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Coordinated Care to Optimize Cardiovascular Preventive Therapies in Type 2 Diabetes
A Randomized Clinical Trial

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IMPORTANCE Evidence-based therapies to reduce atherosclerotic cardiovascular disease risk in adults with type 2 diabetes are underused in clinical practice.

OBJECTIVE To assess the effect of a coordinated, multifaceted intervention of assessment, education, and feedback vs usual care on the proportion of adults with type 2 diabetes and atherosclerotic cardiovascular disease prescribed all 3 groups of recommended, evidence-based therapies (high-intensity statins, angiotensin-converting enzyme inhibitors [ACEIs] or angiotensin receptor blockers [ARBs], and sodium-glucose cotransporter 2 [SGLT2] inhibitors and/or glucagon-like peptide 1 receptor agonists [GLP-1RAs]).

DESIGN, SETTING, AND PARTICIPANTS Cluster randomized clinical trial with 43 US cardiology clinics recruiting participants from July 2019 through May 2022 and follow-up through December 2022. The participants were adults with type 2 diabetes and atherosclerotic cardiovascular disease not already taking all 3 groups of evidence-based therapies.

INTERVENTIONS Assessing local barriers, developing care pathways, coordinating care, educating clinicians, reporting data back to the clinics, and providing tools for participants (n = 459) vs usual care per practice guidelines (n = 590).

MAIN OUTCOMES AND MEASURES The primary outcome was the proportion of participants prescribed all 3 groups of recommended therapies at 6 to 12 months after enrollment. The secondary outcomes included changes in atherosclerotic cardiovascular disease risk factors and a composite outcome of all-cause death or hospitalization for myocardial infarction, stroke, decompensated heart failure, or urgent revascularization (the trial was not powered to show these differences).

RESULTS Of 1049 participants enrolled (459 at 20 intervention clinics and 590 at 23 usual care clinics), the median age was 70 years and there were 338 women (32.2%), 173 Black participants (16.5%), and 90 Hispanic participants (8.6%). At the last follow-up visit (12 months for 97.3% of participants), those in the intervention group were more likely to be prescribed all 3 therapies (173/457 [37.9%]) vs the usual care group (85/588 [14.5%]), which is a difference of 23.4% (adjusted odds ratio [OR], 4.38 [95% CI, 2.49 to 7.71]; $P < .001$) and were more likely to be prescribed each of the 3 therapies (change from baseline in high-intensity statins from 66.5% to 70.7% for intervention vs from 58.2% to 56.8% for usual care [adjusted OR, 1.73; 95% CI, 1.06-2.83]; ACEIs or ARBs: from 75.1% to 81.4% for intervention vs from 69.6% to 68.4% for usual care [adjusted OR, 1.82; 95% CI, 1.14-2.91]; SGLT2 inhibitors and/or GLP-1RAs: from 12.3% to 60.4% for intervention vs from 14.5% to 35.5% for usual care [adjusted OR, 3.11; 95% CI, 2.08-4.64]). The intervention was not associated with changes in atherosclerotic cardiovascular disease risk factors. The composite secondary outcome occurred in 23 of 457 participants (5%) in the intervention group vs 40 of 588 participants (6.8%) in the usual care group (adjusted hazard ratio, 0.79 [95% CI, 0.46 to 1.33]).

CONCLUSIONS AND RELEVANCE A coordinated, multifaceted intervention increased prescription of 3 groups of evidence-based therapies in adults with type 2 diabetes and atherosclerotic cardiovascular disease.

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Visual Abstract

Supplemental content

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Group Information: A complete list of the COORDINATE-Diabetes Site Investigators appears in Supplement 3.

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Atherosclerotic cardiovascular disease is a leading cause of death among adults with type 2 diabetes.[1,2] High-intensity statins,[3] angiotensin-converting enzyme inhibitors (ACEIs),[4] angiotensin receptor blockers (ARBs),[5] sodium-glucose cotransporter 2 (SGLT2) inhibitors,[6] and glucagon-like peptide 1 receptor agonists (GLP-1RAs)[7] reduce cardiovascular risk in those with type 2 diabetes. Guidelines and statements from professional societies recommend each of these therapies for adults with type 2 diabetes and atherosclerotic cardiovascular disease.[8-11]

Given the well-documented underuse of these evidence-based therapies for individuals with type 2 diabetes and atherosclerotic cardiovascular disease in clinical practice,[12,13] we hypothesized that a coordinated, multifaceted intervention of assessment, education, and feedback would increase prescription of these agents. We conducted the Coordinating Cardiology Clinics Randomized Trial of Interventions to Improve Outcomes (COORDINATE)-Diabetes, a cluster randomized clinical trial at cardiology clinics in the US, to assess the effect of the intervention on the proportion of adults with type 2 diabetes and atherosclerotic cardiovascular disease prescribed all 3 groups of recommended therapies (high-intensity statins, ACEIs or ARBs, and SGLT2 inhibitors and/or GLP-1RAs).

Key Points

Question Can a coordinated, multifaceted intervention increase the prescription of 3 evidence-based therapies among adults with type 2 diabetes and atherosclerotic cardiovascular disease?

Findings In a cluster randomized clinical trial of cardiology clinics across the US, participants in the intervention group were more likely to be prescribed all 3 therapies (high-intensity statins, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and sodium-glucose cotransporter 2 inhibitors and/or glucagon-like peptide 1 receptor agonists) after an intervention of assessment, education, and feedback vs those in the usual care group (173/457 [37.9%] vs 85/588 [14.5%], respectively, which is a difference of 23.4%).

Meaning A coordinated, multifaceted intervention increased prescription of 3 groups of evidence-based therapies in adults with type 2 diabetes and atherosclerotic cardiovascular disease.

Methods

Trial Design and Oversight

This cluster randomized clinical trial was conducted at cardiology clinics across the US and the trial design was published.[14] Each clinic was randomly assigned to the intervention or usual care (**Figure 1**), and randomization was stratified by urban location vs suburban or rural location (self-reported by the clinics). Participants provided written informed consent and the trial protocol (Supplement 1) was approved by institutional review boards at the participating sites. Trial oversight was provided by a steering committee and an independent data and safety monitoring committee reviewed study progress and accumulating data (Supplement 2).

Trial Population

Cardiology clinics were eligible if they could identify at least 1 diabetes care clinician (endocrinology or primary care) who could participate in developing local interdisciplinary pathways to improve care. Eligible participants had both type 2 diabetes and atherosclerotic cardiovascular disease, which was defined as coronary artery disease, cerebrovascular disease, or peripheral artery disease. Data on race and ethnicity were collected to adequately describe the study cohort; these data were self-reported based on fixed categories. Those with an estimated glomerular filtration rate less than 30 mL/min/1.73 m^2 or an absolute contraindication to any of the recommended classes of therapies were excluded. Adults with statin-associated adverse effects, such as myalgias, were included. Those already prescribed high-intensity statins and ACEIs or ARBs, and who had a hemoglobin A_{1c} level less than 7% while taking metformin monotherapy alone, were excluded. Those who were already taking SGLT inhibitors or GLP-1RAs also were excluded.

Trial Intervention

The intervention consisted of a suite of strategies provided to clinic personnel by the coordinating center trio of a cardiologist, endocrinologist, and implementation specialist. The implementation specialist had clinical nursing experience as well as experience in facilitating strategies to increase use of evidence-based therapies in clinical health care settings and in research. Prior to the COVID-19 pandemic, the trio traveled to each site to initiate the intervention. After the start of the COVID-19 pandemic, the intervention was conducted virtually. The intervention included the following 6 components.

First, there was a clinic-specific analysis of the barriers to evidence-based care. The trio worked with local care teams to understand care practices, barriers to prescribing evidence-based therapies, and potential resources to overcome barriers.

Second, there was development of local interdisciplinary care pathways to address barriers. Clinic teams created plans to address the locally identified barriers, including strategies emphasizing evidence that SGLT2 inhibitors and GLP-1RAs reduce cardiovascular risk and should be prescribed by cardiologists, engaging pharmacists to support clinical care, and developing pathways to navigate prior authorization and patient assistance programs to cover medication costs.

Third, there was coordination of care between clinicians. Coordination of care, particularly between cardiology, endocrinology, and primary care clinicians, was facilitated at each site and included electronic health record template letters to encourage communication about participating patients.

Fourth, there was clinician education. The educational materials consisted of a review of current practice guidelines, a review of evidence supporting the use of the recommended therapy groups, and practical advice on how to use the therapies in routine care. Education delivery included online videos and slide sets, local grand rounds lectures, and monthly conference calls with all sites to address barriers to care and clinical questions.

Fifth, audit and feedback of quality metrics were used. Each intervention clinic was provided a monthly report of all enrolled participants and whether each was prescribed the recommended therapies. These data were presented to the site for comparison with anonymized data from the other intervention sites (eFigure 1 in Supplement 2). Patient-level trackers allowed clinics to visualize participant progress at 3-month intervals using a color-coded system to denote recommended therapy status (prescribed, in discussion, or not prescribed) (eFigure 2 in Supplement 2).

Sixth, educational materials were provided to the participants. The educational materials included a fact sheet explaining the 3 recommended therapies, a medication passport noting which therapies they were taking and the reasons why or why not (eFigure 3 in Supplement 2), and a placemat designed to encourage adherence to the prescribed medications and healthy lifestyles (eFigure 4 in Supplement 2).

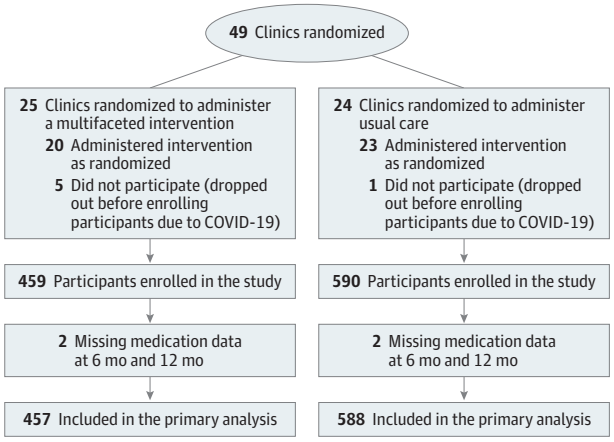
The 6 components were implemented after the sites were randomized. Prior to the site visit (in-person or virtual) by the trial trio, which occurred approximately 30 days to 60 days after site activation, the sites were asked to complete a strategic assessment to identify local barriers and were provided with current guidelines, online videos and slide sets, and educational materials for participants. In addition, the sites were encouraged to enroll at least 2 to 3 participants prior to the site visit to have real clinical cases available for discussion with the trial team.

Clinics in the usual care group were provided current clinical practice guidelines from the American College of Cardiology/American Heart Association and the American Diabetes Association on the management of type 2 diabetes and atherosclerotic cardiovascular disease.

Trial Outcomes

The primary outcome was the proportion of participants who were prescribed all 3 groups of recommended therapies (high-intensity statins, ACEIs or ARBs, and SGLT inhibitors and/or GLP-1RAs) at the last follow-up visit (composite medication score of 3 with 1 point allocated for each drug group). Treatment with high-intensity statins consisted of 40 mg/d to 80 mg/d of atorvastatin or 20 mg/d to 40 mg/d of rosuvastatin. Treatment with ACEIs or ARBs included angiotensin receptor-neprilysin inhibitors. Treatment with SGLT2 inhibitors and/or GLP-1RAs included those with proven cardiovascular efficacy (SGLT2 inhibitors: empagliflozin, dapagliflozin, or canagliflozin; GLP-1RAs: liraglutide, semaglutide, or dulaglutide). Because guidelines and statements from the American College of Cardiology/American Heart Association and the American Diabetes Association at trial initiation did not recommend these agents if the hemoglobin A_{1c} (glycated hemoglobin) level was less than 7%, those with a hemoglobin A_{1c} level less than 7% while taking metformin monotherapy were considered to have met this criterion. However, because statements and guidelines from the American College of Cardiology/American Heart Association and the American Diabetes Association changed during the trial, the prescription of SGLT2 inhibitors and/or GLP-1RAs was encouraged in all eligible participants, independent of hemoglobin A_{1c} level.

Figure 1. Recruitment and Randomization of Sites and Enrollment of Participants in the COORDINATE-Diabetes Cluster Randomized Clinical Trial



COORDINATE indicates Coordinating Cardiology Clinics Randomized Trial of Interventions to Improve Outcomes

Participants who developed allergies or intolerances to therapies during the trial were included. Prescription status was ascertained for each participant via examination of the electronic health record at 3-month intervals in the intervention group and at 6-month intervals in the usual care group (eMethods in Supplement 2). The primary outcome was assessed at the last follow-up visit, and was based on data from either the 6-month visit or the 12-month visit because the data at these visits were similarly collected in both groups. The last follow-up visit was originally planned to be at 12 months for all participants. However, due to the adverse effects from the COVID-19 pandemic on trial enrollment and conduct, the last follow-up visit was modified to be either at 6 months or at 12 months.

The secondary outcomes included the proportion of participants prescribed each recommended therapy and those with a composite medication score of 2 or greater. Additional secondary outcomes included assessments of blood pressure, hemoglobin A_{1c}, and low-density lipoprotein cholesterol (LDL-C). These data were ascertained from electronic health record data when available. A composite clinical outcome of time to first event of any death or hospitalization for myocardial infarction, stroke, decompensated heart failure, or urgent revascularization was assessed using both participant self-report and electronic health record review. All suspected clinical events underwent confirmation by site personnel.

Sample Size and Power Calculation

The trial was designed to randomize 46 clinics with an intended average enrollment of 30 participants per site, an intraclass correlation coefficient of 0.05, and a 2-sided type I error rate of .05, yielding 90% power to detect an absolute difference of 10% in the primary outcome over 12 months of follow-up. However, because of the lower than expected

enrollment due to the COVID-19 pandemic, the target number of sites was reduced to 42 and the average number of participants per site was reduced to 25 without any knowledge of the between-group outcome comparisons. This decreased the power to 85% to detect a 10% absolute difference in the primary outcome. The sample size and power were calculated using R function "n4props" in package "CRT Size" (R Foundation for Statistical Computing).[15,16]

Statistical Analyses

The primary outcome was analyzed using a mixed-effects, repeated-measures model with random intercepts for site to account for the clustering effect, an unstructured covariance for repeated measures over time, a treatment × time interaction term, and adjustment for prespecified baseline factors. To assess whether the effect of the intervention on the primary outcome differed by baseline composite medication score (and hence opportunity for improvement), we used a logistic regression model for the composite medication score at the last follow-up visit with random intercepts for site, risk adjustment, and testing for the interaction between the scores at baseline and after the intervention. Missing medication data were not imputed; the mixed-effects, repeated-measures model effectively accounts for missing and correlated data within participants.[17] The amount of missing data was less than 1.5% for the model covariates. Participants were analyzed by their enrollment group regardless of the actual treatment received.

Secondary outcomes were analyzed using similar methods as the primary outcome analysis to account for clustering. Physical assessments were analyzed using a multivariable, generalized, mixed-effects linear model with random intercepts for site to assess the effect of the intervention after adjustment for prespecified baseline factors among participants with measures at both baseline and at the 6-month and 12-month follow-up visits. Clinical event rates were estimated using Kaplan-Meier cumulative risk.[18] The clinical event outcome was analyzed using a Cox proportional hazards model with a shared frailty to account for the clustering effect and adjustment for prespecified baseline factors.[19]

A 2-sided $P = .05$ was considered significant. All statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc).

Results

Trial Sites and Participants

Between July 2019 and May 2022, 49 cardiology clinics (53% were in urban locations) were randomized; 20 of 25 clinics randomized to the intervention group enrolled participants and 23 of 24 clinics randomized to the usual care group enrolled participants, yielding a total of 43 enrolling sites (**Table 1**, Figure 1, and eFigure 5 and eTable 1 in Supplement 2). There were 459 participants (median, 24 [IQR, 12-35] participants per site) enrolled in the intervention group and 590 participants (median, 25 [IQR, 14-39] participants per site) enrolled in the usual care group. The most common reasons for clinic sites not participating after randomization were due to the COVID-19 pandemic, with clinic sites transitioning to virtual visits only, halting all research activities, or closing completely.

Table 1. Baseline Characteristics of the Clinic Trial Sites

Site characteristics[a]	Intervention (n = 25)	Usual care (n = 24)
No. participants enrolled, median (IQR)	18 (5-31)	24 (14-37)
Urban site, No. (%)	13 (52.0)	13 (54.2)
Academic site, No. (%)	7 (28.0)	8 (33.3)
Cardiology clinicians, median (IQR)	9 (5-16)	11 (9-31)
Baseline composite medication score, median (IQR)	1.6 (1.4-1.7)	1.4 (1.3-1.7)

[a] Presented for all randomized sites. Additional data on the sites that enrolled patients appear in eTable 1 in Supplement 2.

Of the 1049 participants who were enrolled, there were 338 women (32.2%), 173 Black participants (16.5%), 90 Hispanic participants (8.6%), 692 with Medicare coverage (67.4%), 107 with Medicaid coverage (10.4%), and had a median age of 70 years (**Table 2**). The 2 cluster randomized groups were well balanced across most characteristics. Participants in the intervention group at baseline were more frequently taking high-intensity statins compared with the usual care group (66.7% vs 58.3%), taking ACEIs or ARBs (75.2% vs 69.7%, respectively), and had a composite medication score of 2 (59.9% vs 52.0%). By design, none of the participants had a composite medication score of 3 at baseline.

Primary Outcome

The primary outcome analysis was based on 457 participants (99.6%) in the intervention group and 588 participants (99.7%) in the usual care group who had medication data at 6 months or 12 months. A total of 1021 participants (97.3%) had medication data at 12 months.

At the last follow-up visit, participants in the intervention group were more likely than those in the usual care group to be prescribed all 3 recommended, evidence-based therapy groups (high-intensity statins, ACEIs or ARBs, and SGLT inhibitors and/or GLP-1RAs) (173/457 [37.9%] vs 85/588 [14.5%], respectively, which is a difference of 23.4%; odds ratio [OR], 4.46 [95% CI, 2.55-7.80], $P < .001$) (**Table 3**). After adjustment for site and participant baseline characteristics, the intervention effect estimate was similar (adjusted OR, 4.38 [95% CI, 2.49-7.71]). There was no significant interaction ($P = .57$) between the treatment effect of the intervention and baseline composite medication score; thus, the effect of the intervention did not differ by composite medication score at baseline.

A depiction of changes in composite medication scores from baseline to the last follow-up visit, including both initiation and discontinuation of prescriptions by group, appears in **Figure 2** and the changes by baseline composite medication score appear in eTable 2 in Supplement 2. The intervention effect was evident at 6 months (155 of 456 participants in the intervention group [34.0%] vs 62 of 586 participants in the usual

Table 2. Baseline Characteristics of the Participants

Participant characteristics	Intervention (n = 459)	Usual care (n = 590)
Age, median (IQR), y	69 (63-76)	71 (64-77)
Sex, No. (%)		
Male	315 (68.6)	396 (67.1)
Female	144 (31.4)	194 (32.9)
Race, No. (%)[a,b]		
American Indian or Alaska Native	1 (0.2)	6 (1.0)
Asian	17 (3.7)	10 (1.7)
Black	79 (17.2)	94 (15.9)
White	324 (70.6)	480 (81.4)
Other[c]	23 (5.0)	3 (0.5)
Missing	15 (3.3)	1 (0.2)
Hispanic or Latinx ethnicity, No. (%)[a]	52 (11.3)	38 (6.4)
Had health insurance, No. (%)	448 (97.6)	578 (98.0)
Medicare	282 (62.9)	410 (70.9)
Private	151 (33.7)	200 (34.6)
Medicaid	53 (11.8)	54 (9.3)
Did not have health insurance, No. (%)	11 (2.4)	12 (2.0)
Disease history, No. (%)		
Atherosclerotic cardiovascular disease[b]	459 (100)	590 (100)
Coronary artery disease	402 (87.6)	529 (89.7)
Stroke or carotid artery disease	126 (27.5)	148 (25.1)
Peripheral artery disease	80 (17.4)	60 (10.2)
Hypertension	427 (93.0)	555 (94.1)
Hyperlipidemia	414 (90.2)	541 (91.7)
Heart failure	136 (29.6)	159 (26.9)
Atrial fibrillation	75 (16.3)	145 (24.6)
Charlson comorbidity modified index, No. (%)[d]		
1-2 (mild)	17 (3.7)	24 (4.1)
3-4 (moderate)	182 (39.7)	198 (33.6)
≥5 (severe)	260 (56.6)	368 (62.4)
Baseline vitals and laboratory values, median (IQR)		
Systolic blood pressure, mm Hg	130 (120-140) [n = 448]	130 (118-140) [n = 587]
Diastolic blood pressure, mm Hg	74 (68-80) [n = 448]	72 (64-80) [n = 587]
Hemoglobin A_{1c}, %	7.4 (6.7-8.5) [n = 392]	7.3 (6.5-8.1) [n = 462]
Low-density lipoprotein cholesterol, mg/dL	67 (51-85) [n = 373]	68 (53-86) [n = 441]
Baseline composite medication score and hemoglobin A_{1c} level, No. (%)		
0 points (not taking any of the recommended medications)	27 (5.9)	57 (9.7)
1 point		
Taking ACEIs or ARBs	89 (19.4)	128 (21.7)
Taking high-intensity statins	60 (13.1)	78 (13.2)
Taking metformin with a hemoglobin A_{1c} level <7%	8 (1.7)	20 (3.4)
2 points		
Taking high-intensity statins and ACEIs or ARBs	227 (49.5)	242 (41.0)
Taking ACEIs or ARBs and metformin with a hemoglobin A_{1c} level <7%	29 (6.3)	41 (6.9)
Taking high-intensity statins and metformin with a hemoglobin A_{1c} level <7%	19 (4.1)	24 (4.1)

Abbreviations: ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers.

SI conversion factor: To convert low-density lipoprotein cholesterol to mmol/L, multiply by 0.0259.

[a] Race and ethnicity were self-reported by the participant.

[b] May have included more than 1; categories do not sum.

[c] The electronic health record had "other" category; participants could select this category if the preferred race category was not listed.

[d] Defined as the sum of points assigned by (1) age (<50 years, 0 points; 50-59 years, 1 point; 60-69 years, 2 points; 70-79 years, 3 points; or ≥80 years, 4 points), (2) certain diseases: 1 point each for myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular accident (transient ischemic attack), dementia, connective tissue disease, peptic ulcer disease, mild liver disease, moderate to severe liver disease, or uncomplicated diabetes, and (3) other diseases: 2 points each for hemiplegia, kidney insufficiency, or cancer, leukemia, or localized tumor and 6 points each for metastatic solid tumor or HIV.

Table 3. Primary and Secondary Outcomes

	No. (%)		Unadjusted		Adjusted	
	Intervention (n = 457)	Usual care (n = 588)	OR (95% CI)[a]	*P* value	OR (95% CI)[b]	*P* value
Primary outcome						
Prescribed all 3 groups of recommended, evidence-based therapies[c]	173 (37.9)	85 (14.5)	4.46 (2.55-7.80)	<.001	4.38 (2.49-7.71)	<.001
Secondary outcomes						
Prescribed individual groups of recommended therapies						
High-intensity statins	323 (70.7)	334 (56.8)	1.78 (1.07-2.96)	.03	1.73 (1.06-2.83)	.03
ACEIs or ARBs[d]	372 (81.4)	402 (68.4)	1.91 (1.23-2.95)	.004	1.82 (1.14-2.91)	.01
SGLT2 inhibitors and/or GLP-1RAs	276 (60.4)	209 (35.5)	3.11 (2.10-4.59)	<.001	3.11 (2.08-4.64)	<.001
Prescribed ≥2 groups of recommended therapies	361 (79.0)	326 (55.4)	4.78 (2.71-8.44)	<.001	4.68 (2.58-8.51)	<.001
Prescribed all 3 groups of recommended therapies without metformin monotherapy with hemoglobin A_{1c} <7% option	142 (31.1)	50 (8.5)	6.77 (3.51-13.10)	<.001	6.90 (3.55-13.40)	<.001

Abbreviations: ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; GLP-1RAs, glucagon-like peptide 1 receptor agonists; OR, odds ratio; SGLT2, sodium-glucose cotransporter 2.

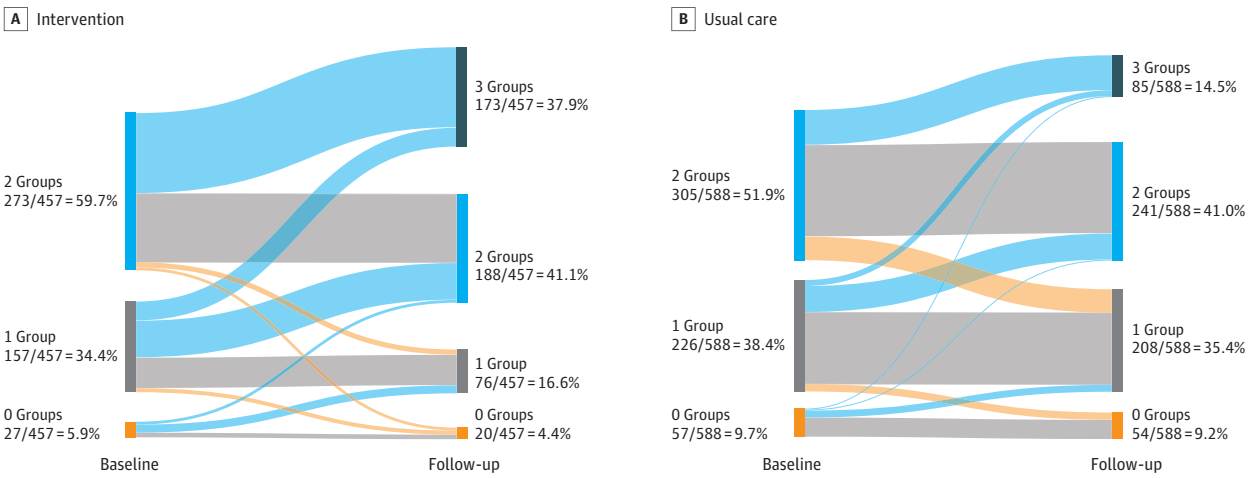
[a] Accounts for the clustering effect, site type (urban vs rural), baseline composite medication score, time, and time × treatment interaction.

[b] Accounts for both the clustering effect and potential confounders, including site type (urban vs rural), participant age, sex, race, baseline composite medication score, Charlson comorbidity index, baseline systolic blood pressure, baseline diastolic blood pressure, time, and time × treatment interaction.

[c] The therapies were high-intensity statins, ACEIs or ARBs, and SGLT2 inhibitors and/or GLP-1RAs (or hemoglobin A_{1c} <7% while taking metformin alone).

[d] A prescription for the angiotensin receptor–neprilysin inhibitor qualified as an ARB.

Figure 2. Comparison Between Composite Medication Scores at Baseline and at the Last Follow-up Visit



The groups were defined as 0, not taking any medication from the 3 recommended, evidence-based therapy groups (high-intensity statins, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and sodium-glucose cotransporter 2 inhibitors and/or glucagon-like peptide 1 receptor agonists); 1, taking medication from 1 of the recommended therapy groups; 2, taking medications from 2 of the recommended therapy groups; and 3, taking medications from all 3 of the recommended therapy groups. The last follow-up visit could have been at 6 months or 12 months.

care group [10.6%]; adjusted OR, 4.87 [95% CI, 2.71-8.76], *P* < .001), and persisted through 12 months (172/449 [38.3%] vs 85/572 [14.9%], respectively; adjusted OR, 3.94 [95% CI, 2.21-7.03], *P* < .001).

Results from the prespecified subgroup analyses appear in eFigure 6 in Supplement 2. In the sensitivity analyses, imputing missing composite scores as failures (n = 4) at the 12-month follow-up visit and using only data from the 6-month follow-up visit (n = 1042), the effect estimates did not differ from the primary outcome analysis (eTable 3 in Supplement 2). Participants were asked at the last follow-up visit if they were currently taking medications from all 3 of the recommended therapy groups (high-intensity statins, ACEIs or ARBs, and SGLT inhibitors and/or GLP-1RAs). Among the 241 participants across both groups who met the primary outcome by having prescriptions for all 3 groups of medications, and who also had participant-reported medication use data at the last follow-up visit, there was 89.2% agreement with participant-reported medication use.

Secondary Outcomes

Participants in the intervention group were more likely than those in the usual care group to be prescribed medications from each of the 3 recommended, evidence-based medication groups (Table 3 and eFigure 7 in Supplement 2). Use of high-intensity statins increased from 66.5% to 70.7% in the

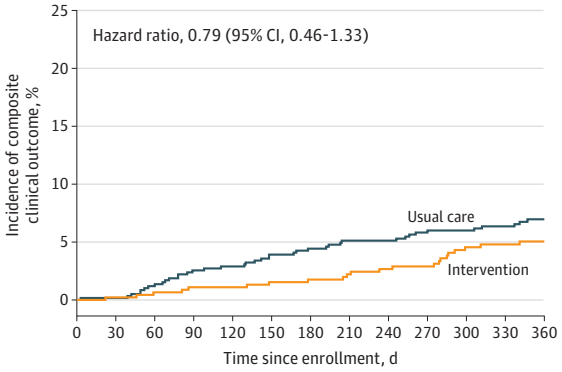
intervention group, but decreased from 58.2% to 56.8% in the usual care group (adjusted OR, 1.73 [95% CI, 1.06-2.83], *P* = .03). Use of ACEIs or ARBs increased from 75.1% to 81.4% in the intervention group, but decreased from 69.6% to 68.4% in the usual care group (adjusted OR, 1.82 [95% CI, 1.14-2.91], *P* = .01). Use of SGLT inhibitors and/or GLP-1RAs increased in the intervention group from 12.3% (reflecting those with hemoglobin A_{1c} <7% while taking metformin alone) to 60.4% vs from 14.5% to 35.5% in the usual care group (adjusted OR, 3.11 [95% CI, 2.08-4.64], *P* < .001). Participants in the intervention group were more frequently prescribed SGLT2 inhibitors compared with the usual care group (34.8% vs 10.9%) or GLP-1RAs (11.2% vs 4.9%, respectively). Few participants in either group were prescribed both SGLT2 inhibitors and GLP-1RAs (0.9% in the intervention group vs 0.7% in the usual care group).

Participants in the intervention group were also significantly more likely to have a composite medication score of at least 2 compared with the usual care group, and to have a composite medication score of 3 when the option of metformin monotherapy with hemoglobin A_{1c} level less than 7% was dropped (Table 3). All of these effects remained similar after adjustment for potential confounders. Participant-reported use of medications at the last follow-up visit was largely concordant with the prescription data. For high-intensity statins, 592 of 615 participants (96.3%) across both groups who had a prescription at the last follow-up visit also reported taking this medication. The concordance was similar with ACEIs or ARBs (717/732 [98.0%]) and SGLT inhibitors and/or GLP-1RAs (436/456 [95.6%]).

The intervention was not associated with measurable reductions in selected atherosclerotic cardiovascular disease risk factors, including systolic blood pressure (adjusted estimate of between-group difference, −2.0 mm Hg [95% CI, −4.3 to 0.4 mm Hg]), diastolic blood pressure (adjusted estimate of between-group difference, −0.4 mm Hg [95% CI, −1.8 to 1.1 mm Hg]), hemoglobin A_{1c} (adjusted estimate of between-group difference, −0.1% [95% CI, −0.3% to 0.3%]), and LDL-C (adjusted estimate of between-group difference, 0.6 mg/dL [95% CI, −5.2 to 6.5 mg/dL]) (eTable 4 in Supplement 2). Blood pressure assessments were available in 82.9% of participants, hemoglobin A_{1c} was available in 48.0%, and LDL-C was available in 43.6%.

Composite clinical events (all-cause death or hospitalization for myocardial infarction, stroke, decompensated heart failure, or urgent revascularization) occurred in 23 of 457 participants (5%) in the intervention group vs 40 of 588 participants (6.8%) in the usual care group (adjusted hazard ratio, 0.79 [95% CI, 0.46-1.33]) (**Figure 3**). Mortality occurred in 6 of 457 participants (1.3%) in the intervention group vs 16 of 588 participants (2.7%) in the usual care group (adjusted hazard ratio, 0.62 [95% CI, 0.24-1.60]).

Figure 3. Kaplan-Meier Cumulative Incidence of the Composite Secondary Clinical Outcome



No. at risk

Usual care	588	587	581	573	571	563	557	546	544	536	531	510	305
Intervention	457	456	453	451	449	447	441	432	427	418	399	381	301

The composite clinical outcome included the first event of death from any cause or hospitalization for myocardial infarction, stroke, decompensated heart failure, or urgent revascularization (coronary, peripheral, or carotid).

Discussion

In this cluster randomized clinical trial of cardiology clinics across the US, a multifaceted intervention aimed at identifying local challenges in prescribing, developing interdisciplinary care pathways, coordinating care between clinicians, educating clinicians about guideline recommendations, reporting real-time data back to clinic personnel, and providing educational materials for participants significantly increased the prescription of the 3 evidence-based therapy groups (high-intensity statins, ACEIs or ARBs, and SGLT2 inhibitors and/or GLP-1RAs) among individuals with type 2 diabetes and atherosclerotic cardiovascular disease.

The results from this trial have several important implications. First, usual dissemination of clinical outcomes evidence alone results in slow uptake of therapies. In a prior analysis of commercially insured individuals with type 2 diabetes and atherosclerotic cardiovascular disease, only 24.7% were taking high-intensity statins, 53.1% were taking ACEIs or ARBs, and only 2.7% of the eligible population were taking all 3 groups of medications (high-intensity statins, ACEIs or ARBs, and SGLT2 inhibitors and/or GLP-1RAs).[12] Similarly, an examination of electronic health record data of 12 large US health systems showed that of 320 000 individuals with type 2 diabetes and atherosclerotic cardiovascular disease, only 4.6% were taking medications in all 3 groups (high-intensity statins, ACEIs or ARBs, and SGLT2 inhibitors and/or GLP-1RAs) and 42.6% were taking none.[13] In the usual care group of the current cluster randomized clinical trial, only 14% of participants were taking recommended medications in all 3 groups (high-intensity statins, ACEIs or ARBs, and SGLT2 inhibitors and/or GLP-1RAs) at the last follow-up visit. This likely reflects an optimistic view of secular trends because site investigators had an interest in participating in a quality improvement program. An absolute increase of 23.4% in prescriptions for all 3 recommended therapies in the intervention group vs the usual care group, which was more than twice the improvement the trial was designed to detect, is clinically meaningful and, based on clinical trial evidence for

these therapies, should result in a substantial improvement in patient outcomes over time.

Second, this trial shows that while clinician behavior has historically proven difficult to change, an intervention with multiple synergistic components can have an effect on clinician prescribing patterns for evidence-based therapies. The intervention in this trial included 6 complementary components. Such multifaceted strategies are likely to be more effective than single-component strategies, as shown in previous trials[20] and summarized by the National Heart, Lung, and Blood Institute (NHLBI) Implementation Science Work Group.[21] Single-component interventions, such as elimination of out-of-pocket costs, have demonstrated real but modest improvements in adherence to prescribing of guideline-based medications.[22,23] Similarly, prompts through the electronic health record can influence prescribing behavior, but the effect may be modest[24,25] compared with that achieved by the multicomponent intervention in the current trial.

Third, even though many prior implementation strategies have been shown to be effective in single-system settings,[26,27] the strategy evaluated in the current trial was successful across multiple clinic sites in the US. This success may be related to the initial assessment of local barriers to delivering evidence-based care, an element that allowed tailoring of the intervention to the specific challenges faced at each clinic site. The NHLBI Implementation Science Work Group concluded that an initial assessment of local needs should anchor implementation efforts.[21] Furthermore, the focus on coordination of care between clinicians was an important component of the intervention in the current trial that may have bolstered its success across diverse settings. The current trial reinforces the potential of team-based care models and interdisciplinary approaches[28,29] to improve secondary prevention management in patients with type 2 diabetes and atherosclerotic cardiovascular disease.

In addition to the ability to tailor the intervention required for each clinic site, the intervention also was designed to be scalable. Moreover, the COVID-19 pandemic forced the intervention to become virtual and thus much less intensive than originally planned. Because the intervention was focused on modifying and improving clinical care as it was delivered, it allowed flexibility and easier adaptation to challenges as clinicians responded to the pandemic.

Limitations

There are several limitations to this trial. First, the trial included selected clinic sites and participants who may not be representative of the broader US patient population. However, the geographic diversity of the clinic sites and the diversity of the participants enrolled should, at least in part, mitigate this concern.

Second, we were only able to collect prescription data in the enrolled cohort and not in the entire patient population at each site, so the potential effect of the intervention on patients who were not enrolled could not be assessed. Sites were randomized before they recruited patients for participant inclusion, which may have influenced the patients selected. At baseline, prescription of individual recommended therapies was different between groups, though this did not have an effect on the primary outcome (because no participants were prescribed all 3 recommended therapies at baseline), and was adjusted for in the prespecified analyses for the secondary outcomes.

Third, the trial was designed to evaluate the effect of the intervention on medication prescription patterns, and it was not designed or powered to detect differences in clinical events.

Fourth, complete biomarker data were not available to accurately determine the effect of the intervention on LDL-C and hemoglobin A_{1c} levels, and therefore these markers cannot be used to estimate adherence to or the effect of the therapies.

Fifth, pharmacy fill data were not available to assess actual adherence to the medications by participants. However, the fact that prescriptions were largely assessed 1 year after enrollment reduces the chance of capture of prescriptions that participants were not taking because medication reconciliation is a standard clinical procedure.

Conclusions

A coordinated, multifaceted intervention increased prescription of 3 groups of evidence-based therapies in adults with type 2 diabetes and atherosclerotic cardiovascular disease.

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