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Second-year results from CINEMA: A novel, patient-centered, team-based intervention for patients with Type 2 diabetes or prediabetes at high cardiovascular risk

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ABSTRACT

Background: The care for patients with type 2 diabetes mellitus (T2DM) necessitates a multidisciplinary team approach to reduce cardiovascular (CV) risk but implementation of effective integrated strategies has been limited.

Methods and Results: We report 2-year results from a patient-centered, team-based intervention called CINEMA at University Hospitals Cleveland Medical Center. Patients with T2DM or prediabetes at high-risk for CV events, including those with established atherosclerotic CVD, elevated coronary artery calcium score ≥100, chronic heart failure with reduced ejection fraction, chronic kidney disease (CKD) stages 2–4, and/or prevalent metabolic syndrome were included. From May 2020 through September 2022, 426 patients were enrolled in the CINEMA program. A total of 227 (54%) completed ≥1 follow-up visit after an initial baseline visit with median (IQR) follow-up time 4 [3–7] months with maximum follow-up time 19 months. Mean age was 60 years, 47 % were women, and 37 % were Black and 85% had prevalent T2DM, 48 % had established ASCVD, 29% had chronic HF, 27% had CKD and mean baseline 10-year ASCVD risk estimate was 25.1 %; baseline use of a SGLT2i or GLP-1RA was 21 % and 18 %, respectively. Patients had significant reductions from baseline in body weight (-5.5 lbs), body mass index (-0.9 kg/m^2), systolic (-3.6 mmHg) and diastolic (-1.2 mmHg) blood pressure, Hb A1c (-0.5 %), total (-10.7 mg/dL) and low-density lipoprotein (-9.0 mg/dL) cholesterol, and triglycerides (-13.5 mg/dL) ($p<0.05$ for all). Absolute 10-year predicted ASCVD risk decreased by ~2.4 % ($p<0.001$) with the intervention. In addition, rates of guideline-directed cardiometabolic medication prescriptions significantly increased during follow-up with the most substantive changes seen in rates of SGLT2i and GLP-1RA use which approximately tripled from baseline (21 % to 57 % for SGLT2i and 18 % to 65 % for GLP-1RA, $p<0.001$ for both).

Conclusions: The CINEMA program, an integrated, patient-centered, team-based intervention for patients with T2DM or prediabetes at high risk for cardiovascular disease has continued to demonstrate effectiveness with significant improvements in ASCVD risk factors and improved use of evidence-based therapies. Successful implementation and dissemination of this care delivery paradigm remains a key priority.

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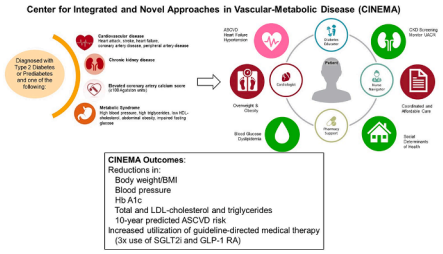

Central Illustration. The Center for Integrated and Novel Approaches in Vascular-Metabolic Disease (CINEMA) Program.
The CINEMA program in the Harrington Heart and Vascular Institute at University Hospitals Cleveland Medical Center is an integrated, patient-centered, team-based intervention for patients with type 2 diabetes and prediabetes at high risk for cardiovascular disease events aimed to improve cardiovascular risk factors and increase utilization of evidence-based therapies to eliminate defects in diabetes care in this high-risk patient population. ASCVD: atherosclerotic cardiovascular disease; BMI: body mass index; CKD: chronic kidney disease; HDL: high-density lipoprotein; LDL: low-density lipoprotein; SGLT2i: sodium-glucose cotransporter-2 inhibitor; GLP1-RA: glucagon-like peptide 1 receptor agonist.

1. Introduction

Management of type 2 diabetes mellitus (T2DM) and its cardiovascular consequences requires a multidisciplinary team approach with a high degree of engagement, education, and collaboration. Historically, it has been demonstrated that adopting such an approach may decrease the risk of cardiovascular and microvascular events by 50 % [1,2]. However, the impact of such team-based approaches in the era of pharmacological therapies such as sodium-glucose cotransporter 2 inhibitor (SGLT2i) and glucagon-like peptide-1 receptor agonist (GLP-1RA) therapy, which are known to not only reduce cardiovascular (CV) events, but also positively impact obesity and chronic kidney disease, is not well studied. The high degree of comorbid high-risk obesity and multi-organ involvement in T2DM and evolving complexities of treatment, necessitate a high level of engagement and coordinated care, that is often either not provided or when provided, results in delayed, fragmented, high-cost, sub-optimal care from both the patient and provider perspectives.

The Center for Integrated and Novel Approaches in Vascular-Metabolic Disease (CINEMA) program in the Harrington Heart and Vascular Institute at University Hospitals (UH) Cleveland Medical Center is an integrated, patient-centered, team-based intervention for patients with T2DM and prediabetes at high risk for CV disease events aimed to improve CV risk factors and increase utilization of evidence-based therapies to eliminate defects in diabetes care in this high-risk patient population. Previously, we presented the year 1 data from a team-based program for T2D at elevated cardiovascular risk, where we found that participation in the program was associated with significant improvements in cardiometabolic risk factors as well as an increase in the prescription rates of SGLT2i and GLP-1RA when indicated [3]. Here, we present the two-year results from the CINEMA program including an in-depth evaluation of lessons learned from the implementation and expansion of the program.

2. Methods

2.1. Programmatic structure

The CINEMA program was founded at University Hospitals, a large healthcare network in Ohio that spans across 11 hospitals and 18 medical centers in the region. The structure of the CINEMA program has been previously reported [3]. The CINEMA team consists of a program administrator; five cardiologists with a special interest and training in the management T2DM, prevention and vascular medicine; two nurse coordinators; a registered dietitian; two certified diabetes care and education specialists (CDCES) to target diet and lifestyle and provide medical nutrition therapy; and a dedicated pharmacist to educate and manage pharmacological therapies. The CINEMA approach mandates careful communication and coordination of all care and visits as needed with primary care and with endocrinology, nephrology, and bariatric surgery providers, to ensure optimization of schedules to reduce the patient's burden, but these providers are not routinely included in CINEMA care visits.

2.2. Patient selection

Upon initiation of the program in May 2020, there were 544,007 patients in the University Hospitals Health System Accountable Care Organization, among whom 57,979 (10.7 %) had diabetes. Of those, 48.7 % had either prevalent cardiovascular disease or chronic kidney disease, with only 15.4 % currently prescribed a SGLT2i or GLP-1 RA. Patients were enrolled in the program through referrals from other medical providers or through self-referral (from the website or webinar, for example); no identification through the electronic health record for direct recruitment to patients was performed. In the first year, most referrals came internally from other cardiology providers (53 %). Other referral sources included internal/family medicine practitioners (26 %), bariatric surgeons (6 %), and "other," including self-referrals (12 %); few referrals came from other sources, such as endocrinology and nephrology. Subsequently, in the second year, the referral patterns shifted such that the majority of referrals came from internal and family medicine (41 %) or cardiology (44 %) with 9 % from endocrinology. Initially, the program was offered at 2 health centers (central and west). Subsequently, 2 additional locations were offered that were strategically located in the Cleveland metro area (central, east, west, and southeast) to provide easier and expanded access for patients.

During the first year of the program, inclusion criteria were restricted to patients with T2DM (defined by self- or physician-report, prevalent medical care for T2DM, and/or glycosylated hemoglobin (Hb A1c) $\geq$6.5 %) and, as defined by the 2021 ADA Professional Practice Committee pathway [4], those with established or at high-risk for atherosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD), and/or chronic heart failure with reduced ejection fraction (HFrEF). These indicators of risk were used for patient selection and inclusion since ASCVD risk assessment using the Pooled Cohort Equations is not routinely performed in this population with type 2 diabetes and prevalent ASCVD.

Due to high demand and patient interest, we broadened our criteria in the second year of the program to also include patients with prediabetes (defined as Hb A1c $\geq$5.7 % but <6.5 %) and those with T2DM or prediabetes and concomitant metabolic syndrome and/or a coronary artery calcium score of $\geq$100 Agatston units. Patients with type 1 diabetes were excluded from the CINEMA program. The CINEMA registry was approved by the University Hospitals Cleveland Medical Center Institutional Review Board, and all participants in the registry provided written informed consent.

2.3. Visit schedule and data collection

The CINEMA program is structured around 2–3 visits with additional follow-up as needed. Unlike the traditional model of care, where the patient travels to different providers in several locations over multiple time points to receive a comprehensive evaluation, CINEMA is unique in that the care team comes to the patient via an in-person or virtual platform in a single initial visit, that attempts to address all aspects of CV and T2DM care. This integrated, team-based approach hybridizes expertise that has been traditionally siloed, by creating a single access point in space and time to engage the patient in his/her own environment (during virtual visits).

All patients undergo standardized assessment of body weight, height,

and laboratory testing including chemistries, lipids, Hb A1c, and urine-albumin creatinine ratio (UACR) using standard assays. Weight, height, and blood pressure are measured, using standard clinic equipment and body mass index is calculated. Laboratory studies are performed for the initial visit and for each subsequent follow-up visit. Baseline laboratory studies are defined as those completed within 3 months prior to or during the initial visit. Follow-up laboratory studies are defined as those completed at the follow-up visit or up to 3 months after the follow-up visit. If laboratory tests are already available within this time frame, they are not repeated. Duplication of testing is minimized since all orders reside in a single electronic health record system and duplicate orders are not performed. Providers seek to determine the patient's overall risk for future CV events and formulate an optimal evidence-based T2DM lifestyle and pharmacologic strategy for reducing CV (including heart failure) and renal events by weighing several patient-specific factors. The team then works with the patient's insurance, pharmacy, and assistance programs to obtain the medication in the most affordable way. UH pharmacy services provides comprehensive management of most medications including home delivery and education around medications including injectables such as GLP-1RA. This includes working around insurance barriers and identification of prescription assistance for patients unable to otherwise obtain these medications. This allows for a high degree of initiation of novel agents and continuation of these therapies in the CINEMA program.

Subsequently, the nurse navigator and CDCES provide continued support, coordination of care, education - including weekly "podcast"-type educational sessions with video broadcast over a virtual meeting platform and peer-led support groups, and additional resources between physician visits. Serious adverse events leading to hospitalization related to the clinical interventions in the program are surveyed. Patients return ~3 months later with repeat clinical and laboratory testing to discuss the patient's progress, review interval medical events, and discuss laboratory results. The patient maintains contact every 3–6 months with the nurse coordinator, dietitian/CDCES, and physician using a combination of telephone and/or a virtual video telehealth platform to ensure continued support, engagement, and metabolic recovery. Patients continue their routine follow-up with primary care and specialty physicians and CINEMA physicians and support staff partner closely with primary care providers to ensure continuity of care to prevent fragmentation and overcome barriers to communication.

2.4. Statistical analysis

Descriptive statistics for the CINEMA patient population were calculated and reported at baseline for those with single and multiple follow-up visits. 10-year predicted atherosclerotic cardiovascular disease (ASCVD) risk was calculated using the Pooled Cohort Equations risk calculator. Baseline differences between groups were assessed using a Wilcoxon-signed rank sum test as several factors were not normally distributed. Normality of biomarkers for analysis was tested and correction for non-normal distribution was performed by applying a Box-Cox transformation on each biomarker or by applying a multilevel generalized linear model that does not assume normality of the data. Changes in biomarkers/risk factor levels and changes in guideline-based medication prescriptions were modeled over time for their longitudinal effects as a function of follow-up visits. Modeling was done by fitting either a Linear Mixed Effects Model (LMEM) or a Generalized Linear Mixed Effects Model (GLMEM), as deemed appropriate, to account for patient random effects as well as longitudinal effects. Analysis of changes in risk factors was also stratified between those with single vs multiple follow-up visits, and by baseline diagnosis of ASCVD, T2DM, CKD, HFrEF, or heart failure with preserved ejection fraction (HFpEF). We assumed no interaction effects, and one random intercept effect per patient. Model specification included adjustment for program week achieved, age, sex, and race/ethnicity to account for confounding factors. For all estimated effects and comparisons, we report individual parameter estimates and 95 % confidence interval. A p-value $p < 0.05$ was considered statistically significant. Statistical analyses were completed using the R package.

3. Results

From May 2020 to September 2022, 426 patients were enrolled in the CINEMA program (Table 1). The mean age was 60 years, 47 % were women, and 37 % were Black. Among those, 85 % had prevalent T2DM, 48 % had established ASCVD, 29 % had chronic HF, and 27 % had CKD. Baseline use of a SGLT2i or GLP-1RA was 21 % and 18 %, respectively. Mean baseline 10-year ASCVD risk estimate for the cohort was 25.1 %. A total of 227 (54 %) completed ≥1 follow-up visit after an initial baseline visit. Differences in baseline characteristics between those with and without a CINEMA follow-up visit were negligible (Table 1).

Median (interquartile range [IQR]) follow-up time in CINEMA was 4 [3–7] months with maximum follow-up time 19 months. ASCVD risk factors generally improved over the follow-up period with the CINEMA intervention. Using a linear mixed effects model adjusted for age, sex, and race/ethnicity, we found significant reductions from baseline in body weight, body mass index, systolic and diastolic blood pressure, Hb A1c, total and low-density lipoprotein cholesterol, and triglycerides ($p<0.05$ for all, Table 2 and Fig. 1). In stratified analyses, findings were similar when the model was additionally adjusted by stratification of several factors: attendance at a single CINEMA follow-up visit or multiple visits (Table S1), prevalent baseline ASCVD (Table S2), prevalent T2DM (Table S3), prevalent CKD (Table S4), or prevalent heart failure (Tables S5 and S6 for HFrEF and HFpEF, respectively). Several reductions in ASCVD risk factors were quantitatively greater among those with prevalent cardiometabolic conditions compared with those without these conditions. These included greater reductions in total- and LDL-cholesterol among those with prevalent ASCVD (p-interaction<0.05 for both) and greater reduction in UACR among those with prevalent CKD (p-interaction<0.001). Absolute 10-year predicted ASCVD risk decreased by ~2.4 % ($p<0.001$) with the intervention. There were no serious adverse events leading to hospitalization related to the clinical interventions in the program.

Among eligible CINEMA patients, rates of guideline-directed cardiometabolic medication prescriptions significantly increased during follow-up (Fig. 2) with the most substantive changes seen in rates of SGLT2i and GLP-1RA use which approximately tripled from baseline (21 % to 57 % for SGLT2i, $p<0.001$; 18 % to 65 % for GLP-1RA, $p<0.001$). Reasons for not initiating a SGLT2i or GLP-1RA included a current prescription at the time of enrollment, contraindication to the medication, and inability to obtain the medication due to lack of insurance coverage/expense. Prescription use rates of additional medications that also increased during the CINEMA intervention included statins ($p<0.001$), renin-angiotensin-aldosterone blockers (including angiotensin converting enzyme inhibitors [ACEi], angiotensin receptor blockers [ARB], angiotensin receptor-neprilysin inhibitors [ARNI], $p<0.001$, and mineralocorticoid receptor antagonists [MRA], $p = 0.003$), metformin ($p = 0.009$), and additional lipid-lowering therapies such as ezetimibe, fenofibrate, and proprotein convertase subtilisin/kexin (PCSK9) inhibitors, $p<0.001$. There was minimal change in insulin use and no significant change in dipeptidyl peptidase 4 inhibitors (DPP4i), sulfonylureas, or thiazolidinediones use (Fig. 2 and Table S7). Dual use of an SGLT2i and GLP-1RA increased from 3.0 % to 37.2 % and triple use of ACEi/ARB/ARNI + statin + SGLT2i + GLP-1RA increased from 2.6 % to 21.6 % between baseline and follow-up ($p<0.001$ for both, Fig. 3 and Table S8).

4. Discussion

The CINEMA program, an integrated, patient-centered, team-based intervention for patients with T2DM or prediabetes at high risk for cardiovascular disease, in its second year, has continued to demonstrate

Table 1
Demographic and Medical Characteristics of CINEMA Patients at Baseline, Overall and Stratified by Follow-Up Status.

	Overall (N = 426)	Follow-Up (N = 231)	No Follow-Up (N = 195)	P-value
Age, years	59.70 (± 11.90)	59.76 (± 11.58)	59.64 (± 12.30)	0.73
Race				0.32
White	246 (57.75%)	128 (55.41%)	118 (60.51%)	
Black	157 (36.85%)	90 (38.96%)	67 (34.36%)	
Other	17 (3.99%)	10 (4.33%)	7 (3.59%)	
Unknown	6 (1.41%)	3 (1.30%)	3 (1.54%)	
Female	200 (46.95%)	111 (48.05%)	89 (45.64%)	0.69
Medical History				
Coronary Artery Disease	204 (47.89%)	109 (47.19%)	95 (48.72%)	0.51
Type 2 Diabetes Mellitus	363 (85.21%)	194 (83.98%)	169 (86.67%)	0.17
Hypertension	343 (80.52%)	195 (84.42%)	148 (75.90%)	0.06
Hyperlipidemia	372 (87.32%)	210 (90.91%)	162 (83.08%)	0.03
Heart Failure Reduced Ejection Fraction	65 (15.26%)	33 (14.29%)	32 (16.41%)	0.45
Heart Failure Preserved Ejection Fraction	60 (14.08%)	31 (13.42%)	29 (14.87%)	0.49
Chronic Kidney Disease	113 (26.53%)	65 (28.14%)	48 (24.62%)	0.40
Current or Former Smoking	222 (52.11%)	118 (51.08%)	104 (53.33%)	0.71
Risk Factor Levels				
Weight, lbs.	233.0 (± 57.47)	234.0 (± 51.67)	231.9 (± 63.79)	0.44
Body mass index, kg/m^2	36.31 (± 8.525)	36.64 (± 8.179)	35.91 (± 8.928)	0.29
Systolic blood pressure, mmHg	133.9 (± 19.45)	135.4 (± 18.03)	132.2 (± 20.91)	0.04
Diastolic blood pressure, mmHg	78.55 (± 11.06)	79.39 (± 10.91)	77.58 (± 11.18)	0.07
Hb A1c,%	7.839 (± 1.958)	7.891 (± 1.903)	7.780 (± 2.023)	0.31
Total cholesterol, mg/dL	161.2 (± 48.77)	163.0 (± 48.93)	159.1 (± 48.65)	0.59
HDL-cholesterol, mg/dL	43.57 (± 12.95)	43.92 (± 12.45)	43.16 (± 13.54)	0.39
LDL-cholesterol, mg/dL	86.10 (± 39.96)	88.36 (± 40.25)	83.39 (± 39.57)	0.26
Triglycerides, mg/dL	172.1 (± 142.5)	169.2 (± 148.0)	175.7 (± 136.0)	0.52
UACR, mg/g	117.6 (± 285.5)	103.2 (± 192.5)	134.3 (± 365.6)	0.72
10-yr ASCVD risk (%)	25.1 (± 15.9)	26.6 (± 18.7)	23.4 (± 15.1)	0.35
Medication Use				
Statin	315 (73.94%)	170 (73.59%)	145 (74.36%)	0.51
ACE/ARB/Entresto	274 (64.32%)	156 (67.53%)	118 (60.51%)	0.19
SGLT-2i	87 (20.42%)	48 (20.78%)	39 (20.00%)	0.54
GLP-1 RA	77 (18.08%)	41 (17.75%)	36 (18.46%)	0.54
DPP4 Inhibitors	26 (6.10%)	13 (5.63%)	13 (6.67%)	0.49
Metformin	208 (48.83%)	113 (48.92%)	95 (48.72%)	0.55
Insulin	138 (32.39%)	83 (35.93%)	55 (28.21%)	0.13
Beta Blockers	200 (46.95%)	112 (48.48%)	88 (45.13%)	0.44
MRA	70 (16.43%)	35 (15.15%)	35 (17.95%)	0.40
Ezetimibe/Fenofibrate/PCSK9 Inhibitor	50 (11.74%)	29 (12.55%)	21 (10.77%)	0.47
Sulfonylurea/Thiazolidinedione	73 (17.14%)	37 (16.02%)	36 (18.46%)	0.43

Data represent mean (± SD) or proportion (%), as appropriate. ACE/ARB/Entresto: Angiotensin-converting enzyme/Angiotensin receptor blockers/Angiotensin Receptor Neprilysin Inhibitor; SGLT2i: Sodium-glucose Cotransporter-2 Inhibitors; GLP1-RA: Glucagon-like peptide 1 receptor agonists; DPP4I: Dipeptidyl peptidase 4 Inhibitor; BB: β-receptor blocker; MRA: Mineralocorticoid receptor antagonist; SU: Sulfonylureas; HbA1c: glycosylated hemoglobin; HDL: high-density lipoprotein; LDL: low-density lipoprotein; PCSK9: Proprotein convertase subtilisin/kexin type 9; UACR: urine albumin creatinine ratio; ASCVD: atherosclerotic cardiovascular disease.

Table 2
Results for key ASCVD risk factors among eligible patients participating in the CINEMA.

Outcome	Estimates	SE	95% CI	p-value
Body weight, lbs.	−5.52	0.54	−6.59 – −4.45	<0.001
Body mass index, kg/m^2	−0.86	0.09	−1.05 – −0.68	<0.001
Systolic blood pressure, mm Hg	−3.62	0.79	−5.18 – −2.07	<0.001
Diastolic blood pressure, mm Hg	−1.18	0.47	−2.11 – −0.25	0.013
HbA1c,%	−0.47	0.06	−0.59 – −0.35	<0.001
Total cholesterol, mg/dL	−10.65	1.96	−14.50 – −6.79	<0.001
HDL cholesterol, mg/dL	0.34	0.34	−0.34 – 1.01	0.32
LDL cholesterol, mg/dL	−9.03	1.64	−12.26 – −5.80	<0.001
Triglycerides, mg/dL	−13.45	4.49	−22.29 – −4.61	0.003
UACR, mg/g	−8.25	7.83	−23.79 – 7.29	0.29

The model is adjusted for age, gender, and race/ethnicity; SE: standard error; 95% CI: confidence interval. Linear Mixed Effect Model (LMEM) model p-values are for trends of change over time. HbA1c: glycosylated hemoglobin; HDL: high-density lipoprotein; LDL: low-density lipoprotein; UACR: urine albumin creatinine ratio.

effectiveness in risk factor reduction and evidenced-based, guideline-directed lifestyle and pharmacological management of high risk cardiometabolic disease (Central Illustration). The current report confirms our previous findings in those with T2DM and CVD and extends the evidence to patients with prediabetes, metabolic syndrome, and those with subclinical ASCVD (i.e., elevated coronary artery calcium). We found that the CINEMA intervention was associated with significant improvements in multiple ASCVD risk factors including body weight, body mass index, systolic and diastolic blood pressure, Hb A1c, total and low-density lipoprotein cholesterol, and triglycerides. Results were consistent regardless of baseline ASCVD, T2DM, CKD, or heart failure status, suggesting generalizability across the spectrum of cardiometabolic conditions. We also found that the CINEMA intervention was associated with improved use of evidence-based therapies, such as SGLT2i, GLP-1RA, with prescription rates increasing approximately 3-fold between baseline and follow-up visits. We also confirmed that cardiometabolic risk factor improvements generally continued with longer duration of program participation, and we previously demonstrated that these results were seen even among patients under the care of an endocrinologist [3].

The cardiometabolic care team model concept for aggressive secondary cardiovascular risk reduction in patients with T2DM and ASCVD has been gaining recognition in recent years. However, implementation of the care model in clinical practice has been sparse. Since our initial CINEMA report, several others from around the United States have been published detailing successes in implementation of coordinated care models for ASCVD risk reduction in patients with T2DM. Initial reports from the Cardiometabolic Center Alliance site St. Luke's Mid-America Heart Institute demonstrated that the use of guideline-directed medical therapies for eligible patients (N = 129) was improved using the cardiometabolic clinic model compared with usual care, including higher rates of SGLT2i and/or GLP-1RA use(5). Moreover, a cluster-randomized clinical trial (COORDINATE-Diabetes) showed that a

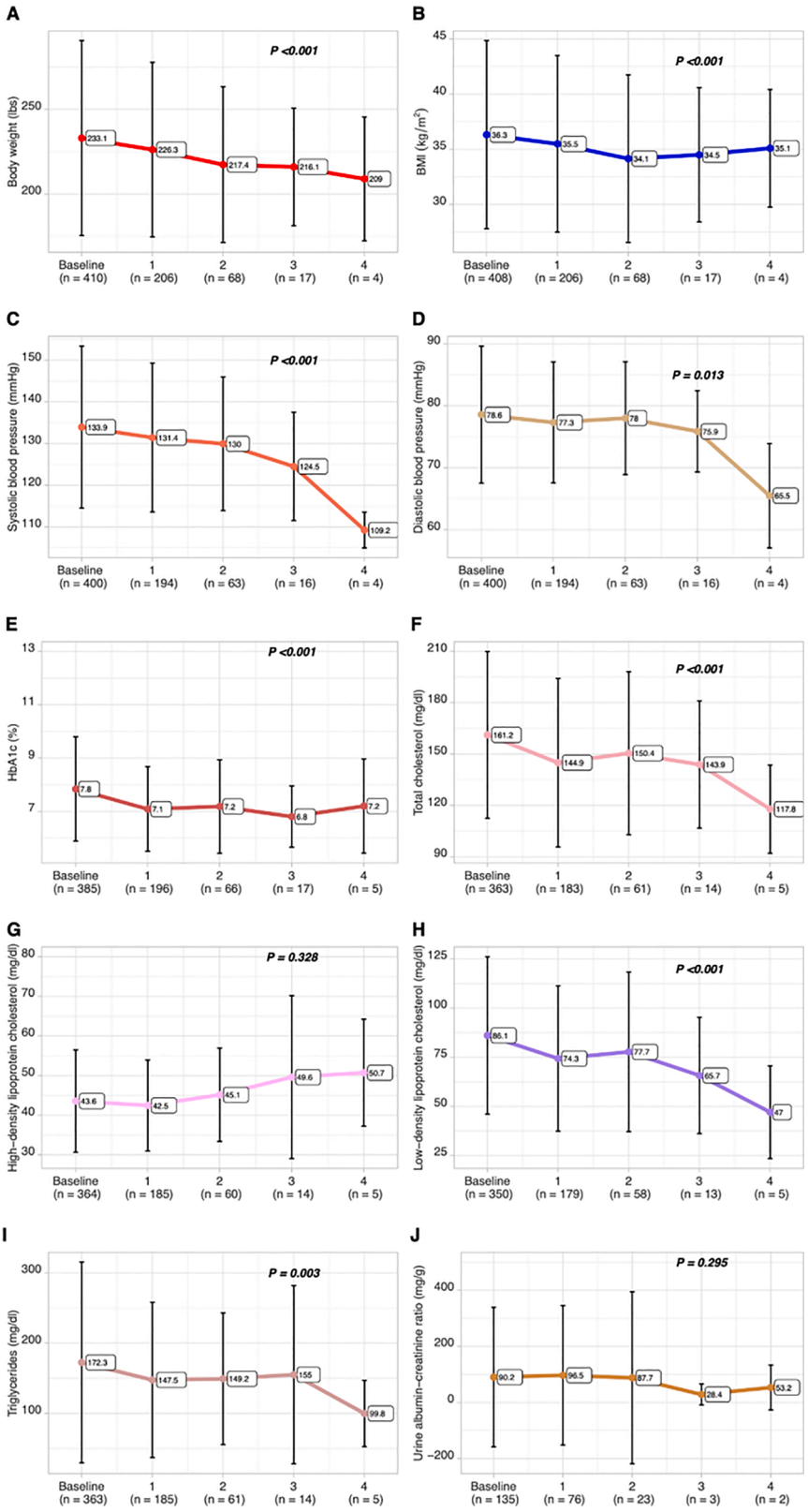

Fig. 1. Changes in key ASCVD risk factors over time among eligible patients participating in the CINEMA program.
The model is adjusted for age, gender, and race/ethnicity; SE: standard error; CI: 95% confidence interval. Linear Mixed Effect Model model p-values are for trends of change over time. A: Body weight, B: BMI: body mass index; C: Systolic blood pressure; D: Diastolic blood pressure; E: Hb A1c: glycosylated hemoglobin; F: Total cholesterol; G: High-density lipoprotein cholesterol; H: Low-density lipoprotein cholesterol; I: Triglycerides; J: Urine albumin-creatinine ratio.

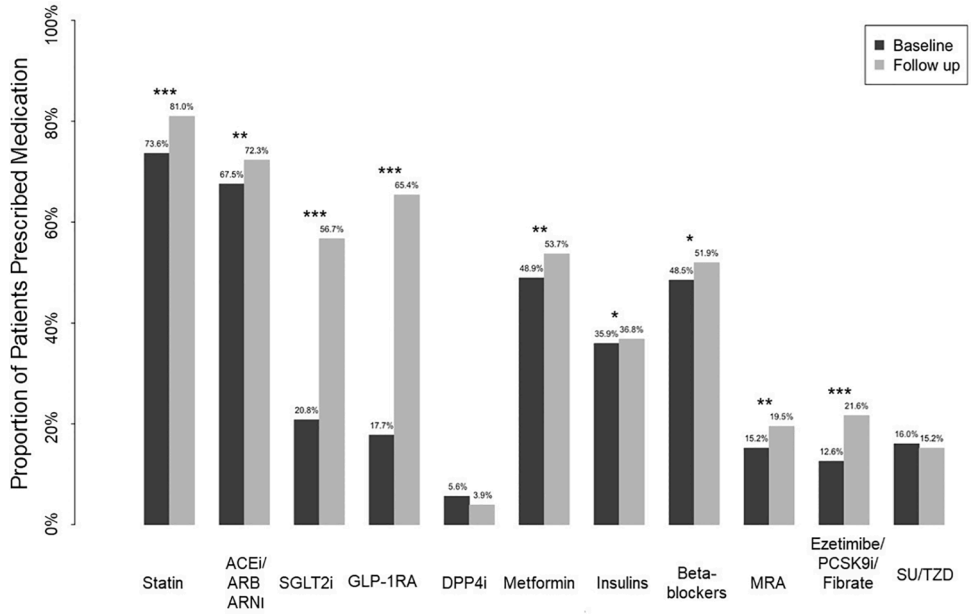

Fig. 2. Changes in rates of guideline-directed cardiometabolic medication prescriptions in CINEMA between baseline and follow-up in eligible patients.
Comparisons between baseline and follow up were assessed using a generalized linear mixed effect model (GLMEM); p-values are for trends of change in medications prescriptions over time from baseline to follow up. * = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$. ACEi/ARB/ARNI: angiotensin-converting enzyme inhibitor/angiotensin receptor blocker/angiotensin receptor neprilysin inhibitor; SGLT2i: sodium-glucose cotransporter-2 inhibitor; GLP1-RA: glucagon-like peptide 1 receptor agonist; DPP4i: dipeptidyl peptidase 4 inhibitor; MRA: mineralocorticoid receptor antagonist; PCSK9i: proprotein convertase subtilisin/kexin type 9 inhibitor; SU: sulfonylurea; TZD: thiazolidinedione.

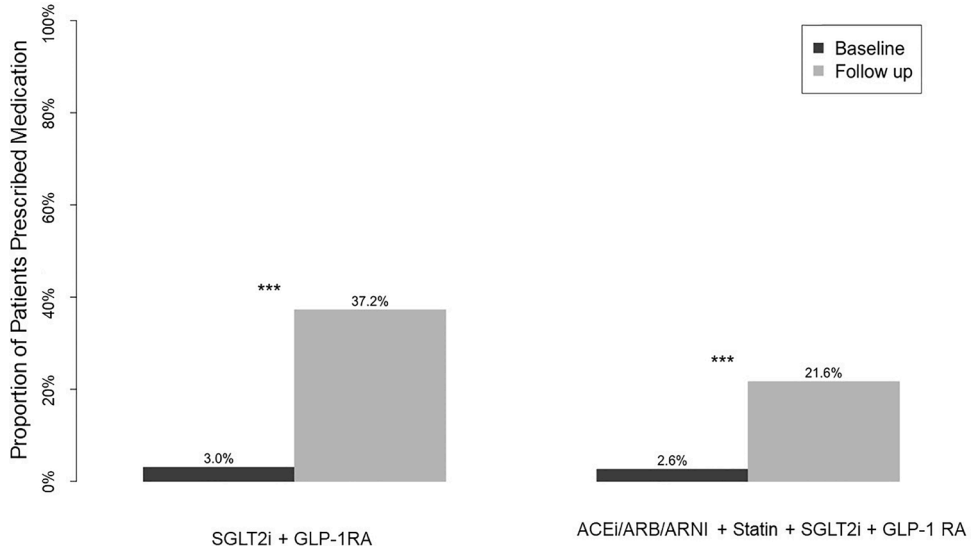

Fig. 3. Changes in rates of guideline-directed cardiometabolic medication bundles in CINEMA between baseline and follow-up in eligible patients.
Comparisons between baseline and follow up were assessed using a generalized linear mixed effect model (GLMEM); p-values are for trends of change in medications prescriptions over time from baseline to follow up. *** = $p < 0.001$. ACEi/ARB/ARNI: angiotensin-converting enzyme inhibitor/angiotensin receptor blocker/angiotensin receptor neprilysin inhibitor; SGLT2i: sodium-glucose cotransporter-2 inhibitor; GLP1-RA: glucagon-like peptide 1 receptor agonist.

coordinated, multifaceted intervention for patients with T2DM and ASCVD led to a 4-fold increase in prescription rates of guideline-directed medical therapies (triple goal of high-intensity statins, ACE or ARB, SGLT2i and/or GLP-1RA) [6] . However, unlike our findings in the CINEMA program, the intervention in COORDINATE-Diabetes was not associated with changes in ASCVD risk factors. To potentially explain the differences seen between these two interventions, it is possible that the COORDINATE intervention was successful in increasing prescription rates but not actual utilization of the medication, especially over the longer term, leading to discontinuation of therapies and no change in ASCVD risk factor levels. This is a known limitation of the study as 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.

Apart from clinical trials, real-world observational data for utilization of evidence-based therapies is less encouraging. A study of ~400,000 patients from 26 major health systems across the US showed that less than 1 in 5 individuals with T2DM and ASCVD are prescribed guideline-endorsed first-line therapies (e.g., SGLT2i and GLP-1RA) with proven CVD risk reduction [7]. It also showed significant disparities

with African American males having as much as 30% lower rates of utilization compared with other demographic groups. The GOULD study prospectively followed 1590 patients with T2DM and ASCVD from 107 US sites between 2016 and 2018 [8]. Overall, only 11% of patients received comprehensive optimal medical therapy (defined as high-intensity lipid-lowering (high-intensity statin, any statin + ezetimibe, proprotein convertase subtilisin/kexin type 9 inhibitor), antithrombotic (antiplatelet or anticoagulant), angiotensin-converting enzyme-inhibitor/angiotensin II receptor blocker/angiotensin receptor neprilysin inhibitor (ACE-I/ARB/ARNI) (excluding glomerular filtration rate [GFR] $<$ 30 ml/min/1.73m^2) and SGLT2i/ GLP-1 RA (excluding GFR $<$ 30 ml/min/1.73m^2 and type 1 diabetes). Patients treated by cardiologists (vs. non-cardiologists) were more likely to be on high-intensity lipid lowering, but less likely to be on an SGLT2i/GLP-1RA, and thus had lower rates of composite optimal medical therapy. Similarly, data from the Diabetes Collaborative Registry including >1 million outpatients from 391 US sites, showed modest improvements in use of SGLT2i and GLP-1RA (7.3 % in 2013 to 28.8 % in 2019) but unexpectedly lower use in patients with ASCVD, heart failure, and CKD, highlighting a treatment-risk paradox [9].

In light of these data, challenges remain for successful implementation of a multifaceted, integrated, patient-centered, team-based intervention for patients with T2DM or prediabetes and high cardiovascular risk. Although several prior implementation strategies have been shown to be effective in single-system settings, scalability and dissemination of programs like CINEMA to other health systems and settings may prove difficult due to lack of system-cohesiveness, infrastructure, and funding. Coordination of care is fundamental to the success of programs such as CINEMA and is facilitated by a strong network of outpatient sites, an integrated electronic medical record, and value-based care through the accountable care organization. Furthermore, incentives to join CINEMA, such as no-copay visits for employees at UH and institutional-led patient assistance programs, increase patient attendance and adherence to lifestyle and pharmacologic therapies. As discussed in our prior report, we acknowledge the concern from a primary care perspective that the specialist-driven cardiometabolic clinic care model may devalue or otherwise further fragment the role of primary care providers in managing comorbid T2DM and ASCVD. To address this concern, we work closely with primary care colleagues and seek to directly address the fragmentation of care and multiple health conditions by working as a partnership. A key element of this partnership is to improve ASCVD prevention by increasing utilization of evidence-based therapies for intensification of care, which appears to be both efficacious and cost-effective [10]. As our and others' experiences demonstrate, use rates of guideline-directed medical therapies in patients with T2DM and ASCVD continues to be relatively low, despite routine primary and endocrinology specialist care, demonstrating an unmet need for aggressive prevention which cardiometabolic specialty programs can provide. As our results demonstrate, CV risk factors levels can be further improved using our cardiometabolic clinic model. Although the cost-effectiveness of our approach cannot be evaluated at this early stage, we hope to provide cost-effectiveness data in future reports with increased program size and duration.

Although we have demonstrated robust improvements in ASCVD risk factors and use of evidence-based therapies for patients with T2DM/ prediabetes and elevated ASCVD risk, we recognize that this report of our CINEMA program has limitations. First, our intervention was implemented in a single academic health system and, as such, our results may not be generalizable to other health settings. Further research into similar programs across diverse geographic areas is warranted. Second, our follow-up duration is relatively brief and therefore we are unable to comment on associations with event-related outcomes such as myocardial infarction, stroke, or CV death in these patients. Third, the rate of retention in the program was relatively modest. The reasons underlying this observation are likely multifactorial and may include "doctor fatigue", access issues with prescribed medications, in addition to others. We did not systematically assess or survey other providers to obtain their feedback about the program goals and outcomes. In order to address these questions, we plan to implement a more systematic implementation science approach to obtaining patient and provider feedback going forward which is ongoing with a program called CINEMA Studio, a patient-led advisory group, aimed at iterative program quality improvement. Finally, since these data represent the initial experience of the program, we are unable to provide a full implementation evaluation of the program using rigorous implementation science assessment tools, an evaluation of cost-effectiveness, or comparison to control patients whom are eligible but do not receive the CINEMA intervention. These methods and further evaluation of outcomes over longer-term follow-up are planned to be added in subsequent evaluations of the program.

In conclusion, the CINEMA program, an integrated, patient-centered, team-based intervention for patients with T2DM or prediabetes at high risk for cardiovascular disease, in its second year, has continued to demonstrate effectiveness with significant improvements in ASCVD risk factors and improved use of evidence-based therapies, such as SGLT2i, GLP-1RA. This novel care paradigm for high-risk patients continues to demonstrate effectiveness in addressing and eliminating defects in cardiometabolic care. Successful implementation and dissemination of this care delivery paradigm remains a key priority.

CRediT authorship contribution statement

Ian J. Neeland: Conceptualization, Methodology, Data curation, Writing – original draft, Writing – review & editing. **Ala' Arafah:** Data curation, Writing – original draft, Writing – review & editing. **Brendan Bourges-Sevenier:** Writing – original draft, Writing – review & editing. **Jean-Eudes Dazard:** Writing – original draft, Writing – review & editing. **Zainab Albar:** Writing – original draft, Writing – review & editing. **Zoe Landskroner:** Writing – review & editing. **Nour Tashtish:** Data curation, Writing – review & editing. **Elke Eaton:** Writing – review & editing. **Janice Friswold:** Writing – review & editing. **Jodie Porges:** Writing – review & editing. **Matthew Nennstiel:** Writing – review & editing. **Amanda Davies:** Writing – review & editing. **Sara Rahmani:** Writing – review & editing. **Quiana S. Howard:** Writing – review & editing. **Katherine Forrest:** Writing – review & editing. **Claire Sullivan:** Writing – review & editing. **Lloyd Greene:** Writing – review & editing. **Sadeer G. Al-Kindi:** Conceptualization, Methodology, Writing – review & editing. **Sanjay Rajagopalan:** Conceptualization, Methodology, Writing – review & editing.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Ian Neeland reports a relationship with Boehringer Ingelheim GmbH that includes: consulting or advisory and speaking and lecture fees. Ian Neeland reports a relationship with Eli Lilly and Company that includes: consulting or advisory and speaking and lecture fees. Ian Neeland reports a relationship with Bayer AG that includes: consulting or advisory and speaking and lecture fees. Ian Neeland reports a relationship with AMRA that includes: consulting or advisory. Sanjay Rajagopalan reports a relationship with Novo Nordisk Inc that includes: consulting or advisory. Sanjay Rajagopalan reports a relationship with Bayer AG that includes: consulting or advisory.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2023.100630.

References

[1] Gaede P, Vedel P, Larsen N, Jensen GVH, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med 2003 Jan 30;348(5):383–93.

[2] https://www.cdc.gov/diabetes/library/spotlights/diabetes-facts-stats.html.

[3] Neeland IJ, Al-Kindi SG, Tashtish N, Eaton E, Friswold J, Rahmani S, et al. Lessons learned from a patient-centered, team-based intervention for patients with Type 2 Diabetes at high cardiovascular risk: year 1 results from the CINEMA program. J Am Heart Assoc 2022 Aug 2;11(15):e024482.

[4] Association AD. 9. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes—2021. Diabetes Care [Internet] 2021 Jan 1;44 (Supplement_1):S111–24. https://doi.org/10.2337/dc21-S009 [cited 2023 Jun 6] Available from:.

[5] Thomas M, Magwire M, Gosch K, Sammour Y, Mehta R, O'Keefe J, et al. Cardiometabolic center of excellence: a novel care delivery model for secondary prevention of cardiovascular disease in Type 2 Diabetes. Circ Cardiovasc Qual Outcomes 2021;14(10). Oct.

[6] Pagidipati NJ, Nelson AJ, Kaltenbach LA, Leyva M, McGuire DK, Pop-Busui R, et al. Coordinated care to optimize cardiovascular preventive therapies in Type 2 diabetes. JAMA 2023;329(15):1261. Apr 18.

[7] Al-Kindi SG, SE Janus, Neeland IJ, Rajagopalan S. Contemporary utilization of GLP1 receptor agonists and SGLT2 inhibitors in patients with diagnosed type 2 diabetes and cardiovascular disease in the United States. J Diabetes Complications 2022;36(7):108224. Jul.

[8] Arnold SV, de Lemos JA, Zheng L, Rosenson RS, Ballantyne CM, Alam S, et al. Use of optimal medical therapy in patients with diabetes and atherosclerotic cardiovascular disease: insights from a prospective longitudinal cohort study. Diabetes Obes Metab 2023;25(6):1750–7. Jun.

[9] Arnold SV, Gosch K, Kosiborod M, Wong ND, Sperling LS, Newman JD, et al. Contemporary use of cardiovascular risk reduction strategies in type 2 diabetes. Insights from the diabetes collaborative registry. Am Heart J 2023;263:104–11. May 8.

[10] Pawaskar M, Bilir SP, Kowal S, Li Q, Weiss T, Davies G. Cost-effectiveness of intensification with SGLT2 inhibitors for type 2 diabetes. Am J Manag Care 2021; 27(8):e269–77. Aug 1.