INDIVIDUALIZED CARE FOR PATIENTS WITH TYPE 2 DIABETES

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- I have no conflicts of interest to disclose

OBJECTIVES

- Understand the importance of patient engagement in relationship to the treatment of DM2
- Be familiar with how a patient's characteristics relate to determining the A1C target goal
- Know which non-insulin medications are best suited for specific health conditions in the DM2 patient

COMMON, EXPENSIVE

- World wide, 347 million people have diabetes
  - 90% have Type 2
  - Likely to double by 2030
- In the US, > 9% have Type 2 DM
- According to the ADA, the total estimated cost of diagnosed diabetes in 2017 is $327 billion
  - In 2012, the total estimated cost was $245 billion
  - 26% increase from 2012 – 2017

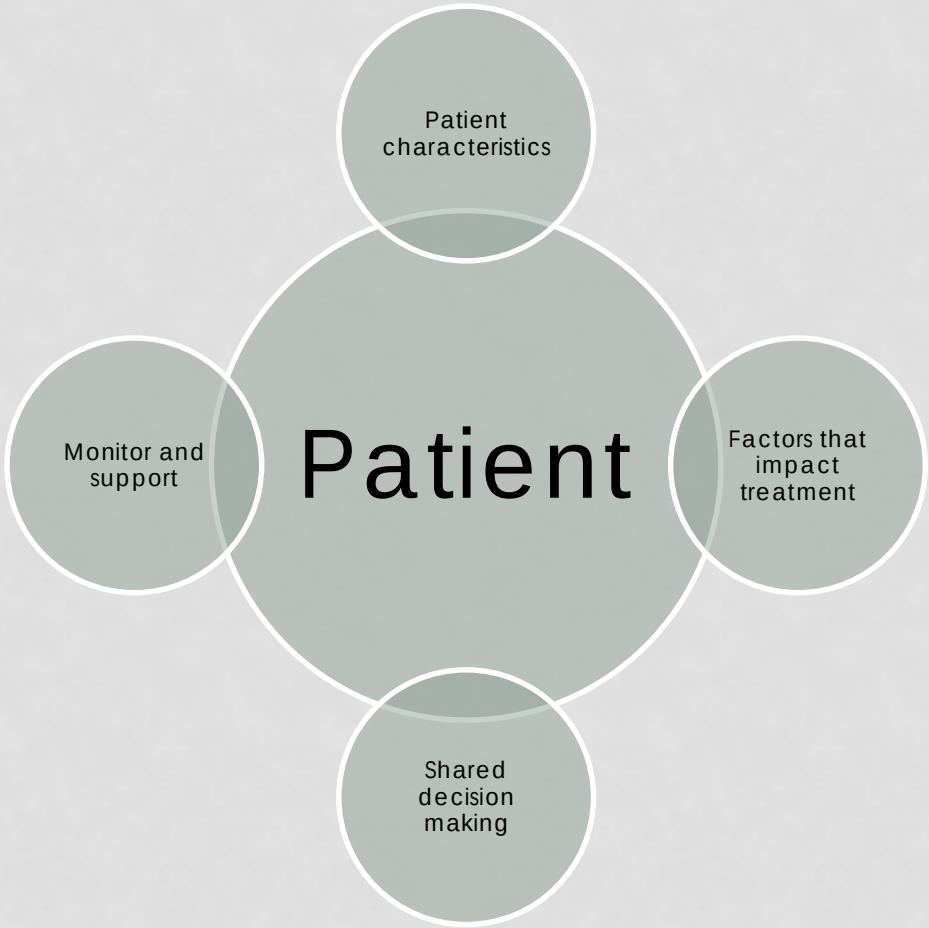
GOALS OF TREATMENT

- Prevent or delay complications
- Maintain/Optimize quality of life

PATIENT CENTERED COLLABORATIVE CARE

- A patient centered communication style that uses person centered and strength based language and active listening, elicits patient preferences and beliefs, and assesses literacy, numeracy, and potential barriers to care should be used to optimize patient health outcomes and health related quality of life.
  - ADA Grade B Recommendation

PLAN OF CARE


Patient characteristics
Monitor and support
Patient
Factors that impact treatment
Shared decision making

PATIENT ENGAGEMENT

- May lead to more responsive services and better care by incorporating the patient's values and preferences into the care plans
  - Compliance
  - Healthy behaviors
  - Creating a therapeutic alliance in clinical encounters


BEFORE I MAKE MY DECISION, I'D LIKE TO ASK FOR YOUR OPINIONS.
IT'S SUPPOSED TO MAKE YOU FEEL "ENGAGED."
AND YOU ACTUALLY PLAN TO LISTEN TO US?
I'M HOPING IT WILL LOOK THAT WAY ON THE OUTSIDE.
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PATIENT CHARACTERISTICS

- Lifestyle
  - “When you are in good company, with family and friends and you are having a dinner you are forced to think of “IT”.” (female, 66, oral therapy)
  - “When you travel, it is very difficult to take the drug, it is also embarrassing.” (male, 68, insulin)
- Motivation
  - “Sometimes I ignore the appointments and I don’t go.” (male, 47, oral therapy)

FACTORS THAT IMPACT TREATMENT

- Impact on weight and hypoglycemia
- Side effect profile of medications
- Complexity of treatment regimen
  - "I think I need to understand better why I need to take this therapy and for how long…many questions pop in my mind and sometimes I search the Internet in order to get answers." (male, 55, oral therapy)
- Cost

SHARED DECISION MAKING

- Involves an educated and informed patient
- Patient preferences
  - Type of Employment
- Motivational interviewing
  - Goal setting
- Empowers the patient

MONITOR AND SUPPORT

- Check for medication side effects
- Glycemic status
- Blood pressure, microalbumin, retinal exam, lipids, etc
- Emotional well being
  - “It is difficult to accept being ill, or at least it has been very hard in the beginning. You feel alone, no one understanding you. I would definitely have appreciated some counseling.” (male, 53, oral therapy)

DIABETES SELF MANAGEMENT EDUCATION AND SUPPORT

- Associated with:
  - Improved diabetes knowledge
  - Self care behavior
  - Lower A1C
  - Lower self reported weight
  - Improved quality of life
  - Reduced all cause mortality risk
  - Reduced health care costs

NUTRITION

- Provided by a registered dietician
- Associated with a decrease in A1C of 0.3 – 2%
- Helpful with weight loss
  - Weight loss of at least 5% is needed to produce beneficial outcomes

A1C GOALS

- A reasonable A1C goal for many non-pregnant adults is < 7%
  - **ADA Grade A**
- Providers might reasonably suggest more stringent A1C goals (< 6.5%) for selected individuals patients if this can be achieved without significant hypoglycemia or other adverse effects
  - **ADA Grade C**
- Less stringent A1C goals (< 8%) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, extensive comorbid conditions, or long standing diabetes in whom the goal is difficult to achieve despite education, monitoring, and multiple meds
  - **ADA Grade B**
- Reassess glycemic targets over time based on criteria or in older adults
  - **ADA Grade E**

A1C GOALS

- ADVANCE
  - Action in Diabetes and Vascular Disease Controlled Evaluation
  - Target of < 6.5% in intensive therapy group vs standard therapy
  - Intensive glycemic control significantly reduced the risk and/or progression of retinopathy, nephropathy, and neuropathy
  - Rates of hypoglycemia were higher in the intensive therapy group
- ACCORD
  - Action to Control Cardiovascular Risk in Diabetes
  - Intensive glycemic control significantly reduced the risk and/or progression of retinopathy, nephropathy, and neuropathy
  - Involved older and middle-aged with long standing DM2 who were at high risk or had established ASCVD
  - Increased mortality in patients randomized to intensive glucose lowering therapy
    - After 5 years, the intensive treatment group had a 20% higher rate of mortality

A1C GOALS

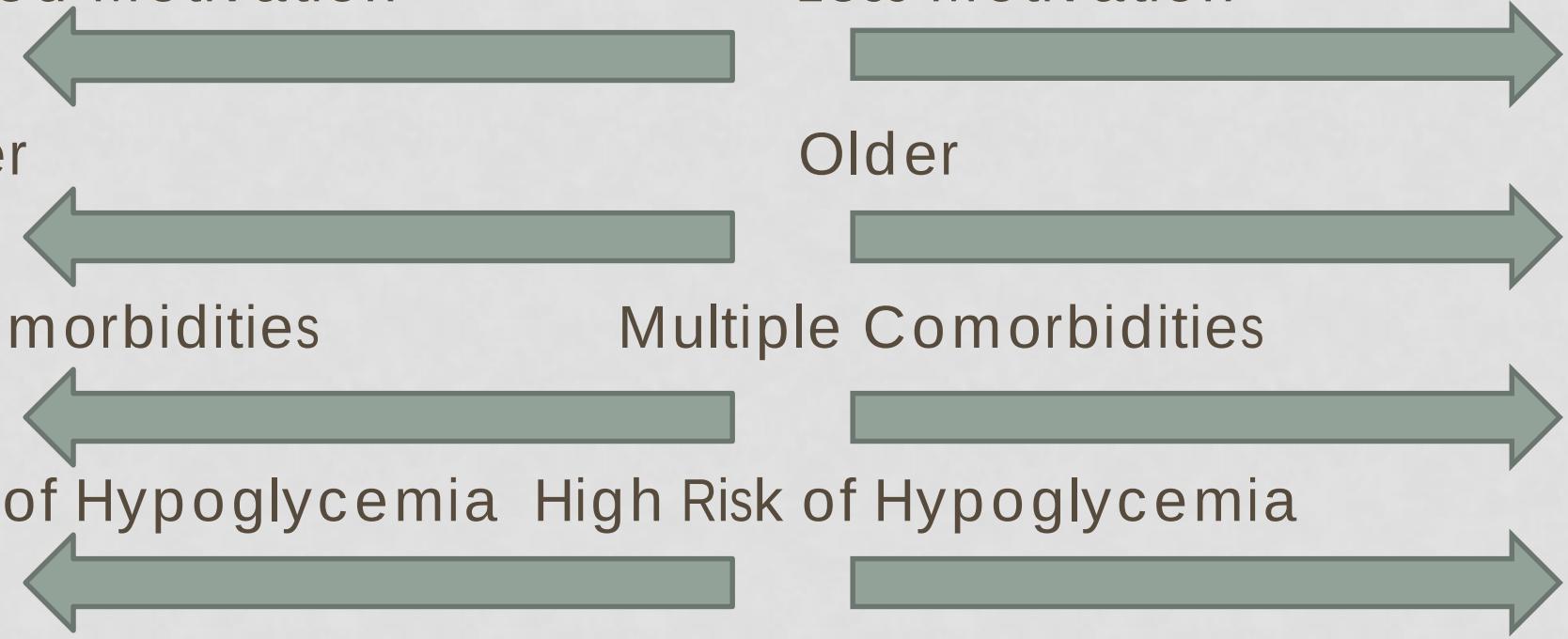
- VADT
  - Veterans Affairs Diabetes Trial
  - Had a higher A1C target for intensively treated patients
  - No between group differences in ASCVD endpoints, CV death, or overall death during the 5.6 year study
  - Observational follow up study, about 10 years
    - About 17% less likely to have a major cardiovascular event if received intensive therapy
    - Mortality risk was about the same

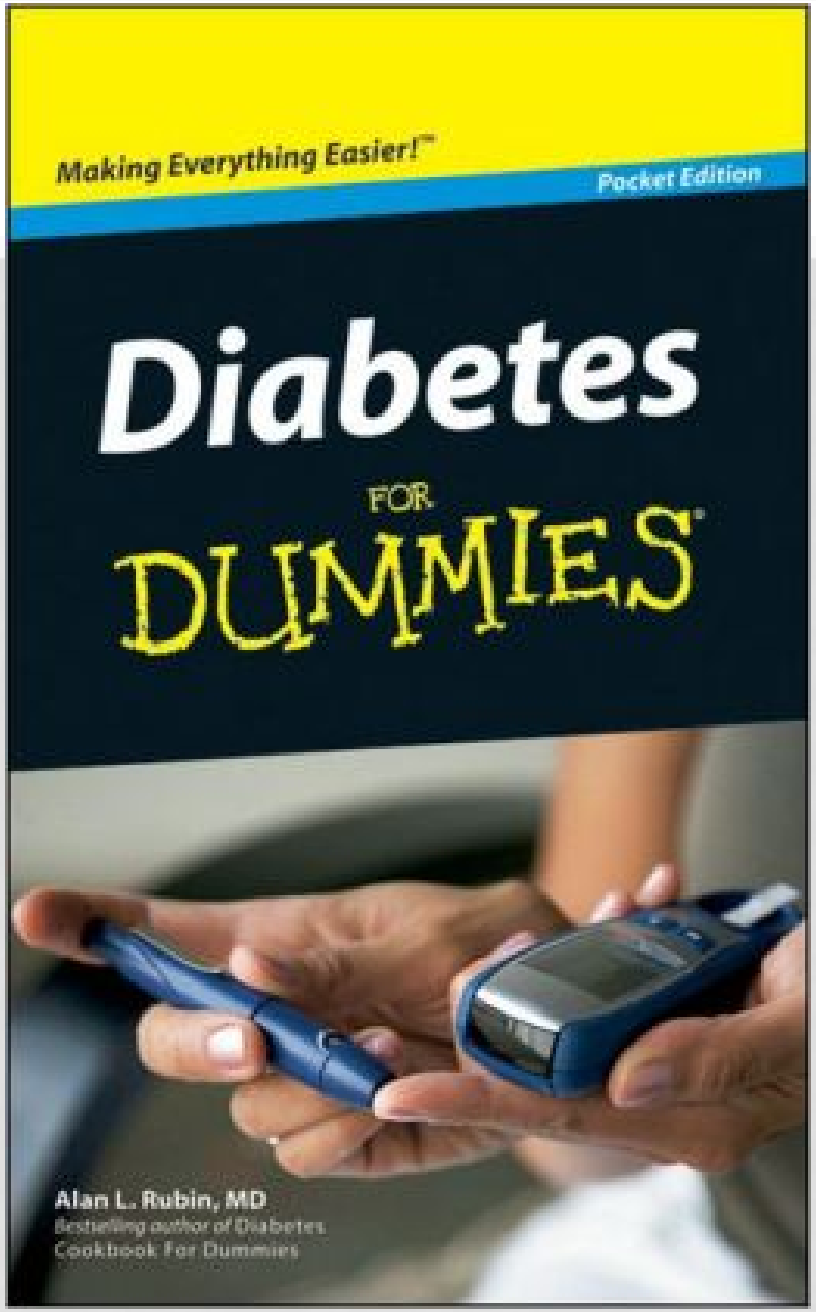
OLDER INDIVIDUALS IN TRIALS

- Older individuals enrolled in diabetes clinical trials are more likely to have better overall health than older individuals in the general population
  - A study may support the concept that intensive strategies for individuals can be effective and safe but for older individuals in poor health aggressive therapy may be harmful without the benefit of reducing complications

A1C TARGET

- Increased Motivation — Less Motivation
- Younger — Older
- Few Comorbidities — Multiple Comorbidities
- No Risk of Hypoglycemia — High Risk of Hypoglycemia




Making Everything Easier!™
Pocket Edition
Diabetes
FOR
DUMMIES
Alan L. Rubin, MD
Bestselling author of Diabetes
Cookbook For Dummies

FIRST LINE THERAPY

- Metformin

METFORMIN

- Low risk of hypoglycemia
- Can promote modest weight loss
- Robust cardiovascular safety
  - United Kingdom Prospective Diabetes Study
    - 32% reduction in any diabetes related end point
    - 42% reduction in diabetes related mortality
    - 36% reduction in all cause mortality
    - 39% reduction in myocardial infarction
    - 50% reduction in fatal myocardial infarction
- Can continue in patients with stable GFR > 30
- Up to 16% of patients may have B12 malabsorption or deficiency

ESTABLISHED ASCVD OR CKD

ASCVD Predominates

- GLP-1RA or SGLT2
- GLP-1RA strongest evidence for CVD benefit liraglutide > semaglutide > exanatide

CHF or CKD Predominates

- SGLT2
- GLP-1RA
  - If SGLT2 not tolerated or GFR less than adequate

GLP-1RA

- Stimulates glucose dependent insulin secretion and suppresses glucagon secretion
- Robust A1C lowering
- Usually associated with weight loss, lipid, and blood pressure reduction
- Low risk of hypoglycemia
- Reduce fluctuations in fasting and post-prandial glucose levels
- Contraindicated in patients with personal/family history of medullary thyroid cancer or MEN2 syndrome
  - Caution with history of pancreatitis
  - Caution with history of gastroparesis or severe GERD
- No renal dose adjustment for liraglutide, semaglutide, and dulaglutide

GLP-1RA

- LEADER
  - Liragulitide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results
  - Liraglutide significantly reduced the risk of nephropathy and death from certain cardiovascular causes
    - FDA approval to reduce the risk of cardiovascular death, non-fatal MI, and non-fatal stroke in adults with DM2 and established cardiovascular disease
- SUSTAIN-6, REWIND
  - Trials with semaglutide and dulaglutide respectively suggest other GLP-1RA also have cardiovascular disease benefits

SGLT2

- Glucosuric effect
- Modest A1C lowering
- Weight loss and blood pressure lowering
- Lower rates of all cause and cardiovascular death and lower risk of hospitalization for heart failure
- Increased risk of amputation
- Mycotic genital infections
- Limited efficacy if GFR <45
- Low hypoglycemia risk
- Caution for dehydration
  - Syncope, hypotension, falls, acute renal impairment

SGLT2

- EMPA-REG
  - Empagliflozin, Cardiovascular Outcomes and Mortality in DM2
  - Significantly reduced the risk of combined cardiovascular outcomes of CV death, MI, and non-fatal stroke as well as reduced hospitalization for HF
  - Reduced secondary renal endpoints
- CANVAS
  - Canagliflozin Cardiovascular Assessment Study
  - Significantly reduced the risk of combined cardiovascular outcomes of CV death, MI, and non-fatal stroke as well as reduced hospitalization for HF
  - Reduced secondary renal endpoints
  - Increased risk of amputation
- DECLARE-TIMI
  - Dapagliflozin Effect on Cardiovascular Events Thrombolysis in Myocardial Infarction
  - Dapagliflozin reduced a composite of CV death and heart failure hospitalizations
  - Did not significantly lower the combined risk of CV death, non-fatal MI, and stroke
- SGLT2 associated DKA
  - Review of 2500 cases 5% of DM1 developed DKA, DM2 ranged from 0.16 – 0.76 per 1000 patient years

GLP-1RA VS SGLT2

- Meta-analysis by T.A. Zilniker et al reviewed data from eight trials and 77,242 patients
  - 42,920 (55.6%) in GLP-1RA trials and 34,322 (44.4%) in SGLT2 trials
  - Both reduced the risk of MACE by 14% in patients with known ASCVD (GLP-1RA also reduced the risk of stroke)
  - Neither reduced the risk of MACE in patients without established ASCVD
  - SGLT2 reduced the relative risk of hospitalization for HF by 31%
  - GLP-1RA had a non-significant 7% relative risk reduction
  - SGLT2 showed relative risk reduction of 45% for the composite of reductions in eGFR, ESKD, and death due to renal causes
  - GLP-1RA reduced microalbuminuria but excluding microalbuminuria had a non-significant relative reduction of 8%

WITHOUT ESTABLISHED ASCVD OR CKD

- Compelling Need
  - Minimize hypoglycemia
  - Minimize weight gain or promote weight loss
  - Cost

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

- DPP4 inhibitors
- GLP-1RA
- SGLT2
- TZD

DPP4 INHIBITORS

- Inhibits DDP4 which increases levels of GLP-1
  - Stimulates insulin secretion and suppresses glucagon secretion
- Modest A1C lowering
- Low risk of hypoglycemia
- Neutral weight change
- Renal dose adjustment
  - Except Linagliptin
- Potential risk of pancreatitis
- Arthralgia
- Possible slight increase in heart failure with saxagliptin and alogliptin

TZD

- Directly reduces insulin resistance
- Relatively potent A1C lowering
- Low risk of hypoglycemia
- Weight gain
- Pioglitazone may have potential ASCVD benefit
- Risk of lower extremity edema and CHF
- Benefit in NASH

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

- GLP-1RA or SGLT2

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- If GLP-1RA or SGLT2 not tolerated or contraindicated; DDP4 (assuming not on a GLP-1RA)

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

- GLP-1RA or SGLT2
- If GLP-1RA or SGLT2 not tolerated or contraindicated; DDP4 (assuming not on a GLP-1RA)
- Caution with TZD, SU, or Basal insulin

IF COST IS A MAJOR ISSUE

- SU or TZD

SULFONYLUREAS

- Relatively potent A1C lowering
  - Lack durability
- Weight gain
- Risk of hypoglycemia
  - Highest risk of any non-insulin therapy
- Concerns regarding cardiovascular safety

SUMMARY

- Engage the patient to improve care
- Select an A1C target that is best for your patient
- Start with metformin (unless compelling reasons)
- Select additional medications based on
  - ASCVD
  - CHF
  - CKD
  - Weight gain
  - Avoidance of hypoglycemia
  - Cost

"Good news.
Your cholesterol has stayed the same,
but the research findings have changed."

SOURCES

- Diabetes Care; ADA Standards Of Medical Care In Diabetes – 2019; Volume 42 Supplement 1
- Consensus Statement By the American Association of Clinical Endocrinologists and American College of Endocrinology On the Comprehensive Type 2 Diabetes Management Algorithm – 2019 Executive Summary; Endocrine Practice, Vol 25 No 1, January 2019
- EMPAREG OUTCOME Investigators, Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New England Journal of Medicine 2015; 373: 2117-2128, Zinman, Wanner, Lachin
- CANVAS Program Collaborative Group. Canagliflozin and cardiovascular and renal events in type 2 diabetes. New England Journal of Medicine 2017; 377:644-657; Perkovic, Mahaffey, et al
- Incidence of hospitalization for heart failure and case fatality among 3.25 million people with and without diabetes. Circulation. 27 June 2018; McAllister, Read, Kerssens
- Treatment of Diabetes in Older Adults: An Endocrine Society Clinical Practice Guideline; LeRoith, Biessels, Braithwaite, Casanueva, Drazin, Halter, Hirsch, McDonnel, Molitch, Murad; The Journal Of Clinical Endocrinology & Metabolism; Volume 104, Issue 5, May 2019 (In Progress)
- Comparison of the Effects of GLP1-RA and SGLT2i; Diabetes In Control, April 9, 2019; Elimairi
- Type 2 Diabetes Mellitus: ACP Releases Updated Guidance Statement on A1C Targets for Pharmacologic Glycemic Control; Am Fam Physician 2018 Nov 1; 98(9): 613 – 614
- How to engage type-2 diabetic patients in their own health management: implications for clinical practice; BMC Public Health. 2014; 14: 648; Graffigna, Barello, Libreri, Bosio