Poster: EPH241

Benzodiazepines and Adrenergic beta2-Agonists: A Synergistic Impact on Health-Related Quality of Life Among Older Adults with Prostate Cancer

Zongliang Yue, PhD[1]*, Xiangzhong Xue, MS[1], and Jingjing Qian, PhD[1]*
[1] Health Outcomes Research and Policy, Harrison College of Pharmacy, Auburn University, AL, USA
Contact: jzq0004@auburn.edu

INTRODUCTION

Prostate cancer is a significant health burden worldwide.

- **One of the most common cancers among men (1/9 men)**
- **Prostate cancer survivors often face the challenge of managing multiple chronic conditions alongside their cancer diagnosis**
- **A higher number of comorbidities is a significant predictor for onset of cancer treatment-related side effects and shorter overall survival**

Polypharmacy is common among older adults with prostate cancer and multiple chronic conditions

- **Polypharmacy are associated with higher mortality in patients diagnosed with cancer compared with patients without multimorbidity and polypharmacy**
- **Polypharmacy leads to potential drug-drug interactions, adverse effects, medication non-adherence, and increased healthcare costs**
- **The association between polypharmacy and HRQoL among older adults with prostate cancer remains unclear**

Contribution:

- **Examined the association between polypharmacy and HRQoL among older adults with prostate cancer**
- **Identified drug class-class pairs on HRQoL and provided insights for future interventions and strategies to improve HRQoL in this population.**

MATERIALS & METHODS

Data Source and Study Design

A retrospective analysis using the 1998-2017 linked Surveillance, Epidemiology, and End Results (SEER) and Medicare Health Outcomes Survey (MHOS) data

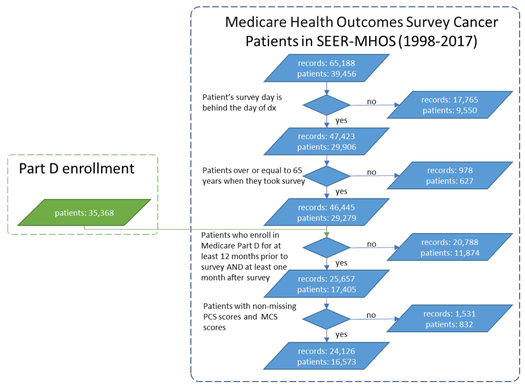

Figure 1. Study sample selection flow chart. SEER-MHOS: Surveillance, Epidemiology, and End Results-Medicare Health Outcomes Survey; dx: diagnosis; PCS: physical component summary T score; MCS: mental component summary T score.

Health-related Quality of Life (HRQoL)

The Veterans RAND 12-Item Health Survey (VR-12) included physical and mental functions. T-score transformation results mean of 50 and a standard deviation (SD) of 10. 3-point (0.3 of a SD) represents a minimally important difference.

Statistical Analysis

Chi-square test was performed to compare each two groups and reported the corresponding p-values. Generalized estimating equations (GEE) were performed to assess the association between polypharmacy and HRQoL.

Drug Class-Class Prioritization

To identify the most relevant drug class-class pairs in terms of HRQoL, as opposed to prevalence, we employed unadjusted odds ratios (OR) with 95% CI for prioritization.

To identify the cohort with severely impaired HRQoL and determine the foreground drug class frequency, we performed z-score normalization for both the PCS and MCS scores and utilized a cutoff of -0.83 z-scores for both the PCS and MCS scores.

We identified the foreground consisting of 1,493 (9% of all) patients with a total of 1,683 (7% of all) survey records. This cohort was compared to the background consisting of 16,092 patients with 23,214 survey records (excluding records with missing values in variables, apart from the MCS and PCS scores, which include the number of unique Part D prescriptions, age, BMI, education, and the count of comorbidities.

Consequently, we utilized unadjusted OR to quantify the association between severely impaired HRQoL's patient records and drug-drug pairs. For each drug class-class pair in the foreground, we calculated its OR using the formula $OR_i = \frac{m_i(N-n_i)}{n_i(M-m_i)}$, where m_i represents the count of surveys with the specific class-class pair in the foreground with the index of i. n_i represents the count of surveys with the specific class-class pair in the background with the index of i, M represents the total number of survey records (1,683 from 1,493 individuals) in the foreground, and N represents the total number of survey records (23,214 from 16,092 individuals) in the background.

RESULTS

I. Sample Characteristics and Associations between Polypharmacy and HRQoL

The polypharmacy was prevalent (about 54%) among Medicare MAO beneficiaries with prostate cancer. Polypharmacy was significantly associated with declined HRQoL (measured with physical and mental functions), especially for beneficiaries with EPP.

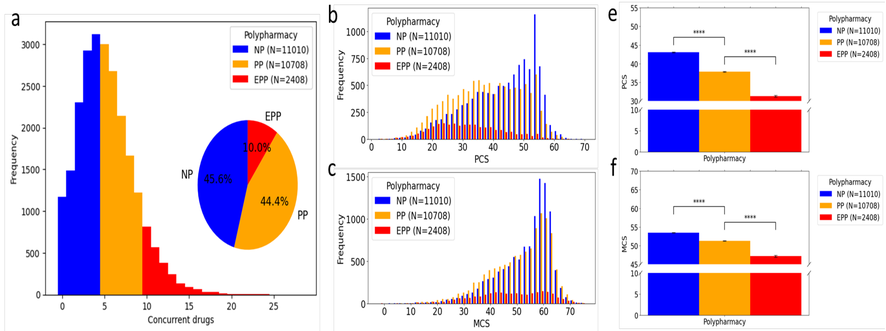

Figure 2. The distribution of concurrent drugs within patient survey records and its potential impact on their health-related quality of life, measured by PCS and MCS scores. (a) The concurrent drug distribution and pie plot of the composition of NP, PP, and EPP in survey records, (b) The comparison of PCS score distribution among the three polypharmacy categories, and (c) The comparison of MCS score distribution among the three polypharmacy categories. The histograms of (a) the physical component summary T score (PCS) and (b) the mental component summary T score (MCS) in the three polypharmacy categories. Each bar on the histogram represents the standard error. Mean PCS score exhibited a decreasing trend across the polypharmacy categories: NP (43.1, 95% CI: 42.9-43.3), PP (37.9, 95% CI: 37.6-38.1), and EPP (31.3, 95% CI: 30.9-31.7). Similarly, mean MCS scores exhibited a decreasing trend across the polypharmacy categories: NP (53.5, 95% CI: 53.3-53.7), PP (51.3, 95% CI: 51.1-51.5), and EPP (47.2, 95% CI: 46.7-47.7). **** indicates the t-test p-value < 0.0001.

The beneficiaries with PP and EPP were more likely to be older, obese or extremely obese, racial/ethnic minorities, residing in South, not married, having lower levels of income and education, smoking, surgery or radiation therapy free, and having more comorbidities than those without polypharmacy (all p<0.001)

Polypharmacy was significantly associated with physical and mental functions based on both unadjusted and adjusted results

Table 1 Unadjusted and adjusted results of the associations between polypharmacy and HRQoL

Polypharmacy	PCS Score MD with 95% CI		MCS Score MD with 95% CI	
	Unadjusted	Adjusted*	Unadjusted	Adjusted*
NP	reference	reference	reference	reference
PP	-4.43 (-4.75, -4.12)	-3.76 (-4.07, -3.44)	-2.05 (-2.34, -1.75)	-1.59 (-1.88, -1.29)
EPP	-9.94 (-10.47, -9.41)	-8.47 (-9.00, -7.94)	-5.57 (-6.15, -4.98)	-4.32 (-4.89, -3.75)

* A multivariate generalized estimating equation (GEE) model, controlling for covariates.
Abbreviations: PCS: Physical Component Summary; MCS: Mental Component Summary; NP: no polypharmacy; PP: polypharmacy; EPP: excessive polypharmacy; CI: Confidence interval; MD: Marginal difference

II. Drug Class-Class Pairs in Patients with Severely Impaired HRQoL

The severely impaired HRQoL patient's survey records exhibited a higher proportion of EPP (25.8%) than those of non-severely impaired patient's EPP (8.6%), and furosemide, omeprazole, and potassium chloride exhibited a relatively high concurrent usage in the severely impaired HRQoL patient's survey records

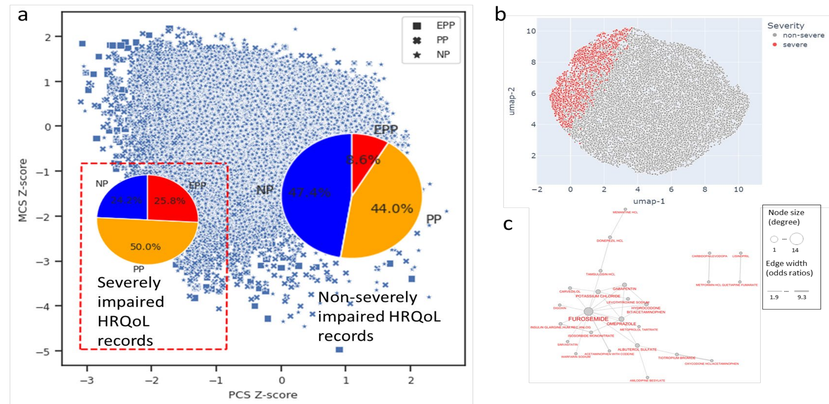

Figure 3. Selection of severely impaired health-related quality of life (HRQoL) survey records. (a) Distribution of z-scores for PCS and MCS, along with a comparison of pie charts between severely impaired HRQoL records and non-severely impaired HRQoL records. The cutoff was set at -0.83 of the z-scores for PCS and MCS, with severely impaired HRQoL records highlighted in the red dashed frame. (b) Uniform Manifold Approximation and Projection for Dimension Reduction (UMAP) plot of severely impaired HRQoL records. To project the survey records into a two-dimensional space, we applied UMAP*. The input of UMAP embedding comprised continuous variables, including weighted (×6) PCS and MCS z-scores, number of concurrent drugs, age, BMI, education, income, and count of comorbidities. (c) Network of drug-drug pairs prioritized by odds ratio in severely impaired HRQoL records. *: McInnes, L.; Healy, J., UMAP: Uniform Manifold Approximation and Projection for Dimension Reduction. ArXiv 2018, abs/1802.03426.

Benzodiazepines and adrenergic beta2-agonists pair were the most impactful drug class pairs associated with HRQoL decline (unadjusted odds ratio=5.1 with 95% CI (1.6, 16.3)).

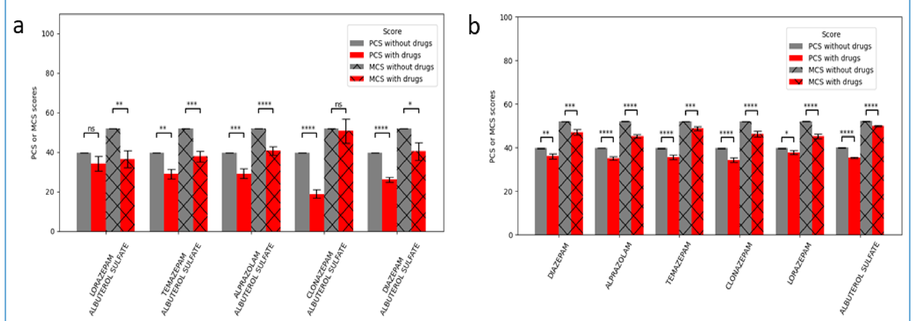

Figure 4. The changes in PCS score and MCS score in relation to the presence or absence of the most influential class-to-class pairs (a, b) benzodiazepines and adrenergic beta2-agonists, on patients' HRQoL. (a) The PCS score and MCS score in the presence or absence of drug-drug pairs, and (b) The PCS score and MCS score in the presence or absence of each single drug. ** indicates the t-test p-value < 0.05. *** indicates the t-test p-value < 0.001. **** indicates the t-test p-value < 0.0001. PCS: physical component summary T score; MCS: mental component summary T score.

ACKNOWLEGMENT

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CONCLUSIONS

- Polypharmacy was significantly associated with declined HRQoL (measured with physical and mental functions), especially for beneficiaries with EPP.
- Beneficiaries with PP and EPP were more likely to be older, obese or extremely obese, racial/ethnic minorities, residing in South, not married, having lower levels of income and education, smoking, surgery or radiation therapy free, and having more comorbidities than those without polypharmacy.
- The most impactful drug class pairs associated with HRQoL among this population was benzodiazepines and adrenergic beta2-agonists.

DISCUSSION

- Closely monitoring concurrent medication use and avoiding inappropriate polypharmacy (e.g., excessive or unnecessary medication use) are critical to ensure older adults' functional stability, reduce adverse events and financial burdens, and improve HRQoL and survival.
- Benzodiazepines have been advised against use among older adults due to high risks of serious adverse effects (i.e., dependence, cognitive deficits, falls, fractures, and mortality) by several major medical and psychiatric organizations.
- Predictive machine learning models to be developed aiming at identifying the specific cohort of patients with drug usage patterns that require close attention.