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ASSOCIATION BETWEEN FUNCTIONAL IMPAIRMENT AND MEDICATION BURDEN AMONG ADULTS WITH HEART FAILURE

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Abstract

Background: Given the inherent risks of taking a high number of medications, balancing the potential benefits and risks of prescribing a high number of medications is important to optimizing outcomes of adults with heart failure (HF). It is not known whether the number of medications taken by adults with HF who have an impairment in their activities of daily living (ADL)—a subpopulation in whom the risks of a high medication burden may outweigh the benefits—differs from those without such an impairment.

Methods: We examined adults aged ≥50 years with self-reported HF from the National Health and Nutrition Examination Survey (2003–2014), a cross-sectional survey that produces national estimates of adults in the United States. We assessed ADL-impairment and medication count based on self-report. ADL-impairment was defined as having difficulty with or being unable to dress, feed, or get in and out of bed. To determine the independent association between ADL-impairment and medication count, we performed sequential Poisson multivariable regression

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Author Contributions:

All authors meet the criteria for authorship stated in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals. Dr. Goyal had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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analyses. All analyses were cross-sectional in nature, and accounted for NHANES' complex survey design.

Results: We studied 947 participants, which represented 4.6 million adults with HF in the United States. The mean age was 70 years. The mean medication count was 7.2 and 74% took 5 medications (i.e., polypharmacy). In a multivariable model, ADL-impairment was not independently associated with medication count. These findings were similar for those with 3 hospitalizations in the prior year, declining health status, and cognitive impairment.

Conclusion: After adjusting for confounders including comorbidity, we found that adults with HF and ADL-impairment take as many medications as those without ADL-impairment. This suggests that providers may not sufficiently consider functional impairment when prescribing medications to adults with HF, and thus may unnecessarily expose individuals to an increased risk for adverse outcomes.

Keywords

polypharmacy; heart failure; functional impairment

INTRODUCTION

Polypharmacy is a well-described phenomenon in geriatrics, with known associations with myriad adverse outcomes^{1,2} including falls,^{3–6} disability,^{7–9} and hospitalizations.^{10–12} Commonly defined as the use of at least 5 medications,^{13,14} polypharmacy is particularly prevalent among adults with heart failure (HF),¹⁵ a condition in which the concurrent use of numerous pharmacologic agents is embraced as the primary therapeutic strategy to improve outcomes.^{16,17} This creates an inherent tension in which more medications may reflect guideline-concordant care, but may also simultaneously increase the risk for drug interactions and adverse drug events.

To optimize the outcomes of adults with HF, it is important for providers to consider key clinical attributes that can impact the risk-benefit balance when prescribing high numbers of medication. Functional impairment represents an important attribute that may identify a subpopulation in HF within whom the risks of taking a high number of medications may outweigh the benefits. Indeed, those with impairments in their activities of daily living (ADLs) like transferring, eating, and/or dressing are known to be at increased risk for adverse drug reactions.⁹ Moreover, given their decreased life expectancy,¹⁸ those with ADL-impairment may not derive the same benefit from pharmacologic therapy as their healthier counterparts. Accordingly, ADL-impairment in HF may help identify a subpopulation that derives limited benefit (and potentially experiences harm) from taking a high number of medications.

Whether adults with HF and ADL-impairment take fewer medications than those without ADL-impairment is unknown. Using National Health and Nutrition Examination Survey (NHANES) data from 2003–2014, we assessed the association of ADL-impairment with the number of medications taken by adults with HF, adjusting for confounding variables

according to the well-established Andersen conceptual framework of health services utilization.¹⁹

METHODS:

Data Source:

We examined NHANES data from 2003–2014. Methodology for participant recruitment and data collection in NHANES has previously been described.²⁰ Briefly, NHANES is a cross-sectional survey with a complex, stratified, multistage probability cluster sampling design that produces aggregate-level national estimates of the adult civilian non-institutionalized United States population. For our study, we combined data releases from the following cycles: 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2012, and 2013–2014.

Study population:

Study subjects included NHANES participants aged ≥50 years old with self-reported HF, defined as responding “Yes” to the question, “Has a doctor or other health professional ever told you that you had congestive heart failure.” HF has been extensively studied in NHANES,^{15,21–23} and the specificity of self-reported HF has previously been shown to exceed 99%.²⁴ We excluded participants with missing data on a.) self-reported HF b.) disability, or c.) number of medications; and those who did not participate in the clinical examination (n=69). Among 61,087 participants surveyed between 2003 and 2014, we included 947 participants in this study (Supplemental Figure S1).

Measurement:

Similar to a prior study,¹⁵ we assessed ADL-impairment based on self-report of having difficulty with or being unable to perform any one of the following: dress themselves, feed themselves, get in and out of bed.

Medication lists were obtained for all NHANES participants during an in-home interview, where participants were also asked to show their medication containers for verification. We determined medication count for each participant by counting the number of medications taken according to self-report. We defined polypharmacy according to the commonly-used definition of ≥5 medications,^{13,14} a threshold associated with worse outcomes.²⁵ We classified medications according to the Multum Lexicon Drug Database.²⁶

We selected covariates according to the Andersen model of healthcare utilization,¹⁹ which incorporates “predisposing,” “enabling,” “need,” and “healthcare utilization” factors into a conceptual model. “Predisposing” factors included age, gender, and race. “Enabling” factors included primary payer of health insurance, highest level of education, total annual household income, marital status, and living alone (defined as “total number of people in household” = 1). “Need factors” included comorbidity count, smoking status, self-reported declining health compared to prior year (reported as same, worse, or better), frailty as defined by hypoalbuminemia (albumin <3.3g/dl)²⁷, and self-reported memory problems (reported as yes or no) as a proxy for cognitive impairment. Of note, NHANES lacked robust measures of frailty during the years of NHANES included in this study. Although a 4-

item frailty phenotype (including exhaustion, low physical activity, weakness, and “shrinking”) has been used in NHANES, factors including exhaustion, low physical activity, and weakness overlap considerably with ADL-impairment.²⁸ “Shrinking,” on the other hand, seems to represent a unique concept, and may be operationalized by serum albumin,²⁷ which is available in NHANES. We accordingly used hypoalbuminemia as a proxy for frailty. Comorbidity count represented a count of the number of comorbid conditions present among the following: hypertension, diabetes, anemia, asthma, chronic bronchitis, emphysema, coronary artery disease, prior myocardial infarction, prior stroke, thyroid disease, liver disease, cancer, chronic kidney disease, dialysis, hypercholesterolemia, and arthritis. We chose comorbid conditions based on their availability in every NHANES cycle included in this study (2003–2014). Finally, “healthcare utilization” factors included number of contacts with ambulatory health care services during the prior year (including emergency room visits that did not lead to an overnight hospitalization) and the number of all-cause hospitalizations (≥ 1 overnight stay) during the prior year.

Statistical Analysis.

We accounted for NHANES’ complex survey design in all analyses. For variance estimation, we used the Taylor linearization method, a method based on first-order Taylor series linear approximation of the derivative of the log-weighted likelihood function.²⁹ We calculated weighted means with standard deviations (SD) for continuous variables and weighted percentages with 95% confidence intervals (CI) for categorical variables to summarize study subject characteristics. We used the t-test and Pearson’s chi-squared test to investigate significant differences between groups. We assessed the trend of medication count over time using survey-weighted linear regression.

To determine the independent association between ADL-impairment and medication count, we performed sequential Poisson multivariable regression analyses, guided by the Andersen model.¹⁹ We first determined the association between ADL-impairment and medication count adjusted only for NHANES cycle. We then added “predisposing factors” (Model 1), followed by “enabling” factors (Model 2). Because comorbidity count is an especially important “need” factor that impacts number of medications,³⁰ we added comorbidity count to the model separately (Model 3), followed by the remainder of the “need” factors (Model 4). Finally, we added “healthcare utilization” factors (Model 5).

To account for missing covariate values in our regression analysis, we employed multiple imputation using chained equations designed for complex survey data.³¹ We performed 50 imputations using sampling of estimates from the posterior distribution of model parameters; we created pooled estimates by fitting regression models within each of the 50 datasets for imputation-specific estimates and then combined them using “Rubin’s rules.”³² In the selected sample, 32% of participants had a missing value for at least one covariate. The variable with the greatest percent missing was primary payer (18%).

To determine whether the independent association between ADL-impairment and medication count differed among those aged ≥ 65 years, a population at especially high risk for adverse drug events requiring medical attention,³³ we performed a sensitivity analysis of sequential Poisson multivariable regression analyses among this group. To determine

whether our results would differ if we included only “chronic” medications as used in a prior NHANES analysis,¹⁵ we performed a sensitivity analysis in which the medication count only included agents taken for at least 2 weeks. To ensure that our models did not result in over-dispersion, we also ran the models with negative binomial regression, revealing nearly identical results.

Finally, we performed Wald tests to determine the presence of effect modification from factors chosen a priori. We performed tests for interactions between ADL-impairment and the following factors: a.) 3 hospitalizations in the prior year, b.) declining self-reported health status, and c.) cognitive impairment.

We used two-sided hypothesis testing, and $p\text{-value} < 0.05$ to determine statistical significance. We managed the data in SAS version 9.4 (SAS Institute, Cary, NC) and performed statistical analysis using STATA version 14 (IBM corporation, Armonk, NY).

RESULTS:

Our study sample of 947 participants represented a non-institutionalized adult population in the United States of approximately 4.6 million adults with HF. The mean age of our cohort was 70 years (95% CI 69.3–70.7), with an even distribution of men and women (Table 1). Other baseline characteristics are shown in Table 1. Of note, those with ADL-impairment more frequently had dual Medicare and Medicaid and were less likely to be married, compared to those without ADL-impairment.

The mean number of comorbid conditions in our sample was 4.7. Those with ADL-impairment had an approximately 25% higher mean count of comorbid conditions (5.6 vs. 4.6, $p < 0.001$). Those with ADL-impairment were more likely to have a history of stroke, asthma, chronic bronchitis, and anemia (Table S1). Those with ADL-impairment were also numerically more likely to have hypoalbuminemia.

Overall, about 50% of the study participants reported that their health status was the same as it had been during the prior year (Table 1). Those with ADL-impairment more frequently reported that their health status had declined over the prior year compared to those without ADL-impairment. The overall prevalence of cognitive impairment in the study sample was 24%, and was more common among those with ADL-impairment. With regard to healthcare utilization over the prior year, 39% of participants had contact with ambulatory healthcare services at least 10 times and 9% were hospitalized at least 3 times. Those with ADL-impairment were more likely to have at least 10 contacts with ambulatory healthcare services, and were also more likely to be hospitalized at least 3 times.

The overall mean medication count in our sample was 7.2 (Table 2). The prevalence of polypharmacy, defined as 5 medications, was 74%. The full distribution of the medication count is shown in Figure 1. Those with ADL-impairment had a higher mean medication count (8.5 vs. 7.0, $p < 0.001$), and more frequently had polypharmacy (82% vs. 73%, $p = 0.003$) compared to those without ADL-impairment. The mean medication count was numerically higher among those with ADL-impairment across all age strata (Figure 2A). Table 2 shows the prevalence of medications according to ADL-impairment. The three most

common medication classes were beta-blockers (61%), diuretics (60%), and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (58%). The prevalence of these agents did not differ according to ADL-impairment. Notably, several agents were more common among those with ADL-impairment. These included proton pump inhibitors and histamine-2 receptor blockers, minerals and vitamins, antidepressants, and non-opioid analgesics.

The prevalence of ADL-impairment for our sample was 11%. Among those with ADL-impairment, 55% reported difficulty with transferring (getting in and out of bed), 22% reported difficulty with eating, and 64% had difficulty dressing themselves. The mean medication count among individuals with ADL-impairment exceeded the mean of those without ADL-impairment in the majority of NHANES cycles (Table S2). Of note, the mean medication count increased over time for those without ADL-impairment (p -for-trend=0.04), but not those with ADL-impairment (p -for-trend=0.67). In a crude model adjusted for survey year only, ADL-impairment was associated with a 23% increase in medication count (Table 3). However, in the fully adjusted model—accounting for “predisposing” and “enabling” factors, “need” factors including comorbidity and frailty, and healthcare utilization factors—ADL-impairment was not independently associated with medication count. In other words, the number of medications taken by adults with ADL-impairment was similar to the number taken by those without ADL-impairment in a fully-adjusted model; this was consistent across all age strata (Figure 2B)

In a sensitivity analysis of participants aged at least 65 years, sequential multivariable regression analysis revealed a similar pattern as that observed in the entire cohort (Table S3). In a second sensitivity analysis, where the medication count only included agents taken for at least 2 weeks, the mean number of medications remained 7.1, and a sequential multivariable regression analysis again revealed a similar pattern as that observed in the entire cohort (Table S4).

None of the a priori specified interactions were significant (Table S5): 3 hospitalizations in the prior year p -for-interaction=0.46; declining health status over prior year p -for-interaction=0.66; cognitive impairment p -for-interaction=0.10.

DISCUSSION:

This analysis from NHANES data revealed that adults with HF take a high number of medications irrespective of ADL-impairment, and that ADL-impairment is not independently associated with number of medications taken despite the known association of ADL-impairment with increased adverse drug events and decreased life expectancy. We additionally found that factors associated with a worse prognosis including recurrent hospitalization, declining health, and cognitive impairment did not modify this association. Together, these findings suggest that providers may not integrate functional impairment and overall prognosis into their prescribing practices, and may unnecessarily be exposing patients with HF to the risks associated with polypharmacy.

The attendant risks of taking a high number of medications are well-described in the geriatric literature with known associations with a number of adverse outcomes^{1,2} including falls,^{3–6} disability,^{7–9} and hospitalizations.^{10–12} Consequently, there is an inherent tension between this observation and providing guideline-concordant care to adults with HF, which frequently includes concurrently prescribing a multitude of medications for HF,^{16,17,34} as well as for other common comorbid cardiovascular and non-cardiovascular conditions. An individualized assessment of the risks and benefits for initiating, titrating, and discontinuing medications is naturally an important component of safe prescribing practice, as the risks and benefits can differ substantially across different subpopulations. Adults with ADL-impairment represent a subpopulation in whom the risks of a high medication burden may exceed its potential benefit. Adults with ADL-impairment are at increased risk for adverse drug events,⁹ and may be less likely to derive long-term benefit from many of their prescribed medications due to a limited life expectancy.¹⁸ Even the benefits of HF medications are not clear in this population, as those with functional impairments and/or limited life expectancy have frequently been excluded from major HF randomized controlled trials.^{35–37} Thus, given their elevated risk for harm and attenuated potential for benefit, we hypothesized that ADL-impairment would be associated with taking fewer medications after controlling for comorbidity and other confounders.

Surprisingly, after adjusting for comorbidity and other confounders using the Andersen framework,¹⁹ we found that ADL-impairment was not independently associated with medication count. In other words, adults with HF who had an impairment in transferring, eating, and/or dressing take just as many medications as those without such impairments, after accounting for comorbidity burden. Although there is the possibility of residual confounding, our findings suggest that providers may not consider functional impairment when prescribing medications to adults with HF, and thus may be exposing a large number of individuals to an increased risk for adverse outcomes.

Given the well-known association between recurrent hospitalizations and decreased survival, we further examined whether ≥ 3 hospitalizations, which is associated with a median survival of under 1 year,³⁸ modified the association between ADL-impairment and medication count. We found no effect. Declining self-reported health, a harbinger of reduced survival,³⁹ also had no effect on this relationship. Finally, cognitive impairment, which is independently associated with adverse drug events,⁴⁰ did not affect this relationship either. Taken together, these data further strengthen the implication that providers may not consider important factors that ultimately affect the risk-benefit ratio of prescribing medications. While much has been written about the importance of incorporating overall prognosis, functional impairment, and cognition into decisions regarding device implantation^{41,42} and/or advanced HF therapies like left ventricular assist devices,⁴³ less is described in the setting of implementing pharmacologic therapy despite its significant population-based implications. It must not be overlooked that medications have attendant risks as well, even if not to the degree of device implantations or surgery. Indeed, adverse drug events cause over 700,000 emergency room visits per year in the United States.⁴⁴ Thus, in addition to ADL-impairment, factors like recurrent hospitalizations which are a marker for advanced disease and overall prognosis, declining self-reported health, and cognitive impairment probably warrant consideration when prescribing medications to adults with HF.

The underlying reasons for our observations are not clear. One possibility that medication number did not differ by ADL status among adults with HF is that prescribers do not appreciate the importance of incorporating functional impairment and/or prognosis into decision-making. Importantly, functional impairment, as it relates to ADLs, may be challenging for clinicians to extricate from the symptoms and physical limitations that frequently result from HF. Consequently, it may not be apparent to clinicians whether more aggressive treatment of HF (and other comorbid conditions) is beneficial or harmful. Another possibility for our findings is that, in the era of subspecialty care where the average adult sees a median of 7 different providers in a year,⁴⁵ physicians are prescribing medications for conditions within the scope of their expertise without consideration for other important patient-based factors like ADL-impairment or total medication burden. Notably, our study revealed that several classes of non-cardiovascular agents were more common among those with ADL-impairment compared to those without. Thus, developing and studying strategies to ensure safe and appropriate use of these agents through improved communication across different specialties and/or implementation of more comprehensive medication reconciliation efforts among subspecialists, like cardiovascular clinicians, are needed. Importantly, our data underscore the need to emphasize the potential risks of a high medication burden to clinicians caring for adults with HF. Consideration for the effect of a high burden of medications on cross-disease or universal health outcomes like health-related quality of life and daily functioning are similarly important, and warrant novel strategies to incorporate these factors into medical decision-making.^{46,47} Future research would benefit from a focus on developing strategies to identify patients at high risk for polypharmacy and its adverse outcomes, as well as strategies to mitigate its effects when polypharmacy is present. Deprescribing has emerged as a potential strategy to reduce medication burden,⁴⁸ but it remains unclear as to which patients would benefit from this strategy and at what point in their disease trajectory it warrants consideration. Whether adults with HF with ADL-impairment, who are at higher risk for adverse drug events and have limited life expectancy, represent a subpopulation in whom deprescribing would be beneficial remains unknown and represents an area for future investigation.

A major strength of this study is its generalizability, as NHANES is a nationally representative sample of the adult non-institutionalized population in the United States. There are also several limitations worth noting. As this was a cross-sectional study, we could not determine the causal relationship between variables. Details of medication dose, frequency, and indication were not available; whether these differed according to ADL-impairment were unknown. Data regarding the severity of various comorbid conditions was not available, and thus could have contributed to residual confounding by indication. Additionally, a number of comorbid conditions, including depression and neuromuscular conditions, were not routinely assessed during the study period and thus were not included in the analysis; these could have had an effect on our findings. NHANES lacks data on hygiene, toileting, and bathing; consequently, our definition of ADL-impairment did not include these, which may have affected the patterns observed in this study. NHANES also lacks a robust unambiguous metric for frailty; although ADL-impairment and hypoalbuminemia can account for several aspects of frailty, we cannot be sure that we fully adjusted for frailty. We also did not have data about the severity (ie, New York Heart

Association class) or subtype of HF. Since the efficacy of pharmacologic therapy for HF with reduced ejection fraction and HF with preserved ejection differ, medication count and its association with ADL-impairment may have differed between HF subtypes. Finally, NHANES data is predominantly ascertained by self-report, which can introduce recall bias. Self-report as a means to identify HF has demonstrated excellent specificity, but limited sensitivity;²⁴ consequently, this cohort may not have included patients with less severe HF. Self-report as a means to identify other comorbid conditions have demonstrated highly variable diagnostic performance metrics,⁴⁹ and thus represents another important limitation.

In conclusion, after adjusting for confounders including comorbidity, we found that adults with HF with ADL-impairment take as many medications as those without ADL-impairment. This observation remained even in the setting of recurrent hospitalizations, declining health, or cognitive impairment. This suggests that providers may not sufficiently consider ADL-impairment, which can be challenging to differentiate from physical limitations related to HF symptoms, and/or prognosis when prescribing medications to adults with HF; and thus may be unnecessarily exposing individuals to an increased risk for adverse outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Impact Statement:

We certify that this work is novel. This study demonstrates that the number of medications taken by adults with heart failure who have an impairment in their activities of daily living—a subpopulation in whom the risks of a high medication burden may outweigh the benefits—does not differ from those without such an impairment. This suggests that providers may not sufficiently consider functional impairment when prescribing medications to adults with heart failure, and thus may be exposing individuals to increased risk for adverse outcomes.

Figure 1. Distribution of medication count.

Polypharmacy, defined as the condition of taking at least 5 medications, occurred in the vast majority (74%) of adults with heart failure.

Figure 2. Mean Medication Count according to ADL-impairment, stratified by Age
A. Unadjusted model: Individuals with ADL-impairment took more medications compared to those without ADL-impairment, across all age strata
B. Fully-adjusted model: After full adjustment, individuals with ADL-impairment took a similar number of medications as those without ADL-impairment, across all age strata

Table 1.Population Characteristics^a, according to ADL impairment

Variable	All (n=947)	No ADL Impairment (n=818)	ADL Impairment (n=129)	P-value
Age, n (%)				0.02
50–64 years	255 (27)	222 (26)	33 (32)	
65–74 years	282 (34)	255 (36)	27 (19)	
75 years	410 (40)	341 (38)	69 (49)	0.07
Women, n (%)	425 (49)	356 (48)	69 (59)	
Race, n (%)				0.12
White	559 (77)	490 (78)	69 (70)	
Black	218 (13)	190 (12.0)	28 (16)	
Other	170 (10)	138 (10)	32 (14)	<0.001
Primary payer, n (%)				
Medicare without Medicaid	484 (66.0)	421 (67)	63 (59)	
Medicaid without Medicare	59 (6)	51 (6)	8 (6)	
Dual Medicare and Medicaid	81 (7)	59 (6)	22 (21)	
Other insurance	107 (15)	99 (16)	8 (9)	0.06
Uninsured	50 (6)	45 (6)	5 (5)	
Education, n (%)				
Below high school	383 (33)	318 (31)	65 (47)	
High school degree, obtained GED or equivalent	462 (54)	409 (55)	53 (44)	0.08
College degree and above	101 (13)	91 (14)	10 (9)	
Household Income, n (%)				
<\$20,000	319 (27)	268 (26)	51 (38)	
\$20,000–\$34,000	238 (27)	204 (28)	34 (25)	
\$35,000–\$74,000	218 (28)	196 (29)	22 (22)	0.008
\$75,000	122 (14)	109 (15)	13 (9)	
Refused to answer	35 (3)	28 (3)	7 (6)	0.44
Married, n (%)	450 (53)	400 (55)	50 (38)	0.008
Lives alone, n (%)	256 (26)	220 (26)	36 (30)	0.44
Count of comorbidities ^b , mean (95% CI) ^c	4.7 (4.5–4.8)	4.5 (4.3–4.7)	5.6 (5.0–6.1)	0.001
Smoking status, n (%)				0.49
Never	389 (40)	336 (40)	53 (41)	
Past	411 (44)	348 (43)	63 (47)	
Current	147 (16)	134 (17)	13 (12)	<0.001
Change in health from last year, n (%)				
Better	208 (22)	184 (23)	24 (21)	
Worse	217 (22)	160 (19)	57 (45)	

Variable	All (n=947)	No ADL Impairment (n=818)	ADL Impairment (n=129)	P-value
Same	520 (55)	473 (58)	47 (34)	
Cognitive impairment	263 (24)	191 (20)	72 (57)	<0.001
Hypoalbuminemia	33 (3)	25 (3)	8 (6)	0.06
Number of contacts with ambulatory services, past year				0.002
0–3	188 (20)	176 (22)	12 (9)	
4–9	374 (41)	328 (42)	46 (34)	
10	384 (39)	313 (37)	71 (56)	
Number of hospitalizations, past year				0.001
<3	852 (91)	746 (93)	106 (81)	
3	93 (9)	70 (7)	23 (19)	

Abbreviations: Activities of daily living (ADLs); Confidence Interval (CI)

^aNumbers are unweighted. Percentages are weighted to represent the United States population.

^bComorbidity count consisted of the following conditions: hypertension, diabetes, anemia, asthma, chronic bronchitis, emphysema, coronary artery disease, history of myocardial infarction, history of stroke, thyroid disease, liver disease, cancer, chronic kidney disease, dialysis, hypercholesterolemia, and arthritis.

Table 2:Medication Count and Classification^a, according to ADL impairment

	All	No ADL Impairment	ADL Impairment	P-value
Mean Medication count (95% CI)	7.2 (6.8–7.5)	7.0 (6.6–7.3)	8.5 (7.7–9.3)	<0.001
Polypharmacy , n (%)	696 (74)	595 (73)	101 (82)	0.003
Heart Failure medications , n (%)				
Beta blockers	578 (61)	505 (61)	73 (61)	0.99
Diuretics	578 (60)	496 (58)	82 (68)	0.10
ACEI or ARB	556 (58)	490 (59)	66 (49)	0.09
Digoxin	121 (13)	108 (14)	13 (9)	0.14
Aldosterone antagonist	102 (11)	88 (10)	14 (13)	0.48
Vasodilators	106 (10)	85 (9)	21 (15)	0.10
Other Cardiovascular medications , n (%)				
Statins	513 (54)	447 (55)	66 (51)	0.56
Anti-arrhythmic agents	236 (26)	202 (26)	34 (24)	0.75
Calcium-channel blockers	243 (22)	208 (22)	35 (23)	0.85
Anti-coagulation agents	190 (21)	162 (21)	28 (23)	0.63
Anti-platelet agents	196 (21)	160 (21)	36 (21)	0.90
Anti-anginal agents	129 (12)	107 (12)	22 (15)	0.43
Non-cardiovascular medications , n (%)				
Anti-diabetic agents	340 (34)	292 (33)	48 (39)	0.38
Proton pump inhibitors and H2-blockers	304 (32)	256 (31)	48 (42)	0.04
Minerals/vitamins	211 (24)	171 (22)	40 (40)	0.003
Anti-depressants	204 (23)	159 (22)	45 (35)	0.03
Thyroid agents	158 (20)	139 (20)	19 (16)	0.48
Bronchodilators	132 (15)	111 (14)	21 (16)	0.65
Opioids	143 (15)	116 (14)	27 (21)	0.08
Non-opioid analgesic	97 (11)	72 (10)	25 (22)	0.01
Benzodiazepines	90 (9)	75 (9)	15 (10)	0.69
Anti-infective agents	76 (9)	61 (8)	15 (16)	0.03
Topical agents	82 (9)	67 (8)	15 (10)	0.52
GU agents	31 (4)	23 (3)	8 (5)	0.47
Anti-psychotics	30 (3)	18 (2)	12 (7)	0.003
Anti-neoplastic agents	17 (2)	11 (1)	6 (8)	0.001

Abbreviations: Activities of daily living (ADLs); Confidence Interval (CI), Angiotensin Converting Enzyme-Inhibitor (ACEI), Angiotensin Receptor Blocker (ARB), Genitourinary Tract (GU),

^a.Numbers are unweighted. Percentages are weighted to represent the U.S. population.

Table 3.

Prevalence Ratios for Association of ADL Impairment and Medication Count

Model	Prevalence Ratio (95% CI)	P-value
ADL impairment ^a	1.23 (1.11 – 1.36)	<0.001
Model 1	1.24 (1.12 – 1.37)	<0.001
Model 2	1.20 (1.08 – 1.34)	0.001
Model 3	1.11 (1.00 – 1.23)	0.04
Model 4	1.07 (0.96 – 1.19)	0.23
Model 5	1.03 (0.93 – 1.14)	0.62

Abbreviations: Activities of daily living (ADLs); Confidence Interval (CI)

^a. Adjusted for NHANES cycle

Model 1-Adjusted for ADL impairment and NHANES cycle plus Predisposing factors (age, gender and race)

Model 2-Adjusted for Model 1 covariates plus Enabling factors (source of health insurance, education, income, marital status, living alone and access to care)

Model 3-Adjusted for Model 2 covariates plus comorbidity count

Model 4- Adjusted for Model 3 covariates plus additional Need factors (smoking status, health compared to last year, hypoalbuminemia, and memory)

Model 5- Adjusted for Model 4 and Healthcare utilization factors (number of contacts with health care system, and number of hospitalizations)