Associations Between Prescription and Supplement Polypharmacy and Cardiometabolic Outcomes Among U.S. Adults: A Cross-Sectional Analysis of NHANES 2017-2018

ABSTRACT

Associations Between Prescription and Supplement Polypharmacy and Cardiometabolic Outcomes Among U.S. Adults: A Cross-Sectional Analysis of NHANES 2017-2018

By

Maysa Osman

April 7th, 2026

Background: Polypharmacy, defined as concurrent use of five or more medications, affects nearly half of U.S. adults and is associated with adverse health outcomes. Most research examines prescription medications only, overlooking dietary supplement use despite its prevalence and potential for interactions. Additionally, little is known about whether polypharmacy-outcome associations differ across racial, ethnic, and socioeconomic groups.

Purpose: This study examined associations between prescription polypharmacy and supplement polypharmacy with three cardiometabolic outcomes (hypertension, hyperlipidemia, hyperglycemia) among U.S. adults, and assessed whether associations varied by race/ethnicity and socioeconomic status.

Methods: Cross-sectional data from 12,290 adults aged 18 years and older in the 2017-2018 National Health and Nutrition Examination Survey were analyzed. Prescription polypharmacy and supplement polypharmacy were defined as concurrent use of five or more prescription medications or dietary supplements, respectively. Self-reported physician diagnoses of hypertension, hyperlipidemia, and hyperglycemia served as outcomes. Survey-weighted logistic regression models adjusted for age, sex, race/ethnicity, education, socioeconomic status, body mass index, and smoking status were used to examine associations. Stratified analyses were conducted by race/ethnicity and socioeconomic status.

Results: Weighted prevalence of prescription polypharmacy was 48.7%, and supplement polypharmacy was 11.3%. After adjustment, adults with hypertension were significantly more likely to have prescription polypharmacy (OR = 3.17, 95% CI: 2.35, 4.28) compared to those without hypertension. Similarly, adults with hyperlipidemia were significantly more likely to have prescription polypharmacy (OR = 1.95, 95% CI: 1.39, 2.73), and adults with hyperglycemia were significantly more likely to have prescription polypharmacy (OR = 3.80, 95% CI: 2.84, 5.08) compared to those without these conditions. Supplement polypharmacy was not significantly associated with any outcome. The likelihood of prescription polypharmacy among those with cardiometabolic outcomes varied by race/ethnicity, with particularly strong associations among Non-Hispanic Black adults with hyperglycemia (OR = 7.07), and remained significant across all socioeconomic strata.

Conclusions: Prescription polypharmacy is highly prevalent and strongly associated with cardiometabolic outcomes. Adults with cardiometabolic conditions are substantially more likely to have prescription polypharmacy. On the other hand, supplement polypharmacy shows no such associations. Important disparities exist across racial/ethnic and socioeconomic groups. Findings support prioritizing prescription medication review in clinical practice and highlight the need for equity-focused medication management approaches.

Associations Between Prescription and Supplement Polypharmacy and Cardiometabolic Outcomes Among U.S. Adults: A Cross-Sectional Analysis of NHANES 2017-2018

By

Maysa Osman

B.S., GEORGIA STATE UNIVERSITY

A Thesis Submitted to the Graduate Faculty

of Georgia State University in Partial Fulfillment

of the

Requirements for the Degree

MASTER OF PUBLIC HEALTH

ATLANTA, GEORGIA

30303

APPROVAL PAGE

Associations Between Prescription and Supplement Polypharmacy and Cardiometabolic Outcomes Among U.S. Adults: A Cross-Sectional Analysis of NHANES 2017-2018

By

Maysa Osman

Dr. Sheryl Strasser

Committee Chair

Dr. Ike Okosun

Committee Member

April 7th, 2026

Date

Acknowledgments

Dr. Sheryl M Strasser, PhD, MPH, MSW, CHES, CPH

Dr. Ike Okosun, PhD, MPH, M.S

TABLE OF CONTENTS

Chapter I
Introduction

1.1 Background

Polypharmacy, commonly defined as the concurrent use of five or more medications, has become more prevalent in the United States. National estimates indicate that approximately 40% of older adults use five or more prescription medications simultaneously, with rates rising substantially over the past two decades (Vennu, 2024). This trend reflects the aging U.S. population and advances in pharmacological management of chronic diseases. Polypharmacy can be appropriate when medications are clinically indicated, but it is associated with increased risk of adverse drug events, drug-drug interactions, medication non-adherence, and higher healthcare costs (Lum et al., 2020).

Cardiometabolic conditions, including hypertension, hyperlipidemia, and hyperglycemia, represent major public health challenges in the United States. These conditions frequently co-occur and share common risk factors, including obesity, physical inactivity, and poor diet quality (Seidu et al., 2023). The relationship between polypharmacy and cardiometabolic health is complex and bidirectional. Individuals with multiple cardiometabolic conditions often require multiple medications for disease management (Franchini et al., 2015), yet polypharmacy itself may contribute to metabolic dysregulation through medication side effects and interactions (Foy et al., 2019; Kalafutova et al., 2014).

Most research on polypharmacy has focused exclusively on prescription medications, overlooking the substantial use of dietary supplements in the U.S. population. National surveys indicate that over 50% of adults use at least one dietary supplement, with prevalence exceeding 70% among older adults (Nahin et al., 2009). Dietary supplements include vitamins, minerals, herbs, amino acids, and other substances intended to supplement the diet. Dietary supplements are not subject to FDA approval for safety and efficacy prior to marketing, and consumers often do not report supplement use to healthcare providers (Gardiner et al., 2015). This creates potential for unrecognized drug-supplement interactions and cumulative medication burden (Kanji et al., 2012). The concurrent use of multiple dietary supplements, known as supplement polypharmacy, has received limited attention in the epidemiological literature. Individuals who use multiple prescription medications may also use multiple dietary supplements, either to manage chronic conditions or believe that supplements provide health benefits (Akilen et al., 2014). However, the prevalence of supplement polypharmacy and its relationship to cardiometabolic outcomes remains poorly characterized.

Disparities in both medication use patterns and cardiometabolic disease burden exist across racial, ethnic, and socioeconomic groups (Vennu, 2024). Non-Hispanic Black adults experience higher rates of hypertension and diabetes compared to other racial groups, while access to medications and healthcare services varies substantially by socioeconomic status. Whether

associations between polypharmacy and cardiometabolic outcomes differ across these population subgroups has not been adequately examined.

1.2 Statement of the Problem

Despite the high prevalence of polypharmacy and cardiometabolic conditions in the U.S., several gaps exist in the literature. First, most studies examine prescription polypharmacy in isolation, failing to account for concurrent use of dietary supplements (Nahin et al., 2009; Loo & Chong, 2021). Second, few studies have investigated whether supplement polypharmacy is independently associated with cardiometabolic outcomes. Third, little is known about whether associations between polypharmacy and cardiometabolic health differ by race/ethnicity or socioeconomic status (Vennu, 2024). Addressing these gaps is essential for developing interventions to reduce medication-related harm and health disparities.

1.3 Purpose of Study

The purpose of this study is to examine associations between polypharmacy and cardiometabolic outcomes among U.S. adults using nationally representative data from the 2017–2018 National Health and Nutrition Examination Survey (NHANES). This study extends prior research by (1) examining prescription and supplement polypharmacy as distinct exposures, (2) investigating associations with three cardiometabolic outcomes (hypertension, hyperlipidemia, and hyperglycemia), and (3) assessing whether these associations vary by race/ethnicity and socioeconomic status.

1.4 Research Questions

This study addresses the following research questions:

1. What is the prevalence of prescription polypharmacy and supplement polypharmacy among U.S. adults?
2. Are prescription polypharmacy and supplement polypharmacy independently associated with hypertension, hyperlipidemia, and hyperglycemia after adjusting for demographic and health-related covariates?
3. Do associations between polypharmacy and cardiometabolic outcomes differ by race/ethnicity and or socioeconomic status?

1.5 Significance of the Study

Findings from this study have several important implications. First, by examining supplement polypharmacy alongside prescription polypharmacy, this research provides a more complete picture of total medication burden in the U.S. population (Agbabiaka et al., 2018). Second, identifying associations between polypharmacy and cardiometabolic outcomes can inform clinical practice guidelines for medication management among patients with chronic conditions (Sangaleti et al., 2023). Third, documenting disparities in these associations by race/ethnicity and

socioeconomic status can guide the development of culturally appropriate interventions to promote medication safety and reduce health inequities.

From a public health perspective, this study contributes to understanding the complex relationship between medication use patterns and chronic disease burden (Cheung et al., 2020). Results may inform policy discussions regarding dietary supplement regulation, medication reconciliation practices, and strategies to optimize medication use in diverse populations (Asher et al., 2017).

Chapter II
Review Of the Literature

2.1 Polypharmacy Epidemiology and Definitions

Polypharmacy is defined as the concurrent use of five or more medications. Polypharmacy is emerging as a public health concern affecting millions of U.S. adults (Vennu, 2024; Cheung et al., 2020). Prevalence estimates vary depending on population characteristics and study settings, ranging from 28.3% among older adults internationally to 46.9% among U.S. adults with at least one cardiometabolic risk factor (Cheung et al., 2020; Vyas et al., 2020). Among individuals with multiple cardiometabolic conditions, polypharmacy rates can exceed 80% (Vyas et al., 2020).

Age represents the strongest demographic predictor of polypharmacy. Adults aged 45-64 years and those 65 years and older are significantly more likely to have polypharmacy compared to younger adults (Vennu, 2024). Women experience slightly higher polypharmacy rates than men, while non-Hispanic Black adults show elevated prevalence (OR = 1.66; 95% CI = 1.51-1.83) compared to non-Hispanic White adults (Vennu, 2024). Geographic factors also influence patterns; individuals with metabolic syndrome in Iran's urban areas showed stronger associations with polypharmacy than with wealth or education (Daneshmand et al., 2024).

2.2 Cardiometabolic Multimorbidity and Medication Burden

Cardiometabolic diseases, such as diabetes mellitus, hypertension, hyperlipidemia, and metabolic syndrome, frequently co-occur within individuals and represent some of the most prevalent chronic conditions globally (Freeman & Gross, 2012; Seidu et al., 2023). This clustering requires complex therapeutic regimens that contribute substantially to polypharmacy. The relationship between cardiometabolic multimorbidity and polypharmacy seems bidirectional: multiple chronic conditions require more medications, and polypharmacy itself may contribute to metabolic dysregulation through iatrogenic effects and drug interactions (Freeman & Gross, 2012; Cheung et al., 2020).

Type 2 diabetes commonly involves hyperlipidemia and hypertension as comorbidities, with each concurrent disorder contributing to the risk of complications and requiring therapeutic intervention (Freeman & Gross, 2012). The simultaneous management of these coexisting conditions commonly results in polypharmacy, which may further complicate treatment through potential drug-drug interactions. Certain antihypertensive agents, particularly beta-blockers and thiazide diuretics, can adversely affect glycemic control, while some diabetes medications influence lipid metabolism (Freeman & Gross, 2012). Conversely, statins have been associated with modest increases in diabetes risk, creating therapeutic dilemmas when managing patients with both conditions (Freeman & Gross, 2012).

In a pooled analysis of 44,818 community-dwelling older adults from Hong Kong and 17 European countries, 34.8% had cardiometabolic multimorbidity and 28.3% experienced polypharmacy (Cheung et al., 2021). Adults with cardiometabolic multimorbidity were substantially more likely to experience polypharmacy compared to those without such conditions. Most importantly, the detrimental effects of polypharmacy attenuated but remained statistically significant with increasing numbers of cardiometabolic diseases, suggesting that polypharmacy poses risks even when clinically indicated for multiple conditions (Cheung et al., 2020). This finding led the authors to conclude that polypharmacy is "less detrimental, yet still detrimental" for adults with cardiometabolic multimorbidity, emphasizing the need to optimize prescribing regardless of disease burden (Cheung et al., 2020).

Defining and measuring cardiometabolic outcomes in medicated populations comes with methodological challenges. McStea et al. (2016) demonstrated that metabolic syndrome prevalence estimates vary substantially depending on whether medication use is incorporated into diagnostic criteria. When standard clinical thresholds alone were used, metabolic syndrome prevalence was 35.1%, but increased to 52.7% when individuals taking relevant medications with controlled biomarkers were included (McStea et al., 2016). This finding highlights the importance of medication-adjusted definitions to avoid underestimating true disease prevalence in treated populations.

2.3 Polypharmacy and Hypertension

Cross-sectional studies document higher polypharmacy prevalence among hypertensive versus normotensive individuals. In Brazilian primary care, 38.1% of older adults with hypertension experienced polypharmacy (Sangaleti et al., 2023). Secondly, European hospitalized hypertensive patients showed significantly higher polypharmacy rates than normotensive individuals ($p = 0.007$) (Diaconu et al., 2021). Hypertensive patients experienced more drug-drug interactions (6.55 ± 5.82 versus 4.93 ± 5.59 per patient, $p = 0.03$) and food-drug interactions (2.64 ± 1.29 versus 2.02 ± 1.73, $p < 0.001$) compared to normotensive individuals (Diaconu et al., 2021).

The relationship between polypharmacy and hypertension is complicated by drug-induced hypertension, an iatrogenic condition affecting a substantial fraction of the hypertensive population (Foy et al., 2019). Multiple medication classes elevate blood pressure through mechanisms including sodium and fluid retention, activation of the renin-angiotensin-aldosterone system, and alteration of vascular tone (Foy et al., 2019). Nonsteroidal anti-inflammatory drugs (NSAIDs), among the most used medications particularly in older adults, commonly interact with antihypertensive agents to impair blood pressure control (Kalafutova et al., 2014). These interactions are classified as moderate severity (class C), yet even minor long-term blood pressure elevations can significantly increase cardiovascular mortality risk (Kalafutova et al., 2014).

Data from the Pars Cohort Study shows 23.7% of individuals with hypertension experienced polypharmacy compared to only 4.7% among those without hypertension ($p < 0.001$) (Zare et al., 2024). The presence of multiple comorbidities amplified this risk; individuals with more than three comorbid conditions had 5.18 times higher prevalence of polypharmacy compared to those with isolated hypertension (Zare et al., 2024).

2.4 The Expanding Role of Dietary Supplements in Polypharmacy

2.4.1 Prevalence and Non-Disclosure

Contemporary definitions of polypharmacy usually focus only on prescription medications, however this approach fails to capture the substantial burden of dietary supplements and herbal products consumed concurrently with pharmaceuticals. Among community-dwelling older adults in the United Kingdom, 78.0% used dietary supplements or herbal medicinal products alongside prescription drugs, with the number of products per person ranging from one to eight (Agbabiaka et al., 2018). Women were significantly more likely than men to be concurrent users (43.4% versus 22.5%, $p = 0.009$) (Agbabiaka et al., 2018). Among U.S. elderly participants in the Ginkgo Evaluation of Memory Study, 74.2% combined at least one prescription drug with one dietary supplement, and 32.5% consumed three or more prescription drugs alongside three or more supplements (Nahin et al., 2009). In cardiovascular disease populations, supplement use reaches even higher levels, with 82.5% of Turkish patients with chronic cardiovascular diseases reporting regular use of dietary herbal supplements (Aykan et al., 2018). Consumption was more prevalent among individuals with hypertension (53.6%) (Aykan et al., 2018).

Most importantly, patients do not disclose supplement use to healthcare providers. Only 21.3% of cardiovascular patients reported their supplement consumption to physicians (Aykan et al., 2018), while similar low disclosure rates were observed among older UK adults (Agbabiaka et al., 2018). This hidden polypharmacy escapes clinical detection, limiting physicians' ability to assess potential interactions and medication burden. Among Malaysian patients with chronic diseases, 55.7% perceived potential interactions between supplements and drugs, 56.0% never consulted healthcare providers about such risks, and 54.0% never sought information about potential interactions (Loo et al., 2021).

2.4.2 Drug-Supplement Interactions

The concurrent use of prescription medications and dietary supplements creates many opportunities for pharmacokinetic and pharmacodynamic interactions. A systematic review examining interactions between commonly used dietary supplements and cardiovascular drugs identified potential concerns across multiple supplement categories; however, evidence was insufficient for most clinical outcomes due to limited long-term studies (Kanji et al., 2012). Low-strength evidence suggested benefits of omega-3 fatty acids on triglyceride levels and garlic supplementation on HDL cholesterol, though safety concerns persist, particularly regarding bleeding risk (Kanji et al., 2012). Common herbal supplements demonstrate different interaction potential. St. John's wort and goldenseal cause clinically important drug interactions and should

generally be avoided by patients receiving pharmacologic therapy (Asher et al., 2017). Other supplements, including curcumin, echinacea, garlic, Asian ginseng, green tea extract, and kava, may interact with specific medications but are likely safe with others (Asher et al., 2017).

Among Malaysian patients with chronic diseases, analysis identified 80 cases of potential drug-supplement interactions, predominantly involving antihypertensive drugs (66.3%) and antidiabetic agents (17.5%), with vitamin B3/niacin (33.8%) and fish oil/omega-3 supplements (26.3%) most commonly implicated (Loo et al., 2021). Hospitalized patients taking cardiac medications face higher risks; among urban inpatients, 19.8% had potentially harmful dietary supplement-prescription medication interactions, but only 25% were asked about supplement use at admission (Gardiner et al., 2015).

2.4.3 Supplements and Cardiometabolic Outcomes

Evidence suggests a complex relationship between dietary supplement use and cardiometabolic health, with findings varying by study design and outcomes examined. Analysis of NHANES data comparing supplement users with non-users found that all supplement user groups demonstrated significantly lower LDL cholesterol after adjusting for demographics, BMI, cardiovascular disease history, and relevant medications (Jacques & Rogers, 2021). Multiple dietary supplement users and long-term users showed higher HDL cholesterol, lower fasting glucose, lower insulin levels, and lower C-reactive protein compared to non-supplement users (Jacques & Rogers, 2021). However, these cross-sectional findings may reflect residual confounding by health-conscious behaviors rather than true supplement effects.

When examining clinical outcomes longitudinally, results are mixed. Among U.S. adults with diabetes, overall dietary supplement use was not associated with all-cause mortality risk (HR = 0.97; 95% CI = 0.87 to 1.08) over a median 6.9-year follow-up (Hua et al., 2023). Subgroup analyses revealed potentially protective effects only for specific supplement classes: amino acid use associated with lower all-cause mortality (HR = 0.66), while fatty acid and glucosamine supplements demonstrated lower cardiovascular disease mortality (Hua et al., 2023)..

2.5 Mechanisms Linking Polypharmacy to Cardiometabolic Outcomes

The relationship between polypharmacy and cardiometabolic outcomes operates through multiple interconnected ways. Drug-drug and drug-supplement interactions represent important mechanisms affecting metabolic parameters. Pharmacokinetic interactions, primarily involving cytochrome P450 enzyme systems, alter drug concentrations and therapeutic effects (Buzea et al., 2022). Pharmacodynamic interactions occur through concurrent binding to identical receptors, opposing physiologic effects, or additive toxicities (Buzea et al., 2022).

Iatrogenic metabolic effects constitute another critical pathway. Many medication classes induce or exacerbate metabolic abnormalities, where medications treating one condition cause adverse effects requiring additional medications (Foy et al., 2019). Polypharmacy may also serve as a marker of disease burden rather than a direct causal factor. Individuals with multiple

cardiometabolic conditions require more medications to manage complex disease states. Figuring out whether polypharmacy contributes to metabolic outcomes or reflects underlying disease severity presents substantial methodological challenges in observational research (Cheung et al., 2020).

2.6 Gaps in Current Literature and Study Rationale

Despite growing research attention to polypharmacy, critical gaps persist. First, most studies examine prescription medications exclusively, failing to capture the substantial burden of dietary supplements consumed by 74-82% of medicated adults (Agbabiaka et al., 2018; Aykan et al., 2018; Nahin et al., 2009). This oversight results in an incomplete assessment of the total medication burden and interaction risks. Second, many studies document polypharmacy in disease-specific populations, particularly heart failure, atrial fibrillation, chronic kidney disease, or psychiatric conditions. Population-based research examining patterns across general adult populations remains limited. Disease-specific cohorts may not generalize to broader populations, particularly younger adults with emerging cardiometabolic risk factors.

Third, research examining polypharmacy and individual cardiometabolic risk factors, hyperlipidemia, hypertension, and hyperglycemia as distinct outcomes is scarce. Most studies focus on cardiovascular disease events or metabolic syndrome as composite endpoints, limiting understanding of how polypharmacy relates to specific metabolic parameters. Fourth, U.S.-based research using nationally representative data is limited. International studies provide valuable insights, yet healthcare systems, prescribing practices, supplement use patterns, and population characteristics differ substantially across countries.

This thesis addresses these gaps by examining polypharmacy patterns, including both prescription medications and dietary supplements, in relation to individual cardiometabolic risk factors among U.S. adults using nationally representative NHANES data. Understanding these relationships is essential for informing clinical practice, patient education, and public health interventions to optimize medication use while minimizing iatrogenic risks.

2.7 Theoretical Basis of the Study

This study is guided by an integrative theoretical framework that combines pharmacoepidemiologic principles with a social determinants of health perspective. This dual framework provides a comprehensive lens for examining how polypharmacy patterns relate to cardiometabolic outcomes while recognizing that these relationships may be shaped by social and economic factors.

2.7.1 Pharmacoepidemiologic Framework

Pharmacoepidemiology examines how medication use patterns in populations affect health outcomes, with particular attention to therapeutic effects, adverse events, and drug interactions (Strom et al., 2019). This framework provides the foundation for understanding relationships

between polypharmacy and cardiometabolic health through three interconnected components: drug utilization patterns, drug-disease associations, and drug interactions.

Drug utilization patterns describe how medications are prescribed, dispensed, and consumed within populations. In the context of cardiometabolic conditions, polypharmacy represents a common pattern arising from the need to manage multiple concurrent risk factors. Understanding which medication classes are used together and whether prescription medications are combined with dietary supplements provides essential context for assessing potential health impacts.

Drug-disease associations examine how medications affect health outcomes, including intended therapeutic effects and unintended adverse consequences. Certain medications can paradoxically worsen the conditions they are meant to treat or induce new metabolic abnormalities. These iatrogenic effects create a prescribing cascade where medications treating one condition cause side effects requiring additional medications (Foy et al., 2019).

Drug interactions represent a critical mechanism through which polypharmacy may affect cardiometabolic outcomes. When multiple medications are consumed concurrently, pharmacokinetic interactions can alter drug metabolism, leading to subtherapeutic or toxic concentrations. Pharmacodynamic interactions occur when drugs have additive, synergistic, or antagonistic effects on physiologic processes (Buzea et al., 2022). The inclusion of dietary supplements alongside prescription medications creates additional interaction possibilities that are poorly characterized despite the high prevalence of concurrent use (Agbabiaka et al., 2018).

2.7.2 Social Determinants of Health Framework

Pharmacoepidemiologic principles explain biological mechanisms linking medications to health outcomes, however they do not fully account for social patterns of medication use and differential health outcomes across population subgroups. Fundamental cause theory posits that social conditions such as race/ethnicity and socioeconomic status operate as fundamental causes of health disparities through multiple mechanisms (Link & Phelan, 1995). These mechanisms include differential access to healthcare resources, quality of care received, medication affordability, health literacy, and ability to navigate complex healthcare systems.

Social determinants may influence polypharmacy prevalence and the nature of polypharmacy experienced. For instance, individuals with higher socioeconomic status may have better access to healthcare and more medications prescribed, while simultaneously receiving higher quality medication management and monitoring. Racial and ethnic minorities may experience both undertreatment of some conditions and overtreatment of others, reflecting systemic disparities in healthcare delivery (Vennu, 2024).

Chapter III
Methodology

3.1 Data Sources and Study Population

This study utilized data from the 2017–2018 National Health and Nutrition Examination Survey (NHANES), a continuous cross-sectional survey conducted by the National Center for Health Statistics. NHANES uses a complex, multistage probability sampling design to obtain a nationally representative sample of the civilian, noninstitutionalized U.S. population. The survey includes household interviews, physical examinations, and laboratory tests conducted at mobile examination centers.

The initial sample included 19,643 participants from the 2017–2018 cycle. The study population was restricted to adults aged 18 years and older with complete data on all study variables. Participants were excluded if they had missing data on prescription medication use, dietary supplement use, cardiometabolic outcomes, or any covariates included in the analysis. After applying these exclusion criteria, the final analytic sample consisted of 12,290 participants.

3.2 Study Measures

Operational definitions and NHANES variable codes for all study measures are presented in Table 3.1.

3.2.1 Independent Variables

The primary exposures of interest were prescription polypharmacy and supplement polypharmacy. Prescription medication use was assessed through the Prescription Medications questionnaire, which asked participants to report all prescription medications taken in the past 30 days. The total count of prescription medications was used to create a binary polypharmacy variable, defined as concurrent use of five or more prescription medications. Dietary supplement use was assessed through the Dietary Supplement questionnaire, which captured all dietary supplements taken in the past 30 days. The total count of dietary supplements was used to create a binary supplement polypharmacy variable, defined as concurrent use of five or more dietary supplements.

3.2.2 Dependent Variables

Three cardiometabolic outcomes were examined: hypertension, hyperlipidemia, and hyperglycemia. Hypertension was defined based on self-reported physician diagnosis (BPQ020: "Ever told you had high blood pressure?"). Hyperlipidemia was defined based on self-reported physician diagnosis (BPQ080: "Ever told you had high cholesterol?"). Hyperglycemia was defined based on self-reported physician diagnosis of diabetes (DIQ010: "Doctor told you have diabetes?"). These self-reported measures have been validated in previous NHANES research and show good concordance with clinical measurements.

3.2.3 Covariates

Demographic and health-related covariates were selected based on prior literature examining polypharmacy and cardiometabolic health. Age was included as a continuous variable measured in years. Sex was coded as a binary variable (male/female). Race/ethnicity was categorized into six groups: Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, Non-Hispanic Asian, and Other/Multiracial. Educational attainment was categorized into five levels: less than 9th grade, 9th–11th grade, high school graduate or GED, some college, and college graduate or higher. Socioeconomic status was categorized by the poverty income ratio into three groups: Low SES, Middle SES, and High SES. Body mass index (BMI) was calculated from measured height and weight data and included as a continuous variable. Smoking status was derived from the Smoking and Cigarette Use questionnaire and categorized into three groups: never smoker, former smoker (smoked at least 100 cigarettes in lifetime but does not currently smoke), and current smoker (currently smokes cigarettes some days or every day).

Table 3.1. Operational Definitions and NHANES Variable Codes for Study Measures

Variable Category	Variable Name	Operational Definition	NHANES Code	Source File
Independent Variables				
Prescription Polypharmacy	Total prescription medication count	Number of prescription medications taken in past 30 days	RXDCOUNT	RXQ_RX_J
	Prescription polypharmacy	Binary: 1 = ≥5 medications; 0 = <5 medications	Derived from RXDCOUNT	
Supplement Polypharmacy	Total dietary supplement count	Number of dietary supplements taken in past 30 days	DSDCOUNT	DSQTOT_J
	Supplement polypharmacy	Binary: 1 = ≥5 supplements; 0 = <5 supplements	Derived from DSDCOUNT	
Dependent Variables				
Hypertension	Self-reported hypertension diagnosis	"Ever told by doctor you had high blood pressure?" Binary: 1 = Yes; 0 = No	BPQ020	BPQ_J
Hyperlipidemia	Self-reported high cholesterol diagnosis	"Ever told by doctor your blood cholesterol was high?" Binary: 1 = Yes; 0 = No	BPQ080	BPQ_J
Hyperglycemia	Self-reported diabetes diagnosis	"Ever told by doctor you have diabetes?" Binary: 1 = Yes; 0 = No	DIQ010	DIQ_J
Covariates				
Age	Age in years	Continuous variable (years)	RIDAGEYR	DEMO_J
Sex	Sex	Binary: 1 = Male; 2 = Female	RIAGENDR	DEMO_J
Race/Ethnicity	Race/ethnicity (6 categories)	1 = Mexican American; 2 = Other Hispanic; 3 = Non-Hispanic White; 4 = Non-Hispanic Black; 6 = Non-Hispanic Asian; 7 = Other/Multiracial	RIDRETH3	DEMO_J
Education	Educational attainment (5 categories)	1 = Less than 9th grade; 2 = 9th–11th grade; 3 = High school/GED; 4 = Some college; 5 = College graduate+	DMDEDUC2	DEMO_J
Socioeconomic Status	Poverty income ratio categories	Low SES (INDFMPIR < 1.0); Middle SES (1.0–2.99); High SES (≥ 3.0)	INDFMPIR	DEMO_J
Body Mass Index	BMI (kg/m²)	Continuous variable calculated from measured height and weight	BMXBMI	BMX_J
Smoking Status	Smoking status (3 categories)	Never smoker; Former smoker (≥100 cigarettes lifetime, not current); Current smoker	SMQ020, SMQ040	SMQ_J
Survey Design Variables				
Survey Weights	2-year MEC exam weights	Survey weights for nationally representative estimates	WTMEC2YR	DEMO_J
Primary Sampling Units	Masked variance pseudo-PSU	Primary sampling units for variance estimation	SDMVPSU	DEMO_J
Strata	Masked variance pseudo-stratum	Strata for variance estimation	SDMVSTRA	DEMO_J

Note: All data files are from NHANES 2017–2018 (Cycle J).

3.3 Statistical Analysis

All analyses accounted for the complex survey design of NHANES using survey weights, primary sampling units, and strata to produce nationally representative estimates. The survey package in R was used to incorporate these design features into all analyses. Descriptive statistics were calculated to characterize the study population. Continuous variables were reported as means with standard deviations, and categorical variables were reported as frequencies and percentages. Weighted prevalence estimates with 95% confidence intervals were calculated for polypharmacy exposures and cardiometabolic outcomes.

Bivariate associations between polypharmacy exposures and cardiometabolic outcomes were assessed using the Rao-Scott chi-square test, which adjusts the Pearson chi-square statistic for the complex survey design. This design-adjusted test produces an F-statistic to account for survey weights, clustering, and stratification (Rao & Scott, 1984). Separate tests were conducted for prescription polypharmacy and supplement polypharmacy with each of the three outcomes. Multivariable logistic regression models were used to examine adjusted associations between polypharmacy and cardiometabolic outcomes. Six separate models were constructed: prescription polypharmacy with each outcome (hypertension, hyperlipidemia, hyperglycemia) and supplement polypharmacy with each outcome. All models adjusted for age, sex, race/ethnicity, education, socioeconomic status, BMI, and smoking status. Results were reported as adjusted odds ratios with 95% confidence intervals.

Stratified analyses were conducted to examine whether associations between polypharmacy and cardiometabolic outcomes varied by race/ethnicity and socioeconomic status. Separate logistic regression models were fit within each racial/ethnic group (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, Non-Hispanic Asian, Other/Multiracial) and each SES category (Low, Middle, High). Stratified models adjusted for age, sex, education, BMI, and smoking status, excluding the stratification variable itself. Statistical significance was set at $p < 0.05$ for all analyses. Missing data were handled using complete-case analysis, with participants excluded if they had any missing values on any study variable. All analyses were conducted using R version 4.5.1 with the survey, haven, dplyr, tidyr, gtsummary, and flextable packages.

3.4 Ethical Considerations

NHANES data collection was approved by the National Center for Health Statistics Research Ethics Review Board, and all participants provided written informed consent. This secondary data analysis used publicly available, de-identified data and was exempt from institutional review board approval

Chapter IV
Results

4.1 Sample Characteristics

The final analytic sample included 12,290 U.S. adults aged 18 years and older from the 2017-2018 National Health and Nutrition Examination Survey (NHANES) with complete data on all study variables. Demographic and clinical characteristics of the sample are presented in Table 1.

The mean age of participants was 59.31 years (SD = 16.17), and 52.4% were female. The sample was racially and ethnically diverse: 43.5% Non-Hispanic White, 23.1% Non-Hispanic Black, 10.1% Mexican American, 10.1% Non-Hispanic Asian, 7.9% Other Hispanic, and 5.3% Other/Multiracial. Educational attainment varied: 20.9% held a college degree or higher, 33.6% had some college education, 25.5% completed high school or obtained a GED, 11.6% completed 9th–11th grade, and 8.5% had less than a 9th-grade education. Regarding socioeconomic status, 34.3% were classified as high SES, 47.4% as middle SES, and 18.2% as low SES based on the poverty income ratio.

The mean body mass index was 30.98 kg/m² (SD = 7.70), indicating the sample was on average classified as obese. Half of the participants (49.9%) reported never smoking, while 33.7% were former smokers and 16.3% were current smokers. Participants reported taking an average of 5.43 prescription medications (SD = 4.19) and 1.84 dietary supplements (SD = 2.18) within the past 30 days. More than half of the sample (54.1%) met criteria for prescription polypharmacy, defined as concurrent use of five or more prescription medications, while 10.4% met criteria for supplement polypharmacy, defined as concurrent use of five or more dietary supplements. Among cardiometabolic outcomes, hypertension was the most prevalent condition, affecting 60.3% of U.S. adults in the sample. Hyperlipidemia affected 51.6%, and hyperglycemia affected 32.9% of adults.

Table 1. Sample Characteristics, NHANES 2017-2018 (N = 12,290)

Characteristic	N = 12,290[1]
Age (years)	59.31 (16.17)
Sex	
Male	5,851 (47.6%)
Female	6,439 (52.4%)
Race/Ethnicity	
Mexican American	1,245 (10.1%)
Other Hispanic	973 (7.9%)
Non-Hispanic White	5,351 (43.5%)
Non-Hispanic Black	2,833 (23.1%)
Non-Hispanic Asian	1,236 (10.1%)
Other/Multiracial	652 (5.3%)
Education	
Less than 9th grade	1,043 (8.5%)
9-11th grade	1,420 (11.6%)
High school/GED	3,132 (25.5%)
Some college	4,132 (33.6%)
College graduate+	2,563 (20.9%)
Socioeconomic Status	
Low SES	2,241 (18.2%)
Middle SES	5,829 (47.4%)
High SES	4,220 (34.3%)
BMI (kg/m²)	30.98 (7.70)
Smoking Status	
Never Smoker	6,138 (49.9%)
Former Smoker	4,146 (33.7%)
Current Smoker	2,006 (16.3%)
Number of Rx Medications	5.43 (4.19)
Number of Dietary Supplements	1.84 (2.18)
Rx Polypharmacy (≥5 medications)	6,650 (54.1%)
Supplement Polypharmacy (≥5 supplements)	1,274 (10.4%)
Hypertension	7,405 (60.3%)
Hyperlipidemia	6,345 (51.6%)
Hyperglycemia	4,039 (32.9%)

[1]Mean (SD) for continuous variables; n (%) for categorical variables.

4.2 Weighted Prevalence of Polypharmacy and Cardiometabolic Outcomes

After accounting for the NHANES complex survey design, the weighted prevalence of prescription polypharmacy was 48.7% (95% CI: 45.1%, 52.3%), while the weighted prevalence of supplement polypharmacy was 11.3% (95% CI: 9.0%, 13.6%).

Among cardiometabolic outcomes, hypertension was the most prevalent condition, affecting 53.8% of U.S. adults (95% CI: 49.9%, 57.7%), followed by hyperlipidemia at 48.9% (95% CI:

44.9%, 52.9%), and hyperglycemia at 24.8% (95% CI: 23.0%, 26.6%). These weighted estimates provide nationally representative prevalence rates for the U.S. adult population aged 18 years and older (Table 2)

Table 2. Weighted Prevalence of Polypharmacy and Cardiometabolic Outcomes, NHANES 2017-2018

Category	Variable	n	Weighted Prevalence	95% CI
Independent Variable	Rx Polypharmacy (≥5 medications)	6,650	48.7%	(45.1%, 52.3%)
Independent Variable	Supplement Polypharmacy (≥5 supplements)	1,274	11.3%	(9%, 13.6%)
Dependent Variable	Hypertension	7,405	53.8%	(49.9%, 57.7%)
Dependent Variable	Hyperlipidemia	6,345	48.9%	(44.9%, 52.9%)
Dependent Variable	Hyperglycemia	4,039	24.8%	(23%, 26.6%)

4.3 Bivariate Associations Between Polypharmacy and Cardiometabolic Outcomes

Design-adjusted Rao-Scott chi-square tests were conducted to examine associations between polypharmacy and cardiometabolic outcomes (Table 3). Prescription polypharmacy showed statistically significant associations with all three cardiometabolic outcomes. Adults with hypertension were significantly more likely to have prescription polypharmacy compared to those without hypertension ($F = 140.69$, $p < 0.001$). Similarly, adults with hyperlipidemia were significantly more likely to have prescription polypharmacy ($F = 94.34$, $p < 0.001$), and adults with hyperglycemia were significantly more likely to have prescription polypharmacy ($F = 211.15$, $p < 0.001$) compared to those without these conditions.

Supplement polypharmacy showed weaker associations with cardiometabolic outcomes. Adults with hypertension were slightly more likely to have supplement polypharmacy ($F = 5.66$, $p = 0.031$), but no significant associations were observed for hyperlipidemia ($F = 1.86$, $p = 0.193$) or hyperglycemia ($F = 1.41$, $p = 0.253$).

Table 3. Bivariate Associations Between Polypharmacy and Cardiometabolic Outcomes, NHANES 2017-2018

Exposure	Outcome	F-Statistic	P-Value
Rx Polypharmacy	**Hypertension**	**140.6900**	**< 0.001**
Rx Polypharmacy	**Hyperlipidemia**	**94.3410**	**< 0.001**
Rx Polypharmacy	**Hyperglycemia**	**211.1500**	**< 0.001**
Supplement Polypharmacy	Hypertension	5.6623	0.031
Supplement Polypharmacy	Hyperlipidemia	1.8609	0.193
Supplement Polypharmacy	Hyperglycemia	1.4112	0.253

Note: P-values and F-statistics were calculated using the Rao-Scott chi-square test to account for the complex survey design

4.4 Adjusted Associations Between Polypharmacy and Cardiometabolic Outcomes

Multivariable logistic regression models were conducted to examine associations between polypharmacy and cardiometabolic outcomes after adjusting for age, sex, race/ethnicity, education, socioeconomic status, BMI, and smoking status (Table 4).

After adjustment for covariates, prescription polypharmacy remained significantly associated with all three cardiometabolic outcomes. Adults with hypertension were significantly more likely to have prescription polypharmacy (OR = 3.17, 95% CI: 2.35, 4.28; p < 0.001) compared to those without hypertension. Similarly, adults with hyperlipidemia were significantly more likely to have prescription polypharmacy (OR = 1.95, 95% CI: 1.39, 2.73; p = 0.001), and adults with hyperglycemia were significantly more likely to have prescription polypharmacy (OR = 3.80, 95% CI: 2.84, 5.08; p < 0.001) compared to those without these conditions. These findings indicate that individuals with cardiometabolic conditions have a substantially higher likelihood of experiencing prescription polypharmacy, with the strongest association observed for hyperglycemia.

In contrast, supplement polypharmacy was not significantly associated with any cardiometabolic outcome after covariate adjustment. Adults with hypertension did not have significantly higher likelihood of supplement polypharmacy (OR = 1.01, 95% CI: 0.63, 1.62; p = 0.973) compared to those without hypertension. Likewise, no significant differences in likelihood of supplement polypharmacy were observed among those with hyperlipidemia (OR = 0.97, 95% CI: 0.55, 1.72; p = 0.925) or hyperglycemia (OR = 0.92, 95% CI: 0.60, 1.42; p = 0.722) compared to those without these conditions.

Table 4. Adjusted Associations Between Polypharmacy and Cardiometabolic Outcomes, NHANES 2017-2018

Exposure	Outcome	Adjusted OR (95% CI)[a]	P-Value
Rx Polypharmacy	**Hypertension**	**3.17 (2.35, 4.28)**	**< 0.001**
Rx Polypharmacy	Hyperlipidemia	1.95 (1.39, 2.73)	0.001
Rx Polypharmacy	**Hyperglycemia**	**3.8 (2.84, 5.08)**	**< 0.001**
Supplement Polypharmacy	Hypertension	1.01 (0.63, 1.62)	0.973
Supplement Polypharmacy	Hyperlipidemia	0.97 (0.55, 1.72)	0.925
Supplement Polypharmacy	Hyperglycemia	0.92 (0.6, 1.42)	0.722

[a]Adjusted for age, sex, race/ethnicity, education, SES, BMI, and smoking status.

4.5 Stratified Analysis by Race/Ethnicity and Socioeconomic Status

Separate logistic regression models were conducted within strata of race/ethnicity and socioeconomic status to examine whether associations between polypharmacy and cardiometabolic outcomes differed across population subgroups. All models were adjusted for age, sex, education, BMI, and smoking status (Table 5).

Among racial/ethnic groups, adults with hypertension were significantly more likely to have prescription polypharmacy compared to those without hypertension in the following groups: Non-Hispanic White (OR = 3.08, 95% CI: 2.06, 4.61; p < 0.001), Non-Hispanic Black (OR = 3.90, 95% CI: 2.50, 6.07; p < 0.001), Non-Hispanic Asian (OR = 2.94, 95% CI: 1.14, 7.57; p =

0.041), Other Hispanic (OR = 3.48, 95% CI: 1.19, 10.21; p = 0.038), and Other/Multiracial (OR = 21.20, 95% CI: 4.33, 103.87; p = 0.002) adults. However, among Mexican American adults, those with hypertension did not have significantly higher likelihood of prescription polypharmacy (OR = 1.21, 95% CI: 0.77, 1.91; p = 0.414) compared to those without hypertension. For hyperlipidemia, adults with this condition were significantly more likely to have prescription polypharmacy in the following groups: Non-Hispanic White (OR = 1.82, 95% CI: 1.13, 2.93; p = 0.014), Non-Hispanic Black (OR = 2.46, 95% CI: 1.53, 3.96; p < 0.001), Other Hispanic (OR = 4.80, 95% CI: 1.72, 13.38; p = 0.003), and Other/Multiracial (OR = 6.38, 95% CI: 1.29, 31.53; p = 0.023) adults. No significant associations were observed among Mexican American (OR = 0.68, 95% CI: 0.35, 1.32; p = 0.238) or Non-Hispanic Asian (OR = 1.57, 95% CI: 0.55, 4.47; p = 0.381) adults. For hyperglycemia, adults with this condition were significantly more likely to have prescription polypharmacy across all racial/ethnic groups: Mexican American (OR = 5.06, 95% CI: 1.80, 14.18; p = 0.002), Other Hispanic (OR = 3.42, 95% CI: 1.11, 10.48; p = 0.031), Non-Hispanic White (OR = 3.44, 95% CI: 2.29, 5.18; p < 0.001), Non-Hispanic Black (OR = 7.07, 95% CI: 4.16, 12.01; p < 0.001), and Non-Hispanic Asian (OR = 6.11, 95% CI: 1.63, 22.85; p = 0.007). The particularly strong association among Non-Hispanic Black adults indicates that Black individuals with hyperglycemia are substantially more likely to experience prescription polypharmacy compared to their counterparts without hyperglycemia.

Supplement polypharmacy showed few significant associations across racial/ethnic strata. Among Mexican American adults, those with hyperlipidemia were more likely to have supplement polypharmacy (OR = 4.12, 95% CI: 1.39, 12.25; p = 0.011) compared to those without hyperlipidemia. For hyperglycemia, Other Hispanic adults with this condition were less likely to have supplement polypharmacy (OR = 0.11, 95% CI: 0.02, 0.79; p = 0.025), while Non-Hispanic Black adults with hyperglycemia were more likely to have supplement polypharmacy (OR = 2.91, 95% CI: 1.31, 6.49; p = 0.009).

Across socioeconomic strata, adults with hypertension were significantly more likely to have prescription polypharmacy in all SES groups: Low SES (OR = 3.73, 95% CI: 2.52, 5.52; p < 0.001), Middle SES (OR = 2.82, 95% CI: 1.81, 4.40; p < 0.001), and High SES (OR = 3.24, 95% CI: 1.80, 5.83; p < 0.001) adults. For hyperlipidemia, adults with this condition were significantly more likely to have prescription polypharmacy among Low SES (OR = 2.56, 95% CI: 1.18, 5.54; p = 0.017) and Middle SES (OR = 2.27, 95% CI: 1.47, 3.49; p < 0.001) adults. Among High SES adults, the association did not reach statistical significance (OR = 1.76, 95% CI: 0.95, 3.26; p = 0.070). For hyperglycemia, adults with this condition were significantly more likely to have prescription polypharmacy across all SES strata: Low SES (OR = 5.33, 95% CI: 3.30, 8.62; p < 0.001), Middle SES (OR = 5.26, 95% CI: 3.25, 8.52; p < 0.001), and High SES (OR = 2.48, 95% CI: 1.38, 4.46; p = 0.002).

Supplement polypharmacy showed limited associations across SES strata. Among Low SES adults, those with hyperlipidemia were less likely to have supplement polypharmacy (OR = 0.30, 95% CI: 0.10, 0.90; p = 0.032). Among High SES adults, those with hyperglycemia were less likely to have supplement polypharmacy (OR = 0.57, 95% CI: 0.34, 0.96; p = 0.032).

Table 5. Stratified Analysis of Polypharmacy and Cardiometabolic Outcomes by Race/Ethnicity and SES, NHANES 2017-2018

Stratification	Stratum	Exposure	Outcome	Adjusted OR (95% CI)[a]	P-Value
Race/Ethnicity	Mexican American	polypharmacy_rx	hypertension	1.21 (0.77, 1.91)	0.414
			hyperlipidemia	0.68 (0.37, 1.25)	0.238
			hyperglycemia	5.06 (2.12, 12.08)	0.002
		polypharmacy_supp	hypertension	1.54 (0.67, 3.57)	0.327
			hyperlipidemia	4.12 (1.59, 10.67)	0.011
			hyperglycemia	0.92 (0.34, 2.47)	0.876
	Other Hispanic	polypharmacy_rx	hypertension	3.48 (1.19, 10.21)	0.038
			hyperlipidemia	4.8 (1.99, 11.59)	0.003
			hyperglycemia	3.42 (1.24, 9.39)	0.031
		polypharmacy_supp	hypertension	0.7 (0.26, 1.93)	0.505
			hyperlipidemia	0.55 (0.14, 2.24)	0.419
			hyperglycemia	0.11 (0.02, 0.62)	0.025
	Non-Hispanic White	**polypharmacy_rx**	**hypertension**	**3.08 (2.06, 4.61)**	**< 0.001**
			hyperlipidemia	1.82 (1.19, 2.78)	0.014
			hyperglycemia	**3.44 (2.38, 4.96)**	**< 0.001**
		polypharmacy_supp	hypertension	1.1 (0.63, 1.93)	0.745
			hyperlipidemia	0.93 (0.45, 1.9)	0.836
			hyperglycemia	0.88 (0.5, 1.56)	0.67
	Non-Hispanic Black	**polypharmacy_rx**	**hypertension**	**3.9 (2.5, 6.07)**	**< 0.001**
			hyperlipidemia	**2.46 (1.73, 3.49)**	**< 0.001**
			hyperglycemia	**7.07 (4.32, 11.58)**	**< 0.001**
		polypharmacy_supp	hypertension	0.98 (0.63, 1.53)	0.938
			hyperlipidemia	1.25 (0.5, 3.09)	0.642
			hyperglycemia	2.91 (1.45, 5.83)	0.009
	Non-Hispanic Asian	polypharmacy_rx	hypertension	2.94 (1.14, 7.57)	0.041
			hyperlipidemia	1.57 (0.59, 4.17)	0.381
			hyperglycemia	6.11 (1.98, 18.88)	0.007
		polypharmacy_supp	hypertension	0.88 (0.33, 2.3)	0.79
			hyperlipidemia	1.71 (0.6, 4.85)	0.33
			hyperglycemia	0.56 (0.23, 1.39)	0.231
	Other/Multiracial	polypharmacy_rx	hypertension	21.2 (4.33, 103.87)	0.002
			hyperlipidemia	6.38 (1.52, 26.67)	0.023
			hyperglycemia	5.55 (1.05, 29.33)	0.062
		polypharmacy_supp	hypertension	0.34 (0.06, 2.08)	0.263
			hyperlipidemia	0.64 (0.16, 2.55)	0.533
			hyperglycemia	0.91 (0.22, 3.82)	0.901
SES	**Low SES**	**polypharmacy_rx**	**hypertension**	**3.73 (2.14, 6.51)**	**< 0.001**
			hyperlipidemia	2.56 (1.29, 5.09)	0.017
			hyperglycemia	**5.33 (3.07, 9.25)**	**< 0.001**
		polypharmacy_supp	hypertension	1.43 (0.3, 6.89)	0.663
			hyperlipidemia	0.3 (0.11, 0.81)	0.032
			hyperglycemia	1.86 (0.38, 9.25)	0.458
	Middle SES	**polypharmacy_rx**	**hypertension**	**2.82 (1.81, 4.39)**	**< 0.001**
			hyperlipidemia	**2.27 (1.63, 3.15)**	**< 0.001**

Stratification	Stratum	Exposure	Outcome	Adjusted OR (95% CI)[a]	P-Value
			hyperglycemia	**5.26 (4, 6.9)**	**< 0.001**
		polypharmacy_supp	hypertension	1.27 (0.74, 2.18)	0.398
			hyperlipidemia	1.74 (0.76, 3.96)	0.208
			hyperglycemia	1.22 (0.65, 2.29)	0.544
	High SES	**polypharmacy_rx**	**hypertension**	**3.24 (1.94, 5.4)**	**< 0.001**
			hyperlipidemia	1.76 (1, 3.13)	0.07
			hyperglycemia	2.48 (1.56, 3.96)	0.002
		polypharmacy_supp	hypertension	0.78 (0.37, 1.64)	0.523
			hyperlipidemia	0.79 (0.4, 1.58)	0.52
			hyperglycemia	0.57 (0.35, 0.91)	0.032

[a]Adjusted for age, sex, education, BMI, and smoking status.

Chapter V
Discussion and Conclusion

5.1 Prevalence of Polypharmacy

This study examined associations between polypharmacy and cardiometabolic outcomes among a nationally representative sample of U.S. adults. The findings demonstrate that prescription polypharmacy is highly prevalent, affecting nearly half of the adult population, and is strongly associated with cardiometabolic conditions. Specifically, adults with hypertension, hyperlipidemia, and hyperglycemia were substantially more likely to have prescription polypharmacy compared to those without these conditions. In contrast, supplement polypharmacy showed no significant associations with cardiometabolic outcomes after adjusting for covariates. Important disparities were observed across racial/ethnic and socioeconomic groups, with particularly strong associations among Non-Hispanic Black adults and consistent patterns across all socioeconomic strata.

5.2 Prescription Polypharmacy and Cardiometabolic Outcomes

After adjusting for demographic and health-related covariates, prescription polypharmacy remained significantly associated with all three cardiometabolic outcomes examined. Adults with hypertension and hyperglycemia were over three times more likely to have prescription polypharmacy compared to those without these conditions. Adults with hyperlipidemia were nearly twice as likely to have prescription polypharmacy. These findings are consistent with previous research documenting strong associations between polypharmacy and cardiometabolic disease (Franchini et al., 2015; Sangaleti et al., 2023).

The observed associations likely reflect multiple underlying mechanisms. First, individuals with more severe or poorly controlled cardiometabolic conditions require more medications for disease management, creating a direct relationship between disease burden and medication count (Diaconu et al., 2021). This explains why adults with these conditions are substantially more likely to experience prescription polypharmacy. Second, certain medications used to treat one condition may contribute to the development of other cardiometabolic problems, further increasing medication requirements. For example, some antihypertensive medications can adversely affect glucose metabolism, while certain antipsychotic and antidepressant medications may contribute to weight gain and metabolic dysregulation (Buzea et al., 2022; Foy et al., 2019). Third, polypharmacy may reduce medication adherence due to regimen complexity, leading to poorer disease control and necessitating additional medications (Vyas et al., 2020).

The cross-sectional design of this study prevents the determination of whether polypharmacy precedes or follows cardiometabolic disease onset. However, the most plausible interpretation is that adults with cardiometabolic conditions require more medications to manage their disease burden, explaining the higher likelihood of polypharmacy observed in this population. The bidirectional nature of this relationship complicates interpretation but does not diminish the public health significance of the findings. Regardless of temporal sequence, the strong associations between cardiometabolic outcomes and prescription polypharmacy highlight the need for careful medication management in this population.

5.3 Supplement Polypharmacy and Cardiometabolic Outcomes

In contrast to prescription polypharmacy, supplement polypharmacy was not significantly associated with any cardiometabolic outcome after covariate adjustment. Adults with hypertension, hyperlipidemia, or hyperglycemia did not have significantly higher likelihood of supplement polypharmacy compared to those without these conditions. This null finding is noteworthy for several reasons. First, it suggests that dietary supplement use, even in high quantities, may not be driven by disease burden in the same way as prescription medication use. While adults with chronic conditions are substantially more likely to have prescription polypharmacy due to medical necessity, they are not more likely to have supplement polypharmacy. This could reflect fundamental differences between supplements and prescription medications in terms of how they are obtained and used. Second, the lack of association may indicate that individuals who use multiple supplements differ systematically from those who use multiple prescription medications. Previous research suggests that supplement users tend to have higher health consciousness, better baseline health status, and more favorable health behaviors (Jacques & Rogers, 2021). These unmeasured factors may explain patterns of supplement use independent of disease status. In other words, supplement polypharmacy may reflect health-seeking behaviors and discretionary health product use rather than disease management needs. Third, the finding raises questions about whether supplement polypharmacy, as currently defined using the prescription medication threshold of five or more products, is an appropriate construct. Dietary supplements vary widely in their ingredients, dosages, and intended purposes, and may require different thresholds or definitions to capture clinically meaningful patterns of use. The one exception to the null findings was a marginal association in bivariate analysis showing that adults with hypertension were slightly more likely to have supplement polypharmacy, which did not persist after multivariable adjustment. This suggests that any apparent relationship between hypertension and supplement polypharmacy was explained by confounding factors such as age, socioeconomic status, or other demographic characteristics.

5.4 Disparities by Race and Ethnicity

Stratified analyses revealed notable variation in the likelihood of prescription polypharmacy across racial/ethnic groups among adults with cardiometabolic conditions. The particularly strong association observed among Non-Hispanic Black adults for hyperglycemia (OR = 7.07)

indicates that Black individuals with hyperglycemia are substantially more likely to experience prescription polypharmacy compared to their counterparts without hyperglycemia. This finding aligns with research documenting racial disparities in diabetes management, disease severity, and medication burden (Kirkman et al., 2012). Several mechanisms may explain these disparities. Black adults experience higher rates of diabetes complications, more severe disease presentation, and poorer glycemic control compared to White adults (Venkat Narayan et al., 2011). More severe disease requires more intensive medication regimens, increasing the likelihood of polypharmacy. Additionally, structural barriers including healthcare access, quality of care, and social determinants of health may contribute to suboptimal disease management, necessitating additional medications (Williams & Mohammed, 2013). The finding that Mexican American adults with hypertension did not show significantly higher likelihood of prescription polypharmacy compared to those without hypertension is unexpected. This may reflect cultural factors in medication use, differences in healthcare utilization patterns, or variations in disease management approaches within this population.

5.5 Disparities by Socioeconomic Status

Across all socioeconomic strata, adults with cardiometabolic conditions were significantly more likely to have prescription polypharmacy. The consistency of associations across SES levels suggests that the relationship between cardiometabolic disease and polypharmacy is universal, affecting individuals regardless of socioeconomic position. However, the particularly strong associations among Low and Middle SES groups for hyperlipidemia highlight potential disparities in disease management and medication burden. Lower SES individuals may face barriers to comprehensive disease management, including limited access to specialists, medication costs, and health literacy challenges. These barriers may result in reactive rather than proactive medication management, where medications are added in response to disease progression rather than preventing complications through lifestyle modifications and early intervention.

5.6 Integration with Existing Literature

The findings of this study contribute to the growing body of evidence on polypharmacy and cardiometabolic health in several ways. First, this study extends previous research by examining both prescription and supplement polypharmacy using a consistent methodological framework and nationally representative data. Second, this study addresses a gap identified by Loo and Chong (2021) regarding the need for population-based studies examining concurrent use of prescription medications and dietary supplements. Previous research has documented high rates of concurrent use (Nahin et al., 2009; Agbabiaka et al., 2018), but few studies have examined whether supplement polypharmacy independently predicts health outcomes. Third, the stratified analyses provide new insights into disparities in associations with more likely outcomes among racial/ethnic and socioeconomic groups. This addresses Vennu's (2024) calls for research examining the social determinants of polypharmacy and its health consequences. The finding

that associations vary substantially across population subgroups suggests that one-size-fits-all approaches to polypharmacy management may be insufficient.

5.7 Limitations of the Study

Several limitations should be considered when interpreting these findings. First, the cross-sectional design does not include causal inference. Prescription polypharmacy was associated with cardiometabolic outcomes, but the temporal sequence cannot be established. Individuals with more severe disease may require more medications, creating reverse causation. Longitudinal studies are needed to determine whether polypharmacy precedes disease onset or progression. Second, all medication use and health outcomes were based on self-report, which may introduce recall bias. Participants may underreport medication use, particularly for supplements that they do not consider medications, or overreport use of medications they believe they should be taking. Similarly, self-reported diagnoses of hypertension, hyperlipidemia, and hyperglycemia may not capture undiagnosed disease or may be subject to differential misclassification across sociodemographic groups. Third, the study used a binary definition of polypharmacy (five or more medications) rather than examining medication count as a continuous variable or using alternative thresholds. This approach aligns with common practice in the literature, but it may obscure dose-response relationships and does not account for qualitative differences in medication regimens. Additionally, the same threshold was applied to both prescription medications and dietary supplements, which may not be equally appropriate for these product types. Fourth, the analyses did not account for specific medication classes, medication duration of use, or prescribing appropriateness. Not all polypharmacy is inappropriate; individuals with multiple chronic conditions may require multiple medications for optimal disease management (Cheung et al., 2020). The inability to distinguish appropriate from inappropriate polypharmacy in this dataset limits the clinical applicability of the findings. Fifth, NHANES excludes institutionalized populations, including nursing home residents and incarcerated individuals, who may have particularly high rates of polypharmacy and different patterns of medication use. The findings may not generalize to these populations.

Sixth, some racial/ethnic subgroups, particularly the Other/Multiracial category, had small sample sizes that resulted in imprecise estimates with wide confidence intervals. Caution is needed when interpreting findings for these groups, and replication in larger samples is needed. Seventh, residual confounding remains possible despite adjustment for multiple covariates. Unmeasured factors such as disease severity, healthcare utilization patterns, health literacy, medication adherence, and genetic factors may influence both polypharmacy and cardiometabolic outcomes. The observed associations may partially reflect these unmeasured confounders instead of the causal effects of polypharmacy. Eighth, the study did not examine potential interactions between prescription and supplement polypharmacy. These two types of polypharmacy were examined separately, but future research should investigate whether concurrent use of both creates synergistic effects on cardiometabolic health beyond their independent effects. Finally, the data are from 2017–2018 and may not reflect current medication

use patterns, particularly given changes in prescribing practices and the introduction of new medications since that time.

5.8 Recommendations

5.8.1 Recommendations for Future Research

Future studies should employ longitudinal designs to establish temporal relationships between polypharmacy and cardiometabolic outcomes. While this cross-sectional study demonstrates that adults with cardiometabolic conditions are more likely to have prescription polypharmacy, prospective cohort studies that follow individuals from disease onset through medication accumulation would provide stronger evidence for understanding this relationship. Such studies should also examine whether specific medication classes or combinations are particularly associated with disease progression or additional medication requirements.

Research should develop and validate measures of supplement polypharmacy that account for the unique characteristics of dietary supplements, including variability in ingredients, dosages, and regulatory oversight. Alternative thresholds or weighted scoring systems that consider the biological activity of different supplements may be needed to better capture clinically meaningful patterns of supplement use. Studies examining drug-supplement interactions in real-world populations are needed to complement the current findings. While this study found that adults with cardiometabolic conditions are not more likely to have supplement polypharmacy, understanding potential interactions between prescription medications and dietary supplements remains important for medication safety.

Qualitative studies exploring medication beliefs, prescribing patterns, and patient-provider communication across diverse populations could inform culturally tailored interventions. Understanding why certain racial/ethnic groups show particularly strong associations between disease and polypharmacy could guide targeted prevention strategies. Future analyses should examine potential interactions between prescription and supplement polypharmacy to determine whether their combined effects differ from their independent effects. This would provide insights into whether individuals using both types concurrently face different patterns or outcomes.

5.8.2 Public Health Intervention Development

Public health intervention development is needed to address threats inherent in prescription polypharmacy. Given the high prevalence (48.7%) observed in this study and the finding that adults with cardiometabolic conditions are 2-4 times more likely to have prescription polypharmacy, this represents a critical area for prevention strategy development. The complexity of managing multiple medications across fragmented healthcare providers, combined with the growing burden of chronic conditions among aging populations, necessitates innovative system-level solutions. A fundamental challenge contributing to polypharmacy is the fragmentation of healthcare delivery. When patients with multiple chronic conditions receive care from multiple specialists, each provider may prescribe medications without being fully aware of the patient's complete regimen. This fragmentation leads to medication accumulation, duplicate therapies, and potentially inappropriate polypharmacy.

Public health interventions must target this structural problem through integrated care models that facilitate collaborative medication management across providers. Health systems should implement shared electronic health record systems with real-time medication synchronization, ensuring every prescriber can see the complete medication picture before adding new therapies. Clinical decision support tools embedded in these systems should flag potential duplications, dangerous interactions, and opportunities for regimen simplification. By breaking down silos between providers, these system-level changes could prevent the uncoordinated medication accumulation that contributes to polypharmacy.

Beyond addressing fragmentation, public health efforts should focus on simplification of medication regimens. Adults managing multiple cardiometabolic conditions face the cognitive burden of remembering multiple medications, navigating different dosing schedules, and managing potential side effects. Population-level strategies to promote simplification include: incentivizing use of fixed-dose combination medications that reduce pill burden, aligning medication schedules to minimize dosing frequency, implementing systematic deprescribing protocols to eliminate unnecessary medications, and creating medication therapy management programs specifically designed for high-risk populations.

The disparities observed in this study demand equity-focused public health interventions. Non-Hispanic Black adults with hyperglycemia showed particularly strong associations (OR = 7.07), indicating they are seven times more likely to have prescription polypharmacy compared to Black adults without hyperglycemia. Community-based programs should be developed and scaled in areas serving predominantly Black and low-SES populations. These programs might include pharmacist-led medication review clinics in community health centers, mobile medication optimization services, and culturally tailored medication education programs delivered through trusted community organizations.

Public health education campaigns should raise awareness about polypharmacy risks and empower individuals to engage in shared decision-making about medications. Messaging should normalize the practice of questioning whether all medications remain necessary and encourage regular medication reviews with healthcare providers. Health literacy programs specifically addressing polypharmacy should provide patients with tools to track their medications, understand potential interactions, and communicate effectively with multiple providers about their complete regimen. Public health surveillance systems should track polypharmacy patterns and outcomes at the population level. Such systems would enable early identification of problematic medication combinations, monitoring of demographic and geographic disparities in medication burden, and evaluation of intervention effectiveness. Data showing that nearly half of U.S. adults experience prescription polypharmacy and that those with cardiometabolic conditions face a higher likelihood of this burden should galvanize public health action and inform resource allocation for prevention programs.

5.8.3 Recommendations for Clinical Practice

Healthcare providers should routinely assess both prescription medication and dietary supplement use during patient encounters. Given that adults with cardiometabolic conditions are substantially more likely to have prescription polypharmacy, medication reconciliation should be prioritized for these patients. This should include explicit questions about supplements, given that patients often do not consider supplements to be medications requiring disclosure (Gardiner et al., 2015). Providers should conduct periodic medication reviews for patients with cardiometabolic conditions and polypharmacy. These reviews should assess the continued necessity of each medication, evaluate for potential drug-drug and drug-supplement interactions, and consider deprescribing when appropriate (Sangaleti et al., 2023). Given the strong likelihood of polypharmacy among adults with multiple cardiometabolic conditions, these reviews should occur at least annually, if not more frequently.

Clinical attention should prioritize prescription polypharmacy, given the strong associations with cardiometabolic outcomes observed in this study. Medication management strategies should be tailored to patient characteristics, including race/ethnicity and socioeconomic status. Providers should be aware that Non-Hispanic Black adults with hyperglycemia, for example, are particularly likely to experience prescription polypharmacy and may benefit from enhanced medication therapy management services. Providers should address barriers to safe medication use, including costs, health literacy, and cultural beliefs. Pharmacists should be engaged as key members of the healthcare team for patients with cardiometabolic conditions and polypharmacy. Pharmacist-led medication therapy management has been shown to improve outcomes in patients with complex medication regimens (Lum et al., 2020).

5.8.4 Recommendation For Policy

Policymakers should consider initiatives to improve coordination of care for patients with multiple chronic conditions who are at high risk of polypharmacy. Given that adults with cardiometabolic conditions are 2-4 times more likely to have prescription polypharmacy, health systems should implement systematic medication reconciliation processes that capture the complete medication picture across all providers. Electronic health record systems should facilitate documentation of all medications and provide clinical decision support for potential interactions and opportunities for medication simplification. Insurance coverage and reimbursement policies should support comprehensive medication therapy management services, particularly for patients with multiple cardiometabolic conditions who are at highest risk of polypharmacy.

Financial barriers to deprescribing or optimizing medication regimens should be addressed. Current reimbursement systems often incentivize prescribing new medications but do not adequately support the time-intensive work of medication review and optimization. Public health agencies should develop and disseminate evidence-based guidance on safe medication use for populations at high risk of polypharmacy, including adults with multiple cardiometabolic conditions, older adults, and individuals with low socioeconomic status. Research funding should prioritize studies examining medication safety and optimization in diverse populations, given the disparities observed in this and other studies (Vennu, 2024).

5.9 Conclusion

This study examined associations between polypharmacy and cardiometabolic outcomes among 12,290 U.S. adults using nationally representative NHANES data. The findings demonstrate that prescription polypharmacy is highly prevalent, affecting nearly half of U.S. adults, and is strongly associated with cardiometabolic conditions. Specifically, adults with hypertension, hyperlipidemia, and hyperglycemia are substantially more likely to have prescription polypharmacy compared to those without these conditions, with odds ratios ranging from 1.95 to 3.80 after adjusting for demographic and health-related factors. These findings indicate that individuals managing cardiometabolic disease face significantly higher likelihood of experiencing the medication burden and complexity associated with polypharmacy. In contrast, supplement polypharmacy, though less common, showed no significant associations with cardiometabolic outcomes. Adults with cardiometabolic conditions were no more likely to have supplement polypharmacy than those without these conditions, suggesting fundamental differences in the drivers of prescription medication versus dietary supplement use. Important disparities were observed across racial/ethnic and socioeconomic groups. Non-Hispanic Black adults with hyperglycemia were particularly likely to have prescription polypharmacy (OR = 7.07), indicating seven times higher odds compared to Black adults without hyperglycemia. Consistent patterns were observed across all socioeconomic strata, though the strength of associations varied by specific condition and SES level.

The cross-sectional design limits causal inference, but the magnitude and consistency of the associations suggest that prescription polypharmacy represents an important marker of cardiometabolic disease burden. The most plausible interpretation is that adults with cardiometabolic conditions require more medications to manage their disease, explaining their substantially higher likelihood of experiencing polypharmacy. Future research employing longitudinal designs, examining specific medication classes and combinations, and testing interventions to optimize medication regimens will be critical for advancing understanding and improving outcomes. From a public health perspective, addressing polypharmacy requires multilevel interventions spanning clinical practice, health systems, and policy. Given that nearly half of U.S. adults experience prescription polypharmacy and that those with cardiometabolic conditions are 2-4 times more likely to face this medication burden, there is an urgent need for system-level solutions that reduce fragmentation of care, simplify pharmaceutical regimens, and ensure equitable access to medication optimization services. This study examines prescription and supplement polypharmacy and investigates disparities across diverse populations, contributing to the evidence base needed to develop targeted, equity-focused strategies to improve medication management and reduce the burden of polypharmacy among adults with cardiometabolic conditions.

References

Agbabiaka, T. B., Spencer, N. H., Khanom, S., & Goodman, C. (2018). Prevalence of drug–herb and drug–supplement interactions in older adults: a cross-sectional survey. British Journal of General Practice.

Akilen, R., Tsiami, A., & Robinson, N. (2014). Individuals at risk of metabolic syndrome are more likely to use a variety of dietary supplements. Advances in integrative medicine, 1(3), 131-137.

Asher, G. N., Corbett, A. H., & Hawke, R. L. (2017). Common Herbal Dietary Supplement-Drug Interactions. American family physician, 96(2), 101–107.

Aykan, D. A., & Aykan, A. C. (2019). Factors associated with the concomitant use of cardiovascular drugs and dietary herbal products: a cross-sectional study. Journal of Cardiovascular Pharmacology and Therapeutics, 24(2), 146-152.

Buzea, C. A., Dima, L., Correll, C. U., & Manu, P. (2022). Drug-drug interactions involving antipsychotics and antihypertensives. Expert Opinion on Drug Metabolism & Toxicology, 18(4), 285–298. https://doi.org/10.1080/17425255.2022.2086121

Cheung, J. T. K., Yu, R., & Woo, J. (2020). Is polypharmacy beneficial or detrimental for older adults with cardiometabolic multimorbidity? Pooled analysis of studies from Hong Kong and Europe. Family practice, 37(6), 793–800. https://doi.org/10.1093/fampra/cmaa062

Daneshmand, Mojdeh, et al. “Polypharmacy and Potentially Inappropriate Medication in Iranian People with Metabolic Syndrome: Epidemiological Aspects and Related Factors, a Multi-Level Cross-Sectional National Study.” Health Science Reports, vol. 8, no. 4, Apr. 2025, https://doi.org/10.1002/hsr2.70600. Accessed 25 Jan. 2026.

Diaconu, C. C., Cozma, M. A., Dobrică, E. C., Gheorghe, G., Jichitu, A., Ionescu, V. A., Nicolae, A. C., Drăgoi, C. M., & Găman, M. A. (2021). Polypharmacy in the Management of Arterial Hypertension-Friend or Foe?. Medicina (Kaunas, Lithuania), 57(12), 1288. https://doi.org/10.3390/medicina57121288

Gardiner, P., Filippelli, A. C., Sadikova, E., White, L. F., & Jack, B. W. (2015). Medication and dietary supplement interactions among a low-income, hospitalized patient population who take cardiac medications. Evidence-Based Complementary and Alternative Medicine, 2015(1), 429826.

Foy, M. C., Vaishnav, J., & Sperati, C. J. (2019). Drug-induced hypertension. Endocrinology and Metabolism Clinics of North America, 48(4), 859–873. https://doi.org/10.1016/j.ecl.2019.08.013

Franchini, M., Pieroni, S., Fortunato, L., Molinaro, S., & Liebman, M. (2015). Poly-pharmacy among the elderly: analyzing the co-morbidity of hypertension and diabetes. Current pharmaceutical design, 21(6), 791–805. https://doi.org/10.2174/1381612820666141024150901

Freeman, J. S., & Gross, B. (2012). Potential drug interactions associated with treatments for type 2 diabetes and its comorbidities: a clinical pharmacology review. Expert review of clinical pharmacology, 5(1), 31–42. https://doi.org/10.1586/ecp.11.64

Hua, R., Lam, C. S., Chu, N., Yang, A., Chow, E., & Cheung, Y. T. (2023). Association between dietary supplement use and mortality among US adults with diabetes: a longitudinal cohort study. Nutrition & Metabolism, 20(1), 33.

Jacques, P. F., & Rogers, G. (2021). A beneficial cardiometabolic health profile associated with dietary supplement use: A cross-sectional study. International Journal for Vitamin and Nutrition Research.

Kalafutova, S., Juraskova, B., & Vlcek, J. (2014). The impact of combinations of non-steroidal anti-inflammatory drugs and anti-hypertensive agents on blood pressure. Advances in clinical and experimental medicine : official organ Wroclaw Medical University, 23(6), 993–1000. https://doi.org/10.17219/acem/37357

Kanji, S., Seely, D., Yazdi, F., Tetzlaff, J., Singh, K., Tsertsvadze, A., ... & Ansari, M. T. (2012). Interactions of commonly used dietary supplements with cardiovascular drugs: a systematic review. Systematic Reviews, 1(1), 26.

Loo, S. C., & Chong, C. P. (2021). Exploring The Concurrent Use and Potential Interactions Between Prescription Drugs and Health Supplement Products Among Patients With Chronic Diseases. Eastern Journal of Medicine, 26(4).

Lum, M. V., Cheung, M. Y. S., Harris, D. R., & Sakakibara, B. M. (2020). A scoping review of polypharmacy interventions in patients with stroke, heart disease and diabetes. International journal of clinical pharmacy, 42(2), 378–392. https://doi.org/10.1007/s11096-020-01028-x

McStea, M., McGeechan, K., Kamaruzzaman, S. B., Rajasuriar, R., & Tan, M. P. (2016). Defining metabolic syndrome and factors associated with metabolic syndrome in a poly-pharmaceutical population. Postgraduate medicine, 128(8), 797–804. https://doi.org/10.1080/00325481.2016.1229103

Nahin, R. L., Pecha, M., Welmerink, D. B., Sink, K., DeKosky, S. T., Fitzpatrick, A. L., & Ginkgo Evaluation of Memory Study Investigators (2009). Concomitant use of prescription drugs and dietary supplements in ambulatory elderly people. Journal of the American Geriatrics Society, 57(7), 1197–1205. https://doi.org/10.1111/j.1532-5415.2009.02329.x

Rao, J. N. K., & Scott, A. J. (1984). On chi-squared tests for multiway contingency tables with cell proportions estimated from survey data. *Annals of Statistics*, 12(1), 46-60.

Sangaleti, C. T., Lentsck, M. H., Silva, D. C. D., Machado, A., Trincaus, M. R., Vieira, M. C. U., Pelazza, B. B., & Colombo, F. M. C. (2023). Polypharmacy, potentially inappropriate medications and associated factors among older adults with hypertension in primary care. Revista brasileira de enfermagem, 76Suppl 2(Suppl 2), e20220785. https://doi.org/10.1590/0034-7167-2022-0785

Santos, A. N. M. D., Nogueira, D. R. C., Gutierrez, B. A. O., Chubaci, R. Y. S., & Oliveira, C. R. B. (2020). Cardiometabolic diseases and active aging - polypharmacy in control. Revista brasileira de enfermagem, 73(2), e20180324. https://doi.org/10.1590/0034-7167-2018-0324

Seidu, B. S., Osman, H., & Seidu, S. (2023). Lifestyle or pharmacotherapy in cardio-metabolic disease prevention. Therapeutic advances in cardiovascular disease, 17, 17539447231177175. https://doi.org/10.1177/17539447231177175

Schulz, M., Trenk, D., & Laufs, U. (2023). Kardiovaskuläre Pharmakotherapie im Alter [Cardiovascular pharmacotherapy in old age]. Herz, 48(4), 325–336. https://doi.org/10.1007/s00059-023-05191-5

Vennu V. Polypharmacy Is Associated with Sociodemographic Factors and Socioeconomic Status in United States Adults. Pharmacy (Basel). 2024 Mar 12;12(2):49. doi: 10.3390/pharmacy12020049. PMID: 38525729; PMCID: PMC10961768.

Vyas, A., Kang, F., & Barbour, M. (2020). Association between polypharmacy and health-related quality of life among US adults with cardiometabolic risk factors. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation, 29(4), 977–986. https://doi.org/10.1007/s11136-019-02377-5

Zailani, I. S., Moshawih, S., Kifli, N., Abd Wahab, M. S., Lee, K. S., & Ming, L. C. (2022). Drug/Natural Products-Related Problems in Elderly. Progress in Drug Discovery & Biomedical Science, 5(1).

Zare, P., Poustchi, H., Mohammadi, Z., Mesgarpour, B., Akbari, M., Kamalipour, A., Abdipour-Mehrian, S. R., Hashemi, E. S., Ghamar-Shooshtari, A., Hosseini, S. A., Malekzadeh, R., Bazrafshan Drissi, H., Malekzadeh, F., & Molavi Vardanjani, H. (2024). Polypharmacy and medication usage patterns in hypertensive patients: Findings from the Pars Cohort Study. Research in social & administrative pharmacy: RSAP, 20(11), 1038–1046. https://doi.org/10.1016/j.sapharm.2024.07.006