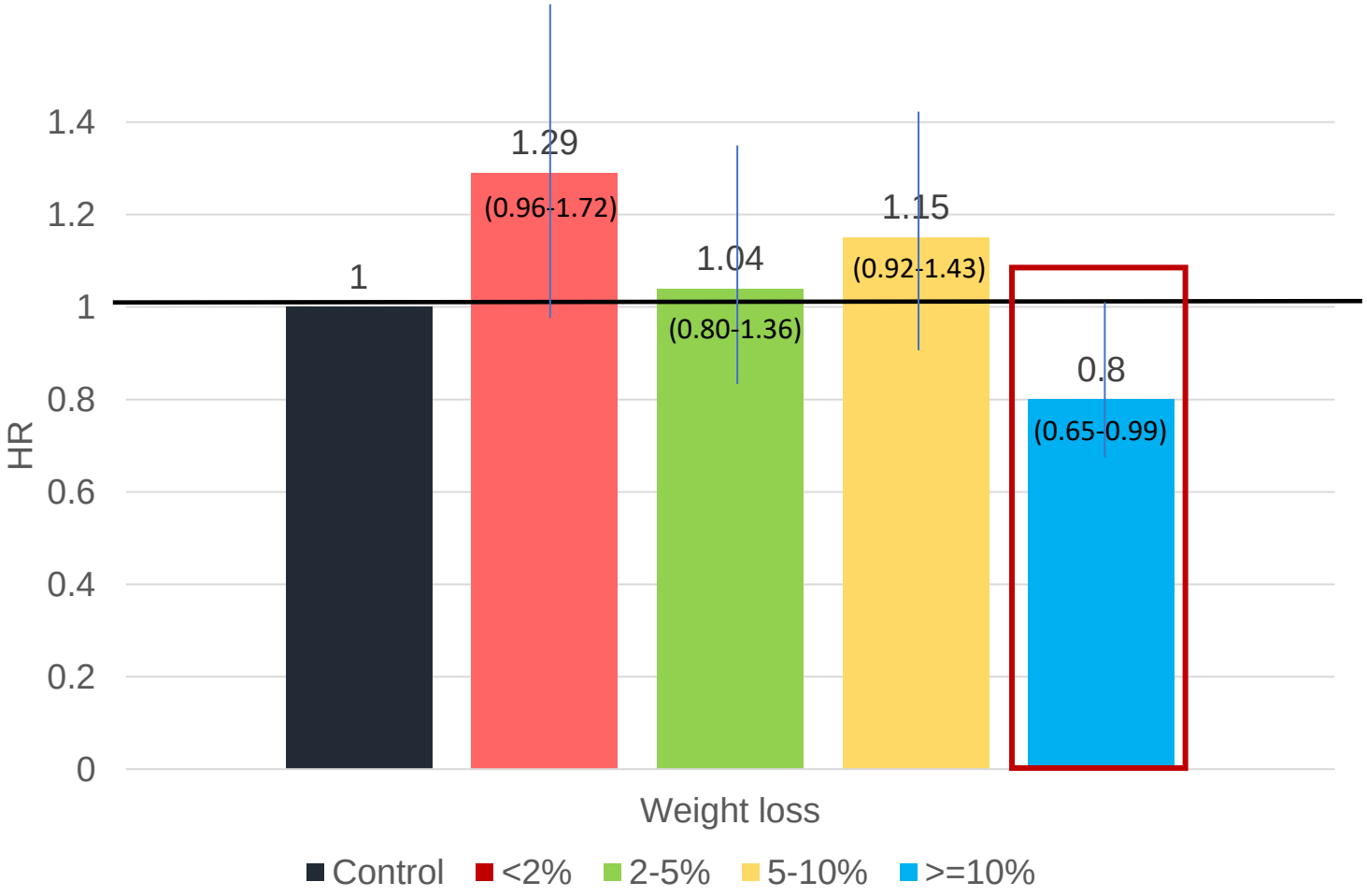
- RCT 5146 patients with T2D
- Intensive lifestyle intervention
  - ✓Weight loss 10%
  - ✓Group and individual counseling weekly over 6 months and decreasing thereafter
  - ✓Goal 1200-1800 kcal/day (30% fat, >15% protein)
  - ✓Meal-replacement products
  - ✓Short-term weight loss medication
  - ✓≥175 minutes of moderate-intensity physical activity/week
- Primary outcome: composite CV death, nonfatal MI, nonfatal stroke or hospitalization for angina
- Trial stopped early based on futility at median 9.6 years
- No significant reduction in CVD events

Look AHEAD Research Group; N Engl J Med. 2013 Jul 11;369(2):145-54.



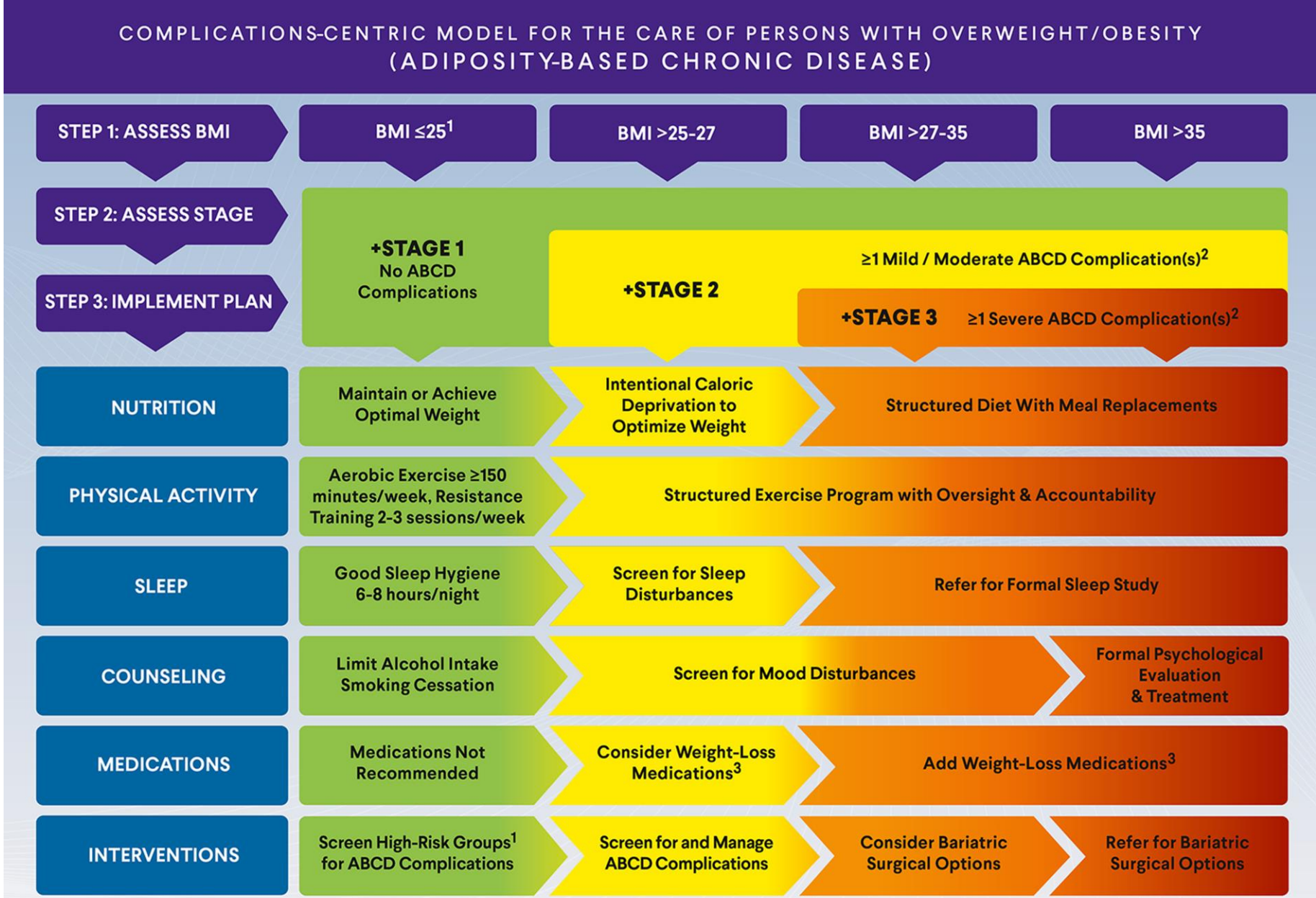
Look AHEAD Research Group; N Engl J Med. 2013 Jul 11;369(2):145-54.

CV events reduced in participants with >10% weight loss



Look AHEAD Research Group. Lancet Diabetes Endocrinol. 2016 Nov;4(11):913-921

Lifestyle Changes for Overweight /Obesity - AACE

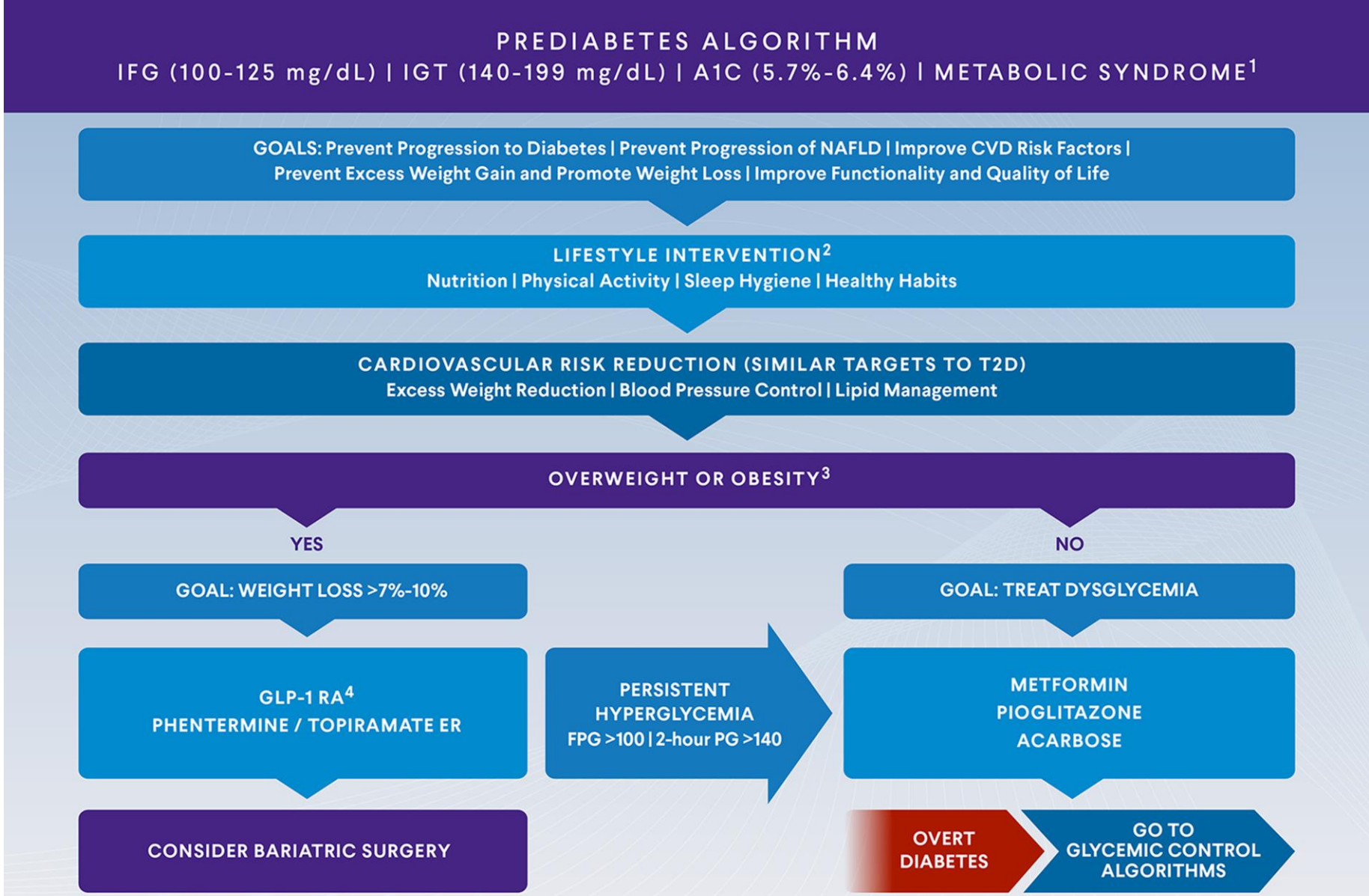


[1]BMI 23 to 25 kg/m^2 may be considered overweight for South Asian, Southeast Asian, and East Asian adults; [2]ABCD complications can include prediabetes, dyslipidemia, hypertension, NAFLD/NASH, ASCVD, CHF and HFpEF, CKD, OSA, OA, asthma/reactive airways disease, GERD, urinary incontinence, PCOS, hypogonadism, and reduced fertility. [3]See PROFILES OF WEIGHT-LOSS MEDICATIONS table.

Algorithm Figure 2-ABCD

AACE Comprehensive Type 2 Diabetes Management Algorithm
Samson SL Endocrine Practice 2023 (29.5): 305-340, doi: 10.1016/j.eprac.2023.02.001

Prediabetes Algorithm - AACE



[1]NCEP ATP III Criteria. [2]See COMPLICATIONS-CENTRIC MODEL FOR THE CARE OF PERSONS WITH OVERWEIGHT/OBESITY. [3]If no overweight or obesity, consider T1D antibody testing for LADA. [4]Indications for weight-loss medications are obesity or overweight BMI >27 kg/m^2 with ABCD complication(s) including prediabetes. Choose GLP-1 RA for approved for weight loss. Also consider other approved weight-loss medications (phentermine [short term], orlistat, naltrexone-ER/bupropion-ER). See also PROFILES OF WEIGHT-LOSS MEDICATIONS table.

Algorithm Figure 3-Prediabetes

AACE Comprehensive Type 2 Diabetes Management Algorithm
Samson SL Endocrine Practice 2023 (29.5): 305-340, doi: 10.1016/j.eprac.2023.02.001

Treatment Options for Overweight and Obesity in T2D

- Nutrition, PA, behavioral counseling for all BMI categories
- Pharmacotherapy*-- BMI 27.0-29.9 (or 25.0-27.4 Asians)
- Metabolic surgery**-- ≥ 30.0 (or ≥27.5 Asians)

*Drugs include Phentermine, Orlistat, combination products (i.e. Phentermine/topiramate ER; Naltrexone/bupropion ER), Liraglutide, Semaglutide, Tirzepatide [not yet approved for wt. loss]

** A variety of medical devices are becoming available for weight loss intervention

American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2023. Diabetes Care. 2023 Jan;46(Suppl 1):S129-S137.

DSMES

- 4 critical times
  - Diagnosis
  - Annually +/- not meeting treatment goals
  - Complicating factors: (health conditions, physical limitations, emotional factors, basic living needs)
  - Transitions in life and care

ADA. Diabetes Care. 2023 Jan;46(Suppl 1):S68-S70.

Association of Diabetes Care & Education

- Core: healthy coping is needed before learning can occur
- Inner ring: basic self-care for all patients
- Monitoring: inform success of inner ring
- Outer ring: behaviors that influence motivation, goal setting, and ability to transform goals into action

Association of Diabetes Care and Education Specialists, Kolb L. An Effective Model of Diabetes Care and Education: The ADCES7 Self-Care Behaviors™. Sci Diabetes Self Manag Care. 2021 Feb;47(1):30-53

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Certified Cardiometabolic Health Professional (CCHP)

Assessment of Comorbidities: Microvascular Complications

James R. Gavin III, MD, PhD
Chief Medical Officer
Healing Our Village, Inc.
Clinical Professor of Medicine
Emory University School of Medicine
Atlanta, GA

UKPDS: Legacy Effect of Earlier Glucose Control

After median 8.5 years post-trial follow-up

N=3277 (out of 4209 originally randomized to intensive vs. standard glucose control)

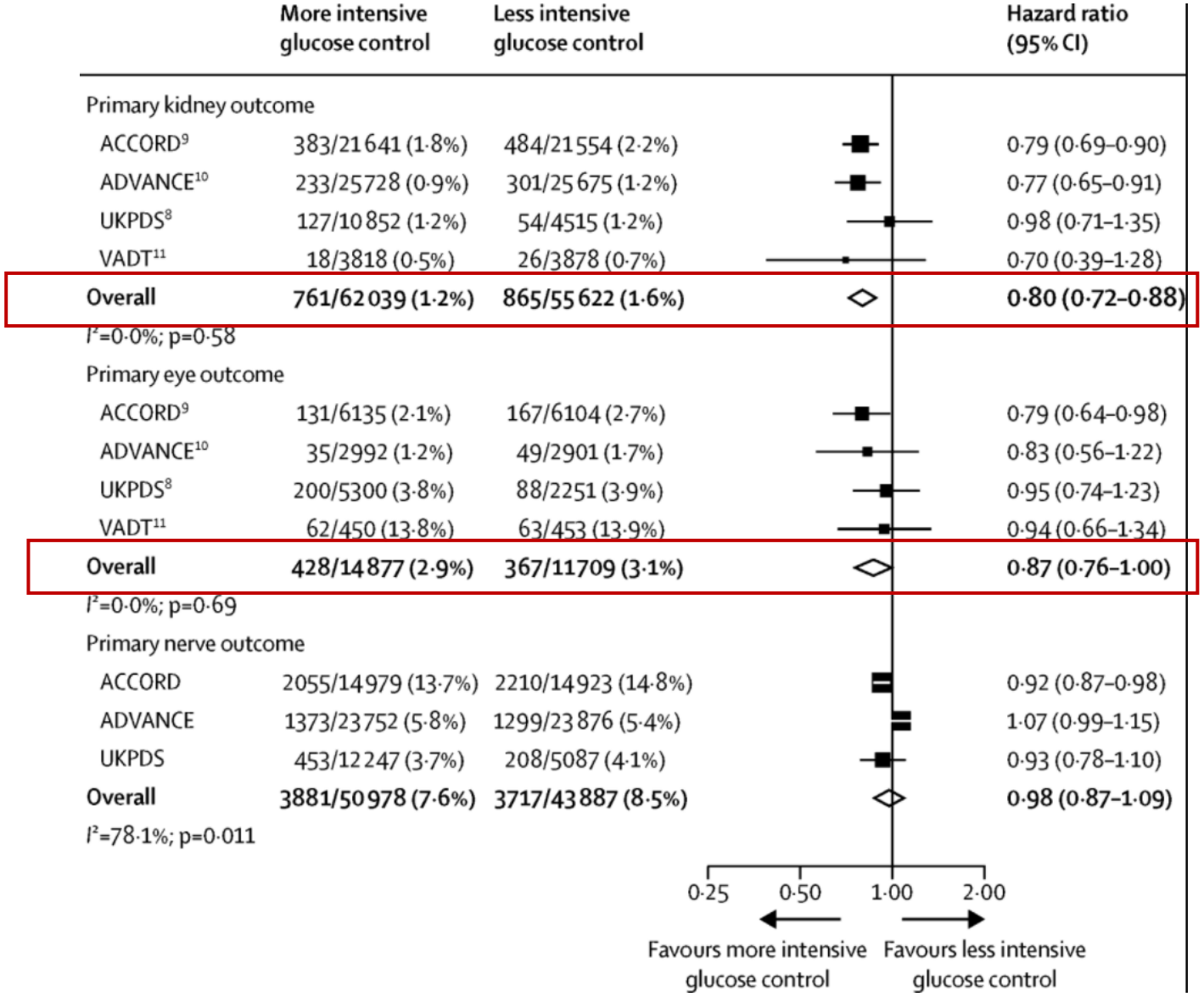
Aggregate Endpoint		1997	2007
Any diabetes related endpoint	*RRR:*	12%	**9%**
P:		0.029	**0.040**
Microvascular disease	*RRR:*	25%	**24%**
P:		0.0099	**0.001**
Myocardial infarction	*RRR:*	6%	**15%**
P:		0.052	**0.014**
All-cause mortality	*RRR:*	6%	**13%**
P:		0.44	**0.007**

Holman et al. N Engl J Med. 2008;359(15):1577-89.

RRR = Relative Risk Reduction, P = Log Rank

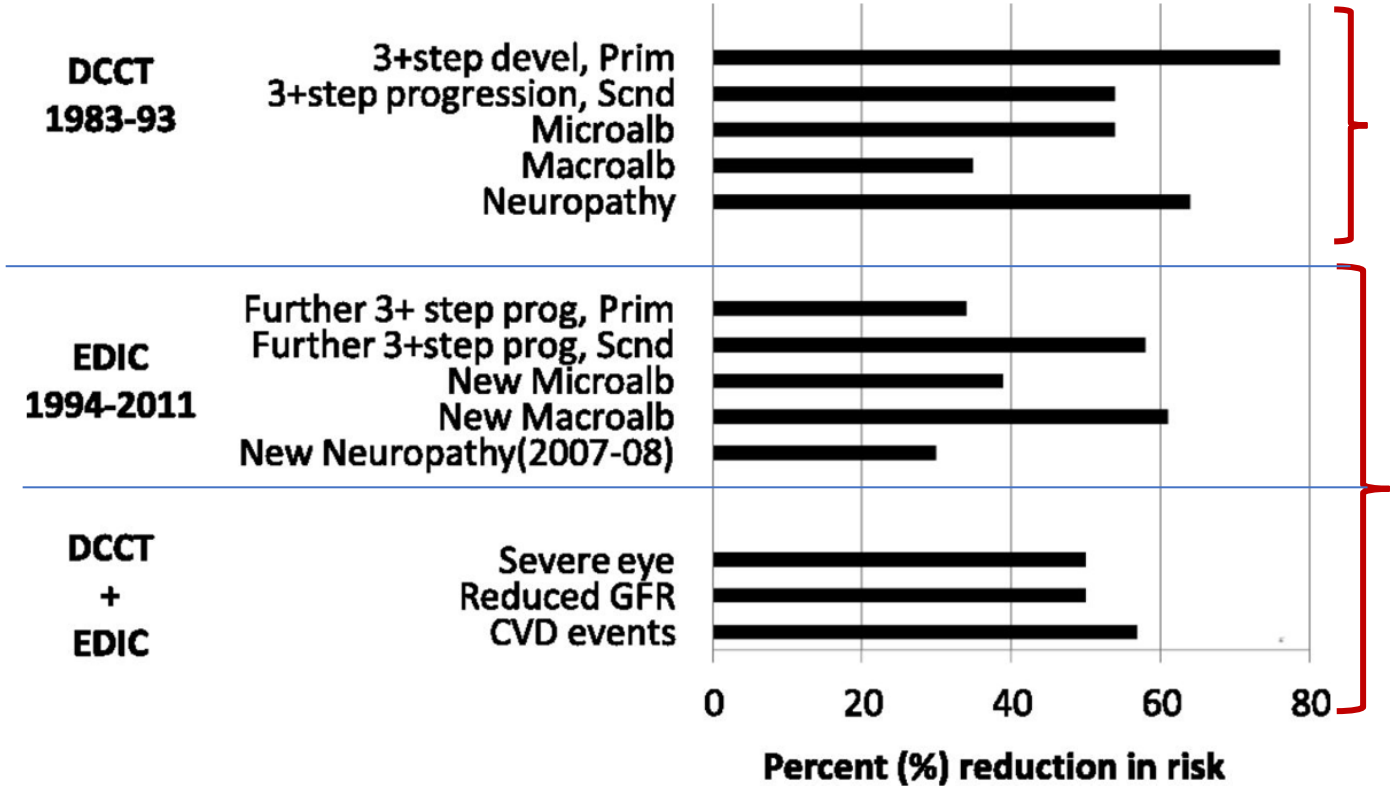
Microvascular Outcomes with Glucose Control in T2D

- Renal outcomes driven by progression to macroalbuminuria



Zoungas et al. Lancet Diabetes Endocrinol. 2017 Jun;5(6):431-437

T1D: Long-term Outcomes of Glucose Control in DCCT-EDIC



DCCT: Randomized study

N=1441, Type 1 diabetes

Intensive: multiple insulin injection (3+/day or pump), BG 70-120 mg/dl premeal, 180 mg/dl post-meal

Conventional: 1-2 injection insulin/day, avoidance of symptoms of hyperglycemia/ hypoglycemia

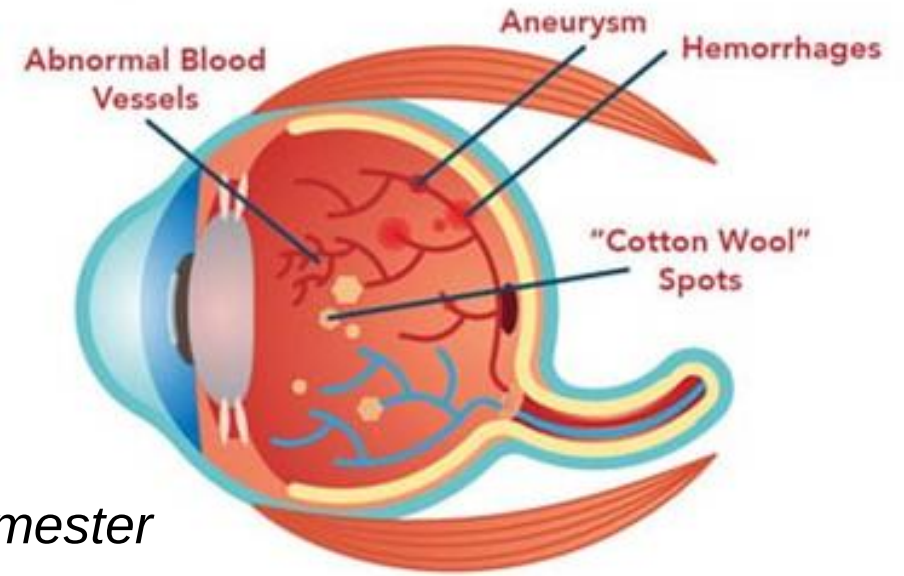
EDIC: Long-term observational follow-up

Demonstrating metabolic memory

Sufficient power to detect difference in CV events did not occur until year 18, with 97% of difference in risk attributable to mean A1c

Nathan et al. Diabetes 2013 Dec; 62(12): 3976-3986.

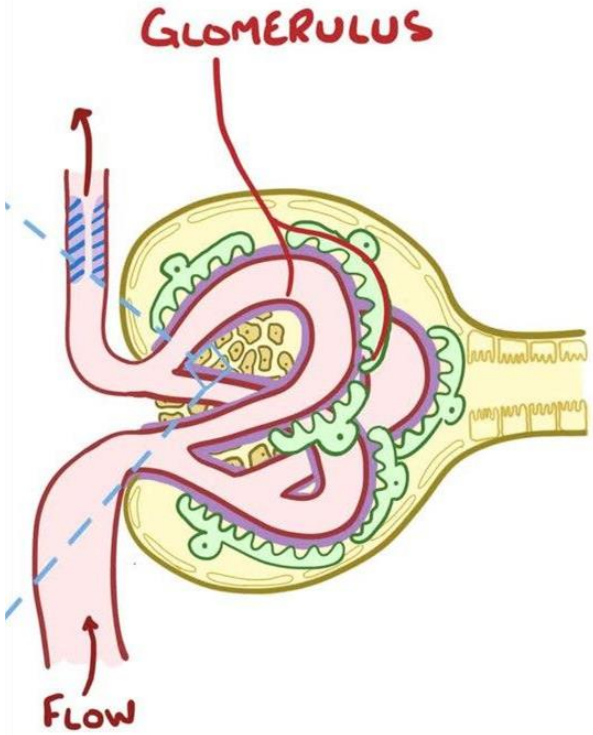
Retinopathy



- Screening: Dilated eye exam
  - *At Dx for T2D, 5 years after diagnosis for T1D*
  - *every 1-2 years if no DR*
  - *annually if +DR*
  - *Before or in first trimester of pregnancy and every trimester*
- Management
  - *Optimize A1c, BP, lipids*
  - *PRP: high risk PDR and some severe NPDR*
  - *Intravitreous EGFR: PDR, central macular edema*

Diabetes Care 2023 Jan; 46(Supplement 1): S204-S205

Nephropathy



- Screening
  - *Annual urine albumin:creatine and eGFR, starting*
    - at diagnosis (T2D)
    - 5 years after diagnosis (T1D)
  - *If UA/cr >30 mg/g or eGFR <50 ml/min/1.73m^2 repeat to confirm*
- Treatment
  - *Optimize BP <140/90 mmHg, <130/80 mmHg now recommended*
  - *ACEI/ARB (do not discontinue for minor change in Creatinine [<30%] in absence of volume depletion)*
  - *eGFR >30 ml/min/1.73m^2, especially if proteinuria consider*
    - SGLT2i (A)
    - GLP1RA (C)
  - *Dietary protein:*
    - Not on HD: 0.8 g/kg/day (RDA)
    - On HD: consider higher intake
  - *Refer to nephrologist if eGFR <30 ml/min/1.73 m^2, rapid progression, or uncertainty in etiology, earlier referrals if albuminuria elevated, regardless of eGFR (per KDIGO heat map)*

Diabetes Care 2023 Jan; 46(Supplement 1): S191-S202

Peripheral Sensory Polyneuropathy (PSPN)

- Assessment
  - *Up to 50% of PSPN is asymptomatic*
  - *Foot exams:*
    - starting at time of Dx of T2D, 5 years after dx of T1D
    - Should include:
      - Temperature or pinprick (small fiber)
      - Vibration (125 Hz tuning fork—large fiber)
    - 10 gm MF: identifies risk for foot ulcer/amputation
  - *Diagnosis of exclusion*
- Management
  - *Foot care/precautions*
  - *Pain:*
    - FDA approved: pregabalin, duloxetine
    - Gabapentin also widely used
    - Tapentadol is FDA approved for PSPN but not recommended first or 2nd line
    - TCA, venlafaxine, carbamazepine, topical capsaicin

Diabetes Care 2023 Jan; 46(Supplement 1): S206-S207

Foot care

- Check your feet every day
- Wash feet (do not soak) daily. Apply lotion but avoid spaces between your toes
- Wear shoes and socks or slippers at all times (check shoes for foreign objects prior to wearing)
- Shoes should fit well
- Trim nails straight across
- Do not remove corns or calluses on your own
- Avoid extreme temperatures: heating pads, electric blankets, space heaters, hot water
- Keep feet dry in cold/rain

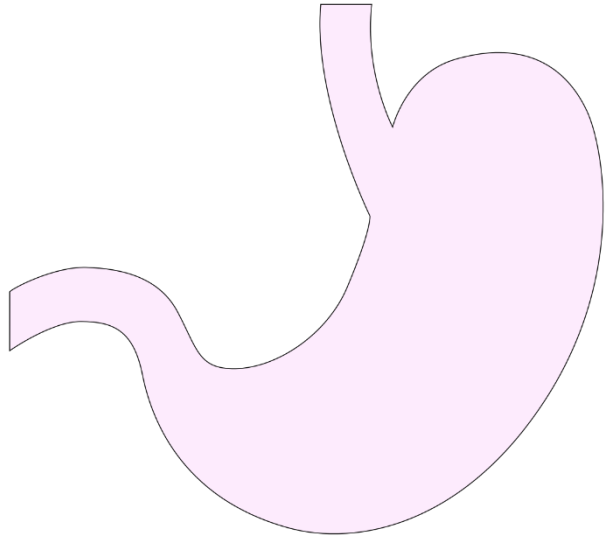
https://www.cdc.gov/diabetes/library/features/healthy-feet.html; Diabetes Care 2023 Jan; 46(Supplement 1): S209-S212

Autonomic neuropathy

- Cardiac AN
  - Associated with ↑ risk of mortality
  - Early: ↓HR variability
  - Late: ↑HR or othostasis (fall in SBP >20 mmHG or DBP >10 mmHg without ↑ HR)
  - Treatment:
    - Salt intake, avoid aggravating medications, compressive garments
    - Medications: midodrine, droxidopa (FDA approved)
    - Supine HTN: short-acting agents at night (guanfacine, clonidine, atenolol, metoprolol, enalapril, isradipine)

Diabetes Care 2023 Jan; 46(Supplement 1): S207

Autonomic neuropathy



- Gastrointestinal
  - Esophageal dysmotility
  - Gastroparesis: may manifest as erratic glucose control
    - Diet: low fiber, low fat, small frequent meals
    - Discontinue aggravating meds: opioids, anticholinergics, TCA, GLP-1RA, pramlintide
    - Metoclopramide (FDA approved) but risk of extrapyramidal signs, limit to 12 weeks
    - Erythromycin (short term due to tachyphylaxis)
    - Gastric stimulation
  - Constipation
  - Diarrhea/Fecal incontinence
- Genitourinary
  - Erectile dysfunction, retrograde ejaculation
  - Female sexual dysfunction
  - Cystopathy

Diabetes Care 2023 Jan; 46(Supplement 1): S207.

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Foundations of Cardiometabolic Health Certification Course

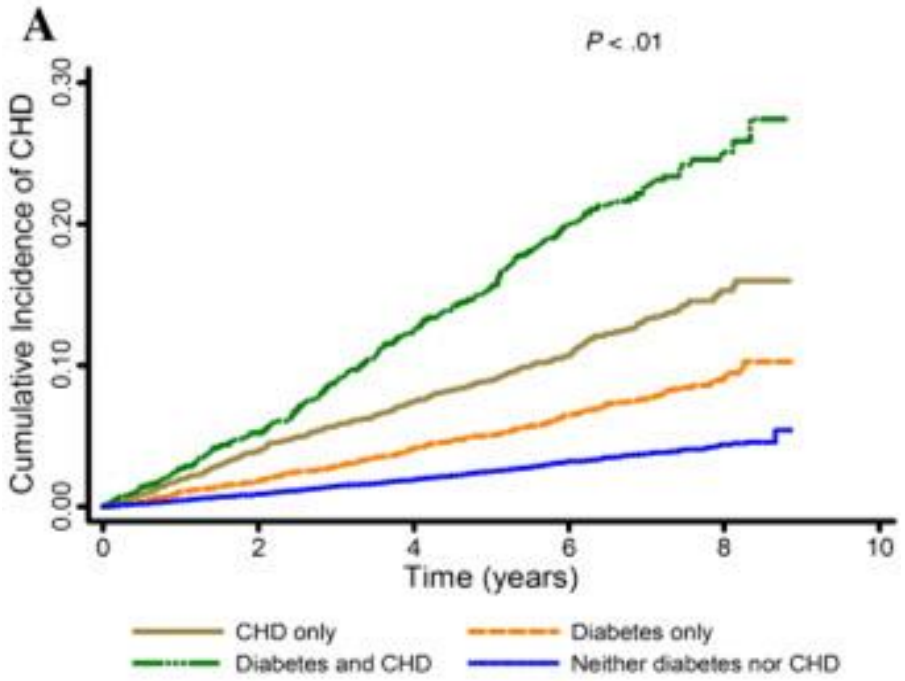
Certified Cardiometabolic Health Professional (CCHP)

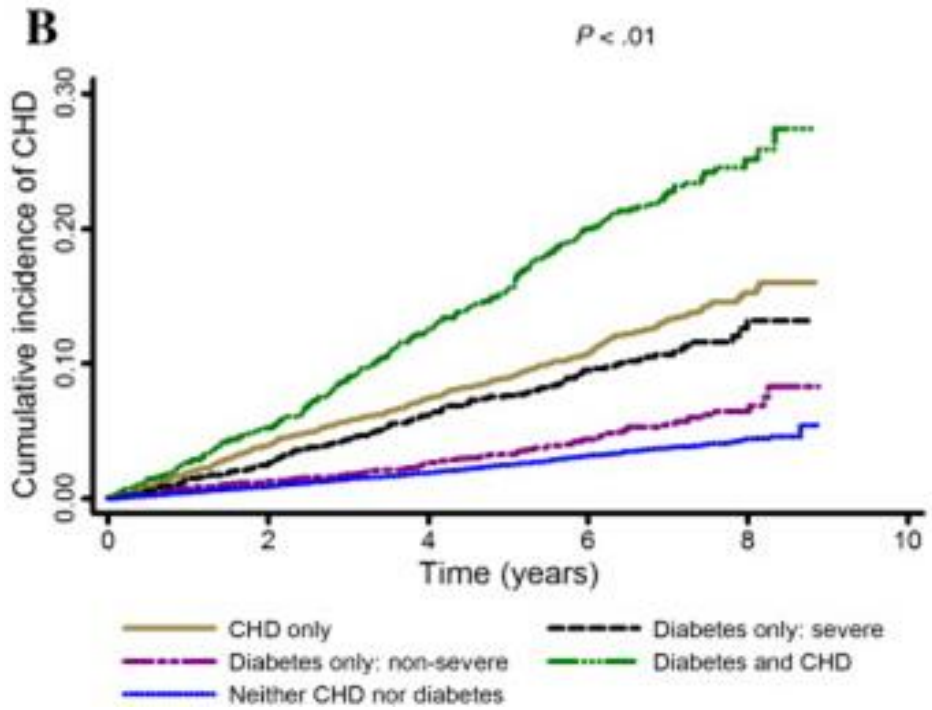
Assessment of Comorbidities: Cardiovascular Disease & Risk Management

James R. Gavin III, MD, PhD
Chief Medical Officer
Healing Our Village, Inc.
Clinical Professor of Medicine
Emory University School of Medicine
Atlanta, GA

Risk of heart disease in persons with and without diabetes mellitus (DM)

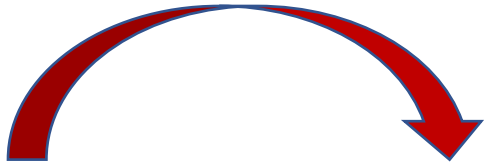
- N=3043
- Risk for MI or CV death was
  - Greatest in persons with DM and known CHD
  - Increased in persons with greater DM burden (insulin requiring or ↑microalbumin)





Mondesir et al. Am Heart J. 2016; 181:43–51.

Diabetes (DM) and heart failure (HF)

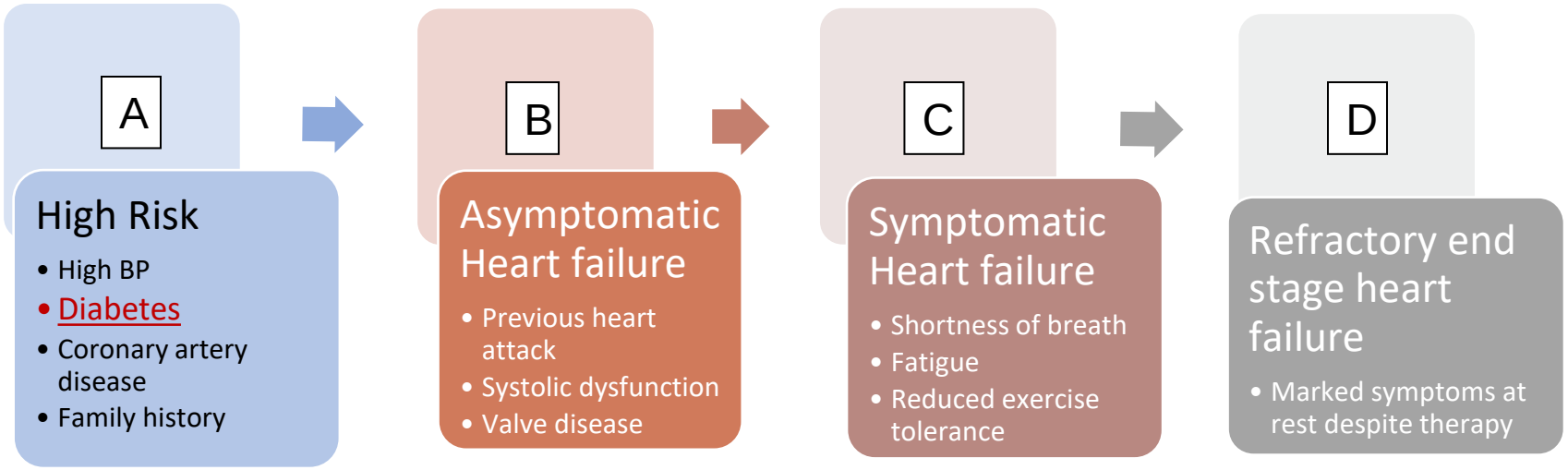


In persons with DM
- There is a 2-fold higher risk of HF
- HF is a leading cause of morbidity and mortality

In persons with HF
- There is a 2-3x higher incidence of DM
- DM coexists in up to 40%
- DM increases the risk of death or hospitalization

Dunlay et al. Type 2 Diabetes Mellitus and Heart Failure: A Scientific Statement From the American Heart Association and the Heart Failure Society of America…Circulation. 2019;140:e294–e324

Stages of Heart Failure



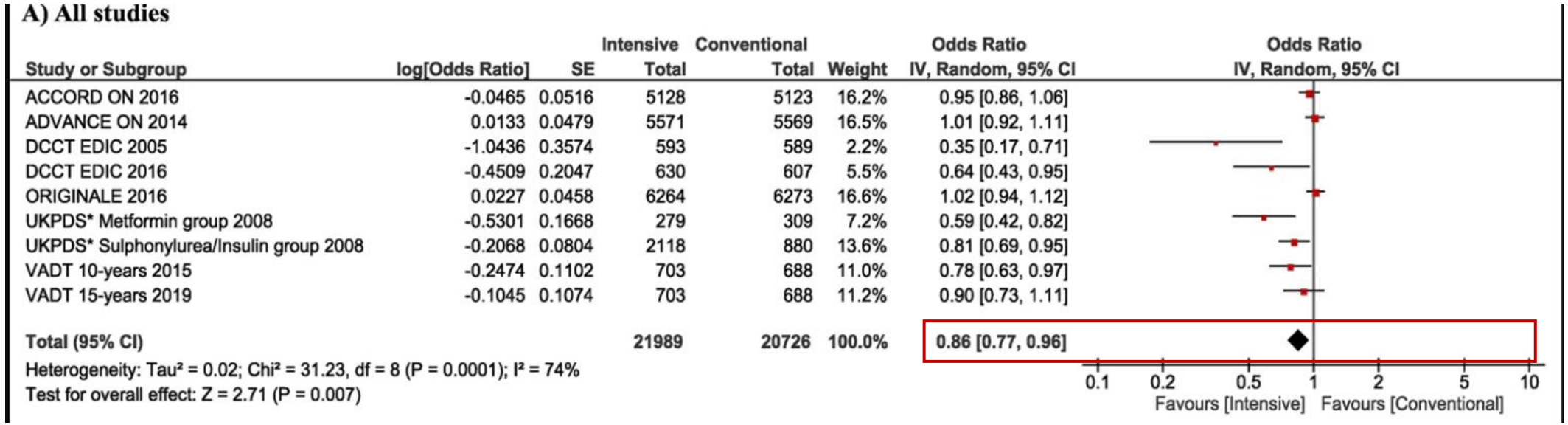
Does Intensive Glucose control reduce CV events?

Cochrane Meta-analysis

Outcome	#Trials	#Participants	Median follow-up (months)	RR (95% CI)	Quality of evidence
All-cause mortality	24	34,325	24	1.0 (0.92-1.08)	moderate
CV mortality	22	34,177	27	1.06 (0.94-1.21)	moderate
Nonfatal MI	14	30,417	60	0.87 (0.77-0.98)	moderate
Nonfatal stroke	13	30,003	54.6	1.0 (0.84-1.19)	moderate
ESRD	8	28,145	93.6	0.87 (0.71-1.06)	moderate
Amputation	11	11,200	65.1	0.65 (0.45-0.94)	low
Severe hypoglycemia	17	28,794	12	2.18 (1.53-3.11)	high

Hemmingsen et al. Cochrane Database Syst Rev. 2013 Nov 11;(11):CD008143.

Glucose control and CV risk—earlier is better



A) All studies

Study or Subgroup	log[Odds Ratio]	SE	Intensive Total	Conventional Total	Weight	Odds Ratio IV, Random, 95% CI
ACCORD ON 2016	-0.0465	0.0516	5128	5123	16.2%	0.95 [0.86, 1.06]
ADVANCE ON 2014	0.0133	0.0479	5571	5569	16.5%	1.01 [0.92, 1.11]
DCCT EDIC 2005	-1.0436	0.3574	593	589	2.2%	0.35 [0.17, 0.71]
DCCT EDIC 2016	-0.4509	0.2047	630	607	5.5%	0.64 [0.43, 0.95]
ORIGINALE 2016	0.0227	0.0458	6264	6273	16.6%	1.02 [0.94, 1.12]
UKPDS* Metformin group 2008	-0.5301	0.1668	279	309	7.2%	0.59 [0.42, 0.82]
UKPDS* Sulphonylurea/Insulin group 2008	-0.2068	0.0804	2118	880	13.6%	0.81 [0.69, 0.95]
VADT 10-years 2015	-0.2474	0.1102	703	688	11.0%	0.78 [0.63, 0.97]
VADT 15-years 2019	-0.1045	0.1074	703	688	11.2%	0.90 [0.73, 1.11]
Total (95% CI)			**21989**	**20726**	**100.0%**	**0.86 [0.77, 0.96]**

Heterogeneity: Tau² = 0.02; Chi² = 31.23, df = 8 (P = 0.0001); I² = 74%
Test for overall effect: Z = 2.71 (P = 0.007)

MACE benefit magnified in

- trials with follow-up >10 years
- DM duration <10 years
- No CVD at baseline

Similar for T1D and T2D

No legacy effect

Prattichizzo et al. Metabolism. 2020 Sep;110:154308.

Severe Hypoglycemia and Mortality Risk in Target Driven Trials

Table 2 Frequency of severe hypoglycemic events and its relationship to mortality [1, 3••, 5, 6, 9•, 14, 17, 20]

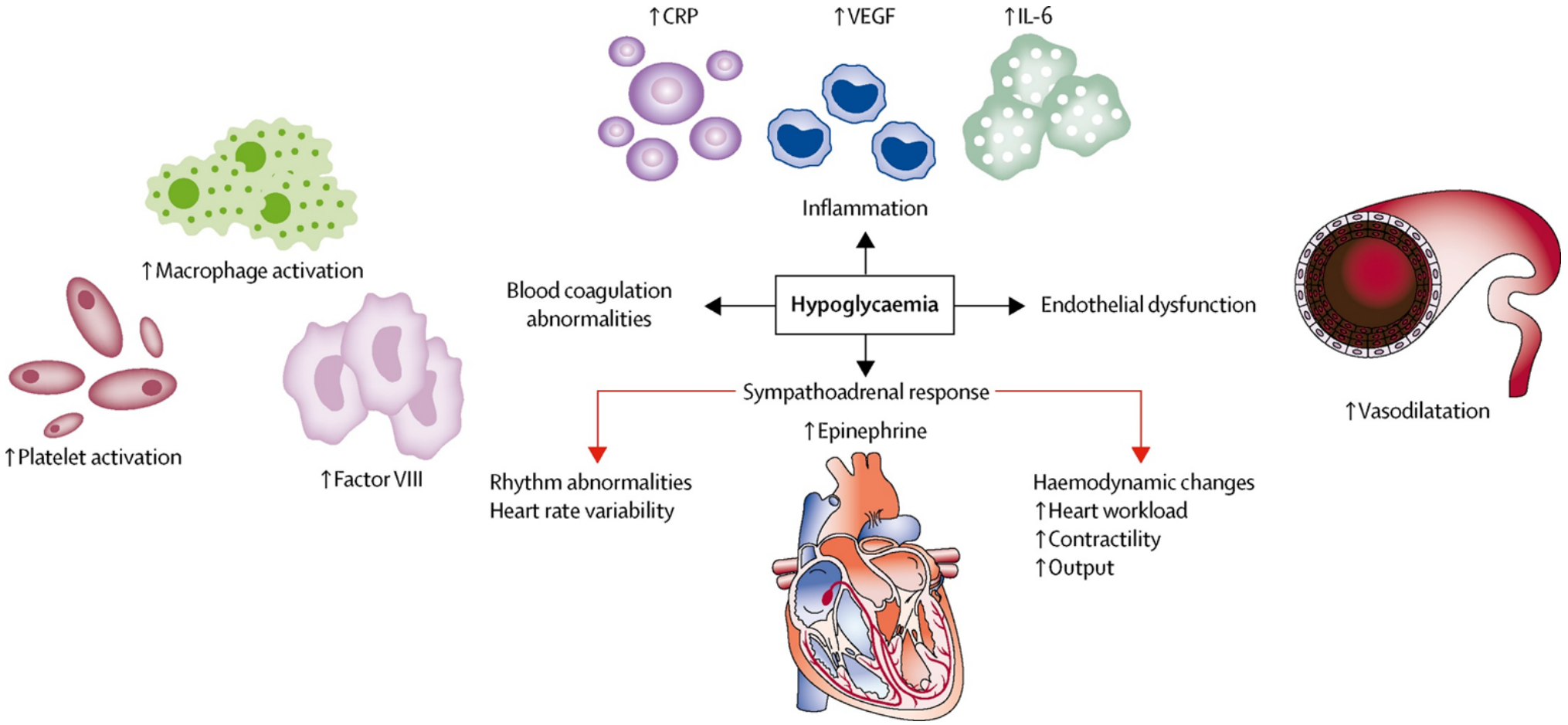
Trial	Severe HE according to treatment group (N / 100 py)		Mortality related to HE (HR; 95 % CI)	Mortality related to HE according to treatment group (HR; 95 % CI - if not indicated otherwise)		
	Standard	Intensive		Standard	Intensive	Comparison
ADVANCE	0.3	0.6	4.28 (2.36–7.75)	5.1 (mortality rate % per year)	3.6 (mortality rate % per year)	*P*=ns
ACCORD	1.0	3.1	1.67 (*P*<0.05)	2.3 (1.46–3.65)	1.41 (1.03–1.93)	*P*<0.01
VADT	1.8	3.8	3.72 (1.34–10.4)	NA	NA	
ORIGIN	0.3	1.0	1.74 (1.39–2.19)	3.13 (2.2–4.46)	1.34 (1.0–1.79)	*P*<0.001
UKPDS	0.4	1.8	NA	NA	NA	
DCCT	19	62	1.36 (0.9–2.07)	NA	NA	

HE hypoglycemic event; *py* patient year

SH is associated with increase in the risk of all-cause mortality, CV mortality, and MACE
Whether the association is causal or because of confounding remains uncertain.

Pistrosch and Hanefeld. Curr Diab Rep 2015;15:117

Mechanism of Hypoglycemia Mediated Harm



International Hypoglycaemia Study Group. Lancet Diabetes Endocrinol. 2019 May;7(5):385-396

Most Excess CV Risk in T2D is Attributed to CV Risk Factors

 # Risk Factors

Control

0

1

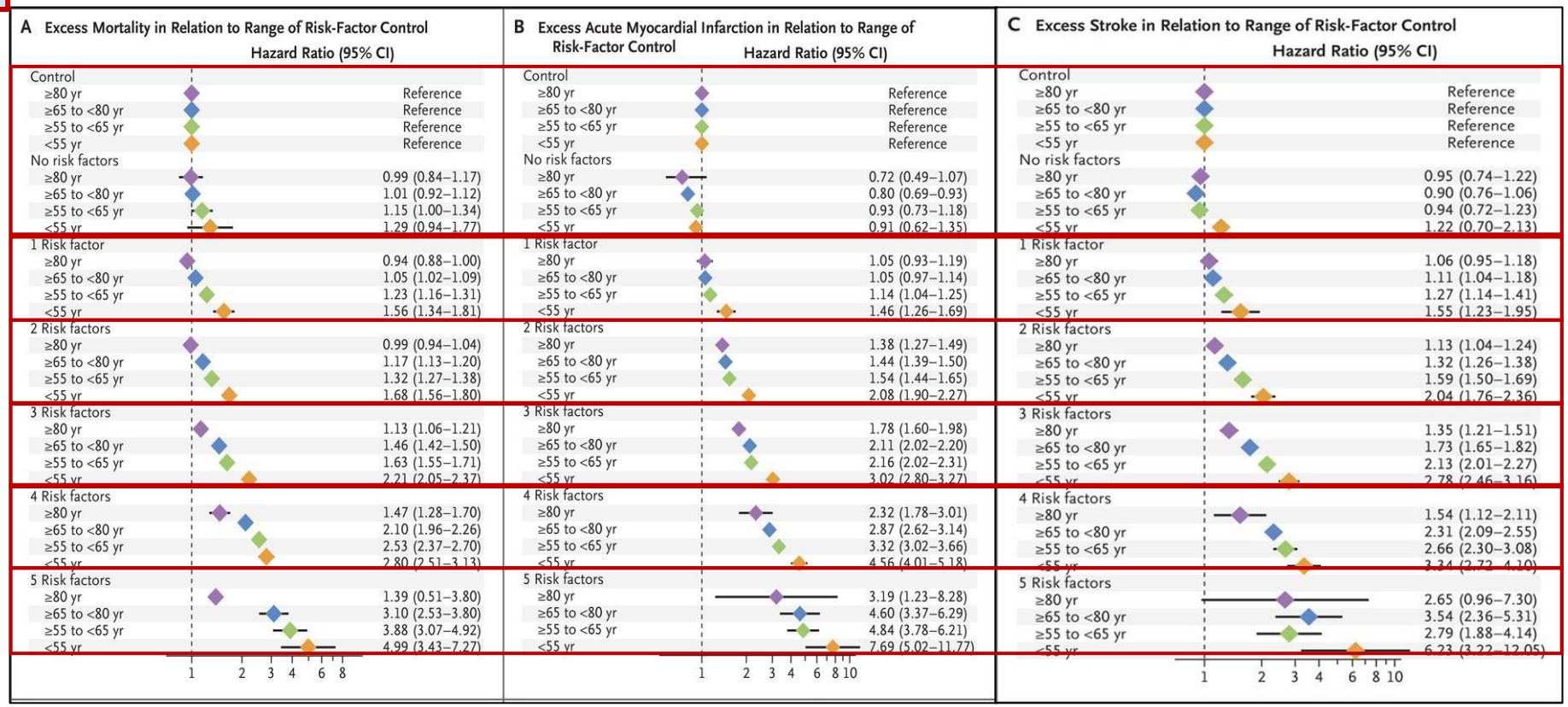
2

3

4

5

Mortality | Myocardial Infarction | Stroke



Swedish National Diabetes Register: N=271,174, Controls N=1,355,870, median f/u 5.7 years

Risk factors: A1c, LDLc, albuminuria, tobacco, BP

Conclusions: Where all 5 risk factors are at target, risk is similar to persons without DM

Rawshani et al. N Engl J Med 2018;379:633-644.

Management of *Stable CAD* in Patients with Diabetes Mellitus: American Heart Association

Antithrombotics

Underlying issue: T2DM is a generalized prothrombotic state caused by both altered coagulation and altered platelet function.

Aspirin alone	Lowest risk of bleeding but high residual platelet reactivity increases cardiovascular risk
Clopidogrel alone	Decreased cardiovascular risk without meaningfully increased risk of bleeding vs aspirin alone
Aspirin+clopidogrel/ticagrelor	Decreased cardiovascular risk with increased risk of bleeding; targets patients with additional risk factor and low risk of bleeding (use risk scores)
Aspirin+low-dose rivaroxaban	Decreased cardiovascular risk with increased risk of bleeding; targets the aberrant coagulation with T2DM

Blood pressure

Underlying issue: Coexisting hypertension increases the risk of MI, stroke, and all-cause mortality.

Target blood pressure	<140/90 mm Hg in most patients; consider <130/80 mm Hg if additional risk factors for stroke or microvascular complications
ACE inhibitor/ARB	First-line therapy because of decreased cardiovascular risk with CAD
Long-acting thiazide diuretic	Good cardiovascular risk reduction but slight increase in glucose
Calcium channel blockers	Good cardiovascular risk reduction and effective antianginal
Aldosterone antagonists	Particularly effective in patients with prior MI or LV dysfunction
β-Blockers	Do not reduce mortality in uncomplicated patients with stable CAD; choose vasodilating β-blocker for less adverse metabolic impact

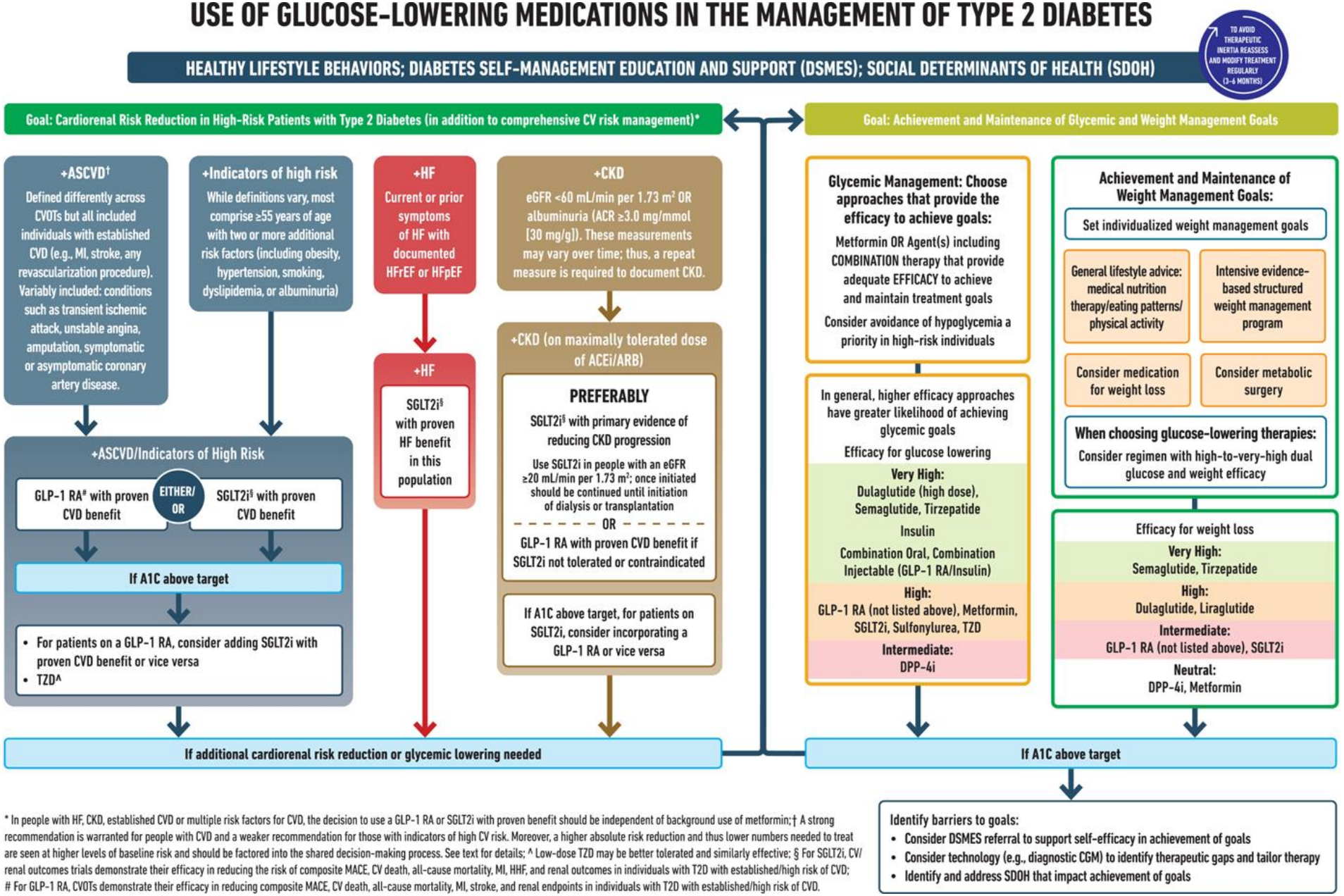
Lipids

Underlying issue: Atherogenic lipid anomalies include hypertriglyceridemia, low HDL-C, and small, dense LDL particles.

High-intensity statins	Cornerstone of lipid therapy and secondary prevention
Ezetimibe and PCSK9 inhibitors	Additional cardiovascular risk reduction when LDL is >70 mg/dL despite maximally tolerated statins
Niacin	Not recommended
Fibrates	Recommended when triglycerides are very high (eg, >500 mg/dL) to reduce the risk of pancreatitis
Icosapent ethyl	Consider for further cardiovascular risk reduction when triglycerides remain elevated (>135 mg/dL) despite maximally tolerated statin

Arnold et al. Circulation. 2020;141(19):e779-e806. doi: 10.1161/CIR.0000000000000766.

USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

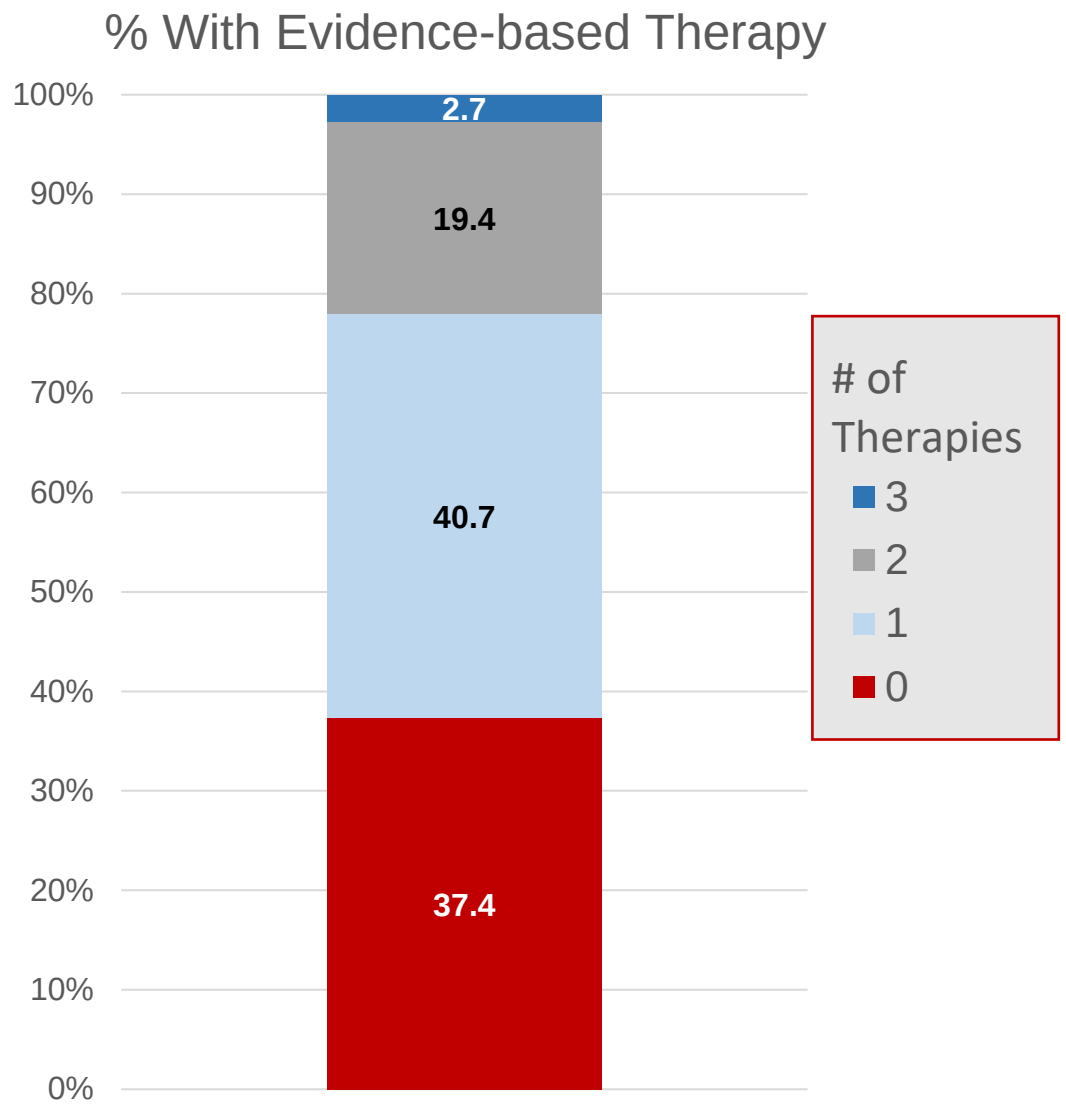


* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction 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 demonstrate 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, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

American Diabetes Association. Standards of Care. Diabetes Care 2023 Jan;46(1):S147

Implementation

- % of patients with CVD on high-intensity statin, ACEI/ARB, SGLT2i/GLP1RA
- Anthem database, N=155,958



Nelson et al. J Am Heart Assoc. 2021 Jan 19;10(2):e016835.

CV Disease—Screening

- Routine screening in asymptomatic adults not generally recommended
  - Coronary CT can be considered in adults >age 40 to assist with risk stratification
    - Need for anti-platelet therapy
    - Statin intensity

ADA. 10. Cardiovascular disease and risk management: Standards of Medical Care in Diabetes 2023. Diabetes Care 2023 Jan;46(Suppl. 1):S172.

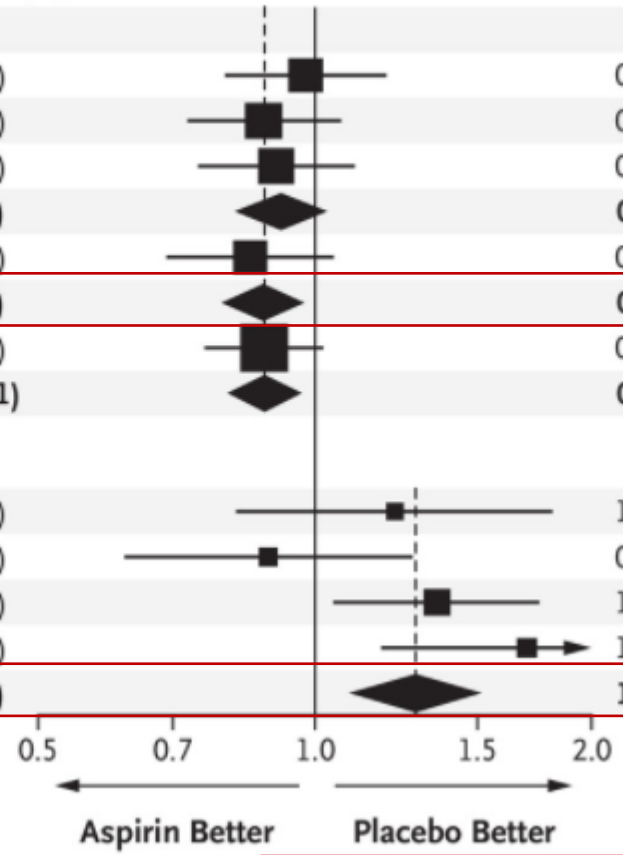
Anti-platelet use

- Secondary prevention:
  - ASA 75-162 mg daily in patients with ASCVD
  - Dual therapy (ASA + P2Y12 inhibitor) 1 or more year post ACS
  - Long-term dual therapy: prior intervention, high risk, low bleeding risk
  - Combination ASA + rivaroxaban: stable CAD or PAD with low bleeding risk
  - BB use 3 years post-MI, in HFrEF
- Primary prevention: consider in patients with very high CV risk and low bleeding risk in the context of shared decision-making
  - men and women 50-70 years with DM ≥1 major risk factor:
    - FH of premature ASCVD
    - HTN
    - Dyslipidemia
    - smoking
    - CKD/albuminuria

ADA. 10. Cardiovascular disease and risk management: Standards of Medical Care in Diabetes 2023. Diabetes Care 2023 Jan;46(Suppl. 1):S170-S172.

ASCEND trial (A Study of Cardiovascular Events in Diabetes): *effect of ASA on serious vascular events*

Type of Event	Aspirin (N=7740)	Placebo (N=7740)	Rate Ratio (95% CI)	P Value
	no. of participants with event (%)			
Vascular Outcomes				
Nonfatal myocardial infarction	191 (2.5)	195 (2.5)	0.98 (0.80–1.19)	
Nonfatal presumed ischemic stroke	202 (2.6)	229 (3.0)	0.88 (0.73–1.06)	
Vascular death excluding intracranial hemorrhage	197 (2.5)	217 (2.8)	0.91 (0.75–1.10)	
Any serious vascular event excluding TIA	**542 (7.0)**	**587 (7.6)**	**0.92 (0.82–1.03)**	
TIA	168 (2.2)	197 (2.5)	0.85 (0.69–1.04)	
Any serious vascular event including TIA	**658 (8.5)**	**743 (9.6)**	**0.88 (0.79–0.97)**	**0.01**
Any arterial revascularization	340 (4.4)	384 (5.0)	0.88 (0.76–1.02)	
Any serious vascular event or revascularization	**833 (10.8)**	**936 (12.1)**	**0.88 (0.80–0.97)**	
Major Bleeding				
Intracranial hemorrhage	55 (0.7)	45 (0.6)	1.22 (0.82–1.81)	
Sight-threatening bleeding in eye	57 (0.7)	64 (0.8)	0.89 (0.62–1.27)	
Serious gastrointestinal bleeding	137 (1.8)	101 (1.3)	1.36 (1.05–1.75)	
Other major bleeding	74 (1.0)	43 (0.6)	1.70 (1.18–2.44)	
Any major bleeding	**314 (4.1)**	**245 (3.2)**	**1.29 (1.09–1.52)**	**0.003**



Mean follow-up 7.4 years

Murphy et al. N Engl J Med. 2018 Oct 18;379(16):1529-1539.

Blood Pressure

- Measure at every visit
- Home BP monitoring in all patients with HTN
- Targets--individualized through shared decision-making process (CV risk, AE, patient preference)
  - <130/80 mmHg
- Therapeutic lifestyle changes
  - DASH diet (reduced sodium, increased potassium)
  - Physical activity
  - Weight loss (if indicated)

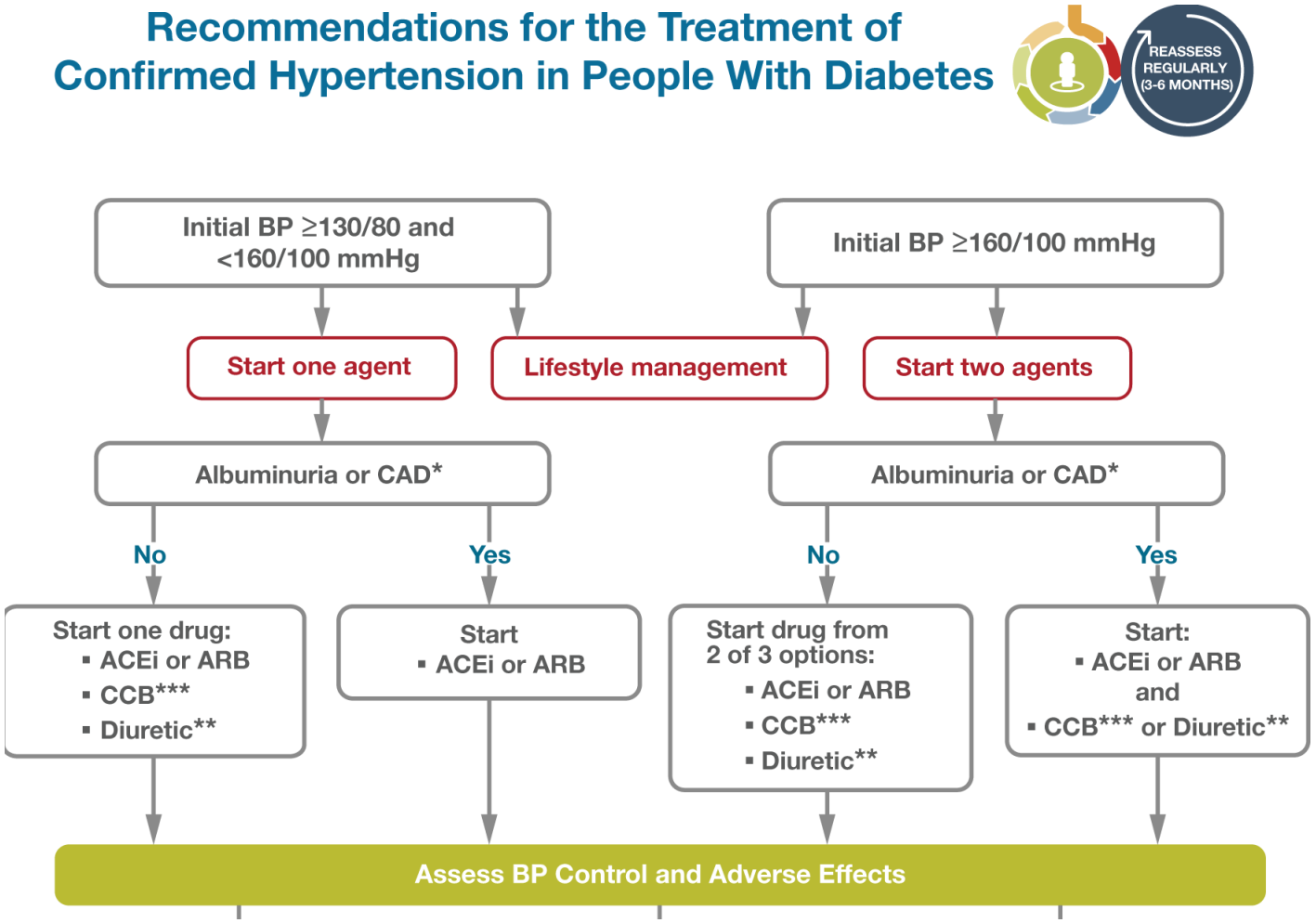
ADA. Diabetes Care 2023 Jan;46(Suppl. 1):S159-S165.

RCT of BP Interventions

Trial	N	N (DM)	Population	Intervention	Outcome
ACCORD BP[1]	4733	4733	T2D, age 40-79 years, CVD or multiple CV RF	SBP <120 vs 130-140	1ary endpoint (composite Nonfatal MI, nonfatal stroke, CV death): No difference Stroke risk reduced 41% AE more common with intervention (creatinine, electrolyte)
ADVANCE BP[2]	11,140	11,140	T2D, age 55+, CVD or multiple CV RF	Perindopril/indapamide vs placebo	1ary endpoint (major macrovascular and microvascular events): reduced 6 year observational followup: attenuated but still significant
HOT[3]	18,790	1,501		DBP ≤80 vs. 90	No benefit in overall population 50% reduction in CVD in DM cohort
SPRINT[4]	9,361	0		SBP <120 vs <140	1ary endpoint (MI, ACS, CVA, HF, CV death): benefit AE more common with intervention (creatinine, electrolyte)

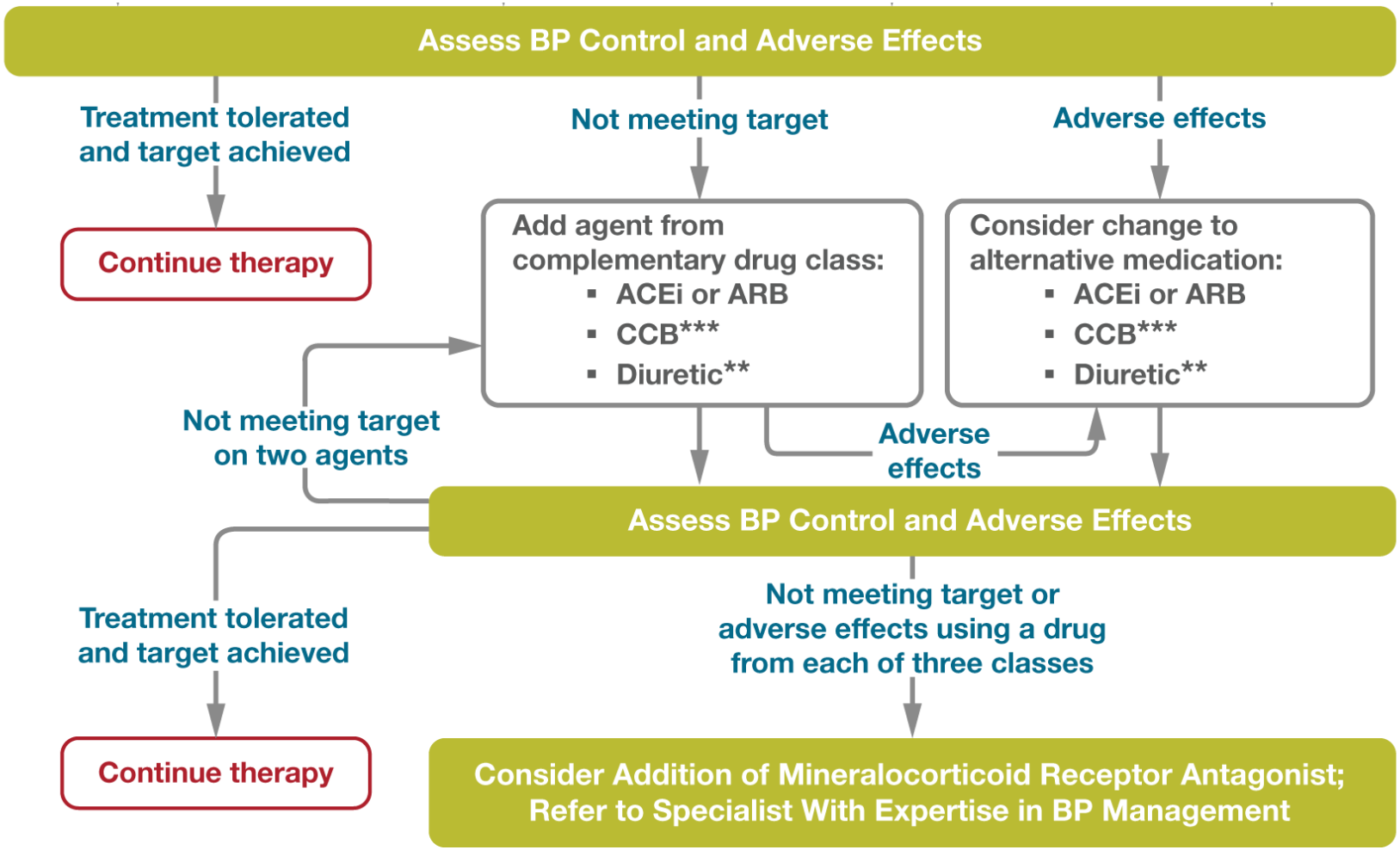
N Engl J Med 2010;362:1575-85 2) Lancet 2007;370:829-40 3) Lancet 1998;351:1755-62 4) N Engl J Med 2015;373:2103-2116

Blood Pressure



Initial pharmacologic therapy: Include drugs with demonstrated CV benefit

ADA. Diabetes Care 2023 Jan;46(Suppl. 1):S164-S165.



Recommendations for the treatment of confirmed hypertension in people with diabetes. *An ACE inhibitor (ACEi) or angiotensin receptor blocker (ARB) is suggested to treat hypertension for patients with coronary artery disease (CAD) or urine albumin-to-creatinine ratio 30–299 mg/g creatinine and strongly recommended for patients with urine albumin-to-creatinine ratio ≥300 mg/g creatinine. **Thiazide-like diuretic; long-acting agents shown to reduce cardiovascular events, such as chlorthalidone and indapamide, are preferred. ***Dihydropyridine calcium channel blocker (CCB). BP, blood pressure. Adapted from de Boer et al. (17).

ADA. Diabetes Care 2023 Jan;46(Suppl. 1):S164-S165.

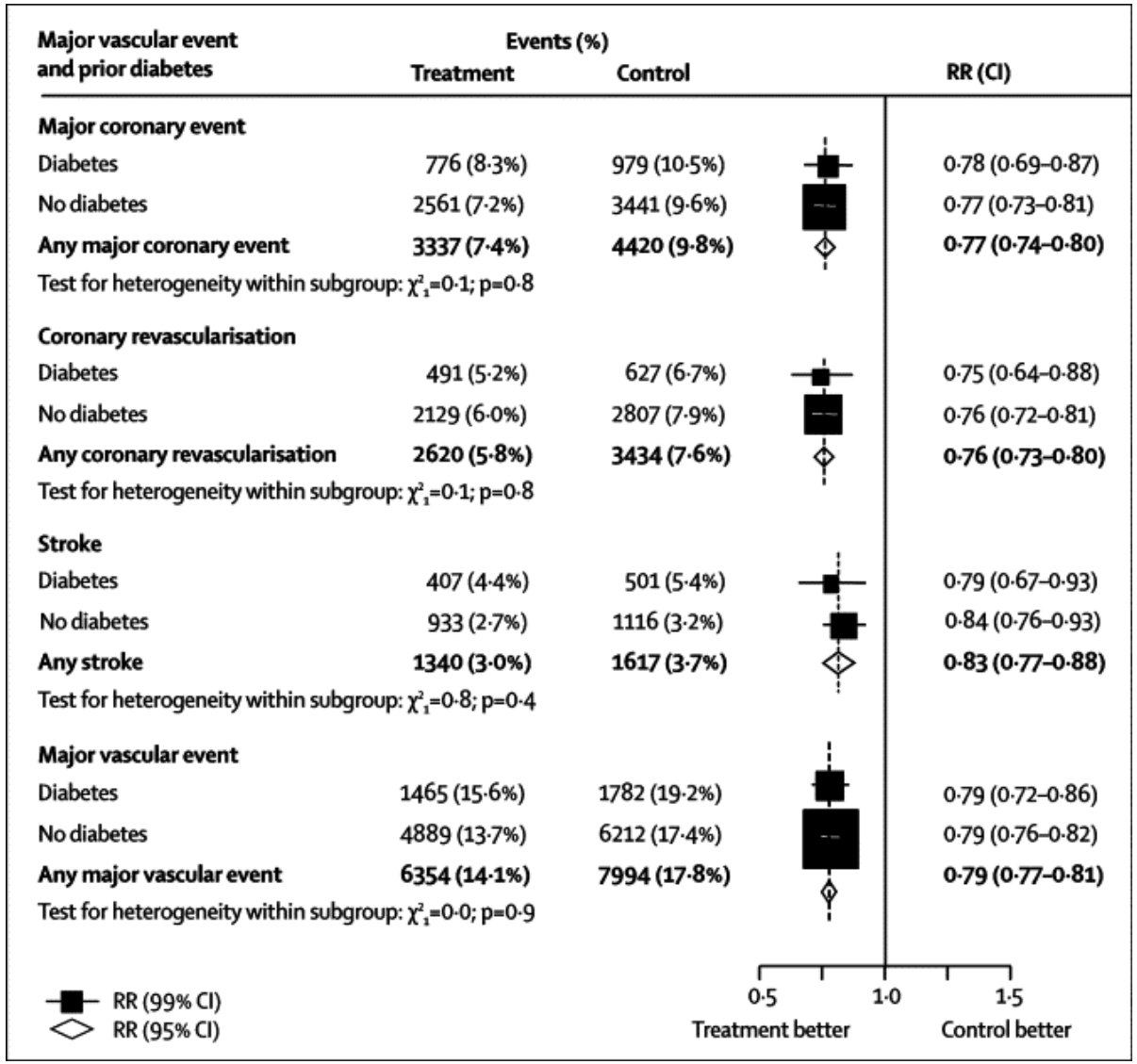
Lipids

- Therapeutic lifestyle changes:
  - Mediterranean or DASH: reduce saturated/trans fat, increase n3 FA, viscous fiber, plant stanols/sterols
  - Physical activity at least 150 minutes/week
- Monitoring
  - Diagnosis/initial evaluation
  - Q5 years (<40 y.o.)
  - 4-12 weeks after addition/change in therapy and annually thereafter

ADA. Diabetes Care 2023 Jan;46(Suppl. 1):S165-S170.

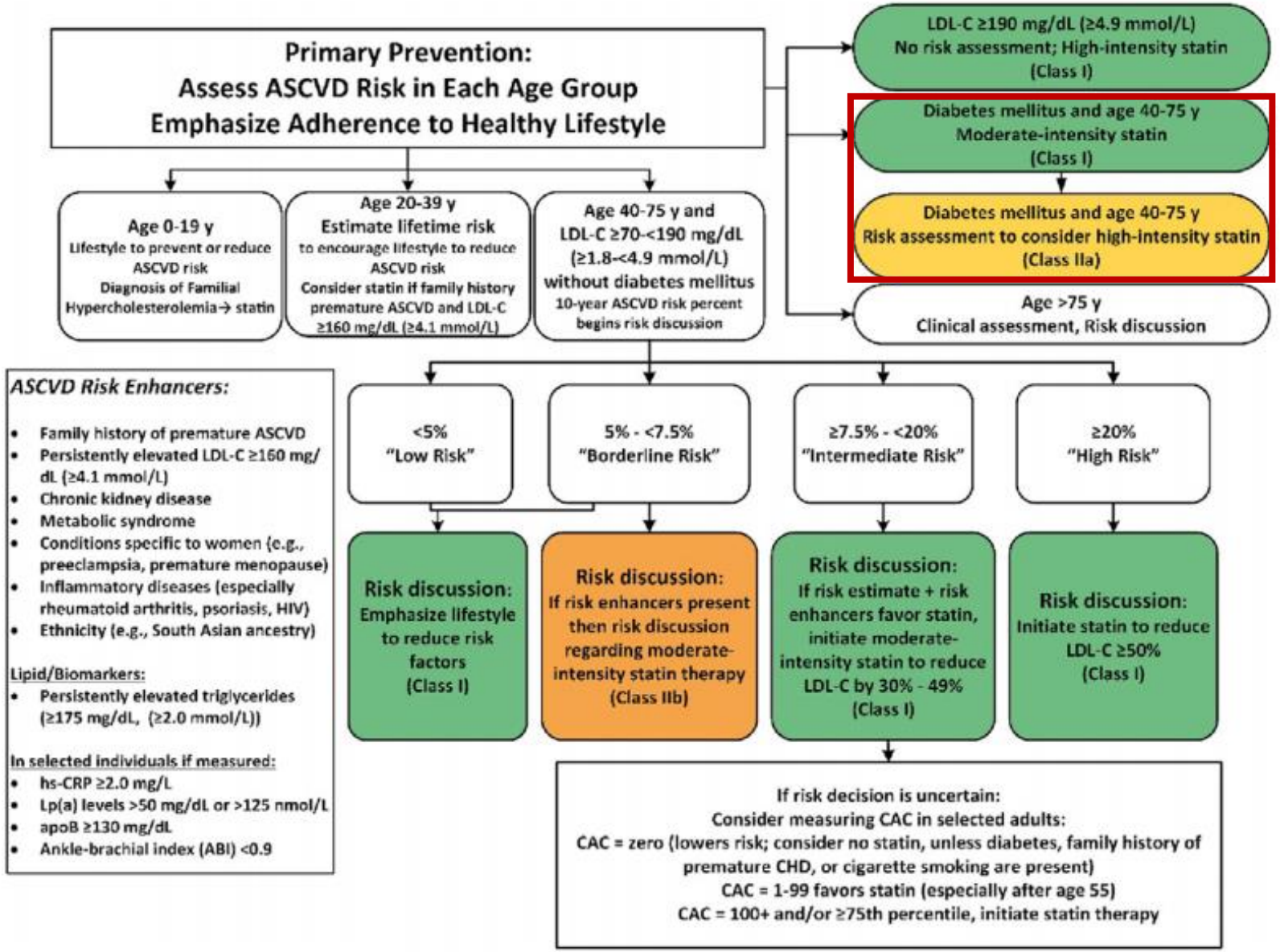
Statin reduces adverse CV events in T2D

Meta-analysis of 18,686 patients with DM randomized to treatment with a HMG-CoA reductase inhibitor



Cholesterol Treatment Trialists' (CTT) Collaborators. Lancet 2008;37:117-125

2019 ACC/AHA guideline on primary prevention of CVD



Arnett et al. Circulation. 2019;140:e563–e595

Diabetes specific risk enhancers

If age <40 years

- Duration ≥10 years (T2D), ≥ 20 years (T1D)
- Albuminuria ≥ 30 mcg/mg creatinine
- eGFR < 60 ml/min/1.73m^2
- Retinopathy
- Neuropathy
- ABI <0.9

Independent of other risk factors

Grundy et al. Circulation 2019;139:e1046-1081

Very High CV Risk

Defined as multiple major ASCVD events or 1 major ASCVD event and multiple high risk conditions

Major ASCVD events

- ACS <12 month
- AMI
- Ischemic stroke
- Symptomatic PAD

High risk conditions

- Age ≥ 65 years
- Heterozygous familial hypercholesterolemia
- CABG/PCI without major ASCVD event
- DM
- HTN
- eGFR 15-59 mL/min/1.73 m2
- Current tobacco use
- LDLc ≥ 100 mg/dl despite maximum statin + ezetimibe
- CHF

Grundy et al. Circulation 2019;139:e1046-1081

Lipid lowering therapy

	Risk factors	Moderate intensity	High intensity	Other
Primary prevention				
Age 20-39	1+	consider		risk enhancers
Age 40-75	Any	yes		
Age 50-70	>1		consider	Lower LDLc 50%
Age >75				*Already on statin:* Continue after discussion of risk/benefits *Not already on statin:* Consider statin after discussion of risk/benefits
CV risk >20%			yes	Lower LDLc 50%
Secondary prevention			yes	
Very high risk				If LDLc >70 mg/dl on maximally tolerated statin, initiate ezetimibe +/- PCSK9i

Grundy et al. Circulation 2019;139:e1046-1081

Statin intensity

High intensity (lower LDLc ≥50%)	**Moderate intensity** (lower LDLc 30-50%)	**Low intensity** (lower LDLc <30%)
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 1-4 mg	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg

ADA. Diabetes Care 2023 Jan;46(Suppl. 1):S165-S169.

Triglycerides and HDL-C

	Evaluate for 2ndary cause	Intensive lifestyle	Medication Therapy	ASCVD or other CV risk factors
TG >150 mg/dl		x		
TG 175-499 mg/dl	x	x		Icosapent ethyl (in addition to statin with LDL-C at goal)
TG >500 mg/dl	x	x	Omega-3 or fibrate	Icosapent ethyl (in addition to statin with LDL-C at goal)
HDL-C <40 mg/dl (M), <50 mg/dl (W)		x		

ADA. Diabetes Care 2023 Jan;46(Suppl. 1):S169.

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Assessment of Comorbidities: Other Comorbidities

James R. Gavin III, MD, PhD
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Autoimmune conditions associated with T1D

- Autoimmune thyroid: screen at diagnosis and periodically thereafter
- Celiac: screen adults with GI symptoms, signs or suggestive lab manifestations (osteoporosis, vitamin d deficiency, iron deficiency)
- Other associated autoimmune disease:
  - Pernicious anemia
  - Autoimmune hepatitis
  - Primary adrenal insufficiency
  - Dermatomyositis
  - Myasthenia gravis
  - Vitiligo

ADA. Diabetes Care 2023 Jan; 46(Supplement 1): S237-S238.

Other Comorbidities

- Cancer:
  - DM associated with increased risk of colon, liver, endometrial, bladder
  - age/sex specific screening
  - Pancreatic: consider if new onset atypical DM (lean, no family history) in middle/older age patient in the presence of weight loss/AP
- Pancreatitis
  - Pancreatitis associated with ↑risk of incident DM and vice versa
  - Exocrine dysfunction present in up to half of persons with DM
  - Link with GLP-1RA but causality not established
- Osteoporosis
  - T1D: ↑risk
  - T2D: ↑fracture risk despite normal BMD
  - Treatment as with general population, use caution with TZDs, SGLT2i
- Auditory impairment ↑risk with DM
- COVID-19—special vigilance with vaccinations, close follow-up, intensive management

ADA. Diabetes Care 2023 Jan; 46(Supplement 1): S56-S63.

Other comorbidities

- Sleep apnea
  - OSA: prevalence in 85% of LOOK-AHEAD trial participants (T2D + obesity)[1]
  - Treatment improves QOL and BP
  - Effect on glucose control unclear
- Periodontal disease[2,3]
  - ↑risk/severity in persons with DM
  - Treatment may improve glucose control
- Male hypogonadism[4]
  - testosterone is lower in men with DM vs. age matched controls, confounded by obesity
  - AM testosterone level (+free testosterone if abnormal) may be considered in the presence of suggestive symptoms
  - Treatment may improve sexual function, well-being, muscle mass and BMD
  - CV risk controversial

ADA. Diabetes Care 2023 Jan; 46(Supplement 1): S56-S63.

1. Foster et al. Diabetes Care. 2009 Jun;32(6):1017-9. 2. Bibbins-Domingo et al. USPSTF. JAMA 2017;317;407-14. 3. Shaw et al. Diabetes Res Clin Pract 2008;81:2-12
4. Bhasin et al. Endocrine Society. J Clin Endocrinol Metab 2018;103:1715-44

“Preparing for a NASH Epidemic: A Call for Action”

- International conference representing 7 professional societies
- Screening for high-risk groups:
  - BMI >35
  - T2D >10 years, >age 50, or metabolic syndrome
  - Elevated ALT

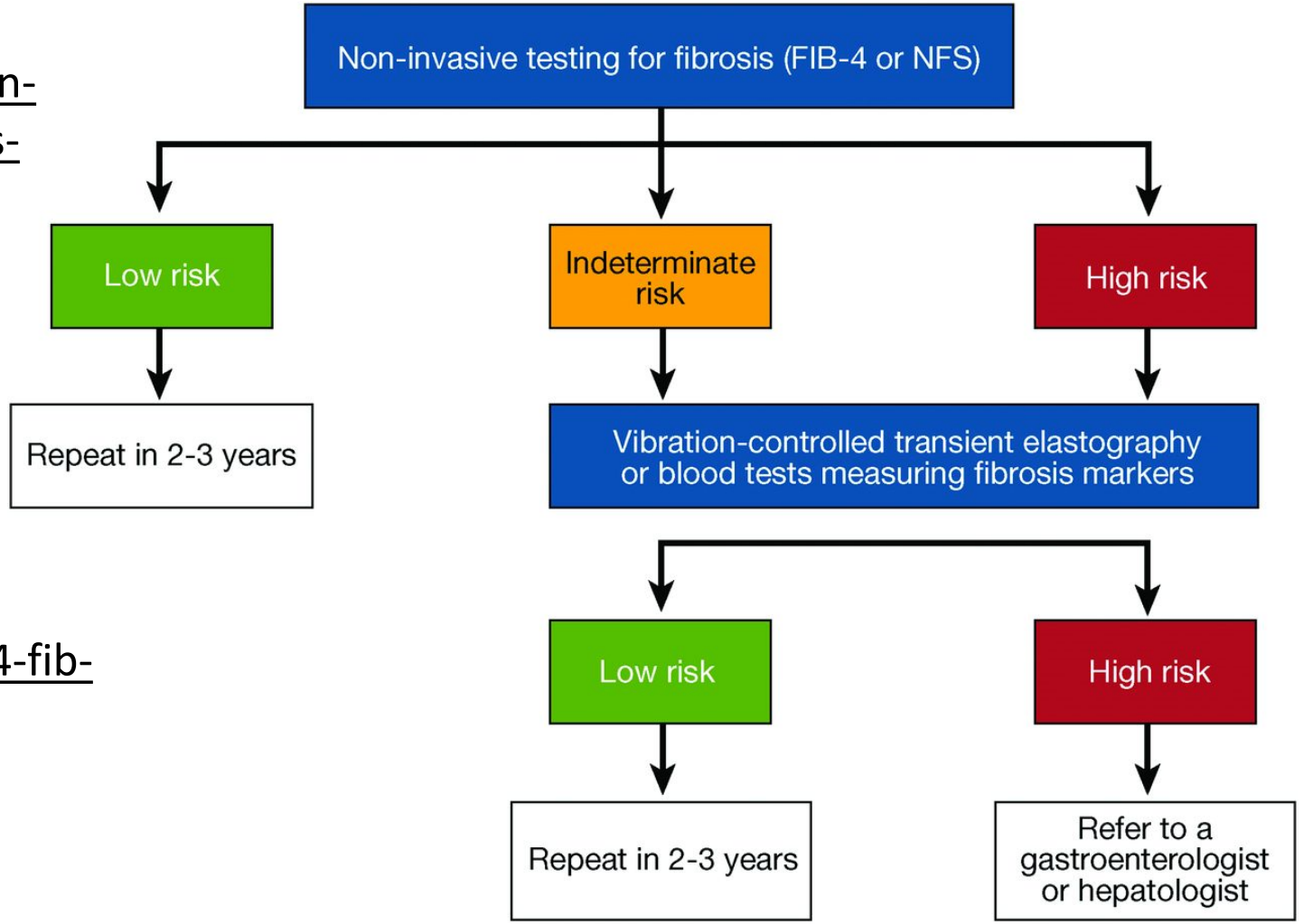
Initial evaluation:

- LFTs often normal
- HBV/HCV serology and viral load
- autoab (ANA, AMA, ASMA)
- Ferritin
- α1AT
- Ultrasound

Kanwal et al. Diabetes Care. 2021 Sep;44(9):2162-2172.

Risk stratification

- Evaluate for advanced fibrosis
  - NAFLD fibrosis score (NFS): https://www.mdcalc.com/nafld-non-alcoholic-fatty-liver-disease-fibrosis-score
    - AGE
    - BMI
    - DM or preDM
    - AST/ALT
    - Platelet
    - albumin
  - Fibrosis-4 Index (Fib-4): https://www.mdcalc.com/fibrosis-4-fib-4-index-liver-fibrosis
    - Age
    - AST/ALT
    - platelet



Kanwal et al. Diabetes Care. 2021 Sep;44(9):2162-2172.

NAFLD Management

	Intensive Lifestyle	Liver directed pharmacotherapy[1]	Diabetes care	CV risk reduction
NAFL	+	-	Standard of care	+
NASH fibrosis (F0-1)	+	-	Standard of care	+
NASH fibrosis (F2-3)	+	+	Pioglitazone or GLP-1RA[2]	+
NASH cirrhosis (F4)	+	+	Individualize[3]	+

1) Vitamin E or clinical trials
2) Among GLP-1RA, semaglutide has best evidence of benefit
3) Evidence very limited and should be individualized, used with caution

Kanwal et al. Diabetes Care. 2021 Sep;44(9):2162-2172.

Immunizations

	Age (years)	Frequency	Comment
HBV	<60 ≥60: discuss with provider	2-3 dose series	
Human papilloma virus (HPV)	<26 27-45: discuss with provider	3 doses every 6 months	
Influenza	All adults	yearly	avoid live attenuated vaccine
Pneumonia (PPSV23 [Pneumovax])	19-64 ≥65	1 dose 2nd dose 5 year after 1st If first dose was PCV13 give PPSV23 in ≥1 year	
Pneumonia (PCV13 [Prevnar])	≥65, discuss with provider	1 dose	Indicated for immune compromise, cochlear implant, CSF fluid leak
Tetanus, diphtheria, pertussis (TDAP)	All adults	10	Pregnant women should have extra dose
Zoster (Shingrix)	≥50	2-dose series	Even if previously vaccinated

www.cdc.gov/vaccines/

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Assessment of Comorbidities: Mental Health

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DM and Mental health

- Depression
  - Depression associated with ↑risk of DM and vice versa
  - Screen annually and at time of complications
  - Co-treatment as part of multi-disciplinary team improves BG control and self-care
- Schizophrenia
  - ↑ risk for DM
  - Disordered thinking and judgement reduces self-care behaviors and ability to make healthcare decisions
  - Antipsychotic medications:
    - Atypical antipsychotics: screen for DM at 4 months and annually
    - 2nd generation: monitor weight, glucose control and lipids in persons with DM

ADA. Diabetes Care. 2023 Jan;46(Suppl 1):S82-S86.

Mental health

- Anxiety
  - Compounded by injections, not meeting BG targets, complications
  - Fear related to hypoglycemia→avoidance behaviors
  - OCD: can manifest as excessive DM self-management
- Disordered eating
  - Includes omission of insulin for the purpose of weight loss
- Diabetes distress: negative psychological reaction related to emotional burden and worries specific to managing a complicated, demanding chronic disease
  - Linked to ↑A1c, ↓ self-efficacy, diet, exercise, medication taking
  - DSMES effective to reduce DM distress
  - Behavioral health provider

ADA. Diabetes Care. 2023 Jan;46(Suppl 1):S81-S85.

Indications for referral to mental health provider

- DM distress + impaired self-care despite DSMES
- +Depression screen
- Eating disorder
- Intentional omission of medication to cause weight loss
- + screen for anxiety, fear of hypoglycemia
- Serious mental illness
- Youth with self-care difficulties, recurrent hospitalization, distress
- Cognitive impairment
- Declining ability to perform self-care
- Prior to bariatric/metabolic surgery

ADA. Diabetes Care. 2023 Jan;46(Suppl 1):S79-S81.

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Considerations for Older Adults

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Older age

- Dementia
  - DM associated with ↑risk for Alzheimer, vascular
- Screen for conditions that may impact self-management & QOL
  - Cognitive impairment: age 65+, annual
  - Hypoglycemia: assess every visit, consider CGM
  - Polypharmacy
  - Depression
  - Urinary incontinence
  - falls

American Diabetes Association. Diabetes Care 2023;46(Suppl. 1):S216–S229.

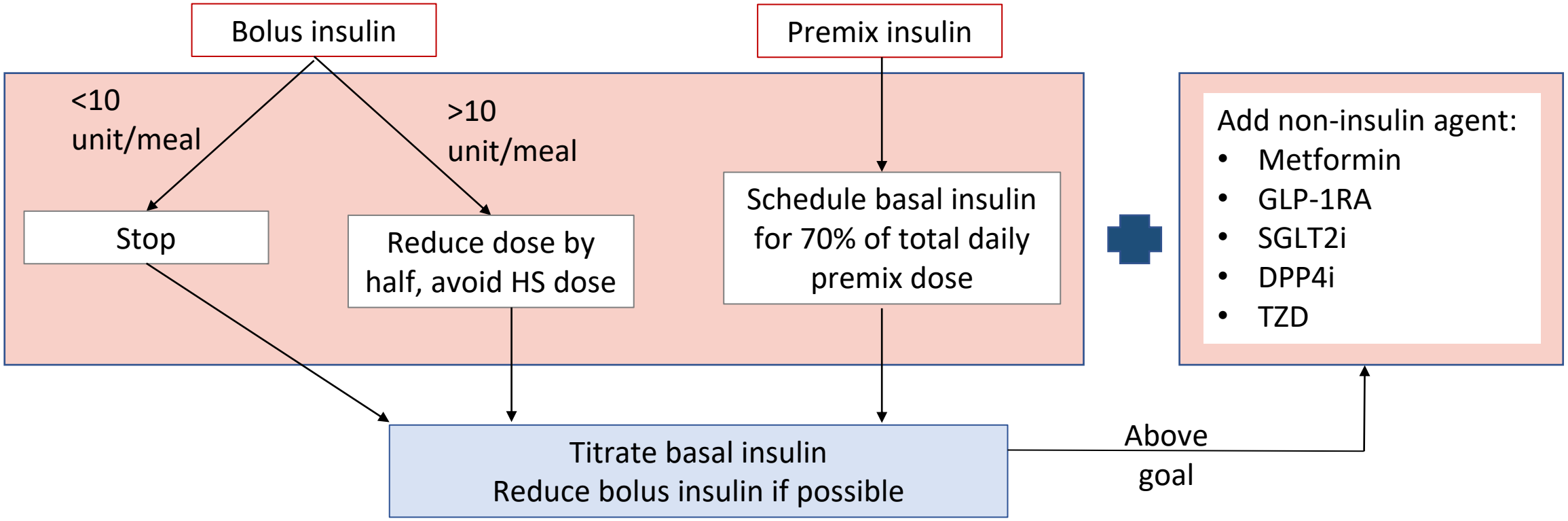
Goals for Older Adults

	Co-morbidity	A1c goal (%)*	Fasting goal (mg/dl)	HS goal (mg/dl)	BP (mmHg)	Lipids
Healthy	few	<7.0-7.5	80-130	80-180	<130/80	Statin unless contraindicated or not tolerated
Complex/ intermediate	• Multiple (3+) comorbidity • Mild-moderate cognitive impairment • 2+ instrumental ADL impairment	<8.0	90-150	100-180	<130/80	Statin unless contraindicated or not tolerated
Very complex/ poor	• Long-term care • End-stage chronic illness • Mod-severe cognitive impairment • 2+ ADL impairment	Avoid reliance on A1c, avoid hypoglycemia, symptomatic hyperglycemia	100-180	110-200	<140/90	Consider likelihood of benefit with statin

Categories provide a general framework only and should take patient and caregiver preferences into consideration. ***Lower goal may be considered if achievable without recurrent or severe hypoglycemia or undue treatment burden**

American Diabetes Association. Diabetes Care 2023 Jan;46(Suppl. 1):S216–S229.

De-intensifying complex insulin regimens



- Lifestyle changes remain the cornerstone of management.
- In the presence of insulin, consistent carbohydrate intake recommended.
- Add non-insulin therapy, reduce/stop mealtime insulin where possible (success more likely with lower doses, better glucose control, shorter duration of DM; insulin requirements may decrease with advanced chronic kidney disease).

American Diabetes Association. Diabetes Care 2023;46(Suppl. 1):S222-S223.

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Social Determinants of Health and Diabetes Care

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Social determinants of health

ADA recommendations:

- Assess
  - Food insecurity
  - Housing insecurity/homeless
  - Financial barriers
  - Social support, consider racism/discrimination
  - Language or literacy barriers
- Refer to community resources
- Provide support from lay health coaches, navigators, community health workers, preferably with similar lived experience

Hill-Briggs et al. Diabetes Care 2020; DOI: 10.2337/dci20-0053

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The Evolving Treatment Paradigm and Chronic Care Models in Diabetes

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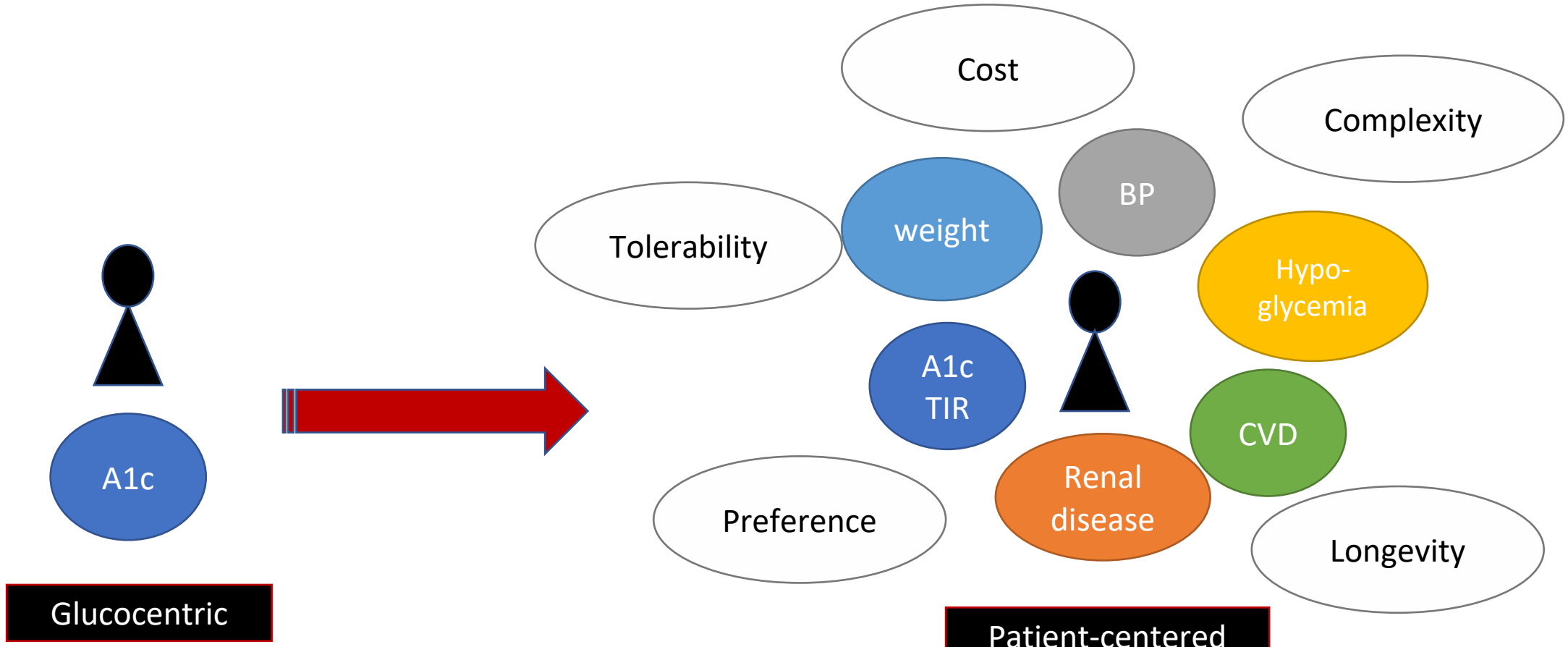
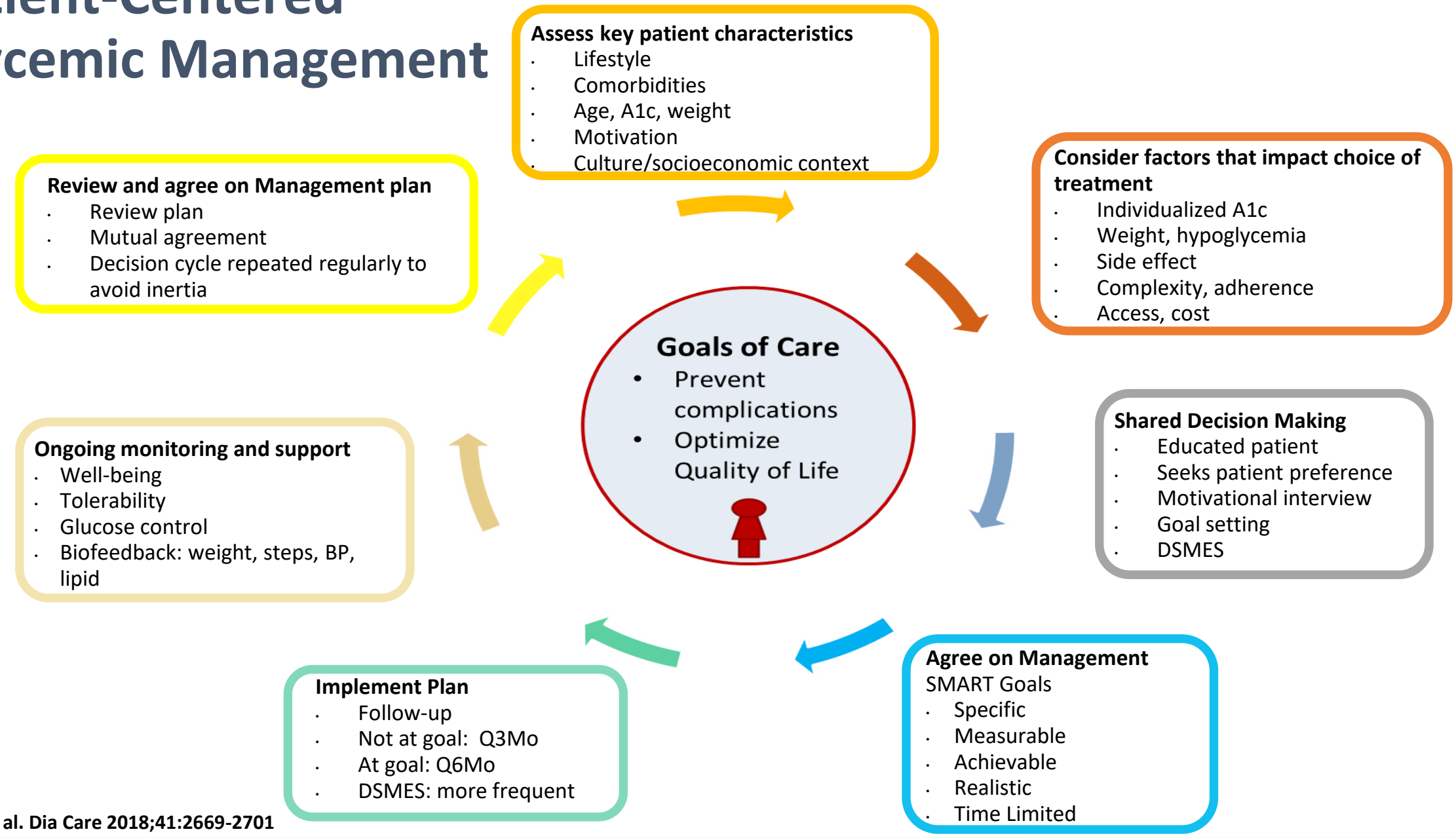
A shift in Treatment Paradigm



- Phase 3 studies

- Composite endpoints
- Outcomes trials
- Real World data

Patient-Centered Glycemic Management



Davies et al. Dia Care 2018;41:2669-2701

Language

Use language that is

- neutral, nonjudgmental, and based on facts, actions or biology
- Free from stigma, respectful, inclusive, imparts hope
- Person-centered
- Fosters collaboration

Avoid	Use instead
Diabetic	Person with diabetes
Test	Monitor
Control	Manage
Suffering from diabetes	Living with diabetes
Good/bad/poor glycemic control	A1c, A1c level, glycemic target
Compliance or adherence	Engagement, medication-taking
Obese patient, morbidly obese	Weight, BMI
Refuse	Decline

Dickinson JK et al., Diabetes Care, 2017.

Chronic Care Model

- 6 core elements
  - Delivery system design: reactive→ proactive
  - Self-management support
  - Decision support
  - Clinical information systems
  - Community resources and policies
  - Health systems

American Diabetes Association Standards of Care; Diabetes Care 2021 Jan; 44(Supplement 1): S7-S14.

Diabetes Centers of Excellence: 6 Pillars

Nonexclusive Focus on High Risk Individual and "Open Door Policy"	Communication across the medical neighborhood	Comprehensive Care	Learning health care system	Outcome assessment	Education and Dissemination
•High risk: *T1D* *Poor Control* *Hypo unaware* *Complications* *Transplant* *CF* *Atypical Complications* •Physician extender	•Pre-consultation exchanges •Telemedicine •Shared Management	•Collaborative sessions •Co-locating specialties	•Clinical Research •Registry •Quality Improvement •Co-locating specialties	•Goal directed measures (A1c, LDLc, BP) •Complications •Resource utilization •PRO	•Conferences •Small group •Expert courses •Itinerant endocrinologist

- *Community engagement and population health strategies
- *Cost of care models
- *Transdisciplinary and disease-focused research teams

Drazin, et. Al J Clin Endocrinolo Metab March 2018, 103:809-812