Diabetes Update 2019

Lisa S. Usdan, MD, FACE
University of Tennessee Methodist Physicians

Assistant Professor of Medicine, Department of Endocrinology
University of Tennessee Health Science Center

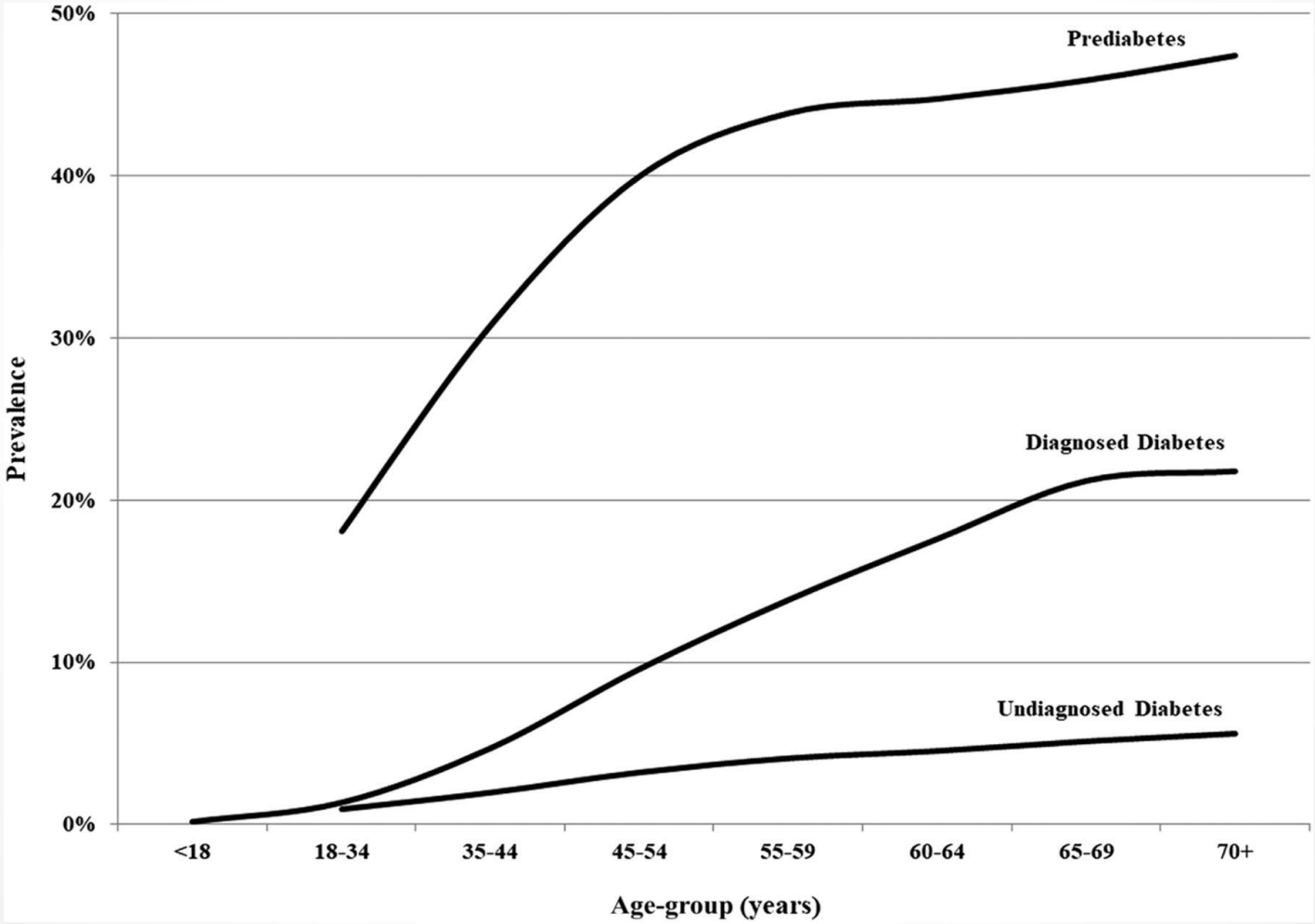
Objectives

1. Review current treatment guidelines for patients with diabetes mellitus

1. Review strategies for optimizing diabetes control using current pharmacotherapies and lifestyle modifications

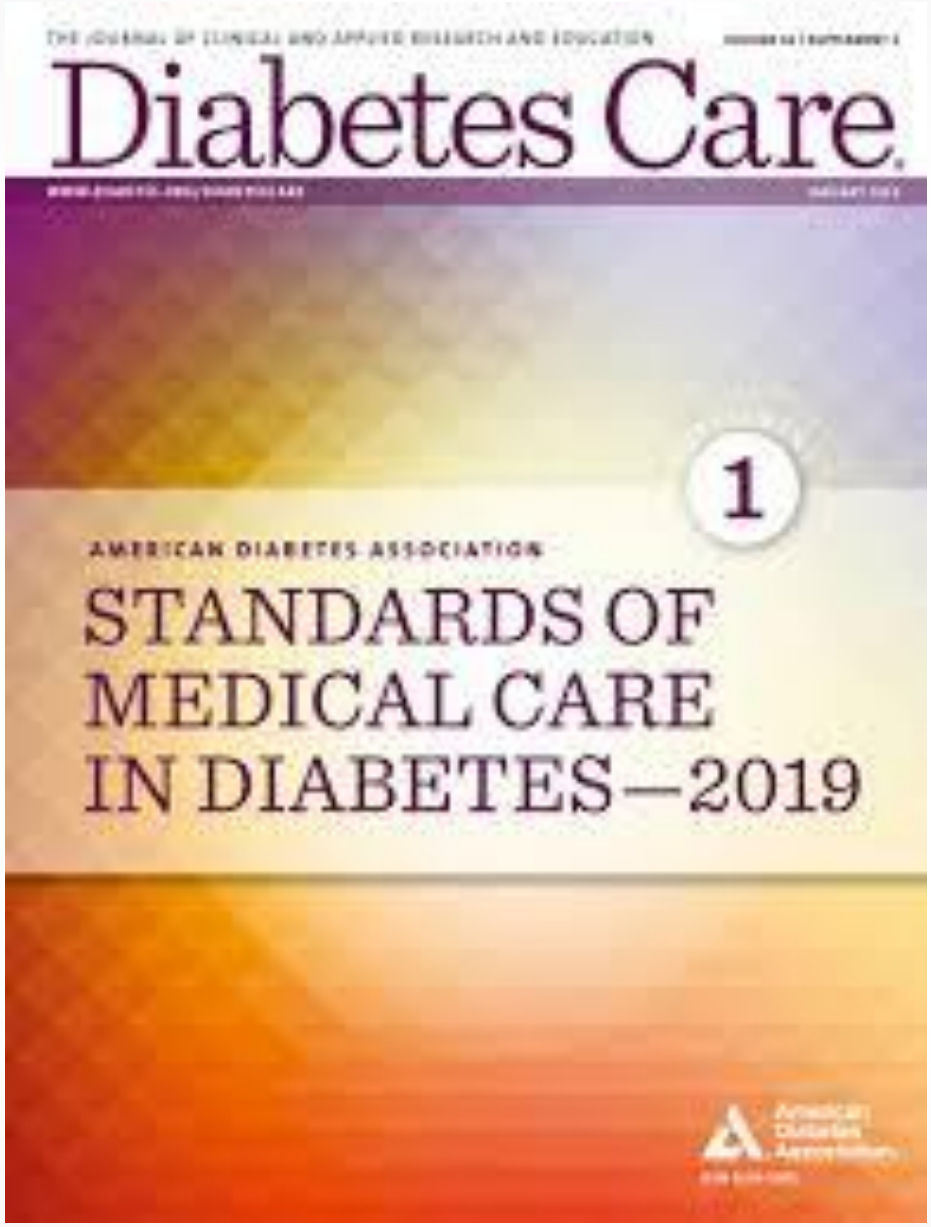
1. Discuss cardiovascular and renal outcomes associated with available diabetes medications

Prevalence of Diabetes & Prediabetes in US (2017)



Timothy M. Dall et al. Dia Care 2019;42:1661-1668

American Diabetes Association.


Diabetes Care
1
AMERICAN DIABETES ASSOCIATION
STANDARDS OF MEDICAL CARE IN DIABETES—2019

Improving Care & Promoting Health In Populations

- Importance of Getting to Goal
  - NHANES Data shows ↓ in national A1c 7.6% (1999-2002) to 7.2% (2007-2010)
  - More oder adults reach goal than younger adults
  - **A1c < 7% leads to ↓ in end stage microvascular complications**
- Cost of Diabetes
  - Annual Cost of Diagnosed Diabetes 2017:
    - $237 Billion– direct medical costs
    - $90 Billion– decreased productivity
    - Increased by >25% from 2012 to 2017
- Patient Centered Care
- Diabetes Self Care and Management

Diabetes Care 2019;42(Suppl.1):S7-S126 https://doi.org/10.2337/dc19-S001

Criteria for Diagnosis of Diabetes

Fasting Plasma Glucose ≥ 126 mg/dL (fasting is defined as no caloric intake for at least 8 hours)

OR

2 hour Plasma Glucose ≥ 200 during OGTT (using 75 gm test)

OR

A1c ≥ 6.5%

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis & random sugar ≥ 200

In absence of unequivocal hyperglycemia, diagnosis requires 2 abnormal tests from the same or separate samples

Hemoglobin A1c

- Use standardized methods for testing to prevent misdiagnosis or missed diagnosis
- Be suspicious of inconsistencies (between plasma glucose levels and A1c readings)
- Be aware of conditions affecting A1c:
  - Hemoglobinopathies
  - Pregnancy (2^{nd} & 3^{rd} Trimesters and Post Partum Period)
  - G6PD Deficiency
  - HIV
  - Hemodialysis
  - Recent change in blood volume (loss or transfusion)
  - Erythropoietin therapy

Diagnostic Criteria for Prediabetes and Diabetes

Test	Prediabetes	Diabetes
A1c	5.7-6.4%	≥ 6.5%
Fasting Plasma Glucose (mg/dL)	**100-125** **Impaired Fasting Glucose**	≥ 126
Oral Glucose Tolerance Test – 2 hours post 75 gm OGTT	**140-199** **Impaired Glucose Tolerance**	≥ 200
Random Plasma Glucose		≥ 200

Results should be confirmed with repeat testing on OGTT unless unequivocal hyperglycemia noted.
Random blood sugars are only diagnostic with symptoms of hyperglycemia or hyperglycemic crisis.
WHO & other organizations define IFG > 110

Criteria for Testing for Diabetes/Prediabetes

1. Overweight/Obese adults with one or more of the following risk factors
   - 1st Degree Relative with Diabetes
   - High-risk Race/Ethnicity (African American, Latino, Native American, Asian American, or Pacific Islander)
   - History of CVD
   - Hypertension
   - HDL < 35 and/or a Triglyceride > 250
   - Women with Polycystic Ovarian Syndrome
   - Physical Inactivity
   - Other Clinical Conditions Associated with Insulin Resistance
2. Those with Prediabetes should be tested Q1 year
3. Women with history of GDM should be tested Q3 years
4. For all others begin testing at 45
5. If normal, retest at a minimum of 3 years or with change in health status

Classification of Diabetes

Type 1 Diabetes	Autoimmune Destruction of β Cells Absolute Insulin Deficiency
Type 2 Diabetes	Progressive Loss of β Cell Insulin Secretion Often in setting of insulin resistance
Gestational Diabetes	Diagnosed in 2nd or 3rd Trimester of Pregnancy
Specific Types	Monogenic Diabetes (MODY) Diseases of Exocrine Pancreatic Function Chemical/Drug Induced Diabetes - Glucocorticoids - Post Transplant Diabetes - Therapy of other Comorbidities

Staging of Type 1 Diabetes

	Stage 1	Stage 2	Stage 3
Characteristics	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• New Onset Hyperglycemia • Symptomatic
Diagnostic Criteria	• Multiple Autoantibodies • No IGT or IFG	• Multiple Autoantibodies • Dysglycemia • FPG 100-125 • 2hPPG 140-199 • A1c 5.7-6.4% or ≥10% increase in A1c	• Clinical Symptoms • Diabetes by Standard Criteria

Adapted from Table 2.1 Staging of Type 1 Diabetes
ADA Standards of Medical Care in Diabetes 2019

Autoantibodies in T1DM

- Islet Cell
- GAD65
- Insulin
- Tyrosine Phosphatases
  - IA-2
  - IA-2β

Type 1 Risk Assessment Clinical Research Study

www.trialnet.org

Idiopathic Type 1 Diabetes

- No association with HLA linkage but strongly heritable
- No evidence of B cell autoimmunity
- Most often seen in African/Asian ancestry
- Insulinopenic
- Prone to DKA
- May only have intermittent insulin requirements

Type 2 Diabetes

- 90-95% of all cases of Diabetes
- Relative insulin deficiency with insulin resistance
- Spontaneous DKA RARE, but can be seen with stress/drugs:
  - Infection
  - Concomitant Meds: Corticosteroids, Antipsychotics, SGLT2 inhibitors
- Usually undiagnosed for many years due to gradual presentation of hyperglycemia

Mechanisms of Hyperglycemia in T2DM

- Beta Cell Dysfunction
- Insulin Resistance (liver, fat, & muscle)
- Increased Sympathetic Tone
- Increased SGLT2 Effect
- Alpha Cell Dysfunction (increased glucagon)
- Decreased Amylin
- Decreased Incretin
- Immune Dysregulation/Inflammation
- Microbiome Changes

Miller, E. et al. Type 2 Diabetes: Evolving concepts and treatment. Cleveland Clinic Journal of Mediicne 2019: 86(7): 494-504.

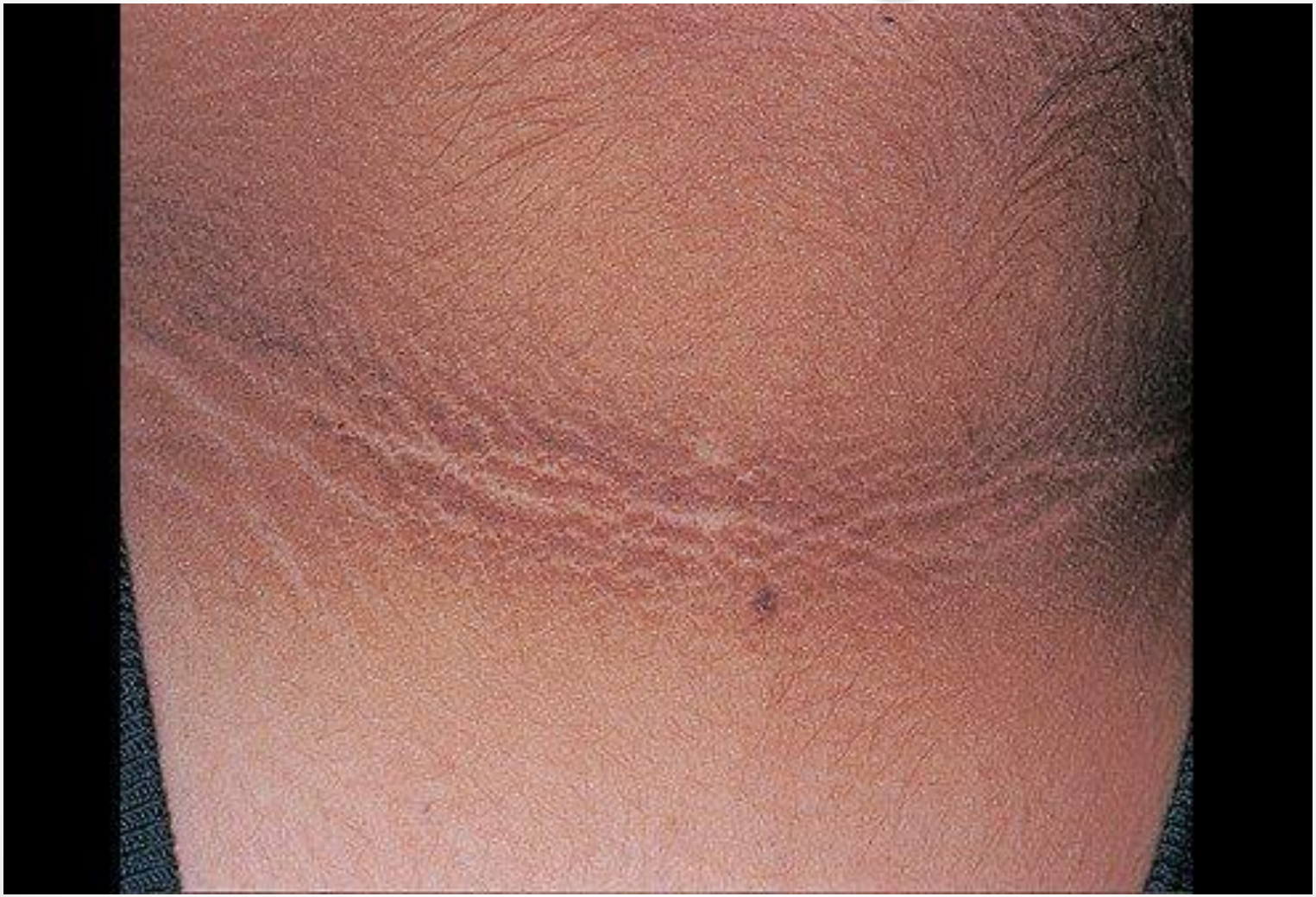
Prevention/Delay of T2DM

- Annual Monitoring in Prediabetes
- Lifestyle Modifications
  - Diabetes Prevention Program
    - Weight loss 7%
    - Increase Physical Activity to 150 min/week
    - Nutrition Counseling/Calorie Reduction
    - Utilization of Technology (Apps)
    - Tobacco Cessation
- Pharmacologic Therapies
  - Some drugs approved for DM have been show to help decrease conversion to DM but none explicitly approved for Prediabetes
  - Reasonable to recommend Metformin in prediabetes with high risk for progression to Diabetes
- Assessment and Treatment of CV Risks
- Education

Evaluation & Assessment of Comorbidities

- BMI
- BP/Vitals
- Eye Evaluation
- Skin Exam
  - Insulin Resistance Markers– Acanthosis Nigricans & Acrochordans
  - Lipodystrophy
  - Necrobiosis Lipoidica Diabeticorum
- Foot Exam
- Lab Assessment
- Immunizations
- Hyperglycemia/Hypoglycemia

Acanthosis Nigricans



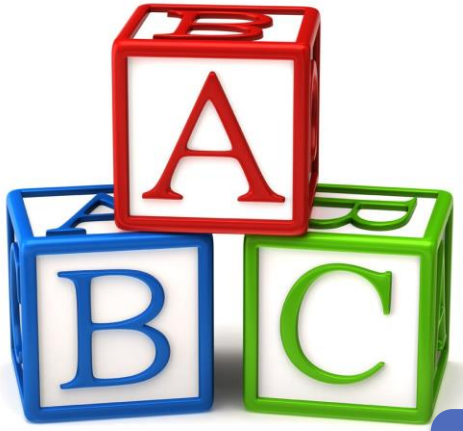
- From: www.medicinenet.com

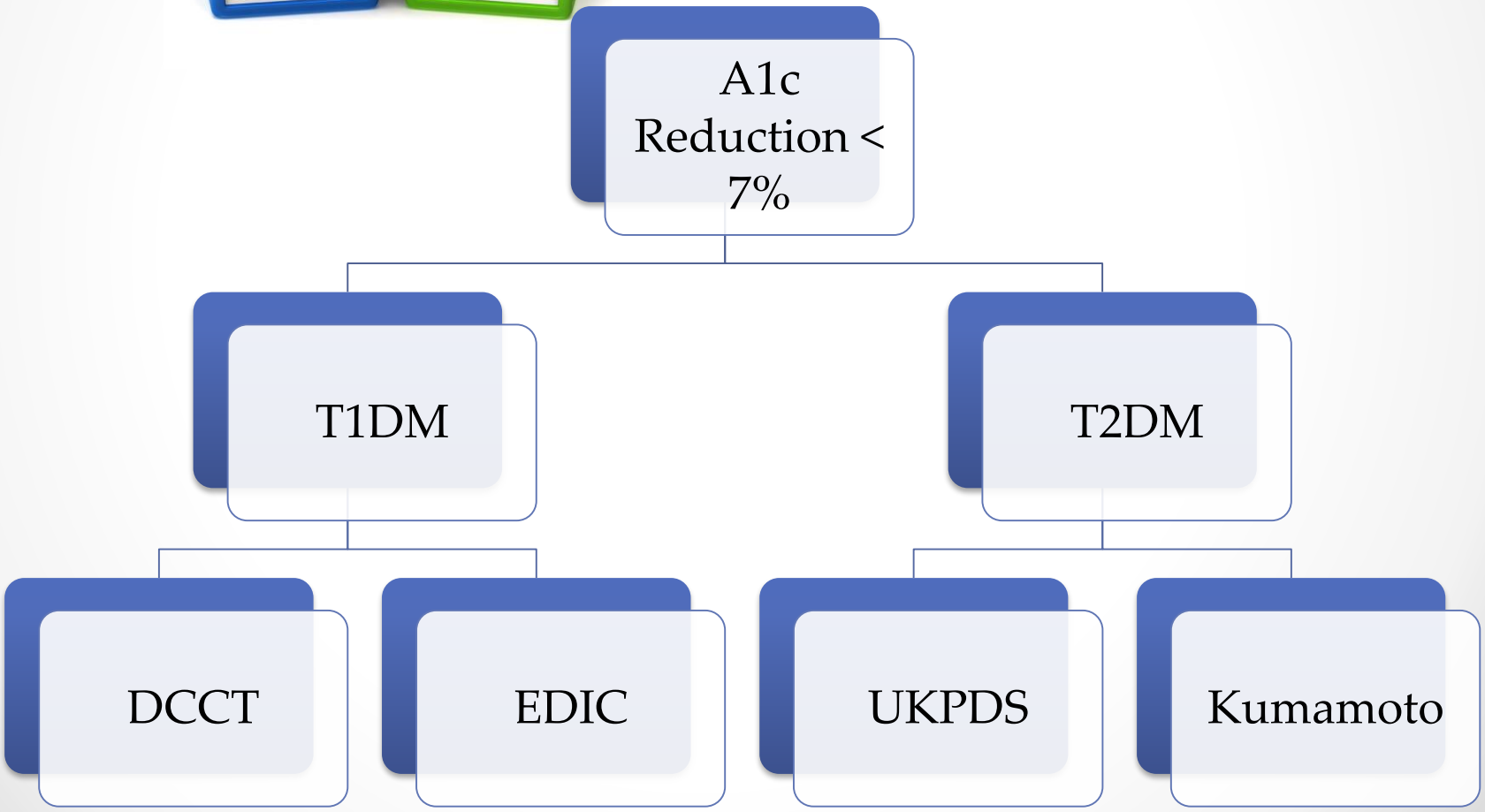
Insulin-Mediated Lipohypertrophy

Verma R. N Engl J Med 2017;377:573-573.

A1c Goals in Diabetes

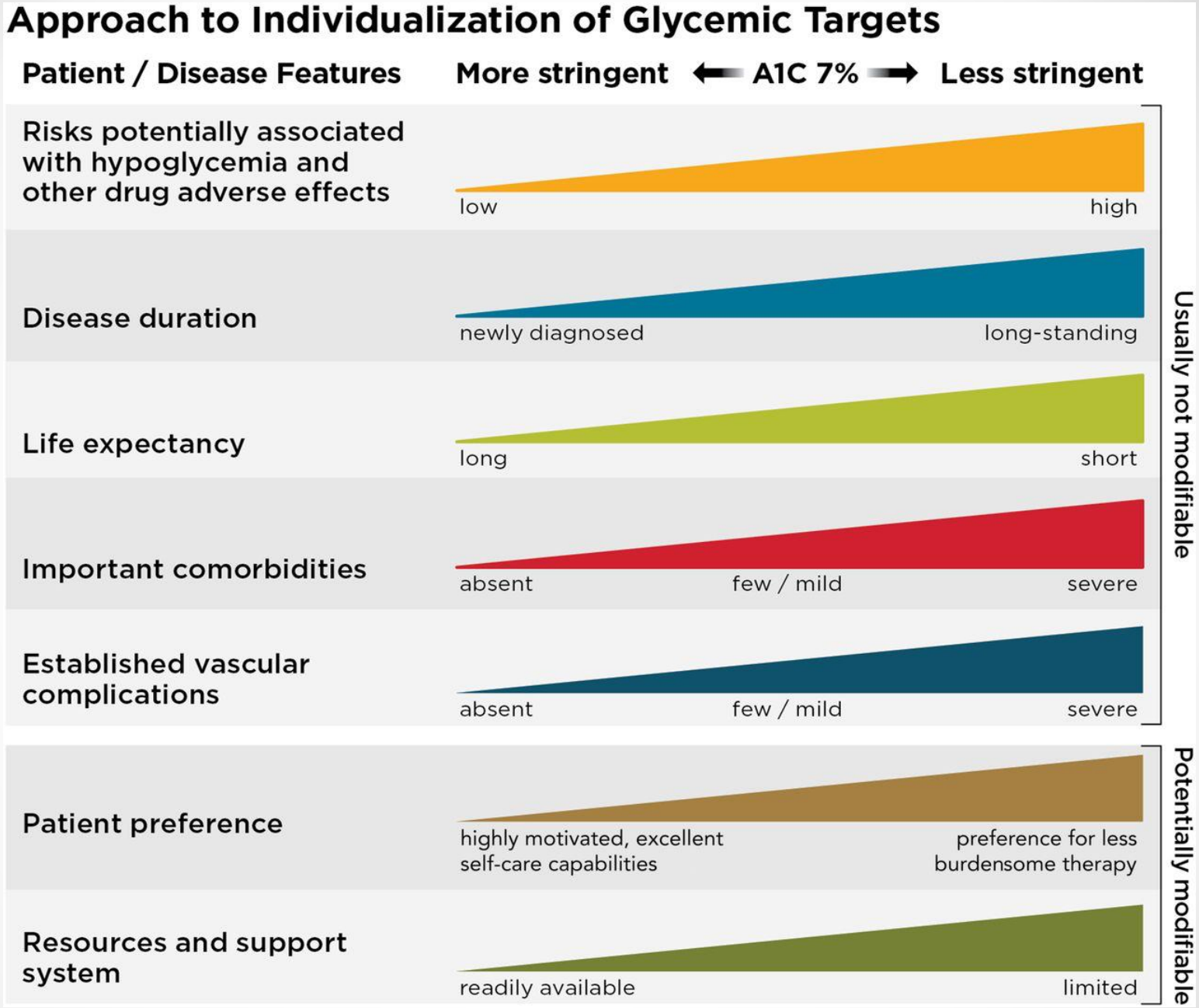
< 6.5%	< 7%	< 8 %
Stricter goals for: - otherwise healthy - few other comorbidities - lower hypoglycemia risk	Reasonable goal for many non-pregnant adults	Looser goals for: - Complicated medical histories, - significant hypoglycemia risk - limited life expectancy - advanced microvascular or macrovascular complications

The  's of A1c Trials



Finding the Perfect Fit

- ACCORD, ADVANCE, and VADT Trials
  - Too low is not always best
  - Increase Mortality from Risk of Hypoglycemia
  - Trials suggested no significant reduction in CVD outcomes with intensive glucose control



- Diabetes Care 2019 Jan; 42(Supplement 1): S61-S70. https://doi.org/10.2337/dc19-S006

Recommended Glycemic Goals for Most Non-Pregnant Adults

A1c	**< 7.0%**
Preprandial Glucose	80-130 mg/dL
Peak Postprandial Glucose	< 180 mg/dL

Hypoglycemia

- Assess at risk individuals at every visit for symptomatic and asymptomatic low sugars
- Hypoglycemia Unawareness indicates need for treatment reevaluation/de-intensification
- Review Treatment Plans with Patient and Family
  - Glucose always preferred if able to take PO
    - 15-15-15 Rule
  - Glucagon
    - IM
    - Intranasal

Classification of Hypoglycemia

Level of Hypoglycemia	Description
Level 1	Glucose < 70 and glucose ≥ 54
Level 2	Glucose < 54
Level 3	Severe event with altered mental/physical status and requiring assistance

- From Diabetes Care 2019; 42(Suppl.1):S61-S70

Lifestyle Management

Critical Times to Address

1. Diagnosis
2. Annually
3. Complications
4. Life Transitions

Goals of Nutrition Therapy

- Promote healthy eating patterns
  - Higher quality nutrients
  - Emphasis on appropriate portion size
- Approach ideal body weight
  - Weight loss
  - Maintenance
- Achieve metabolic goals
  - A1c
  - Blood Pressure
  - Lipids
- Delay/prevent complications of diabetes
- Maintain pleasure and social nature of eating
- There is no single best way to eat

Medical Nutrition Therapy

- Individualized Diet Plan
  - Eating Patterns
  - Macronutrient Distribution
- Energy Balance
- Carbohydrates
- Protein
- Fat
- Dietary Supplements
- Alcohol
- Sodium
- Nonnutritive Sweeteners

Nonnutritive Sweeteners

- May be useful at reducing overall ingested calories and carbohydrates
- Avoid excess
- Potential influence on microbiome
- May lead to further “sweets” cravings

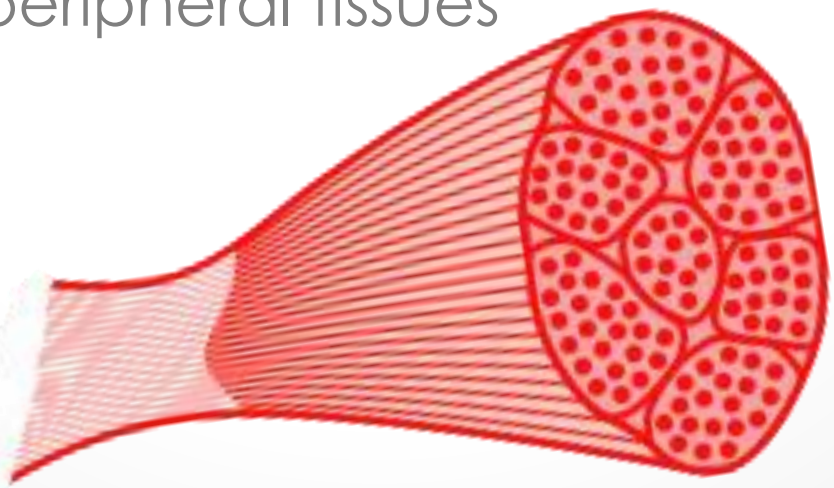
Physical Activity

- Most adults should participate in 150 minutes or more of moderate to vigorous intensity aerobic activity each week
- Resistance Exercise for 2-3 sessions/week on non consecutive days
- Avoid prolonged sitting
- Flexibility and balance training

  2-3 times/week for older adults

How Exercise Helps?

- Glycogen used for fuel in early exercise
- As blood sugars decrease → insulin secretion decreases
- Glucagon rises → stimulates TG use for muscle fuel
- Increased GLUT4 expression→ increased glucose sensitivity in peripheral tissues



Pharmacologic Therapies

Type 1 Diabetes

- Basal/Bolus Insulins
  - Basal Dose ~ 50% TDD
  - Prandial Dose Based on Pre Meal Sugar + Ingested CHO
- Multiple Daily Injections
- Insulin Pump Therapy
- Non Insulin Treatments
  - Pramlintide
- Pancreas/Islet Transplants

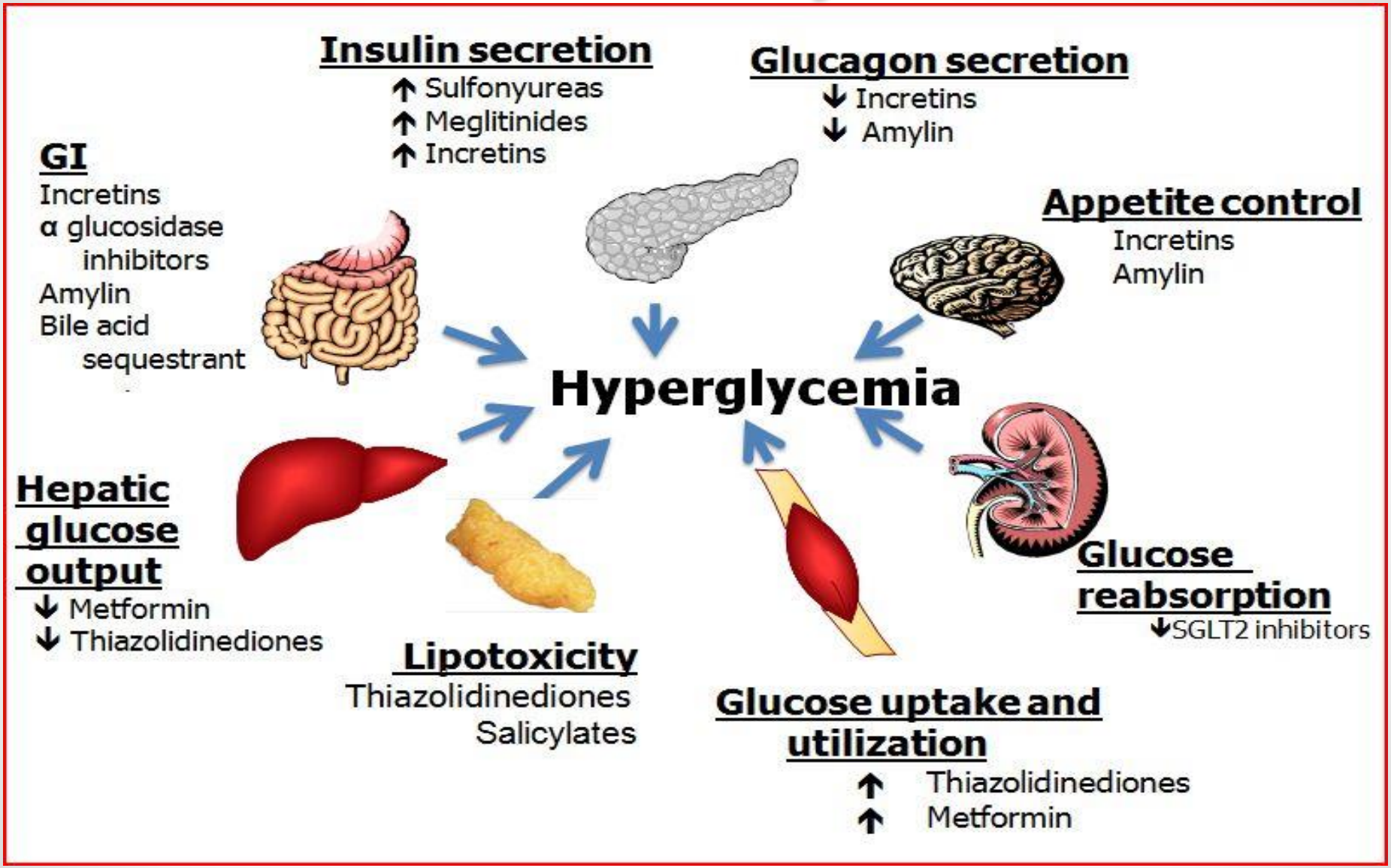
Type 2 Diabetes

- Oral Hypoglycemics
- Non Insulin Injectables
- Insulins
  - Basal
  - Prandial

Non Insulin Therapies for Diabetes

- Biguanides (Metformin)
- Sulfonylureas
- Meglitinides
- Alpha Glucosidase Inhibitor
- Thiazolidinediones
- GLP-1 Receptor Agonists
- DPP-4 Inhibitors
- SGLT2 Inhibitors
- Dopamine 2 Agonists
- Amylin Mimetics
- Bile Acid Sequestrants

Where do they work?



- http://diabetesmanager.pbworks.com/w/page/17680289/

Galega officinalis (French Lilac)

Gila Monster (*Heloderma suspectum*)

Effects of GLP-1 Agonists

Glycemic

- Corrects deficient GLP-1 state of T2DM (and likely T1DM)
- Promotes insulin secretion in glucose dependent fashion
- Decreases Glucagon Levels
- Slows Gastric Emptying

Non-Glycemic

- Slows Gastric Emptying
- Natriuresis
- Vasodilation
  - ↓ BP
  - ↑ HR
- Increase Satiety
- Improves Lipid Profiles
- Weight Loss

Differences in Available GLP Agonists

Short Acting Agents

- Greater effect on Gut- delays gastric emptying
- Reduce post prandial hyperglycemia
  - **Exenatide**
  - **Lixisenatide**

Long Acting Agents

- Greater effect at pancreatic level:
  - ↓ Glucagon
  - ↑ Insulin
- Targets fasting hyperglycemia
  - **Liraglutide**
  - **Exenatide ER**
  - **Dulaglutide**
  - **Semaglutide**

Owens DR et al. Differential effects of GLP-1 receptor agonists on components of dysglycemia in individuals with T2DM. Diabetes Metab. 2013 Dec;39(6): 485-96.

SGLT-2 Inhibitors

- Phlorizin isolated in 1835 from apple tree bark
- Use as hypoglycemic was limited due to non selectivity and side effects
- Approved in US in 2013
- Associated with weight loss
  - Diuretic properties
  - Glucosuria leading to loss of 100-300 calories/day

Adapted from www.diabetesincontrol.com- "History of the SGLT2 Inhibitor Drug Class." Jan. 17, 2014

Concentrated Insulins

Benefits of Concentrated Insulins

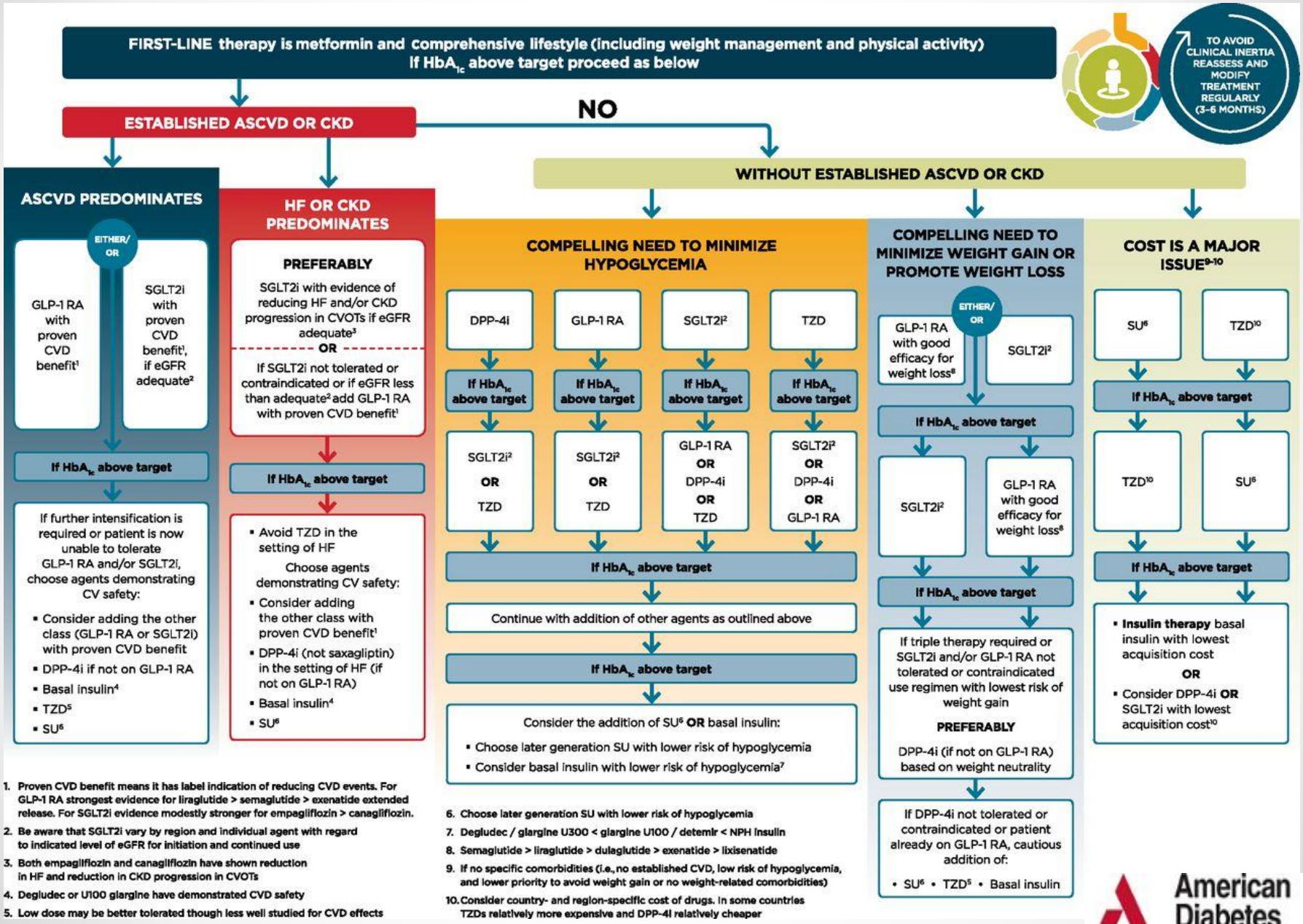
- Decreased Hypoglycemia
  - Nocturnal
  - Severe
  - Overall
- Increased flexibility in dosing due to longer duration of action
- Less need for frequent adjustments
- Less variability in activity
- Less risk of "stacking"
- Equivalent or less weight gain

Garber, AJ et al. Endocrine Practice Nov 2016 Vol 22 Supplement 5. "Basal Insulin 4.0: Updating your clinical practice with ultralong acting insulins and insulin combination therapy

Currently Used Basal Insulins

Insulin	Concentration	Duration of Action
NPH	U100	16 hours
Glargine	U100	~24 hours
Detemir	U100	~24 hours
Glargine	U300	> 36 hours
Degludec	U100 or U200	> 42 hours

Glucose-lowering medication in type 2 diabetes: overall approach.

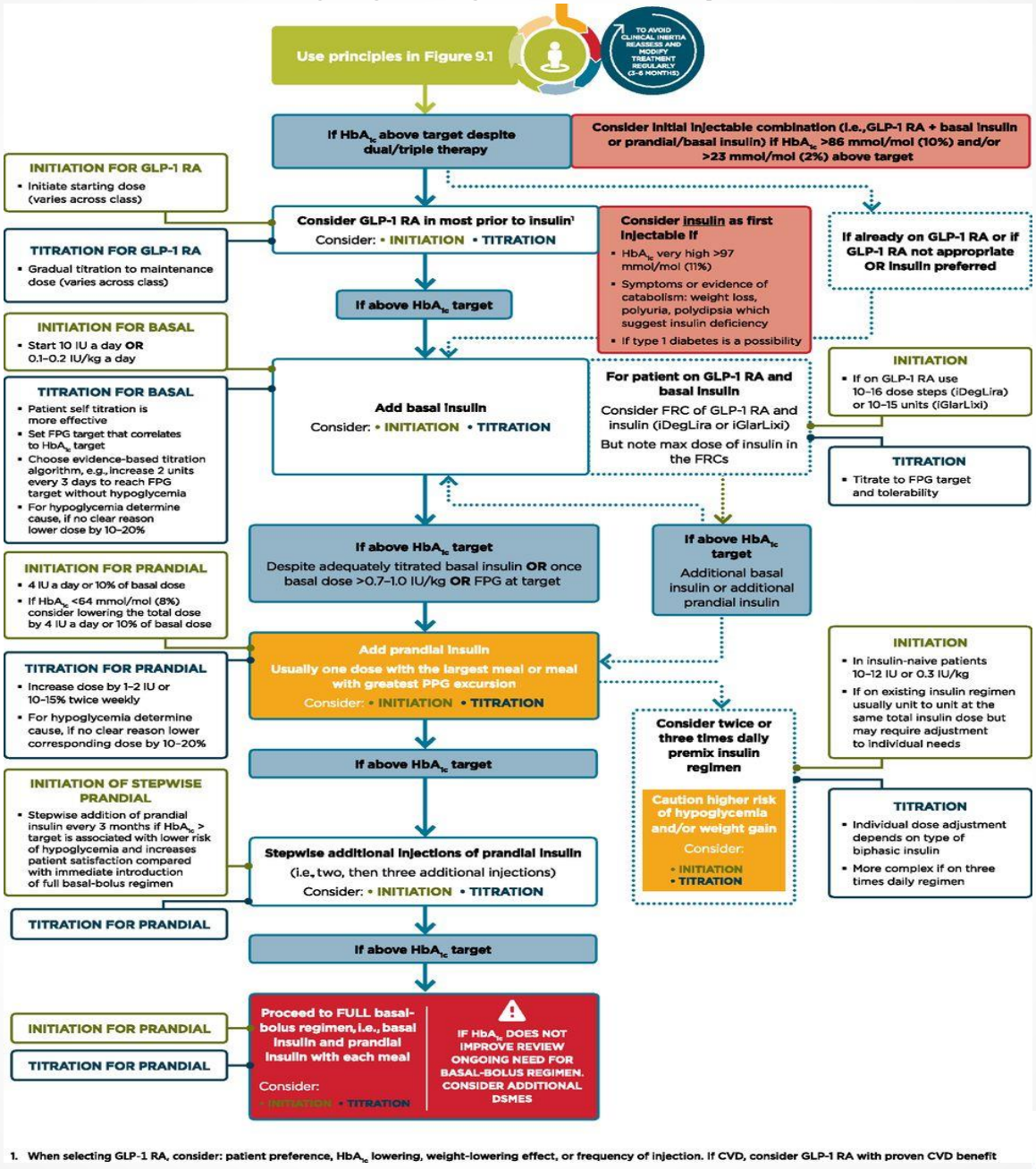


1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for liraglutide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU with lower risk of hypoglycemia
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

American Diabetes Association

American Diabetes Association Dia Care 2019;42:S90-S102

Intensifying to injectable therapies.



1. When selecting GLP-1 RA, consider: patient preference, HbA_{1c} lowering, weight-lowering effect, or frequency of injection. If CVD, consider GLP-1 RA with proven CVD benefit

American Diabetes Association Dia Care 2019;42:S90-S102

American Diabetes Association.

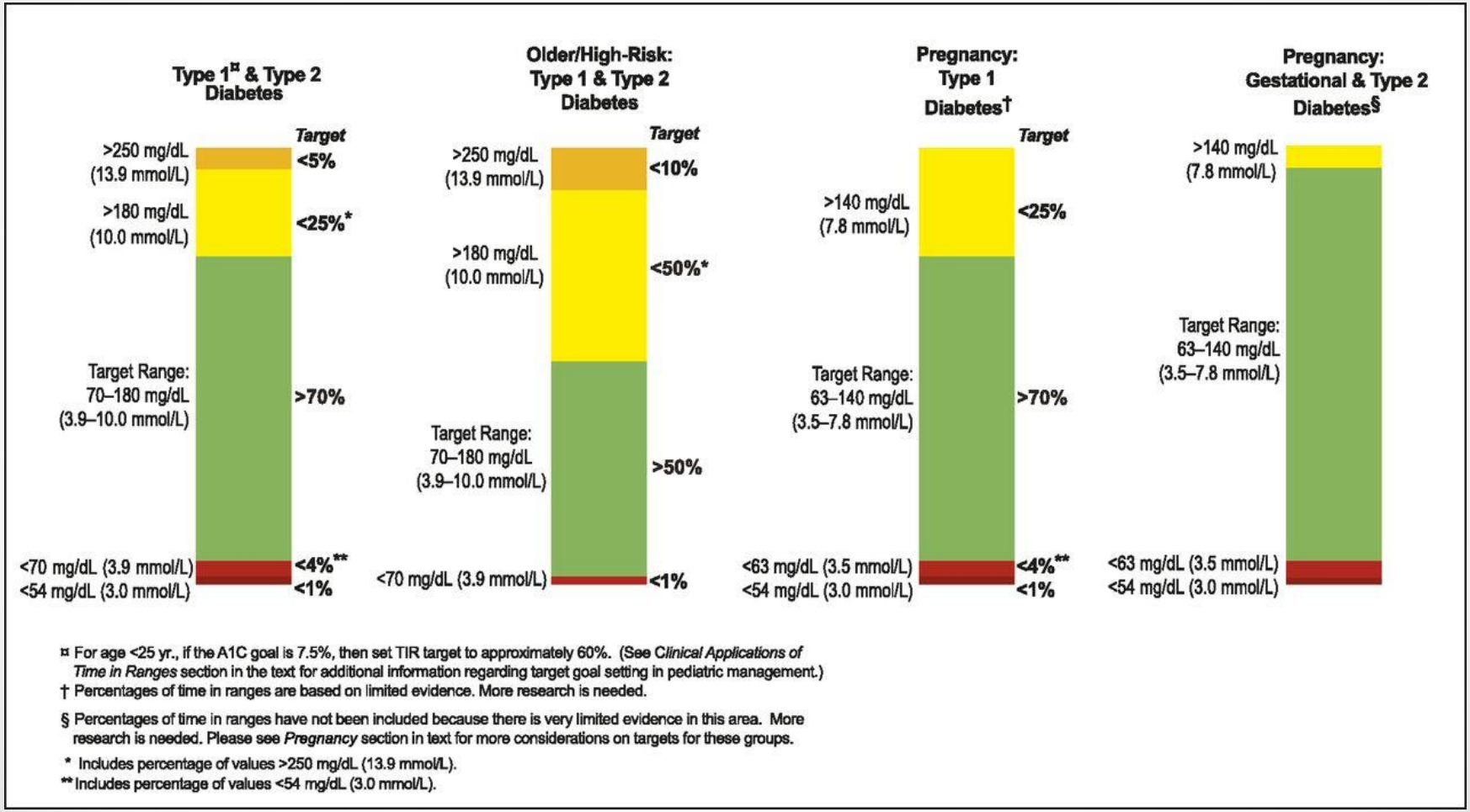
Diabetes Technology

The first insulin pump created by Dr. Arnold Kadish in California in 1963 which delivered both insulin and glucagon.

From: www.medscape.org

Continuous Glucose Monitoring Sensors

CGM-based targets for different diabetes populations.



¤ For age <25 yr., if the A1C goal is 7.5%, then set TIR target to approximately 60%. (See *Clinical Applications of Time in Ranges* section in the text for additional information regarding target goal setting in pediatric management.)

† Percentages of time in ranges are based on limited evidence. More research is needed.

§ Percentages of time in ranges have not been included because there is very limited evidence in this area. More research is needed. Please see *Pregnancy* section in text for more considerations on targets for these groups.

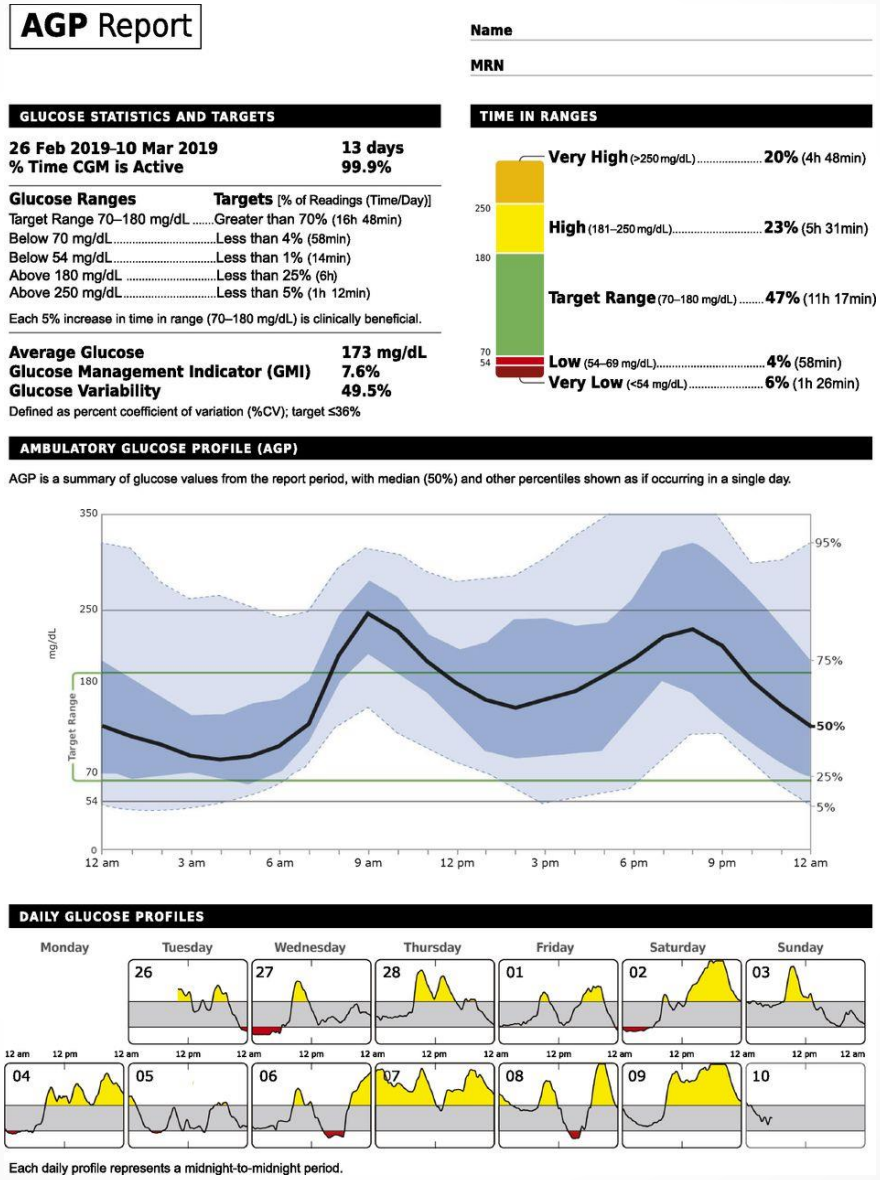
* Includes percentage of values >250 mg/dL (13.9 mmol/L).

** Includes percentage of values <54 mg/dL (3.0 mmol/L).

Tadej Battelino et al. Dia Care 2019;42:1593-1603

American Diabetes Association.

Ambulatory Glucose Profile



AGP Report

Name

MRN

GLUCOSE STATISTICS AND TARGETS

26 Feb 2019–10 Mar 2019	**13 days**
% Time CGM is Active	**99.9%**

Glucose Ranges	**Targets** [% of Readings (Time/Day)]
Target Range 70–180 mg/dL	Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)

Each 5% increase in time in range (70–180 mg/dL) is clinically beneficial.

Average Glucose	**173 mg/dL**
Glucose Management Indicator (GMI)	**7.6%**
Glucose Variability	**49.5%**

Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES

250
180
70
54

Very High (>250 mg/dL) **20%** (4h 48min)
High (181–250 mg/dL) **23%** (5h 31min)
Target Range (70–180 mg/dL) **47%** (11h 17min)
Low (54–69 mg/dL) **4%** (58min)
Very Low (<54 mg/dL) **6%** (1h 26min)

AMBULATORY GLUCOSE PROFILE (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.

DAILY GLUCOSE PROFILES

Each daily profile represents a midnight-to-midnight period.

Tadej Battelino et al. Dia Care 2019;42:1593-1603

American Diabetes Association.

Obesity Management for the Treatment of T2DM

- Lifestyle
  - Dietary Goals→ >5% weight loss and maintained
  - Intense Behavioral Therapy
    - Focus on diet, exercise, and behavioral strategies
    - ≥ 16 sessions in 6 months
- Pharmacotherapy
- Metabolic Surgery

From: texashillcountry.com

Drug	% Weight Loss	Side Effects	Safety Considerations
Phentermine	5.5-6.1	Dry Mouth Insomnia Dizziness Irritability	Severe HTN CI with MAOI
Orlistat	5.6-9.6	Abdominal Pain Gas Fecal Urgency Back Pain Headache	Malabsorption Cholelithiasis Nephrolithiasis Liver Injury
Lorcaserin	4.5	Headache Nausea Fatigue Dizziness	Serotonin & Neuroleptic Malignant Syndrome Monitor for Depression/SI Worsening HTN Avoid with kidney/liver disease
Phentermine /Topiramate ER	7.8-9.8	Constipation Paresthesia Insomnia Xerostomia	Birth Defects Cognitive Impairment Acute Angle Glaucoma
Naltrexone/Bupropion ER	5.0	GI Symptoms Heachache Xerostomia Insomnia	CI with uncontrolled HTN or Seizures CI with chronic opioids Acute Angle Glaucoma BLACK BOX: SI
Liraglutide	2.0-6.0	Hypoglycemia GI Symptoms	Acute pancreatitis BLACK BOX: Risk of thyroid C cell tumors & CI with h/o MTC or MEN 2

Metabolic Surgery Recommendations

- Metabolic surgery should be recommended as an option to treat T2DM in appropriate candidates with BMI ≥ 40& in adults with BMI 35-39.9 who do not achieve durable weight loss and improvement in comorbidities with reasonable nonsurgical methods
- Metabolic surgery may be considered as an option for adults with T2DM and BMI 30-34.9 who do not achieve durable weight loss and improvement in comorbidities with reasonable nonsurgical methods

From: Obesity Management for the Treatment of T2DM: Standards of Medical Care in Diabetes– 2019. Diabetes Care 2019;42(Suppl.1):S81-89

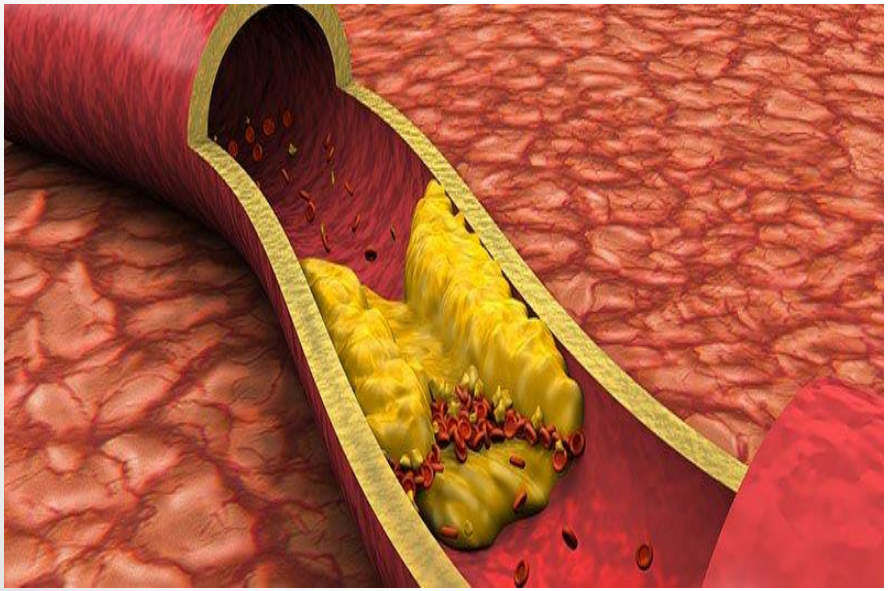
CV Disease & Risk Management

- Achieve BP goals:
  - _DM +HTN with higher ASCVD risk /10 yr atherosclerotic CVD risk > 15% consider target BP < 130/80
  - DM + HTN with lower risk for CVD.10 yr atherosclerotic risk < 15% use goal BP < 140/90
  - Antihypertensive therapy reduces risk of CVA, retinopathy &albuminuria
- Lifestyle Interventions
  - DASH Diet
  - Mediterranean Diet
  - Physical Activity
- Lipids
  - High Intensity Statin- DM + ASCVD or 10 year risk > 20%
  - Moderate Intensity Statin- DM Age > 40 without additional CV RF
  - No Statin Age < 40 without ASCVD or risk < 20%
  - Consider PCSK9 or Ezetimibe if LDL remains ≥ 70

High & Moderate Intensity Statin Therapies

High Intensity

- Atorvastatin 40-80 mg
- Rosuvastatin 20-40 mg



From: verywellhealth.com

Moderate Intensity

- 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

CV Outcome Trial Summary

- EMPA-REG
  - Empagllflozin reduced risk of MI, CVA and CV death by 14% & CV death by 38%
- CANVAS
  - Canagliflozin reduced risk of CV death, MI, & CVA vs Placebo
  - Increased risk of lower limb amputation with Canagliflozin
- LEADER
  - Liraglutide reduced risk of MI, CVA or CV death as compared to placebo
- SUSTAIN-6
  - Semaglutide results consistent with LEADER
- ELIXA
  - Lixisenatide was non-inferior to placebo but not superior at reducing CV outcomes
- EXSCEL
  - Exenatide Qweek showed non-inferiority but not superior to primary end point

From: Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes– 2019. Diabetes Care 2019;42(Suppl.1):S103-S123

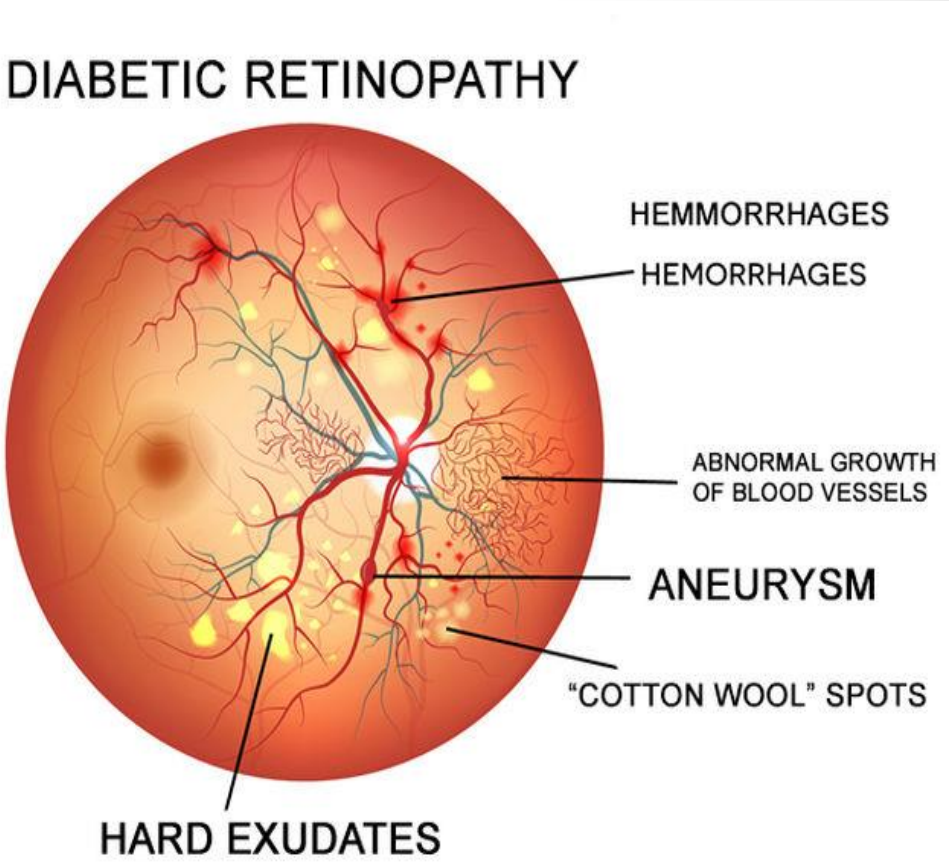
Microvascular Complications-- CKD

- Asses spot urine/creatinine ratio annually
- Optimize glycemic & BP control (< 140/90)
- Consider SGLT2i or GLP1 agonist in T2DM as may reduce progression of CKD
- Consider ACE/ARB in patients with albumin/Cr > 30 (strongly encouraged if > 300)
- Periodically monitor K and Cr
- Refer for renal evaluation when needed

- **ACE/ARB therapy not recommended for primary prevention of CKD in patients with DM with normal BP and normal eGFR and normal microalbumin/creatinine ratio
- ** Combined use of ACE and ARB not recommended

Microvascular Complications-- Retinopathy

- Optimize lipids, BP, and glycemic control
- Refer to ophthalmologist
- Women planning pregnancy should be followed closely Treatments include:
  - Laser Photocoagulation
  - anti-VEGF Therapies



From: https://www.contouravisionindia.com/single-post/What-causes-diabetic-retinopathy

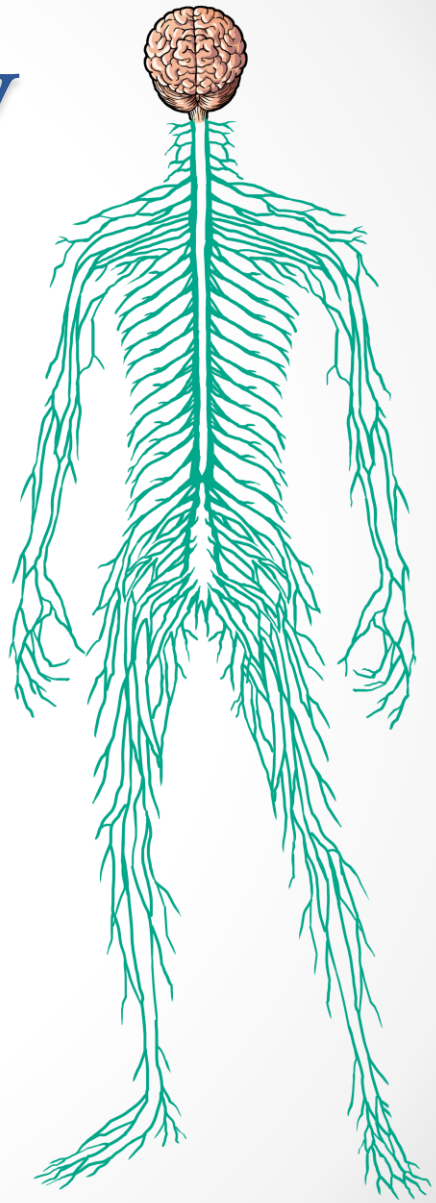
Microvascular Complications-- Neuropathy

- Begin assessing at diagnosis in T2DM
  - Small fiber function with temperature/pin prick sensation
  - Large fiber function with tuning fork
  - Protective sensation with 10 gm Monofilament
- Optimize glucose control to delay diagnosis and prevent progression of neuropathy in T2DM
- Pharmacologic options:
  - Pregabalin
  - Duloxetine
  - Gabapentin

From webmd.com

Diabetic Autonomic Neuropathy

- Hypoglycemia Unawareness
- Tachycardia at Rest
- Orthostatic Hypotension
- Gastroparesis
- Constipation/Diarrhea
- Fecal Incontinence
- Erectile Dysfunction
- Neurogenic Bladder
- Sudomotor dysfunction



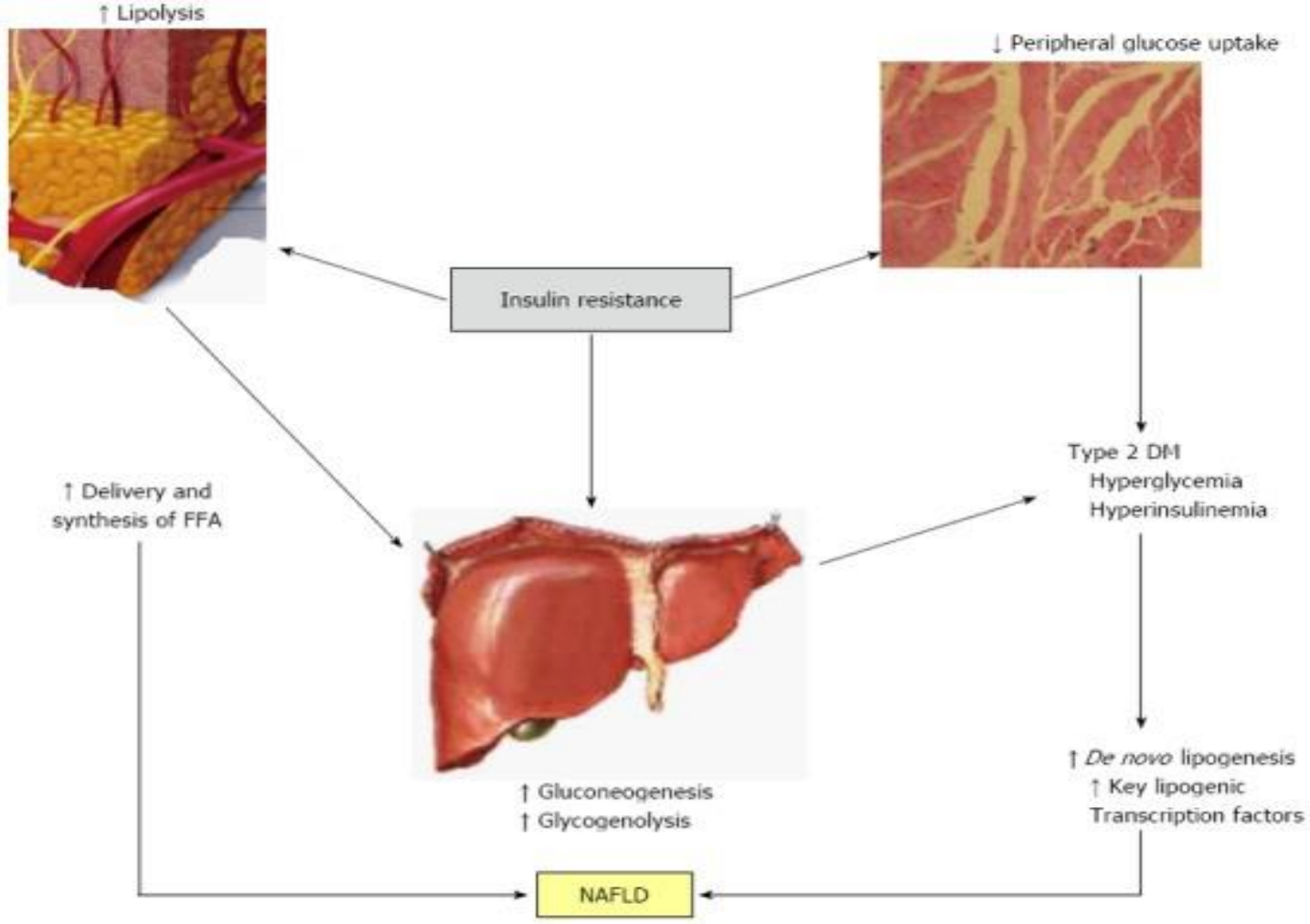
From: www.skillscommons.org

Foot Care in Diabetes

- Perform annual comprehensive foot exam
  - Skin Inspection
  - Foot Deformities
  - Neurological Testing (monofilament + one more test)
  - Vascular Assessment- check pulses
- Inspect those with sensory loss or prior ulceration or amputation at EVERY visit
- Encourage Tobacco Cessation
- Educate on self foot care

From: Diabetes Care 2011 Sep; 34(9): 2123-2129. https://doi.org/10.2337/dc11-0844

Insulin Resistance in NAFLD



Leite, NC et al Non-alcoholic fatty lievr disease and diabetes: from physiopathological interplay to diagnosis and treatment. World J Gastroenterology July 2014;20(26): 8377-8392

Diabetes in Older Adults

- Prevalence of Diabetes in Older Adults
  - ¼ of all Adults > 65 years have Diabetes
  - ½ of all older adults have Prediabetes
- Assess Diabetes Self Management Skills
- Hypoglycemia Risk
- Consider Adjustment of Glycemic/Lipid/BP Goals:

Healthy Individuals	**A1c < 7.5%**
Complex Comorbidities Mild to Moderate Impairment of Cognition and Effects on ADL	**A1c < 8.0%**
Complex Health Issues and Functional Status	**A1c < 8.5%**

Diabetes in Older Adults

- Metformin
  - OK for GFR > 30 but not to be used with ESRD and should be used cautiously with CHF or impaired hepatic function
- Thiazolidinediones
  - Use caution (if at all) with or at risk for CHF or high falls/fracture
- Sulfonylureas
  - Use caution due to increase hypoglycemia risk
  - Glyburide contraindicated in older adults (due to longer duration)
- Incretins (DPP4/GLP agents)
- SGLT2 agents
- Insulins

Patients Perceptions on Need for Aggressiveness of DM Therapy

Hypothetical Patient Factor	Study Participant Perception Relative to Guideline Recommendations
Duration of DM - 5 years - 15 years	Discordant
DM Complications - None - Severe	Discordant
Comorbidities - None - Many	Discordant
Life Expectancy - 5 years - 15 years	Concordant
Adverse Event Risk - High Risk - Low Risk	Concordant

Adapted from Schoenborn, NL et al. Patient perceptions of diabetes guideline frameworks for individualizing glycemic targers. JAMA Internal Med. Sep 16, 2019. Doi:10.1001/jamainternmed.2019.3806

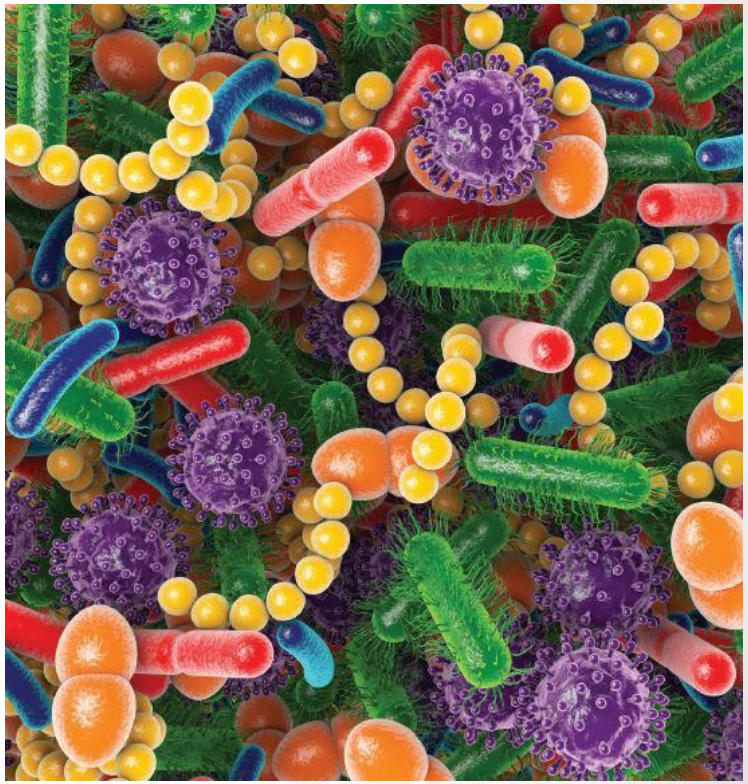
Summary of Revisions: Standards of Medical Care in Diabetes-2019

- Diagnosis
  - Inclusion of 2 abnormal test results from the SAME sample
  - Additions to conditions affecting A1c accuracy
- Prevention/Delay
  - Nutritional Updates
  - Tobacco Cessation
- Comorbidity Assessment
  - Avoidance of Clinical Inertia
  - Hypoglycemia Risk Assessment
  - ASCVD Risk
  - Fatty Liver
- Lifestyle Management
  - Macronutrient Patterns to be Individualized
  - Decrease Sweetened and Artificially Sweetened Beverages
  - Sodium Consumption
- Glycemic Targets
  - Fluidity of A1c Goals
- Diabetes Technology
- Obesity Management for Treatment of T2DM
  - Health Trackers
  - Recommendations for Metabolic Surgery
- Pharmacologic Therapies
- CV Disease & Risk
- Microvascular Complications & Foot Care
- Older Adults
- Diabetes in the Hospital

Diabetes Care 2019;42(Suppl.1):S4-S6 https://doi.org/10.2337/dc19-srev01

Gut Microbiome

- Important Microbial Roles in Gut:
  - Breakdown of indigestible fibers
  - Biosynthesis of amino acids and vitamins
  - Neurotransmitter/Hormone Production
- Therapeutic Targets for Diabetes and Obesity
  - Alterations in microbiome composition
  - Genetic alteration to bacteria
  - Targeting specific regions of colonic delivery
  - Pro/Pre Biotics and Personalized Nutrition
- Changes in microbiome composition following bariatric surgery



From prescriber.co.uk

Brunkwall, L et al. The gut microbiome as a target for prevention and treatment of hyperglycaemia in T2DM: from current human evidence to future possibilities. Diabetologia (2017)60:943-951.

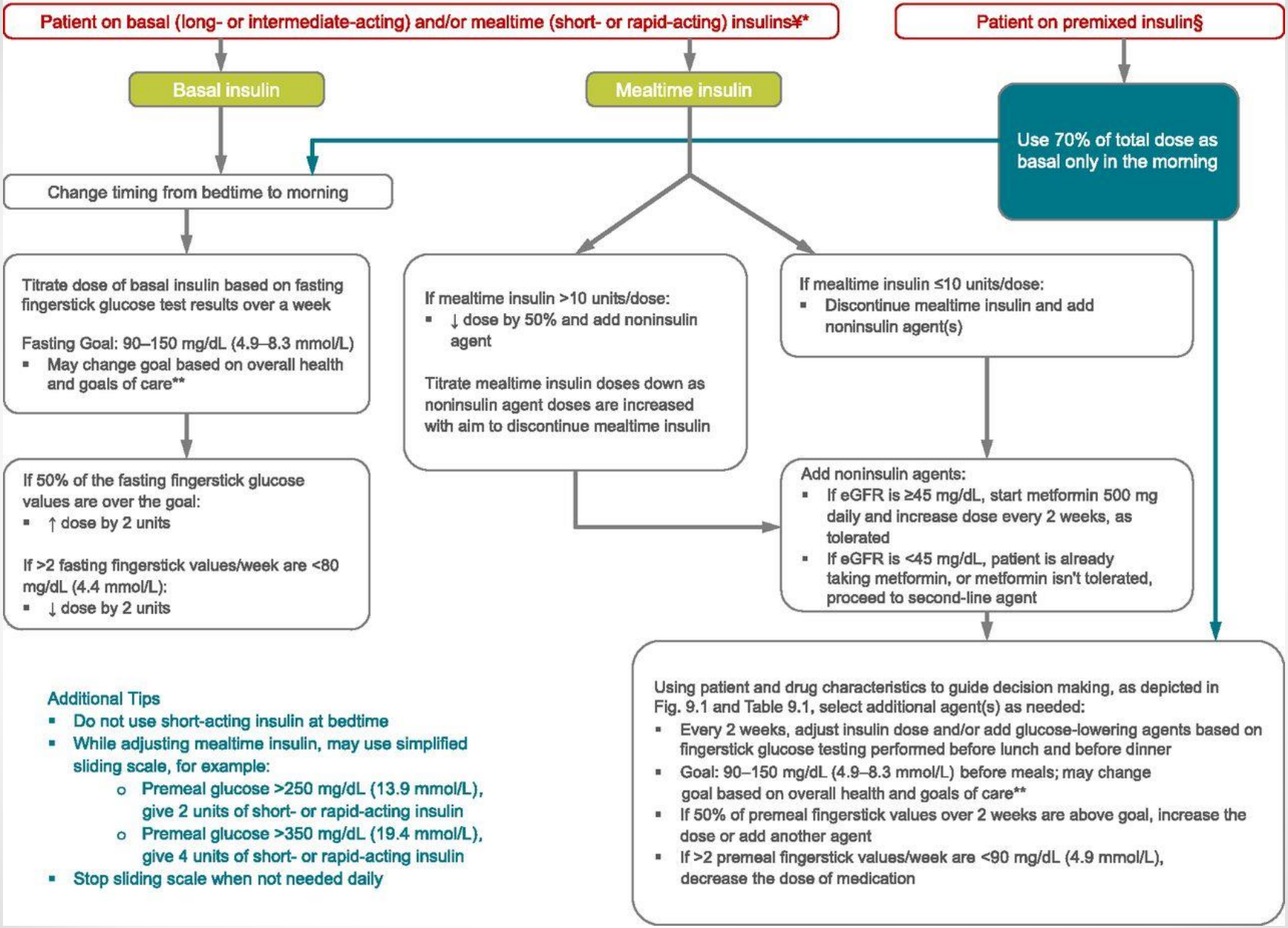
Changes to Gut Microbiome in Diabetes

- ↓ **Butyrate** producing bacteria seen in DM
  - may be improved with metformin treatment
- ↑ **Branched Chain Amino** Acids associated with increase in Insulin Resistance
- ***Akkermansia muciniphil*** = a potential biomarker of Glucose Intolerance
- **Prevotella** genus is associated with ↑ fiber diets
  - May enhance digestion of complex polysachharides

Inpatient Diabetes Care

- A1c Status
- Treat persistent hyperglycemia ≥ 180 with insulin
  - Glucose Targets on Insulin 140-180
  - More stringent goals (110-140) for select patients if low risk of hypoglycemia
- Preferred Therapies for Hyperglycemia in Hospital:
  - Basal/Prandial/Correction Doses of Insulin
  - Discourage "sliding scale" as sole treatment
  - Restart PO agents prior to D/C when patient is eating normally
- Avoid Hypoglycemia
  - Begin treating < 70
  - Recognize common triggers
    - ↓ PO intake, ↓ corticosteroids, NPO status

Simplification of Complex Insulin Therapy



American Diabetes Association Dia Care 2019;42:S139-S147

American Diabetes Association.