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Disparities in Combination Drug Therapy Use in Older Adults with Coronary Heart Disease

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Abstract

Background—Despite evidence of effective combination drug therapy for secondary prevention of coronary heart disease (CHD), older adults remain undertreated.

Objective—To describe time trends (1992–2003) in the adoption of combination cardiac drug therapies (beta blockers, angiotensin-converting enzyme inhibitors [ACE] or angiotensin II receptor blockers [ARB], and lipid-lowering agents) among older adults with CHD and to identify factors associated with not using combination therapy.

Design—Cross-sectional time-series.

Participants—Nationally representative sample of adults aged ≥ 65 years with CHD (unweighted $n=6,331$; weighted $n=20.1$ million) included in the 1992–2003 Medicare Current Beneficiary Survey

Main Outcome Measurements—The outcome measure is low-intensity cardiac pharmacotherapy (no drug or single drug therapy with beta-blockers, ACE/ARBs, or lipid-lowering agents) compared to combination therapy (≥ 2 cardiac drugs) for secondary CHD prevention.

Results—Use of combination drug therapy in older adults with CHD increased 9-fold during the study period (6% in 1992 to 54% in 2003). Adjusted analyses demonstrate that suboptimal drug therapy was independently associated with advanced age (relative risk [RR] 1.18 [95% confidence interval: 1.14–1.23]) for persons ≥ 85 years vs 65–74 years; being black (RR 1.05 [95% CI: 1.01–1.10]) or Hispanic (RR 1.12 [95% CI: 1.06–1.21]) vs being non-Hispanic white.

Conclusions—Combination drug therapy use for secondary CHD prevention increased in older adults over the last decade, but improvements were not uniform. The oldest-old, non-Hispanic blacks and Hispanics experienced slower adoption of optimal medical therapy to improve their long-term prognosis for CHD.

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Conflict of Interest

Dr. Briesacher has received an unrestricted grant from and has served as a consultant for Novartis Pharmaceuticals in the last 3 years.

Background

Care for coronary heart disease (CHD) has changed considerably over the past two decades. Evidence demonstrating the efficacy of multiple cardiac medications for the secondary prevention of CHD has resulted in evolving clinical guidelines that intensified pharmacotherapy for patients with CHD throughout the 1990s.¹⁻³ Initial guidelines recommended the use of aspirin and beta-blockers in most patients with CHD², and later guidelines extended treatment to four therapies - aspirin, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors or angiotensin II-receptor blocking agents (ARB), and lipid-lowering agents.^{3, 4} However, the adoption of effective medications has been slow for several high-risk CHD patient groups, including older adults⁵⁻⁸. Understanding underuse of effective cardiac medications by older adults is limited because prior studies were not able to account for other important patient-level factors that influence physician prescribing for older adults, such as limited income⁹, lack of prescription drug benefits¹⁰, or patient frailty.¹¹ It therefore remains important to describe and understand factors affecting trends in the use of combination drug therapies for the secondary prevention of CHD in the vulnerable population of older adults with CHD and to examine whether advanced age alone, after accounting for age-related confounders, explains underuse in this population.

The aims of this study were to examine a more than decade-long trend in the use of a combination of ACE/ARBs, beta blockers, and lipid-lowering medications for the secondary prevention of CHD among a national sample of older adults in the United States between 1992 and 2003 and to identify factors associated with the use of no therapy or single drug therapy for the secondary prevention of CHD while accounting for potential age-related confounders (including annual income, lack of prescription drug benefits, and functional impairment).

METHODS

Data Source

The Medicare Current Beneficiary Survey (MCBS) was utilized for this investigation. The MCBS is a continuous annual face-to-face survey of a nationally-representative sample of approximately 15,000 Medicare beneficiaries. Information is collected regarding demographic characteristics, income, living arrangements, health and functional status, healthcare behaviors, health insurance coverage, health care utilization and expenditures, and access to medical care. The sample is drawn from Medicare enrollment data according to a multi-stage sampling design. Respondents are interviewed in person three times a year using Computer Assisted Personal Interviewing (CAPI), resulting in very high response rates (about 85%).¹²

Study Sample

Beneficiaries were included in the study sample if they were aged 65 years, lived in the community, had a history of CHD, and had a full year of observation for measuring annual medication use. Individuals with CHD were identified as having 2 or more physician or hospital claims records with a diagnosis of CHD (*International Classification of Diseases, Ninth Revision [ICD-9], code 410.xx-414.xx*). We excluded individuals in managed care organizations (n=8,135) since Medicare claims were not available for identifying potential cases of CHD. In addition, we used data from only the first year of observation to generate independent observations across years. The final sample size by year of observation was: 1,659 in 1992, 297 in 1993, 273 in 1994, 565 in 1995, 547 in 1996, 494 in 1997, 444 in 1998, 449 in 1999, 395 in 2000, 377 in 2001, 408 in 2002, and 423 in 2003. The final weighted population in 1,000s was: 5,126 in 1992, 965 in 1993, 649 in 1994, 1,900 in 1995,

1,898 in 1996, 1,649 in 1997, 1,353 in 1998, 1,389 in 1999, 1,220 in 2000, 1,242 in 2001, 1,333 in 2002, and 1,432 in 2003, for a total of 20.1 million beneficiaries across all years.

Measures of Health and Socioeconomic Status

We used the adapted Charlson comorbidity score that predicts mortality and health service utilization as our main measure of disease burden.¹³ We also measured frailty with the activities of daily living score (ADLs) [categorized as independent, instrumental ADL impairment only, 1–2 ADL impairments, ≥ 3 ADL impairments]. We examined annual household income in the following categories (< \$10,000; \$10,001–\$20,000; \$20,001–\$30,000; \geq \$30,000) adjusted to 2003 dollars using the Consumer Price Index. The two lowest income categories roughly correspond to the 100% and 200% federal poverty thresholds, respectively.¹⁴ We also measured socioeconomic status as the following: race/ethnicity (non-Hispanic black, non-Hispanic white, Hispanic, other self-reported race/ethnicity) and highest level of education achieved (less than high school, high school graduate, greater than high school). Residence in a metropolitan versus rural region was identified in the MCBS using United States federal government definitions of residence in a metropolitan statistical area of high or low population density. Prescription drug coverage was defined as being present if there was any prescription paid for by third party insurance or the respondent reported having drug coverage.

Measures of Drug Therapy

The cardiac medications examined in this study included ACE inhibitors or angiotensin II-receptor blockers, beta blockers, and lipid-lowering agents. The utilization of ACEs and ARBs were combined into a single category which included single or combination products. Beta blockers were defined as all beta-blockers available as single or combination products and included alpha beta-blockers. Lipid-lowering agents were defined as the utilization of statins, niacin, gemfibrozil, and other antihyperlipidemics. We were unable to study aspirin use since this and other over-the-counter medications are not recorded in the MCBS. The outcome measure is low-intensity pharmacotherapy (no drug or single drug therapy with beta-blockers, ACE/ARBs, or lipid-lowering agents) compared to combination therapy (≥ 2 cardiac drugs) for secondary CHD prevention. The term low-intensity pharmacotherapy is used to refer to the use of no drug or single drug therapy for the rest of the paper because use of combination drug therapy, though not inappropriate, was not widely indicated for most patients prior to the 2001 American College of Cardiology/American Heart Association secondary prevention guidelines³. Prescription medication use is based on self-report, but is verified through insurance receipts or pill bottle counts during in-home interviews. Patients were defined as receiving a cardiac medication if any prescription for that medication was reported during the year under study.

Statistical Analysis

We initially calculated the unadjusted prevalence of low-intensity pharmacotherapy and combination cardiac drug use in each study year. We subsequently calculated the unadjusted prevalence of low-intensity (0–1) and combination (≥ 2) cardiac drug use at selected time periods (1992–93; 1997–98; 2002–03) according to patient demographic and health status-related characteristics. To construct national estimates, we used sample weights included in the MCBS file and the Taylor expansion method for weighting and variance calculation recommended by the MCBS technical documentation.¹⁵

To evaluate the relative impact of patient characteristics on the receipt of combination cardiac drug use by older adults with CHD over time, we developed multivariable regression models using generalized estimating equations (GEE). The dependent variable was the dichotomous outcome of low-intensity pharmacotherapy use across all years compared to

combination pharmacotherapy use across all years. The independent variables included patient demographics (sex, age, annual income, race, level of educational attainment, rural/metropolitan residence), health status (number of comorbidities, functional status), possession of prescription drug insurance, and year of study observation.

To account for the complex survey design, we developed two GEE models. The primary model corrected for clustering due to the sampling design but did not incorporate the sampling weights. The secondary model incorporated the cross-sectional sampling weights but could not accommodate a variance correction due to clustering. A comparison of the parameter estimates for each model showed stable and nearly identical results, so we have presented only the results from our primary model with the correct standard errors. Using a method described by McNutt¹⁶ to estimate relative risk ratios in studies of common outcomes, we specified the GEE models using a Poisson distribution with a log link and independent working correlation structure.

All analyses were performed in Stata SE 10.0 (Stata Corporation, College Station, TX). This study was reviewed and approved by the institutional review board of the University of Massachusetts Medical School.

RESULTS

Characteristics of Study Population

Approximately 20.1 million beneficiaries (unweighted $n=6,331$) are represented in our study sample. Approximately 1.7 million beneficiaries are represented in each observation year. The average age of patients with CHD was 77.8 years. The majority of our study sample were female (52.0%), white (89.2%), had an annual income $< \$20,000$ (52.4%), had a greater than high school education (57.8%), lived in a metropolitan area (73.7%), and had prescription drug benefits (57.7%). The proportion with prescription drug benefits increased over the period under study from 42.7% in 1992 to 75.3% in 2003. A large proportion of the study sample had a comorbidity score of ≥ 4 (47.0%), 68% were functionally independent, and 8% had ≥ 3 ADL impairments.

Trends in the Use of Combination Drug Therapy

Increases were observed in the use of each of the cardiac drugs examined by elders with CHD during the more than decade-long period under study (Figure 1), including ACE/ARB's (21% in 1992–53% in 2003), beta-blockers (18%–51%) and lipid-lowering drugs (8%–53%). There were also marked increases in the use of combination therapy over time (Figure 2). Approximately 6% of beneficiaries with CHD were treated with combination pharmacotherapy in 1992; in 2003, approximately 54% reported using a multidrug regimen.

Profile of Patients Using Effective Cardiac Drugs

Table 1 shows how the use of cardiac drugs, particularly combination therapies, changed over time for certain vulnerable subgroups. For example, in 2002–2003, approximately one-third of the oldest-old (≥ 85 years) received combination therapies compared to approximately 3 in every 5 of those 65–74 years old. In 2002–2003, 39.37% of the poor (annual income $< \$10,000$) used combination therapy compared to 54.4% of higher income beneficiaries.

For all age subgroups, the increase in combination therapy was greater than 5-fold between 1992 and 2003 (Table 1). However, the absolute change in the prevalence of combination therapy was smaller for the 85 year olds (28.7%) compared to the 75–84 year olds (47.4%) and 65–74 year olds (49.8%); additionally, the overall prevalence of combination

pharmacotherapy in our most recent study year (2003) remained lowest for the oldest-old (32.2%). The relative difference in combination pharmacotherapy for the youngest-old compared to the oldest-old was almost 2.5-fold (8.7% vs 3.5%) in 1992–1993, and 1.8-fold (58.5% vs 32.3%) in 2002–2003.

Different trends in combination pharmacotherapy were also observed for some racial groups. For example, blacks had a lower relative and absolute difference in combination pharmacotherapy between 1992 and 2003, with only a 5-fold relative increase and 35% absolute difference over the observed period. In contrast, whites had an 8.7-fold relative increase, and a 47.5% absolute increase, in combination therapy over time. In some demographic categories, the gaps in multidrug use observed in the early period narrowed over time. For example, there was a 200% relative difference in the use of combination cardiac pharmacotherapy among patients with educational attainment above high school compared to those with less than a high school education in 1992–1993 that closed to less than 10% in 2002–2003. These trends were not, however, noted according to age.

Factors Associated with Use of Low-Intensity Pharmacotherapy

In the multivariable model of adjusted relative risks of the receipt of low-intensity pharmacotherapy, advancing age, being non-Hispanic black or Hispanic, being poor and having ≥ 3 ADL impairments each increased the likelihood of using suboptimal therapy for the secondary prevention of CHD (Table 2). The strongest effect was observed for advanced age, with an increased adjusted relative risk (RR) for both 75–84 year olds and the ≥ 85 year olds compared to 65–74 year olds (RR = 1.10 [95% confidence interval (CI) 1.07–1.13] and RR = 1.18 [95% CI 1.14–1.23], respectively). A strong association was also seen for being Hispanic (RR = 1.13 [95% CI 1.06–1.21]) and black (RR 1.05 [95% CI 1.01–1.10]) relative to being non-Hispanic white. Being a woman or having a comorbidity score ≥ 4 was independently protective against the use of low-intensity cardiac therapy (RR 0.96 [95% CI 0.94–0.98] and RR 0.94 [95% CI 0.91–0.97], respectively). No association was observed with possession of prescription drug benefits and receipt of low-intensity cardiac medication therapy.

DISCUSSION

Our study of a nationally-representative sample of older adults shows encouraging trends in the use of combination drug therapy for the secondary prevention of CHD. However, we also found evidence of key subgroups at risk for underuse of combination pharmacotherapy. Of concern was the relationship between lack of combination cardiac drug therapy and advanced age, even after adjustment for important confounding factors associated with advanced age such as functional disability, comorbidity burden, and limited income. Of particular concern is underuse of combination pharmacotherapy in 2003, when consensus on CHD prevention unambiguously recommended multidrug therapy. Because the population of older adults is rapidly growing, because CHD is the leading cause of morbidity and mortality in the elderly, and because this population is at overall increased risk of mortality from CHD^{5, 17}, narrowing the gap between recommended therapy and actual practice in the population remains vitally important.

Although reassuring increases in combination cardiac drug therapy occurred between 1992 and 2003, the rate of increase was smaller for some subgroups, including the oldest-old and blacks. In addition, gaps in combination drug therapy that existed during the earliest years under study continued to exist during the most recent study years for several subgroups of older adults, including ethnic minorities. Conversely, gaps in the use of combination drug therapies according to educational attainment appeared to narrow over time.

Other studies have reported lower use of combination drug therapy for patients with CHD of advanced age.⁸ We observed a dose-response relationship between advancing age and combination drug therapy, where the young-old group (65–74 year olds) were least likely to receive low-intensity cardiac therapy and the oldest-old (age \geq 85 years) were most likely to receive low-intensity therapy. The findings of our national cross-sectional sample of US adults are consistent with the results of other investigations that have identified the suboptimal receipt of effective drug therapy in older adults.^{6,18}

Some investigators suggest that limited life-expectancy should be considered when examining prescribing aggressiveness for older patients.¹⁹ Since biologic age is an insufficient marker of life-expectancy, we also examined the relationship between functional disability and the use of combination medical therapy. In this analysis, which adjusted for clinical and demographic factors, we found that severe ADL impairment increased the likelihood of low-intensity therapy (RR 1.08). One interpretation of these data is that physicians may be less likely to prescribe combination therapy for frail older adults with CHD. These data may also suggest that, even after adjustment for functional ability and comorbidity score, advanced age alone is associated with low-intensity pharmacotherapy for CHD. These findings are in agreement with the results of another study showing that older adults, even those at the highest risk of cardiac mortality, are at risk for underuse of effective cardiac medications such as statins.⁵

Older adults have additional challenges to drug acquisition, including limited income and poor access to prescription drug benefits prior to Medicare Part D. For example, the median annual income for persons 65 years and older was slightly more than \$14,000 in 2001.⁹ Not surprisingly, many older adults report cost-related nonadherence to medications.¹⁰ When we examined the relationship between income and combination medical therapy for CHD, we found that after adjustment for inflation, lower income did not appear to be associated with receipt of low-intensity drug therapy. This is in contrast to the results of other studies showing that patients with higher annual income had greater use of guideline recommended therapies in the management of diabetes mellitus.¹¹ Further, we failed to observe an independent association between possession of prescription drug benefits and use of combination drug therapy for CHD prevention. This is likely explained by the increasing availability of prescription drug benefits in our population between 1992–2003. These findings are similar to documented trends in drug benefit access.^{20,21} Given the strong association between possession of prescription drug benefits and time, and the strong effect of time on the use of combination drug therapy in our study, it is not surprising that we did not find an independent association between drug benefits and combination cardiac therapy after adjusting for time.

We also found relationships between non-aging related factors and the use of combination drug therapy for CHD. Being non-white (non-Hispanic black and Hispanic) was associated with a greater risk of less than optimal treatment, a finding others have reported.²² Given the strong upward trend in combination cardiac therapy over time, and adjustment for time trends in our analysis, our findings suggest that race, advanced age and being poor contribute to lags in the adoption of combination drug therapy for CHD prevention.

It is important recall that secondary prevention guidelines for CHD changed during the observation period for our study. While combination drug therapy in 2003 was the standard of care, it was arguably cutting edge and aggressive in the earlier time points of our observation period. In this context, our findings suggest that older adults are less likely to receive standard care in 2003, and less likely to receive aggressive pharmacotherapy for CHD in the 1990s.

We consider the implications of our findings after addressing several caveats. First, we were unable to examine previous adverse events or contraindications to the receipt of selected medications, but argue that these likely occurred non-differentially between our comparison groups, and over time, and had little effect on our findings. Furthermore, medication use in our study was based on self-report and previous MCBS studies suggest underreporting on the order of approximately 5% of filled prescriptions.²³ Because measures were based on actual medication containers and receipts, and not only self-report, this measurement bias is likely to be non-differential by drug coverage or other groups of interest. We also excluded beneficiaries who were members of managed care organizations, thereby limiting the generalizability of our findings to this population. This selection criterion may have contributed to an underestimation of the prevalence of combination cardiac drug use in our study, since managed care organizations strongly promote the use of guideline-recommended drugs for chronic diseases.²⁴ Finally, we were unable to determine whether medications were not received because of a patient preference or physician assessment of limited benefit due to limited life-expectancy.

In summary, approximately 1 in every 5 elderly Medicare beneficiaries received no therapy for CHD prevention despite the presence of CHD and approximately one third received single drug therapy for the secondary prevention of CHD in 2003. As the Center for Medicare and Medicaid Services develops additional measurements for assessing quality of medication use, including under- and over-use of medications, attention needs to be focused on subgroups at risk for underuse identified in our study. These high risk groups include elders over the age of 75 years and racial minorities. Clinical reminder systems and decision support in electronic medical records might be one means of alerting physicians to evaluate the quality of cardiac care for these at risk groups. Policy makers and prescribers need to be mindful of those falling through the prescribing gap.

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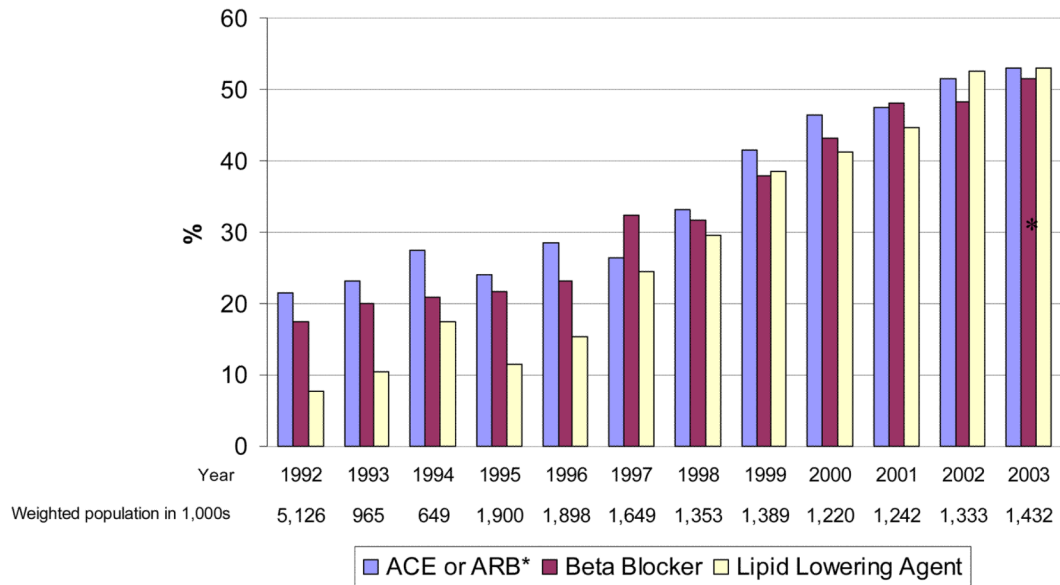


Figure 1.

Time trends in the use of selected cardiac medications by elderly Medicare beneficiaries with coronary heart disease. The proportion of beneficiaries taking ACE (angiotensin-converting enzyme) inhibitors or angiotensin II receptor blockers, beta blockers, and lipid lower agents are presented in each year from 1992–2003.

*ACE (angiotensin-converting enzyme inhibitors); ARB (angiotensin II receptor blockers)

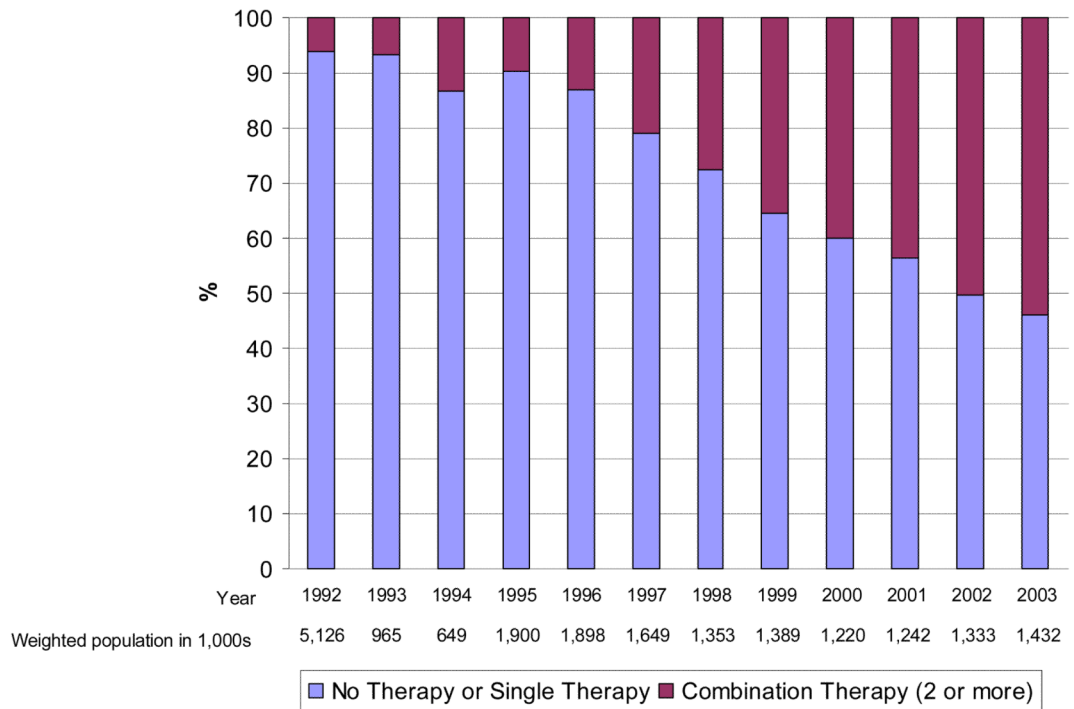


Figure 2. Time trends in the adoption of combination cardiac medication therapy by elderly Medicare beneficiaries with coronary heart disease. The proportion of beneficiaries combination therapy, and no therapy or single therapy are presented in each year from 1992–2003.

Table 1

Receipt of cardiac medications in patients with coronary heart disease (CHD) according to patient characteristics and time period (Medicare Current Beneficiary Survey).*

| <i>Characteristic</i> | Percent (%) of beneficiaries receiving low-intensity pharmacotherapy[†] for CHD | | |
|--------------------------------------|---|---|---|
| | 1992–1993 (weighted n=6.1 million) | 1997–1998 (weighted n=3.0 million) | 2002–2003 (weighted n=2.8 million) |
| Age | | | |
| 65–74 years | 91.3 | 70.6 | 41.5 |
| 75–84 years | 95.5 | 78.4 | 48.1 |
| ≥ 85 years | 96.5 | 87.9 | 67.8 |
| Gender | | | |
| Male | 94.2 | 77.8 | 45.7 |
| Female | 93.3 | 74.6 | 50.1 |
| Race/Ethnicity | | | |
| White | 93.8 | 74.7 | 46.3 |
| Black | 92.1 | 85.2 | 57.2 |
| Hispanic | 99.8 | 93.5 | 58.5 |
| Other [‡] | 97.1 | 86.1 | 67.5 |
| Educational Level | | | |
| No high school | 96.2 | 81.1 | 50.1 |
| High school | 93.0 | 72.9 | 55 |
| Above high school | 41.4 | 75.1 | 45.5 |
| Geography | | | |
| Rural | 92.7 | 75.8 | 43 |
| Metro | 94.1 | 76.3 | 49.6 |
| Annual Income | | | |
| <\$10,000 | 95.8 | 84.5 | 60.7 |
| \$10,001–20,000 | 93.9 | 75.8 | 44.9 |
| \$20,001–30,000 | 93.2 | 74.1 | 53.8 |
| >\$30,000 | 92.4 | 72.4 | 45.6 |
| Prescription Drug Benefit | | | |
| Absent | 94.9 | 78.0 | 49.7 |
| Present | 92.4 | 75.0 | 47.1 |
| Comorbidity Score | | | |
| 0–1 | 94.5 | 77.9 | 53.3 |
| 2–3 | 94.5 | 78.2 | 51.9 |
| ≥ 4 | 92.6 | 74.3 | 44.6 |
| Functional Status[§] | | | |
| Independent | 93.5 | 73.9 | 46.1 |
| Instrumental ADL impairment only | 92.7 | 77.9 | 49.8 |
| 1–2 ADL impairments | 93.1 | 74.1 | 46.4 |
| ≥ 3 ADL Impairments | 96.7 | 90.1 | 59 |

* Weighted percents.

† Low-intensity pharmacotherapy defined as no drug or single drug therapy with beta-blockers, ACE/ARBs, or lipid-lowering agents.

‡ Other includes American Indian/Alaskan Native, Asian and other race/ethnicity specified by respondent.

¶ ADL - activities of daily living

Table 2

Factors associated with use of low-intensity pharmacotherapy by older adults with coronary heart disease (weighted n=20.1 million beneficiaries)

| <i>Use of low-intensity pharmacotherapy</i> [*] | |
|---|--|
| Characteristic | Adjusted [†] Relative Risk (95% CI) |
| Age (65–74 years) [‡] | |
| 75–84 | 1.10 (1.07–1.13) |
| ≥ 85 | 1.18 (1.14–1.23) |
| Gender (Male) [‡] | |
| Female | 0.96 (0.94–0.99) |
| Race/Ethnicity (White Non-Hispanic) [‡] | |
| Black Non-Hispanic | 1.05 (1.01–1.10) |
| Hispanic | 1.13 (1.06–1.21) |
| Other [¶] | 1.00 (1.00–1.18) |
| Educational Level (Above high school) [‡] | |
| No high school | 1.01 (0.98–1.04) |
| High school | 1.03 (1.01–1.06) |
| Geography (Metropolitan) [‡] | |
| Rural | 0.99 (0.96–1.02) |
| Annual Income (≥ \$30,000) [‡] | |
| ≤\$10,000 | 1.04 (1.00–1.09) |
| \$10,001–20,000 | 1.02 (0.99–1.06) |
| \$20,001–30,000 | 1.02 (0.98–1.06) |
| Prescription Drug Benefits (Present) [‡] | |
| None | 1.01 (0.99–1.04) |
| Comorbidity score (0–1) [‡] | |
| 2–3 | 0.98 (0.95–1.01) |
| ≥ 4 | 0.94 (0.91–0.97) |
| Functional Status (Independent) [‡] | |
| IADL impairment only | 1.01 (0.96–1.05) |
| 1–2 ADL impairments | 1.01 (0.98–1.04) |
| ≥ 3 ADL impairments | 1.08 (1.05–1.12) |

* Low-intensity pharmacotherapy defined as no drug or single drug therapy with beta-blockers, ACE/ARBs, or lipid-lowering agents.

[†] Multivariable generalized estimating equation models, including adjustment for study year. Numbers in boldface are statistically significant at P<0.05.

[‡] Indicates the reference group.

[¶] Other includes American Indian/Alaskan Native, Asian and other race/ethnicity specified by respondent.