

CPGs On Diabetes Mellitus, Focus on Older Adults

T.S. Dharmarajan MD, MACP, FRCPE, AGSF

Professor of Medicine

Albert Einstein College of Medicine, Bronx, NY

Vice Chairman, Department of Medicine

Clinical Director, Geriatric Medicine

Program Director, Geriatric Medicine Fellowship Program

Montefiore Medical Center (Wakefield Campus), Bronx, NY

Learning Objectives

- **Understand the current Clinical Practice Guidelines pertinent to Type 2 diabetes mellitus**
- **Discuss presentations of diabetes in older adults and the approaches in patients with cognitive and functional challenges**
- **Determine glycemic goals for individualized, patient-centered care**
- **Understand management relating to care settings, comorbidity and life expectancy**

Speaker Disclosures

T.S. Dharmarajan MD has disclosed that he has no financial relationship(s) whatsoever, with regards to his presentation

The material in this presentation is derived from

Standards of Medical Care in Diabetes (ADA), 2019

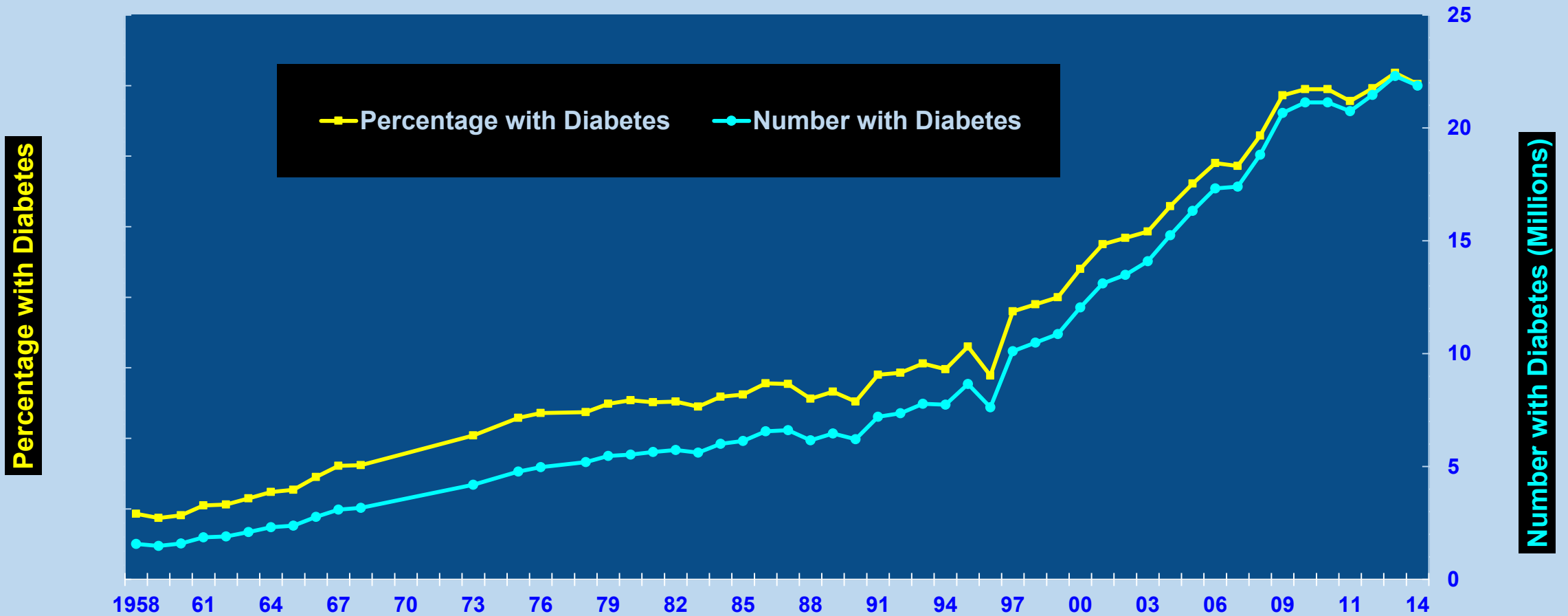
Endocrine Society Clinical Practice Guidelines, 2019

American Medical Directors Association CPGs

American Geriatrics Society Guidelines

And Current Literature

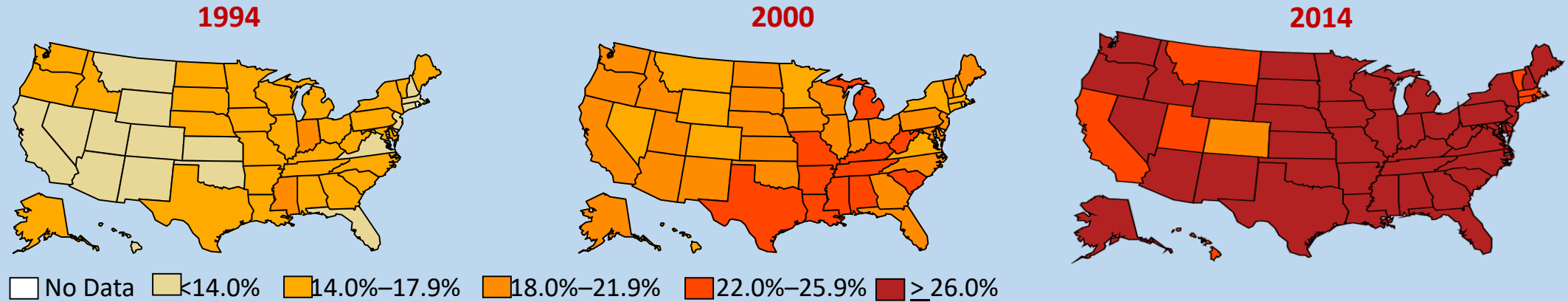
Number and percentage of U.S. Population with Diagnosed Diabetes, 1958 - 2014



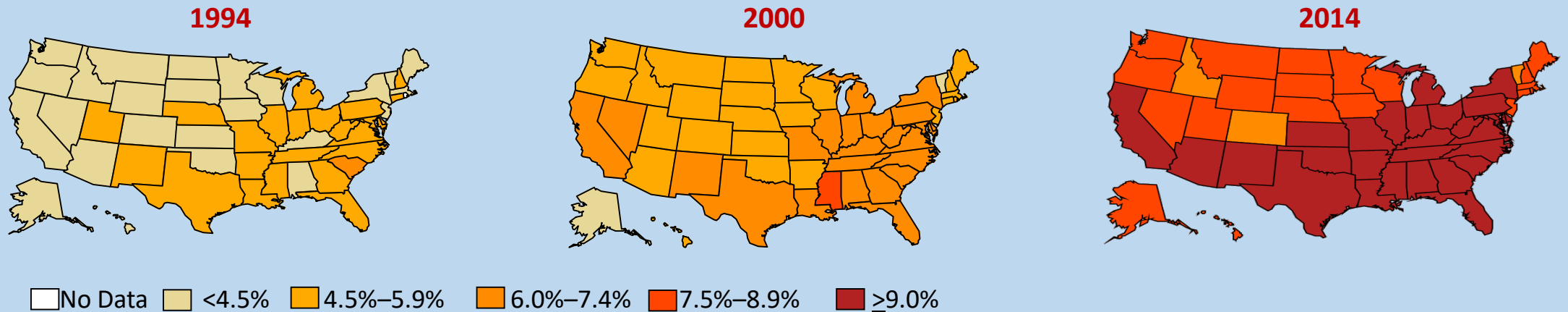
CDC's Division of Diabetes Translation. United States Diabetes Surveillance System available at <http://www.cdc.gov/diabetes/data>

Age-adjusted Prevalence of Obesity and Diagnosed Diabetes Among US Adults

Obesity (BMI ≥ 30 kg/m²)



Diabetes Mellitus



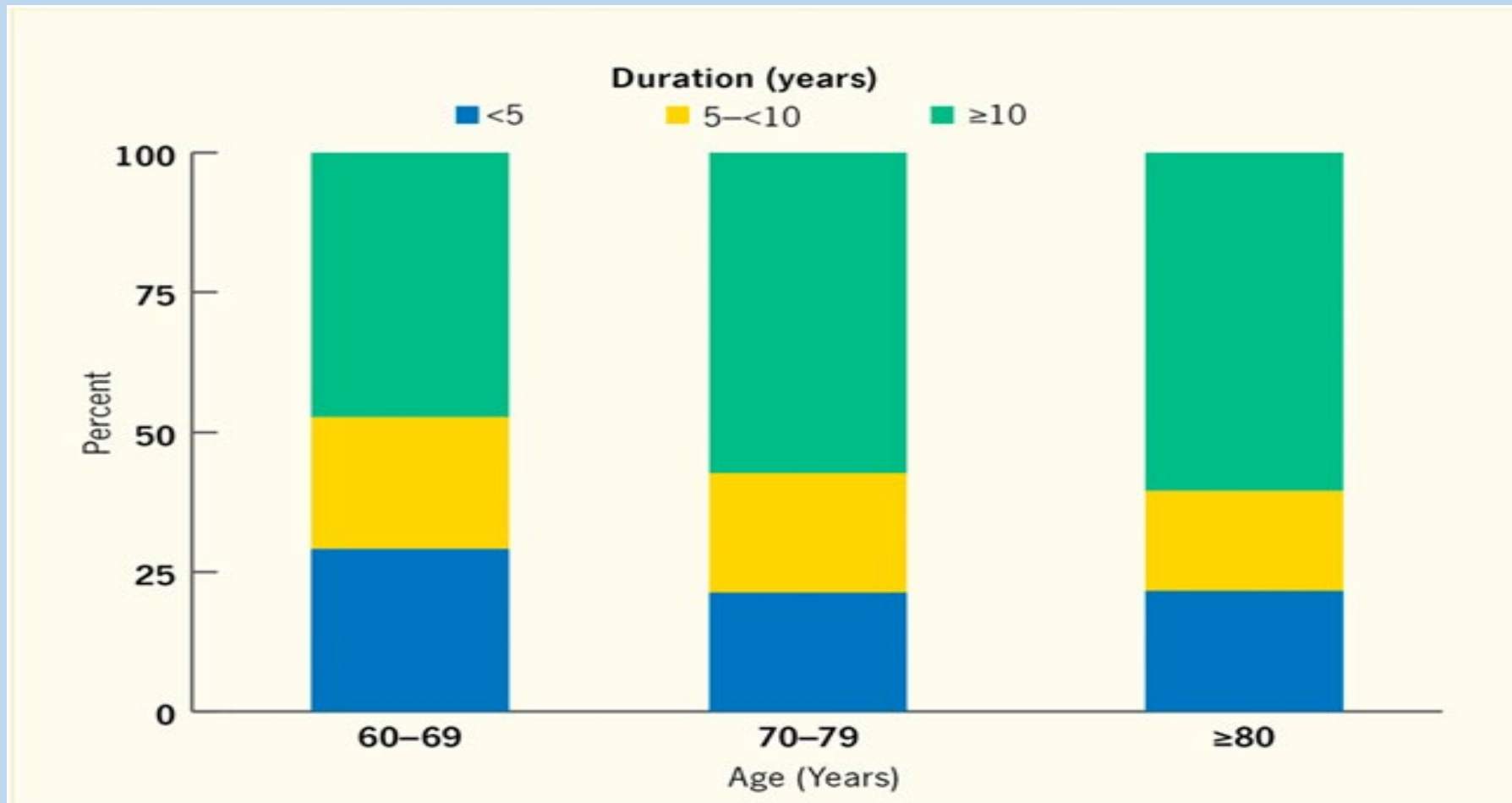
Diabetes in the Old: Consequences to Economy

- **In the Medicare-eligible population, the diabetes population is expected to rise from 8.2 million in 2009 to 14.6 million in 2034**
- **This equates an estimated rise from \$45 billion to \$171 billion in the costs of care rendered**

T2Diabetes is an Age Related Disease

Duration of T2D in Over 60 years Age Categories, U.S.

Treatment of Diabetes in Older Adults: Endocrine Society CPG
J Clin Endocrinol Metabol. 2019;104:1520-74



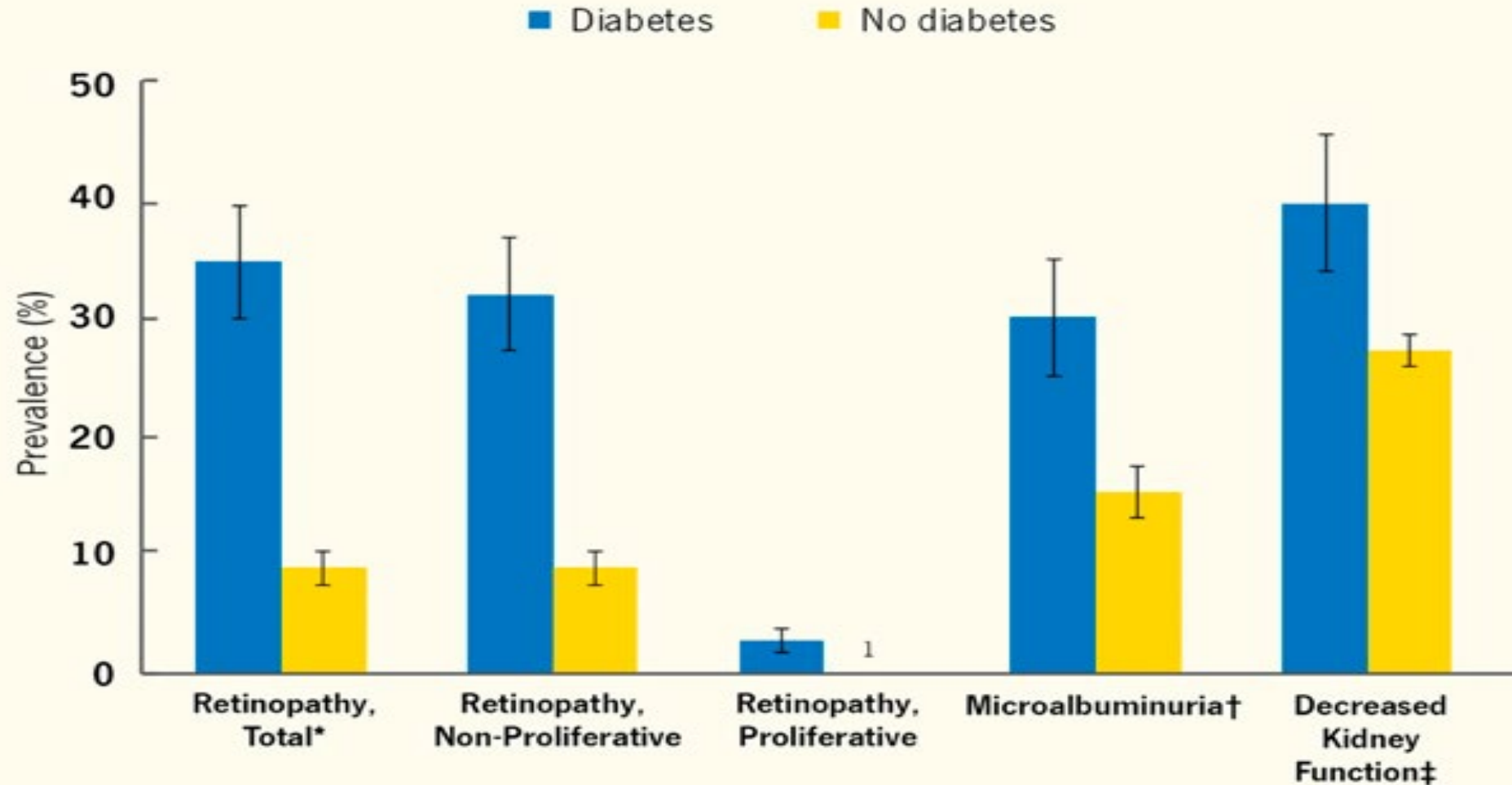
Epidemiology of Type 2 Diabetes in the U.S.

- **T2D is an age related disease, prevalence 33% in those >65 years; over 90% of these adults have T2D**
- **And nearly 50% of older adults meet criteria for prediabetes**
- **New diagnosis: incidence highest in the 65 - 79 years age group**
- **Prevalence higher in Black Americans and Hispanic Americans**
- **Outcomes:10-year reduction in life expectancy**

Microvascular Complications by Diabetes Status, Adults, over 60 years, U.S.

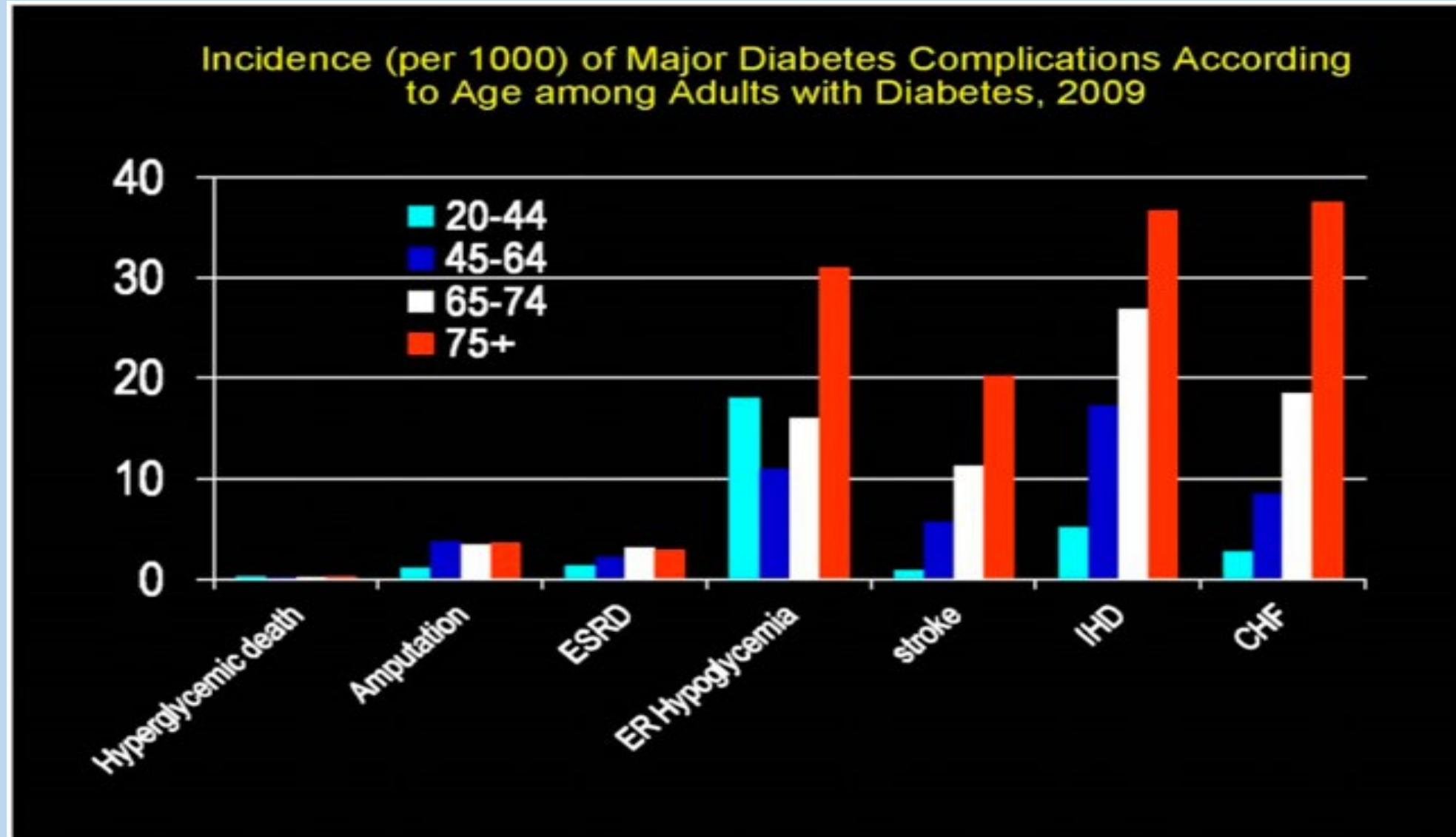
Treatment of Diabetes in Older Adults: Endocrine Society CPG

J Clin Endocrinol Metabol. 2019;104:1520-74



Diabetes Complications and Age

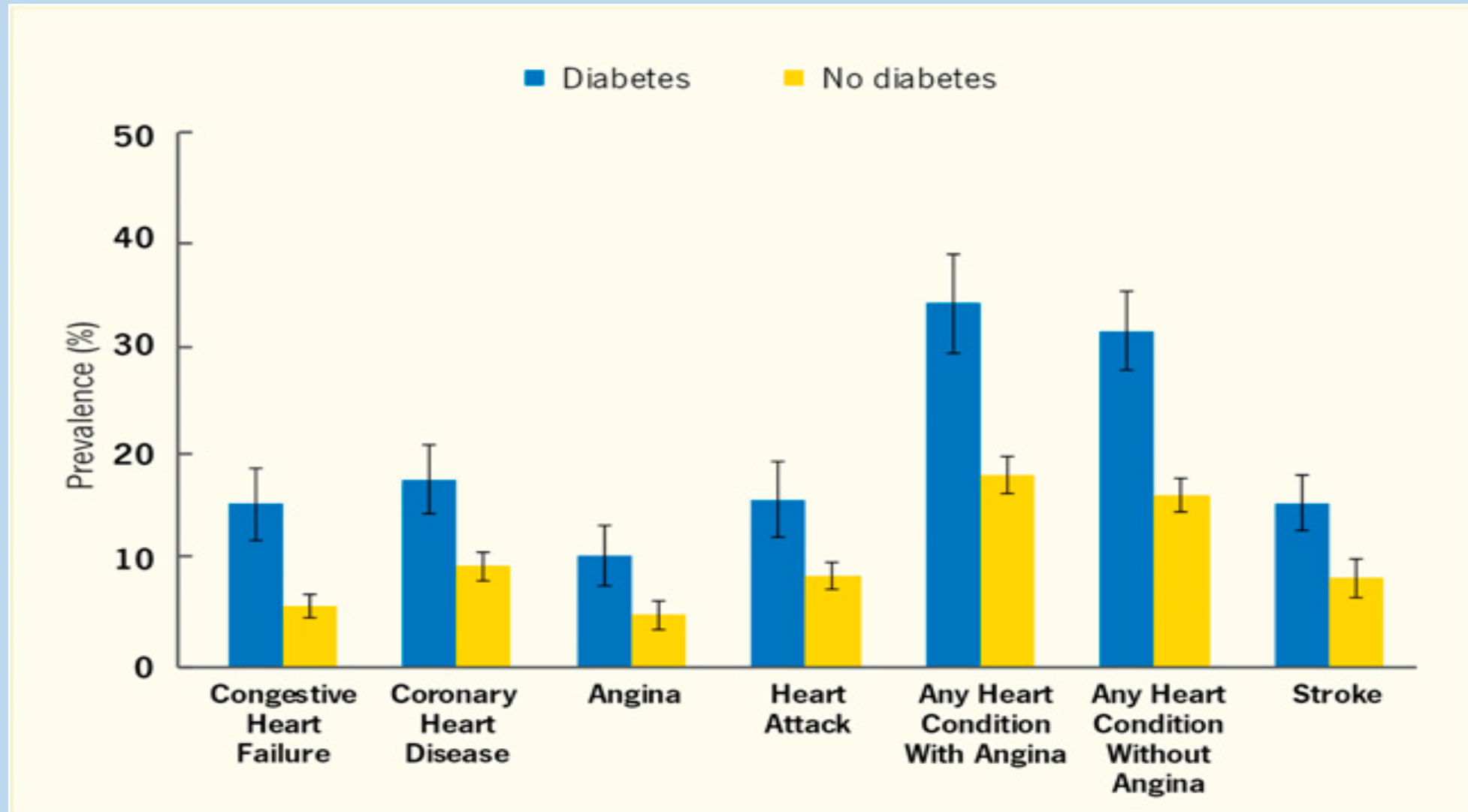
Treatment of Diabetes in Older Adults: Endocrine Society CPG
J Clin Endocrinol Metabol. 2019;104:1520-74



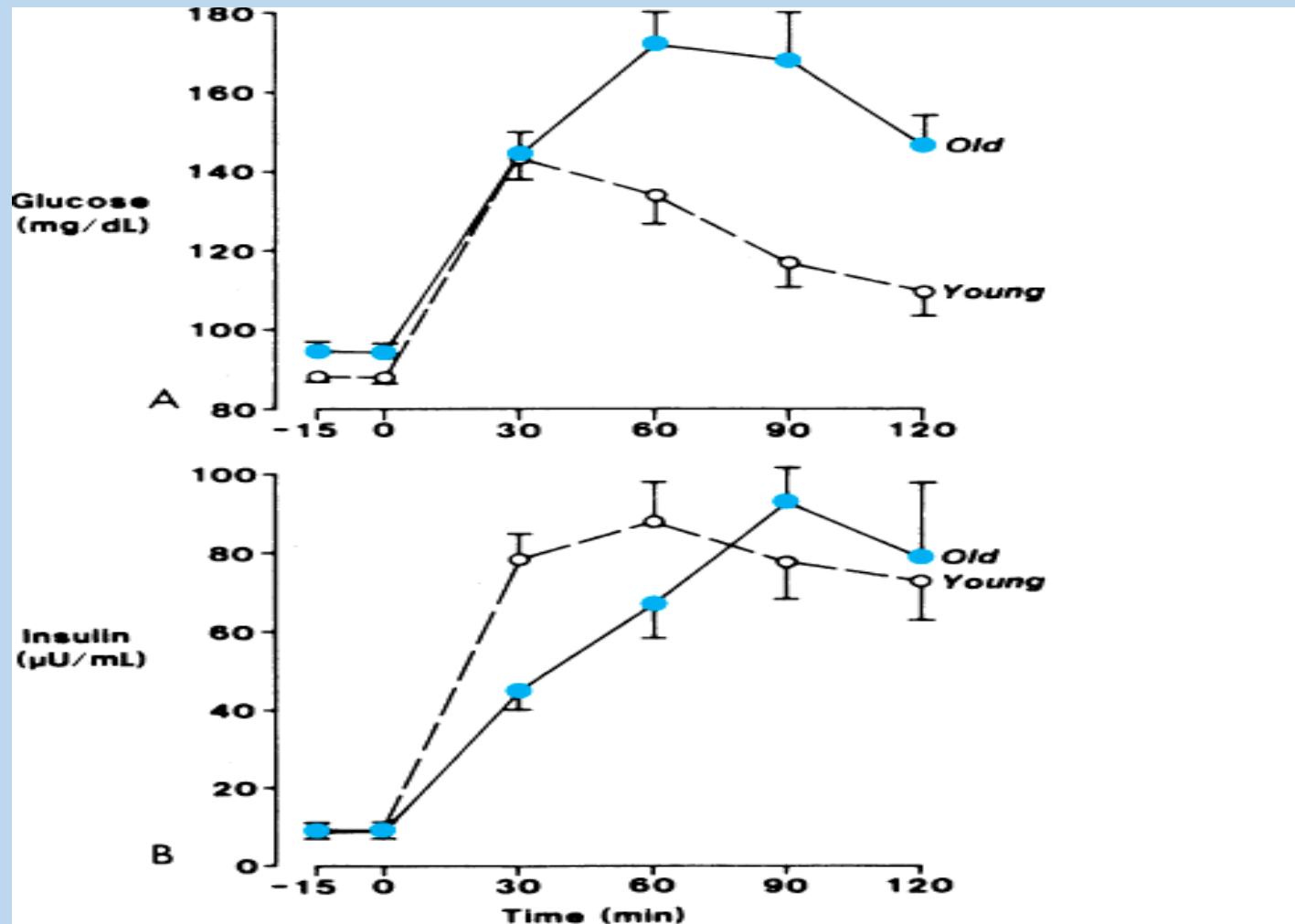
Cardiovascular Complications by Diabetes Status, Adults, over 60 years, U.S.

Treatment of Diabetes in Older Adults: Endocrine Society CPG

J Clin Endocrinol Metabol. 2019;104:1520-74

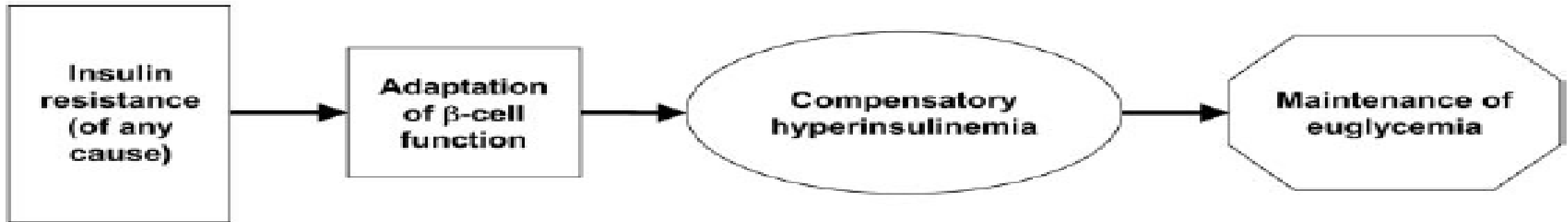


Effect of Aging in Blood Glucose and Insulin Level



With aging, the fasting glucose level is elevated with delayed recovery after glucose intake

Normal Adaptation to Insulin Resistance



- **Aging is associated with:**
 - ✓ Decline in β -cell function
 - ✓ Decline in insulin sensitivity
 - ✓ Increase in body adiposity furthers insulin resistance
 - ✓ Age-related impairment of intracellular insulin signaling and reduction in insulin-mediated mobilization of glucose transporters

Evidence Grading System, ADA

A	<ul style="list-style-type: none">• Clear evidence from well-conducted, generalizable RCTs, that are adequately powered, including• Evidence from a well-conducted multicenter trial or meta-analysis that incorporated quality ratings in the analysis;• Compelling non-experimental evidence;• Supportive evidence from well-conducted RCTs that are adequately powered
B	<ul style="list-style-type: none">• Supportive evidence from a well-conducted cohort studies• Supportive evidence from a well-conducted case-control study
C	<ul style="list-style-type: none">• Supportive evidence from poorly controlled or uncontrolled studies• Conflicting evidence with the weight of evidence supporting the recommendation
E	<ul style="list-style-type: none">• Expert consensus or clinical experience

Designation of Quality and Strength of Evidence (AGS)

Evidence	Description
Quality	
Level I	Evidence from at least 1 properly RCT
Level II	Evidence from at least 1 well-designed clinical trial without randomization, from cohort or case-controlled study
Level III	Evidence from respected authorities based on clinical experience, descriptive studies or reports of expert committees
Strength	
A	Good evidence to support; “clinicians should do this all the time”
B	Moderate evidence to support; “clinicians should do this most of the time”
C	Poor evidence, “clinicians may or may not follow the recommendation”
D	Moderate evidence against the use; “clinicians should not do this”
E	Good evidence against the use; “clinicians should not do this”

Criteria for the Diagnosis of Diabetes

- **FPG ≥ 126 /mg/dL (7 mmol/L) (fasting = no calories for >8 hrs)**
- **Or 2 hour plasma glucose ≥ 200 mg/dL (glucose load equal to 75 g glucose in water)**
- **Or A1C $\geq 6.5\%$**
- **Or in a patient with classic symptoms of hyper or hypoglycemia, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L)**
- **Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186**

Criteria for Testing for Diabetes or Prediabetes In Asymptomatic Adults

- All adults who are overweight (BMI ≥ 25 kg/m²) & those with additional risks:
 - ❖ Physical inactivity
 - ❖ First degree relative with diabetes
 - ❖ High risk race / ethnicity (African Amer, Latino, Native Amer, Asian Amer)
 - ❖ Hypertension
 - ❖ HDL Cholesterol < 35 mg/dL and or a TG level > 250 mg/dL
 - ❖ Women with polycystic ovary syndrome (or delivered a baby > 9 lb)
 - ❖ A1C $\geq 5.7\%$
 - ❖ Other: history of CVD, severe obesity, acanthosis nigricans
- Testing begins at age 45 years
- If A1C is normal, repeat testing at a minimum 3 year intervals
- For those with pre-diabetes, annual testing is recommended
- Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

Strategies And Team Concepts That Improve Care

- **A patient centered communication style incorporating patient preferences, literacy and cultural barriers**
- **Care systems should support team based care**
- **Patient centered approach: include plan to reduce CV risk by addressing BP, lipid control, smoking prevention / cessation, weight management, physical activity and life style**
- **Management applies through all stages of life and locations**
- **Address psychosocial care, with patient centered approach**
 - ❖ **Optimize both provider and team approach**
 - ❖ **Support patient behavior change**
 - ❖ **Address patient adherence and barriers**
- **Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186**

Tailor Treatment to the Vulnerable Patient

- Ethnic / Cultural / Sex / Socioeconomic differences / disparities
 - ❖ Strong social support improves outcomes
 - ❖ Tailor to incorporate culture, religion, language and literacy elements
- Food Insecurity (unreliable availability of nutritious food)
 - ❖ Propose solutions for homelessness, poor literacy etc (A)
- Cognitive Dysfunction
 - ❖ Tailor treatment to avoid hypoglycemia (A)
 - ❖ If DM + CV risk, benefits of statins may outweigh risks in dementia
 - ❖ If second generation antipsychotics are used, changes in weight, glycemic and lipid levels need to be monitored and regimen assessed periodically (C)
- Mental Illness
 - ❖ Diabetes is 2 – 3 times higher in those with schizophrenic / bipolar disorders
 - ❖ Treatment of depression may improve glycemic control

Case 1: Diabetes Management

- 85 year old female resident in a nursing home has moderate dementia, and is evaluated based on the nurse's information that the patient's diabetes control is not optimal. The patient is often agitated.
- She is on metformin 850 mg twice a day for her diabetes for the past year.
- Her A1c 3 months ago was 8.3% and her thrice a day glucose finger sticks range from 140 mg to 265 mg%. The last serum creatinine is 1.4 mg%.
- Which one of the following would be your order for diabetes management?
 1. Increase the dose of metformin to 850 mg thrice daily
 2. Add a sulfonyl urea to her regimen
 3. Consider a basal bolus insulin regimen
 4. Decrease the frequency of finger stick testing
 5. Stop the A1c testing

Case 1: Diabetes Management

- 85 year old female resident in a nursing home has moderate dementia, and is evaluated based on the nurse's information that the patient's diabetes control is not optimal. The patient is often agitated.
- She is on metformin 850 mg twice a day for her diabetes for the past year.
- Her A1c 3 months ago was 8.3% and her thrice a day glucose finger sticks range from 140 mg to 265 mg%. The last serum creatinine is 1.4 mg%.
- Which one of the following would be your order for diabetes management?
 1. Increase the dose of metformin to 850 mg thrice daily
 2. Add a sulfonyl urea to her regimen
 3. Consider a basal bolus insulin regimen
 4. Decrease the frequency of finger stick testing
 5. Stop the A1c testing

The Need to Address Several Domains

1. Aspirin
2. Smoking
3. Hypertension
4. Glycemic control
5. Lipids
6. Eye Care
7. Foot Care
8. Nephropathy Screening
9. DM Self-Management Education and Support
10. Depression
11. Polypharmacy
12. Cognitive Impairment
13. Urinary Incontinence
14. Injurious Falls
15. Pain

ARE YOU AT RISK FOR TYPE 2 DIABETES?



Diabetes Risk Test

- 1 How old are you?**
 Less than 40 years (0 points)
 40—49 years (1 point)
 50—59 years (2 points)
 60 years or older (3 points)
- 2 Are you a man or a woman?**
 Man (1 point) Woman (0 points)
- 3 If you are a woman, have you ever been diagnosed with gestational diabetes?**
 Yes (1 point) No (0 points)
- 4 Do you have a mother, father, sister, or brother with diabetes?**
 Yes (1 point) No (0 points)
- 5 Have you ever been diagnosed with high blood pressure?**
 Yes (1 point) No (0 points)
- 6 Are you physically active?**
 Yes (0 points) No (1 point)
- 7 What is your weight status?
(see chart at right)**

Write your score
in the box.

Add up
your score.

Height	Weight (lbs.)		
4' 10"	119-142	143-190	191+
4' 11"	124-147	148-197	198+
5' 0"	128-152	153-203	204+
5' 1"	132-157	158-210	211+
5' 2"	136-163	164-217	218+
5' 3"	141-168	169-224	225+
5' 4"	145-173	174-231	232+
5' 5"	150-179	180-239	240+
5' 6"	155-185	186-246	247+
5' 7"	159-190	191-254	255+
5' 8"	164-196	197-261	262+
5' 9"	169-202	203-269	270+
5' 10"	174-208	209-277	278+
5' 11"	179-214	215-285	286+
6' 0"	184-220	221-293	294+
6' 1"	189-226	227-301	302+
6' 2"	194-232	233-310	311+
6' 3"	200-239	240-318	319+
6' 4"	205-245	246-327	328+
	(1 Point)	(2 Points)	(3 Points)

You weigh less than the amount in the left column (0 points)

Adapted from Bang et al., Ann Intern Med 151:775-783, 2009. Original algorithm was validated without gestational diabetes as part of the model.

If you scored 5 or higher:
 You are at increased risk for having type 2 diabetes. However, only your doctor can tell for sure if you do have type 2 diabetes or prediabetes (a condition that precedes type 2 diabetes in which blood glucose levels are higher than normal). Talk to your doctor to see if additional testing is needed.

Type 2 diabetes is more common in African Americans, Hispanics/Latinos, American Indians, and Asian Americans and Pacific Islanders.

Higher body weights increase diabetes risk for everyone. Asian Americans are at increased diabetes risk at lower body weights than the rest of the general public (about 15 pounds lower).

For more information, visit us at diabetes.org or call 1-800-DIABETES (1-800-342-2383)

Lower Your Risk

The good news is that you can manage your risk for type 2 diabetes. Small steps make a big difference and can help you live a longer, healthier life. If you are at high risk, your first step is to see your doctor to see if additional testing is needed. Visit diabetes.org or call 1-800-DIABETES (1-800-342-2383) for information, tips on getting started, and ideas for simple, small steps you can take to help lower your risk.

Comprehensive Diabetes Medical Evaluation

- **History: onset, history of DKA, etc**
- **Eating patterns, weight history, physical activity**
- **Assessment of Functional Status (living independently?)**
- **Comorbidities: depression, smoking, alcohol, substance use**
 - ❖ P/E: include ht, wt, BMI, BP
 - ❖ **Fundoscopy**
 - ❖ **Skin exam**
 - ❖ **Thyroid exam**
 - ❖ **Foot exam**: inspection, doralis pedis, posterior tibial, DTRs, proprioception, vibration and monofilament sensation
- **Laboratory evaluation to address**
 - ❖ **A1C, lipid profiles, TSH, renal function, urine albumin / creatinine ratio**
 - ❖ **B12 levels if on metformin**
- **Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186**

Additional Considerations: 1

- **Smoking Cessation**
 - ❖ Avoidance of use cigarettes or tobacco products; routine component of diabetic care (A)
- **Address: cognitive function, depression screening and anxiety (B)**
 - ❖ Annual testing after testing at initial visit in adults >65 years (B)
 - ❖ These states render management difficult; risk for hypoglycemia?
- **Blood pressure control to <130 / 80 mm Hg (2017 HTN guidelines)**
- **BP <140/90 in those with DM and low 10 yr ASCVD risk (ADA / Endo CPGs) (A)**
- **Assessment for diabetic retinopathy (initial and follow up)**
- **Assessment for peripheral neuropathy**
- **Renal Function:**
 - ❖ Monitor eGFR every 6 months (quarterly when eGFR <45 ml/min);
 - ❖ Monitor electrolytes, Hgb, calcium, phosphorus, PTH and albumin
 - ❖ Referral to a Nephrologist must be a consideration
 - ❖ Dosage adjustment of medications where appropriate for renal function
- **Screen for abdominal aortic aneurysm by ultrasound (Endocrinology CPG)**
- Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

Additional Considerations: 2

- **Immunizations (C)**

- ❖ Pneumococcal vaccination, as applicable
- ❖ Influenza vaccine
- ❖ Herpes zoster vaccine
- ❖ Tetanus toxoid
- ❖ Consider hepatitis B vaccine

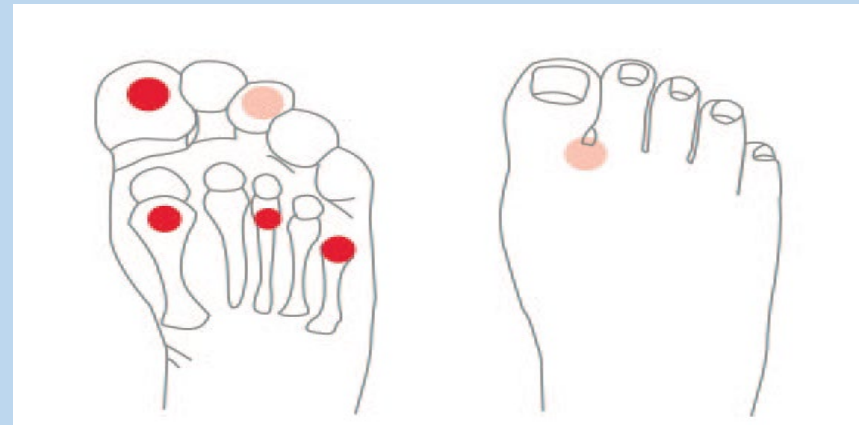
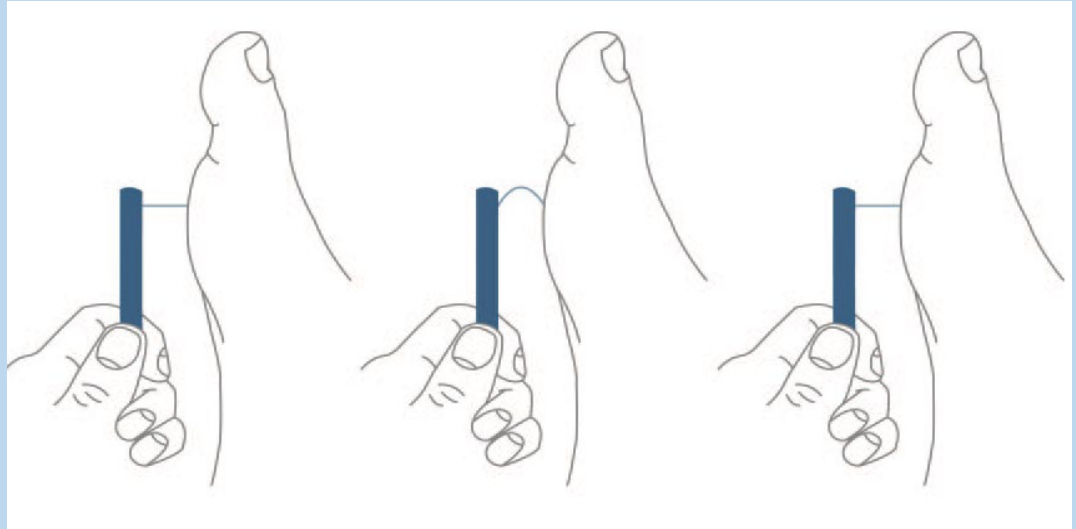
- **Antiplatelet agents**

- ❖ Aspirin 75 – 162 mg/d in those with history of diabetes and history of ASCVD: a **secondary prevention** strategy (A)
- ❖ Aspirin 75 – 162 mg/d as a **primary prevention** strategy in those with diabetes and increased CV risk, after discussion of risks vs benefits (C)

- Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

Recommend: Foot Care

- To perform the 10-g monofilament test, place the device perpendicular to the skin; Apply pressure until monofilament buckles.
- Hold in place for 1 second and release.
- The monofilament test should be performed at the highlighted sites while the patient's eyes are closed.



Peripheral Neuropathy is Common! Screen

- **Assess for peripheral neuropathy after diagnosis of T2DM, 5 years after diagnosis of T1DM, and at least annually thereafter (B)**
- **Assessment should include history and 10 gram monofilament testing (most useful) + vibration sensation (large-fiber function), temperature or pinprick (small-fiber function) (B)**
- **Use a 128 Hz tuning fork for vibration test**
- **Two normal tests (and no abnormal test) rule out loss of protective sensation**
- **Further, symptoms of autonomic neuropathy should be assessed**
- **Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186**

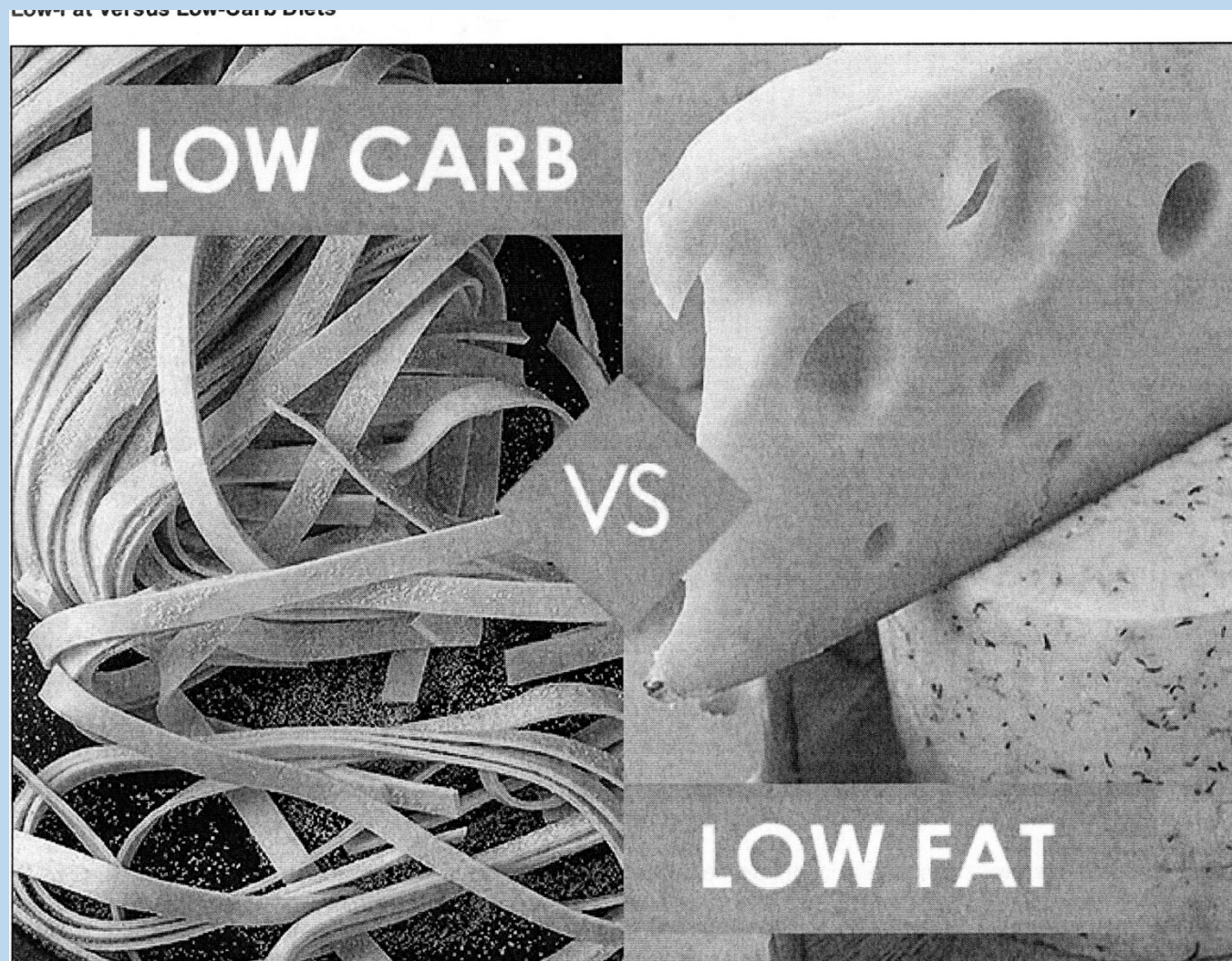
Cognitive Impairment and Depression

- Cognitive impairment should be assessed during initial evaluation period and **with any significant decline in clinical status.**
- Increased difficulty with self care should be considered a change in clinical status (IIIA)
 - ❖ **Annual screen for mild cognitive impairment or dementia in adults >65 (B)**
 - ❖ **If there is evidence of cognitive impairment and delirium is excluded, an initial evaluation designed to identify reversible conditions should be performed (IIIA)**
- **DM patients are at greater risk of depression and should be screened for during initial evaluation period (first 3 months) and if there is any unexplained decline in clinical status (IIB)**

Injurious Falls

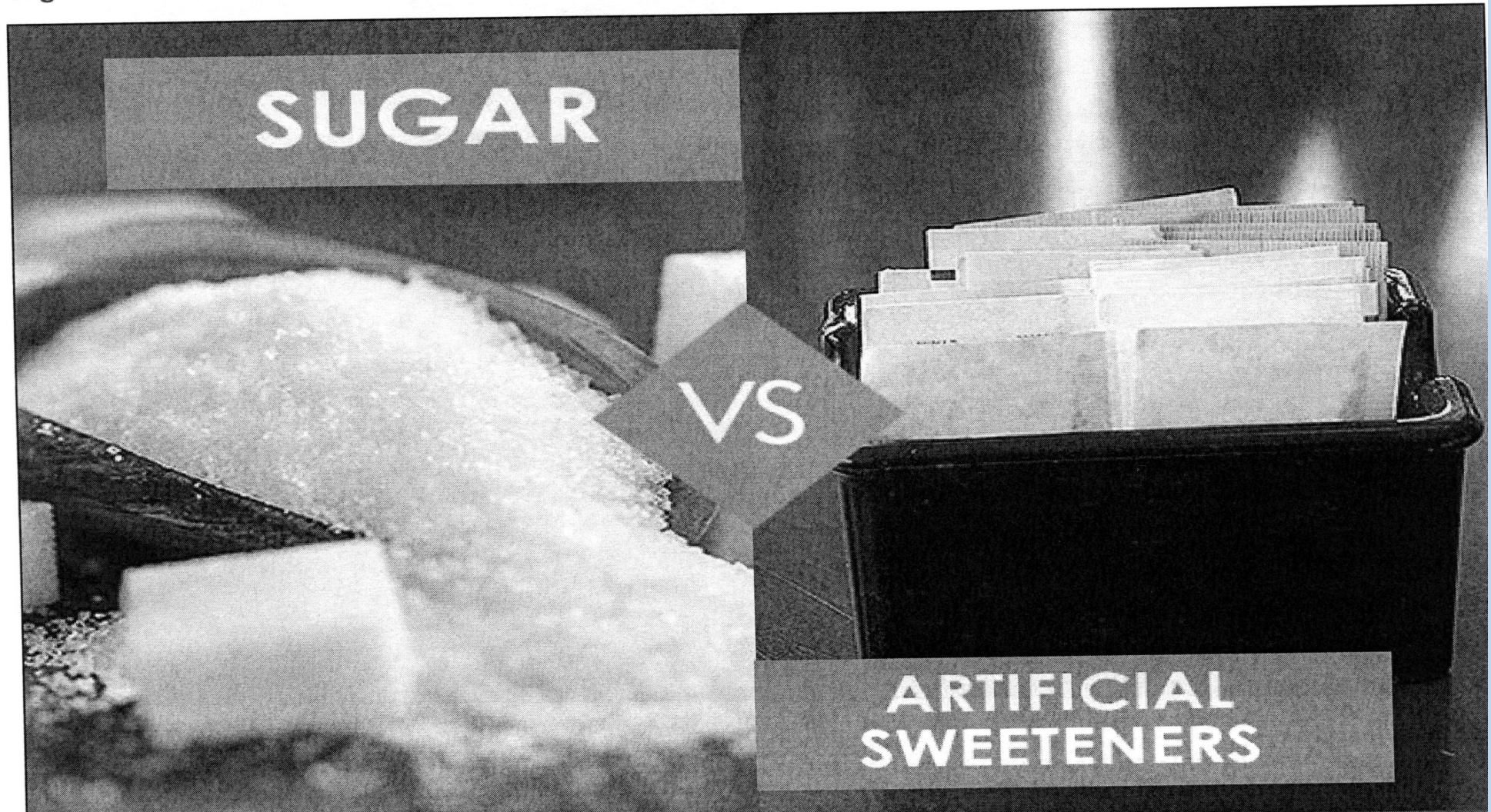
- **Falls should be asked every 12 months or more frequently if needed (IIIB)**
- **If patient presents with evidence of falls, the clinician should document a basic fall evaluation, including an assessment of injuries and**
- **Conduct an examination for potentially reversible causes of falls (i.e. medications, environmental factors, comorbidity) (IIIB)**

Nutrition: Does it Make a Difference?



Nutrition: Does it Make a Difference?

Sugar Versus Artificial Sweeteners



Medical Nutrition Therapy

- There is no “one-size fits all eating pattern” for all diabetic patients: individualize to personal preferences and health status
 - Promote healthful eating patterns, emphasize nutrient dense foods
 - Replace refined carbohydrates and added sugars with whole grains, legumes, vegetables and fruits
 - Minimize use of terms such as “diabetic diet”, or “no added sugar”; and minimize use of restricted diets
 - Provide a regular diet with a variety of foods, consistent amount of carbohydrates and meals / snacks
 - Avoid sugar sweetened beverages and added sugar
 - Non-nutritive sweeteners (with no cal) may be a substitute for nutritive sweeteners (with cal) such as honey, sugar, most syrups; they do not have significant effect on glucose control, but reduce overall calorie intake
-
- Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186
 - AMDA. Diabetes Management in the Long-Term Care Setting. Clinical Practice Guideline. Columbia, MD: 2015

Nutrient Dense Foods

- **Foods that carry the greatest amount and variety of nutrients and are relatively low in calories (generous nutrients but low calories). E.g.**
 - ❖ **Among super healthy greens, kale is king**
 - ❖ **Spinach: vitamins and minerals**
 - ❖ **Almonds: minerals, vitamins, fiber**
 - ❖ **Fish: not all are equal: salmon has highest omega-3**
 - ❖ **Garlic: vitamins, minerals and more**
 - ❖ **Tomatoes: vitamins and lycopene**
 - ❖ **Among fruits, berries, esp. blueberries: vitamins, minerals, antioxidants**
 - ❖ **Dark chocolate (cocoa): minerals, antioxidants**

Nutrition, cont'd

- **Mediterranean style diet rich in monounsaturated fats can help glucose metabolism (and lipid control), rather than a low fat diet**
- **Eating foods with long chain omega 3 fatty acids such as fatty fish, nuts and seeds help prevent CVD (B)**
- **But no evidence for beneficial role for omega-3 dietary supplements(A)**
- **There is no evidence that dietary supplementation with vitamins, herbals or minerals can improve health in diabetes; no role for antioxidants such as vitamins E, C or carotene (C)**
- **Nuts, berries, yogurt, coffee and tea associated with less diabetes risk**

Nutrition Therapy Summary: 2019 Recommendations

Standards of Medical Care in Diabetes: Diabetes Care. 2019; S1-S186

- **Carbohydrates (A, B)**
 - ❖ Nutrient dense carbohydrates that are high in fiber
 - ❖ Avoid sugar sweetened beverages (including fruit juices) and foods with added sugar
- **Fats (A, B)**
 - ❖ Ideal total fat intake inconclusive; adopt Mediterranean style diet rich in mono, polyunsaturated fats
 - ❖ Eating long chain n-3 fatty acids (fatty fish) beneficial, no evidence for n-3 supplements
 - ❖ Nuts and seeds (ALA) are recommended
- **Protein (B)**
 - ❖ There is no evidence that adjusting protein intake (typical 1-1.5 g/kg) will improve health in absence of diabetic kidney disease; ideal amount is inconclusive, based on research
 - ❖ Ingested proteins increase insulin response, without increasing plasma glucose conc. Hence, avoid carbohydrate sources high in protein while addressing hypoglycemia
- **Micronutrients (C)**
 - ❖ Supplements with vitamins and minerals do not improve outcomes who do not have deficiencies
- **Non-nutritive sweeteners (B)**
 - ❖ Have potential to reduce calorie and carb intake if substitute for sugar sweeteners

Type of Carbohydrate

- **Fiber rich products in diet (25 - 35 g / day)**
 - ❖ Soluble fiber preferred over insoluble fiber
- **Low glycemic index foods**
- **Be aware of the glycemic load**
- **Complex, not Simple carbs**
- **Prefer raw foods and foods cooked with shorter cooking time**

ADA Standards of Medical Care in Diabetes. Diabetes Care. 2017;40 (suppl 1): S33-43

Glycemic Index and Glycemic Load

- **Glycemic index (GI) is a value based on how slowly or quickly foods increase the blood glucose levels.**
 - ❖ **Low GI foods tend to release glucose slowly and steadily, while high GI foods release glucose rapidly**
- **Glycemic load gives a more accurate picture of real-life impact on blood sugar; it is determined by multiplying the gms of carbohydrate in a serving by the GI and dividing by 100.**
 - ❖ **A glycemic load of 10 or below is considered low; 20 or above is high**
- **A good example is watermelon: has a high GI (80) but has so little carbohydrate (6 g) that its glycemic load is just 5**

Glycemic Index and Glycemic Loads of Common Foods

Source: Harvard Health publications, Feb 2015

Food	Glycemic Index (glucose =100)	Glycemic Load per serving
Cakes, banana / sponge	42 - 57	12 - 17
Apple muffins	44 - 48	9 - 13
Waffles, Aunt Jemima	76	10
Bagel	72	25
White wheat bread	75	11
Whole wheat bread	69	9
Pumpernickel bread	56	7
100% whole grain bread	51	7
Corn tortilla	52	12
Wheat tortilla	30	8

Glycemic Index and Glycemic Loads of Common Foods

Source: Harvard Health publications, Feb 2015

Food	Glycemic Index (glucose =100)	Glycemic Load per serving
Coca Cola	63	16
Apple juice, unsweetened	41	12
Orange juice, unsweetened	50	12
Tomato juice (no sugar)	38	4
All-Bran cereal	44	9
Cornflakes, avr	81	20
Cream of Wheat, Instant	74	22
Oatmeal, avr	55	13
Instant oatmeal, avr	79	21
Raisin Bran	61	12

Glycemic Index and Glycemic Loads of Common Foods

Source: Harvard Health publications, Feb 2015

Food	Glycemic Index (glucose =100)	Glycemic Load per serving
Couscous	65	9
Quinoa	53	13
White rice	72	29
Brown rice	50	16
Parboiled Converted white rice (Uncle Ben's)	38	14
Crackers	74	13
Ice cream, regular, avr	62	8
Ice cream, premium	38	3
Milk, full fat or skim, avr	31	4
Yogurt, reduced fat, with fruit, avr	33	11

Glycemic Index and Glycemic Loads of Common Foods

Source: Harvard Health publications, Feb 2015

Food	Glycemic Index (glucose =100)	Glycemic Load per serving
Apple, avr	36	5
Banana, raw, avr	48	11
Dates, dried, avr	42	18
Grapefruit	25	3
Grapes, black	59	11
Oranges, avr	45	5
Peach, avr	42	5
Pear, avr	38	4
Raisins	64	28
Watermelon	72	4

Glycemic Index and Glycemic Loads of Common Foods

Source: Harvard Health publications, Feb 2015

Food	Glycemic Index (glucose =100)	Glycemic Load per serving
Beans (black, navy, kidney)	30 - 39	7 - 12
Chickpeas	10	3
Lentils	28	5
Cashews	22	3
Peanuts	13	1
Fettucini	32	15
Macaroni, spaghetti	46 - 58	24 - 26
Potato chips, avr	56	12
Pretzels	83	16
Microwave popcorn	65	7

Glycemic Index and Glycemic Loads of Common Foods

Source: Harvard Health publications, Feb 2015

Food	Glycemic Index (glucose =100)	Glycemic Load per serving
Green peas	54	4
Carrots	39	2
Baked potato	111	33
Boiled / mashed potato	82 - 87	17 - 21
Sweet potato	70	22
Hummus	6	0
Chicken nuggets	46	7
Pizza, plain	80	22
Pizza Super Supreme	36	9
Honey, avr	61	12

Exercise, Exercise, Exercise!



Physical Activity

- **Physical activity:**
 - ❖ Term includes all movements that increase energy use
 - ❖ **Exercise is a more specific form of structured physical activity**
 - ❖ No routine pre-exercise testing recommended
 - ❖ Assess patients for contraindications
- **Adults with diabetes to perform at least 150 min/wk of moderate intensity aerobic physical activity (50 – 70% max HR); bouts should last at least 10 minutes, with a goal of 30 mins or more/day (A)**
- **Activity most days a week with no more than 2 consecutive days without activity**
- **If no contraindications, resistance training 2 – 3 times a week (B)**
- Standards of Medical Care in Diabetes – 2019. ADA Position Statement. Diabetes Care. 2019; S1 - S186

Physical Activity (2)

- All adults, and particularly those with T2D, **should decrease sedentary behavior and extended time sitting (for >90 min) (B)**
- **Prolonged sitting should be interrupted every 30 min for blood glucose benefits, particularly in adults with T2D (C)**
- **Flexibility training and balance training are recommended 2 – 3 times/week for older adults with diabetes.**
- **Yoga and tai chi may be included based on individual preferences for flexibility, muscular strength, and balance (C)**

Case 2: Hemoglobin A1C

- **Background:** Hemoglobin A1C is measured to identify the three-month average plasma glucose concentration; it is a three-month average because the RBC lifespan is 120 days. All red cells do not undergo lysis simultaneously; hence A1C is interpreted as a 3 month measure.
- **All of the following regarding A1C as a marker for screening for diabetes and as a measure for glucose control are true except:**
 1. A1C testing may be performed every 6 months or less often in patients who meet treatment goals
 2. A1c testing may be performed every 3 months for poorly controlled diabetes failing to meet treatment goals
 3. A1C interpretation is affected by common disorders such as CKD, thyroid disease, anemia and RBC life span (e.g. hemolysis)
 4. A1C levels are not subject to inter-individual variations or heritability, making it a reliable marker

A1C Testing

Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

- A1C should be performed **by a lab that is certified** by the NGSP and standardized to the Diabetes Control and Complications Trial (DCCT) (B)
- **Discrepancy between A1C and plasma glucose raises possibilities of interference**

A1C Testing and Glycemic Targets

- A1C testing may be performed twice a year in those who meet treatment goals (with stable glycemic control): (E)
- Perform quarterly in those with changes in treatment and not at goals (E)
- **A1C levels are affected (discordance) by several factors that affect the life of the red cell**, such as splenectomy, hemolytic anemia, iron deficiency anemia, thyroid status, hypertriglyceridemia, CKD, ESRD, alcoholism, vitamin C, etc.
- **Inter-individual variations do occur, unrelated to blood glucose levels; seen in diabetic nephropathy, relating to heritability (or genes) causing glycation gaps**
- **Fructosamine: linkage to average glucose and prognostic significance not as clear as A1C**

O'Keefe JT et al. HbA1c in the evaluation of diabetes mellitus. JAMA. 2016; 315:615-6

A1C Goals

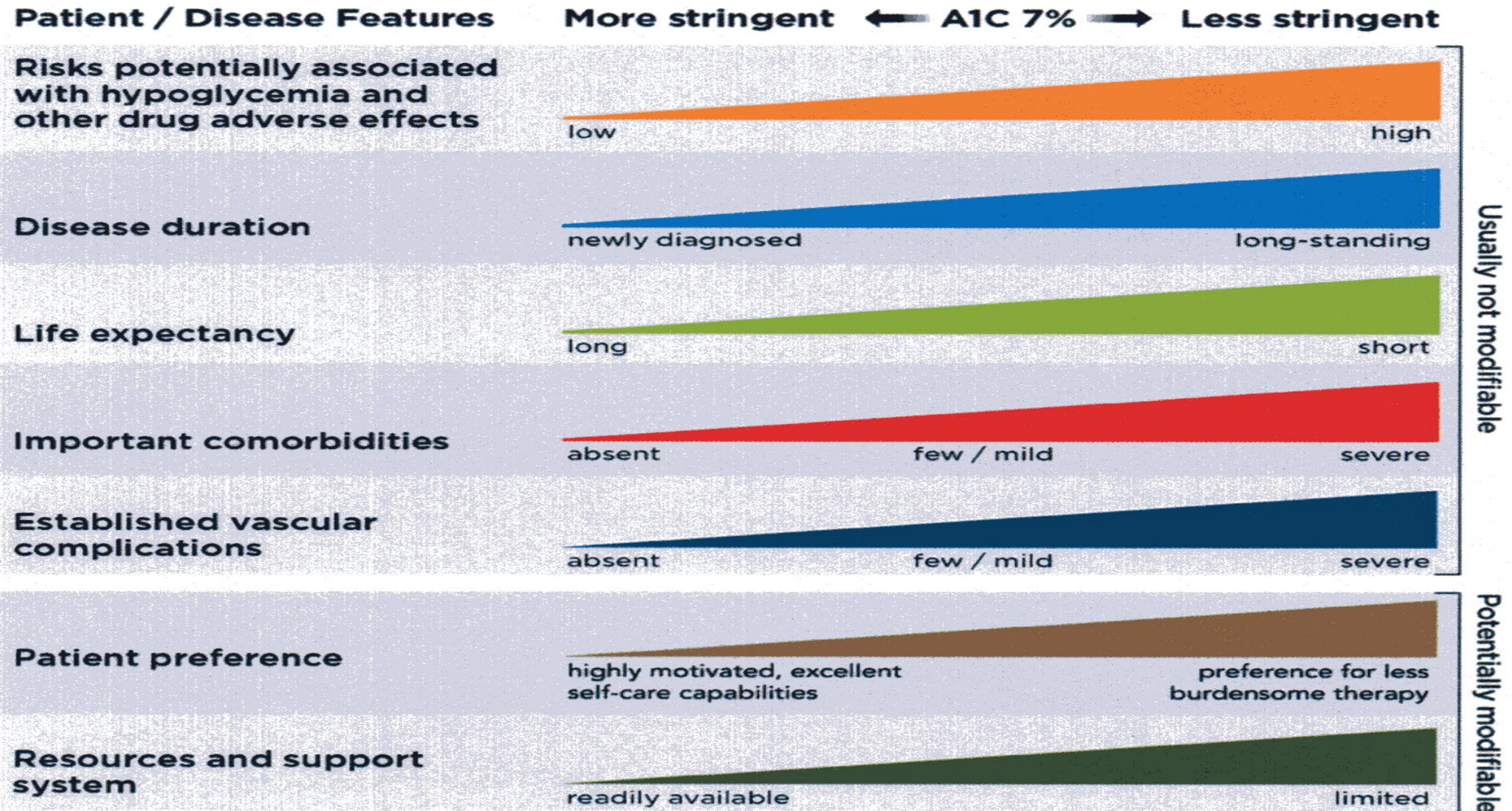
Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

- Reasonable target for non-pregnant adults <7% (A)
- More stringent goals (<6.5%) (C)
 - ❖ those with short duration of diabetes
 - ❖ long life expectancy and
 - ❖ those only on life style or metformin therapy
- Less stringent goals (<8%) (B)
 - ❖ history of severe hypoglycemia
 - ❖ limited life expectancy
 - ❖ extensive comorbidity

Management of Hyperglycemia and A1C Targets

Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

Approach to Individualization of Glycemic Targets



Case 2: Hemoglobin A1C

- **Background:** Hemoglobin A1C is measured to identify the three-month average plasma glucose concentration; it is a three-month average because the RBC lifespan is 120 days. All red cells do not undergo lysis simultaneously; hence A1C is interpreted as a 3 month measure.
- **All of the following regarding A1C as a marker for screening for diabetes and as a measure for glucose control are true except:**
 1. A1C testing may be performed every 6 months or less often in patients who meet treatment goals
 2. A1c testing may be performed every 3 months for poorly controlled diabetes failing to meet treatment goals
 3. A1C interpretation is affected by common disorders such as CKD, thyroid disease, anemia and RBC life span (e.g. hemolysis)
 4. A1C levels are not subject to inter-individual variations or heritability, making it a reliable marker

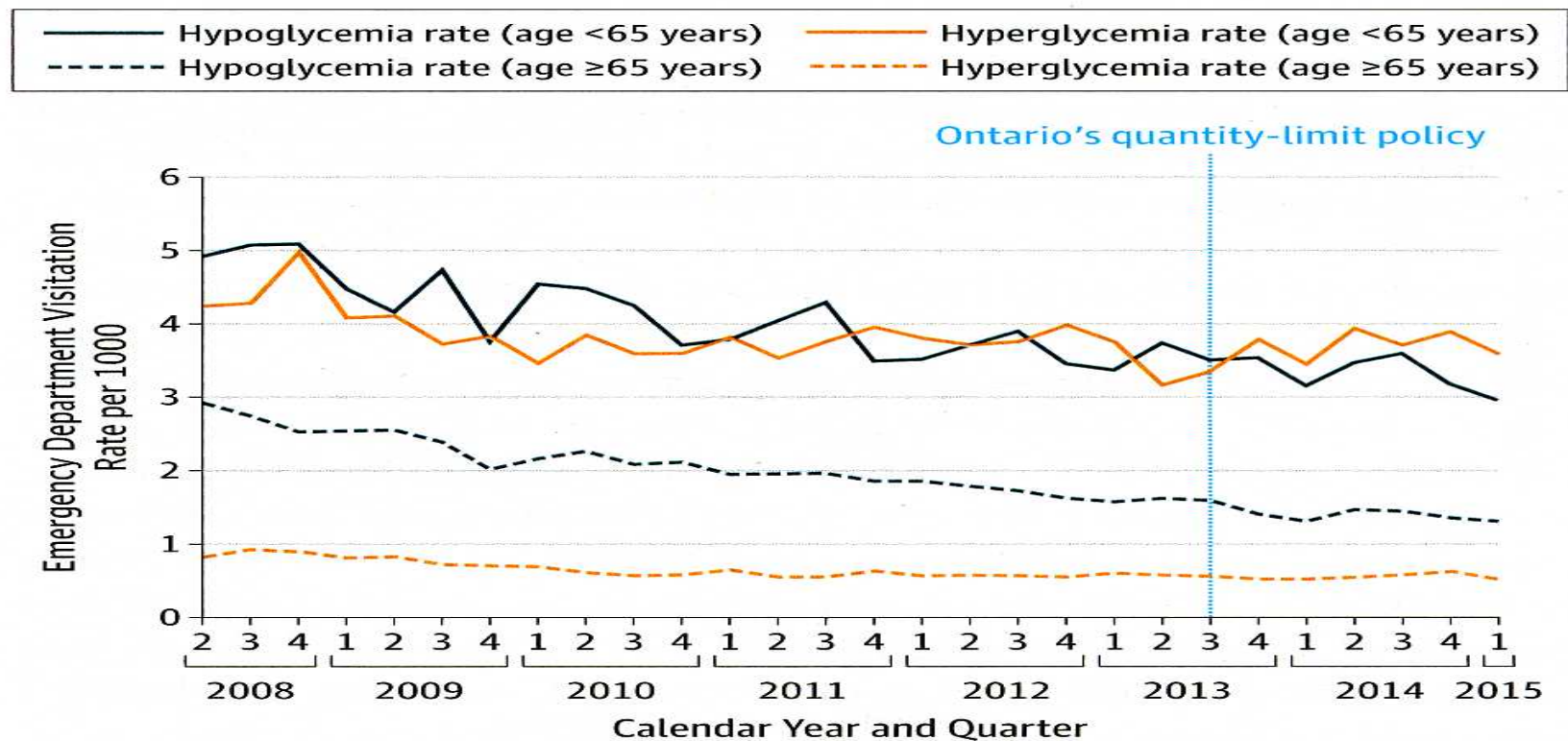
Monitoring Blood Glucose Levels

- Overall effect of glucose monitoring on blood glucose levels is small
- No evidence to suggest that blood glucose monitoring by itself influences QOL or long term diabetic outcomes
- Evidence for optimal frequency or timing of glucose monitoring in PA/LTC settings is sparse
- Frequency and timing is best individualized, and may be more frequent when diabetes is poorly controlled

Association of a Blood Glucose Test Strip Quantity-Limit Policy with Patient Outcomes. A population-based study.

Gomes T et al. JAMA Intern Med. 2017;177:61-66

Figure 1. Rates of Emergency Department Visits for Hyperglycemia and Hypoglycemia Among ODB-Eligible Patients With Diabetes in Ontario



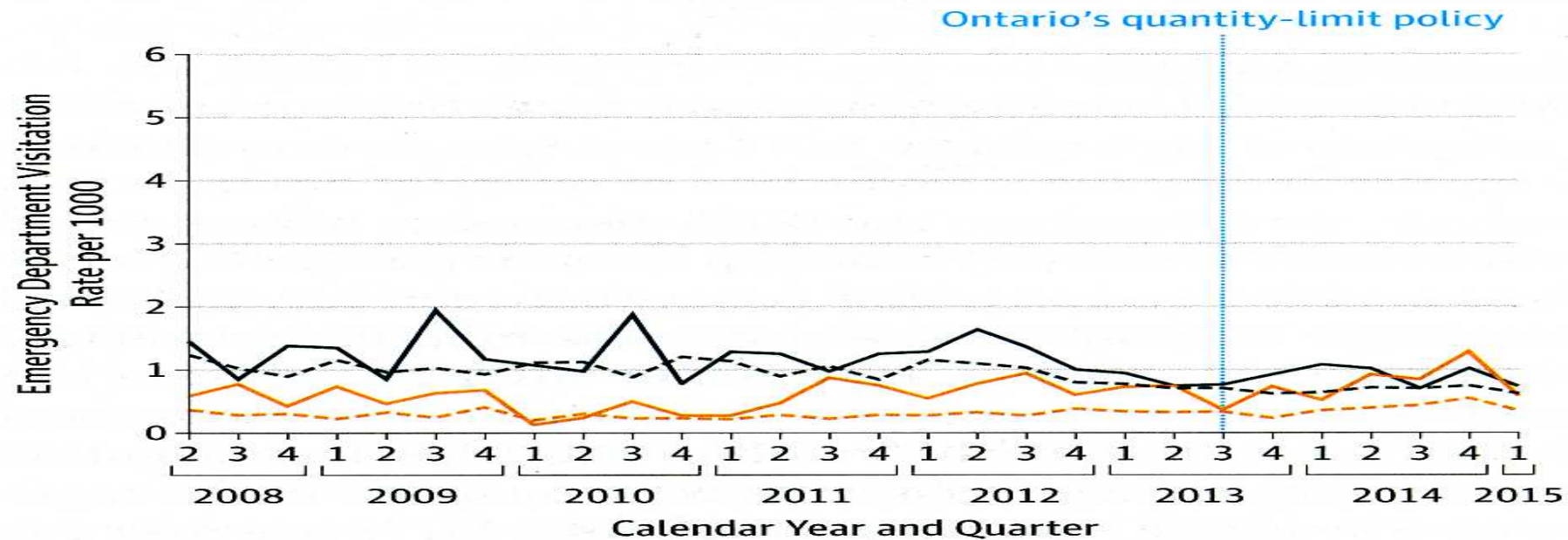
ODB indicates Ontario drug benefit.

Association of a Blood Glucose Test Strip Quantity-Limit Policy with Patient Outcomes. A population-based study.

Gomes T et al. JAMA Intern Med. 2017;177:61-66

Figure 5. Rates of Emergency Department Visits for Hyperglycemia and Hypoglycemia Among the High BGTS User Cohort

— Hypoglycemia rate (age <65 years) — Hyperglycemia rate (age <65 years)
- - - Hypoglycemia rate (age ≥65 years) - - - Hyperglycemia rate (age ≥65 years)



BGTS indicates blood glucose test strips.

Recommendations: Glucose Monitoring

- **Most patients on multiple-dose insulins or insulin pump therapy, or at the onset of insulin therapy should monitor blood glucose periodically (B)**
- **Individualize: may mean several times a day**
 - ❖ **Prior to meals**
 - ❖ **At bedtime**
 - ❖ **Prior to exercise**
 - ❖ **When one suspects low blood glucose or fluctuations**
 - ❖ **After treating low blood glucose until normoglycemic**
 - ❖ **Occasionally postprandially**

Classification of Hypoglycemia

Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

- **Level 1: Glucose <70 mg/dl and ≥ 54 mg/dl**
- **Level 2: Glucose <54 mg/dl**
- **Level 3: Severe event with altered mental or physical status requiring assistance (increased risk of dementia)**

- **Hypoglycemia unawareness, or one or more episodes of level 3 hypoglycemia, warrant re-evaluation of treatment**

Hypoglycemia and Diabetes

A Report of the ADA and the Endocrine Society. Diabetes Care 2019

- **Acute hypoglycemia in DM leads to confusion, seizures, coma and even death**
- **However, response varies with each patient who has hypoglycemia**
- **Patients with recurrent hypoglycemia do not experience symptoms from an adrenergic response to a fall in glucose, until glucose levels are lower and lower**
- **Eventually they develop “hypoglycemia associated autonomic failure”**
- **Older adults also tend to have a decline in β adrenergic receptor function, as well as counter regulatory hormone responses (through glucagon, growth hormone and others)**

Hypoglycemia and Diabetes

A Report of the ADA and the Endocrine Society. Diabetes Care 2019

- First sign is confusion in many (neuroglycopenic), relying on “focus on assistance”; neuroglycopenic symptoms are more prevalent in the old (glucagon response is often absent and there is autonomic failure)
- **Point: Neurological manifestations are more common than autonomic symptomatology in hypoglycemia (in the old)**
- Further, age related decline in renal and hepatic function interfere with drug metabolism, a rationale to avoid use of glyburide, some newer drugs and insulin sliding scales (= hypoglycemia)
- **Enquire about symptomatic and asymptomatic hypoglycemia at encounters (C)**
 - ❖ Treatment: glucose (15 - 20 g) preferred; or glucagon / carbs (E)
 - ❖ Raise glycemic targets in patients with unawareness, e.g. cognitively impaired (in whom vigilance is recommended)

Hypoglycemia in the Frail Elderly: Presentation

AMDA. Diabetes Management in the Long-Term Care Setting. Clinical Practice Guideline. Columbia, MD: 2015

- **Altered behavior and mental function**
 - **Altered level of consciousness (drowsiness, lethargy)**
 - **Confusion, disorientation**
 - **Falls**
 - **General weakness**
 - **Irritability**
 - **Poor concentration**
 - **Seizures**
 - **Stroke**
-
- **Hunger**
 - **Increased sweating**
 - **Palpitations**

Hypoglycemia and Overtreatment in the Old: What does the Literature State?

- **Intensive glucose lowering treatment in Type 2 DM increases (doubles) risk of severe hypoglycemia (JAMA Intern Med. 2016;176:969-78)**
- **A1C over-testing and associated overtreatment in stable Type 2 DM leads to waste and patient burden (BMJ. 2015;8:351)**
- **Current CPGs emphasize the need to avoid hypoglycemic episodes in older adults even in the absence of symptoms (Clin Interv Aging. 2014;9:1963-80)**
- **Better glycemic levels are not necessarily associated with better clinical outcomes, calling for individualized glycemic control in the elderly (J Amer Med Dir Assoc. 2014;15:757-62)**

JAMA Clinical Guideline Synopsis, 2018

Clinical Review & Education

JAMA Clinical Guidelines Synopsis

Glycemic Control in Nonpregnant Adults With Type 2 Diabetes

Elizabeth L. Tung, MD, MS; Andrew M. Davis, MD, MPH; Neda Laiteerapong, MD, MS

GUIDELINE TITLE Hemoglobin A_{1c} Targets for Glycemic Control With Pharmacologic Therapy for Nonpregnant Adults With Type 2 Diabetes Mellitus: A Guidance Statement Update From the American College of Physicians

DEVELOPER/FUNDING SOURCE American College of Physicians (ACP)

RELEASE DATE March 2018

PRIOR VERSION September 2007

TARGET POPULATION Nonpregnant adults with type 2 diabetes

MAJOR RECOMMENDATIONS

- Personalize hemoglobin A_{1c} (HbA_{1c}) goals for patients with type 2 diabetes based on discussions of benefits and harms of pharmacotherapy; patient preferences, health, and life expectancy; treatment burden; and costs of care.
- Aim for an HbA_{1c} level between 7% and 8% in most patients with type 2 diabetes.
- Consider deintensifying pharmacologic therapy in patients with type 2 diabetes and HbA_{1c} levels less than 6.5%.
- Treat patients with type 2 diabetes to minimize hyperglycemia symptoms and avoid targeting an HbA_{1c} level in patients with a life expectancy of less than 10 years due to advanced age, nursing home residence, or end-stage chronic conditions.

Case 3: Overall Management of a patient with Diabetes

- A 75 year old male resident, prior smoker, receives care in the PA/LTC setting. His hypertension is under reasonable control based on the last JNC recommendations, on lisinopril 10 mg /d and a thiazide. His last A1C three months ago is 7.5%, on metformin and glipizide. The blood pressure is 145/85 mm Hg. The lipid levels are: LDL 125 mg%, HDL 50 mg% and triglycerides 170 mg%. He has stage 3 CKD. Based on his last testing, he has mild cognitive impairment.
 - He is functionally active, walks daily, had no hospitalizations for 3 years.
 - Based on the above which is the next step that you would recommend?
1. Add another antihypertensive agent if the ACE inhibitor dose cannot be increased.
 2. Consider adding a statin based on his age and risk factors
 3. Increase the intensity of diabetes management by adding insulin.
 4. As he is doing well, make no changes to management, but regulate the diet and intensify his physical activity

Lipid Management

Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

- Obtain lipid profile at time of diagnosis of diabetes, at initiation of statin therapy, and 4 to 12 weeks after initiation or change in dose (E)
- Life style modification: weight loss and reduction of saturated and trans-fats; increase fiber & plant sterols and omega-3 fatty acids (Mediterranean or DASH diet) (A)
- Optimize glycemic control esp. in those with high TG levels
- Decision on high or moderate intensity therapy to be made based on age, presence of diabetes (age 40 – 75 years) and 10 year ASCVD risk >20% (high intensity), and lifestyle (A)
- Combination therapy with statins and fibrates or niacin does not improve outcomes (B)

Statin Treatment in T2 Diabetes (2019 ADA CPGs)

Age	Risk Factors	Statin Intensity
< 40 years	10 year ASCVD risk : None	None
	10 year ASCVD risk : High	Moderate or high statins; consider PCSK9 Inhibitors
40–75 years	None	Moderate
	ASCVD risk factors	High
	ACS & LDL \geq 70 or with history of ASCVD who can't tolerate high dose statin	Moderate and ezetimibe and consider PCSK9 inhibitors
> 75 years	None	Moderate
	ASCVD risk factors or ASCVD	Moderate or high
	ACS & LDL \geq 70 or with history of ASCVD who can't tolerate high dose statin	Statin, ezetimibe and PCSK9 Inhibitors

Case 3: Overall Management of a patient with Diabetes

- A 75 year old male resident, prior smoker, receives care in the PA/LTC setting. His hypertension is under reasonable control based on the last JNC recommendations, on lisinopril 10 mg and a thiazide. His last A1C three months ago is 7.5%, on metformin and glipizide. The blood pressure is 145/85 mm Hg. The lipid values are: LDL 125 mg%, HDL 50 mg% and triglycerides 170 mg%. He has stage 3 CKD. Based on his last testing, he has mild cognitive impairment.
 - Is functionally active, walks daily, had no hospitalizations for 3 years.
 - Based on the above which is the next step that you would recommend?
1. Add another antihypertensive agent if the ACE inhibitor dose cannot be increased.
 2. Consider adding a statin based on his age and risk factors
 3. Increase the intensity of diabetes management by adding insulin.
 4. As he is doing well, make no changes to management, but regulate the diet and intensify his physical activity

Guidelines from AGS for Improving Care: Review the Medications

- **Older adults with DM should be advised to maintain an updated medication list for review annually (11A)**
- **Medication list review more often is particularly important in older adults with DM who manifest falls, depression, impaired cognition or urinary incontinence**

Awareness of Medications that Promote Weight Gain

Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

- **Review, minimize or offer alternatives where possible**
 - ❖ **Antipsychotics**
 - ❖ **Antidepressants (TCAs)**
 - ❖ **SSRIs**
 - ❖ **Glucocorticoids**
 - ❖ **Anticonvulsants (gabapentin)**
 - ❖ **Sedating antihistamines**
 - ❖ **Anticholinergics**

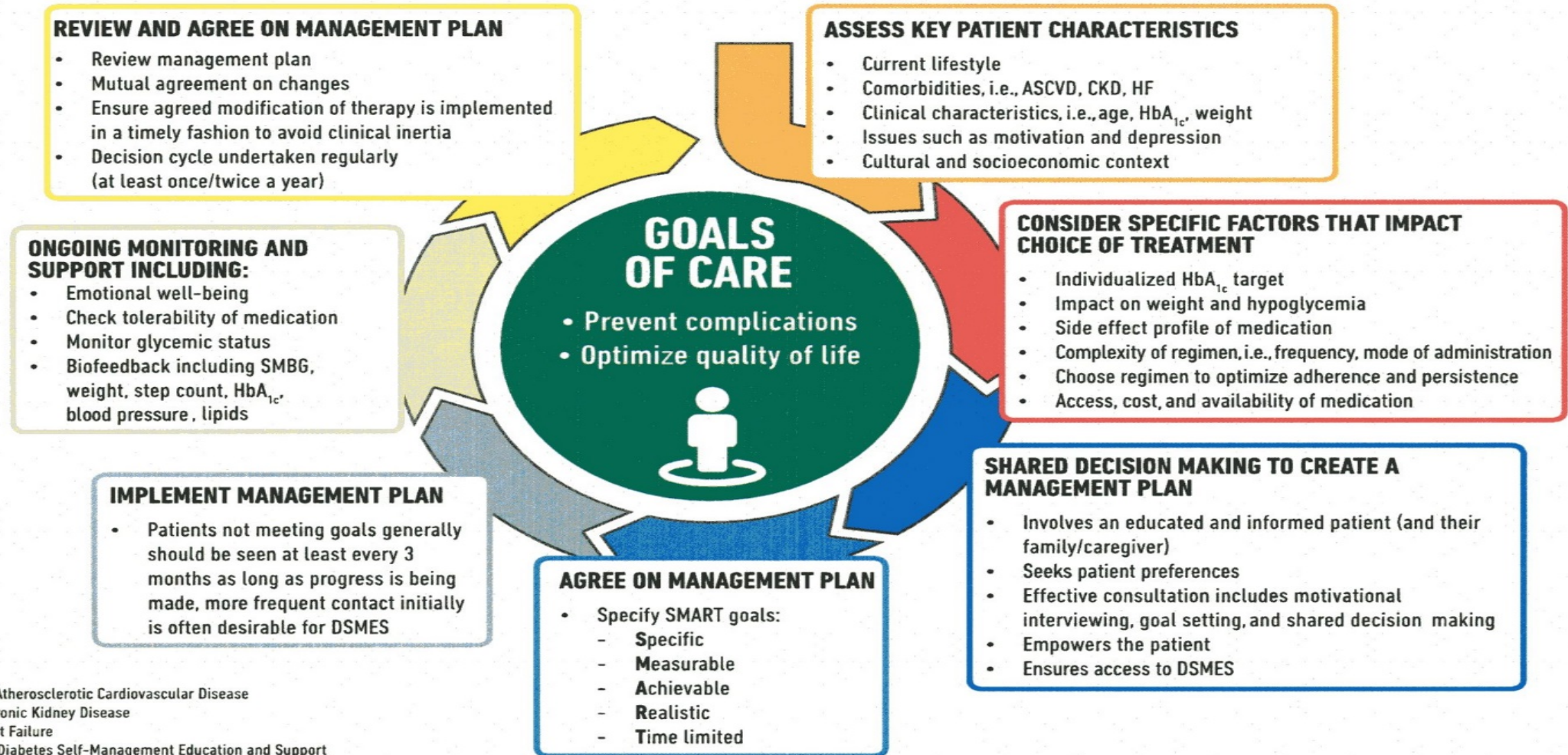
Hospital and Pre-Op Settings

Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

- **Insulin therapy should be initiated for persistent hyperglycemia ≥ 180 mg/dl, target 140 – 180 mg/dl (A)**
- **Sole use of sliding scale in the inpatient hospital setting is strongly discouraged (A)**
- **Perioperative Care**
 - ❖ **Withhold metformin & other oral hypoglycemic agents on day of surgery**
 - ❖ **Give half the NPH, or 60 - 80% of long acting or basal insulin**
 - ❖ **Monitor glucose every 4 to 6 hours while NPO and dose with short or rapid acting insulin as needed**
 - ❖ **Tighter control of blood glucose does not improve outcomes**

Medical Evaluation and Assessment of Comorbidities

Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186



ASCVD = Atherosclerotic Cardiovascular Disease

CKD = Chronic Kidney Disease

HF = Heart Failure

DSMES = Diabetes Self-Management Education and Support

SMBG = Self-Monitored Blood Glucose

ADA Position Statement, 2019: Metformin Therapy

- **Metformin should be considered to prevent Type 2 diabetes in those with pre-diabetes and those with a BMI \geq 35, those aged <60 years and prior gestational diabetes (A)**
 - ❖ No dosage reduction down to a reduction of eGFR >45 ml/min
 - ❖ Reduction to 1000 mg daily if eGFR is \geq 30 to 44 ml/min
- **Long term use of metformin is associated with vitamin B12 deficiency; hence periodic measure of B12 levels should be considered in such patients, especially if they have anemia or neuropathy (B)**
- Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

FIRST-LINE therapy is metformin and comprehensive lifestyle (including weight management and physical activity)
if HbA_{1c} above target proceed as below



ESTABLISHED ASCVD OR CKD

NO

WITHOUT ESTABLISHED ASCVD OR CKD

ASCVD PREDOMINATES

EITHER/
OR

GLP-1 RA
with
proven
CVD
benefit¹

SGLT2i
with
proven
CVD
benefit¹,
if eGFR
adequate²

If HbA_{1c} above target

If further intensification is required or patient is unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety:

- Consider adding the other class (GLP-1 RA or SGLT2i) with proven CVD benefit
- DPP-4i if not on GLP-1 RA
- Basal insulin⁴
- TZD⁵
- SU⁶

HF OR CKD PREDOMINATES

PREFERABLY

SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate³

OR

If SGLT2i not tolerated or contraindicated or if eGFR less than adequate² add GLP-1 RA with proven CVD benefit¹

If HbA_{1c} above target

- Avoid TZD in the setting of HF
- Choose agents demonstrating CV safety:
- Consider adding the other class with proven CVD benefit¹
- DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA)
- Basal insulin⁴
- SU⁶

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

DPP-4i

GLP-1 RA

SGLT2i²

TZD

If HbA_{1c} above target

If HbA_{1c} above target

If HbA_{1c} above target

If HbA_{1c} above target

SGLT2i²

OR

TZD

OR

TZD

GLP-1 RA

OR

DPP-4i

OR

TZD

SGLT2i²

OR

DPP-4i

OR

GLP-1 RA

If HbA_{1c} above target

Continue with addition of other agents as outlined above

If HbA_{1c} above target

Consider the addition of SU⁶ OR basal insulin:

- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia⁷

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

EITHER/
OR

GLP-1 RA with good efficacy for weight loss⁸

SGLT2i²

If HbA_{1c} above target

SGLT2i²

GLP-1 RA with good efficacy for weight loss⁸

If HbA_{1c} above target

If triple therapy required or SGLT2i and/or GLP-1 RA not tolerated or contraindicated use regimen with lowest risk of weight gain

PREFERABLY

DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:

- SU⁶ • TZD⁵ • Basal insulin

COST IS A MAJOR ISSUE⁹⁻¹⁰

SU⁶

TZD¹⁰

If HbA_{1c} above target

TZD¹⁰

SU⁶

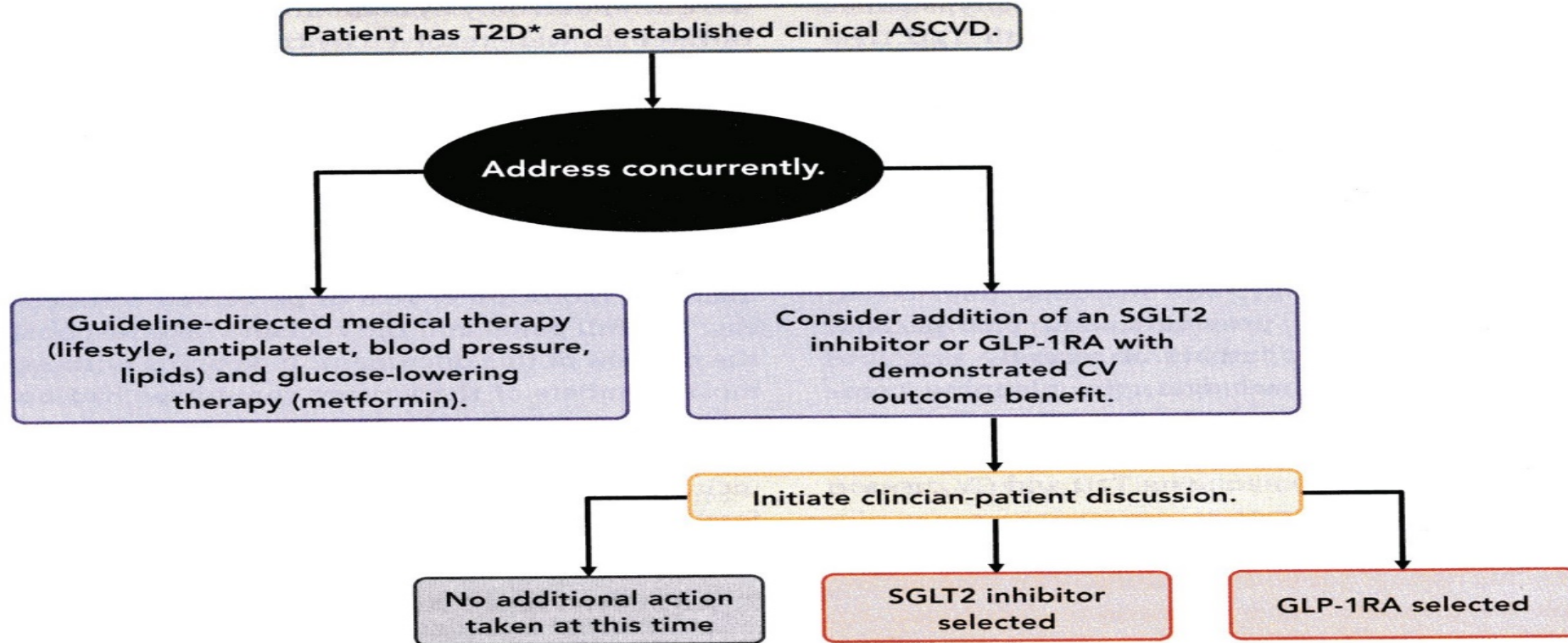
If HbA_{1c} above target

- Insulin therapy basal insulin with lowest acquisition cost
- OR
- Consider DPP-4i OR SGLT2i with lowest acquisition cost¹⁰

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

FIGURE 1 Summary Graphic



*Most trials of SGLT2i and GLP-1RA required baseline A1C $\geq 7\%$ (Example: EXSCEL Trial required HbA1c $\geq 6.5\%$), and most patients were already on metformin as first-line therapy if tolerated and not contraindicated

Abbreviations: ASCVD = atherosclerotic cardiovascular disease; CV = cardiovascular; GLP-1RA = glucagon-like peptide-1 receptor agonist; SGLT2 = sodium-glucose cotransporter-2; T2D = type 2 diabetes.

CENTRAL ILLUSTRATION Normal Glucose Reabsorption in the Kidney

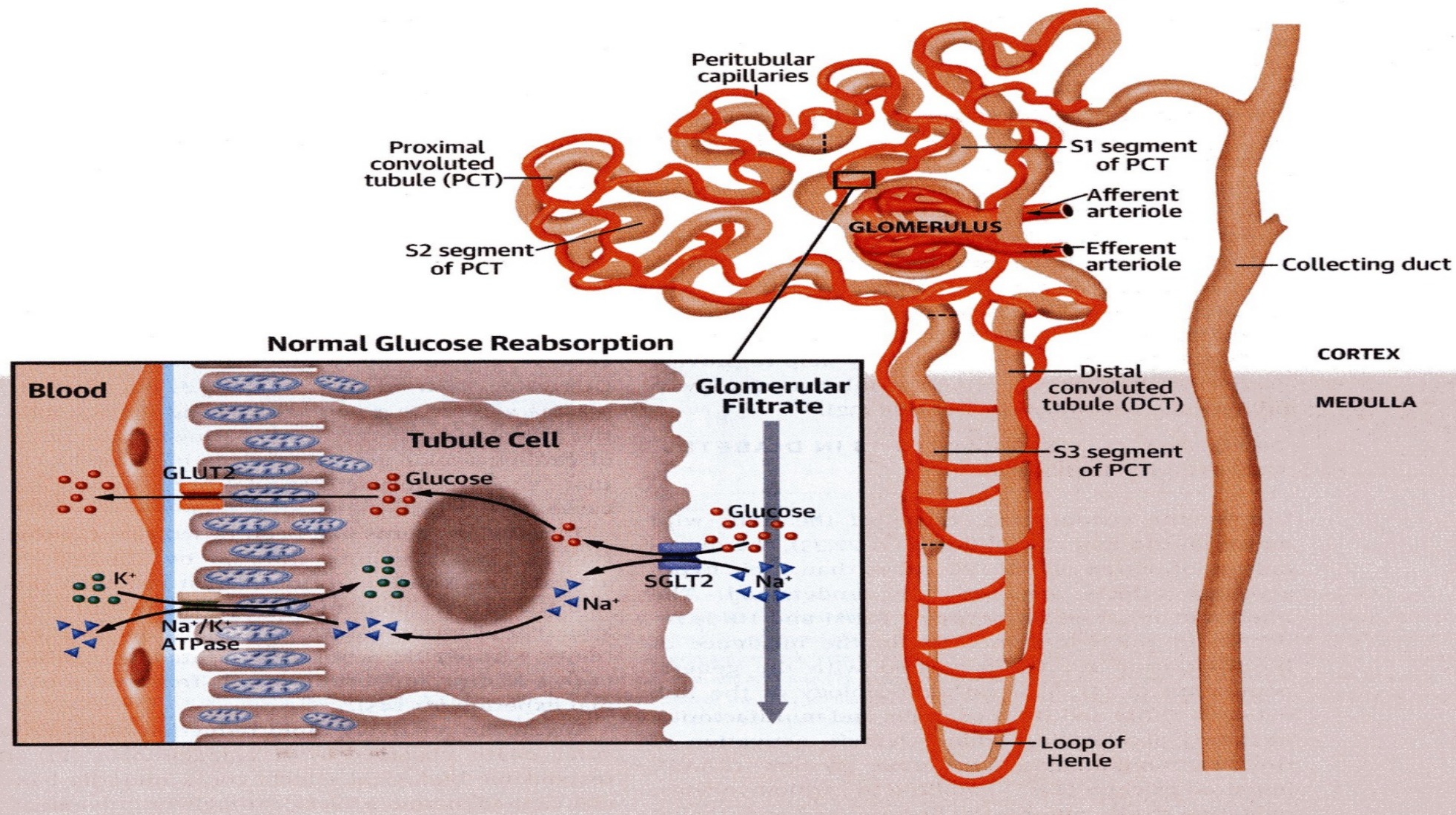
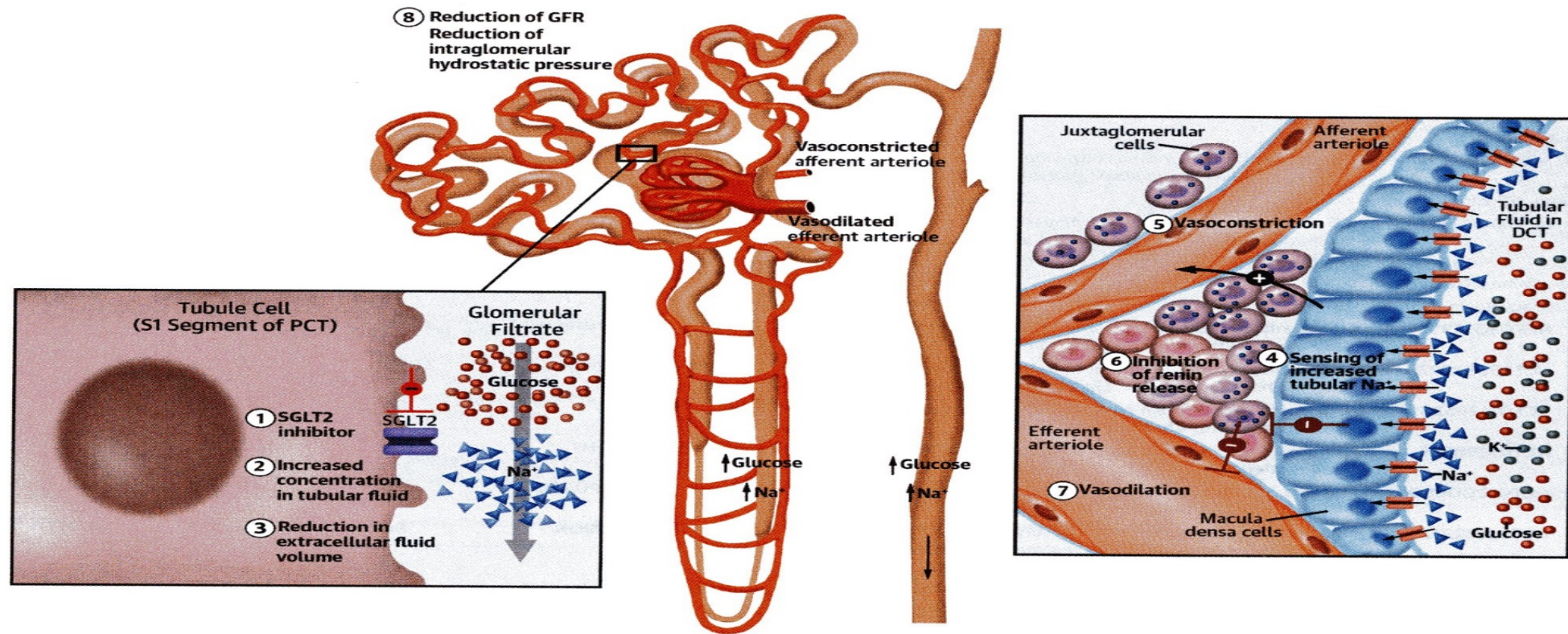


FIGURE 1 Changes After SGLT2 Inhibition



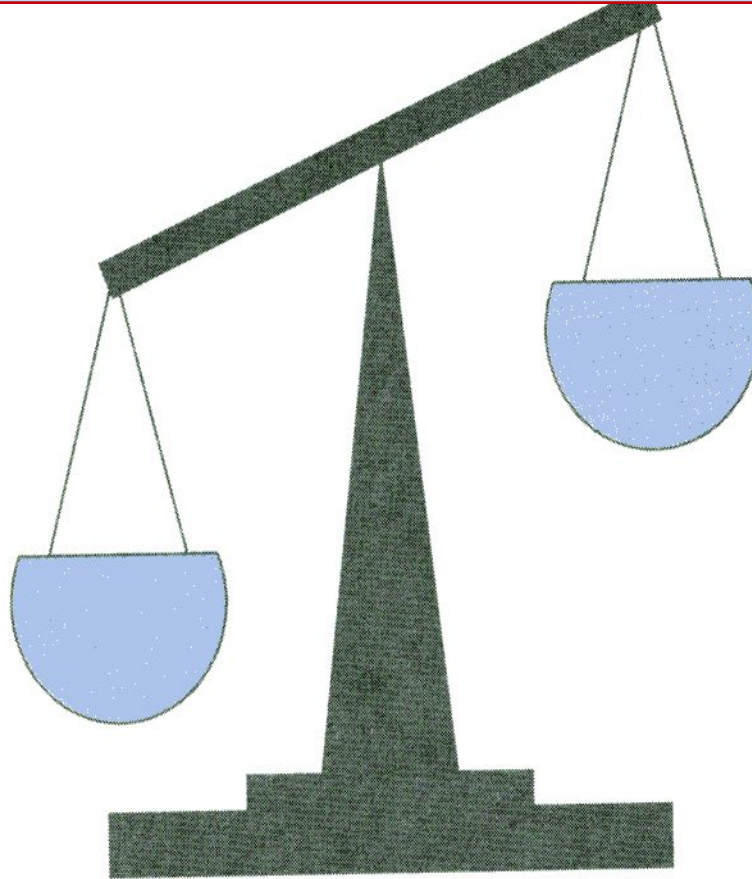
Inhibition of sodium-glucose co-transporter 2 (SGLT2) (1) results in excretion of glucose and sodium (Na⁺) (2) in the urine. As a result of loss of body salt, the extracellular fluid volume contracts (3) and leads to a decrease of atrial natriuretic peptides, which may result in vasoconstriction of the afferent arterioles. Because glucose reabsorption is coupled with Na⁺ absorption, the macula densa senses an increased Na⁺ concentration (4), enhancing the activation of the tubuloglomerular feedback causing vasoconstriction of the afferent arteriole, which is driven primarily by adenosine-mediated signal cascades (5). The macula densa inhibits the release of renin from the juxtaglomerular cells (6), enhancing the dilation of the efferent arteriole (7). Vasoconstriction of the afferent and vasodilation of the efferent arterioles reduce the glomerular filtration rate (GFR) initially, but the reduction of the intraglomerular hydrostatic pressure represents the renoprotective effects of this drug class (8). DCT = distal convoluted tubule; K⁺ = potassium; PCT = proximal convoluted tubule.

Effects of SGLT2 Inhibitors

Zelniker TA, Braunwald E. JACC. 2018;72:1852

Favorable effects

- Reduction of pre-load (diuretic effects)
- Reduction of afterload (blood pressure, arterial stiffness)
- Improvement of mitochondrial efficiency
- Delay of decline in eGFR
- Delay of micro- and macroalbuminuria
- Weight loss
- Reduction in epicardial adipose tissue
- Improvement in glycemia
- Reduction in uric acid



Unfavorable effects

- Amputations (in particular toe, metatarsal)
- Volume depletion/Hypotension
- Diabetic ketoacidosis
- Fractures
- Urinary and genital infections

Favorable and unfavorable effects that have been reported for sodium-glucose co-transporter (SGLT2) inhibitors. eGFR = estimated glomerular filtration rate.

SGLT2 Inhibitors (Empagliflozin)

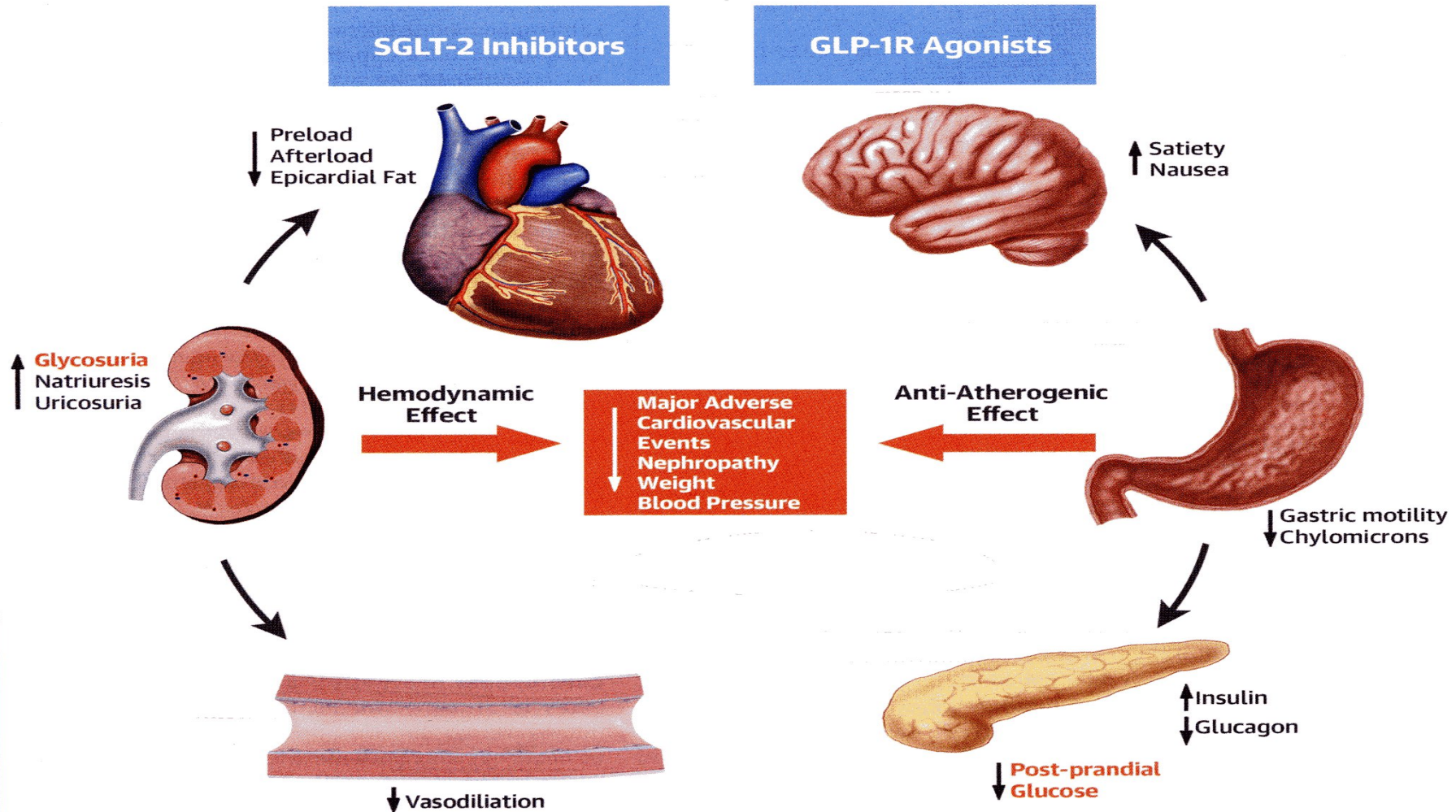
JACC 2018;72: 3200-23

Favorable	Unfavorable
Dose 10 mg to 25 mg once daily (long half life)	Do not initiate if eGFR* <45 ml/min
Improves glycemic control in adults with T2D	Contraindicated if eGFR* <30 ml or on dialysis
Reduces risk of CV death in T2D and CVD	Causes volume depletion
Reduces progression of kidney disease	Genital infections
Administered orally	Euglycemic ketosis
Prevents HF hospitalization; reduces BP	In osteoporosis, caution with canagliflozin
Highest selectivity for SGLT2 over SGLT1	Needs moderately preserved renal function

Drugs and CVD Risk Reduction In Type 2 Diabetes

Newman et al. JACC 2018; 14: 1859

CENTRAL ILLUSTRATION Potential Pathways of Cardiovascular Benefit From Use of SGLT2 Inhibitors and GLP-1 Receptor Antagonists for Patients With T2D



GLP-1RAs (Liraglutide)

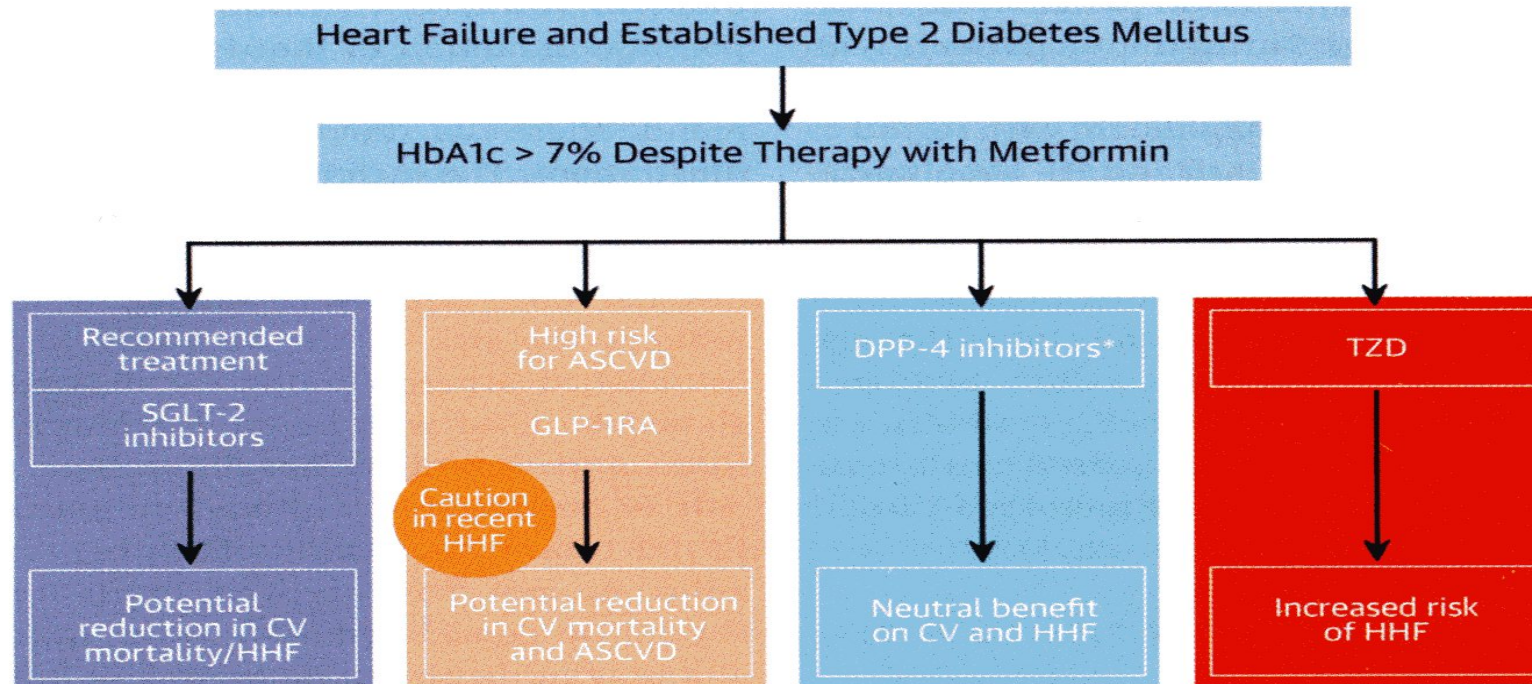
JACC 2018;72: 3200-23

Favorable	Unfavorable
Dose 0.6 to 1.8 mg SC daily (or weekly)	No dose adjustment for renal or hepatic impairment (no data for ESRD)
Improves glycemic control in adults with T2D	Contraindication for some in ESRD
Reduces risk of MI, CVA or CV death in adults with T2D and CV disease	Caution with family history of medullary thyroid cancer and MEN2
Weight loss, LDL reduction (↓ atherogenesis)	Caution in pancreatitis, gastroparesis
Blood pressure reduction	Nausea and vomiting (delays gastric emptying)
Anti-inflammatory action (upregulates nitric oxide)	Administered as injection

Drugs and HF Treatment Strategy In Type 2 Diabetes

JACC 2018; 16: 813-22

CENTRAL ILLUSTRATION Oral Antihyperglycemic Treatment Strategy in Patients With Diabetes and Heart Failure

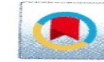


Sharma, A. et al. *J Am Coll Cardiol HF*. 2018;6(10):813-22.

*Saxagliptin and alogliptin may increase the risk for heart failure hospitalization. ASCVD = atherosclerotic cardiovascular disease; CV = cardiovascular; DPP = dipeptidyl dipeptidase; GLP-1RA = glucagon-like peptide-1 receptor agonists; HbA_{1c} = hemoglobin A_{1c}; HHF = hospitalization for heart failure; SGLT = Sodium-glucose co-transporter; TZD = thiazolidinediones.

CLINICAL RESEARCH

Comparison of New Glucose-Lowering Drugs on Risk of Heart Failure in Type 2 Diabetes



A Network Meta-Analysis

Caroline K. Kramer, MD, PhD,^{a,b} Chang Ye, MSc,^a Sara Campbell, MD,^a Ravi Retnakaran, MD^{a,b,c}

ABSTRACT

OBJECTIVES The authors conducted a systematic review and network meta-analysis of placebo-controlled, randomized clinical trials in the post-Food and Drug Administration (FDA) guidance era to formally compare the effects of 3 new classes of glucose-lowering drugs on hospitalization for heart failure (HF) in type 2 diabetes mellitus.

BACKGROUND The 2008 FDA Guidance for Industry launched an era of cardiovascular outcome trials for new glucose-lowering drugs in T2DM, including glucagon-like peptide (GLP)-1 agonists, dipeptidyl peptidase (DPP)-4 inhibitors, and sodium glucose co-transporter (SGLT)-2 inhibitors.

METHODS We searched Embase, PubMed, Cochrane Library, and clinicaltrials.gov between December 1, 2008, and November 24, 2017, for randomized placebo-controlled trials, and performed network meta-analyses by Bayesian approach using Markov-chain Monte Carlo simulation method to compare the effects of glucose-lowering drugs on risk of HF hospitalization and estimate the probability that each treatment is the most effective.

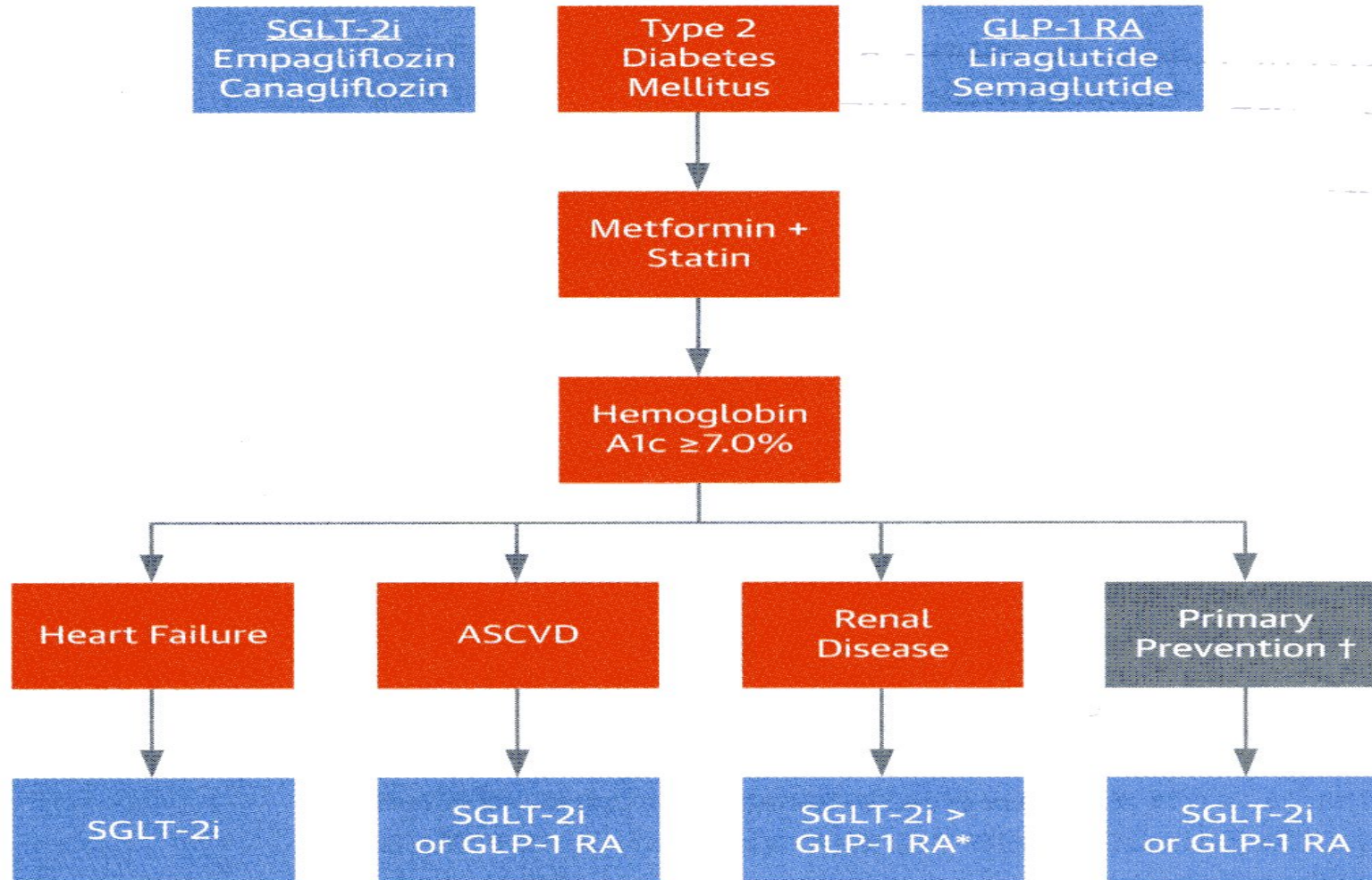
RESULTS Nine studies were identified, yielding data on 87,162 participants. In the network meta-analysis, SGLT-2 inhibitors yielded the greatest risk reduction for HF hospitalization compared with placebo (relative risk [RR]: 0.56; 95% CrI [credibility interval]: 0.43 to 0.72). Moreover, SGLT-2 inhibitors were associated with significant risk reduction in pairwise comparisons with both GLP-1 agonists (RR: 0.59; 95% CrI: 0.43 to 0.79) and DPP-4 inhibitors (RR: 0.50; 95% CrI: 0.36 to 0.70). Ranking of the classes revealed 99.6% probability of SGLT-2 inhibitors being the optimal treatment for reducing the risk of this outcome, followed by GLP-1 agonists (0.27%) and DPP-4 inhibitors (0.1%).

CONCLUSIONS Current evidence suggests that SGLT-2 inhibitors are more effective than either GLP-1 agonists or DPP-4 inhibitors for reducing the risk of hospitalization for HF in type 2 diabetes mellitus. (J Am Coll Cardiol HF 2018;6:823-30)
© 2018 by the American College of Cardiology Foundation.

Drugs and CVD Risk Reduction In Type 2 Diabetes

Newman et al. JACC 2018; 14: 1866

FIGURE 5 A New Algorithm for CVD Risk Reduction in Type 2 Diabetes



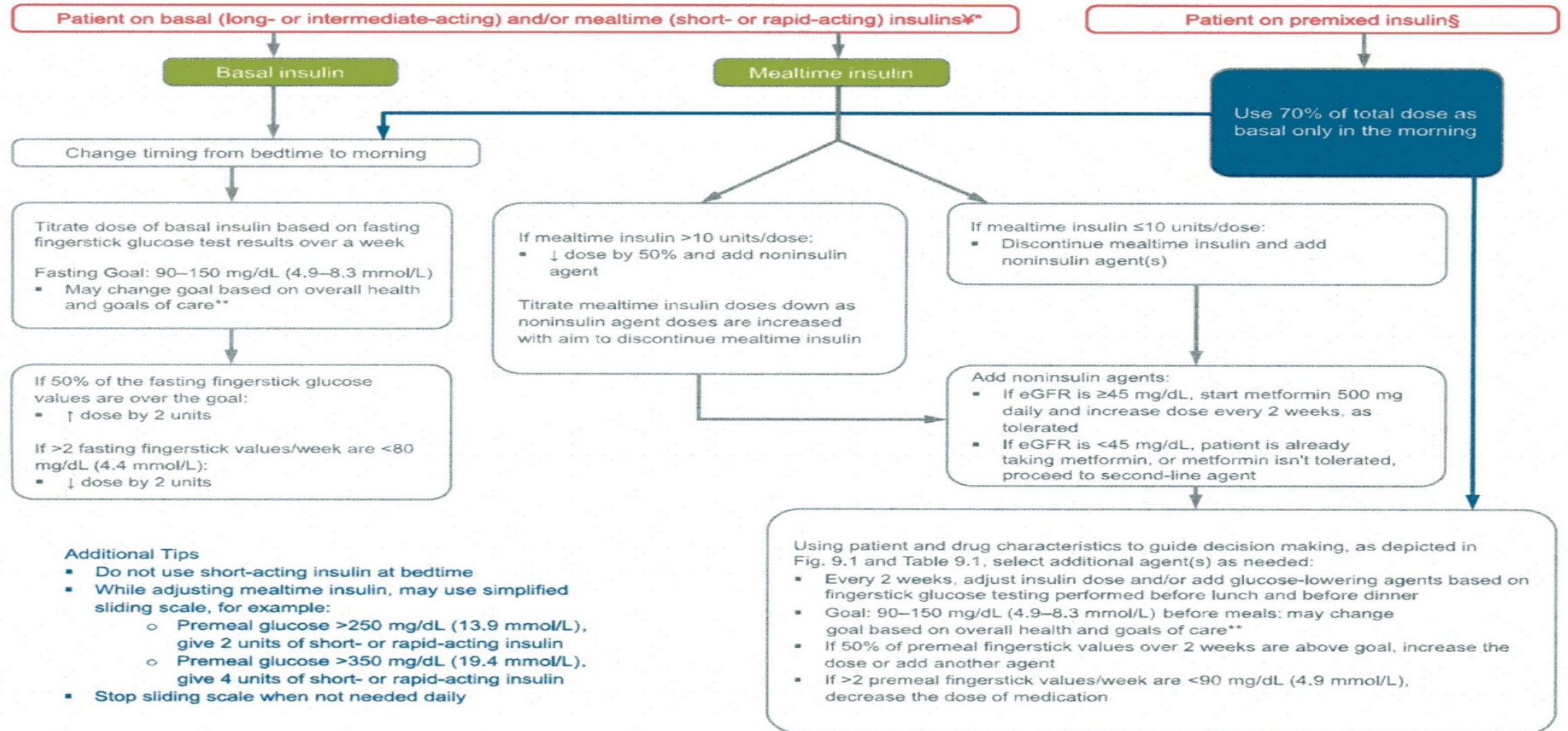
Antihyperglycemic Medications for T2 Diabetes

Medication	CV and HF effects	Efficacy	Hypo-glycemia	Comments
Metformin	CV: benefit? HF: neutral	High	No	Contraindicated for eGFR <30 ml/mt Vitamin B12 deficiency possible
Sulfonylureas	neutral	High	Yes	Glyburide not recommended
SGLT-2 Inhibitors	CV: benefit HF: benefit	Intermediate	No	Renal benefits for progression of CKD Renal dose adjustment required Risks: GU infections, fractures, DKA, low BP
GLP-1 RAs	CV: benefit HF: neutral	High	No	Renal dose adjustment GI effects; diarrhea, nausea, pancreatitis
DPP-4 inhibitors	CV: neutral HF: risk	Intermediate	No	Renal dose adjustment for most Risk for acute pancreatitis
Thiazolidinediones	HF: high risk	High	No	No dose adjustment Not recommended in CKD, HF (fluid retention)
Insulins	Neutral	Highest	Yes	Lower dose with decline in eGFR

Insulin Therapy

Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

Simplification of Complex Insulin Therapy



Sliding Scale Insulin

- SSI is a reactive way of treating hyperglycemia, where insulin is given only after glucose levels are elevated
- SSI does not prevent or reduce glucose fluctuations
- SSI does not meet physiological needs; and it does not prevent hyperglycemia: it is a reactive approach
- SSI use increases nursing time and patient discomfort
- However, SSI may be used short term: e.g. following admission to a PA/LTC facility, acute illness or unstable situations, and for newly recognized diabetes, but it should not remain in effect indefinitely
- In general, SSI regimens may be re-evaluated in a week and altered to fixed daily insulin doses that minimize use of correction doses

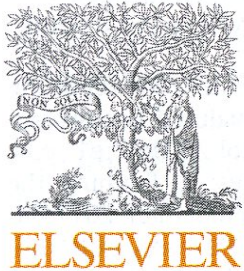
Minimize Excessive Reliance on Sliding Scale Insulin

- In spite of benefits, SSI use often appears the sole mode of control
- Avoid the tendency to use “one size fits all” regimens
- Beers criteria (2015) mention that use of SSI is associated with higher risk of hypoglycemia without improvement in hyperglycemia, regardless of care setting (strong recommendation)
- AMDA CPGs recommend that patients on SSI be re-evaluated within 1 week and converted to fixed daily insulin doses that minimize the need for correction doses
- Finally, clinical judgment along with ongoing clinical assessment are important in decision-making to treat hyperglycemia

- AMDA. Diabetes Management in the Long-Term Care Setting. Clinical Practice Guideline. Columbia, MD: 2015
- Pandya N, Wei W, Kilpatrick BS, et al. "The Burden of Sliding Scale Insulin". JAGS Dec 2013
- Dharmarajan TS, Mahajan D, Zambrano A et al. Sliding scale insulin vs basal bolus insulin in long term care. A 21 day randomized controlled trial comparing efficacy safety and reliability. J Am Med Dir Assn. 2016; 17: 206-13.

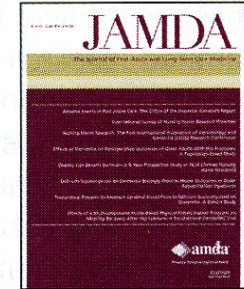
Sliding Scale Insulin or Basal-Bolus Insulin?

JAMDA 17 (2016) 206–213



JAMDA

journal homepage: www.jamda.com



Original Study

Sliding Scale Insulin vs Basal-Bolus Insulin Therapy in Long-Term Care: A 21-Day Randomized Controlled Trial Comparing Efficacy, Safety and Feasibility



CrossMark

Thiruvinvamalai S. Dharmarajan MD, MACP, AGSF^{a,*}, Dheeraj Mahajan MD, CMD^{b,c,d,e},
Annie Zambrano PA-C^{b,c,d,e}, Bikash Agarwal MD, CMD, FACP^f,
Rachel Fischer DNP^f, Zahra Sheikh MD, MPH^g, Anna Skokowska-Lebelt MD^h,
Meenakshi Patel MD, FACP, MMM, CMD^{i,j}, Rebecca Wester MD^k,
Naga P. Madireddy MD^l, Naushira Pandya MD, CMD, FACP^m, Florence T. Baralatei MDⁿ,
Jackie Vance RN^o, Edward P. Norkus PhD, FACN^a

Sliding Scale Insulin vs Basal Bolus Insulin Therapy in LTC: A 21 day Randomized Controlled Trial

Dharmarajan TS, Mahajan D, Zambrano A et al. Sliding scale insulin vs basal bolus insulin in LTC. J Am Med Dir Assn. 2016; 17: 206-13

- **Study compared efficacy of SSI (control) with BBI (intervention)**
- **14 LTC facilities in the U.S., residents with type 2 DM**
- **110 residents recruited; 75 completed study**
- **Age 80 ± 8 yrs, 66% female**
- **Both groups were similar in age, gender, co-morbidity**
- **Conclusions**
 - ❖ **BBI therapy produced significantly lower average FBG after 21 days when compared to SSI therapy**
 - ❖ **Rates of hypo and hyperglycemia were similar**
 - ❖ **Switching to BBI therapy was Feasible, Safe and Effective**

Diabetes Care in PA / LTC

- A quarter or more of residents in PA/LTC facilities have DM
- Goals of glycemic control should relate to patient's health, preferences, values, goals of care, benefits, life expectancy
- Use an inter-professional approach (collaborate with nursing, pharmacist and family)
- The routine and prolonged use of sliding scale insulin (SSI) is not recommended as the primary or sole treatment

Older Adults Requiring Palliative Care

- **When palliative care is needed, strict BP control is not necessary**
- **Withdrawal of therapy may be appropriate**
- **Intensity of lipid management can be relaxed; withdrawal of lipid-lowering therapy may be appropriate**
- **Preservation of comfort and quality of life are primary goals**

A Framework for Considering Treatment Goals for Glycemia in Older Adults with Diabetes, Based on Health Status

Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

Patient Characteristics And Health Status	Rationale	Reasonable A1C goal	Fasting or pre-prandial glucose mg/dL	Bedtime glucose mg/dL
Healthy	Longer remaining life expectancy	< 7.5 %	90-130	90-150
Complex intermediate illness (multiple coexisting)**	Intermediate remaining life expectancy ; high treatment burden, hypoglycemia, falls	< 8.0 %	90-150	100-180
Very complex and poor health	Limited remaining life expectancy makes benefit uncertain	< 8.5 %	100-180	110-220

Framework for Diabetes Management Goals, Based on Location

Standards of Medical Care in Diabetes – 2019. Diabetes Care. 2019; S1-S186

Location	Considerations	Rationale	A1C
Community dwelling patients at SNF for rehab	Rehab Potential Goal to discharge home	Optimal glycemic control Verify cognition status Address glucose excursions	A1C <7.5% Avoid relying on A1C in acute illness Follow BG trends
Patients residing in LTC and short term rehab Complex illness	Limited life expectancy Frequent health changes impact BG	Limited benefits for intensive glycemic control Maintain function; address cognition; de-intensify therapy? Focus on QOL	<8.0% Use caution Interpreting A1C if glucose excursions are wide
Patients at end of life	Avoid invasive Diagnostic / Therapeutic procedures with little benefit	No benefit for glycemic control; avoid hyperglycemia Deintensification /Deprescribe	No role for A1C

Summary: AGS Guidelines to Improve Care in T2D

- No longer recommends aspirin for primary prevention of CVD
- Aspirin 81 mg/d for older adults with DM and CVD (Secondary)(1A)
- **BP control to <140/90 mm Hg (2017 Hypertension CPGs: <130/80)**
 - ❖ BP control to lower values is not associated with better outcomes
 - ❖ A diabetic patient on ACEI or ARB should have renal function and K measured 1 to 2 weeks after initiation of therapy, and again with dosage change and yearly
- **Emphasis: treat dyslipidemias with statins, target vs. individualize?**
- **Customize A1c goals to burden: comorbidity, function, life expectancy**
 - ❖ Target 7.5 – 8% in general; 7-7.5% in healthy old; higher levels (8-9%) for those with co-morbidities, poor health, limited life expectancy (11A)
 - ❖ There is potential harm in lowering A1C to <6.5% in older adults with DM (11A)
 - ❖ **No evidence that tight glycemic control (<6.5%) with drugs is beneficial**

Summary 2: Comments (ADA Position Statement)

- **Hypoglycemia risk is the most important factor in determining glycemic goals due to the catastrophic consequences in this population. (B)**
- **Simplified treatment regimens preferred and better tolerated (E)**
- **Sole use of SSI should be generally avoided (C)**
- **Liberal diet plans are associated with improvement in food and beverage intake in this population. To avoid unintentional weight loss, restrictive therapeutic diets should be minimized (B)**
- **Physical activity and exercise are important in all patients and depend on the current level of the patient's functional abilities (C)**

Thank You!

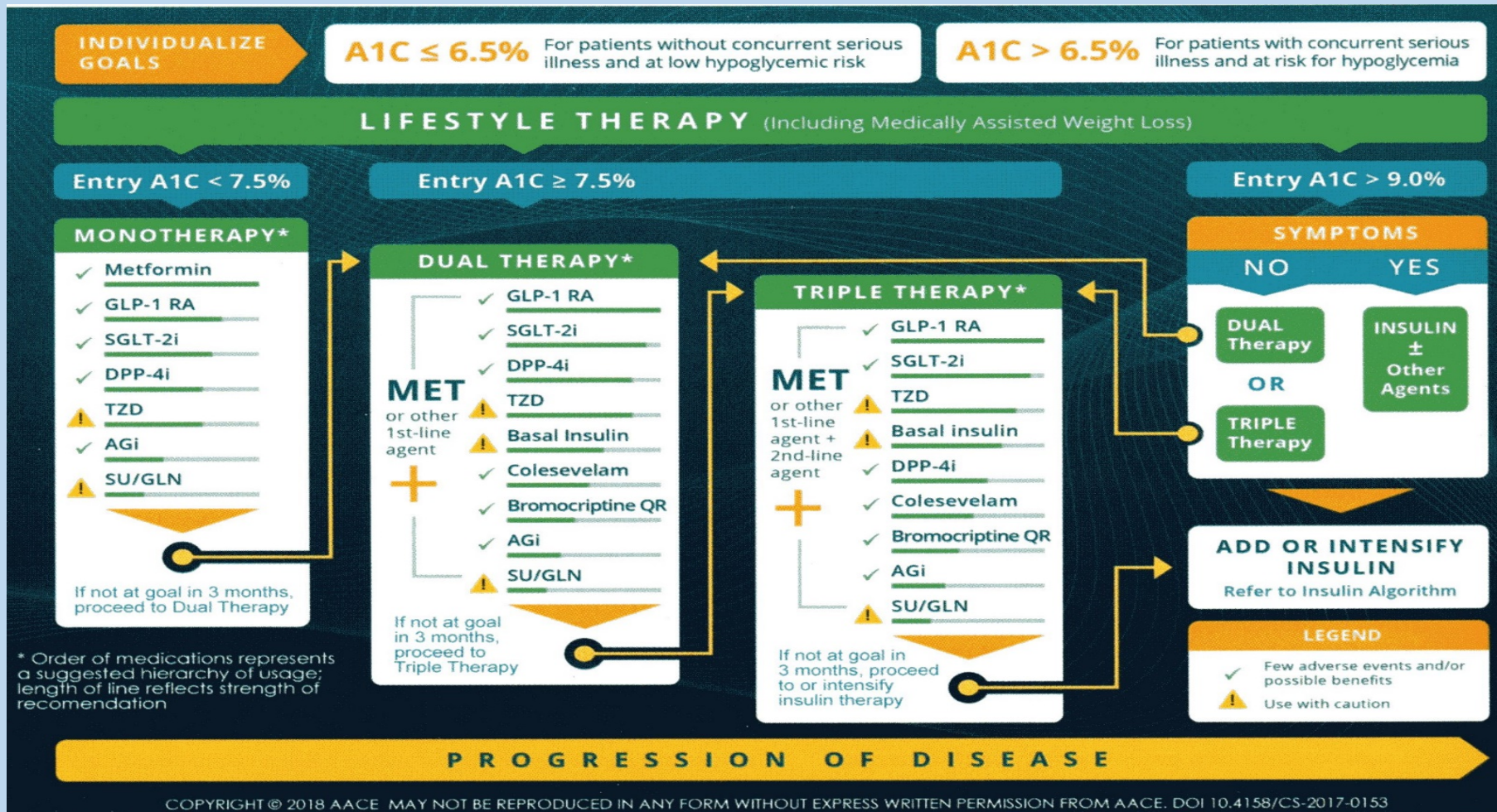


Figure 1. 2018 AACE/ACE glycemic control algorithm. Reprinted with permission from American Association of Clinical Endocrinologists © 2018. Endocr Pract. 2018;24:90-120. AACE: American Association of Clinical Endocrinologists; ACE: American College of Endocrinology