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Geographic Region and Racial Variations in Polypharmacy in the United States

Winn Cashion[1], **William McClellan**[1], **George Howard**[2], **Abhinav Goyal**[1], **David Kleinbaum**[1], **Michael Goodman**[1], **Valerie Prince**[3], **Paul Muntner**[4], **Leslie A. McClure**[2], **Ann McClellan**[1], and **Suzanne Judd**[2]

[1]Emory University Rollins School of Public Health, Department of Epidemiology, 1518 Clifton Rd Atlanta GA 30322

[2]University of Alabama at Birmingham, Department of Biostatistics, 1665 University Boulevard Birmingham AL 35294-0022

[3]Samford University McWhorter School of Pharmacy, 800 Lakeshore Dr. Birmingham AL 35229

[4]University of Alabama at Birmingham, Department of Epidemiology, 1665 University Boulevard Birmingham AL 35294-0022

Abstract

Purpose—Medications can have unintended effects. High medication use populations may benefit from increased regimen oversight. Limited knowledge exists concerning racial and regional polypharmacy variation. We estimated total medication distributions (excluding supplements) of American black and white adults and assessed racial and regional polypharmacy variation.

Methods—REasons for Geographic And Racial Differences in Stroke (REGARDS) cohort data (N=30,239 U.S. blacks/whites ages ≥45 years) were analyzed. Home pill-bottle inspections assessed the last two weeks' medications. Polypharmacy (≥ 8 medications) was determined by summing prescription and/or OTC ingredients. Population-weighted logistic regression assessed polypharmacy's association with census region, race, and gender.

Results—The mean ingredient number was 4.12 (SE = 0.039), with 15.7% of REGARDS using ≥8 ingredients. In crude comparisons, women used more medications than men, and blacks and whites reported similar mean ingredients. A cross-sectional, logistic model adjusting for demographics, socioeconomics, and comorbidities showed increased polypharmacy prevalence in

Corresponding author: Winn Cashion, Depart. Epidemiology, Rollins School of Public Health, 431 Briarvista Way NE, Atlanta, GA 30329-3620, wcashio@emory.edu, Phone: 413-478-5906, Fax: 404-727-8737.

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whites vs. blacks (OR, [95% CI]: 0.63, [0.55–0.72]), women (1.94, [1.68–2.23]), and Southerners {broadly Southeasterners and Texans} (1.48, [1.17–1.87]) vs. Northeasterners {broadly New England and upper Mid-Atlantic}. Possible limitations include polypharmacy misclassification and model mis-specification.

Conclusion—Polypharmacy is common. Race and geography are associated with polypharmacy variation. Further study of underlying factors explaining these differences is warranted.

Keywords

pharmacoepidemiology; medications; REGARDS; polypharmacy; geographic variations; and race

INTRODUCTION

Adult Americans take many prescription and over-the-counter (OTC) medications[1], each year purchasing approximately four billion prescriptions.[2] There are over 300,000 distinct OTC products.[3] Over $300 billion is spent annually in the United States on prescriptions.[4]

In addition to pharmaceuticals' well-established benefits, medication errors also occur, the most frequent class of medical error.[5] Based on a meta-analysis, if categorized as a disease, adverse drug reactions (ADRs) are estimated to be up to the fourth leading cause of death.[6]

Polypharmacy, broadly conceptualized as high medication use, encapsulates the dual potential for poly-therapeutic effects and/or poly-toxicities.[7] Unfortunately, polypharmacy has no universally accepted definition.[8] Polypharmacy sometimes has negative connotations, suggesting inappropriate/excessive medication use; however, it can also reflect appropriate care for patients with multiple health conditions and/or conditions requiring multiple medications. Nevertheless, polypharmacy has been associated with adverse health events, including cognitive decline,[9,supp ref] falls,[10,supp ref] ADRs,[11] and drug-drug interactions.[12]

Although some data on America's medication use have begun emerging,[13] population-based medication variation according to geography and race merit further elucidation. Large-scale, national studies assessing multivariable-adjusted racial and/or geographic polypharmacy variations in the general black and white adult population are, to our knowledge, largely unavailable. Here we use data from a large, population-based cohort to characterize cross-sectional racial and geographic polypharmacy patterns in the United States.

MATERIAL and METHODS

Study Design and Population

We used the **RE**asons for **G**eographic **A**nd **R**acial **D**ifferences in **S**troke (REGARDS) cohort study data.[14] REGARDS utilized a two-stage survey design, with simple random sampling within strata defined by three geographic areas [stroke buckle (coastal plains of the Carolinas and Georgia)/stroke belt (eight Southern states: North Carolina, South Carolina, Georgia, Tennessee, Alabama, Mississippi, Arkansas, Louisiana)/stroke nonbelt (the rest of the continental United States)], two race categories (black/white), age groups, and sex (male/

female).[14] After excluding 58 participants with data anomalies or missing medication information, the analytic cohort included 30,181 community-dwelling black and white Americans ages ≥45 years residing in the contiguous United States. The population-based cohort was sampled from Genesys'[15] commercial database, with oversampling of blacks and "stroke belt"[16,17] residents.

Detailed REGARDS methodology is presented elsewhere.[14] Briefly, a study pamphlet was mailed to potential participants; a telephone interviewer then called to inquire about participation. Individuals were excluded for non-black/non-white race, ongoing cancer treatment, poor English proficiency, cognitive impairment judged by the telephone interviewer, having a medical condition preventing long-term follow-up, or current nursing home residence or presence on a nursing home waiting list. The cooperation rate (number of study participants enrolled divided by the number who were contacted and met inclusion criteria) was 49%.[18,19] For those agreeing to participate, the interviewer obtained verbal informed consent and began a computer-assisted telephone interview (CATI).

CATI-derived data included information about demographics, socioeconomic status (SES) including education (nine levels ranging from never attended/kindergarten only to graduate/professional school) and annual income (nine levels ranging from < $5,000 to > $150,000), and comorbidities (cardiovascular disease history, hypertension, diabetes, dyslipidemia, and chronic kidney disease). Each participant's race was self-reported as black or white. Following the CATI, an in-home exam was conducted. Participants were asked to collect all medicines used in the previous two weeks prior to the exam. Blood pressure was measured during the in-home exam. Blood samples were analyzed at a central laboratory, and the results were used to estimate glomerular filtration rate to define chronic kidney disease. Institutional Review Boards reviewed the research at all participating institutions, and signed informed consent was obtained.

Drug Data Collection/Classification and Polypharmacy Definition

Cohort members were called prior to in-home exam and reminded to assemble their medications. Health professionals trained in the study protocol examined each medication provided (i.e. "pill bottle inspection") and recorded the name (generic/brand) on a standardized form with space for up to 20 medication names. All rendered medications taken in the past two weeks (including medications administered ophthalmically, dermally, via injection, etc.) were recorded. Neither dosage nor use frequency/history was recorded. These records were processed into an electronic database of 34,776 distinct recorded medication names.

All medications were assigned a generic name (e.g., acetaminophen instead of Tylenol) by a research pharmacist and graduate students using primarily data from *Drugs.com*.[20] For combination formulations (e.g., 3 ingredient-component antihypertensive), the drug count was the total number of ingredients. For 1.62% of recorded medications, a generic name could not be assigned, and these were marked as "unknown." Each "unknown" medication was assumed to correspond to one drug ingredient.

Polypharmacy status was expressed as a binary variable, indicating whether or not ≥ 8 total ingredients (excluding supplements) were documented. This cut-point was chosen *a priori*, because it is an approximate midpoint between possible thresholds of 5 or 10 medications[21,supp ref] and because it corresponds to the highest quintile of medication-use (21.1%) in the REGARDS cohort. To study whether the associations examined were sensitive to the polypharmacy definition, an alternative analysis was conducted in which the polypharmacy threshold was set at ≥ 5 instead of ≥ 8. Some participants had the same ingredient listed multiple times, whether due to different medication formulations (e.g., long-, medium-, and short-acting insulin) or using the same medicine twice (e.g., two acetaminophen-containing, multi-component analgesics); in such cases the total ingredient sum counted the medication as many times as it was recorded.

Because of their heterogeneity and limited regulatory oversight (the Food and Drug Administration's purview is very different for prescription/OTCs than with supplements),[22] supplements (vitamins/minerals, herbal preparations, and nutraceuticals) were not considered. Some vitamins and minerals are available both as supplements and prescriptions; we tried to distinguish the prescription forms which counted towards polypharmacy (e.g., isotretinoin) from the OTC-available forms (e.g., vitamin A) that were considered supplements.

On the standardized medication form, there was a box to check if the medication inventory were complete of all medications used within the previous two weeks. Of the 20,586 participants who reported medication use and checked the box, 98.3% indicated that their medication inventories were complete.

Statistical Analysis

Sampling fractions from region-age-race-sex strata were used to provide weighted, nation-level estimates. Analyses for this report incorporated sampling weights using Statistical Analysis Software (SAS) 9.3 survey procedures.

Medication counts and their distributions were determined from participants' two-week total medication (prescriptions/OTCs) ingredient sums. Logistic regression was used to assess the multivariable-adjusted association between the independent variables listed in Table 1 and polypharmacy. The three exposures of interest were: race [black, white], census-defined regions [South, West, Midwest, Northeast], and gender [female, male]. The covariates were as follows:

Demographics: age [45–54, 55–64, 65–74, 75–84, 85+ years]

SES: education [< High School (HS), ≥ HS]; income [<$20k, $20–34k, $35k–74k, ≥ $75k, "refused"])

C**omorbidities:** chronic kidney disease [yes/no: self-reported dialysis or estimated glomerular filtration rate ≤ 60 mL/min/1.73m^2]; cardiovascular disease history [yes/no: self-reported MI (myocardial infarction), bypass, angioplasty, stenting or electrocardiogram MI evidence or self-reported stroke]; diabetes [yes/no: fasting glucose ≥ 126 mg/dL, non-fasting ≥ 200 mg/dL, or self-reported use of anti-hyperglycemic medication

or insulin]; hypertension [yes/no: systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or self-reported antihypertensive use]; and dyslipidemia [yes/no: total cholesterol ≥ 240 mg/dL, low-density lipoprotein ≥ 160 mg/dL, high-density lipoprotein ≤ 40 mg/dL, or self-reported use of lipid-lowering medication].

Sampling weights allowed geographic estimates following the census regions[23] boundaries (Figure 1) of South, Midwest, West, and Northeast.

Three distinct logistic regression models were constructed. The level of statistical significance was $\alpha = 0.05$. For all models, census region, race, and gender were the exposures of interest and polypharmacy was the outcome. Model 1 adjusted for age categories. Model 2 also adjusted for education and income. Model 3 included all variables used in Model 2 and added comorbidities (chronic kidney disease, hypertension, dyslipidemia, diabetes, and cardiovascular disease history). Model collinearity was checked using the SAS macro's condition indices/variance decomposition proportions.[supp ref] All models were *a priori* no-interaction models.

RESULTS

Characteristics of the Cohort and Their Medications

A total of 171,573 drug names were obtained and transcribed from the medication inventories conducted during in-home visits. Among sampling-weighted, non-supplemental medications, 91.8% were single-ingredient drugs and 16.0% of transcribed medications were available OTC. The mean age of participants was 65 years; 42% were black; 45% were male; 68% resided in the South (Table 1). The prevalences of dyslipidemia and hypertension were both nearly 60%, and the prevalence of diabetes was 22%.

The Midwest had the highest proportion of black cohort members. The West had the highest proportion of cohort members with at least a HS education and with an annual income ≥ $75,000. There was relatively little regional variability with regards to comorbidities.

Among black cohort members, a greater proportion was female and fewer had completed HS relative to whites. Black cohort members reported lower incomes and had higher rates of diabetes and hypertension relative to whites.

Males reported higher incomes than females. Males also had higher prevalences of dyslipidemia and cardiovascular disease history.

Prevalence of Medication Use and Mean Ingredient Counts

Overall, 27,060 participants (89.7%) used ≥ 1 medication ingredient(s) in the two weeks preceding the in-home visit. Figure 2 shows sampling-weighted ingredient sum prevalence distribution in the entire analytic cohort (national estimate) and according to gender, race, and census region. As these are sampling-weighted calculations, they represent national estimates for black and white adults age ≥ 45 years.

For the overall national estimate, less than 15% of participants reported taking no medications in the preceding two weeks. The prevalence of polypharmacy (≥8 drug ingredients) was 15.7%. The mean (standard error [SE]) ingredient count was 4.12 (0.039).

Females had higher mean ingredient counts [4.53 (0.057)] than males [3.66 (0.054)]. Females also had a higher rate of polypharmacy (18.4%) than males (12.7%).

Mean ingredient counts (blacks = 4.08, whites = 4.13) and polypharmacy proportions (blacks = 16.3%, whites = 15.7%) were similar regardless of race (Figure 2).

The South's mean number of total ingredients was 4.53 (SE = 0.057), substantially higher than that of the West (3.90, [0.099]), the Midwest (3.87, [0.082]), and the Northeast (3.83, [0.12]). Similarly, the polypharmacy prevalence in the South (19.3%) was higher than in the West (13.9%), the Midwest (13.5%), and the Northeast (13.0%).

Multivariable Race- /Census Region- /Gender-Polypharmacy Associations

The multivariable-adjusted odds ratios (ORs) for the three exposures of interest (race, census region, and gender) in the three models constructed are shown in Table 2. Analogous sensitivity analyses using the alternate polypharmacy definition did not yield substantially different ORs. Crude, sampling-weighted odds ratios (ORs) and 95% confidence intervals (CI) are also shown.

In the crude analysis and in all multivariable models, polypharmacy was more common in the South than the Northeast, with ORs (95% CIs) ranging from 1.61 (1.32–1.96) in the crude analysis to 1.48 (1.17–1.87) in Model 3. The point estimates for the Midwest and West (relative to the Northeast) were all non-significant.

In crude analysis and in models that did not adjust for comorbidities, there was no statistically significant difference in the prevalence of polypharmacy among blacks compared to whites. However, in Model 3 (which adjusted for demographics, SES factors, *and* comorbidities), blacks were statistically significantly (OR = 0.63; 95% CI: 0.55–0.72) less likely to have polypharmacy.

For gender, in crude analyses and multivariable-adjusted analyses, women were more likely than men to have polypharmacy. The association was strongest in Model 3 (OR = 1.94; 95% CI: 1.68–2.23).

DISCUSSION

Medications are a cornerstone of medical care, and medication regimens are often exceedingly complex, making managing polypharmacy a major challenge across multiple domains (e.g., patients, physicians, pharmacists, insurers, etc.). While not the focus of this research, an obvious implication is that an improved understanding of medication patterns may foster more economical and efficacious drug utilization, while minimizing risks (e.g., embedded electronic medical record software applications to suggest regimen simplification in cases of therapeutic redundancies or pop-up reminders to try to minimize anti-cholinergic burdens in geriatrics).

Consistent with other large studies, the overwhelming majority of REGARDS participants were taking medication(s).[1,13] This widespread medication use highlights the need for nurses, physicians, pharmacists, and allied health providers to remain cognizant to patients' medication regimens, retaining awareness that new signs/symptoms may be medication-induced. Paradoxically, polypharmacy may indicate lost therapeutic opportunities, as polypharmacy is a risk factor for underprescribing,[24] so polypharmacy should not be considered synonymous with overprescribing. Although many REGARDS cohort member's drugs may be appropriately prescribed and properly used, the high mean ingredient count (4.12) and a significant proportion using ≥ 8 ingredients (15.7%) may indicate increased risks for ADRs and drug interactions.[11,12] In this study, however, we could not distinguish "appropriate" from "inappropriate" polypharmacy.

Our most important findings were that, after adjustment for demographics, SES factors, and comorbidities, whites and Southern residents had significantly greater prevalence of polypharmacy. To our knowledge, this is the first time that a multivariate model of the American adult population ages 45 and older has reported findings of racial and geographic medication use differences.

This analysis of REGARDS medication use has several strengths. First, the large sample (N=30,239 for the total cohort, 58 participants were excluded in the presented analyses), allowed for detailed subgroup comparisons. Additionally, medication use was assessed rigorously through pill-bottle verification by trained health professionals. Furthermore, raw drug data coding by trained staff using a systematic strategy for ascertaining misspelled medications' identities ensured accurate classification. Finally, despite considerable effort, 1.62% of collected medications could not be assigned a generic name ("unknowns"). These unknowns were not excluded but instead were assumed to represent a single non-supplemental ingredient.

This study also has a number of limitations. Data were not collected on medication dose or use frequency/history, which would help distinguish sporadic from persistent polypharmacy. However, defining polypharmacy by ingredient sums (excluding supplements) may be the most biologically plausible approach, since supplements do not undergo the same regulation and often contain many "active" ingredients (e.g., multivitamin). Polypharmacy misclassification could occur at multiple steps—not all medications were assembled or medications not used in the previous two weeks were included, medication transcription mistakes, electronic medication list scanner errors, and generic assignment misclassification. Some residual selection bias from sampling-weight misspecification could occur. The reasons for medication use are multifactorial and variable; the polypharmacy models may be mis-specified (e.g., important confounders and effect modifiers may have been omitted or the models may have been "overfit" with variables not needed to correct for confounding by indication).

In crude comparisons, blacks and whites had similar mean ingredient counts and polypharmacy prevalences. However, upon multivariable adjustment that included comorbidities, blacks had less polypharmacy than whites. The lack of a crude race-polypharmacy association (but a significant adjusted association) may be attributable to

blacks' greater comorbidities. To our knowledge, this is the first time a multivariable-adjusted model has reported racial polypharmacy disparities for the general, biracial American adult (≥ 45 years) population.

Our findings are consistent with Dwyer *et al*.[25] who reported that "black/other" nursing home residents were less likely than whites to be exposed to polypharmacy. Among two cohorts of hospitalized elderly with heart failure from 1998–2001, Masoudi *et al.* also reported higher mean multivariable-adjusted prescription counts at hospital discharge among whites than blacks.[26] By contrast, Hanlon *et al.* found no crude black-white difference in polypharmacy among Veterans Affairs nursing home extended-stay residents.[supp ref] Similarly, in a study of community-dwelling American adults, Qato *et al*. reported no statistically significant racial differences in a multivariable model of "no regular medication use," although this study had a significantly smaller sample than REGARDS.[13]

In geographic analyses, the South had the highest prevalence of polypharmacy compared to all other census regions. To our knowledge, no previous studies have reported significant, multivariable, American regional variation in aggregate medication use. The reasons for higher medication utilization in the South relative to the rest of the country are unclear. Regional variation in healthcare has been reported by others,[27,supp ref] and prescribing quality geographic differences have been documented.[supp ref]

Aparasu *et al*. documented crude, but not multivariable, regional variation in elderly office visit polypharmacy.[28] Similarly, Perry and Turner reported crude mean prescription count regional variation among National Health and Nutrition Examination Survey III 65+ year olds.[29] Additionally, Gupta *et al.* noted intrastate geographic variation with prescription count in Louisiana geriatric Medicaid beneficiaries.[30] Other researchers have investigated different dimensions of medication use geographic variation (e.g., inter- and intra-regional variation abroad and urban/rural variation).[supp ref] Moreover, although not a composite pharmacological assessment like polypharmacy, some United States data on the spatial distributions of use of specific medication classes are available.[supp ref]

CONCLUSIONS

In summary, this research documents a high frequency of polypharmacy in the United States and shows that polypharmacy is not equally distributed across racial groups and census regions. The geographic variation should be explored at the community level; further investigation into factors that explain the observed polypharmacy racial disparities is merited. Also, future studies should investigate potential consequences of polypharmacy including direct toxicity, drug interactions, and ADRs. Finally, it should be noted that as polypharmacy is appropriate and the standard of care for some patients, higher prevalences of polypharmacy in the South and among whites should not be equated with excessive medication use in these groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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WC had full access to all study data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Abbreviations/Acronyms

ADR	adverse drug reaction
CATI	computer-assisted telephone interview
CI	confidence interval
HS	high school
MI	myocardial infarction
OTC	over-the-counter
REGARDS	REasons for Geographic And Racial Differences in Stroke
SAS	statistical analysis software
SE	standard error
SES	socioeconomic status

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Highlights

- There is a high frequency of polypharmacy (using ≥ 8 total prescription and/or OTC ingredients) among American adults.
- Polypharmacy is not equally distributed across racial groups and census regions.
- Future research should investigate potential deleterious consequences of polypharmacy (e.g., drug interactions)
- However, it should be noted that polypharmacy is appropriate and the standard of care for some patients. As such, higher prevalences of polypharmacy in the South and among whites should not *a priori* be equated with excessive medication use in these groups.

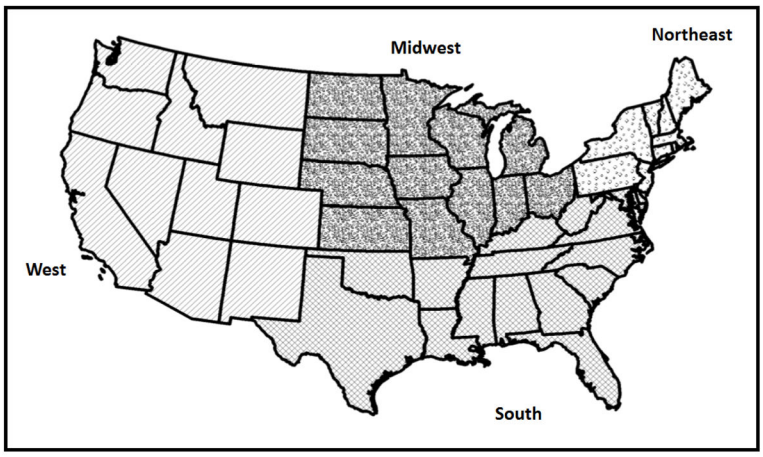

Figure 1. Census Regions Used
The four census regions are shown.

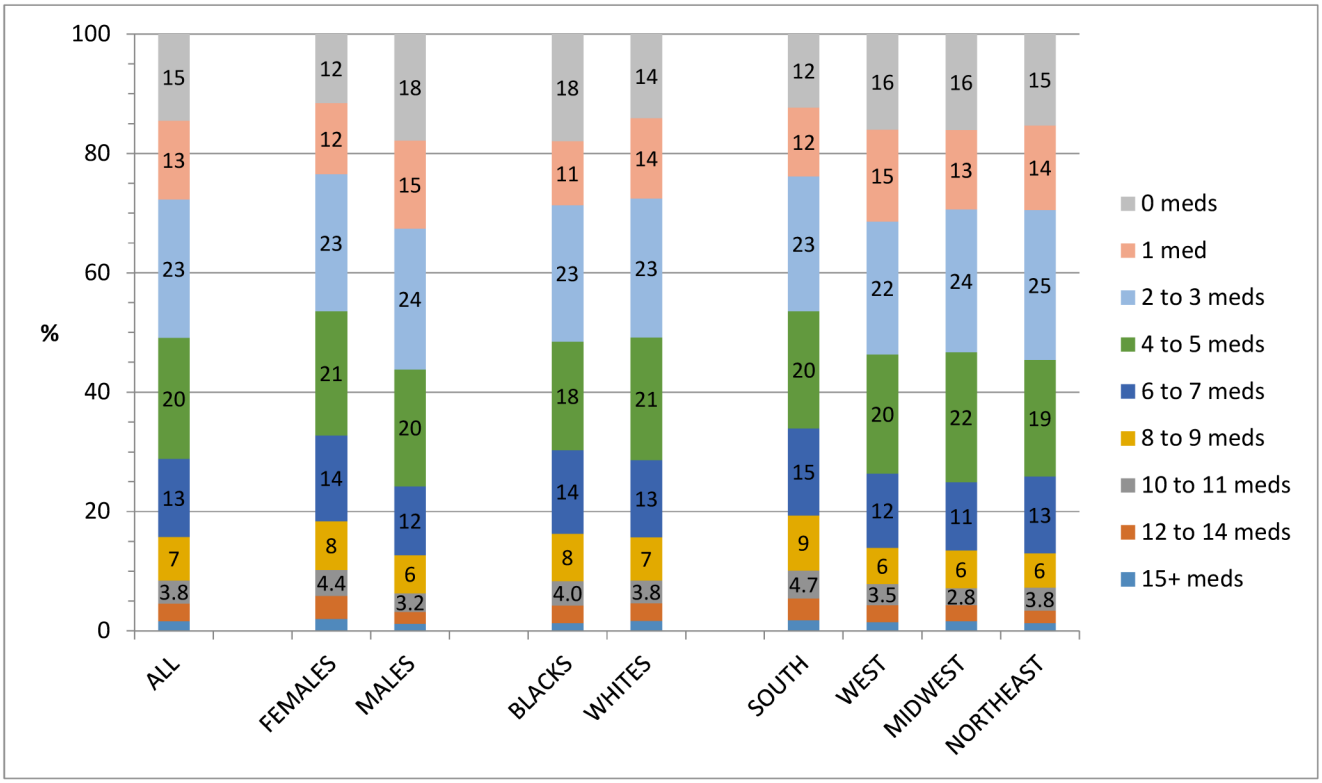

Figure 2. Ingredient Sum Prevalence Distribution for Entire Cohort and According to Gender, Race, and Geographic Region, *Adjusted* for Sampling Weights

The percent corresponding to the respective total ingredient sums (excluding supplements) is found within the labeled bars. Because of space constraints, these percentages are not shown for the 12–14 meds and 15+ meds categories.

Meds: total ingredient sum

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Table 1

REGARDS Cohort's (Sampling-Unweighted) Covariate Distribution According to Census Region, Race, and Gender

Covariate	Cov. Val.	Tot. N	Census Region %*				Race %*		Gender %*	
			NE	MW	W	S	B	W	M	F
Age	85+	590	2.14	2.15	3.15	1.72	1.66	2.16	2.06	1.87
	75–84	4,580	17.2	16.0	18.2	14.3	13.0	16.7	16.3	14.3
	65–74	9,685	30.9	32.2	31.5	32.3	31.2	32.8	33.7	30.8
	55–64	11,539	40.6	38.7	34.2	38.5	40.1	36.9	37.5	38.9
	45–54	3,787	9.20	10.9	12.9	13.2	14.1	11.5	10.5	14.2
Region	South	20,386	-	-	-	100	64.6	69.6	66.4	68.5
	West	2,953	-	-	100	-	9.09	10.3	9.48	10.0
	Midwest	4,689	-	100	-	-	18.5	13.5	16.7	14.6
	Northeast	2,153	100	-	-	-	7.82	6.64	7.50	6.84
Race	Black	12,513	45.5	49.3	38.5	39.7	100	-	35.0	46.7
	White	17,668	54.5	50.7	61.5	60.3	-	100	65.0	53.3
Gender	Female	16,630	52.8	51.8	56.5	55.9	62.1	50.2	-	100
	Male	13,551	47.2	48.2	43.5	44.1	37.9	49.8	100	-
Education	≥ HS	26,364	88.7	86.7	95.6	86.3	80.0	92.7	88.5	86.6
	< HS	3,792	11.3	13.3	4.40	13.7	20.0	7.33	11.5	13.4
Income	< $20k	5,478	17.4	18.8	10.2	19.2	26.9	12.0	12.1	23.1
	$20k – $34k	7,306	22.6	26.6	20.5	24.4	26.4	22.7	23.3	24.9
	$35k – $74k	8,914	29.6	28.7	33.2	29.2	25.2	32.6	34.3	25.7
	≥ $75k	4,754	18.3	13.9	24.4	14.6	8.88	20.6	21.0	11.4
	Refused	3,729	12.0	12.0	11.7	12.6	12.7	12.1	9.30	14.8
Dyslipidemia	Yes	17,228	57.5	58.7	57.1	60.0	55.3	62.1	67.2	52.8
	No	11,817	42.5	41.3	42.9	40.0	44.7	37.9	32.8	47.2
Diabetes	Yes	6,398	21.7	21.1	18.0	22.8	30.9	15.8	22.9	21.3
	No	22,654	78.3	78.9	82.0	77.2	69.1	84.2	77.1	78.7
Hypertension	Yes	17,846	57.6	60.0	52.9	60.2	71.3	50.7	58.3	60.0

Covariate	Cov. Val.	Tot. N	Census Region %*				Race %*		Gender %*	
			NE	MW	W	S	B	W	M	F
	No	12,262	42.4	40.0	47.1	39.8	28.7	49.3	41.7	40.0
CVD Hist.	Yes	6,501	21.2	24.0	18.8	22.1	20.9	22.8	28.2	16.9
	No	23,019	78.8	76.0	81.2	77.9	79.1	77.2	71.8	83.1
CKD	Yes	3,295	10.7	12.0	11.4	11.4	12.1	10.9	11.4	11.4
	No	25,583	89.3	88.0	88.6	88.6	87.9	89.1	88.6	88.6

Tot. N: Cohort N--For example, there were 590 cohort members age 85+.

*Column percent

B: Black; **CKD**: Chronic Kidney Disease; **CVD**: Cardiovascular Disease; **F**: Female; **HS**: High School; **M**: Male; **MW**: Midwest; **NE**: Northeast; **S**: South; **W**: West; **W**: White; -: Not Applic.

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Table 2

Results from Sampling-*Weighted*, *Multivariable-Adjusted* Logistic Regression Models of Polypharmacy Associations

Exposures		Sampling-Weighted Polypharmacy Model ORs (95% CI)			
		Crude (CI)	**Model 1[*] (CI)**	**Model 2[†] (CI)**	**Model 3[‡] (CI)**
Region	Northeast	**Ref**	**Ref**	**Ref**	**Ref**
	Midwest	1.04 (0.83–1.31)	1.07 (0.86–1.34)	1.03 (0.82–1.29)	1.01 (0.78–1.32)
	West	1.08 (0.86–1.37)	1.08 (0.86–1.37)	1.14 (0.90–1.45)	1.23 (0.93–1.62)
	South	**1.61** (1.32–1.96)	**1.59** (1.30–1.94)	**1.51** (1.23–1.85)	**1.48** (1.17–1.87)
Race	White	**Ref**	**Ref**	**Ref**	**Ref**
	Black	1.05 (0.96–1.15)	1.07 (0.97–1.18)	0.90 (0.81–1.00)	**0.63** (0.55–0.72)
Gender	Male	**Ref**	**Ref**	**Ref**	**Ref**
	Female	**1.55** (1.39–1.73)	**1.50** (1.34–1.68)	**1.35** (1.20–1.51)	**1.94** (1.68–2.23)

Statistically Significant Estimates are Bolded

For model covariate possible values see Table 1

[*]Adjusted for Demographics (Age, Race, Gender, Region)

[†]Adjusted for Demographics + SES Factors (Education, Income)

[‡]Adjusted for Demographics + SES Factors + Comorbidities (Chronic Kidney Disease, Hypertension, Dyslipidemia, Diabetes, Cardiovascular Disease History)

CI: confidence interval

OR: odds ratio for being polypharmacy (≥ 8 total ingredients) positive

Ref: reference group