Chronic Care Roundtable Meeting

Medication Care Paths for Type 2 Diabetes and Advanced Complications

November 13, 2019

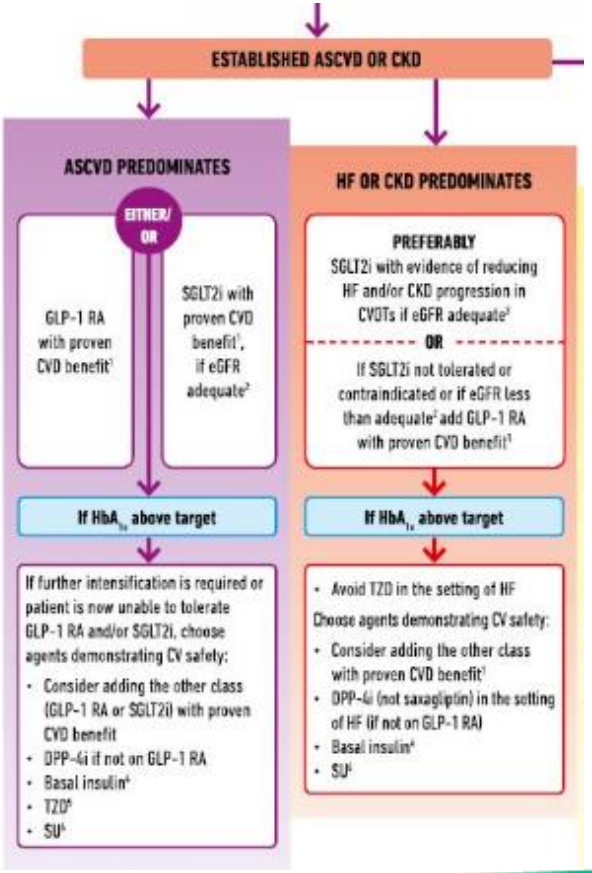
AMGA Foundation

AMGA

John W. Kennedy, M.D.
President, AMGA Foundation
Chief Medical Officer, AMGA

Thank You

ADA Diabetes Guidelines Algorithm



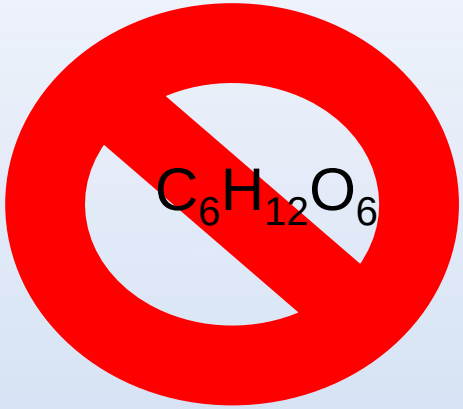
Implementing an algorithm or care path for use of SGLT-2i for Patients with Type 2 Diabetes and CKD despite ACEI/ARB

Evan Norfolk MD
Chair Nephrology, Geisinger
November 13, 2019

Geisinger

Outline

- The Science
- The Government
- Geisinger
- Guidelines
- Population Health Tools
  - Computers
  - Communication
  - Staff
- Developing a Care pathway



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Average Clinic Patient

63 yo male w/ hx of CAD, GERD, PVD, Obesity, HTN. Hx of DM 2 x 9 years has known retinopathy, and neuropathy. At least one trip to the cath lab

Presents to nephrology in 2016

No hx of NSAIDS/ No fx renal disease

Meds Atorvastatin, Gabapentin, Lasix, Lisinopril, Hydralazine Amlodipine, Insulin glargine, and insulin Aspart, ASA

Labs:

Year	CR	eGFR	ACR
2013	1.0	>60	600
2015	1.3	58	
2016	2.4	28	7500
2017	3.0	21	8000
2018	…		

Medicare Spending on ESRD

1% Medicare population

$35.4 Billion dollars 2016

7% Medicare FFS Costs

SOURCE: 2018 U.S. Renal Data System Annual Data Report.

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Epidemiology and Dx

DM 2 is 7th leading cause of mortality in US

DKD - Leading cause of CKD-> ESRD

50% of cases of ESRD

Diabetic w/ risk of developing DKD

- 33% type I 50% type II

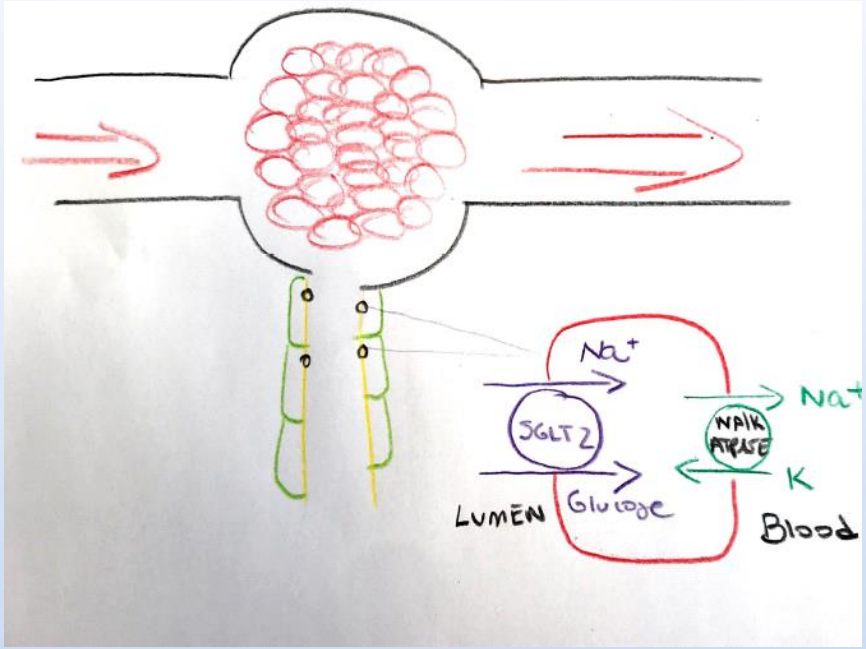
Mortality:

- DKD 3-12 x increased beyond that of DM
- 90% die before ESRD

Diagnosis

- ACR > 30 mg/g
- Albuminuria > 30 mg/ day
- Decreased GFR

Sodium Glucose Co-Transporter



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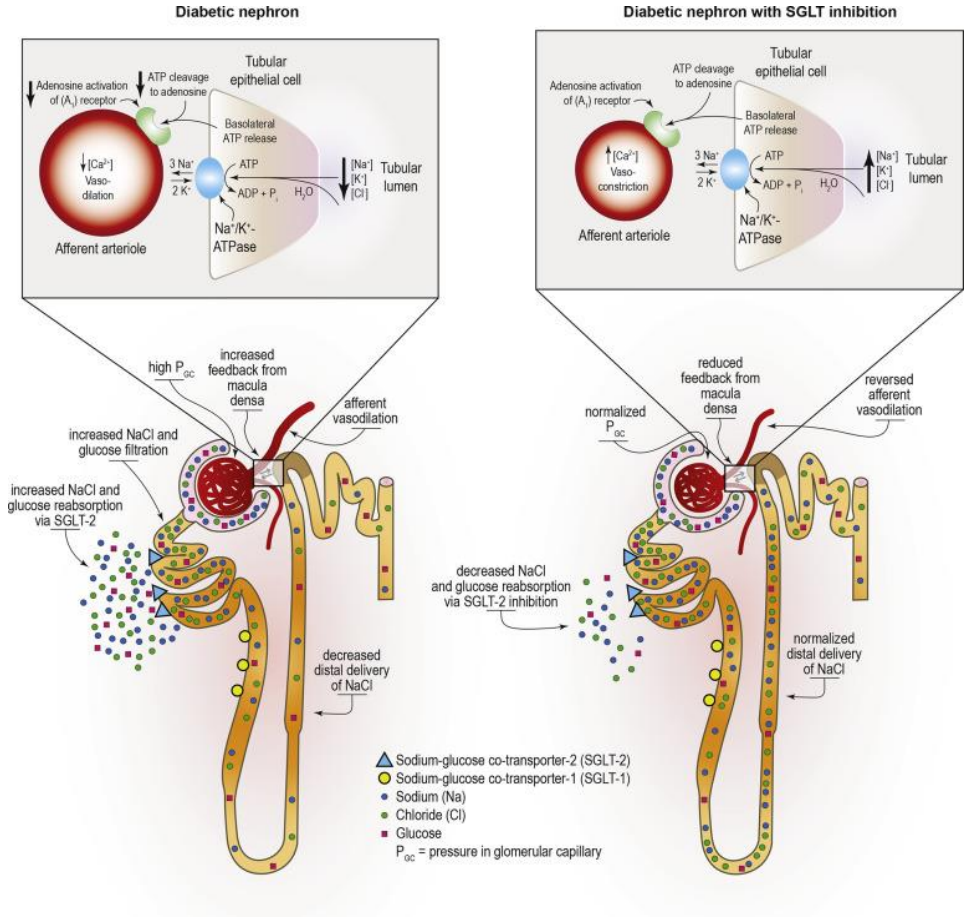
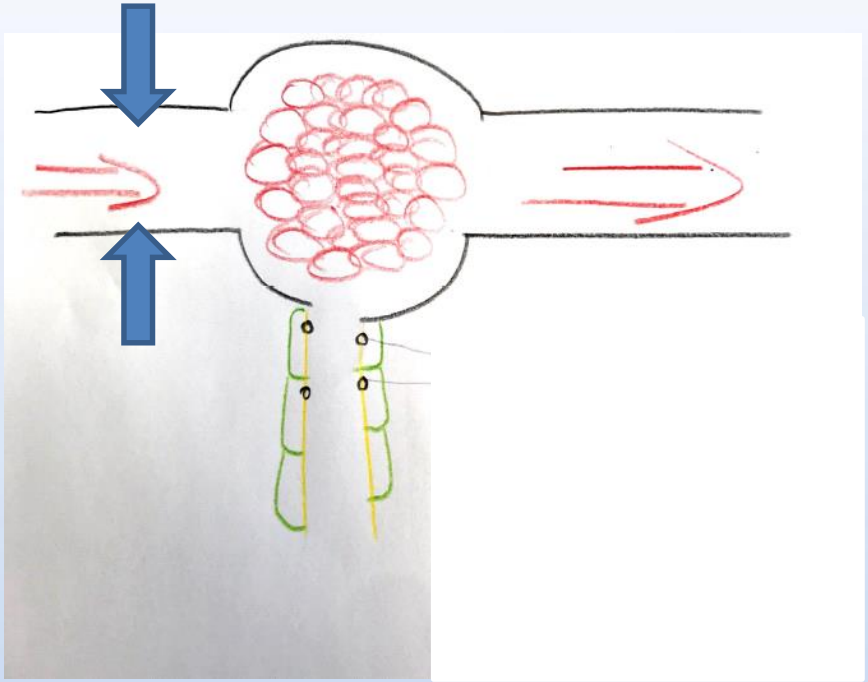
SGLT-2 Inhibitor – Renal Protection Against Hyperfiltration

- SGLT-2 blocks Na/Glucose -> natriuretic response -> TGF-> Afferent vasoconstriction -> Decreased Intraglomerular Hypertension
  - Decreased hyperfiltration / Improved dynamics
  - Decreased albuminuria
- Ace/arb -> efferent vasodilation
- Combination- – Combined impact on intraglomerular pressure
  - Initial drop in GFR which plateaus over time



SGLT2 Inhibition for the Prevention and Treatment of Diabetic Kidney Disease: A Review
Alicic, Radica Z., American Journal of Kidney Diseases, Volume 72, Issue 2, 267-277

SGLT2i - Renal protective Effect



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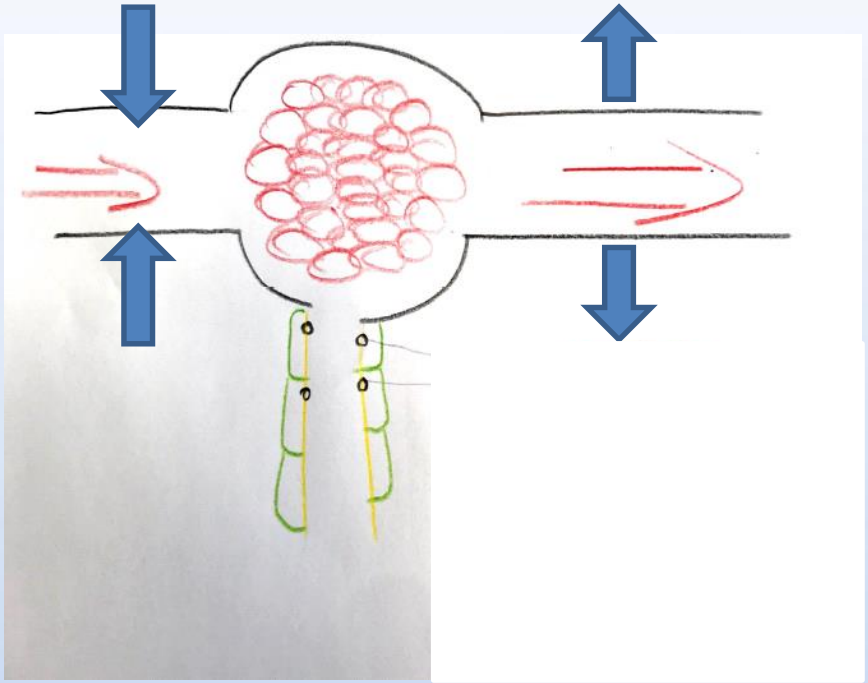
SGLT2i - Renal protective Effect w Ace-I



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Benefits of SGLT2 Inhibitors

- Wt loss
  - Glucosuria: loss of 60-100g glucose/day
  - 5 to 7 lbs after 3 months
  - plateaus after 6 months
- Renal protective (normalization of hyperfiltration)
  - Decreased albuminuria
  - Decreased Hyperfiltration
- Blood pressure decrease 5 mm Hg/ 2 mm Hg
  - Empagliflozin, dapagliflozin, canagliflozin (class effect)
  - Empagliflozin only agent with decreased nocturnal SBP
  - Mechanism: improved endothelial fx, vascular compliance by blocking oxidative stress

SGLT-2 Inhibitor Effect On Serum Glucose

Normal Renal Fx:	Hba1c decreased by 1%
eGFR 60-90	Decreased A1C 0.7% (Empagliflozin)
eGFR 30-60	Decreased A1C by 0.4 %

SGLT-2 inhibitors in DKD – Benefits

Decrease serum uric acid

Decreased SNS

Hyperglycemia

- Decreased fasting and post prandial hyperglycemia
  - enhanced B Cell function
  - decreased insulin sensitivity

Effect on A1C

- Normal Renal Fx –> decreased 1%
- Decreased eGFR -> blunted effect
- **Renal protective effects not due to improved glycemic control**

Diuretic effect -> Natriuresis

SGLT-2 Adverse Effects

Genital Candida Infections Most common adverse effect

- Equally M=F

Canagliflozin

- Increased bone fractures
- Increased incidence LE amputations (Legs/ Feet/ Toes)
- Not seen with empagliflozin/ dapagliflozin

SGLT-2 Adverse Effects

Urinary Infections

Polyuria

Postural Hypotension

DKA – Canagliflozin - 73 cases of DKA/ Ketosis – March 2013- May 2015; Not seen in large clinical trials; FDA Warning

AKI- Canagliflozin, Dapagliflozin

Fournier gangrene

- Necrotizing fasciitis 12 cases over 5 years in 1.7 million patients

What to tell patients about the agent?

Concern for DKA

- Mainly in insulin or sulfonylureas if decrease or discontinued
- Increased risk if volume depletion

Watch for groin infections

Current SGLT-2i on the Market

First approved for use in approx. 2013-14

Dapagliflozin	Farxiga
Empagliflozin	Jardiance
Canagliflozin	Invokana
Ertugliflozin	Steglatro

SGLT2i Use and eGFR Recommendations 2019

		eGFR
Dapagliflozin	Avoid Starting	< 60
	Not Recommended	*30-60*
	Discontinue	<60 Persistently
	Contraindicated	<30
Empagliflozin	No renal dosing	> 45
	Stop if	<45
	Contraindicated	<30
Canagliflozin	Dose adjust	45-60
	Do not start if	30-45
	Stop if	<45 Persistently
	Contraindicated	<30
Ertugliflozin	Avoid starting	*30-60*
	Not recommended if	30-60
	Discontinue if	<60 Persistently
	Contraindicated	<30

eGFR < 30

Lack of glycemic effect

Lack renal outcomes

Lack safety data

Lower eGFR trials needed

Studies

	Year of Publication	Powered for Renal Outcome
EMPA- REG	2015	No
Canvas / Canvas-R	2017	No
Declare-Timi58	2018	No
Credence Trial	2019	Yes
Dapa CKD	Est. November 2020	Yes

Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Patients – Removing Excess Glucose (EMPA-REG Outcome Trial) -2015

7020 pt w/ DM 2 w/ CAD + PVD or Cerebrovascular Disease- randomized to Empagliflozin 10mg, 25 mg vs Placebo

Baseline eGFR > 30

- 26% had eGFR <60
- 40% population had proteinuria

Primary endpoint- cardiovascular death, nonfatal MI, nonfatal stroke

- Sig decreased by Empagliflozin
- Early decrease risk of cardiovascular death (38%) and CHF hospitalizations (35%)
  - Not accounted for by decrease in MI or CVA as there rates were unchanged.

Terminated 3.1 years due to Empagliflozin benefits

All Cause Mortality decreased (32%)

Heart failure most sensitive outcome

Empa-Reg Endpoint (Empagliflozin) -2015

44% Risk Reduction in doubling of serum Cr

38% Risk Reduction decrease in ACR

55% Risk Reduction decreased of RRT

Empagliflozin resulted in decrease in loss of eGFR by 0.9 ml/min/yr

Significantly reduced rate of death from Cardiovascular causes, hospitalization, heart failure and death

14% reduction major adverse cardiovascular events

Increased risk genital infections

Urosepsis

Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes (Canvas/Canvas-R) -2017

Two trials; 10,142 patients w/ DM2 and CAD

RCT canagliflozin vs Placebo for 188 Wk (3 yr/ 7 mth)

Primary endpoint composite Cardiovascular death, nonfatal MI, nonfatal CVA.

Primary outcome lower w/ canagliflozin

Renal outcomes not statistically significant but possible benefit of canagliflozin

- Decreased progression of albuminuria
- Improved composite outcome of a sustained 40% decreased in eGFR, RRT, or Renal related deaths

Adverse effects Canvas/Canvas-R

Increased bony fracture

Increased risk amputations (toes/ feet/ legs) doubled

- not seen w/ empagliflozin or dapagliflozin
- EMPA- Reg- retrospective analysis no increase in lower limb amputation

Declare TIMI 58 (Dapagliflozin Effect on CardiovascuLAR Events) - 2018

17,160 Pts with T2DM, 2/3 no prior cardiovascular disease

Hypothesis DM 2 rx w/ dapagliflozin decreased endpoints

- Primary safety endpoint – MACE (cardiovascular death, myocardial infarction, or ischemic stroke)
- Primary efficacy endpoint MACE + composite cardiovascular death or Heart failure w/ hospitalization
- Secondary outcomes were a renal composite (≥40% decrease in eGFR to < 60, New ESRD, death from renal or cardiac or any cause of death.

Dapagliflozin

No decrease in adverse cardiovascular events

- Reduced reduce the risk of CHF hospitalization
- Reduced renal composite outcome
  - 40% decrease in eGFR, ESRD, or renal death

No major safety concerns.

Declare Timi 58 (from NEJM)

Followed for 4.2 years

Results:

- Dapagliflozin was noninferior to placebo regarding MACE
- lower rate of cardiovascular death or hospitalization for heart failure

- Adverse
  - DKA more common than placebo
  - Genital infections leading to discontinuation of the agent.

Canagliflozin and renal outcomes in type 2 DM and Nephropathy (Credence Trial) 2019

4401 patients double blind RCT DM 2 w/ albuminuria to canagliflozin 100 mg vs placebo

Cohort :

- eGFR 30-90and albuminuria (UACR > 300 mg/g)- high risk for renal failure
- All on Ace./ARB for one month prior to randomization (max labeled dose or dose not associated w/ side effect) ; No dual RAS blockade
- Categories of gfr 30-45; 45-60 / 60-90; gfr < 30 excluded

Primary endpoint composite Renal end pt (CKD5. ESRD, Renal tx,), doubling of cr, death from renal or cardiovascular causes

Stopped early 2.62 years

Canagliflozin and renal outcomes in type 2 DM and Nephropathy (Credence Trial) 2019

Primary Outcome

- 30% lower relative risk w/ canagliflozin than placebo of primary composite outcome: ESRD, doubling cr, renal or cardiovascular death
- 32% lower Relative Risk of ESRD

NNT TO PREVENT ONE DIALYSIS = 16

Canagliflozin also had lower risk cardiovascular death, mi , CVA , hospitalization for CHF, composite cardiovascular death, mi, or CVA (not all on RAS blockade)

No difference in amputations or fractures

- Unclear if amputation was due to different populations or protocols (they looked at feet more closely here)

Rates DKA low but higher in canagliflozin vs placebo 11/2200 vs 1/2197

Credence - Nonhemodynamic mechanisms of renal protection

Decreased inflammation – NLRP3- inflammasome in cell

Decreased oxidant stress by 60%

Blunted intrarenal angiotensinogen levels

Credence- glucose lowering is minimal in eGFR of 30-44 mL/min

Credence- Canagliflozin updated FDA Indications

September 30, 2019: Updated indication for adults w/ DKD and proteinuria

- Reduce the risk of ESRD
- Reduce risk of worsening of kidney function
- Reduce risk of cardiovascular death
- Reduce risk of hospitalization for CHF

- Only DM2 agent approved to treat DMD and decrease risk of CHF hospitalizations

A Study to Evaluate the Effect of Dapagliflozin on Renal Outcomes and Cardiovascular Mortality in Patients With Chronic Kidney Disease (Dapa-CKD)

- 4000 pts - RTC - dapagliflozin versus placebo, to see effect on CKD, or cardiovascular or renal death.
- 4 year study- Start date – 2/ 2017
- Primary Outcome first occurrence of any of the components of the composite
  - ≥50% sustained decline in eGFR
  - ESRD
  - CV death
  - renal death
- Est Completion Nov 2020

Summary SGLT-2I Science

4 agents approved for DM2/ CKD

Efficacy to lower a1c depends on agent

- Greater reduction occurred w/ empagliflozin

Canagliflozin, dapagliflozin and empagliflozin decreased reduction in urine ACR compared to placebo

eGFR decrease after starting med

- 4-5 ml/min/1.73 m2 decreased

Generally returns to baseline or when med stopped

Advancing American Kidney Health Initiative- July 2019

Renal disease #9 cause of death

100,000 pts on tx waiting list

20% of Medicare dollars - $114 billion/yr are spent on kidney disease

Goals:

- fewer patients developing ESRD (25% decrease by 2030)
- fewer Americans receiving dialysis in dialysis centers / Increase kidneys available for transplant.
- 80% incident ESRD patients on home modality or transplant
- Double the number of kidneys for transplant by 2030

CMII 4 Payment models

- goal of align incentives for providers

AAKH

ESRD Treatment Choices – Mandatory model- Enroll 50% dialysis providers in new model w/ incentive to encourage home modality –

- Payment changes on Medicare claims from January 1, 2020 through June 30, 2026.

Home modality:

- Currently 12% home dialysis penetration
- Target- 80% transplant or home dialysis

Transforming organ donation and transplant process

- Reform the organ procurement and management
- Compensate lost wages and child care expenses
- Increase the number of available organs

Encourage prize competitions through public-private partnership

HHS will launch a public awareness campaign about kidney disease

- 40% CKD patients are unaware

Kidney X

Public-private partnership between HHS, FDA and ASN to accelerate innovation in the prevention, diagnosis, and treatment of kidney diseases.

Encourage development of wearable/implantable artificial kidneys

Accelerating the development of drugs, devices, biologics and other therapies across the spectrum of kidney care

disruptive technologies via competitive, non-dilutive funding to innovators

Coordination clearer and less expensive path to bringing products to daily care .

Urgency - spotlighting immediate needs

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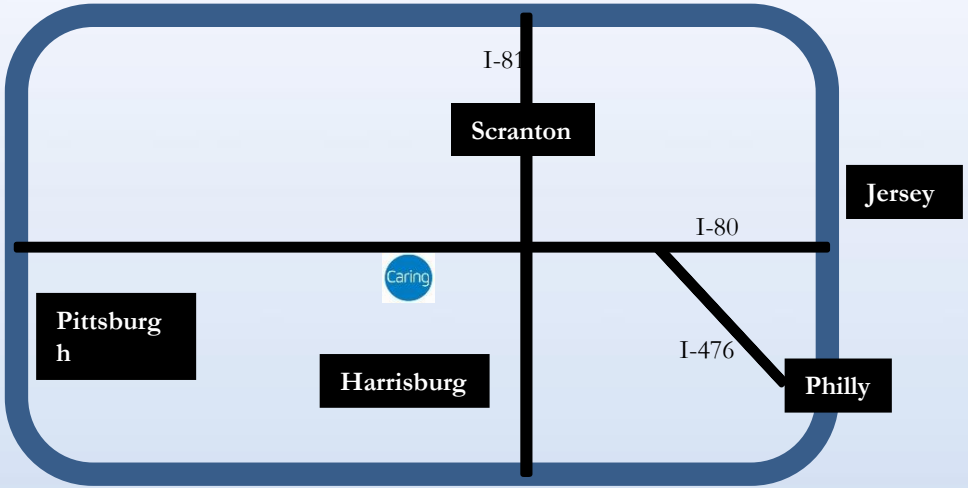
Pennsylvania



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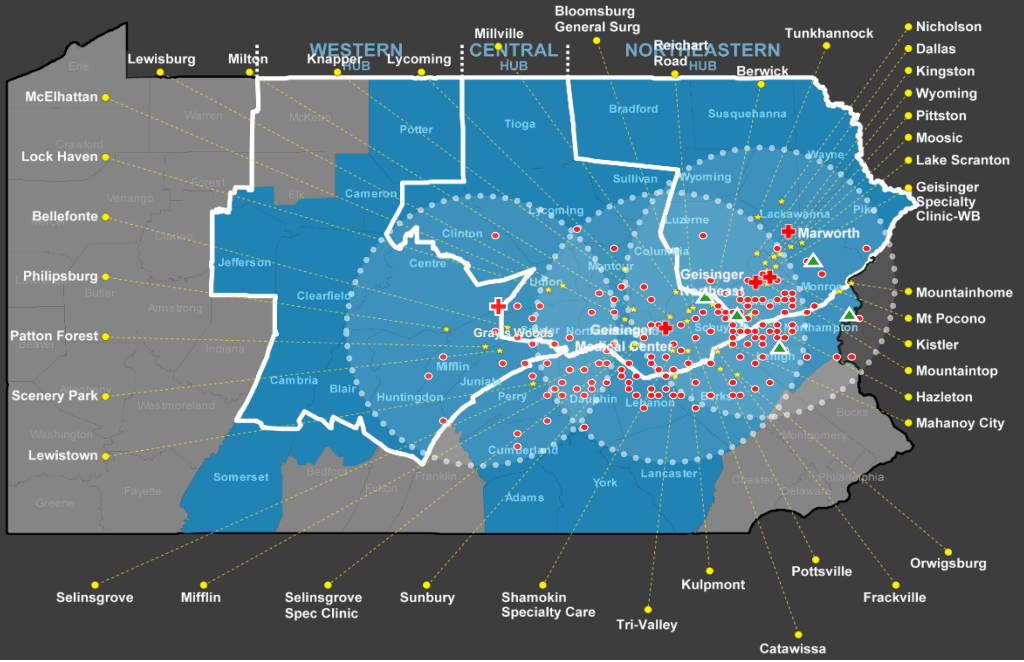
What is Geisinger?

- Largest Rural Health Care System in the U.S.
- Approximately 4.6 million people in service area
  - > 100,000 inpatient admissions/year
  - >6.7 million outpatient encounters/year
- 1900+ Physicians, 1200+ Advanced Practitioners
- 100+ Community Practice sites
- 12 Hospitals
- 500,000 + member health plan
- 2 Research Centers
- Medical School - Geisinger Commonwealth School of Medicine
- Healthcare IT and Informatics
  - EPIC Ambulatory (1996)
  - EPIC Inpatient (2007)

Geisinger Medical Center
Danville Campus

Geisinger

Geisinger Health System



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Nephrology Staff

- Twelve Staff Physicians
  - Two transplant nephrologists
  - Two clinical investigator
- Four mid-level providers
- Two nephrology fellows
- Five case managers
- Four renal pharmacists

Geisinger Organizational Culture

- Physician leadership drives changes in clinical practice
- Culture:
  - Value = Quality/Cost
  - Re-engineering /Transforming Care
  - Data, Metrics, Outcomes

Example of Disease Management – Anemia

Initial hypothesis – That traditional mode of care, that is ESA oversight and management primarily by physicians, was not leading to optimal care

- Appropriate interval labs were being missed
- Appropriate interval ESA adjustments were being missed
- Appropriate adjuvant therapy (IV iron) was not being optimally utilized

Fundamental Design- MTM

Pharmacist responsible for

- Obtaining insurance authorization for ESA therapy
- Ensuring timely appropriate labs and review of same
- Ensuring timely, appropriate adjustment in ESA therapy
- Arranging IV Iron therapy as indicated by protocol
- Discussion with physician, patient parameters that don't fit into protocol

Program inception September 2003 – Since 2006 all pts with CKD 3 or greater with ESA requirements enrolled in program

Nephrology paid by system for oversight of program

Outcomes Show Improvement

Expanded dose interval
Average ESA dose
Time in goal Tsat
Site of administration
Hemoglobin Time in goal
Days to Goal

Pop health tools and issues

- Identifying at risk patients
- Protocols and pathways
- EHR Alerts
- Ask a Doc tools
- Specialty clinic- use of
  - Pharmacists
  - Case management
- Access & Affordability

At risk patients

What is problem you want to solve?

Is solution evidence based? / how strong is the evidence?

DO YOU HAVE PROVIDER AGREEMENT ON GOALS?

- If algorithm -> will everyone use it?
- Exclusion patients- ie: Hypertension goals, Hba1c

Can you easily identify the patients ?

- Meaningful Use

Tracking a population

Patients lists

Manually

- outside of electronic record
- in electronic record

Automatically

Identifying Patients

Data issues

- Problem list - garbage basket (shared); Is it being used?
- Diagnoses -ICD10 and sub-diagnoses
- Meds
  - Is the med list accurate?
  - Are you receiving external data feeds?
- Labs
  - Discrete data? - external papers
  - Trending of data
- Can you pull all data into one place
- NLP

When to intervene?

Reports- How long does it take to obtain data to identify the target patients ?

- Can you query system in real time?
- Do you need an analyst to write reports? (timeframe/ money)
- Are you dependent on EHR vendor?
- What happens when you want to tweak the report?
  - Do have consensus ?

Identifying patients before the visit for labs?

Identify at visit and making an intervention?

Alerts – Point of Care

Identify care gaps during the visit to make provider aware

Who receives the alert?

- Nursing staff work on protocols - Eg: flu shot; Working to the top of license?
- Provider alerts

System alerts

- Do they appear during the correct part of the workflow?
- Is verbiage cumbersome?
- Do they provide adequate information?
- Is it actionable?
- Are you measuring provider reaction to alert? Are they ignoring alert?
  - If so why?

Populations Workflows

- Clinic based workflows
  - Before clinic
  - During clinic visits
  - After clinic visits
- Active patient population followed by providers
- Attribution
- Patient population at large

EHR alerts

Patient has Type 2 diabetes mellitus with kidney complication, without long-term current use of insulin (E11.29) With Type 2 diabetes mellitus with stage 3 chronic kidney disease (N18.3) with persistent proteinuria (R80.1). Confirm patient is on first line therapy then consider use of Dapagliflozin, Empagliflozin, Canagliflozin, or Ertugliflozin.

Pt w/ DM CKD and Proteinuria on Metformin. Consider SLGT2i.

Pt w/ DM CKD and Proteinuria on Metformin. Consider SLGT2i.
Last Hba1c: 8.4 (8/15/19)
Last eGFR 59 (8/15/19)
Last ACR 35 (1/6/ 19)

Pt w/ DM CKD and Proteinuria on Metformin. Consider SLGT2i.

Last Hba1c: 8.4 (8/15/19)

Last eGFR 59 (8/15/19)

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Order Empagliflozin

Order Canagliflozin

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Pt w/ DM CKD and Proteinuria on Metformin. Consider SLGT2i.

Last Hba1c: 8.4 (8/15/19)

Last eGFR 59 (8/15/19)

Last ACR 35 (1/6/ 19)

Order Empagliflozin

Order Canagliflozin

Will not add (Enter Reason)

Order Med from Alt Class

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Pt w/ DM CKD and Proteinuria on Metformin. Consider SLGT2i.
Last Hba1c: 8.4 (8/15/19)
Last eGFR 59 (8/15/19)
Last ACR 35 (1/6/ 19)

Insurance covers **Canagliflozin**

Order Empagliflozin

Order Canagliflozin

Will not add (Enter Reason)

Order Med from Alt Class

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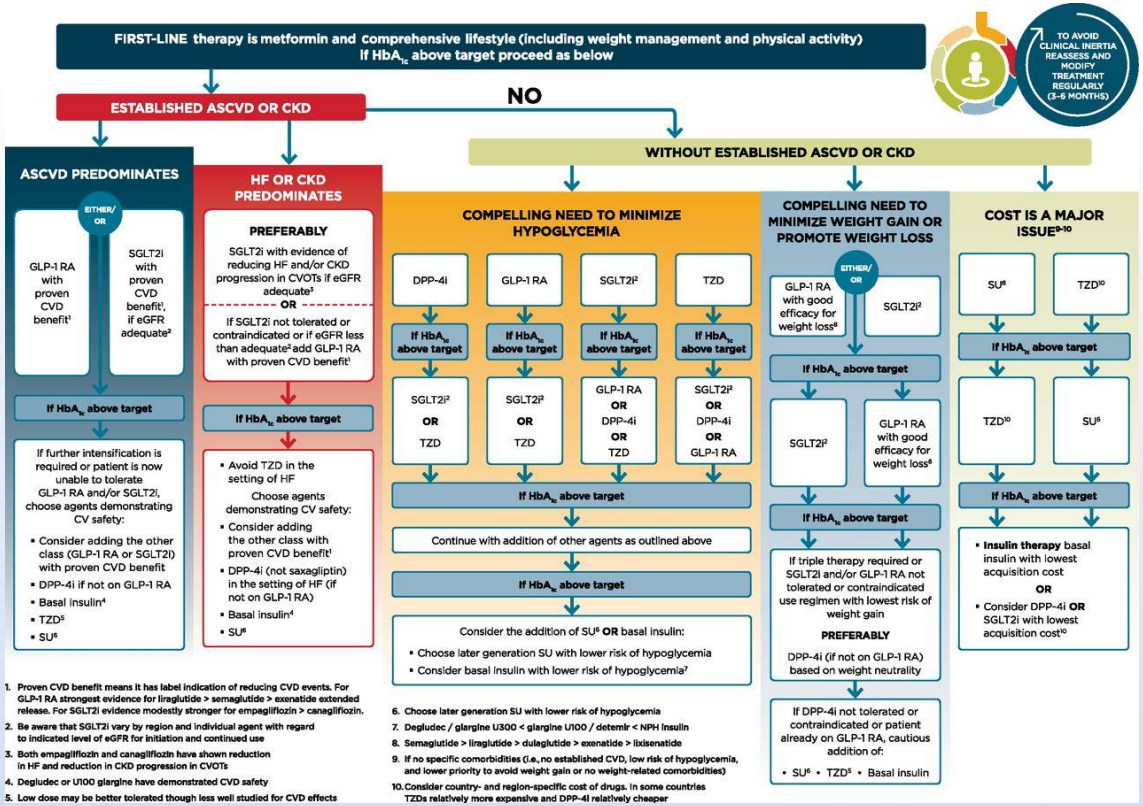

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Electronic Health Record DM 2 Order Set

- Nutrition Referral (lifestyle changes)
- Wellness Coach Referral (lifestyle changes)
- ↓ Metformin (First Line therapy if eGFR > 45)
  - eGFR > 60 Metformin 1000 mg po daily
  - eGFR 45-59 Metformin 500 mg po daily
- Second Line- ASPVD Main Risk- GLP-1
- Second Line- CKD/ CHF Main Risk- SGLT2i
- Second Line - Cost Constraints Sulfonylureas/ TZD
- Third Line -SGLT2i (If already on Metformin/GLP1)
- 2nd or Third Line - DPP-4 (if GLP-1 Contraindicated)
- Basal insulin

Scorecard

Outcomes Clinic 1

	Jan-18	Feb-18	Mar-18	Apr-18	May-18
Process measures					
Measure of urine ACR	70	71	74	77	79
Measure of Hba1C	75	77	79	85	88
Use of ace/arb if DM microalbuminuria	30	35	37	32	35
Blood pressure at target (140/90)	40	47	48	48	41
SGLT-2i use in DM2 w/ +ACR	8	10	11	10	10
Outcome Measures					
Admission	8	6	7	3	4
30 Day readmission	4	4	4	6	7

Outcomes Clinic 1

	Jan-18
Measure of urine ACR	70
Measure of Hba1C	75
Use of ace/arb if DM microalbuminuria	30
Blood pressure at target (140/90)	40
SGLT-2i use in DM2 w/ +ACR	10
Outcome Measures	
Admission	8
30 Day readmission	4

Are you reviewing the data?

- Is the data pushed ?
- Do you need to retrieve it ?

Do you have targets ?

Are you giving the providers the data?

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Dr. Smith Scorecard

	Jan-18	Feb-18	Mar-18
Process measures			
Measure of urine ACR	15	17	18
Measure of Hba1C	75	77	79
Use of ace/arb if DM microalbuminuria	5	6	7
Blood pressure at target (140/90)	40	47	48
SGLT-2i use in DM2 w/ +ACR	0	0	0
Admission	8	6	7
30 Day readmission	4	4	4

Why is one providers data not consistent?

- Labs scanning issue?
- Priorities to provider?
  - Overwhelmed / too many alerts
  - Doesn't care measure
- Carrot/ Stick

Ask a doc – Est. circa 2014

- Geisinger's program to easily route questions to a specialty (35 specialties) Specialist replies in predefine time
- Easy inline workflow in electronic health record
- Specialist can review pt record and conveniently documents reply and route answer in patient's chart
- No need to figure out who to call
- Reduce scheduling of unnecessary face-to-face consultations with specialists
- Helps specialist to triage urgent cases which need to be seen urgently – right care/ right patient/ right time
- > 99% completion rate

Ask a doc -Outcomes

Decreased turnaround time between primary and specialty physicians
- 6½ hours compared to traditional referrals, which could take weeks to month

14% reduction in total cost of care in first month of program

20% reduction in cost in 2nd month

74% drop in specialist visits.

84 % of Geisinger PCP use it routinely

Over 17,000 consults thus far

10% of all Geisinger referrals to participating specialties

Opened up almost 4,000 additional face-to-face specialty slots in 2018

Ask-A –Doc

How to best leverage this tool for use of SGLT-2?

Nephrologist Thoughts on SGLT2i Use...

Directly Ordered: yes 4 no 5 **Request others order: yes 4 no 5**

“I would feel wary of prescribing it in patients with diabetic foot ulcers/severe PVD, frequent UTIs, or poorly controlled diabetes/poor compliance.”

“I am not very familiar with them and I have to study more about it”

“generally uncomfortable prescribing diabetes meds since I'm not primarily responsible for DM management, worry about side effects and clear communication to other team members about changes, would favor this be driven by pharmacy in our dept”

“occasionally ask MTM/PCP to consider these; have definitely had MTM approach me about “

“The main issue is practical. DM is managed by PCP and MTM Clinic for vast majority. To start this “drug might mean we have to stop/adjust other drugs”

“Have asked PCP and MTM clinic to start.. but lot of them gets stopped for various reasons---- Pre renal AKI, yeast infections, DKA etc. “

“Multiple times [have asked for them to be started]..got good response from PCPs and endocrine”

“I think it is challenging to start managing a diabetic medication which is also being managed by PCP. Who takes responsibility for managing the patient’s diabetes? I also don’t think there is enough time in most clinic visits to take this on. MTM management I believe would be the best. ”

Nephrologist Thoughts... (2)

we should be using them in the appropriate population. That being said, I'm not sure we should be the ones prescribing them. They are becoming the "new anti-RAAS" therapy, and for good reason.

However, a nephrologist prescribing an SGLT2i can open a can of worms in my opinion (side effects, monitoring, need for adjustment in other components of DM regimen, etc.). They SHOULD be standard of care in our department for the right group of patients, but

I think utilizing the MTM pharmacist is the best way to make that happen. If we see a candidate for an SGLT2i, we should refer to MTM DM pharmacist or message them if they already follow. Same goes for Endocrine if they are following.

MTM Pharmacist - SGLT-2 Considerations

- Connected EHR
  - Physical location/ Modes of communication
- Algorithms
- Tailor meds
  - SGLT2i and diuretics
  - Discontinuation SGL2i
- Labs
  - Glycemic effect
  - Follow-up cr

- Education
- Med interactions: Sulfonylureas / insulin
- Compliance
- Med List Accuracy
- Work w/ physician
- Document in EHR
- Pharmacist Salary?

Summary – Science

SGLT-2 Inhibitors are cardiorenal risk reduction agents w/ glucose lowering as side effect

Only class of drug since RAS blockers to show decreased progression of CKD

Canagliflozin now shown to further slowed CKD when combined with RAS

Glucose lowering effect is blunted w/ lower eGFR

Use only until eGFR =30

Summary- Algorithm

- Consensus
  - Patient population
  - Provider Workflow
  - System tools
- Electronic pathways
- MTM Pharmacist
- Scorecards- Process measures
  - Data review
  - Attribution
  - Giving providers back their data
  - Improving process measures
- Outcome data review

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Geisinger

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AMGA
Advancing High Performance Health

Patients with Type 2 Diabetes and Chronic Kidney Disease

Nikita Stempniewicz

AMGA Foundation Chronic Care Roundtable

November 2019

AMGA's Distinguished Data and Analytics Collaborator

Background

Clinical guidelines (ADA) recommend measuring urine albumin, e.g., urine albumin to creatinine ratio (uACR), and estimated glomerular filtration rate (eGFR) ***at least once per year in all patients with type 2 diabetes***

- Powerful predictors of future health care costs and utilization, and cardio-vascular and kidney outcomes
- Allow providers to screen, diagnosis, and risk stratify chronic kidney disease (with a known risk relationship)

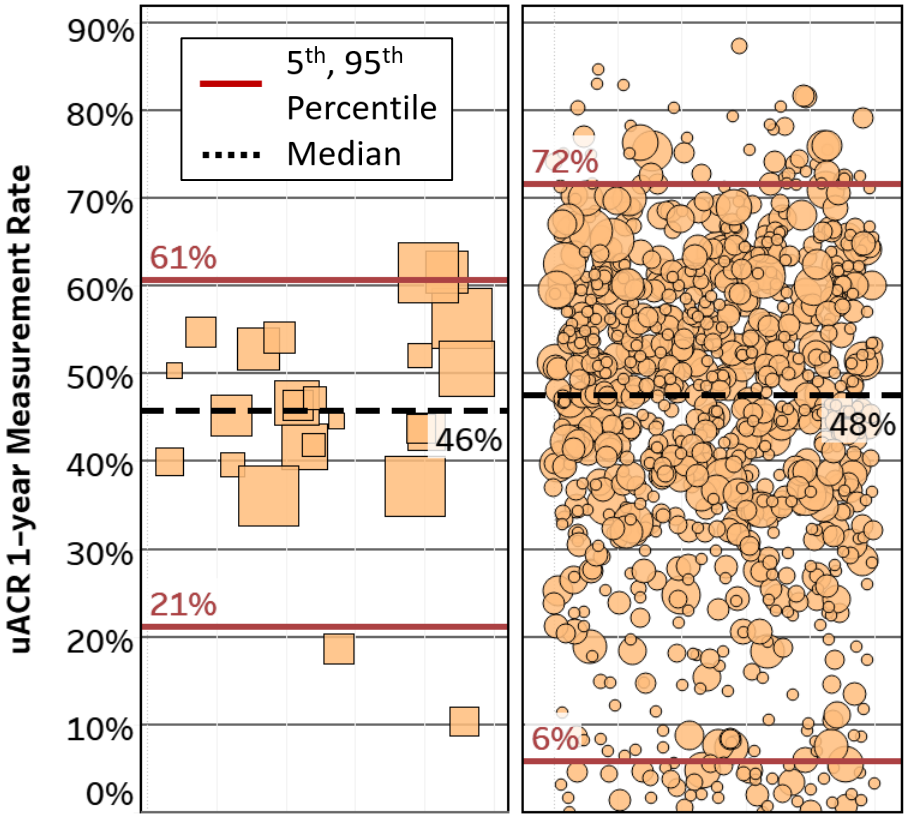
Prognosis of CKD by GFR and albuminuria category

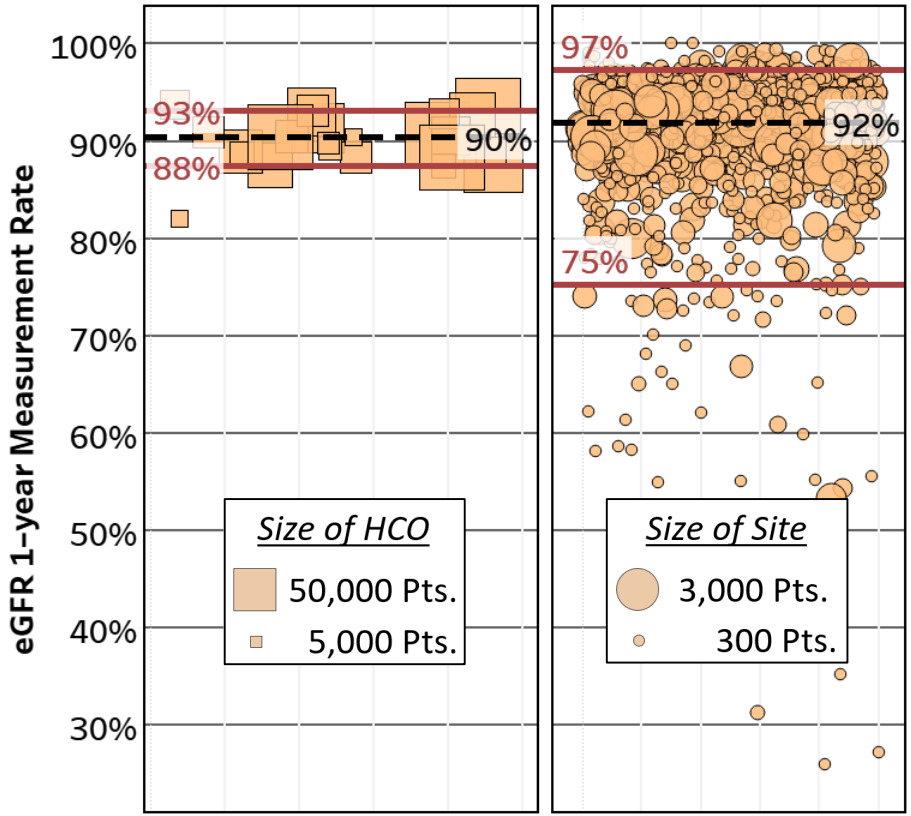
GFR categories (ml/min/ 1.73 m^2) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk. KDIGO 2012

uACR and eGFR Measurement by Org. and Site of Care

- 520,000 patients aged 18 – 85, with ≥ 1 visit with a PCP in 2018, no ESRD, and a Dx for T2DM





https://www.asn-online.org/education/kidneyweek/2019/program-abstract.aspx?controlId=3236557

uACR and eGFR Measurement by Org. and Site of Care

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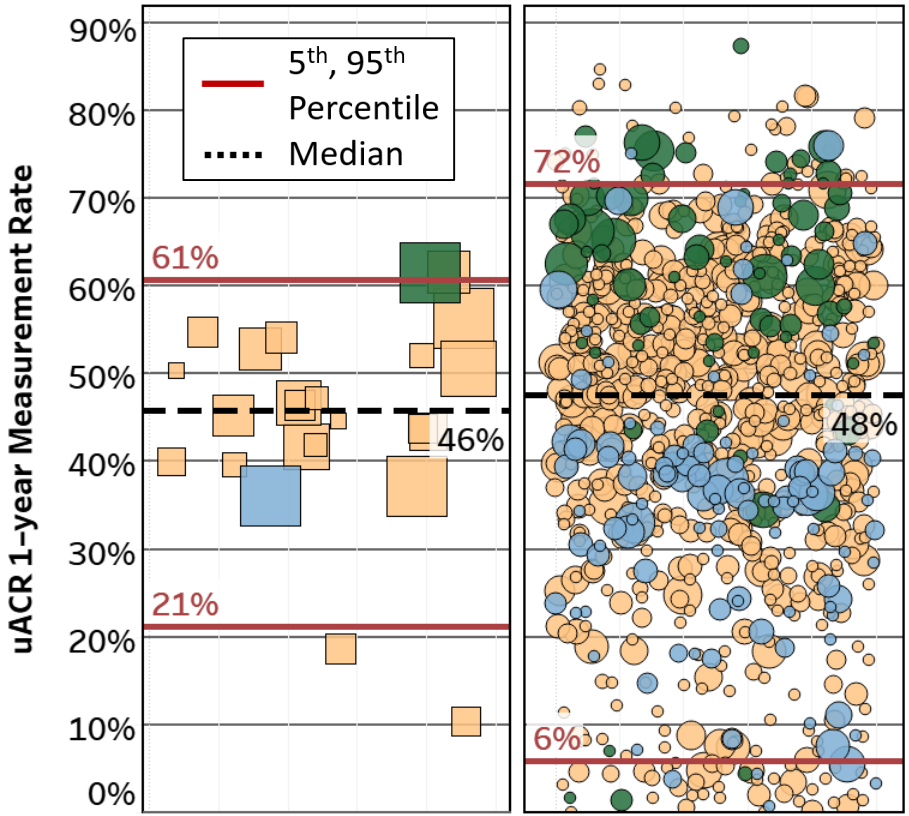
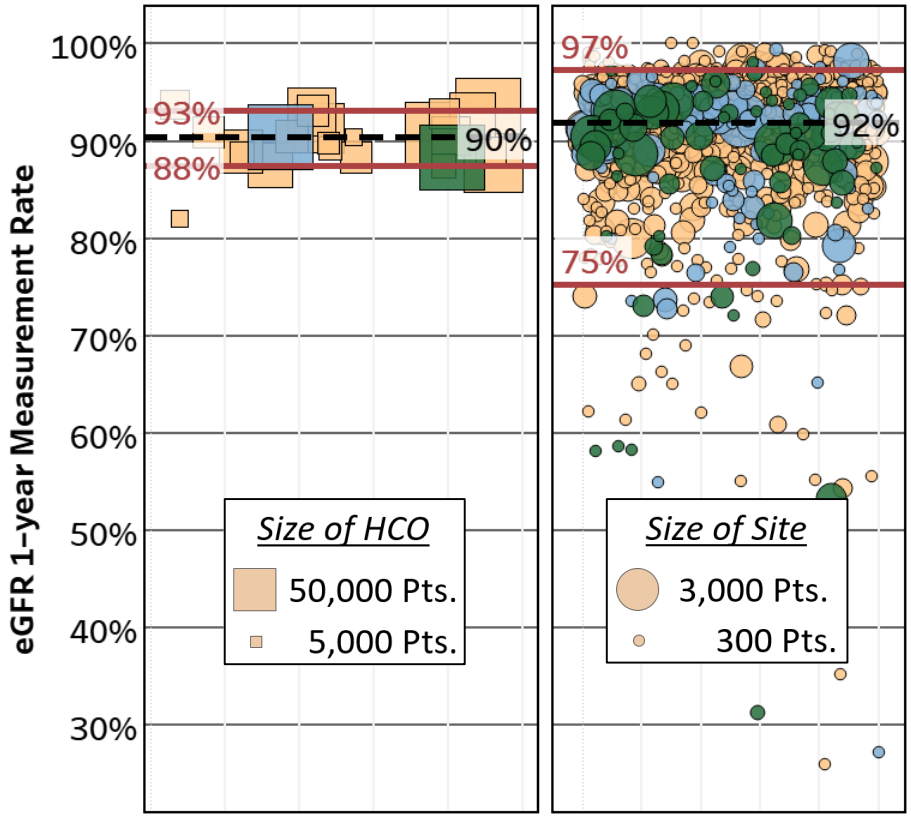




https://www.asn-online.org/education/kidneyweek/2019/program-abstract.aspx?controlId=3236557

Quality Measures for CKD in T2DM

- **Medical Attention for Nephropathy (current measure):** Percentage of patients who had a nephropathy screening test or evidence of nephropathy
  - any urine protein test **OR**
  - diagnosis of nephropathy **OR**
  - visit with a nephrologist **OR**
  - prescribing ACE-i or ARB

- **Kidney health evaluation (proposed replacement):** Received a kidney health evaluation
  - eGFR **AND**
  - Urine Albumin-Creatinine Ratio (uACR)

https://www.kidney.org/sites/default/files/nkf-kidney-health-evaluation-measure-worksheet.pdf

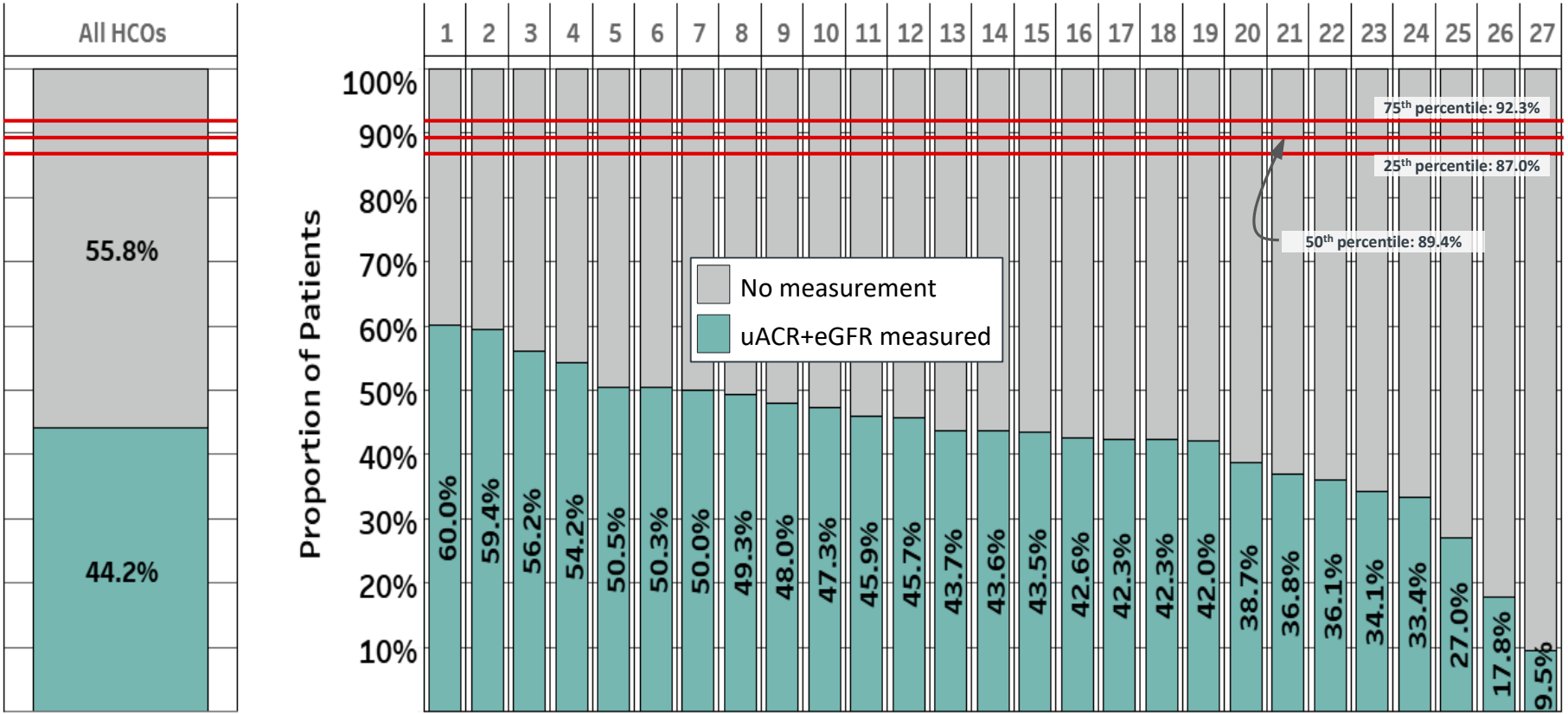
Issues with Medical Attention for Nephropathy Measure

- eGFR not included, an important test for CKD detection and risk stratification
- “Topped-out” at most health systems, false sense of optimal kidney care for people with diabetes

Patients w/ uACR + eGFR – By Organization

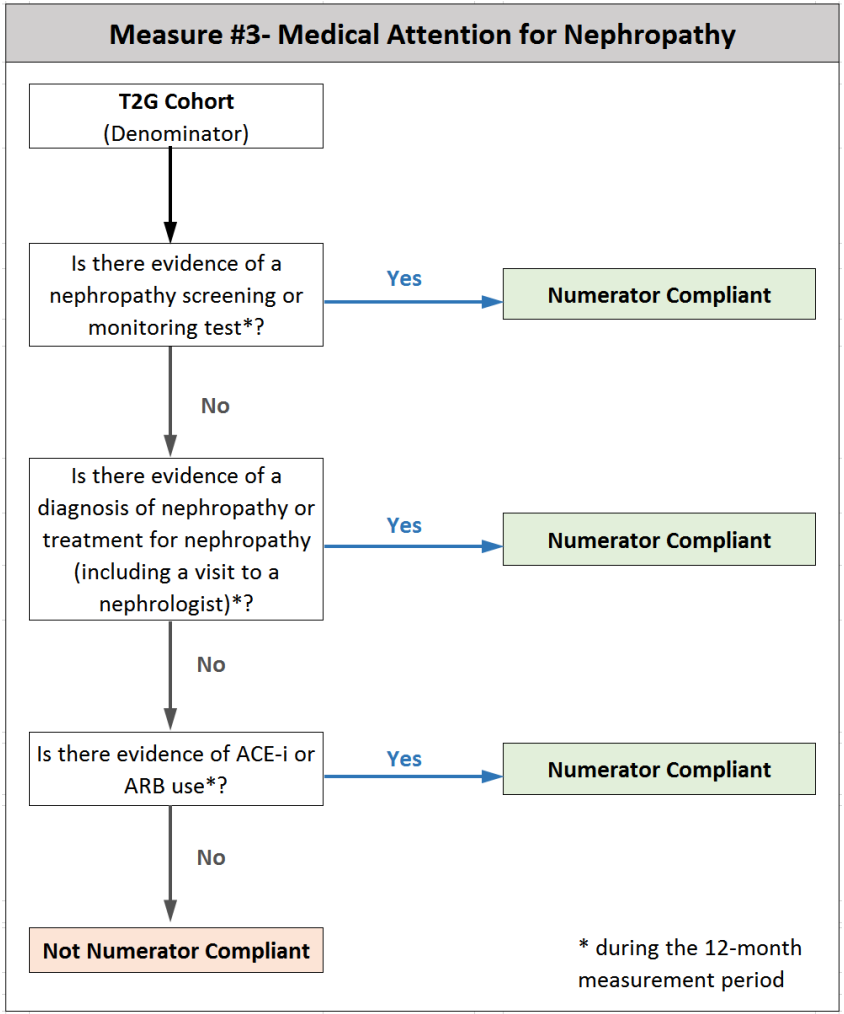
618,000 patients aged 18-89, with ≥ 1 visit with a PCP in 2018, and a Dx for DM (T1 or T2)

Medical Attention for Nephropathy in current NCQA Comprehensive Diabetes Care group: Red lines show 25th, 50th, and 75th percentiles of performance (2018 Q4) among 90 AMGA member organizations in Together to Goal,® AMGA Foundation's campaign to improve care for 1 million people with type 2 diabetes.



Issues with Current Medical Attention for Nephropathy Measure

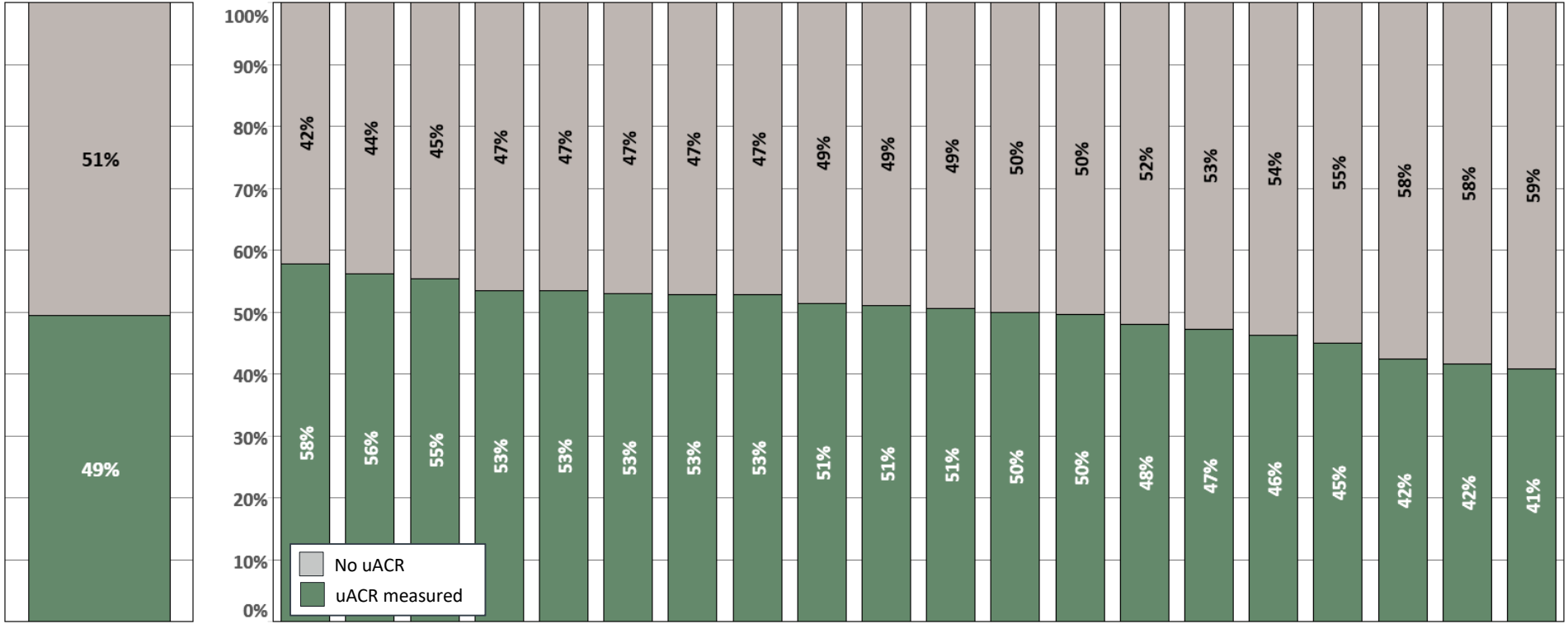
- eGFR not included, an important test for CKD detection and risk stratification
- “Topped-out” at most health systems, false sense of optimal kidney care for people with diabetes
- Convoluted measure: can meet the numerator in multiple ways, which may or may not have been a deliberate attempt to address nephropathy



- 685,000 patients with type 2 diabetes receiving care at 24 different health care organizations
  - patients age 18 – 75, with a diagnosis of type 2 diabetes, and ≥ 2 visits in the last 18 months with a PCP, cardiologist , endocrinologist, or nephrologist
- Urine protein measurements
  - kidney health evaluation measure: albumin to creatinine ratio only
  - medical attention for nephropathy: includes a broader set of urine protein measurements (e.g,. including qualitative measurements with a dipstick)

uACR Measurement Rates

- 685,000 patients age 18 – 75 with type 2 diabetes and at least 2 visits with a PCP, cardiologist, endocrinologist, or nephrologist.
- Overall, 49% of patients (in green) had a urine albumin to creatinine test in the 12 month measurement period.
- Rates ranged from 41 – 58% across individual organizations.

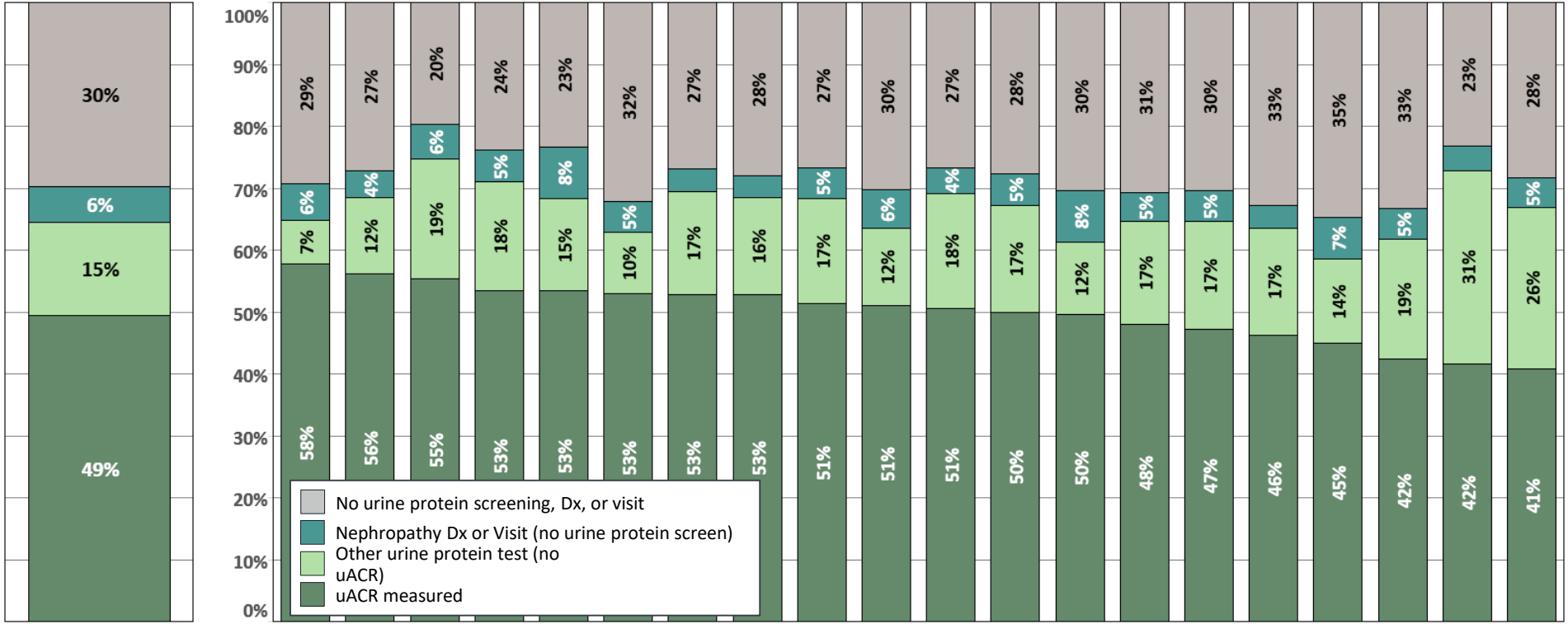


Urine Protein Test for Nephropathy Screening or Monitoring

- 685,000 patients age 18 – 75 with type 2 diabetes and at least 2 visits with a PCP, cardiologist, endocrinologist, or nephrologist.
- Overall, 15% of patients (in light green) had a urine protein test in the 12 month measurement period other than uACR.
- Rates ranged from 7 – 31% across individual organizations.

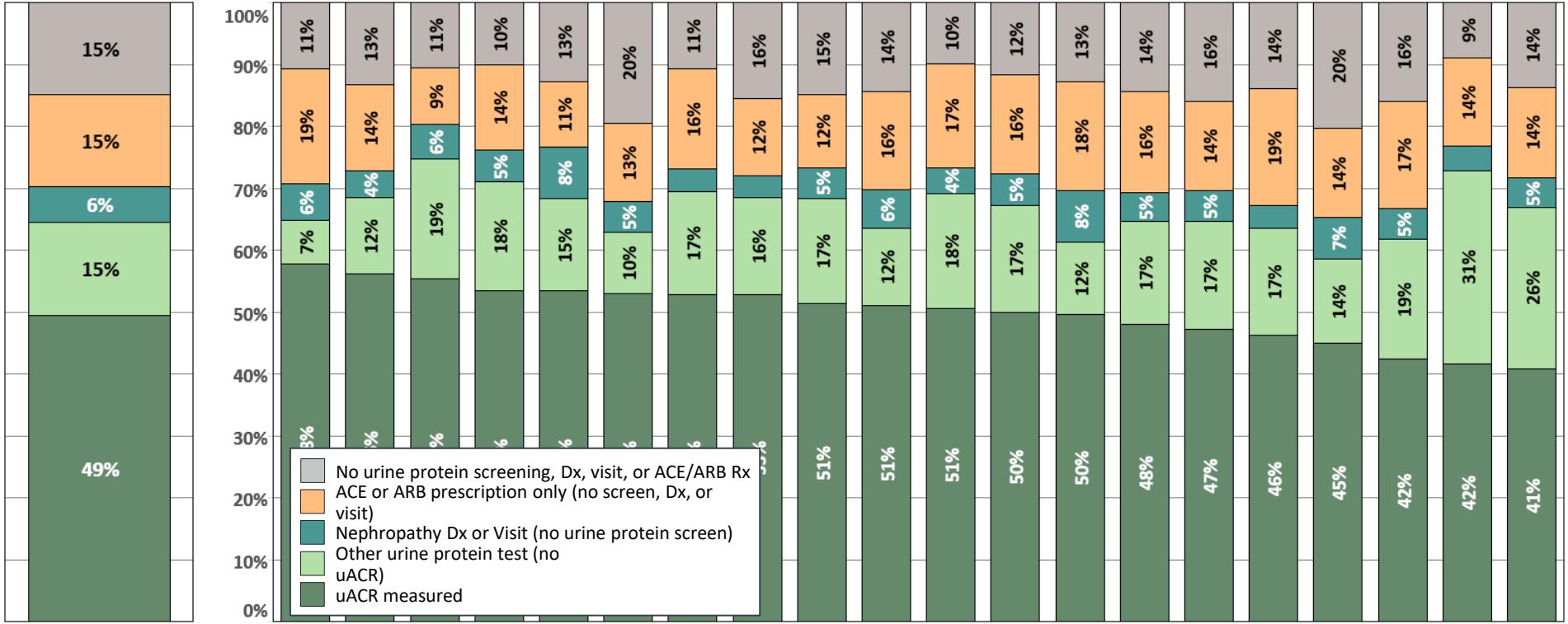
Diagnosis or Treatment of Nephropathy or Visit with Nephrologist

- Overall, 6% of patients (in teal) had a diagnosis for nephropathy, treatment for nephropathy, or a visit with a nephrologist, and no urine protein test.
- Rates ranged from 3 – 8% across individual organizations.



ACE or ARB Prescriptions

- Overall, 15% of patients (in orange) had an ACE or ARB prescription and no urine protein test, nephropathy Dx, nephropathy treatment, or visit with a nephrologist.
- Rates ranged from 12 – 19% across individual organizations.



Pushback on Including ACE/ARBs

- While the evidence shows that ACE/ARBs are beneficial among patients with T2DM and albuminuria, the medical attention to nephropathy measure only requires a prescription, with or without evidence of albuminuria
- ~ 15% of patients met the measure for use of ACE-i/ARB only
  - < 1% of patients who met the measure solely on ACE-i/ARBs use had a Dx for microalbuminuria [1]
  - ~ 75% had a diagnosis for cardiovascular disease (e.g., hypertension) [1]
- *"Use of these medications does not obviate the need for a nephropathy screening in diabetics. Inclusion of these medications as numerator compliance leads to overreporting and may contribute to underscreening of a population at risk."* [1]

[1]Krause TM, Ganduglia-Cazaban C, Finkel KW. Rates for HEDIS Screening for Diabetic Nephropathy Quality Measure May Be Overstated. *Manag Care.* 2018;27(8):45-49.

Key Points

- Most patients with T2DM have eGFR measured, consistent with guideline recommendations.
- uACR measurement rates were moderate and variable across organizations.
- Measurement rates varied widely within organizations, many with one or more site of care among the highest and lowest performers across sites at all organizations.
- Current medical attention for nephropathy may be giving false sense of optimal kidney care for people with T2DM
- Proposed kidney health evaluation measure helps identify opportunities for improvement at all organizations, which would likely stimulate more consistent use of evidence-based therapy and more accurate risk prediction, reducing complications in this high-risk population.

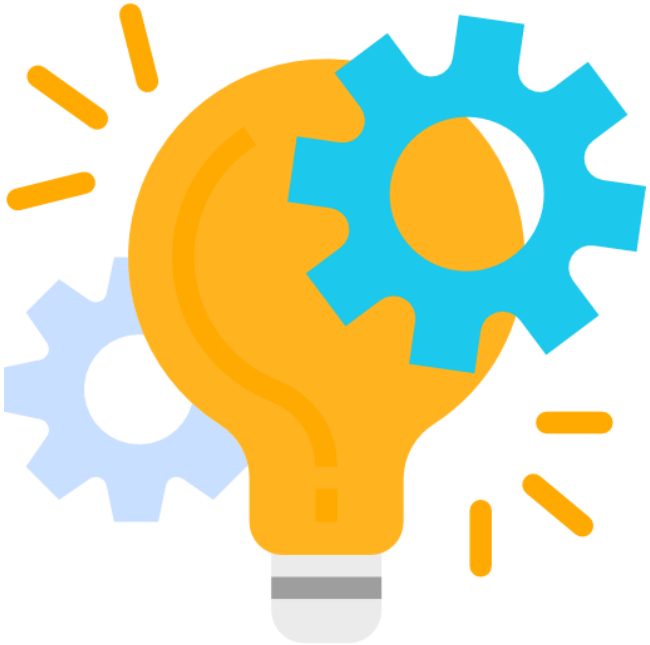
Next Steps

- Working with NKF and NCQA to evaluate the kidney health evaluation measure, to replace the medical attention for nephropathy measure in NCQA's Comprehensive Diabetes Care measure set
  - Examine performance and disparities
  - Describe association of evidence based interventions with meeting quality measure
    - Use of kidney protective drugs, nephrology consultation, Statin therapy, diabetes and blood pressure control
  - Compare to same for current medical attention to nephropathy measure
  - Goal: NQF endorsement of new measure
- Working with AMGA members to understand trends and barriers in measurement for uACR and eGFR among patients with type 2 diabetes

Breakout Groups

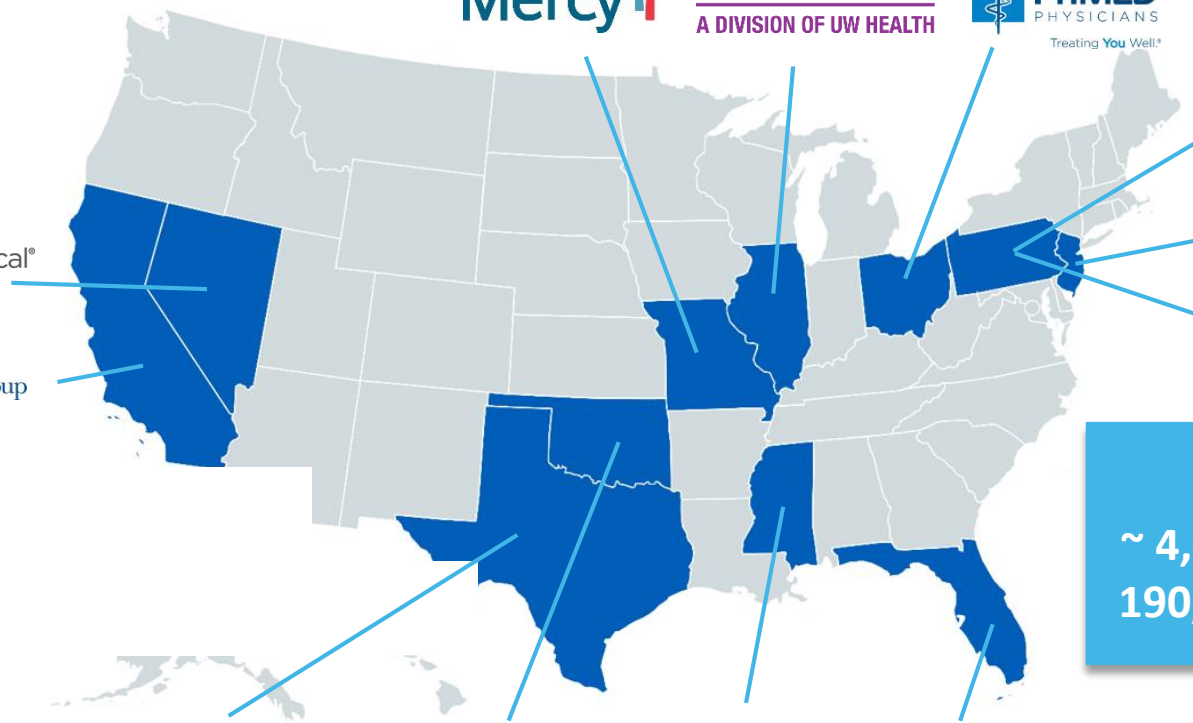
- Group 1 – Curie Room
- Group 2 – Edison G
- Group 3 – Edison EF *(Stay here)*

Together 2 Goal® Innovator Track



- Cardiovascular Disease Cohort
  - Concluded June 2019
- Eye Care Cohort
  - Concluded September 2019
- 12 month programs

CVD Cohort



Mercy
SwedishAmerican
A Division of UW Health
PriMED Physicians
Treating You Well.
Geisinger
Summit Medical Group
Premier Medical Associates
Southwest Medical
Part of OptumCare
SHARP Rees-Stealy Medical Group
Kelsey-Seybold Clinic
Your Doctors for Life
utica park clinic
Hattiesburg Clinic
Watson Clinic LLP
Quality Healthcare for Every Generation

12 groups
~ 4,000 FTE Physicians
190,000+ T2D Patients

CVD Cohort Measures

- 1: Non-Tobacco User

- 2a: Daily aspirin for 2º prevention
- 2b: Daily aspirin for 1º prevention

Daily Aspirin or Anti-Platelet Agent

- 3a: Any statin
- 3b: High-intensity statin
- 3c: Measured LDL < 70

Lipid Management for Secondary Prevention

CVD Cohort Outcomes

- **1,700** additional patients with **tobacco-free status**
- **600** additional patients with **documented aspirin therapy (secondary prevention)**
- **1,000** additional patients with **documented aspirin therapy (primary prevention)**
- **775** additional patients with a **Rx for any statin**
- **1,900** additional patients with a **Rx for high-intensity statin**
- **1,640** additional patients with **LDL < 70 mg/dL**

Eye Care Cohort

10 groups
~4,000 FTE Physicians
160,000 T2D Patients

Eye Care Cohort Measure

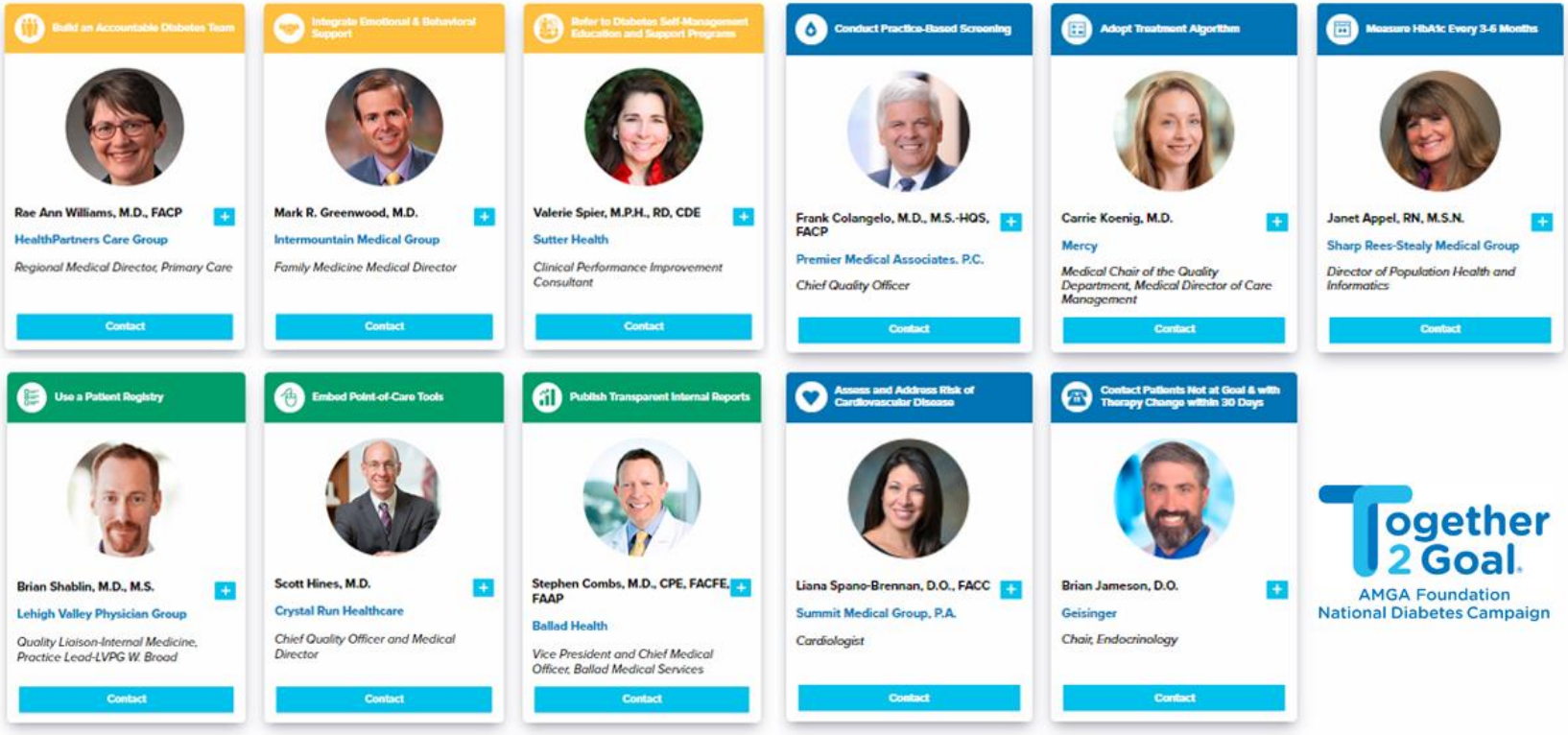
- Patients with documented screening for diabetic retinal disease

  - ✓ Increase the **number of screenings** conducted (*screening new patients that are at risk who have not been screened before*)
  - ✓ Increase **documentation** of eye screenings (*could entail improving the capture of external or internal exams that previously weren't recorded in the health record*)

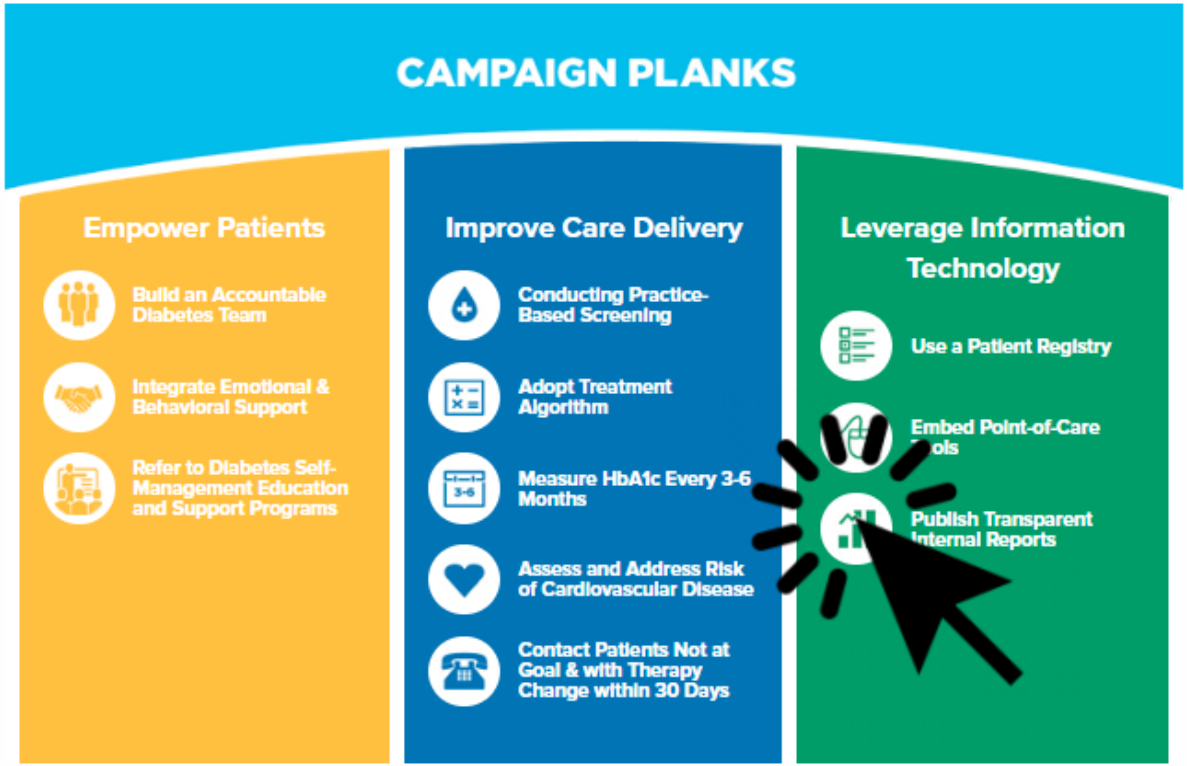
Eye Care Cohort Outcomes

- **8,600** additional patients with documented screening
  - absolute improvement ranged from 2% to 21%
  - relative improvement ranged from 5% to 45%

Plank Mentors



Interactive Campaign Planks



National Day of Action – Nov. 7, 2019

T2G Talk & Taste Events

- Watch a Plank Mentor video
- Discuss as a team
- Recognize exceptional staff
- Celebrate successes
- Enjoy a healthy meal!

Wrap Report coming soon!

New Partnerships

1,082,000

336,000

AMGA
Advancing High Performance Health

T2G Patient Lives Improved

Baseline through Year 3

Nikita Stempniewicz, Cori Rattelman, Caitlin Shaw, John Cuddeback

September 2019

Tracking Achievement

Together2Goal
AMGA Foundation
National Diabetes Campaign

AMGA

Population Measures

- Proportion of patients in control (%)
  - A1c < 8.0
  - BP < 140/90
  - Statin Rx
  - Nephropathy
  - Bundle
- Cross-sectional
- Reported quarterly
- Ages 18 – 75

Patients Improved

- Number of patients with sustained improvement
  - New diagnosis of type 2 diabetes
  - Improve on at least one measure
- Longitudinal
- Reported annually
  - Year 3 concluded 2019 Q1
- Ages 18 – 89
- Number of patients with sustained control on bundle measure

HbA1c < 8.0 – 2016 Q1 (Baseline)

850,000 patients with type 2 diabetes, across 70 AMGA member organizations

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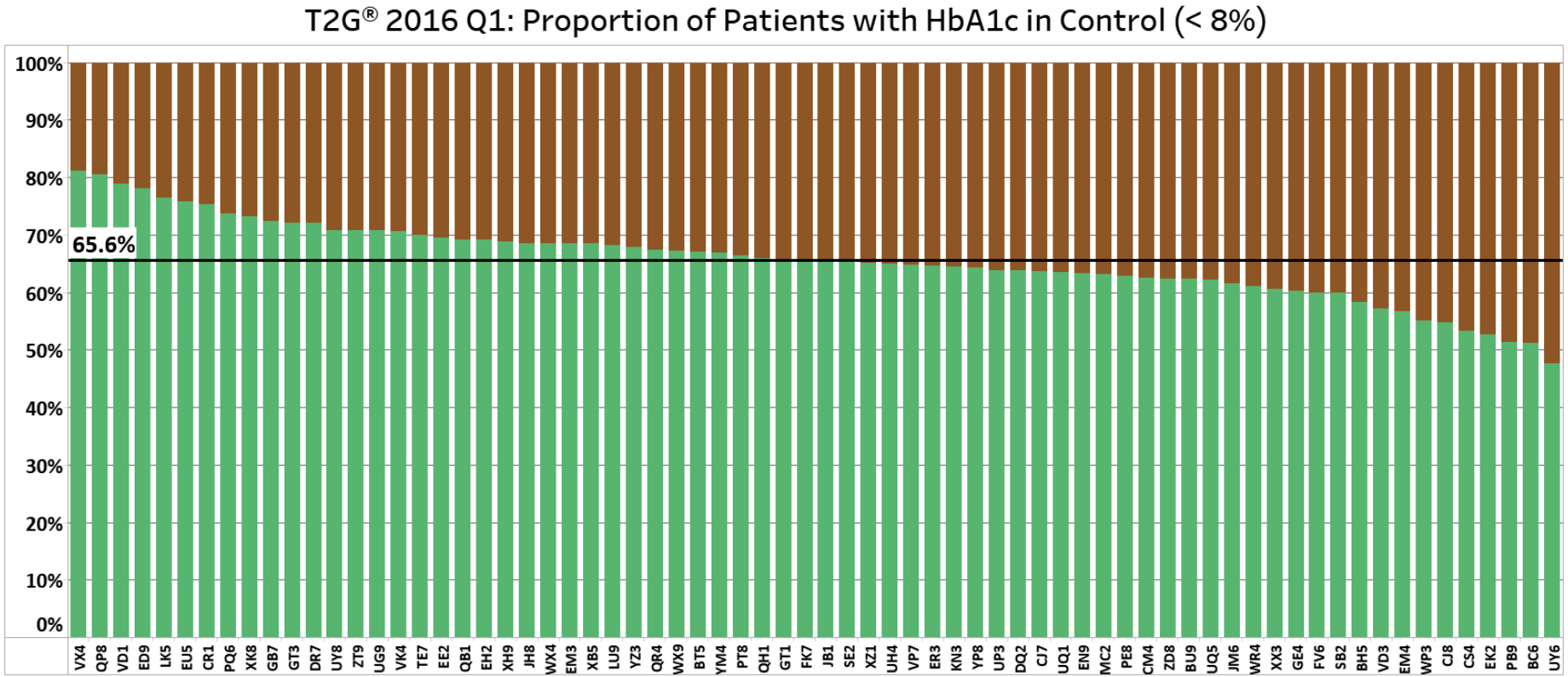
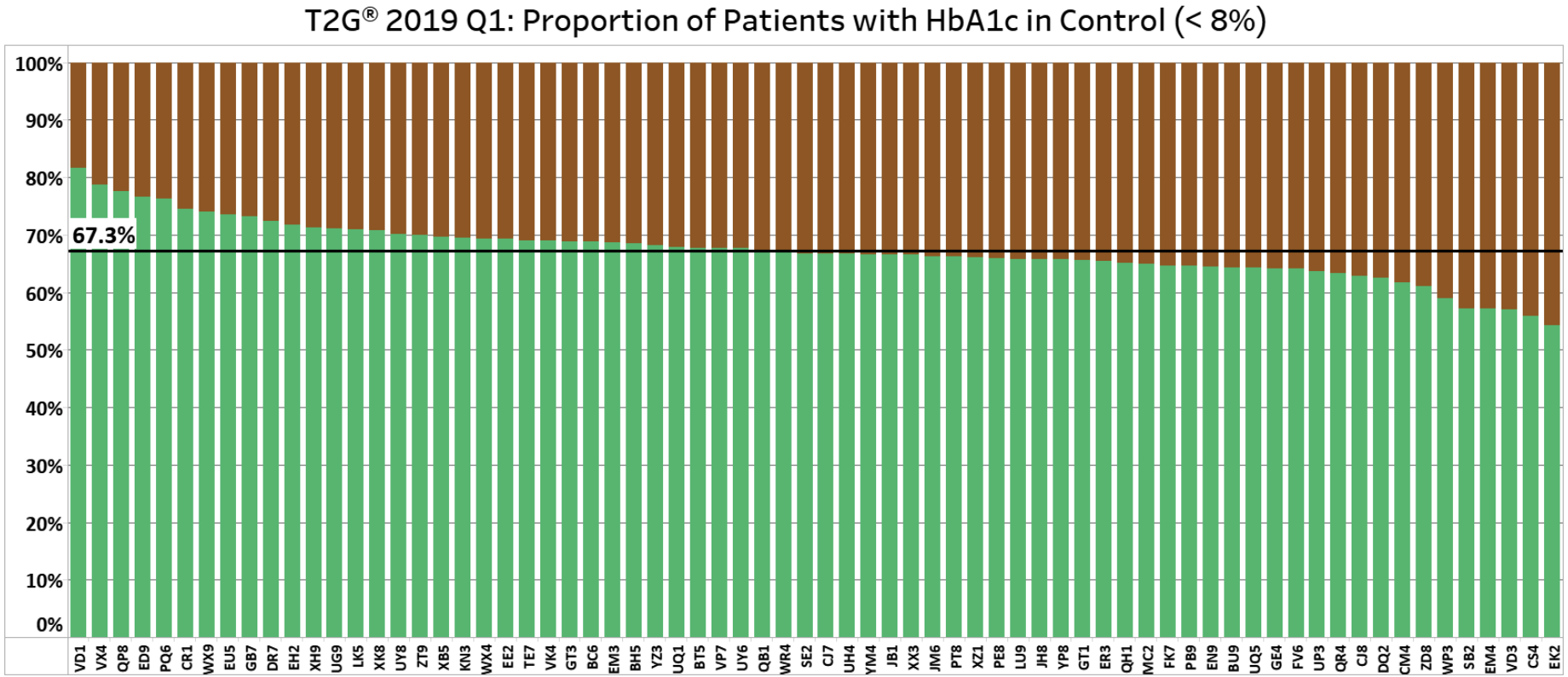


HbA1c < 8.0 – 2019 Q1 (Year 3)

1,010,000 patients with type 2 diabetes, across 70 AMGA member organizations

Together2Goal
AMGA Foundation
National Diabetes Campaign

AMGA

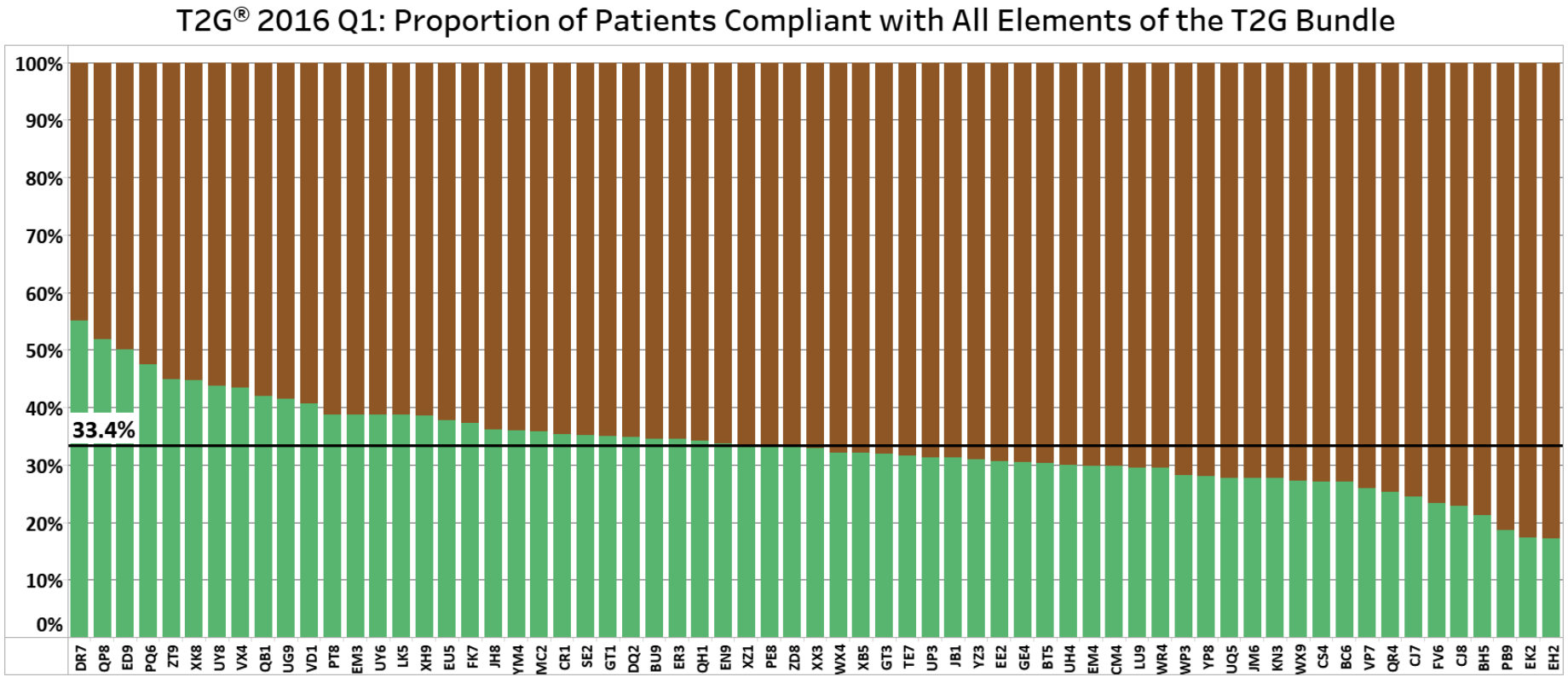


T2G Bundle – 2016 Q1 (Baseline)

790,000 patients with type 2 diabetes, across 65 AMGA member organizations

Together2Goal
AMGA Foundation
National Diabetes Campaign

AMGA



T2G Bundle – 2019 Q1 (Year 3)

930,000 patients with type 2 diabetes, across 65 AMGA member organizations

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AMGA Foundation
National Diabetes Campaign

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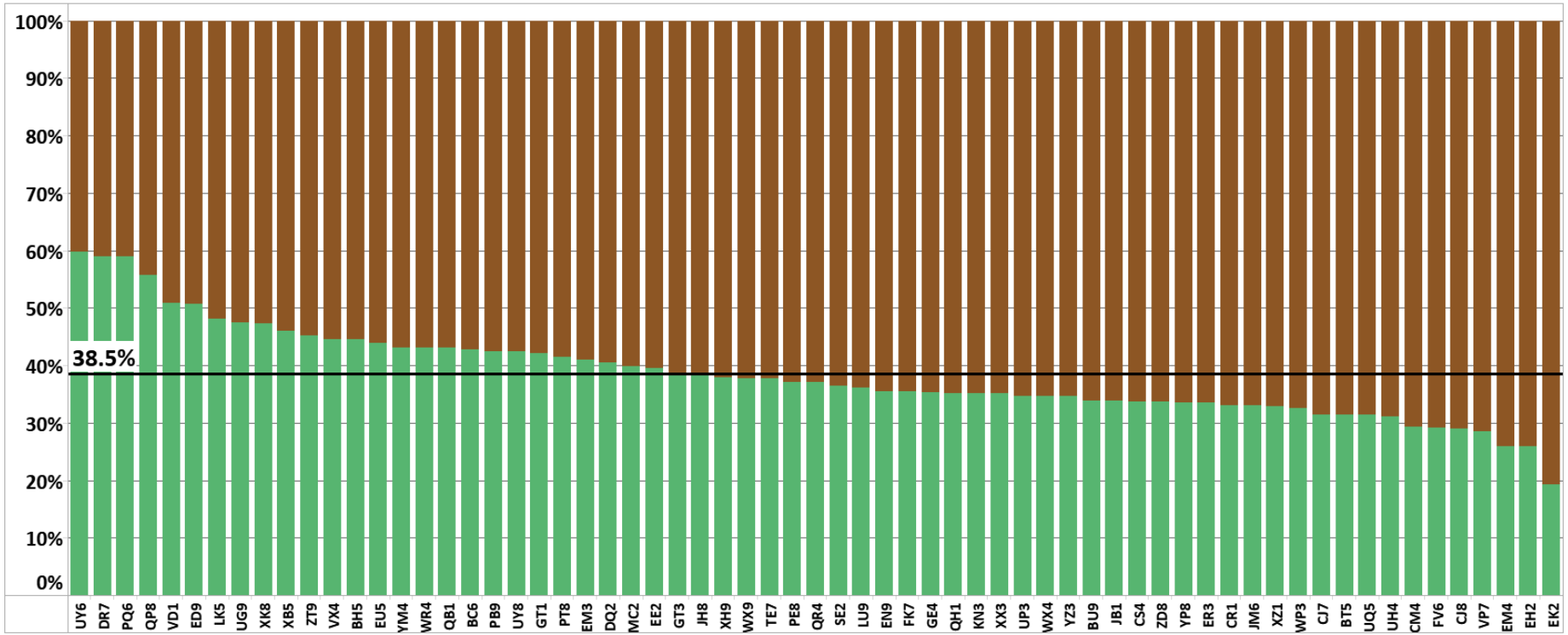
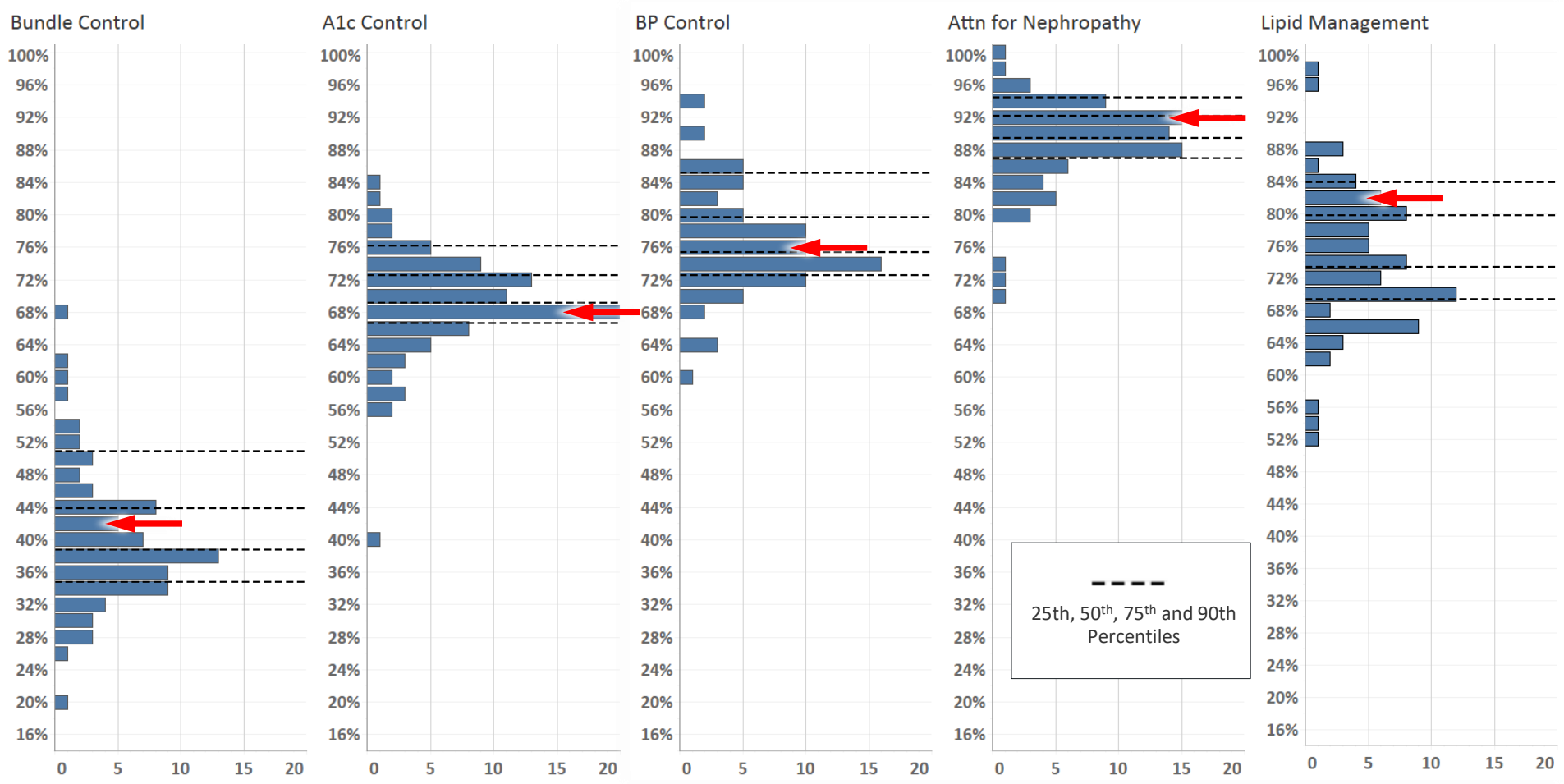
T2G® 2019 Q1: Proportion of Patients Compliant with All Elements of the T2G Bundle



Distribution of Measure Performance Rate



Number of Health Care Organizations (Reporting for 2018Q4)

Measures – Population-level "Control" Rates: 2016 Q1 → 2019 Q1

- 70 organizations reporting measures for 3 years (65 Core Track + 5 Basic Track)
- Average performance rate (group weighted) from baseline (2016 Q1) to year 3 (2019 Q1)

	2016 Q1	2017 Q1	2018 Q1	2019 Q1	Δ 2016–2019
T2DM prevalence	13.8%	13.6%	13.8%	14.2%	
HbA1c < 8.0	65.6%	66.4%	67.5%	67.3%	+1.6%
BP < 140/90	72.9%	74.0%	75.3%	75.9%	+3.0%
Nephropathy	85.9%	87.0%	87.9%	88.5%	+2.6%
Lipid management	68.7%	69.5%	71.5%	73.3%	+4.5%
T2G Bundle	33.4%	34.9%	37.5%	38.5%	+5.1%

Opportunities for Improvement

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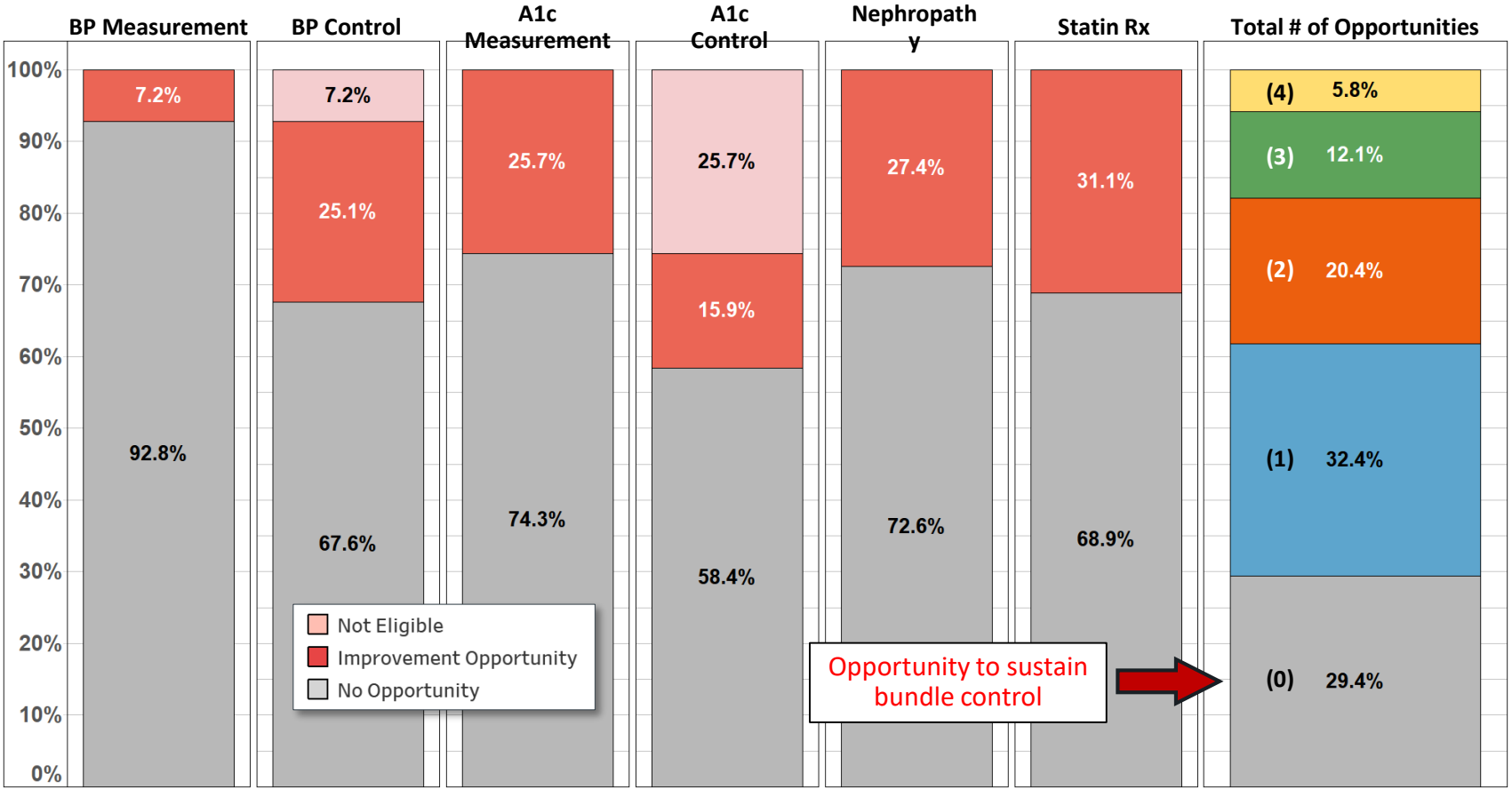
- Patients with no prior diagnosis
  - New diagnosis for type 2 diabetes (on claim* or problem list)
    - Review clinical data for existing evidence that's diagnostic or strongly suggestive of type 2 diabetes
    - Practice-based screening
- Patients with a diagnosis of type 2 diabetes
  - If A1c is not measured (during measurement period), measure A1c
  - If A1c ≥ 8.0, bring A1c into control
  - if BP is not measured, measure BP
  - If BP ≥ 140/90, bring BP into control
  - If no medical attention to nephropathy, screen/diagnose or refer to a nephrologist
  - If no statin prescribed and LDL ≥ 70 mg/dL, prescribe (or re-try) a statin

* We require Dx codes on claims to be associated with a face-to-face encounter with a provider, to ensure we don't pick up a code for diabetes that's used in a "rule-out" sense, on a claim for a lab test intended as screening for diabetes. This use of the code is technically not correct, but it's a common error.

Have Dx: Opportunities for Improvement

Campaign baseline data (2016 Q1): Broader population, i.e., patients age 18 – 75 with ≥ 1 visit (instead of ≥ 2 visits required in T2G)



Improvement Calculation

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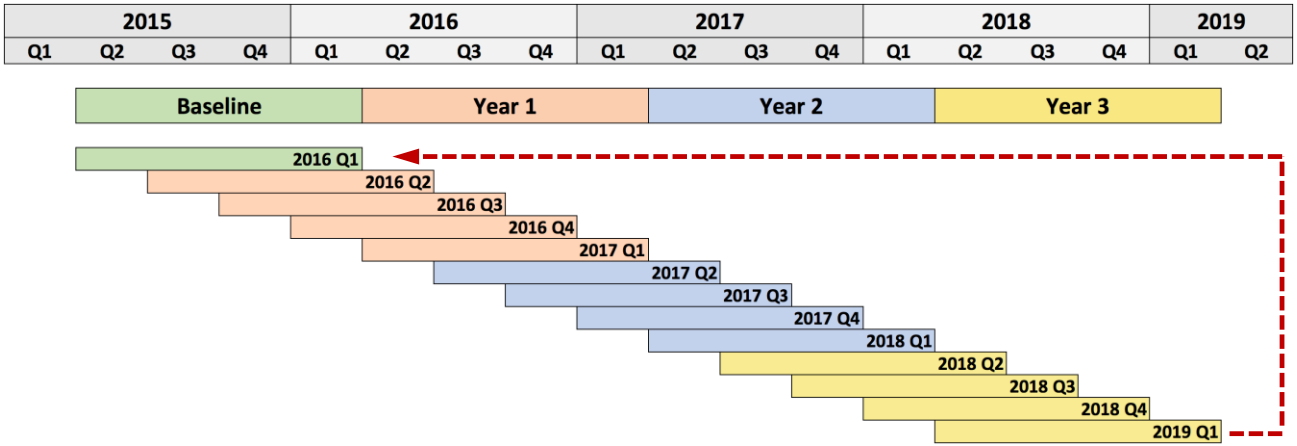
	A1c		BP		Lipid		Nephropathy		Bundle		Improvement
	Baseline	Year 3	Baseline	Year 3	Baseline	Year 3	Baseline	Year 3	Baseline	Year 3	Baseline → Year 3
Example A	✔	✔	✗	✔	✔	✔	✔	✔	✗	✔	✔
Example B	✔	✔	✗	✔	✗	✔	✔	✔	✗	✔	✔
Example C	✔	✗	✗	✔	✔	✔	✔	✔	✗	✗	✗
Example D	✔	✔	✗	✔	✗	✗	✔	✔	✗	✗	✔
Example E	✔	✗	✗	✔	✗	✔	✔	✔	✗	✗	✔
Example F	✔	✗	✗	✔	✗	✔	✔	✗	✗	✗	✗
Example G	✔	✔	✔	✔	✔	✔	✔	✔	✔	✔	✗

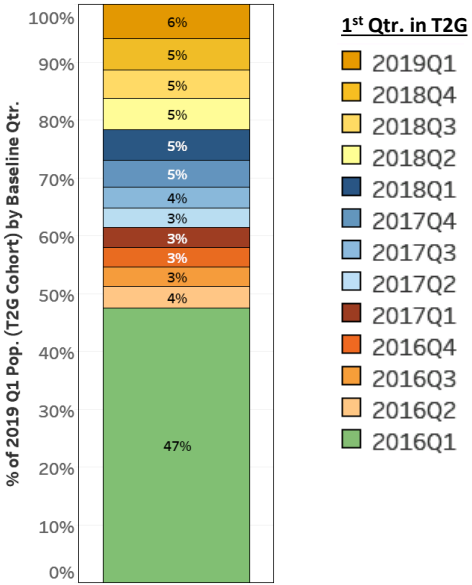
Improvement is assessed for each patient, then summarized for all patients in the T2G denominator

- Example A – Moving from out-of-control (✗) to in-control (✔) on any measure counts as improvement, provided it is not offset by movement from in-control to out-of-control on another measure (see Example D)
- Example B – Moving from out-of-control to in-control on multiple measures improves performance, but it counts the same as a single measure toward improvement
- Example C – Moving from out-of-control to in-control does not count as improvement if it is "offset" by regression (moving from in-control to out-of-control) on another measure
- Example D – Remaining out-of-control diminishes performance on the respective measure, but it does not offset improvement on another measure
- Examples E and F – Improvement on two measures is not offset by regression on one other measure, but it is offset by regression on two other measures
- Example G – Remaining in-control (✔) maintains performance on the respective measure, but it does not count as improvement for the campaign

Improvement Calculation

- Compare data from Year 3 (2019 Q1) to Baseline (2016 Q1)
- Look backward, to ensure that any improvements are sustained through end of measurement period
  - 47% of patients in T2G Cohort in 2019 Q1 were in T2G Cohort at Baseline (2016 Q1)
- Evaluate these patients for improvement in measures, from baseline to year 3





Improvement Calculation

- For remaining current T2G Cohort patients, evaluate cohorts quarterly—check how they entered the T2G Cohort
  - Patient new in T2G Cohort but Active in a prior quarter → established patient, newly diagnosed (diagnosis counts as improvement)
  - Patient new in T2G Cohort and in Active Population → new patient, already diagnosed (diagnosis does not count as improvement)
    - Evaluate these patients for improvement in measures, from cohort entry to current
- Consider patients who were active during the campaign, but not in the most recent quarter
  - Include improvements among patients who were active in ≥ 2 quarterly reporting periods but not the most recent quarter
    - Evaluate these patients for improvement in measures, from cohort entry to exit
- Lives improved includes only the AMGA members who are reporting data quarterly on the campaign measures
- For patients with bundle control at cohort entry or baseline, check to see if they sustained bundle control
  - These patients are not eligible for any improvements toward the campaign goal

Patients with Improved Care

Together2Goal
AMGA Foundation
National Diabetes Campaign

AMGA

- Among **1,780,000** patients with T2DM age 18 – 75, included in 2019 Q1 population
  - **735,000** patients with improved care, through the end of year 3 of the campaign (2019 Q1)
  - **223,000** patients with sustained bundle control for ≥ 1 year
    - These patients had all measures in control at baseline, i.e., they were not eligible for any improvements and have no overlap with the 735,000 patients above

- Among **3,100,000** patients with T2DM age 18 – 89, included in 2019 Q1 population or in ≥ 2 reporting periods during campaign
  - **1,082,000** patients with improved care, through the end of year 3 of the campaign (2019 Q1)
  - **336,000** patients with sustained bundle control for ≥ 1 year

- About 1/3 of improvements are people who have a new diagnosis of type 2 diabetes
- About 2/3 are patients who already had a diagnosis and achieved a net improvement in control, among the 4 measures that make up the T2G bundle

1,082,000

336,000

AMGA

Advancing High Performance Health

Update: Adoption of new therapies and guidelines in the management of patients with T2DM and CVD

Clinical Inertia can take place across all stages of chronic disease

GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH

FIRST-LINE THERAPY IS METFORMIN AND COMPREHENSIVE LIFESTYLE (INCLUDING WEIGHT MANAGEMENT AND PHYSICAL ACTIVITY)
IF HbA_{1c} ABOVE TARGET PROCEED AS BELOW

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

ESTABLISHED ASCVD OR CKD

ASCVD PREDOMINATES

EITHER/OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1], if eGFR adequate[2]

If HbA_{1c} above target

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

- Consider adding the other class (GLP-1 RA or SGLT2i) with proven CVD benefit
- DPP-4i if not on GLP-1 RA
- Basal insulin[4]
- TZD
- SU[6]

HF OR CKD PREDOMINATES

PREFERABLY
SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate[3]

OR

If SGLT2i not tolerated or contraindicated or if eGFR less than adequate[2] add GLP-1 RA with proven CVD benefit[1]

If HbA_{1c} above target

- Avoid TZD in the setting of HF

Choose agents demonstrating CV safety:

- Consider adding the other class with proven CVD benefit[1]
- DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA)
- Basal insulin[4]
- SU[6]

NO

WITHOUT ESTABLISHED ASCVD OR CKD

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

DPP-4i	GLP-1 RA	SGLT2i[2]	TZD
If HbA_{1c} above target			
SGLT2i[2] **OR** TZD	SGLT2i[2] **OR** TZD	GLP-1 RA **OR** DPP-4i **OR** TZD	SGLT2i[2] **OR** DPP-4i **OR** GLP-1 RA

If HbA_{1c} above target

Continue with addition of other agents as outlined above

If HbA_{1c} above target

Consider the addition of SU[6] **OR** basal insulin:

- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia[7]

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

EITHER/OR

- GLP-1 RA with good efficacy for weight loss[8]
- SGLT2i[2]

If HbA_{1c} above target

- SGLT2i[2]
- GLP-1 RA with good efficacy for weight loss[8]

If HbA_{1c} above target

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

PREFERABLY

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

COST IS A MAJOR ISSUE[9-10]

- SU[6]
- TZD[10]

If HbA_{1c} above target

- TZD[10]
- SU[6]

If HbA_{1c} above target

- **Insulin therapy** basal insulin with lowest acquisition cost

OR

- Consider DPP-4i **OR** SGLT2i with lowest acquisition cost[10]

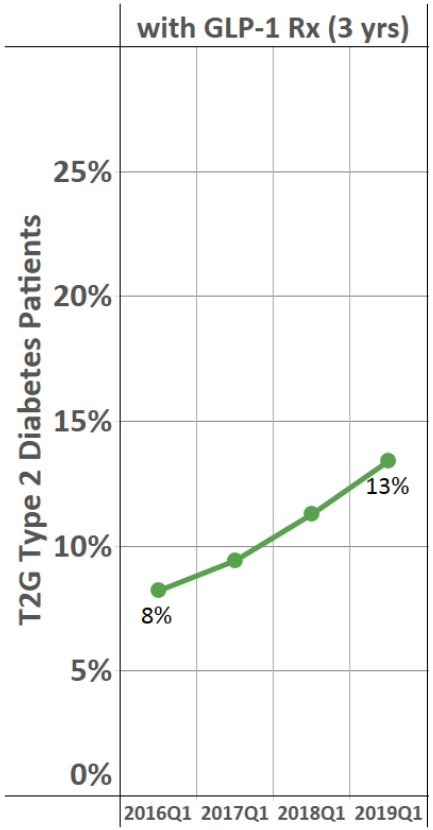
Davies M, D'Alessio D, et. al. Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care Sep 2018, dci180033; **DOI:** 10.2337/dci18-0033

Medication uptake: Patients with prescription for GLP-1 RA, SGLT2i, or DPP-4i

- 4 cohorts of patients with type 2 DM across 22 AMGA member organizations
- Observed for existing or new Rx of novel antidiabetic agents: GLP-1 RA, SGLT2i, or DPP-4i during four 36-month periods ended
  - 2016 Q1 (n=361,496)
  - 2017 Q1 (n=375,246)
  - 2018 Q1 (n=399,137)
  - 2019 Q1 (n=443,224)

Data for AMGA members using an Optum population health analytics platform. Optum is AMGA's Distinguished Data and Analytics Collaborator and is a Principal Corporate Collaborator for Together 2 Goal.

Medication uptake: Patients with prescription for GLP-1 RA, SGLT2i, or DPP-4i



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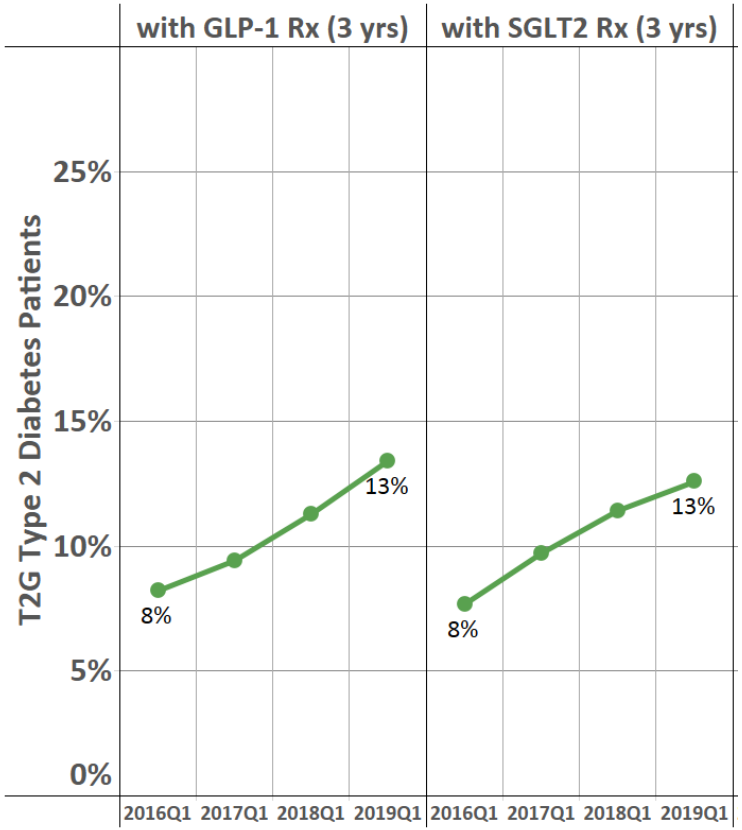

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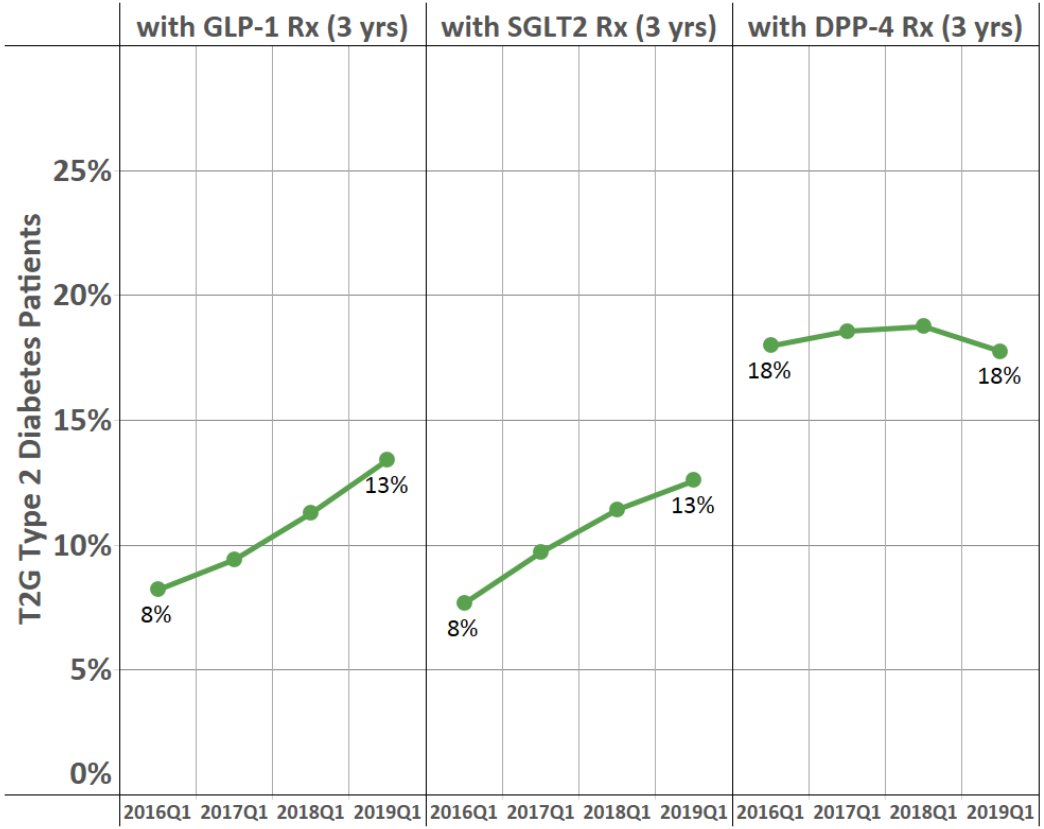

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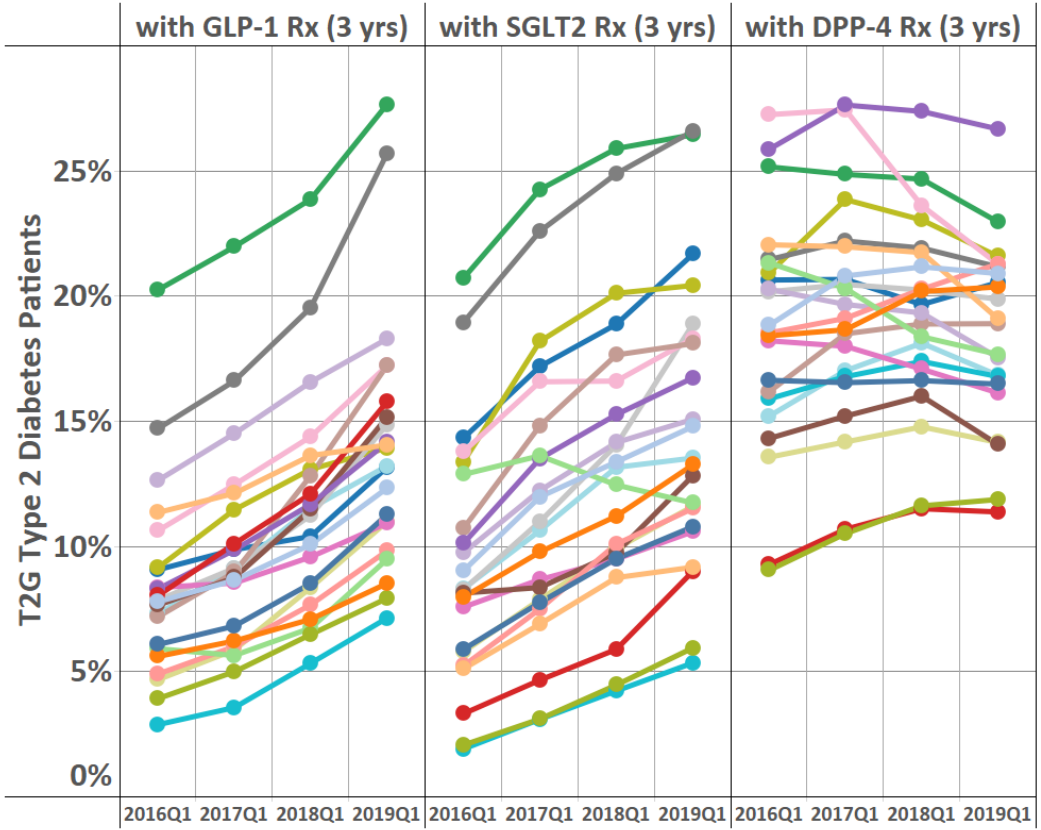
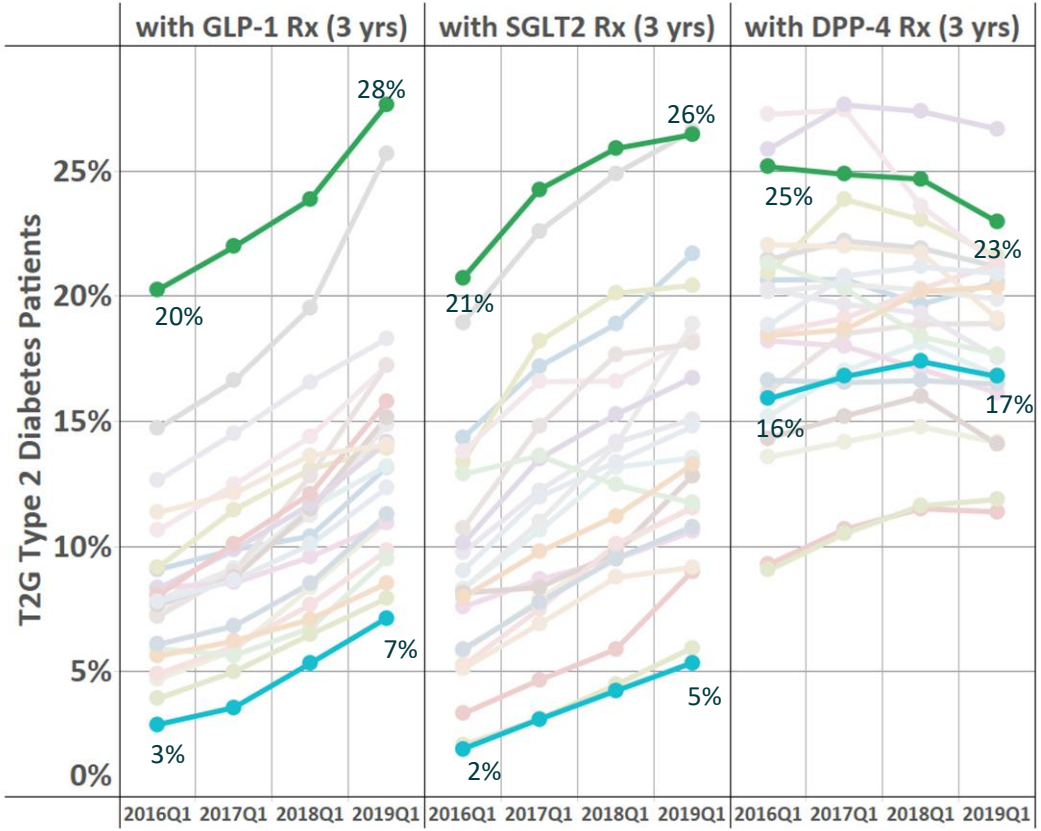
Medication uptake: Patients with prescription for GLP-1 RA, SGLT2i, or DPP-4i
By organization



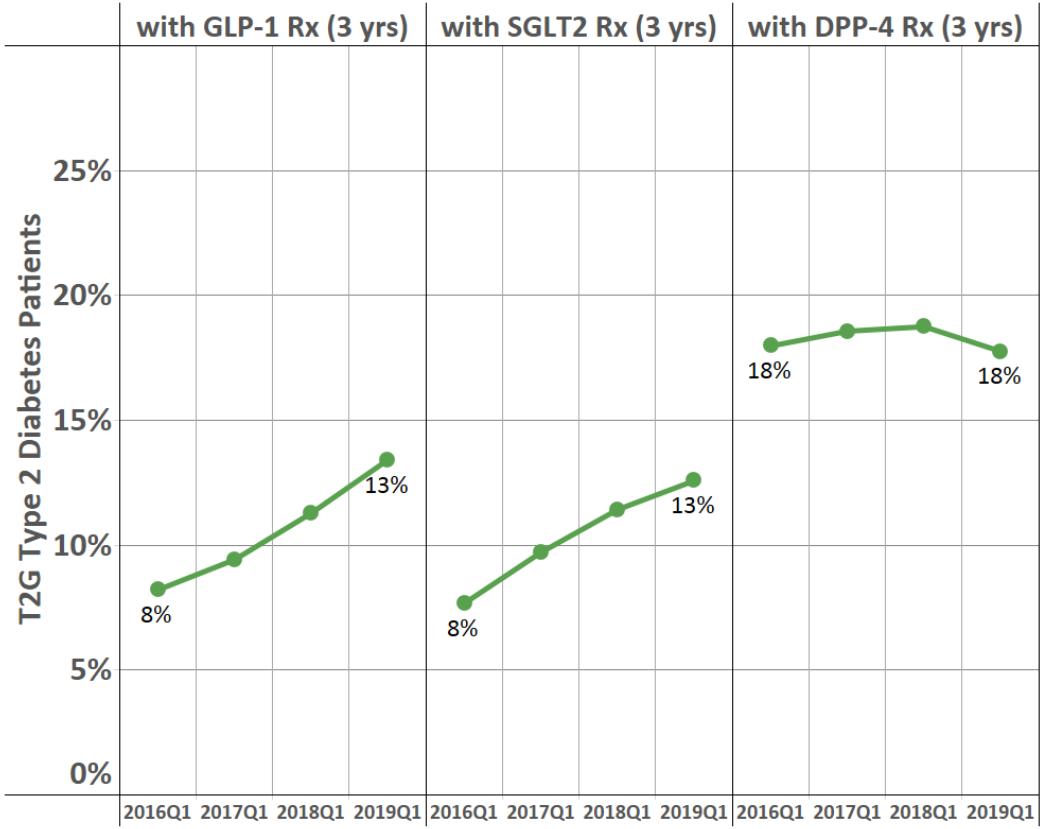
- Each colored line represents the prescription rate at one of 22 AMGA member organizations

Medication uptake: Patients with prescription for GLP-1 RA, SGLT2i, or DPP-4i By organization



- Each colored line represents the prescription rate at one of 22 AMGA member organizations
- Significant variation in rates but pattern of medication uptake is consistent across organizations

Medication uptake: Patients with prescription for GLP-1 RA, SGLT2i, or DPP-4i by CVD status

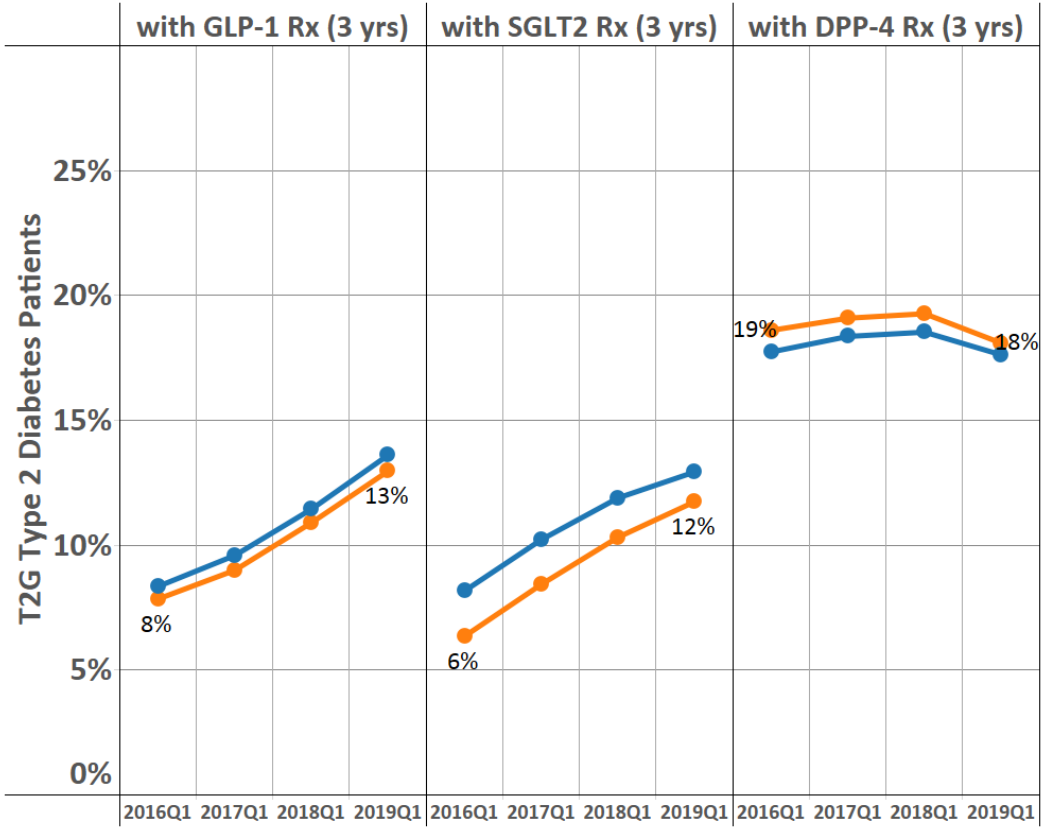


- Prevalence of CVD among these type 2 DM patients ranges from 28% in 2016Q1 to 30% in 2019Q1

CVD for T2G – HEDIS Value Sets
(diagnoses, events, or procedures):

- Ischemic vascular disease
- Myocardial infarction
- Coronary artery bypass graft
- Percutaneous coronary intervention
- Other revascularization procedure

Medication uptake: Patients with prescription for GLP-1 RA, SGLT2i, or DPP-4i by CVD status



- Prevalence of CVD among these type 2 DM patients ranges from 28% in 2016Q1 to 30% in 2019Q1
- Patients with CVD are no more likely to be prescribed GLP-1 or SGLT2 than patients without

	2016Q1	2017Q1	2018Q1	2019Q1
No CVD	261,853	268,312	280,753	311,902
CVD	99,643	106,934	118,384	131,322

CVD for T2G – HEDIS Value Sets
(diagnoses, events, or procedures):

- Ischemic vascular disease
- Myocardial infarction
- Coronary artery bypass graft
- Percutaneous coronary intervention
- Other revascularization procedure

Adoption of guidelines: Among patients with A1c ≥ 8.0, proportion with new Rx for GLP-1 RA, SGLT2i, or DPP-4i, by CVD status

Patients with baseline DM medication regimen excluding: DPP-4, SGLT2i, GLP-1 and insulin

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and A1c ≥ 8.0

EOD 3/31/2019

	2016Q1	2017Q1	2018Q1	2019Q1
No CVD	10,834	11,396	11,300	12,371
CVD	2,712	2,870	2,910	3,248

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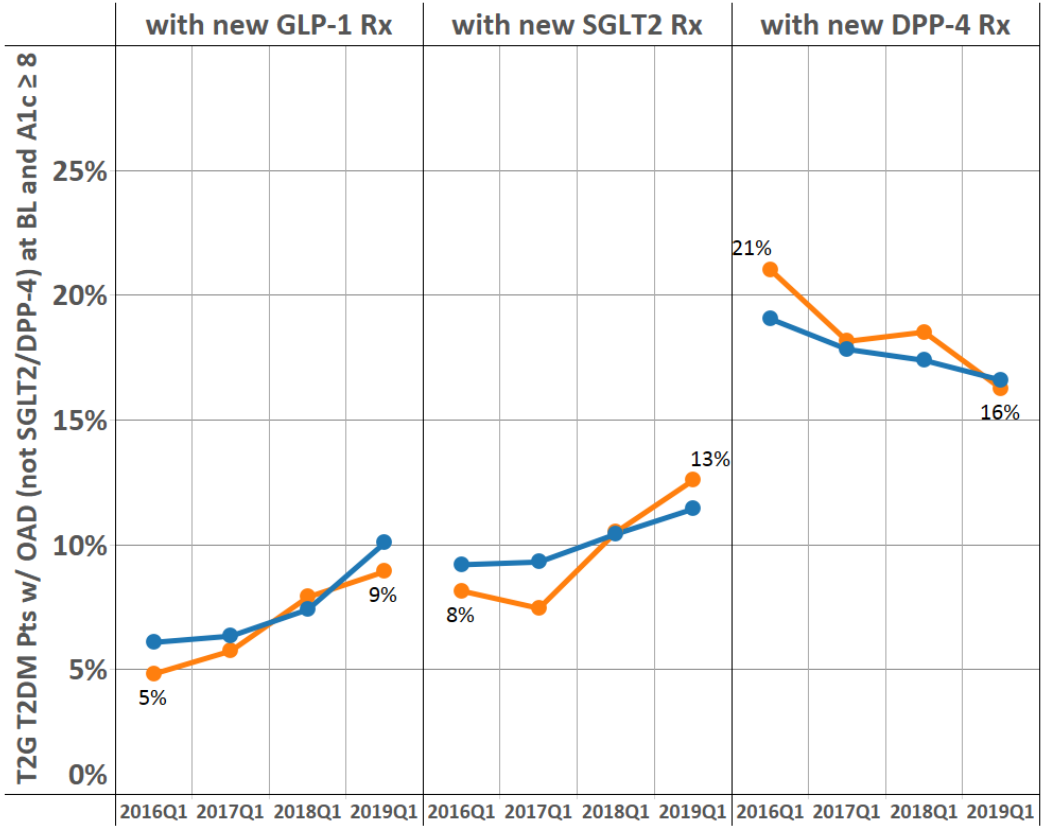

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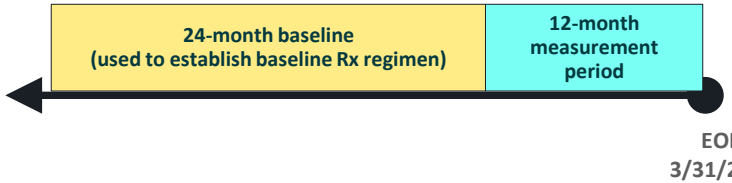

	2016Q1	2017Q1	2018Q1	2019Q1
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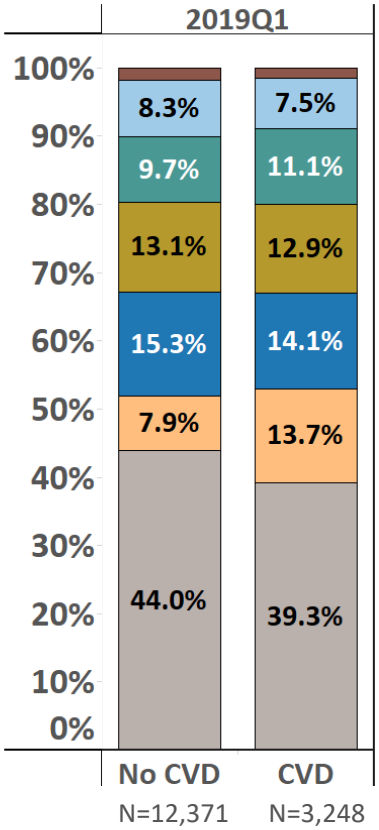
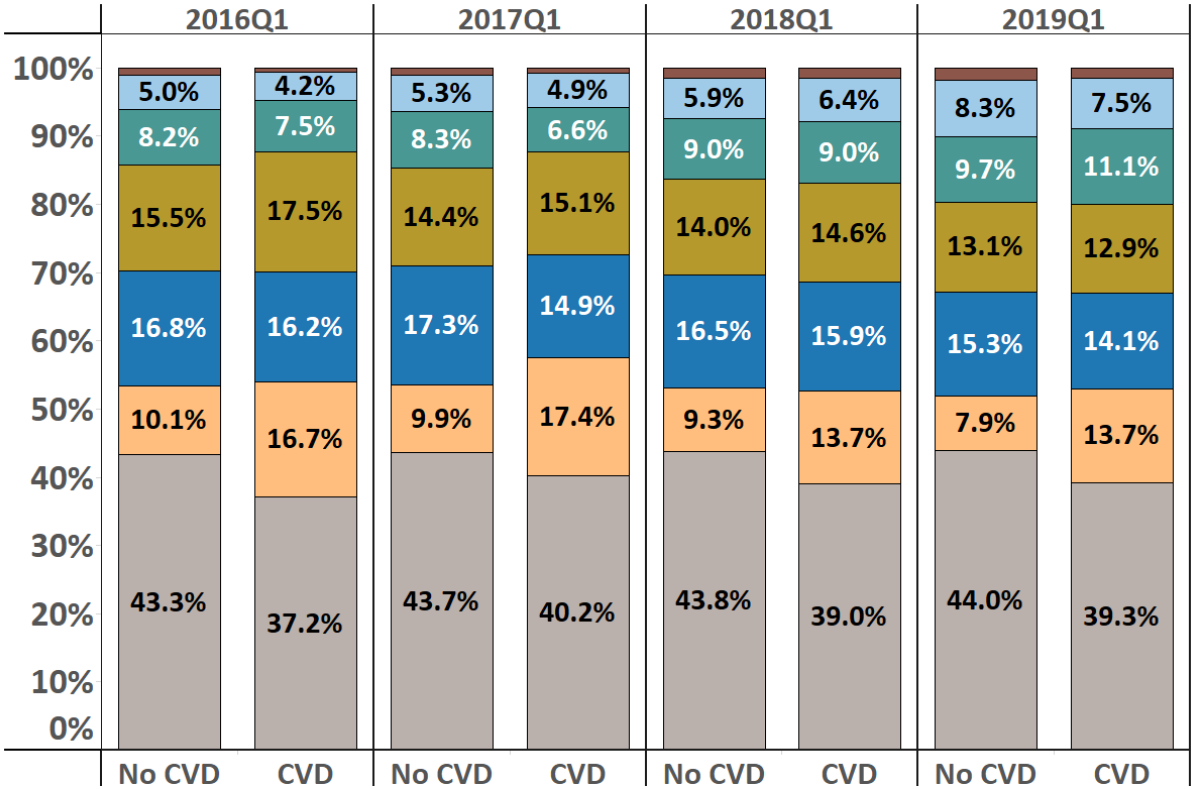
T2DM patients with BL medication excluding DPP-4i, SGLT2i, GLP-1, and insulin *and* A1c ≥ 8.0



Each patient counted only once, based on the following order of interventions:

- added GLP-1 and SGLT2
- added GLP-1
- added SGLT2
- added DPP-4
- added Sulfonylurea, TZD, or Metformin
- added Insulin ONLY
- No change

T2DM patients with BL medication excluding DPP-4i, SGLT2i, GLP-1, and insulin *and* A1c ≥ 8.0



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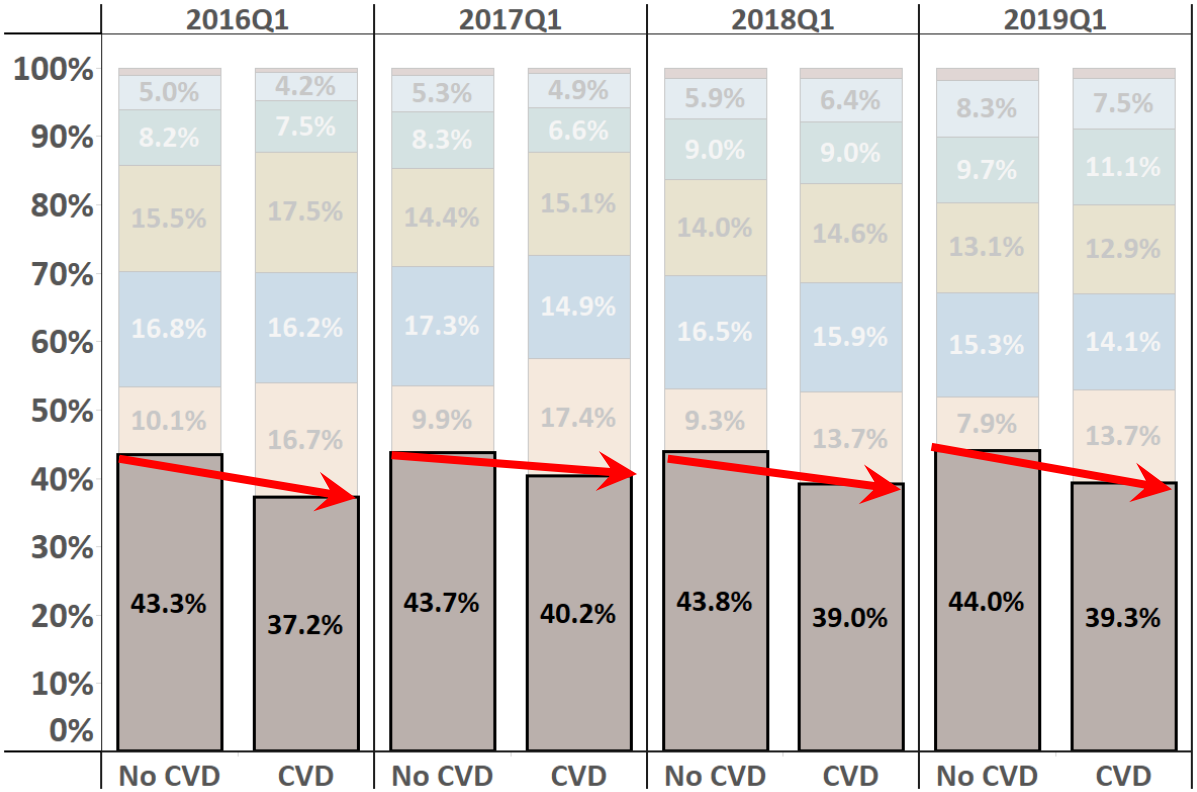

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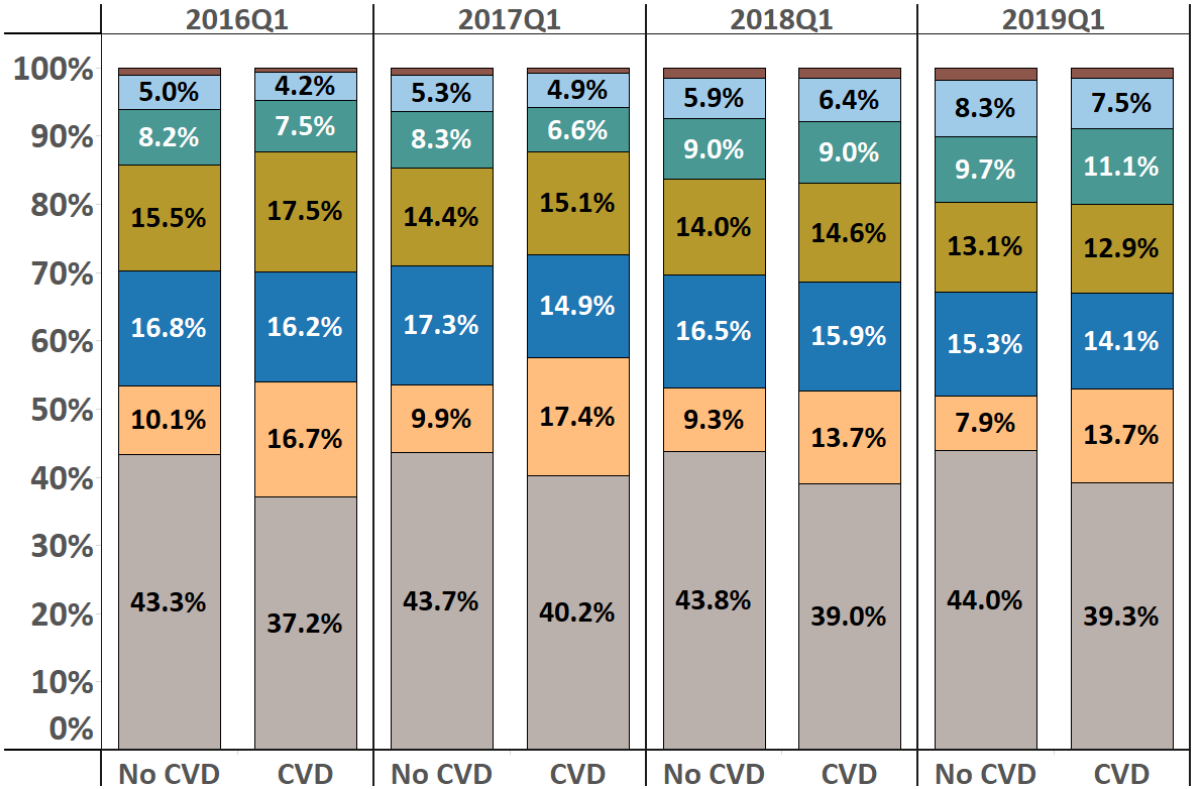

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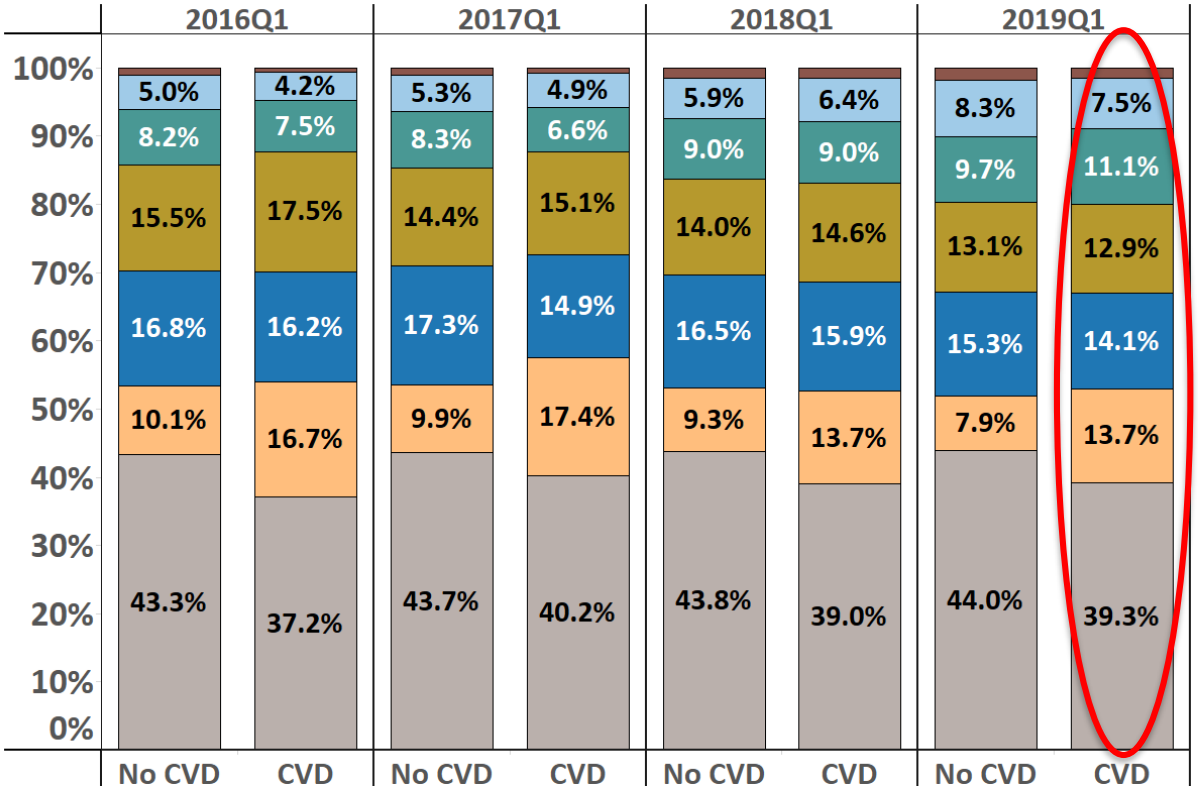

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- No change

2019Q1 measurement period: Potential clinical inertia among T2DM/CVD patients with BL medication excluding DPP-4i, SGLT2i, GLP-1, and insulin *and* A1c ≥ 8.0

Each patient counted only once, based on the following order of interventions:

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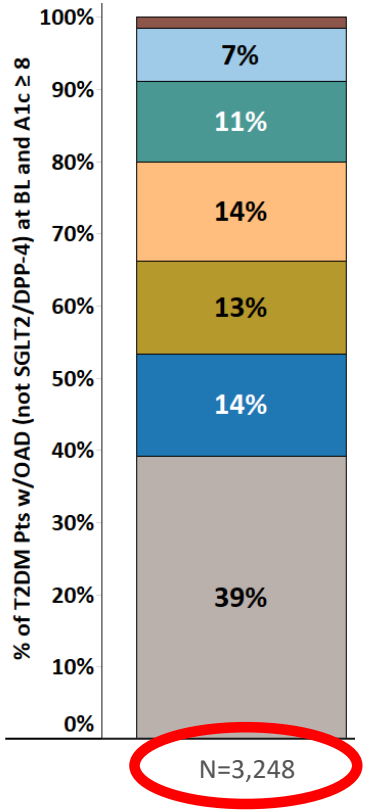
- added Insulin ONLY
- No change



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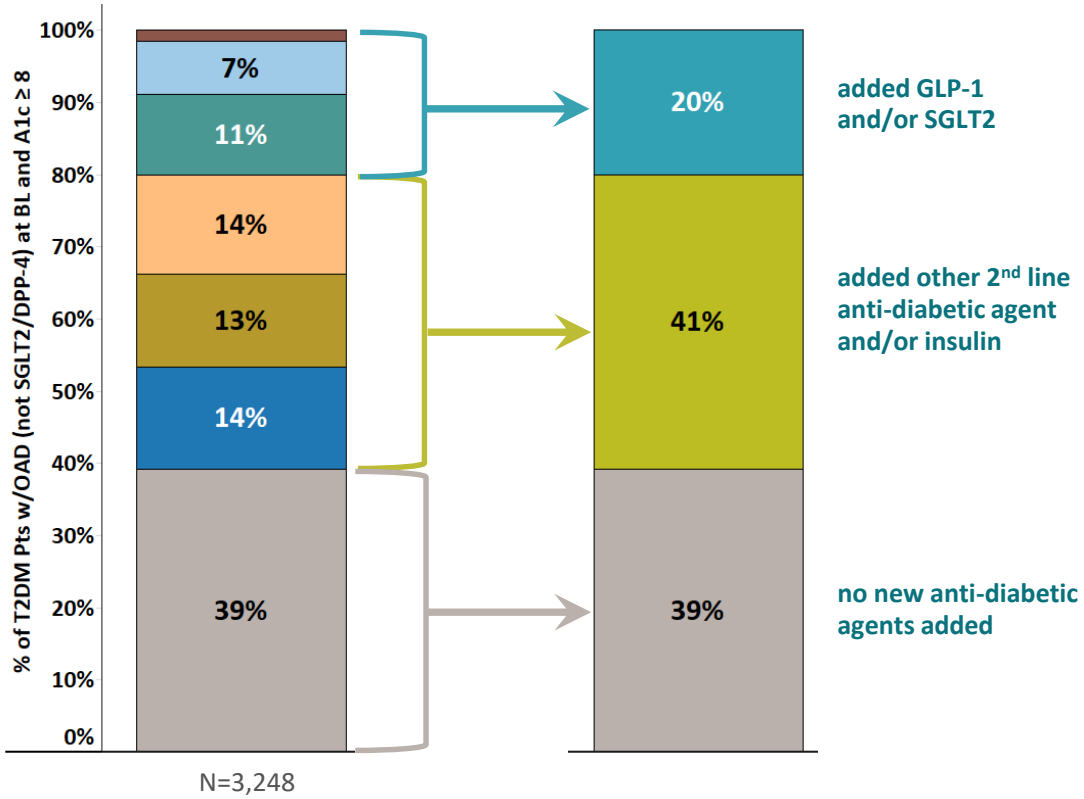
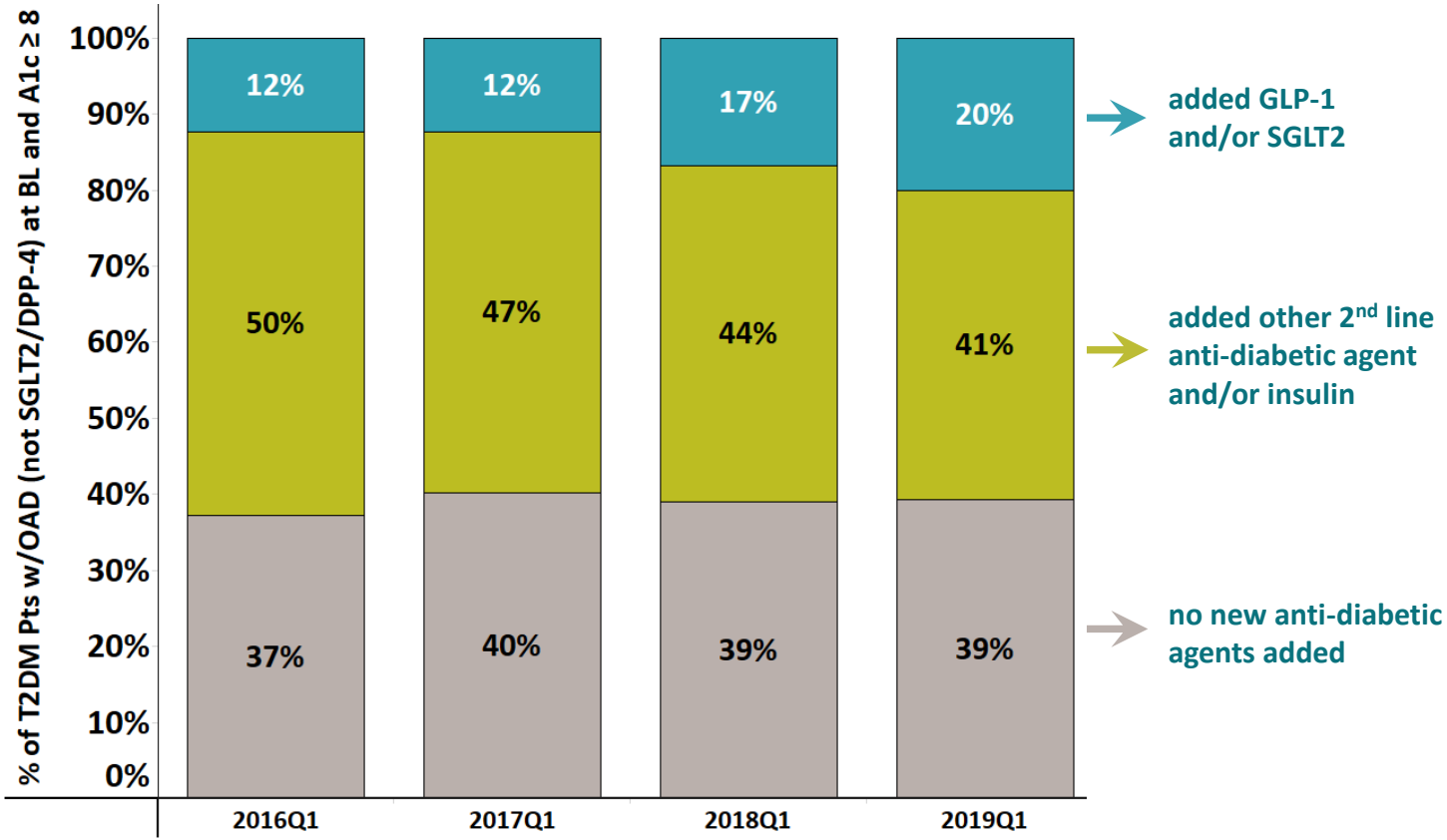
- added Insulin ONLY
- No change



Adoption of guidelines: 2016Q1 to 2019Q1



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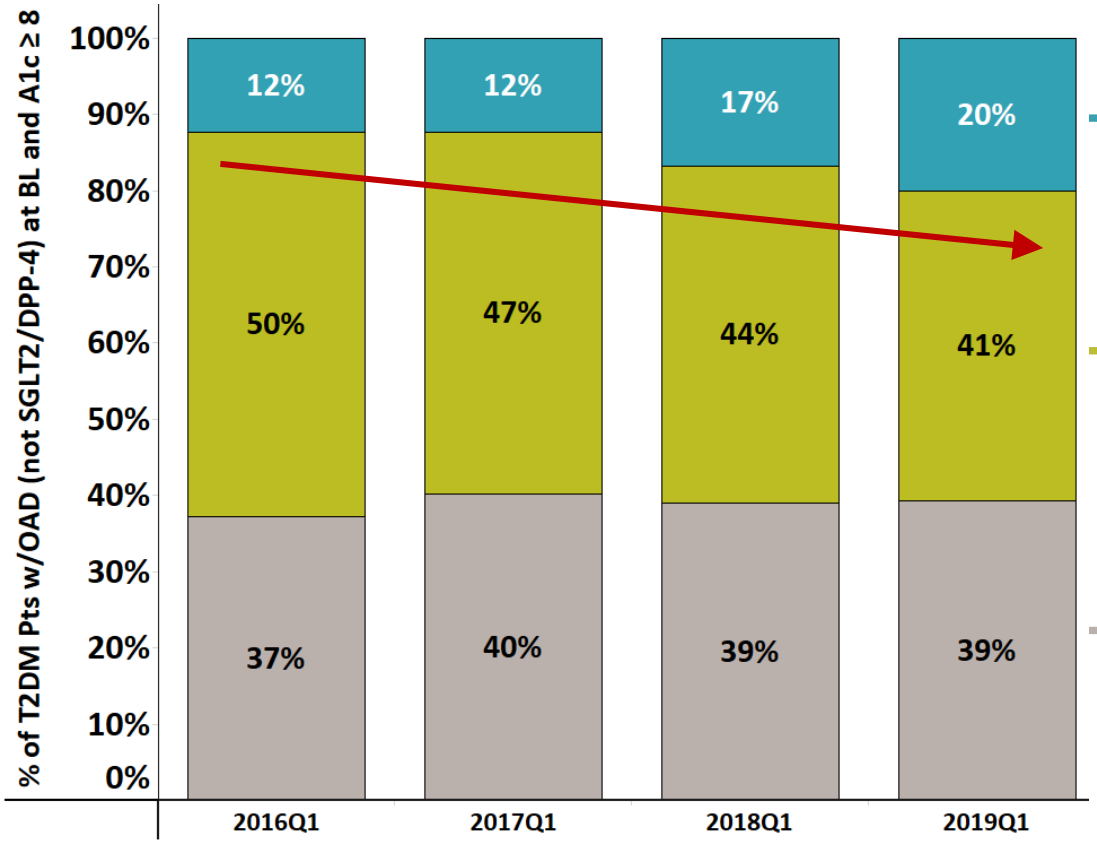


added GLP-1 and/or SGLT2

added other 2nd line anti-diabetic agent and/or insulin

no new anti-diabetic agents added

Potential clinical inertia if ASCVD dominates for these patients: Fell from 87.7% to 80.0%

Summary

- Among patients with type 2 diabetes (T2DM), Rx for GLP-1 and SGLT2 continue to increase, but still only 13% in 2019 Q1 (vs. 18% for DPP-4)
  - Up ~ 5% since 2016Q for both GLP-1 and SGLT2
  - Flattening out for DPP-4
  - Same patterns observed at individual organizations but with significant variation in Rx rates (range for 2019Q1: 7 to 28% for GLP-1 Rx and 5 to 26% for SGLT2 Rx)

- Patients with T2DM and evidence of CVD are no more likely to be prescribed GLP-1 or SGLT2 than patients without
  - That is changing for those patients who are also not at goal (A1c > 8)

- Potential clinical inertia in adopting new Rx guidelines may be as high as 80%
  - But falling nearly 8% since 2016 Q1

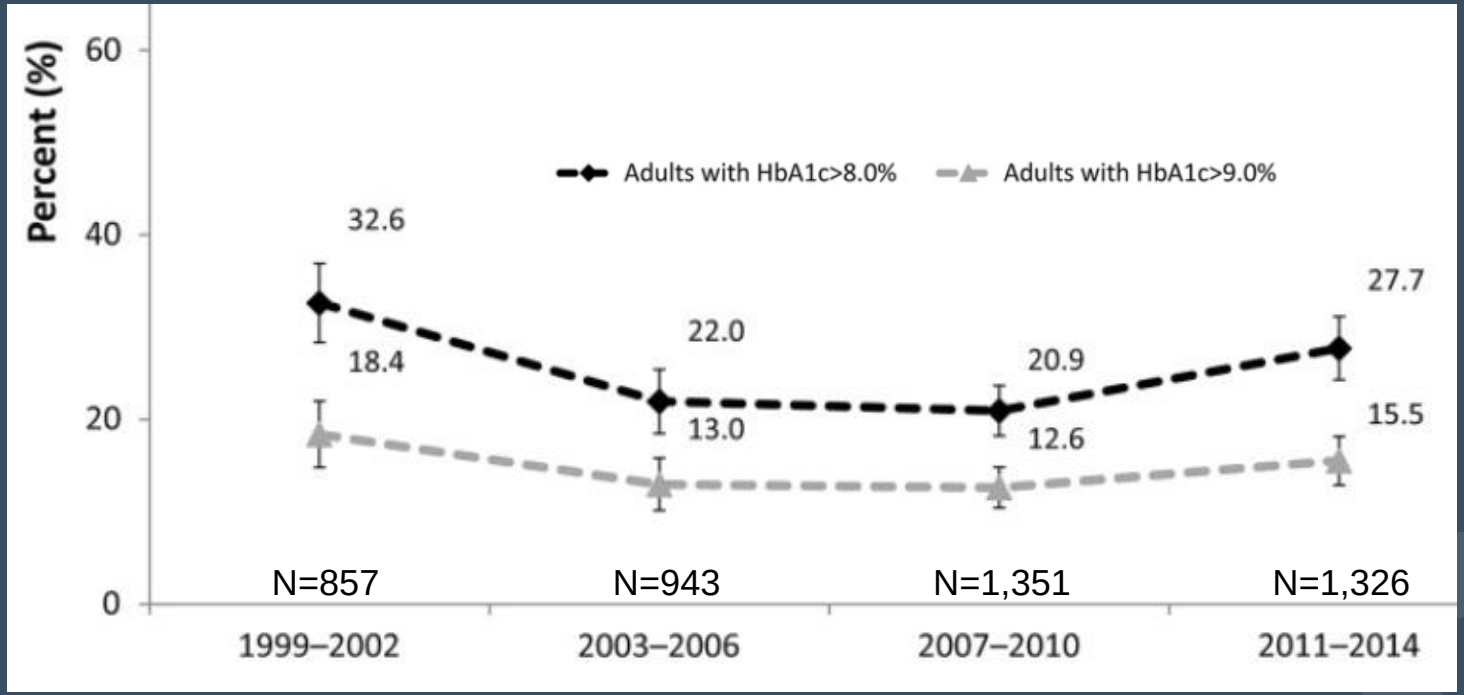
AMGA Foundation

Panel Discussion:
Implementing Medication Care Paths for Type 2 Diabetes and Cardiovascular Disease and Congestive Heart Failure

T2D Management:
Therapeutic Inertia, Newer Therapies, and Intensification Tools, Oh My!

Kevin M Pantalone, DO, ECNU, FACE
Director of Diabetes Initiatives
Department of Endocrinology
Endocrinology and Metabolism Institute
Cleveland Clinic

How Are We Doing?

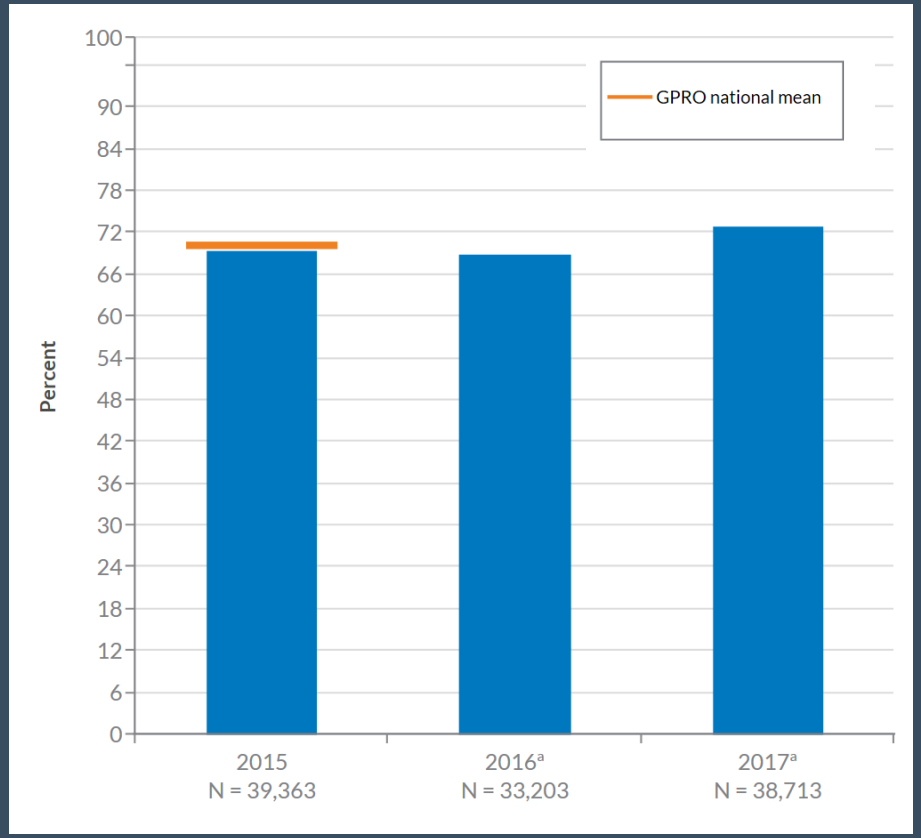


Carls G et al. Diabetes Ther. 2017; 8(4): 863–873.

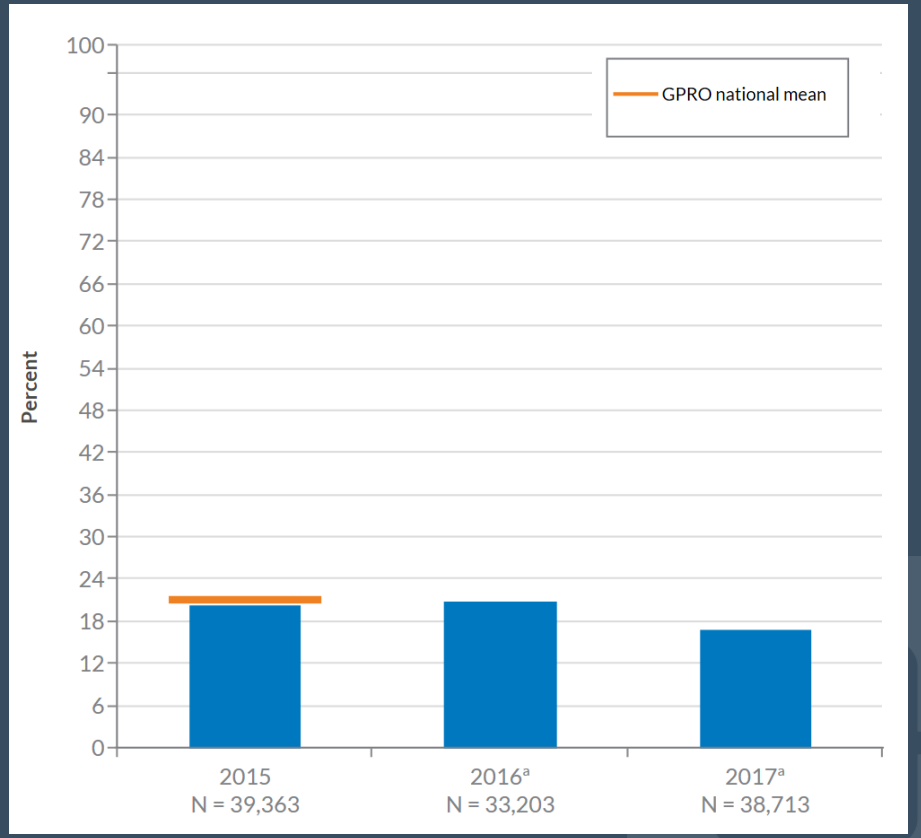
Based on NHANES respondents
Weighted to represent US adults with diabetes

Cleveland Clinic

ACO 22 DM Patients with A1C < 8%



ACO 27 DM Patients with A1C ≥ 9%



Therapeutic Inertia Summit

Overcoming Therapeutic Inertia

American Diabetes Association®

Overcoming Therapeutic Inertia

The American Diabetes Association has launched a new initiative focused on Overcoming Therapeutic Inertia. Phase 1 of this multi-year activity kicked-off on November 28th, 2018 in Arlington, Virginia with a Summit.

This important meeting brought together over 120 members of the diabetes health care eco-system, including interprofessional primary care providers, diabetes specialists, health systems, payors, industry and patient advocacy groups. The objective was to identify and assess issues related to therapeutic inertia, address barriers, and develop solutions and next steps that will have a significant impact on long-term outcomes.

Summary of Proceedings

https://professional.diabetes.org/sites/professional.diabetes.org/files/media/ada_therapeutic_inertia_interior_final.pdf

Newly-diagnosed T2D, Cleveland Clinic

- After at least 3 months of metformin monotherapy:
  - Baseline A1C >7%
    - 38% did not undergo early intensification (≤ 6 months)
  - Baseline A1C >7.5%
    - 31% did not undergo early intensification
  - Baseline A1C >8%
    - 28% did not undergo early intensification

Pantalone KM et al. Diabetes Care. 2016 Sep;39(9):1527-34.

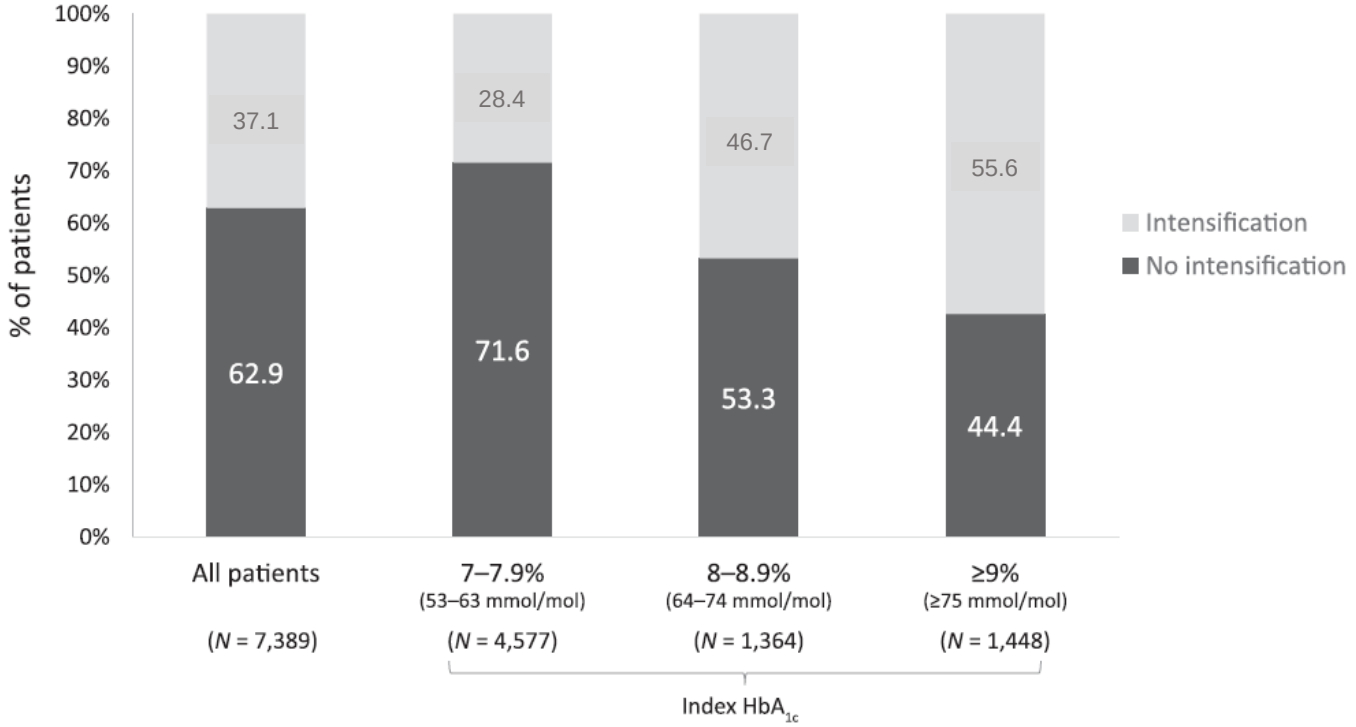
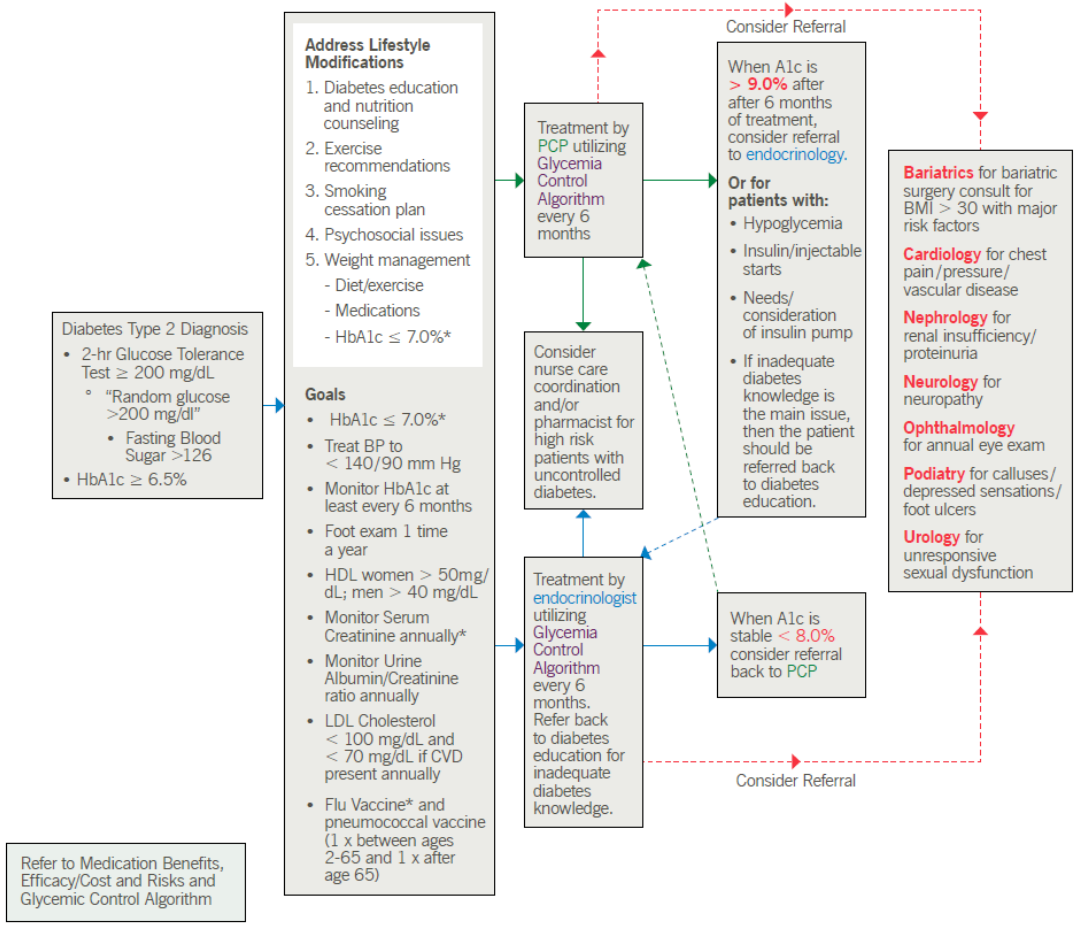


Figure 1—Rates of intensification and nonintensification of antihyperglycemic therapy observed among 7,389 patients with T2D during a 6-month period following an $HbA_{1c} \geq 7\%$ (≥ 53 mmol/mol). All patients had been using a stable regimen of two OADs for at least 6 months preceding the index HbA_{1c}.

Pantalone KM et al. Diabetes Care. 2018 Jul;41(7):e113-e114.

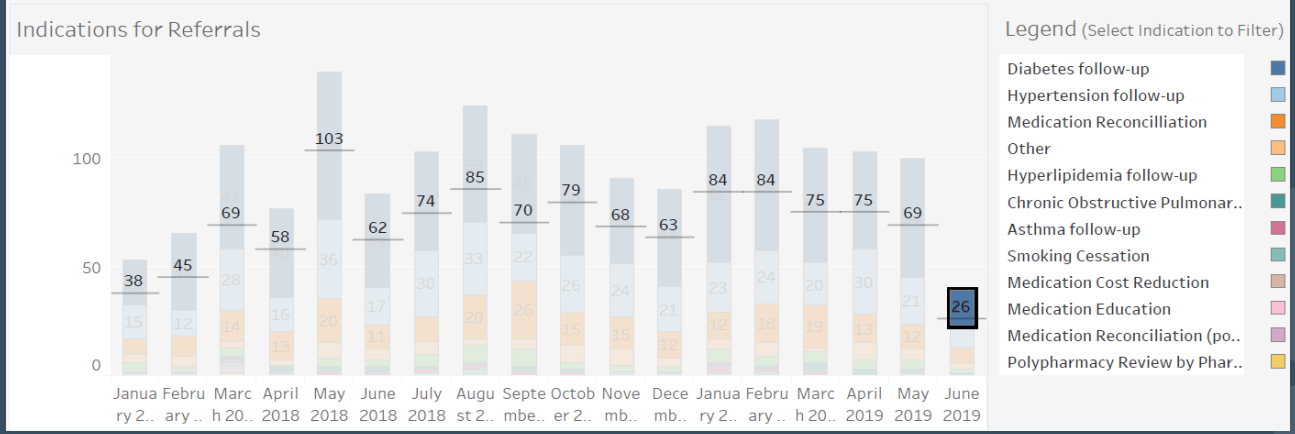
APPENDIX 1: CLEVELAND CLINIC TYPE 2 DIABETES CARE PATH OVERVIEW

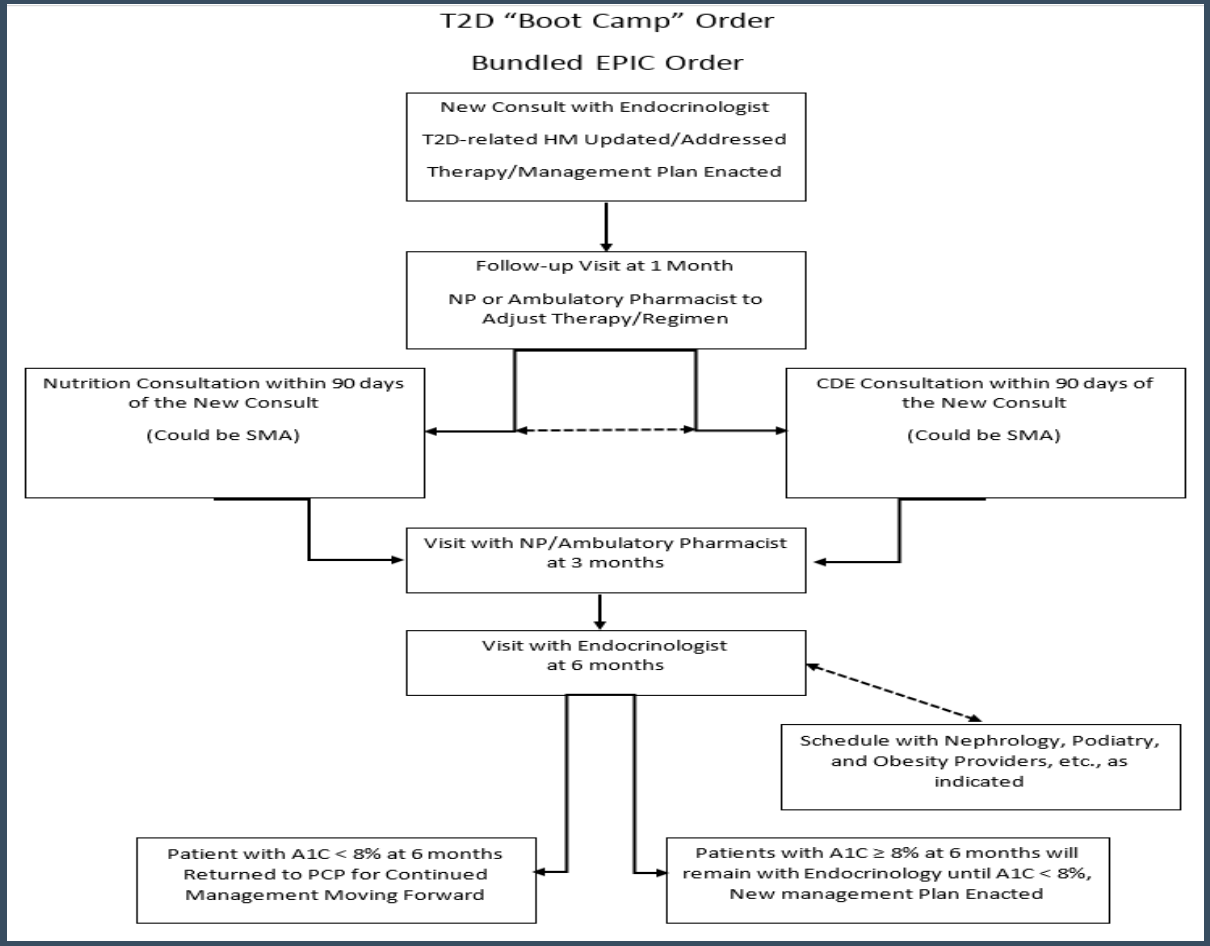


*Individualized based on age, hypoglycemic unawareness and complications (e.g., CAD, ESRD, prolific nephropathy)

Ambulatory Pharmacist Referrals

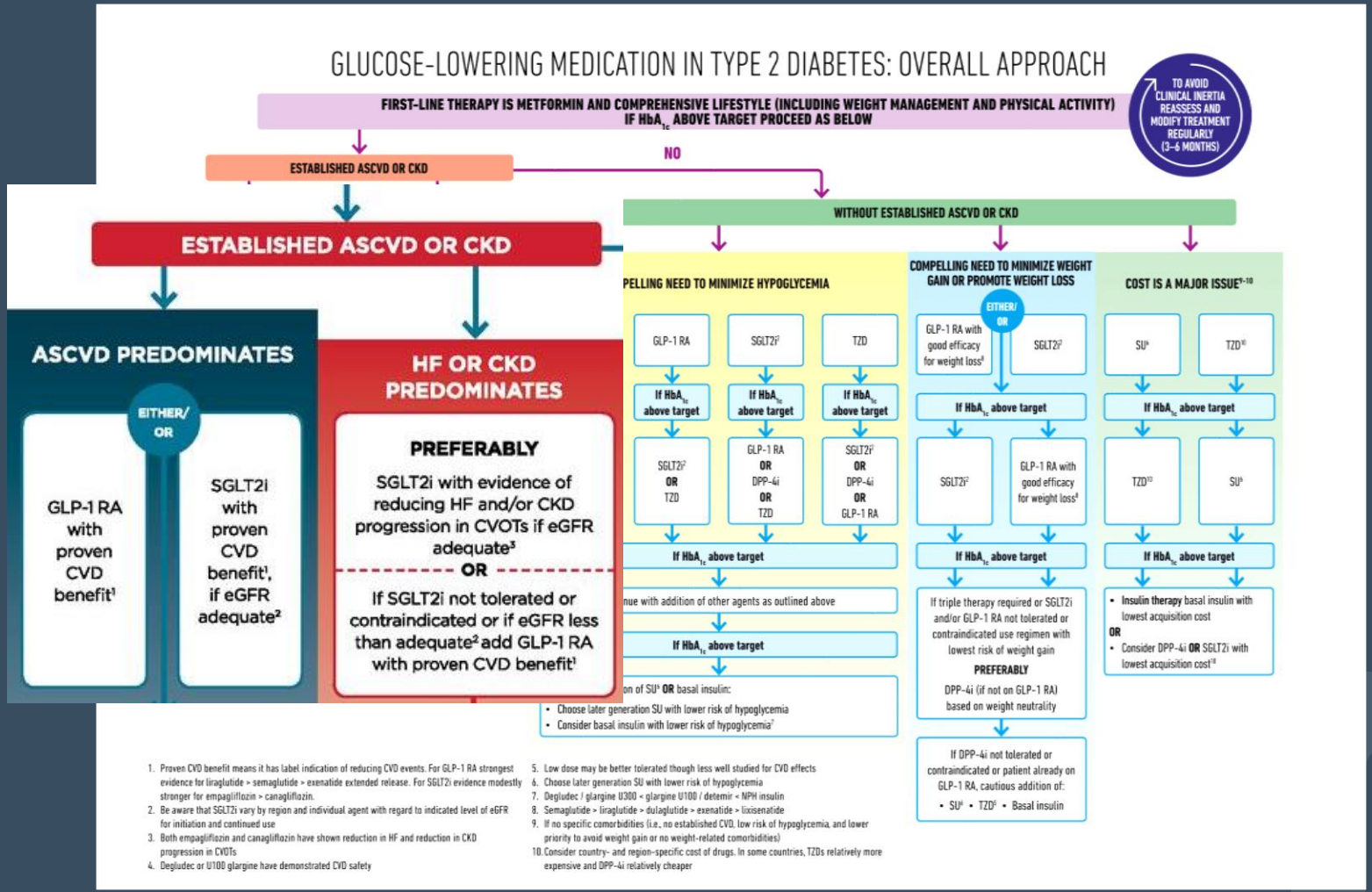
Expand/Collapse	2018												2019					
	Jan..	Febr..	Mar..	April	May	June	July	Aug..	Sept..	Oct..	Nov..	Dec..	Jan..	Febr..	Mar..	April	May	June
Main Campus Internal Medicine (G10)	38	45	69	59	103	62	74	85	70	79	68	63	84	85	75	75	70	26
Stephanie Tubbs Jones Health Center	52	50	62	47	54	42	45	58	56	76	51	56	55	67	61	49	56	15
Lorain FHC	26	35	26	40	27	46	28	45	63	55	49	56	67	32	61	41	44	16
Solon FHC	32	30	47	63	56	46	17	19	36	44	52	44	55	35	24	57	48	18
Independence FHC	11	11	14	22	28	25	49	47	29	32	29	24	36	43	38	40	32	15
Wooster FHC	9	12	26	34	38	36	42	42	27	36	34	35	42	44	43	9	7	3
Strongsville FHC	9	15	19	41	32	33	21	26	33	46	32	23	32	20	39	39	33	8
Beachwood FHC	10	14	15	31	31	32	27	35	20	23	36	29	38	41	26	34	39	3
Willoughby Hills FHC									36	71	65	47	62	27	48	43	37	16
Twinsburg FHC	2	5	2		4	2	1	15	45	48	23	42	64	53	37	46	38	9
Richard E. Jacobs FHC	2	1		2	1	2	1		39	82	33	31	33	27	39	34	27	5
Chestnut Commons (Elyria FHC)										60	39	36	43	32	37	26	56	10




T2D "Boot Camp" Order
Bundled EPIC Order
New Consult with Endocrinologist
T2D-related HM Updated/Addressed
Therapy/Management Plan Enacted
Follow-up Visit at 1 Month
NP or Ambulatory Pharmacist to Adjust Therapy/Regimen
Nutrition Consultation within 90 days of the New Consult
(Could be SMA)
CDE Consultation within 90 days of the New Consult
(Could be SMA)
Visit with NP/Ambulatory Pharmacist at 3 months
Visit with Endocrinologist at 6 months
Schedule with Nephrology, Podiatry, and Obesity Providers, etc., as indicated
Patient with A1C < 8% at 6 months Returned to PCP for Continued Management Moving Forward
Patients with A1C ≥ 8% at 6 months will remain with Endocrinology until A1C < 8%, New management Plan Enacted

Patients That Remain Poorly Controlled

- Leverage new approaches to engage
  - Virtual visits
  - SMAs (T2D)
  - E-consults
  - Remote monitoring (CDE)
  - CDE chronic care coordinators
  - Local care with access to services

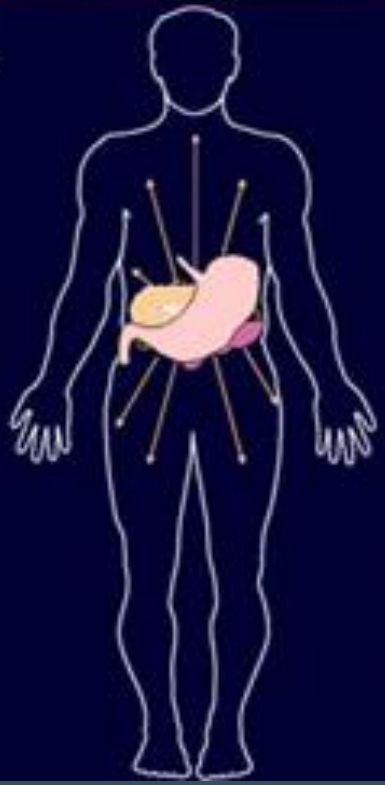


Davies MJ et al. Diabetes Care 2018 Dec; 41(12): 2669-2701.

GLP-1
Mechanisms of Action

Upon ingestion of food...

GLP-1 is secreted from the L-cells in the jejunum and ileum



This in turn...

- Stimulates glucose-dependent insulin secretion
- Suppresses glucagon secretion
- Slows gastric emptying
- Improves insulin sensitivity
- Reduces food intake

Long-term effects demonstrated in animals

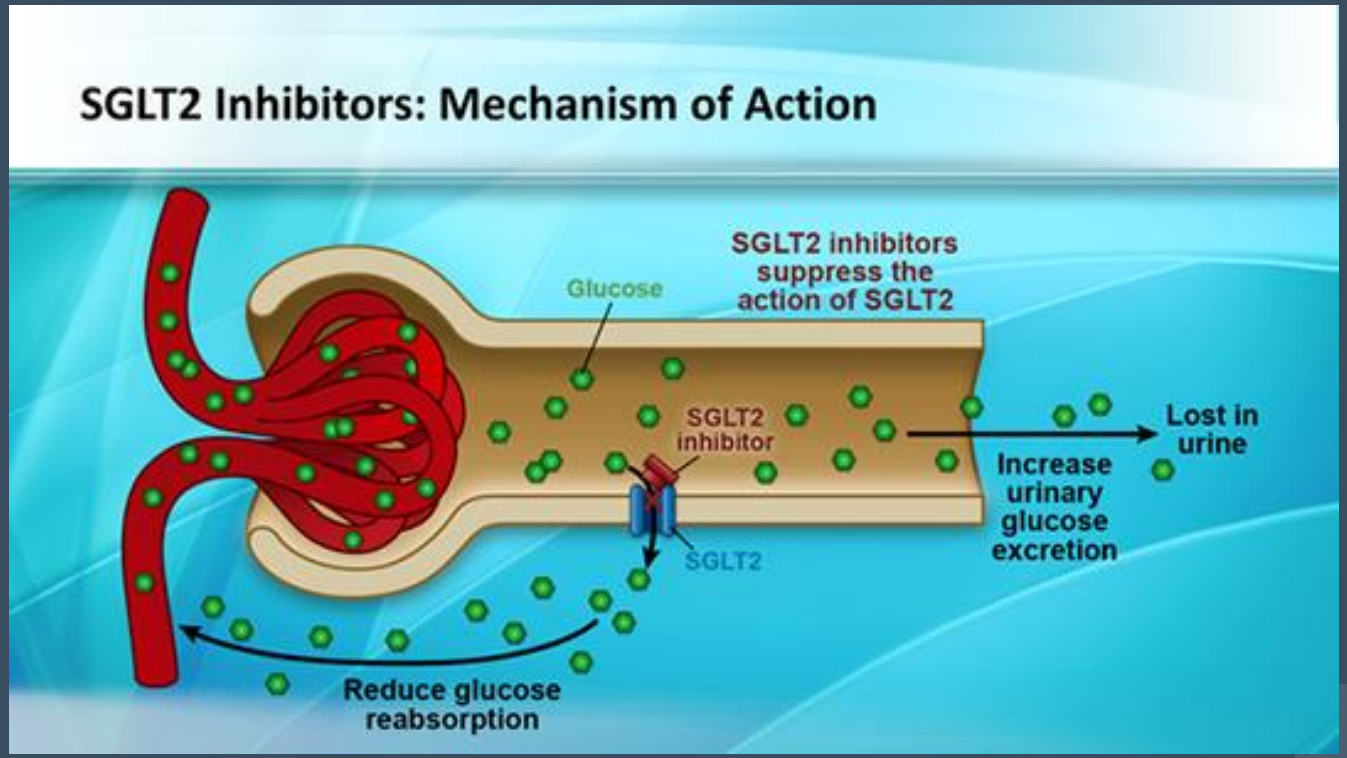
- Increases β-cell mass and maintains β-cell function

Drucker DJ. Diabetes Care. 2003;26:2929-2940.

GLP-1RAs

- Benefits
  - Weight loss
  - Low (no) risk of hypoglycemia
  - Improved glycemic control
  - Reduction in systolic BP
  - CV risk reduction
  - ? In-vivo increase B-cell growth/replication
    - Durability
  - ? Kidney protection

- Side Effects/Adverse Reactions/Warnings
  - Nausea, vomiting, diarrhea, injection site reactions
  - Acute pancreatitis
  - Thyroid C-cell tumors, including medullary thyroid carcinoma (MTC)



Combo SGLT2 and DPP-4 Inhibitors: Complementary Mechanisms of Action
Authors: John Anderson, MD; Vivian Fonseca, MD, FRCP
https://www.medscape.org/viewarticle/837818_transcript

SGLT-2 Inhibitors

- Benefits
  - Weight loss
  - Low (no) risk of hypoglycemia
  - Improved glycemic control
  - Reduction in systolic BP (~ 5 mmHg)
  - CV risk reduction
  - Reduction in risk of hospitalization for heart failure
  - Renal risk reduction/kidney protection (Canagliflozin, CREDENCE)
    - Also observed to varying degrees in studies with other SGLT-2i (CVOTs)

- Risks/Negatives
  - Slight increase in LDL cholesterol
  - Hypotension
    - Intravascular volume contraction
  - UTIs, genital mycotic infections
  - Fournier's gangrene (???)
  - Bladder cancer (???), Breast cancer (???)
  - Increase risk of DKA (largely in DM-1/insulin dependent DM-2)
  - Bone loss and increase in fracture risk (Canagliflozin)
  - Amputations (Canagliflozin, ? Ertugliflozin)

Cleveland Clinic EMR

Table 2 Antidiabetic medication treatment patterns stratified by cardiovascular disease (CVD) status

Medication[a]	No established CVD N = 54,659	Established CVD N = 40,910	P value[†]
No OAD	17,984 (32.9%)	17,137 (41.9%)	< 0.001
OAD	36,675 (67.1%)	23,773 (58.1%)	
1 OAD	23,166 (63.2%)	14,889 (62.6%)	< 0.001
2 OAD	9540 (26.0%)	6574 (27.7%)	< 0.001
≥ 3 OAD	3969 (10.8%)	2310 (9.7%)	< 0.001
Insulin	6211 (11.4%)	7472 (18.3%)	< 0.001
GLP-1RA	2978 (5.4%)	1685 (4.1%)	< 0.001
Liraglutide	1683 (3.1%)	916 (2.2%)	< 0.001
SGLT-2i	2265 (4.1%)	1042 (2.5%)	< 0.001
Empagliflozin	462 (0.8%)	209 (0.5%)	< 0.001
Canagliflozin	1348 (2.5%)	691 (1.7%)	< 0.001
Other ADD	1101 (2%)	853 (2.1%)	0.444

OADs: biguanide (metformin), sulfonylurea, thiazolidinedione, dipeptidyl-peptidase-4 inhibitor, alpha-glucosidase inhibitor, sodium–glucose co-transporter-2 inhibitor

Other ADD-other antidiabetic drug: pramlintide, name brand bromocriptine (Cycloset®), colesevelam, nateglinide or repaglinide

ADD antidiabetic drug, *CVD* cardiovascular disease, *GLP-1RA* glucagon-like peptide-1 receptor agonist, *OAD* oral antidiabetic drug

Large US Administrative Claims Database

TABLE 2 Antidiabetes medication treatment patterns stratified by atherosclerotic cardiovascular disease (ASCVD) status

Medication	Non-ASCVD N = 659 498	ASCVD N = 543 938
OAD only, n (%)	340 485 (77.0)	243 967 (73.6)
1 OAD	189 412 (55.6)	138 907 (56.9)
2 OAD	103 133 (30.3)	73 194 (30.0)
≥3 OAD	47 940 (14.1)	31 866 (13.1)
Insulin ± OAD, n (%)	61 278 (13.9)	61 452 (18.5)
GLP-1RA ± OAD, n (%)	27 481 (6.2)	16 430 (5.0)
Insulin + GLP-1RA ± OAD, n (%)	13 095 (3.0)	9805 (3.0)
Any GLP-1RA use, n (%)	40 576 (9.2)	26 235 (7.9)
Exenatide	3202 (7.9)	2260 (8.6)
Exenatide ER	10 291 (25.4)	6358 (24.2)
Albiglutide	2086 (5.1)	1240 (4.7)
Dulaglutide	5174 (12.8)	3169 (12.1)
Liraglutide	23 006 (56.7)	15 009 (57.2)
Any SGLT2i use, n (%)	51 997 (11.8)	29 103 (8.8)
Canagliflozin	35 891 (69.0)	20 350 (69.9)
Dapagliflozin	11 170 (21.5)	5836 (20.1)
Empagliflozin	6530 (12.6)	3791 (13.0)

Pantalone KM et al. Cardiovasc Diabetol. 2018 Apr 10;17(1):54.
Weng W et al. Endocrinol Diabetes Metab. 2019 May 22;2(3):e00076.

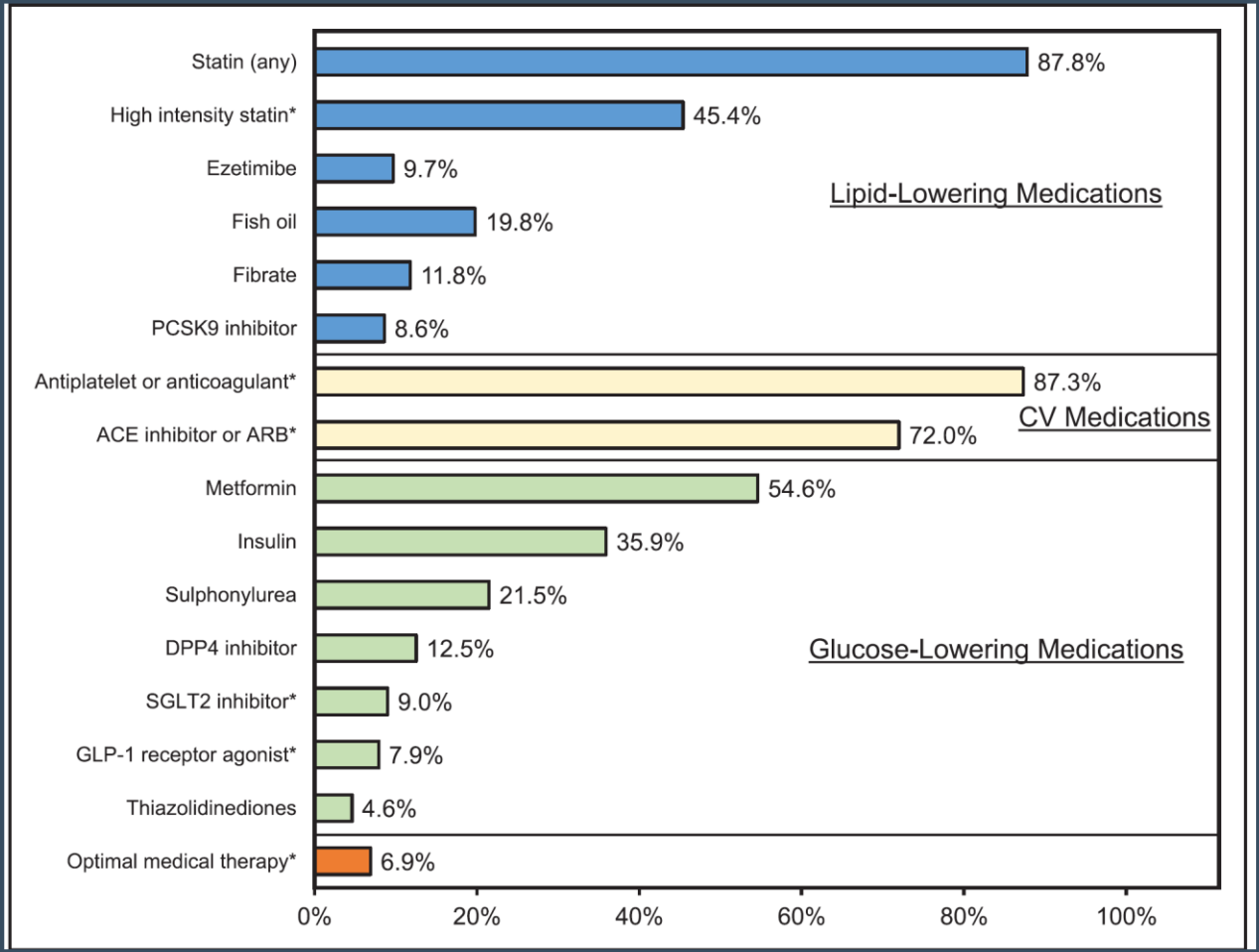


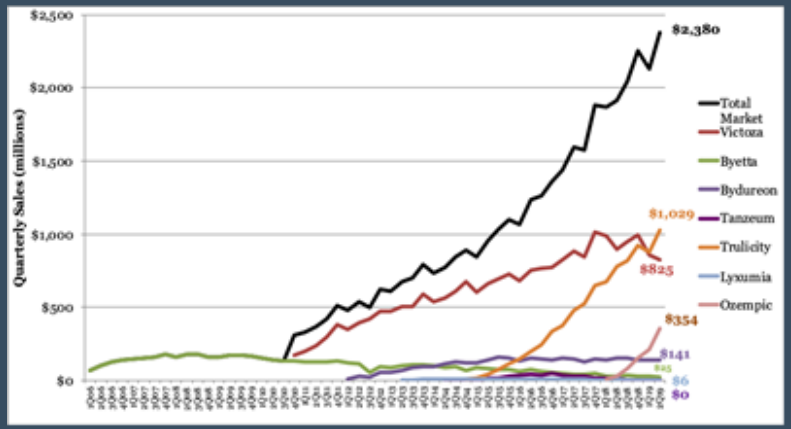
Figure. Use of cardiovascular and glucose-lowering medications among patients with diabetes mellitus and atherosclerotic cardiovascular disease.

*Components of optimal medical therapy: high-intensity statin, antiplatelet agent or anticoagulant (excluding triple therapy), ACE inhibitor or ARB (excluding glomerular filtration rate <30 mL/[min·1.73 m^2]), and SGLT2 inhibitor or GLP1 receptor agonist (for type 2 diabetes mellitus; excluding glomerular filtration rate <30 mL/[min·1.73 m^2]). ACE indicates angiotensin converting enzyme; ARB, angiotensin II receptor blocker; CV, cardiovascular; DPP4, dipeptidyl peptidase-4; GLP1, glucagon-like peptide 1; PCSK9, proprotein convertase subtilisin/kexin type 9; and SGLT2, sodium-glucose cotransporter-2.

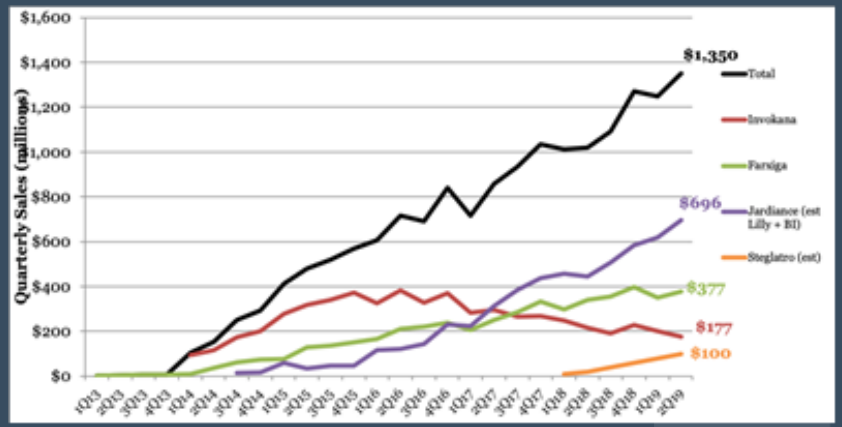
Arnold SV et al. Circulation. 2019 Aug 13;140(7):618-620.

Growth

GLP-1RA
24% YOY and 12% sequentially to $2.4 billion



SGLT-2i
25% YOY and 7% sequentially to $1.3 billion



Kelly L. Close <kelly_close@closeconcerns.com>

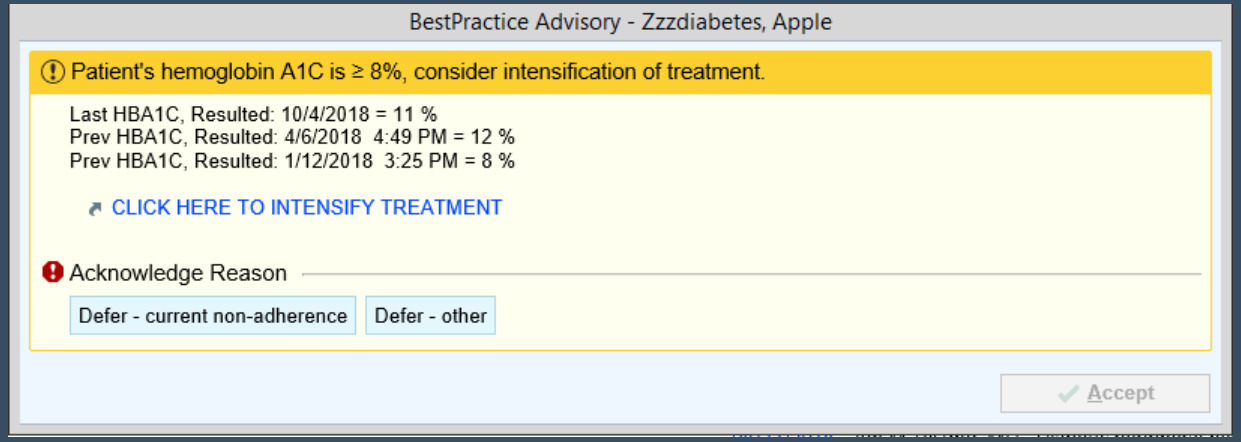
Current Initiatives

- EHR-based T2D Intensification Tool
  - Leverage EHR in real-time
  - Facilitate care and improve outcomes

- Attempt to make T2D Care Path “Functional”
  - Follow progress with Care Path Dashboard

- Engage and collaborate with PCPs

BPA



1) Age ≥ 18 years
AND
2) A1C Greater than or Equal to 8 in the last 6 months
AND
3) No current T1D problem on the Problem List
AND
4) Patient is not currently Pregnant

Diabetes Mellitus Type 2 Smartform

Pertinent Patient Data

Weight (today)	292.1 lbs, 132.5 kg	Weight (last)	286.6 lbs, 130.0 kg (1/2/2019)	HbA1C	9.9 (1/2/19)	eGFR - Other	
Height (today)	5' 0"	Height (last)	5' 0" (1/2/2019)	Blood Creatinine	1.1 (12/31/18)	eGFR - AA	
BMI (today)	57.1 kg/m²	BMI (last)	56.0 kg/m² (1/2/2019)				

Medication Categories

Select Patient Goals: Cardiovascular Risk Reduction | Low Hypoglycemia Risk | Weight Loss | Cost | A1C Lowering

Applicable Medications

Metformin	Patient has Metformin Allergy
GLP-1 Receptor Agonists	
SGLT-2 Transport Inhibitors	Patient currently on a SGLT-2 Transport Inhibitor
DPP-4i	
Alpha-glucosidase inhibitor	

Health Maintenance Checks

HM

TOPIC	STATUS	LAST COMPLETION DATE	DUE DATE
DILATED RETINAL EXAM	Overdue		5/6/1994
DIABETIC FOOT EXAM	Overdue		5/6/1994
ONE PNEUMOVAX PRIOR TO AGE 65	Overdue		5/6/2000
LDL CHOLESTEROL	Overdue		5/6/2002
INFLUENZA	Overdue		9/1/2018
HBA1C	Not Due	1/2/2019	4/2/2019
URINE ALBUMIN:CREATININE RATIO	Information not on file		

Upon diagnosis of diabetes before age 65, Pneumovax 23 should be administered. At age 65, Prevnar 13 pneumoccocal vaccine should be administered and one year later, Pneumovax 23 should be administered only if the initial Pneumovax 23 shot was > 5 years ago. The second Pneumovax 23 Injection should be administered at least 5 years after the first dose.

Health Maintenance Orders

Use speed buttons to pre-populate SmartSet

Health Maintenance Consults	Ophthalmology	Podiatry	
Health Maintenance Labs	HbA1C	HbA1C (POC)	Lipid Panel
	Urine Albumin Creatinine Ratio		
Health Maintenance Immunizations	Influenza Vaccine	Pneumococcal 23 (Pneumovax)	

Other Orders

Use speed buttons to pre-populate SmartSet

Diabetes Care Path Consults	Primary Care (HbA1C < 8 last 6 months)	Weight Management (BMI > 30)
	eConsult Endocrinology (provider-to-provider)	Diabetes Ambulatory Clinic Pharmacy
Diabetes Annual Education	Nutrition Therapy	Diabetic Education

TO PROCEED WITH ORDERS, CLICK HERE

Diabetes Care Path Links

Insulin Intensification Algorithm

Care Path Guide
- Medication Table (p. 12)
- Type 2 Diabetes Goal Based Algorithm (p. 14)

Restore | Close | Previous | Next

Insulin Initiation and Titration

Determine A1c goal

Candidate for starting insulin therapy?

See How

Start with **basal** insulin if:

- Inadequate control on 2 or 3 oral hypoglycemic agents.
  - or 2 oral agents + GLP1 analog.
- Inadequate control with 1-2 oral agents (w/wo GLP1 analog therapy) and contraindications to other therapies.
- Inadequate control with 2 oral agents & inability to afford brand name medications.

Start **basal-bolus** insulin regimen if:

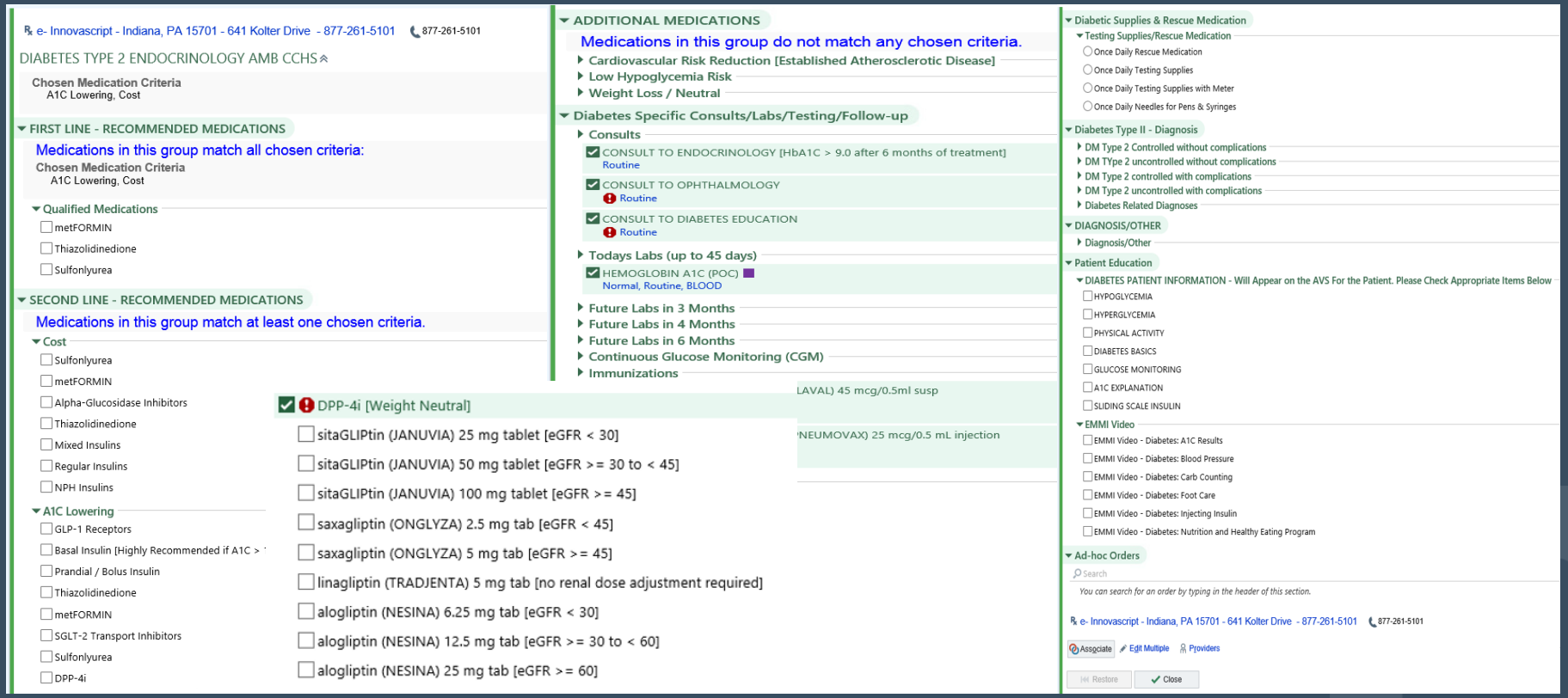
See How

Severe symptomatic hyperglycemia:

- Polyuria, polydipsia and polyphagia.
- Blood glucose ≥ 300 mg/dl.
- HgA1c ≥ 10%.

- Insulin analogs are available to qualified patients per patient's assistance programs.
- NPH and pre-mixed human insulin types are the cheapest, followed by pre-mixed insulin analogs (See candidates):
  - Greater weight gain.
  - Higher frequency of hypoglycemia.
  - Re-assess/relax A1c goal if those types of insulin were to be used.
  - See how and see pre-mixed insulin and human insulin types

Smartset

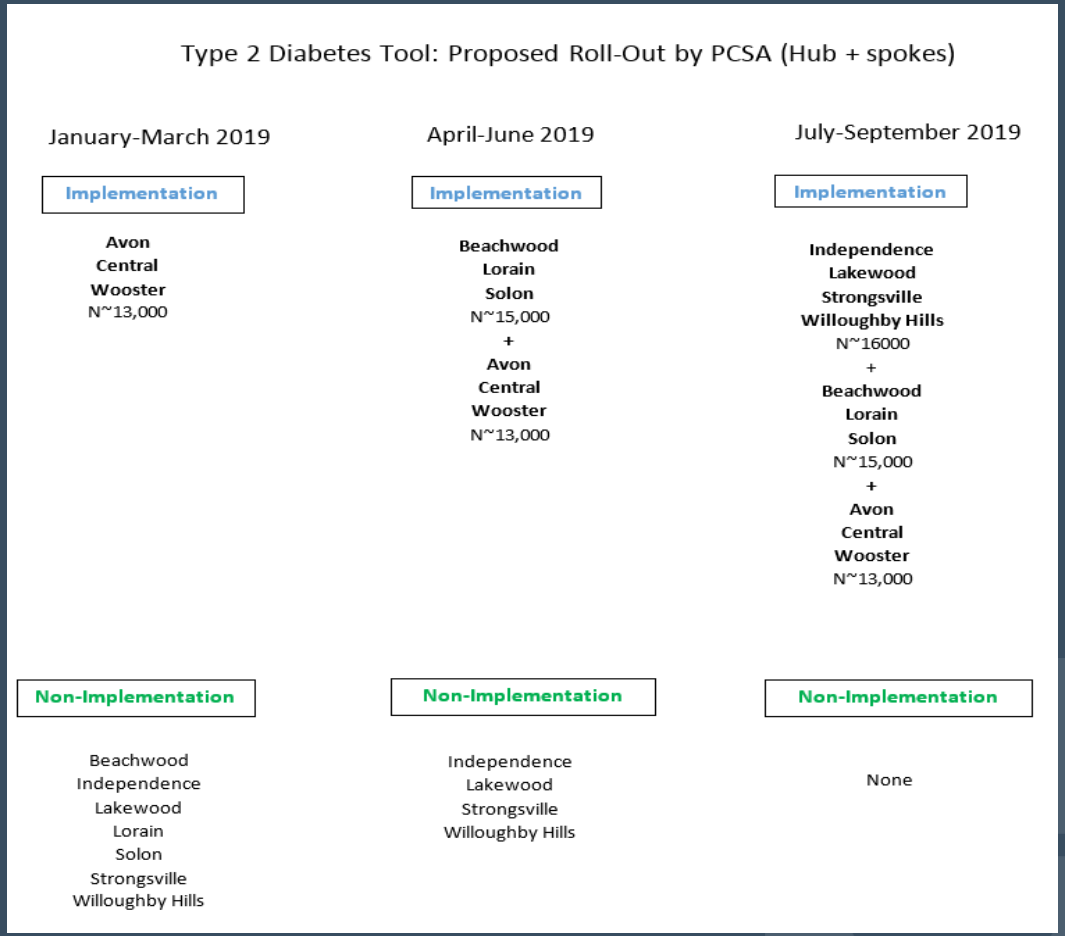

e- Innovascript - Indiana, PA 15701 - 641 Kolter Drive - 877-261-5101
877-261-5101
DIABETES TYPE 2 ENDOCRINOLOGY AMB CCHS
Chosen Medication Criteria
A1C Lowering, Cost
FIRST LINE - RECOMMENDED MEDICATIONS
Medications in this group match all chosen criteria:
Chosen Medication Criteria
A1C Lowering, Cost
Qualified Medications
metFORMIN
Thiazolidinedione
Sulfonlyurea
SECOND LINE - RECOMMENDED MEDICATIONS
Medications in this group match at least one chosen criteria.
Cost
Sulfonlyurea
metFORMIN
Alpha-Glucosidase Inhibitors
Thiazolidinedione
Mixed Insulins
Regular Insulins
NPH Insulins
A1C Lowering
GLP-1 Receptors
Basal Insulin [Highly Recommended if A1C >
Prandial / Bolus Insulin
Thiazolidinedione
metFORMIN
SGLT-2 Transport Inhibitors
Sulfonlyurea
DPP-4i
ADDITIONAL MEDICATIONS
Medications in this group do not match any chosen criteria.
Cardiovascular Risk Reduction [Established Atherosclerotic Disease]
Low Hypoglycemia Risk
Weight Loss / Neutral
Diabetes Specific Consults/Labs/Testing/Follow-up
Consults
CONSULT TO ENDOCRINOLOGY [HbA1C > 9.0 after 6 months of treatment]
Routine
CONSULT TO OPHTHALMOLOGY
Routine
CONSULT TO DIABETES EDUCATION
Routine
Todays Labs (up to 45 days)
HEMOGLOBIN A1C (POC)
Normal, Routine, BLOOD
Future Labs in 3 Months
Future Labs in 4 Months
Future Labs in 6 Months
Continuous Glucose Monitoring (CGM)
Immunizations
LAVAL) 45 mcg/0.5ml susp
NEUMOVAX) 25 mcg/0.5 mL injection
DPP-4i [Weight Neutral]
sitaGLIPtin (JANUVIA) 25 mg tablet [eGFR < 30]
sitaGLIPtin (JANUVIA) 50 mg tablet [eGFR >= 30 to < 45]
sitaGLIPtin (JANUVIA) 100 mg tablet [eGFR >= 45]
saxagliptin (ONGLYZA) 2.5 mg tab [eGFR < 45]
saxagliptin (ONGLYZA) 5 mg tab [eGFR >= 45]
linagliptin (TRADJENTA) 5 mg tab [no renal dose adjustment required]
alogliptin (NESINA) 6.25 mg tab [eGFR < 30]
alogliptin (NESINA) 12.5 mg tab [eGFR >= 30 to < 60]
alogliptin (NESINA) 25 mg tab [eGFR >= 60]
Diabetic Supplies & Rescue Medication
Testing Supplies/Rescue Medication
Once Daily Rescue Medication
Once Daily Testing Supplies
Once Daily Testing Supplies with Meter
Once Daily Needles for Pens & Syringes
Diabetes Type II - Diagnosis
DM Type 2 Controlled without complications
DM TYpe 2 uncontrolled without complications
DM Type 2 controlled with complications
DM Type 2 uncontrolled with complications
Diabetes Related Diagnoses
DIAGNOSIS/OTHER
Diagnosis/Other
Patient Education
DIABETES PATIENT INFORMATION - Will Appear on the AVS For the Patient. Please Check Appropriate Items Below
HYPOGLYCEMIA
HYPERGLYCEMIA
PHYSICAL ACTIVITY
DIABETES BASICS
GLUCOSE MONITORING
A1C EXPLANATION
SLIDING SCALE INSULIN
EMMI Video
EMMI Video - Diabetes: A1C Results
EMMI Video - Diabetes: Blood Pressure
EMMI Video - Diabetes: Carb Counting
EMMI Video - Diabetes: Foot Care
EMMI Video - Diabetes: Injecting Insulin
EMMI Video - Diabetes: Nutrition and Healthy Eating Program
Ad-hoc Orders
Search
You can search for an order by typing in the header of this section.
e- Innovascript - Indiana, PA 15701 - 641 Kolter Drive - 877-261-5101
877-261-5101
Associate
Edit Multiple
Providers
Restore
Close

Roll-out Plan

- E-Learning Module
- Walk-through Video
- Clinical Systems Support
- Physician Specialist Support

Retrospective Study

- Outcomes



T2D Carepath Dashboard

Care Path | Care Path Details | Provider Summary Report | Patient Summary Report | Definitions

Type 2 Diabetes Care

Month: June 2019 - Institute: All - Location: All - Provider: All

Goal Category Name	Metric Name	Actual	N	Last Update
Process of Care	% Intensified – Primary Care	8.8%	1,484	07/18/19
	% Intensified – Endocrinology	38%	457	07/18/19
Cost and Utilization	HbA1c < 8%	72.80%	50,846	07/12/19
	HbA1c > 9%	16.82%	50,846	07/12/19
	Count of Diabetes Cases	50846	50,846	07/12/19
	Referral to Primary Care	36.44%	5,743	07/12/19

- Count of Diabetes Cases


Cleveland Clinic
Every life deserves world class care.

SGLT2 Inhibitors

A Change In Paradigm And Call To Arms

Paula Pinell-Salles MD FACC

November 14, 2019

Outline

- Burden of disease
- ADA/AHA/ACC guideline updates
- SGLT2i pharmacology
- SGLT2i and cardiovascular protection
- SGLT2i and renal protection
- Barriers to wide-spread implementation
- Expanding indications and ongoing Research
- SGLT2i in HF reduced EF

Burden of disease

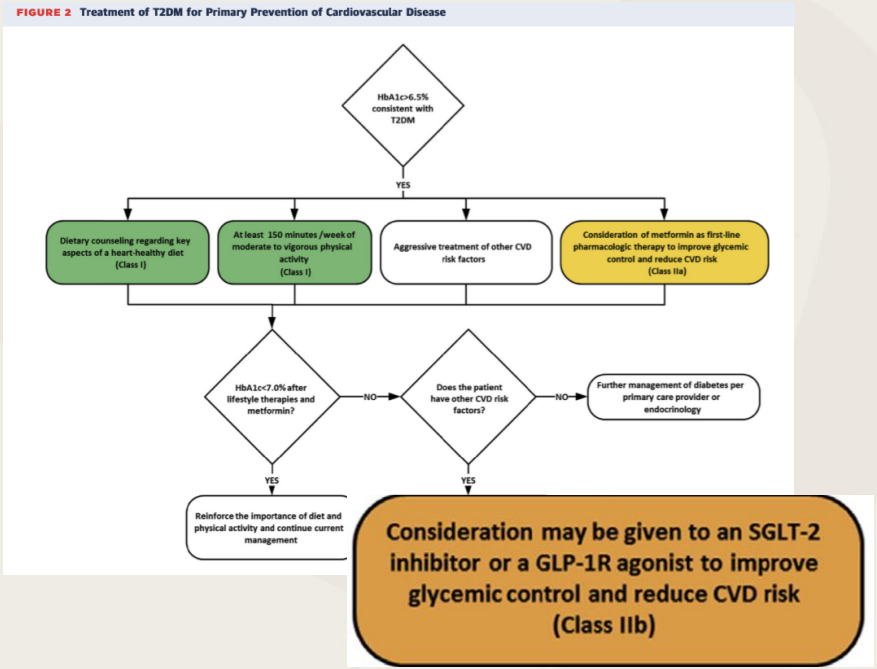
- Prevalence 30.3 million
- Incidence 1.4 million

- **ASCVD** leading cause of morbidity and mortality
- Cost $37.3 billion in cardiovascular-related spending per year

- Leading cause of **ESRD** (44%)
- Hemodialysis costs average $90,000 annually per patient, $28 billion overall and 69% higher among diabetics

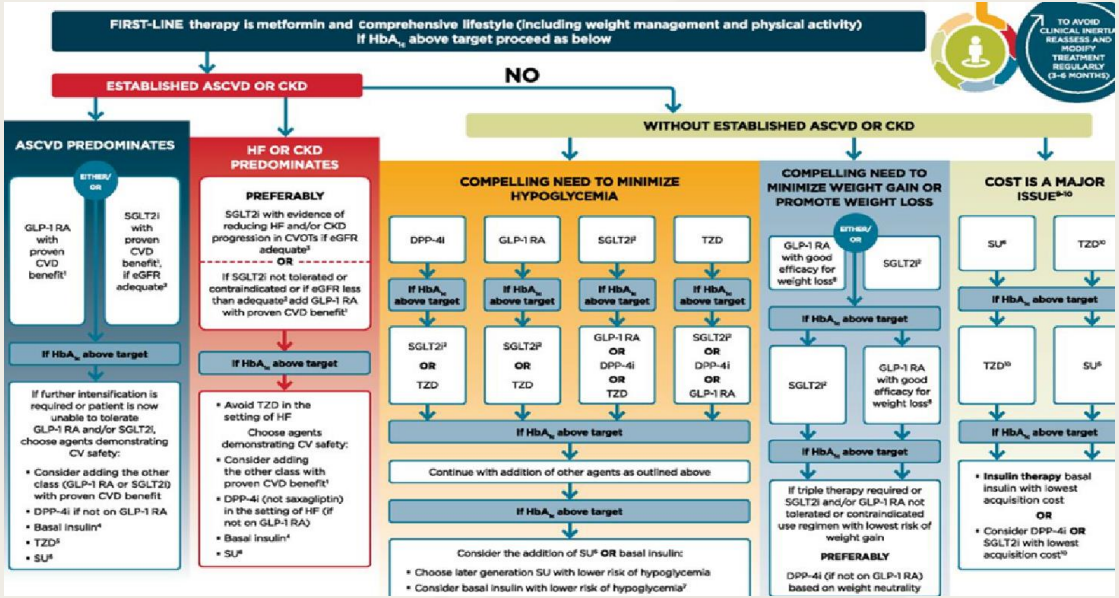
- Overall **heart failure hospitalization** > 900,000 annually with 25% readmission within first month, cost $30 billion annually
- Incident heart failure hospitalization twofold higher in diabetic patients

2019 ACC/AHA
Guideline on the Primary Prevention of Cardiovascular disease



2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary Sept, 2019

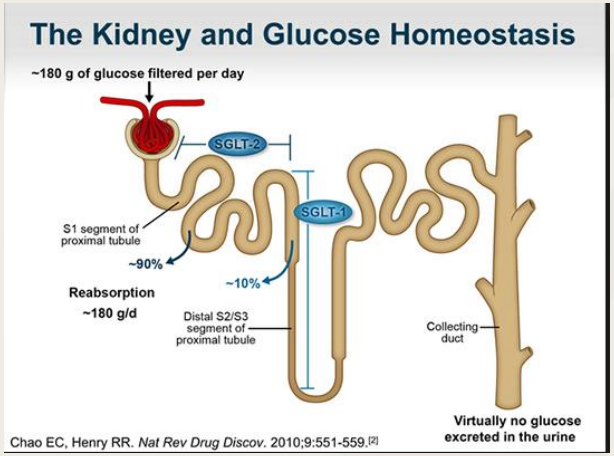
ADA Guidelines for Diabetic Management 2018



SGLT2 Inhibitors

Pharmacology

SGLT2 Inhibitor Mechanism of Action



- **Hypoglycemia rare**
- **Osmotic diuresis**

- **Euglycemic DKA (delayed diagnosis)**
- **Hypovolemia and hypotension**
- **Yeast and genitourinary infections**

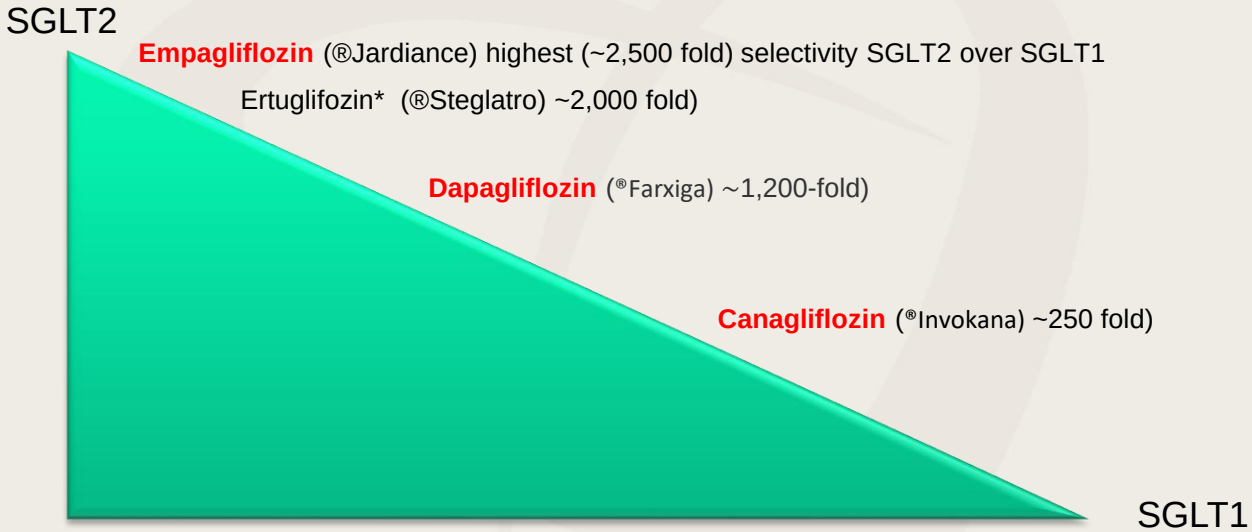
- **Drops Hba1c 0.8**

- ✓ **Decrease SBP 4mm**
- ✓ **Decrease DBP 2mm**
- ✓ **Weight loss 2-4 kg**

CONTRAINDICATED :
Type I DM
Type II DM prone to DKA

CAUTION :
Diuretic use
RAAS Inhibitor use
eGFR< 60mL/min

Medscape: SGLT2 Inhibitors in the Modern Era: Why and Where?

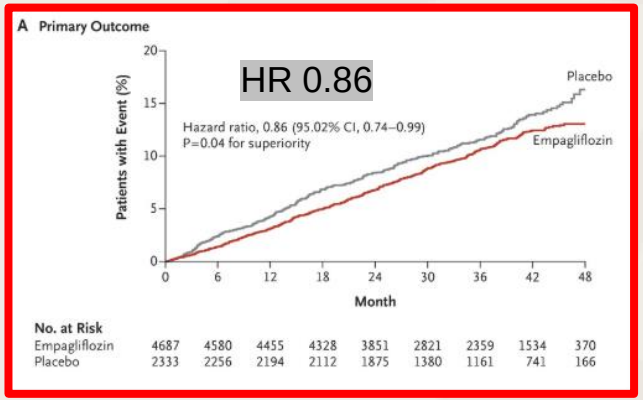


*neutral in cardiovascular outcomes studies

SGLT2 Inhibitors

Cardiovascular outcomes

Empagliflozin reduced primary composite of CV death, nonfatal MI and CVA



7,020 patients
Median follow up 3.1 years
Mean age 63

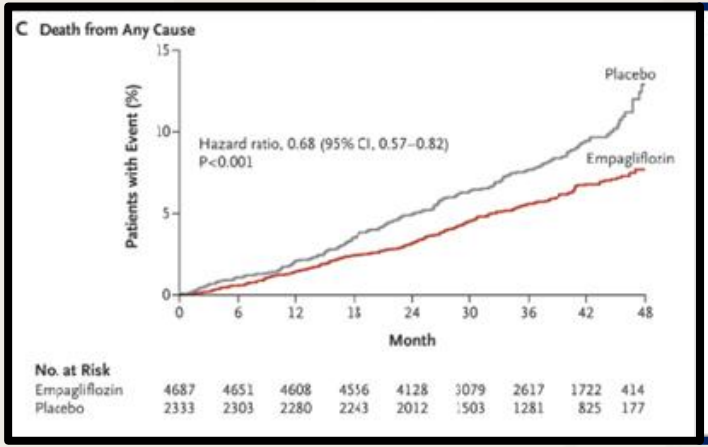
Type 2 DM with A1C 7-10
Avg A1C 8.1
48% insulin
57% 10+ year diagnosis

Established CVD with high risk of CV events
ACS> 2mo prior
LM or 2vCAD
1vCAD w abnormal MPI or unstable angina w/in 12 mo
CVA (ischemic or hemorrhagic) > 2 mo prior
Occlusive PAD with ABI< 0.9, prior intervention or > 50%

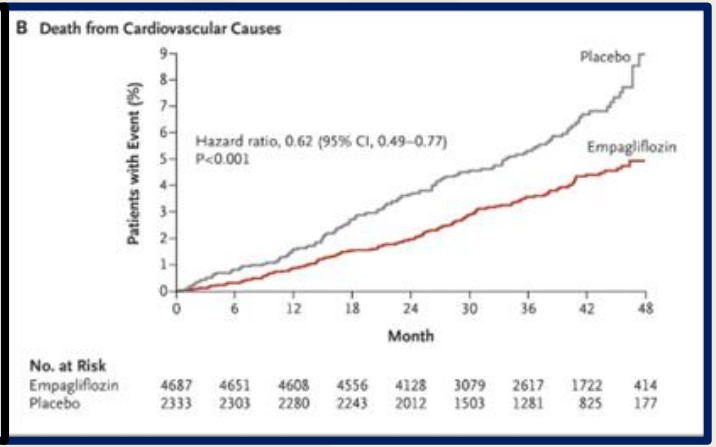
EMPA-REG OUTCOMES TRIAL. NEJM 2015; 373:2117-2128

Empagliflozin reduced all-cause and CV death

All Cause Mortality HR 0.68



CV Death HR 0.62



NNT 39 for 3 years to prevent 1 death

NNT 46

EMPA-REG OUTCOMES TRIAL. NEJM 2015; 373:2117-2128

FDA NEWS RELEASE

FDA approves Jardiance to reduce cardiovascular death in adults with type 2 diabetes

For Immediate Release: December 02, 2016

Canagliflozin reduced primary composite of CV death, nonfatal MI and CVA

2 combined trials CANVAS and CANVAS-R
10,142 patients
Median follow up 2.4 years
Mean age 63

Type 2 DM with Hba1c 7.0-10.5

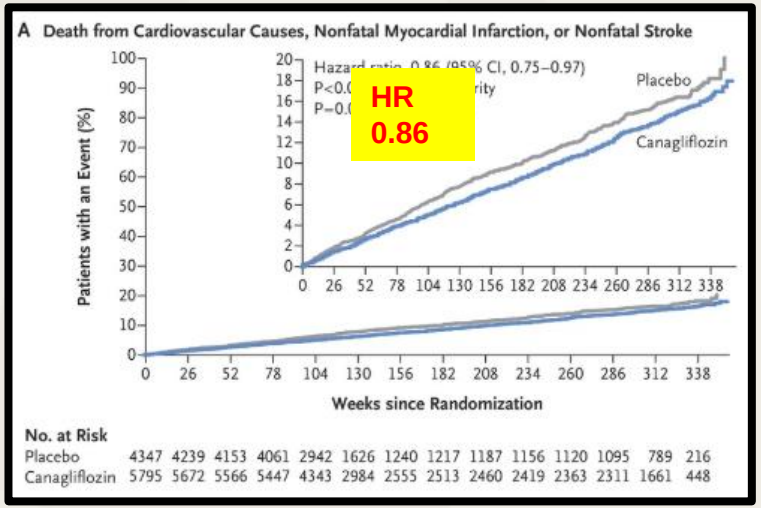
- 57% 10+ yr diagnosis
- Average A1C 8.2
- 50% on insulin

symptomatic ASCVD and >30 yo ***(66%)***

OR

> 50 yo AND ≥ 2 risk factors

DM ≥ 10 years duration
SBP≥ 140mm Hg despite BP Rx
Active smoking
Micro- or macro- albuminuria
HDL< 38.7 mg/dL

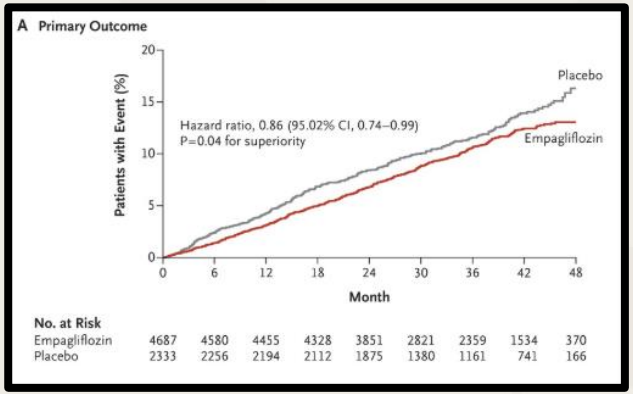


CANVAS trial. NEJM 2017; 377:644-657

Reduced Primary Composite
CV death, nonfatal MI or CVA

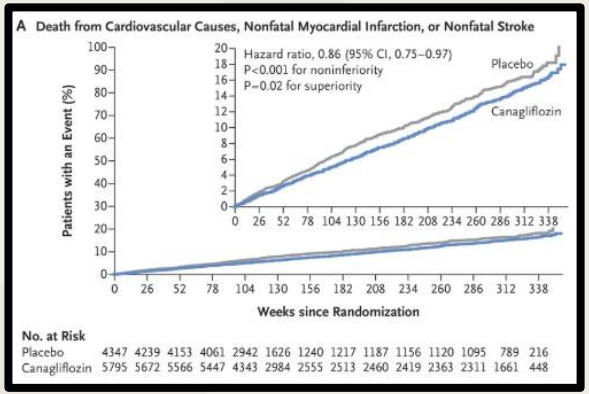
HR 0.86

Empaglifozin



EMPA-REG outcomes trial. NEJM 2015; 373:2117-2128
Event rate: 37.4 vs 43.4/1000 patient years

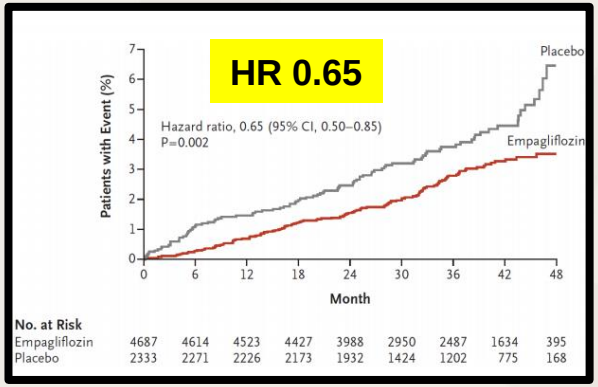
Canafliglozin



CANVAS trial. NEJM 2017; 377:644-657
Event rate: 26.93 vs 31.48/1000 patient years

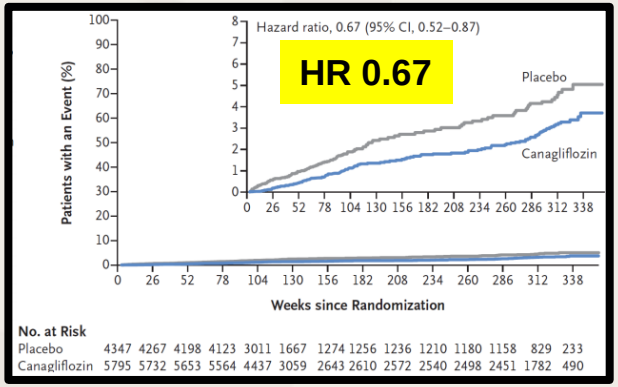
Reduced Hospitalization for CHF

Empagliflozin



EMPA-REG Outcomes Trial. NEJM 2015; 373:2117-2128

Canagliflozin



Canvas Trial. NEJM 2017; 377:644-657

Dapagliflozin Reduced Hospitalization for CHF

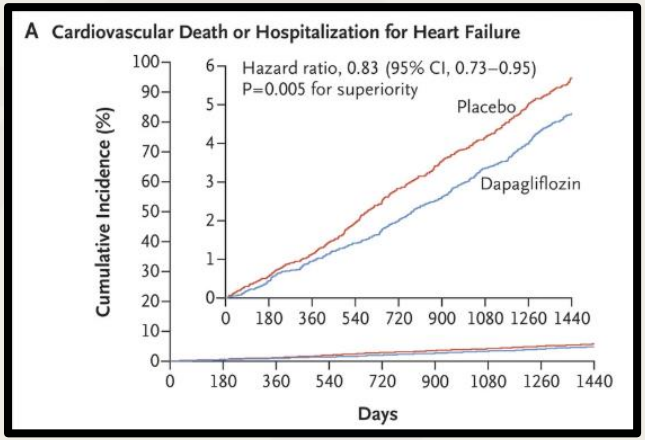
17, 160 patients
Median follow up 4.2 years
Mean age 64

- **Type 2 DM with a1c ≥ 6.5**
  Average A1C 8.3
  41% insulin

Established ASCVD
Prior MI/revascularization with LM/2vCAD
Prior TIA/CVA or carotid revascularization
Prior LE revascularization, amputation or symptoms w ABI< 0.9

OR

2 risk factors in men ≥ 55 or women≥ 60
LDL> 130 or on lipid lowering therapy
BP> 140/90 or on Rx
Current tobacco use ≥ 5 cigarettes/d for ≥ 1 year



Composite driven by decreased HF hospitalization HR 0.73

No subgroup difference related to
- History of HF (10%)
- Established ASCVD (40%)

DECLARE-TIMI 58. NEJM.org Nov 10 2018

SGLT2i and Cardiovascular Outcomes: Meta-analyses of RCTs parallel large propensity matched registries

- **MACE reduction only in those with established ASCVD (HR 0.86)**
  - *MACE reduction limited to reduced cardiovascular death and nonfatal MI*
  - No reduction in CVA risk
- **Reduced composite of CV death or HF hospitalization in all (HR 0.77)**
  - *HF hospitalization reduction similar in all irrespective of prior HF or ASCVD*

Journal of the American College of Cardiology
Volume 71, Issue 11 Supplement, March 2018

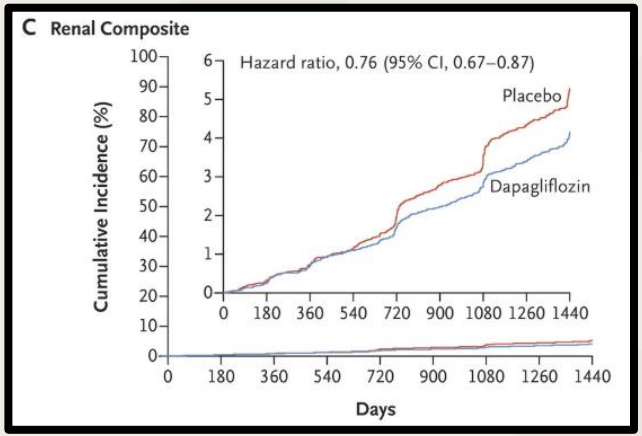
Lancet. 2019 Jan 5;393(10166):31-39.

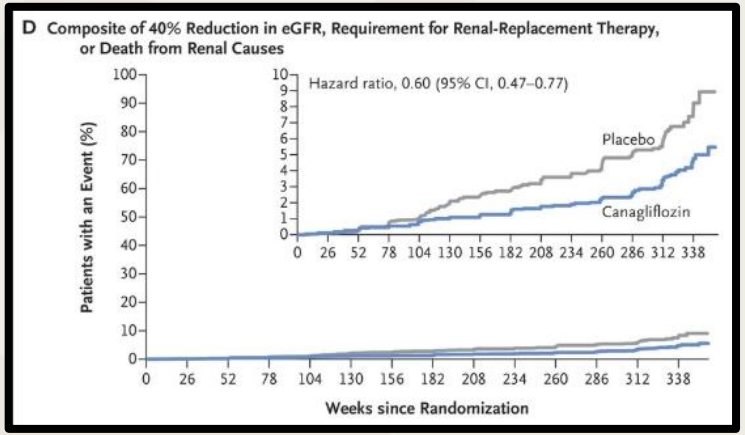
SGLT2 Inhibitors

Renal outcomes

Reduced **Renal Composite outcome***

***ESRD (HD, kidney transplant or eGFR< 15mL/min/1.73m2), doubling of serum creatinine, or death from renal or cardiovascular outcomes**





DECLARE-TIMI 58 NEJM.org Nov 11 2018

CANVAS-R NEJM 2017; 377:644-657

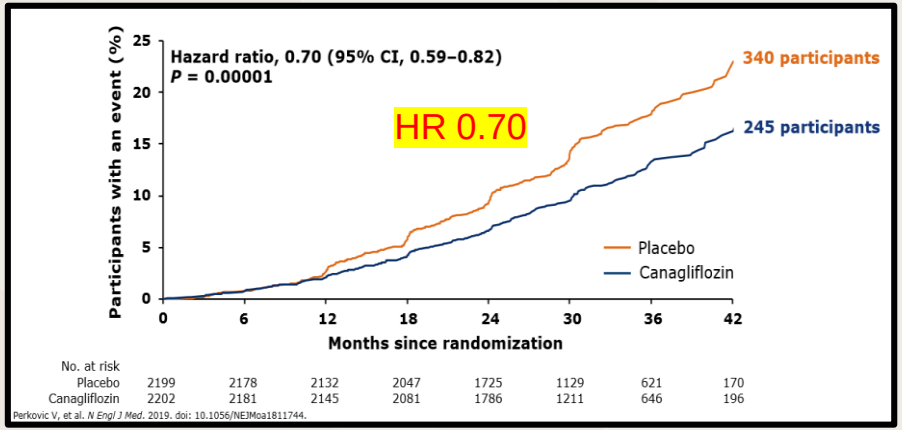
Canagliflozin reduced primary composite outcome in patients with CKD

4,395 patients
Median follow up 3.6 years
Age> 30 (Mean age 63)

Type 2 DM with AIC 6.5-12.0

- Average AIC 8.3
- Mean duration DM 16 yr
- 66% on insulin
- ASCVD 51%

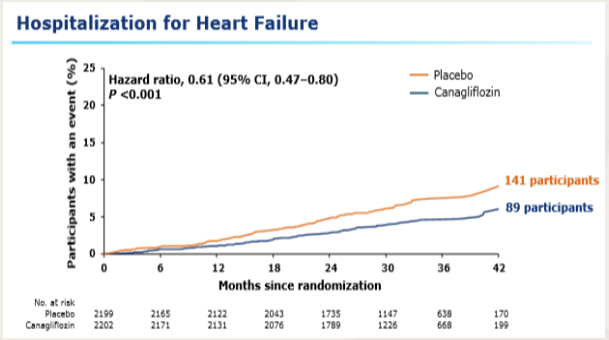
ACE or ARB
eGFR 30-90mL/min/1.73m2
UACR 300-5000mg/g

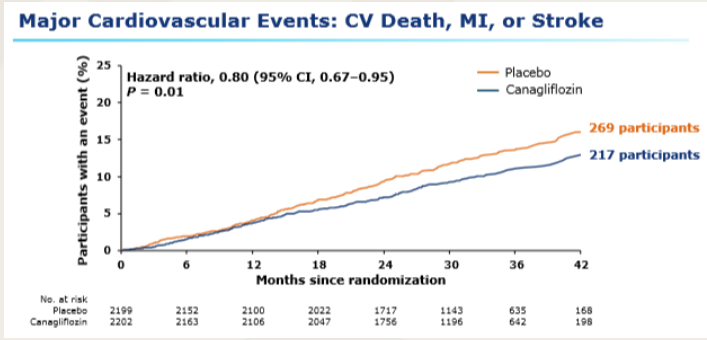


NNT 28 in 2.5 year follow up

CREDENCE. NEJM 2019; 380. 24;2295-2306

Canagliflozin reduced MACE and hospitalization for HF **among diabetics with CKD**





ADA updated recommendations on Diabetes and CKD June, 2019:

- Urinary albumin and eGFR should be assessed at least annually in DM type 2
- **SGLT2i use preferred if eGFR> 30 especially if albuminuria > 300mg/d to lower renal and CV risk**

SGLT2 Inhibitors

Barriers to Use

Barriers to SGLT2i Use

As little as $0 copay, max savings $250, 12 mo use, exp 12/31/2019

Canagliflozin (Invokana)

$497/mo

https://www.Invokana.com/patient-support/savings-card for commercially insured patients

As little as $0 copay, max savings $200 per mo, $3000 per year, 12 mo use, exp 12/31/2019

Dapagliflozin (Farxiga)

$495/mo

https://www.farxigasavingsrx.com/welcome.html online savings card

For commercially insured as little as $0 copay, max savings $378 per mo

For uninsured, save up to $150 per mo.

Barriers to SGLT2i Use

Euglycemic DKA

Blood glucose < 200mg/dL, plasma bicarbonate < 15mEq/L
Type I diabetics: intrinsic insulin indeficiency

SGLT2i results in lower blood glucose, decrease circulating insulin, *increase glucagon*
Enhanced lipolysis, ketogenesis. Decreased ketone reabsorption and ketonemia
Increased insulin resistance due to **stress or extended fasting** can transform drug-induced ketogenic state to ketoacidosis
triggers: heavy alcohol consumption, decreased caloric intake, pregnancy

Hold during hospitalizations and when npo/ limited po intake
Maintain high index of suspicion and assess for DKA even if glc< 250 if symptoms present (e.g. nausea, abdominal pain)

Adverse effects

Hypovolemia, dehydration
Hypotension
Hypoglycemia (rare)

- UTI

Yeast infections
Perineal infections (Fournier's gangrene, extremely rare)

- Amputation risk*
- Fracture risk*

Barriers to SGLT2i Use

* CANVAS only. Not in other SGLT2i even in PVD subgroups, not in meta-analyses or further canagliflozin studies

System-based solutions

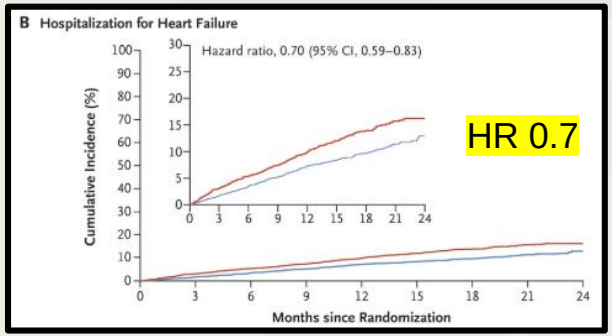
Clinical education and research
Get with the guidelines (GWG) initiatives targeting system wide coordination(PCP, urgent cares and ER, subspecialists especially endocrinologist, cardiologist, nephrologist)
Lessons re initiation of medication at discharge (e.g. BB, ACE/ARB, ARNI in HF)
Optimizing EMR for guideline implementation and data collection (akin to EPIC with GWTG)
Patient education

Drug cost and Insurance coverage
Continued FDA fast-tracking of expanding indications
Ongoing safety monitoring and reporting through EMR and registries

SGLT2 Inhibitors

Expanding clinical indications

Dapagliflozin *in HF reduced EF patients* reduced HF hospitalization



NNT 27 for 18 mos

4,744 patients
NYHA class II-IV
EF of 40% or less
Median follow up 18.2 mos

Mean EF 31%
NYHA class II 67%, class III 32%
Diabetes *NOT* inclusion criteria

41.8% diabetic
27% insulin

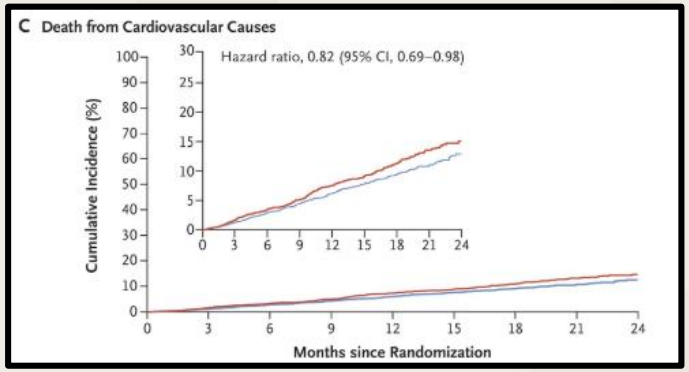
92% ACE/ARB/ARNI
93% diuretic

40% eGFR<60

DAPA-HF. NEJM Sept 19, 2019

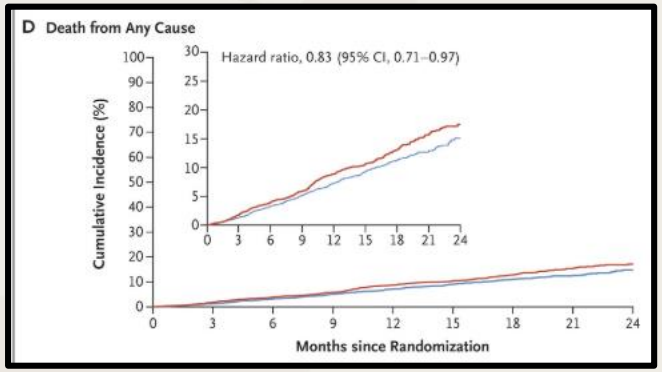
Dapagliflozin *in HF reduced EF patients*

Reduced CV death HR 0.82



NNT 52 for 18 mo

Reduced all cause death HR 0.83



NNT 43

DAPA-HF. NEJM Sept 19, 2019

Guideline directed medical therapy for HF

Reduced EF

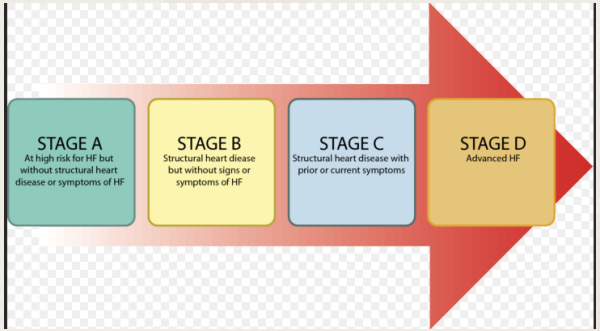
- ACE inhibitor/ ARB
- Beta blockers
- Mineralocorticoid Receptor Agonists
- Sacubitril/neprilisyn
- Cardiac Resynchronization therapy

Preserved EF

- ~~ACE inhibitor/ ARB~~
- ~~Beta blockers~~
- ~~Mineralocorticoid Receptor Agonists~~
- ~~Sacubitril/neprilisyn~~
- ~~Cardiac Resynchronization therapy~~

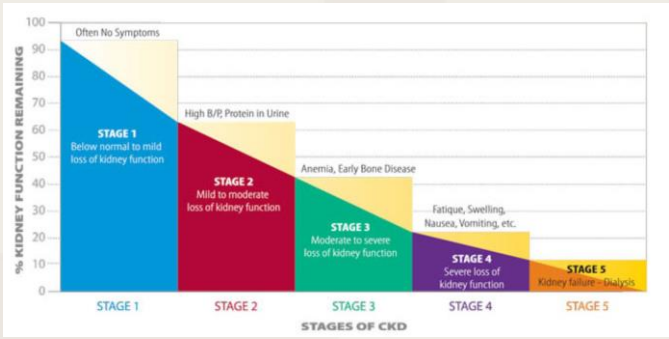
Continuum of disease progression

Heart failure stages



DAPA HF : greatest benefit in class II HFrEF

Progression of CKD



CREDENCE: greatest benefit in eGFR 45-60

Future Research:
FDA **Fast Track Designation**

- ✓ *Farxiga* to reduce the risk of CV death, or the worsening of heart failure in adults with heart failure with reduced ejection fraction (HFrEF) or preserved ejection fraction (HFpEF) based on the Phase III DAPA-HF and DELIVER trials

- ✓ *Farxiga* to delay the progression of renal failure and prevent CV and renal death in patients with chronic kidney disease (CKD) based on the Phase III DAPA-CKD trial.

Discussion

Breakout Groups

- Group 1 – Curie Room
- Group 2 – Edison G
- Group 3 – Edison EF *(Stay here)*

AMGA Foundation

Insight Showcase

AMGA Foundation

Morning Sessions

Insight Showcase

Type 2 Diabetes and Kidney Disease

"You put 16 people on this drug (canaglifozin), you'll prevent one patient from going on dialysis. This is the newest thing that can really prevent renal disease. That's huge."

"It's the people, it's the right drugs, it's communication and it's data."

"Much more variance at the site of care level than at the organizational level. At AMGA we try and find commonalities across organizations for top performers and share with them so they can achieve those better rates at all their sites of care."

Insight Showcase

Affordability, Implementation and Ownership

“We have to go from “the diabetes” to “my diabetes.”

“Industry needs to be a part of the solution but they need to fit the workflow of the primary care provider.”

“Top three challenges are education, education and education.”

AMGA Foundation

Afternoon Sessions

Insight Showcase

T2G, Therapeutic Inertia, Type 2 Diabetes and CVD

1,082,000 patients with improved care!

“90% of patients with diabetes are managed by their primary care provider who are overwhelmed. Patients trust their pharmacists more than their physicians.”

“We need license to prescribe this class of drugs more broadly. As a cardiologist, I am shy of prescribing these for fear of hypoglycemia. As we get expanded clinical indications and more comfort as cardiologists prescribing this in even non diabetic populations, maybe I’ll feel more comfortable.”

Insight Showcase

Implementing Medication Care Paths

"More education on patient portals is needed for example, what a specific lab measurement means."

"Are we in the value based world or are we still doing widgets?"

Thank You for a Great Day!