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# The association between comprehensive medication review and medication adherence among medicare beneficiaries with chronic obstructive pulmonary disease

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## ARTICLE INFO

## ABSTRACT

*Background:* Medicare Part D plans are required to provide Medication therapy management (MTM) services to eligible beneficiaries to optimize medication utilization. Comprehensive medication review (CMR) is a core element of the MTM program. Despite the availability of advanced medical treatment for patients with chronic obstructive pulmonary disease (COPD), medication adherence to maintenance medications poses a continued challenge for patients with COPD.
*Objective:* To examine the effects of CMR on medication adherence among patients with COPD.
*Methods:* Medicare data for 2016–2017 linked to Area Health Resource Files were analyzed. The study population was Medicare beneficiaries with COPD. The intervention group consisted of beneficiaries who received CMR in 2017 but not in 2016. Patients who were eligible for MTM services but did not receive these services in 2016 or 2017 made up the control group. Propensity score matching was used to select an intervention and control group with balanced characteristics. The study outcome was adherence to COPD medications with the proportion of days covered at or above 80%. A difference-in-differences approach was adopted in the logistic regression analyses with an interaction term between the status of CMR receipt and the year 2017.
*Results:* The study sample included 25,564 patients with COPD. The proportions of adherent patients were similar in the control group in both years but increased significantly from 60.08% in 2016 to 69.38% in 2017 in the intervention group ($P < .001$). The odds of medication adherence in the intervention group increased from 2016 to 2017 by 59% more than in the control group (adjusted odds ratio = 1.59, 95% confidence interval = 1.48–1.71).
*Conclusions:* Receiving CMR was associated with improved adherence to COPD medications among Medicare beneficiaries. Policymakers should ensure that Medicare beneficiaries with COPD receive CMR.

## 1. Introduction

Chronic obstructive pulmonary disease (COPD) is a group of chronic lung diseases characterized by limited lung airflow and persistent respiratory symptoms.[1] In the United States (U.S.), COPD is one of the most common chronic conditions; with a 6.0% prevalence rate, it was the sixth-highest cause of mortality in 2021.[2,3] As chronic lung disease progresses gradually, COPD is more prevalent in the elderly; 13.0% of Medicare beneficiaries were estimated to live with COPD in 2021.[4] The treatment of patients with COPD includes inhaled/oral medications and

preventative measures, and its focus is controlling symptoms and reducing exacerbations and mortality.[5]

Adherence to medication treatments is essential to manage COPD effectively. The COPD medications commonly used in the U.S. include bronchodilators (beta2-agonist, anticholinergics) and inhaled corticosteroids.[5,6] Good adherence to these drugs has been proven to decrease the likelihood of exacerbations and increase life expectancy and patients' quality of life with COPD.[7,8] Nonadherence to drugs for COPD has been linked to an increased risk of exacerbations, which can result in expensive healthcare services, such as emergency care visits and the use of intensive care units, and death.[9–14] Therefore, nonadherence to COPD medications significantly burdens the healthcare system, costing $30 billion yearly in direct healthcare expenditure in the U.S..[9–14] However, adherence to COPD medications remains suboptimal; the adherence rate to inhaled medications has been reported to range between 20% and 60% among patients with COPD.[15,16] Previous studies have identified several barriers to adherence to inhaled medications among patients with COPD, including the complexity of the medication regimens, difficulties in learning the proper techniques to administer the medications, and challenges in effectively managing the simultaneous use of multiple medications due to the presence of other chronic conditions.[17–21]

Beginning in 2006, Medicare Part D insurance plans were mandated to initiate medication therapy management (MTM) services for qualifying beneficiaries.[22] The goals of MTM programs are to increase medication utilization quality and lower the incidence of adverse drug events, thus optimizing therapeutic outcomes.[23] The Centers for Medicare and Medicaid Services (CMS) provides a broad guideline of eligibility criteria for MTM programs (i.e., individuals with multiple chronic conditions, taking several Part D drugs, and experiencing Part D drug expenditures over a pre-determined threshold), but plans can determine their specific eligibility criteria within the guideline.[22] For example, CMS required Part D plans to enroll Medicare beneficiaries with the following characteristics in 2023 - a minimum of 3 identified chronic conditions, taking no less than 8 Part D-covered medications, and spending $4935 or more on medications in 2022.[23] Once enrolled in the MTM program, beneficiaries can receive an annual comprehensive medication review (CMR) service along with other services. During a CMR appointment, pharmacists review all prescriptions and over-the-counter medications taken by the patients and then provide consultation on medication utilization to the patients accordingly.[24] After the encounter, CMR recipients receive a written summary of the consultation in a standardized format that contains a personal medication record and an action plan to improve medication utilization and therapeutic outcomes.[24] It has been found previously in the U.S. and other countries that MTM programs, including CMRs, are associated with higher medication adherence rates, reduced healthcare costs, and decreased racial/ethnic disparities in medication nonadherence rates.[25–27]

Despite the benefits of the MTM programs, since their initiation, low enrollment rates of approximately 10% of Part D enrollees persist, although CMS expected 25% of Part D enrollees to be eligible.[22,28,29] CMS has tried to expand the program by lowering eligibility criteria, such as reducing the required number of chronic diseases and Part D drugs.[22] However, it has yet to successfully improve MTM enrollment, likely due to Part D plans lacking financial incentives toward MTM programs.[22] An obstacle for the MTM program to achieve its full potential may be insufficient evidence showing the effectiveness of MTM programs on clinical outcomes, which is associated with the long-time inaccessibility of data for Medicare MTM enrollment to researchers. This is an important topic that has received little attention. Accordingly, this study examined whether CMRs have increased the rate of adherence to COPD medications among the Medicare population with COPD.

## 2. Methods

Medicare data from 2016 to 2017 and the Area Health Resources Files were analyzed.[30–32] The Medicare data comprised the Master Beneficiary Summary File, Parts A/B claims, MTM Data File, and Part D Event File. The databases provided information on beneficiary demographic characteristics, coverage status for various Medicare benefits, chronic disease diagnosis, utilization and costs for medications of interest, MTM enrollment, and the status of CMR receipt.[30,31] To supplement beneficiaries' demographic characteristics, the Area Health Resources Files were linked to the Medicare databases to provide community-level socioeconomic characteristics and the availability of healthcare services.[32] Data from 2016 and 2017 were utilized because they were the latest available to the authors at the time of the analysis.

The study population was Medicare beneficiaries aged at least 65 in 2016 who were alive in 2017 and continuously covered by Medicare Parts A/B/D in the fee-for-service system during the study periods. Enrollees of Medicare Advantage plans were excluded. In addition to these criteria, only Medicare beneficiaries who had a COPD diagnosis in both 2016 and 2017 were included. Patients with COPD were identified based on ICD-10 diagnosis codes using the CMS algorithm available from the CMS Chronic Conditions Data Warehouse.[33]

Andersen's Behavioral Model of Health Services Use was the theoretical framework used to classify the determinants of patients' utilization of health services into three distinct categories: predisposing, enabling, and need factors.[34] The demographic and social characteristics at both individual and community levels were considered predisposing factors. Race/ethnicity, gender, and age were the individual-level predisposing factors. The community-level predisposing factors were the proportions of married-couple families and individuals with high school education or above. The enabling factors comprised the community-level average income level, the uninsured population, the metropolitan statistical area, the Health Professional Shortage Area, and census regions. To account for patients' perceived or actual health conditions, a need factor was included in the analyses: a risk adjustment summary score. Employing the CMS methodology, this score was computed with free software available through CMS, which was developed to adjust for payment to Medicare Advantage plans.[35,36] This score was calculated based on patients' diagnoses information and demographic factors.[35,36] A higher score signified worse health status and indicated that an individual was likely to incur greater healthcare costs.[35,36]

CMR receipt in 2017 was the intervention of the study. The intervention group included Medicare beneficiaries enrolled in MTM and received a CMR in 2017 but not in 2016. The control group included beneficiaries who were eligible for but not enrolled in MTM programs and did not receive CMR in either year. To ensure that control patients did not benefit from an MTM program, the control group was not identified among the MTM enrollees. The MTM eligibility thresholds for 2016 and 2017 were used to identify the control group. According to the CMS guidelines for 2016, the thresholds for MTM eligibility were a minimum of 3 chronic diseases, at least 8 medications covered by part D, and a medication cost of no less than $3507.[37] The 2017 thresholds were the same as in 2016, except the minimum medication cost threshold was $3919.[38] Although plans had the option of using less restrictive eligibility thresholds than the CMS guidelines, most Part D plans adopted those recommended by CMS.[39,40] Therefore, individuals exceeding these thresholds were considered the control group.

Information regarding the quantity of Part D-covered medications and their associated costs were obtained from the 2016–2017 Part D Event File.[41] Beneficiaries' chronic disease count was identified through Parts A and B claims by applying the ICD-10 codes for 25 chronic diseases relevant to Medicare beneficiaries.[42] The propensity score matching (PSM) strategy was employed to ensure that individuals in both groups shared comparable characteristics. The propensity score, representing the predicted likelihood of receiving CMR, was obtained using a logistic regression that incorporated variables specified by the theoretical model. The nearest-neighbor matching algorithm without replacement was adopted, as it produces the most balanced groups among all matching methods.[43] Individuals in the control and

intervention groups were matched at a 3:1 ratio to increase the total analytical sample size. A higher ratio was not utilized, as the literature has indicated that efficiency gains are poor beyond the 3:1 level.[44] The difference in sample sizes between the two study groups after matching does not affect the robustness of the empirical findings, provided that the underlying characteristics of the two groups are comparable.[45]

An indicator variable for adherence to COPD medications was the outcome variable of the study. The adherence measure used was initially developed and created by the Pharmacy Quality Alliance (PQA), an independent, nonprofit organization committed to addressing issues in medication utilization for Medicare Part D. Based on the PQA measure manual, the adherence measure for COPD medications assessed the adherence to long-acting inhaled bronchodilator medications, which included the following medication categories: anticholinergics, beta-agonists, and combination products.[46] Medications were identified with National Drug Codes. The proportion of days covered was applied to measure adherence to COPD medications. It was calculated by the number of days covered by at least one COPD prescription over the total number of days of the measurement period. For the intervention group, because the CMR service date was available, the start date of the measurement period was the initiation date for the first COPD prescription after the patient received CMR. For the control group, the measurement period started from the first prescription date of any COPD medications to the end of the year. Beneficiaries were deemed adherent to COPD medications if the proportion of days covered was greater than or equal to 80%.[46]

Medicare data were accessed via the CMS Virtual Research Data Center, with all data analyses carried out using SAS v9.4 (Cary, NC). The Institutional Review Board at the corresponding author's institution deemed this study exempt on February 20, 2020 (approval number 20–07197-XM).

Using data from 2016, a comparison of the baseline characteristics was made between the intervention and control groups both prior to and following the matching. Categorical and continuous variables were compared utilizing a Chi-square test and a *t*-test, respectively. Using a Chi-square test, the proportions of beneficiaries adhering to their COPD medications were compared between the two study groups.

In the adjusted multivariable analysis, a difference-in-differences method was adopted in the logistic regression with an interaction term of two dummy variables: a dummy variable for the year 2017 and a dummy variable for the CMR receipt. This method compared the changes in medication adherence from before to after CMR receipt between the intervention and control groups. The validity of the difference-in-differences approach does not depend on the baseline values of the outcome variable being the same between the study groups.[47,48] The estimated coefficient on the above interaction term captured the effects of receiving CMR on a beneficiary's adherence to COPD medications. An odds ratio of more than one would imply that CMR receipt was related to improved adherence to COPD medications. To account for the potential correlation between individuals in the same county, standard errors at the county level were clustered.

## 3. Results

Prior to propensity score matching, a total of 93,911 beneficiaries were identified for the control group and 6391 for the intervention group. The intervention group was 100% matched in the matching. Therefore, the final study sample consisted of 25,564 COPD patients, including 19,173 in the control group and 6391 in the intervention group, in a ratio of 3:1. The baseline characteristics of the study sample before and after the matching are shown in Table 1. Significant differences in the following characteristics between the two study groups were observed before the matching: age, race/ethnicity, county-level proportions of high school education and income per capita, metropolitan statistical area, and risk adjustment summary score (*P* < .0001). The intervention and control groups were not statistically significantly

**Table 1**

Baseline Characteristics for Intervention and Control Groups in 2016 Before and After Propensity Score Matching[a].

| Characteristics | After Matching Intervention (n = 6391, 25%) Number | % | Control (n = 19,173, 75%) Number | % | Before Matching Control (n = 93,911) Number | % |
|---|---|---|---|---|---|---|
| Predisposing Factors | | | | | | |
| Age, mean (SD)[b] | 75.76 (6.63) | | 75.70 (6.86) | | 76.14 (6.94) | |
| Male | 2410 | 37.71 | 7283 | 37.99 | 35,289 | 37.58 |
| Race/Ethnicity[b] | | | | | | |
| Non-Hispanic White | 5522 | 86.40 | 16,647 | 86.83 | 81,368 | 86.64 |
| Black (African American) | 493 | 7.71 | 1428 | 7.45 | 5295 | 5.64 |
| Hispanic | 176 | 2.75 | 501 | 2.61 | 3482 | 3.71 |
| Asian/Pacific Islander | 115 | 1.80 | 336 | 1.75 | 2321 | 2.47 |
| Other | 85 | 1.33 | 261 | 1.36 | 1445 | 1.54 |
| Proportion of Married-Couple Families, mean (SD)[c] | 0.73 (0.07) | | 0.73 (0.07) | | 0.73 (0.07) | |
| Proportion of High School Education and above, mean (SD)[b, c] | 0.87 (0.06) | | 0.87 (0.05) | | 0.87 (0.05) | |
| Enabling Factors | | | | | | |
| Income Per Capita (in $1000), mean (SD)[b, c] | 46.69 (14.78) | | 46.68 (14.13) | | 48.89 (16.71) | |
| Proportion of the Uninsured, mean (SD)[c] | 0.10 (0.04) | | 0.10 (0.04) | | 0.10 (0.04) | |
| Metropolitan Statistical Area[b, c] | 4585 | 71.74 | 13,690 | 71.40 | 72,620 | 77.33 |
| Health Professional Shortage Area[c] | 5753 | 90.02 | 17,223 | 89.83 | 85,004 | 90.52 |
| Census Regions[c] | | | | | | |
| Northeast | 1491 | 23.32 | 4531 | 23.63 | 21,761 | 23.17 |
| Midwest | 1496 | 23.41 | 4553 | 23.75 | 20,455 | 21.78 |
| South | 2266 | 35.46 | 6696 | 34.92 | 35,824 | 38.15 |
| West | 1138 | 17.81 | 3393 | 17.70 | 15,871 | 16.90 |
| Need Factor | | | | | | |
| Risk Adjustment Summary Score, mean (SD)[b] | 2.48 (1.50) | | 2.46 (1.57) | | 2.32 (1.46) | |

SD = standard deviation.

All characteristics were similar between the intervention and control groups after matching (*P* > .05).

[a] The intervention group was 100% matched.

[b] These characteristics significantly differed between the intervention and control groups before matching (*P* < .0001).

[c] County-level characteristics.

different in any of the characteristics after the matching (*P* > .05).

The proportions of adherent patients in the two study groups based on the unadjusted analysis are shown in Fig. 1. The proportions of patients who adhered to COPD medications were similar in 2016 and 2017 in the control group (68.88% in 2016 and 68.11% in 2017, *P* > .05). In the intervention group, these proportions increased significantly from 60.08% in 2016 to 69.38% in 2017 (*P* < .0001).

According to the adjusted analysis, CMR receipt was associated with positive changes in the odds of adherence to COPD medications (Table 2). The adjusted odds ratio for the interaction term between CMR receipt and the year 2017 was 1.59 (95% Confidence Interval or CI = 1.48–1.71). Results indicated that the odds of medication adherence in the intervention group increased by 59% more than in the control group
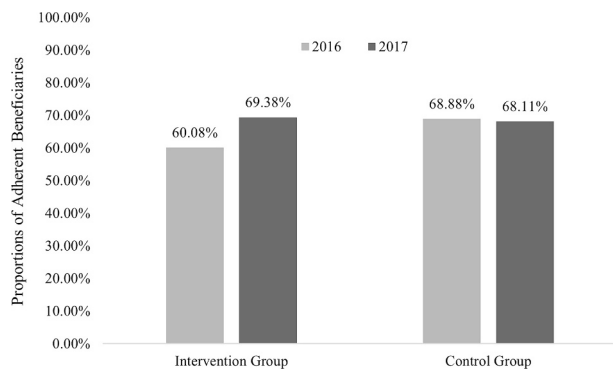
**Fig. 1.** Proportions of Adherent Patients in Intervention and Control Groups in 2016 and 2017. The intervention group experienced a significant increase from 2016 to 2017 ($P < .0001$), whereas the control group exhibited similar proportions in the two study years ($P > .05$).

**Table 2**

Adjusted Difference-in-Differences Estimates of the Effects of Comprehensive Medication Review on Adherence to Medications for Chronic Obstructive Pulmonary Disease among Medicare Beneficiaries ($N = 25,564$).

| Characteristics | Odds Ratio | 95% Confidence Interval |
|---|---|---|
| Year 2017 | 0.97 | 0.94–1.01 |
| CMR Receipt | 0.68 | 0.64–0.72 |
| CMR Receipt × Year 2017 | 1.59 | 1.48–1.71 |
| Predisposing Factors | | |
| Age | 0.999 | 0.996–1.002 |
| Male | 1.06 | 1.005–1.109 |
| Race/Ethnicity | | |
| Black (African American) | 0.77 | 0.71–0.84 |
| Hispanic | 0.75 | 0.65–0.87 |
| Asian/Pacific Islander | 1.02 | 0.76–1.39 |
| Other | 0.997 | 0.82–1.22 |
| Proportion of Married-couple Families[a] | 0.93 | 0.57–1.52 |
| Proportion of High School Education and Above[a] | 2.05 | 1.06–3.95 |
| Enabling Factors | | |
| Income Per Capita (in $1000)[a] | 1.002 | 0.9998–1.0042 |
| Proportion of the Uninsured[a] | 0.60 | 0.28–1.27 |
| Metropolitan Statistical Area[a] | 0.96 | 0.91–1.02 |
| Health Professional Shortage Area[a] | 0.98 | 0.90–1.07 |
| Census Regions[a] | | |
| Midwest | 0.95 | 0.88–1.02 |
| South | 0.80 | 0.74–0.87 |
| West | 0.98 | 0.90–1.06 |
| Need Factor | | |
| Risk Adjustment Summary Score | 0.89 | 0.88–0.90 |

Reference groups: Female, non-Hispanic white, the year 2016, control group (CMR non-recipients), non-metropolitan statistical area, non-health professional shortage area, and northeast region

[a] County-level characteristics.

from 2016 to 2017.

In the adjusted model, several other factors were also significantly associated with the odds of adherence to COPD medications. Factors negatively associated with adherence to COPD medications included Black race, Hispanic ethnicity, South region, and a higher risk score. For instance, Black patients had 23% lower odds of medication adherence than White patients (OR = 0.77, 95% CI = 0.7–0.84). The proportion of people with a high school education and above in a county was positively associated with adherence to COPD medications (OR = 2.05, 95% CI = 1.06–3.95).

## 4. Discussion

Compared to non-CMR recipients, CMR recipients experienced a

considerably higher increase in adherence to COPD medications from 2016 to 2017. This finding adds critical empirical evidence to the literature on the benefits of MTM programs in improving medication adherence. Although this study used 2016–2017 data, findings with data from more recent years are expected to be similar due to the lack of major MTM program change.[23]

Previous research has found that MTM programs can improve medication adherence rates, highlighting the value of such intervention in medication management led by pharmacists or other qualified providers.[25,26] Results from this study also reconfirmed the benefits of CMRs (a required component of the MTM services) on the population of interest. As stated above, one possible reason for this population's low medication adherence rate is the complexity of COPD medication regimens. Patients with COPD are, on average, prescribed a combination of 6.3 oral and inhaled medications with different dosing patterns.[17,18] Further, patients with COPD often do not understand their inhaled medications and the technique to use them.[17,19] Also, older patients with COPD are likely to have other chronic conditions, thus simultaneously taking medications for those conditions.[20] Older patients may find it challenging to manage several medications adequately.[21] Since pharmacists and other MTM providers may help alleviate medication management issues through CMRs, patients with COPD would benefit significantly from these services. Both new COPD patients and those who have been on COPD medications for some time were included in the current study. Among new patients, learning proper medication administration through the education received in CMRs could help to increase medication adherence. For patients who had been on COPD medication for a longer time, CMRs may address any ongoing issues with adherence. Future studies are needed to test the economic implications of these findings.

Results from this study suggest that MTM programs may alleviate medical and economic tolls on individuals with COPD and society through improved medication adherence. However, the low rate of MTM enrollment has impeded the MTM program from reaching its full potential. A key barrier to enhancing MTM enrollment is the need for more financial incentives for Part D sponsors.[22] Since its inception, the costs associated with MTM services are built into sponsors' annual CMS bids for a prospective contract. Part D plans are not reimbursed separately from CMS for the MTM services.[49] Under the current policy design, it is reasonable to expect that stand-alone prescription drug plans (PDPs) may keep down the overall enrollment rate of the MTM programs because such plans are only at risk for prescription medication expenditures.[49] However, research has revealed no discernible gap in the enrollment rate between PDPs and Medicare Advantage prescription drug plans (MAPDs).[28] These results also have demonstrated the necessity of a direct budget line allocated to MTM programs.

In addition to expanding the pool of beneficiaries eligible for MTM programs, the results of benefits of CMRs support the further improvement in the CMR completion rate. The percentage of CMR recipients among MTM enrollees during the reported period is a measure in Medicare Part D Star Ratings, a quality improvement program for the Medicare program.[50] The CMR completion rate was first introduced in 2013 as a display measure and was adopted as a Medicare Part D Star Ratings regular measure in 2016.[51] Although the CMR completion rate has continued to grow, there is still improvement to be made, particularly for PDPs. For example, in 2022, the average CMR completion rate for MAPDs was 83%, while that of PDPs was 54%.[50] The low rate among PDPs is critical to address because 47.3% of Part D beneficiaries (23.1 million) were enrolled in this plan type in 2022.[52] Based on the 2021 prevalence estimate of 13.0% for COPD among Medicare enrollees, a large number of patients with COPD did not receive a CMR.[4] These patients are likely to experience COPD exacerbations and incur higher healthcare costs due to the poor management of the disease.[11,12] Policymakers should devise strategies to improve the CMR completion rate to reduce avoidable medical and financial burdens.

Some individual- and county-level characteristics were associated

with medication adherence among patients with COPD. For example, minority status (especially Black and Hispanic patients) was associated with a lower adherence rate to COPD medications. It has been reported that racial and ethnic minorities were more likely than non-Hispanic Whites to show higher medication non-adherence in general.[53] Other factors were also found to be associated with lower medication adherence, such as being situated in the Southern region and bearing a higher risk adjustment score. Low medication adherence among patients with chronic disease (e.g., diabetes, hypertension, or hyperlipidemia) has been observed in the southern region.[54] Results from this study suggest that such a pattern of low medication adherence in the Southern region also applies to patients with COPD. Further, individuals with a higher risk score are likely to experience multiple chronic diseases and complex drug regimens, which is related to lower medication adherence.[33,55] Therefore, the inverse relationship between the risk score and medication adherence among COPD patients is understandable. On the other hand, residing in a county with a higher percentage of people attaining a minimum of a high school education was positively linked to medication adherence among COPD patients. This is also expected because greater levels of education and health literacy have been found to be associated with higher adherence.[56]

This study has the following limitations. First, beneficiary-level information in the Medicare data only included some basic demographics such as age, gender, and race/ethnicity. Although the Medicare data were supplemented with county-level socioeconomic variables obtained from the Area Health Resources Files, these variables may not be perfect proxies for individual-level socioeconomic characteristics. Second, adherence to COPD medications was measured based on the proportion of days covered derived from Medicare beneficiaries' prescription fills recorded but not actual medication intake. However, the proportion of days covered has been regarded as a valid proxy for medication adherence in research and has been adopted in CMS Parts C and D Star Ratings.[51] Further, picking up a prescription does not equate to taking the medication as instructed. Thirdly, the intervention and control groups did not have equivalent baseline adherence rates. Fourthly, this study only included a Medicare fee-for-service population, which restricts the generalizability of the findings to other populations, such as Medicare Advantage enrollees, Medicaid enrollees, and the uninsured population. Finally, the CMS-designated values for the number of chronic conditions a patient must have and Part D medications the patient must take to determine the intervention and control groups was applied. However, there exists variation in eligibility criteria across different Part D plans. Hence, the current findings may not generalize to beneficiaries in different plans. Despite these limitations, these results make a significant contribution to the literature by investigating the effectiveness of CMRs on medication adherence among Medicare fee-for-service beneficiaries with COPD.

## 5. Conclusions

Medicare fee-for-service beneficiaries who received a CMR were found to experience improved adherence rates to medication therapies. The study findings speak to the need to reform the program design to enhance MTM enrollment and the completion rate of CMR among the Medicare population. Such expansion strategies help MTM programs cover more patients with COPD and prevent COPD-related adverse health outcomes that poor management of the disease can cause. Furthermore, offering CMRs to MTM enrollees may help avoid the utilization and costs of alternative healthcare services such as hospitalization and emergency room visits through improved medication adherence. Future research is warranted to explore the effects of CMRs on these outcomes among COPD patients.

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## CRediT authorship contribution statement

**Xiangjun Zhang:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Yongbo Sim:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Chi Chun Steve Tsang:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Junling Wang:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Funding acquisition, Formal analysis, Conceptualization. **Christopher K. Finch:** Writing – review & editing, Writing – original draft, Methodology, Conceptualization.

## Declaration of competing interest

**Xiangjun Zhang**: None; **Yongbo Sim**: None; **Chi Chun Steve Tsang**: None; **Christopher K. Finch**: None; **Junling Wang**: Received funding from AbbVie, Curo, Bristol Myers Squibb, Pfizer, and Pharmaceutical Research and Manufacturers of America (PhRMA) and serves as the Chair of the Value Assessment-Health Outcomes Research Advisory Committee of the PhRMA Foundation.

## Data availability

The data analyzed for this article are available from the Virtual Research Data Center managed by the Centers for Medicare & Medicaid Services with strict access restrictions.

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