

Biomedical outcomes and cardiovascular risks in Chinese adults with type 2 diabetes in the metabolic management center program: A longitudinal comparative study

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Keywords

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ABSTRACT

Aims: To assess the extent to which biomedical outcomes and cardiovascular risk profile were improved in the management of Chinese patients with type 2 diabetes enrolled in the metabolic management center (MMC) program.

Materials and Methods: We performed propensity score matching of diabetic patients in the MMC program for at least 12 months to those with diabetes under usual primary care, based on age, sex, fasting plasma glucose (FPG) level, and diabetes duration. Difference-in-difference analysis was conducted to compare changes in biomedical outcomes, attainment of treatment targets, and cardiovascular disease (CVD) risk reduction.

Results: Of 557 pairs of diabetic patients matched 1:1 ($n = 1,114$), the MMC cohort exhibited greater improvements in FPG (-0.84 mmol/L, 95% confidence interval [CI] -1.22 to -0.46 , $P < 0.001$), diastolic blood pressure [BP] (-2.08 mmHg, 95%CI -3.21 to -0.94 , $P < 0.001$), body mass index [BMI] (-0.29 kg/m², 95%CI -0.51 to -0.07 , $P = 0.009$), low-density lipoprotein cholesterol (0.13 mmol/L, 95%CI 0.04 – 0.23 , $P = 0.008$), high-density lipoprotein cholesterol (0.05 mmol/L, 95%CI 0.01 – 0.08 , $P = 0.017$), and 10-year CVD risk (Framingham CVD risk, -0.94% , 95%CI -1.71 to -0.17 , $P = 0.017$; atherosclerotic CVD risk, -0.77% , 95%CI -1.34 to -0.20 , $P = 0.009$) when compared to the usual primary care cohort after adjustment for confounders. More patients in the MMC cohort achieved treatment targets with lifestyle modifications than their counterparts under primary care.

Conclusions: Enrolment in the MMC program appears promising in the management of FPG, BP, BMI, lifestyle, and CVD risk in diabetic patients, suggesting the necessity of incorporating the MMC program into routine primary care.

INTRODUCTION

Diabetes is a prevalent metabolic disorder characterized by hyperglycemia, resulting from a clustering of both genetic and environmental risk factors¹. The prevalence data from the

WHO Global Health Observatory showed that 11.2% of adults in China were affected by diabetes in 2022², and the number is projected to reach 12.5% by 2045³. The rising tide of diabetes, along with its associated macrovascular (e.g., hypertension, coronary artery disease, and stroke) and microvascular complications (e.g., retinopathy and nephropathy), as well as increased

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risk of cancer attributable to diabetes, imposes a significant economic burden on both healthcare systems and patients^{4–8}. Diabetes-related healthcare costs in China amounted to 165 billion purchasing-power parity-adjusted dollars, representing a significant public health challenge⁹.

The Chinese government has launched a publicly funded program to deliver the national basic public health (BPH) service package since 2009¹⁰. This is a nationwide standard package of primary care services delivered by community health centers for all citizens¹¹, in particular for hypertensives, type 2 diabetics, and older adults who have a complex care need for health risk screening, individualized health education, regular check-ups, and follow-up evaluation¹². This aims to help address the gaps in diabetes care through a systematic preventive approach with a comprehensive management of body mass index (BMI), blood pressure (BP), lipid profile, and lifestyles, on top of the clinical focus on achieving glycemic control targets^{13,14}. Despite the paradigm shift in diabetes management from tertiary care to primary care providers, nationwide data in China revealed low achievement of clinical targets in adults with self-reported diabetes¹⁵. Provider-level barriers such as a shortage in primary care professionals, lack of coordinated care across clinical settings, and inadequate communication between physicians and patients, are often associated with suboptimal control of diabetes in routine clinical practice, which necessitate quality improvement strategies¹⁶.

An innovative approach is to develop technology competency to allow for remote monitoring and patient empowerment to improve health outcomes beyond glycemic control in the management of diabetes¹⁷. The national metabolic management center (MMC) program, initiated by the Chinese Medical Doctor Association in 2016, was designed as a 'one-stop-center delivering a standardized model' approach. Patients with type 2 diabetes (T2D) referred from primary care to the MMC program are offered one-stop care that encompasses registration, testing, evaluation, prescriptions, and health education¹⁸, with the potential to overcome barriers embedded in traditional specialty-based clinical settings. Multi-functional examination equipment is used in the MMC program to meet patients' need for one-stop hospital services, thus streamlining the screening process for diabetic complications and alleviating the treatment burden. The use of electronic medical record system and advanced Internet of Things (IoT) technology also enables the delivery of a wide spectrum of out-of-hospital services, for example, medication reminders, doctor-patient communication, revisit appointments, and so forth, to facilitate daily management of diabetes. The MMC innovation is anticipated to optimize diabetes care following standardized procedures in disease management.

In the real-world settings, evidence on the effectiveness of the MMC program in Chinese patients with diabetes is largely lacking. This study aimed to assess the extent to which health outcomes with respect to biomedical parameters and

cardiovascular risk profile were improved in the management of patients with T2D in the MMC program.

MATERIALS AND METHODS

Study design

This is a longitudinal comparative study of biomedical outcomes, achievement of treatment targets, and estimated 10-year cardiovascular disease (CVD) risk reduction in patients with T2D enrolled in the MMC program on top of usual primary care, compared to their counterparts with T2D under usual primary care. The usual primary care was provided by community health centers, including free-of-charge annual check-up and general health education in the national context of public health service delivery in China¹².

Setting and data source

The MMC program has been implemented at a tertiary-level hospital in Guangzhou, China, in January 2019. The MMC management team was composed of specialists from endocrinology and cardiovascular departments of the hospital, where a standardized procedure was implemented for patients diagnosed with T2D. At the initial clinical encounter, patients were guided by clinical staff to complete a series of evaluation. First, a patient account was registered, with information drawn from a questionnaire survey on patients' demographic information, medical history, and self-management practice. Second, an onsite health examination (diabetes, lipid metabolism, cardiovascular conditions, and the function of vital organs including both liver and kidney) was conducted. Third, patients attended a 60 min diabetes education session, during which, patients were instructed to use the MMC Butler mobile application for diabetes self-management. Fourth, individualized treatment plans were discussed with patients based on check-up results. Patients were scheduled to have follow-up visits at the MMC encounter every 3 months to receive care following the aforementioned standardized procedure. Examinations and laboratory tests were all performed at the MMC center. During the follow-up interval period, domiciliary blood glucose control was monitored by the management team and personalized feedback were provided via the MMC mobile application. Computerized routine data of the MMC cohort patients were retrieved from the MMC standardized data management system.

The source population of the usual primary care cohort were patients with T2D living in the same neighborhood, who were regular users of primary care but were not program participants of the MMC. In contrast to the MMC 'one-stop center' approach, services delivered across diverse specialty settings are not integrated in the usual primary care context. Thus, patients with diabetic complications that require specialist care may often need to attend different departments with multiple hospital visits for various examinations and repeated investigations. Computerized routine data of primary care were retrieved from an information platform where health records were

documented electronically by healthcare practitioners at community health centers.

Participants and sample size

The eligibility criteria of study participants were as follows: (1) aged 18 years and older; (2) service users of primary care; (3) having a clinical diagnosis of T2D¹⁹; and (4) with no CVD complications at baseline. Patients with missing data of variables at baseline and at 12-month follow-up were excluded from the analysis. A total of 1,269 patients enrolled in the MMC program since January 2019, of whom 585 were eligible for matching. A control cohort of T2D patients under usual primary care were propensity-score matched on baseline characteristics using 1:1 nearest-neighbor matching, with calipers of width equal to 0.2 of the standard deviation of the logit of the propensity score²⁰, to account for selection bias and baseline differences between MMC and non-MMC patients in age, sex, FPG levels, and duration of diabetes. Baseline data of the usual primary care cohort were derived from annual check-up in 2019 or 2020, whichever is earlier, and patients' outcomes were assessed at 12 months.

A sample size calculation was performed to ensure a sufficient number of patients included in the analysis, with conservative estimates based on previous studies^{21,22}. We aimed to detect a minimum relative difference of 5% in the proportion of T2D patients achieving glycemic control targets between the MMC cohort and the usual primary care cohort at 12-month follow-up. Based on a closed-cohort study design, a minimum of 652 patients were needed (i.e., 326 patients per cohort) using PASS 2021 software, with a two-sided 5% significance level and 90% power²². The final sample included a total of 1,114 patients, that is, 557 patients in MMC and usual primary care cohorts, respectively. Unmatched subjects were excluded from the analysis (Figure S1).

Study variables and measurements

The primary outcome was the change in FPG at 12 months. Secondary outcomes were changes in other biomedical parameters including BP, BMI, lipid profile, and CVD risk reduction. Changes in biomedical outcomes were assessed by mean values and by the proportions of patients who achieved treatment targets in FPG (<7 mmol/L), systolic/diastolic blood pressure (SBP/DBP, <130/80 mmHg), BMI (<24 kg/m²), total cholesterol (TC, <4.5 mmol/L), triglyceride (TG, <1.7 mmol/L), low-density lipoprotein cholesterol (LDL-C, <2.6 mmol/L), and high-density lipoprotein cholesterol (HDL-C, >1.0 mmol/L for men and >1.3 mmol/L for women), according to the Chinese National Guidelines for the Prevention and Control of Diabetes in Primary Care²³. BMI was calculated as body weight (in kg) divided by height squared (in m²). Demographic information, clinical parameters, medical history, and treatment modalities were retrieved from computerized MMC data management system (for MMC cohort) and national BPH information platform (for usual primary care cohort). The estimated 10-year CVD

risk was calculated from Framingham risk equations for total CVD risk²⁴, and from the risk assessment equations for atherosclerotic cardiovascular disease (ASCVD) risk²⁵. We used baseline age to take into account the age effect on CVD risk estimation at both baseline and 12 months.

Statistical analysis

Descriptive statistics were presented as mean \pm standard deviation (SD) or *n* (percentage) for continuous and categorical variables, respectively. The two-sample *t* test or the chi-square test, where appropriate, was used for MMC vs usual primary care group comparisons at baseline. We conducted paired *t* test to compare within-group differences in biomedical measurements between baseline and 12 months. The McNemar test was employed to compare differences in paired proportions of patients achieving treatment targets between baseline and 12 months. We adopted a difference-in-difference approach to compare between-group changes in biomedical outcomes, achievement of treatment targets, and CVD risk reduction. Further, generalized linear mixed models were conducted for comparison after adjustments were made for confounders. Model 1 was adjusted for demographic characteristics and lifestyle at baseline and 12 months. Model 2 was further adjusted for outcome measurements at baseline. Variable selection was determined based on our previous knowledge while taking into account the availability and completeness of data captured in the real-world setting. All *P* values were two-sided, with a significance level set at <0.05. Analyses were performed with SAS (version 9.4; SAS Institute Inc, Cary, United States) and R (version 4.0.2; Core Team, Vienna, Austria).

RESULTS

Baseline characteristics of participants

The propensity score matching resulted in the selection of 557 pairs of T2D patients strictly matched 1:1 (*n* = 1,114) with no statistically significant differences in all parameters considered for the propensity score, that is, age, sex, FPG value, and duration of diabetes between MMC and usual primary care cohorts (all *P* > 0.10). The two cohorts demonstrated similar SBP/DBP levels and proportion of patients reaching BP targets and had comparable proportions of smokers and drinkers (Table 1). The MMC cohort had a better lipid profile but lower proportions meeting targets for FPG and BP. The estimated 10-year Framingham CVD risk and ASCVD risk were higher in patients under usual primary care.

Changes in biomedical outcomes

Over 12 months follow-up, we observed significant reduction on FPG levels (-0.73 ± 3.98 mmol/L, *P* < 0.01), DBP (-2.58 ± 11.58 mmHg, *P* < 0.01), BMI (-0.24 ± 2.20 kg/m², *P* < 0.05), TC (-0.14 ± 1.43 mmol/L, *P* < 0.05) relative to baseline, while patients under usual primary care had significant reductions on LDL-C (-0.01 ± 0.79 mmol/L, *P* < 0.01) and HDL-C (-0.05 ± 0.31 mmol/L, *P* < 0.01) compared with

Table 1 | Baseline characteristics of the MMC and usual primary care cohort patients

| Variables | Mean \pm SD or <i>n</i> (%) | | <i>P</i> |
|--------------------------------------|-------------------------------|---------------------------------|----------|
| | MMC (<i>N</i> = 557) | Usual care (<i>N</i> = 557) | |
| Demographics | | | |
| Age | 59.91 \pm 8.32 | 59.41 \pm 9.97 | 0.363 |
| Sex | 311 (55.83) | 319 (57.27) | 0.629 |
| Smokers | 106 (19.03) | 94 (16.88) | 0.349 |
| Drinkers | 105 (18.85) | 82 (14.72) | 0.065 |
| Clinical characteristics | | | |
| FPG (mmol/L) | 7.91 \pm 3.60 | 7.64 \pm 3.21 | 0.191 |
| SBP (mmHg) | 133.20 \pm 16.64 | 132.70 \pm 17.64 | 0.631 |
| DBP (mmHg) | 78.70 \pm 9.82 | 78.57 \pm 9.70 | 0.826 |
| BMI (kg/m ²) | 25.10 \pm 3.67 | 24.96 \pm 3.42 | 0.518 |
| TC (mmol/L) | 5.19 \pm 1.37 | 5.50 \pm 1.38 | <0.001 |
| TG (mmol/L) | 2.03 \pm 1.57 | 2.23 \pm 1.95 | 0.050 |
| LDL-C (mmol/L) | 2.82 \pm 0.97 | 3.15 \pm 0.97 | <0.001 |
| HDL-C (mmol/L) | 1.55 \pm 0.46 | 1.40 \pm 0.41 | <0.001 |
| Duration of diabetes (months) | 76.02 \pm 78.27 | 78.32 \pm 68.71 | 0.603 |
| Achievement of treatment target | | | |
| FPG <7 mmol/L | 272 (48.83) | 334 (59.96) | <0.001 |
| SBP/DBP < 130/80 mmHg | 179 (32.14) | 214 (38.42) | 0.028 |
| BMI < 24 kg/m ² | 221 (39.68) | 231 (41.47) | 0.542 |
| TC <4.5 mmol/L | 170 (30.52) | 133 (23.88) | 0.013 |
| TG <1.7 mmol/L | 314 (56.37) | 270 (48.47) | 0.008 |
| LDL-C < 2.6 mmol/L | 233 (41.83) | 160 (28.73) | <0.001 |
| HDL-C > 1.0/1.3 mmol/L for men/women | 462 (82.94) | 392 (70.38) | <0.001 |
| Estimated CVD risk | | | |
| 10-year Framingham CVD risk | 8.82 \pm 7.11 | 10.06 \pm 8.89 | 0.010 |
| 10-year ASCVD risk | 7.42 \pm 6.26 | 8.65 \pm 8.33 | 0.005 |

ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MMC, metabolic management center; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol; TG, triglyceride.

baseline (Table 2). The difference-in-difference analysis showed that the MMC cohort experienced greater improvements in FPG (-0.84 mmol/L, 95% confidence interval [CI] -1.22 to -0.46 , $P < 0.001$), DBP (-2.08 mmHg, 95%CI -3.21 to -0.94 , $P < 0.001$), BMI (-0.29 kg/m², 95%CI -0.51 to -0.07 , $P = 0.009$), LDL-C (0.13 mmol/L, 95%CI 0.04 – 0.23 , $P = 0.008$), and HDL-C (0.05 mmol/L, 95%CI 0.01 – 0.08 , $P = 0.017$) when compared to the usual primary care cohort after adjustment for confounders (Table 3).

Changes in treatment modalities and lifestyle

The proportions of patients on oral antidiabetic drugs (OAD) and on insulin remained relatively stable in both cohorts

Table 2 | Paired differences between baseline and 12 months follow-up in each cohort

| Variables | Mean \pm SD or % | |
|--|---------------------------|---------------------------------|
| | MMC (<i>N</i> = 557) | Usual care (<i>N</i> = 557) |
| Biomedical parameters | | |
| FPG (mmol/L) | $-0.73 \pm 3.98^{**}$ | 0.11 ± 3.64 |
| SBP (mmHg) | -1.16 ± 18.71 | -1.24 ± 17.58 |
| DBP (mmHg) | $-2.58 \pm 11.58^{**}$ | -0.50 ± 10.24 |
| BMI (kg/m ²) | $-0.24 \pm 2.20^*$ | 0.05 ± 1.59 |
| TC (mmol/L) | $-0.14 \pm 1.43^*$ | -0.07 ± 1.01 |
| TG (mmol/L) | -0.09 ± 1.37 | -0.08 ± 1.32 |
| LDL-C (mmol/L) | 0.03 ± 0.94 | $-0.10 \pm 0.79^{**}$ |
| HDL-C (mmol/L) | -0.01 ± 0.38 | $-0.05 \pm 0.31^{**}$ |
| Achievement of treatment target | | |
| FPG <7 mmol/L | 5.75 (0.31, 11.18)* | -5.39 (-10.39 , 0.38)* |
| SBP/DBP < 130/80 mmHg | 6.46 (1.54, 11.39)* | -2.33 (-7.34 , 2.68) |
| BMI < 24 kg/m ² | 3.05 (0.02, 6.09)* | 0.90 (-1.61 , 3.41) |
| TC <4.5 mmol/L | 1.97 (-2.43 , 6.38) | 1.80 (-1.39 , 4.98) |
| TG <1.7 mmol/L | -1.97 (-6.41 , 2.46) | 3.23 (-0.10 , 6.56) |
| LDL-C < 2.6 mmol/L | -1.26 (-5.75 , 3.23) | 7.72 (3.97, 11.47)** |
| HDL-C > 1.0/1.3 mmol/L for men/women | -1.80 (-5.48 , 1.89) | -3.23 (-6.60 , 0.13) |
| Estimated CVD risk | | |
| 10-year Framingham CVD risk | -0.40 ± 5.57 | $0.54 \pm 5.61^*$ |
| 10-year ASCVD risk | -0.17 ± 3.53 | $0.60 \pm 3.65^{**}$ |

* $P < 0.05$. ** $P < 0.01$. ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MMC, metabolic management center; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol; TG, triglyceride.

between baseline and 12 months, although a greater proportion of MMC patients had insulin therapy (Figure 1). We observed a significant reduction in the proportion of smokers (19.03% vs 7.18%, $P < 0.001$) and drinkers (18.85% vs 5.03%, $P < 0.001$) among T2D patients enrolled in the MMC program at 12 months. Likewise, smoking (16.88% vs 14.72%, $P = 0.034$) and drinking (14.72% vs 10.59%, $P < 0.001$) prevalence declined in T2D patients under usual primary care over a 12-month period, but with a slight attenuation of the magnitude of reduction (Figure 1 and Table S1).

Achievement of treatment targets

Compared to baseline, there were increased patients achieving treatment targets with respect to the control of FPG (5.75%,

Table 3 | Changes in biomedical outcomes and cardiovascular risks between the MMC and usual primary care cohorts at 12 months

| Variables | Unadjusted D-in-D Estimates (95% CI) | <i>P</i> | Model 1 | <i>P</i> | Model 2 | <i>P</i> |
|--|--------------------------------------|----------|-----------------------|----------|-----------------------|----------|
| Biomedical parameters | | | | | | |
| FPG (mmol/L) | −0.84 (−1.28, −0.40) | <0.001 | −0.84 (−1.27, −0.42) | <0.001 | −0.84 (−1.22, −0.46) | <0.001 |
| SBP (mmHg) | 0.08 (−2.44, 2.59) | 0.953 | 0.08 (−2.41, 2.56) | 0.953 | 0.07 (−1.84, 1.99) | 0.940 |
| DBP (mmHg) | −2.08 (−3.51, −0.65) | 0.004 | −2.08 (−3.50, −0.65) | 0.004 | −2.08 (−3.21, −0.94) | <0.001 |
| BMI (kg/m ²) | −0.29 (−0.78, 0.20) | 0.245 | −0.29 (−0.78, 0.20) | 0.244 | −0.29 (−0.51, −0.07) | 0.009 |
| TC (mmol/L) | −0.07 (−0.27, 0.13) | 0.469 | −0.07 (−0.27, 0.12) | 0.466 | −0.07 (−0.21, 0.06) | 0.290 |
| TG (mmol/L) | −0.01 (−0.25, 0.24) | 0.954 | −0.01 (−0.25, 0.24) | 0.954 | −0.01 (−0.16, 0.14) | 0.925 |
| LDL-C (mmol/L) | 0.13 (−0.01, 0.28) | 0.068 | 0.13 (−0.01, 0.27) | 0.067 | 0.13 (0.04, 0.23) | 0.008 |
| HDL-C (mmol/L) | 0.05 (−0.01, 0.11) | 0.137 | 0.05 (−0.01, 0.11) | 0.125 | 0.05 (0.01, 0.08) | 0.017 |
| Achievement of treatment target | | | | | | |
| FPG <7 mmol/L | 11.13 (3.34, 18.92) | 0.005 | 11.13 (3.44, 18.83) | 0.005 | 11.25 (3.81, 18.69) | 0.003 |
| SBP/DBP < 130/80 mmHg | 8.80 (1.04, 16.55) | 0.026 | 8.80 (1.08, 16.52) | 0.026 | 8.84 (1.50, 16.19) | 0.018 |
| BMI < 24 kg/m ² | 2.15 (−4.85, 9.16) | 0.546 | 2.15 (−4.84, 9.15) | 0.546 | 2.25 (−2.87, 7.37) | 0.389 |
| TC <4.5 mmol/L | 0.18 (−6.47, 6.82) | 0.958 | 0.18 (−6.43, 6.79) | 0.958 | 0.21 (−5.68, 6.09) | 0.945 |
| TG <1.7 mmol/L | −5.21 (−12.67, 2.26) | 0.171 | −5.21 (−12.67, 2.25) | 0.171 | −5.18 (−11.76, 1.41) | 0.123 |
| LDL-C < 2.6 mmol/L (1.8 mmol/L for having ASCVD) | −8.98 (−16.10, −1.85) | 0.014 | −8.98 (−16.08, −1.88) | 0.013 | −8.96 (−15.05, −2.87) | 0.004 |
| HDL-C > 1.0/1.3 mmol/L for men/women | 1.44 (−5.01, 7.88) | 0.662 | 1.44 (−4.97, 7.84) | 0.660 | 1.40 (−4.31, 7.11) | 0.630 |
| Estimated CVD risk | | | | | | |
| 10-year Framingham CVD risk | −0.94 (−2.06, 0.18) | 0.100 | −0.94 (−1.80, −0.09) | 0.031 | −0.94 (−1.71, −0.17) | 0.017 |
| 10-year ASCVD risk | −0.76 (−1.70, 0.17) | 0.109 | −0.76 (−1.39, −0.14) | 0.016 | −0.77 (−1.34, −0.20) | 0.009 |

Model 1 was adjusted for age, sex, smoking, and drinking at baseline and 12 months. Model 2 was adjusted for age, sex, smoking, drinking, treatment modalities at baseline and 12 months, and outcome measurements at baseline. ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; DBP, diastolic blood pressure; D-in-D, difference-in-difference; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MMC, metabolic management center; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

$P < 0.05$), BP (6.46%, $P < 0.01$), and BMI (3.05%, $P < 0.05$) in the MMC cohort. However, in the usual primary care cohort, the proportions reaching FPG control target significantly dropped at 12 months (Table 2). Compared to usual primary care cohort, we observed a significantly marked increments in the proportion of patients reaching treatment targets in MMC cohort, with respect to the control of FPG (11.13%, $P = 0.005$) and BP (8.80%, $P = 0.026$). These differences remained significant after adjustment for confounders (Table 3).

Estimated 10-year CVD risk reduction

At follow-up, the usual primary care cohort exhibited significant increases in the Framingham CVD risk ($0.54 \pm 5.61\%$, $P < 0.05$) and ASCVD risk ($0.60 \pm 3.65\%$, $P < 0.01$), while the MMC cohort demonstrated a reduction, albeit non-significant, in both Framingham and ASCVD risk (Table 2). However, reductions in CVD risk became significant after adjusting for confounding factors. The MMC cohort showed significantly larger reductions in both Framingham CVD risk (-0.94% , 95% CI -1.71 to -0.17 , $P = 0.017$) and ASCVD risk (-0.77% , 95% CI -1.34 to -0.20 , $P = 0.009$) when compared to the usual primary care cohort (Table 3).

DISCUSSION

In this longitudinal comparative study, we assessed the extent to which biomedical outcomes and cardiovascular risks were improved in the management of Chinese patients with T2D enrolled in the MMC program on top of routine primary care compared to their counterparts under usual primary care. Using propensity score matching and difference-in-difference analysis, the MMC cohort demonstrated greater improvements in levels of FPG, DBP, BMI, LDL-C, and HDL-C, had a higher proportion of patients with glycemic control and lifestyle modifications, and showed a larger reduction in 10-year CVD risk compared to the usual primary care cohort.

Optimizing blood glucose control is pivotal for reducing risks of diabetic microvascular and cardiovascular complications, and preventing the progression of early diabetic microangiopathy, thereby reducing diabetes-related mortality^{26–29}. As an emerging model for diabetes care in China, the effectiveness of the MMC program in blood glucose control has not yet been extensively studied. The findings of our study align with those of a previous small-scale study in China, which reported a greater magnitude of improvement in FPG levels at 12 months³⁰. This could be attributed to variations in baseline blood glucose levels, where statistical effects such as regression to the mean

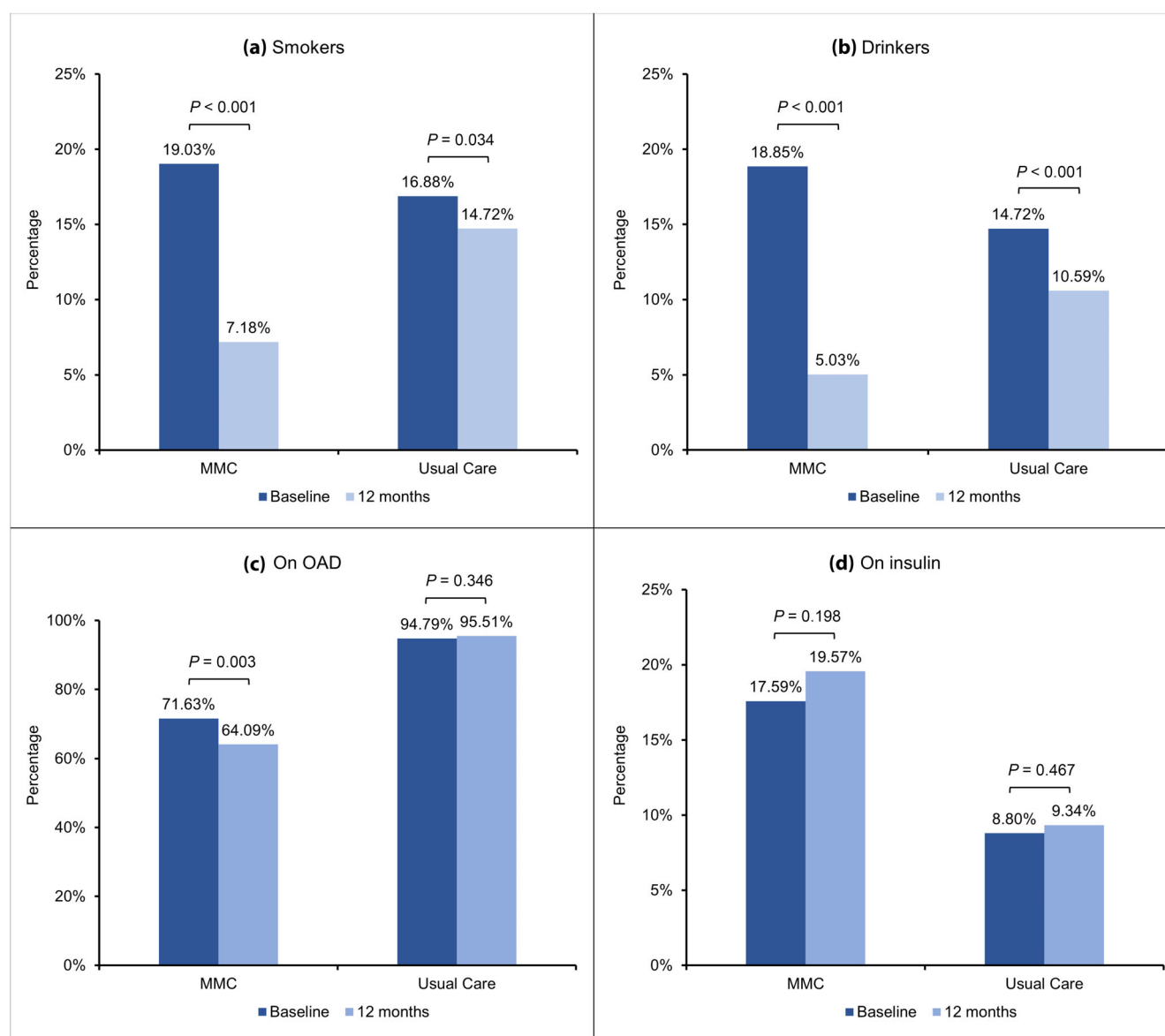


Figure 1 | Changes in treatment modalities and lifestyle in the MMC and usual primary care cohorts between baseline and 12 months. MMC, metabolic management center; OAD, oral antidiabetic drugs.

may yield an exaggerated estimate such that those with higher baseline FPG levels exhibited larger improvements. In our cohort, patients had a much lower baseline FPG levels (i.e., 7.91 mmol/L vs 10.24 mmol/L reported in that study³⁰), which may limit the potential for more pronounced reductions. Meanwhile, our study showed a significantly marked increments in the proportion of patients achieving FPG treatment targets in the MMC cohort as compared to usual primary care, implying the clinical advantage of MMC in enhancing glycemic control.

In contrast to the hospital ward setting, patients' compliance with medication regimens, lifestyle modifications, blood glucose monitoring, and self-management is often suboptimal in the

real-world setting^{31,32}. This presents a significant and persistent challenge to achieving optimized long-term care for patients with diabetes. The MMC program embraces the cutting-edge IoT technology to facilitate a coordinated data collection and analysis platform that incorporates key domains such as rapid detection tests, disease diagnostic procedures, and patient education, thereby ensuring standardized and efficient management of endocrine and metabolic diseases¹⁸. By integrating virtual and in-person health care with continuing diabetes education, the MMC program helps guide patients to adopt tailored management plans in response to their complex health needs. Evidence suggests that this approach is associated with an

increased capacity for addressing limited health literacy, treatment nonadherence, and suboptimal glycemic control³⁰. A multifactorial approach to risk factor management, including lifestyle change, healthy weight maintenance, and treatment for BP and lipid profile alongside blood glucose control, is crucial to reduce the risk of CVD and mortality in patients with T2D^{23,33,34}. Consistent with previous findings that advocate multidisciplinary management^{30,35}, our results revealed that the MMC program had reduced smoking and drinking prevalence, with greater improvements in weight loss during follow-up.

We employed both the estimated 10-year risks of ASCVD (first non-fatal myocardial infarction, non-fatal stroke, coronary revascularization, or CVD death) and total CVD to evaluate whether MMC enrollees could experience risk reductions^{24,25}. We observed significant between-group differences in CVD risk reductions, where the MMC cohort demonstrated significantly larger reductions in both Framingham CVD risk and ASCVD risk. Previous studies suggested that the UKPDS risk engine might be more sensitive in estimating coronary heart disease risk in Chinese diabetic population^{36,37}. However, due to the limited availability of glycated hemoglobin (HbA1c) data in routine primary care settings, this index was not adopted in the present study. Further investigation with HbA1c data at regular follow-up shall provide more evidence on CVD risk improvement under the MMC program implementation.

Efficient collaboration across different specialty departments is essential for effective patient management. Previous studies demonstrated that multidisciplinary interventions involving both physicians and nurses often resulted in effective control of blood glucose^{35,38–40}. In contrast, interventions that overly focused on single discipline treatment paradigms are less likely to exert beneficial impact on biomedical outcomes and cardiovascular risk reductions^{35,41}. The MMC program embraces a patient-centered, multidisciplinary collaborative approach to support the engagement of specialized human resources and partnering with communities to maximize the professional expertise and value of each discipline. Ongoing efforts to monitor the program output indicators, such as incidence of diabetes-related complications, will continue to inform optimal management of diabetes.

Our study has several limitations that require caution in interpreting the results. First, we did not adopt a randomized controlled trial design as it was not feasible to accomplish blinding of care providers and patients in our study setting. Thus, we cannot rule out the possibility that potential confounders may influence the process of care delivered to study participants, despite comparable baseline characteristics between the two cohorts. It is worth noting that care delivered outside the randomized trial setting may not be as effective as that observed in real-world environments⁴². It is therefore reasonable to assume that the between-group differences seen in our study could be more evident in the context of a randomized trial. Second, residual bias may exist because of confounding by unmeasured factors, such as dietary intake, physical activity,

family history of chronic diseases, and patterns of healthcare utilization. Third, a significant proportion of missing data on HbA1c in routine primary care settings precluded the comparison of HbA1c control in our study. Last but not least, our study participants were drawn from a highly urbanized region in southern China, which may affect the generalizability of our findings to the entire T2D patient population.

In conclusion, we provided comparative, longitudinal evidence suggesting that enrolment in the MMC program appears promising in the management of FPG, BP, BMI, lifestyle, and CVD risk in diabetic patients, suggesting the necessity of incorporating the MMC program into routine primary care.

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DISCLOSURES

The authors declare no conflict of interest.

Approval of the research protocol: The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. Biomedical Research Ethics Review Committee of the School of Public Health at Sun Yat-Sen University, Approval No. SPH2019032.

Informed consent: All informed consent was obtained from the subjects.

Registry and the registration no. of the study/trial: N/A.

Animal studies: N/A.

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DATA AVAILABILITY STATEMENT

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Flow chart of study participants.

Table S1. Comparison of treatment modalities and lifestyle between the MMC and usual primary care cohorts at baseline and 12 months.