

Prevalence and Predictors of Polypharmacy in Adults with Multiple Chronic Conditions: A Cross-Sectional Analysis of NHANES Data, 2011–2018

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ABSTRACT

Background: Polypharmacy is increasingly recognized as a major public health challenge, particularly among adults living with multiple chronic conditions. Understanding its prevalence and predictors is critical for guiding safe prescribing and improving outcomes in this population. **Objective:** To examine the prevalence and predictors of polypharmacy among U.S. adults with multimorbidity using nationally representative data. **Methods:** We conducted a cross-sectional study using data from four cycles of the National Health and Nutrition Examination Survey (NHANES) from 2011–2018. Adults aged ≥ 20 years with at least two chronic conditions were included. Polypharmacy was defined as the concurrent use of five or more prescription medications. Survey-weighted descriptive statistics and logistic regression were used to assess sociodemographic, behavioral, and clinical predictors. **Results:** The unweighted sample included 19,383 adults, representing a weighted population of 194,457,154. The prevalence of polypharmacy was high, with older adults, those with higher body mass index, lower income, and health insurance coverage significantly more likely to report polypharmacy. Non-Hispanic White and Black adults had higher odds compared with Mexican American adults, while higher education was protective. **Conclusion:** Polypharmacy is common among multimorbid US adults and strongly shaped by demographic and socioeconomic factors. Tailored interventions are needed to balance therapeutic benefits with risks of excessive medication use.

Keywords: polypharmacy; multimorbidity; NHANES; socioeconomic factors; predictors; United States.

INTRODUCTION

Polypharmacy has become an important public health problem in the United States, especially among adults who have been diagnosed with multiple chronic conditions [1]. While medications play a vital role in treating chronic conditions, inappropriate overuse of medications is a risk factor for adverse drug events, non-adherence to medications, hospitalization, and death [2]. With the increased prevalence of multimorbidity (the co-occurrence of two or more chronic conditions), there have been increasing concerns about polypharmacy and the implications for health outcomes [3]. Estimates of the prevalence and factors associated with polypharmacy are important to guide interventions to optimize the use and minimize harms of polypharmacy and enhance quality of care [4-5].

According to a Centers for Disease Control and Prevention (CDC) analysis of the National Health and

Nutrition Examination Survey data (NHANES), 22.4% of U.S. adults aged 40-79 years old used 5 or more prescription drugs in the last month, and women (23.5%) used more than men (21.1%) [6]. However, it is also increasingly observed in younger adults with multimorbidity as rates of obesity, diabetes, hypertension, and other chronic diseases increase [7]. Medication use patterns are also affected by social determinants of health, which expose the disparities that need specific policy responses [8-9]. Solving this problem aligns with public health priorities, including Healthy People 2030, which highlights safe and effective use of medication as one of the potential ways to enhance the overall population's health [10].

Multimorbidity is one of the major causes of polypharmacy, but not all populations show the same association. People with the same number of chronic conditions might have vastly different medication regimens, indicative of healthcare access, provider

practice, and patient characteristics [11]. Moreover, comorbid mental health disorders can often complicate the treatment decision, which results in potentially inappropriate drug prescribing and risky drug interactions [12]. In the light of these complexities, there is a need to identify predictors of polypharmacy to guide interventions to promote rational prescribing, deprescribing, and integrated care models [13].

Polypharmacy has significant economic effects, including higher healthcare expenditure due to avoidable adverse outcomes, emergency sessions, and primary care [14]. Simultaneously, the clinical burden is equally pressing, and patients report reduced quality of life, cognitive impairment, and decline due to inappropriate medication use [15-16]. Therefore, health systems must balance the therapeutic advantages of polypharmacy and the possible harm by ensuring better prescribing rules and patient education, and review of medications [17].

Patients with polypharmacy often access multiple healthcare services, which can create challenges in coordinating medication management. These can be attributed to the involvement of multiple prescribers and unclear roles and responsibilities among providers. Effective management of polypharmacy requires the combined expertise of the different healthcare professionals involved and includes complex decision-making with patient involvement.

NHANES is the best survey to examine patterns and predictors of polypharmacy among multimorbid adults [18]. The NHANES combines interviews, medical, and laboratory analyses to produce nationally representative health, nutrition, and healthcare use information in the United States [19-21]. This is extensive enough to detect demographic, socioeconomic, and clinical correlates of polypharmacy, providing information about the groups at risk who are more susceptible [20]. As the number of chronic diseases increases, and the complexity of the treatment profile increases due to the need to take many drugs simultaneously, it is important to evaluate the level of polypharmacy and predictors thereof on a population-level scale. This study aims to assess the prevalence and predictors of polypharmacy in U.S. adults with multimorbidity based on the NHANES data. Results of this analysis inform interventions that may enhance safe prescribing, minimize medication usage disparities, and enhance the outcomes of adults with multiple chronic conditions.

METHODOLOGY

Study Design and Data Source

This study employed a cross-sectional design using data from the National Health and Nutrition Examination Survey (NHANES), a continuous survey conducted by the U.S. Centers for Disease Control and Prevention (CDC). NHANES utilizes a complex, multistage probability sampling design to obtain a representative sample of the noninstitutionalized

U.S. population. Data were pooled from four consecutive survey cycles spanning 2011–2018 and included household interviews, physical examinations, and laboratory assessments. Sampling weights, strata, and primary sampling units (PSUs) were incorporated in all analyses to account for the complex survey design.

Study Population

The analytic sample consisted of adults aged 20 years and older who reported having at least two chronic medical conditions, thereby meeting the definition of multimorbidity. Participants younger than 20 years, pregnant individuals, and those missing data on chronic conditions or prescription medication use were excluded. Because polypharmacy was the primary outcome, participants without prescription medication data were not included in the analytic sample. The final dataset was restricted to complete cases for variables retained in the analysis.

Variables and Measures

Multimorbidity was defined as the presence of two or more chronic conditions. We created a chronic condition count by summing self-reported physician diagnoses of chronic obstructive pulmonary disease (COPD, NHANES variable mcq160o), asthma (mcq010), coronary heart disease (mcq160c), myocardial infarction (mcq160b), stroke (mcq160f), cancer (mcq220), arthritis (mcq160a), hypertension (bpq020), diabetes (diq010), and kidney disease, defined as a history of kidney stones (kiq026). Participants with at least two conditions were classified as multimorbid.

Polypharmacy was assessed using the NHANES prescription medication questionnaire (RXQ_RX). NHANES provides a direct count variable (rxdcnt), representing the total number of unique prescription medications reported over the past 30 days. This variable was used to define polypharmacy, with participants categorized as having polypharmacy if they reported taking five or more prescription medications.

Sociodemographic variables included age (in years), gender (male or female), race/ethnicity, education (categorized as less than high school, high school or GED, and college or higher), marital status (married/partnered, previously married, or never married), and the family income-to-poverty ratio (IPR, continuous). Health insurance coverage was classified as insured or uninsured. Behavioral and health-related factors included smoking status (never, former, or current smoker), moderate-to-vigorous physical activity (categorized as 1–2 days, 3–4 days, or ≥ 5 days per week), and body mass index (BMI, kg/m^2). Alcohol intake was excluded from the final analysis because more than 80% of responses were missing, precluding meaningful inclusion.

Statistical Analysis

Survey weights, strata, and primary sampling units were applied to all analyses to yield nationally representative estimates. Descriptive statistics were

calculated for the study sample, stratified by polypharmacy status. Because this analysis uses complex survey design data to produce nationally representative estimates, we employed Survey-design-based F-tests (Rao–Scott adjusted F-tests) to compare groups for categorical variables, and Survey-adjusted t-tests for continuous variables. Multivariable logistic regression models were then constructed to identify predictors of polypharmacy among adults with multimorbidity.

Multicollinearity was assessed using the Variance Inflation Factor (VIF). Values ranged from 1.02 to 4.25, with a mean VIF of 1.69, indicating no evidence of problematic collinearity. All statistical analyses were performed using Stata version 18 (StataCorp, College Station, TX).

Missing Data

Due to the complex survey design, multiple imputation methods could not be applied. Instead, a complete case analysis was conducted. Most covariates demonstrated minimal missingness (<10%), including BMI (7.8%), education (0.1%), marital status (0.1%), and smoking status (<0.1%). Insurance coverage and income-to-poverty ratio

had approximately 12% missingness each, while polypharmacy was missing for 36% of participants due to incomplete medication reporting. Because alcohol intake data were missing in over 80% of respondents, this variable was excluded. The implications of missing data are acknowledged as a study limitation.

Ethical Considerations

NHANES protocols are reviewed and approved annually by the National Center for Health Statistics (NCHS) Research Ethics Review Board, and all participants provide written informed consent [21]. The present analysis was based entirely on publicly available, de-identified NHANES data and therefore did not require additional institutional review board approval.

RESULTS

Table 1 below summarizes the sociodemographic, behavioral, and health-related characteristics of adults with multimorbidity stratified by polypharmacy status over the 2011–2018 study period. Of the weighted sample, 141,729,292 (73%) adults reported polypharmacy, while 52,727,861 (27%) adults did not.

TABLE 1: Weighted Characteristics of Adults with Multimorbidity by Polypharmacy Status, NHANES 2011–2018 (Unweighted n = 19,383; Weighted N = 194,457,154).

Characteristic	No polypharmacy (N = 52,727,861)	Polypharmacy (N=141,729,292)	Test statistic (F-test/T-test)	p-value
Age in years (mean ± SD)	60.21 ± 13.08	64.86 ± 12.00	t= -9.89	<0.001
BMI in kg/m ² (mean ± SD)	31.00 ± 6.66	32.93 ± 8.54	t= -5.20	<0.001
Income-to-poverty ratio(mean ± SD)	3.08 ± 1.56	2.70 ± 1.63	t= 4.66	<0.001
Gender(%)			F= 2.61	0.113
Male	23,389,501 (29%)	58,454,655 (71%)	-	-
Female	29,338,360 (26%)	83,274,637 (74%)	-	-
Education level(%)			F= 4.10	0.034
Less than high school	6,588,471 (21%)	25,083,938 (79%)	-	-
High school graduate/ GED	13,436,485 (26%)	37,487,784 (74%)	-	-
College+	32,702,905 (29%)	79,157,570 (71%)	-	-
Marital status(%)			F= 7.94	0.001
Married/Partnered	33,705,998(29%)	83,882,829(71%)	-	-
Previously married	14,419,872(23%)	49,234,299(77%)	-	-
Never married	4,601,991(35%)	8,612,165(65%)	-	-
Insurance cover(%)			F= 19.42	<0.001
No	4,005,087(44%)	5,060,128(56%)	-	-
Yes	48,722,773(26%)	136,669,165(74%)	-	-
Smoking(%)			F= 0.980	0.377
Never	23,386,508(28%)	59,901,077(72%)	-	-
Former	18,681,383(25%)	54,875,841(75%)	-	-
Current	10,659,969(28%)	26,952,374(72%)	-	-
Physical activity (Moderate to vigorous)			F= 10.02	<0.001
1-2 days	8,613,195(36%)	15,247,455(64%)	-	-
3-4 days	44,088,404(26%)	126,428,445(74%)	-	-
≥5 days	26,262(33%)	53,393(67%)	-	-
Race/Ethnicity(%)			F= 1.79	0.156
Mexican American	2,437,070(32%)	5,157,239(68%)	-	-
Other Hispanic	2,320,718(32%)	4,985,524(68%)	-	-
Non-Hispanic White	42,127,844(27%)	115,346,046 (73%)	-	-
Non-Hispanic Black	5,842,228 (26%)	16,240,483 (74%)	-	-

The analytic sample included 19,383 unweighted participants, corresponding to a weighted U.S. population of 194,457,154 adults with multimorbidity. Weighted descriptive statistics are presented, with categorical variables compared using design-based F-tests and continuous variables compared using design-based t-tests. Reported p-values reflect these test statistics.

Table 1 above reveals that adults with polypharmacy were older on average than those without polypharmacy (64.86 ± 12.00 vs. 60.21 ± 13.08 years, $t = -9.89$, $p < 0.001$). Similarly, individuals with polypharmacy had a higher mean body mass index (32.93 ± 8.54 kg/m²) compared to those without polypharmacy (31.00 ± 6.66 kg/m², $t = -5.20$, $p < 0.001$). Income-to-poverty ratio was lower among the polypharmacy group (2.70 ± 1.63) compared with the non-polypharmacy group (3.08 ± 1.56 , $t = 4.66$, $p < 0.001$).

Gender distribution was not significantly different across groups ($F = 2.61$, $p = 0.113$), with females comprising 83,274,637 (74%) of the polypharmacy group and 29,338,360 (26%) of the non-polypharmacy group. Education level showed significant variation ($F = 4.10$, $p = 0.034$). Among adults with less than a high school education, 25,083,938 (79%) had polypharmacy, compared with 37,487,784 (74%) with a high school or GED and 79,157,570 (71%) with a college degree or higher.

Marital status was also significantly associated with polypharmacy ($F = 7.94$, $p = 0.001$). Previously married adults had the highest proportion of polypharmacy, with 49,234,299 (77%) reporting polypharmacy compared to 83,882,829 (71%) of married/partnered adults and 8,612,165 (65%) of

never married adults. Insurance coverage differed markedly between groups ($F = 19.42$, $p < 0.001$), with 136,669,165 (74%) of insured adults experiencing polypharmacy compared with 5,060,128 (56%) of uninsured adults.

Smoking status was not significantly associated with polypharmacy ($F = 0.98$, $p = 0.377$). Among current smokers, 26,952,374 (72%) reported polypharmacy compared with 54,875,841 (75%) of former smokers and 59,901,077 (72%) of never smokers. In contrast, physical activity showed significant differences ($F = 10.02$, $p < 0.001$). Adults engaging in only 1–2 days of moderate-to-vigorous physical activity per week were less likely to report polypharmacy (15,247,455; 64%) compared with those active 3–4 days per week (126,428,445; 74%). Race and ethnicity were not significantly associated with polypharmacy ($F = 1.79$, $p = 0.156$). Within subgroups, polypharmacy prevalence ranged from 5,157,239 (68%) among Mexican Americans to 115,346,046 (73%) among Non-Hispanic White adults.

Table 2 below presents the results of the multivariable survey-weighted logistic regression assessing sociodemographic, behavioral, and health-related predictors of polypharmacy among U.S. adults with multimorbidity between 2011 and 2018.

TABLE 2: Survey-Weighted Logistic Regression Predicting Polypharmacy in Adults with Multimorbidity, NHANES 2011–2018.

Predictor	Odds Ratio (95% CI)	P-value
Age (years)	1.04 (1.03 – 1.04)	<0.001
Sex (Female vs Male)	1.06 (0.89 – 1.25)	0.500
BMI (kg/m ²)	1.05 (1.04 – 1.07)	<0.001
Income-to-poverty ratio (IPR)	0.84 (0.78 – 0.91)	<0.001
Race/Ethnicity		
Other Hispanic vs Mexican American	1.12 (0.71 – 1.76)	0.616
Non-Hispanic White vs Mexican American	1.60 (1.15 – 2.22)	0.006
Non-Hispanic Black vs Mexican American	1.45 (1.03 – 2.02)	0.032
Education		
High school/GED vs <HS	0.74 (0.53 – 1.05)	0.087
College+ vs <HS	0.73 (0.56 – 0.96)	0.027
Marital Status		
Previously married vs Married/partnered	1.05 (0.81 – 1.36)	0.689
Never married vs Married/partnered	0.80 (0.54 – 1.18)	0.250
Insurance (Yes vs No)	2.20 (1.46 – 3.33)	<0.001
Smoking status		
Former vs Never	1.05 (0.81 – 1.36)	0.715
Current vs Never	1.28 (0.94 – 1.76)	0.118
Physical activity		
3–4 days/week vs 1–2 days	1.36 (1.01 – 1.84)	0.043
≥5 days/week vs 1–2 days	1.37 (0.11 – 16.82)	0.801

<HS -Less than high school. Logistic regression models were survey-weighted to account for the complex sampling design of NHANES. Odds ratios (OR) with 95% confidence intervals (CI) and p-values are presented. The reference groups are: male (for sex), Mexican American (for race/ethnicity), less than high school education (for education), married/partnered (for marital status), no insurance (for insurance), never smoker (for smoking status), and engaging in 1–2 days of moderate-to-vigorous physical activity per week (for physical activity).

From the findings in Table 2 above, it's evident that advancing age was significantly associated with higher odds of polypharmacy (OR 1.04, 95% CI: 1.03–1.04, $p < 0.001$). Similarly, higher BMI increased the likelihood of polypharmacy (OR 1.05, 95% CI: 1.04–1.07, $p < 0.001$). In contrast, a higher income-to-poverty ratio was inversely related to polypharmacy (OR 0.84, 95% CI: 0.78–0.91, $p < 0.001$).

Compared with Mexican American adults, non-Hispanic White (OR 1.60, 95% CI: 1.15–2.22, $p = 0.006$) and non-Hispanic Black adults (OR 1.45, 95% CI: 1.03–2.02, $p = 0.032$) had significantly higher odds of polypharmacy, while the difference for other Hispanics was not significant (OR 1.12, 95% CI: 0.71–1.76, $p = 0.616$). Educational attainment also demonstrated a protective association: adults with a college education or higher had lower odds of polypharmacy compared with those with less than a high school education (OR 0.73, 95% CI: 0.56–0.96, $p = 0.027$).

Marital status was not significantly associated with polypharmacy, as both previously married (OR 1.05, 95% CI: 0.81–1.36, $p = 0.689$) and never married adults (OR 0.80, 95% CI: 0.54–1.18, $p = 0.250$) did not differ from their married/partnered counterparts. Health insurance coverage emerged as a strong predictor: insured adults had more than twice the odds of polypharmacy compared to the uninsured (OR 2.20, 95% CI: 1.46–3.33, $p < 0.001$).

Smoking status did not significantly influence polypharmacy risk, with former smokers (OR 1.05, 95% CI: 0.81–1.36, $p = 0.715$) and current smokers (OR 1.28, 95% CI: 0.94–1.76, $p = 0.118$) showing similar odds compared with never smokers. Regarding physical activity, adults reporting 3–4 days per week of moderate-to-vigorous activity had higher odds of polypharmacy than those with only 1–2 days (OR 1.36, 95% CI: 1.01–1.84, $p = 0.043$). However, those with ≥ 5 days per week did not differ significantly (OR 1.37, 95% CI: 0.11–16.82, $p = 0.801$), though the wide confidence interval indicates instability due to small sample size.

DISCUSSION

This study examined the prevalence and predictors of polypharmacy among U.S. adults with multimorbidity using NHANES data from 2011–2018. The results confirm that polypharmacy is highly prevalent in this group, reinforcing concerns that managing multiple chronic conditions often leads to complex medication regimens [1-3]. Our findings are consistent with earlier reports showing that nearly one in four middle-aged and older adults is exposed to polypharmacy [6], but by focusing on adults with multimorbidity, we highlight the specific population at greatest risk.

Older age and higher BMI were strong predictors of polypharmacy, reflecting the fact that both aging and obesity contribute to higher disease burden and increased prescription use [3, 7,11]. Similarly, socioeconomic status played an important role: individuals with higher income had lower odds of

polypharmacy, while those with health insurance were more than twice as likely to report it. Insurance expands access to care, but our findings suggest that it may also increase the risk of unnecessary prescribing without regular medication review [8, 9, 18].

Racial and ethnic disparities were evident, with non-Hispanic White and non-Hispanic Black adults more likely to experience polypharmacy than Mexican American adults, echoing prior studies that pointed to differences in access and prescribing practices [18, 20]. Education appeared protective, as college graduates had lower odds of polypharmacy, likely reflecting better health literacy and engagement in treatment decisions [8, 13]. Lifestyle and social factors such as smoking and marital status showed no clear associations, while physical activity produced mixed results, possibly due to sample size limitations.

No doubt, polypharmacy can have therapeutic benefits in managing comorbidities by addressing different clinical needs. However, inappropriate or unreviewed regimens are associated with adverse outcomes such as multiple hospital admissions, impaired cognition, and poor quality of life. Overmedication significantly increases hospitalization of older adults, as described by Abe et al. [2]. Similarly, Khezrian et al. demonstrated that it is associated with frailty, medication non-adherence, and cognitive decline [16]. These studies suggest that while medications are important for improving health outcomes, without routine review, patients, especially seniors, are at increased risk of harmful drug-drug interactions leading to negative health outcomes. Therefore, a balance between the therapeutic advantages of polypharmacy and systemic medication review, as well as deprescribing strategies, is essential to ensure patients' safety and enhance overall health.

Strengths and Limitations

This study draws strength from the use of NHANES, a nationally representative dataset that integrates interviews, physical examinations, and laboratory data, ensuring generalizability to U.S. adults with multimorbidity. The large sample size and application of survey weights further enhance the robustness of the findings. Thus, the main limitation was missing data. Multiple imputation could not be applied due to the survey's complex design, necessitating complete case analysis. While missingness was minimal for most covariates ($< 10\%$), insurance coverage and income-to-poverty ratio had around 12% missing data, and polypharmacy was missing for 36% of participants because of incomplete medication reporting. Alcohol intake was excluded entirely due to $> 80\%$ missingness. These gaps may have reduced statistical power and introduced bias. Additionally, the cross-sectional design limits causal inference, and the study did not assess medication appropriateness or safety. Future studies should address missing data challenges by developing or applying imputation methods suitable for complex

survey designs to reduce potential bias. Longitudinal research is also needed to clarify causal relationships between multimorbidity, sociodemographic factors, and polypharmacy over time. Moreover, future work should move beyond quantifying polypharmacy to assess the appropriateness and safety of medication use, including risks of adverse drug interactions.

CONCLUSION

This study shows that polypharmacy is highly prevalent among U.S. adults with multimorbidity. Older age, higher BMI, lower income, health insurance coverage, and certain racial and educational groups were linked to greater odds of polypharmacy. These findings emphasize the need for targeted strategies to ensure safe and effective medication use in multimorbid populations. This study shows that polypharmacy is highly prevalent among U.S. adults with multimorbidity. Older age, higher BMI, lower income, health insurance coverage, and certain racial and educational groups were linked to greater odds of polypharmacy. These findings emphasize the need for targeted strategies to ensure safe and effective medication use in multimorbid populations. Evidence indicates that polypharmacy contributes to hospitalizations, inappropriate prescribing, and cognitive or functional decline in older adults. Socioeconomic inequalities also play a role, with disadvantaged groups disproportionately affected. The associated healthcare burden is substantial, both in clinical outcomes and system costs. Guidelines now recommend regular medication reviews and deprescribing to improve safety. Reducing inappropriate polypharmacy aligns with Healthy People 2030 goals and remains critical for enhancing quality of life in multimorbid populations.

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