

Health outcomes and costs associated with polypharmacy in Washington state, 2022

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August 27, 2024

Summary

- 16% of adults aged 65 and older experienced polypharmacy (five or more prescriptions).
 - Prevalence increases with age.
 - Prevalence higher with multiple chronic conditions.
- Polypharmacy was strongly associated with adverse drug events, hospitalization, and emergency department (ED) utilization.
- Polypharmacy was associated with \$17,733 higher annual medical cost (including pharmacy) compared to seniors without polypharmacy.
- Depression, dementia, managed care and low income (dual eligibility) all influenced the effects of polypharmacy. All but managed care were strongly associated with higher odds of polypharmacy and adverse drug events.
- Medicare Advantage as primary payer was associated with slightly lower odds of polypharmacy and lower cost and utilization, but higher risk of adverse drug events.

Background

Polypharmacy – the concurrent use of multiple medications – is a growing concern in an aging population experiencing multiple overlapping health issues (1). Seniors can struggle to manage multiple prescriptions, each on their own schedule, leading to underdosing, overdosing and lack of adherence (2) (3). Managing multiple medications can be especially difficult for people with intellectual disabilities (4) (5). Financial constraints may also lead to non-adherence for seniors struggling to afford multiple high-cost prescriptions. Non-adherence, accidental overdosing or drug interactions can lead to serious health consequences and reduced quality of life (5) (6) (7) (8) (9).

In this study, we explore factors associated with polypharmacy in Washington state using data from the Washington All-Payer Claims Database (WA-APCD) for 2022. We examine the relationship between polypharmacy and diagnosed dementia or depression – two conditions which could make it difficult to manage medication. We also consider the patients' primary sources of insurance. Dual Medicaid/Medicare eligibility is generally an indicator of limited financial means. Managed care (Medicare Advantage) was created, in part, to better coordinate care, and so might be expected to

reduce polypharmacy or mitigate its effects. We then examine the relationships of polypharmacy with adverse drug events, health care utilization and total cost.

Study population

The study population consisted of 952,375 WA-APCD members aged 65 and older with continuous pharmacy coverage during 2022 and continuous medical coverage during 2021 and 2022. Continuous pharmacy coverage in 2022 was required to assess polypharmacy; continuous medical coverage in 2022 was required to assess associated health outcomes. Continuous medical coverage in 2021 was required to assess pre-existing chronic conditions. Demographic breakdown of the study population is given in Table 1. At the start of 2022, 47% of the study population had Medicare Advantage as their primary insurance, 42% had Medicare fee-for-service and 9% had private commercial insurance. 13% of the study population had dual Medicare/Medicaid coverage at some point during 2022.

Methods

We operationally defined polypharmacy as five or more distinct prescriptions during 2022. National Drug Codes (NDC) were grouped by product so that generic and name brand equivalents were considered the same drug, and changes in dosage or packaging were not treated as distinct prescriptions. While not universal, a five-or-more-prescription cutoff is common in the literature (6) (5).

We used logistic regression to assess the association of polypharmacy as a dependent variable with diagnosis of dementia, diagnosis of depression, Medicare Advantage as primary medical insurance and dual Medicare/Medicaid coverage as independent variables (four separate analyses).

We used logistic regression to assess the association between polypharmacy as an independent variable with adverse drug events, inpatient admission and emergency department visits (three separate dependent variables) during 2022. For each dependent variable, we examined interactions between polypharmacy and dementia, depression, Medicare Advantage and with dual coverage (four separate analyses for each dependent variable).

Adverse drug events were defined following Hohl et al. 2013 (10). The authors used full chart review to classify diagnosis codes according to their likelihood of being an adverse drug event. We chose a conservative approach, including only diagnoses with the descriptions “induced by medication/drug,” “induced by medication or other cause,” “poisoning by medication/drug,” or “poisoning by medication or other cause.” The authors found that this code set had low sensitivity (6.8%) but high specificity (98%) in identifying adverse drug events. More inclusive code sets captured a few more events, but also picked up far more false positives.

We used simple linear regression to assess the association between polypharmacy as independent variable and total medical cost and total pharmacy cost for 2022 as dependent variables. We examined interactions between polypharmacy and diagnosis of dementia, diagnosis of depression, Medicare Advantage as primary medical insurance and with dual Medicare/Medicaid coverage in their association with medical and pharmacy cost.

All models controlled for age (three categories: 65–74, 75–84, 85+); sex; and number of preexisting conditions (among diabetes, cancer, hypertension or ischemic heart disease). Chronic conditions were defined according to the Center for Medicare and Medicaid Services (CMS) Chronic Conditions Warehouse (CCW). Because of strong collinearity between age, sex, and chronic conditions, we used a principal component decomposition to control for these variables.

Results

Polypharmacy

Overall, 16.7% of the study population were identified with polypharmacy. Polypharmacy prevalence was higher among women (18.0%) than men (14.9%). Polypharmacy prevalence increased with age, up to 21.6% for age 85 and older. Polypharmacy prevalence increased with the number of chronic conditions up to 52.4% for members with all four conditions. (Figure 1)

Polypharmacy was strongly positively associated with dual coverage (Odds ratio 2.8), diagnosis of depression (Odds ratio 2.3) and diagnosis of dementia (Odds ratio 1.8). Polypharmacy was inversely associated with Medicare Advantage as primary payer (Odds ratio 0.9). All associations were statistically significant with $p < .001$. (Figure 2)

Associated Health Conditions

Seniors with polypharmacy had 2.9 times higher odds of an adverse drug event, 2.5 times higher odds of having an ED visit, and 3.0 times higher odds of a hospital admission at some point during the year compared to seniors without polypharmacy (Figure 3). All associations were statistically significant with $p < .001$.

Because of strong associations between polypharmacy and the factors listed above, we also examined interactions between polypharmacy and dementia, depression, Medicare Advantage, and with dual coverage. In all but one case (polypharmacy x Medicare Advantage with adverse drug events) the interaction was statistically significant with $p < .001$. When significant interactions exist, the effect of one factor must be considered in the context of the other.

Figure 4 shows the association with adverse drug effects of polypharmacy interacting with (a) dementia, (b) depression, (c) dual coverage, and (d) Medicare Advantage. For example, in Figure 4a, we see that the odds ratio of adverse drug events in seniors with polypharmacy alone, without dementia, was 1.6 – less than the overall ratio of 2.9. The odds ratio for seniors with dementia but not polypharmacy was 2.9, and the odds ratio for seniors with both polypharmacy and dementia was 3.7. If there were no interaction, the odds ratios for each condition would be independent, and the odds ratio for the combined effect would be the product $1.6 \times 2.9 = 4.6$. So, some of the association between polypharmacy and adverse drug events reflects the association with dementia, and vice versa. Figures 4, 5, and 6 can be interpreted similarly. Note: in figure 4d, the interaction was not significant ($p=.234$), so the odds ratios operate independently.

Cost

Polypharmacy was associated with an additional \$10,733 total annual medical costs and \$7,003 total annual pharmacy cost, including insurance paid and out-of-pocket cost, compared to members without polypharmacy. When other factors are considered, we again find significant interactions between polypharmacy and dementia, depression, dual coverage, and Medicare Advantage. Figure 7 shows the association between polypharmacy and cost, taking these other factors into account.

Conclusions

Our results show that a large fraction (16%) of seniors in Washington are managing five or more prescriptions. The fraction is even higher among older and sicker segments of the population. Seniors with polypharmacy, in turn, had higher odds of also experiencing adverse drug events, hospitalization, or emergency department visits, and had higher medical and pharmacy costs.

Seniors with dementia or depression – conditions which we hypothesized would make it much more difficult to manage medications – had around twice the odds of experiencing polypharmacy. These conditions, interacting with polypharmacy, were also associated with elevated risk of adverse drug events, hospitalization, and emergency department utilization, and higher cost.

Seniors with dual Medicaid/Medicare eligibility – in most cases an indicator of low financial means – had nearly three times higher odds of experiencing polypharmacy. Dual eligibility, interacting with polypharmacy, was associated with higher risk of adverse drug events and higher hospital and emergency department utilization, as well as higher cost despite Medicaid's lower reimbursement.

The results for Medicare Advantage did support the hypothesized mitigating effects of managed care on utilization and cost, but not on adverse drug events. Medicare Advantage patients had 10% lower odds of polypharmacy. In interactions with polypharmacy, Medicare Advantage was associated with lower hospital and emergency department utilization and lower cost. However, Medicare Advantage was associated with 80% higher odds of adverse drug events, independent of whether polypharmacy was involved. This was the only result where there was no significant interaction with polypharmacy. Further research is required to determine why reduction in utilization and cost is not accompanied by improved health in this case.

It must be noted that in a cross-sectional study such as this, no causal relationships can be inferred. While it is plausible that poorly managed polypharmacy can lead to adverse drug events, we cannot conclude that from the data. Similarly, all we can say is that Medicare Advantage was *associated* with lower cost. It could be that some unmeasured aspect of the Medicare Advantage population made their care less expensive, having nothing to do with managed care itself.

Polypharmacy is a complex issue with no simple solution that will apply in all cases. Deprescribing interventions may reduce the number of prescriptions, but evidence on unintended adverse outcomes is limited (11). Seniors managing multiple chronic health issues may genuinely require a complex regimen of multiple medications. Many seniors who might benefit from reduced prescriptions resist deprescribing efforts entirely, while others would be amenable with better communication and patient involvement

(12). A close relationship with a trusted primary care provider is clearly needed to coordinate prescriptions across multiple specialists and manage potential adverse events.

Strengths and limitations

WA-APCD does not receive claims from the Veteran's Administration or most self-insured plans. While most members had Medicare as primary insurance, some commercial secondary coverage may be under-represented.

Medical claims are primarily intended for billing purposes, not medical evaluation or public health surveillance. Diagnosis codes that do not affect billing may not show up on claims. Attempts to identify health conditions and treatments based on claims alone can be difficult. While we can count the number of prescriptions, it could be ill-advised to try to assess the appropriateness of prescriptions for individual patients. Similarly, the low sensitivity of Hohl et al. (10) index for adverse drug events reflects the limitations of claims data compared with comprehensive chart review.

While our analyses controlled for age and sex, and a limited number of pre-existing conditions, there are many other possible confounding factors we may have failed to consider.

Table 1: Study population demographics

	Member count	Percent
Total	952,375	100
Female	536,952	56.4
Male	415,418	43.6
Age 65–74	570,586	59.9
Age 75–84	289,340	30.4
Age 85+	92,061	9.7
Three or more chronic conditions	181,427	19.0
Primary medical coverage at start of year		
Commercial	94,204	9.9
Medicaid fee-for-service	1,972	0.2
Medicaid managed care	3,572	0.4
Medicare Advantage	448,767	47.1
Medicare fee-for-service	403,534	42.4
Medicare supplemental	326	0.0
Dual coverage at some time in the year		
No dual coverage	827,391	86.9
Dual coverage	124,984	13.1

Figure 1: Prevalence of polypharmacy in the study population by age, sex, and number of chronic conditions

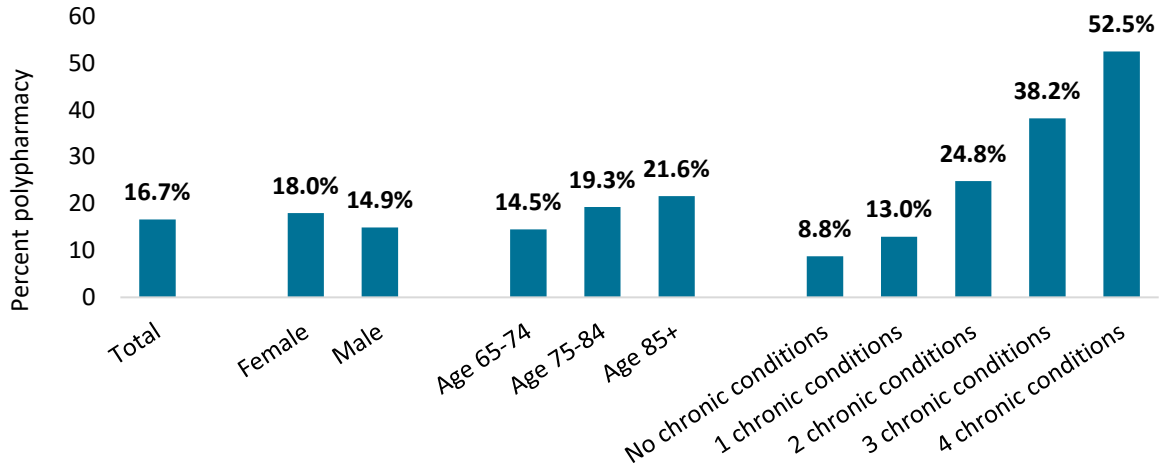


Figure 2: Odds ratios of polypharmacy, controlling for age, sex, and chronic conditions

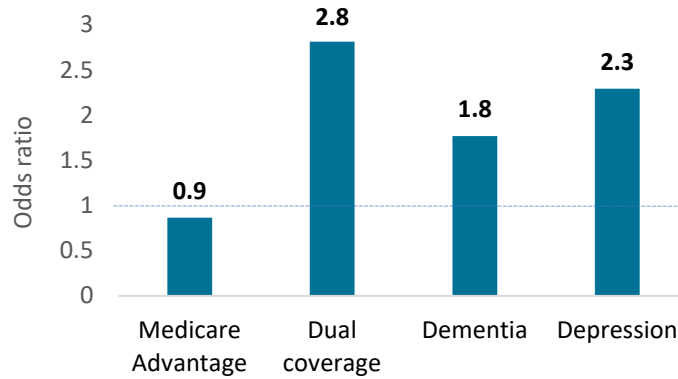


Figure 3: Odds ratios of associated health outcomes for members with polypharmacy, controlling for age, sex, and number of chronic conditions

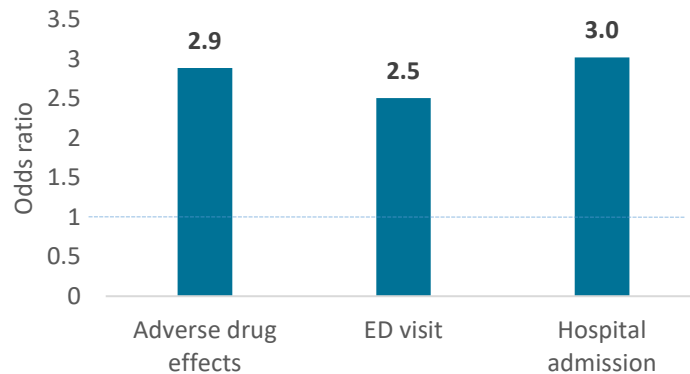
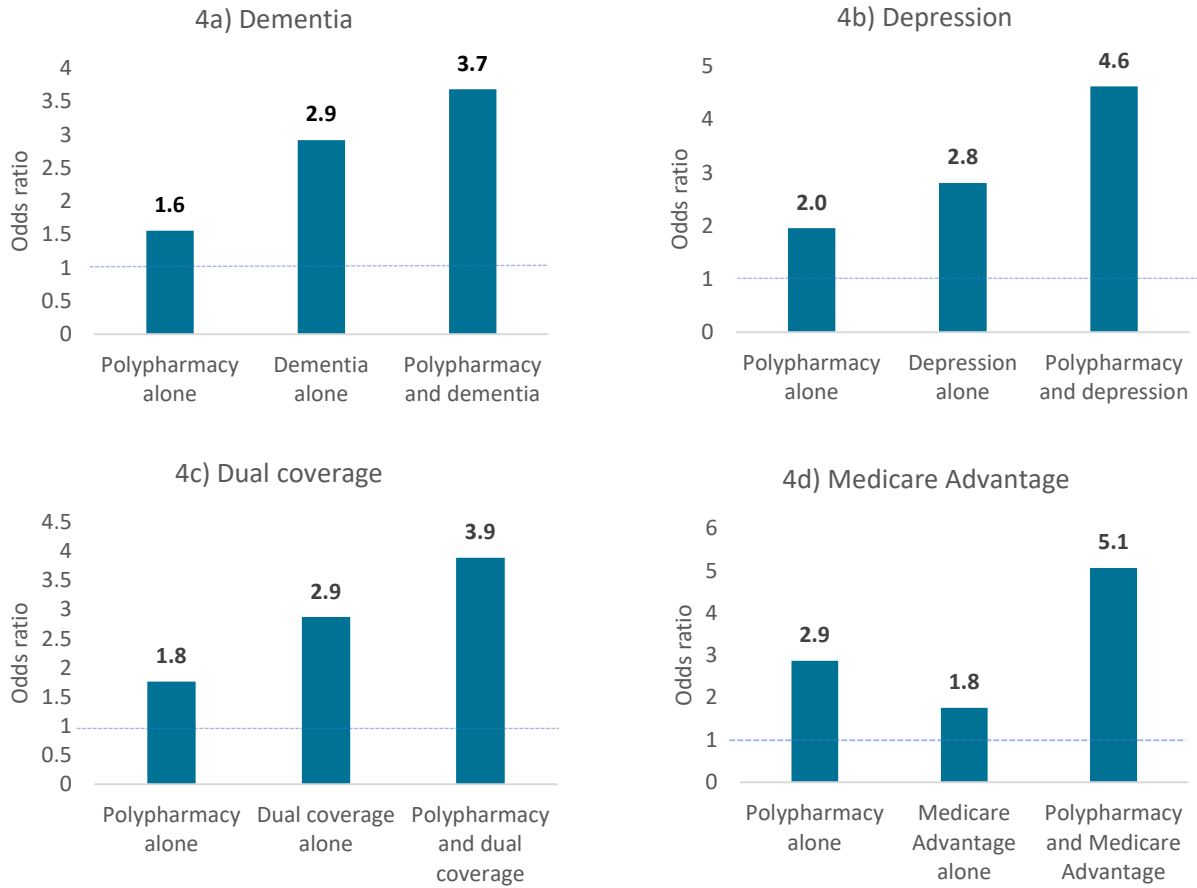


Figure 4: Odds ratio of adverse drug events by interaction of polypharmacy with a) dementia, b) depression, c) dual coverage, and d) Medicare Advantage coverage, controlling for age, sex, and chronic conditions



**Figure 5: Odds ratio of ED visit by interaction of polypharmacy with
a) dementia, b) depression, c) dual coverage, d) Medicare Advantage coverage,
controlling for age, sex, and chronic conditions**

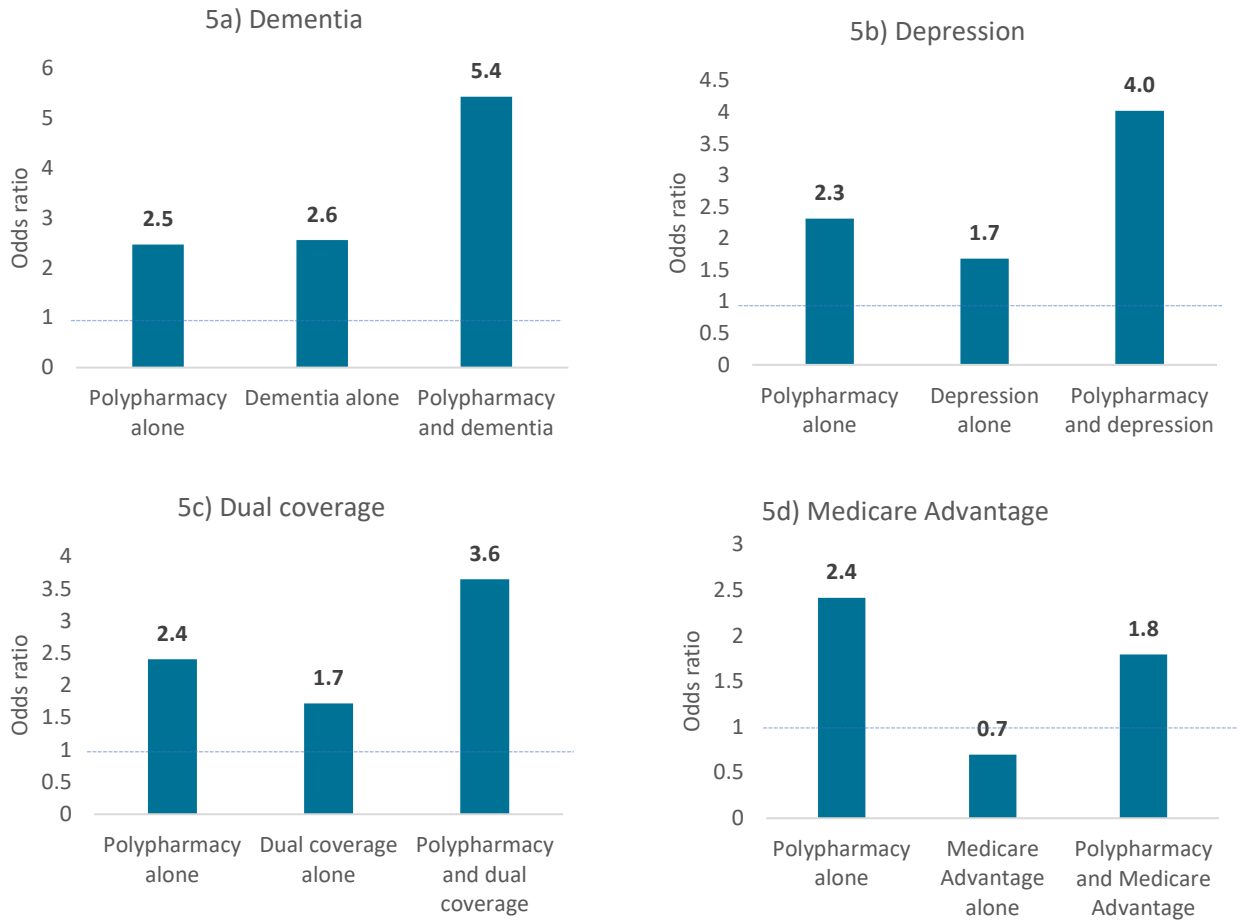


Figure 6: Odds ratio of inpatient hospital stay by interaction of polypharmacy with a) dementia, b) depression, c) dual coverage, and d) Medicare Advantage coverage, controlling for age, sex, and chronic conditions

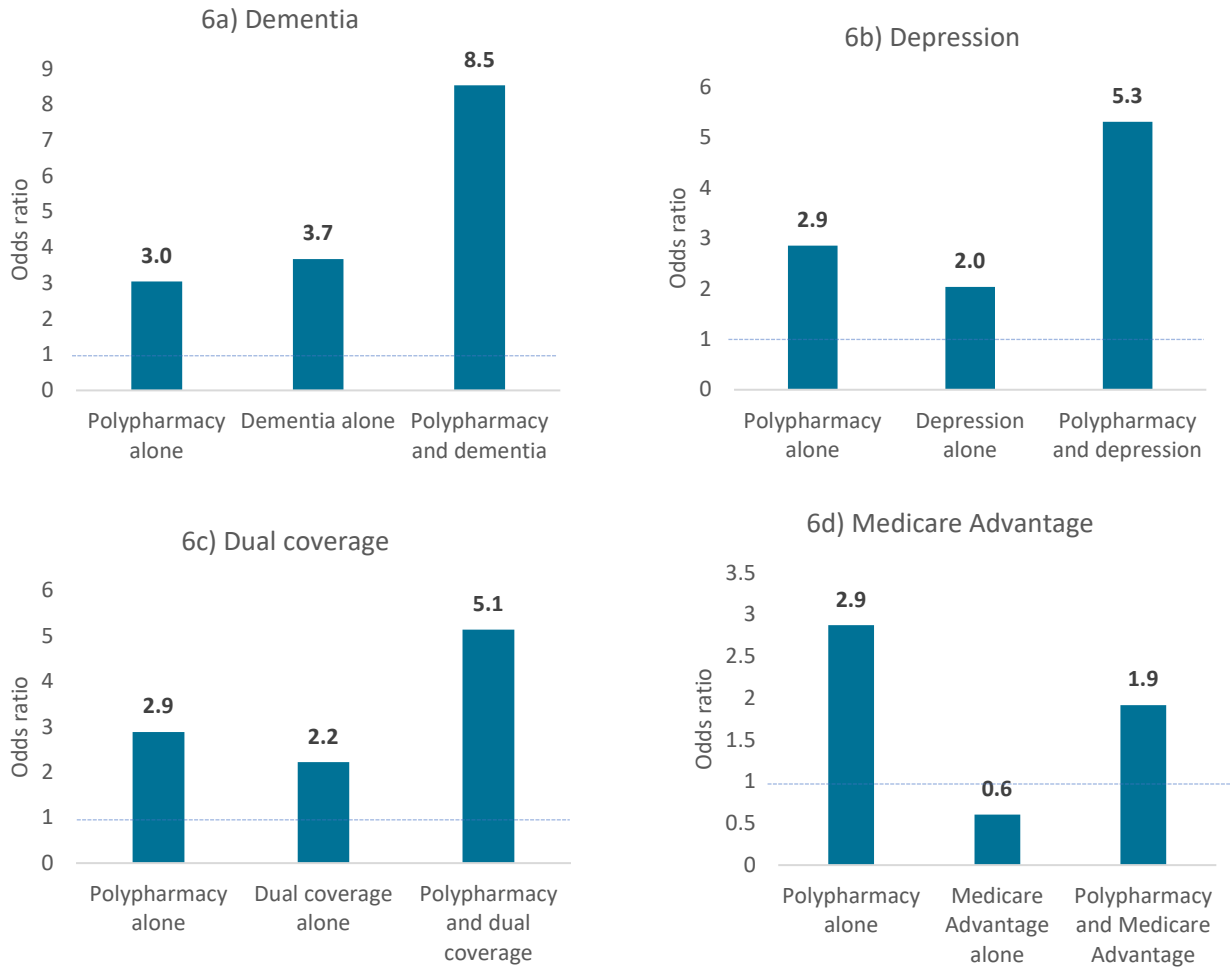
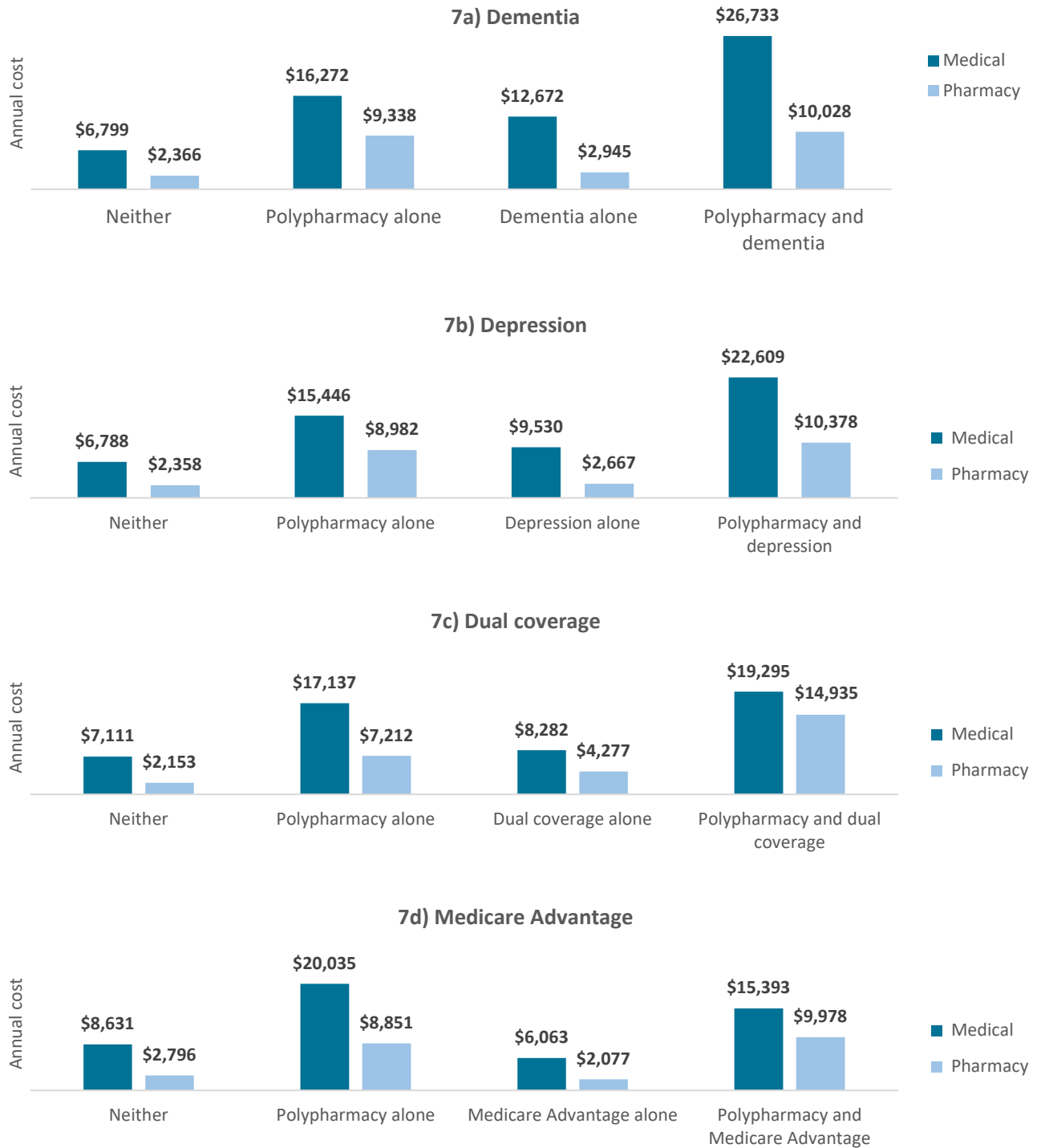


Figure 7: Annual medical and pharmacy cost by interaction of polypharmacy with a) dementia, b) depression, c) dual coverage, and d) Medicare Advantage coverage, controlling for age, sex, and chronic conditions



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Appendix: Statistical models

- **Model 1: Logistic regression with polypharmacy as outcome**
 - Polypharmacy = <dementia> + PC1 + PC2 + PC3
 - Repeat for <depression>, <dual>, <Medicare Advantage>
 - 4 combinations

- **Model 2: Logistic regression with health outcomes and polypharmacy as predictor**
 - <adverse effect> = polypharmacy+ PC1 + PC2 + PC3
 - Repeat for <ED visit>, <IP stay>
 - 3 combinations

- **Model 3: Logistic regression with health outcomes including interactions**
 - <adverse effect> = polypharmacy + {dementia} + polypharmX{dementia} + PC1 + PC2 + PC3
 - Repeat for <ED visit>, <IP stay>
 - Repeat for {depression}, {dual}, {Medicare Advantage}
 - 12 combinations

- **Model 4: Linear regression with cost as outcome, including interactions.**
 - <Annual medical cost> = polypharm + {dementia} + polypharmX{dementia} + PC1 + PC2 + PC3
 - Repeat for <annual Rx cost>
 - Repeat for {depression}, {dual}, {Medicare Advantage}
 - 8 combinations