Mount Sinai Health Partners:
Frontline Excellence in Ambulatory Chronic Disease Management

Module 2: Chronic Kidney Disease and Hypertension

Wednesday, April 14, 2021

Course Director
Arshad K. Rahim, MD, MBA, FACP

Provided by
Mount Sinai Health Partners (MSHP) and the Icahn School of Medicine at Mount Sinai

Mount Sinai Health Partners

Accreditation Statement

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Visit our CME portal at https://mssm.cloud-cme.com/

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Go to "***My CME***" button on the top right

Click "***Evaluations and Certificates***" – online evaluation will be open at the end of the course. There will be one tab for each day.

Faculty Disclosures (1 of 2)

It is the policy of Icahn School of Medicine at Mount Sinai to ensure objectivity, balance, independence, transparency, and scientific rigor in all CME-sponsored educational activities. All faculty participating in the planning or implementation of a sponsored activity are expected to disclose to the audience any relevant financial relationships and to assist in resolving any conflict of interest that may arise from the relationship. Presenters must also make a meaningful disclosure to the audience of their discussions of unlabeled or unapproved drugs or devices. This information will be available as part of the course materials.

Please find below the compiled information we have received on disclosure of relevant financial relationships from activity faculty and planners. The following faculty/planners have reported that they have no relevant financial relationships to disclose:

Roy Cohen, MD
Arshad K. Rahim, MD, MBA, FACP
Lisa Bloch, MS

Faculty Disclosures (2 of 2)

In this upcoming presentation, one of the available early disease screening tests to assess for CKD progression is KidneyIntelX, and is based on technology developed by Mount Sinai faculty and licensed to RenalytixAI, Inc.

- Mount Sinai faculty members are co-founders and equity owners in the company
- The Icahn School of Medicine at Mount Sinai has equity ownership in RenalytixAI plc

Dr. Joji Tokita receives research support from Renalytix AI (i.e. test which estimates risk of kidney disease progression).

Dr. Steven Coca is a co-founder of Renalytix AI (i.e. test which estimates risk of kidney disease progression), as well as consultant/advisor and independent contractor. Dr. Coca's financial relationship with Renalytix AI, a publicly-traded company, includes ownership, stock, and stock options.

Frontline Excellence in Ambulatory Chronic Disease Management

Module 2: Chronic Kidney Disease and Hypertension
April 14, 2021

6:00 - 6:05 pm

Welcome and Opening

Arshad K. Rahim, MD, MBA, FACP

6:05 - 6:40 pm

Identifying and Managing Chronic Kidney Disease, Importance of Aggressively Managing Early Stage Disease, New Screening Options

- ✓ CKD Burden in general population
- ✓ Correct Classification
- ✓ Risk stratify early in course of CKD (one option is Kidney IntelX)
- ✓ Management Options and Checklist

Joji Tokita, MD

Steven G. Coca, DO

Frontline Excellence in Ambulatory Chronic Disease Management

Module 2: Chronic Kidney Disease and Hypertension
April 14, 2021

6:40 - 6:50 pm	**Audience Q&A**
6:50 - 7:20 pm	**Management Update on Hypertension** Roy Cohen, MD
7:20 – 7:30 pm	**Audience Q&A and Closing Remarks**

Identifying and Managing CKD, Importance of Aggressively Managing Early Stage Disease, New Screening Options

Joji Tokita, MD
Clinical Director, Division of Nephrology
Associate Professor of Medicine (Nephrology)
Icahn School of Medicine at Mount Sinai

Steven Coca, DO, MS
Associate Chair for Clinical and Translational Research, Department of Medicine
Associate Professor of Medicine (Nephrology)
Icahn School of Medicine at Mount Sinai

Mount Sinai Health Partners

Case Discussion

A 61 year old woman with type 2 diabetes mellitus for 8 years, CAD, S/P PCI to LCx 2 years ago, BMI 32, hypertension, stage G3aA3 CKD (eGFR 52 ml/min, albuminuria 800 mg/g), presents for nephrology consultation

- Medications
  - metformin 1000 mg twice daily, lisinopril 40 mg daily, atorvastatin 20 mg dail, amlodipine 10 mg daily, chlorthalidone 25 mg daily

- She saw a commercial on TV for a drug that is supposed to reduce her chance of dying from a CV event and her friend from church told her she started this medication because she heard that it also “protects the kidneys long-term” but might “dry them up too”. She can’t remember the name of the medication.

Case Discussion (continued)

- She also mentions that she has good insurance through work and has a small co-pay
- Examination is normal except for obesity and 1+ LE edema
- **Vitals**
  - BP 136/77 mmHg, P 72/min
- **Labs**
  - HbA1C 7.4%, K 4.9 mEq/L, BUN 32, Creat 1.6 mg/dL
- **Urinalysis**
  - SG 1.017, pH 5.5, 2+ protein. 2+ glucose, LE negative, blood negative

Poll — Next Step

1) From what is presented, is this patient strictly eligible for an SGLT2 inhibitor?
   – Yes or No?

2) Do you think she is a good candidate for an SGLT2 inhibitor?
   – Yes or No?

3) Will you:
   a) Write the prescription for SGLT2 inhibitor?
   b) Defer the decision entirely to her nephrologist or endocrinologist?

Outline

- ❑ CKD Burden in the general population is underappreciated
- ❑ Correct Classification Using Urine Albumin to Creatinine Ratio (UACR)
- ❑ Risk stratify early in course of CKD (beyond GFR) and take action to prevent progression
- ❑ Options include Aggressive Blood Pressure Management (<130/80), use ACE/ARB to max dose if possible, use SGLT2i!
  - ❑ This will also save the heart!
- ❑ Use the Mount Sinai CKD Checklist and/or refer to Nephrology

CKD is a Worldwide Public Health Crisis

Affects 850 Million Individuals Globally

Chronic Kidney Disease

37M Americans currently estimated with CKD

20% Of the CMS budget is related to CKD or ESRD

90% 9 out of 10 adults with CKD don't know they have it

Diabetic Kidney Disease

~60M

Adults in the U.S. expected to be diagnosed with diabetes by 2060

1 in 3

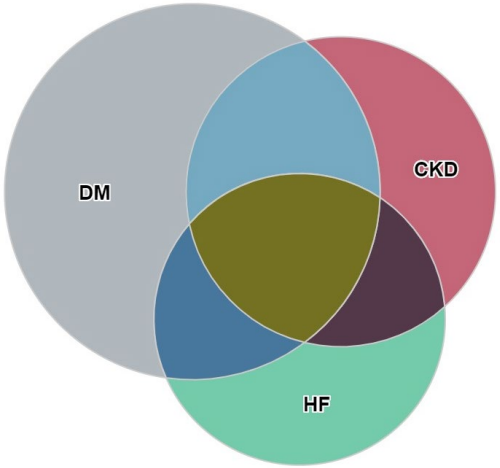
Adults with diabetes develop CKD

Major Overlap Between Kidney Disease, Type 2 DM, and CVD

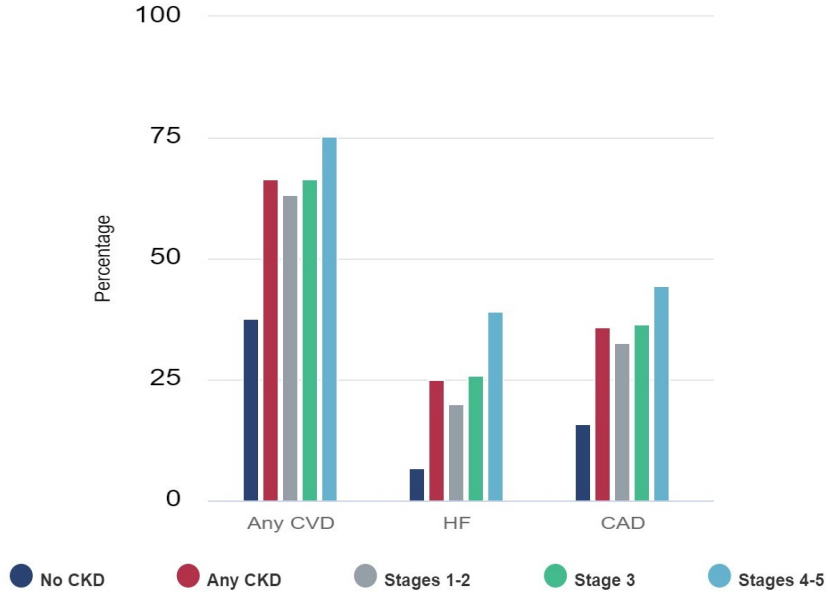
Management of CKD Vital for Improving Outcomes

Annual Medicare Spending on CKD, DM2, Heart Failure

$295 Billion



Increase in Risk for Cardiovascular Disease by CKD

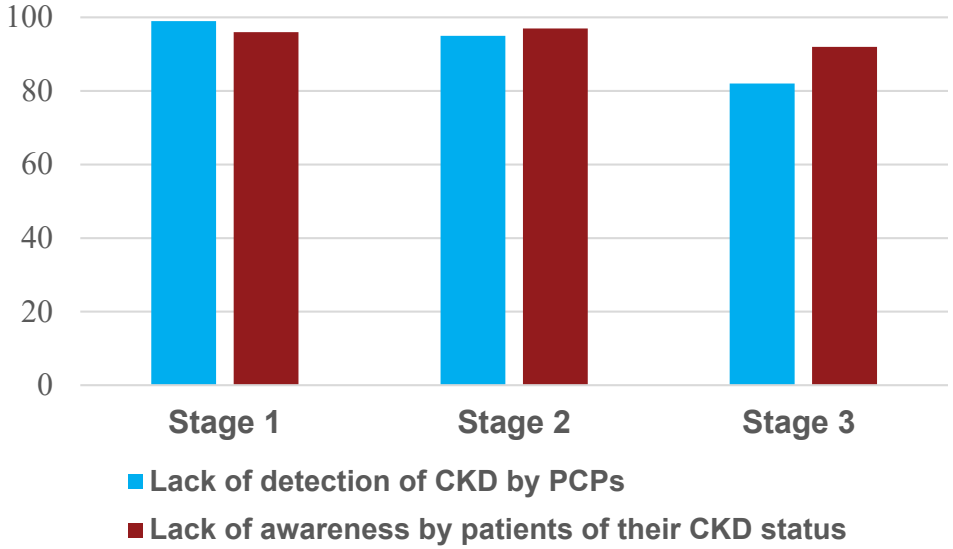


United States Renal Data System (USRDS). USRDS Annual Report, 2020

CKD is Missed in Early Stages

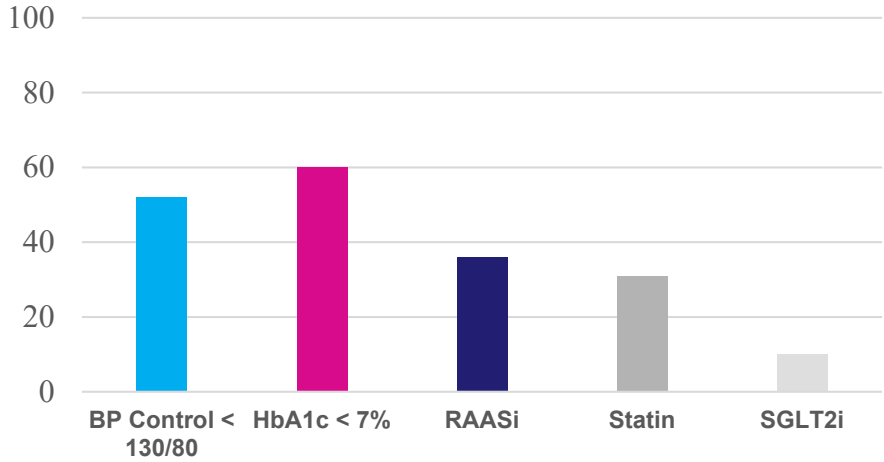
There is a Huge Opportunity to Improve the Quality of CKD Care to Prevent Progression to ESKD

Inadequate Detection of CKD by Physicians
Lack of Awareness of CKD by Patients



Source: PCP Data: Szczech LA, et al. Plos One 2014
Patient Awareness Data: NHANES 2018 Data

Inadequate Treatment of CKD by Physicians

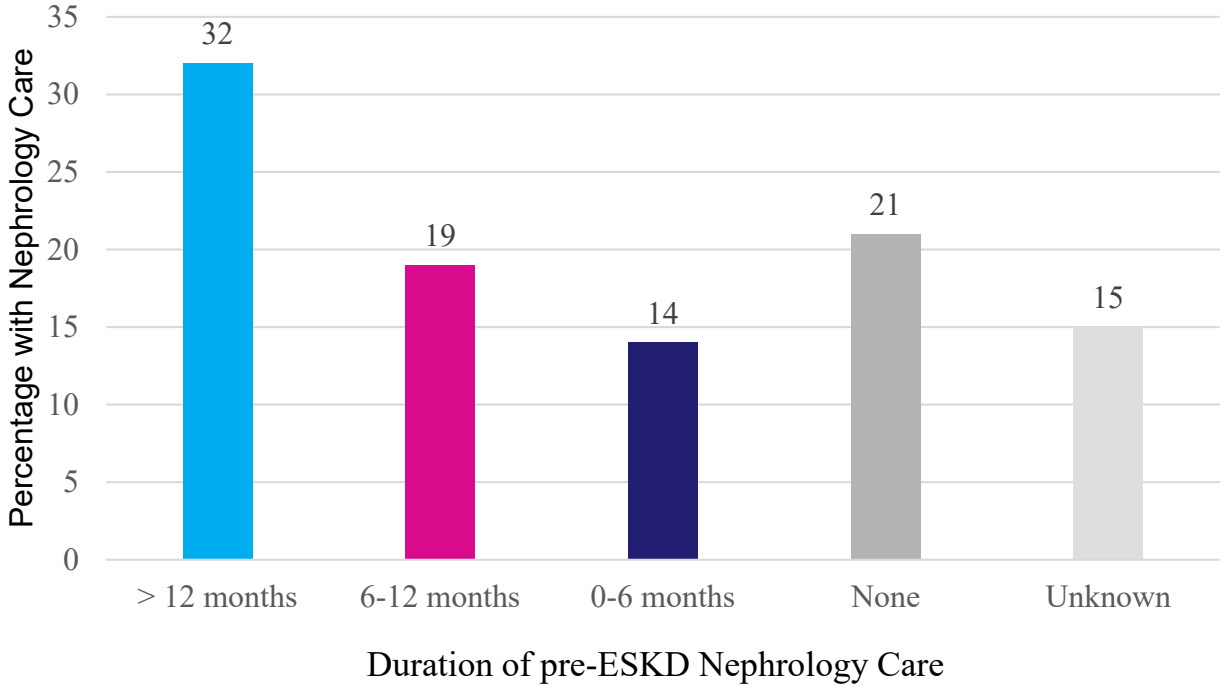


Sri Lekha Tummalapalli, Neil R. Powe and Salomeh Keyhani
CJASN August 2019, 14 (8) 1142-1150

An Assessment of Early-Stage CKD Care in the US

Late and Inadequate Referrals in US

Only 32% of Patients Starting Long-term Dialysis Were Under the Care of Nephrologist for > 1 Year



USRDSAnnual Data Report 2018

Outline

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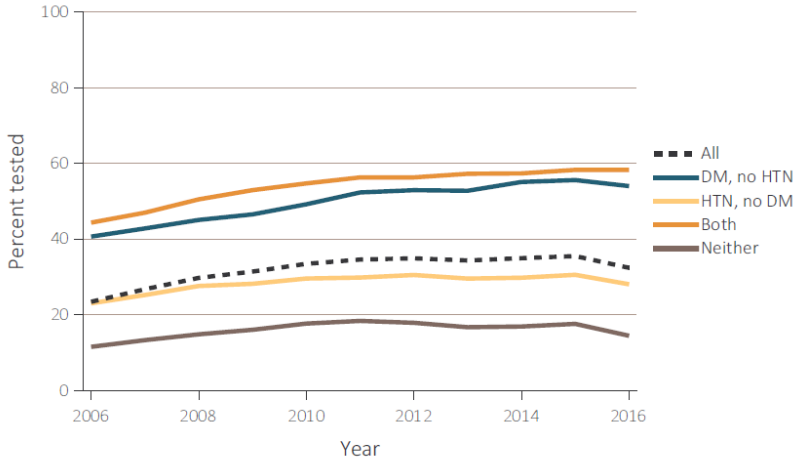
Use of UACR: Underutilized, but Necessary for Classification of CKD, and part of Guidelines and HEDIS Measures

Nearly 50% of patients with CKD Do NOT Get Urine Albumin Testing



GFR categories (ml/min per 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	⩾90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

Even with eGFR and UACR Testing, There are Still Nuances to Consider

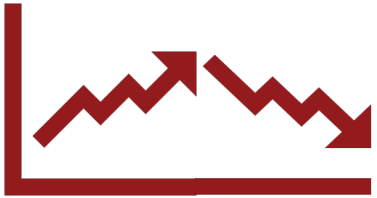
High biological variability of UACR and eGFR

Intra-individual variability:
UACR 55-125%
eGFR 16-20%

Lack of precision in eGFR by race

NKF/ASN have dropped race from eGFR calculation

Hyperfiltration precedes DKD progression



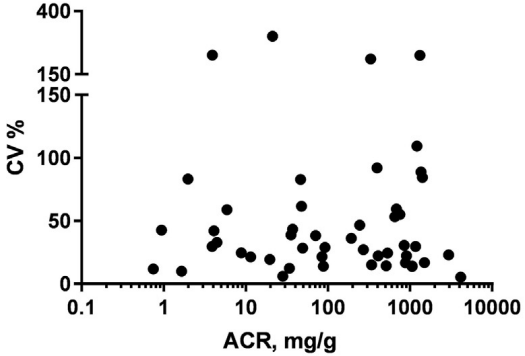
Hyperfiltration masks early DKD while kidney injury continues

Most kidney protective drugs decrease kidney function over first 1-2 years of Rx

RAAS inhibitors and SGLT2i both result in drops in eGFR

Significant Intra-Individual Variability in UACR Within Short-time Period

Random UACR X 2 taken
< 4 weeks apart



CVw = 30%

124% increase

Given a median CV_w = 30%, an increase from baseline of 124% or a decrease of 55% can be expected by chance

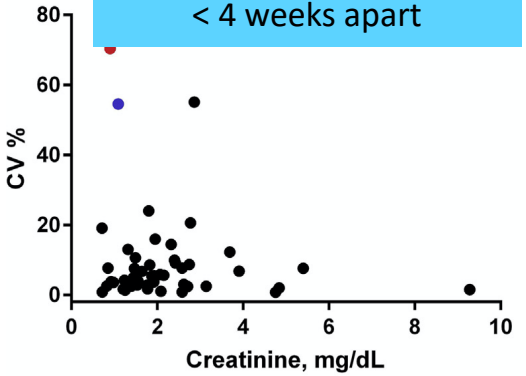
55% decrease

Abbreviations: CVw= Within person coefficient of variation

Am J Kidney Dis. 2018. 72(4): 538-546

Significant Intra-Individual Variability in eGFR Within Short Time Period (Continued)

Serum Creatinine X 2 taken
< 4 weeks apart



CVw = 5.4%

20% increase

Given a median CV_w in SCr of 5.4%, an increase in eGFR from baseline of 20% or a decrease of 16% can be expected by chance

16% decrease

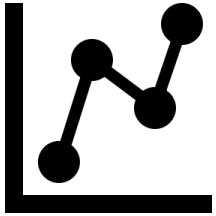
Am J Kidney Dis. 2018. 72(4): 538-546

Abbreviations: CVw= Within person coefficient of variation

Issues with Current Standard of Care

Measures of Kidney Function

High Biological Variability



Lack of precision by race

Hyperfiltration precedes DKD progression

Most kidney protective drugs decrease kidney function over first 1-2 years of Rx

Implications for Black Adults in US due to Dropping AA from Calculation of eGFR

Instantaneous

eGFR Calculation (CKD-EPI)

$GFR = 141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018[\text{if female}] \times 1.159[\text{if black}]$

$\kappa = 0.7$ if female
$\kappa = 0.9$ if male

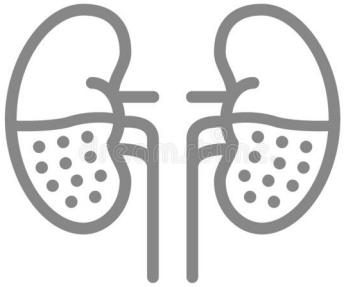
$\alpha = -0.329$ if female
$\alpha = -0.411$ if male

min = The minimum of Scr/κ or 1
max = The maximum of Scr/κ or 1

Scr = serum creatinine (mg/dL)

No change in true biology or disease

New CKD



20% Relative Increase
1.2m new "cases" CKD

Progression of CKD

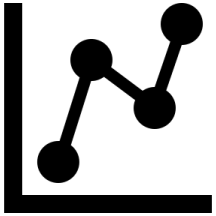
29% Relative Increase
1.5m with worse stage of CKD

Diao JA, et al. Clinical implications of removing race from estimates of kidney function (Research Letter). *JAMA* [published online ahead of print]. doi: 10.1001/jama.2020.22124

Issues with Current Standard of Care

Measures of Kidney Function

High Biological Variability

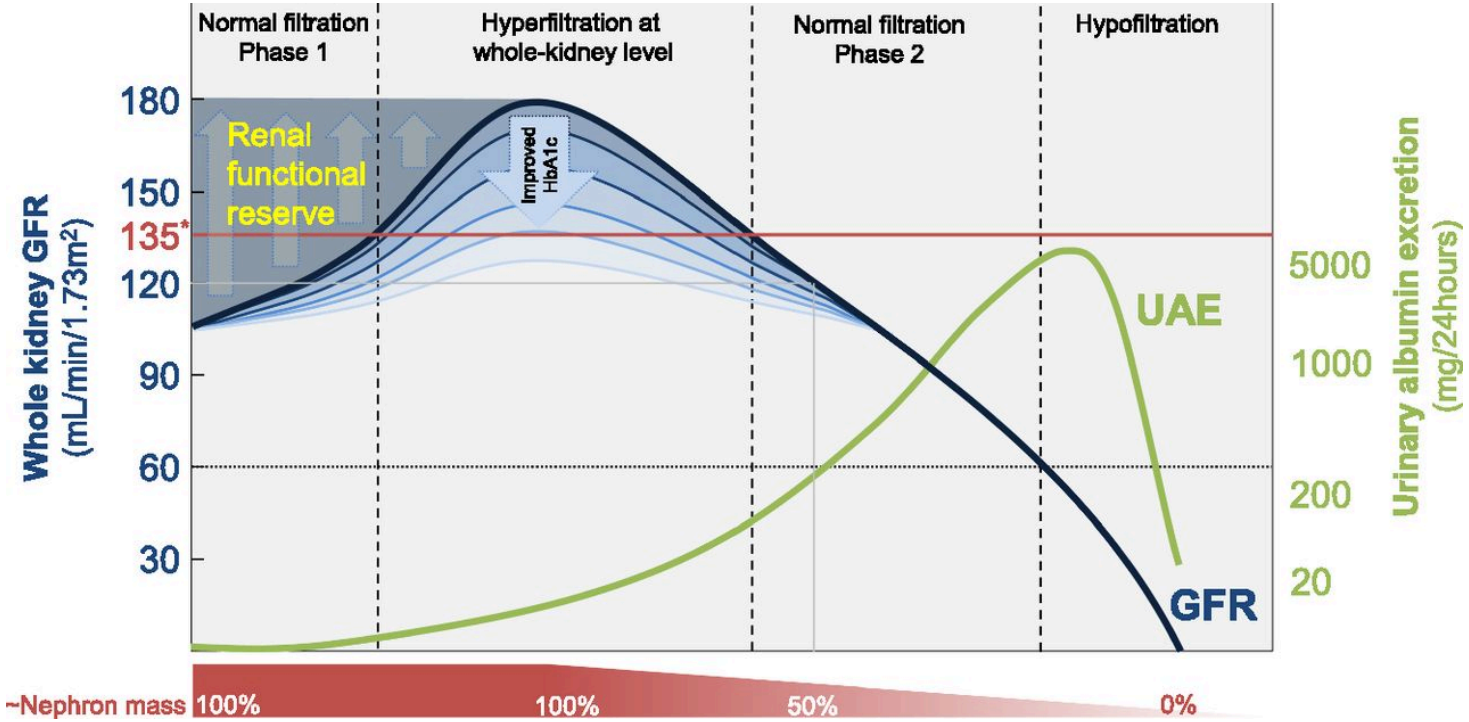


Lack of precision by race

Hyperfiltration precedes DKD progression

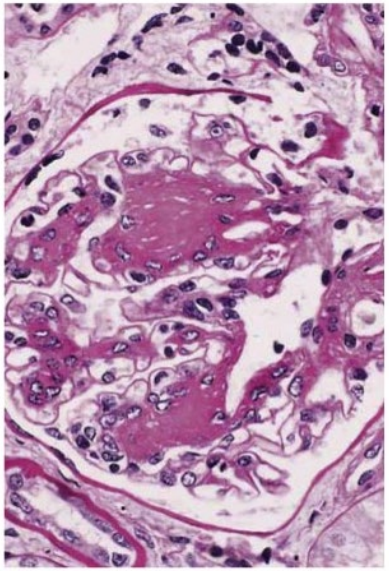
Most kidney protective drugs decrease kidney function over first 1-2 years of Rx

Hyperfiltration in Early Stages of DKD Provides False Sense of Security

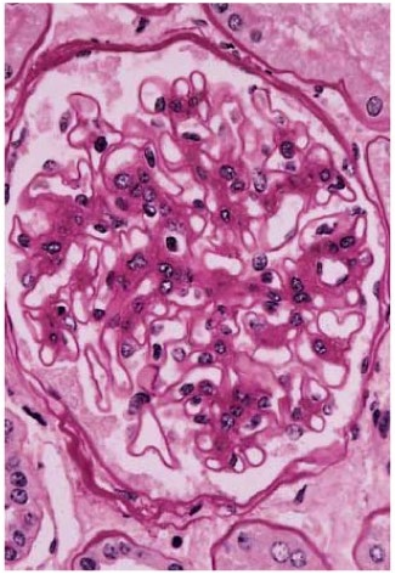


Can lose half of nephron mass with no decrement in GFR

Marked Kidney Damage in Individuals with Diabetes and Normal Levels of Kidney Function



eGFR 84 ml/min/1.73 m^2



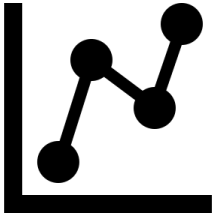
eGFR 110 ml/min/1.73 m^2

N Engl J Med 1998; 339:69-75

Issues with Current Standard of Care

Measures of Kidney Function

High Biological Variability

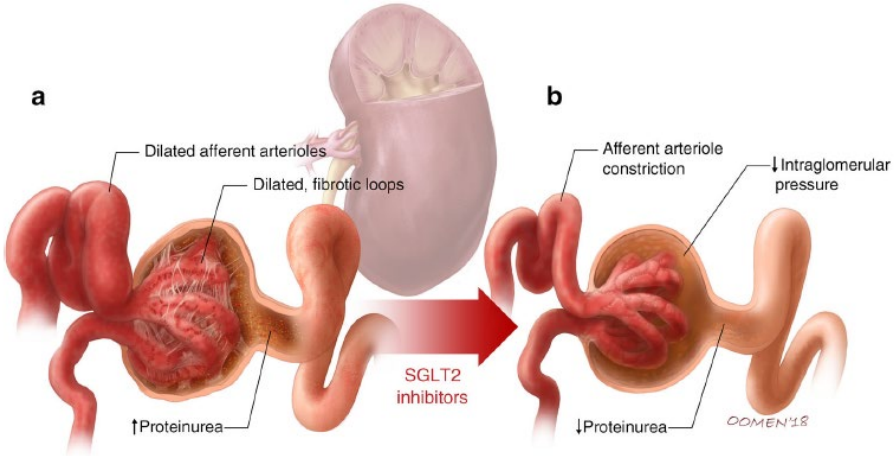


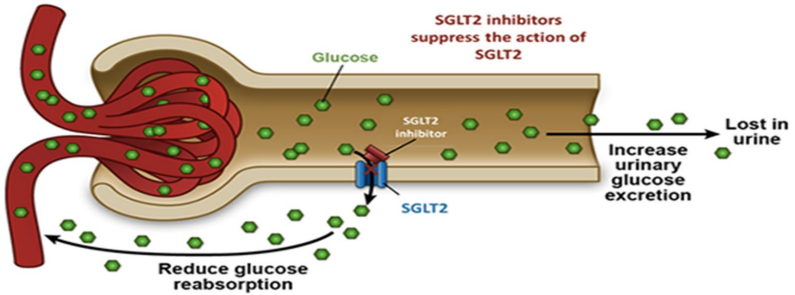
Lack of precision by race

Hyperfiltration precedes DKD progression

Most kidney protective drugs decrease kidney function over first 1-2 years of Rx

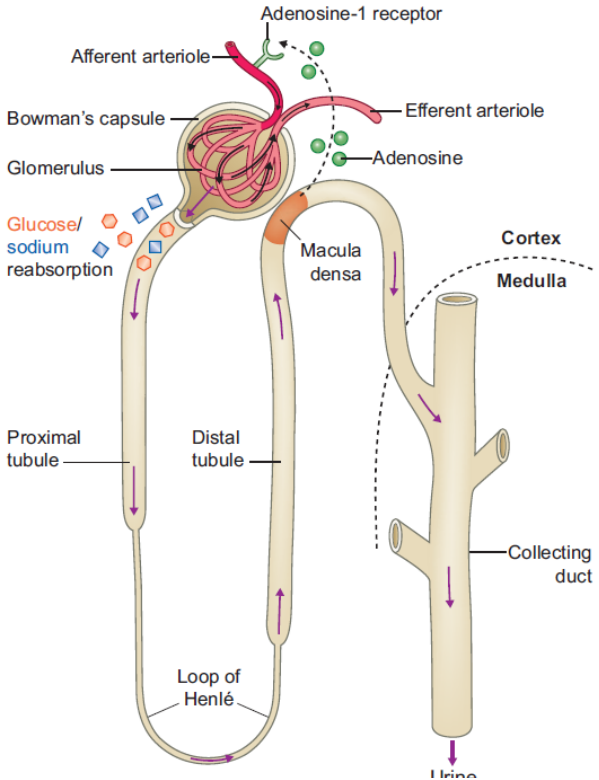
The Goal for DKD is to Decrease Intraglomerular Pressure





Wright EM, et al. *Physiol Rev*. 2011;91:733-794.

Verma and McMurray Diabetiologica 2018

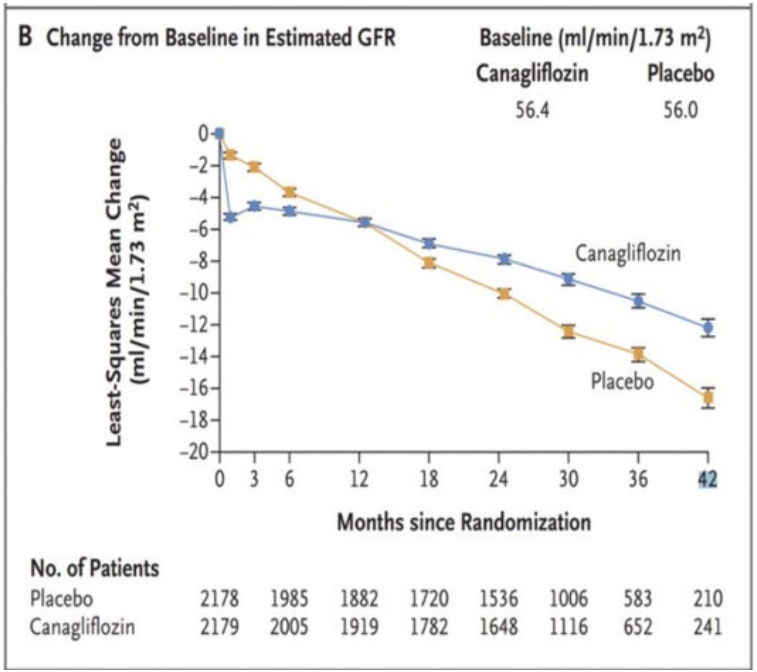


Heerspink H. Nephrol Dial Transplant 2019

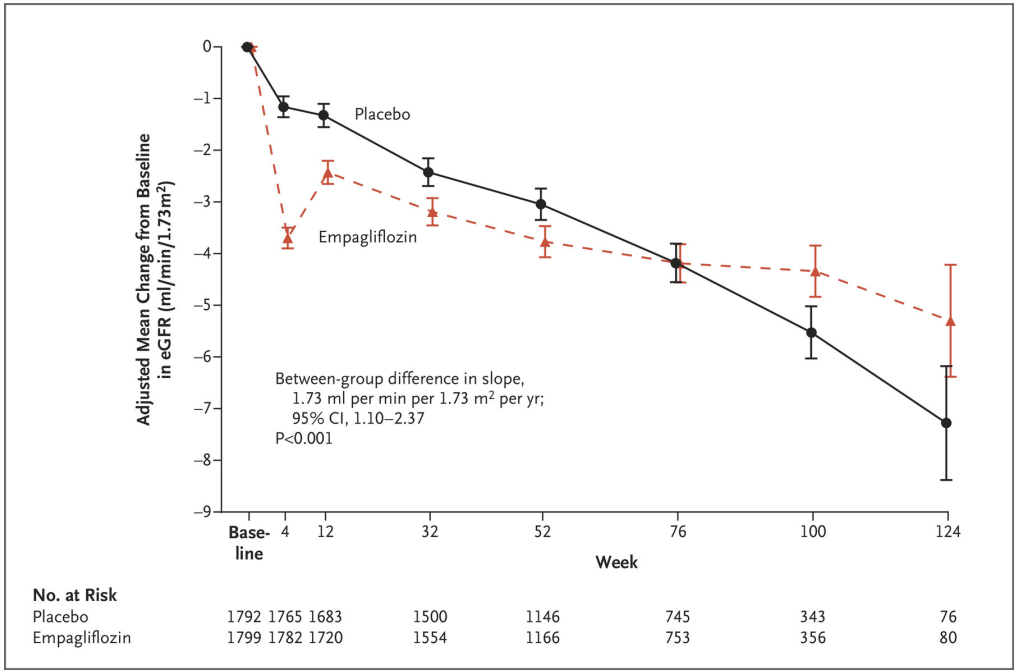
Acute eGFR Decline After SGLT2 Inhibitors

Cross-over and Better Trajectory Doesn't Occur until 12+ Months Later

CREDENCE (NEJM 2019)

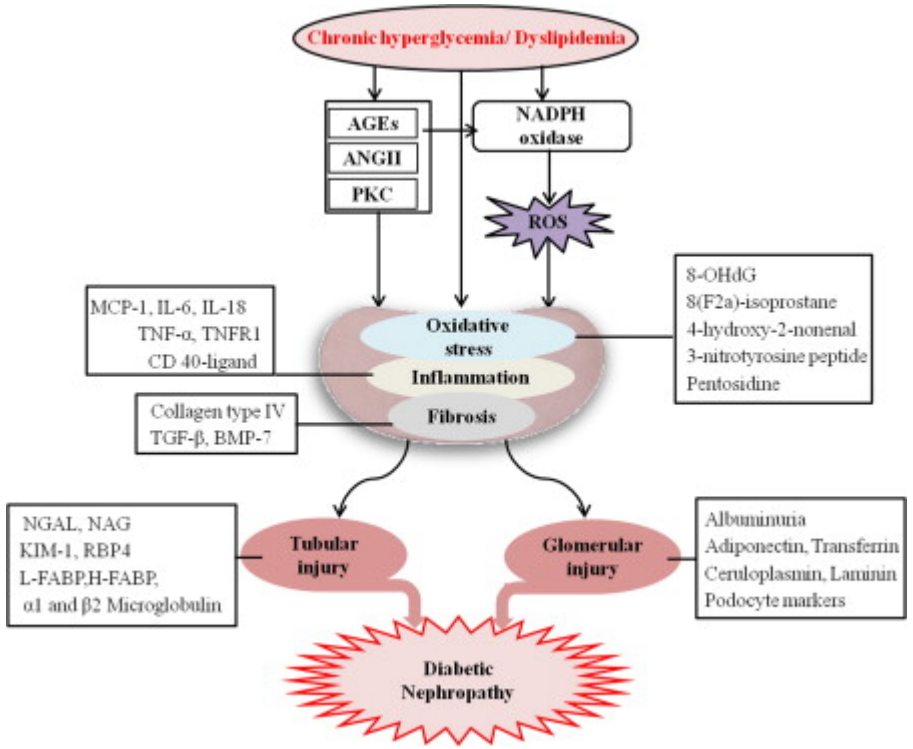


EMPEROR-Reduced (NEJM 2020)

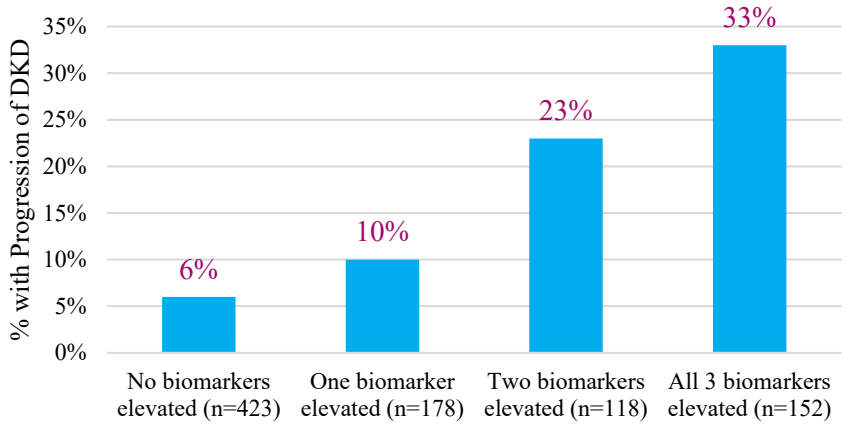


One Screening Option Involves New Biomarkers for Diabetic Kidney Disease

Integrated with Pathophysiology of DKD and Strongly Prognostic for Progression



Risk for DKD Progression in Mount Sinai Bio*Me* by Number of Plasma Biomarkers* Elevated



***Plasma TNFR1, TNFR2, KIM1**

Chauhan et al. Kidney360 2020;1:731-739

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KidneyIntelX™: A New "Bioprognostic" That Combines Biomarkers Plus Clinical Variables into An Easy to Read Report with Risk Score and Care Path

Indicated for T2D / CKD Stages 1, 2, 3

Standard blood draw

Biomarkers sTNFR1, sTNFR2, KIM-1

+

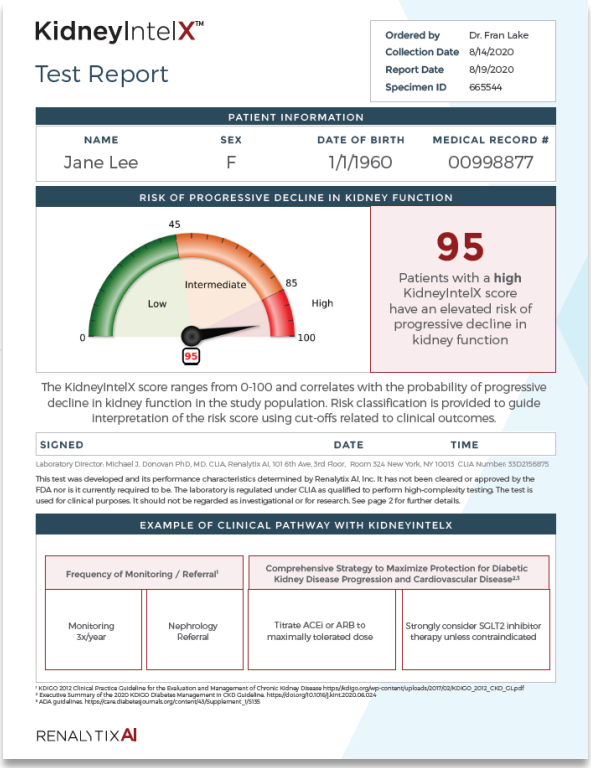
Standard EHR Elements*

Longitudinal patient data assessed

*eGFR, UACR, serum calcium, HbA1c, systolic BP, platelets, AST

Machine Learning Algorithm Harmonizes Data

Actionable Risk Assessment



FDA Breakthrough designation De novo 510K

CMS Medicare price determination: $975 & CPT code 0105U

State & CLIA Authorized laboratories in UT and NY

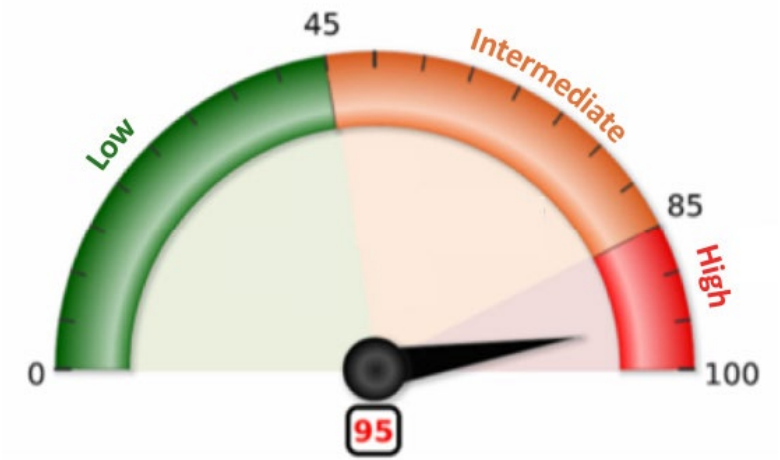
FDA Final 510K submission

CMS Medicare Coverage of Innovative Technology – Final Ruling

KidneyIntelX is First Tool to Enable Early-Stage Progression Risk Assessment in Early DKD Stages 1, 2, 3

93%

Low scoring patients have a **93% chance** of **not** experiencing progression*



69%

High scoring patients have a **2 out of 3 chance** of experiencing progression*

MAINTAIN	MONITOR	ACT
Low	**Intermediate**	**High**
Low-risk patients (~50%) are not likely to progress to ESKD and should continue to be monitored annually	Intermediate-risk patients (~35%) require more primary care follow-up (2-3 times annually) and may need a specialist referral	High-risk patients (~15%) are significantly more likely to progress to ESKD and require more aggressive lifestyle changes, medication regimens, and immediate referrals

*Data from Validation Study in Subgroup with UACR available
Chan L, et al. Diabetologia 2021 (in press)

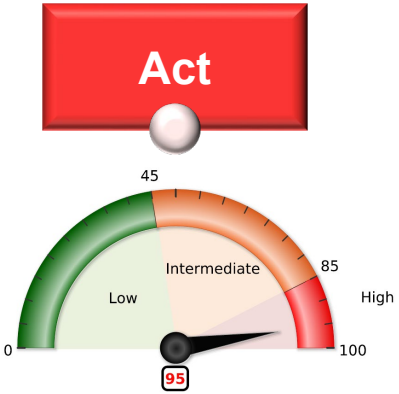
KidneyIntelX Risk Score Promotes Patient-Centered Care and Engagement

Low Risk

Frequency of Monitoring[1]	Strategy to Reduce Diabetic Kidney Disease Progression and Cardiovascular Disease[2,3]
Monitoring 1x/year	Maintain current level of treatment with ACEi/ARB, antihypertensives, and anti-hyperglycemic agents unless BP or glucose are uncontrolled

Intermediate Risk

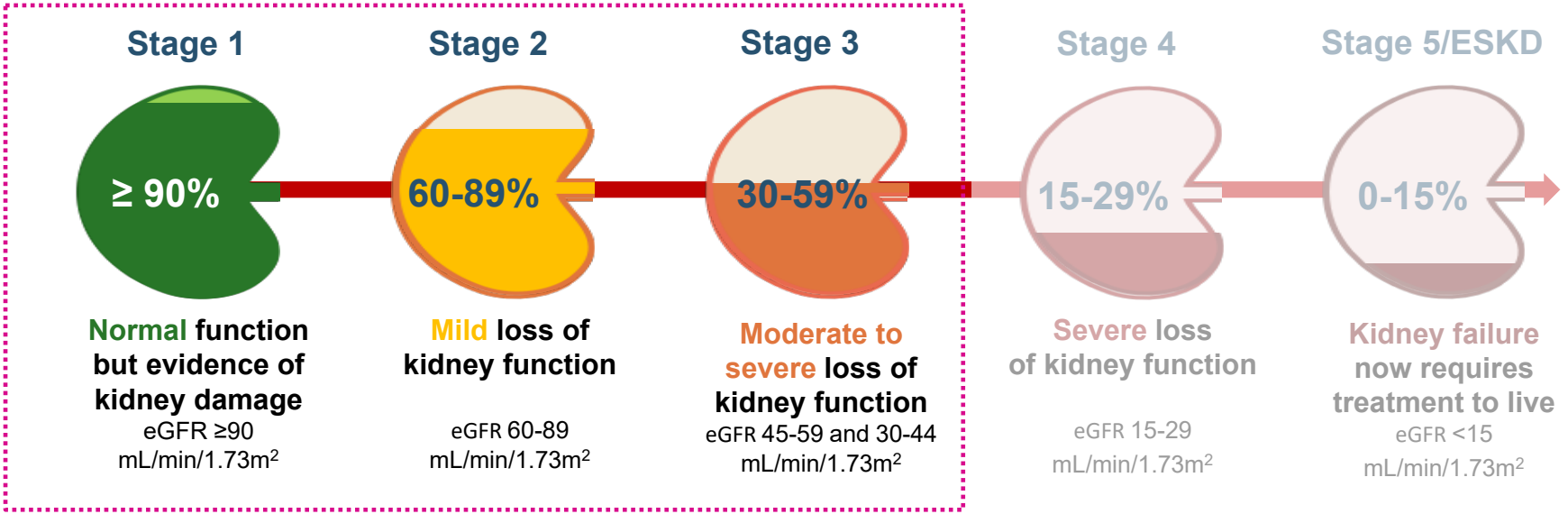
Frequency of Monitoring[1]	Strategy to Reduce Diabetic Kidney Disease Progression and Cardiovascular Disease[2,3]	
Monitoring 2x/year	Treat with ACEi or ARB and antihypertensives	Consider SGLT2 Inhibitors if clinically indicated



High Risk

Frequency of Monitoring / Referral[1]		Comprehensive Strategy to Maximize Protection for Diabetic Kidney Disease Progression and Cardiovascular Disease[2,3]	
Monitoring 3x/year	Nephrology Referral	Titrate ACEi or ARB to maximally tolerated dose	Strongly consider SGLT2 inhibitor therapy unless contraindicated

There is Time to Intervene Prior to CKD Progression When It Is Irreversible



OPPORTUNITY TO SHIFT DKD CARE UPSTREAM

FUTURE: ***Earlier Intervention = Better Outcomes***

CURRENT: Treat at costly end-stage

36

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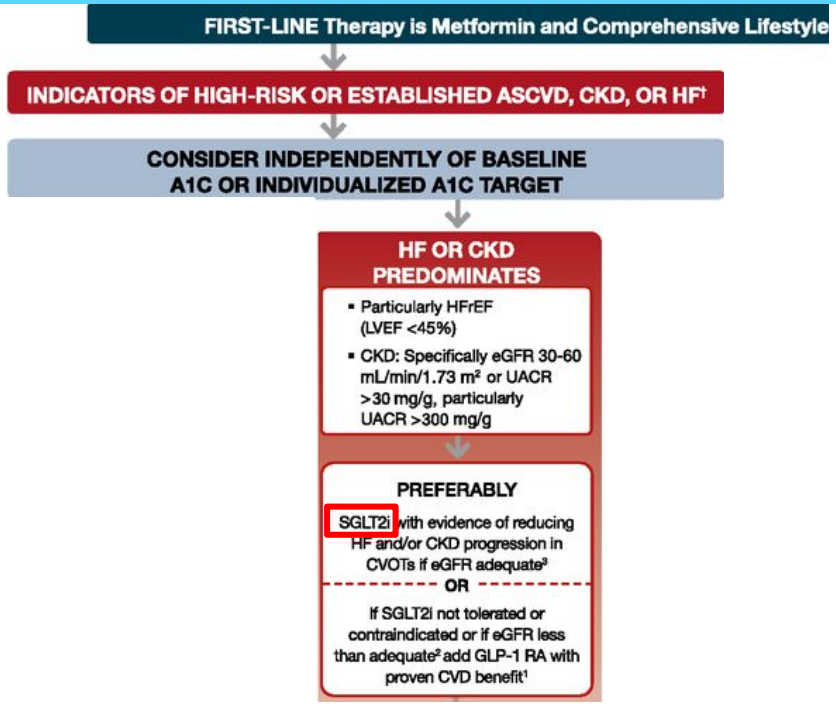
  - ❑ **This will also save the heart!**
- ❑ Use the Mount Sinai CKD Checklist and/or refer to Nephrology

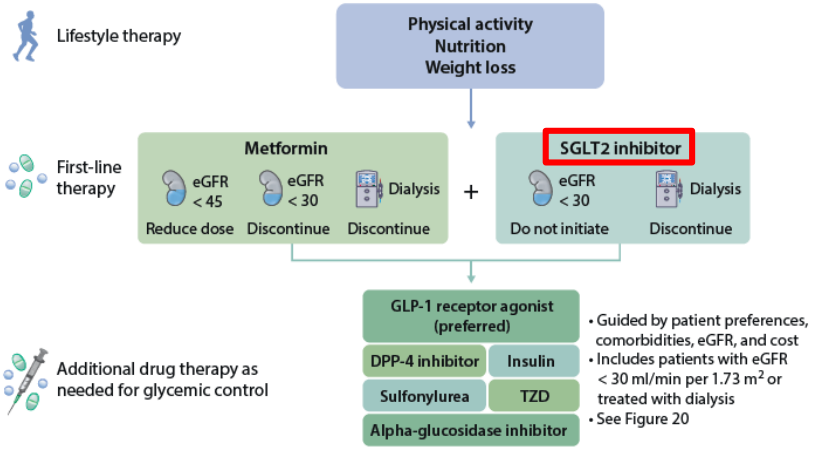
Four Pillars of Diabetic Kidney Disease Management in 2021

Metformin/Lifestyle + SGLT2i (ADA 2020 and KDIGO 2020)

2020 ADA Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes



2020 KDIGO Clinical Practice Guidelines for Diabetes Management in CKD



4.2 Sodium–glucose cotransporter-2 inhibitors (SGLT2i)

Recommendation 4.2.1: We recommend treating patients with T2D, CKD, and an eGFR ≥30 ml/min per 1.73 m² with an SGLT2i *(1A)*.

Acronyms: Chronic Kidney Disease (CKD), American Diseases Association (ADA), Kidney Disease: Improving Global Outcomes (KDIGO)

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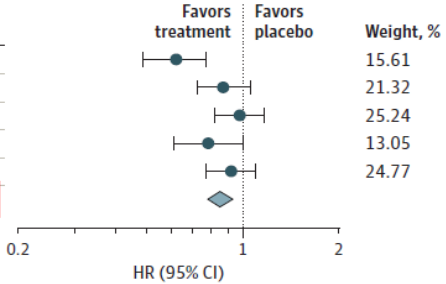
SGLT2i Are Powerful Medications for Improved CV and Kidney Outcomes

Figure 2. Effects of Sodium-Glucose Cotransporter 2 Inhibitors on Cardiovascular Death

A Overall CV death

	Treatment		Placebo		
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)
EMPA-REG OUTCOME	172/4687	12.4	137/2333	20.2	0.62 (0.49-0.77)
CANVAS program	NA/5795	11.6	NA/4347	12.8	0.87 (0.72-1.06)
DECLARE-TIMI 58	245/8582	7.0	249/8578	7.1	0.98 (0.82-1.17)
CREDENCE	110/2202	19.0	140/2199	24.4	0.78 (0.61-1.00)
VERTIS CV	341/5499	17.6	184/2747	19.0	0.92 (0.77-1.10)
Fixed-effects model (Q = 11.22; *df* = 4; *P* = .02; I^2 = 64.3%)					0.85 (0.78-0.93)

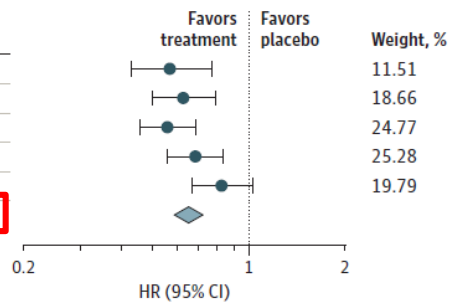


15% Reduction in CV Death

Figure 4. Effects of Sodium-Glucose Cotransporter 2 Inhibitors on Kidney-Related Outcomes

A Overall kidney outcomes

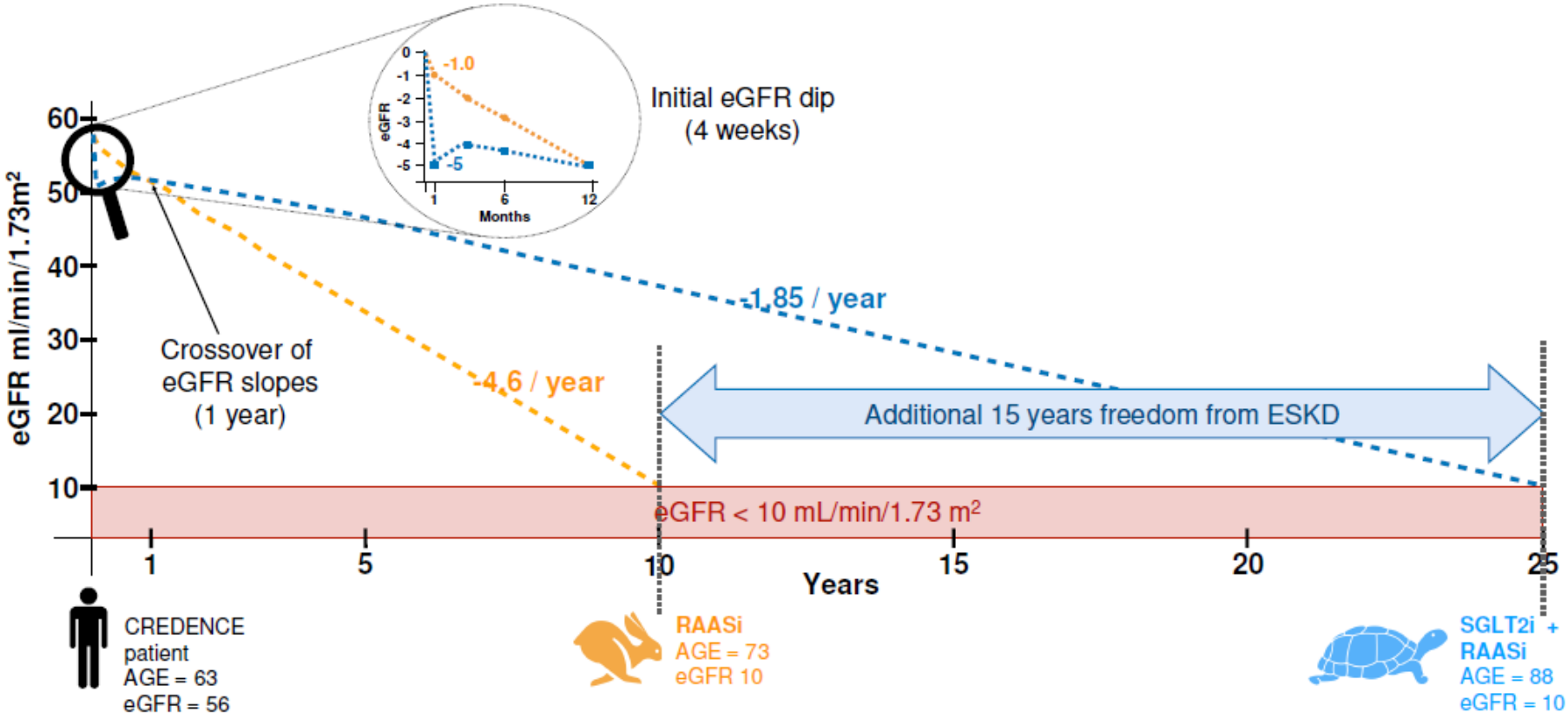
	Treatment		Placebo		
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)
EMPA-REG OUTCOME	81/4645	6.3	71/2323	11.5	0.54 (0.40-0.75)
CANVAS program	NA/5795	5.5	NA/4347	9.0	0.60 (0.47-0.77)
DECLARE-TIMI 58	127/8582	3.7	238/8578	7.0	0.53 (0.43-0.66)
CREDENCE	153/2202	27.0	224/2199	40.4	0.66 (0.53-0.81)
VERTIS CV	175/5499	9.3	108/2747	11.5	0.81 (0.64-1.03)
Fixed-effects model (Q = 7.96; *df* = 4; *P* = .09; I^2 = 49.7%)					0.62 (0.56-0.70)



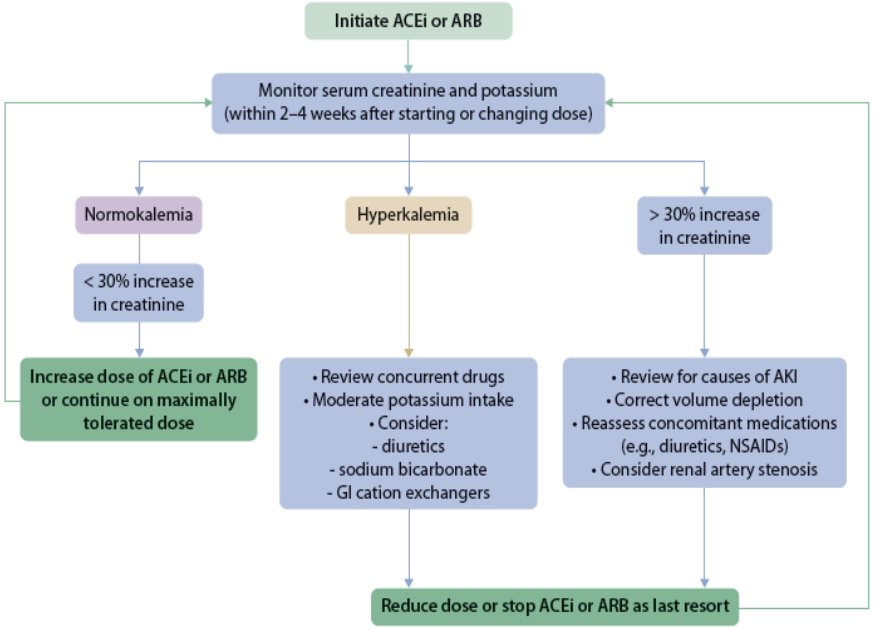
38% Reduction in Kidney Outcomes

JAMA Cardiol. 2021;6(2):148-158. doi:10.1001/jamacardio.2020.4511

SGLT2i Inhibitors May Delay ESKD by 15 Years



ACEi/ARB Initiation, Titration, and Mitigation Strategies for Hyperkalemia: KDIGO 2020



1.2 Renin–angiotensin system (RAS) blockade

Recommendation 1.2.1: We recommend that treatment with an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) be initiated in patients with diabetes, hypertension, and albuminuria, and that these medications be titrated to the highest approved dose that is tolerated *(1B)*.

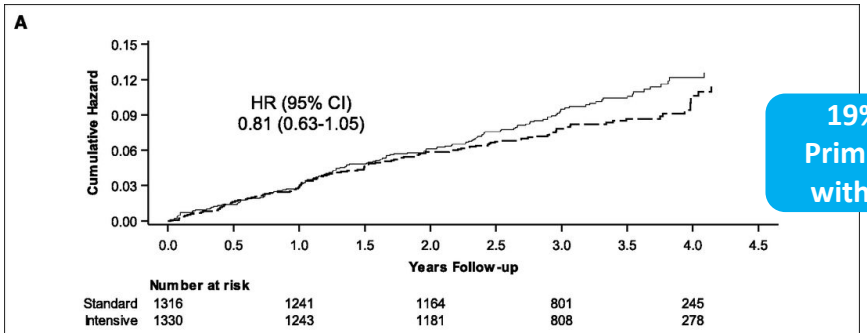
BP Targets in CKD (SBP < 120): KDIGO 2021 Guidelines

Chapter 3: Blood pressure management in patients with CKD, with or without diabetes, not receiving dialysis

3.1. Blood pressure targets

Recommendation 3.1.1: We suggest that adults with high BP and CKD be treated with a target systolic blood pressure (SBP) of <120 mm Hg, when tolerated, using standardized office BP measurement (*2B*).

Kaplan-Meier curves for primary cardiovascular outcome in SPRINT participants with CKD



19% Reduction in Primary CV Endpoint with Target SBP 120

JASN September 2017, 28 (9) 2812-2823; DOI: https://doi.org/10.1681/ASN.2017020148

Outline

- ❑ CKD Burden in the general population is underappreciated
- ❑ Correct Classification Using Urine Albumin to Creatinine Ratio (UACR)
- ❑ Risk stratify early in course of CKD (beyond GFR) and take action to prevent progression
- ❑ Options include Aggressive Blood Pressure Management (<130/80), use ACE/ARB to max dose if possible, use SGLT2i!
  - ❑ This will also save the heart!
- ❑ **Use the Mount Sinai CKD Checklist and/or refer to Nephrology**

				Persistent Albuminuria Categories						
				A1	A2	A3				
				Normal-Mildly Increased	Moderately Increased	Severely Increased				
				<30 mg/g	*30-300 mg/g*	*>300 mg/g*	*BMD**	*NA Intake***	*Diabetes Treatment****	
GFR Categories (ml/min/1.73m²)	Stage 1	Normal or High	≥90	1 visit/yr if CKD	1 visit/yr	2 visits/yr		<4 g (<2 g/d if HTN or DM)	Metformin	SGLT-2i
	Stage 2	Mildly Decreased	60-89	1 if CKD	1	2				
	Stage 3a	Mild-Moderately Decreased	45-59	1	2	3				GLP-1 RA
	Stage 3b	Moderately-Severely Decreased	30-44	2	3	3	Assess for Bone Mineral Disorder			
	Stage 4	Severely Decreased	15-29	3	3	4+		<3 g (<2 g/d if HTN or DM)		
	Stage 5	Kidney Failure	<15	4+	4+	4+				
Hypertension without DM				ACE/ARB, CCB, Diuretic	ACE/ARB Suggested	ACE/ARB				
Hypertension-with DM, GFR>60				ACE, ARB, CCB, Diuretic	ACE/ARB					
Hypertension w DM, GFR<60				ACE/ARB						

Note: Risk of progression based on GFR and severity of albuminuria indicated by color (green-very low, yellow-low, orange-moderate, red-high, deep red-very high). Note: Frequency of follow-up based upon GFR and severity of albuminuria (visits per year)

* Bone Mineral Disorder (BMD): Time to initiate monitoring for BMD, based on GFR

** Daily sodium intake based on GFR

*** Appropriate use of SGLT-2, GLP-1 RA, and metformin based on GFR. SGLT-2 preferred. Use GLP-1 RA if SGLT-2 not tolerated or GFR <30

**** Recommended hypertension treatment based on severity of microalbuminuria and presence/absence of DM. Use highest tolerated dose

Checklist for Chronic Kidney Disease Management

for Front Line Providers

Screening/ Management	Clinical Targets	Frequency of Testing / Visits	Next Steps for Uncontrolled/Positive Findings
Estimate GFR and albuminuria	GFR ≥90 Urine ACR <30 mg/g	Stages 1-2: Annually Stage 3: Semiannual Stages 4/5: Quarterly	Determine if progressive Estimate risk for progression (Kidney Failure Risk Equation or KidneyIntelX in diabetics)
Nutrition	Protein Intake Stage 5: 0.6-0.8 g/kg/d Sodium intake Stages 3/4-5: <4g/<3 g d Stages 3-5 w Htn: <2 g/d	Annually and as needed	Provide dietary counseling (Nutritionist or CDE) Protein composition recommended: 50% High Biologic Value (foods that contain high protein includes poultry, fish, eggs), 50% plant-based (e.g. lentils, tofu, chickpeas)
Blood Pressure Control	Target Blood Pressure: <130/80	Monthly until controlled, then every 3-6 months	Lifestyle modification, Home BP monitoring Non-Diabetic: ACR <30 mg/g: Use ACE/ARB, CCB, Diuretic ACR 30-299 mg/g: Use of ACE/ARB suggested ACR >300 mg/d: Use ACE/ARB Diabetic: ACR<30: Use ACE/ARB, CCB, and/or Diuretic ACR >30 or GFR<60: Use ACE/ARBR <60: ACE/ARB
Diabetes Mellitus Management	HbA1c <7% (range <6.5-8%) Urine ACR <30 mg/g	Controlled: q 6 mon Poorly controlled: q 3 mon	Intensify medications to optimize control With CKD, both metformin and SGLT-2i as first line therapy Use GLP-1 RA if intolerant to SGLT-2i or GFR <30

Continued on next slide

Screening/ Management	Clinical Targets	Frequency of Testing / Visits	Next Steps for Uncontrolled/Positive Findings
Lipid Management	LDL <130 or <100 based on ASCVD risk	Annually	Lifestyle modification Statin therapy for Stage 3-5 (Non-Dialysis)
Metabolic Acidosis	Sodium Bicarbonate >22 meq/l	Stage 1-2: Annual Stage 3: q 6 mon Stages 4/5: q 3 mon	If bicarbonate <22 mEq/l, add sodium bicarbonate (650 mg TID) or sodium citrate (30 ml/d)
Anemia	Hgb level ≥13 mg/dl men, ≥12 women	Stage 3: Annual Stages 4-5:q 3 mon On ESA : q 3 mon	Replete iron orally or IV if iron deficient (FeS04 325 mg TID, Fe gluconate 2-3 mg/kg/d BID-TID) Erythropoiesis Stimulating Agents if refractory
Bone Metabolic Disease	Normal Calcium and Phopshate concentrations	Screening at GFR <45 Stage 3A/3B: q 6-12mon Stage 4: q 3-6 mon Stage 5: q 1-3 mon	Correct hypocalcemia if <7.5 mg/dl (adjusted for albumen), symptomatic, or severe hyperPTH Treat hyperphosphatemia with diet (~900 mg/d) and phosphate binders if >6 mg/dl
	Vitamin D	Screening to establish baseline and as needed	Correct as without CKD, if Phosp/calcium normal. Calcitriol or synthetic vitamin D analogs if progressive hyperparathyroidism
	Parathyroid hormone level	Stage 3A/3B: Baseline Stage 4: q 6-12 mon Stage 5: q 3-6 mon	Correct modifiable factors Calcitriol/Vit D analogues for severe progressive disease
Hyperkalemia	Serum Potassium	Stage 1-2: Annual Stage 3: q 6 mon Stages 4/5: q 3 mon	Low potassium diet, Reduce or eliminate contributing meds, Correct acidosis Sodium polystyrene, Patiromer, or Sodium zirconium cyclosilicate
Behavioral Health	Depression Screen: PHQ 2/9	Annual Screening	Initiate treatment and/or refer
Immunizations	• PPSV 23 • Hepatitis B • Influenza	Once if GFR <30 or at higher risk, repeat in 5y Complete Hep B series when GFR <30 and at risk of progression. Annual	Consider administration of PV 13 at 65yrs Check HepBs Ab to confirm immunity

Q&A

Hypertension: Management Update

Roy Cohen, MD

Associate Professor of Medicine, General Internal Medicine, Icahn School of Medicine at Mount Sinai

Director of Population Health, Department of Medicine, Mount Sinai

Hypertension Definition

Blood pressure = or >140/90

- Multiple organizations[1] have published guidelines with differing definitions and workflows for the evaluation and treatment of hypertension
- The HEDIS[2] performance measure for controlling HBP defines HTN as a blood pressure **at or above 140/90** – standard used by Medicare and our value-based insurers
  - Mount Sinai will continue to use this definition for charting, billing and performance review purposes.
- ACC/AHA 2019 guidelines[3] place critical emphasis on ASCVD risk
  - Measure atherosclerotic cardiovascular disease (ASCVD) risk for **all patients with blood pressure at or above 130/80**, regardless of stage.
  - Incorporating this risk assessment process into treatment goals to drive outcomes.

[1]including the ACC, AHA, ACP, AAFP and the European Society of Cardiology

[2] CMS Healthcare Effectiveness Data and Information Set

[2]3https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2019/03/07/16/00/2019-acc-aha-guideline-on-primary-prevention-gl-prevention

Burden of Disease

Screen patients for hypertension and use evidence-based guidelines to inform team-based treatment strategies

- Hypertension is a major cause of morbidity and mortality and 20% of adults with HTN in the US were unaware of the condition in 2019
- 37 million adults in the US are taking medication for hypertension and among those 53% have uncontrolled BP
- The incidence of ASCVD and all-cause mortality scales with blood pressure increases above 130/80 for those advised to start or already taking anti-hypertensive medications
- Individuals with HBP face on average nearly $2000 more in annual health care expenses than those without HBP

Ethnicity, Race & Hypertension

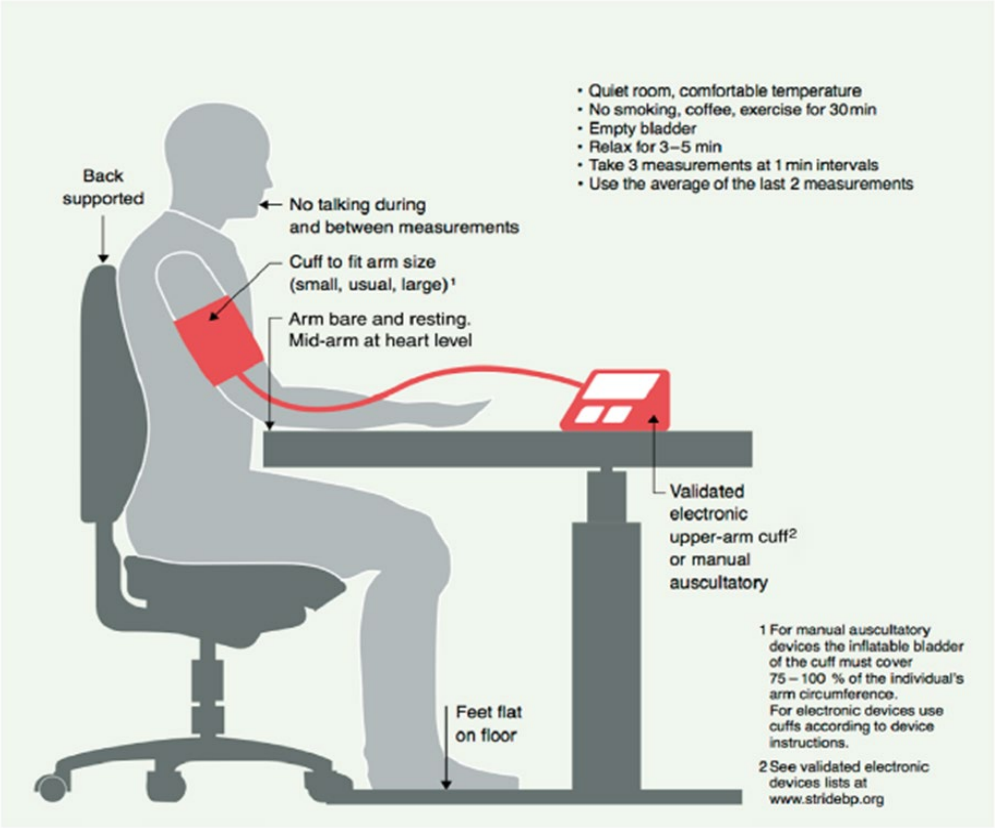
HTN prevalence, treatment and control rates vary significantly according to ethnicity

- Differences may have a genetic component, but lifestyle and social determinants of health likely impact health behaviors such as access to healthy food/diet, and stress
- Patients of African descent
  - Develop hypertension and associated organ damage at younger ages
  - Have a higher frequency of resistant and nighttime hypertension
  - Are at higher risk than other ethnic groups for kidney disease, stroke, HF, and mortality

Ethnicity, Race & Hypertension (continued)

- East Asian populations have a greater likelihood of salt-sensitivity accompanied with mild obesity. When compared to Western populations, East Asian people present a higher prevalence of stroke (particularly hemorrhagic stroke) and non-ischemic HF
- Morning hypertension and nighttime hypertension are also more common in Asia, compared with European populations.
- South Asian populations originating from the Indian subcontinent have a particularly high risk for CV and metabolic diseases, including CAD and type 2 DM.
- With large hypertensive populations residing in India and China, clinical trials in these populations are required to advise whether current treatment approaches are ideal

Blood Pressure Measurement



Blood Pressure Measurement (continued)

Initial evaluation

- Measure BP in both arms, preferably simultaneously
- If there is a consistent difference between arms >10 mm Hg in repeated measurements, use the arm with the higher BP. If the difference is >20 mm Hg consider further investigation.

Standing blood pressure

- Measure in treated hypertensive patients after 1 min and again after 3 min when there are symptoms suggesting postural hypotension and at first visit in the elderly and people with diabetes

Out-of-Office blood pressure measurement

- Out-of-office & SMBP measurements are recommended to confirm the diagnosis of hypertension and for titration of medications
- **Out-of-office BP measurements at home or with 24-hour ABPM are more reproducible than office measurements, more closely associated with hypertension induced organ damage and the risk of cardiovascular events and can identify both white coat and masked hypertension phenomena**

Case Discussion

42-year-old woman evaluated during routine visit for recent BP elevation at her workplace

- The patient doesn't feel fully rested upon awakening in the AM but otherwise feels well and review of systems is unremarkable
- FHX is significant for HTN in her father, mother and 2 siblings, CVA in her father and CHF in her mother. She takes no medications
- On PE, the average of two BP measurements is 128/78. BMI is 30. The remainder of the exam is normal.
- Lab results include Bicarb 24, Cr 0.9, K 4.0, Urine A/C ratio of 10
- EKG reveals NSR and voltage criteria for LVH

Poll — Next Step

Which of the following is the appropriate next step to perform?

1. TSH measurement
2. Home BP or 24-hour ambulatory BP monitoring
3. Polysomnography
4. Plasma aldosterone/renin activity ratio

High Blood Pressure Monitoring Guidance

Provide recommendations for the frequency of home BP monitoring

- (e.g., daily versus three times weekly)

Inform patient that individual BP readings may vary substantially

Provide guidance for provider notification of high BP readings

- (e.g., call/contact office/PCP if above 180/100)

Set office follow-up date with PCP or team member to review BP monitoring diary

- (e.g., 2-4 weeks)

Diagnosis and Classification

- Hypertension can be diagnosed and confirmed using office-bases visits, home or ambulatory BP monitoring over 1-4 week intervals
- Diagnosis can be made on a single visit if BP is ≥ 180/110 mm Hg and there is evidence of CVD
- Criteria for diagnosis differ by site and modality

Criteria for Hypertension Based on Office-, Ambulatory (ABPM)-, and Home Blood Pressure (HBPM) Measurement	
	SBP/DBP, mmHg
Office BP	≥140 and/or ≥90
HBPM	≥135 and/or ≥85
ABPM	
24-hour average	≥130 and/or ≥80
Daytime (awake) average	≥135 and/or ≥85
Nighttime (asleep) average	≥120 and/or ≥70

Risk Assessment to Inform Treatment Goals

More than 50% of hypertensive patients have additional CVD risk factors

The presence of one or more additional CVD risk factors proportionally increases the risk of coronary, cerebrovascular, and renal diseases in hypertensive patients

The most common risk factors are:

- Diabetes (15%–20%), lipid disorders (elevated LDL-C and triglycerides (30%), overweight- obesity (40%), metabolic syndrome (40%), hyperuricemia (25%),

- Peripheral arterial disease, CVA including Lacunar infarcts as well as smoking, high alcohol intake, sedentary lifestyle

Risk Stratification Key Steps

- Calculate the 10-year risk of a first atherosclerotic cardiovascular disease event using race and sex-specific pooled cohort equations to better stratify atherosclerotic cardiovascular disease risk
  - (e.g. http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/)

- This risk tool is best validated among non-Hispanic whites and non-Hispanic blacks living in the United States and it may over- or under-estimate risk in other groups.

- Clinicians may consider use of another risk prediction tool if validated in a population with similar characteristics to the evaluated patient

- Patients with BP 130-139/80-89 and a 10-yr risk for ASCVD risk > 10% can be treated with medical therapy while those with a risk < 10% should be managed with non-pharmacological therapy

Risk Stratification

- Patients should know their current cardiovascular risk
  - How it relates to decisions about their therapy
  - How it relates to the setting of therapeutic goals
- Engage patients in SDM discussions about personalized ASCVD risk estimates and their implications on the perceived benefits of preventive strategies, including:
  - Lifestyle habits
  - Goals
  - Medical therapies
- Collaborative decisions are more likely to
  - address potential barriers to treatment options
  - increase long term adherence to medications and lifestyle modifications

Classification of HTN Risk with Additional Risk Factors and HMOD

Simplified Classification of Hypertension Risk According to Additional Risk Factors, Hypertension-Mediated Organ Damage (HMOD), and Previous Disease*				
Other risk factors, HMOD, or disease	**High-Normal SBP 130-139 DBP 85-89**		**Grade 1 SBP 140-159 DBP 90-99**	**Grade 2 SBP ≥ 160 DBP ≥ 100**
No other risk factors	Low		Low	Moderate / High
1 or 2 risk factors	Low		Moderate	High
≥ 3 risk factors	Low	Moderate	High	High
HMOD, CKD 3+ DM, CVD	High		High	High

*Example based on a 60-year old male patient. Categories of risk will vary according to age and sex.

Work-Up

- Labs should include a BMP, lipids, U/A and EKG
- Perform additional investigations, when indicated, to assess and confirm suspicion of HMOD (HTN-Mediated Organ Damage), coexistent diseases and/or secondary hypertension. These include:
  - Fundoscopy, TTE, Carotid Duplex, Kidney/Renal Artery imaging
- Elevated serum uric acid (UA) is common in patients with hypertension.
  - Patients with gout with a uric acid > 6mg/dl, should be treated with diet, urate influencing drugs (losartan, fibrates, atorvastatin) or urate lowering drugs

Treatment

- Therapeutic strategy must include:
  - Lifestyle modifications
  - BP control to target
  - Effective treatment of other risk factors to optimize reduction of residual cardiovascular risk
- **A reduction in BP of 20/10 mm Hg is associated with a 50% decrease in cardiovascular risk**
- The combined treatment of hypertension, HMOD and additional cardiovascular risk factors reduces the rate of CVD beyond BP control
- Treat to a BP goal of < 130/80 those with:
  - ASCVD risk of ≥ 10%
  - DM
  - CKD 3+,
  - CKD post-transplant
  - HF
  - Stable ischemic CAD and PAD
  - Secondary stroke prevention including Lacunar infarcts

Lifestyle Changes

Salt Reduction	Healthy Diet	Healthy Beverages
Moderation of Alcohol Consumption	Weight Reduction	Smoking Cessation
Regular Physical Activity	Reduce Stress Induce Mindfulness	Reduce exposure to pollution and cold weather

See appendix for more details

Substance/Medication Exacerbators/Inducers

- NSAIDs
- Combined oral contraceptive pills
- Anti-depressants (TCAs and SNRIs, not SSRIs)
- Daily Acetaminophen use
- Steroids
- Sympathomimetics: pseudoephedrine, cocaine, amphetamines
- Antimigraine serotonergics
- Erythropoeitin
- Calcineurin inhibitors (Cyclosporin, Tacrolimus)
- Antiangiogenesis and kinase inhibitors (Cancer chemotherapeutics)
- 11 s-hydroxysteroid dehydrogenase type 2 inhibitors
- Alcohol & Herbals (ma-huang, ginseng at high doses, liquorice, St. John's wort, yohimbine)

Case Discussion

52 year-old man is evaluated during a follow-up visit for elevated BP identified for the first time during his last visit

- He reports back pain of several week's duration after an episode of heavy lifting at work. History is also notable for seasonal allergies. He currently takes Motrin BID for back pain and Claritan as needed for allergies.
- On PE, his pulse is 52, the average of 2 BP measurements is 143/91 and BMI is 27. The remainder of the exam is normal.
- EKG is normal and 10 yr ASCVD estimate is 8.5%

Poll – Next Step

In addition to F/U with you or a team member in 1-2 months, which is the appropriate management?

1. Begin Amlodipine
2. Begin HCTZ
3. D/C Motrin
4. D/C Claritan

Ideal Medication Characteristics

- Treatments should be evidence-based in relation to benefits & morbidity/mortality prevention
- Use of a once-daily regimen whenever possible which provides 24-hour blood pressure control
- Affordable and/or cost-effective relative to other agents & well tolerated
- For older adults (≥65 y of age) with HTN or any patient with a high burden of comorbidity and frailty or limited life expectancy:
  - Clinical judgment, patient preference, and a team-based approach to assess risk/benefit are reasonable for decisions regarding intensity of BP lowering and choice of antihypertensive drugs

Medications

- First-line pharmacological therapy is recommended as a single pill or combination pill or pills including a ACE/ARB, CCB or thiazide-like diuretic
- Co-morbid illness often dictates medication preference, ACE/ARB for DM
- As a general rule, 75% of a medication's effect occurs at 50% of it's maximal dose
- A combination of two agents at moderate dose is often more successful at achieving BP goals than one at maximal dose for those with BP greater than 20/10 above goals
- **Use an ARB (not an ACE) in black patients**, as angioedema is about three times more likely to occur with ACE inhibitors among black patients

Case Discussion

54 year-old man is evaluated during a follow-up visit for treatment of persistently elevated BP. He takes no medication.

- PE reveals a well-developed, muscular man in NAD
- BP is 165/98 and pulse is 70/min; other vitals are normal
- BMI is 28. Cardiac exam is unremarkable.
- Lab results include
- Bicarb of 27
- Creatinine 1.3
- Potassium 4.5
- eGFR > 60.
- EKG NSR and voltage criteria for LVH

Poll – Next Step

Which of the following is the most appropriate treatment?

1. Metoprolol & Doxazosin both once daily
2. Hydralazine TID
3. Amlodipine/benazepril combination daily
4. Telmisartan and chlorthalidone -- both once daily

Medication Adherence

- Evaluate at each visit and prior to escalation of antihypertensive treatment
- Reduce polypharmacy – use single pill combinations
- Prescribe once-daily dosing rather than multiple-times-per-day dosing
- Link adherence behavior with daily habits
- Provide adherence feedback to patients
- Home BP monitoring
- Reminder packaging of medications
- Empowerment-based counseling for self-management
- Electronic adherence aids such as mobile phones or short messages services
- Team approach (i.e. pharmacists) to improve monitoring for adherence

Resistant Hypertension

Affects 10% of hypertensive individuals and increases the risk of CAD, chronic HF, CVA, ESRD and all-cause mortality

- Resistant hypertension is defined as seated office BP >140/90 in a patient treated with three or more antihypertensive medications at optimal (or maximally tolerated) doses including a diuretic and excluding:
    - Pseudo-resistance (poor BP measurement technique, white coat effect, non-adherence and suboptimal choices in antihypertensive therapy),
    - Substance/drug-induced hypertension and secondary hypertension
- Approximately 50% of patients diagnosed with resistant hypertension have pseudo-resistance rather than true resistant hypertension

Treatment-Resistant Hypertension

Optimize lifestyle and medications.

- Add a low dose of spironolactone as the 4th line agent in those whose serum potassium is <4.5 mmol/L and whose eGFR is >45 ml/min to achieve BP targets
- If spironolactone is contraindicated or not tolerated, eplerenone, amiloride, doxazosin, clonidine, and beta-blockers are alternatives, or any available antihypertensive class not already in use
- If the GFR < 30 or the patient is volume overload, initiate loop diuretic

Secondary Hypertension

A specific cause of secondary hypertension can be identified in 5-10% of hypertensive patients

- Early diagnosis of secondary hypertension and the institution of appropriate targeted treatment have the potential to cure hypertension in some patients or improve BP control/reduce the number of prescribed antihypertensive medications in others
- The most common types of secondary hypertension in adults are:
  - Renal parenchymal (CKD) & renovascular DX
  - Primary aldosteronism
  - Chronic sleep apnea
  - Substance/drug-induced
- Other less common causes include:
  - Cushings Disease & Syndrome
  - Pheochromocytoma
  - Thyroid Disease
  - Coarctation of aorta

Screening for Secondary HTN

- Patients with early onset hypertension (<30 years of age) in particular in the absence of hypertension risk factors (obesity, metabolic syndrome, familial history etc.)
- Those with true resistant hypertension
- Individuals with sudden deterioration in BP control
- Hypertensive urgency and emergency
- Those presenting with high probability of secondary hypertension based on strong clinical clues

Clinical Integration / Team-Based Care

Endocrinology / CDEs

- For A1c > 9, despite 6 months of adherent therapy
- Recurrent hypoglycemia
- Continuous subcutaneous insulin infusion (insulin pump) therapy

Cardiology

- For treatment of concomitant cardiac disease (CAD, HF), and orthostatic hypotension.
- Optimize treatment of lipid disorders

Nephrology

- To clarify the cause of CKD and assistance managing related complications
- All Stage 4 CKD (eGFR <30)
- KidneyIntelX™ medium or high risk score
  - Diagnostic blood test that predicts risk of progressive decline in kidney function in patients with type 2 diabetes and existing Diabetic Kidney Disease at stages 1-3 (eGFR 30-59 or UACR ≥ 30)

Clinical Integration / Team-Based Care (continued)

- MSHS Disease Management Services
- Certified Diabetes Education Disease Management Team (Wellness coaches)
- Clinical Pharmacist for uncontrolled chronic diseases, such as:
  - HTN, HF, DM, asthma, COPD, depression, behavioral health
  - High utilizers, Post D/C and Polypharmacy, Med Rec & Adherence
- Care Management for multiple no-shows, unexplained non-adherence to medications, testing or treatment
  - Demonstrated difficulty managing new or ongoing symptoms and/or disease processes
  - Frequent admissions or ED visits that may be preventable with more support
  - Complex family dynamics that deplete the provider
  - Difficulty accessing needed community-based care and a high “worry score”, patients that you areare most worried about between visits
- Behavioral Health treatment and referrals
  - Patients diagnosed with depression/other BH disorders should be treated,--either locally or referred for psychiatric services
- Remote Patient Monitoring program -- Connected Hearts

Appendix

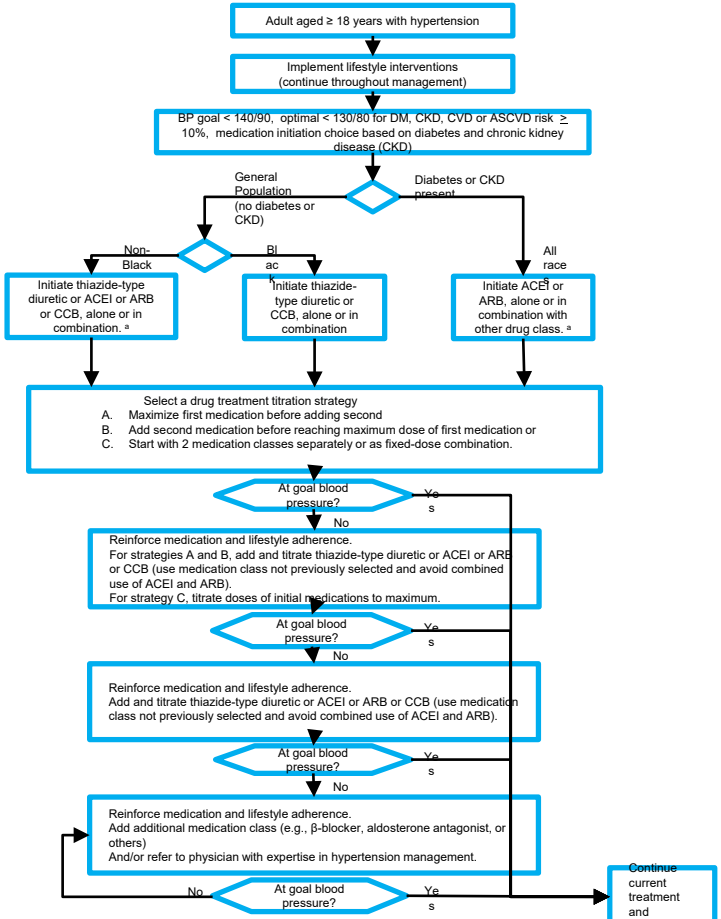
Lifestyle Changes

Salt reduction	There is strong evidence for a relationship between high salt intake and increased blood pressure. • Reduce salt added when preparing foods, and at the table • Avoid or limit consumption of high salt foods such as soy sauce, fast foods, and processed foods, including breads and cereals high in salt
Healthy diet	• Eat a diet that is rich in whole grains, fruits, vegetables, polyunsaturated fats, and dairy products, and reduce food high in sugar, saturated fat, and trans fats, such as the DASH diet (www.dashforhealth.com) • Increase intake of vegetables high in nitrates known to reduce BP, such as leafy vegetables and beetroot • Other beneficial foods and nutrients include those high in magnesium, calcium, and potassium such as avocados, nuts, seeds, legumes, and tofu
Healthy beverages	• Moderate consumption of coffee, green and black tea. • Other beverages that can be beneficial include karkadé (hibiscus) tea, pomegranate juice, beetroot juice, and cocoa.
Moderation of alcohol consumption	• Positive linear association exists between alcohol consumption, blood pressure, the prevalence of hypertension, and CVD risk. • The recommended daily limit for alcohol consumption is 2 standard drinks for men and 1.5 for women (10 g alcohol/standard drink). Avoid binge drinking
Weight reduction	• Body weight control is indicated to avoid obesity. • Abdominal obesity should be managed. • Ethnic-specific cutoffs for BMI and waist circumference should be used. Alternatively, a waist-to-height ration <0.5 is recommended for all populations.

Lifestyle Changes (continued)

Smoking cessation	• Smoking is a major risk factor for CVD, COPD, and /cancer. • Smoking cessation and referral to smoking cessation programs are advised
Regular physical activity	• Studies suggest that regular aerobic and resistance exercise may be beneficial for both the prevention and treatment of hypertension • Moderate intensity aerobic exercise (walking, jogging, cycling, yoga, or swimming) for 30 minutes of 5-7 days or HIIT (high intensity interval training) which involves alternating short bursts of intense activity with subsequent recovery periods of lighter activity • Strength training can also help reduce blood pressure. Performance of resistance/strength exercises 2-3 days per week
Reduce stress and induce mindfulness	• Chronic stress has been associated to high blood pressure later in life. • Randomized clinical trials examining the effects of transcendental meditation/mindfulness on blood pressure suggest that this practice lowers blood pressure (more research needed on chronic stress' effect on BP • Stress should be reduced and mindfulness or meditation introduced into the daily routine
Reduce exposure to air pollution and cold temperature	• Evidence from studies support a negative effect of air pollution on blood pressure in the long-term

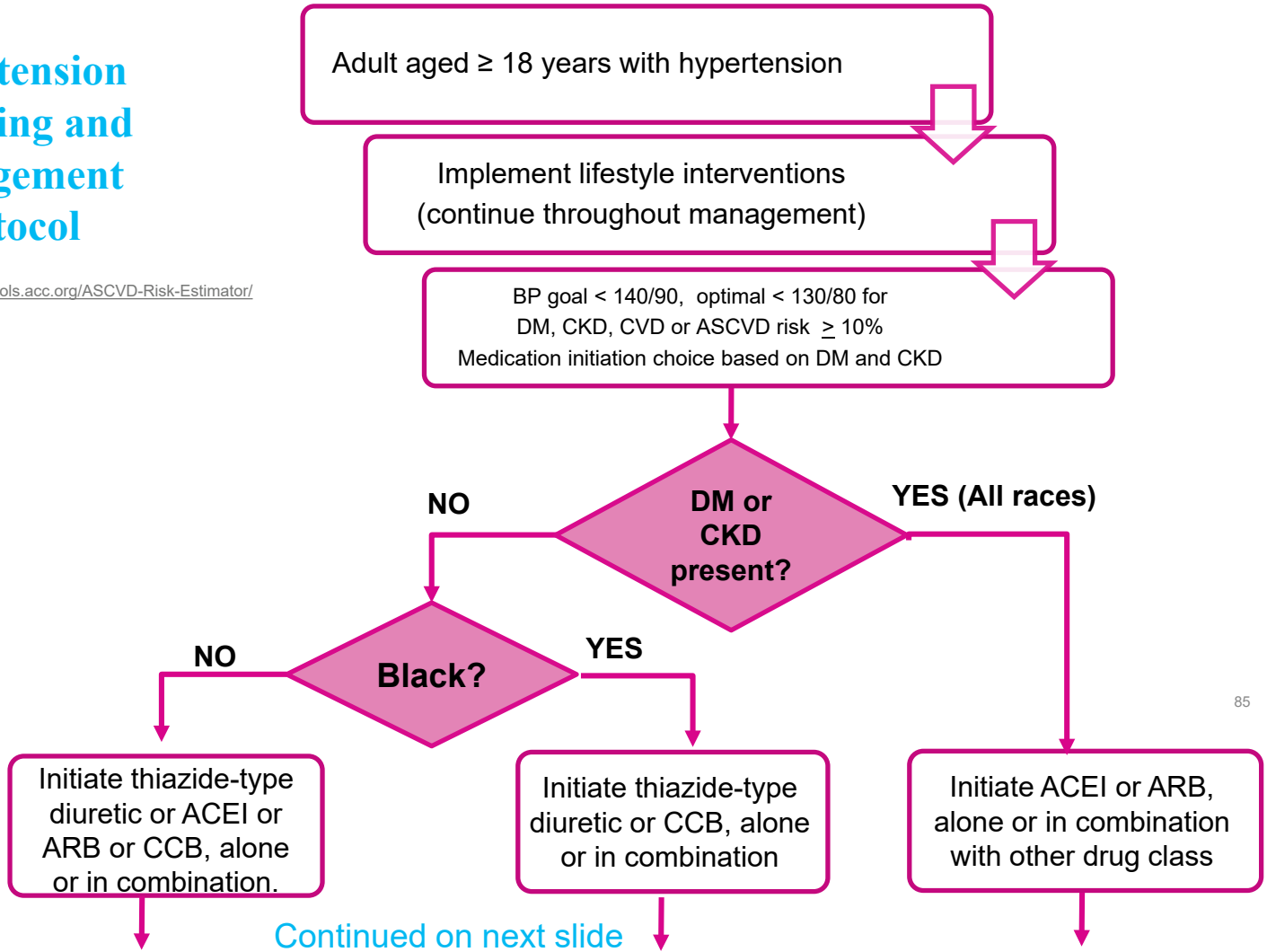
HYPERTENSION SCREENING AND MANAGEMENT PROTOCOL



❖ Risk calculator http://tools.acc.org/ASCVD-Risk-Estimator/

Hypertension Screening and Management Protocol

❖ Risk calculator http://tools.acc.org/ASCVD-Risk-Estimator/



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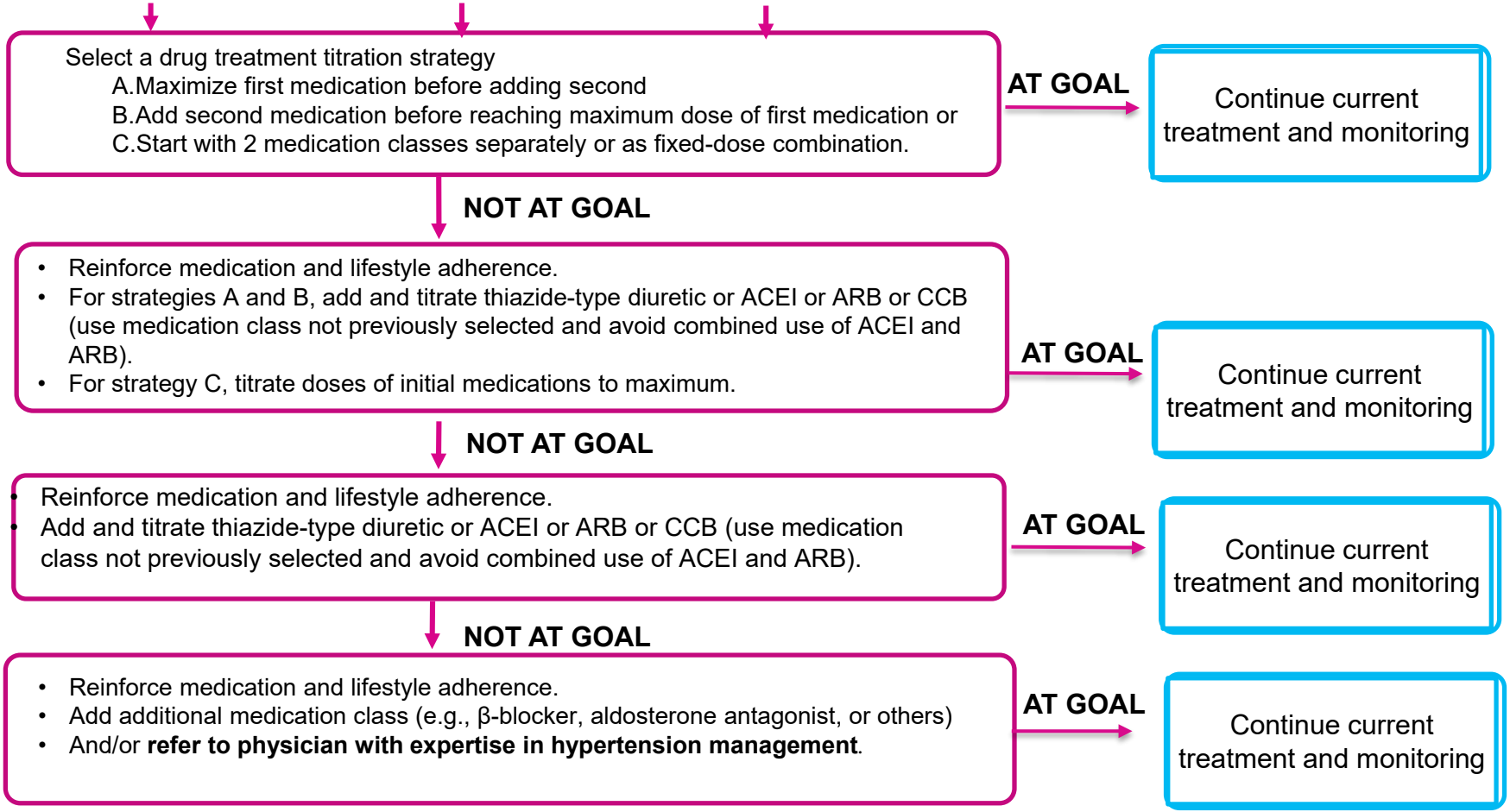
Hypertension Screening and Management Protocol (continued)



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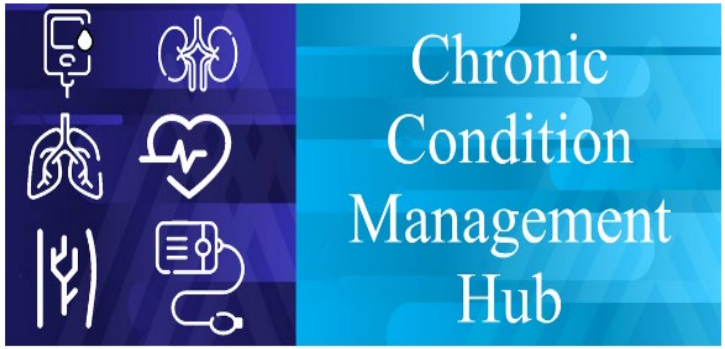
Q&A



https://mshp.mountsinai.org/web/mshp/quick-guides