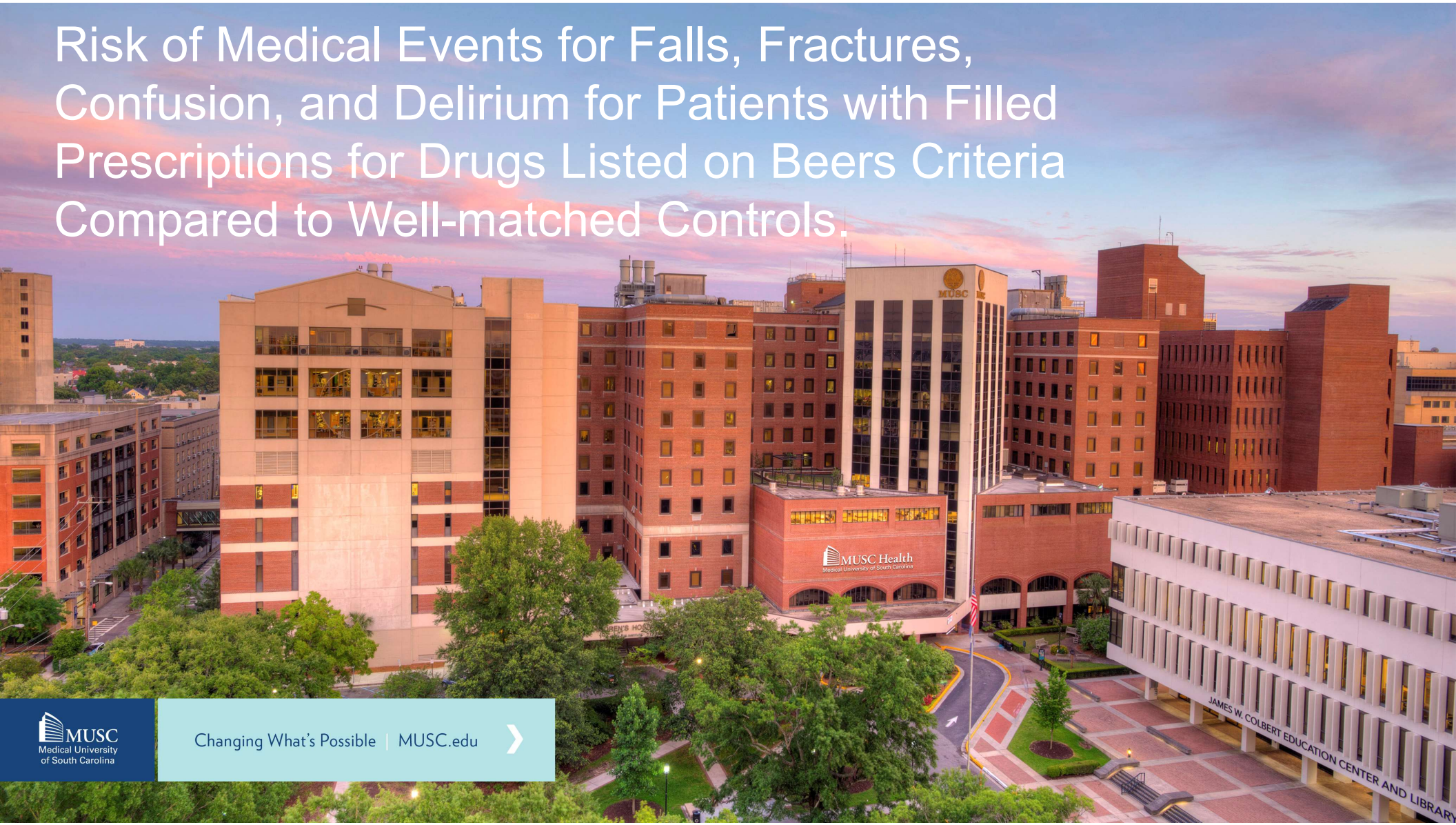
# Risk of Medical Events for Falls, Fractures, Confusion, and Delirium for Patients with Filled Prescriptions for Drugs Listed on Beers Criteria Compared to Well-matched Controls.

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# Doctoral Project Defense

## Doctorate of Health Administration

## College of Health Professions

# Background and Need

# Background and Need

- The population of the United States is aging with the life-expectancy of elderly individuals also increasing
- Thus, Medicare must serve:
  - More patients with chronic conditions who require medication management, and
  - More frail patients needing multiple medications for comorbid conditions.
- Studies have found that 60% of elderly patients take 5 or more medications, while 20% of elderly patients take 10 or more medications
  - Elderly patients taking 10 or more medications are at a 6x increase of experiencing a fall
- Many medications routinely used in younger patients are not safe for the elderly
- The Beers Criteria contains more than 27 drug classes which are NOT recommended for use in older patients

# Background and Need

- Studies exist confirming a relationship between the use of Beers Criteria medications and risk of falls, fractures, confusion, and delirium with unplanned hospitalizations in elderly populations
- Cognitive impairment, multimorbidity, and medication related balance and gait problems are just a few of the common medication side effects
- Commonly used medication may place patients at risk for fall or delirium events:
  - Benzodiazepines leading to falls and fractures, and
  - Diphenhydramine leading to confusion and delirium
- Falls are one of the leading causes of injuries, fractures, and unplanned hospitalizations in the elderly linked to prescription medication use
  - Aside from physical effects, there are a number of psychological effects on the patient that also occur with falls
  - Because of the large number of medications which can cause balance and gait problems, medication management is the most manageable risk intervention

# Literature Review

# Literature Review, Falls and Fractures in the Elderly

Weiner et al. 1998:

- Elderly patients using CNS-active medications were at a higher risk of fall from those not

Neutel et al. 2002:

- Elderly patients taking multiple drugs were at a higher risk of experiencing an injurious fall
- Patients starting a new benzodiazepine or antipsychotic prescription were at a *very high* risk of injurious fall

Tinetti et al. 2006:

- Healthcare expenditures for a single fall event, $24,330
- Overall healthcare burden caused by falls in patients ≥65 years old, $5.7 billion

Hammond and Wilson, 2013

- Polypharmacy has been independently linked to falls in elderly individuals

# Literature Review, Falls and Fractures in the Elderly

Gelbard et al. 2014:

- 72.5% of elderly patients that experienced an injurious fall had at least one comorbidity
- Non-ground level falls are typically cause more injury and lead to a longer length of stay

Ambrose et al. 2015:

- Falls account for 87% of fractures in the elderly associated with impaired balance and gait, polypharmacy, and a prior history of falls

Chiu et al. 2015:

- Patients with an anxiety diagnosis were 4.7 times more likely to experience a fall than those without

Allali et al. 2017:

- GOOD Initiative: "**G**ait, c**O**gniti**O**n, and **D**ecline"

# Literature Review, Benzodiazepine Use in the Elderly

## Ray et al. 2000

- Greatest risk of falls in the elderly occur within the first seven days of a new benzodiazepine prescription (OR = 2.96) but remain elevated after

## Bogunovic and Greenfield, 2004

- Benzodiazepines usage in the elderly may contribute to psychomotor impairment increasing the risk of falls and automobile accidents for elderly that may still operate motor vehicles

## Kragh et al., 2011

- Fall-Risk Increasing Drugs

## Puustinen et al., 2011

- BZD usage in the elderly was found to be associated with dizziness, a reduced ability to walk, and shorter nighttime sleep

# Literature Review, Confusion and Delirium

Morrison et al., 2003:

- A study of 541 hip fracture patients found those who received opioid analgesics post-surgery were at a 2.4 higher risk of developing delirium than with other analgesic medications

Puustinen et al., 2011

- Use of opioids and the concurrent use of opioid and benzodiazepine medications were all associated with cognitive decline in the elderly population

Hein et al., 2014

- 25% of community-dwelling elderly individuals developed delirium on hospitalization, polypharmacy increased this risk by 2.3x

Kalisch Ellett et al., 2016

- Opioids are overused and used inappropriately in the elderly population – risk of delirium related hospitalizations in community-dwelling elderly was 2.4x greater with the use of 2 or more CNS-acting medications

# Literature Review, Confusion and Delirium

## Swart et al. 2017:

- Research in the area of opioids and delirium in the elderly is limited and should be further investigated
- This research should include a comparative investigation between the different types of opioids and their effect on delirium in the elderly

## Motter et al. 2018

- Anticholinergic drugs appear on 16/22 potentially inappropriate medication lists

## Mueller et al. 2018:

- Cognitively-impaired elderly individuals using more than 4 medications had an increased risk of unplanned emergency department visits

# Problem Statement

- However, studies have not compared well-matched groups of patients who were exposed and not exposed to drugs affecting balance and cognition with the risk of admissions for falls, fractures, confusion, or delirium, while still controlling for other Beers Criteria medications, frailty, and comorbid conditions.

# Research Questions

Two research areas we will examine specifically are:

1. Admissions for falls and/or fractures in patients taking medications on the Beers Criteria which are not recommended because of their effect on balance and gait, and
2. Admissions for confusion and/or delirium in patients taking medications on the Beers Criteria which not recommended because of their effect because on cognition and a person's ability to live independently.

# Methodology

# Study Design and Sample

- This is a retrospective cohort study using propensity-score matched patients in an exposed and non-exposed group
- The Beers classification and propensity-score matching was performed by Roland (2018), as follows:
  - Data was selected and extracted from the 2013 Truven Marketscan® Administrative Claims database
  - Individuals were required to be ≥65 years old and living independently,
  - PIM use was identified by the presence of a medication listed on the 2012 revision of the AGS Beers Criteria, and
  - For inclusion in the “experimental” arm of the study, patients were required to have been prescribed a PIM in the timeframe of 1/1/2013 to 3/31/2013

# Dataset

- This study uses an augmented version of the dataset from Roland (2018)
- Data augmentations performed for the purposes of our study:
  - Data extraction for hospital admissions and ED visits for falls and delirium, and
  - Creation of drug sub-group specifications for:
    - Medication classes associated with falls,
    - Medication classes associated with delirium and confusion, and
    - A residual group named “other Beers drugs”
- The final dataset contained 2,595,254 patients;
  - Patients who took any Beers Criteria medications in Q1 2013 (n = 1,297,627), and
  - Patients taking no Beers Criteria medications in Q1 2013 (n = 1,297,627)

# Definition of Variables

The dataset matching and control variables includes:

- Patient demographics (age, gender, geographic region, # insured days/year),
- Charlson Comorbidity indicators,
- 26 of 29 Elixhauser Comorbidity indicators,
- Frailty measure indicators, score, and categories,
- Beers Criteria medication classes (# of Rxs and Rx days), and
- Hospital admission information (# of admissions, length of stay, total cost, inpatient cost, outpatient cost, and Rx cost)

# Beers Criteria Categories

Falls and fractures:

- Antipsychotics,
- Barbiturates,
- Benzodiazepines,
- Sedatives,
- Tricyclic antidepressants, and
- [Other Beers, No Beers]

Delirium and confusion:

- Antihistamines,
- Antipsychotics,
- Benzodiazepines,
- Narcotics, and
- [Other Beers, No Beers]

# Inclusion Conditions

## Falls and Fractures:

- Accidental falls involving:
  - Stairs or steps (E880)
  - Ladders or scaffolding (E881)
  - From/out of a building/structure (E882)
  - Holes or other surface openings (E883)
  - One structure level to another (E884)
  - Slipping, tripping, or stumbling (E885)
  - Collision, pushing, or shoving, by or with another person (E886)
  - Fracture, unspecified (E887)
  - Other fall, unspecified (E888)

## Delirium:

- Admissions involving:
  - Drug-induced delirium (292.81)
  - Delirium, other known cause (293.0)
  - Subacute delirium (293.1)
  - Reactive confusion (298.2)
  - Psychosis, unspecified (298.9)
  - Hallucinations (780.1)
  - Altered mental status (780.97)

# Analysis

Statistical analysis compared the presence of any Beers Criteria medication (categorical by medication class) and the absence of any Beers medications

Descriptive statistics:

- Pearson Chi-square tests will be used for the comparison of categorical variables
- T-tests were used for the comparison of normally distributed continuous variables and Mann-Whitney U/Wilcoxon nonparametric tests for non-normally distributed continuous variables

Multivariable modeling using logistic regression was used to compare the risks of falls and fractures, and delirium and confusion admissions

The total expenditure cost was compared using a gamma-distributed, log-linked multivariable model to accommodate the distribution of the total cost data

# Results

# Our Patient Sample

| | Patients without Beers Medications | Patients with Beers Medications |
|---|---|---|
| Age, years | 74.06 ± 6.9 | 73.93 ± 6.8 |
| Female | 750,416 (57.8%) | 757,171 (58.3%) |
| Charlson Score | 0.07 ± 0.5 | 0.09 ± 0.6 |
| Frailty Score | 0.353 ± 2.2 | 0.451 ± 2.4 |
| Length of Stay, days | 6.11 ± 9.4 | 6.63 ± 9.8 |
| Delirium Admissions | 25,727 (2.0%) | 43,117 (3.3%) |
| Falls Admissions | 26,255 (2.0%) | 32,725 (2.5%) |
| Total Treatment Costs | $ 8,580 ± 30,962 | $ 14,987 ± 36,033 |

Data expressed as mean ± standard deviation (SD) or otherwise indicated as Number (%). All differences significant at α = 0.05.
n = 2,595,254

# Characteristics of Falls and Fractures Patients

| | Patients without Falls Admissions | Patients with Falls Admissions |
|---|---|---|
| Age, years | 73.91 ± 6.8 | 77.52 ± 7.1 |
| Female | 1,468,759 (57.9%) | 38,838 (65.8%) |
| Charlson Score | 0.08 ± 0.6 | 0.19 ± 0.8 |
| Frailty Score | 0.37 ± 2.3 | 1.78 ± 3.5 |
| Length of Stay, days | 6.32 ± 9.6 | 7.84 ± 10.7 |
| Fall Drug Days | 0.86 ± 21.7 | 2.82 ± 37.7 |
| Taking Any Beers ℞ | 1,264,902 (49.9%) | 32,725 (55.5%) |
| Total Treatment Costs | $ 11,424 ± 33,350 | $ 27,244 ± 45,144 |

Data expressed as mean ± standard deviation (SD) or otherwise indicated as Number (%). All differences significant at α = 0.05.
n = 2,595,254

# Characteristics of Delirium Patients

| | Patients without Delirium Admissions | Patients with Delirium Admissions |
|---|---|---|
| Age, years | 73.87 ± 6.8 | 78.34 ± 6.9 |
| Female | 1,468,454 (58.1%) | 39,133 (56.8%) |
| Charlson Score | 0.08 ± 0.5 | 0.34 ± 1.1 |
| Frailty Score | 0.33 ± 2.2 | 2.91 ± 4.3 |
| Length of Stay, days | 5.86 ± 8.5 | 9.86 ± 14.4 |
| Delirium Drug Days | 39.6 ± 84.80 | 71.82 ± 107.36 |
| Taking Any Beers ℞ | 1,254,510 (49.7%) | 43.117 (62.2%) |
| Total Treatment Costs | $ 10,868 ± 31,546 | $ 45,380 ± 72,459 |

Data expressed as mean ± standard deviation (SD) or otherwise indicated as Number (%). All differences significant at α = 0.05.
n = 2,595,254

# Results: Falls and Fractures

| | Patients with No Fall Admissions (n = 2,536,274) | Patients with Fall Admissions (n = 58,980) |
|---|---|---|
| Antipsychotics | 58,753 (2.3%) | 4,008 (6.8%) |
| Barbiturates | 9,878 (0.4%) | 231 (0.4%) |
| Benzodiazepines | 354,080 (14.0%) | 10,598 (18.0%) |
| Sedatives | 94,429 (3.6%) | 2,040 (3.5%) |
| Tricyclic antidepressants | 33,999 (1.3%) | 898 (1.5%) |
| Other Beers Medications | 715,763 (28.2%) | 14,950 (25.4%) |
| No Beers Medications | 1,271,372 (50.1%) | 26,255 (44.5%) |

# Results: Delirium and Confusion

| | Patients with No Delirium admissions (n = 2,536,274) | Patients with Delirium Admissions (n = 58,980) |
|---|---|---|
| Antihistamines | 45,907 (1.8%) | 1,231 (1.8%) |
| Antipsychotics | 52,187 (2.1%) | 10,574 (15.4%) |
| Benzodiazepines | 351,640 (14.0%) | 13,038 (19.0%) |
| Narcotics | 1,514 (0.1%) | 27 (0.04%) |
| Other Beers Medications | 803,262 (31.8%) | 18,247 (26.5%) |
| No Beers Medications | 1,271,900 (50.5%) | 25,727 (37.8%) |

# Regression Results: Falls and Fractures

| Beers Category | Odds Ratio | 95% CI | *p*-value |
|---|---|---|---|
| Antipsychotics | 1.935 | [1.865, 2.007] | <.0001 |
| Benzodiazepines | 1.372 | [1.341, 1.405] | <.0001 |
| Barbiturates | 1.290 | [1.13, 1.472] | 0.953 |
| Sedatives | 1.184 | [1.13, 1.239] | 0.0002 |
| Tricyclic Antidepressants | 1.333 | [1.245, 1.427] | 0.2426 |
| Other Beers Medication | 1.073 | [1.051, 1.095] | <.0001 |

Model c-statistic: 0.725
All Beers Criteria categories values are in comparison to the No Beers group.

# Regression Results: Delirium

| Beers Category | Odds Ratio | 95% CI | *p*-value |
|---|---|---|---|
| Antipsychotics | 5.122 | [4.985, 5.263] | <.0001 |
| Benzodiazepines | 1.801 | [1.762, 1.841] | 0.005 |
| Antihistamines | 1.416 | [1.335, 1.503] | 0.003 |
| Narcotics | 1.05 | [1.065, 1.544] | 0.0103 |
| Other Beers Medications | 1.221 | [1.197, 1.245] | <.0001 |

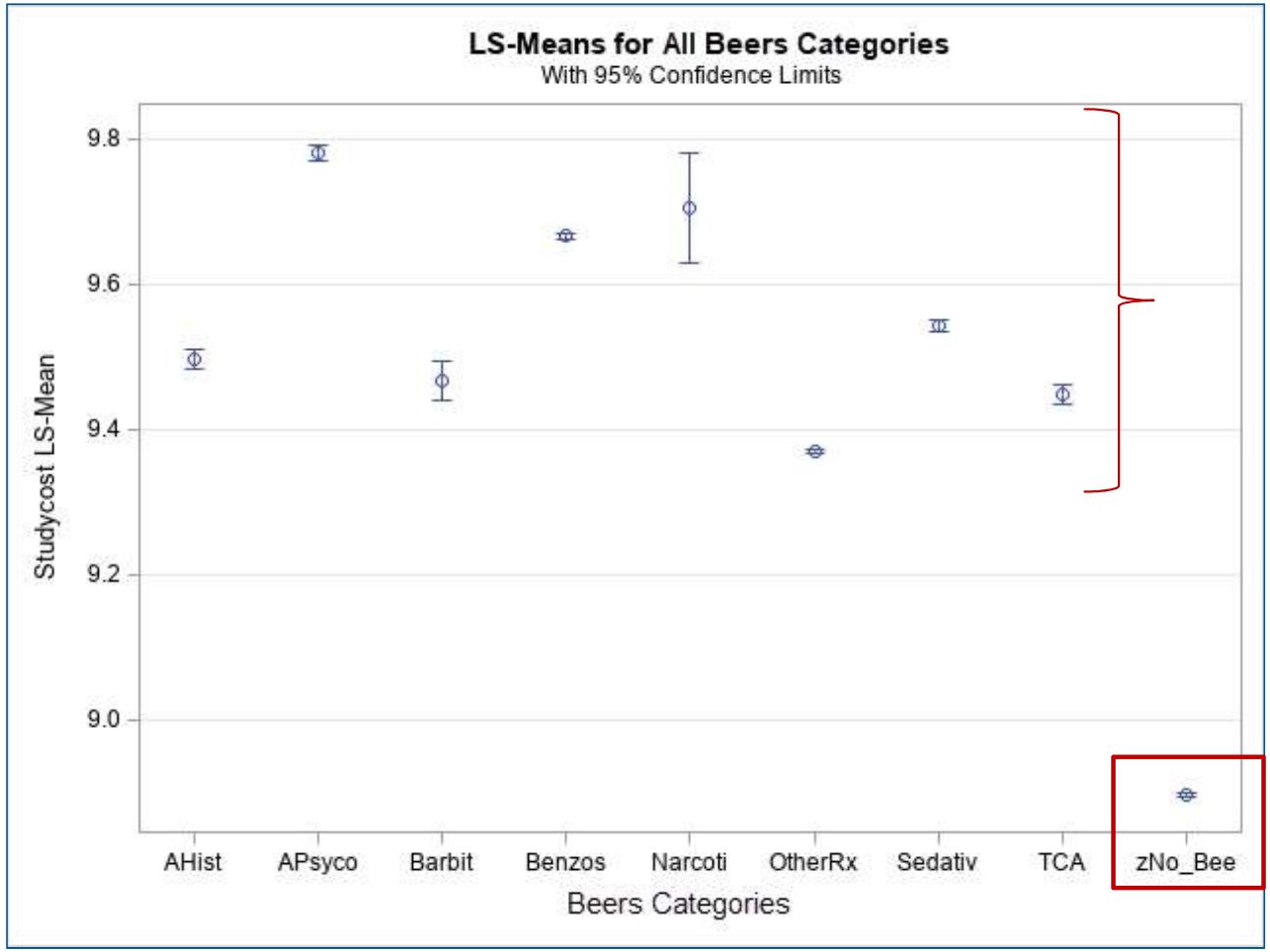
Model c-statistic: 0.80

All Beers Criteria categories values are in comparison to the No Beers group.

# Regression Results: Total Study Costs

| Beers Criteria Class | Exponentiated ($e^{\beta}$) | 95% CI |
|---|---|---|
| Antihistamines | 13,308 | [13132, 13487] |
| Antipsychotics | 17,692 | [17500, 17886] |
| Barbituates | 12,926 | [12584, 13276] |
| Benzodiazepines | 15,782 | [15712, 15853] |
| Narcotics | 16,393 | [15201, 17679] |
| Sedatives | 13,957 | [13836, 14080] |
| Tricyclic Antidepressants | 12,690 | [12508, 12874] |
| Other Beers Medications | 11,726 | [11688, 11765] |
| No Beers Medications[a] | 7,311 | [7293, 7328] |

[a] Reference group
All comparisons to the reference group were significant at $p < .0001$


LS-Means for All Beers Categories
With 95% Confidence Limits
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Beers Categories

# Discussion

# Discussion: Falls and Fractures

Patients who experienced falls and fractures compared with those who did not:

- Average age 77.52 vs. 73.91 years
- Charlson Score 0.19 vs. 0.08
- Length of stay 7.84 vs. 6.32 days

Most frequent Beers Criteria classes involved:

- Benzodiazepines (n=10,598) and
- Antipsychotics (n=4,008)

Increased risk of a falls/fracture admission:

- Antipsychotics are associated 1.9x [1.865, 2.007]
- Benzodiazepines are associated 1.4x [1.341, 1.405]
- TCA's are associated 1.3x [1.245, 1.427]

# Discussion: Confusion and Delirium

Patients who experienced confusion and delirium compared with those who did not:

- Average age 78.34 vs. 73.87 years
- Charlson Score 0.34 vs. 0.08
- Length of stay 9.86 vs. 5.86 days

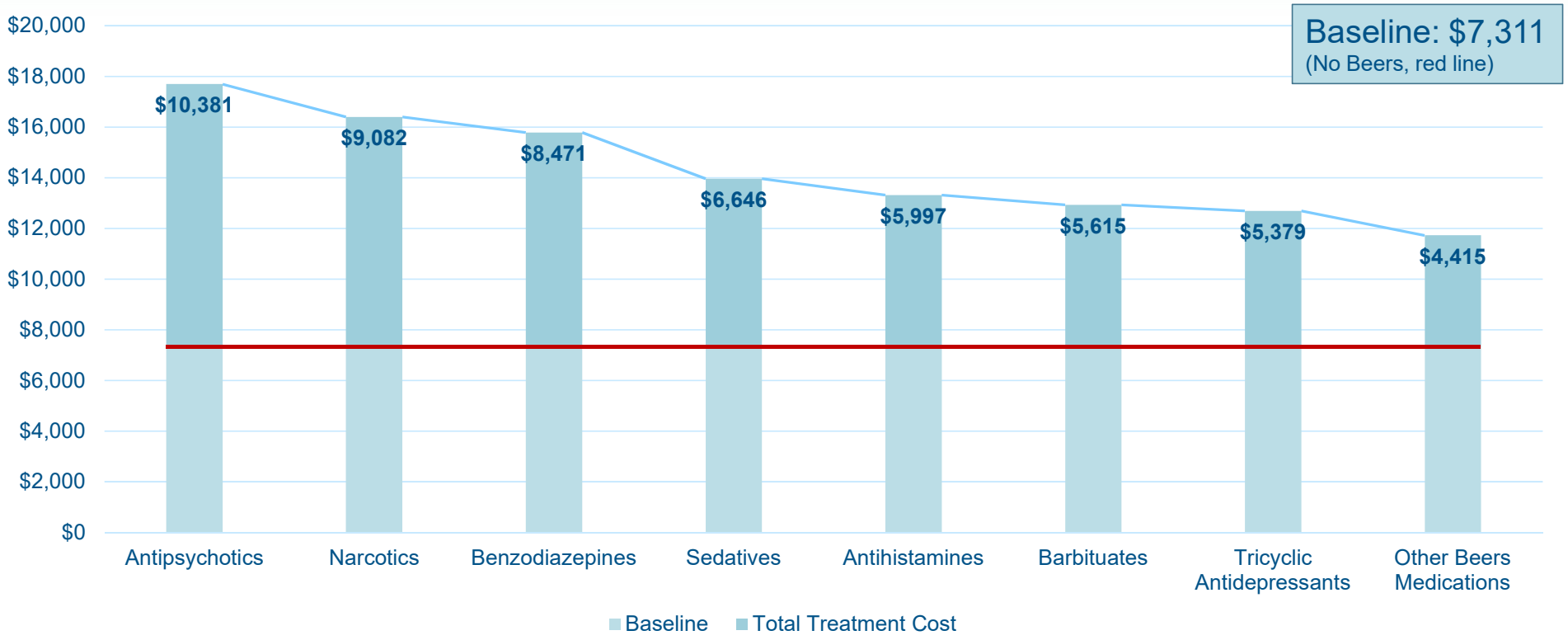
Most frequent Beers Criteria classes involved:

- Benzodiazepines (n=13,038) and
- Antipsychotics (n=10,574)

Increased risk of a falls/fracture admission:

- Antipsychotics are associated 5.1x [4.985, 5.263]
- Benzodiazepines are associated 1.8x [1.762, 1.841]
- Antihistamines are associated 1.4x [1.338, 1.503]

# Effect of Beers Medication Class on Treatment Cost



# Overall Findings

Patients in both groups were older, had a longer length of stay, and a higher Charlson Score

Antipsychotics and benzodiazepines most frequently prescribed to patients who experienced a fall/fracture or delirium/confusion admission

Risk of admission:

- Antipsychotics and benzodiazepines were associated with the greatest risk increase of admission both falls and fractures, and delirium and confusion

Overall treatment costs:

- Antipsychotics were associated with the highest expected cost of admission and benzodiazepines third, independent of the admission type
- Narcotics, specifically for the delirium patients, was the second highest contributor to the expected cost of admission

# Limitations

## Data from the Roldan (2018) study:

- Only included community-dwelling individuals ≥65 years old, this would exclude those who are institutionalized or in nursing homes/assisted living
- Excluded costs relating to skilled nursing, long-term, palliative, or hospice care

## Use of Truven Marketscan® Administrative Claims data:

- MarketScan is a convenience, not a randomized, sample
- Coding of billing data within the dataset, while unlikely, may be incorrect and unexpected exclusion of patients could occur
- Data is generally aggregated from larger employers providing commercially-provided health insurance

# Future Research and Study Conclusions

# Future Research

1. Examining specific medications versus an entire class
2. Examining combinations of drug classes and their effects on falls, fractures, delirium, and confusion
3. Examining risks of falls, fractures, confusion, and delirium outside of community-dwelling individuals, i.e. short-term rehab facilities, long-term care, and skilled nursing facilities

# Conclusion

Falls and fracture patients using antipsychotics are at twice the risk for hospitalization than their well-matched controls.

Delirium and confusion patients using antipsychotics are at more than a five times risk for hospitalization than their well-matched controls.

For all patients:

- Antipsychotics were associated with an increase of $10,381 over the non-Beers baseline
- Benzodiazepines were associated with an increase of $8,471 over the non-Beers baseline

Specifically for the delirium patients, narcotics were associated with an increase of $9,082 over the non-Beers baseline.

Further research and investigation into antipsychotic use in the elderly is warranted.

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