



COORDINATE Diabetes: Rationale and Design

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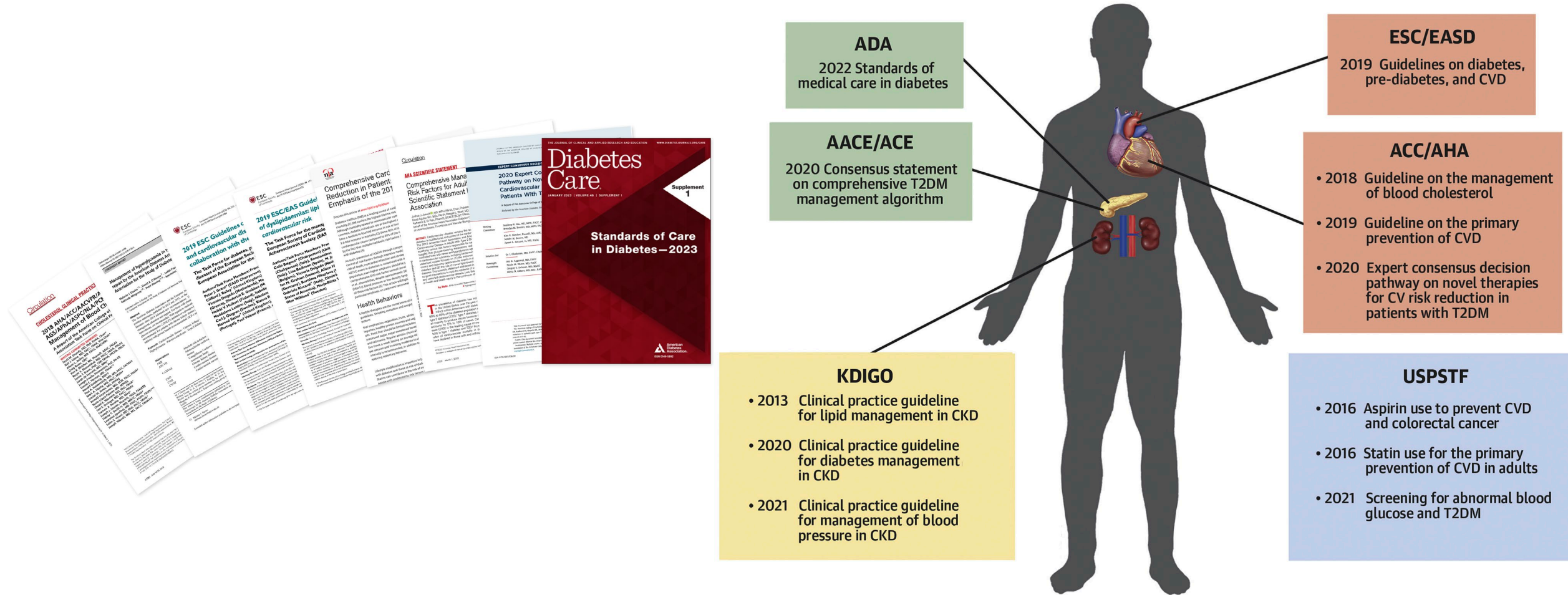
Duke Clinical Research Institute



Disclosures

- Research support from Amgen, Boehringer Ingelheim, Egglund's Best, Eli Lilly, Novartis, Novo Nordisk, Verily Life Sciences
- Consultation/Advisory Panels for Bayer, Boehringer Ingelheim, CRISPR Therapeutics, Eli Lilly, Esperion, AstraZeneca, Merck, Novartis, and Novo Nordisk.
- Executive Committee member for trials sponsored by Novo Nordisk and by Amgen.
- Medical advisory board for Miga Health

Interdisciplinary consensus



ADA
2022 Standards of medical care in diabetes

ESC/EASD
2019 Guidelines on diabetes, pre-diabetes, and CVD

AACE/ACE
2020 Consensus statement on comprehensive T2DM management algorithm

ACC/AHA

- 2018 Guideline on the management of blood cholesterol
- 2019 Guideline on the primary prevention of CVD
- 2020 Expert consensus decision pathway on novel therapies for CV risk reduction in patients with T2DM

KDIGO

- 2013 Clinical practice guideline for lipid management in CKD
- 2020 Clinical practice guideline for diabetes management in CKD
- 2021 Clinical practice guideline for management of blood pressure in CKD

USPSTF

- 2016 Aspirin use to prevent CVD and colorectal cancer
- 2016 Statin use for the primary prevention of CVD in adults
- 2021 Screening for abnormal blood glucose and T2DM

Multifactorial Risk Reduction

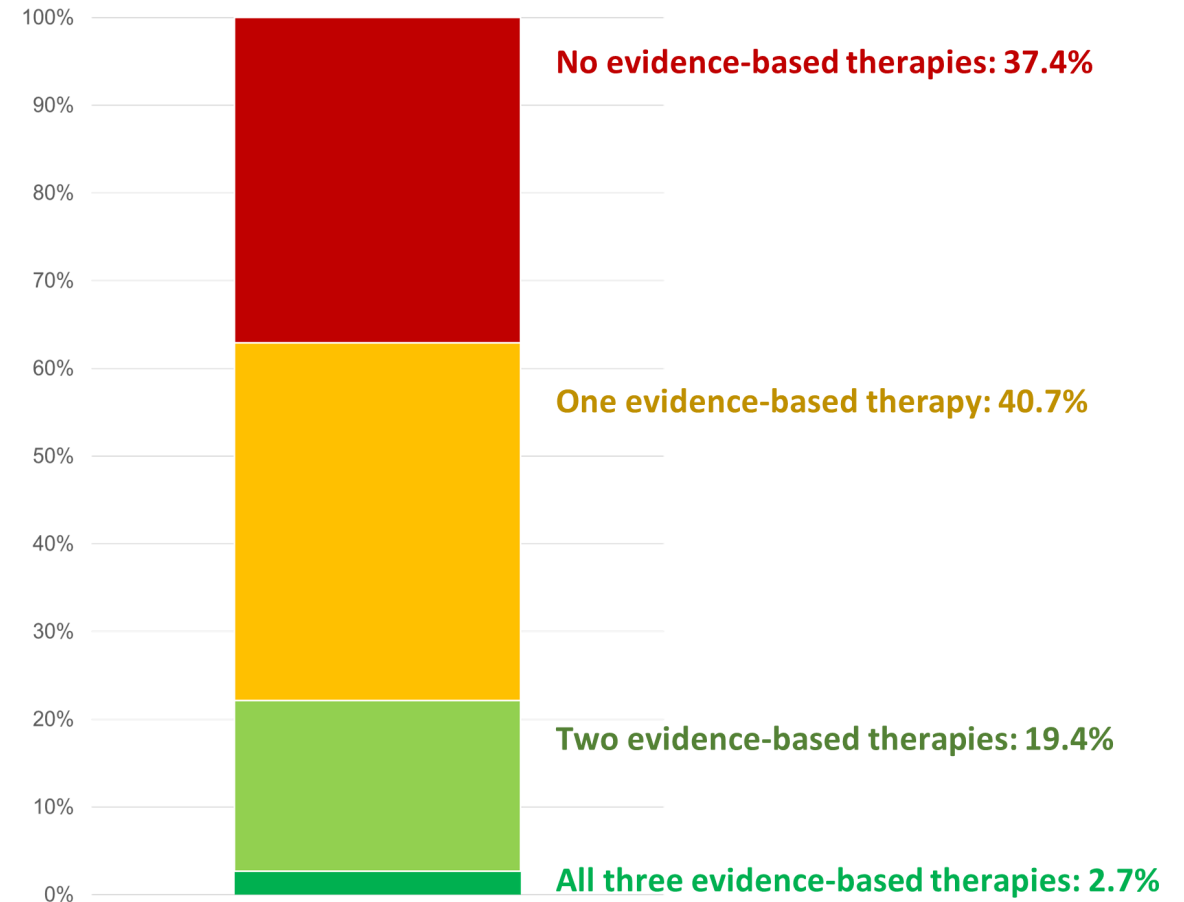


Several therapies are proven to reduce ASCVD risk among patients with T2DM, however these are substantially under-used in clinical practice

- Among 155,958 commercially-insured patients with T2DM and ASCVD:
 - 24.7% on high-intensity statin
 - 53.1% on ACEi/ARB
 - 9.9% on SGLT2i or GLP1RA

Overall

- **2.7% on all 3 groups of therapies**
- **37.4% on NONE of these groups of therapies**



COORDINATE-Diabetes



Objective

To test the impact of a clinic-level, multifaceted intervention on the prescription of 3 key groups of evidence-based therapies.

Coordinate-Diabetes Study Organization



COORDINATING CENTER:



STUDY TEAM:

Chris Granger, MD
Hussein Al-Khalidi, PhD
Jennifer Green, MD
Lisa Kaltenbach, MS
Monica Leyva, MHA, RCIS
Renato Lopes, MD, PhD
Adam Nelson, MBBS, MBA, MPH, PhD
Neha Pagidipati, MD, MPH
Laura Webb, BS, CCRP
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STEERING COMMITTEE:

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Matthew A. Cavender, MD, MPH
Tanya Szesny Gaynor, MPAS, PA-C
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Ildiko Lingvay, MD, MPH, MSCS
Melissa Magwire, RN, MSN, CDE
Darren McGuire, MD
Jonathan Pak, PharmD, MBA
Rodica Pop-Busui MD, PhD
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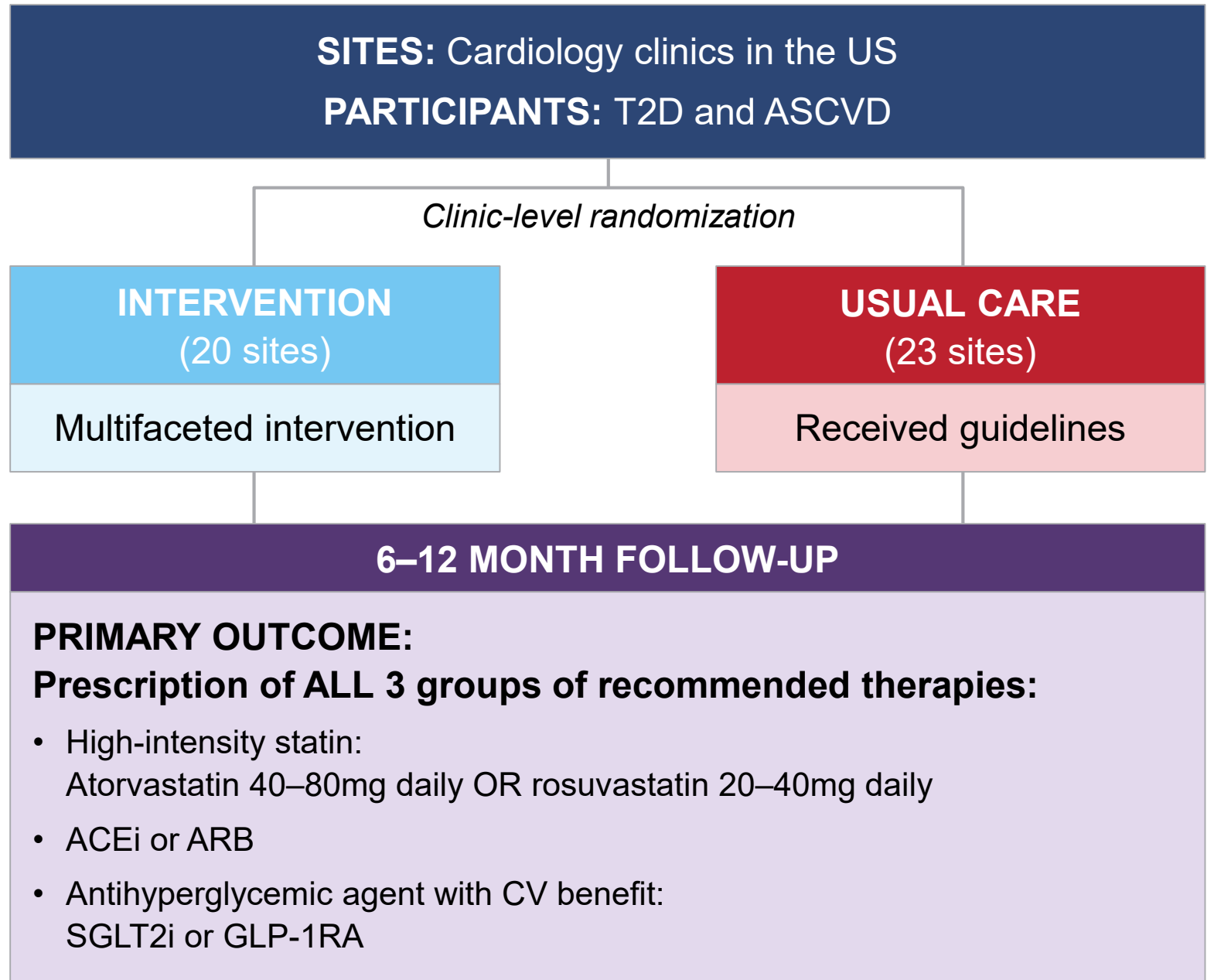
DATA AND SAFETY MONITORING BOARD:

John H. Alexander, MD, MHS
Bernard J. Gersh, MB, ChB, DPhil

SPONSORS:

Boehringer Ingelheim
Pharmaceuticals
Eli Lilly and Company

Study Design



Participating Sites



INCLUSION CRITERIA

- Cardiology clinic with **at least three cardiology providers (MD, DO, or APPs)**
- Able to identify at least 1 local diabetes care specialist to collaborate with

Participant Population



INCLUSION CRITERIA

- Diagnosis of type 2 diabetes
- History of at least one:
 - Coronary artery disease
 - Peripheral arterial disease
 - Cerebrovascular disease

EXCLUSION CRITERIA

- Already prescribed at baseline:
 - All 3 evidence-based therapies
 - SGLT2i or GLP-1RA
- Absolute contraindication to any of the 3 evidence-based therapies

Primary Outcome



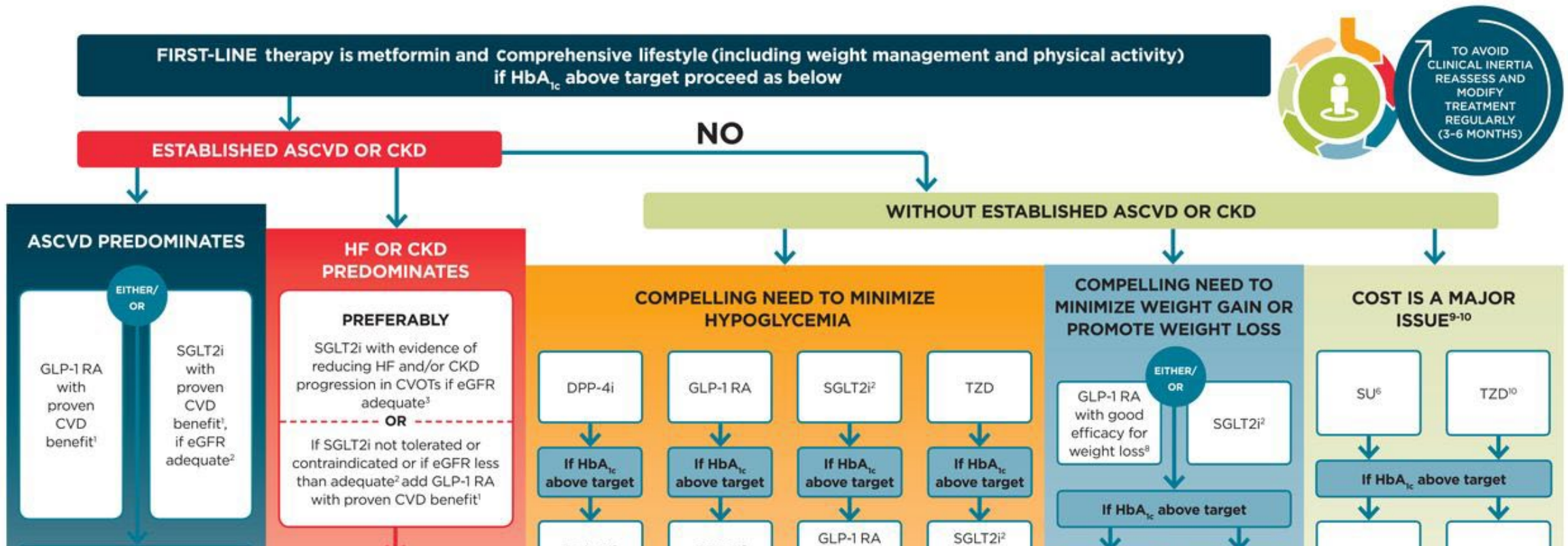
Proportion of individuals achieving society- and guideline-recommended management for T2DM and CVD at last follow-up visit for all of the following (composite score of 3):

- An anti-hyperglycemic agent with evidence for CV benefit (i.e. SGLT-2i or GLP-1RA)
 - Acceptable alternative: metformin monotherapy with HbA1c < 7%
- ACEi/ARB/ARNI
- High-intensity statin: atorvastatin 40-80mg daily OR rosuvastatin 20-40mg daily

Antihyperglycemic Agents with CV Benefit



2019 ADA Standards of Care



Secondary Outcomes



- Proportion of individuals receiving each group of therapies
- Proportion of individuals achieving a composite score of ≥ 2
- Intermediate Outcomes:
 - Change from baseline: sBP, dBP, HbA1c, LDL-C
 - Proportion of individuals with: sBP<130 mmHg, HbA1c<7%, LDL-C<70 mg/dL
- Clinical time-to-event outcomes
 - Composite of all-cause death; hospitalization for: MI, stroke, decompensated heart failure, or urgent revascularization (coronary, peripheral, carotid)

Statistical Analysis



Initially powered at 90%

to detect 10% difference in primary outcome between arms (46 clinics, 30 patients/clinic)



Modified to have 85% power

(42 clinics, 25 patients/clinic) due to difficulties with recruitment during the COVID-19 pandemic

Primary and secondary outcomes

analyzed using a mixed model for repeated measures model, accounting for clustering effect, and with adjustment for baseline factors as potential confounders

Clinical event outcomes

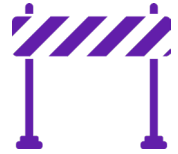
analyzed using a multivariable Cox proportional hazards model

Multifaceted Intervention



1.

**Assessment
of local practices
and barriers**



Clinic-specific
assessment of
barriers to prescribing
the recommended
therapies

2.

**Development of strategies to
overcome those barriers**



Development
of care pathways
to address barriers



Clinician
education



Coordination
of care between
clinicians



Participant educational
materials

3.

**Audit and
feedback**



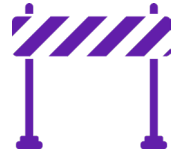
Audit and
feedback of
quality metrics

Multifaceted Intervention



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Assessment of Local Barriers



			
Barriers to evidence-based care	SITE #	Organizational approach	
Strategic Objective	Current Standing	Opportunity for DM/CVD Patient Care	Action Plan
1.1 Are there any current efforts to improve quality of patient care overall in the clinic?			
1.2 Does the clinic have a quality improvement team focused on patient management and improving outcomes in general, or for specific patient populations?			
1.3 Is there a process by which cardiology providers can communicate with other providers of patients with diabetes and cardiovascular disease?			
1.4 Do opportunities for education about current ACC/AHA guidelines exist for providers in the clinic?			
1.5 Do opportunities for education about new evidence or therapies (not yet in guidelines) exist?			

SITE VISIT SUMMARY REPORT			
Site #		Facility Name	
Date		Duke Team	
Time		Site Team	
Initial Assessment	<i>Insert information regarding the clinic etc.</i>		
Best Practices	<i>What are they doing well</i>		
Strengths	<i>e.g. Leadership, research team, resources</i>		
Potential Gaps	<i>Gap analysis information and additional information gleaned from the visit</i>		
Challenges	<i>Perceived and site identified</i>		
Attendees	<i>List of attendees from sign-in sheet</i>		

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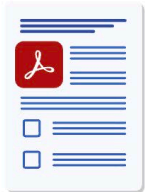
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Clinician Education



Provider Education: Train care providers on best practices.

Download the following resources:



- [SGLT2/GLP1RA management and cost assistance reference](#)
- [Injectable diabetes meds reference](#)
- [Oral diabetes meds reference](#)
- [Non-Vitamin K anticoagulants reference](#)

[Module 1: Aims of COORDINATE](#)

[Module 2: COORDINATE Background](#)

[Module 3: SGLT-2i / GLP-1RA](#)

[Module 4: High intensity statins](#)

[Module 5: ACE Inhibitors / ARBs](#)

COORDINATE-Diabetes
@CoordinateDm
Cluster randomized trial of an intervention to improve care for patients with diabetes and atherosclerotic cardiovascular disease
Joined October 2019

COORDINATE DIGEST

A newsletter brought to you by the COORDINATE-Diabetes trial team

SEPTEMBER 2021

Top stories this month

29
New patients enrolled in August and 968 overall.

43
Activate sites!

Top enroller for August — Ambarish Pandey from UTSW who enrolled 9 patients in their first month!!!

Dr Caroline Richardson and Dr Rodica Pop-Busui were involved in a study recently showing the benefits of continuous glucose monitors. Click [here](#)

Trial status

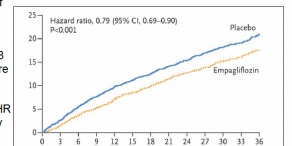


- With 43 sites activated and enrolling, we now have 968 patients in the study that represents over 90% of our target!
- The time to make improvements in care is... NOW!**
- The best time to make a change to guideline-directed care is at the enrollment visit when both you and the patient are motivated!
 - As each patient approaches 12 months, this is a key time to assure patients are on each component: high-intensity statin, ACE/ARB, SGLT-2i/GLP-1RA...

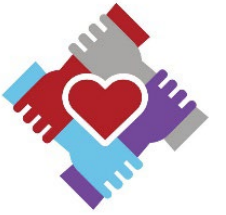
Updates from the European Society of Cardiology Congress:

EMPEROR-Preserved trial shows benefit for empagliflozin in HFpEF!

Presented as a Hot Line clinical trial at the European Society of Cardiology and simultaneously published in *NEJM*. [EMPEROR-Preserved](#) is the study of empagliflozin vs placebo to improve outcomes for patients with heart failure with preserved ejection fraction with or without diabetes (HFpEF, LVEF >40%). The trial recruited 5,988 patients, mean age 72 years of which 45% were female. After a median followed up of 26.2 months, empagliflozin reduced the risk of CV death or heart failure hospitalization by 21% (HR 0.79, 95%CI 0.69-0.90, p<0.001) driven mainly by reduced rates of HF hospitalization (8.6 vs. 11.8%). There was no significant difference in the rates of hypoglycemia or hypotension between placebo and empagliflozin treated patients, further supporting the safety of this drug among patients with high degrees of comorbidity. **This trial establishes empagliflozin as the first drug proven to improve outcome in HFpEF. It extends the role of empagliflozin to patients across the spectrum of heart failure, regardless of presence of diabetes and regardless of ejection fraction!**

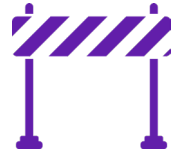


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Audit and Feedback



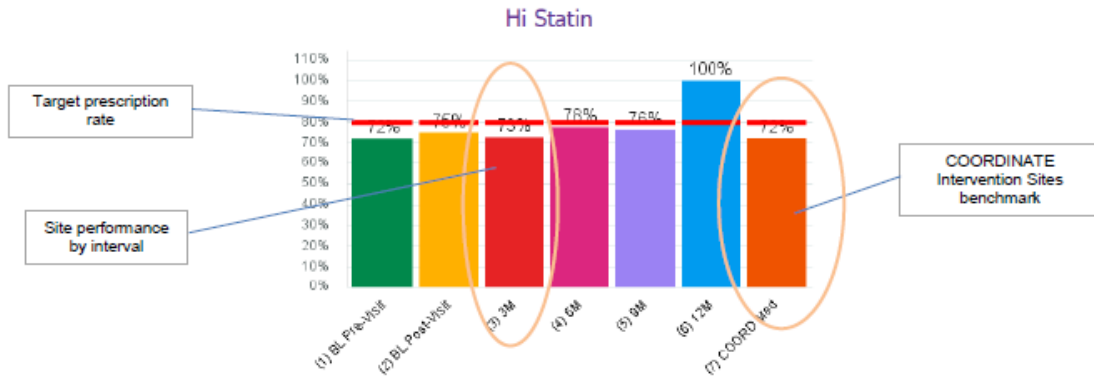
COORDINATE-Diabetes Report Interpretation Guide

The COORDINATE-Diabetes Intervention Report describes your site's quarterly performance on prescribing key medication classes to patients with diabetes and cardiovascular disease who have been enrolled in the study. These metrics are based on the American Diabetes Association Standard of Medical Care in Diabetes (2020). The metrics of interest are a prescription for ACE inhibitor, ARB, or ARNI; high-intensity statin; and SGLT2 inhibitor or GLP1RA.

Using data submitted and saved as Complete, these medications are reported as separate measures and as a Composite Score ("All 3") that presents a global view of your site's performance. The Composite score is comprised of the three individual medication guideline metrics.

In order to help you to evaluate your site's treatment of patients with cardiovascular disease and diabetes, the COORDINATE-Diabetes reports provide three benchmarks. The first and most important benchmark is your site's performance over time. Assuming your system of data collection remains constant, this benchmark enables you to best judge the success of your quality improvement initiatives. Additionally, we encourage you to compare your site results against the benchmark of all Intervention sites participating in COORDINATE-Diabetes, noted by a bar depicting the intervention site median for the specified therapy; and the target rate for all medication prescriptions, noted by a bar at the 80% rate.

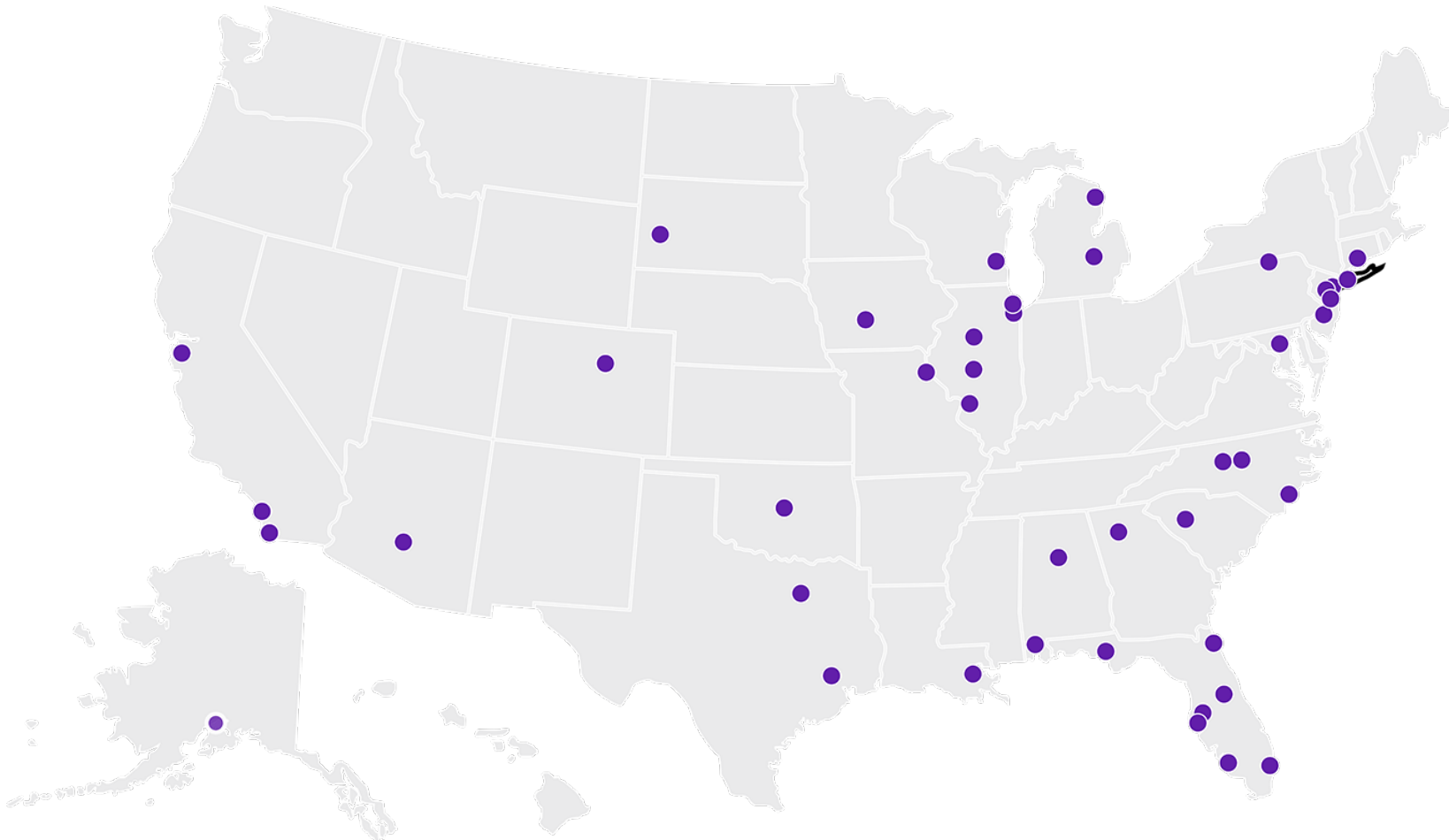
In general, missing data is assumed to be "No" in the report calculations. It is important to note that patients with missing data for medications are included in the denominators; thus missing variables may have an adverse impact on metric performance.



COORDINATE Medication Prescriptions Target ≥ 80%



Enrolling Sites



43

enrolling sites

24 (14,36)

participants enrolled

Baseline composite medication score (median):

1.6

intervention

1.4

usual care

Participant Baseline Characteristics



	Intervention (N=459)	Usual care (N=590)
Age, median (25 th , 75 th)	69 (63, 76)	71 (64, 77)
Female	31.4%	32.9%
Race: White	70.6%	81.4%
Black	17.2%	15.9%
Asian/other	8.9%	3.2%
Insurance:	97.6%	98.0%
- Medicare	62.9%	70.9%
- Private	33.7%	34.6%
- Medicaid	11.8%	9.3%
Prior coronary artery disease	76.0%	84.7%
Prior stroke/carotid artery disease	27.5%	25.1%
Prior peripheral arterial disease	17.4%	10.2%
Hypertension	93.0%	94.1%
Dyslipidemia	90.2%	91.7%

Participant Baseline Characteristics



	Intervention (N=459)	Usual care (N=590)
Atrial fibrillation	16.3%	24.6%
Heart failure	29.6%	24.6%
Charlson comorbidity ≥ 5	56.6%	62.4%
Diabetes complications:		
- DKA	0.4%	1.2%
- Retinopathy	6.8%	4.7%
- Neuropathy	24.0%	27.1%
- Gastroparesis	3.3%	1.4%
Clinical/laboratory		
Systolic blood pressure, mmHg	131	130
Body mass index, kg/m ²	32.2	32.4
LDL-C, mg/dL	72.8	73.2
eGFR, mL/min/1.73m ²	68	65
HbA1c, %	7.7	7.5

Participant Baseline Characteristics



	Intervention (N=459)	Usual care (N=590)
Composite medication score: 0	5.9%	9.7%
1	34.2%	38.3%
2	59.9%	52.0%
High-intensity statin use	66.7%	58.3%
ACEi/ARB use	75.2%	69.7%



COORDINATE Diabetes: Results

Christopher Granger, MD

Donald F. Fortin, MD, Distinguished Professor of Medicine



Duke Clinical Research Institute



Disclosures

- Research contracts: Anthos, Apple, Alnylam, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Daiichi Sankyo, Janssen, Novartis, GSK, Medtronic Foundation, Philips, Pfizer, The Medicines Company, FDA, NIH
- Consulting/Honoraria: Abiomed, AstraZeneca, Bayer, BMS, Boston Scientific, GSK, Janssen, Pfizer, Lilly, Daiichi Sankyo, Novartis, Novo Nordisk, Boehringer Ingelheim, Medtronic, Medtronic Foundation
- Equity: tenac.io
- For full listing see www.dcri.duke.edu/research/coi.jsp

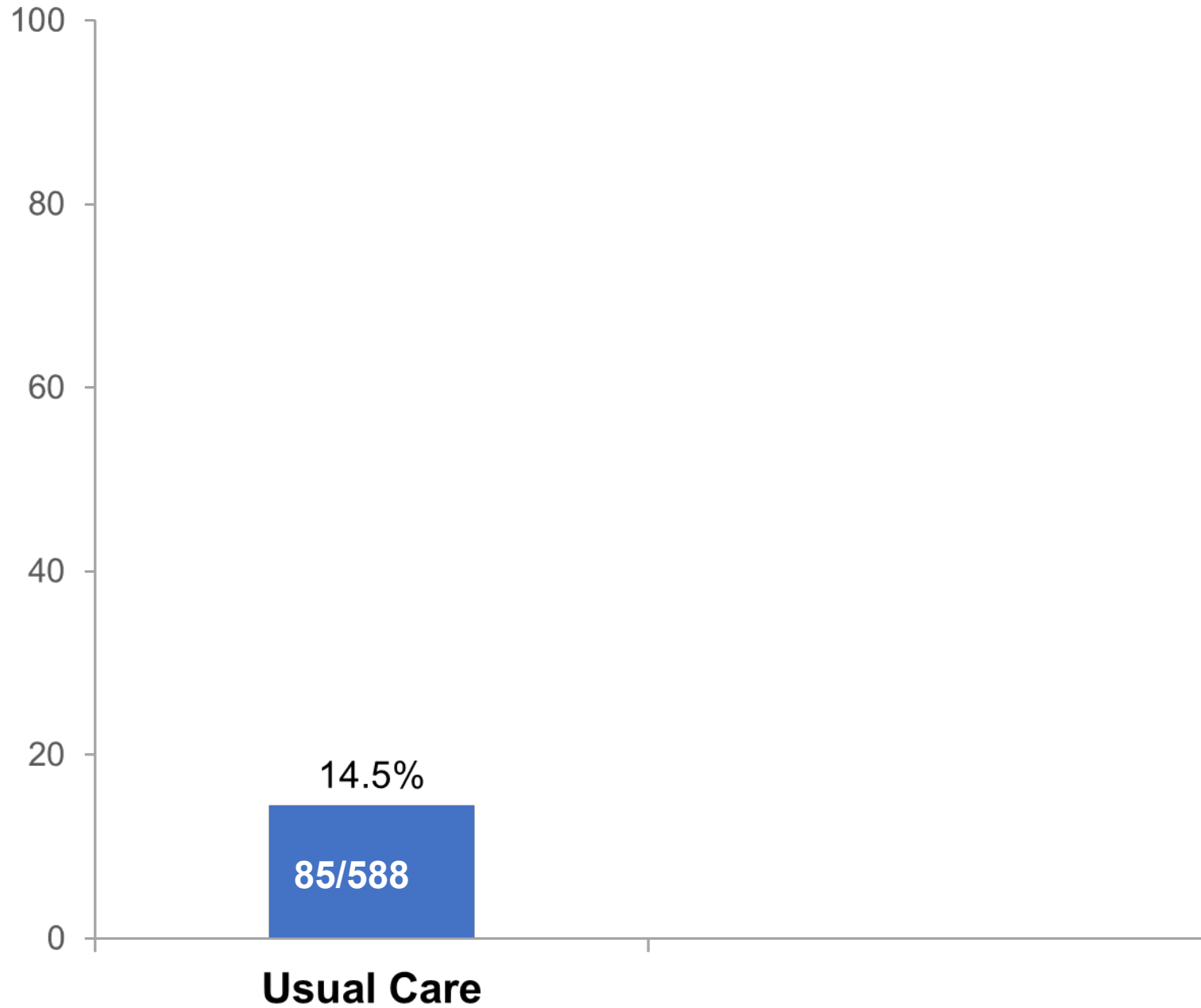
Primary Outcome



Primary Outcome



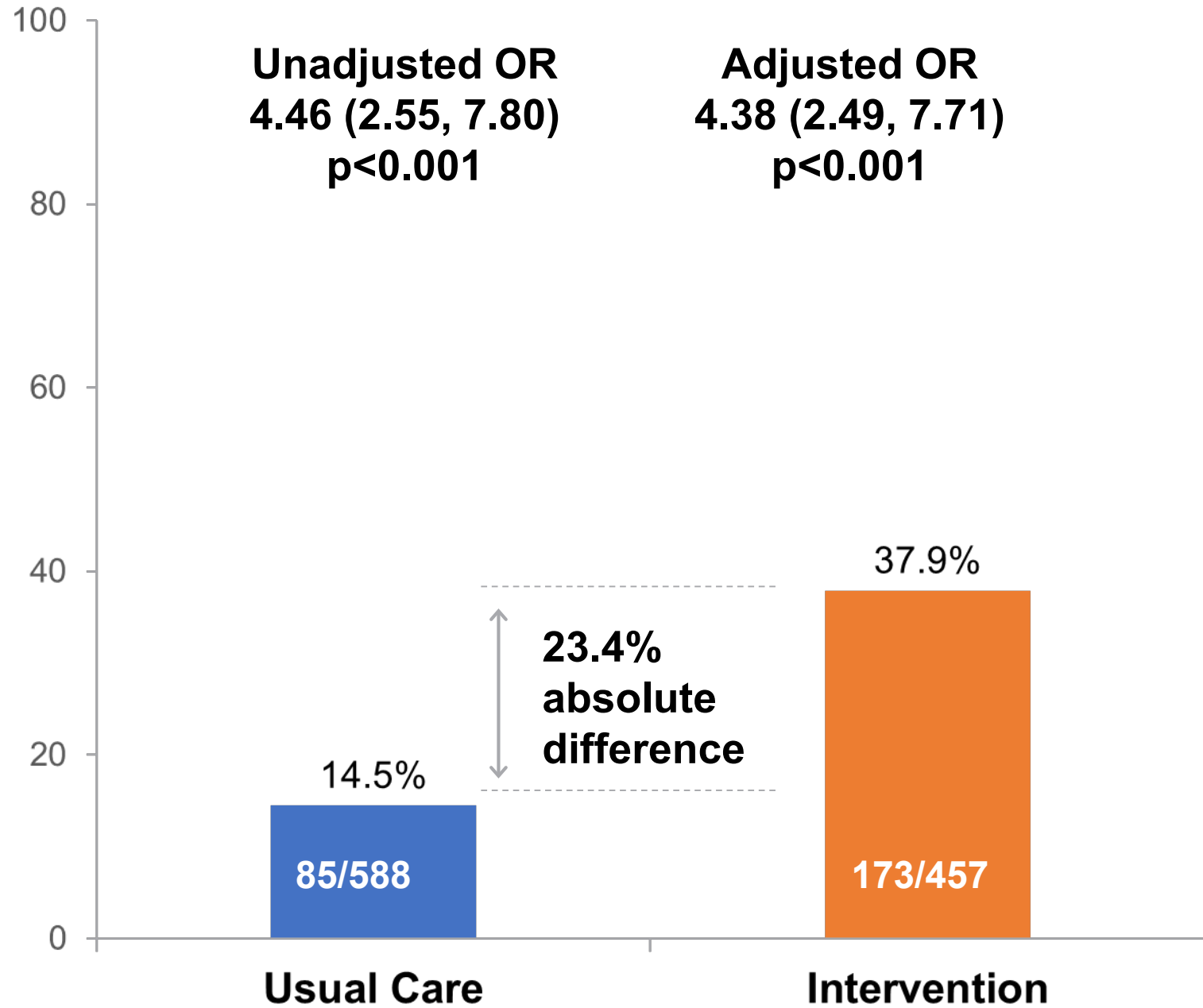
Participants prescribed
all 3 therapies (%)



Primary Outcome



Participants prescribed
all 3 therapies (%)



Secondary Outcomes



Outcome	Usual care No. (%) (N=588)	Intervention No. (%) (N=457)	Adjusted Odds ratio (95% CI)	P value
Prescribed at last follow up:				
High-intensity statin	334/588 (57)	323/457 (71)	1.73 (1.06 to 2.83)	0.029
ACEi/ARB	402/588 (68)	372/457 (81)	1.82 (1.14 to 2.91)	0.013
SGLT2i or GLP-1RA*	209/588 (36)	276/457 (60)	3.11 (2.08 to 4.64)	<0.001

Adjusted for clustering effect, site type (urban vs. non-urban), age, sex, race, baseline composite score, Charlson comorbidity index, baseline systolic BP, baseline diastolic BP, time, and time-by-treatment interaction

*Or HbA1c<7% on metformin alone



Absolute greater use of medications, intervention vs control

High intensity statins	14%
ACEi/ARB	13%
SGLT2i/ GLP-1RA	25%

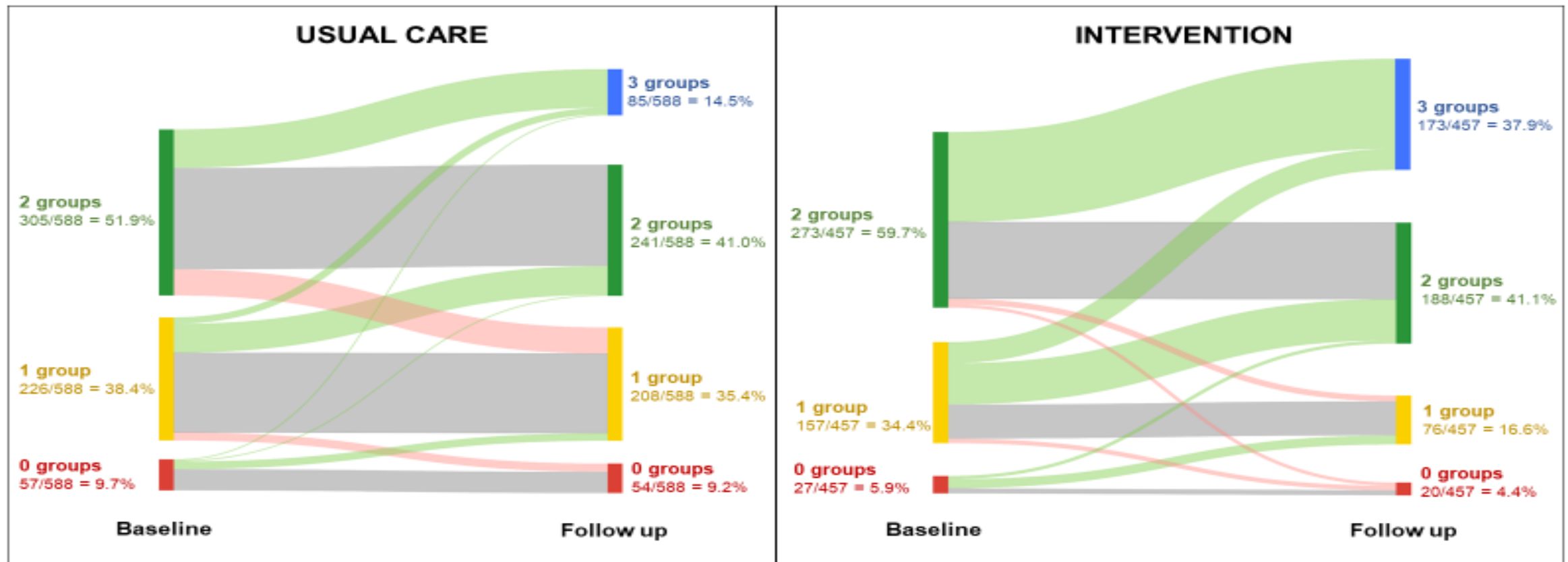


Diabetes medication use at end of trial

	Usual care	Intervention
SGLT2i	10.9%	34.8%
GLP-1RA	4.9%	11.2%
Both	0.7%	0.9%

Changes in composite medication scores

Fighting Clinical Inertia



Secondary Outcomes: Risk Factor Control



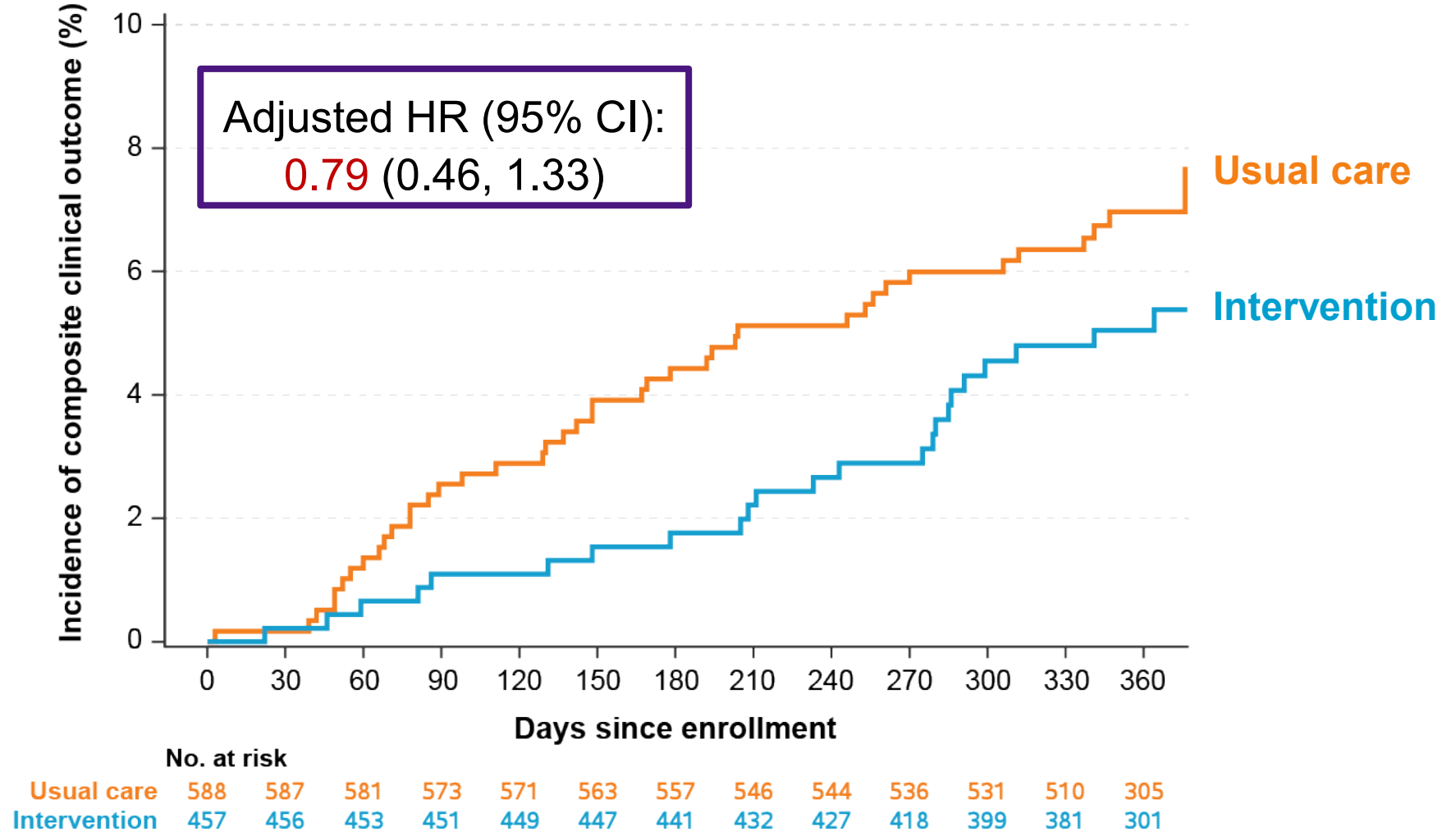
	% Available	Intervention (n=459)	Usual care (N=590)	Adjusted difference in differences [†]	
		Difference	Difference	Estimate (95% CI)	P value
sBP	82.9%	-2.31	0.91	-1.99 (-4.34, 0.36)	0.0961
HbA1c	48.0%	-0.17	-0.00	-0.05 (-0.34, 0.25)	0.7495
LDL-C	43.6%	-4.14	-5.30	0.61 (-5.24, 6.46)	0.8379

† Adjusted for site type (urban vs. non-urban), patient age, sex, race, baseline composite score, Charlson comorbidity index, baseline systolic BP

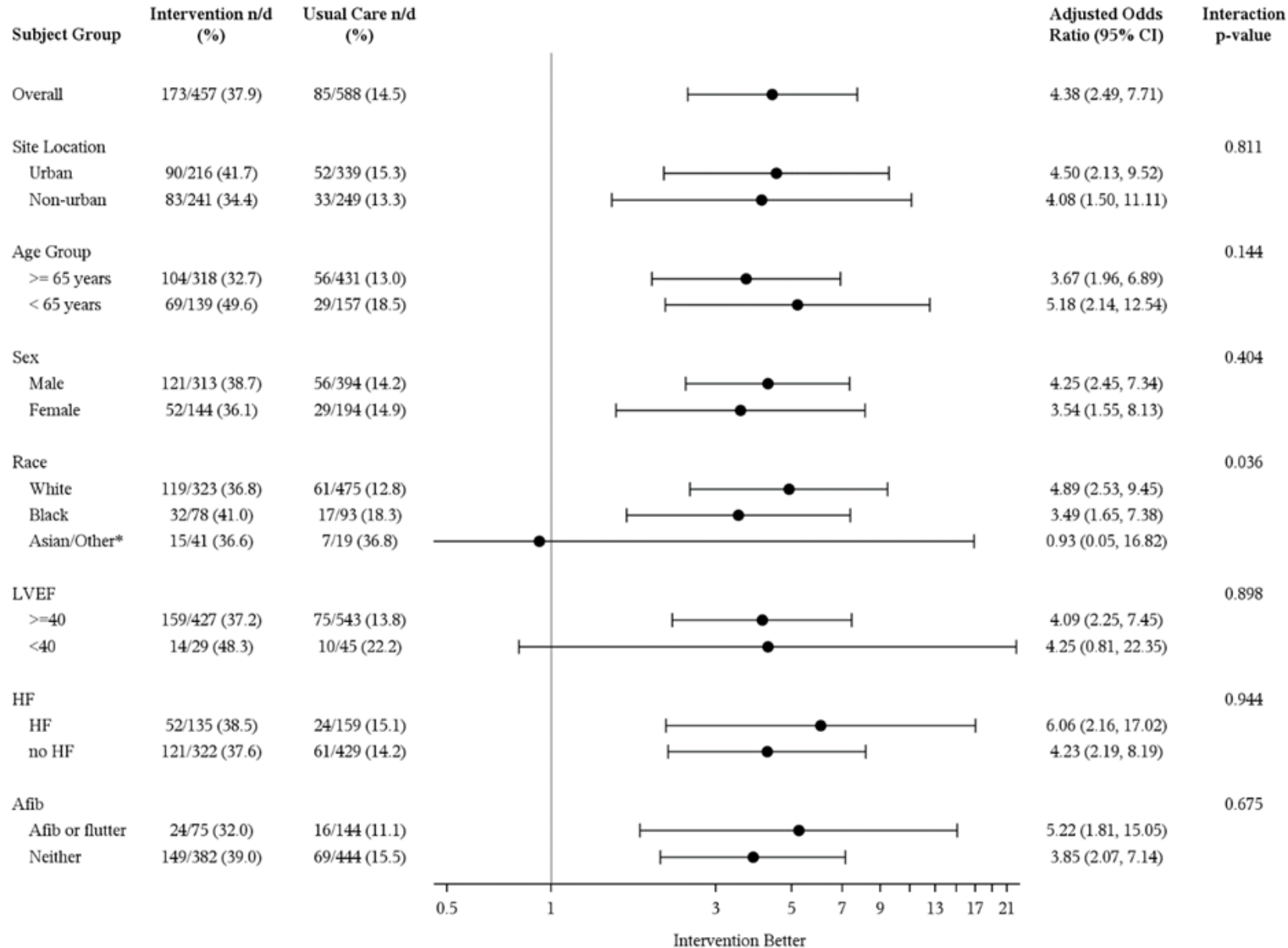
Secondary Outcomes: Clinical Events



Composite outcome:
All-cause mortality or hospitalization for MI, stroke, decompensated HF, or urgent revascularization (coronary, carotid, peripheral)



Consistency across clinic and patient subgroups



Most patients who had a prescription reported taking the medication



Patient reported “yes” to taking this therapy at last follow-up	EHR indicated a prescription for this therapy
High-intensity statin	96.3%
ACEi/ARB	98.0%
Antihyperglycemic agents with CV benefit	95.6%

Limitations



- Selected sites and patients may not be representative of broader US or international population
- We focused on a cohort, rather than on the entire clinic population
- Because of the COVID pandemic, the intervention was delivered remotely and was thus less intensive than originally designed

Conclusions



A coordinated, multifaceted intervention
increased prescription of 3 groups of
evidence-based therapies in adults
with T2D and ASCVD

Questions



- Were we able to get cardiologists to write the prescriptions for SGLT2i and GLP-1RA?

Yes

- Was the effect consistent across different clinics?

There was heterogeneity, but when we looked at tertiles of final performance, ALL of those in bottom tertile were usual care sites

- Was the intervention resource-intensive?

No, the intervention was simple but depended on a champion to promote the efforts

Clinical Implications



- Evidence-based therapies are under-used in clinical practice, and there is little high-quality data on how to improve this.
- This multifaceted intervention is effective in increasing the prescription of evidence-based therapies in adults with T2D and ASCVD.
- The next step is to scale this intervention across cardiology practices in order to improve the quality of care being delivered broadly.



“Humanity’s greatest advances are not in its discoveries – but in how those discoveries are applied ...”

*Bill Gates, June 7, 2007
Harvard Commencement Address*

Selected randomized trials showing successful implementation: Average of 50 centers, 1000 patients, with a 6 to 50% improvement in guideline-directed medication use

Virtual Care Team Guided Management of Patients With Heart Failure During Hospitalization



JACC 2023

Ankeet S. Bhatt, MD, MBA, ScM,^{a,b,*} Anubodh S. Varshney, MD,^{c,*} Alea Moscone, MPH,^d Brian L. Claggett, PhD,^a

Electronic Alerts to Improve Heart Failure Therapy in Outpatient Practice

A Cluster Randomized Trial

JACC 2022

Lama Ghazi, MD, PhD,^a Yu Yamamoto, MS,^a Ralph J. Riello, PHARM,^a Claudia Coronel-Moreno, MPH,^a

Cluster-Randomized Trial Comparing Ambulatory Decision Support Tools to Improve Heart Failure Care



JACC 2023

Amrita Mukhopadhyay, MD,^a Harmony R. Reynolds, MD,^a Lawrence M. Phillips, MD,^a Arielle R. Nagler, MD,^b

Safety, tolerability and efficacy of up-titration of guideline-directed medical therapies for acute heart failure (STRONG-HF): a multinational, open-label, randomised, trial

Lancet 2022

Alexandre Mebazaa, Beth Davison, Ovidiu Chioncel, Alain Cohen-Solal, Rafael Diaz, Gerasimos Filippatos, Marco Metra, Piotr Ponikowski,

A multifaceted intervention to improve treatment with oral anticoagulants in atrial fibrillation (IMPACT-AF): an international, cluster-randomised trial

Lancet 2017

Dragos Vinereanu, Renato D Lopes, M Cecilia Bahit, Denis Xavier, Jie Jiang, Hussein R Al-Khalidi, Wensheng He, Ying Xian, Andrea O Ciobanu,

Coordinated Care to Optimize Cardiovascular Preventive Therapies in Type 2 Diabetes

A Randomized Clinical Trial

JAMA 2023

Neha J. Pagidipati, MD, MPH; Adam J. Nelson, MBBS, MPH, MBA, PhD; Lisa A. Kaltenbach, MS; Monica Leyva, RCIS, MHA; Darren K. McGuire