Navigating the Intersection: Diabetes, Cardiovascular Health, Kidney Function, and GLP-1 Therapies

November 12, 2024

John W. Kennedy, MD
President, AMGA Foundation
Chief Medical Officer, AMGA

Thank You Chronic Care Roundtable Partners

Chronic Care Roundtable Theme

This meeting will address several critical healthcare topics, starting with the impact of GLP-1 receptor agonists on cardiovascular and renal health, integration of technology in diabetes care, and the importance of early screening for chronic kidney disease. Additionally, we will examine diabetes care through a health equity lens and the importance of community involvement.

Speakers

CKM Session:

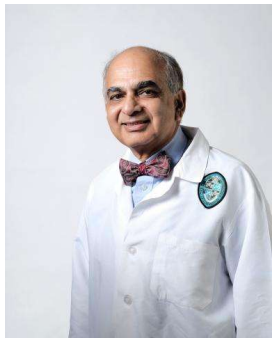
Kenny J. Cole, MD, MS
System VP, Clinical Improvement
Medical Director, Digital Medicine
Ochsner Health

Hot Topics Moderator:

Nancy Beran, MD, MHCDS, FACP, CPE
Vice President and Chief Quality Officer, Northwell Health

Health Equity Session:

Yeng M. Yang, MD, MBA, FAAP
Internal Medicine/Pediatrics, Urgent Care
HealthPartners Park Nicollet



Innovation and Technology Session:

Vivian Fonseca, MD, FRCP
Asst. Dean for Clinical Research
Chief, Endocrinology, Professor, Tullis-Tulane Alumni Chair—Diabetes
Tulane University School of Medicine

Lizheng Shi, PhD, MsPharm, MA
Endowed Regents Professor
Director, Health Systems Analytics Research Center
Tulane University School of Medicine

Kenny J. Cole, MD, MS

System VP, Clinical Improvement
Medical Director, Digital Medicine
Ochsner Health
Diabetes & Cardiovascular-Kidney-Metabolic (CKM) Syndrome Session

CKD and CKM Syndrome

Chronic Kidney Disease and
Cardiovascular Kidney Metabolic Syndrome

Kenny Cole, MD, MS
System VP, Clinical Improvement
Medical Director, Digital Medicine
Ochsner Health

OchsnerHealth

KDIGO Heat Map

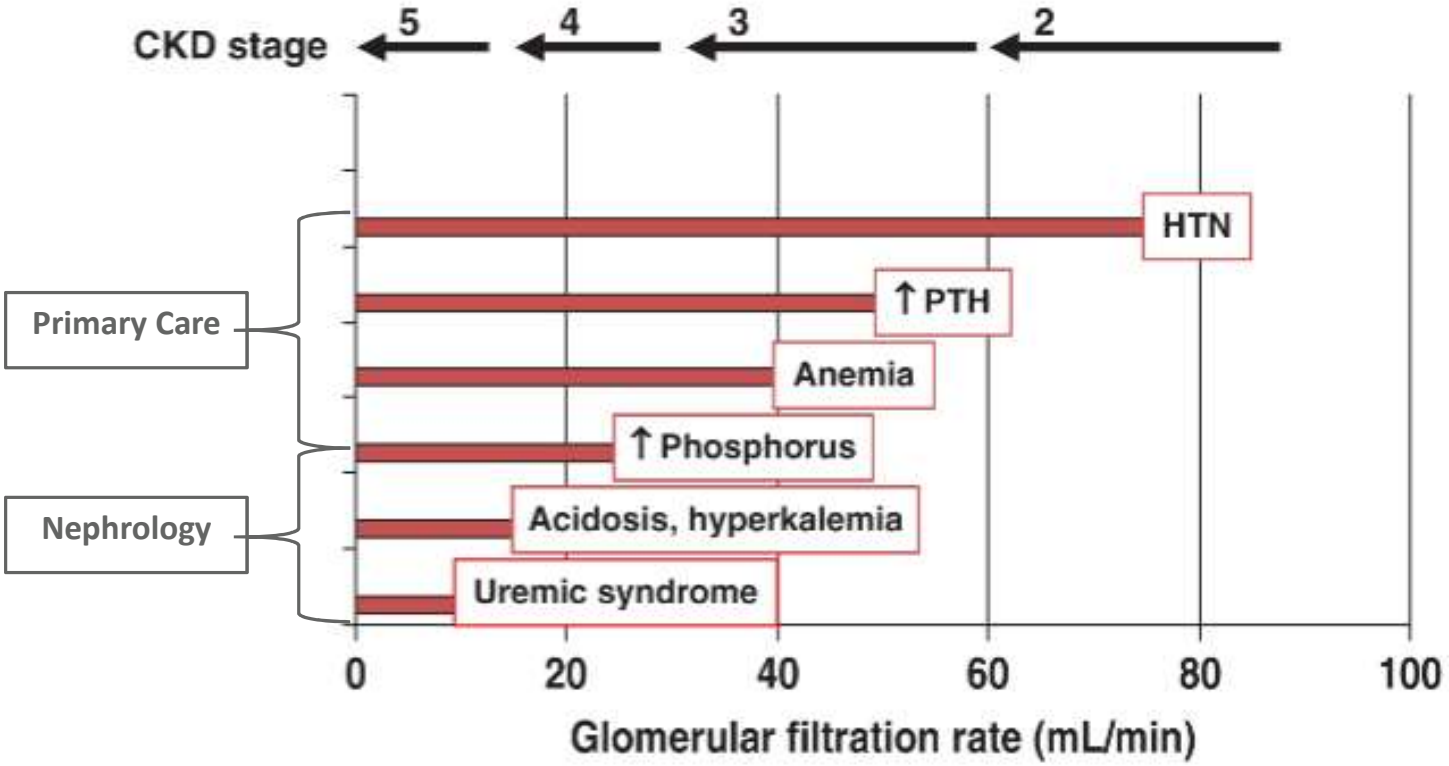
Use this heat map to help monitor progression versus improvement in kidney function objectively via improvements in albuminuria and/or eGFR to assess performance of digital CKM solution

CKD is classified based on:
Cause (C)*
GFR (G)†
Albuminuria (A)†

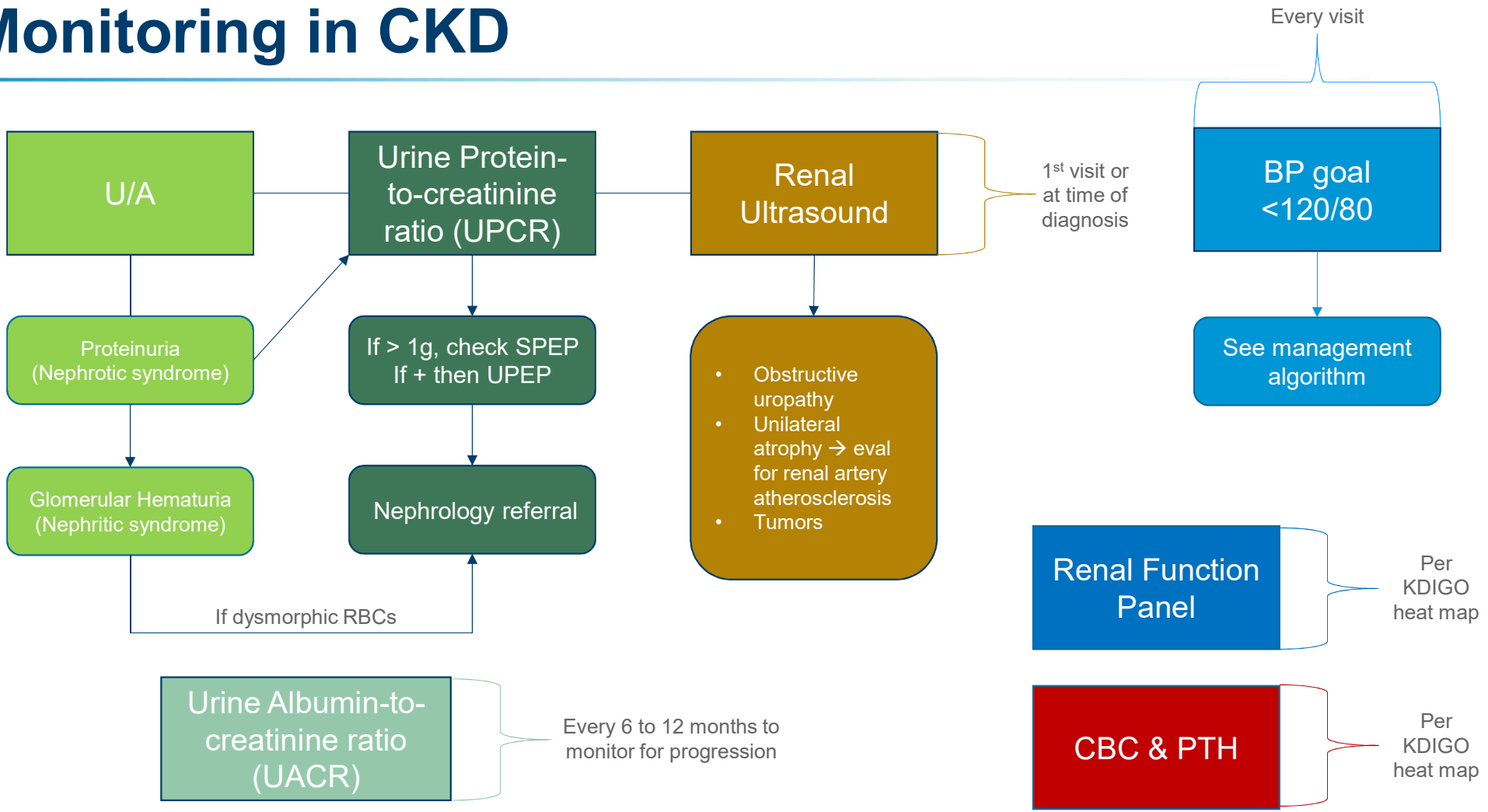
GFR categories (mL/min per 1.73 m²) Description and range				Albuminuria categories Description and range		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
	G1	Normal or high	≥90	Screen 1	Treat 1	Treat and refer 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat and refer 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat and refer 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat and refer 3	Treat and refer 3
	G4	Severely decreased	15–29	Treat and refer† 3	Treat and refer† 3	Treat and refer 4+
	G5	Kidney failure	<15	Treat and refer 4+	Treat and refer 4+	Treat and refer 4+

Low risk (if no other markers of kidney disease, no CKD)
Moderately increased risk
High risk
Very high risk

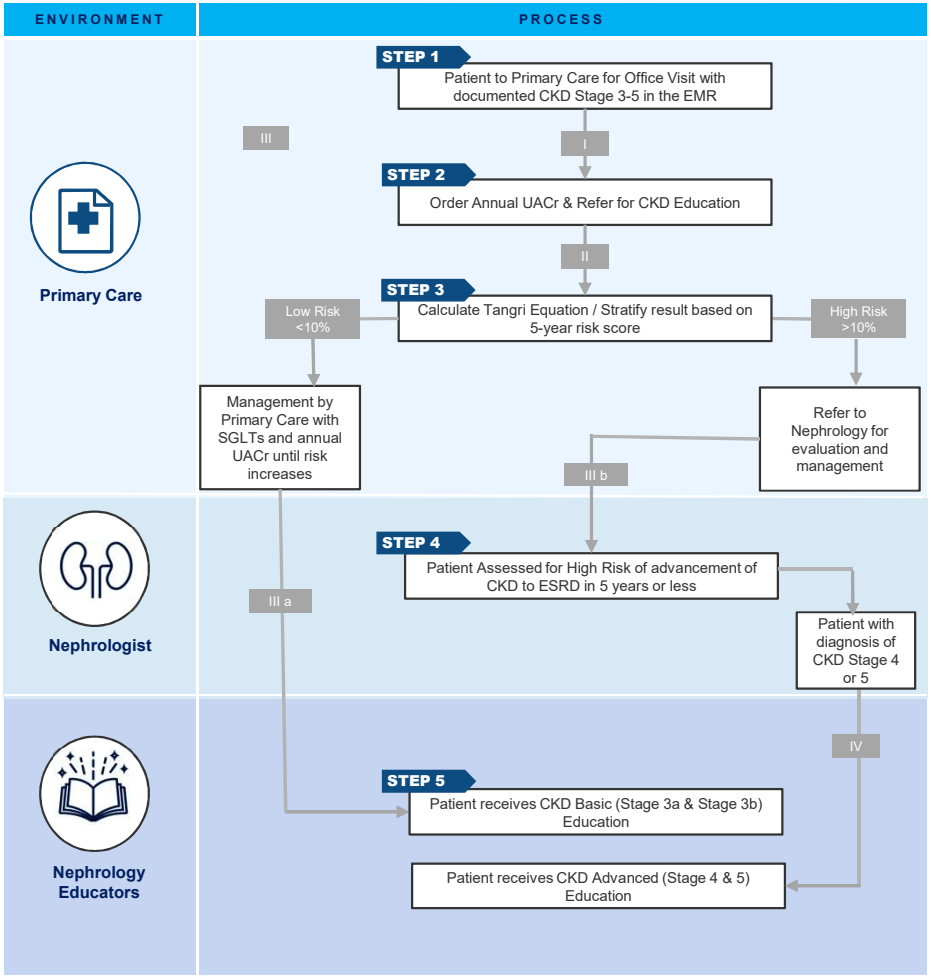
Complications of CKD



Monitoring in CKD



CKD Care Pathway



Pathway Decision Node Criteria

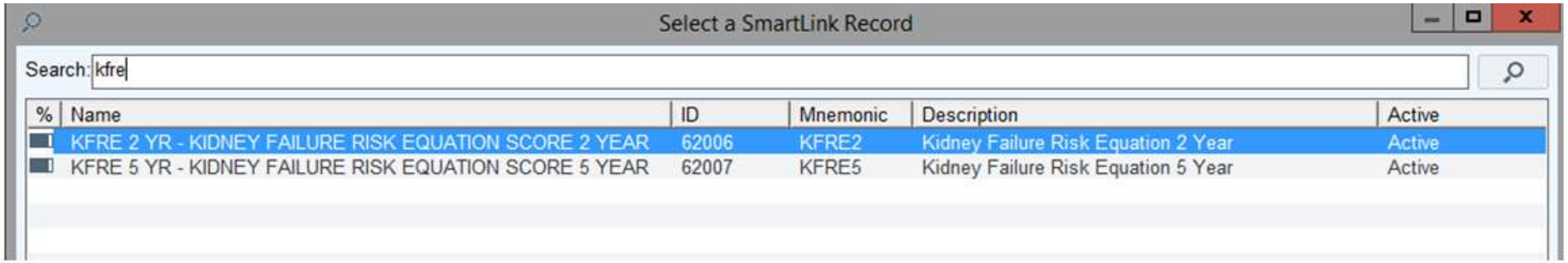
Process Step	Decision Criteria Definition
i.	***Proceed if ≥1 of the following criteria apply:*** • Patient with confirmed diagnosis of CKD Stage 3-5 • HCC capture/re-capture

ii.	***Order annual UACr:***
	• Applies to all patients with a diagnosis of CKD Stage 3-5
	• Document result in Epic Health Maintenance
	• Utilize the written order guideline for appropriate level of care
	
	Refer for CKD education
	• Level of CKD Basic Education Class
	  • Stage 3 class (virtual or in-person)
	  • Stage 4-5 class (virtual or in-person)
	• Consider referral into Digital CKD Program after launch in 3Q 2024

iii a. & b.	***Calculate Tangri / KDIGO*** • <10% @ 5% Risk → Medical Management by Primary Care with SGLTs • >10% @ 5% Risk → Refer to Nephrology for assessment and future management • Consider referring into the Digital CKD Program
iv.	***Refer to Nephrology for assessment and future management*** • Assess and confirm CKD stage level • Refer to Nephrology Educators as indicated • Consider referring into the Digital CKD Program
v.	***Patient receives CKD Education*** • Based on Stage of CKD, patient participates in CKD education classes • Consider referring into the Digital CKD Program

Tangri Risk Equation – EPIC integration

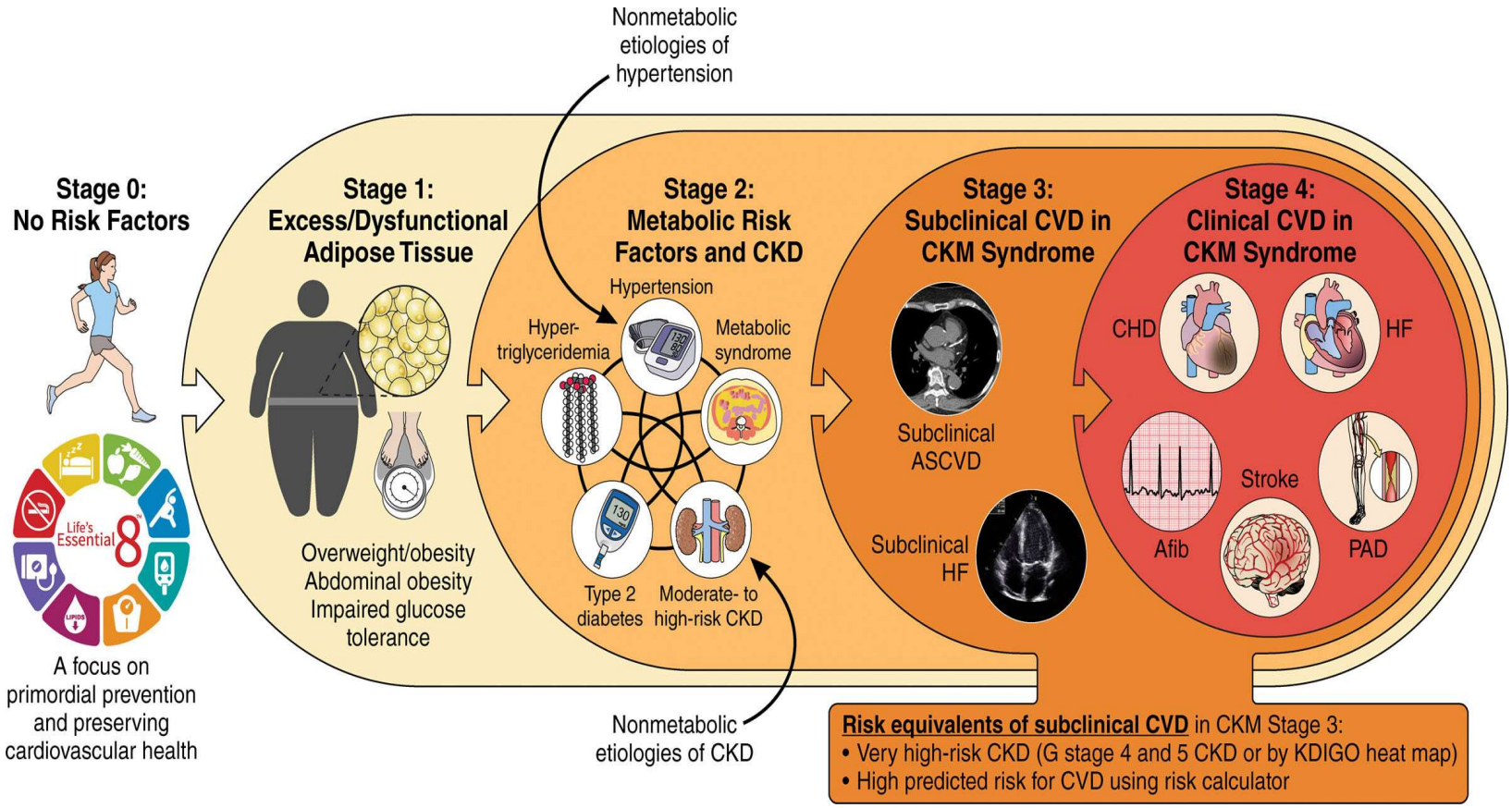
- EPIC Dot Phrases - .KFRE2 & .KFRE5



CKM Syndrome

Cardiovascular-Kidney-Metabolic Syndrome

Ochsner Health



Chiadi E. Ndumele. Circulation. Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association, Volume: 148, Issue: 20, Pages: 1606-1635, DOI: (10.1161/CIR.0000000000001184)

Stage 0 of CKM Syndrome

Stage 0 → Stage 1 → Stage 2 → Stage 3 → Stage 4

No risk factors

1. Healthy diet
2. Physical activity
3. Normal blood glucose
4. Healthy weight
5. Healthy lipids
6. Healthy BP
7. Nonsmoker
8. Healthy sleep

New Connected Health Solution deployed around Life's Essential 8

Patient entered data remotely collected via questionnaire + EMR data + remote monitoring data

- Maximum score is 100
- Can be collected at periodic intervals where patient can change the number through their own behavior

May require some assistance from health coach +/- dietitian

We can measure effectiveness of our health maintenance remote patient management interventions based on the AHA Life's Essential 8 Heart Health score

Stage 0 of CKM Syndrome

Stage 0 → Stage 1 → Stage 2 → Stage 3 → Stage 4

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1. Healthy diet
2. Physical activity
3. Normal blood glucose
4. Healthy weight
5. Healthy lipids
6. Healthy BP
7. Nonsmoker
8. Healthy sleep

Stage 0 = absence of risk factors for chronic conditions

Objectively quantifiable by a heart health score and capable of signaling when a risk factor becomes apparent that could trigger deployment of one or more digital solutions

Stage 1 of CKM Syndrome

Stage 0 | Stage 1 | Stage 2 | Stage 3 | Stage 4

No risk factors

1. Healthy diet
2. Physical activity
3. Normal blood glucose
4. Healthy weight
5. Healthy lipids
6. Healthy BP
7. Nonsmoker
8. Healthy sleep

Central obesity
Waist circumference
- > 88 cm women
- > 102 cm men

Overweight/obesity
- BMI 25-29.9
- BMI ≥ 30

Prediabetes
- A1c 5.7 to 6.4

Impaired FBG
- FBG 100-125

Impaired glucose tolerance
- Abnormal OGTT

Digital Weight Management Solution

- Performance assessed by objective rates of improvement in waist circumference, weight reduction (aiming for 5-10% reduction), A1c, and fasting blood glucose
- Also, via % of patients improving from stage 1 to 0 or worsening from stage 1 to 2

Can track improvement/regression to stage 0 as well as worsening/progression from stage 1 to 2

Once patients are diagnosed with CKD, that diagnosis remains in their record and they cannot go back to stage 1 CKM syndrome, but they can improve within stage 2 CKM syndrome based on their chart location within the KDIGO heat map

For example, a patient can go from CKD G3b/A3 within the heat map to stage G3a/A1 with appropriate therapy, but are still stage 2 CKM syndrome

Stage 2 of CKM Syndrome

Stage 0 | Stage 1 | Stage 2 | Stage 3 | Stage 4

No risk factors

1. Healthy diet
2. Physical activity
3. Normal blood glucose
4. Healthy weight
5. Healthy lipids
6. Healthy BP
7. Nonsmoker
8. Healthy sleep

Central obesity

Waist circumference
- > 88 cm women
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Overweight/obesity
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Prediabetes
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Impaired glucose tolerance
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Metabolic risk factors + CKD
- HTN
- DM2
- Hypertriglyceridemia
- Metabolic syndrome
- Moderate- to high-risk CKD (see KDIGO heat map)

Existing digital solutions for HTN, DM2, Dyslipidemia New digital solution for CKD

Bundled as new digital CKM solution

Performance assessed by:
- Individual control rates
- Statin Tx for DM2 (with % reduction for primary prevention or targeted LDL goal for secondary prevention)
- Bundled control rates (% of BP at goal x % of controlled A1c x % of targeted LDL goal + nonsmoking status)
- % of patients maintained in stage 2 versus progressing to stage 3
- Targeted reductions in albuminuria and eGFR (measured via UACR and eGFR position changes on KDIGO heal map, moving between moderate and higher risk)
- ED visits/K
- Admissions/K
- Readmission rate
- Total cost of care (PMPM)

Can track improvement/regression to stage 0 as well as worsening/progression from stage 1 to 2

Stage 3 of CKM Syndrome

Stage 0 | Stage 1 | Stage 2 | Stage 3 | Stage 4

No risk factors

1. Healthy diet
2. Physical activity
3. Normal blood glucose
4. Healthy weight
5. Healthy lipids
6. Healthy BP
7. Nonsmoker
8. Healthy sleep

Central obesity
Waist circumference
- > 88 cm women
- > 102 cm men

Overweight/obesity
- BMI 25-29.9
- BMI ≥ 30

Prediabetes
- A1c 5.7 to 6.4

Impaired FBG
- FBG 100-125

Impaired glucose tolerance
- Abnormal OGTT

Metabolic risk factors + CKD
- HTN
- DM2
- Hypertriglyceridemia
- Metabolic syndrome
- Moderate- to high-risk CKD (see KDIGO heat map)

Subclinical CVD
Subclinical ASCVD
- CAC score > 0
- Calcifications on imaging

Subclinical HF
- AHA Stage A or B HF

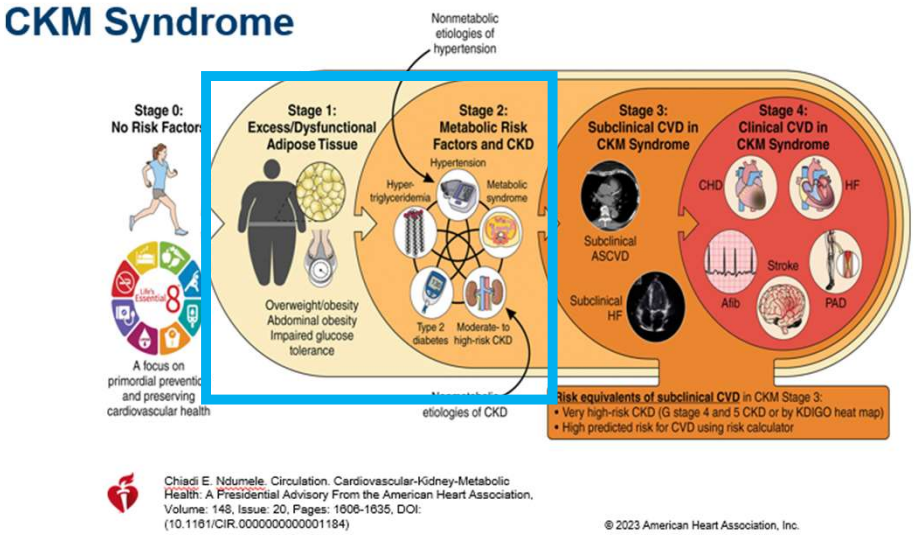
Existing digital solutions for HTN, DM2, Dyslipidemia
New digital solution for CKD
New digital solution for HF

Can track improvement/regression to stage 0 as well as worsening/progression from stage 1 to 2

Irreversible, but can slow progression from 3 to 4

Clinical Excellence: Unified Scope Planning

- Transition from program specific disease management goals to comprehensive medication management services for **cardiometabolic conditions** based on compelling indications including chronic kidney disease, heart failure, hyperlipidemia and ASCVD risk reduction
  - **Patient must have hypertension, diabetes or obesity to enroll**
  - Improved Best Practice pathways for HTN, DM and obesity management with enhanced review for complication comorbidities
  - Comprehensive health coaching and patient education organized around Life's 8 Essential Behaviors
  - New enhanced RD consult model scaled across all programs
  - Ability for patients to "dial up" care by reaching out for a health coach or dietitian consult
- Therapy goals include **disease control** (HTN, DM), **close care gaps** (ASCVD reduction, albuminuria management, HFrEF: DM, statin, MRA, MRA titration, SGLT2 use, ACE/ARB, ACE/ARB HF), **lab monitoring** (increased frequency of labs based on acuity).



Chiadi E. Ndumele. Circulation. Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association, Volume: 148, Issue: 20, Pages: 1606-1635, DOI: (10.1161/CIR.0000000000001184)

Ochsner digital medicine

SGLT2 inhibitors in CKD

Ochsner Health

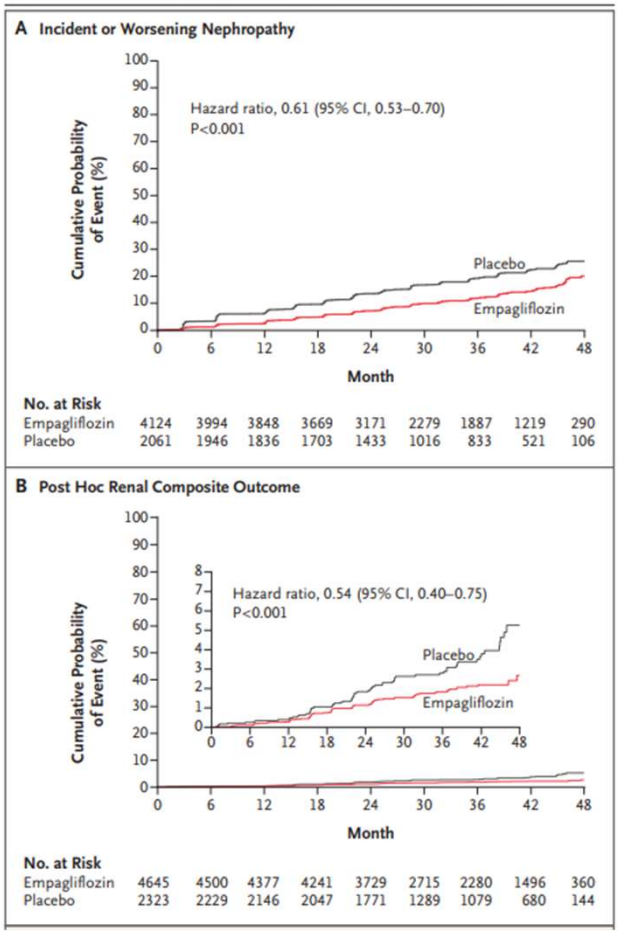
SGLT2 inhibitors

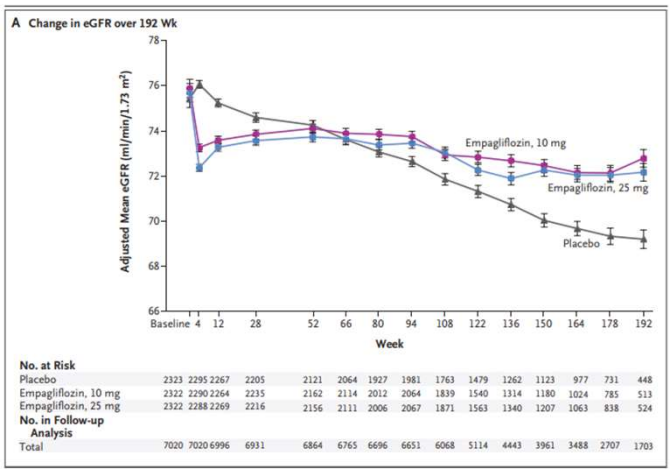
- Na-glucose co-transporter inhibitor leading to both natriuresis and glycosuria
- Acts like a diuretic, improves blood pressure, associated with cardiovascular risk reduction, and reduced heart failure admissions
- **Patient education**
  - May cause more frequent urination → stay well hydrated
  - May lower BP → watch for orthostasis if on BP medications
  - Increased risk of fungal infection and vulvovaginal yeast infections → consider stopping if 3 or more infections occur
  - Adequate hygiene in skin folds of patients with a large pannus
- Euglycemic DKA
  - More common in LADA rather than true type 2 DM
  - More common in patients where insulin dose was decreased significantly to make way for SGLT2i
- GLP1 RA more potent glucose lowering and more weight loss than SGLT2i

EMPA-REG OUTCOME (Empagliflozin)

Findings: In patients with type 2 diabetes and high cardiovascular risk, empagliflozin was associated with slower progression of kidney disease and lower rates of clinically relevant renal events than was placebo when added to standard of care

- Incident or worsening nephropathy 12.7% in the empagliflozin group vs 18.8% in the placebo group (hazard ratio in the empagliflozin group, 0.61; 95% confidence interval, 0.53 to 0.70; P<0.001)
- Doubling of the serum creatinine level occurred in 70 of 4645 patients 1.5% in the empagliflozin vs 2.6% in the placebo group, a significant relative risk reduction of 44%
- Renal-replacement therapy was initiated 0.3% in the empagliflozin group vs 0.6% in the placebo group, representing a 55% lower relative risk in the empagliflozin group



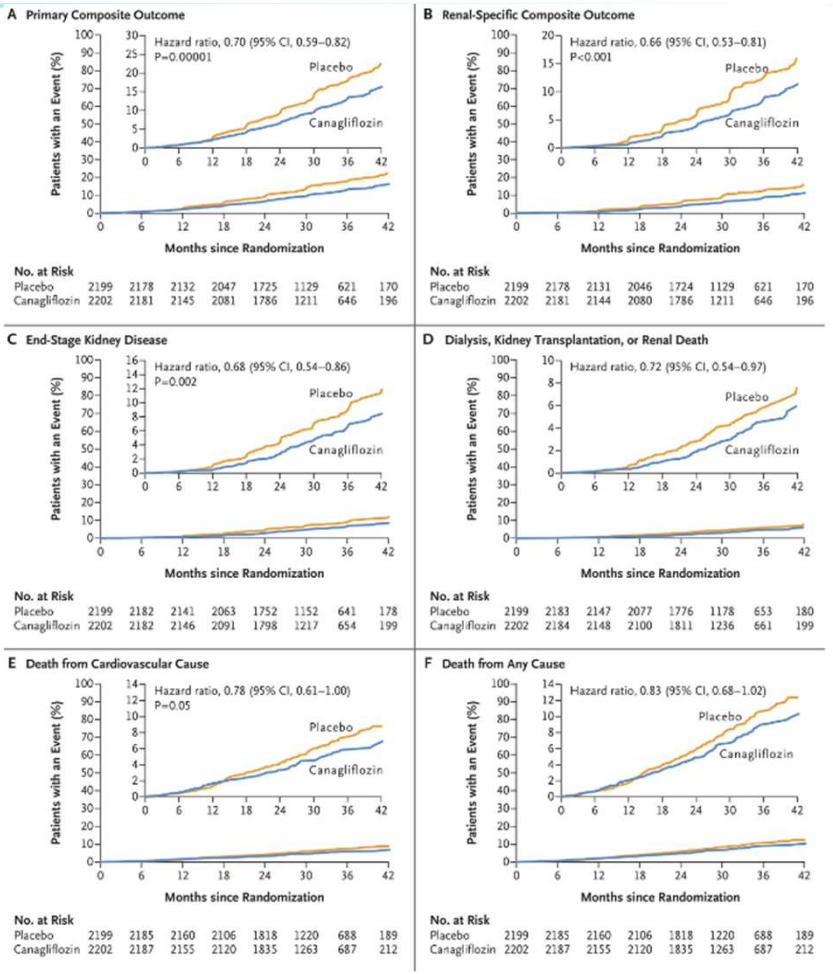


Wanner et. Al. N Engl J Med 2016;375:323-334

CREDENCE (Canagliflozin)

In patients with type 2 diabetes and kidney disease, the risk of kidney failure and cardiovascular events was lower in the canagliflozin group than in the placebo group at a median follow-up of 2.62 years.

- Relative risk of the primary composite outcome of ESKD, doubling of the serum creatinine level, or renal or cardiovascular death was significantly lower in the canagliflozin group was 30% lower than in the placebo group (hazard ratio, 0.70; 95% confidence interval [CI], 0.59 to 0.82; P=0.00001)
- Relative risk of the renal-specific composite of ESKD, a doubling of the creatinine level, or death from renal causes was lower by 34% (hazard ratio, 0.66; 95% CI, 0.53 to 0.81; P<0.001)
- Relative risk of ESKD was lower by 32% (hazard ratio, 0.68; 95% CI, 0.54 to 0.86; P=0.002)
- Canagliflozin group also had a lower risk of cardiovascular death, myocardial infarction, or stroke (hazard ratio, 0.80; 95% CI, 0.67 to 0.95; P=0.01) and hospitalization for heart failure (hazard ratio, 0.61; 95% CI, 0.47 to 0.80; P<0.001)

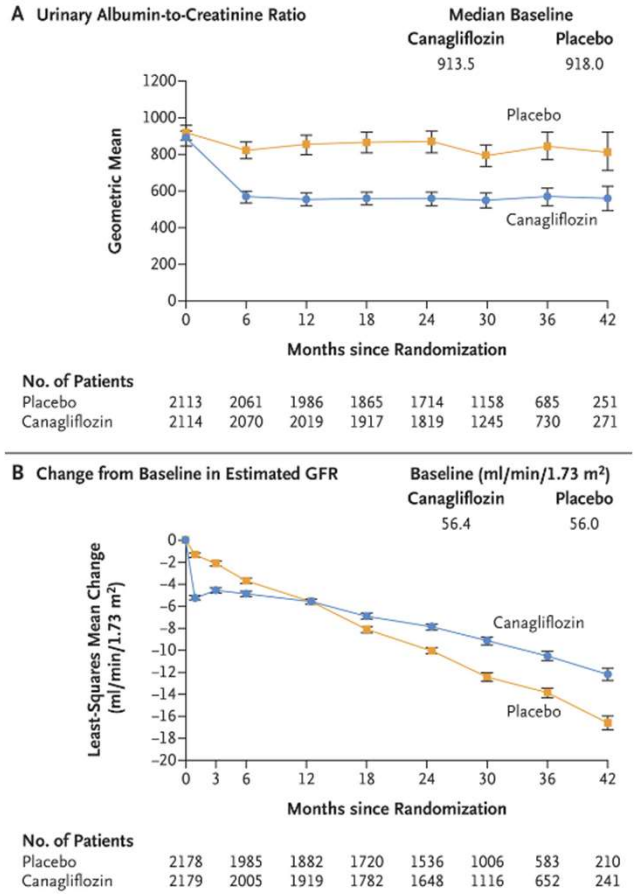


Perkovic et al. NEJM 2019;380:2295-2306

CREDENCE (Canagliflozin)

Levels were lower in the canagliflozin group for
- SBP ~3.3 mm Hg
- DBP ~.8 mm Hg

- Urinary albumin-to-creatinine ratio (UACR) was lower by 31% (95% CI, 26 to 35) on average during follow-up in the canagliflozin group
- Change in the estimated GFR slope was less in the canagliflozin group than in the placebo group (–3.19±0.15 vs. –4.71±0.15 ml per minute per 1.73 m^2 per year), for a between-group difference of 1.52 ml per minute per 1.73 m^2 per year (95% CI, 1.11 to 1.93)

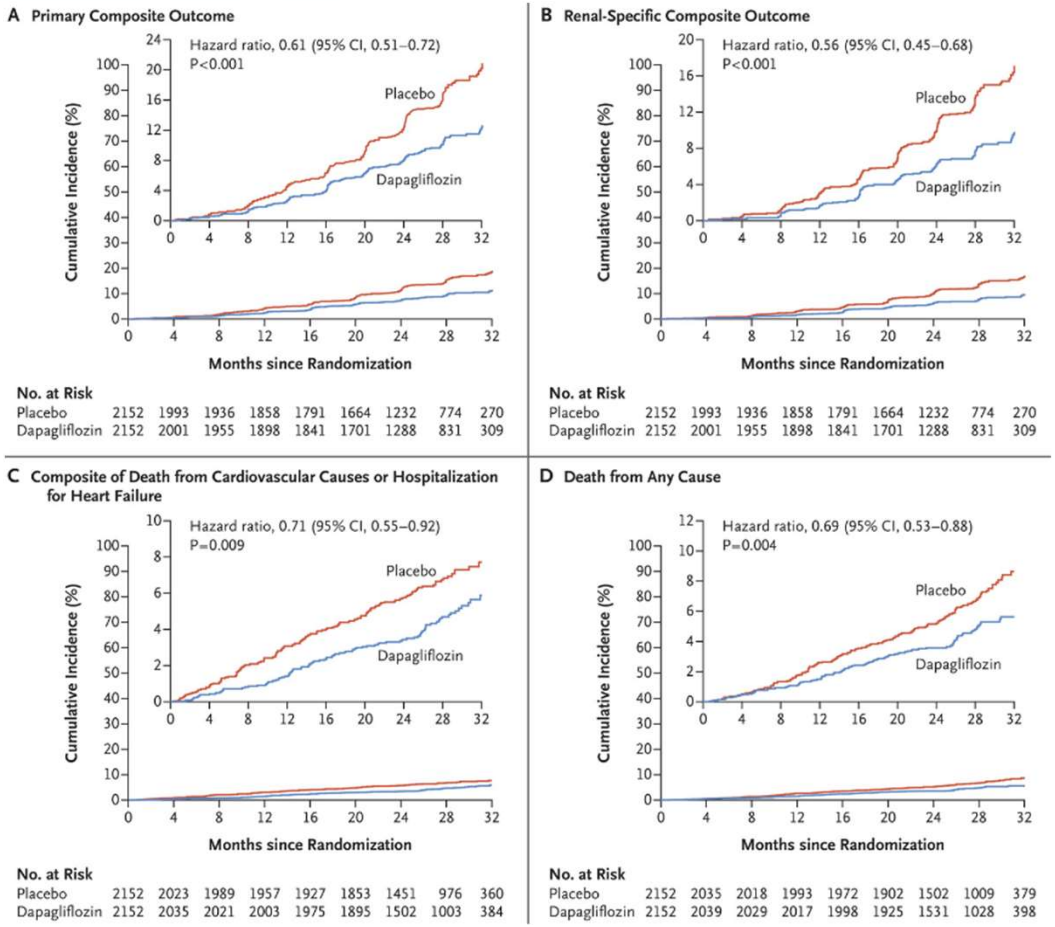


Perkovic et al. N Engl J Med 2019;380:2295-2306

DAPA-CKD (Dapagliflozin)

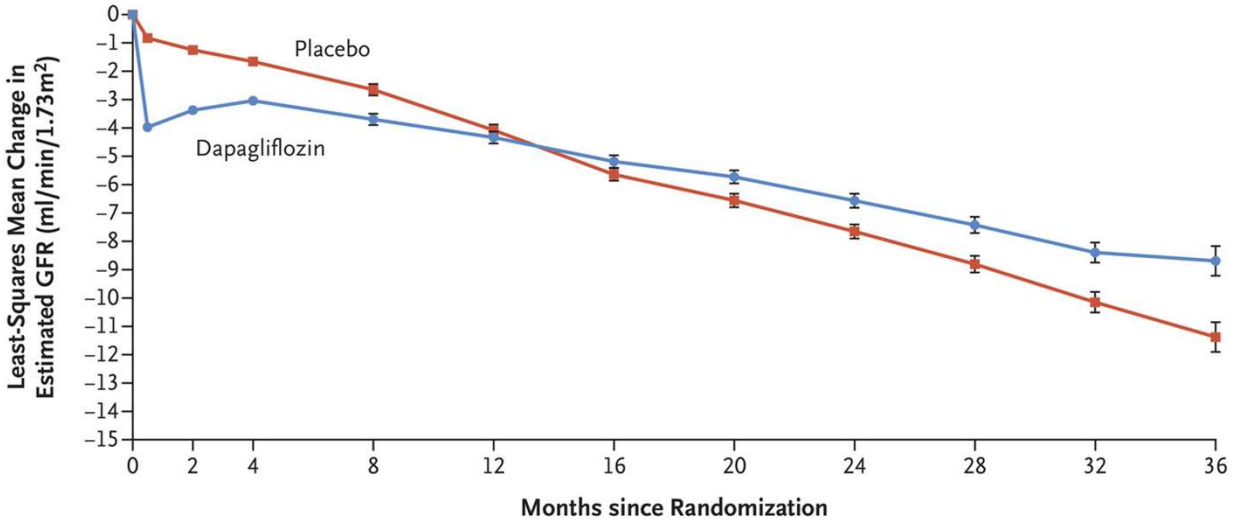
Among patients with chronic kidney disease, regardless of the presence or absence of diabetes, the risk of a composite of a sustained decline in the estimated GFR of at least 50%, end-stage kidney disease, or death from renal or cardiovascular causes was significantly lower with dapagliflozin than with placebo

- Primary composite outcome of a sustained decline in the estimated GFR of at least 50%, end-stage kidney disease, or death from renal or cardiovascular causes occurred in 9.2% in the dapagliflozin group 14.5% in the placebo group (hazard ratio, 0.61; 95% confidence interval [CI], 0.51 to 0.72; P<0.001)
- The incidence of each secondary outcome was lower in the dapagliflozin group than in the placebo group



Hiddo et. al. N Engl J Med 2020;383:1436-1446

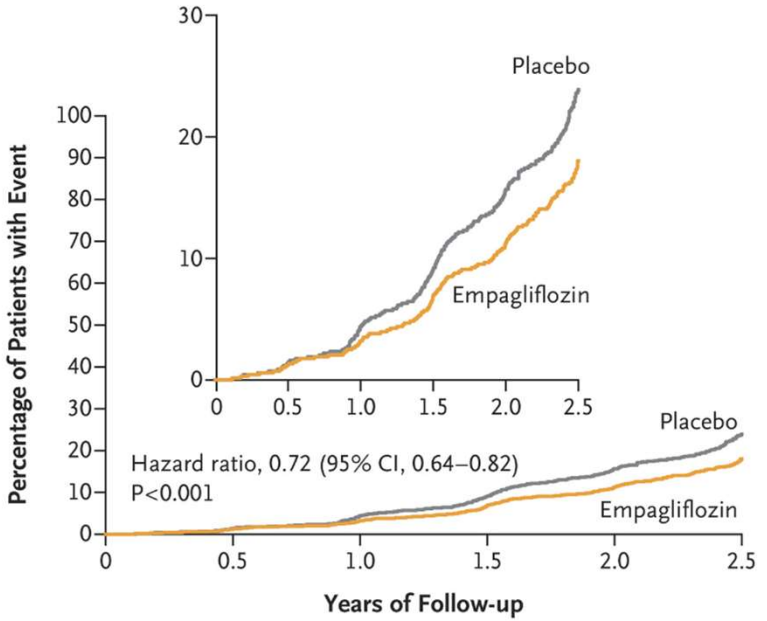
DAPA-CKD (Dapagliflozin)



EMPA KIDNEY

Among a wide range of patients with chronic kidney disease who were at risk for disease progression, empagliflozin therapy led to a lower risk of progression of kidney disease or death from cardiovascular causes than placebo

- Progression of kidney disease or death from cardiovascular causes occurred in 13.1% in the empagliflozin group and in 16.9% in the placebo group (hazard ratio, 0.72; 95% confidence interval [CI], 0.64 to 0.82; P<0.001)
- After we controlled the familywise error rate for the three key secondary outcomes, the rate of first and subsequent hospitalizations from any cause was lower in the empagliflozin group than in the placebo group (24.8 vs. 29.2 hospitalizations per 100 patient-years; hazard ratio, 0.86; 95% CI, 0.78 to 0.95; P=0.003)



No. at Risk						
Placebo	3305	3250	3129	2243	1496	592
Empagliflozin	3304	3252	3163	2275	1538	624

EMPA-KIDNEY Collaborative Group N Engl J Med 2023;388:117-127

GLP1 Receptor Agonists

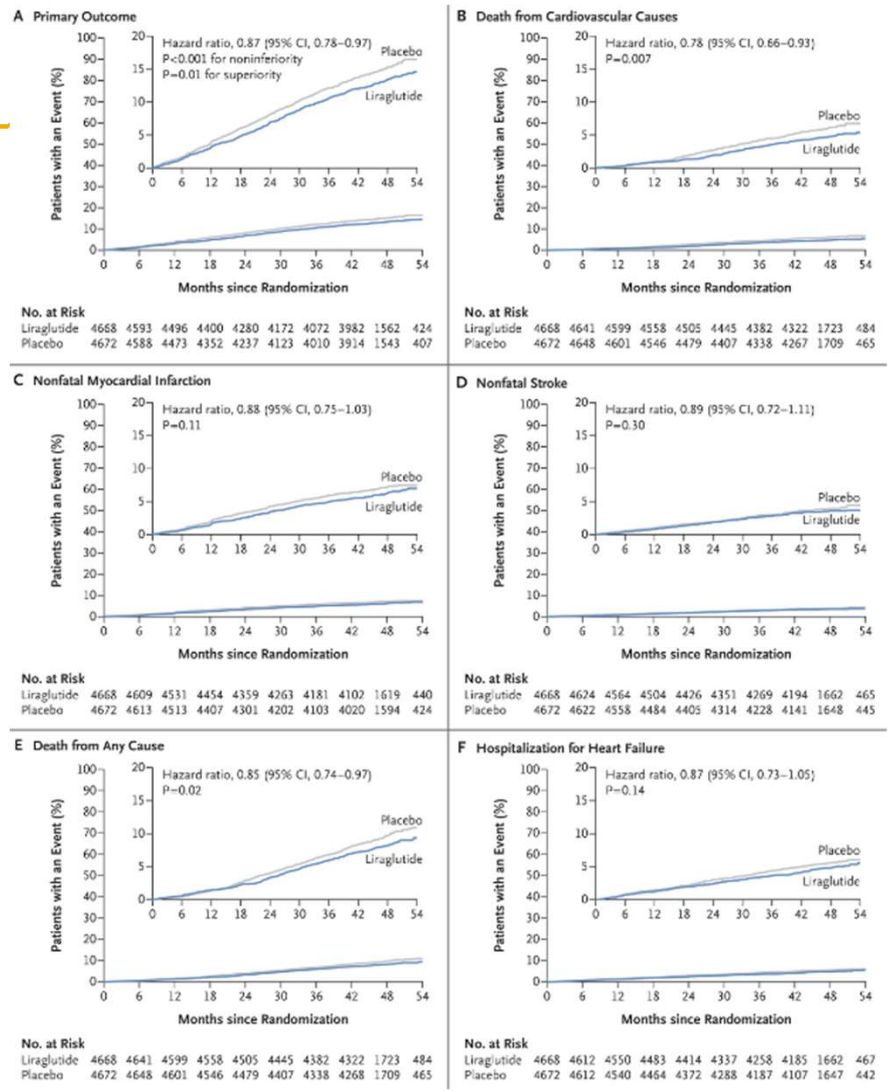
Ochsner Health

The Leader Trial

Findings: In the time-to-event analysis, the **rate of** the **first occurrence of death from cardiovascular causes**, nonfatal myocardial infarction, or nonfatal stroke **among patients with type 2 diabetes** mellitus was **lower with liraglutide than with placebo**

Major inclusion criteria:

- ✓ **Age ≥ 50 years with at least one cardiovascular coexisting condition:**
  - ✓ Coronary heart disease
  - ✓ Cerebrovascular disease
  - ✓ Peripheral vascular disease
  - ✓ Chronic kidney disease of stage 3 or greater, or
  - ✓ Chronic heart failure of NY Heart Association class II or III)
- ✓ **Age ≥ 60 years or more with at least one cardiovascular risk factor:**
  - ✓ Microalbuminuria or proteinuria
  - ✓ Hypertension and left ventricular hypertrophy
  - ✓ Left ventricular systolic or diastolic dysfunction
  - ✓ Ankle–brachial index < 0.9



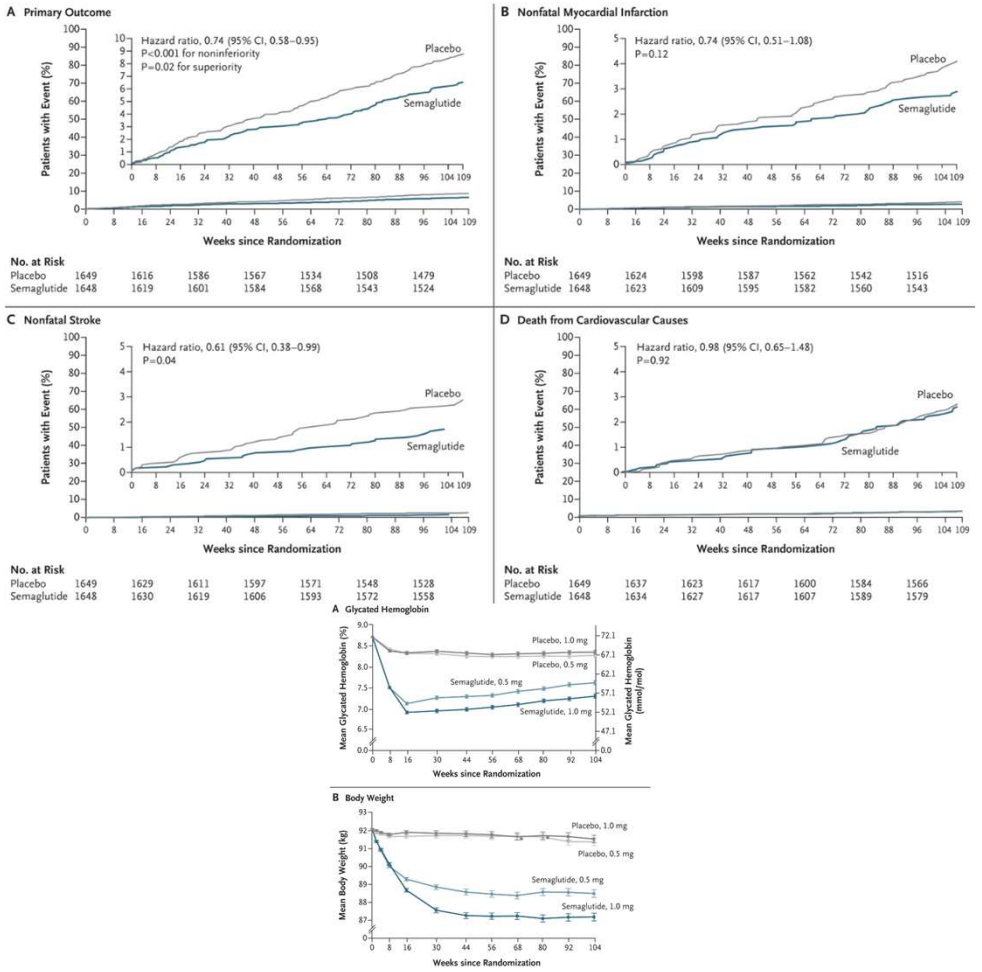
Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes
Marso, et al. for the LEADER Steering Committee on behalf of the LEADER Trial Investigators
N Engl J Med 2016;375:311-322

Sustain 6 Trial

Findings: In **patients with type 2 diabetes** with **high cardiovascular risk**, the **rate of cardiovascular death**, nonfatal myocardial infarction, or nonfatal stroke was **significantly lower among patients receiving semaglutide** than among those receiving placebo, an outcome that confirmed the noninferiority of semaglutide

Key inclusion criteria:

- ✓ **Age ≥ 50 years with established cardiovascular disease:**
  - ✓ Previous cardiovascular, cerebrovascular, or peripheral vascular disease
  - ✓ Chronic heart failure (NY Heart Association class II or III)
  - ✓ Chronic kidney disease of stage 3 or higher
- ✓ **Age ≥ 60 years with at least one cardiovascular risk factor**



Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes
Steven P. Marso, M.D., et.. al. for the SUSTAIN-6 Investigators
N Engl J Med 2016;375:1834-1844

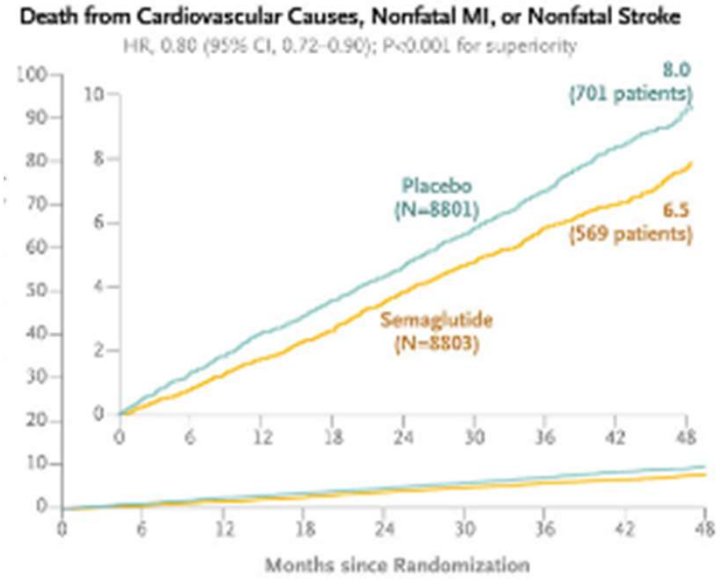
SELECT Trial

Findings: In **patients** with **preexisting cardiovascular disease** and **overweight or obesity** but **without diabetes**, **weekly** subcutaneous **semaglutide** at a dose of 2.4 mg was superior to placebo in **reducing the incidence of death from cardiovascular causes**, nonfatal myocardial infarction, or nonfatal stroke at a mean follow-up of 39.8 months

Key inclusion criteria:

- ✓ Age ≥ 45 years
- ✓ BMI ≥ 27
- ✓ Established cardiovascular disease

Cardiovascular disease = previous myocardial infarction, previous stroke or symptomatic peripheral arterial disease



Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes
Lincoff, M.D. et. al. for the SELECT Trial Investigators
N Engl J Med 2023;389:2221-2232

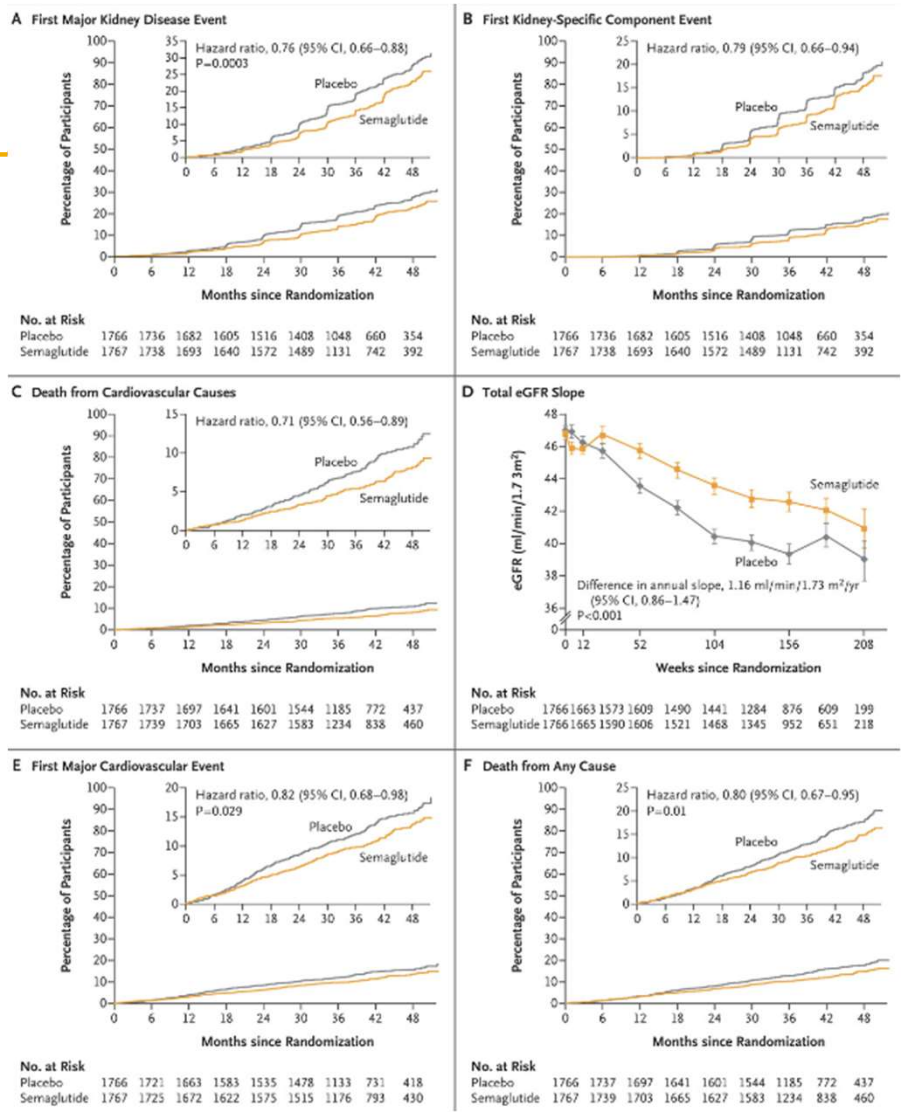
The FLOW Trial

Findings: **Semaglutide reduced** the **risk** of clinically important **kidney outcomes** and **death from cardiovascular causes** in **patients with type 2 diabetes** and **chronic kidney disease**

Key inclusion criteria:

- ✓ Adults with type 2 diabetes (glycated hemoglobin level, ≤10%) with:
  - ✓ High-risk chronic kidney disease and receiving a stable maximal labeled dose (or the maximal dose without unacceptable side effects) of RAS inhibitors (angiotensin-converting–enzyme inhibitor or angiotensin-receptor blocker)

Kidney disease = eGFR of 25 to 75 ml per minute with a urinary albumin-to-creatinine ratio > 300 and < 5000 if the eGFR was ≥ 50 ml per minute or a urinary albumin-to-creatinine ratio > 100 and < 5000 if the eGFR was 25 to < 50 ml per minute



Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes
Perkovic et. al. for the FLOW Trial Committees and Investigators
N Engl J Med 2024;391:109-121

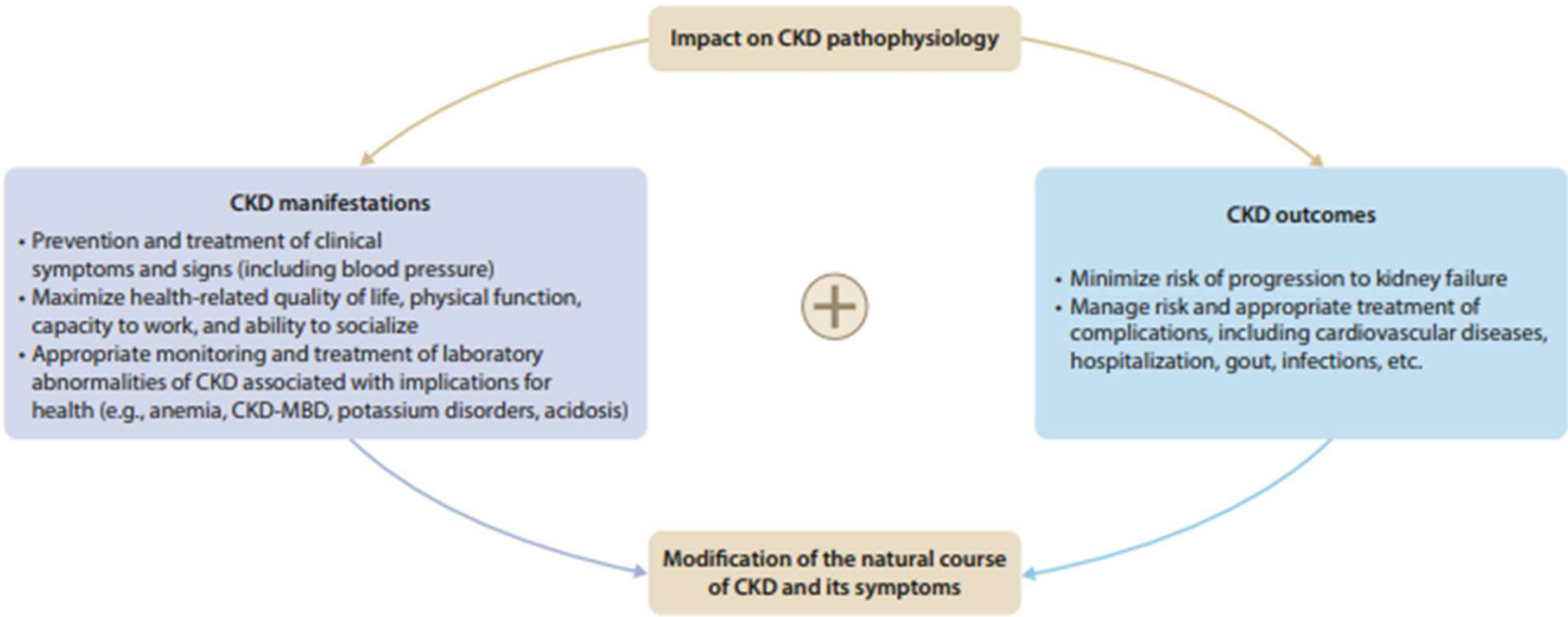
CKD Management

Medication management

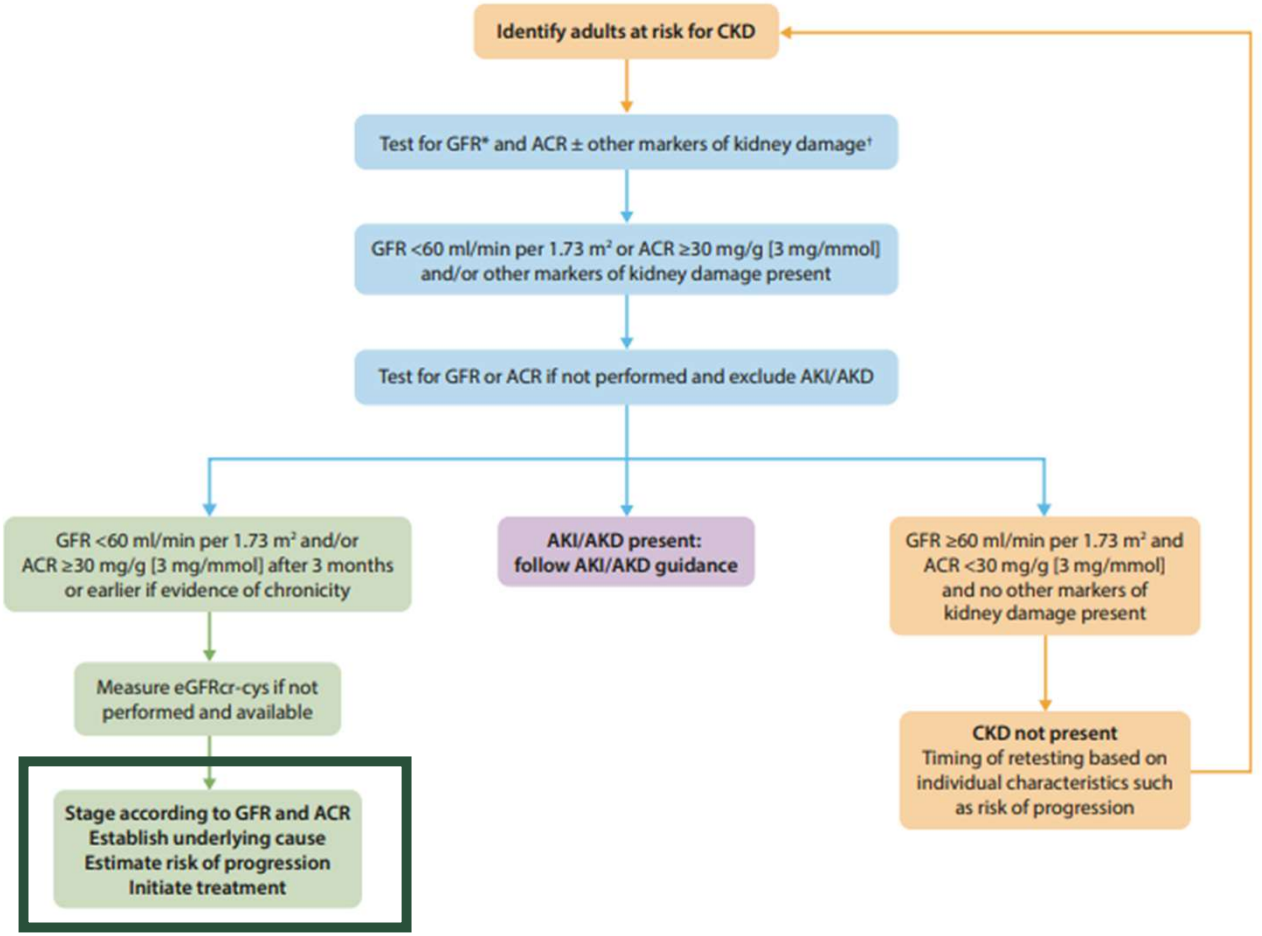
- Preserve eGFR
- Reduce or stabilize albuminuria
- Improve CVD risk

Ochsner Health

From Upstream Manifestations to Downstream Outcomes



Screening Algorithm for CKD



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Cause (C)*
GFR (G)†
Albuminuria (A)†

GFR categories (mL/min per 1.73 m²) Description and range				Albuminuria categories Description and range		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
	G1	Normal or high	≥90	Screen 1	Treat 1	Treat and refer 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat and refer 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat and refer 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat and refer 3	Treat and refer 3
	G4	Severely decreased	15–29	Treat and refer† 3	Treat and refer† 3	Treat and refer 4+
	G5	Kidney failure	<15	Treat and refer 4+	Treat and refer 4+	Treat and refer 4+

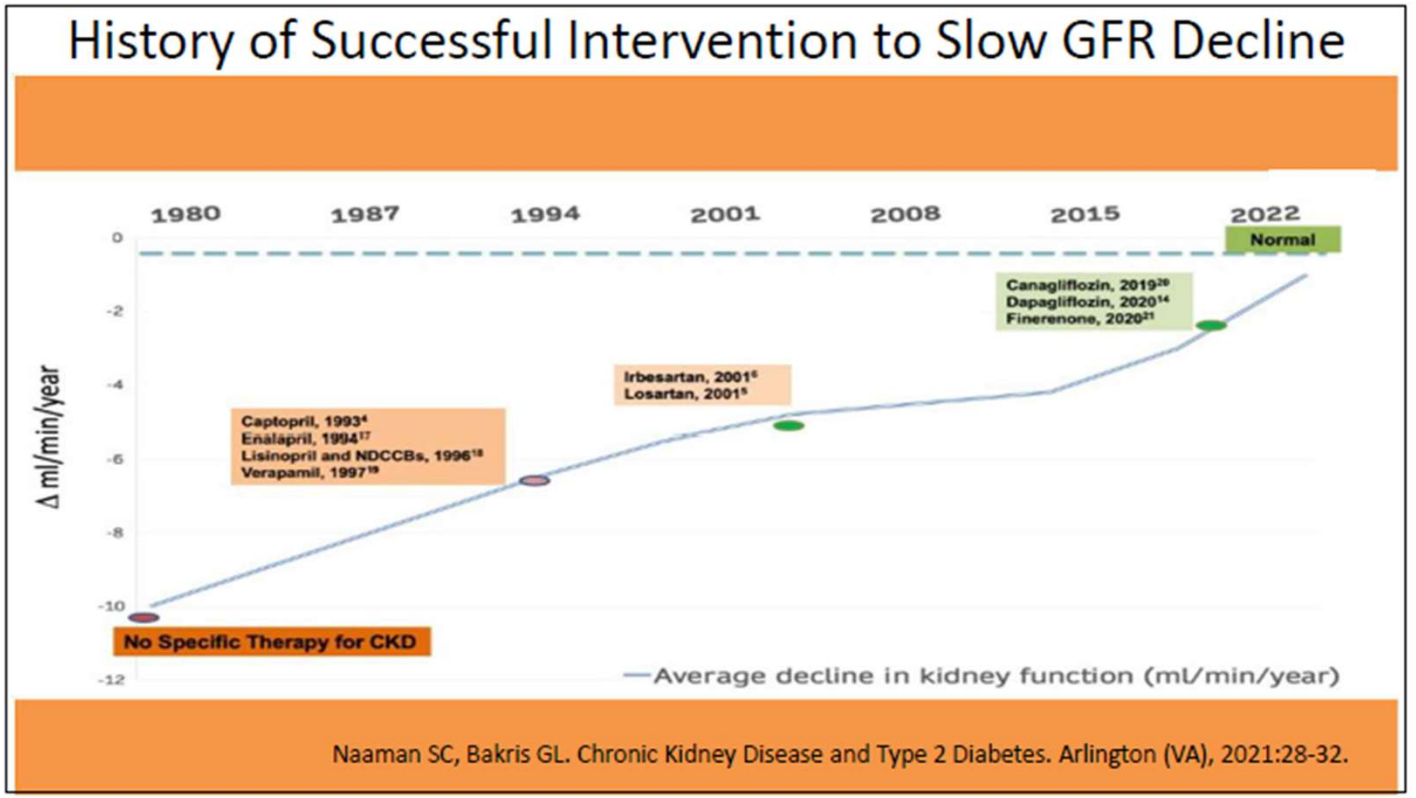
Low risk (if no other markers of kidney disease, no CKD)
Moderately increased risk
High risk
Very high risk

Slowing CKD Progression

Avg ↓ in eGFR (mL/min/year)

- No specific Tx = 10
- ACE inhibitor = ~7
- ARB = ~5
- SGLT2 inhibitor = ~2 to 3
- NS-MRA = ~1 to 2

Lower number is better!



ACE = angiotensin converting enzyme

ARB = angiotensin receptor blocker

SGLT2 = sodium-glucose Cotransporter 2

NS-MRA = nonsteroidal mineralocorticoid receptor antagonist

Importance of UACR

- Progressive risk of multiple adverse outcomes with declining eGFR and rising UACR
- Depicts the rising risk of given outcome with progression down and to the right of the KDIGO heat map

Overall	Urine albumin-creatinine ratio, mg/g					Urine albumin-creatinine ratio, mg/g				
eGFRcr	<10	10–29	30–299	300–999	1000+	<10	10–29	30–299	300–999	1000+
	All-cause mortality: 82 cohorts 26 444 384 participants; 2 604 028 events					Myocardial infarction: 64 cohorts 22 838 356 participants; 451 063 events				
105+	1.6	2.2	2.9	4.3	5.8	1.1	1.4	2.0	2.7	3.8
90–104	ref	1.3	1.8	2.6	3.1	ref	1.3	1.6	2.2	3.2
60–89	1.0	1.3	1.7	2.2	2.8	1.1	1.3	1.6	2.2	3.1
45–59	1.3	1.6	2.0	2.4	3.1	1.4	1.7	2.0	2.8	3.7
30–44	1.8	2.0	2.5	3.2	3.9	1.9	2.0	2.4	3.2	4.3
15–29	2.8	2.8	3.3	4.1	5.6	2.7	3.1	3.1	4.2	5.1
<15	4.6	5.0	5.3	6.0	7.0	4.6	5.6	4.8	6.0	6.0
	Cardiovascular mortality: 76 cohorts 26 022 346 participants; 776 441 events					Stroke: 68 cohorts 24 746 436 participants; 461 785 events				
105+	1.4	2.0	3.0	4.1	5.4	1.2	1.6	2.2	3.1	4.3
90–104	ref	1.3	1.9	2.7	3.6	ref	1.3	1.6	2.4	3.1
60–89	1.0	1.4	1.7	2.4	3.2	1.1	1.3	1.7	2.2	3.0
45–59	1.4	1.7	2.2	2.8	3.8	1.4	1.6	1.9	2.3	2.9
30–44	2.0	2.3	2.8	3.7	4.6	1.6	1.7	2.0	2.4	3.0
15–29	3.2	3.1	3.5	5.0	6.5	1.8	2.1	2.1	2.7	3.0
<15	6.1	6.4	6.4	7.3	8.2	3.2	2.8	2.9	3.2	3.8
	Kidney failure with replacement therapy: 57 cohorts 25 466 956 participants; 158 846 events					Heart failure: 61 cohorts 24 603 016 participants; 1 132 443 events				
105+	0.5	1.2	2.9	7.7	25	1.2	1.7	2.7	4.2	6.9
90–104	ref	1.8	4.3	12	43	ref	1.3	2.0	2.8	4.2
60–89	2.3	4.9	10	27	85	1.1	1.4	1.9	2.7	4.2
45–59	13	19	37	89	236	1.6	1.8	2.4	3.4	5.0
30–44	50	58	115	240	463	2.2	2.5	3.1	4.2	6.5
15–29	283	301	443	796	1253	3.6	3.5	4.1	5.8	8.1
<15	770	1040	1618	2297	2547	5.1	5.7	5.8	7.9	9.9
	Acute kidney injury: 49 cohorts 23 914 614 participants; 1 408 929 events					Atrial fibrillation: 50 cohorts 22 886 642 participants; 1 068 701 events				
105+	1.0	1.6	2.4	3.7	5.5	1.1	1.3	1.7	2.4	3.5
90–104	ref	1.4	2.1	3.2	5.0	ref	1.2	1.5	1.9	2.3
60–89	1.6	2.2	3.1	4.3	6.7	1.0	1.2	1.4	1.7	2.2
45–59	3.5	4.0	5.1	6.9	9.0	1.2	1.3	1.5	1.8	2.4
30–44	5.6	5.9	6.8	8.6	11	1.4	1.5	1.7	2.0	2.4
15–29	8.3	8.0	8.5	9.9	10	1.9	1.8	2.0	2.6	3.0
<15	8.5	11	7.9	5.5	5.7	2.6	2.5	3.1	3.6	4.2
	Hospitalization: 49 cohorts 25 426 722 participants; 8 398 637 events					Peripheral artery disease: 54 cohorts 24 830 794 participants; 378 924 events				
105+	1.4	1.7	2.1	2.1	2.3	0.9	1.4	1.9	2.8	5.0
90–104	ref	1.1	1.3	1.5	1.7	ref	1.3	1.9	2.8	4.3
60–89	1.0	1.1	1.3	1.5	1.8	1.0	1.3	1.8	2.5	3.8
45–59	1.3	1.3	1.5	1.7	2.1	1.5	1.7	2.1	2.9	4.2
30–44	1.5	1.5	1.6	1.9	2.3	2.0	1.9	2.5	3.6	5.0
15–29	1.8	1.8	1.9	2.4	2.8	3.3	3.3	3.8	5.7	8.1
<15	2.7	2.8	3.0	3.2	3.8	9.1	9.0	9.6	13	14

Holistic Approach to CKD Treatment

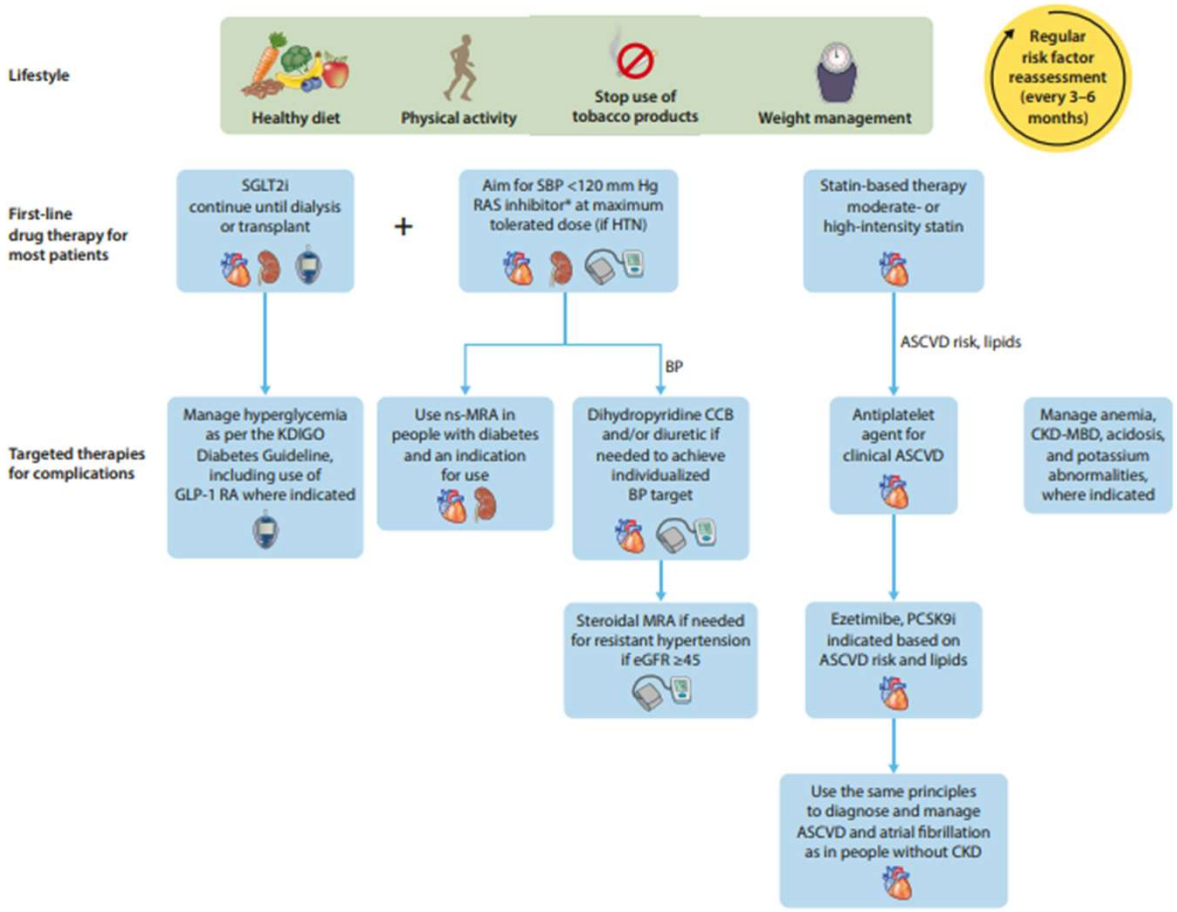
Pharmacotherapeutic Nephroprotection
SGLT2i +/- GLP1RA

+

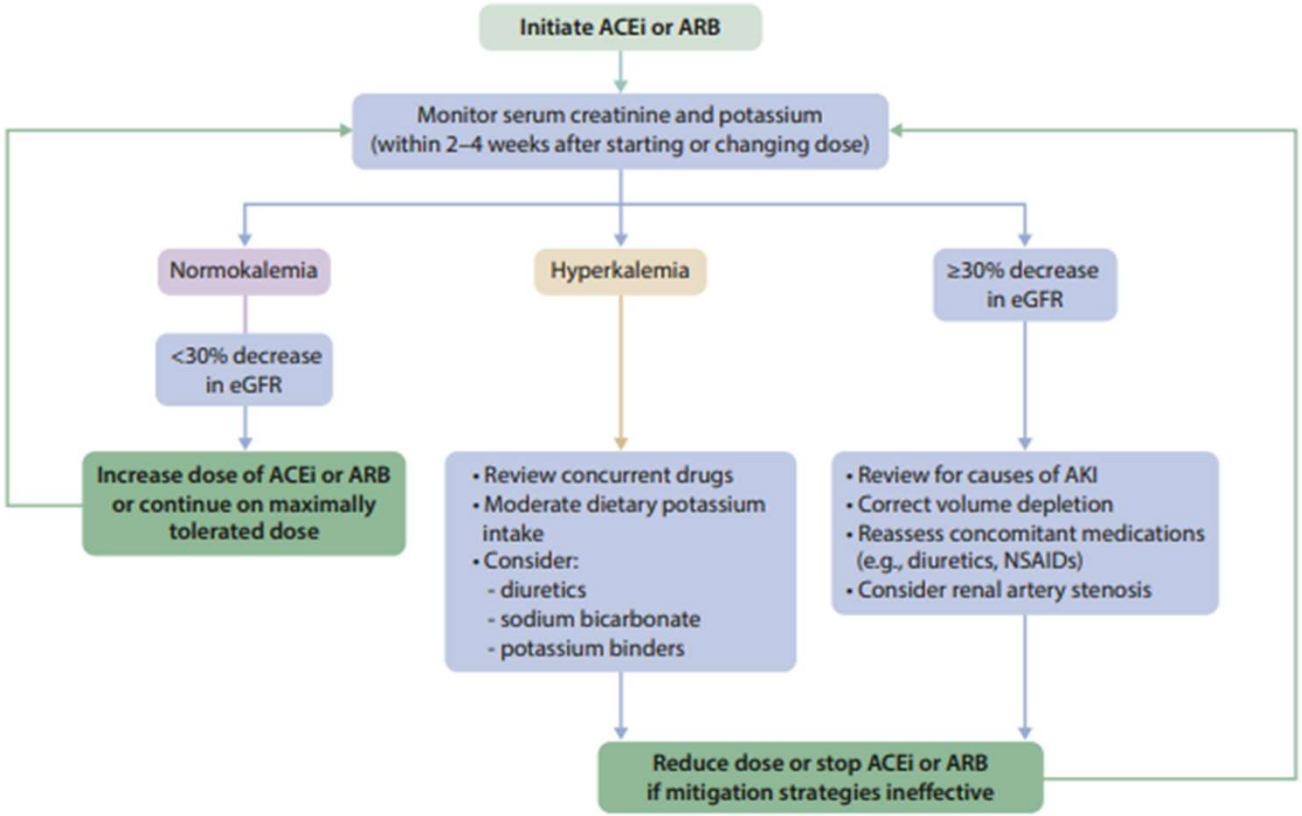
BP control
SBP < 120

+

Lipids
ASCVD Risk Reduction
Statin therapy
2° Prevention



Monitoring K and eGFR after starting RAAS blockers



Nonsteroidal MRA – Finerenone

- A nonsteroidal MRA may be added to a RASi and an SGLT2i for treatment of T2D and CKD in adults
- To mitigate risk of hyperkalemia, select people with consistently normal serum potassium concentration and monitor serum potassium regularly after initiation of a nonsteroidal MRA

K^+ ≤4.8 mmol/l

- Initiate finerenone
  - 10 mg daily if eGFR 25–59 ml/min/1.73 m^2
  - 20 mg daily if eGFR ≥60 ml/min/1.73 m^2
- Monitor K^+ at 1 month after initiation and then every 4 months
- Increase dose to 20 mg daily, if on 10 mg daily
- Restart 10 mg daily if previously held for hyperkalemia and K^+ now ≤5.0 mmol/l

K^+ 4.9–5.5 mmol/l

- Continue finerenone 10 mg or 20 mg
- Monitor K^+ every 4 months

K^+ >5.5 mmol/l

- Hold finerenone
- Consider adjustments to diet or concomitant medications to mitigate hyperkalemia
- Recheck K^+
- Consider reinitiation if/when K^+ ≤5.0 mmol/l

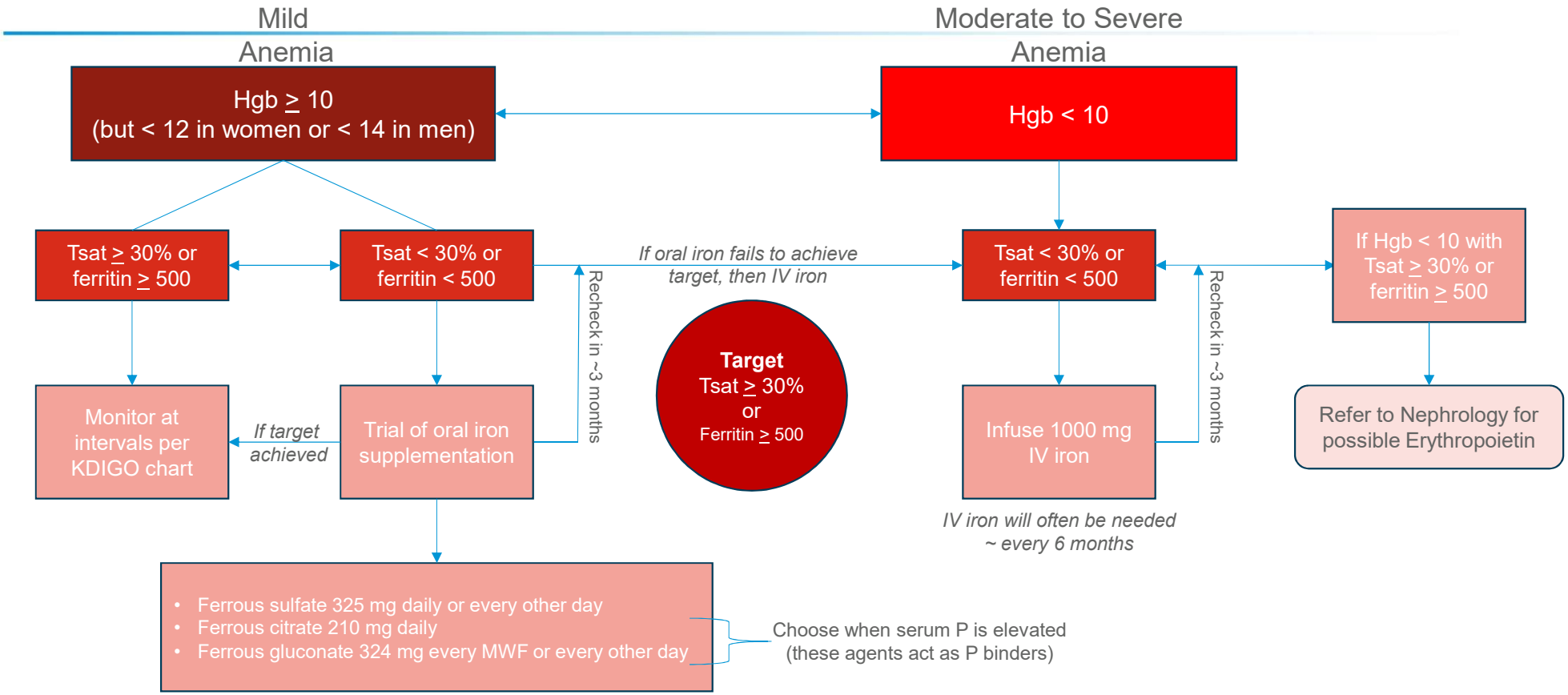
Anemia of CKD Workflow

Ochsner Health

Anemia of CKD

- Check these labs at intervals indicated per KDIGO heat map
  - **CBC**
  - **Iron & TIBC (Tsat = Transferrin Saturation = Iron/TIBC)**
  - **Ferritin**

- If Hgb < 10, but Tsat and ferritin are normal, and no other obvious cause of anemia is found, then check **erythropoietin level**


Mild Anemia
Moderate to Severe Anemia
Hgb ≥ 10 (but < 12 in women or < 14 in men)
Hgb < 10
Tsat ≥ 30% or ferritin ≥ 500
Tsat < 30% or ferritin < 500
If oral iron fails to achieve target, then IV iron
Tsat < 30% or ferritin < 500
If Hgb < 10 with Tsat ≥ 30% or ferritin ≥ 500
Recheck in ~3 months
Target Tsat ≥ 30% or Ferritin ≥ 500
Monitor at intervals per KDIGO chart
If target achieved
Trial of oral iron supplementation
Infuse 1000 mg IV iron
Recheck in ~3 months
Refer to Nephrology for possible Erythropoietin
IV iron will often be needed ~ every 6 months
• Ferrous sulfate 325 mg daily or every other day
• Ferrous citrate 210 mg daily
• Ferrous gluconate 324 mg every MWF or every other day
Choose when serum P is elevated (these agents act as P binders)

CKD-MBD Workflow

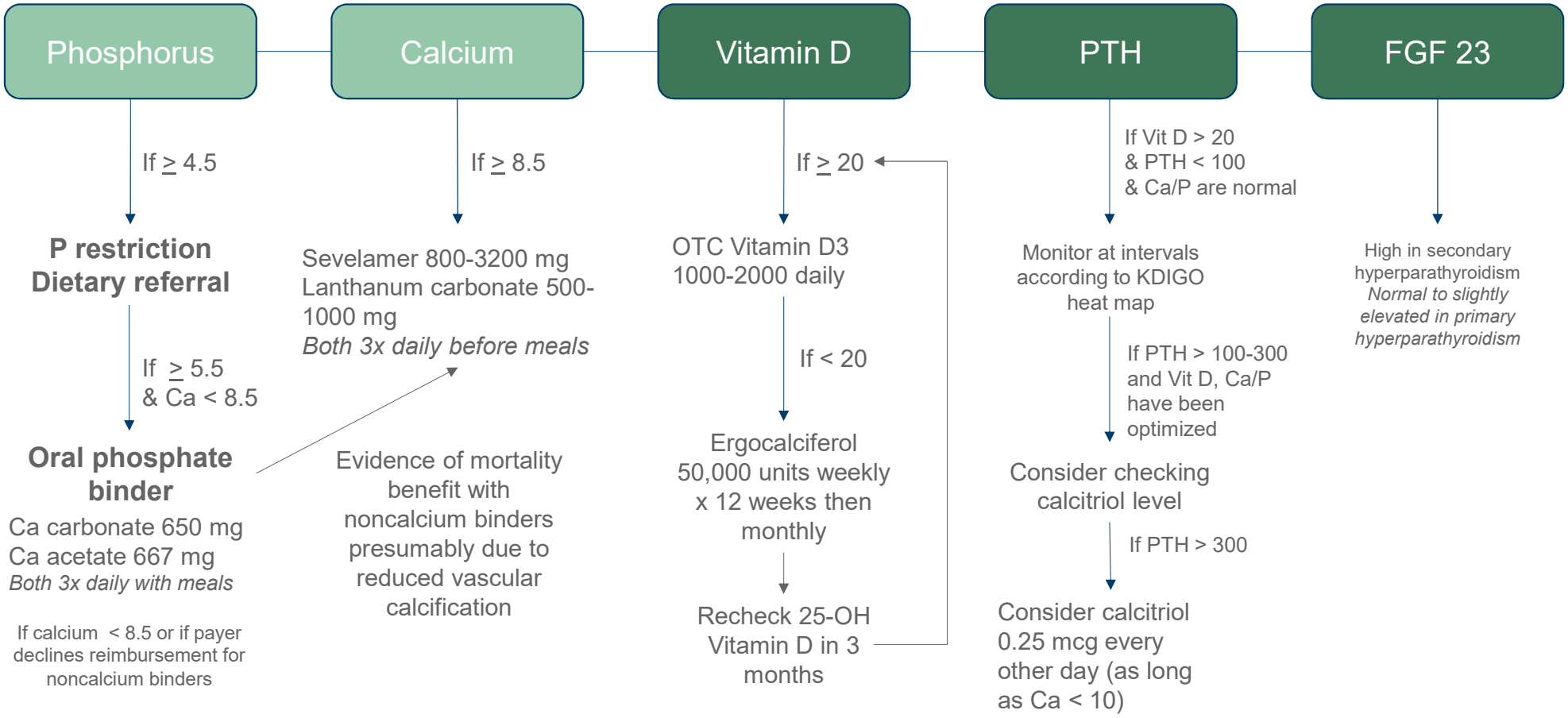
Ochsner Health

CKD-MBD

- Check these labs at intervals indicated per KDIGO heat map
  - **Phosphorus**
  - **Calcium**
  - **25-OH Vitamin D**
  - **PTH**

- In cases where there is difficulty discriminating between primary hyperparathyroidism and secondary hyperparathyroidism, then consider checking calcitriol and FGF-23
  - Calcitriol – high in primary, low in secondary
  - FGF-23 – normal or slightly elevated in primary, high in secondary

Lab monitoring & management in CKD-MBD



Depiction of Smart Phrase in Epic

Assessment & Plan:

UACR

Microalb/Creat Ratio

Date	Value	Ref Range	Status
09/06/2024	127.4 (H)	0.0 - 30.0 ug/mg	Final

Acid-base

CO2

Date	Value	Ref Range	Status
08/06/2024	26	23 - 29 mmol/L	Final

Blood Pressure (Goal < 130/80)

BP Readings from Last 3 Encounters:

04/09/24	114/70
03/15/24	118/76
10/20/23	102/67

Renal Function Panel

BMP

Lab Results

Component	Value	Date
NA	141	08/06/2024
K	4.1	08/06/2024
CL	107	08/06/2024
CO2	26	08/06/2024
BUN	20	08/06/2024
CREATININE	1.3	08/06/2024
CALCIUM	10.6 (H)	08/06/2024
ANIONGAP	8	08/06/2024
EGFRNORACEVR	>60.0	08/06/2024

Mineral Bone Disorder

Lab Results

Component	Value	Date
PTH	79.7 (H)	09/06/2024
CALCIUM	10.6 (H)	08/06/2024
PHOS	3.6	02/29/2024

66-year-old man with DM, HTN, Hyperlipidemia, ASCVD, Obesity, Primary Hyperparathyroidism, and CKD

Meds: Semaglutide 1 mg, Empagliflozin 10 mg, Zetia/Simvastatin 10/40 mg, Amlodipine/Valsartan 10/320 mg

Anemia

Lab Results

Component	Value	Date
WBC	6.08	08/06/2024
HGB	14.7	08/06/2024
HCT	44.9	08/06/2024
MCV	88	08/06/2024
PLT	180	08/06/2024

Lab Results

Component	Value	Date
IRON	55	08/25/2023
TRANSFERRIN	252	08/25/2023
TIBC	373	08/25/2023
FESATURATED	15 (L)	08/25/2023

Lab Results

Component	Value	Date
FERRITIN	67	08/25/2023

DM

Lab Results

Component	Value	Date
HGBA1C	6.0 (H)	09/06/2024

Lipid Management

Lab Results

Component	Value	Date
LDLCALC	55.8 (L)	03/07/2024

KFRE2 & KFRE5

KFRE 2-Year: 0.2% at 9/6/2024 9:26 AM
Calculated from:
Serum Creatinine: 1.3 mg/dL at 8/6/2024 1:57 PM
Urine Albumin Creatinine Ratio: 127.4 ug/mg at 9/6/2024 9:26 AM
Age: 66 years
Sex: Male at 9/6/2024 9:26 AM
Has CKD-3 to CKD-5: Yes

KFRE 5-Year: 0.6% at 9/6/2024 9:26 AM
Calculated from:
Serum Creatinine: 1.3 mg/dL at 8/6/2024 1:57 PM
Urine Albumin Creatinine Ratio: 127.4 ug/mg at 9/6/2024 9:26 AM
Age: 66 years
Sex: Male at 9/6/2024 9:26 AM
Has CKD-3 to CKD-5: Yes

CKD stage G2/A2 eGFR >60 mL/min
KDIGO Heat Map Color yellow
Lab monitoring Interval Frequency once annually

Depiction of Smart Phrase in Epic

UACR

Microalb/Creat Ratio

Date	Value	Ref Range	Status
04/25/2024	262.1 (H)	0.0 - 30.0 ug/mg	Final

Acid-base

CO2

Date	Value	Ref Range	Status
07/16/2024	20 (L)	23 - 29 mmol/L	Final

Blood Pressure (Goal < 130/80)

BP Readings from Last 3 Encounters:

08/09/24	128/76
05/03/24	136/84
03/22/24	138/86

Renal Function Panel

BMP

Lab Results

Component	Value	Date
NA	138	07/16/2024
K	4.3	07/16/2024
CL	109	07/16/2024
CO2	20 (L)	07/16/2024
BUN	21	07/16/2024
CREATININE	1.4	07/16/2024
CALCIUM	10.3	07/16/2024
ANIONGAP	9	07/16/2024
EGFRNORACEVR	42.8 (A)	07/16/2024

Mineral Bone Disorder

Lab Results

Component	Value	Date
PTH	170.4 (H)	04/25/2024
CALCIUM	10.3	07/16/2024
CAION	1.36	01/26/2011
PHOS	3.0	04/25/2024

61-year-old woman with DM, HTN, Hyperlipidemia, Primary hyperparathyroidism, and CKD

Meds: Metformin ER 2000 mg, Empagliflozin 25 mg, Semaglutide 1 mg, Tresiba 26 units, Amlodipine/Valsartan 10/320 mg, Spironolactone 50 mg, Atorvastatin 40 mg

Anemia

Lab Results

Component	Value	Date
WBC	6.42	03/21/2024
HGB	12.4	03/21/2024
HCT	40.1	03/21/2024
MCV	71 (L)	03/21/2024
PLT	159	03/21/2024

Lab Results

Component	Value	Date
IRON	84	03/21/2024
TRANSFERRIN	260	03/21/2024
TIBC	385	03/21/2024
FESATURATED	22	03/21/2024

Lab Results

Component	Value	Date
FERRITIN	60	03/21/2024

DM

Lab Results

Component	Value	Date
HGBA1C	7.3 (H)	05/22/2024

Lipid Management

Lab Results

Component	Value	Date
LDLCALC	73.2	07/16/2024

KFRE2 & KFRE5

KFRE 2-Year: 1.5% at 7/16/2024 7:25 AM
Calculated from:
Serum Creatinine: 1.4 mg/dL at 7/16/2024 7:25 AM
Urine Albumin Creatinine Ratio: 262.1 ug/mg at 4/25/2024 7:20 AM
Age: 61 years
Sex: Female at 7/16/2024 7:25 AM
Has CKD-3 to CKD-5: Yes

KFRE 5-Year: 4.7% at 7/16/2024 7:25 AM
Calculated from:
Serum Creatinine: 1.4 mg/dL at 7/16/2024 7:25 AM
Urine Albumin Creatinine Ratio: 262.1 ug/mg at 4/25/2024 7:20 AM
Age: 61 years
Sex: Female at 7/16/2024 7:25 AM
Has CKD-3 to CKD-5: Yes

CKD stage G3b/A2 eGFR 43 mL/min
KDIGO Heat Map Color red
Lab monitoring Interval Frequency 3x annually

Appendix

Ochsner Health

Life's Essential Eight Data

Profile and Health Behaviors

Profile

- Gender
- Age

Diet

- # of servings of vegetables per week
- # of servings of red meat, hamburger, bacon, sausage, per week
- # of servings of butter or cream per week
- # of servings of whole grains per week
- # of times per week fast food consumed
- # of servings of fruit per week
- # of servings of fish or shellfish/seafood per week
- # of servings of beans per week
- # of commercial sweets, candy bars, pastries, cookies, or cakes per week
- # of servings of sugar sweetened beverages per week

Needs to be inputted with the assistance of health coach or a dietitian

Physical Activity

- # of minutes of moderate intensity activity per week

Life's Essential Eight Data

Health Behaviors (continued) and Health Factors
Nicotine exposure • Smoking status Sleep duration • # of hours of sleep per 24-hour period
Health Factors Blood pressure Blood sugar (FBG or A1c) Cholesterol (Total and HDL) Body composition (height and weight) -- BMI

Life's Essential Eight Data

Social Context

- Steady employment
- Highest level of education completed
- Access to medical care
- Opportunities in neighborhood to be physically active
- Friend or family member who patient can talk with about their health
- In past 12 months, food bought not lasting long enough without money to buy more
- Health insurance coverage
- Have a PCP
- Access to neighborhood grocery store with fresh produce easily available
- History of experiencing discrimination or bullying based on race/ethnicity

Life' Essential Eight Data

Well-being

Physical & Mental Health (1st three questions of PROMIS-10)

- Patient reported general health
- Patient reported physical health
- Patient reported mental health

Collection of the entire set of data enables the calculation of Life's Essential Eight **Heart Health Score**

- Importance is that it empowers people to have agency and control over these variables through changes in their own behavior
- Behavioral modification can be enabled by embedded mental health resource support, nutritional support counseling, and health coaching to help patients overcome struggles that impede their progress toward health-related goal attainment
- Barriers, obstacles, and challenges to behavioral change need to be identified and include impaired self efficacy, low health literacy/numeracy, low tech literacy, maladaptive coping mechanisms, mental health disturbances, impaired social determinants, and history of adverse childhood experiences

My Life Check® | Welcome (heart.org)

Hypertension Algorithm

First and Second Agents

Calcium channel blocker

Primary -- Amlodipine 2.5 mg or 5 mg once daily
Secondary -- Diltiazem extended release 180 mg or 240 mg in patients with tachyarrhythmia or for antiproteinuric effect

and/or

Angiotensin receptor blocker

Primary – Olmesartan 10 mg or 40 mg; Valsartan 80 mg or 160 mg once daily; Candesartan 8 to 32 mg; Telmisartan 40 to 80 mg
Monitor BMP (K and creatinine) 2 to 4 weeks after starting drug and after dosage adjustments

Third Agent

Thiazide and/or Loop Diuretic

Primary – Chlorthalidone 12.5 mg or 25 mg once daily or Indapamide 1.25 mg or 2.5 mg or 5 mg daily
Monitor BMP frequently (Na, K, creatinine) 2 to 4 weeks after starting drug and after dosage adjustments
Secondary – HCTZ 12.5 mg or 25 mg once daily
(HCTZ 12.5 mg in frail, elderly, or vulnerability to gout attacks)
Thiazides remain effective even at eGFR < 30 mL/min, but need higher dosages

and/or

If volume overloaded/expanded (such as in CKD4)
Primary – Torsemide 10 mg or 20 mg once daily
Monitor BMP frequently (Na, K, creatinine) 2 to 4 weeks after starting drug and after dosage adjustments
Shorter acting agents (like bumetanide and furosemide) are not as effective for BP control because of increased BP lability but need to be dosed twice daily if used for BP control (dosed early AM and 6 to 8 hours later)

Hypertension Algorithm

Fourth Agent

Mineralocorticoid Antagonist

Primary – Spironolactone 12.5 mg or 25 mg once daily
Monitor BMP frequently (Na, K, creatinine) 2 to 4 weeks after starting drug and after dosage adjustments
Secondary – Eplerenone 25 mg once daily up to 50 mg bid
(if intolerance to spironolactone or if gynecomastia develops)

or

In cases of resistant HTN not due to primary aldosteronism, consider defect of the ENaC channel
Primary – Amiloride 2.5 mg x first few days then titrate up to 5 mg twice daily over 2 to 3 weeks
Monitor BMP frequently (Na, K, creatinine) 2 to 4 weeks after starting drug and after dosage adjustments

Fifth Agent

Beta-blocker or alpha-beta blocker
(*Only if history of MI or HF or tachyarrhythmia*)
Guanfacine
Transdermal Clonidine

Carvedilol 6.25 mg or 12.5 mg or 25 mg twice daily
Or Metoprolol succinate 25 to 100 mg (aim for HR 55-60)
(In patients with atrial fibrillation or other tachyarrhythmias, heart failure, history of MI, CAD/stable angina, ascending aortic aneurysm)
Guanfacine 1 mg to 2 mg daily *(especially with ADHD)*
Catapres patch TTS 1 to 3 weekly

Try to avoid hydralazine and minoxidil whenever possible
Avoid alpha-blockers (except in BPH)
Avoid short acting oral clonidine
Short acting alpha blockers like oral clonidine or the –zosins cause too much BP lability) However, can consider them in patients with BPH and prazosin has some effectiveness in patients suffering from PTSD

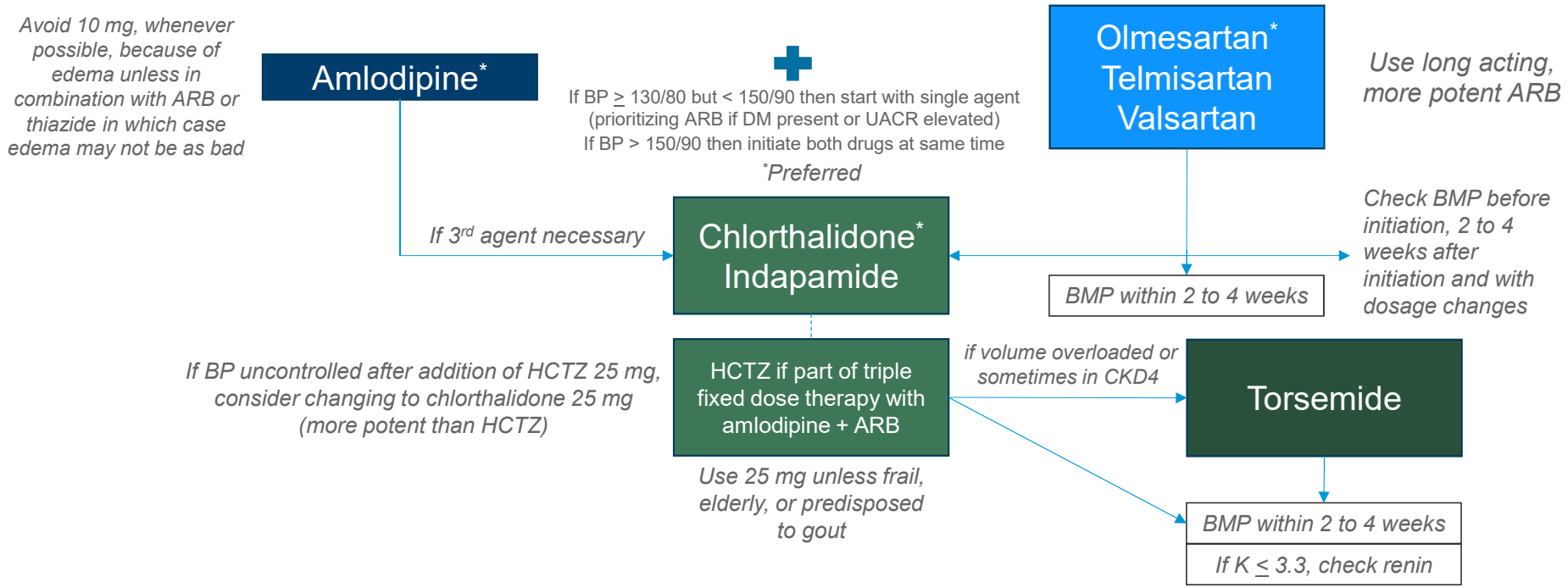
Hyperaldosteronism

- ~1 out of every 12 persons with HTN
- 20% of all cases of resistant HTN

Primary Aldosteronism
Untreated hypertension with sustained BP >150/100 mm Hg on three separate occasions
Resistant hypertension (>140/90 mm Hg) on three-drug therapy including a diuretic
Controlled blood pressure on four or more antihypertensives including a diuretic
Hypertension associated with spontaneous or diuretic-induced hypokalemia
Hypertension and an incidentally discovered adrenal mass
Hypertension and sleep apnea
Hypertension with a family history of either early-onset hypertension or cerebrovascular accident before age 40 years
Hypertension in the setting of a first-degree relative with PA

Hypertension Algorithm – 1st 3 agents

Primarily target RAAS Driven Mechanism



BP remains uncontrolled despite 3 drugs where regimen includes a diuretic **= resistant hypertension**

Hypertension Algorithm – Resistant Hypertension

BP remains uncontrolled despite 3 drugs where regimen includes a diuretic **= resistant hypertension**

For all patients

Quantify alcohol intake (> 2 drinks in men, or > 1 drink in women or age ≥ 65)

Consider STOP BANG to assess risk for OSA or adherence to CPAP if already on it

Check plasma renin activity and plasma aldosterone concentration

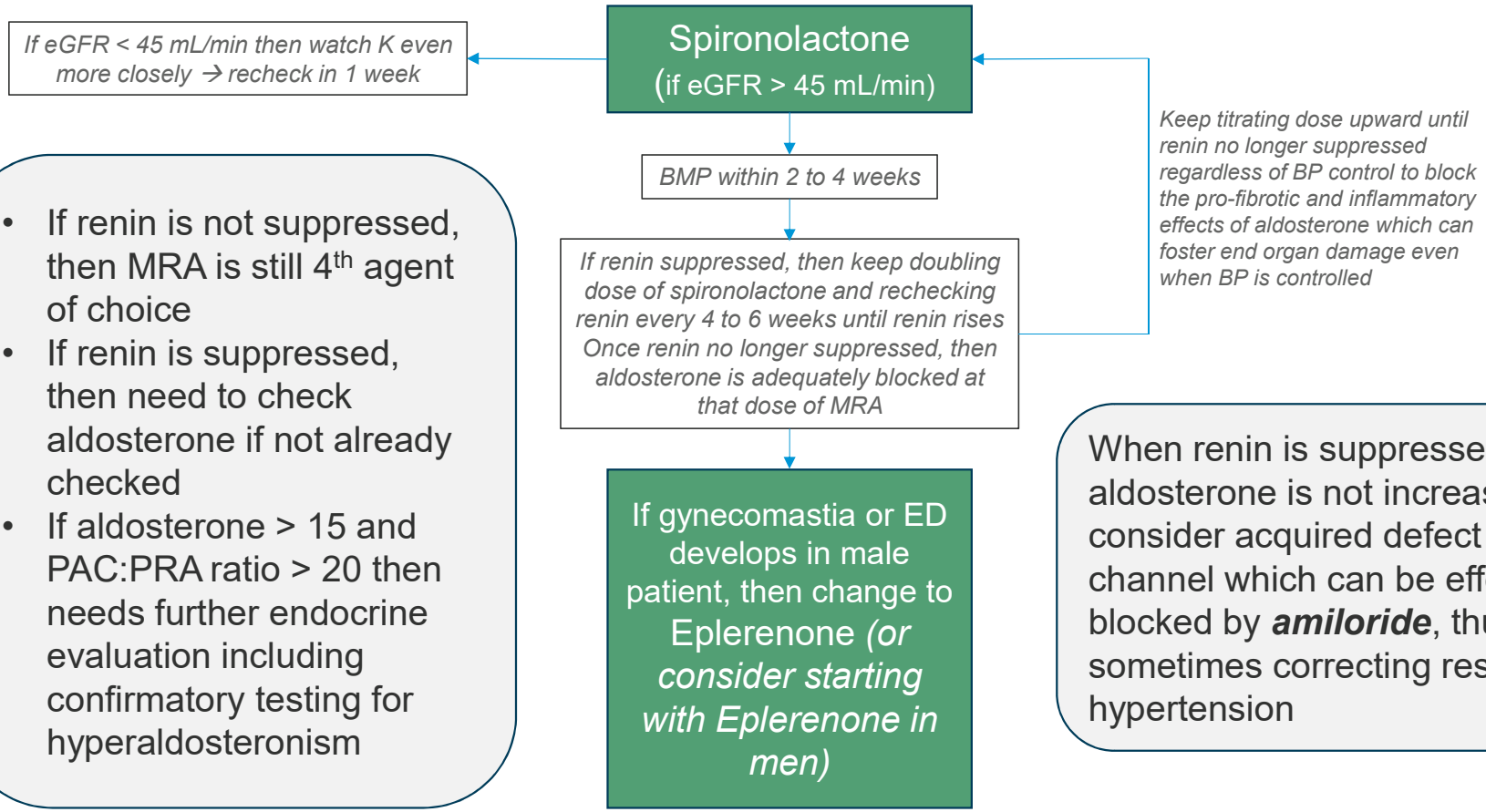
For select patients

If moon facies, supraclavicular fat pads, buffalo hump, or abdominal striae → consider evaluation for Cushing's Disease (24-hour urinary free cortisol and/or 1-mg dexamethasone suppression test

If hyperadrenergic "spells" such as flushing, palpitations, headaches, diaphoresis → consider pheochromocytoma (plasma free metanephrines)

If abdominal bruit or > 30% increase in serum creatinine following addition of ACE or ARB, then consider renovascular hypertension

Hypertension algorithm – 4th choice agent

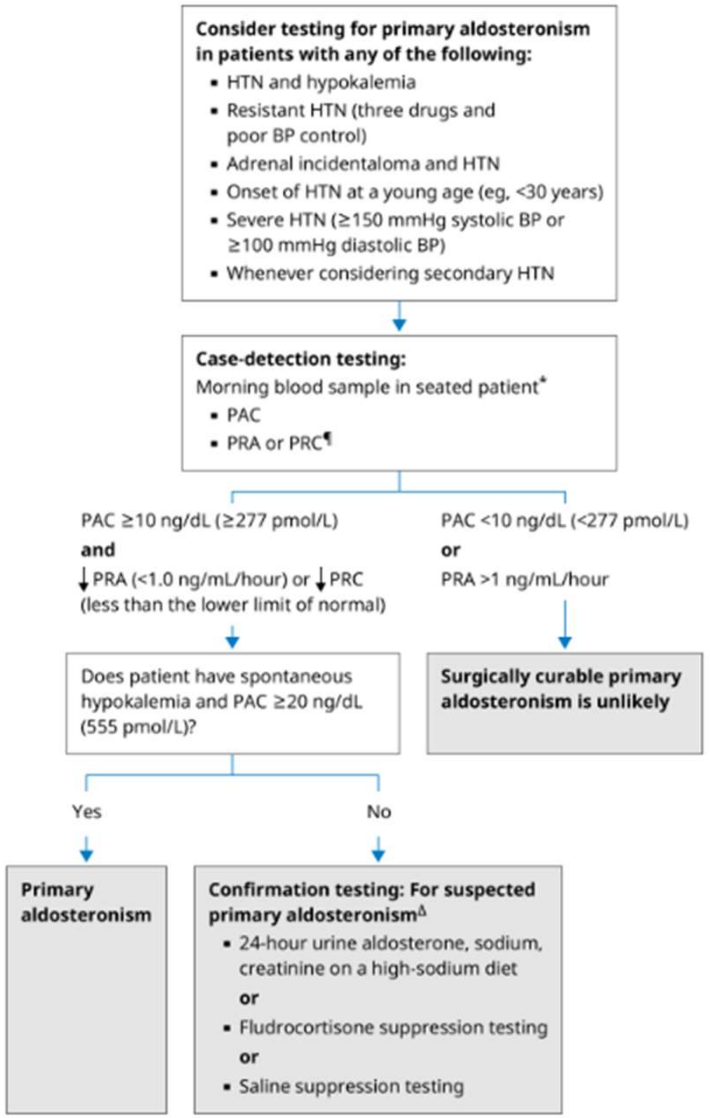


- If renin is not suppressed, then MRA is still 4th agent of choice
- If renin is suppressed, then need to check aldosterone if not already checked
- If aldosterone > 15 and PAC:PRA ratio > 20 then needs further endocrine evaluation including confirmatory testing for hyperaldosteronism

When renin is suppressed but aldosterone is not increased, then consider acquired defect of ENaC channel which can be effectively blocked by ***amiloride***, thus sometimes correcting resistant hypertension

If PA confirmed, then order CT of adrenals looking for adrenal mass and refer to Endocrine (if adrenal mass is present then next step is adrenal venous sampling to evaluate for possible aldosterone producing adenoma)

Caution: Even if testing does not confirm PA, patient may still suffer from aldosterone excess (termed apparent mineralocorticoid excess), which should still be managed medically with an MRA (i.e., Spironolactone or Eplerenone)



Hypertension agent – 5th choice agent choices

Beta-blockers are relatively poor anti-hypertensive agents and there is some evidence of increased mortality of using beta-blockers for treatment of hypertension without definitive indication

Try to avoid minoxidil and short acting agents such as hydralazine, oral clonidine, or other alpha-blockers, when possible, but in some cases can be utilized as 6th line agents

Carvedilol
Bisoprolol
Metoprolol succinate

→ *Primarily if tachyarrhythmia such as AF or SVT, but also including >10% PVCs on 24 hour-Holter, history of MI or known CAD with angina, ascending aortic aneurysm, or HFrEF*

or

Guanfacine

→ *Especially if ADD*

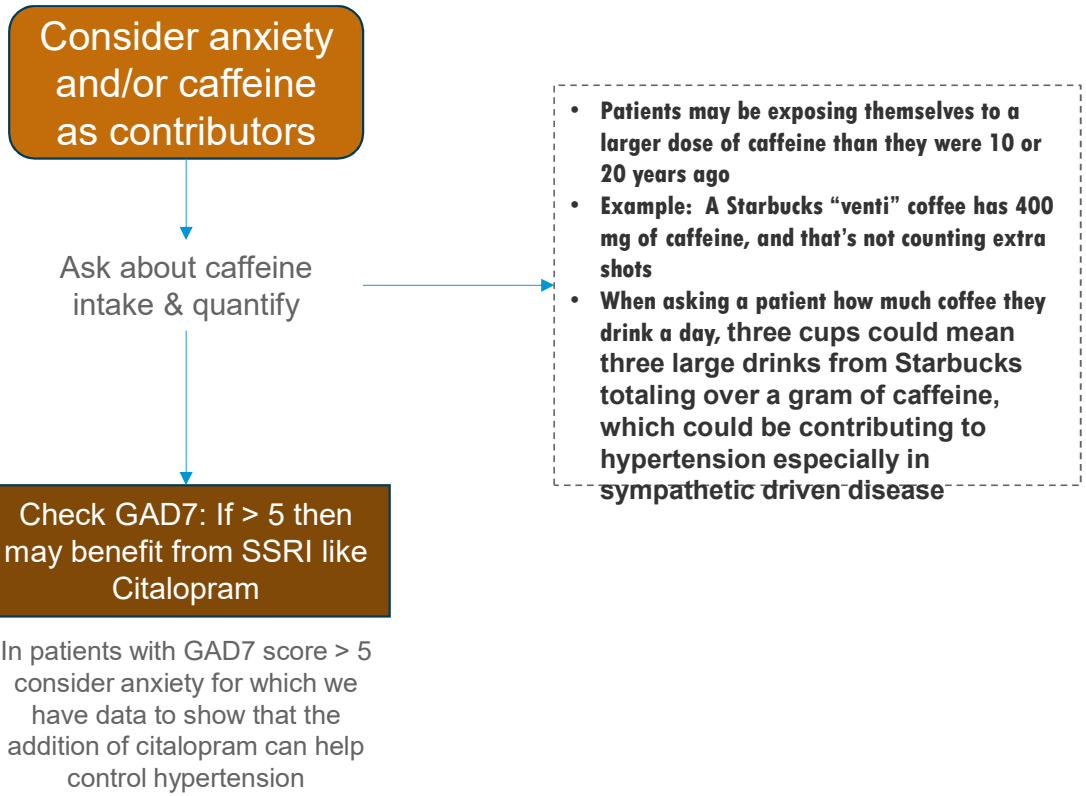
or

Transdermal clonidine

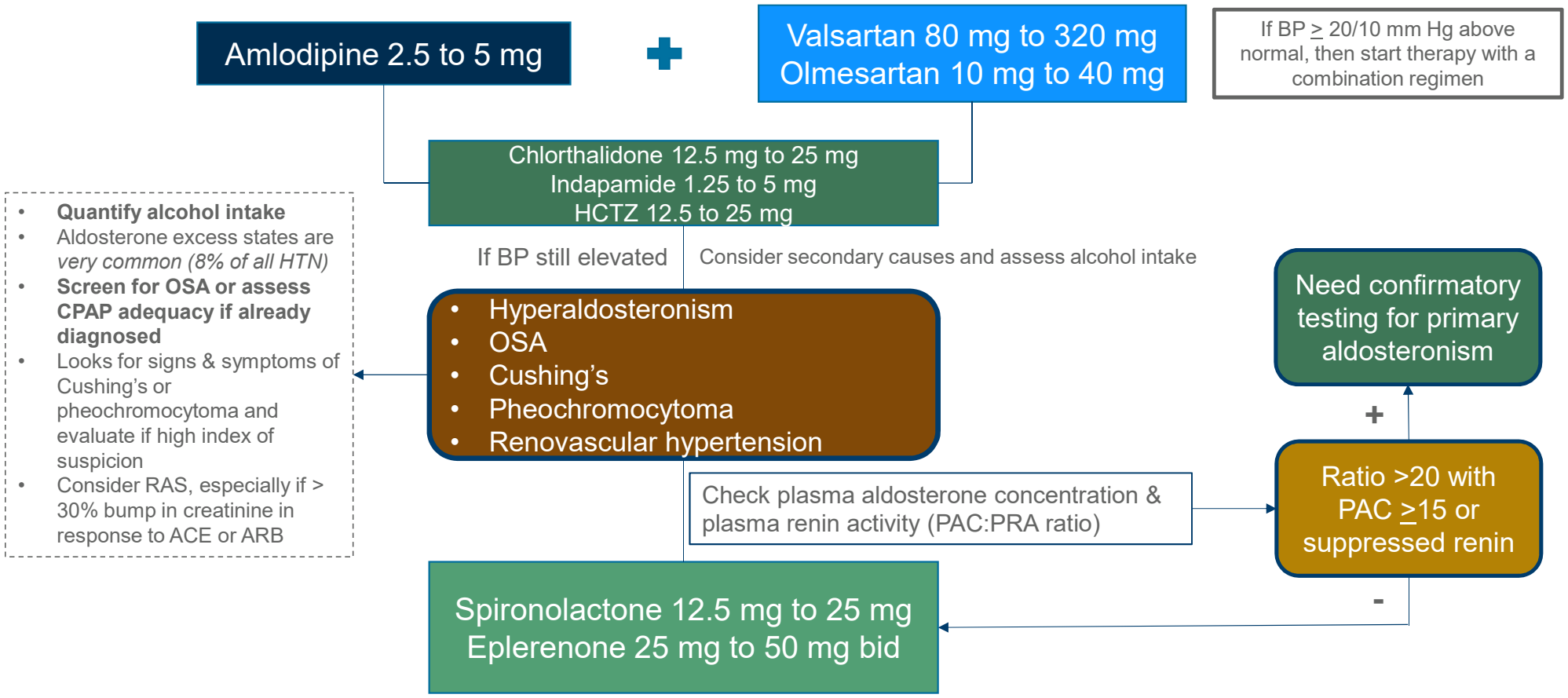
→ *Especially if need to wean off beta-blocker in a patient without definitive therapeutic indication*

Sympathetic Driven Mechanism of Hypertension

- Some providers use beta-blockers in these cases (but there is some evidence of increased mortality when beta-blockers are used in the absence of a more compelling indication)
- Some providers use “as needed” agents, such as hydralazine or clonidine to be taken for specified high readings (should be done very cautiously in select patients only)
- Ideally, we should strive for longer acting agents that achieve sustained control without predisposition to BP lability



Hypertension Algorithm



CKD

- Chronic kidney disease (CKD) is ***defined as abnormal kidney structure or function present for >3 months***
- CKD is stratified into stages 1 to 5 based on the level of estimated glomerular filtration rate (eGFR)
- Stage G1 does not have a reduction in eGFR and therefore is defined by the presence of anatomical defects or markers of kidney damage such as albuminuria, hematuria, or electrolyte abnormalities
- **Stage G2 is characterized by eGFR 60-89 in the presence of albuminuria, hematuria, or electrolyte abnormalities**
- Because **albuminuria** is associated with **increased renal and cardiovascular morbidity and mortality**, the Kidney Disease: Improving Global Outcomes (KDIGO) group further subdivides the eGFR-based kidney stages by degree of albuminuria

CKD and Hypertension

- **KDIGO suggests a target blood pressure of <120 mm Hg**, if tolerated in patients with hypertension and CKD, whereas the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) blood pressure guideline recommends a target blood pressure of <130/80 mm Hg
- KDIGO recommends starting an ACE inhibitor or angiotensin receptor blocker (ARB) for patients with hypertension, CKD, and increased albuminuria
- ARBs have fewer side effects than ACE inhibitors and are increasingly preferred as first line choices of therapy
- Newer ARBs such as Olmesartan or Telmisartan are more potent than older ARBs such as Losartan, and also have longer half-lives enabling effective once daily dosing
- Chlorthalidone is more effective than HCTZ for managing HTN
- When eGFR falls < 30 mL/min, thiazides can still be used
  - May require increased dose of thiazide
  - Or change to long-acting loop diuretic such as Torsemide

Laboratory monitoring in CKD 3

- **First visit or time of diagnosis → try to identify the cause**
  - **U/A** – looking for structural damage such as proteinuria, pyuria (especially with negative culture and absence of UTI symptoms), or hematuria (if RBCs present, dysmorphic → glomerulonephritis; no dysmorphia → think lower urinary tract)
  - **Urine for protein-to-creatinine ratio (UPCR) –** (looking not just for albuminuria but also for other proteins [globulins, Bence Jones for Myeloma, Amyloid, etc.])
  - **Blood pressure →** impact on protecting kidneys is mild to moderate, but impact on preventing heart attacks, heart failure, and strokes is super impressive!
  - **Renal Ultrasound →** looking for evidence of obstructive uropathy, unilateral atrophy indicative of renal artery atherosclerosis, or tumors
  - **Look for potential nephrotoxins**
- **BMP ~** one to four times per year (see chart on CKD stages)
- **Annually** (if normal → more frequently if abnormal)
  - **Urine for albumin-to-creatinine ratio (UACR)**
  - **CBC and PTH**
  - Anemia is mostly iron deficiency rather than erythropoietin deficiency → elevated hepcidin levels block GI iron absorption and mobilization of iron stores (may need IV iron)
  - Make sure bone marrow can respond to erythropoietin → **check TSH, B_{12}, ferritin, iron, and TIBC**

When to Refer to Nephrology

- eGFR < 30 mL/min = CKD 4
- WBC casts or pyuria without evidence of infection (worrisome for interstitial nephritis)
- Significant proteinuria
  - UPCR > 1g warrants further evaluation and possible biopsy; consider
    - Don’t miss myeloma (possible oncology referral)
    - Nephrotic syndromes (Minimal change, Membranous, Membranoproliferative, FSGS, Diabetic, HIV, Amyloidosis)
  - UPCR > 2g warrants a biopsy unless they are a diabetic with steady progression of proteinuria over time
- Glomerular hematuria or RBC casts
    - Nephritic syndromes
      - ANCA-associated vasculitides (Crescentic, GPA, MPA, eGPA)
      - Anti-GBM disease
      - Immune complex (Post-infectious or infectious, SLE, IgA, Cryoglobulinemic, MPGN)
- Uncontrolled BP/refractory hypertension

Preparations of IV Iron

- Iron sucrose (Venofer) 200 mg weekly x 5 weeks to complete 1000 mg total
- Ferric gluconate (Ferrelcit) 125 mg weekly x 8 weeks to complete 1000 mg total
- Ferric carboxymaltose (Injectafer)
  - If ≥ 50 kg then 750 mg x 2 at least 7 days apart (max dose 1500 mg per treatment course)
  - Alternative: 15 mg/kg x one dose with a max dose of 1000 mg
  - If < 50 kg then 15 mg/kg x one dose with a second dose at least 7 days later
- Fermoxytol (Feraheme) 510 mg x 2 doses, 3 to 8 days apart or 1020 mg as a single dose (60-minute monitoring period recommended)

Yeng M. Yang, MD, MBA, FAAP
Internal Medicine/Pediatrics
Urgent Care
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Empowering Communities: *Tackling Diabetes Through Culturally Responsive and Equitable Care*

Yeng M. Yang, MD, MBA, FAAP (She/Her)

HealthPartners-Internal Medicine-Pediatrics

Medical Advisor, Co-Chair Health Equity, Inclusion & Anti-Racist Cabinet

Regional Medical Director, Primary Care North East Region

(Arden Hill, Brookdale, Brooklyn Center, Hugo, Lino Lakes, Maplewood, Roseville, White Bear Lake, & Woodbury)

Disclosures

Yeng Yang, MD, MBA has no relevant financial relationships with ineligible companies.

Objectives

1. Review the contribution of systemic racism and bias to health inequities in marginalized communities.
2. Review the MN & HealthPartners example of health care disparities in diabetes
3. Understand the principles of culturally responsive care and its role in promoting health equity.
4. Share an example of how to incorporate culturally responsive diabetes care in diverse communities.

ADA calls for health equity with Bill of Rights

- *"The ADA Health Equity Bill of Rights envisions a future without unjust health disparities."*

  -ADA

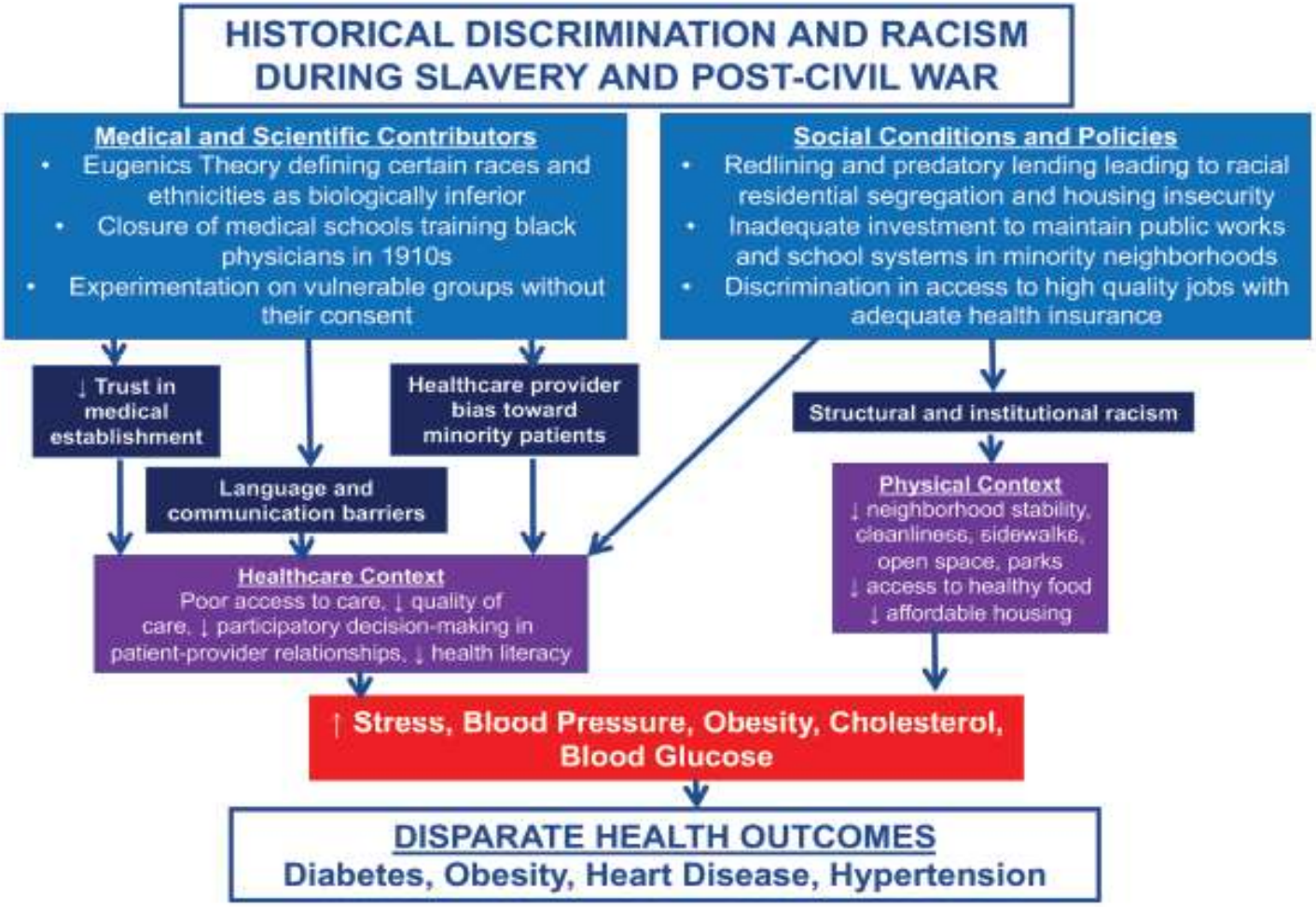
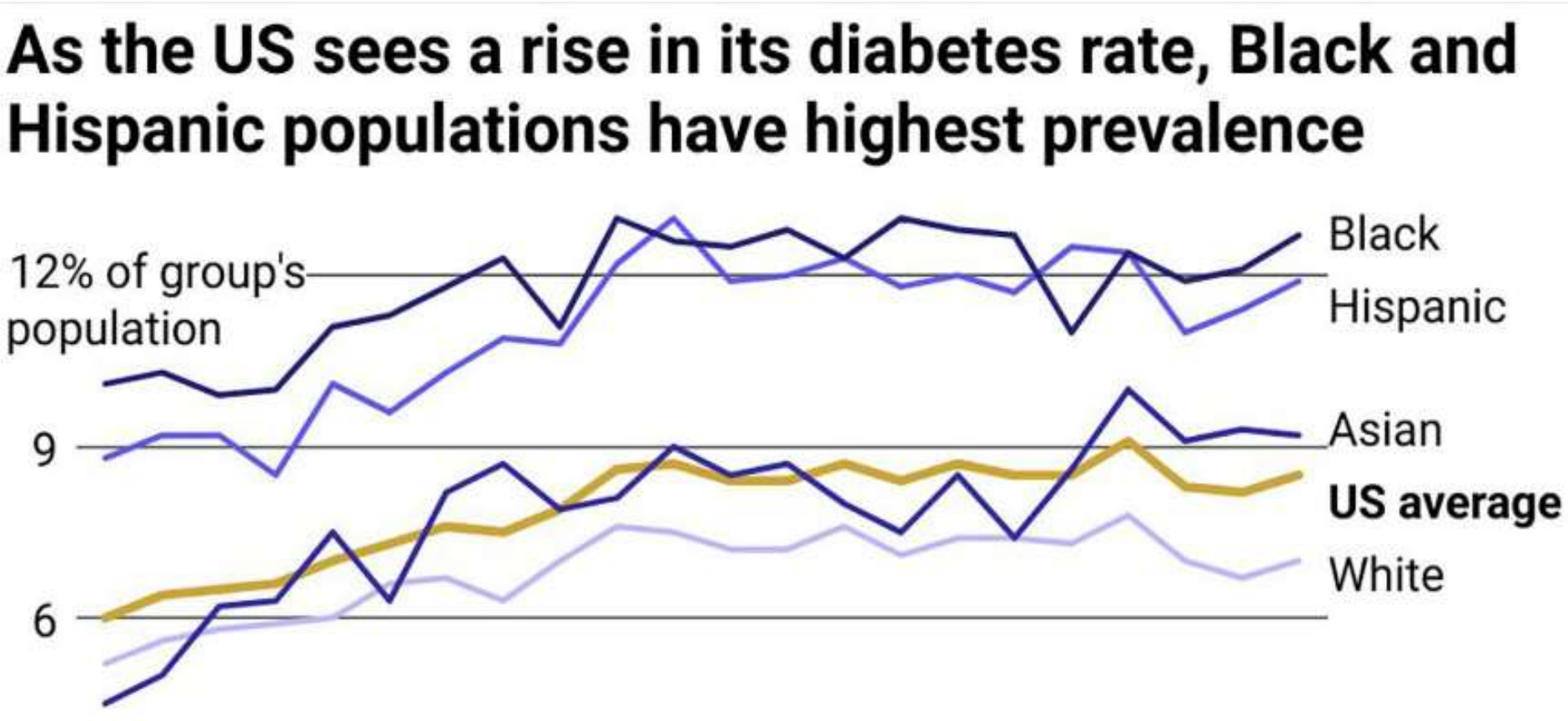


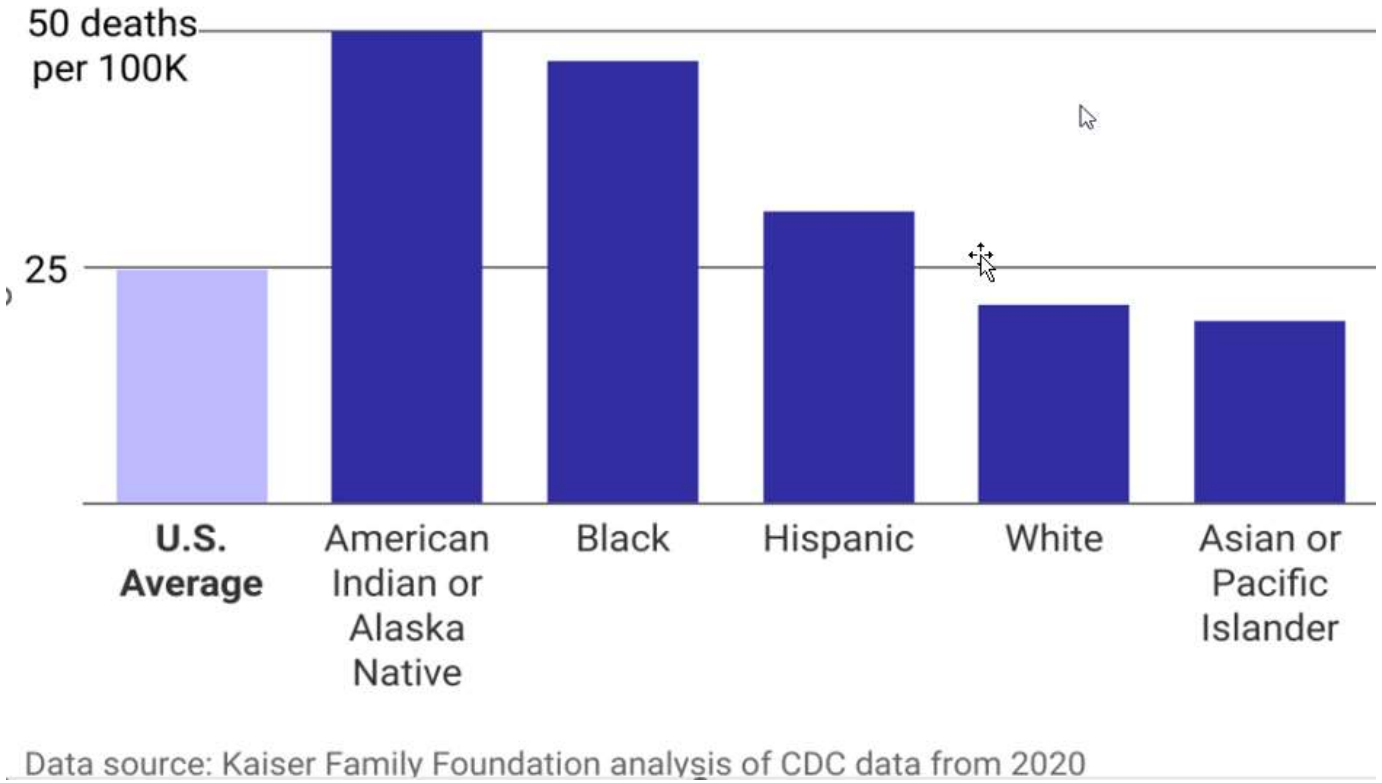
Figure 1. Medical, scientific, and social policy contributors to health and health care disparities in African Americans in the United States.

Prevalence



Source: CDC

Indigenous and Black Americans Have Highest Diabetes Death Rates



Data source: Kaiser Family Foundation analysis of CDC data from 2020

Factors contributing to health care disparities?

2003-IOM report on widespread racial/ethnic health care disparities highlighting role of system level determinants (access and utilization) and micro-level interactions. What is micro-level interactions?

- Research evaluating micro-level interactions between patients and physicians continue to point to physician bias as the driving force behind treatment disparities.

Racially/ethnically discordant health care provider	
NH White	23%
NH Black	77%
Hispanic	79%

Cholesterol lowering intervention study 2020			
Interventions	NH White	NH Black	Hispanic
Lifestyle Modification Recommendations	1X	2X	2X
Lipid Lowering Rx	-	43% lower odds	43% lower odds

Bacon, Ethnicity & Heath, 2020

Physicians' perceptions of patients are influenced by patients' race & SES

- SES has fairly linear relationship with physician's rating of patient's:
  - ✓ Intelligence
  - ✓ Desire for physical activities
  - ✓ Active lifestyle
  - ✓ Medication adherence
  - ✓ Cardiac rehab participation
  - ✓ Career demands, and
  - ✓ Need to care for family members.
- SES tracks well with personal attributes such as likeability and likely for patients being someone physicians might be friends with.

If black and poor, worse perceived by physicians and can lead to less exchange of information between patient & physician, prescription for aggressive treatments.

Van Ryn & Burke, Social Science & Medicine 2000

Glycemic Control & Patient-Clinician Language Concordance

- Among LEP patients, Latinos with DM, those who switched from a non-language concordant to a language concordant patient-clinician dyad (i.e., Spanish-speaking) had significant improvement in glycemic control
- Language concordant care is a critical element of delivering equitable care
  - Can be facilitated by providing certified interpretation services in the preferred language of care

Parker, JAMA Intern. Med. 2017

Do we need all diverse patients to be cared for by diverse clinicians?

NO

- Not enough diverse clinicians around
- **TRUST building is KEY to equitable and great outcomes**
  - BP control study comparing concordance W/W, AA/AA vs W/AA dyads
  - Little difference in medication adherence
- **Increasing TRUST was associated with significantly better adherence**

  (No White pts and AA clinician dyad in study)

Schoenthaler, Ethn Health October 2014

MN & HealthPartners data

We are making progress but still have disparity gaps

HealthPartners® Clinic

MN Community Measure results by race/ethnicity 2023

MEASURE	STATEWIDE RATE	RACE						ETHNICITY	
		Asian	Black	Indigenous	Multi Racial	Native Hawaiian	White	Hispanic/ Latinx	Not Hispanic/ Latinx
Optimal Diabetes Care	**44.6%**	48.1% ▲	34.7% ▼	25.5% ▼	36.1% ▼	40.2% ▼	46.4% ▲	37.7% ▼	45.2% ▲

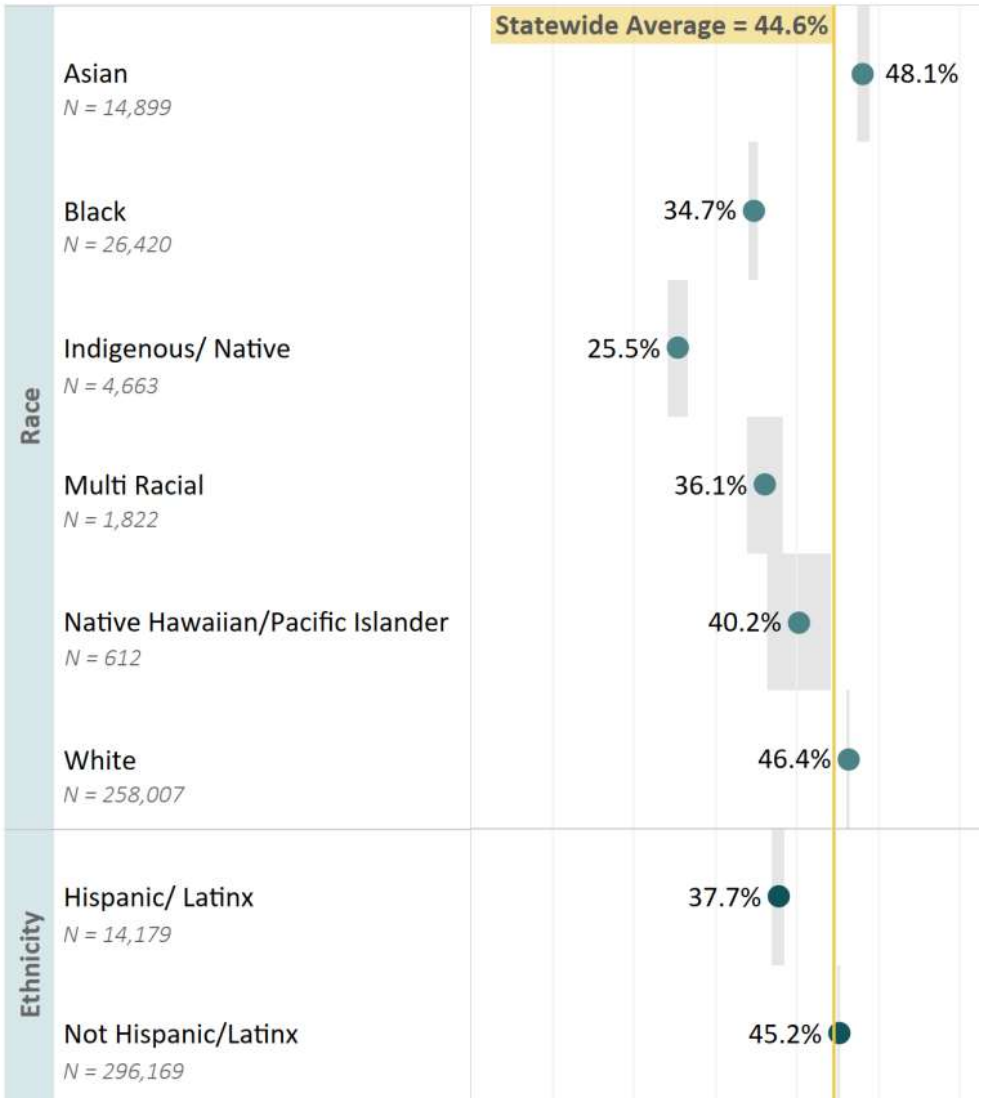
TOP PERFORMERS

Included if eligible for at least 5 measures

- ● Above average
- ○ Below average or average
- < Not reportable

QUALITY MEASURE		CentraCare Health	Central Pediatrics	Child and Teen Medical Center	Entira Family Clinics	Essentia Health	Health Partners Clinics	Mankato Clinic, Ltd.	Park Nicollet Health Services	Pediatric & Young Adult Medicine
MEASURES REPORTED BY MEDICAL GROUPS DDS/PIPE	Adolescent Depression: Follow-up PHQ-9/9M at 12 Months	●	●	○	●	●	●	●	●	○
	Adolescent Depression: Remission at 12 Months	●	○	●	○	●	○	○	○	●
	Adolescent Mental Health and/or Depression Screening	●	●	●	○	●	○	●	○	●
	Adult Depression: Follow-up PHQ-9/9M at 12 Months	○	○	<	●	●	●	●	●	<
	Adult Depression: Remission at 12 Months	○	○	<	●	●	●	●	●	<
	Colorectal Cancer Screening	●	-	-	●	●	●	●	●	-
	Optimal Asthma Control - Adults	●	●	●	●	●	●	●	●	●
	Optimal Asthma Control - Children	○	●	●	●	●	●	○	●	●
	Optimal Diabetes Care	●	-	-	●	●	●	●	○	-
	Optimal Vascular Care	○	-	-	●	●	●	○	○	-

2022 measurement year

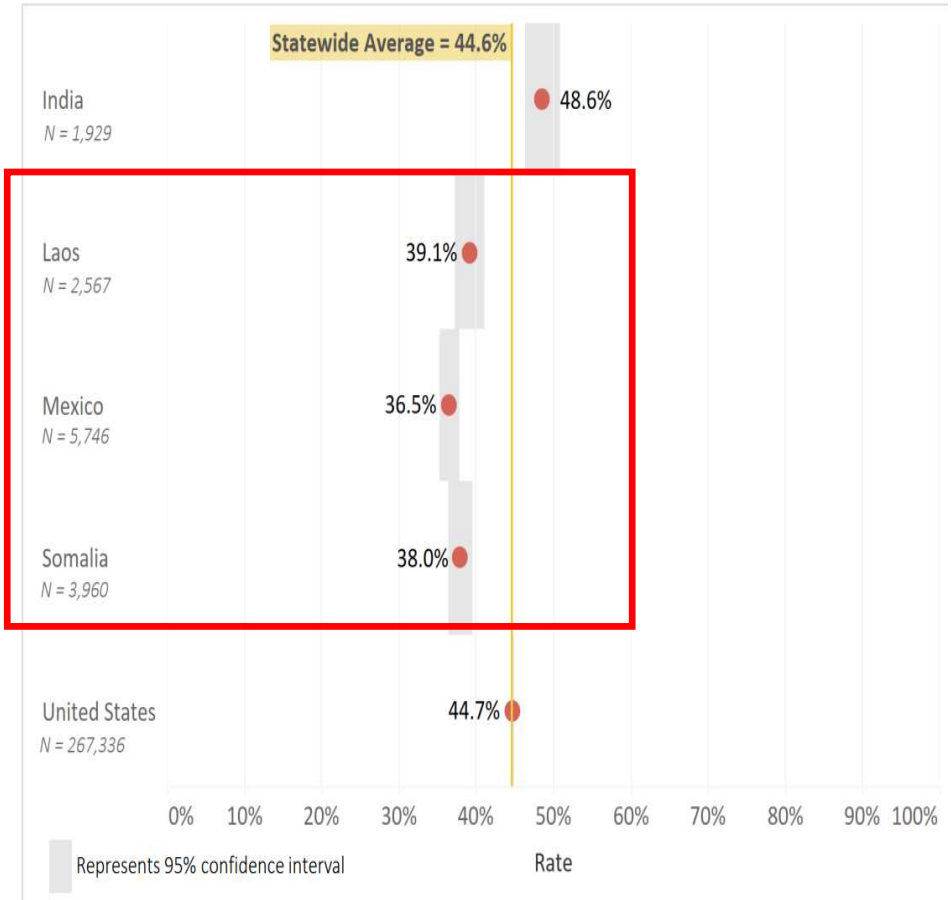


OPTIMAL DIABETES CARE

Country of Origin Summary

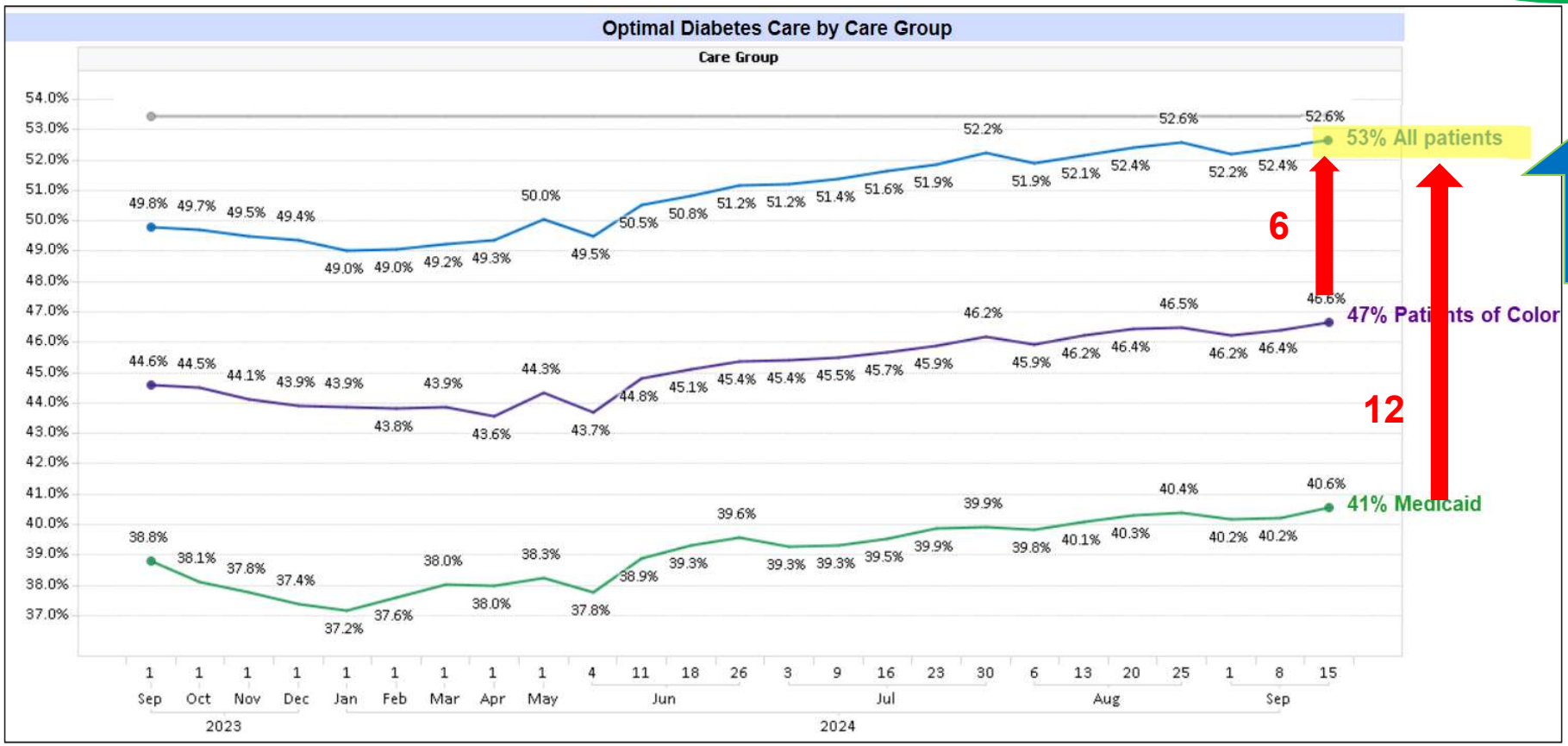
2022 measurement year

MNCM 2023 report reflecting 2022 data



HP Optimal Diabetes Care YTD 9.24

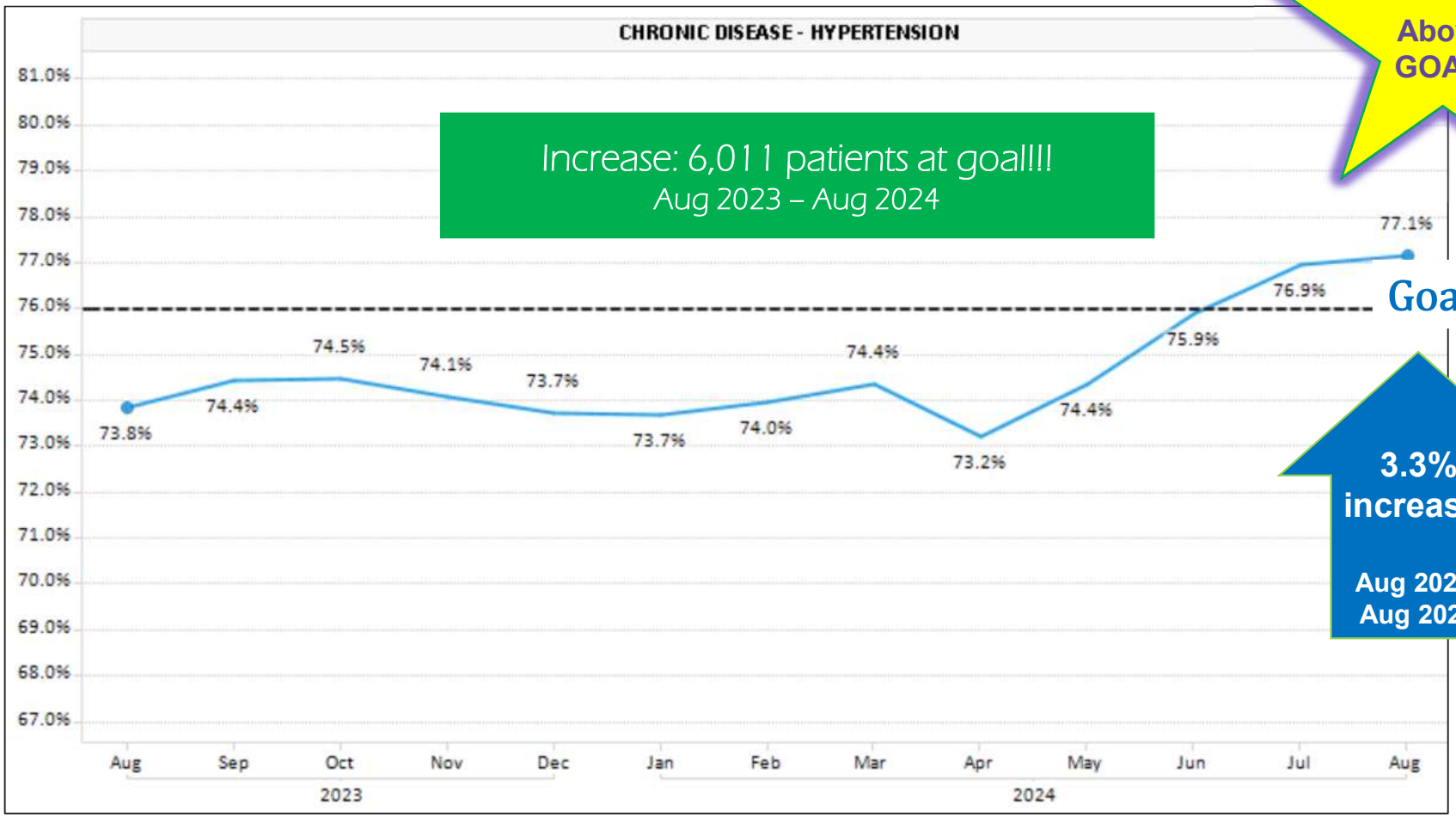
Goal 53.4%



All Patients 62,967 | Patients of Color 18,625 | Payor (Medicaid) 8188

Diabetes Components

Hypertension Care Group Improvement!



Increase: 6,011 patients at goal!!!
Aug 2023 – Aug 2024

Above GOAL!

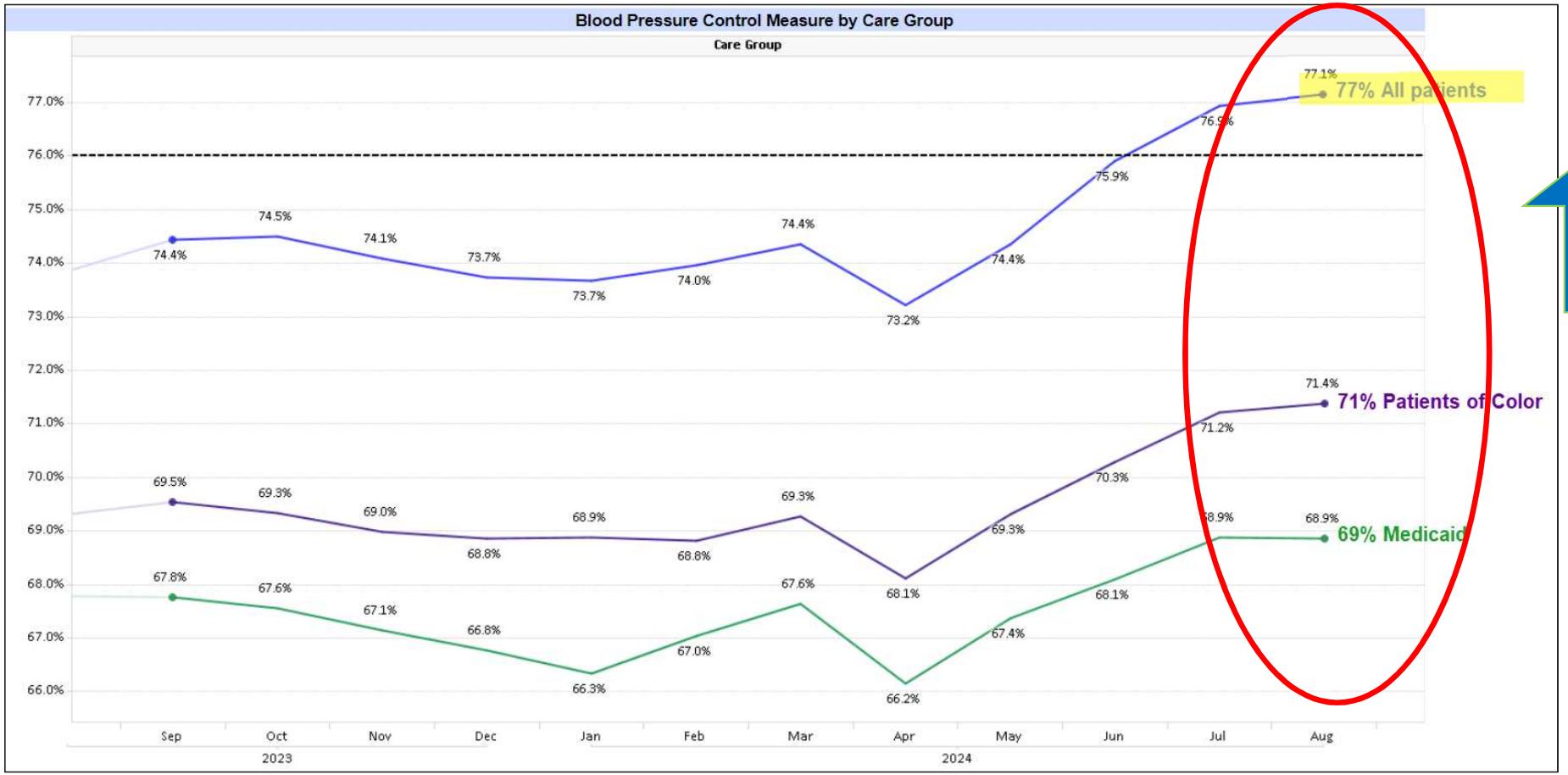
Goal 76%

3.3% increase!

Aug 2023-Aug 2024

Hypertension

Goal 76%



3.3% increase!

All Patients 160,376 | Patients of Color 27,950 | Payor (Medicaid) 11,976

Track My Health BP Outreach 2024

Go live: 6/26/2024

Automated, quarterly MyChart outreach to collect patient reported blood pressure readings.

TMH BP Messages

- Total Sent: 22,071
- Reminders sent: 16,646
- Questionnaires submitted: 3624

BP Submissions 3273

- **76%** Normal /Low: BP <140/90 (2484)
- **20%** Moderate: BP 140/90-159/99 (651)
- **3%** Moderately High: 160/100 - 179-109 (110)
- **1%** Extremely High: >=180/110 (28)

Patient Population:

- Ages 18-85 AND
- Diagnosis of diabetes, vascular, and/or hypertension AND
- No blood pressure in the last 12 months or most recent BP is 140/90 and greater AND
- No upcoming qualifying appt in the next 60 days

Data from 9/17/24

2025 Planning and Priorities – Expert Panel

Discussion and Recommendations:

Work in Progress

- **Mobile Check in BPs** automatic file into Epic - **NOW LIVE!!**
- **BP Follow Up Guidelines** updates (BP Check only and Pt Reported BP) DONE
  Track my Health **BP outreach** 2024 - increase outreach (quarterly 2025)
- **E-visits**
- **Referral back to Primary Care from Specialty** - elevated BP (HTN FU REF 768)
- **BP Decision Support Tool** - SmartSet
- **PREVENT Risk equation** - Priority Wizard
- Updates to **Epic Chronic Condition RWB** for Care Teams
- **MOC –** Diabetes (24 clinicians) Hypertension (52 clinicians)
- **CGM downloading & Epic documentation** – Tom and Erin
- **Patient Education –** Tracy

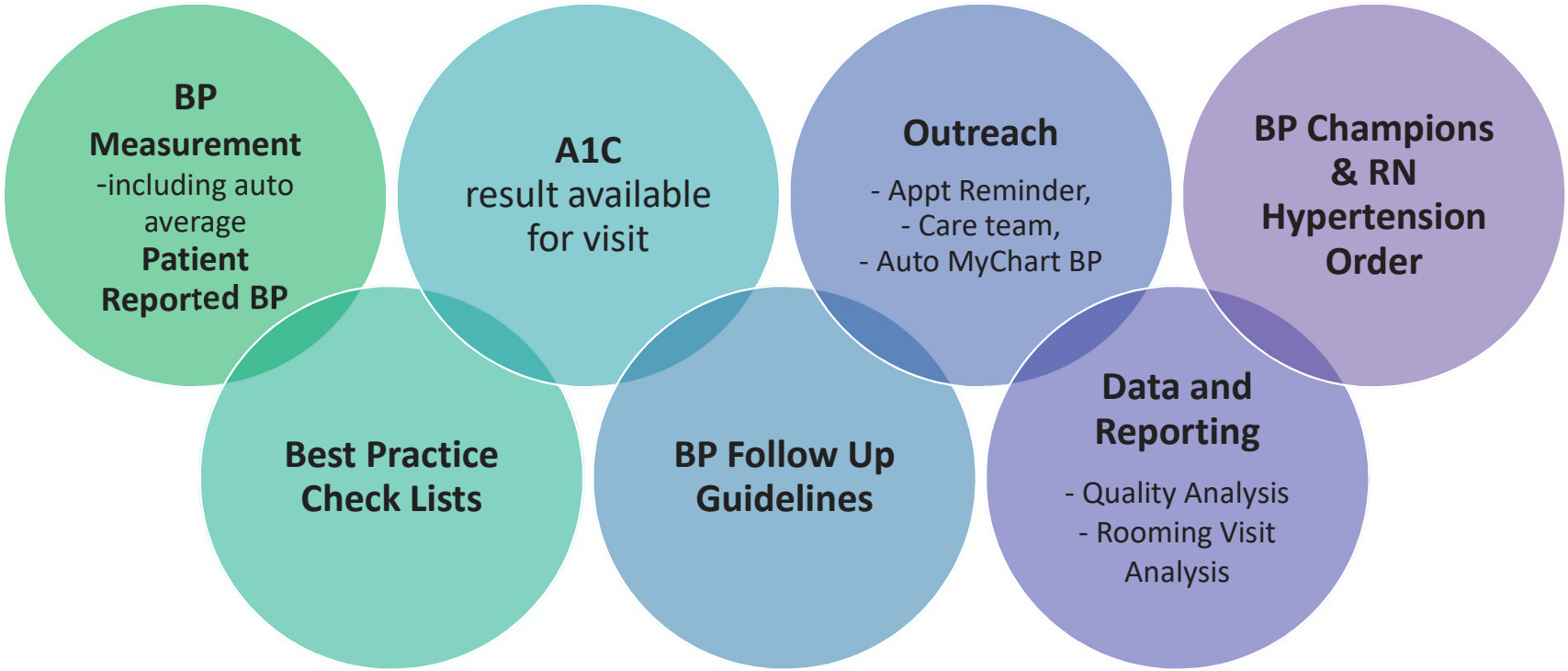
New Requests – Hot Topics

- Data/reporting transition to Power BI - 2025
- Reminder to bill CGM interpretation

Parking Lot – Not started

- **Checking accuracy** of patient's home BP monitors
- **Documenting home BP monitor** use in Epic
- Capturing **individual BP goals** in Epic
- **Diabetes HMA** – ability to remove if error in dx
- **Hgb A1c HMA** - automate based on last Hgb A1c result

Key QI drivers of improvement



What does this tell us?

- **Quality improvement is not enough!**

✓ Incorporate Health Equity Lens in quality improvement efforts
  - *Incorporate the National Standards for CLAS in Health and Health Care.*

✓ Multidimensional approach

✓ Bias training-Focus on patient-clinician TRUST building and communication

✓ Culturally responsive/informed care
  - Human-Centered design principles

✓ Health literacy

✓ Care must be expanded beyond the walls of clinics and hospitals

Golden, J. Clinical Endocrinology & Metabolism 2021

Hypertension MOC-CME: Reducing Health Disparities & Improving Hypertension Management

Brookdale, Brooklyn Center, Woodbury part of the AMGA Health Equity QuiC efforts in 2023-2024.

HealthPartners Clinic

Organizational Approach to Hypertension Management Focus on Disparity

Hypertension MOC-CME:

Reducing Health Disparities &

Improving Hypertension Management

Clinician role and use of organizational tools to support improving hypertension management and health outcomes based on payor and race populations that can be applied broadly to all patient populations.

Clinic Emphasis on Patients with Hypertension:

Focus on how clinics engage with their hypertensive patients and support patient education.

Utilize all available resources, especially within the clinic itself, to achieve local, organizational, and state goals related to hypertension management.

Compensation for clinicians tied to meeting specific care goals at the clinic level, not through individual patient panels.

Importance of Patient/Clinic Interactions and SDOH:

Understand social drivers of health (SDOH) to enhance shared decision making for primary care teams in improving hypertension control.

SDOH-related interventions include:

Addressing transportation issues by incorporating more phone/video visits.

Template for incorporating culturally responsive care to improve diabetes

Somali Study Case

HealthPartners Clinic

Why does culturally responsive care matter?

- Health disparity exist in most metrics (DM/VASC/HTN)
- Traditionally marginalized communities have low trust in health care system
- Patients fear that they will need to give up their cultural staple foods (Rice)
- Previous poor experiences with DM/nutrition education themselves or through friends and families (word of mouth)
- Hear from patients that previous practice in DM education and nutrition education do not always translate to their eating cultures
- Not all clinicians feel comfortable enough to advise patients on their cultural foods.
- Clinicians may make unsupported assumptions that patients from diverse backgrounds won't go if referred.

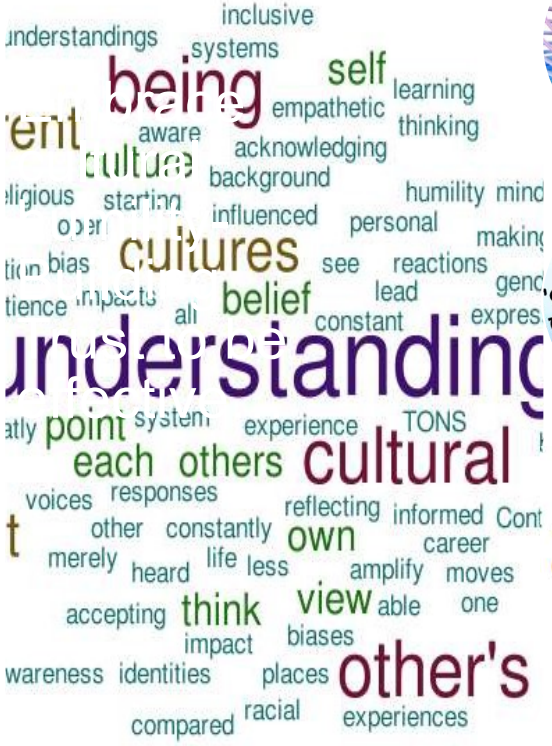
What is culturally informed/responsive care?

Approach to Culturally responsive care

Engage & co-design with communities

- Emphasize collaboration and partnership
- Avoid placing greater value on the opinions/voice/expertise of the medical providers:
  - Regard community knowledge and ability of community members/patients
  - Share authority, listen and be flexible and understanding of diverse traditions, religions, beliefs, ideas and expertise.
- Share educational communication in relevant languages and beyond written text (e.g., verbal presentations/recordings & infographics)

Approach to culturally informed care: *when working cross-culturally, mistakes will happen, so…*



Being flexible

Take responsibility for mistakes

Be open to learning/adapting as culture & languages evolve

Our Approach To Creating Culturally Responsive Care

01

Literature search for guidance – how to create culturally informed patient education, in concert with health literacy.

02

Human-Centered Design Principles; Co-design with Community– Engaged with the local Somali, Hmong, and Ethiopian communities (focus groups & ongoing consultation)

03

Surveyed primary care clinicians on their perspectives of clinical challenges working with diverse populations and connecting them with diabetes/nutrition education

Principles for Designing Patient Education

P.E.A.R.L

P = Plain language & understandability

E = Explicit data, statistics & graph

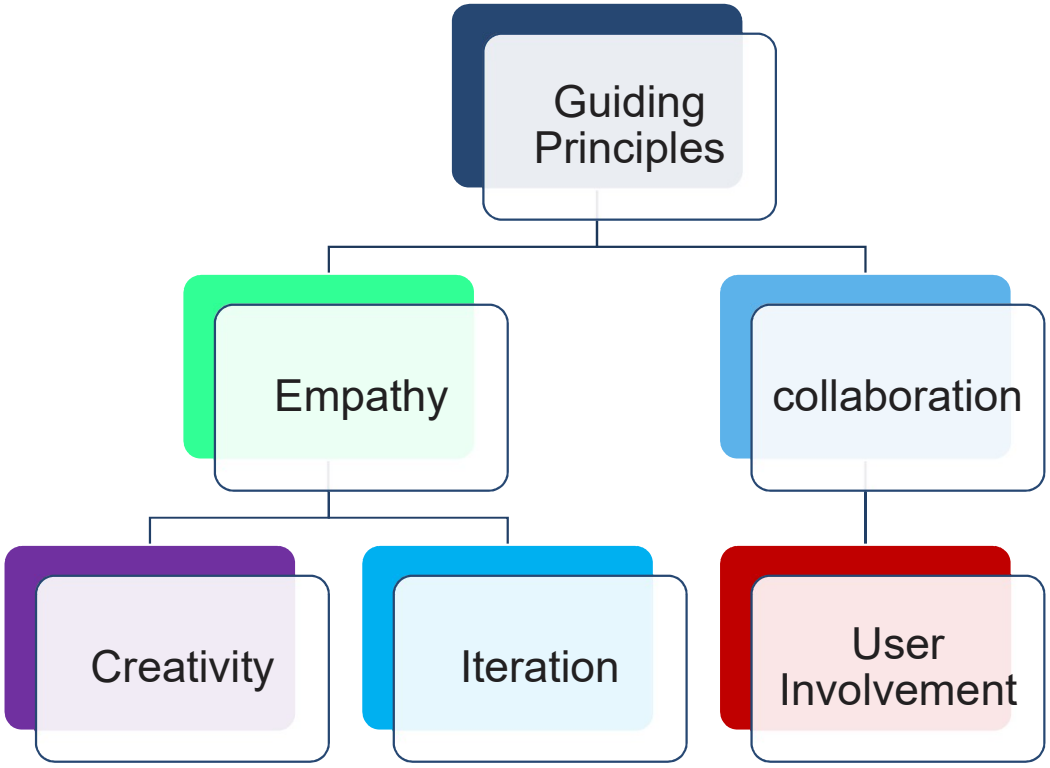
A = Affirmative framing

R = Representative content

L = Local Connection

Haynes, et al, 2022, Oct

Human-Centered Design Basics



Benefits of the human-centered design approach

- Improved user satisfaction
- Increased adoption rates
- Reduced development costs
- Improved innovation

Kitch, Bryan May 2023

IHI Equity Learning Lab Project ('23): *Preventative & Chronic Disease Management*

"Open Faces: Moving Forward Together" IHI project with the Somali community

Lessons:

- Open to working together to build trust with open hearts.
- Trusted messengers to endorse information
- Prefer patient education in recorded and video formats

Patient Education-Community focused groups

2-2 Hour focus groups

1. Hmong
2. Somali
3. Ethiopian

**Note: Community members were provided with a meal and nominal gift cards provided by a grant*

Focused on

1. What the understanding of diabetes is within each community
2. What they are looking for in education about diabetes
3. How they would like to receive patient education (modalities)

Focus Groups: Ethiopian (Amharic), Hmong, Somali

HealthPartners Clinic

Focus Groups: Ethiopian (Amharic), Hmong, Somali

HealthPartners Clinic

Lessons from patient focus groups

- Lack of Trust without the endorsement of trusted messengers
- Health literacy is variable among different populations:
  - ✓ More pictorial representation and less written words
  - ✓ Verbal (recorded) instructions/education
- Language access is needed for some
- Understanding diabetes is difficult
- Patients have difficulty adapting western-based diet to other food cultures; education material need to reflect various food cultures.
- Label reading on food packages is difficult
- Carbohydrate-based education does not translate well.
- Communities fear that clinicians & DM educators will force medications first

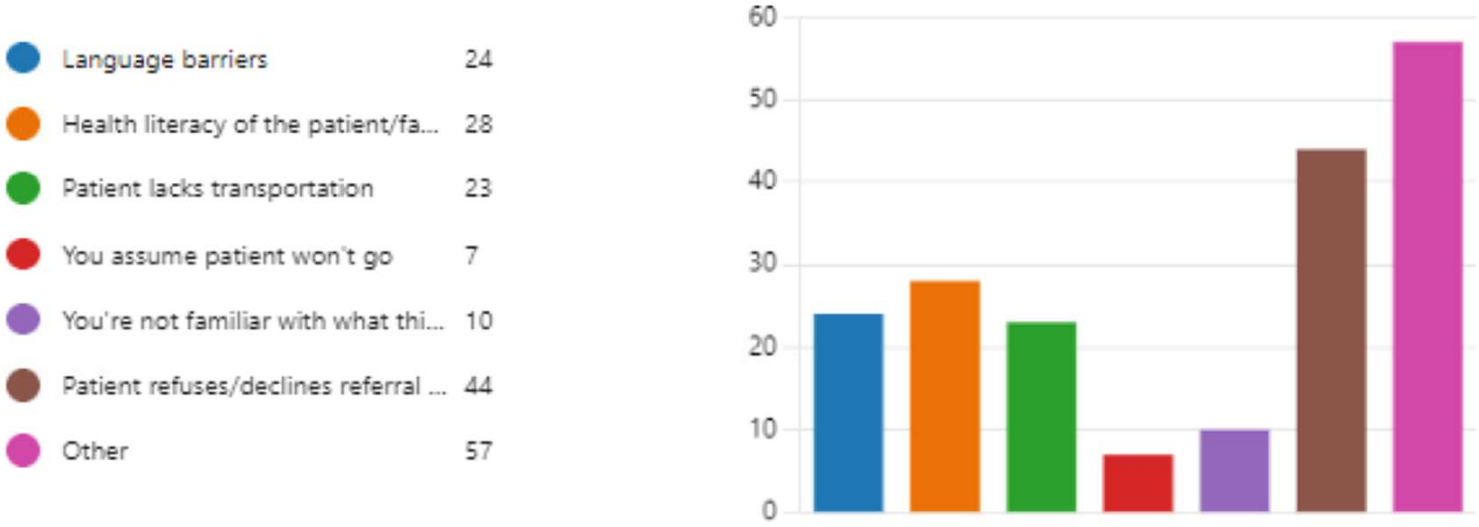
Primary Care Clinician Survey

Thank you to primary care clinicians primary care service line across our enterprise who took this survey to give us feedback

HealthPartners Clinic

2. What are common obstacles/barriers that prevent you from referring your patients of color to diabetes and nutrition education now?

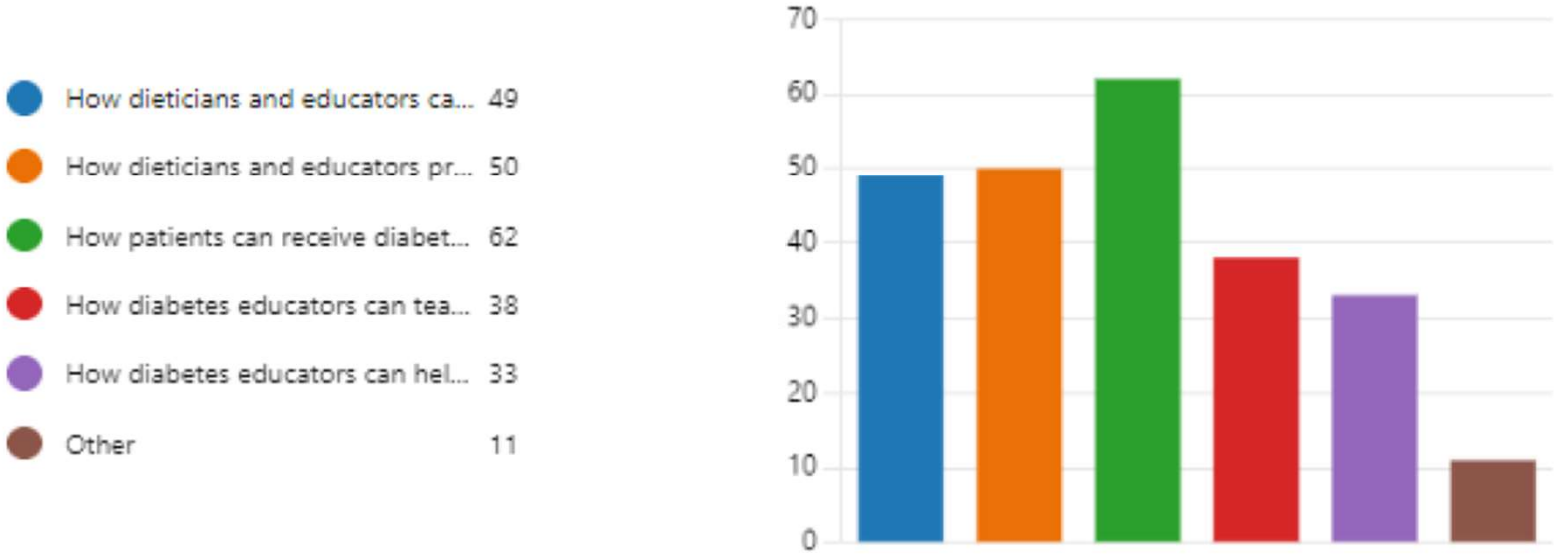
More Details



1. Language barriers
2. Health literacy of the patient/family
3. Patient lacks transportation
4. You assume patient won't go
5. You're not familiar with what this service offers
6. Patient refuses/declines referral - if you chose this please check the "Other" option below and type in reasons the patients decline.
7. Other

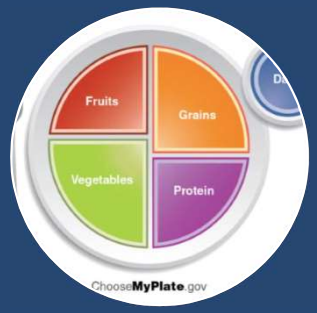
3. What would you like to learn about diabetes and nutrition education and working with diabetes and nutrition educators?

More Details

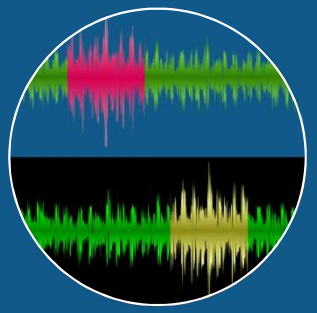


1. How dieticians and educators can co-manage patients with clinicians, including follow-up visits until goals are met
2. How dieticians and educators practice cultural curiosity in helping patients create a healthy eating plan
3. How patients can receive diabetes and nutrition education tailored to their food culture
4. How diabetes educators can teach patients how to use continuous glucose monitoring to better manage their diabetes
5. How diabetes educators can help patients understand their treatment options

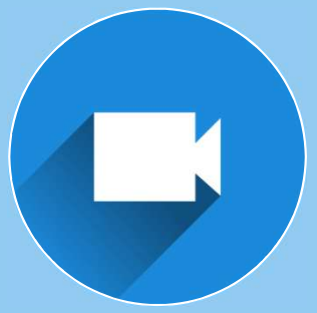
Phase I: 4 Projects for Somali patients; 1 for clinicians



MyMeal Handout



Recorded patient education on diabetes



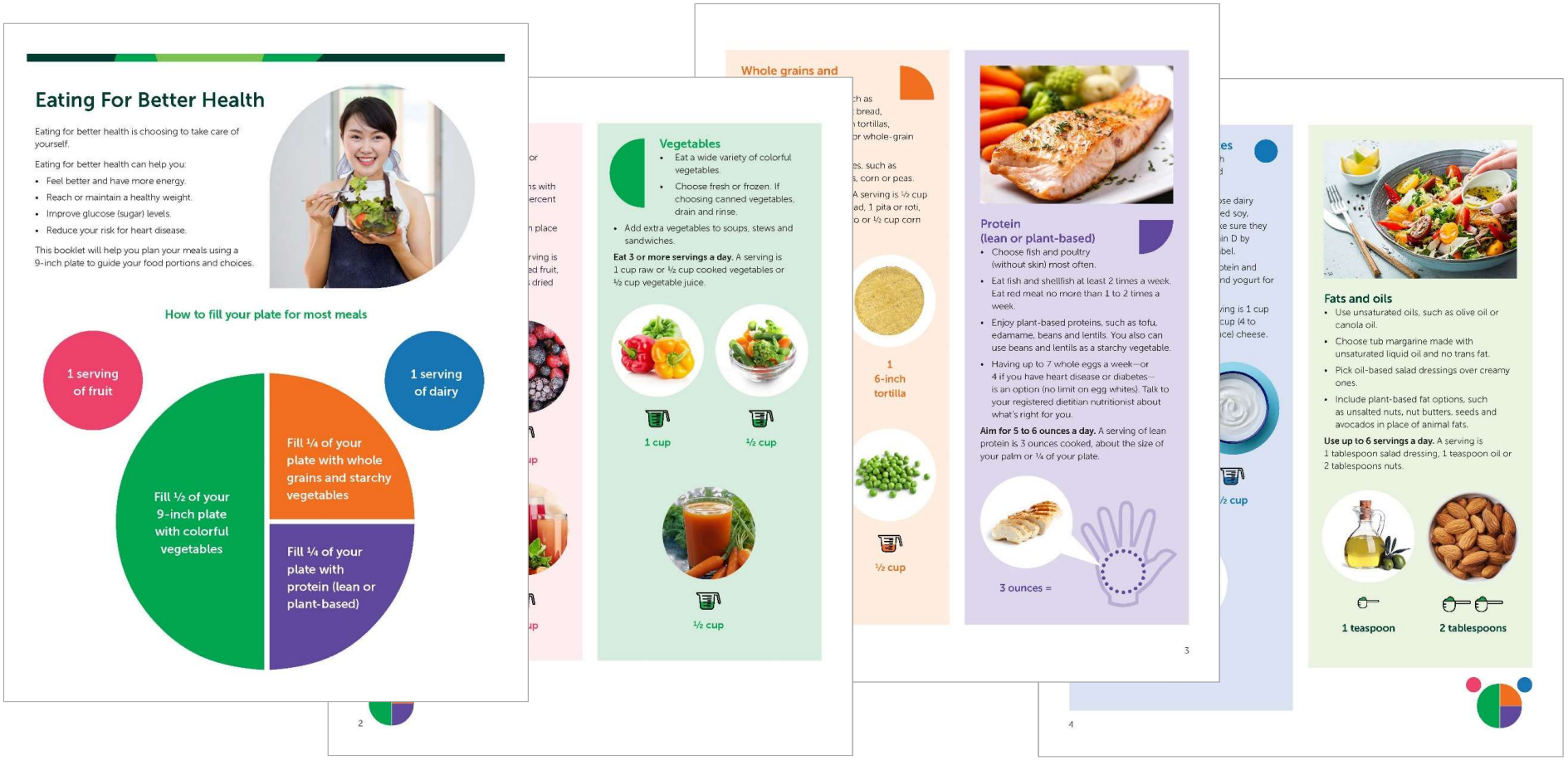
Video of what to expect at a diabetes educ. session

Video of healthy foods for managing diabetes

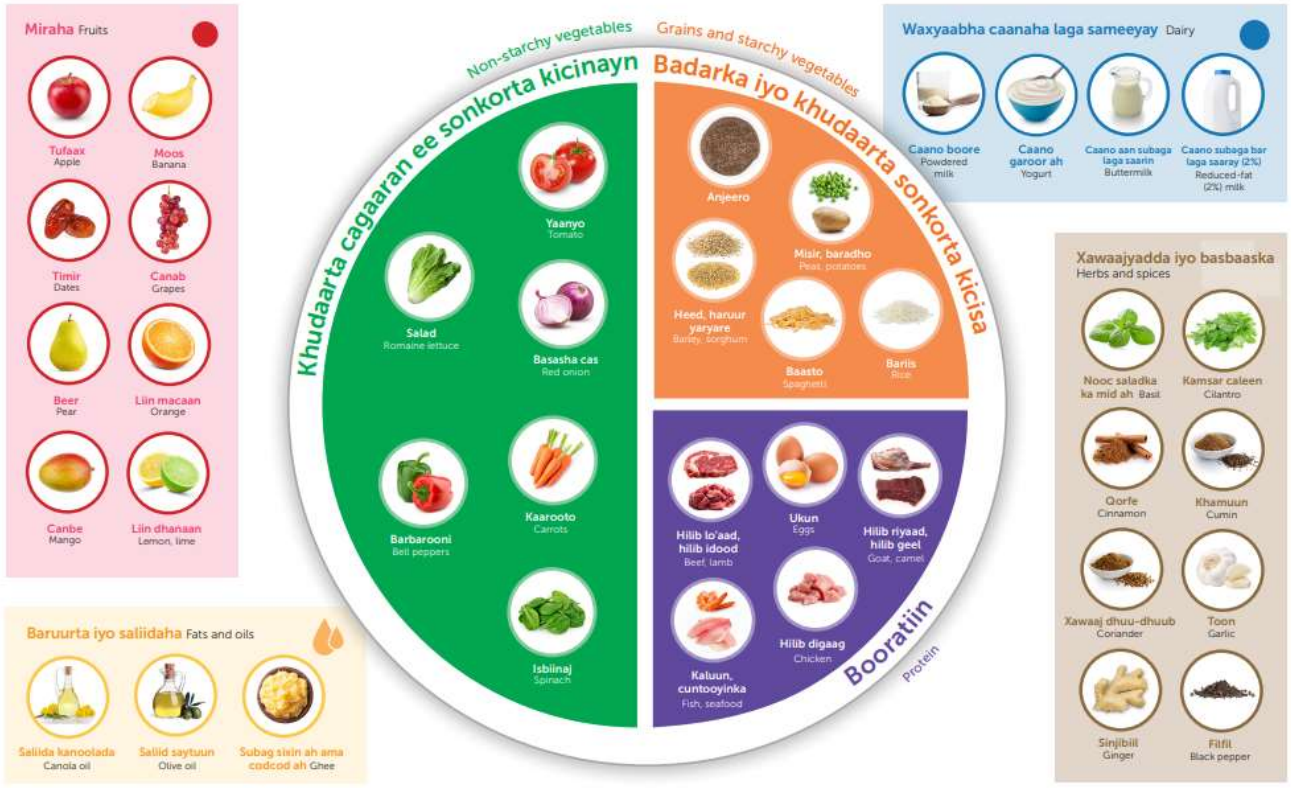
Clinician Education & Tip Sheet

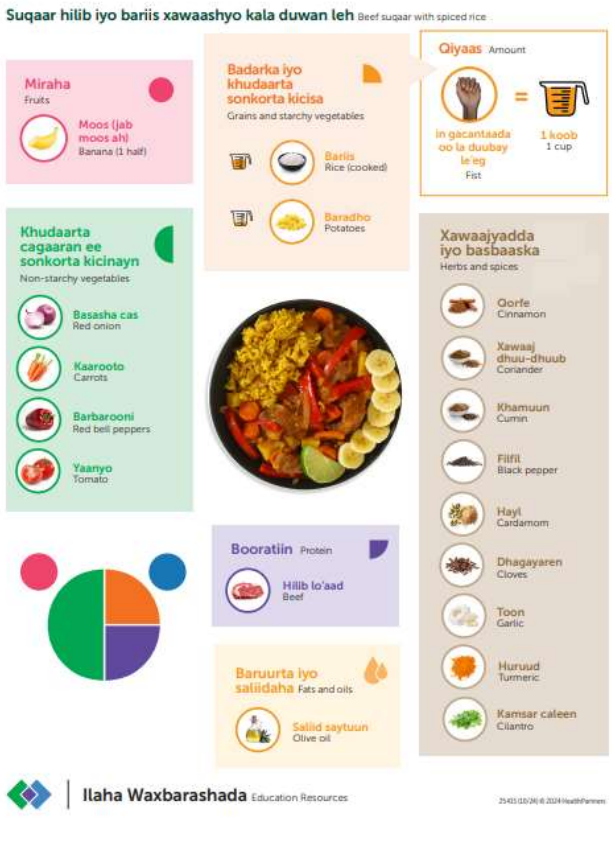
Educational Resources for Patients & Clinicians

Current nutrition education



Project #1: MyPlate → MyMeal





Diabetes and Nutrition Education for Patients from Different Food Cultures

November 2024

How can you help patients from different food cultures better understand and manage their diabetes? Refer them to a diabetes educator or a dietitian! Follow the tips below to set up your patients for success.

Why refer patients to diabetes or nutrition education?

After 2 visits, patients:

- Have an average A1C reduction of **1.6%**.

These visits also provide:

- Better patient access.
- More time to educate patients in a longer visit.

Which patients can benefit from education visits?

All patients can benefit from education visits, including patients with limited English proficiency. Interpreters are available for visits, both in-person and virtual. See box below for referral codes.

How to refer your patients

- **Diabetes educators** focus on general diabetes management, including healthy coping and eating, starting and adjusting diabetes medication, diabetes tech support and problem solving. Use **REF583** for referrals to a diabetes educator.
- **Dietitians** focus on nutrition and food choices to manage diabetes. Use **REF024** for referrals to a dietitian. Refer patients with prediabetes to a dietitian (not to a diabetes educator).

How can I encourage my patients to go to an education visit?

Know your patients' history.

Many patients from different food cultures (or their families and friends) are discouraged after receiving advice based on a Western diet or having other negative health care experiences.

Build trust.

Acknowledging these experiences allows for a better understanding between you and your patients.

Share culturally informed resources.

Culturally specific education resources are being developed for you and your patients (see other side).

Explain how the visit will make a difference.

Use these talking points when referring your patients (adapt to your speaking style):

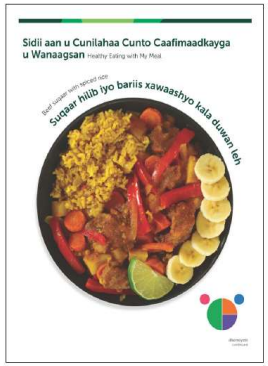
- **To a diabetes educator:** *"I would like you to visit with a diabetes educator. The educator can help you learn how to manage your diabetes, including how to monitor your blood sugar, solve problems and create an eating plan that includes food from your [Somali/Hmong/etc.] culture."*
- **To a dietitian:** *"Many of my patients from the [Somali/Hmong/etc.] community enjoy their visits with the dietitian because they have more time to explain and teach you about healthy eating and diabetes. They'll respect your food culture and you can discuss what works well for your family."*

continued

Tips for referring your patients to a diabetes educator or nutritionist	
Acknowledge their fears	Don't be afraid to bring up examples. For example, "I've seen that my patients from the Hmong community are hesitant to go to these visits because they think we'll tell them they can't have rice, which is a staple food in their culture."
Reassure them	Tell them that the education is tailored to their culture. They'll still be able to eat rice, injera or other cultural foods important to them.
Ask (practice cultural humility)	Try: "What concerns do you have about going to this appointment?" Help patients feel more in control of these visits and give an opportunity for patients and their family to speak openly.
Share information	Resources for your patients are available on myPartner. See below.
Follow up	After the visit, ask about their experience and listen for any concerns or questions. Read the educator's or dietitian's notes so you know what was discussed.

Resources for your patients

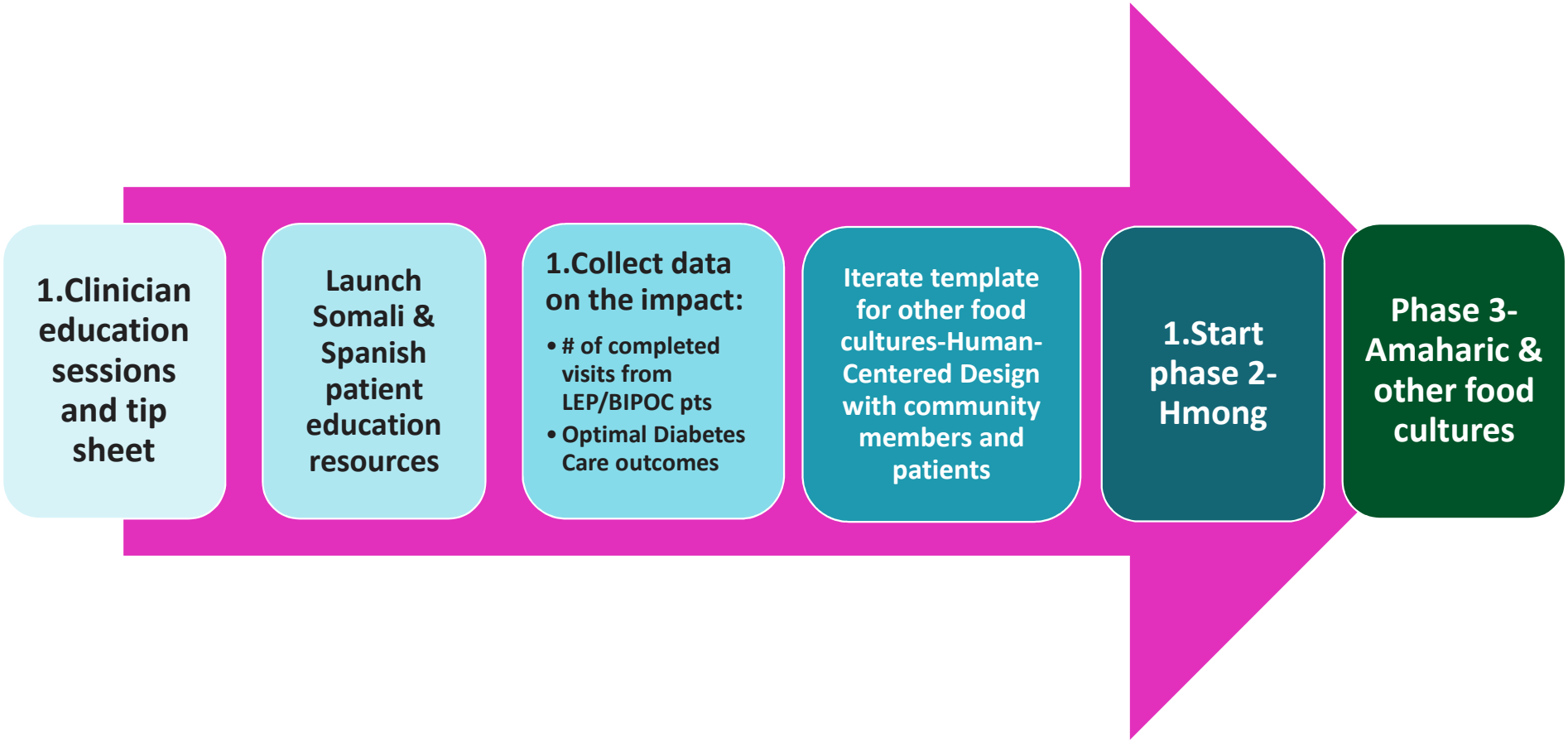
Find the latest patient resources, including videos, patient education handouts and more on myPartner. Go to **Departments** > **Clinician & Patient Education Services** > **Clinical guidance** > **Diabetes, vascular and hypertension care.**



What's new in DM/nutrition education that is culturally informed? *(video=7:05 min)*

https://youtu.be/EmY0m2KW0a4

Next Steps



Key take aways

- We do a great job over all in quality improvement
- Health care disparity/inequity persists
- Our past approach is not enough for all patient populations
- We need to meet patients and communities where they are at
- Using human-centered design principles, co-designing with our patients and communities and iterate over time improves adherence
- Practice culturally responsive care
- Build trust wherever and whenever you can because it pays dividends

Appendix

Examples of health disparity in endocrinology

References

HealthPartners Clinic

What about endocrinology specific case examples of health care disparity?

2.26% disparity in Adjusted Mean A1C in Black v. White Young Adults-SDOH composed the largest component of glycemic disparity in DM I

- Identifiable disparities include technology use, diabetes stress, self-management
- Implicit bias in prescribing technology for Black vs Hispanic vs White patients must be considered
  - Studies in statin, psychotropic meds, opioids for pain control suggest that prescribing practices create racial ethnic disparities.
- Black YA has societal/cultural legacy of mistrust of healthcare system, systemic racism leading to diabetes tress and lower self management due to lower social & disease related support in low SES communities

Agarwal JCEM, Aug 2020

References

Agarwal, Shivani et al, August 2020. “Racial-Ethnic inequity in Young Adults with Type I Diabetes.” JCEM 105(8); e2960-e2969.

Artiga, Samantha, Orgera, Kendal. March 4, 2020. “Health and Health Care: Five Key Questions and Answers.” *KFF*

Bacon, Emily. 2020. “Racial/Ethinic differences in treatment recommendations: lifestyle changes and medication prescriptions for high cholesterol.” 25(2); 273-388.

Bailey, Zinzi D., et al. April 8, 2017. “Structural racism and health inequities in the USA: evidence and interventions.” *The Lancet* 389: 1453-1463.

Ben, Jehonathan et al. December 18, 2017. “Racism and health service utilization: A systematic review and meta-analysis.” *Plos One 1-22 @ https://doi.org/10.1371/journal.pone.0189900.*

Braverman P, Arkin E, Orleans T, Proctor D and Plough A. May 1, 2017. “What is Health Equity?” Robert Wood Johnson Foundation.

Burton, Elan et al. 2020. “COVID-19: Health Disparities and social determinants of health.” *International Social Work 63(6):771-776.*

Byrd, Angel S. et al. 2018. “Racial Disparities in Obesity Treatment.” Curr Obes Rep. 7(2); 130-138.

Carratala, Sofia, Maxwell, Connor. May 7, 2020. “Health Disparities by Race and Ethnicity..” *Center for American Progress*

Chadha, Noor et al. 2018 “Toward the abolition of biological race in medicine.” The Institute for Healing and Justice in Medicine.

Chung, Siukyung et al. 2020. “Patient-Reported Experiences in Discussing Prescribed Medications with a Health Care Provider: Evidence for Racial/Ethnic Disparities in a large Health Care Delivery System.” *Population Health Management* 23(1): 78-84.

Collins, Sara, Gunja, Munira Z, and Aboulafia, Gabriella N. August 19, 2020. *“ U.S. Health Insurance Coverage in 2020: A Looming Crisis in Affordability”* The Commonwealth Fund

Freeman, Lauren, Stewart, Heather. 2019. “Microaggressions in Clinical Medicine.” *Kennedy Institute of Ethics Journal* 28(4): 411-449.

Foronda, Cynthia et al. 2016. “ Cultural Humility: a Concept Analysis” *J. Transcultural Nursing* 27(3):210-217

Golden, Sheita et al. 2021. “Casting a Health Equity Lens on Endocrinology and Diabetes.” J. Clinical Endocrinology & Metabolism 106(4); e`909e1916.

References

Hagiwara, Nao, et al. 2019. "Detecting implicit racial bias in provider communication behaviors to reduce disparities in healthcare: Challenges, Solutions, and future directions for provider communication training. "*Patient Education and Counseling* 102(2019): 1738-1743.

Institute for Healing and Justice. "*Towards the Abolition of Biological Race in Medicine and Public Health: Transforming Clinical Education, Research, and Practice"* https://www.instituteforhealingandjustice.org/section-1-racism-not-race-causes-health-disparities.

Johnson, Rachel L, et al. December 2004. "Patient Race/Ethnicity and Quality of Patient-Physician Communication During Medical Visits." *American J of Public Health* 94(12): 2084-2090.

Milner, Adrienne, Frantz, Berkeley, and Braddock, Jomilis Henry. Sept 25, 2020. "We need to talk about racism-in all of its forms-to understand COVID-19 disparities." *Health Equity* 4(1): 1-8.

MNCM.org; mnhealthscores.com "2019 Minnesota Health Care Disparities by Insurance Type." May 2020.

Paul-Emile, Kimani et al. 2020 *"Addressing Patient Bias Toward Health Care Workers: Recommendations for Medical Centers*." Annals of Internal Medicine 173: 468-473.

Russell, Tonya. July 11, 2020. "Racism in care leads to health disparities, doctors and other experts say as they push for change." *The Washingtong Post.*

Roswell, Robert et al. December 2020 "Cultivating Empathy Through Virtual Reality: Advancing Conversations About Racism, Inequity, and Climate in Medicine." *Academic Medicine* 95(12):1882-1986.

Saluga, Bani, Bryant, Zenobia. November 2020. "How Implicit Bias Contributes to Racial Disparities in Maternal Morbidity and Mortality in the United States." *J of Women's Health 00(00): 1-4.*

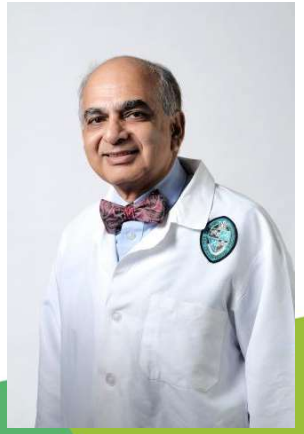
Schoenthaler, Antoinette, et al. 2014. "Patient-physician Racial/Ethnic Concordance and Blood Pressure Control: The role of trust and medication adherence." 19(5); 565-578.

References

Van Ryn, Michelle, Burke, Jane. “The effect of patient race and socio-economic status on physicians’ perceptions of patients.” *Social Science & Medicine 50(200): 813-828.*

Vyas, Darshali A, Eisenstein, Leo G., Jones, David S. August 27, 2020. “Hidden in Plain Sight-Reconsidering the use of Race Correction in Clinical Algorithms.” *N Engl J Med* 383(9): 874-882.

Zimmerman, Frederick J, Anderson, Nathanial W. June 28, 2019. “Trends in Health Equity in the United States by Race/Ethnicity, sex, and income, 1993-2017.” *Jama Network Open 2(6): e196386.doi:10.1001/jamanetworkopen.2019.6386.*



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Using Modern Risk Engines and ML/AI to Predict Diabetes Complications

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Tulane University

Disclosure

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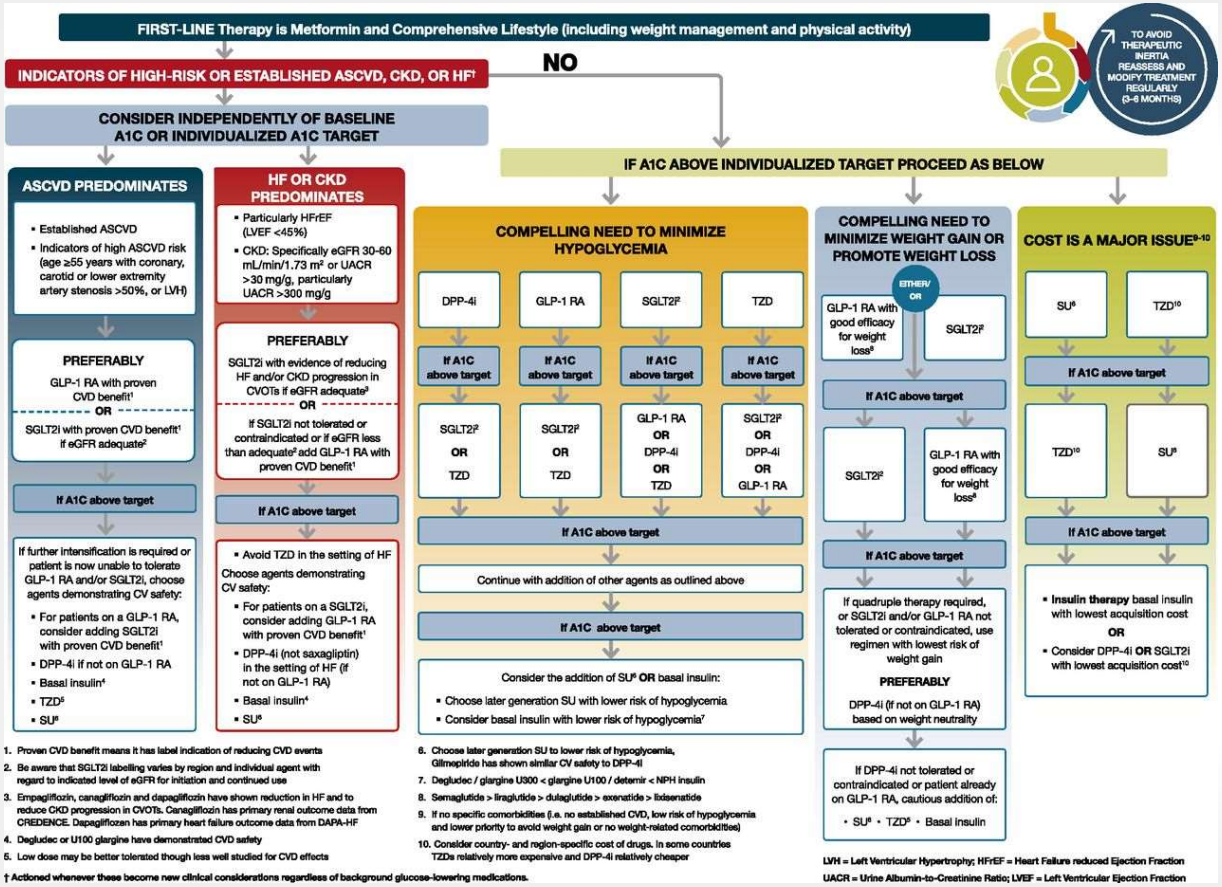
Stock: BRAVO4Health, Insulin Algorithms



Glucose-lowering Medication in Type 2 Diabetes: Overall Approach

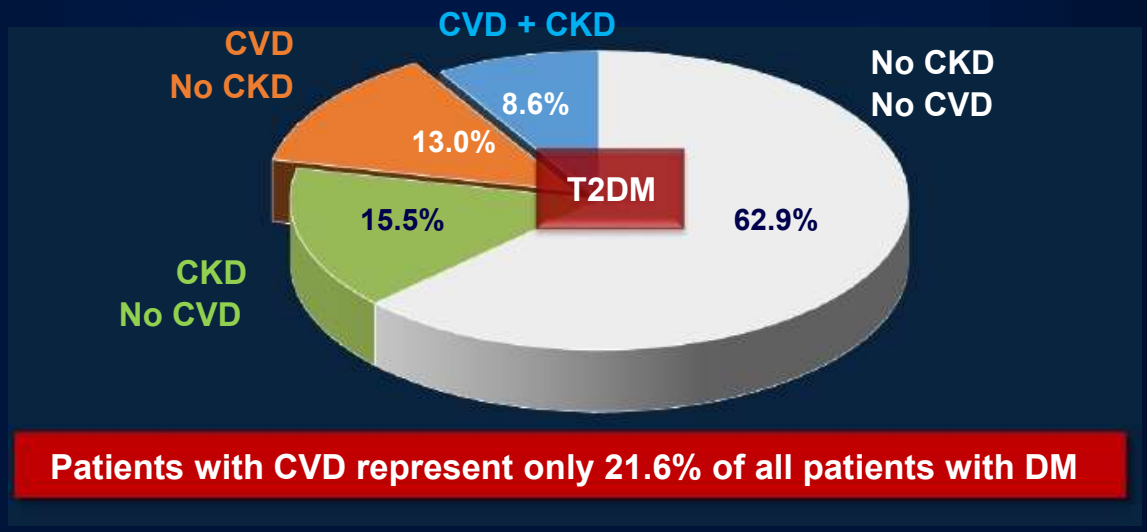
Pharmacologic Approaches to Glycemic Management: *Standards of Medical Care in Diabetes - 2020. Diabetes Care* 2020;43(Suppl. 1):S98-S110

Prevalence and Co-Prevalence of Comorbidities in T2DM (Q-EMR)

N=1.39 million

Total CKD: 24.1%

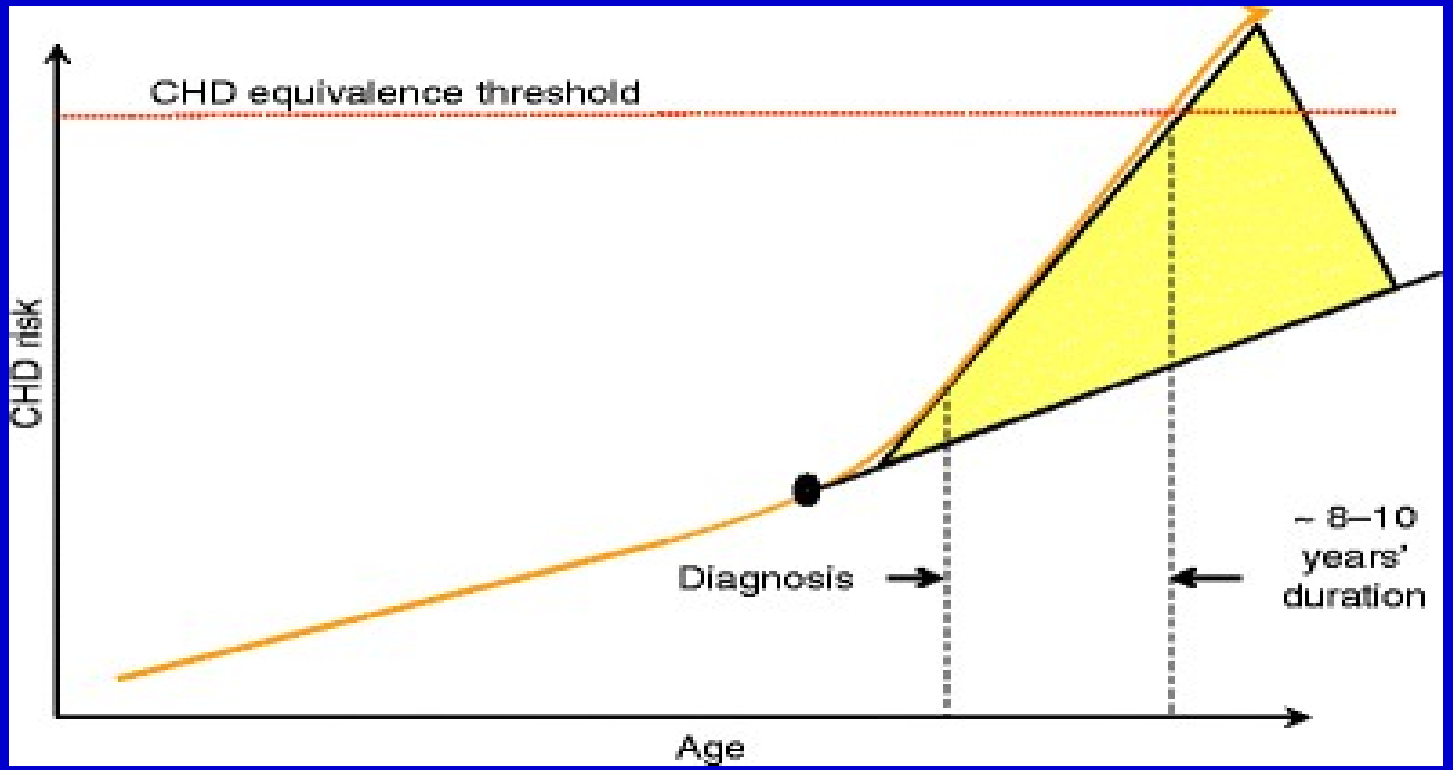
Total CVD: 21.6%



CKD was defined based on the presence of an ICD-9-CM diagnosis code or, if a code was not present, an estimated glomerular filtration rate (eGFR) <60mL/min/1.73m^2 using the most recent measurement prior to the index date. If not already estimated in the database, eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) study equation.

Iglay K, et al. *Curr Med Res Opin* 2016;32:1243-52.

Diabetes: Not Always a CVD risk Equivalent



Sattar N; Diabetologia 2013

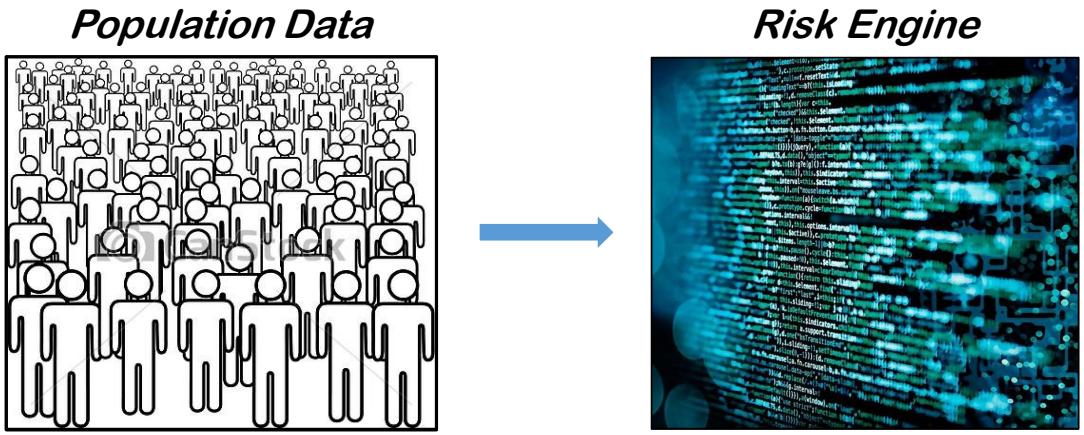
Can We Be More Accurate in Individual Risk Prediction?

Can This lead to Better Individualization of Goals?

Would Better Targeting of Goals lead to better Outcomes?

Characteristics of DM Subtypes

• What is a risk engine?



- To simulate the progression of diabetes, an algorithm with a set calculation equations, derived from a large trial population (e.g., UKPDS).
- It evolves by new knowledge and new data cohorts (e.g., ACCORD/BRAVO)
- It improves by analytics tools (e.g., machine learning)

The components of the score are:

- **Age**
- **Gender**
- **Total cholesterol in mmol/L**
- **Cigarette smoking**
- **High density lipoprotein (HDL) cholesterol in mmol/L**
- **Systolic blood pressure in mmHg**
- **Medication for hypertension.**

CHD risk at 10 years calculated but "risk" is arbitrary
Framingham risk equations are unable to provide:

1. **Accurate estimations of absolute risk in individuals from different populations.**
2. **Risk estimates do not have the flexibility to incorporate regional, socioeconomic, and temporal differences in disease rates.**
3. **Unable to predict outcomes in patients with diabetes – it overestimated the risks in the EPIC-Norfolk study,.**

UKPDS OUTCOMES MODEL 2

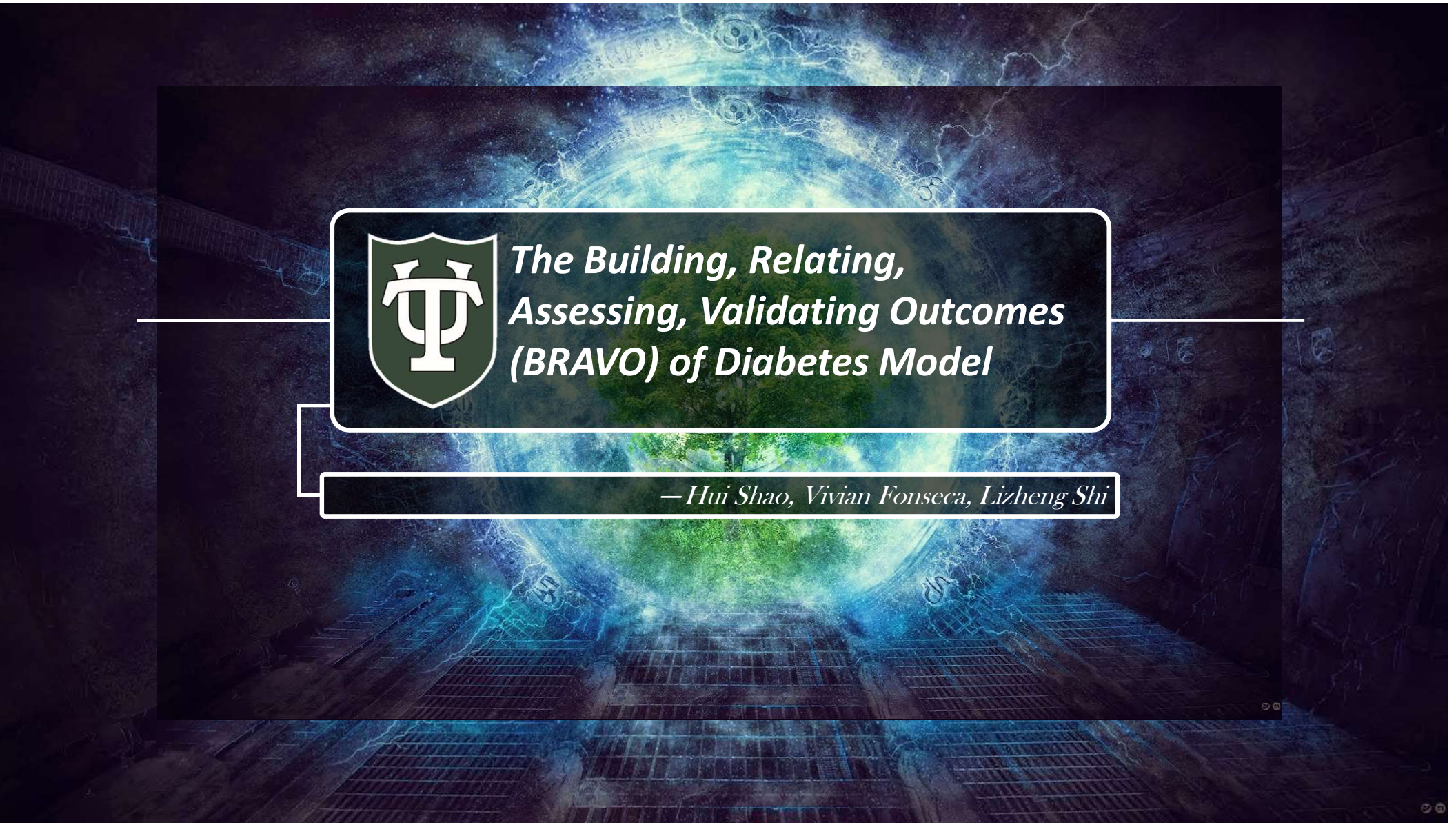
- Model equations were based on a median 17.6 years of follow-up and up to 89,760 patient-years of data- double the number of events
- Greater precision and a larger number of significant covariates.
- Internally valid over 25 years
- Predicts event rates for complications, which are lower than those from the existing model.
- Based on a small English Population with recent onset Diabetes
- Is it applicable to a US based multi- ethnic population?

UKPDS Risk Engine is Outdated

Applying UKPDS Risk Engine to Predict ACCORD Cohort

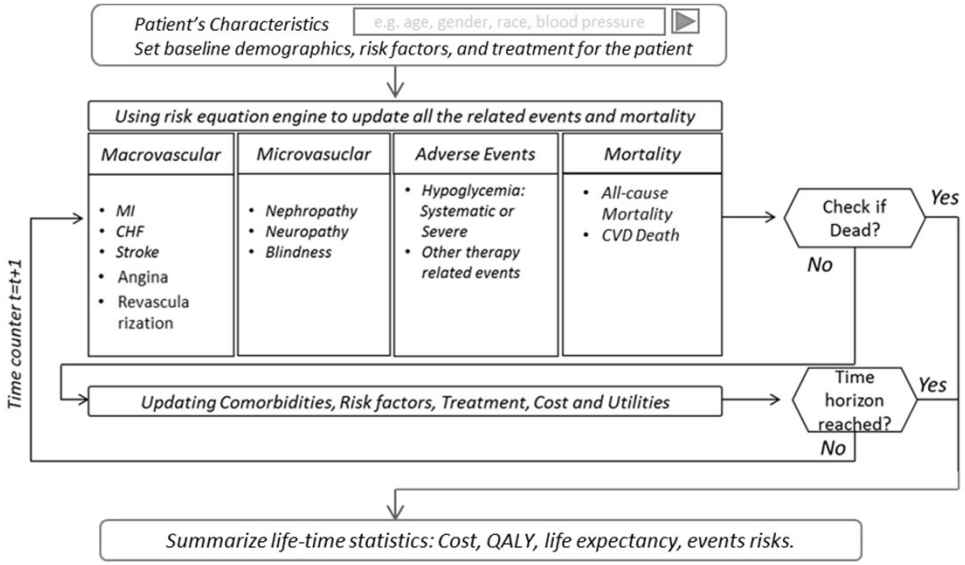
	ACCORD (Standard Glucose)		
	Observed	UKPDS	Relative Bias*
Stroke	1.40%	2.30%	164.29%
Non-Fatal	1.20%	1.80%	150.00%
Fatal	0.20%	0.50%	250.00%
MI	4.90%	6.50%	132.65%
Non-Fatal	4.60%	2.60%	56.52%
Fatal	0.30%	3.90%	1300.00%
CHF	4.00%	2.20%	55.00%
Non-Fatal	3.50%	2.00%	57.14%
Fatal	0.50%	0.20%	40.00%
ESRD	3.00%	0.50%	16.67%
Blind	8.10%	1.35%	16.67%
All Cause Mortality	4.00%	10.30%	257.50%
CVD Mortality	1.30%	4.60%	353.85%

* Relative Bias= Predicted(UKPDS)/Observed


The Building, Relating, Assessing, Validating Outcomes (BRAVO) of Diabetes Model
—Hui Shao, Vivian Fonseca, Lizheng Shi

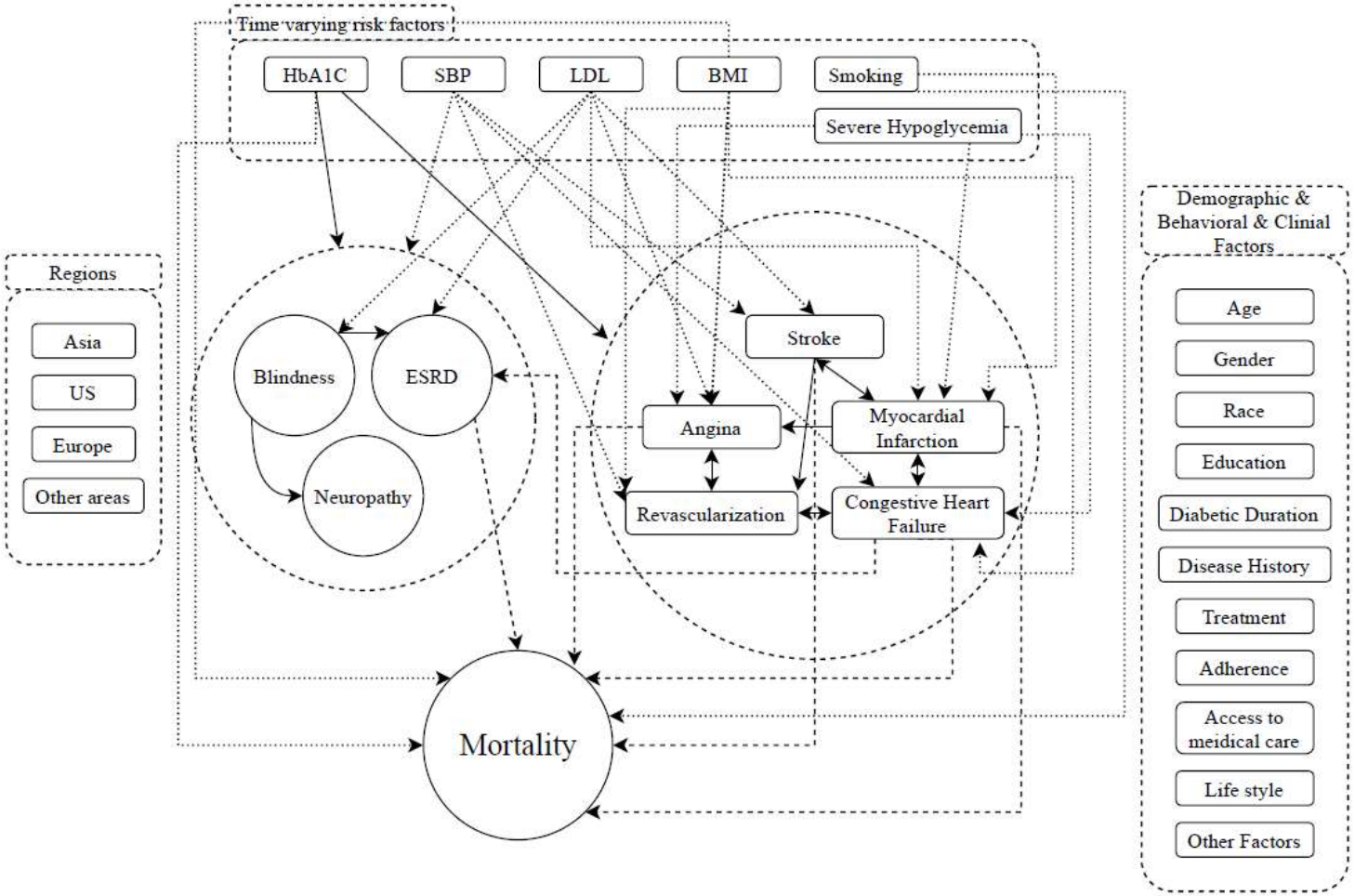
- Overview
  - Based on ACCORD trial.
  - Patient-Level Microsimulation Model.
- Features
  - Predict both primary and secondary CVD events.
  - Microvascular Events
  - Key biomarkers (e.g., HbA1c, LDL-c) progress over time.
  - QALY function decrements associated with complications.
  - Globalization module: predict patients from other regions.
- Potential applications

What is the BRAVO Diabetes Model?



- Person-level, real-time, microsimulation model.
- Simulate risk for diabetes complications and mortality for patients with diabetes.
- Life expectancy, risks of different events, life-time costs and cumulative QALY can be predicted to assist decision making.

What is the BRAVO Diabetes Model?



PREDICTION MODELS COMPARISON

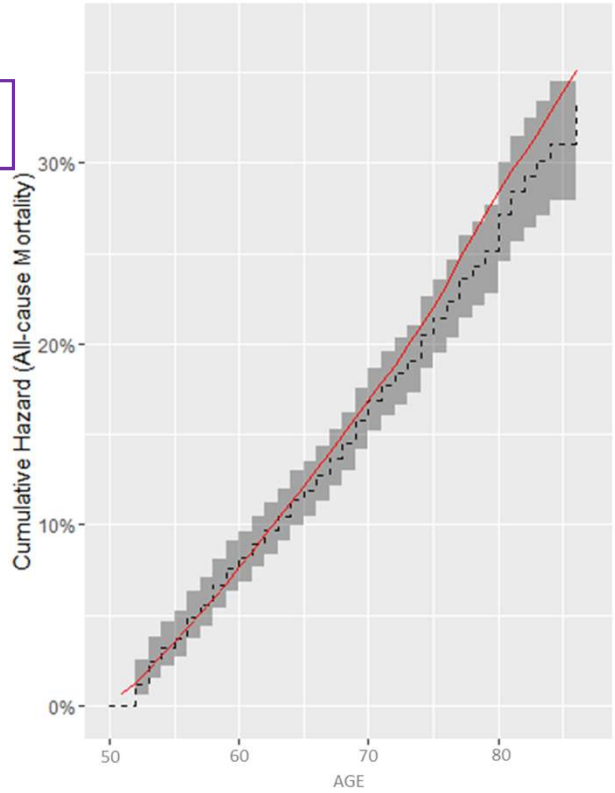
Differences between BRAVO model, Framingham equation and ASCVD equation

	Framingham	ASCVD	BRAVO
Infer clinical decision (e.g. risk stratification, and patient heterogeneity)			
• predict risk of general cardiovascular event as one outcome	**Yes**	**Yes**	**Yes**
• predict risks of different cardiovascular event types (i.e., MI, CHF)			**Yes**
• predict risks of microvascular complications (i.e., ESRD, Blindness)			**Yes**
• Short-term outcomes prediction (<=10 years)	**Yes**	**Yes**	**Yes**
• Long-term or lifetime outcomes prediction		**Yes**	**Yes**
• Cost estimation over a specified time period			**Yes**
• QALY estimation over a specified time period			**Yes**
• Take into account impact of treatment			**Yes**
Support discrete-time event simulation and cost-effectiveness analysis			
• Person-level microsimulation			**Yes**
• Allow 1st (stochastic) order uncertainty			**Yes**
• Allow 2nd order uncertainty			**Yes**
• Allow time-varying risk factors			**Yes**
• Allow inter-related diabetes complications			**Yes**
Global Calibration Module, allow cross-country prediction			**Yes**

All Cause Mortality

Prediction equation for All-cause Mortality

Variables	Coefficient	S.E.	HR	95% CI	
				Lower	Upper
HbA1c	-0.674	0.516	0.510	0.185	1.401
HbA1c^2	0.047	0.033	1.048	0.982	1.118
BMI	0.018	0.009	1.018	1.000	1.036
Smoking	0.688	0.154	1.990	1.471	2.691
Female	-0.551	0.116	0.576	0.459	0.724
Education	-0.317	0.126	0.728	0.569	0.932
MI History	0.196	0.118	1.217	0.965	1.533
Stroke History	0.324	0.165	1.383	1.001	1.911
CHF History	0.777	0.139	2.175	1.656	2.856
Angina History	0.417	0.128	1.517	1.181	1.950
Stroke_Event	1.229	0.369	3.418	1.658	7.044
CHF Event	1.745	0.185	5.726	3.984	8.228
Log(Scale)	2.444	0.099			
Log(Shape)	-6.391	2.113			



Functional Form: *Gompertz*

- *Previous study found U shape between HbA1c and mortality*
- *7.17% is the optimal point for HbA1c (U shape)*

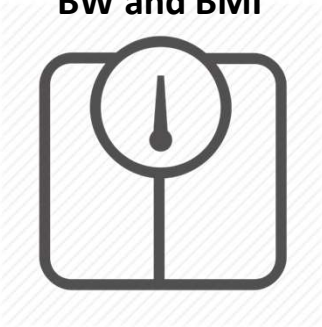
C-Statistics

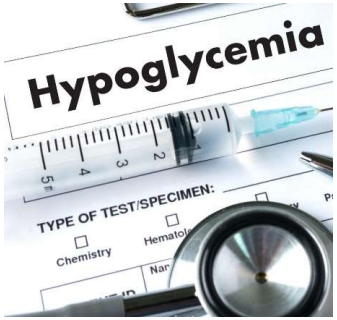
	BRAVO	UKPDS[1]	RECODe[2]	ASCVD[3]	QRISK[4]
All-Cause Death	0.79 (0.77, 0.81)	0.72	0.70 (0.68, 0.72)		
CVD Death	0.80 (0.78. 0.83)	0.70	0.74 (0.71, 0.77)		
Nonfatal MI	0.79 (0.77, 0.80)	0.58	0.69 (0.67, 0.70)	10-year CVD 0.65 (0.60, 0.69)	10-year CVD 0.78
Nonfatal CHF	0.80 (0.78, 0.82)	0.71	0.75 (0.73, 0.77)		
Nonfatal Stroke	0.79 (0.76, 0.82)	0.66	0.70 (0.66, 0.74)		

1. Keng MJ, Leal J, Mafham M, et al. Performance of the UK Prospective Diabetes Study Outcomes Model 2 in a Contemporary UK Type 2 Diabetes Trial Cohort. Value Health. 2022 Mar;25(3):435-442. doi: 10.1016/j.jval.2021.09.005.
2. Basu S, Sussman JB, Berkowitz SA, et al. Development and validation of Risk Equations for Complications Of type 2 Diabetes (RECODe) using individual participant data from randomised trials. Lancet Diabetes Endocrinol. 2017 Oct;5(10):788-798. doi: 10.1016/S2213-8587(17)30221-8.
3. Kuragaichi T, Kataoka Y, Miyakoshi C, et al. External validation of pooled cohort equations using systolic blood pressure intervention trial data. BMC Res Notes. 2019 May 14;12(1):271. doi: 10.1186/s13104-019-4293-1.
4. Collins GS, Altman DG. An independent external validation and evaluation of QRISK cardiovascular risk prediction: a prospective open cohort study. BMJ. 2009 Jul 7;339:b2584. doi: 10.1136/bmj.b2584.

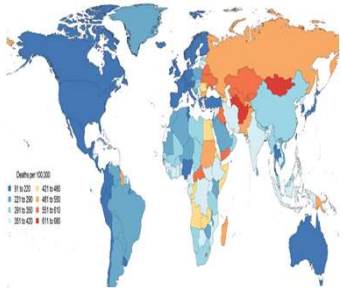
COMPARED TO OTHER MODELS, THE BRAVO MODEL INCLUDES FOUR KEY ASPECTS:

BW and BMI





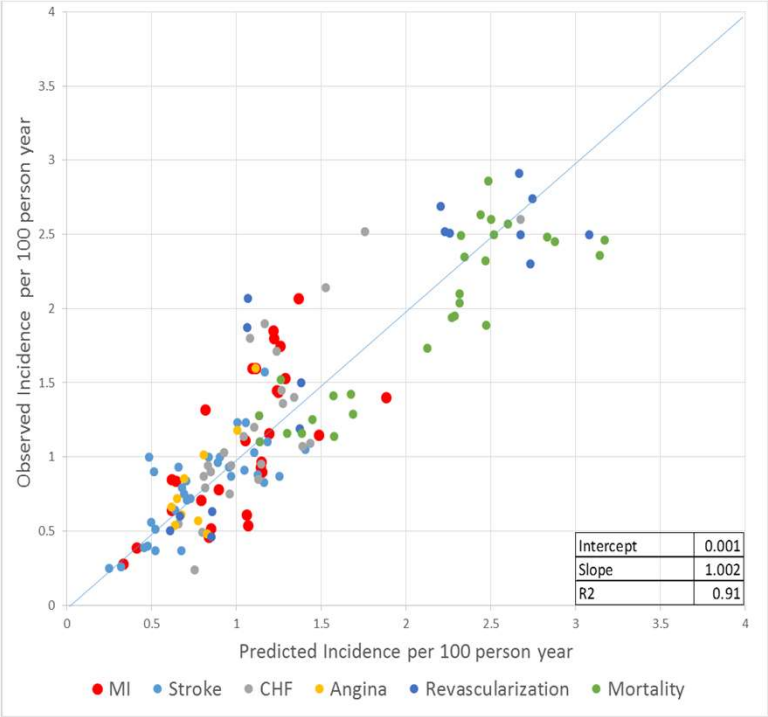
Globalization



Utility and QALY

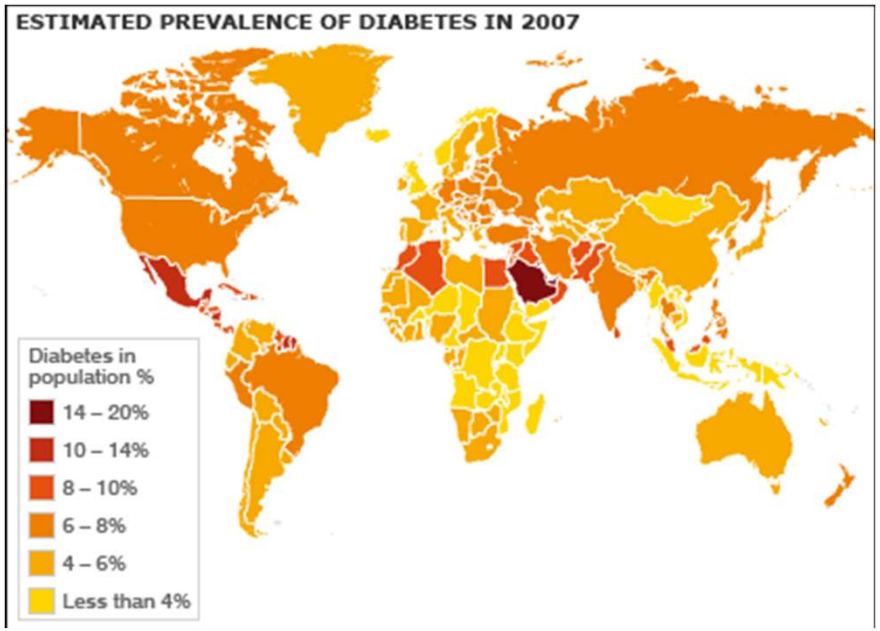
- Better capturing impact of body weight on cardiovascular risks, cost and QALY.
- Better capturing impact of hypoglycemia.
- Has a globalization module to calibrate regional variation of cardiovascular risks.
- Has both utility and QALY equations developed from the same study cohort. .

The BRAVO Diabetes Model has high Prediction Accuracy



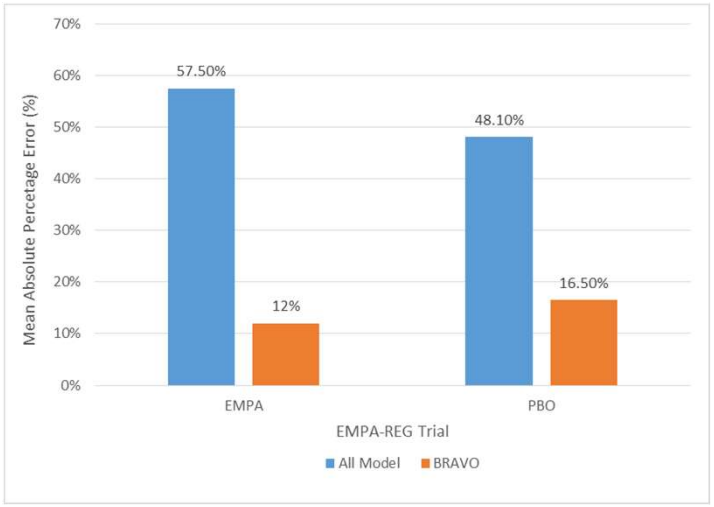
- The Globalized BRAVO Model has been externally validated using 18 large clinical trials.
- Results show high prediction accuracy (R2=0.91).

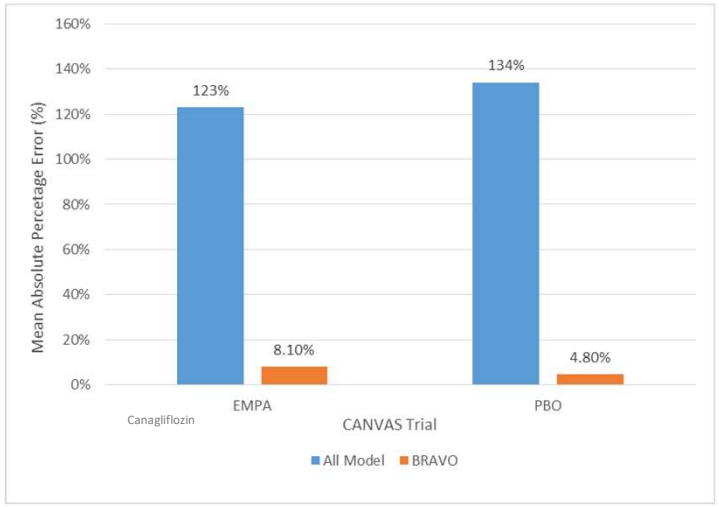
Regional Variation



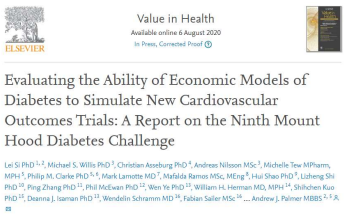
- The BRAVO model has been calibrated against 18 multinational large RCT studies conducted after 2000.
- Regional variation in CVD outcomes were included as an important risk factor in the simulation.

- The International Diabetes Simulation Model Bi-annually Competition: The Mount Hood Challenge





- In EMPA-REG trial, the average prediction errors across 12 models were 57.50% (Treatment) and 48.1% (Placebo), while the prediction error of BRAVO model was 12.0% and 16.5%, respectively.
- In CANVAS trial, the average prediction errors across 12 models were 123% (Treatment) and 134% (Placebo), while the prediction error of BRAVO model was 8.1% and 4.8%, respectively.


Value in Health
Available online 6 August 2020
In Press, Corrected Proof

Evaluating the Ability of Economic Models of Diabetes to Simulate New Cardiovascular Outcomes Trials: A Report on the Ninth Mount Hood Diabetes Challenge

What Does BRAVO Diabetes Model Do?

Risk Stratification

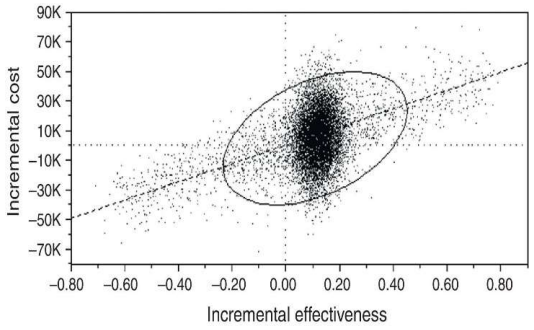
—For Healthcare System

Diabetes Management

—For Clinical Practice

Cost-effectiveness Analysis

—For Pharmacoeconomics & Policy Making



Program Evaluation

—Health Care Providers

From: **Potential Gains in Life Expectancy Associated With Achieving Treatment Goals in US Adults With Type 2 Diabetes**

JAMA Netw Open. 2022;5(4):e227705. doi:10.1001/jamanetworkopen.2022.7705

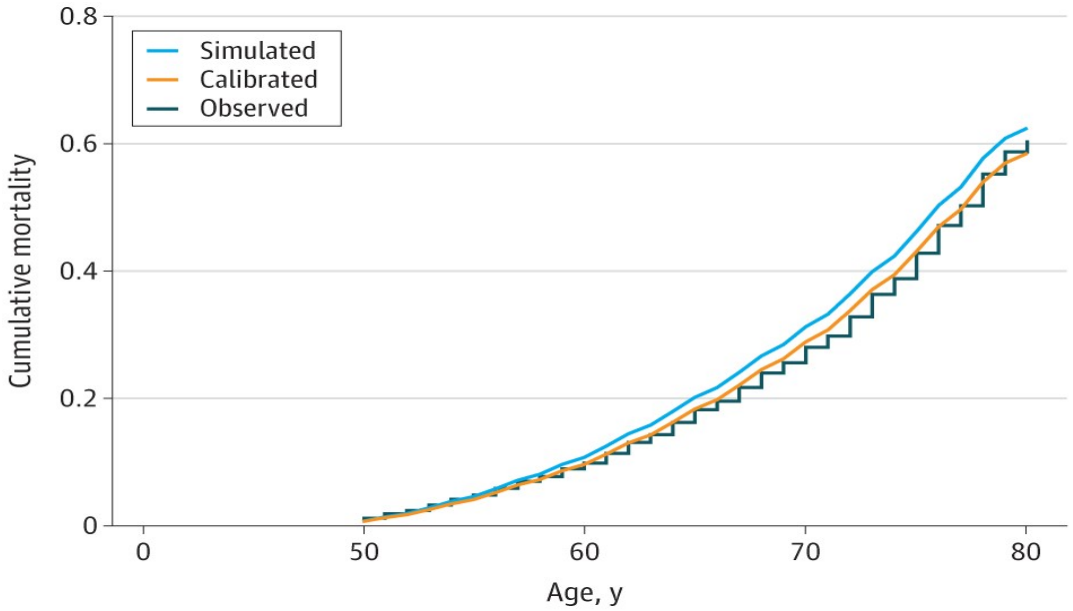
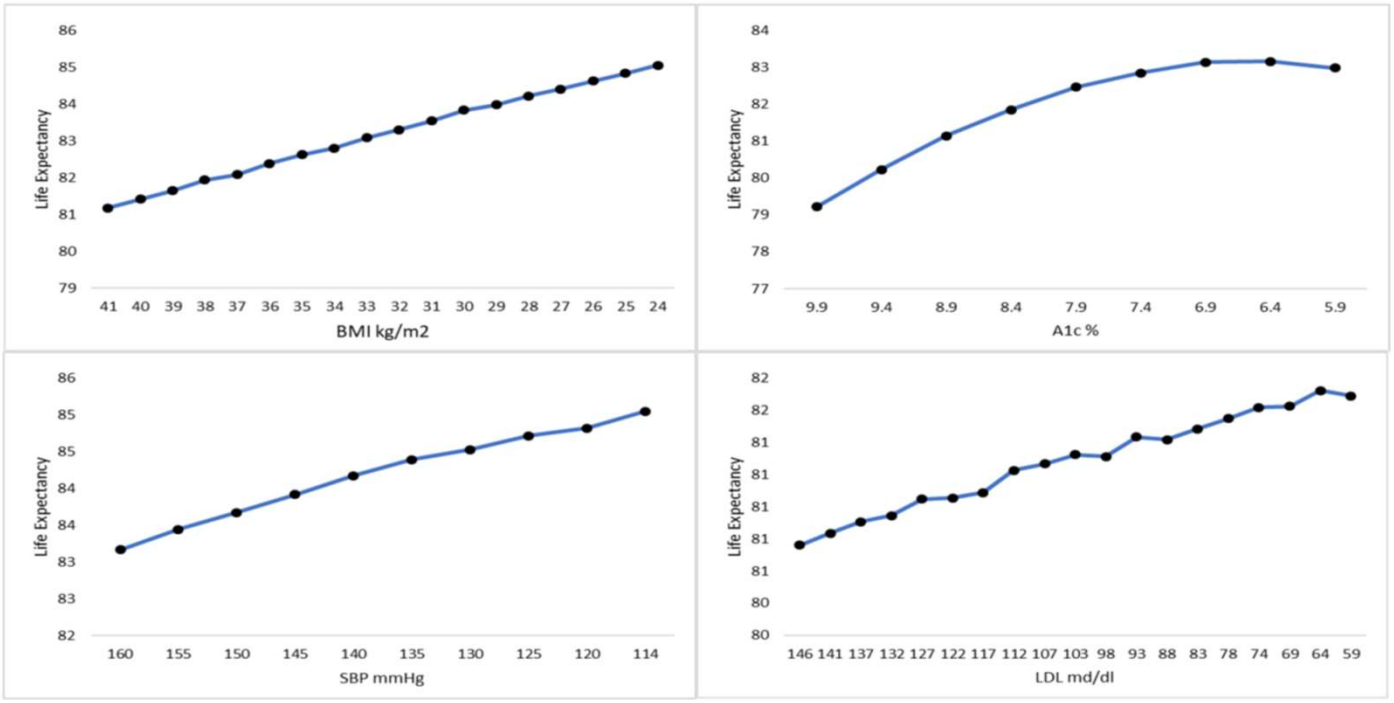


Figure Legend:

Cumulative Mortality Over 30 Years in Individuals With Type 2 Diabetes at Age 51 to 55 Years

Study No.1 Life Expectancy Associated with Biomarker Control

eFigure 3 Life-Expectancies Associated With Different Levels of BMI, A1c, SBP, and LDL.



- JAMA Network Open 2022

From: **Potential Gains in Life Expectancy Associated With Achieving Treatment Goals in US Adults With Type 2 Diabetes**

JAMA Netw Open. 2022;5(4):e227705. doi:10.1001/jamanetworkopen.2022.7705

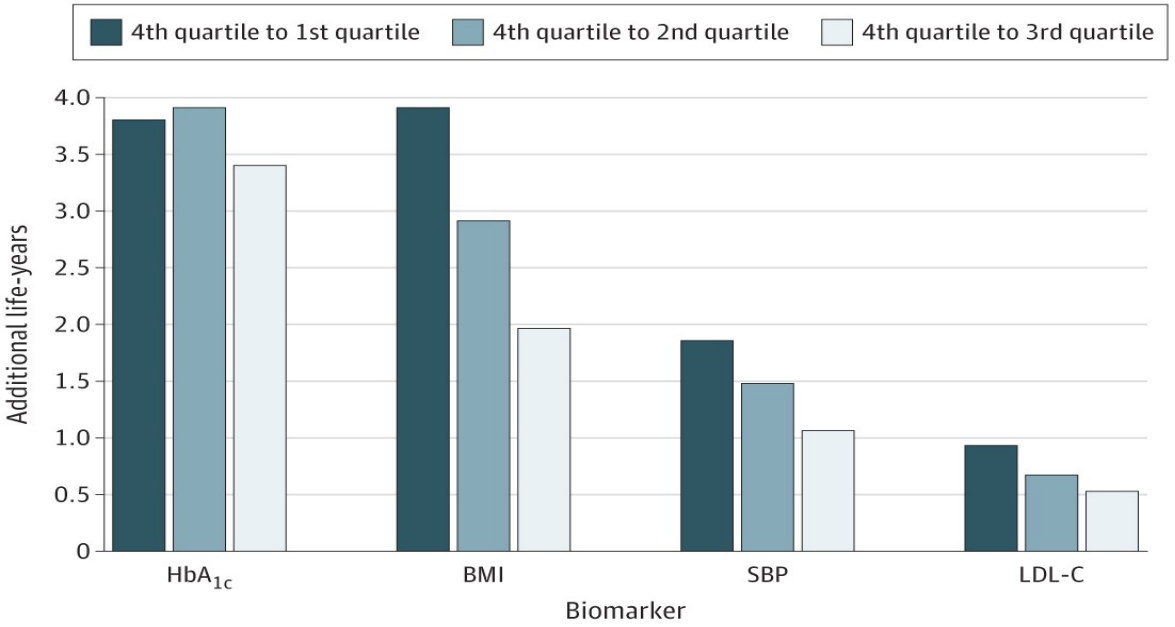


Figure Legend:

Gains in Life-Years Associated With Different Levels of Biomarkers in Individuals With Type 2 DiabetesThe mean values of biomarkers for the first, second, third, and fourth quartile were as follows: glycated hemoglobin (HbA_{1c}), 5.9%, 6.8%, and 7.7% vs 9.9% (to convert to proportion of total hemoglobin, multiply by 0.01); systolic blood pressure (SBP), 114.1 mm Hg, 128.1 mm Hg, and 139.1 mm Hg vs 160.4 mm Hg; low-density lipoprotein cholesterol (LDL-C), 58.9 mg/dL, 84.0 mg/dL, and 107.0 mg/dL vs 146 mg/dL (to convert to mmol/L, multiply by 0.0259), and body mass index (BMI, calculated as weight in kilograms divided by height in meters squared), 24.3, 28.6, and 33.0 vs 41.4.

From: **Potential Gains in Life Expectancy Associated With Achieving Treatment Goals in US Adults With Type 2 Diabetes**

JAMA Netw Open. 2022;5(4):e227705. doi:10.1001/jamanetworkopen.2022.7705

	Age, y	SBP, mm Hg	BMI = 25									BMI = 30									BMI = 35								
			HbA_{1c} (7%)			HbA_{1c} (8%)			HbA_{1c} (10%)			HbA_{1c} (7%)			HbA_{1c} (8%)			HbA_{1c} (10%)			HbA_{1c} (7%)			HbA_{1c} (8%)			HbA_{1c} (10%)		
Women	51-60	180	27.6	27.2	26.6	26.6	26.0	25.3	22.4	21.5	20.5	26.2	25.7	25.1	25.1	24.6	23.8	21.0	20.2	19.4	24.7	24.2	23.7	23.6	23.1	22.4	19.6	18.9	18.2
		160	28.8	28.5	28.1	28.1	27.6	27.1	24.1	23.4	22.7	27.6	27.3	26.8	26.8	26.3	25.8	22.8	22.3	21.5	26.2	25.9	25.5	25.3	24.9	24.4	21.5	21.0	20.3
		140	29.6	29.4	29.2	29.0	28.7	28.3	25.4	24.9	24.4	28.5	28.3	28.0	27.8	27.5	27.2	24.2	23.8	23.3	27.4	27.1	26.8	26.6	26.3	25.9	22.9	22.5	22.0
		120	30.1	30.0	29.8	29.6	29.4	29.2	26.3	26.0	25.6	29.2	29.0	28.8	28.6	28.3	28.1	25.1	24.8	24.5	28.1	27.9	27.7	27.5	27.2	27.0	24.0	23.7	23.3
	61-70	180	20.4	19.9	19.3	19.4	18.8	18.1	15.6	14.9	14.0	19.0	18.6	18.1	18.1	17.6	17.0	14.5	13.9	13.2	17.7	17.3	16.9	16.8	16.3	15.8	13.5	12.9	12.3
		160	21.7	21.4	20.9	20.9	20.5	19.9	17.2	16.7	15.9	20.4	20.1	19.8	19.6	19.2	18.8	16.1	15.6	15.0	19.1	18.8	18.5	18.3	18.0	17.5	15.0	14.6	14.0
		140	22.6	22.3	22.0	21.9	21.6	21.2	18.3	18.0	17.5	21.4	21.1	20.9	20.8	20.4	20.1	17.3	17.0	16.5	20.2	20.0	19.8	19.5	19.3	18.9	16.3	15.9	15.5
		120	23.2	23.0	22.8	22.6	22.4	22.1	19.2	19.0	18.5	22.1	22.0	21.7	21.5	21.3	21.1	18.2	17.9	17.6	21.0	20.8	20.6	20.4	20.2	19.9	17.1	16.9	16.6
	71-80	180	12.7	12.2	11.8	11.9	11.4	10.9	9.1	8.5	7.9	11.7	11.3	10.9	10.9	10.6	10.1	8.4	7.9	7.3	10.7	10.4	10.1	10.0	9.7	9.3	7.6	7.3	6.8
		160	13.7	13.4	13.0	13.0	12.7	12.3	10.3	9.9	9.3	12.7	12.5	12.2	12.1	11.8	11.5	9.5	9.1	8.7	11.8	11.5	11.3	11.1	10.9	10.6	8.8	8.5	8.1
		140	14.4	14.2	14.0	13.9	13.6	13.3	11.2	10.9	10.5	13.5	13.3	13.1	13.0	12.8	12.5	10.4	10.1	9.8	12.6	12.4	12.2	12.1	11.9	11.6	9.6	9.4	9.1
		120	14.9	14.8	14.6	14.5	14.3	14.1	11.8	11.6	11.3	14.1	14.0	13.8	13.6	13.4	13.2	11.0	10.9	10.6	13.2	13.1	12.9	12.8	12.6	12.5	10.3	10.1	9.9
Men	51-60	180	23.3	22.9	22.4	22.4	21.9	21.1	18.4	17.7	17.0	22.1	21.6	21.1	21.1	20.6	20.0	17.3	16.7	16.0	20.7	20.2	19.9	19.8	19.3	18.8	16.2	15.6	15.0
		160	24.4	24.1	23.7	23.6	23.3	22.7	19.9	19.4	18.7	23.2	22.9	22.5	22.4	22.0	21.6	18.8	18.3	17.7	21.9	21.6	21.3	21.1	20.8	20.4	17.6	17.2	16.7
		140	25.1	24.9	24.7	24.5	24.3	23.8	20.9	20.6	20.1	24.0	23.8	23.5	23.4	23.1	22.8	19.8	19.5	19.0	22.8	22.6	22.3	22.2	21.9	21.6	18.7	18.4	18.0
		120	25.7	25.4	25.2	25.1	24.9	24.6	21.6	21.3	21.0	24.6	24.4	24.2	24.0	23.8	23.6	20.6	20.3	20.0	23.5	23.3	23.2	22.9	22.7	22.5	19.6	19.3	19.0
	61-70	180	16.3	15.9	15.4	15.5	15.0	14.4	12.2	11.7	11.0	15.2	14.9	14.4	14.4	14.0	13.5	11.4	10.9	10.3	14.1	13.8	13.4	13.4	13.0	12.6	10.5	10.1	9.6
		160	17.2	16.9	16.6	16.6	16.2	15.8	13.4	13.0	12.4	16.2	15.9	15.6	15.5	15.3	14.9	12.5	12.2	11.7	15.1	14.9	14.6	14.4	14.2	13.9	11.7	11.3	10.9
		140	17.8	17.7	17.4	17.3	17.1	16.8	14.2	14.0	13.5	16.9	16.7	16.5	16.3	16.1	15.9	13.4	13.1	12.8	15.9	15.7	15.5	15.3	15.2	14.9	12.6	12.3	12.0
		120	18.3	18.2	18.0	17.9	17.7	17.5	14.8	14.6	14.4	17.4	17.3	17.1	16.9	16.8	16.5	14.0	13.8	13.6	16.5	16.3	16.2	16.0	15.8	15.6	13.2	13.0	12.8
	71-80	180	10.2	9.9	9.5	9.6	9.2	8.8	7.2	6.8	6.3	9.4	9.1	8.8	8.8	8.5	8.1	6.7	6.3	5.9	8.6	8.4	8.1	8.1	7.8	7.5	6.1	5.8	5.5
		160	10.9	10.7	10.4	10.4	10.2	9.8	8.1	7.8	7.3	10.2	9.9	9.7	9.6	9.4	9.1	7.5	7.2	6.9	9.4	9.2	9.0	8.9	8.7	8.5	6.9	6.7	6.4
		140	11.4	11.3	11.1	11.0	10.8	10.5	8.6	8.5	8.8	10.7	10.5	10.4	10.2	10.1	9.9	8.1	7.9	7.7	10.0	9.8	9.7	9.5	9.4	9.2	7.5	7.3	7.2
		120	11.8	11.7	11.5	11.4	11.3	11.1	9.1	8.9	8.8	11.1	11.0	10.8	10.7	10.6	10.4	8.5	8.4	8.2	10.4	10.3	10.2	10.0	9.9	9.8	8.0	7.8	7.7
			70	100	130	70	100	130	70	100	130	70	100	130	70	100	130	70	100	130	70	100	130	70	100	130	70	100	130
			LDL-C, mg/dL																										

Life expectancy, y

Shortest — Longest

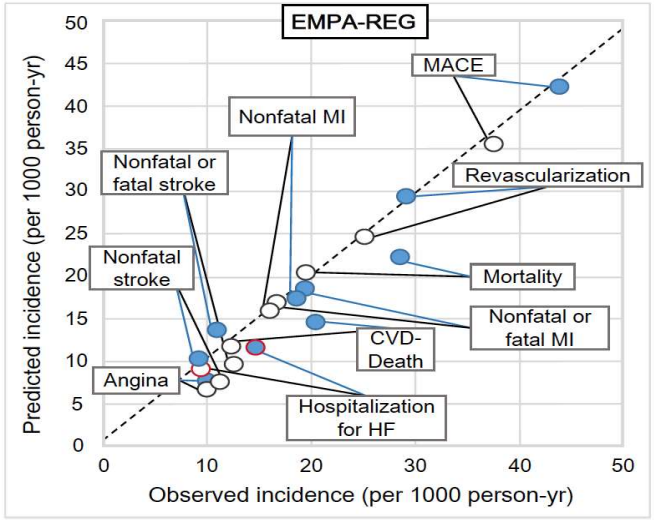
Study No.1 Life Expectancy Associated with Biomarker Control

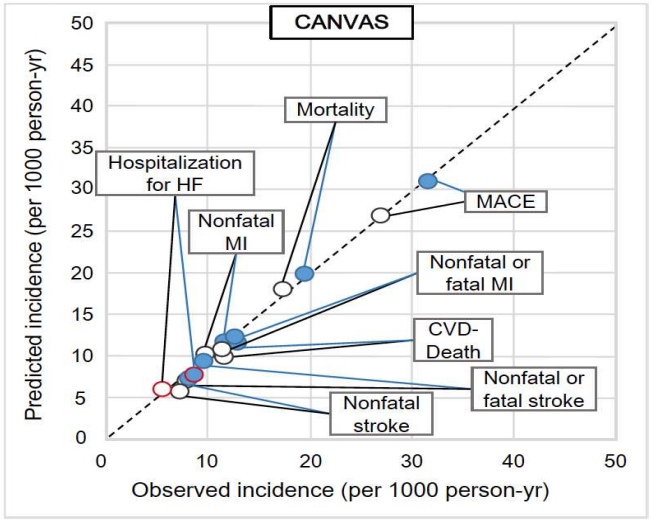
	Age	SBP (mmHg)	BMI=25 (kg/m2)									BMI=30 (kg/m2)									BMI=35 (kg/m2)								
			Hba1c (7%)			Hba1c (8%)			Hba1c (10%)			Hba1c (7%)			Hba1c (8%)			Hba1c (10%)			Hba1c (7%)			Hba1c (8%)			Hba1c (10%)		
Women	50-60	180	27.6	27.2	26.6	26.6	26.0	25.3	22.4	21.5	20.5	26.2	25.7	25.1	25.1	24.6	23.8	21.0	20.2	19.4	24.7	24.2	23.7	23.6	23.1	22.4	19.6	18.9	18.2
		160	28.8	28.5	28.1	28.1	27.6	27.1	24.1	23.4	22.7	[illegible]								21.5	26.2	25.9	25.5	25.3	24.9	24.4	21.5	21.0	20.3
		140	29.6	29.4	29.2	29.0	28.7	28.3	25.4	24.9	24.4	28.5	28.3	28.0	27.8	27.5	27.2	24.2	23.8	23.3	27.4	27.1	26.8	26.6	26.3	25.9	22.9	22.5	22.0
		120	30.1	30.0	29.8	29.6	29.4	29.2	26.3	26.0	25.6	29.2	29.0	28.8	28.6	28.3	28.1	25.1	24.8	24.5	28.1	27.9	27.7	27.5	27.2	27.0	24.0	23.7	23.3
	60-70	180	20.4	19.9	19.3	19.4	18.8	18.1	15.6	14.9	14.0	19.0	18.6	18.1	18.1	17.6	17.0	14.5	13.9	13.2	17.7	17.3	16.9	16.8	16.3	15.8	13.5	12.9	12.3
		160	21.7	21.4	20.9	20.9	20.5	19.9	17.2	16.7	15.9	20.4	20.1	19.8	19.6	19.2	18.8	16.1	15.6	15.0	19.1	18.8	18.5	18.3	18.0	17.5	15.0	14.6	14.0
		140	22.6	22.3	22.0	21.9	21.6	21.2	18.3	18.0	17.5	21.4	21.1	20.9	20.8	20.4	20.1	17.3	17.0	16.5	20.2	20.0	19.8	19.5	19.3	18.9	16.3	15.9	15.5
		120	23.2	23.0	22.8	22.6	22.4	22.1	19.2	19.0	18.5	22.1	22.0	21.7	21.5	21.3	21.1	18.2	17.9	17.6	21.0	20.8	20.6	20.4	20.2	19.9	17.1	16.9	16.6
	70-80	180	12.7	12.2	11.8	11.9	11.4	10.9	9.1	8.5	7.9	11.7	11.3	10.9	10.9	10.6	10.1	8.4	7.9	7.3	10.7	10.4	10.1	10.0	9.7	9.3	7.6	7.3	6.8
		160	13.7	13.4	13.0	13.0	12.7	12.3	10.3	9.9	9.3	12.7	12.5	12.2	12.1	11.8	11.5	9.5	9.1	8.7	11.8	11.5	11.3	11.1	10.9	10.6	8.8	8.5	8.1
		140	14.4	14.2	14.0	13.9	13.6	13.3	11.2	10.9	10.5	13.5	13.3	13.1	13.0	12.8	12.5	10.4	10.1	9.8	12.6	12.4	12.2	12.1	11.9	11.6	9.6	9.4	9.1
		120	14.9	14.8	14.6	14.5	14.3	14.1	11.8	11.6	11.3	14.1	14.0	13.8	13.6	13.4	13.2	11.0	10.9	10.6	13.2	13.1	12.9	12.8	12.6	12.5	10.3	10.1	9.9
Men	50-60	180	23.3	22.9	22.4	22.4	21.9	21.1	18.4	17.7	17.0	22.1	21.6	21.1	21.1	20.6	20.0	17.3	16.7	16.0	20.7	20.2	19.9	19.8	19.3	18.8	16.2	15.6	15.0
		160	24.4	24.1	23.7	23.6	23.3	22.7	19.9	19.4	18.7	23.2	22.9	22.5	22.4	22.0	21.6	18.8	18.3	17.7	21.9	21.6	21.3	21.1	20.8	20.4	17.6	17.2	16.7
		140	25.1	24.9	24.7	24.5	24.3	23.8	20.9	20.6	20.1	24.0	23.8	23.5	23.4	23.1	22.8	19.8	19.5	19.0	22.8	22.6	22.3	22.2	21.9	21.6	18.7	18.4	18.0
		120	25.7	25.4	25.2	25.1	24.9	24.6	21.6	21.3	21.0	24.6	24.4	24.2	24.0	23.8	23.6	20.6	20.3	20.0	23.5	23.3	23.2	22.9	22.7	22.5	19.6	19.3	19.0
	60-70	180	16.3	15.9	15.4	15.5	15.0	14.4	12.2	11.7	11.0	15.2	14.9	14.4	14.4	14.0	13.5	11.4	10.9	10.3	14.1	13.8	13.4	13.4	13.0	12.6	10.5	10.1	9.6
		160	17.2	16.9	16.6	16.6	16.2	15.8	13.4	13.0	12.4	16.2	15.9	15.6	15.5	15.3	14.9	12.5	12.2	11.7	15.1	14.9	14.6	14.4	14.2	13.9	11.7	11.3	10.9
		140	17.8	17.7	17.4	17.3	17.1	16.8	14.2	14.0	13.5	16.9	16.7	16.5	16.3	16.1	15.9	13.4	13.1	12.8	15.9	15.7	15.5	15.3	15.2	14.9	12.6	12.3	12.0
		120	18.3	18.2	18.0	17.9	17.7	17.5	14.8	14.6	14.4	17.4	17.3	17.1	16.9	16.8	16.5	14.0	13.8	13.6	16.5	16.3	16.2	16.0	15.8	15.6	13.2	13.0	12.8
	70-80	180	10.2	9.9	9.5	9.6	9.2	8.8	7.2	6.8	6.3	9.4	9.1	8.8	8.8	8.5	8.1	6.7	6.3	5.9	8.6	8.4	8.1	8.1	7.8	7.5	6.1	5.8	5.5
		160	10.9	10.7	10.4	10.4	10.2	9.8	8.1	7.8	7.3	10.2	9.9	9.7	9.6	9.4	9.1	7.5	7.2	6.9	9.4	9.2	9.0	8.9	8.7	8.5	6.9	6.7	6.4
		140	11.4	11.3	11.1	11.0	10.8	10.5	8.6	8.5	8.8	10.7	10.5	10.4	10.2	10.1	9.9	8.1	7.9	7.7	10.0	9.8	9.7	9.5	9.4	9.2	7.5	7.3	7.2
		120	11.8	11.7	11.5	11.4	11.3	11.1	9.1	8.9	8.8	11.1	11.0	10.8	10.7	10.6	10.4	8.5	8.4	8.2	10.4	10.3	10.2	10.0	9.9	9.8	8.0	7.8	7.7
			70	100	130	70	100	130	70	100	130	70	100	130	70	100	130	70	100	130	70	100	130	70	100	130	70	100	130
			LDL (mg/dl)																										

Life Expectancy (Years)

Shortest — Longest

BRAVO: PREDICTION OF RESULTS OF SGLT2I CVOTs





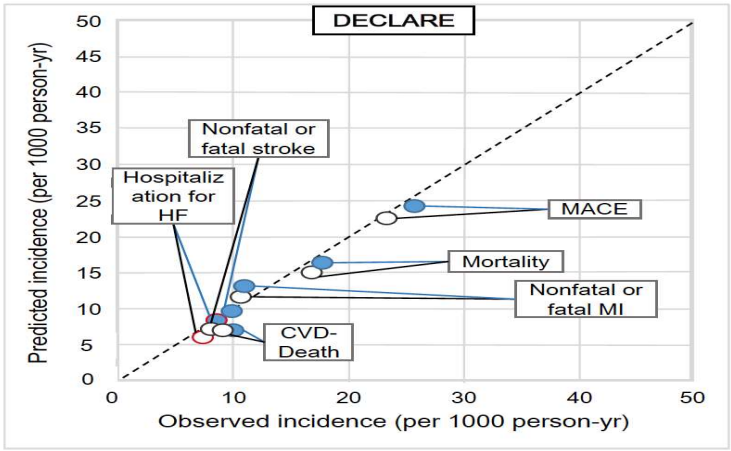


Table 3 Population-level health and economic outcomes associated with the Medicare Senior Savings Model (SSM)									
Time Horizon ->		5-years				20-years			
Overall Population under Medicare SSM (Subgroups #1, #2, and #3)	Diabetes-related Complications	No SSM	SSM	Cases Averted	Relative Risk Reduction[1]	No SSM	SSM	Cases Averted	Relative Risk Reduction[1]
	Stroke	69,397	67,383	2,014	-2.9%	184,152	180,539	3,513	-1.9%
	Myocardial Infarction	72,532	71,597	935	-1.3%	199,297	196,759	2,538	-1.3%
	Congetive Heart Failure	58,259	57,944	315	-0.5%	186,211	185,032	1,179	-0.6%
	End-stage Renal Disease	49,921	49,577	344	-0.7%	148,339	146,738	1,601	-1.1%
	Blind	158,128	156,011	2,117	-1.3%	407,151	403,734	3,417	-0.8%
	Severe Pressure Sensation Loss	286,583	282,166	4,417	-1.5%	667,586	657,790	9,796	-1.5%
	All Cause Mortality	349,529	348,397	1,132	-0.3%	1,249,083	1,247,754	1,329	-0.1%
	Health Outcomes (population-level)			Increment[2](95% CI)[3]	% change[4]			Increment[2] (95% CI)[3]	% change[4]
	Life years (millions)	7.01	7.01	3,220 (1,226, 5,215)	+0.04%	18.14	18.17	32,204 (32,046, 32,361)	+0.17%
	Quality-adjusted life years gained (millions)	4.12	4.12	3,381 (2,004, 4,758)	+0.08%	8.58	8.60	20,932(20,869, 20,995)	+0.25%
	Economic Outcomes (population-level)								
	OOP payment on Insulin (Billions)	5.82	2.26	-3.56 (-3.70, -3.42)	-61.1%	15.06	5.79	-9.27 (-9.69, -8.85)	-61.6%
	Total Insulin Cost (Billions)	38.95	42.40	3.45 (3.23, 3.67)	+8.9%	99.65	108.87	9.22 (7.58, 10.85)	+9.3%
	Total Medical Cost (Billions)	155.38	158.22	2.84 (1.94, 3.75)	+1.8%	422.20	427.76	5.56 (4.86, 6.25)	+1.3%
	Total Insulin Cost (Billions, 70% Rebate for Insulin)	11.69	12.72	1.04 (0.97, 1.10)	+8.9%	29.90	32.66	2.77 (2.28, 3.26)	+9.3%
	Total Medical Cost (Billions, 70% Rebate for Insulin)	128.12	128.54	0.42 (-0.35, 1.19)	+0.3%	352.45	351.55	-0.9 (-1.57, -0.24)	-0.3%
All costs were standardized in 2018 USD									
[1] Relative Risk Reduction:(1- incidence (with SSM))/Incidence (without SSM)									
[2] Increment: outcome (with SSM) – outcome (without SSM).									
[3] 95% simulation confidence interval (CI)									
[4] Change: Increment /outcome (without SSM)									

- We used the BRAVO model to evaluate the long-term economic and health impact of the $35 monthly insulin copayment cap policy.
- **Diabetes Care**

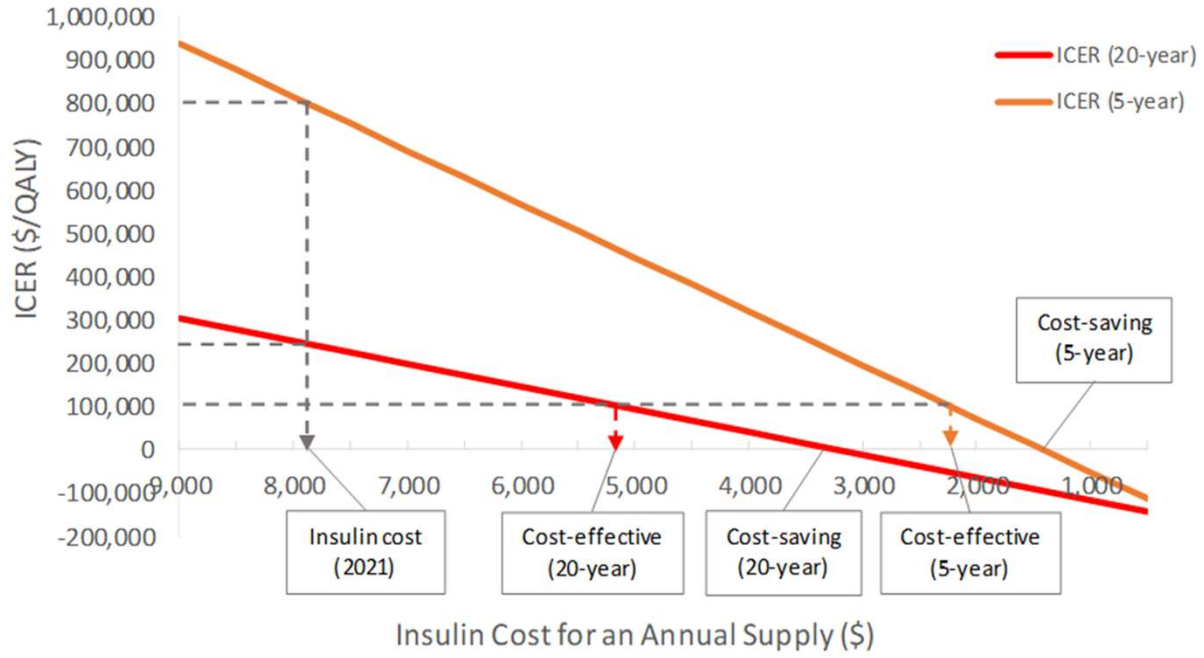


Figure 1. The incremental cost-effectiveness ratios of the $35 insulin copay cap policy

Notes: ICER: incremental cost-effectiveness ratio. A policy with an ICER under $100,000/QALY is considered cost-effective.

- We used the BRAVO model to evaluate the long-term economic and health impact of the $35 monthly insulin copayment cap policy.
- **Diabetes Care**

- SGLT2 inhibitors for heart failure prevention
- A risk reduction of 40%.

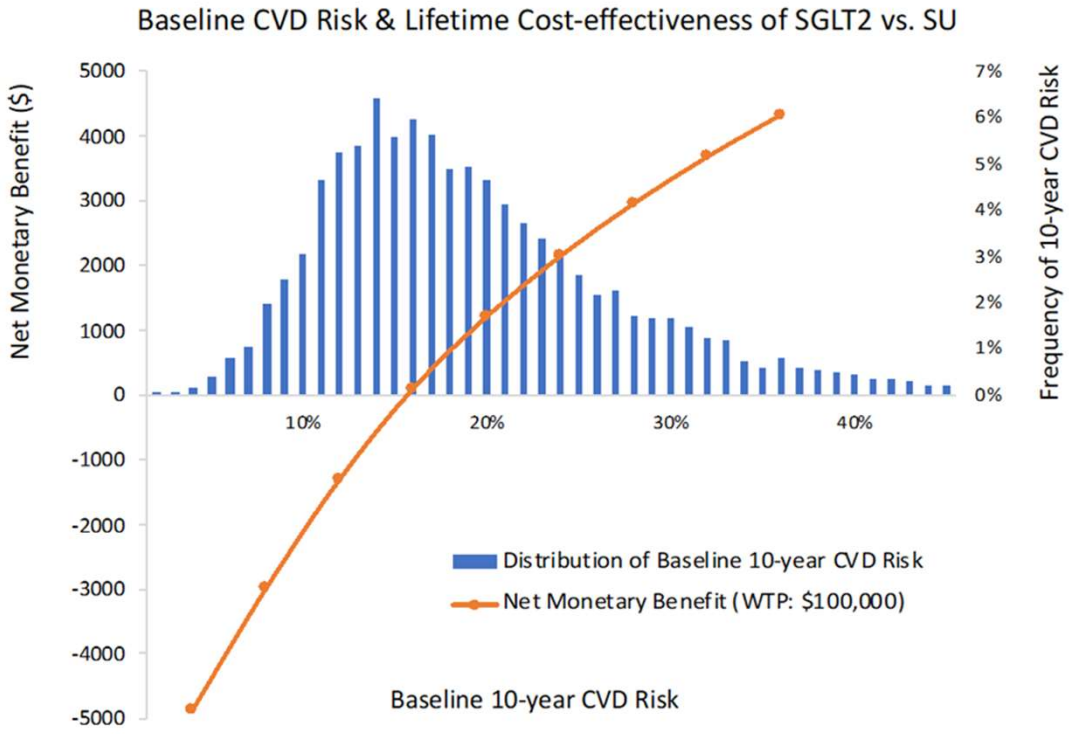
☑ 50% risk for Heart failure without SGLT2i

☑ 30% risk for Heart failure with SGLT2i

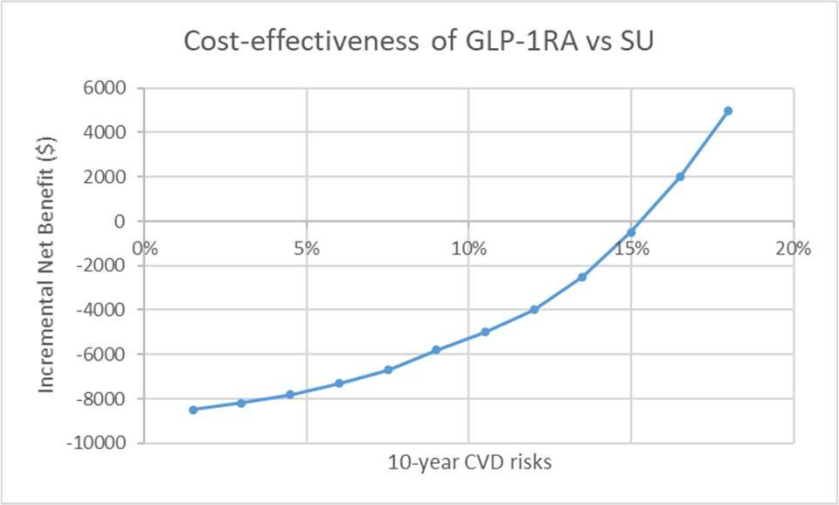
20% risk reduction= 4 additional years to live = 2.5 QALY.

☑ 1% risk for Heart failure without SGLT2i

☑ 0% risk for Heart failure with SGLT2i



The association between baseline cardiovascular disease risk and the cost-effectiveness of SGLT2 vs. SU among individuals with diabetes with the HbA1c higher than 7%.



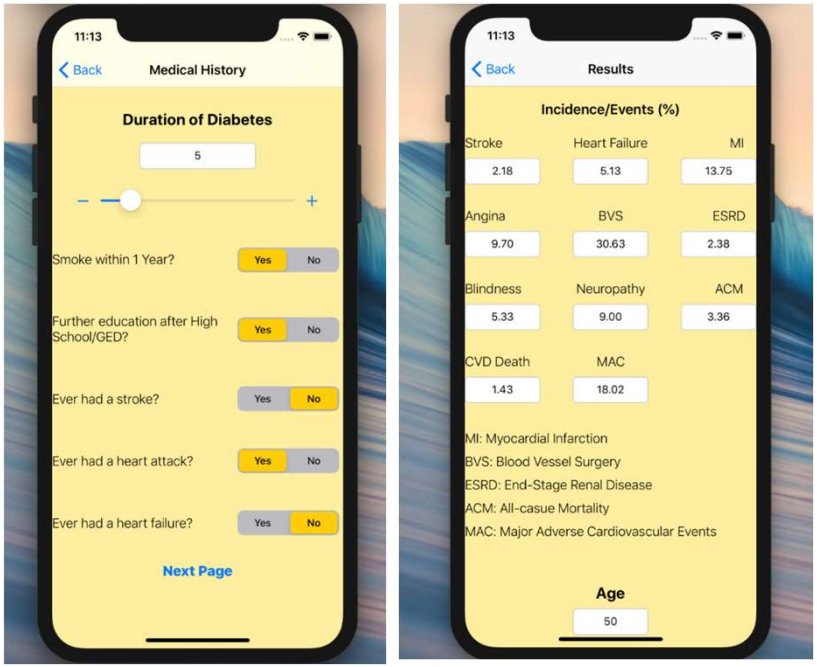
- National Health and Nutrition Examination Survey (NHANES)
- **Model: the BRAVO diabetes microsimulation model**
- Incremental Net Benefit > $0 = GLP-1RA is cost-effective

https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/

Individualized Treatment

- A patient walks into a clinic.
- Physician consider alternative treatment plans.
- Based on individual's characteristics, the BRAVO model potenitally simulates future outcomes
  - complications, mortality, risk of hypoglycemia, etc.
- A transparent platform for shared decision making.

Point Of Care Tool



- Present the future risk of complications based on patient's health status at the point of care
- Show the benefit patients could obtain by reducing biomarkers to the recommended level.
- http://www.bravo4health.com/

Incident HF Risk Prediction and Risk Score

Variable	Hazard (95% CI)
HbA1c	1.072 (0.953-1.205)
SBP	
SBP<120	
SBP: 120-140	1.139 (0.823-1.577)
SBP: >140	1.751 (1.233-2.486)
BMI	1.045 (1.025-1.066)
HDL	0.978 (0.967-0.990)
Age at T2DM diagnosed	
18-45	
45-65	2.026 (1.460-2.810)
>65	4.940 (2.926-8.334)
college education	0.520 (0.379-0.714)
MI_history	1.677 (1.287-2.185)
Revasc_history	1.915 (1.482-2.476)
albuminuria history	1.635 (1.290-2.073)
hypertension duration	1.012 (1.002-1.022)
log(uacr)	1.232 (1.155-1.315)
Cardiovascular medications	1.758 (1.305-2.368)
hospitalization this year	1.953 (1.304-2.923)
ER room visit	
0	
1	1.122 (0.720-1.747)
2 or more	2.234 (1.246-4.007)
nerve problems history	1.452 (1.123-1.877)
ESRD	1.934 (1.118-3.349)
log(scale)	6.31
log(shape)	0.567
Brier score	0.006400832
C-statistics	0.838 (0.821-0.855)
EVENT	299

An integer-based scoring algorithm (0~100) for the risk of 5-year HF incidence.

- 9,649 diabetes patients without HF history were used for model development, with a median follow-up of 5 years and 299 CHF events .
- The CHF risk model included college education, age at T2DM diagnosed, HbA1c, systolic blood pressure, BMI, HDL, urine albumin-to-creatinine ratio, hypertension duration, myocardial infarction history, albuminuria history, revascularization history, neuropathy history, end-stage renal disease, cardiovascular medication, hospitalization, and ER visit as predictors.
- The model demonstrated good discrimination (C-index 0.838 [95% CI 0.821-0.855]) and calibration (Brier Score 0.0064 [95% CI 0.006-0.007]) performance in the internal ACCORD data.
- The 5-year HF incidence of in a graded fashion from 1% risk in quintile 1 (risk score ≤ 28) to 20% in quintile 5 (risk score ≥ 54).

Predicting incident heart failure among patients with type 2 diabetes mellitus: The DM-CURE risk score

TABLE 3 Risk groups by quintiles

Estimate of risk	Point	Risk category
<1%	≤14	Low
<5%	15-23	
5%-10%	24-27	
10%-20%	28-33	Intermediate
>20%	>33	High

Lin Y et al Diabetes, Obesity and Metabolism; 2022; 24: 2203-2211

Prognostic Risk Score for Chronic Kidney Disease and Progression in Type 2 Diabetes Population Using ACCORD and ACCORDION Trial

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School of Public Health and Tropical Medicine

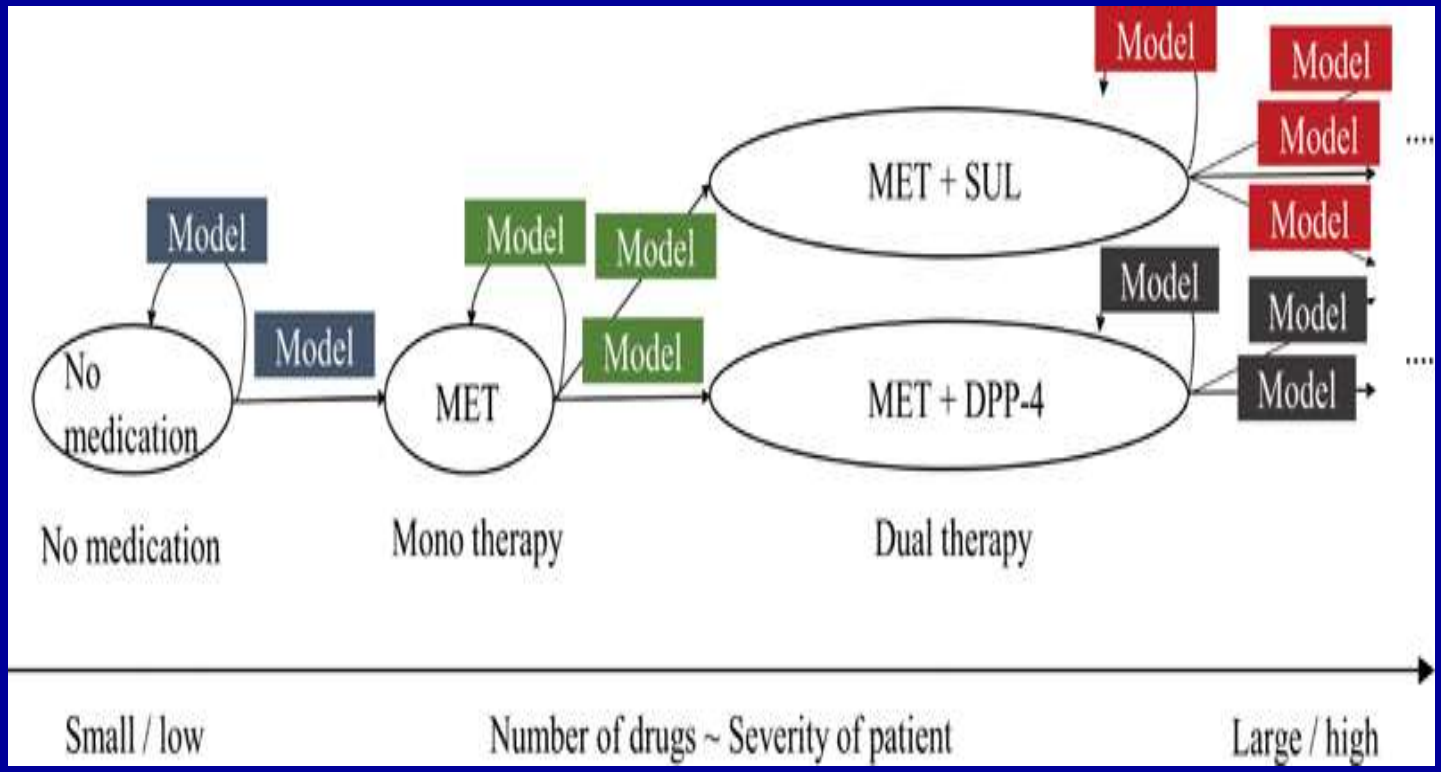
a global commitment to public health

CKD progression

CKD progression
50% decline, or 25 mL/min/1.73 m^2 decline in eGFR from baseline, or onset of ESKD
N=6,982
Event=3,346
median follow-up: 4 years

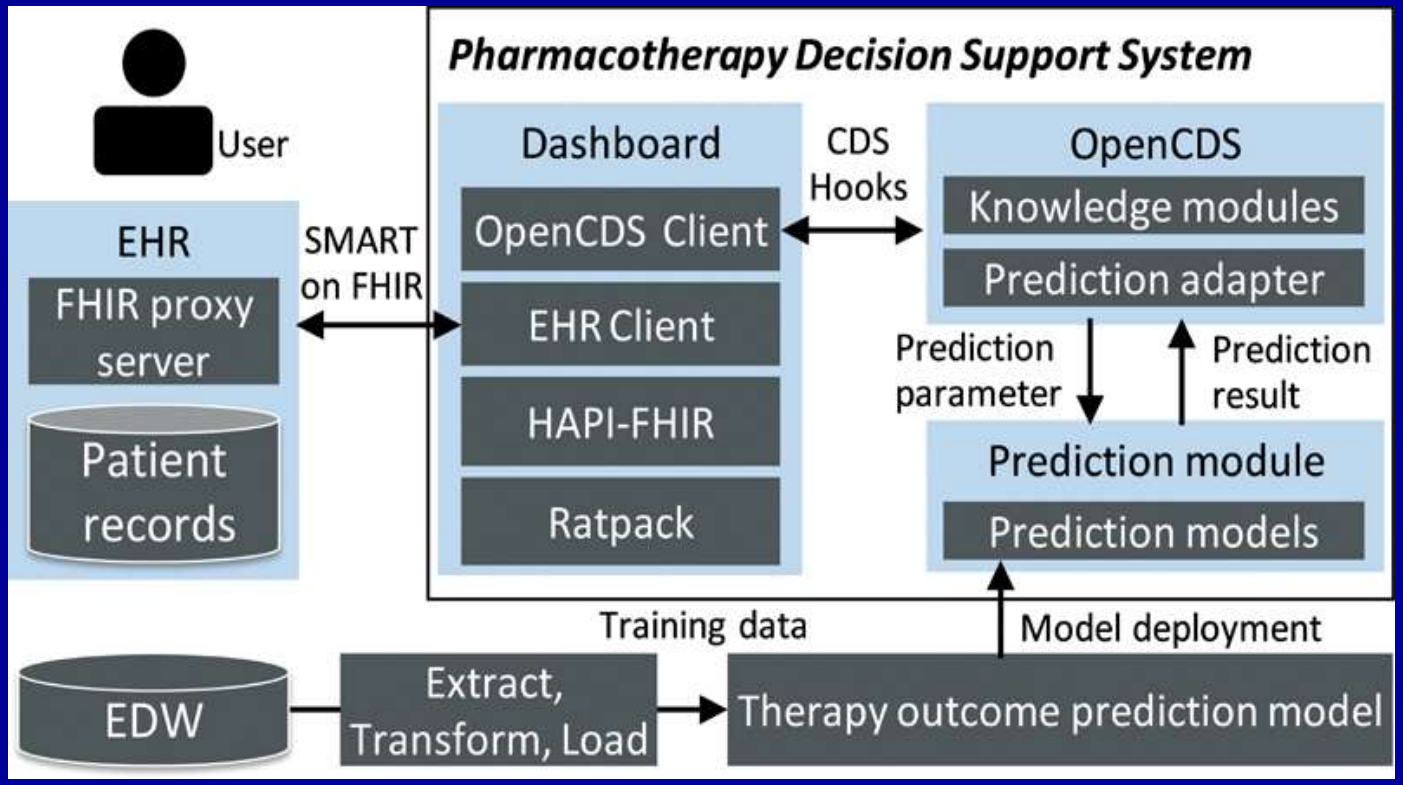
Variables		Coeffcient	95% CI	Hazard Ratio	95% CI
Female sex		**-0.181**	**(-0.267--0.095)**	**0.835**	**(0.765-0.910)**
Age at diabetes diagnosis (yrs)		0.004	(-0.002-0.010)	1.004	(0.998-1.010)
Current smoker		**0.505**	**(0.189-0.821)**	**1.657**	**(1.209-2.272)**
SBP (mmHg)					
	SBP≤120	0		1	
	120<SBP≤140	**0.318**	**(0.165-0.471)**	**1.374**	**(1.180-1.601)**
	SBP>140	**0.682**	**(0.457-0.907)**	**1.977**	**(1.579-2.478)**
DBP (mmHg)					
	DBP≤80	0		1	
	80<DBP≤90	**0.153**	**(0.024-0.282)**	**1.166**	**(1.024-1.326)**
	DBP>90	**0.215**	**(-0.001-0.431)**	**1.24**	**(0.999-1.538)**
Every 10-unit higher in heart rate (bpm)		0.02	(-0.017-0.057)	1.021	(0.983-1.059)
HbA1c (%)		**0.102**	**(0.069-0.135)**	**1.107**	**(1.071-1.145)**
Every 10-unit higher in ALT (mg/dL)		**0.076**	**(0.027-0.125)**	**1.079**	**(1.027-1.133)**
Every 10-unit higher in eGFR (ml/min/1.73 m^2)		**-0.329**	**(-0.345--0.313)**	**0.72**	**(0.708-0.731)**
Every 100-unit higher in UACR (mg/g)		**0.008**	**(0.002-0.014)**	**1.008**	**(1.002-1.014)**
Retinopathy event in previous year		**0.124**	**(0.018-0.230)**	**1.132**	**(1.018-1.258)**
Hospitalization in previous year		**0.297**	**(0.168-0.426)**	**1.346**	**(1.183-1.532)**
Interaction: SBP*Smoke					
	0	0		1	
	1	-0.341	(-0.719-0.037)	0.711	(0.487-1.038)
	2	-0.424	(-0.802--0.046)	0.655	(0.448-0.955)
Interaction: SBP*ALT		-0.037	(-0.072--0.002)	0.964	(0.930-0.998)

Pharmacotherapy Decision Support



Tarumi S et al Methods Inf Med. 2021 Jun;60(S 01):e32-e43. doi: 10.1055/s-0041-1728757

Pharmacotherapy Decision Support



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Pharmacotherapy Decision Support

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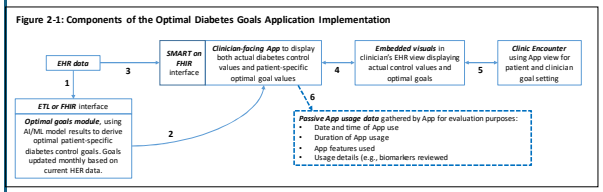
A POC SMART-on-FHIR Application to Support Patient-Specific Diabetes Control Goals

Tulane (Lizheng Shi/Vivian Fonseca) Contact: lshi1@tulane.edu; www.bravo4health.com

Problem Description

- Research problem being addressed: Recent research, including extensive Tulane work, has demonstrated that optimal diabetes control goals vary by individual patient (age, race, and comorbidities).
- State goal of the research: Implement a clinician decision support application to establish patient-specific goals (e.g., HbA1c, blood pressure, lipids) for better diabetes management.

Proposed Approach



Relevance to Health Outcomes

- Relevance: Patients who meet all three goals (HbA1c, BP, and LDL-C) have better outcomes than those who meet only one or two. Using an ML approach, we then worked to determine optimal goals for the best outcomes and now are applying AI algorithms to individualize goals using a POC SMART-on-FHIR application.
- Significance: To strengthen EHR-related research infrastructure and explore ways of using the FHIR standard to capture, integrate, and exchange clinical data for research, to facilitate future clinical trials and observational studies
- Target Industry: Health systems, telehealth providers; health plans

SMART: Substitutable Medical Applications and Reusabl Technologies
FHIR: Fast Healthcare Interoperability Resources.

Preliminary Research & Needs

- Expertise: Health system, informatics, clinical sciences
- Relevant prior work (or data) The proposed intervention will build on our experience with the ADA's Diabetes INSIDE program. Using data from the EHR, we informed clinicians via dashboards about their patients who were not meeting goals, and we provided patient-centered tutorials to physicians to help meet goals. The intervention resulted in significant improvements in goal achievement, particularly for those most in need
- Needs (i.e., collaboration, data, infrastructure): Commercialization

EHR integration

- **Fast Health Interoperability Resources (FHIR)**
  - "is a standard describing data formats and elements and an application programming interface (API) for exchanging electronic health records"

- **Substitutable Medical Applications and Reusable Technologies (SMART on FHIR)**
  - "a standard framework that allows the development of 'interchangeable healthcare applications' regardless of EHR".

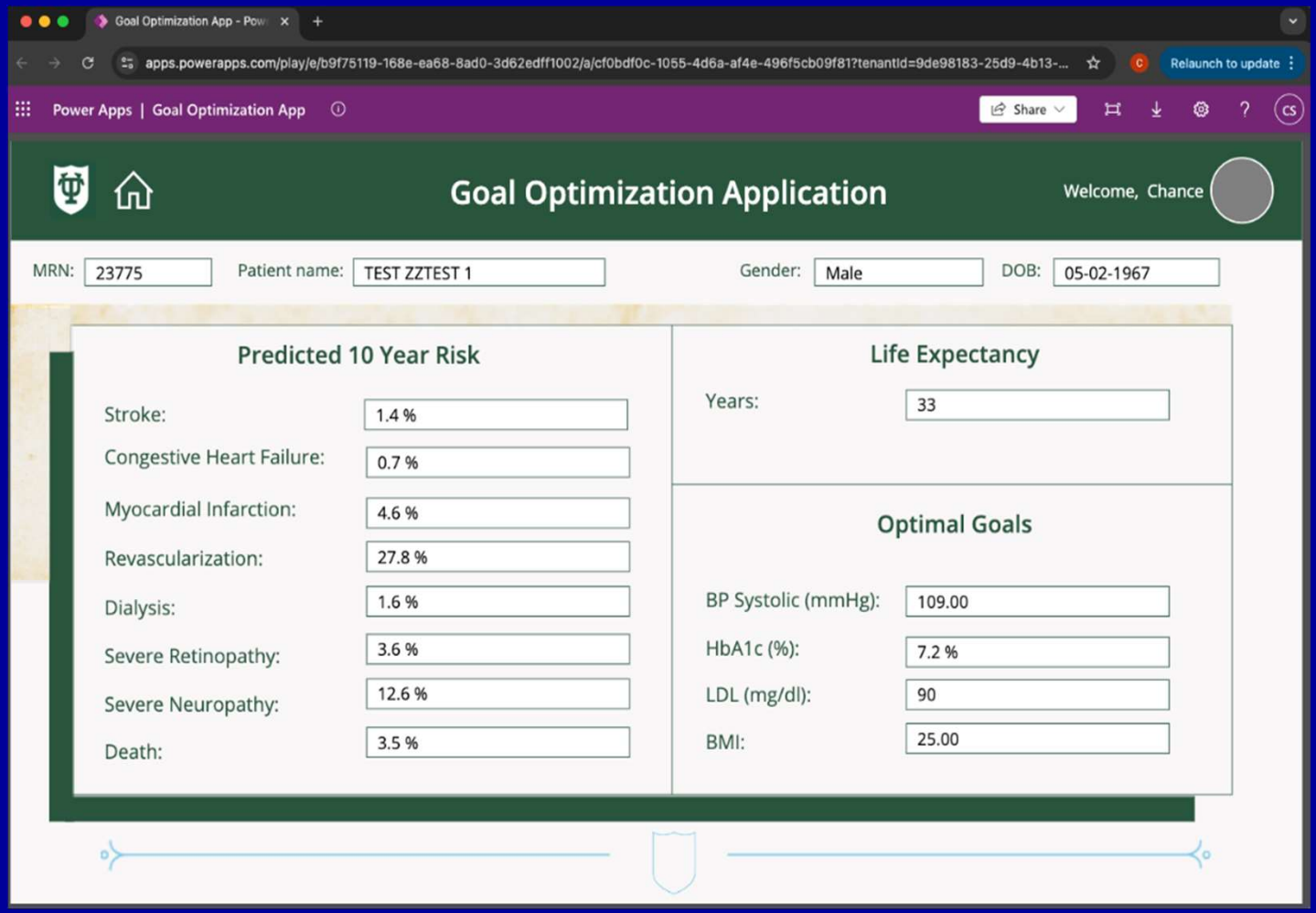
- **Challenges:**

-Very few EHRs are capable of handling SMART on FHIR (Epic, Cerner, AllScripts, some others)

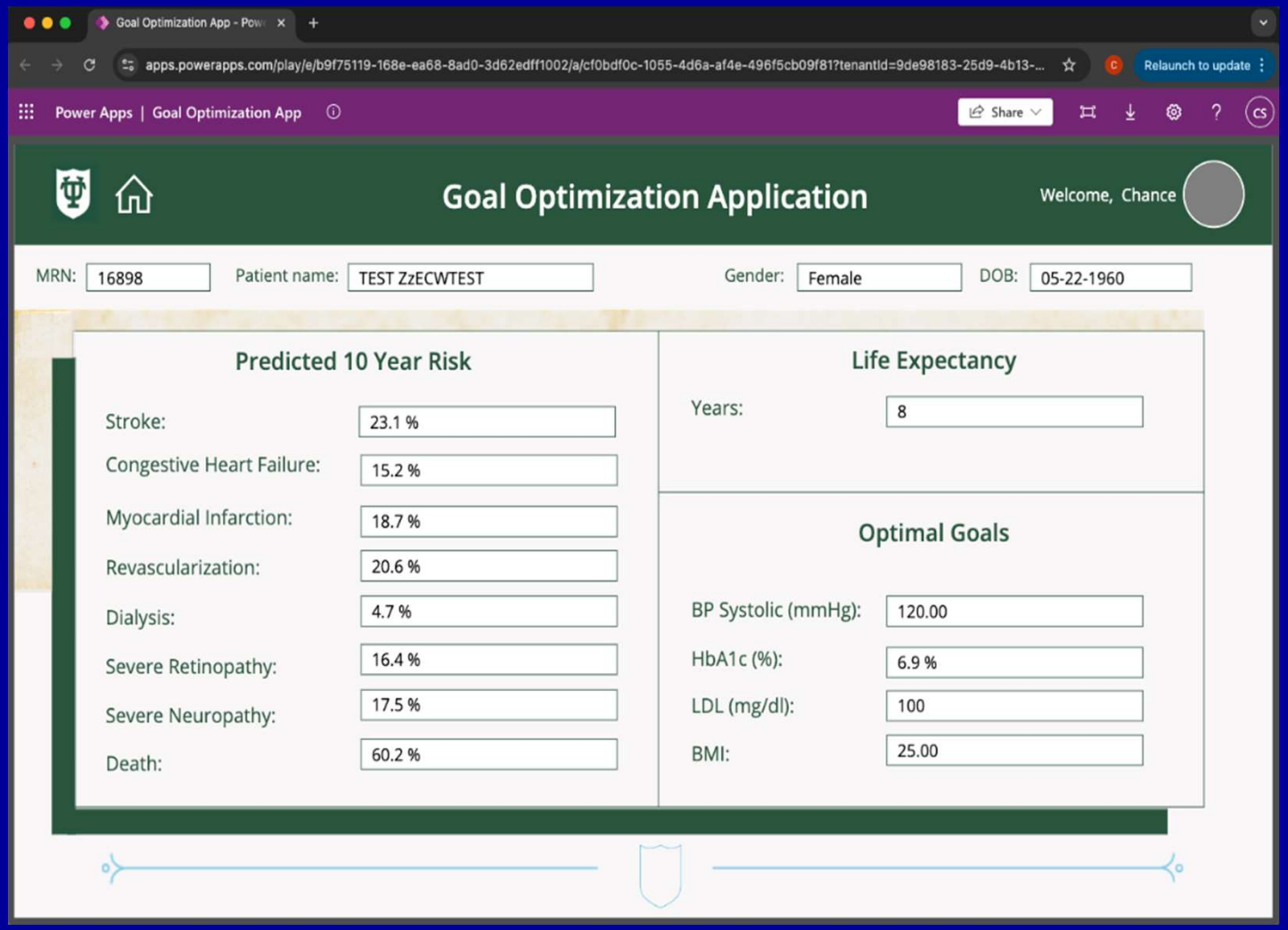
-The ones that can, have limited FHIR data domains available

-In some situations, you can have a SMART on FHIR app that is using some data from the EHR, but complementary data coming from another source

Risk Prediction for a low- risk patient



Risk Prediction for a high-risk Patient



GenAI to Guide Disease Management

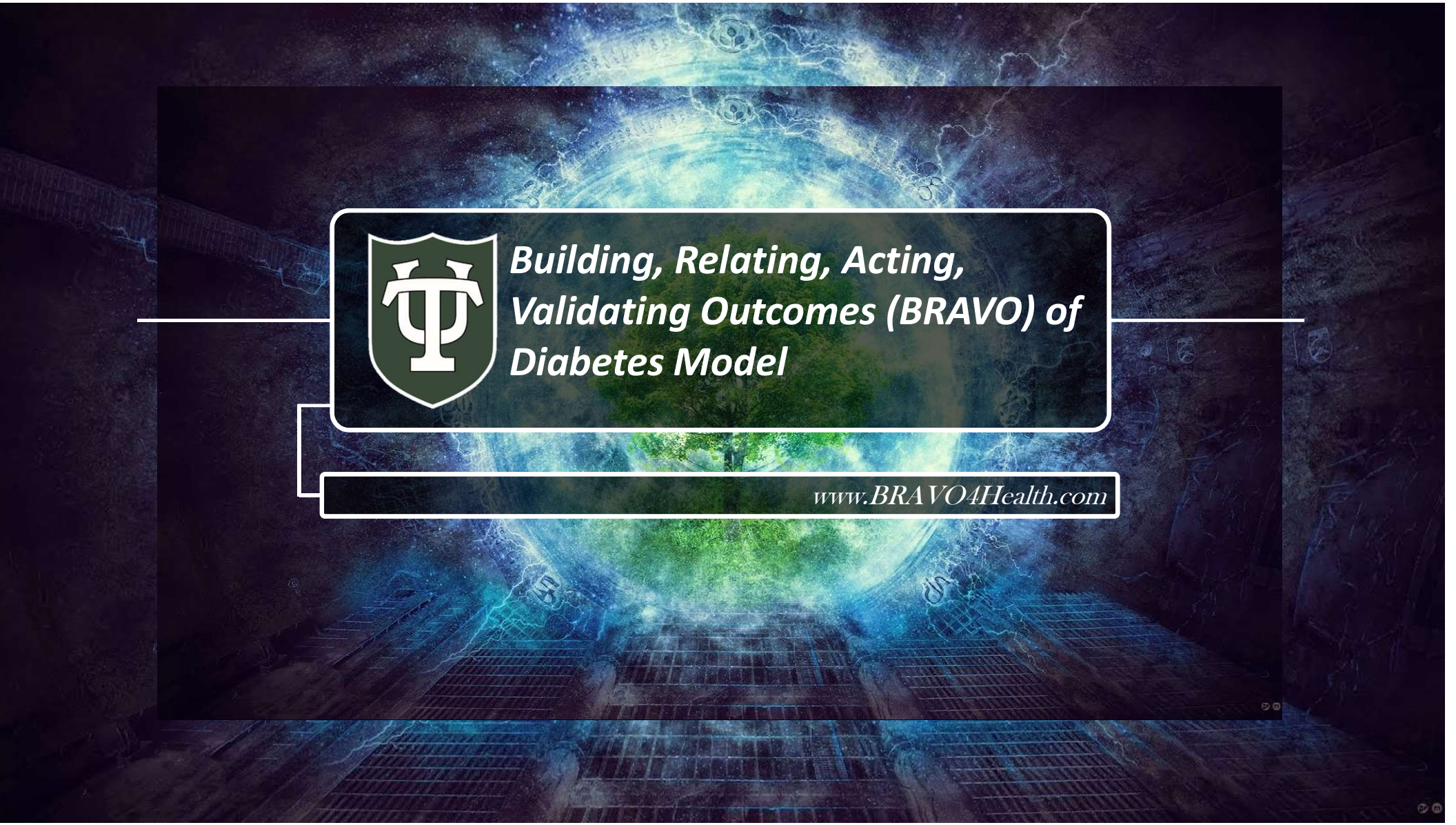
- Based on your current health status, the predicted 10-year risk for various complications is as follows: Stroke (13.7%), Congestive Heart Failure (3.2%), Myocardial Infarction (5.0%), Revascularization (20.4%), Dialysis (3.2%), Serious Severe Retinopathy (9.2%), Severe Neuropathy (25.3%), and Death (33.6%). Your life expectancy is estimated to be 13.538 years.

- To improve your health outcomes, it is recommended to strive for optimal goals in the following parameters: BP Systolic (120.0), HbA1c (7.0), LDL (90.0), and BMI (25.0). Meeting these goals could potentially increase your life expectancy by 1.247 years.

- By focusing on achieving these optimal goals, you can reduce your risk for complications and improve your overall health and longevity. It is important to work closely with your healthcare team to develop a personalized plan to reach these goals and enhance your quality of life.

Conclusion

- The BRAVO diabetes model for the US diabetes cohort has a good internal/external validity.
- And it is also capable of accurately predict diabetes comorbidities in other US and non-US based population.
- The model can be extrapolated over lifetime and provide long-term outcomes.
- Several currently active studies


Building, Relating, Acting, Validating Outcomes (BRAVO) of Diabetes Model
www.BRAVO4Health.com