Leading Predictors and their Associations with Combination Pain Therapy in Older Adults with Cancer: Application of Machine Learning Approaches

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INTRODUCTION

- In 2017, 26.8% of older adults filled at least one opioid prescription.[1-3]
  - 1 in 3 of Medicare Part D beneficiaries
- Opioid toxicity[3,4]: 14.1 per 100,000
  - Older adults with fastest growing rates of[2-4]:
    - Misuse
    - Hospitalizations
    - Death
- Opioid prescribing rates highest in cancer patients[4-6]
  - ~80% of patients with advanced cancer report pain[7]
- Concern with combination pain therapy and narcotic prescribing in older adults with cancer
  - Primary risk factors for opioid overdose and death: concomitant opioid and benzodiazepine (BZD) use[8,9]
  - Link between sedatives (gabapentinoids) and risk of falls and death in older adults with cancer[8,9]

OBJECTIVES

- Determine the association of socioeconomic, biological, and clinical characteristics to opioid and combination therapy pain management.
- Examine the leading predictors of combination pain therapy using machine learning approaches.

METHODS

DATA SOURCES
- **SEER**: largest, national patient registry that trends and monitors incidence, survival, and burden
  - 5% Medicare cancer sample
  - Zip-level population characteristics
  - Census-tract level population characteristics\
- Medicare fee-for-service (FFS) claims
  - Inpatient/outpatient, prescription drug, home health, durable medical equipment, hospice

NIH NATIONAL CANCER INSTITUTE
Surveillance, Epidemiology, and End Results Program

STUDY DESIGN
- Retrospective cohort analysis of older (≥ 66 years old) cancer survivors

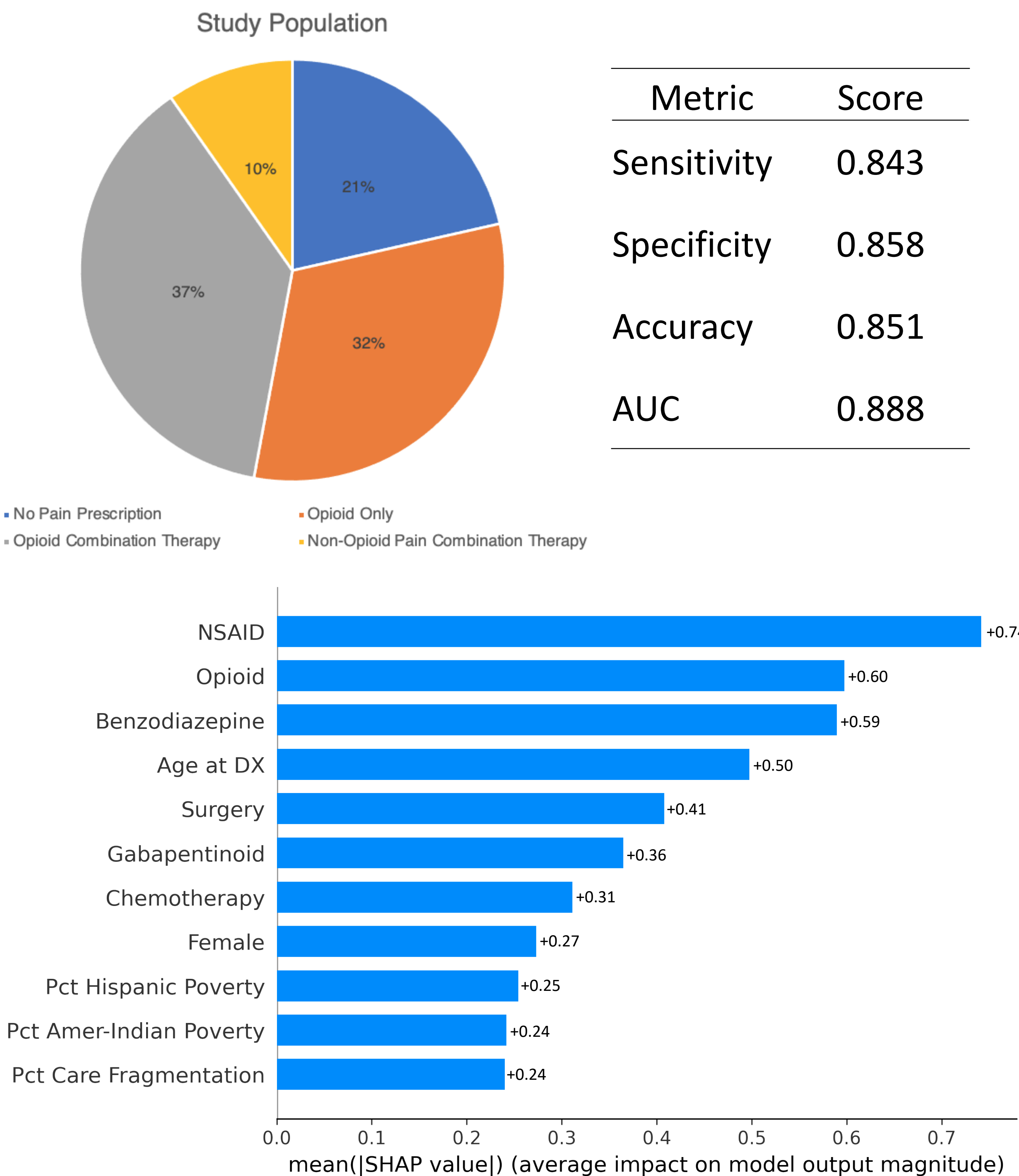| Inclusion Criteria	Exclusion Criteria
• Diagnosed with: breast, colorectal, lung, or prostate cancers • Other: cervical, melanoma, NHL, ovarian, pancreatic, thyroid, and uterine cancer • Combination pain therapy: opioid with non-steroidal anti-inflammatory drugs (NSAID), BZD, gabapentinoids, and/or skeletal muscle relaxants (SMR) • Incident primary cancer • Enrolled continuously in Medicare Part A, B, and D	• Diagnosed at autopsy • Male for female-centric cancers and vice-versa

METHODS (CTD.)

INDEPENDENT & DEPENDENT VARIABLES
- Independent variables: socioeconomic and clinical demographics, healthcare utilization, and cancer type/stage/treatment
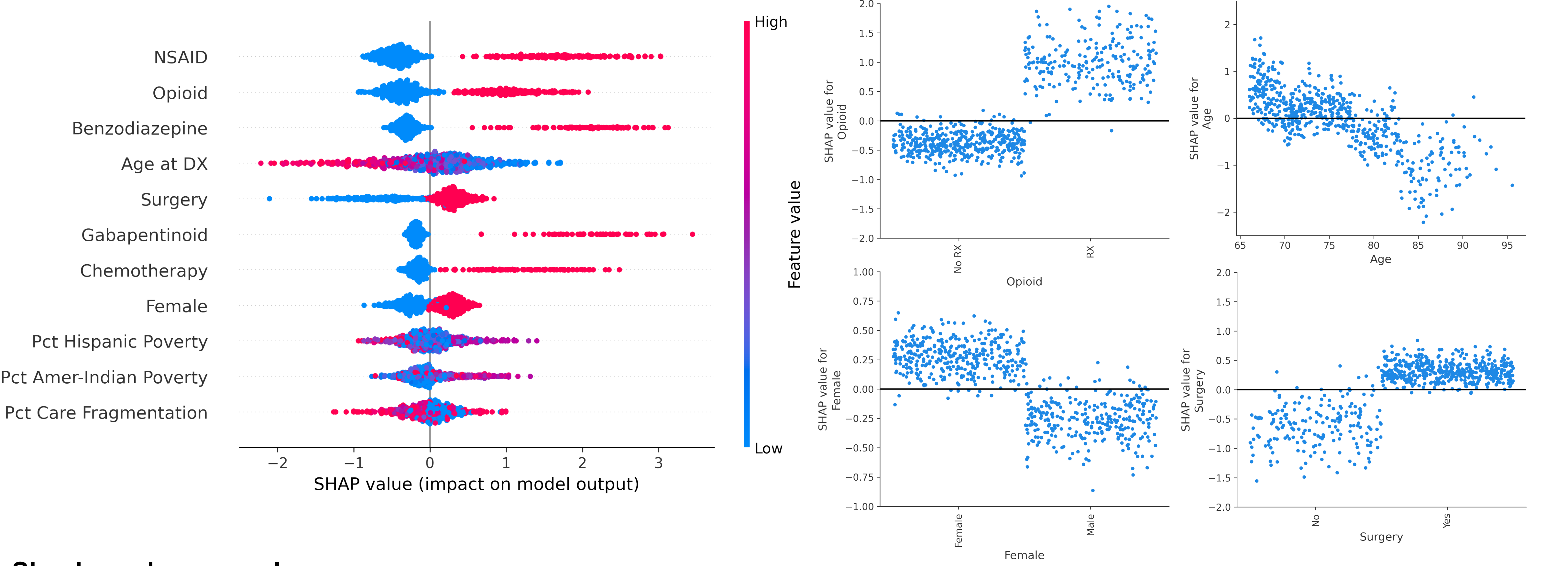- Dependent variable: combination pain therapy

ANALYSES – Machine Learning Methods
- **eXtreme Gradient Boosting (XGBoost),** a decision-tree based algorithm
- Shapley values and plots for interpretable machine learning
- Model validity: assessed with sensitivity, specificity, accuracy, and area under the curve (AUC)
- Leading predictors: identified via shapley values
- Python 3.9.7

RESULTS (N = 2,673)

Study Population

■ No Pain Prescription	■ Opioid Only
■ Opioid Combination Therapy	■ Non-Opioid Pain Combination Therapy

Metric	Score
Sensitivity	0.843
Specificity	0.858
Accuracy	0.851
AUC	0.888

mean(|SHAP value|) (average impact on model output magnitude)

- NSAID +0.74
- Opioid +0.60
- Benzodiazepine +0.59
- Age at DX +0.50
- Surgery +0.41
- Gabapentinoid +0.36
- Chemotherapy +0.31
- Female +0.27
- Pct Hispanic Poverty +0.25
- Pct Amer-Indian Poverty +0.24
- Pct Care Fragmentation +0.24

RESULTS (CTD.)

Shapley values reveal:
- Baseline pain therapy use, female sex, surgery, and chemotherapy were positively associated with opioid combination therapy.
- **Age** had a negative but **complex relationship** with opioid combination therapy.
- There were **complex interactions** between age and care fragmentation, and between types of baseline pain therapies used.
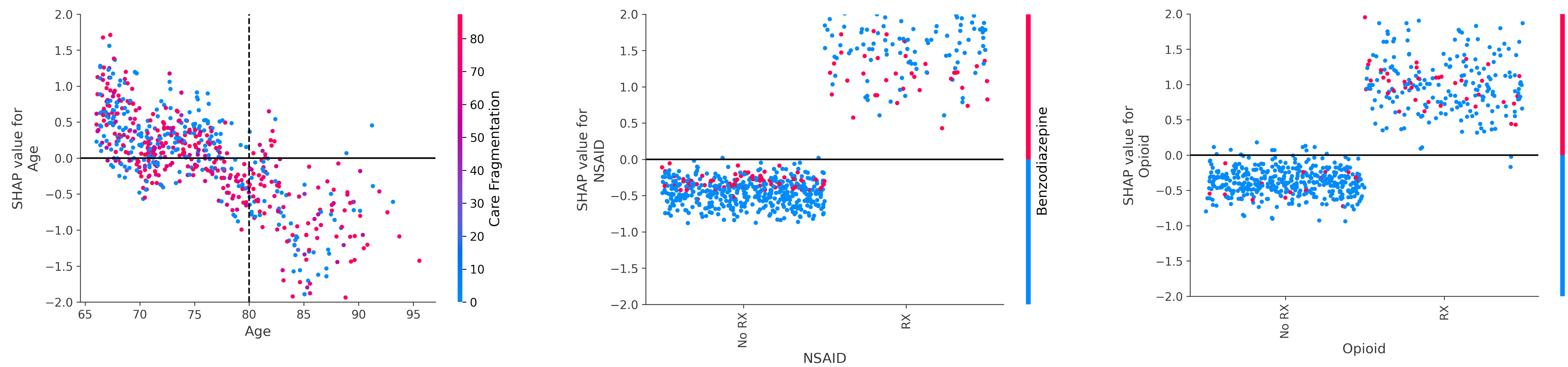
CONCLUSIONS

- Novel, interpretable machine-learning methods are valuable in conducting health services and outcomes research.
- Pain therapies before diagnosis were the leading predictors of combination therapy use after diagnosis.
- Providers need to weigh risks and benefits of prescribing opioid combination therapy to minimize use in older adults with cancer.
- Shapley values reveal that age, care fragmentation, and zip-code level percent of Hispanics and American-Indians living in poverty have complex relationships with opioid combination therapy use.
- Programs and policies that improve social determinants of health may decrease combination opioid therapy and avoid consequent morbidity and mortality.

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