Recent clinical practice guidelines for improving kidney outcomes: BP goals, kidney protective medications, and nutrition goals

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ECHO

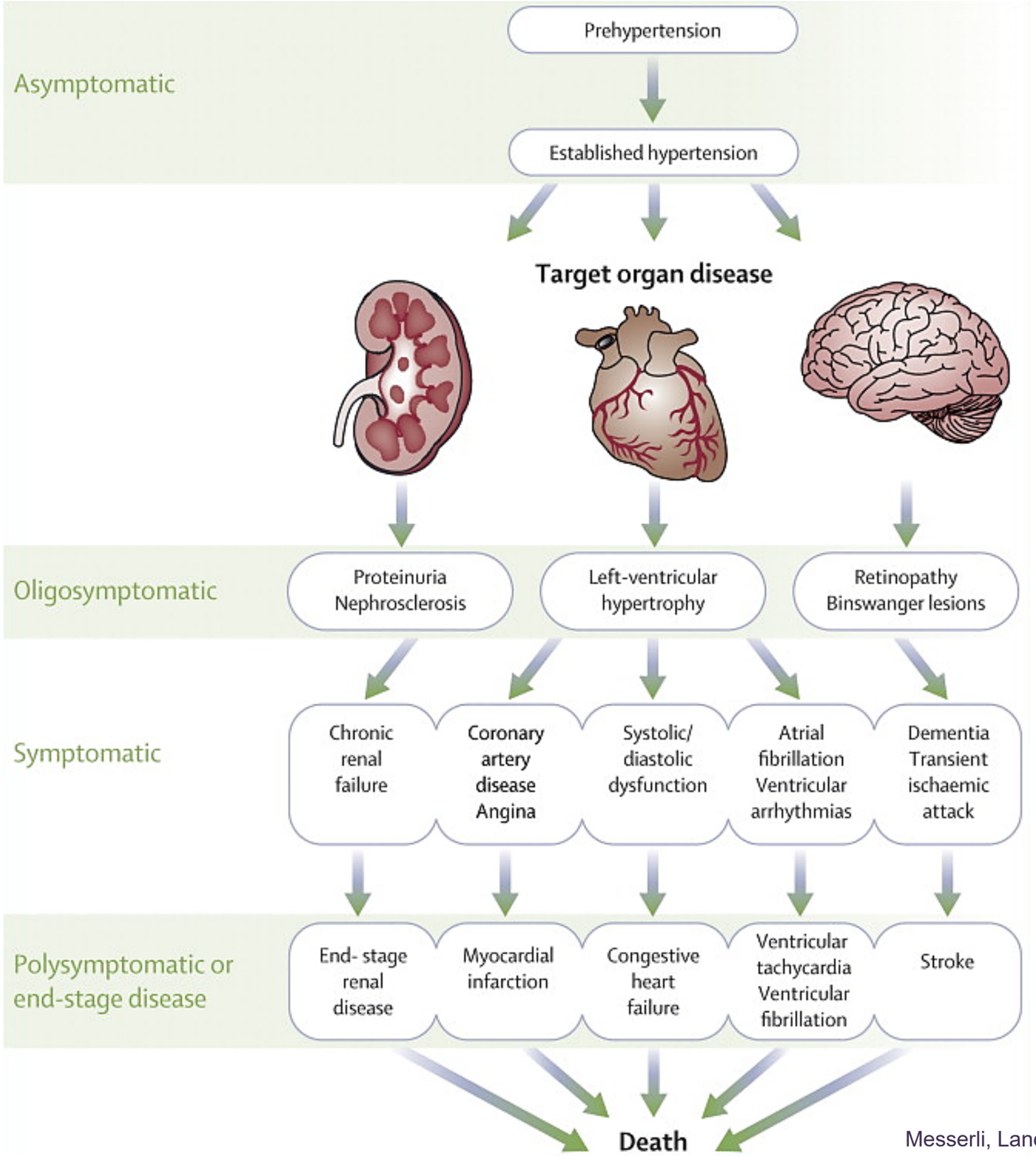
Objectives

- Explain different BP goals in kidney disease from leading societies on kidney disease and diabetes
  - ACC/AHA, ADA, KDIGO, KDOQI
- Be able identify those that should initiate kidney protective medications based on CM and kidney risk based on algorithm from guidelines
- Discuss the controversy over new nutrition goals for those with kidney disease
- Brief mention of new two test HEDIS Kidney Health Evaluation for Patients with Diabetes (KED) screening measure

Disclosures

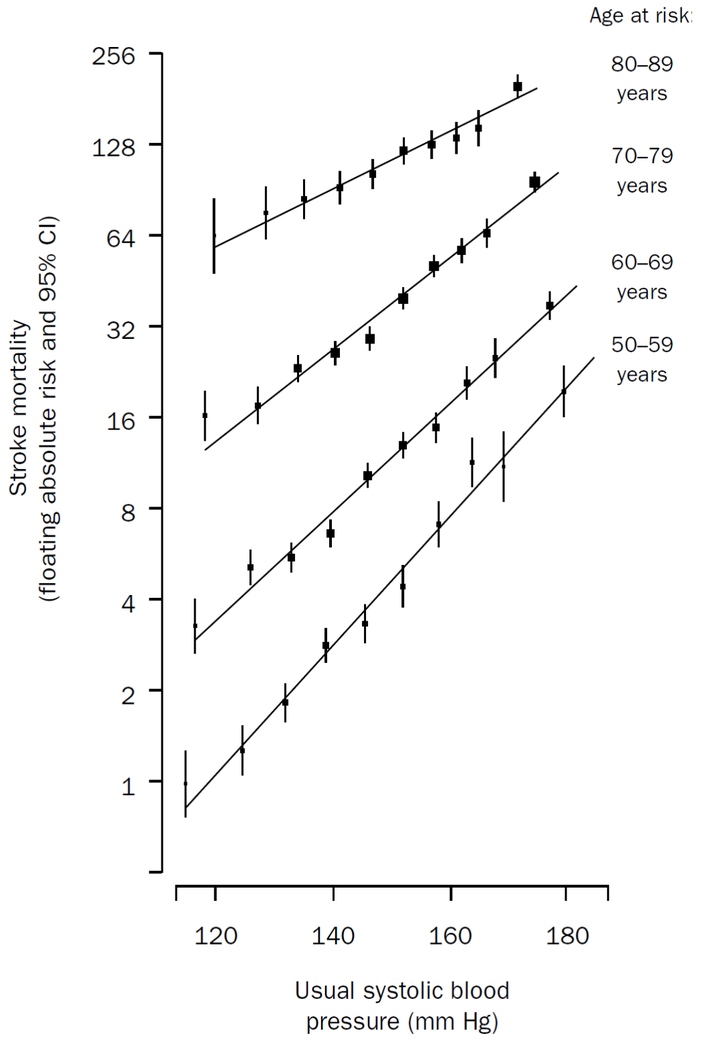
Matthew B. Rivara, MD
has nothing to disclose

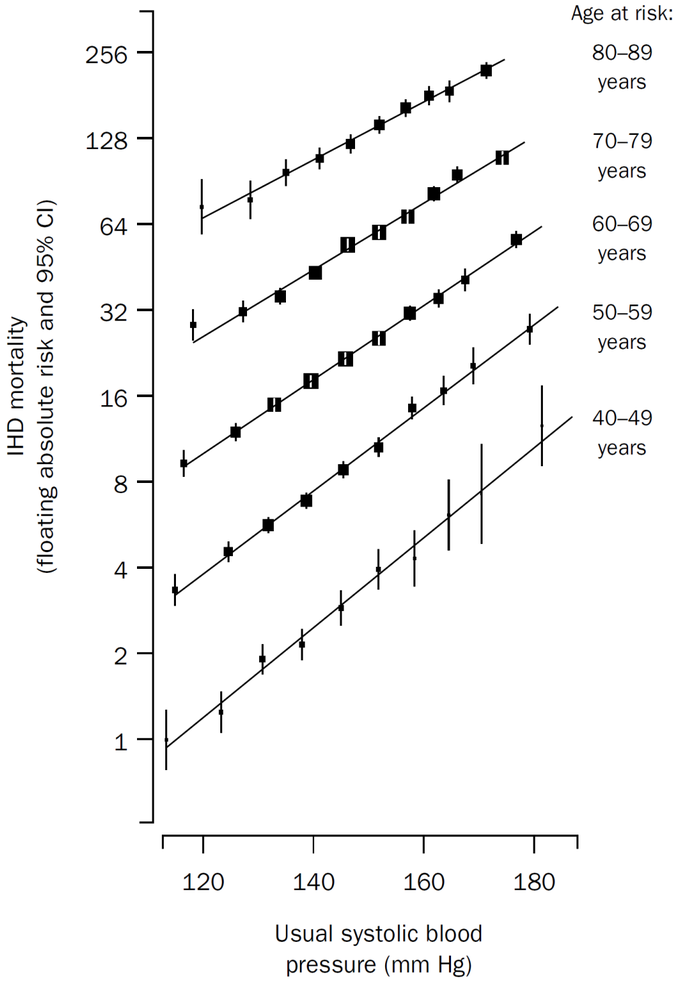
Why do we care about hypertension?



Messerli, Lancet, 2007

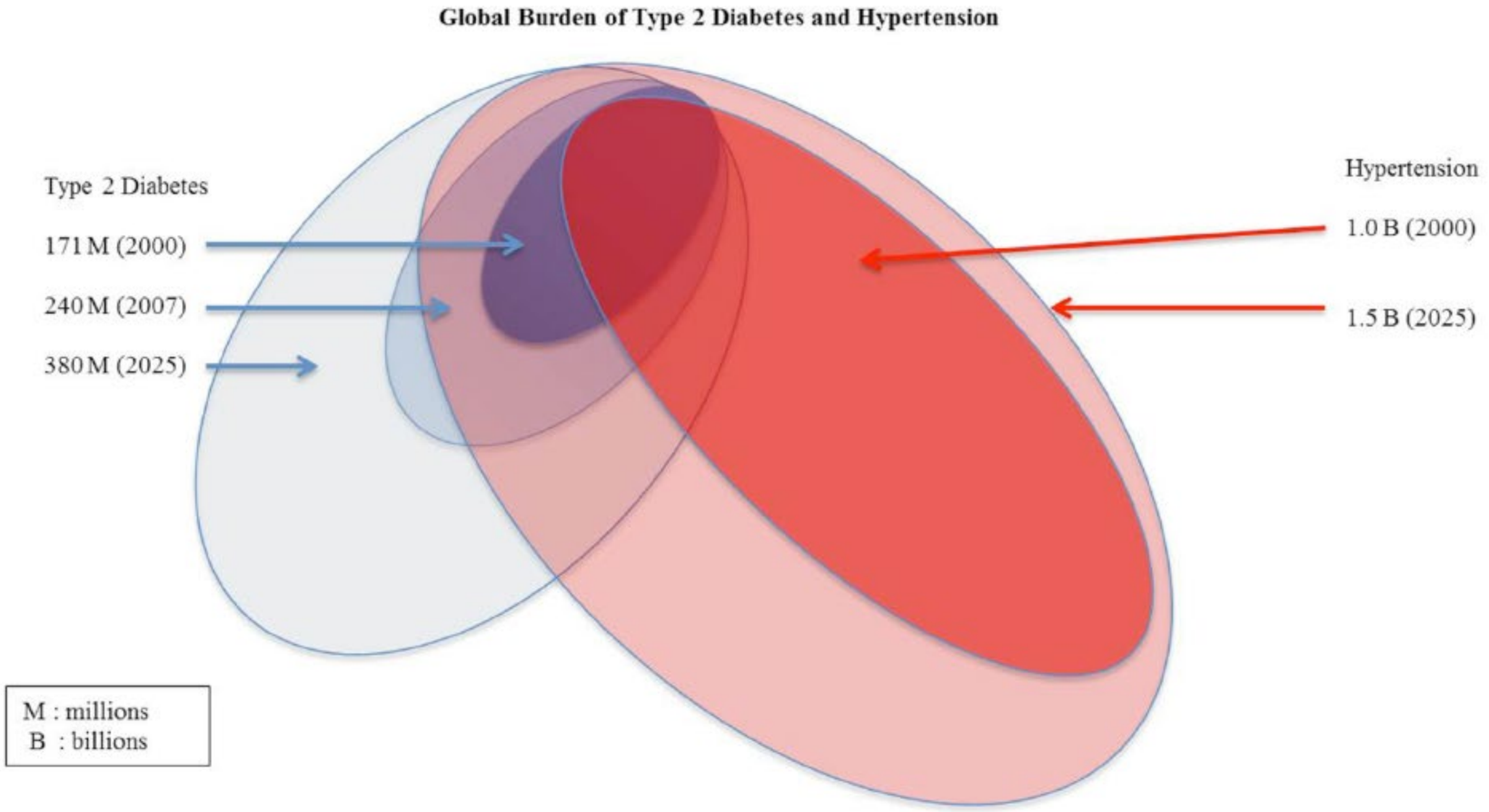
Association of HTN with adverse outcomes





Lewington et al, Lancet 20032;360(9349):1903 -13

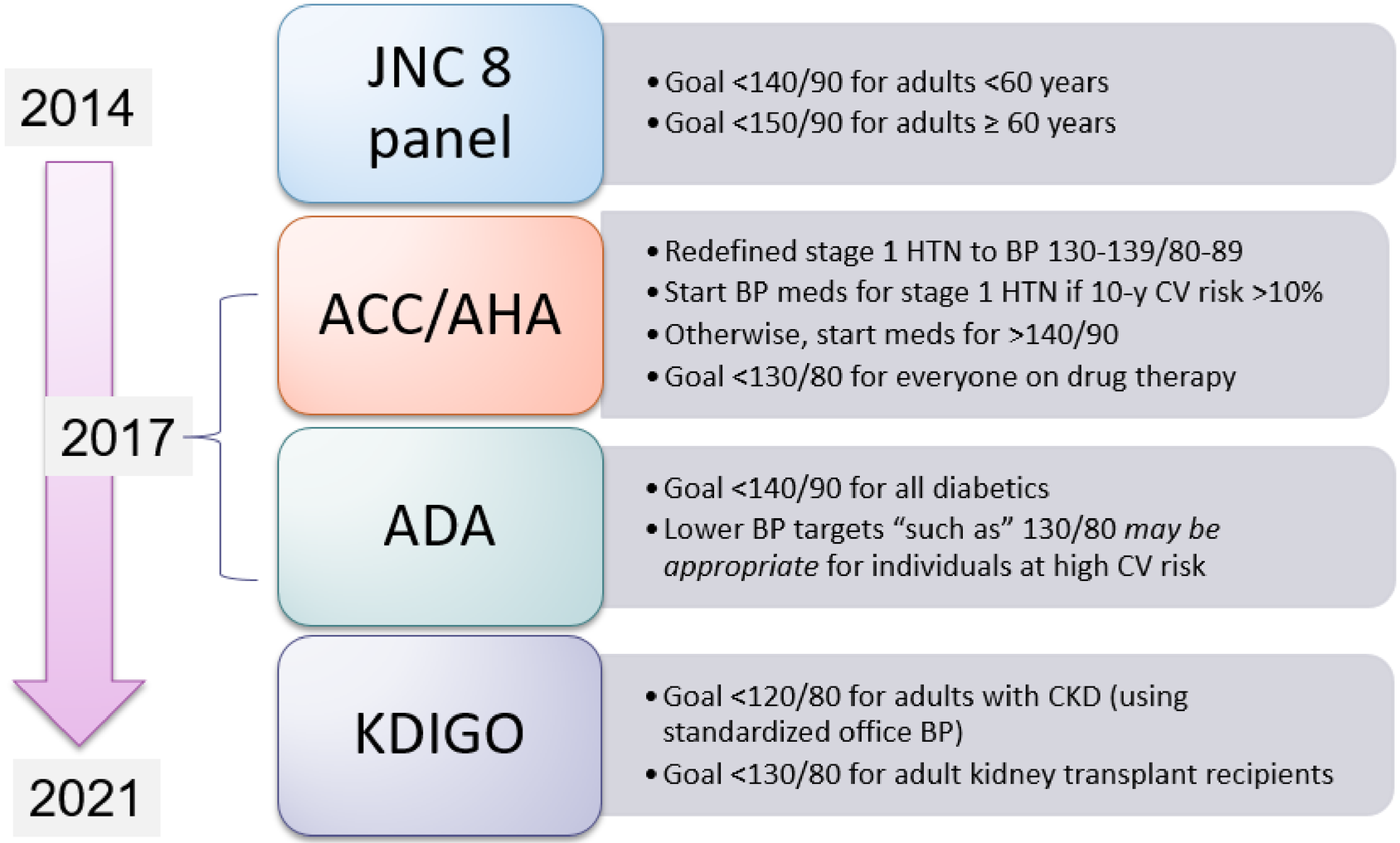
Enormous burden of comorbid diabetes and HTN



- Approximately 50-75% of individuals with type 2 DM have comorbid HTN
  - ~40% for 20 -44 years of age
  - ~60% for 45 -64 years of age
  - ~80% for ⩾65 years of age
- In patients with hypertension without diabetes at baseline, ~2% of individuals develop diabetes each year

Franchini et al. Curr Pharm Des 2015; 21
Kearney PM, et al. Lancet 2005; 365(9455): 217-23.
Roumie CL et al. Hypertension 2020;75:331-338

A dizzying time for HTN treatment goals…



Clinical Practice Guideline

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

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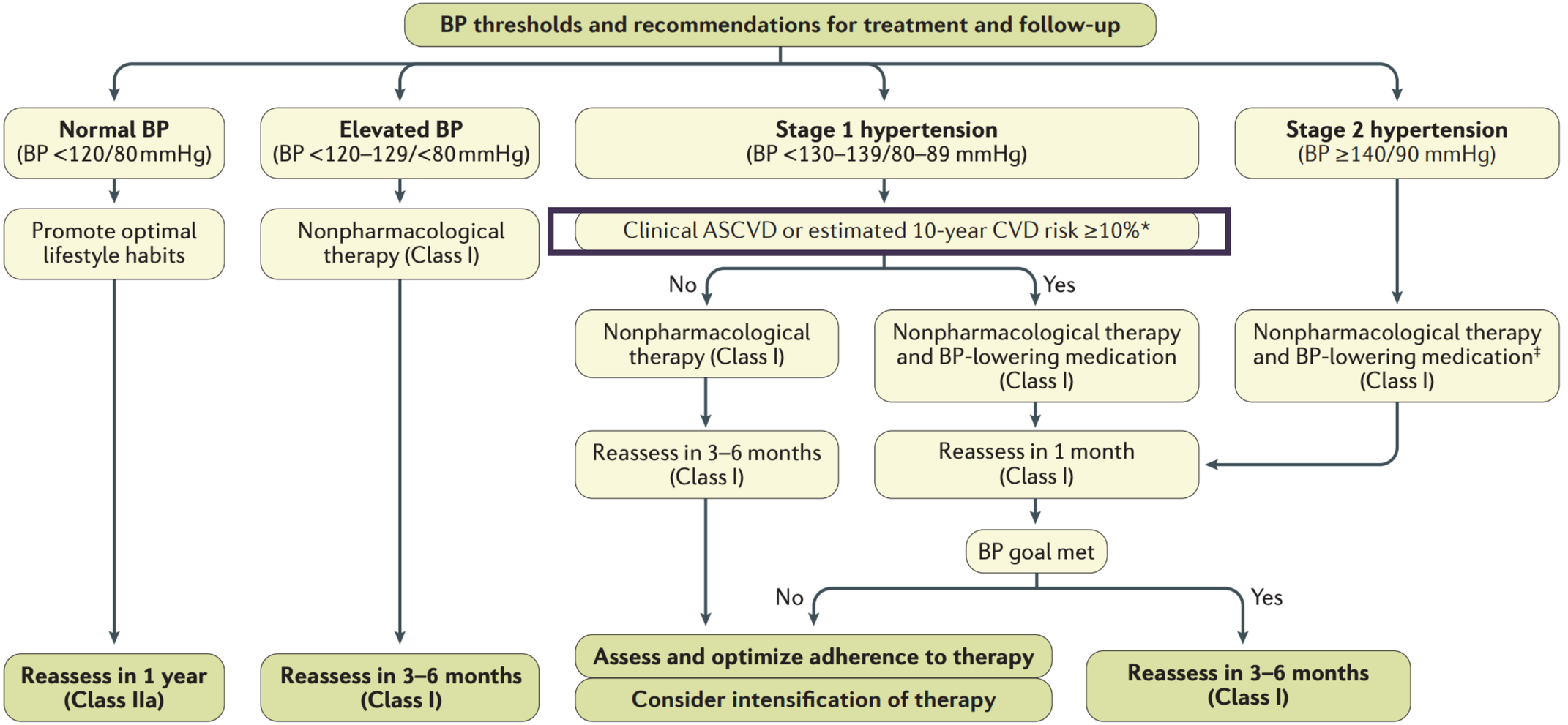
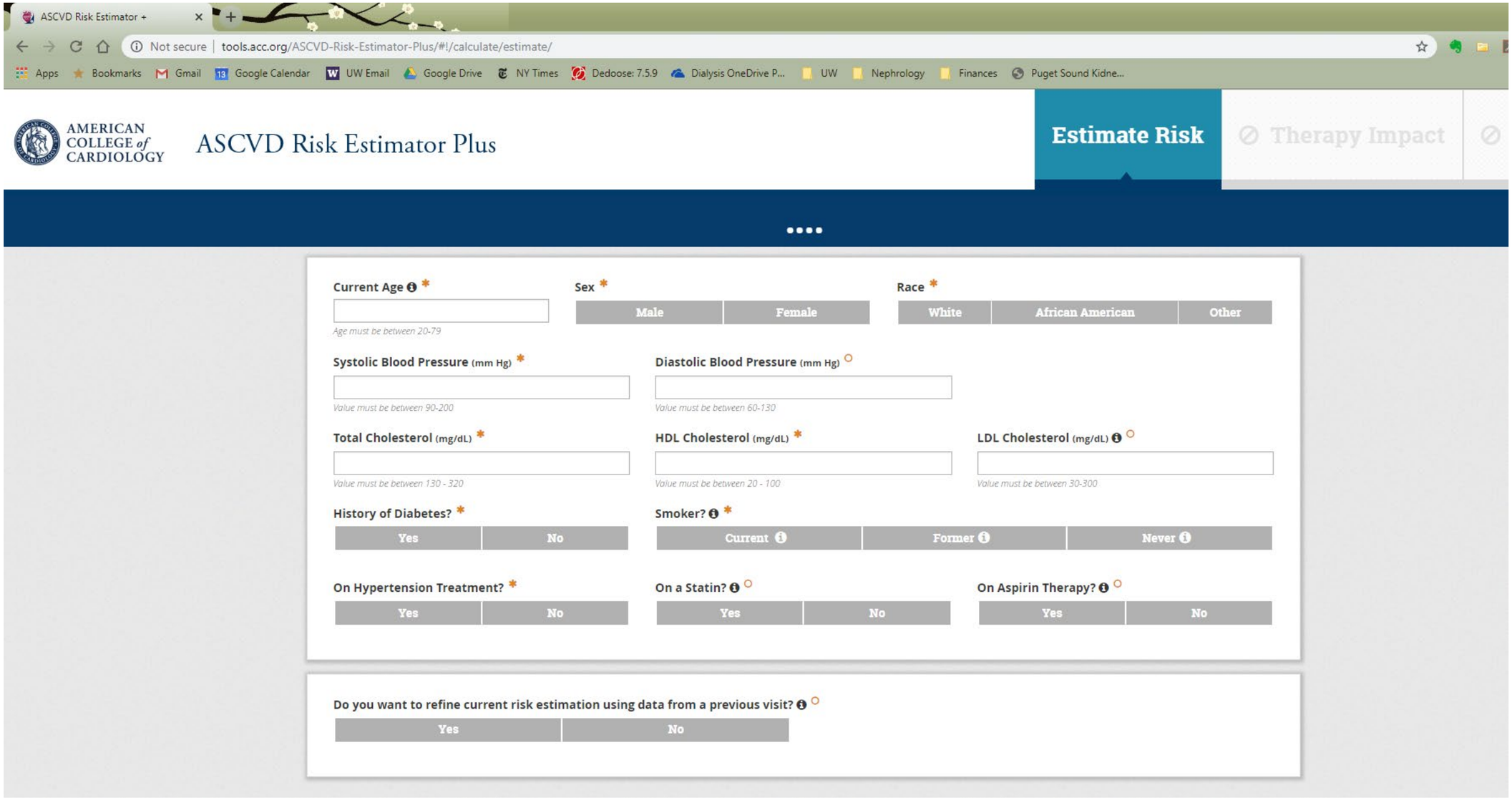


Slide courtesy of Cary Paine, MD

Oparil Nature Reviews 2018



http://tools.acc.org/ASCVD-Risk-Estimator-Plus/

Kidney Disease Improving Global Outcomes (KDIGO)

- **Recommendation 1.1:**
  - "We recommend standardized office BP measurement in preference to routine office BP measurement for the management of high BP in adults."
- **Recommendation 3.1.1:**
  - "We suggest that adults with high BP and CKD be treated with a target systolic blood pressure (SBP) or <120 mm Hg, when tolerated, using standardized office BP measurement (2B)."

Cheung AK, et al. Kidney Int 2021;99:559 -69

Digression to talk about standardized office BP

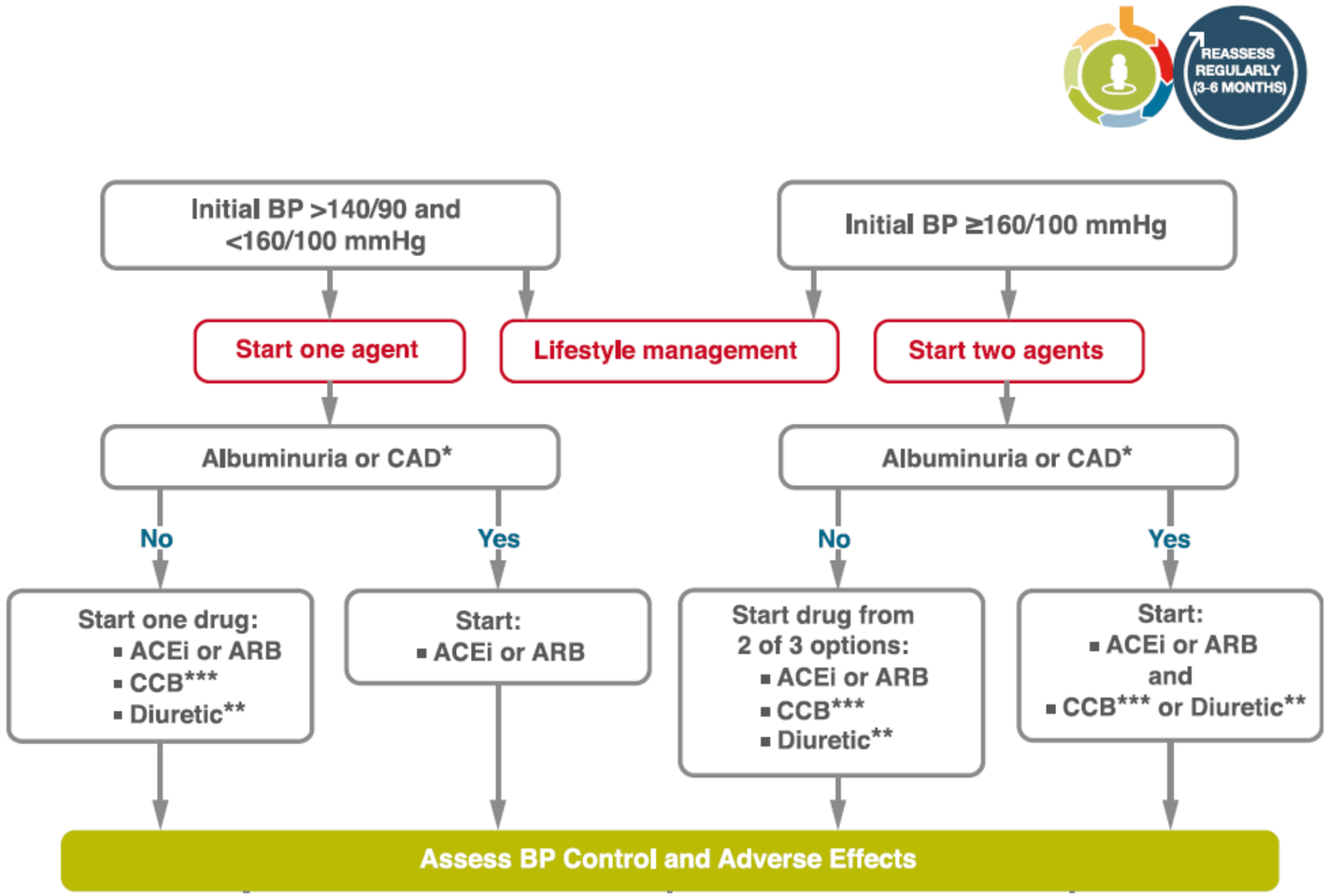
- Average of 2 or more BPs should be obtained by trained operator using appropriate sized cuff
- The patient should have adequate time to relax in quiet room (5-10 minutes) alone

Factors affecting accuracy of blood pressure measure

Factor	Magnitude of systolic/diastolic blood pressure discrepancy (mm Hg)
Talking or active listening	10/10
Distended bladder	15/10
Cuff over clothing	5-50/
Cuff too small	10/2-8
Smoking withing 30 minutes of measurement	6-20/
Paralyzed arm	2-5/
Back unsupported	6-10/
Arm unsupported, sitting	1-7/5-11
Arm unsupported, standing	6-8/

Handler, Perm J 2009

Recommendation for the Treatment of Confirmed Hypertension in People with Diabetes



ADA guidelines 2021

For individuals with DM2 and HTN at higher CV risk, a BP target of <130/80 mm Hg may be appropriate if it can be safely attained

Diabetes Care 2022;45(Suppl. 1):S144 –S174

Why are the contemporary BP targets so much lower than previously?

"I'm afraid you've had a paradigm shift."

What data do we have supporting this?

Image: The New Yorker, Published 12/17/01

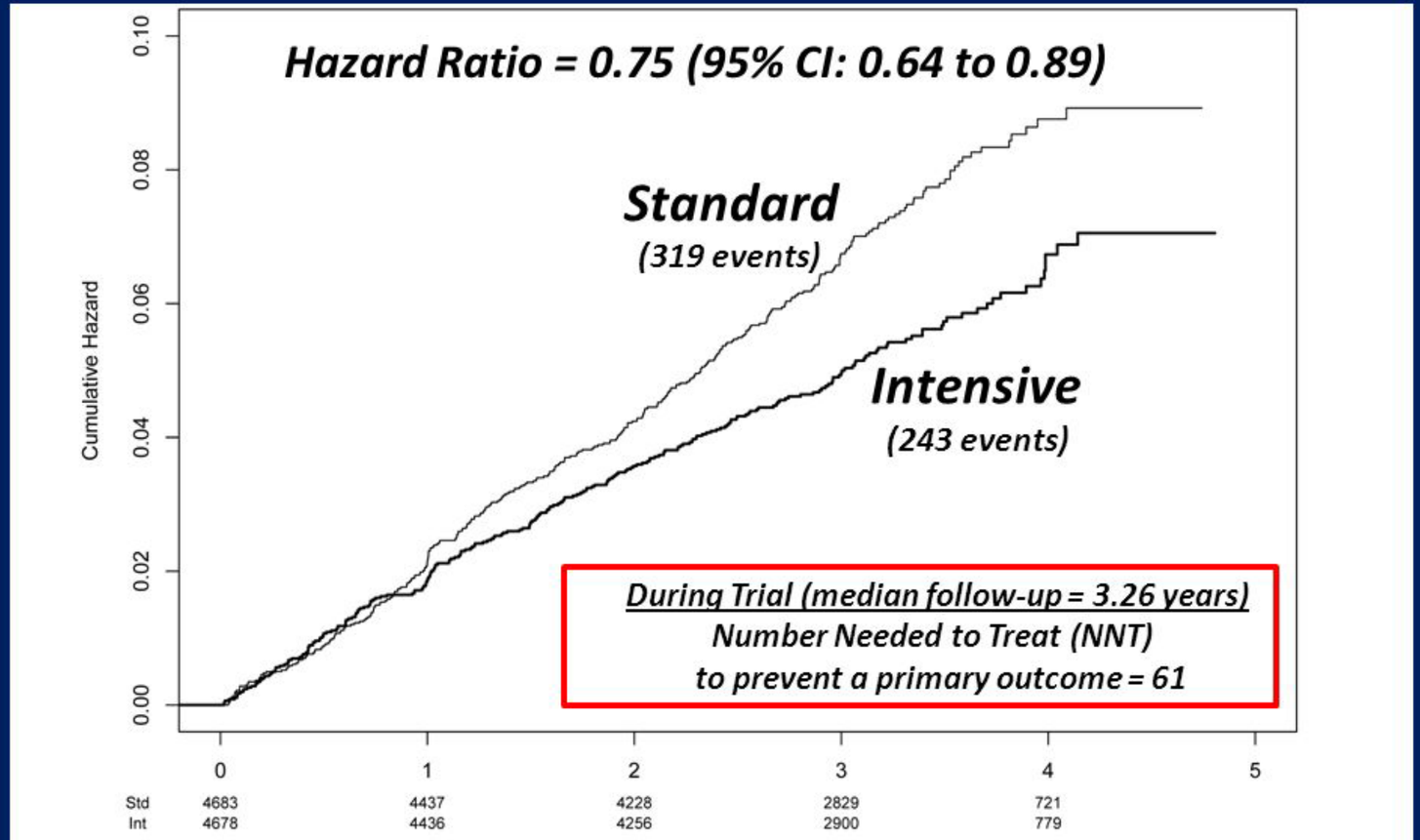
SPRINT Trial

- **Systolic Blood Pressure Intervention Trial**
  - Published Nov. 2015 in NEJM
  - Multicenter RCT, 9,361 non-diabetic patients ⩾ 50 years of age without a history of prior stroke who were at elevated risk for CV events.
    - Clinical CVD (prior MI, revascularization, ACS, AAA>5cm)
    - Subclinical CVD (CAC score, ABI, LVH on ECG or TTE)
    - CKD (eGFR 20-60)
    - Framingham score >15%
    - Age ≥ 75
  - Randomized to:
    - **Intensive, target SBP <120**
    - **Standard, target SP 135-139**

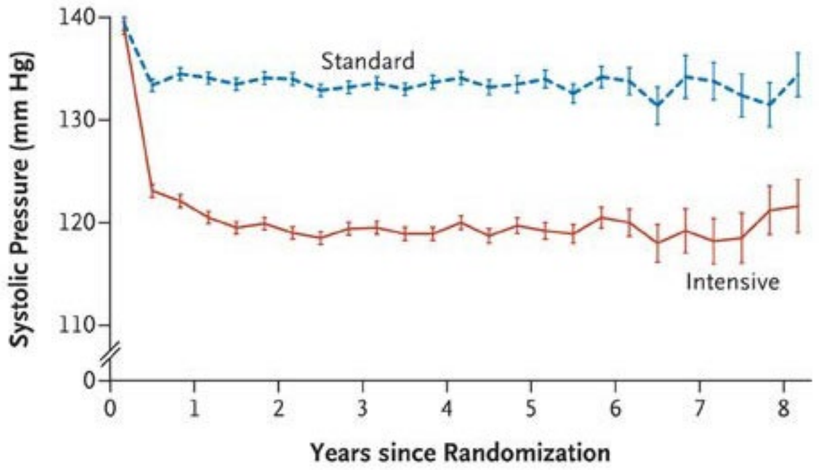
Primary outcome: MI, other ACS, stroke, CHF, or death from CV cause

SPRINT Results

SPRINT Primary Outcome
Cumulative Hazard



So, from ADA guidelines, why not <130/80 mm Hg or lower in all diabetics? – the ACCORD BP study

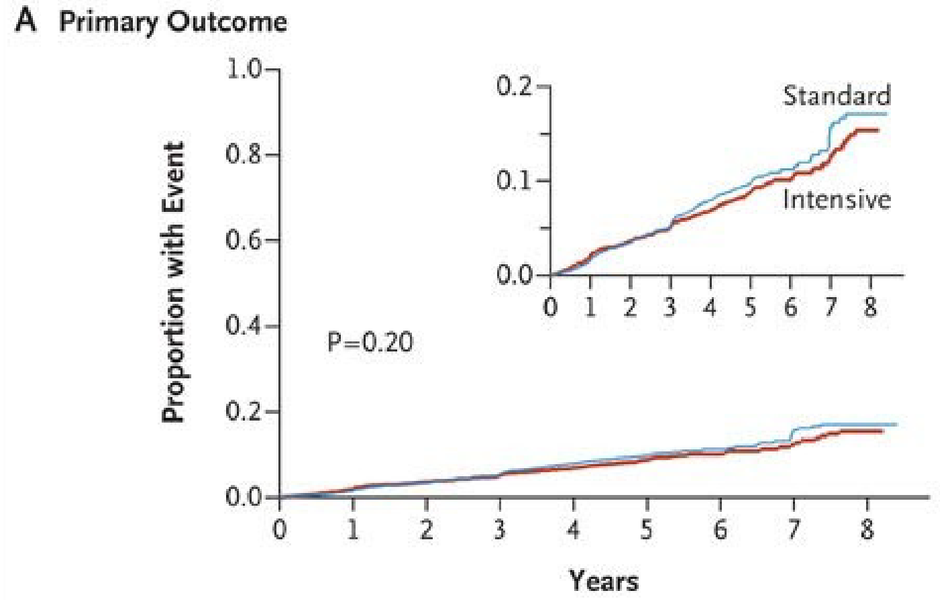


Mean No. of Medications Prescribed								
Intensive	3.2	3.4	3.4	3.5	3.5	3.5	3.4	3.4
Standard	1.9	2.1	2.1	2.2	2.2	2.3	2.3	2.3
No. of Patients								
Intensive	2174	2071	1973	1792	1150	445	156	156
Standard	2208	2136	2077	1860	1241	504	203	201

4733 patients with DM2, creatinine <1.5mg/dL

Assigned to SBP <120 mm Hg vs <140 mm hg

Primary outcome: MI, stroke, death from CV cause



No. at Risk									
Intensive	2362	2273	2182	2117	1770	1080	298	175	80
Standard	2371	2274	2196	2120	1793	1127	358	195	108

ACCORD study group, NEJM 2010;362:1575-85

Summary of recent BP guidelines

	ACC/AHA	KDIGO	KDOQI	ADA
Year	2017	2021	2021	2021
Standardized BP measurement	Yes	Yes	Yes	Yes
Overall SBP treatment target	<120 mm Hg	< 130 mm Hg	<130 mm Hg	N/A
BP target (CKD)	<120 mm Hg	<120/80 mm Hg *	<120/80 * mm Hg	<130/80 mm Hg; lower if UACR ⩾ 30 mg/g
BP target (DM)	<120 mm Hg	<120/80 mm Hg*	<130/80 mm Hg	High CV risk: <130/80 mm Hg; lower CV risk: <140/90 Hg

* When using standardized office BP only

Drawz PE, et al. AJKD 2022;79(3):311-327

How to navigate all the guidelines. My approach…

- I target BP < 130/80 mm Hg for most patients, irrespective of diabetes status
- For patients with CKD, I use measurements obtained with automated office BP (AOBP) or reliable home BP readings only to cautiously lower BP towards 120 mm Hg.
- I **do not** recommend targeting systolic BP <120 mm Hg unless using standardized office BP or reliable hom ebP
- In patient who have a systolic BP <130 mm Hg but diastolic >80 mm Hg , I do not further increase anti -hypertensive agent intensity

https://www.ncbi.nlm.nih.gov/books/NBK278938/#!po=14.5833

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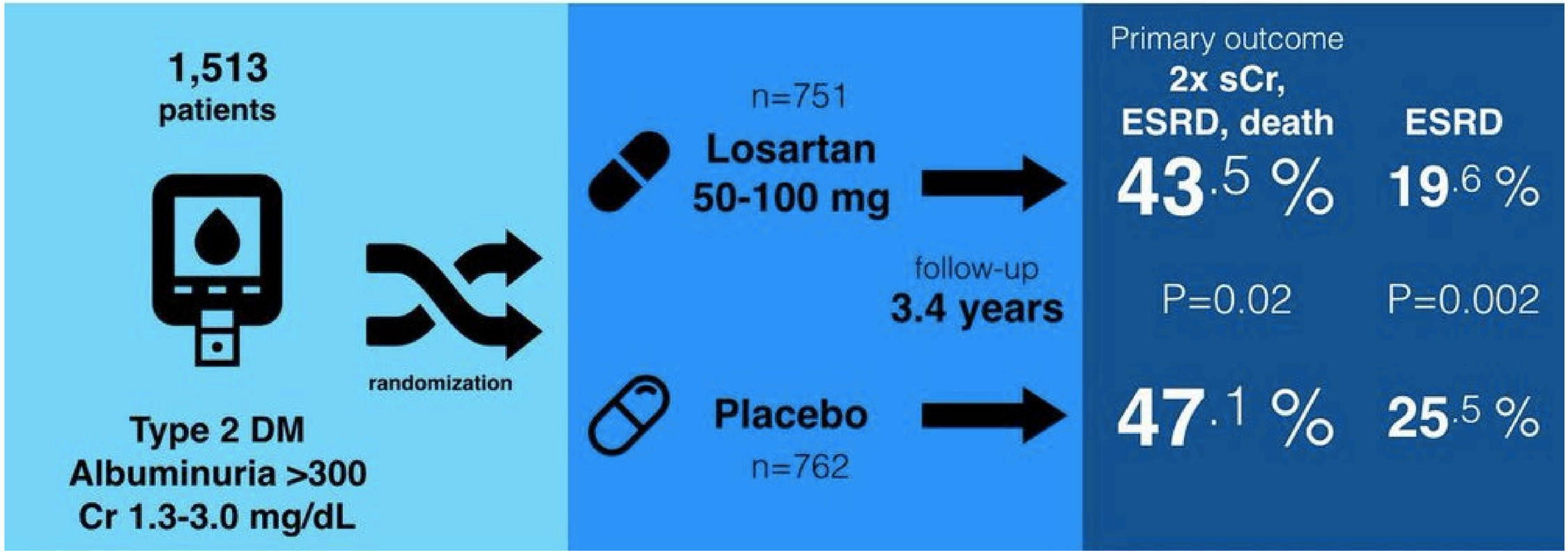
What are “kidney protective” medications?

- ACE inhibitors/Angiotensin Receptor Blockers (ACEIs/ARBs)
- Sodium-glucose Cotransporter -2 inhibitors (SGLT2i)
  - canagliflozin, dapagliflozin, and empagliflozin
- Glucagon-like Peptide-1 Receptor (GLP-1) agonists
  - Dulaglutide, exenatide, semaglutide, liraglutide
- What about metformin?
- What about mineralocorticoid receptor antagonists (MRAs)
  - spironolactone, eplerenone, finerenone

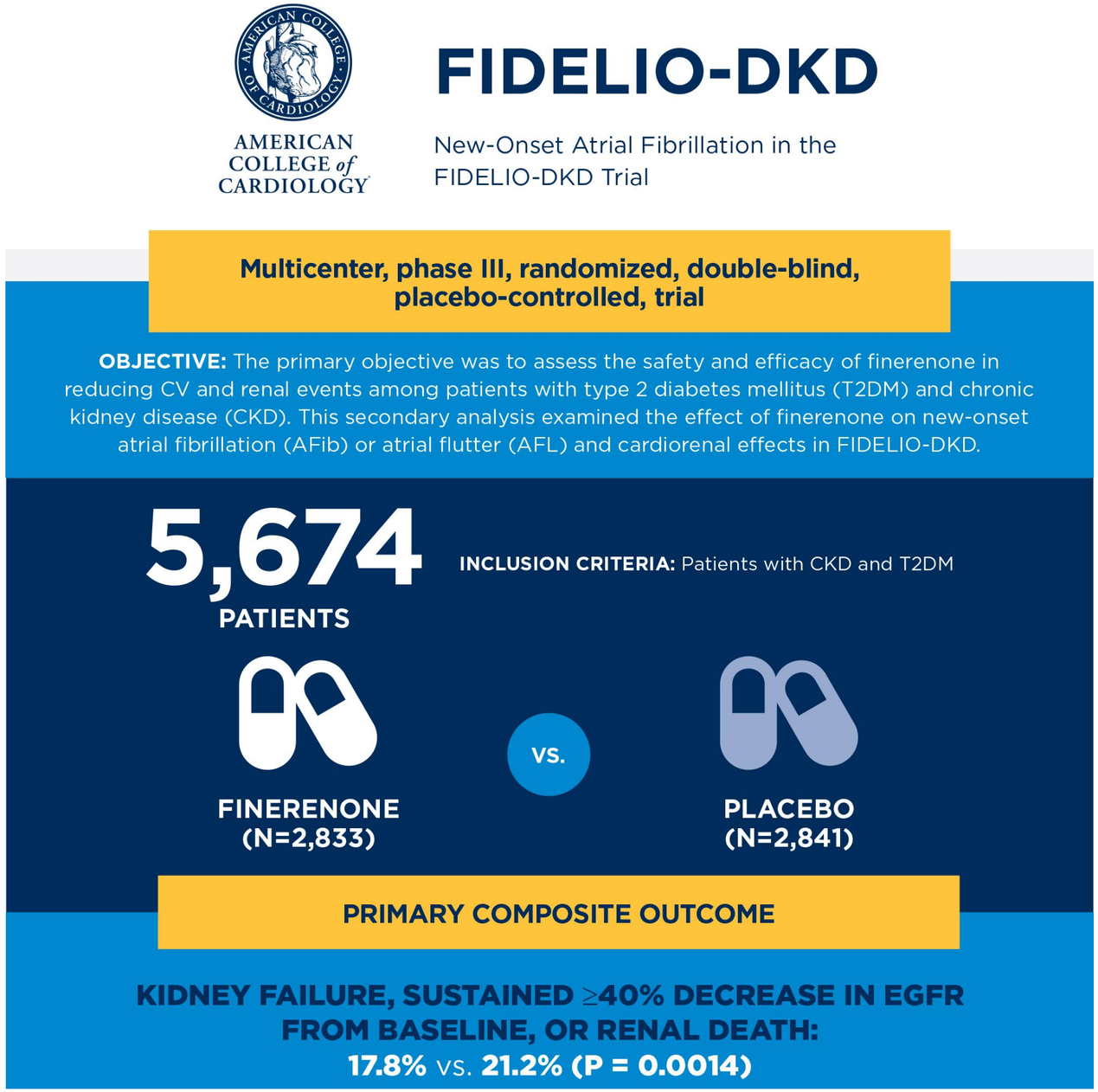
Effects of Losartan on Renal and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Nephropathy (RENAAL)



Brenner BM, et al. NEJM 2001;3454;861-869

What about MRAs?

- MRAs classically avoided in CKD due to risks of hyperkalemia
- Finerenone is a new selective non-steroidal MRA that *may* have less hyperkalemia than spironolactone or eplerenone
  - No comparative effective trials
- Fidelio DKD randomized patients with CKD and DM2 to finerenone vs placebo for 2.5 years
  - eGFR 25 to <60



Albuminuria Lowering Effect of Dapagliflozin, Eplerenone and Their Combination in Patients with Chronic Kidney Disease: A Randomized Cross-Over Clinical Trial

METHODS

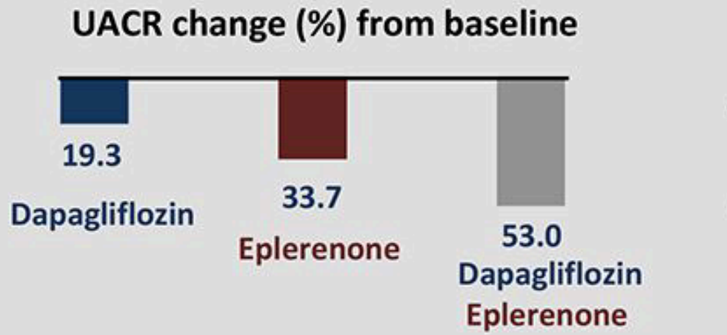
46 patients

- Age ≥18 years
- UACR 100-3500 mg/24-hour
- eGFR >30 - <90 mL/min/1.73m^2
- Stable (>4 weeks) dose of ACEi **or** ARB

Dapagliflozin 10 mg → **Eplerenone** 50 mg → **Eplerenone** 50 mg **Dapagliflozin** 10 mg

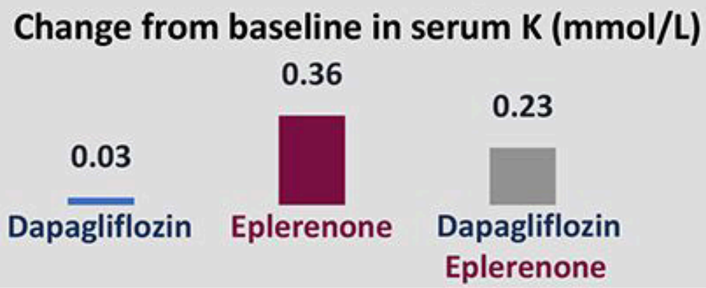
4-weeks treatment in random order with 4-weeks wash-out in between

OUTCOMES



combination vs. dapa: p<0.001

combination vs. eple: p=0.0127



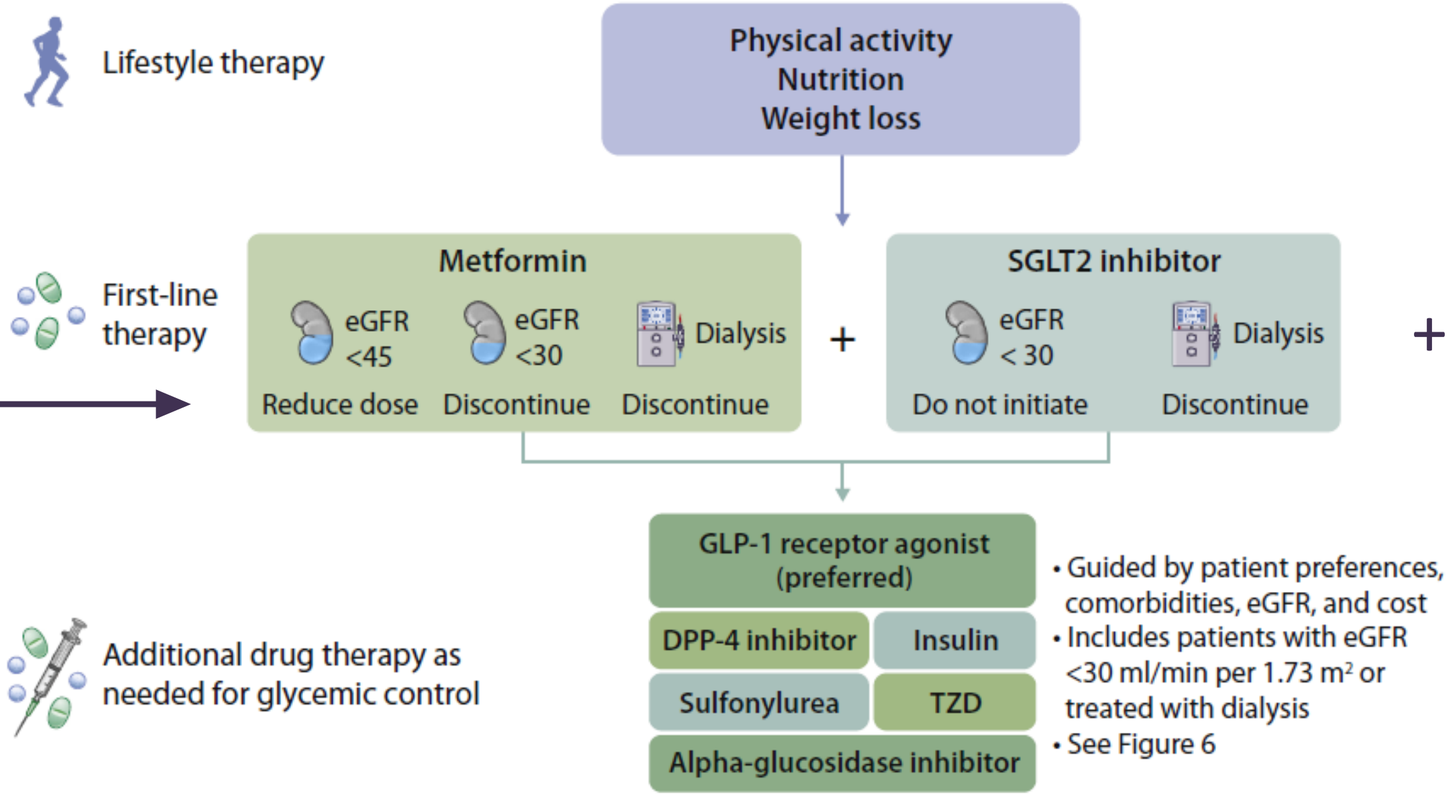
combination vs. dapa: p<0.0018

combination vs. eple: p=0.0296

Conclusion: Dapagliflozin in combination with eplerenone reduced albuminuria to a greater extent than either Drug alone. Compared to eplerenone, dapagliflozin-eplerenone combined decreased serum potassium.

Provenzano et al. JASN 2022;33(8):1569-80

Putting it together – patients with DM2 and CKD



Metformin recommended first line due to low cost, low risks of hypoglycemia, prevents weight gain, reduces CV events. No clear benefit for kidney outcomes

? MRAs – not in guidelines (yet)

De Boer IH, et al. Kidney Int 2020;90:839-848

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KDOQI Clinical Practice Guidelines for Nutrition in CKD – 2020 Update

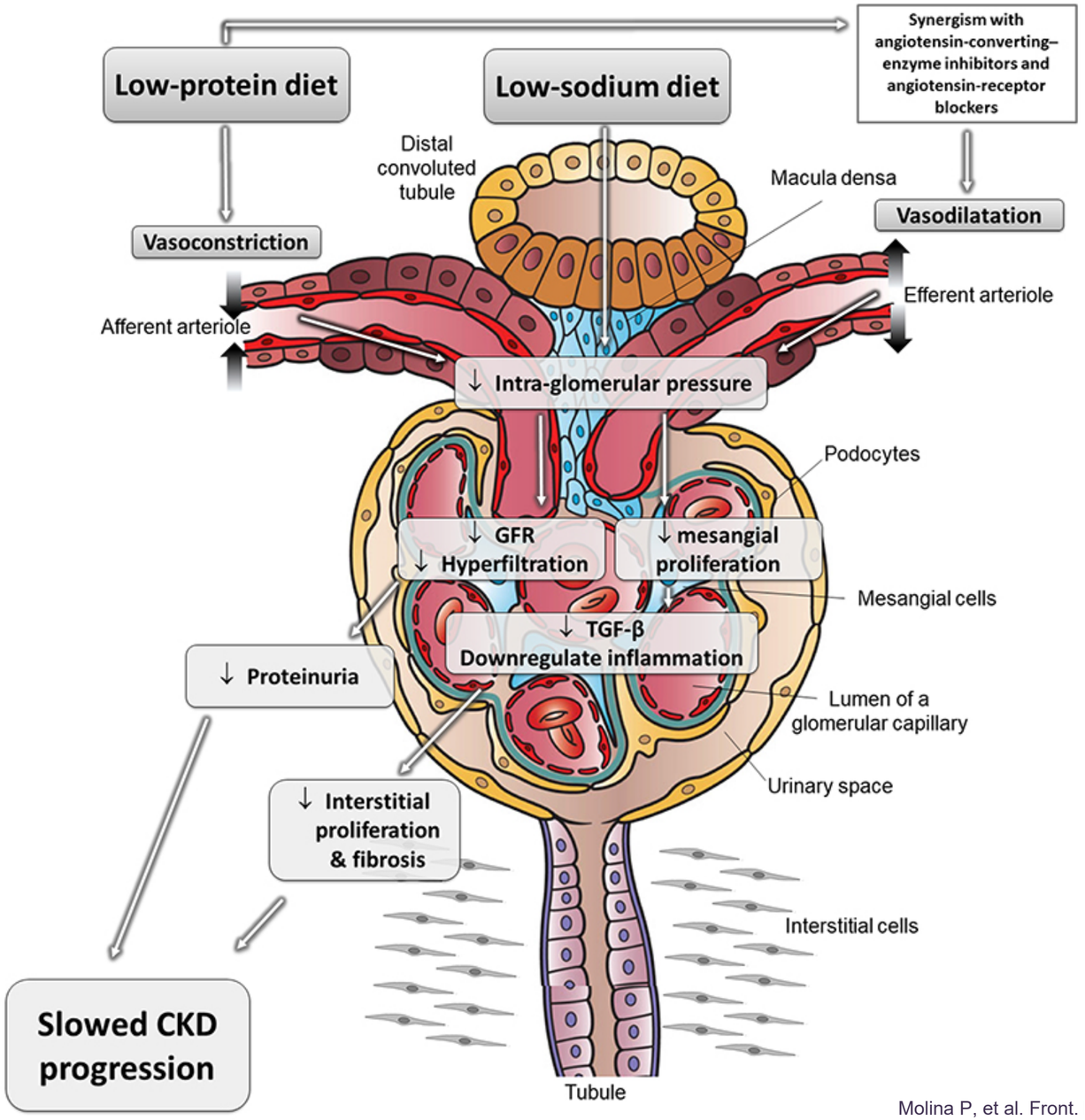
- Statement 3.0.1: In adults with CKD 3-5 who are metabolically stable, we recommend protein restriction to reduce risk for ESRD (2C)
  - 0.55-0.6g dietary protein/kg body weight/day

- Statement 3.0.2: In adults with CKD 3-5 AND diabetes, it is reasonable to prescribe, under close supervision, a dietary protein intake of 0.6-0.8 g/kg body weight/day (OPINION).

- Statement 6.5: In adults with CKD 3-5, we recommend limiting sodium intake to <2.3g/d to reduce BP, improve volume control, and reduce proteinuria.

Effects of nutritional interventions to slow progression of CKD

- Excess load of amino acids can increase intraglomerular pressure by dilating the afferent arteriole.
- Glomerular hyperfiltration can contribute to progression of CKD
- Thus, lower protein intake can lead to constriction of afferent arteriole, leading to lower glomerular hyperfiltration



Molina P, et al. Front. Med. 2021

Concerns about low protein diets

- **Adherence**
  - Adherence to low protein diets is low
  - Can require trained dietitian to develop individualized dietary programs
  - Registered dietitians not universally available

- **Effectiveness:**
  - KDIGO guideline: “the certainty of the evidence is low or very low…it is possible, though not yet unequivocally proved, that nutritional interventions slow disease progression…”
  - No studies cited in the guidelines recommend low -protein diets for diabetic patients assessed patients with type 2 DM

Nutritional guidance for patients with CKD – my approach

- I recommend normal protein diets for my patients (0.8 -1.2 g/kg/day)
- I don't have a different recommendation for patients with/without diabetes
- I recommend low salt diets (<2.3g/day) for patients with proteinuria or hypertension
- In general, I do not recommend dietary phosphate restriction

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HEDIS Kidney Health Evaluation for Patients with Diabetes (KED) screening measure

- HEDIS = Healthcare Effectiveness Data and Information Set
  - Comprehensive set of standardized performance measures designed to evaluate health plans – focus on preventive care
- In 2020, a new HEDIS measure was released related to kidney health evaluation – the KED measure, and is part of HEDIS measurement year 2022
- What is KED measure?
  - The percentage of adults (age 18-85) with DM1 or DM2 that have been assessed using the Kidney Profile (eGFR and uACR) in a 12-month period.

Credit: National Kidney Foundation

Why? Why not screen only for microalbuminuria?

- The KED measure was developed in partnership with the National Kidney Foundation
  - Aimed at earlier diagnosis – historically, <50% of people with diabetes have eGFR AND albuminuria assessed
- US Preventive Services Taskforce last reviewed CKD screening in 2012, and at that time stated that evidence was lacking.
- ***Since then***, much new evidence for "kidney protective medicines" in patients with diabetes:
  - SGLT2i
  - GLP-1 agonists
  - MRAs
- Thus, identifying patients with DM2 and CKD can now change management and reduce adverse kidney outcomes

Key Points

- Clinical guidelines for BP targets in patients with and without diabetes are confusing.
  - Focus on standardized office BP measurement
  - Goal BP of <130/80 reasonable for most patients
- We are in a new era of “kidney protective” medications for patients with CKD and especially for DM + CKD:
  - Metformin and SGLT2i for most
  - ACEI/ARBs for hypertensive patients
  - GLP-1 agonists if additional glycemic control needed
  - Consider MRAs after above
- Protein restriction in CKD is controversial

Questions?

KIDNEY RESEARCH INSTITUTE

A collaboration between
Northwest Kidney Centers and UW Medicine

Division of Nephrology
University of Washington

Case Notes Session 11 Case 11

Sept. 7, 2022

RECAP

- 69 y/o with uncontrolled T2DM c/b PN, 3A CKD (eGFR 55) with recurrent pancreatitis, possible gastroparesis and HTN and hyperlipidemia. Her BMI is 29.0 (wt kg 73)

- Uncontrolled DM(last a1c 10) in setting of abd pain and limited engagement in healthcare and some issues with cost of medications

Current Medication(s) (including dose frequency):

Medication	Dose	Frequency
Lantus	17 units	QHS
Humalog	10-10-15 units	TID
Lisinopril	20mg	Daily
Freestyle Libre 2 Sensor	1 ea	Q14d

Individual Patient Characteristics

- BMI 29.6 (73.0kg)= so + insulin resistance
- GFR =55 /CKD 3A
- Age 69
- A1c 10.1-14 – slight improvement recently
- Medicare insurance
- CKD
- Gastroparesis and Chronic pancreatitis
- Hyperlipidemia
- HTN

First question:

Does this person produce insulin?

- Type 1 or Type 2?
- Insulinopenic or Insulin resistant ?

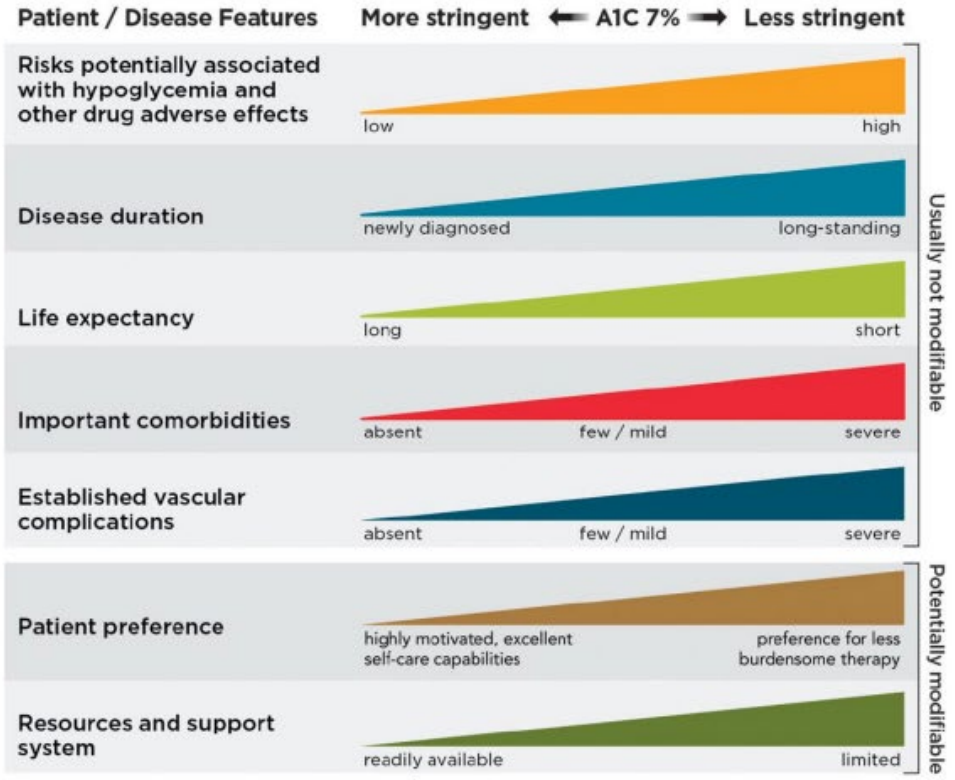
Type 2- most likely but given pancreatitis could be relatively insulinopenia

-C-peptide may not change management so may not be indicted

Second Question:

- **What is her A1c Goal?**
- 7.0%-7.5 (over time)

Individualizing Glycemic Targets



American Diabetes Association.

Figure 6.1—Depicted are patient and disease factors used to determine optimal A1C targets. Characteristics and predicaments toward the left justify more stringent efforts to lower A1C; those toward the right suggest less stringent efforts. A1C 7% = 53 mmol/mol. Adapted with permission from Inzucchi et al. (40).

Non-Pharm Intervention

- First Clinical Question: Nutritional Management of gastroparesis and/or recurrent pancreatitis?

Clinical Guideline: Management of Gastroparesis

- Markedly uncontrolled (> 200 mg/dl) glucose levels may aggravate symptoms of gastroparesis and delay gastric emptying. (Strong recommendation)
- Optimization of glycemic control should be a target for therapy;. (Moderate recommendation

Am J Gastroenterol. 2013 January ; 108(1): 18–38.
doi:10.1038/ajg.2012.373

General dietary recommendations for gastroparesis

- Eat smaller, more frequent meals
- Eat less fatty foods
- Avoid fiber
- Avoid foods that cannot be chewed well
- Foods that are generally encouraged include:

Table 3:

Foods that are encouraged

- Breads, Cereals, Crackers, ground or pureed meats
- Vegetables – cooked and, if necessary, blenderized/strained
- Fruits – cooked and, if necessary, blenderized/strained
- Juices, Beverages, Milk products, if tolerated

537-Dietary and Nutritional Recommendations for Patients with Gastroparesis - IFFGD

Non-Pharm Intervention

- Second Clinical question: Cost of medications and meal support for meal/ food in > age 65 population

Non-Pharm Intervention

- 3rd Clinical question: Accessing CGM data and alarm fatigue

Uploading CGM device

OVERVIEW

What you will need:

- Your FreeStyle Libre 2 reader
- Your USB cable
- Access to a valid email address
- Access to your web browser

Steps to share glucose data:

This guide will walk you through the following 3 steps:

STEP 1: Create a LibreView account online
STEP 2: Link to your doctor's practice
STEP 3: Upload data to share

Note the FreeStyle Libre 2 system is not for use with the FreeStyle LibreLink* app.

If you already have a LibreView† account, you can use it to sign-in on your web browser.

FreeStyle Libre 2 reader and sensor

FreeStyle Libre 2 reader USB cord

Visit LibreView.com on a web browser from your computer

*The FreeStyle LibreLink app is only compatible with certain mobile devices and operating systems. Please check the website for more information about device compatibility before using the app.

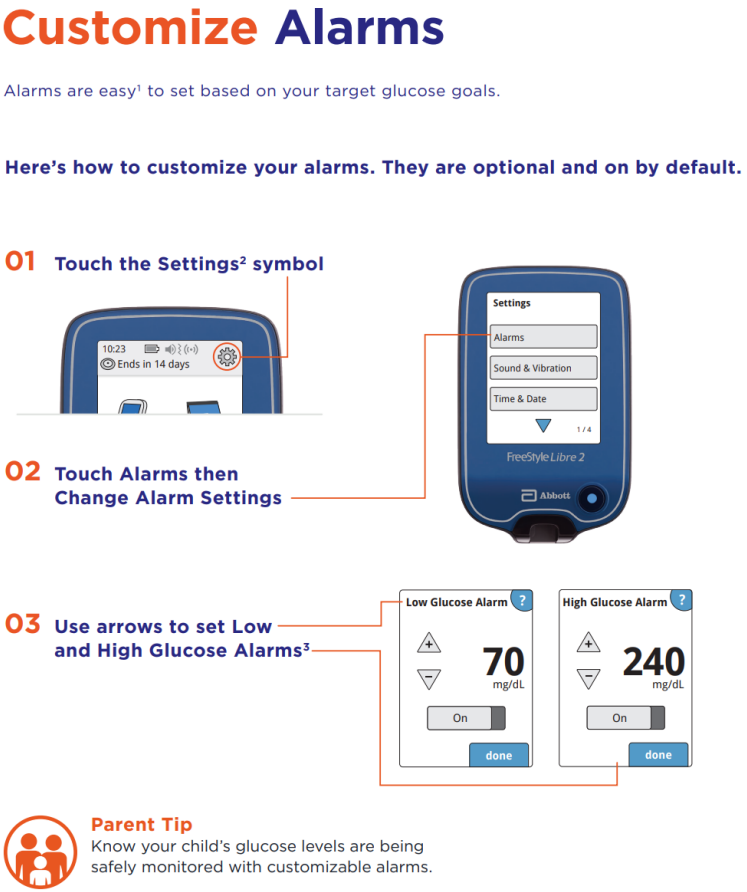
†LibreView is developed, distributed, and supported by Newyu, Inc. The LibreView data management software is intended for use by both patients and healthcare professionals to assist people with diabetes and their healthcare professionals in the review, analysis and evaluation of historical glucose meter data to support effective diabetes management. The LibreView software is not intended to provide treatment decisions or to be used as a substitute for professional healthcare advice.

[ADC-24579v2.indd (myfreestyle.com)]

[How to Use Dexcom Products User Guide, Quick Start Tutorials | Dexcom]

Alarms for CGM

- 240 mg/L is default high glucose alarm
- 70mg/dl is default low glucose alarm



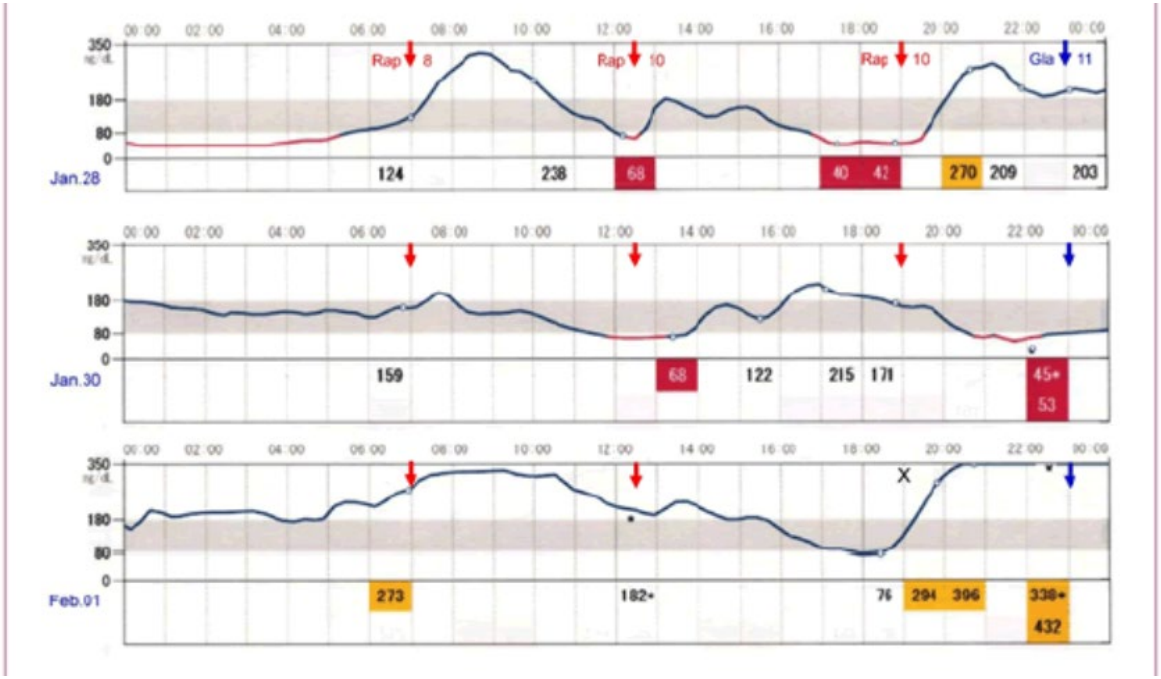
[FreeStyle Libre 2 Get Started Guide.pdf (myfreestyle.com)]

Pharm Intervention

Forth clinical question: Insulin management and use of insulin sparing agents

Insulin dose calculation : BMI 29/ Weight 73kg and GFR 55

- - Basal dose 0.1-0.5 u/kg
- 17/73= .23 u/kg (22 units would be 0.3 u/kg)



endocrinology-research-and-metabolism-monitoring-1-2-10-g002.png (579×537) (imedpub.com)

Prandial/Meal insulin and correction/sensitivity

- On 10/10/ 15 units with meals –
- 35 units daily= 35/73=0.3 u/kg

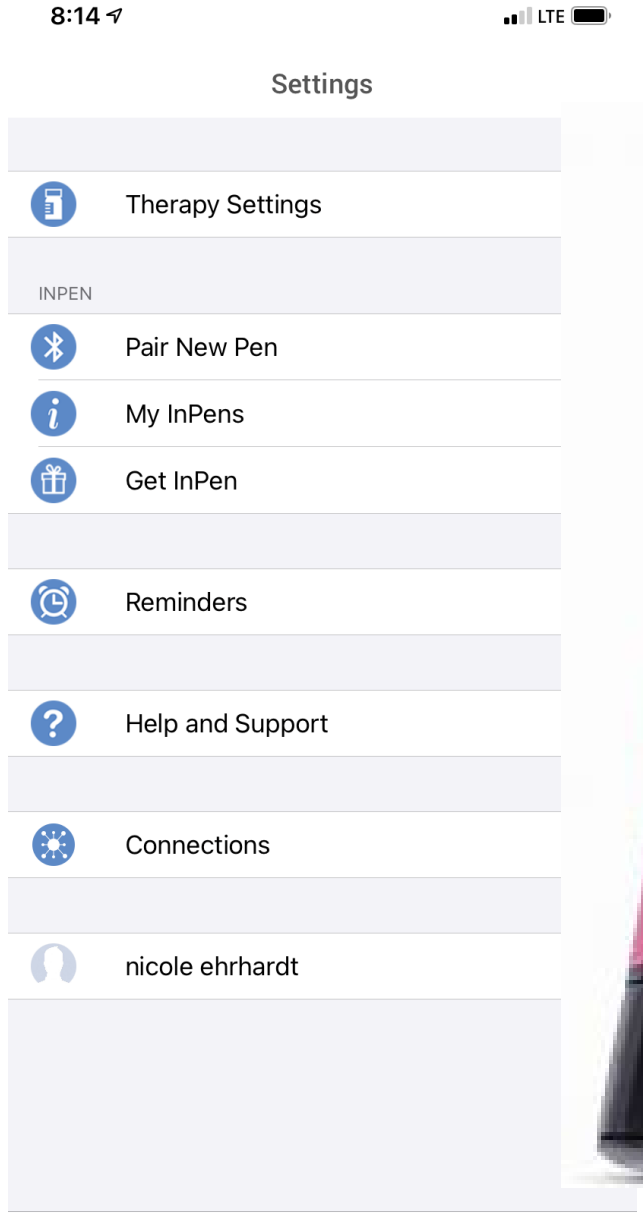
Post prandial goal is <180 2 hours ADA
AACE <160 1 hour and 140 2 hour after

Predicated sensitivity: 17+35= 52
-1700/52=32 1 unit over every 30 >150
Or simple 2 units for > 200 4units for 260 and >300 6 units

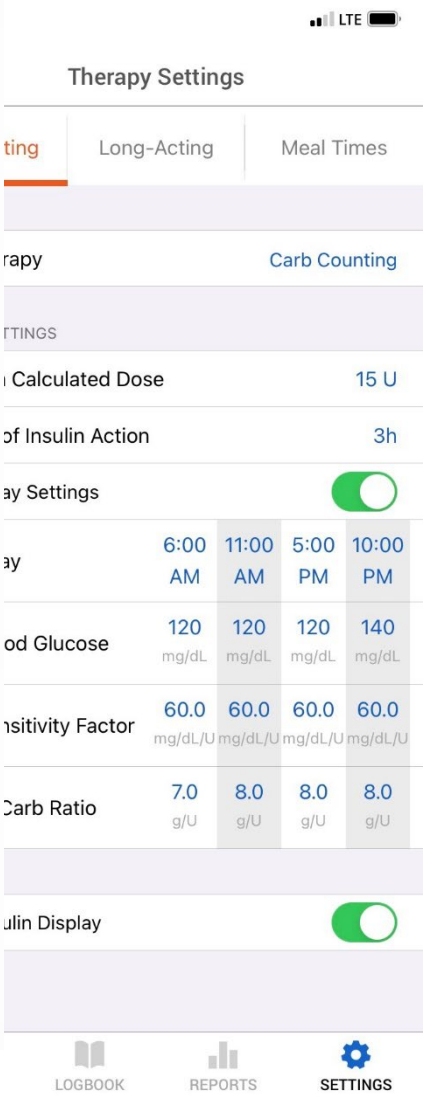
Overcoming Barriers to Taking Insulin

- Most important discuss:
- In a non-judgmental way total dose of insulin currently taking

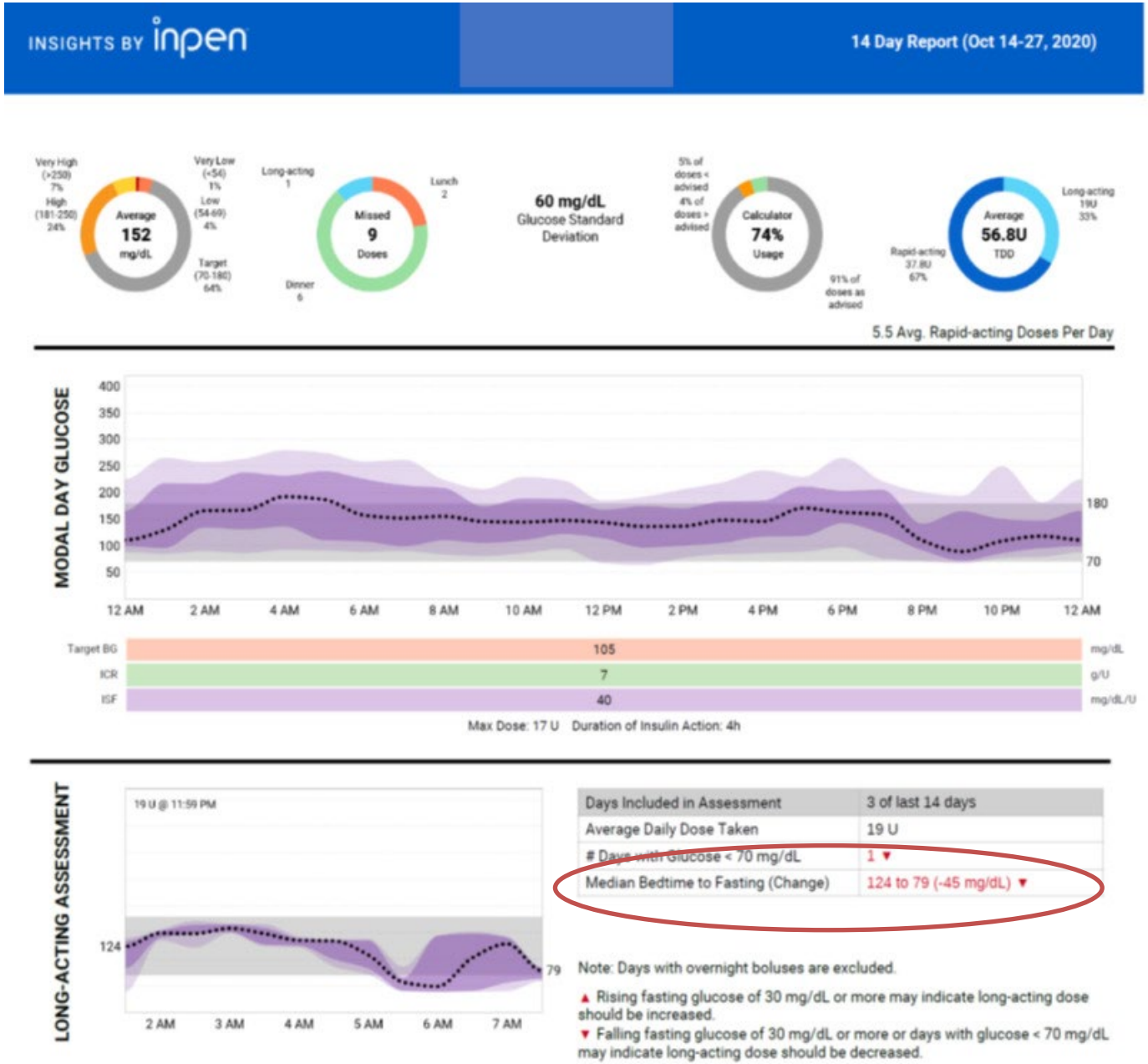
INPEN


8:14
LTE
Settings
Therapy Settings
INPEN
Pair New Pen
My InPens
Get InPen
Reminders
Help and Support
Connections
nicole ehrhardt
HOME
LOGBOOK
REPORTS
SETTINGS


Last Glucose
156 mg/dL
Last Dose
5.5 U
6.7 U
Active Insulin (IOB)
HOME
LOGBOOK
REPORTS
SETTINGS


LTE
Therapy Settings
ting
Long-Acting
Meal Times
rapy
Carb Counting
TTINGS
Calculated Dose
15 U
of Insulin Action
3h
ay Settings
ay
6:00 AM
11:00 AM
5:00 PM
10:00 PM
od Glucose
120 mg/dL
120 mg/dL
120 mg/dL
140 mg/dL
nsitivity Factor
60.0 mg/dL/U
60.0 mg/dL/U
60.0 mg/dL/U
60.0 mg/dL/U
Carb Ratio
7.0 g/U
8.0 g/U
8.0 g/U
8.0 g/U
ulin Display
HOME
LOGBOOK
REPORTS
SETTINGS

INPEN


INSIGHTS BY inpen
14 Day Report (Oct 14-27, 2020)
Very High (>250) 7%
High (181-250) 24%
Average 152 mg/dL
Very Low (<54) 1%
Low (54-69) 4%
Target (70-180) 64%
Long-acting 1
Missed 9 Doses
Lunch 2
Dinner 6
60 mg/dL Glucose Standard Deviation
5% of doses < advised
4% of doses > advised
Calculator 74% Usage
91% of doses as advised
Average 56.8U TDD
Long-acting 19U 33%
Rapid-acting 37.8U 67%
5.5 Avg. Rapid-acting Doses Per Day
MODAL DAY GLUCOSE
400
350
300
250
200
150
100
50
180
70
12 AM
2 AM
4 AM
6 AM
8 AM
10 AM
12 PM
2 PM
4 PM
6 PM
8 PM
10 PM
12 AM
Target BG 105 mg/dL
ICR 7 g/U
ISF 40 mg/dL/U
Max Dose: 17 U Duration of Insulin Action: 4h
LONG-ACTING ASSESSMENT
19 U @ 11:59 PM
124
79
2 AM
3 AM
4 AM
5 AM
6 AM
7 AM
Days Included in Assessment | 3 of last 14 days
Average Daily Dose Taken | 19 U
Days with Glucose < 70 mg/dL | 1 ▼
Median Bedtime to Fasting (Change) | 124 to 79 (-45 mg/dL) ▼
Note: Days with overnight boluses are excluded.
▲ Rising fasting glucose of 30 mg/dL or more may indicate long-acting dose should be increased.
▼ Falling fasting glucose of 30 mg/dL or more or days with glucose < 70 mg/dL may indicate long-acting dose should be decreased.

V-GO

- The V-Go series of Wearable Insulin Delivery Devices
- Deliver: 20 Units of Insulin (0.83 U/hr), 30 Units of insulin (1.25 U/hr), or 40 Units of insulin (1.67 U/hr)
- On-demand bolus:

  2 Unit increments (up to

  36 Units per one 24-hour

  time period)

https://www.go-vgo.com/hcp

CeQur

- Insulin patch
- 3 day wear
- 200 units of insulin

[Healthcare Professionals | Insulin Patch | CeQur Simplicity (myceqursimplicity.com)]

Pharm Intervention

Clinical question 5 : Use of insulin sparing agents in setting of CKD 3A and chronic abd pain

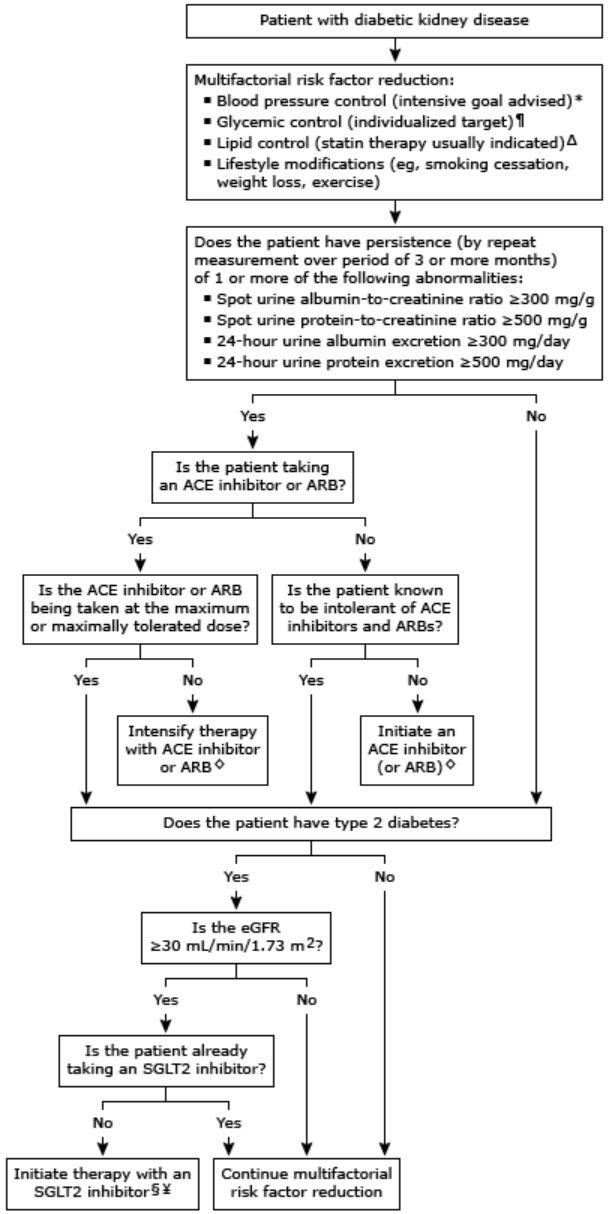
CKD and Diabetes

Pt has eGFR 55 and Micro/Alb ratio 30

-ACE/ARB:
Pt is on 20 lisinopril

- SGLT2-I
- Mineralocorticoid receptor antagonists (MRAs)

Overview of the management of diabetic kidney disease



CE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; eGFR: estimated glomerular filtration rate; SGLT2: sodium-glucose co-transporter 2.

Δ Graphic 123083 Version 1.0

Clinical Guideline: Pain Management of Gastroparesis

- Tramadol
- Tapentadol
- Gabapentin
- Pregabalin
- Nortriptyline

*however, their effect on gastric emptying is still unclear

Am J Gastroenterol. 2013 January ; 108(1): 18–38.
doi:10.1038/ajg.2012.373

ACC/AHA ASCVD Risk Calculator

19.3%

10-year risk of heart disease or stroke

On the basis of your age alone, the USPSTF guidelines suggest you **would not benefit from starting aspirin** for heart disease and stroke risk reduction.

On the basis of your age, your calculated risk for heart disease or stroke over 7.5%, and diabetes, the ACC/AHA guidelines suggest you should be on a **high intensity statin**.

Based on your age, your blood pressure is **well-controlled**.

Demography	Cholesterol	Blood pressure	Risk factors
Age: 69	Total: 214	Systolic: 125	Diabetes: yes
Gender: female	HDL: 70	Diastolic: 72	Smoking: no
Race: not African-American		On medication: yes	

Notes and further reading

- **Moderate intensity statin** may be atorvastatin 10mg, pravastatin 40mg, or simvastatin 20-40mg. **High intensity statin** may be atorvastatin 40mg-80mg.
- AHA/ACC guidelines stress the importance of lifestyle modifications to lower cardiovascular disease risk in all patients. This includes eating a heart-healthy diet, regular aerobic exercises, maintenance of desirable body weight and avoidance of tobacco products.
- Before initiating statin therapy, clinicians and patients ought to engage in a discussion which considers addressing risk factors such as smoking and optimal lifestyle, the potential for ASCVD risk reduction benefits, adverse medication effects, drug-drug interactions, and patient preferences for treatment.
- **ASCVD Risk Enhancers** may be used to inform treatment decision making and include family history of premature ASCVD with onset less than 55 years of age in a first degree male relative or less than 65 years of age in a first degree female relative, chronic kidney disease, metabolic syndrome, certain conditions specific to women (eg preeclampsia), inflammatory disease (especially rheumatoid arthritis, psoriasis, HIV), ethnicity (eg South Asian ancestry), persistently elevated LDL-C greater than 160 mg/dL, persistently elevated triglycerides of greater than 175 mg/dL, high-sensitivity C-reactive protein greater than 2 mg/L, coronary artery calcification score greater than 75th percentile for age, sex, and ethnicity, or ankle-brachial index less than 0.9.

https://www.cvriskcalculator.com/

Questions?