

# Medication Nonadherence, Mental Health, Opioid Use, and Inpatient and Emergency Department Use in Super-Utilizers

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Optimal adherence to essential prescription medications is critical for the treatment of chronic conditions.<sup>1-3</sup> Medication nonadherence is a major barrier to achieving treatment goals, especially among high-risk patient populations.<sup>4</sup> These include so-called super-utilizers—patients with disproportionately high inpatient and emergency department (ED) use—who generally have multiple chronic conditions and use multiple concurrent medications to treat these conditions.<sup>5-8</sup> The cost of caring for super-utilizers is high, with estimates that they represent only 3% to 5% of the US population but account for 30% to 50% of total spending.<sup>5,9</sup>

Findings of previous studies conducted among Medicare beneficiaries have shown that optimal medication adherence is associated with lower inpatient and ED use.<sup>10,11</sup> Evidence shows that depression is associated with higher incidence of hospitalizations among patients who are high utilizers of medical care, and our previous studies have highlighted high rates of chronic pain and opioid use in this vulnerable population.<sup>12-14</sup> However, the impact of these factors on healthcare utilization among medically underserved communities is not well understood. This study builds on previous research by focusing on more vulnerable Medicare beneficiaries from a medically underserved metropolitan area in the South who are predominantly African American, younger, and disabled.<sup>13</sup>

This study was conducted using baseline data from the SafeMed Program, a care transitions program focusing on medication management and funded by the CMS Health Care Innovation Awards (HCIA).<sup>6</sup> SafeMed targeted super-utilizers from medically underserved areas (MUAs) with ambulatory care-sensitive chronic conditions (hypertension, type 2 diabetes, congestive heart failure [CHF], coronary artery disease [CAD], chronic obstructive pulmonary disease [COPD], or asthma) for which outpatient care improvements can reduce inpatient utilization.<sup>15-18</sup> Using longitudinal 2-year Medicare data for the period prior to the SafeMed intervention, we examined whether medication nonadherence, mental health diagnosis, and opioid medication use were associated with inpatient and ED use in super-utilizers. We also examined whether tobacco use disorder, polypharmacy, number of prescribers, and access to outpatient care

## ABSTRACT

**OBJECTIVES:** To examine whether mental health conditions, opioid use, and medication nonadherence are associated with inpatient and emergency department (ED) use among Medicare super-utilizers from medically underserved areas.

**STUDY DESIGN:** Retrospective panel study.

**METHODS:** The study included Medicare super-utilizers (≥3 hospitalizations or ≥2 hospitalizations with ≥2 ED visits in 6 months) served by a health system in a medically underserved area in the South from February 2013 to December 2014 with at least 1 filled prescription for hypertension, type 2 diabetes, cardiovascular, and/or chronic obstructive pulmonary disease/asthma medications. We used random effects negative binomial models to assess whether mental health diagnosis, opioid use, and medication nonadherence were associated with preventable and overall hospitalizations and ED visits stratified by age (18-64 vs ≥65 years).

**RESULTS:** Overall chronic disease medication nonadherence was associated with more frequent hospitalizations and ED visits for both younger (hospitalizations: incidence rate ratio [IRR], 1.31; 95% CI, 1.16-1.47; ED visits: IRR, 1.33; 95% CI, 1.14-1.55) and older (hospitalizations: IRR, 1.34; 95% CI, 1.20-1.49; ED visits: IRR, 1.18; 95% CI, 1.02-1.38) beneficiaries. Mental health diagnosis was significantly associated with higher hospitalizations and ED visits among both age groups. Although associations between opioid medication use and inpatient and ED use were inconsistent and not significant in most cases, we found that 7 or more days' supply of opioids was associated with lower preventable hospitalizations in Medicare beneficiaries 65 years or older.

**CONCLUSIONS:** The study findings highlight the importance of improving medication adherence and addressing behavioral health needs in Medicare super-utilizers.

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were associated with hospitalizations and ED visits in this vulnerable population.

## METHODS

### Design and Setting

This study was a retrospective panel analysis of the baseline data for Medicare beneficiaries from a MUA served by a hospital system in Memphis, Tennessee, and meeting the SafeMed Program eligibility criteria during the enrollment period from February 2013 to December 2014.<sup>6</sup> For each patient, we reviewed 2 years of data prior to SafeMed enrollment. The dates of this 2-year baseline period varied for each patient based on their enrollment date for the SafeMed Program. For instance, if a patient was enrolled in the SafeMed Program in February 2013, the 2-year evaluation period was from February 2011 to February 2013. The data for each patient were divided into four 6-month patient-periods, with the last 6-month period serving as the qualifying period for the SafeMed Program.<sup>6</sup> The panel design enabled us to examine changes in hospitalizations, ED visits, and nonadherence over time. **eAppendix Figure 1** (eAppendix available at [ajmc.com](http://ajmc.com)) shows the study design.

### Data

The study used Chronic Conditions Data Warehouse files including pharmacy and medical claims for all fee-for-service Medicare beneficiaries with parts A, B, and D coverage. Data on hospitalizations were obtained using Medicare Provider Analysis and Review files. Data on observation stays and ED visits were obtained using Medicare outpatient revenue center files. Part D drug event files were used to assess medication nonadherence, and diagnosis codes present in the inpatient, outpatient, or Part B claims were used to assess chronic conditions. Medicare beneficiary summary files (parts A, B, and D) were used to assess demographic factors. Patient identifier and claim identifier were used as linking variables.

### Study Population

The final study sample (N = 1092) included adult super-utilizers ( $\geq 3$  hospitalizations or  $\geq 2$  hospitalizations with  $\geq 2$  ED visits in 6 months) with a diagnosis of at least 1 of the previously mentioned ambulatory care-sensitive conditions, with continuous eligibility for Medicare parts A, B, and D and who had filled at least 1 of 17 type 2 diabetes, cardiovascular, or COPD/asthma drug classes during the 2-year period. The list of therapy classes is presented in **eAppendix Table 1**. The study sample was divided into 2 groups: (1) Medicare beneficiaries aged 18 to 64 years who are eligible due to their disability<sup>19</sup> and (2) Medicare beneficiaries 65 years or older. The study excluded patients with insulin fills because adherence cannot be reliably calculated using claims data.<sup>20</sup>

## TAKEAWAY POINTS

Nonadherence to essential chronic medications and mental health diagnosis were associated with higher hospitalizations and emergency department use among Medicare super-utilizers.

- ▶ This study builds on previous research conducted among Medicare patients by focusing on a more vulnerable Medicare population from a medically underserved metropolitan area in the South with patients who are predominantly African American, younger, disabled, and super-utilizing.
- ▶ This study has important implications for policy makers and institutions involved in improving the quality of care and reducing costs for super-utilizers.
- ▶ The study findings highlight the importance of improving medication adherence and addressing behavioral health needs in Medicare super-utilizers.

### Measures

The outcomes included overall and preventable inpatient stays and ED visits, measured for each 6-month period. Hospitalizations and ED visits for hypertension, type 2 diabetes, CHF, CAD, COPD, or asthma were considered preventable based on the Agency for Healthcare Research and Quality (AHRQ) Prevention Quality Indicators chronic composite measures.<sup>21</sup> Preventable hospitalizations and ED visits were identified using the primary diagnosis documented during an encounter. Medication nonadherence was measured as interval-based average proportion of days covered (PDC).<sup>22,23</sup> Using the PDC approach,<sup>22</sup> patients were followed continuously from the first 6-month period in which they had 2 or more fills for a drug class through the fourth 6-month period. The numerator was number of days of medication supply, and the denominator was number of days during the interval from the index date to the last day of that period. We used the first day of medication fill as the index date only if patients had 2 or more fills for a drug class for the first time in a period. If patients filled 2 or more medications for a drug class in any of the previous periods, the denominator was 180 days. For the numerator, if the days' supply extended into the next period, it contributed to both periods. We did not double-count the days when patients refilled their medications before the previous prescription ran out. We subtracted the inpatient days from the denominator. We calculated an overall average PDC at the patient level by adding the PDC for each drug class and then dividing by the number of drug classes for each patient. Nonadherence was defined as PDC less than 80%. Nonadherence was also measured by disease category for type 2 diabetes, cardiovascular, and COPD/asthma drug classes.

We identified patients with mental health diagnosis if they had depression/anxiety (*International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 296.2, 296.3, 298.0, 300, 309.1, or 311*), bipolar disorder, schizophrenia, or other psychotic disorders (*ICD-9-CM code 295, 297, 298, 293.81, 293.82, 296.0, 296.1, 296.4, 296.5, 296.6, 296.7, 296.8, or 296.9*) in the current period or any prior period. Opioid medication use was defined by whether or not patients had 7 or more days' supply of opioids in each 6-month period.

## TRENDS FROM THE FIELD

**TABLE 1.** Characteristics Among Younger (<65 years) and Older (≥65 years) Medicare Beneficiaries<sup>a</sup>

Characteristics	<65 Years n = 468	≥65 Years n = 624	P <sup>b</sup>
Female, n (%)	242 (51.7)	400 (64.1)	<.001
Race/ethnicity, n (%)			<.001
Non-Hispanic white/other	107 (22.9)	235 (37.7)	
Non-Hispanic black	361 (77.1)	389 (62.3)	
Eligibility status, n (%)			
Disabled	407 (87.0)	–	–
End-stage renal disease	209 (44.7)	115 (18.4)	<.001
Non-dual-eligible, non-LICS	43 (9.2)	255 (40.9)	<.001
Non-dual-eligible, LICS	48 (10.3)	50 (8.0)	
Dual-eligible, LICS	377 (80.6)	319 (51.1)	
Chronic conditions, n (%)			
Diagnosis of hypertension	464 (99.2)	622 (99.7)	.24
Diagnosis of type 2 diabetes	358 (76.5)	426 (68.3)	.003
Diagnosis of congestive heart failure	336 (71.8)	463 (74.2)	.38
Diagnosis of coronary artery disease	309 (66.0)	476 (76.3)	<.001
Diagnosis of asthma	162 (34.6)	215 (34.5)	.96
Diagnosis of chronic obstructive pulmonary disease	236 (50.4)	347 (55.6)	.09
Number of chronic conditions, n (%)			
1 chronic condition	18 (3.8)	13 (2.1)	.33
≥2 chronic conditions	450 (96.2)	611 (97.9)	
Charlson Comorbidity Index score, mean (SD)	7.1 (3.4)	6.7 (3.0)	.03
Diagnosis of mental health conditions, <sup>c</sup> n (%)	277 (59.2)	329 (52.7)	.03
Diagnosis of anxiety	151 (32.3)	164 (26.3)	.03
Diagnosis of depression	194 (41.5)	159 (25.5)	<.001
Diagnosis of other mental health conditions <sup>d</sup>	74 (15.8)	51 (8.2)	<.001
Diagnosis of tobacco use disorder, n (%)	209 (44.7)	142 (22.8)	<.001

LICS indicates low-income cost-sharing subsidy.

<sup>a</sup>This study was conducted using baseline data from the SafeMed Program, a care transitions program focusing on medication management that targeted Medicare super-utilizers from a medically underserved area served by a hospital system in Memphis, Tennessee.

<sup>b</sup>Statistical significance at  $P < .05$ .

<sup>c</sup>Mental health condition was defined as diagnosis of depression, anxiety, schizophrenia, other psychotic disorders, or bipolar disorders (≥1 diagnosis claim present in Medicare inpatient, outpatient, or Part B claims) in the 2-year study evaluation period.

<sup>d</sup>Diagnosis of other mental health conditions included schizophrenia, other psychotic disorders, and bipolar disorders.

### Other Factors

Baseline factors included age, gender, race, dual Medicare-Medicaid eligibility, and low-income cost-sharing subsidy (LICS) receipt. Because the income threshold for receiving a LICS is higher than the threshold for Tennessee Medicaid, we created a variable with 3 groups: non-dual-eligible, non-LICS; non-dual-eligible, LICS; and dual-eligible, LICS. Other factors included tobacco use disorder, cancer, Charlson Comorbidity Index score,<sup>24</sup> 1 or more physician office visits, unique medications filled, and unique prescribers.

### Statistical Analysis

For multivariate analyses, observations from the four 6-month periods were pooled using patient-period as the unit of analysis. Random effects negative binomial models were used as multivariate models. Along with medication adherence and opioid use (time-varying factors), we were interested in mental health diagnosis that did not vary much with time. Therefore, we used random effects models. Additionally, negative binomial models were used, given that the utilization outcomes were overdispersed count variables.<sup>25</sup> Separate models for beneficiaries aged 18 to 64 years and those 65 or older were estimated to understand associations specific to these Medicare groups. Lagged effects of all independent factors were included in the models to account for potential endogeneity. Thus, mental health, opioid use, medication nonadherence, and all other covariates were measured in a period before the outcomes were measured. Multivariate analyses were conducted to examine the association between nonadherence and inpatient and ED utilization by disease category.

### Sensitivity Analysis

Realizing that medication switching between drug classes may be common after hospitalizations, we measured adherence using an alternative method. Patients were included in the 6-month period if they had (1) at least 2 fills for a drug class for the first time in the period or (2) at least 1 fill in the period if they previously had at least 2 fills for that drug class.

## RESULTS

**Table 1** shows that among 1092 study subjects, nonelderly disabled beneficiaries were more likely to be African Americans, be low-income dual-eligible, and have higher rates of mental health diagnosis compared with older Medicare beneficiaries ( $P < .05$  for all). Among both age groups, the most common primary discharge diagnoses were for COPD, CHF, chronic kidney disease (CKD), pneumonia, and hypertensive CKD (data not shown). Opioid fill rates were high in all 4 study periods but were highest in the fourth 6-month period when all patients met the super-utilizer definition, with 64.1% of elderly and 75.8% of nonelderly Medicare patients filling 1 or more opioid medications. Additionally, overall nonadherence rates increased from the first period to the fourth period (**eAppendix Table 2**).

**Table 2** shows the multivariate associations among elderly Medicare beneficiaries. Nonadherent patients had significantly higher overall and preventable inpatient and ED visits compared with adherent patients. Mental health diagnosis was significantly associated with higher overall inpatient and overall and preventable ED visits, whereas 7 or more days' supply of opioids was significantly associated with lower preventable hospitalizations.

**Table 3** displays the same results among nonelderly Medicare beneficiaries. As observed with older beneficiaries, nonadherence and mental health diagnosis were also associated with significantly higher hospitalizations and ED visits in this younger age group.

Additionally, tobacco use disorder was significantly associated with higher hospitalizations and ED visits.

**eAppendix Table 3** shows that inpatient and ED visits were significantly higher for nonadherent patients compared with adherent patients for all disease categories. In sensitivity analyses using the alternative PDC definition, we found similar patterns of nonadherence over time (**eAppendix Figure 2** [A and B]). Additionally, multivariate results were similar in terms of significance and directionality to our main analyses (**eAppendix Table 4**; **eAppendix Table 5**).

## DISCUSSION

In our retrospective study of super-utilizing Medicare beneficiaries, we found higher hospitalizations and ED visits among nonadherent patients. Similar associations were found across the 3 disease categories and in both age groups. These findings are consistent with those of a previous study that found that Medicare patients with COPD who were adherent to their chronic medications experienced fewer hospitalizations.<sup>11</sup> Our work extends these findings to super-utilizing patients who were more disadvantaged than average elderly Medicare patients: More were dual-eligible, disabled, with multiple comorbidities, and nonadherent to their essential chronic disease medications.<sup>13</sup>

This analysis reinforced previous findings that super-utilization is dynamic and changes with time.<sup>5,14</sup> Less than 20% of nonelderly and less than 10% of elderly Medicare beneficiaries were super-utilizers in the first three 6-month periods (**eAppendix Table 2**). The current study also demonstrates that nonadherence worsens over time as patients approach super-utilizer status (**eAppendix Figure 2** [A and B]). This suggests that it may be helpful to identify and address medication nonadherence earlier among patients with ambulatory care-sensitive conditions who are at risk of becoming super-utilizers.

Similar to previous studies,<sup>5,26</sup> we found high rates of mental health conditions and tobacco use disorders, especially among nonelderly Medicare patients. Mental health diagnosis was significantly associated with high inpatient and ED utilization among both age groups, whereas tobacco use disorder was a significant risk factor for high inpatient and ED utilization among nonelderly beneficiaries. These findings suggest that Medicare super-utilizers may benefit from

psychosocial interventions that provide assistance with mental health, tobacco cessation, and social support.

Results of this study show high opioid use in these super-utilizers. A substantial amount of opioid utilization is likely driven by the high prevalence of chronic pain in super-utilizers, as documented in a previous study.<sup>14</sup> Efforts to address opioid use among super-utilizers may include alternative strategies for managing chronic pain. Although associations between opioid medication use and inpatient and ED use were inconsistent and not significant in most cases, we found that receipt of 7 or more days' supply of opioids

**TABLE 2.** Factors Associated With Inpatient Stays and ED Visits Among Medicare Beneficiaries 65 Years or Older (n = 1757 patient-periods)<sup>a</sup>

Characteristics	Inpatient Stays		ED Visits	
	Overall IRR (95% CI)	ACSC IRR (95% CI)	Overall IRR (95% CI)	ACSC IRR (95% CI)
Medication nonadherence <sup>b</sup>	<b>1.34</b> (1.20-1.49)	<b>1.32</b> (1.05-1.66)	<b>1.18</b> (1.02-1.38)	<b>1.17</b> (1.01-1.36)
Diagnosed mental health condition <sup>c</sup>	<b>1.25</b> (1.09-1.40)	1.11 (0.84-1.47)	<b>1.47</b> (1.22-1.77)	<b>1.48</b> (1.24-1.78)
≥7-day supply of opioids	0.92 (0.82-1.02)	<b>0.72</b> (0.56-0.92)	0.93 (0.79-1.10)	0.93 (0.79-1.10)
Female (ref: male)	0.98 (0.88-1.10)	1.04 (0.79-1.38)	1.17 (0.96-1.43)	1.15 (0.95-1.41)
Race				
White/others (ref)	-	-	-	-
Non-Hispanic black	<b>0.81</b> (0.73-0.91)	<b>0.53</b> (0.39-0.72)	<b>1.25</b> (1.01-1.55)	1.19 (0.96-1.47)
Eligibility status				
Non-dual-eligible, non-LICS (ref)	-	-	-	-
Non-dual-eligible, LICS	1.20 (0.99-1.44)	<b>1.86</b> (1.15-3.02)	<b>1.41</b> (1.01-1.96)	<b>1.43</b> (1.03-1.99)
Dual-eligible, LICS	1.11 (0.99-1.25)	<b>1.64</b> (1.21-2.22)	<b>1.45</b> (1.17-1.80)	<b>1.46</b> (1.18-1.81)
Diagnosed tobacco use disorder	1.04 (0.91-1.19)	1.40 (1.00-1.94)	1.05 (0.82-1.34)	1.04 (0.82-1.33)
Charlson Comorbidity Index score	<b>1.14</b> (1.13-1.16)	<b>1.18</b> (1.13-1.23)	<b>1.11</b> (1.08-1.14)	<b>1.12</b> (1.09-1.15)
Diagnosed cancer	<b>0.82</b> (0.72-0.93)	<b>0.63</b> (0.46-0.88)	0.89 (0.71-1.11)	0.85 (0.68-1.06)
Number of unique medications filled	0.99 (0.98-1.00)	1.00 (0.99-1.02)	1.00 (0.99-1.01)	0.99 (0.98-1.01)
Number of unique prescribers	1.01 (0.99-1.04)	1.05 (1.00-1.11)	1.02 (0.98-1.05)	1.01 (0.97-1.05)
Physician office visits	<b>0.98</b> (0.97-0.99)	<b>0.97</b> (0.94-0.99)	<b>1.03</b> (1.02-1.05)	<b>1.12</b> (1.09-1.15)

ACSC indicates ambulatory care-sensitive condition; ED, emergency department; IRR, incidence rate ratio; LICS, low-income cost-sharing subsidy; ref, reference.

<sup>a</sup>We used multivariable random effects negative binomial models. The unit of analysis was patient-period. The models included lagged effects of all the above factors. All statistically significant (P < .05) results are indicated in bold.

<sup>b</sup>Medication nonadherence, defined as proportion of days covered, was based on 17 index drug classes.

<sup>c</sup>Diagnosed mental health condition was defined as diagnosis of depression, anxiety, schizophrenia, other psychotic disorders, or bipolar disorders (≥1 diagnosis claim present in Medicare inpatient, outpatient, or Part B claims) in the 2-year study evaluation period.

## TRENDS FROM THE FIELD

**TABLE 3.** Factors Associated With Inpatient Stays and ED Visits Among Medicare Beneficiaries Younger Than 65 Years (n = 1242 patient-periods)<sup>a</sup>

Characteristics	Inpatient Stays		ED Visits	
	Overall IRR (95% CI)	ACSC IRR (95% CI)	Overall IRR (95% CI)	ACSC IRR (95% CI)
Medication nonadherence <sup>b</sup>	<b>1.31</b> <b>(1.16-1.47)</b>	<b>1.54</b> <b>(1.13-2.09)</b>	<b>1.33</b> <b>(1.14-1.55)</b>	<b>1.28</b> <b>(1.10-1.50)</b>
Diagnosed mental health condition <sup>c</sup>	<b>1.25</b> <b>(1.11-1.41)</b>	1.06 (0.77-1.48)	<b>1.41</b> <b>(1.18-1.69)</b>	<b>1.42</b> <b>(1.18-1.72)</b>
≥7-day supply of opioids	1.11 (0.98-1.25)	0.94 (0.68-1.30)	1.10 (0.92-1.33)	1.11 (0.92-1.33)
Female (ref: male)	1.07 (0.96-1.21)	0.79 (0.54-1.15)	1.06 (0.87-1.29)	1.08 (0.88-1.32)
Race/ethnicity				
White/others (ref)	-	-	-	-
Non-Hispanic black	0.99 (0.86-1.13)	0.91 (0.58-1.41)	1.21 (0.96-1.53)	1.10 (0.86-1.40)
Eligibility status				
Non-dual-eligible, non-LICS (ref)	-	-	-	-
Non-dual-eligible, LICS	1.08 (0.83-1.40)	1.34 (0.59-3.02)	1.23 (0.80-1.90)	1.26 (0.81-1.97)
Dual-eligible, LICS	1.02 (0.82-1.28)	1.49 (0.73-3.01)	1.38 (0.95-2.01)	1.43 (0.97-2.10)
Diagnosed tobacco use disorder	<b>1.24</b> <b>(1.10-1.40)</b>	<b>1.72</b> <b>(1.21-2.43)</b>	<b>1.27</b> <b>(1.04-1.53)</b>	<b>1.30</b> <b>(1.07-1.59)</b>
Charlson Comorbidity Index score	<b>1.10</b> <b>(1.08-1.12)</b>	<b>1.10</b> <b>(1.04-1.17)</b>	<b>1.04</b> <b>(1.01-1.07)</b>	<b>1.08</b> <b>(1.05-1.11)</b>
Diagnosed cancer	0.98 (0.84-1.14)	0.78 (0.48-1.29)	1.23 (0.97-1.56)	1.15 (0.90-1.46)
Number of unique medications filled	<b>0.98</b> <b>(0.97-0.99)</b>	0.99 (0.97-1.01)	<b>0.98</b> <b>(0.97-0.99)</b>	<b>0.98</b> <b>(0.97-0.99)</b>
Number of unique prescribers	1.02 (1.00-1.04)	1.01 (0.96-1.06)	<b>1.06</b> <b>(1.04-1.09)</b>	<b>1.05</b> <b>(1.03-1.08)</b>
Physician office visits	0.99 (0.98-1.00)	0.98 (0.95-1.01)	1.01 (0.99-1.02)	1.01 (1.00-1.02)

ACSC indicates ambulatory care-sensitive condition; ED, emergency department; IRR, incidence rate ratio; LICS, low-income cost-sharing subsidy; ref, reference.

<sup>a</sup>We used multivariable random effects negative binomial models. The unit of analysis was patient-period. The models included lagged effects of all the above factors. All statistically significant ( $P < .05$ ) results are indicated in bold.

<sup>b</sup>Medication nonadherence, defined as proportion of days covered, was based on 17 index drug classes.

<sup>c</sup>Diagnosed mental health condition was defined as diagnosis of depression, anxiety, schizophrenia, other psychotic disorders, or bipolar disorders (≥1 diagnosis claim present in Medicare inpatient, outpatient, or Part B claims) in the 2-year study evaluation period.

was associated with lower preventable hospitalizations in elderly Medicare beneficiaries. This finding suggests that adequately treated pain may lead to lower hospitalizations in elderly Medicare patients. Policies that encourage limiting use of opioid medications to short courses of fewer than 7 days may be beneficial if complemented with proven alternative methods of chronic pain management.

There were weak but significant associations between outcomes and other factors including physician office visits, polypharmacy, and number of prescribers. Although having 1 or more physician office visits was associated with lower hospitalizations, it was significantly

associated with higher ED visits among elderly Medicare beneficiaries. Polypharmacy was protective, whereas having a higher number of prescribers was associated with higher utilization among nonelderly Medicare beneficiaries. These findings should be interpreted with caution given the weak associations for these factors.

This study has important implications for policy makers and institutions involved in improving care and reducing healthcare costs for super-utilizers. Our study findings suggest that early medication adherence support is needed to address medication nonadherence. Hospitals and payers may evaluate programs aimed at improving medication adherence among this population. Furthermore, our findings of an association between mental health diagnosis and utilization highlight the importance of mental health care and social support. Given the complex medical and social needs of Medicare super-utilizers, future studies should examine programs that address these barriers. Moreover, disabled nonelderly Medicare patients, who have higher rates of comorbidities, mental illness, tobacco use disorder, and opioid use compared with elderly Medicare beneficiaries, merit particular targeting and social support.

### Limitations

The PDC measure is an indirect method that may not accurately capture medication use and is not accurate for measuring insulin adherence. Excluding patients on insulin limits the generalizability to insulin users. The study did not account for medication switching between therapy classes. However, examining medication adherence using an alternate method that did not follow patients continuously over time allowed for checking the reliability of the main adherence measure. Additionally, pharmacy claims data capture only medication fills and not prescriptions written by the provider. Evidence suggests that patients receiving 90-day supplies and prescriptions through mail-order pharmacy have higher PDC.<sup>27</sup> Although we did not have information on mail-order pharmacy in the prescription drug event file, we found that only about 10% of drug claims were 90-day fills. The variable Pharmacy Service Type Code indicating the type of pharmacy that dispensed the prescription was not available. Because mental health conditions are often underdiagnosed,<sup>28,29</sup> our definition based on diagnosis might not reflect the true prevalence in super-utilizers. The study findings may be generalizable only

to similar populations and settings across the country because they are based on super-utilizers living in Memphis, Tennessee. Additionally, because this study included fee-for-service Medicare beneficiaries, the results may not be generalizable to beneficiaries on Medicare Advantage plans. Given their high inpatient and ED utilization and high rates of comorbidities, our patient population was much sicker than beneficiaries on Medicare Advantage plans. Although we adjusted for comorbidities and other factors that affect utilization, other unobserved factors that were not available in claims data may not have been accounted for in this study. Because we used data from the CMS/HCIA-funded SafeMed Program, we had access to data for only super-utilizing patients who were potentially eligible for this program. This may limit the generalizability of this study. Finally, although we defined hospitalizations and ED visits for ambulatory care-sensitive conditions as preventable using the AHRQ definition, not all hospitalizations for these conditions are preventable.

## CONCLUSIONS

Overall medication nonadherence was associated with more hospitalizations and ED use among Medicare super-utilizers, who are patients with disproportionately high inpatient and ED use. We found similar associations for type 2 diabetes, cardiovascular, and COPD/asthma disease categories. Mental health diagnosis was associated with higher inpatient and ED use among both age groups. The associations between opioid medication use and inpatient and ED use were inconsistent and not significant in most cases. The exception was 7 or more days' supply of opioid medications, which was significantly associated with lower preventable hospitalizations among elderly Medicare super-utilizers. The study findings suggest the importance of early monitoring and addressing of medication nonadherence and behavioral health needs among Medicare super-utilizers. More research is needed to examine programs that target medication nonadherence and behavioral health among Medicare super-utilizers. ■

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**eAppendix Table 1.** List of Type-2 Diabetes, Cardiovascular, and COPD/Asthma Drug Classes<sup>a</sup>

<b>Type-2 diabetes oral hypoglycemic medications</b>	sulfonylureas, biguanides, thiazolidinediones, meglitinides, and dipeptidyl peptidase-4 inhibitors
<b>Cardiovascular disease medications</b>	angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARB), statins, antiplatelet agents, beta-blockers, calcium channel blockers, diuretics, alpha-1 blockers, central alpha-2 agonists, and direct vasodilators
<b>COPD/asthma drug classes</b>	anticholinergic inhalers, inhaled corticosteroids alone or in combination with long-acting beta-agonists (LABA), and other COPD/asthma medications (theophylline and leukotriene modifiers)

<sup>a</sup> The study sample included adult super-utilizers ( $\geq 3$  hospitalizations or  $\geq 2$  hospitalizations with  $\geq 2$  ED visits in 6 months), diagnosed with  $\geq 1$  of the above mentioned ambulatory care sensitive conditions, with continuous eligibility for Medicare Part A, B, and D, and who had filled  $\geq 1$  of 17 type-2 diabetes, cardiovascular, or COPD/asthma drug classes, during the 2-year period.

**eAppendix Table 2.** Comorbidities, Medication Use, and Health Services Utilization in Each 6-Month Patient-Period among Younger (ages < 65) and Older (ages 65+) Medicare Beneficiaries, (n=1,092)

<b>Characteristics</b>	<b>Period 1</b>	<b>Period 2</b>	<b>Period 3</b>	<b>Period 4</b>
<b>Medicare Beneficiaries &lt;65 years, N=468</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>
Overall medication nonadherence <sup>a</sup>	188 (47.7)	282 (66.7)	312 (72.7)	354 (79.0)
Opioids with $\geq 7$ -day supply	237 (50.6)	261 (55.8)	249 (53.2)	284 (60.7)
No. of unique medications filled, mean (SD)	5.2 (7.1)	5.4 (7.5)	6.6 (7.5)	9.8 (8.9)
No. of unique prescribers, mean (SD)	5.1 (3.4)	5.4 (3.5)	5.4 (3.6)	6.7 (3.7)
Health services utilization				
$\geq 1$ physician office visits	393 (84.0)	393 (84.0)	391 (83.6)	392 (83.8)
No. of inpatient stays, mean (SD)	1.0 (1.7)	1.1 (1.8)	1.0 (1.7)	3.3 (1.3)
No. of emergency department visits, mean (SD)	1.2 (2.8)	1.3 (3.1)	1.4 (2.9)	2.3 (3.5)
Super-utilizers	80 (17.1)	88 (18.8)	68 (14.3)	468 (100.0)
<b>Medicare Beneficiaries <math>\geq 65</math> years, N=624</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>
Overall medication nonadherence <sup>b</sup>	190 (33.5)	285 (48.5)	363 (60.3)	418 (68.3)
Opioids with $\geq 7$ -day supply	252 (40.4)	255 (40.9)	247 (39.6)	323 (51.8)
No. of unique medications filled, mean (SD)	5.5 (6.5)	5.6 (6.6)	6.3 (6.8)	8.7 (8.3)
No. of unique prescribers, mean (SD)	3.9 (2.4)	4.0 (2.3)	4.1 (2.5)	5.1 (2.5)
Health services utilization				
$\geq 1$ physician office visits <sup>b</sup>	507 (81.3)	510 (81.7)	518 (83.0)	523 (83.8)
No. of inpatient stays, mean (SD)	.56 (1.0)	.50 (1.0)	.56 (1.0)	3.0 (.5)
No. of emergency department visits, mean (SD)	.47 (1.2)	.60 (1.1)	.58 (1.2)	1.2 (1.6)
Super-utilizers	43 (6.9)	50 (8.0)	43 (6.9)	624 (100.0)

<sup>a</sup> Medication nonadherence defined as proportion of days covered (PDC) was based on seventeen index drug classes.

Sample size for medication nonadherence:

- Medicare beneficiaries <65 years (Period 1: N=394, Period 2: N=423, Period 3: N=429, Period 4: N=448)
- Medicare beneficiaries  $\geq 65$  years (Period 1: N=567, Period 2: N=588, Period 3: N=602, Period 4: N=612)

<sup>b</sup> Physician office visits were identified using Part B claims and were defined as “location, other than a hospital, skilled nursing facility (SNF), military treatment facility, community health center, State or local public health clinic, or intermediate care facility (ICF),

where the health professional routinely provides health examinations, diagnosis, and treatment of illness or injury on an ambulatory basis.”

**eAppendix Table 3.** Association of Medication Adherence with Inpatient Stays and Emergency Department Visits by Disease Category <sup>a</sup>

Therapy Class	Inpatient Stays		ED Visits <sup>e</sup>	
	IRR <sup>f</sup> (95% CI)	P Value <sup>g</sup>	IRR <sup>f</sup> (95% CI)	P Value <sup>g</sup>
Diabetes Medications <sup>b</sup>				
Nonadherence (overall sample)	1.32 (1.14-1.53)	<b>&lt;.001</b>	1.21 (1.01-1.48)	<b>.04</b>
Nonadherence (<65 years)	1.24 (0.98-1.58)	.07	1.24 (0.98-1.57)	.07
Nonadherence (≥65 years)	1.30 (1.07-1.57)	<b>.008</b>	1.17 (0.92-1.50)	.21
Cardiovascular Disease Medications <sup>c</sup>				
Nonadherence (overall sample)	1.42 (1.25-1.61)	<b>&lt;.001</b>	1.26 (1.13-1.40)	<b>&lt;.001</b>
Nonadherence (<65 years)	1.33 (1.19-1.50)	<b>.001</b>	1.26 (1.13-1.40)	<b>&lt;.001</b>
Nonadherence (≥65 years)	1.42 (1.19-1.69)	<b>&lt;.001</b>	1.23 (1.06-1.44)	<b>.007</b>
COPD <sup>h</sup> or Asthma Medications <sup>d</sup>				
Nonadherence (overall sample)	1.20 (1.02-1.42)	<b>.03</b>	1.34 (1.02-1.74)	<b>.03</b>
Nonadherence (<65 years)	1.04 (0.80-1.36)	.78	1.24 (0.84-1.84)	.29
Nonadherence (≥65 years)	1.48 (1.01-2.18)	<b>.04</b>	1.38 (0.96-1.99)	.08

<sup>a</sup> We used multivariable random effects negative binomial models. The adjusted models included lagged effects of medication nonadherence, race, dual low-income status, gender, Charlson comorbidity index, diagnosed mental health conditions, tobacco use disorder, opioid medication filled, number of medications filled, number of different prescribers, and ≥1 physician office visits.

<sup>b</sup> Diabetes Medications: Overall sample: 794 patient-periods, <65 years: 293 patient-periods, ≥65 years: 501 patient-periods.

<sup>c</sup> Cardiovascular Disease Medications: Overall sample: 2,925 patient-periods, <65 years: 1,195 patient-periods, ≥65 years: 1,730 patient-periods.

<sup>d</sup> COPD or Asthma Medications: Overall sample: 560 patient-periods, <65 years: 222 patient-periods, ≥65 years: 338 patient-periods

<sup>e</sup> Emergency department visits

<sup>f</sup> Incidence Rate Ratio

<sup>g</sup> Significant at  $P < 0.05$ .

<sup>h</sup> Chronic obstructive pulmonary disease.

**eAppendix Table 4.** Factors Associated with Inpatient Stays and Emergency Department Visits among Medicare Beneficiaries  $\geq 65$  years Using Alternative Criteria\* (N=1,737 patient-periods) <sup>a</sup>

Characteristics	Inpatient Stays		ED Visits <sup>b</sup>	
	Overall IRR <sup>c</sup> (95% CI)	ACSC IRR <sup>c</sup> (95% CI)	Overall IRR <sup>c</sup> (95% CI)	ACSC IRR <sup>c</sup> (95% CI)
Medication nonadherence <sup>d</sup>	<b>1.26 (1.14-1.40)</b>	<b>1.32 (1.04-1.66)</b>	<b>1.16 (1.00-1.34)</b>	1.15 (0.98-1.34)
Diagnosed mental health condition <sup>e</sup>	<b>1.50 (1.34-1.68)</b>	1.12 (0.85-1.48)	<b>1.48 (1.23-1.77)</b>	<b>1.49 (1.24-1.79)</b>
$\geq 7$ day supply of opioids	1.01 (0.90-1.12)	<b>0.74 (0.58-0.95)</b>	1.09 (0.92-1.28)	0.94 (0.79-1.11)
Female (Ref: Male)	0.99 (0.89-1.10)	1.02 (0.77-1.35)	1.05 (0.88-1.27)	1.18 (0.96-1.44)
White/Others (ref)	--		--	
Non-Hispanic Black	<b>0.88 (0.78-0.98)</b>	<b>0.53 (0.39-0.71)</b>	<b>1.26 (1.02-1.57)</b>	1.19 (0.96-1.48)
Non-Dual Non-LICS (ref) <sup>f</sup>				
Non-Dual LICS	1.17 (0.96-1.42)	<b>1.81 (1.12-2.94)</b>	1.39 (1.00-1.94)	<b>1.41 (1.01-1.97)</b>
Dual LICS	1.13 (1.00-1.28)	<b>1.62 (1.20-2.19)</b>	<b>1.43 (1.15-1.77)</b>	<b>1.44 (1.16-1.78)</b>
Diagnosed tobacco use disorder	1.11 (0.96-1.28)	1.38 (1.00-1.92)	1.01 (0.80-1.27)	1.05 (0.82-1.34)
Charlson comorbidity index	<b>1.08 (1.06-1.10)</b>	<b>1.18 (1.13-1.24)</b>	<b>1.05 (1.02-1.08)</b>	<b>1.12 (1.09-1.16)</b>
Diagnosed cancer	<b>0.83 (0.73-0.94)</b>	<b>0.64 (0.46-0.89)</b>	0.88 (0.70-1.10)	0.83 (0.67-1.04)
Number of unique medications filled	0.99 (0.98-0.99)	1.00 (0.98-1.02)	1.00 (0.99-1.01)	0.99 (0.98-1.01)
Number of unique prescribers	1.02 (0.99-1.04)	1.07 (1.01-1.13)	1.02 (0.98-1.05)	1.01 (0.97-1.05)
Physician office visits	<b>0.98 (0.97-0.99)</b>	<b>0.96 (0.94-0.99)</b>	<b>1.03 (1.02-1.05)</b>	<b>1.03 (1.02-1.05)</b>

<sup>a</sup> We used multivariable random effects negative binomial models. The unit of analysis was patient-period. The models included lagged effects of all the above factors. All statistically significant results are indicated in bold.

<sup>b</sup> Emergency Department visits

<sup>c</sup> Incidence Rate Ratio.

<sup>d</sup> Medication nonadherence defined as proportion of days covered (PDC) was based on seventeen index drug classes.

<sup>e</sup> Diagnosed mental health condition was defined as diagnosis of depression, anxiety, schizophrenia, other psychotic disorders, or bipolar disorders (at least 1 diagnosis claim present in Medicare inpatient, outpatient, or Part B claims) in the 2-year study evaluation period

<sup>f</sup> Low-income cost sharing subsidy

**eAppendix Table 5.** Factors Associated with Inpatient Stays and Emergency Department Visits among Medicare Beneficiaries <65 years Using Alternative Criteria\* (N=1,210 patient-periods) <sup>a</sup>

Characteristics	Inpatient Stays		ED Visits <sup>b</sup>	
	Overall IRR <sup>c</sup> (95% CI)	ACSC IRR <sup>c</sup> (95% CI)	Overall IRR <sup>c</sup> (95% CI)	ACSC IRR <sup>c</sup> (95% CI)
Medication nonadherence <sup>d</sup>	<b>1.26 (1.13-1.41)</b>	<b>1.46 (1.08-1.96)</b>	<b>1.24 (1.06-1.44)</b>	<b>1.23 (1.05-1.43)</b>
Diagnosed mental health condition <sup>e</sup>	<b>1.21 (1.07-1.36)</b>	1.10 (0.79-1.51)	<b>1.39 (1.15-1.68)</b>	<b>1.37 (1.14-1.66)</b>
≥7 day supply of opioids	1.11 (0.98-1.26)	0.92 (0.66-1.27)	1.12 (0.93-1.35)	1.14 (0.94-1.37)
Female (Ref: Male)	1.06 (0.94-1.19)	0.80 (0.55-1.16)	1.05 (0.85-1.30)	1.04 (0.84-1.29)
White/Others (ref)	--		--	
Non-Hispanic Black	0.98 (0.85-1.14)	0.87 (0.56-1.35)	1.19 (0.93-1.53)	1.15 (0.90-1.47)
Non-Dual Non-LICS (ref) <sup>f</sup>				
Non-Dual LICS	1.06 (0.82-1.38)	1.28 (0.57-2.87)	1.28 (0.81-2.04)	1.25 (0.79-1.98)
Dual LICS	1.01 (0.80-1.26)	1.49 (0.74-3.01)	1.42 (0.95-2.11)	1.39 (0.93-2.06)
Diagnosed tobacco use disorder	<b>1.25 (1.10-1.41)</b>	<b>1.75 (1.24-2.46)</b>	<b>1.30 (1.06-1.59)</b>	<b>1.31 (1.07-1.61)</b>
Charlson comorbidity index	<b>1.07 (1.05-1.09)</b>	<b>1.10 (1.04-1.16)</b>	<b>1.08 (1.05-1.11)</b>	<b>1.08 (1.05-1.11)</b>
Diagnosed cancer	0.96 (0.82-1.12)	0.81 (0.49-1.33)	<b>1.28 (1.01-1.64)</b>	1.20 (0.94-1.53)
Number of unique medications filled	<b>0.98 (0.97-0.99)</b>	0.99 (0.97-1.01)	<b>0.98 (0.97-0.99)</b>	<b>0.98 (0.97-0.99)</b>
Number of unique prescribers	1.02 (0.99-1.03)	1.02 (0.97-1.07)	<b>1.05 (1.03-1.08)</b>	<b>1.05 (1.02-1.07)</b>
Physician office visits	0.99 (0.98-1.00)	0.98 (0.96-1.02)	1.01 (0.99-1.02)	1.01 (0.99-1.02)

<sup>a</sup> We used multivariable random effects negative binomial models. The unit of analysis was patient-period. The models included lagged effects of all the above factors. All statistically significant results are indicated in bold.

<sup>b</sup> Emergency Department visits

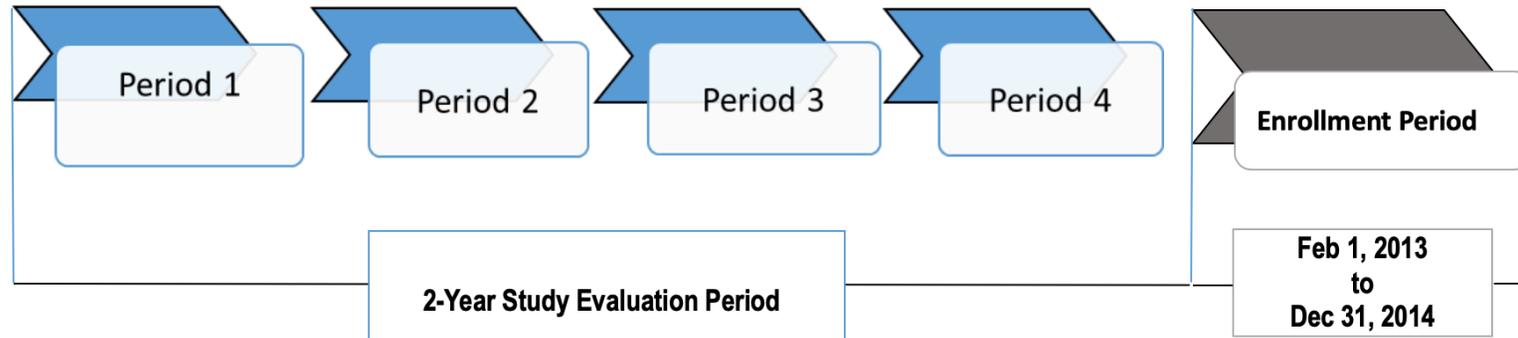
<sup>c</sup> Incidence Rate Ratio.

<sup>d</sup> Medication nonadherence defined as proportion of days covered (PDC) was based on seventeen index drug classes.

<sup>e</sup> Diagnosed mental health condition was defined as diagnosis of depression, anxiety, schizophrenia, other psychotic disorders, or bipolar disorders (at least 1 diagnosis claim present in Medicare inpatient, outpatient, or Part B claims) in the 2-year study evaluation period

<sup>f</sup> Low-income cost sharing subsidy

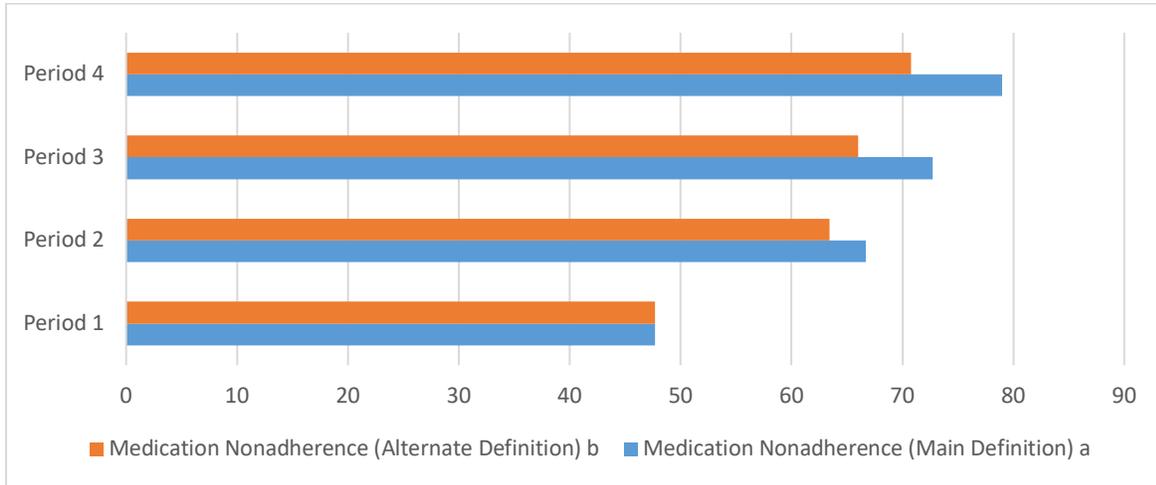
**eAppendix Figure 1. Study Design<sup>a</sup>**



<sup>a</sup> This study was a retrospective panel analysis of the baseline data for Medicare beneficiaries meeting the SafeMed Program eligibility criteria during the enrollment period from February 2013-December 2014. For each patient, we reviewed 2 years of data prior to SafeMed enrollment. The dates of this 2-year baseline period varied for each patient based on their enrollment date for the SafeMed Program. For instance, if a patient was enrolled in the SafeMed Program in February 1, 2013, the 2-year evaluation period was from February 12, 2011 to February 1, 2013. The data for each patient were divided into four 6-month patient-periods, with the last 6-month period serving as the qualifying period for the SafeMed Program.

### eAppendix Figure 1

#### A. Medication Nonadherence Rates (proportion of patients with PDC<80%) among Medicare Beneficiaries <65 Years Using Main and Alternate PDC definitions.



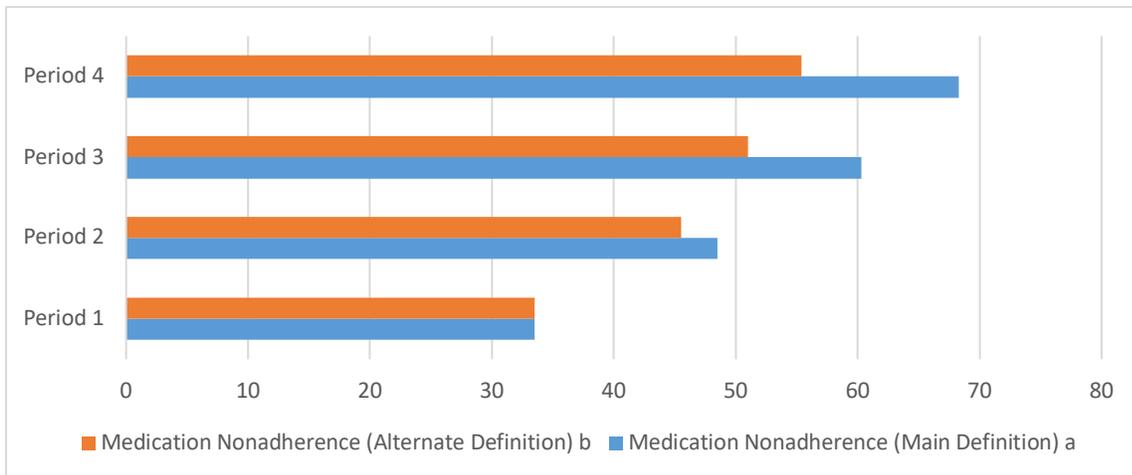
<sup>a</sup> Patients were continuously followed once they filled  $\geq 2$  medications for a drug class.

Sample size for main definition: Period 1: N=394, Period 2: N=423, Period 3: N=429, Period 4: N=448.

<sup>b</sup> Alternate Definition: Patients who filled  $\geq 2$  medications for a drug class in any of the previous periods were required to have at least one fill for that drug class in the current period.

Sample size for alternate definition: Period 1: N=394, Period 2: N=415, Period 3: N=415, Period 4: N=438.

#### B. Medication Nonadherence Rates (proportion of patients with PDC<80%) among Medicare Beneficiaries $\geq 65$ Years Using Main and Alternate PDC definitions.



<sup>a</sup> Patients were continuously followed once they filled  $\geq 2$  medications for a drug class.

Sample size for main definition: Period 1: N=567, Period 2: N=588, Period 3: N=602, Period 4: N=612.

<sup>b</sup> Patients who filled  $\geq 2$  medications for a drug class in any of the previous periods were required to have at least one fill for that drug class in the current period.

Sample size for alternate definition: Period 1: N=567, Period 2: N=583, Period 3: N=592, Period 4: N=607