

Unraveling the Multilevel Factors Influencing Transition to Radical Treatment in Medicare Beneficiaries Newly Diagnosed with Low-Risk and Favorable Intermediate-Risk Prostate Cancer Initiating Active Surveillance: A Fine-Gray and Cause-Specific Hazard Modeling Approach

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Background

- Active surveillance (AS) is guideline-recommended strategy for managing low-risk (LR) and favorable intermediate-risk (FIR) localized prostate cancer (LIPCa: cT1-cT2c, cN0, cM0, ≤Gleason pattern, 3 + 4), reducing overtreatment and complications from radical treatment (RT), including radical prostatectomy, radical radiotherapy, and systemic therapy.¹
- However, persistence under AS remained low (i.e., 23% to 39%), with high dropout rates over time, with a trend towards switching to more curative treatment.²

Objective

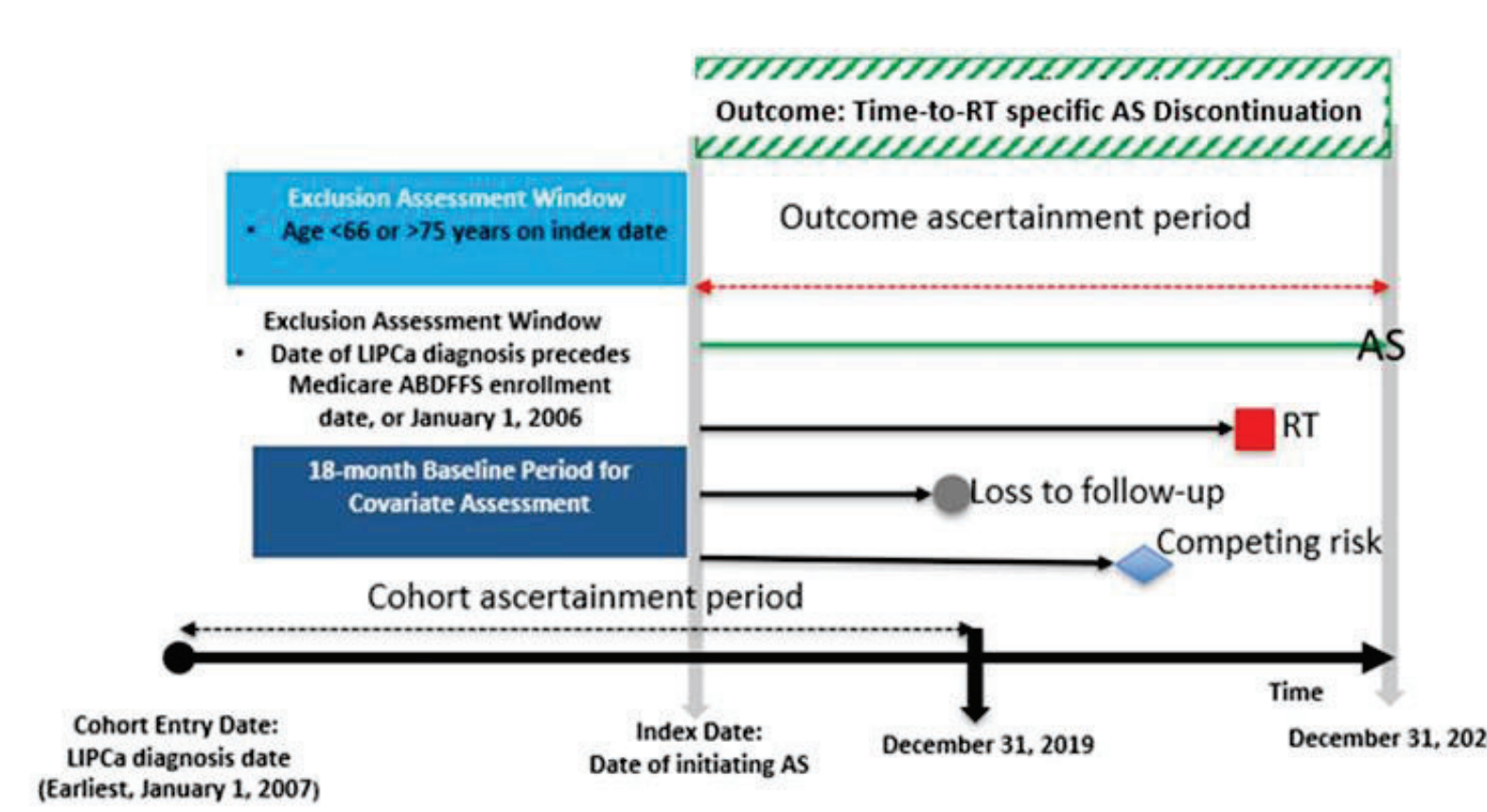
- This study quantified the association between patient-level, Census tract-level social determinants of health (SDoH), physician- and practice-level factors and the transition from AS to RT among the Medicare Fee-for-Service (FFS) beneficiaries with LIPCa.

Methods

Study Design and Population:

- Retrospective cohort study (Figure 1) using Surveillance, Epidemiology, and End Results (SEER)-Medicare data (2006-2020) linked to PolicyMap Census tract-level SDoH measures.^{3,4}
- Patients, aged 66 to 75 years, with incident LIPCa (cT1-cT2c, cN0, cM0 with Gleason scores ≤3+4) - identified using clinical tumor-node-metastasis (TNM) staging and American Urological Association (AUA) risk stratification¹ (2007-2019).
- A modified validated claims-based algorithm⁵ was used to identify AS initiation at the end of 18 months of diagnosis.
- AS initiation definition: No curative treatment within 18 months after the date of initial LIPCa diagnosis and comorbidity score < 3.
- 18 months pre-index date continuous enrollment for Medicare Part A, B, and D coverage required - for confirmatory testing, and covariate assessment. The index date was defined as the date of initiating AS.

Figure 1. Visualizing A Retrospective Cohort Design



Population: Medicare beneficiaries with newly diagnosed LIPCa aged 66 to 75 years who initiated AS within 18 months of diagnosis.
AS: Active surveillance; RT: Radical treatment; LIPCa: Low-favorable intermediate-risk prostate cancer.
Primary explanatory factors: Risk group/Age.
Other explanatory factors: other individual-level factors, Census tract-level SDoH, physician, and practice-level factors.
Index date: The date of the first day after the 18-month treatment initiation window constituted the index date for the AS cohort.

Pre-Index Date Multilevel Factors

- Patient-level:** Risk group, and age group in years, sociodemographic information; tumor-level (i.e., Clinical T stage, Gleason grade group [GG], prebiopsy PSA level); clinical (e.g., Charlson Comorbidity Index (CCI), hyperlipidemia, obesity, benign prostatic hyperplasia (BPH), alcohol use disorder, confirmatory biopsy type, year of treatment initiation).
- Census tract-level SDoH measures:** Education, household income, poverty, Yost index, homeowners cost burden, food insecurity, internet access, and public transportation access.⁶
- Physician/Practice-level:** Physician specialty and Medicare LIPCa case volume (average cumulative Medicare volume, ACMV).⁷

Statistical Analysis

- Fine-Gray subdistribution hazard model, accounting for competing risks, was fit.⁸
- Variable specification: Informed by data-driven insights, published literature, and clinical guidance.⁷
- Subdistribution hazard ratios (sdHRs; 95% confidence intervals [CIs]) reported.
- A p-value of 0.05 or less was considered statistically significant.
- Sensitivity analyses: Cause-specific hazard models, including a frailty model, and risk-stratified subgroups.
- All statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

Results

- Among 2,826 AS initiators (median follow-up: 4.2 years; 95% CI: 4.0-4.3), **34.1% transitioned to RT**, with a plurality of AS initiators transitioning to **radiation (40.6%)** and **systemic therapies (33.1%)** (Figure 2).
- Patients with **LR (vs. FIR: asdHR: 0.815; 95% CI: 0.696-0.955)** disease, those who were **unmarried** (vs. married: asdHR: 0.803; 95% CI: 0.667-0.967), or **preexisting BPH** (vs. no BPH: 0.835; 95% CI: 0.726-0.961), had a lower incidence of RT transitions (Figure 3).
- Conversely, patients with **prior AMI** (vs. no AMI: 1.823; 95% CI: 1.017-3.270) or those who initiated AS in **more recent years** ([2014-2015: 1.453; 95% CI: 1.072-1.968; 2016-2018: 1.590; 95% CI: 1.179-2.143] vs. 2007-2009), had a higher incidence of RT transitions.
- While patients with **LR disease and preexisting DM** (vs. no DM: asdHR: 0.726, 95% CI: 0.557-0.945) had lower incidence of RT transitions, those patients with **LR disease and preexisting hyperlipidemia** (vs. no hyperlipidemia: asdHR: 1.283, 95% CI: 1.059-1.553) had higher incidence of RT transitions.
- Being managed by **radiation** (vs. urologist: asdHR: 1.955; 95% CI: 1.372-2.784) and **surgical** (vs. urologist: asdHR: 2.735; CI: 1.005-7.442) oncologists increased RT transitions, while being managed at a **high-volume** (vs. low-volume: asdHR: 0.850; CI: 0.738-0.980) practice reduced the incidence of RT transitions.
- Sensitivity analyses findings were consistent with the base case results.

Figure 2. Radical Treatment Transitions Among Patients with LIPCa who initiated AS, Overall and by Treatments, 2007-2020

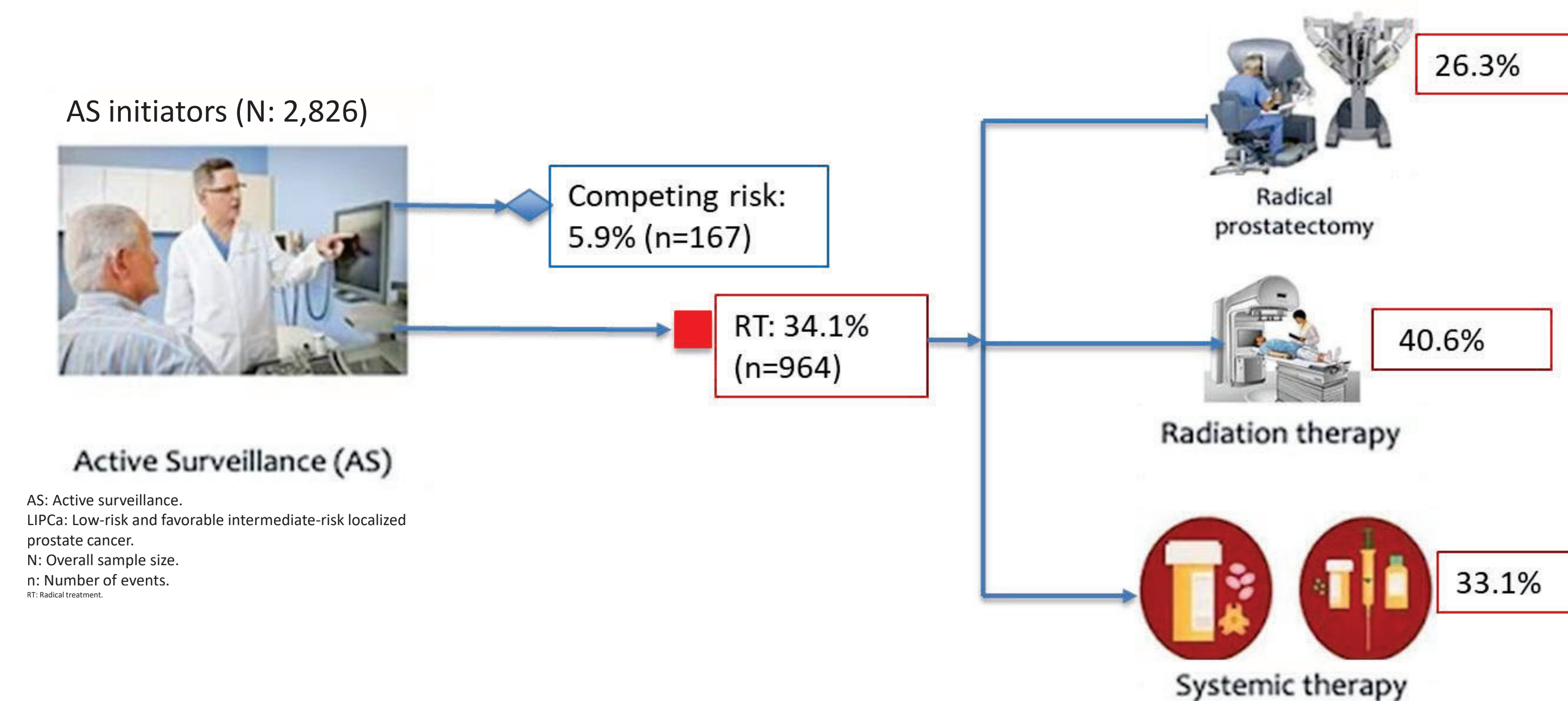
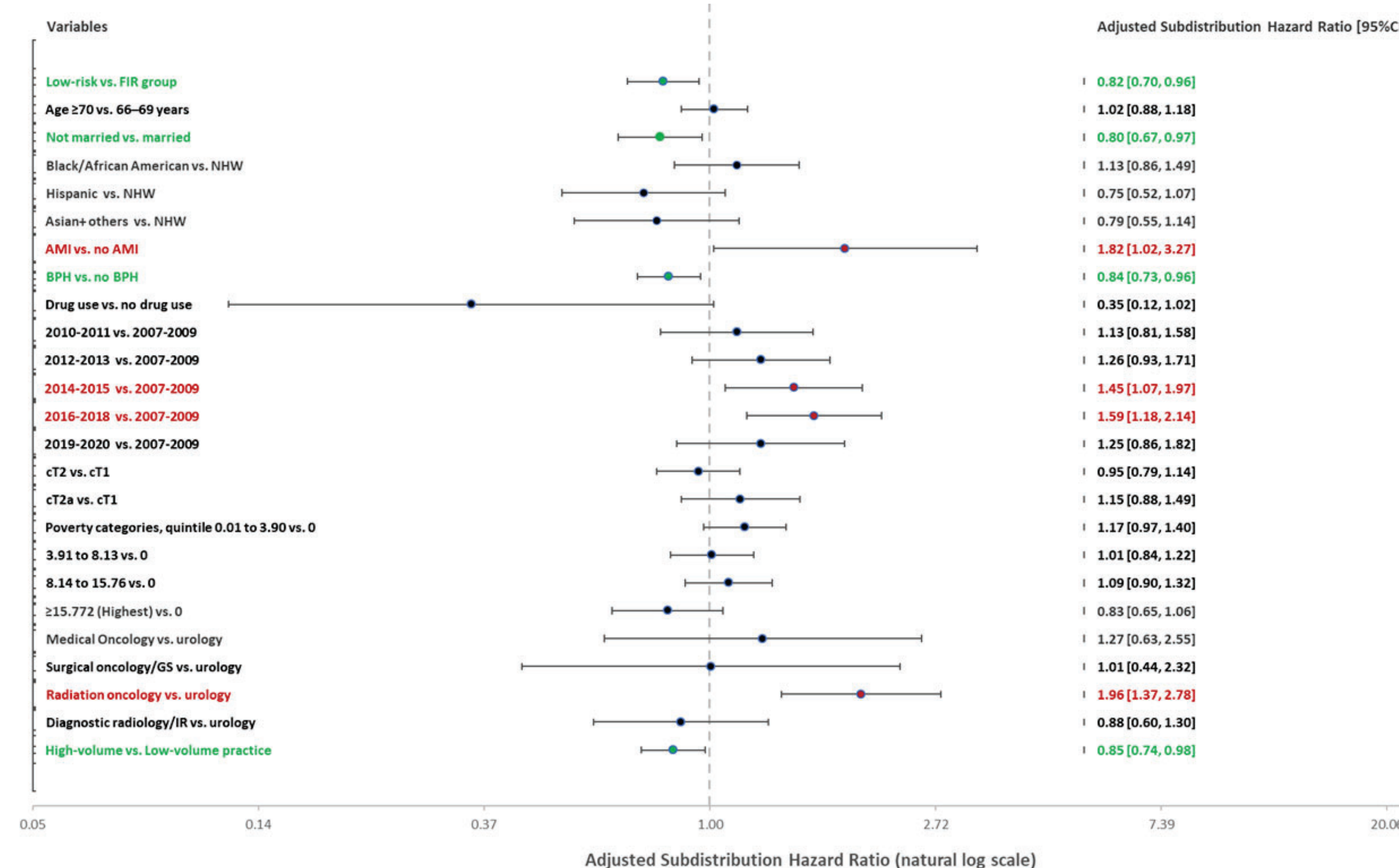


Figure 3. Factors Associated with RT Transitions Among Patients diagnosed with LIPCa Who Initiated AS, 2007-2020



Discussion

- In this retrospective cohort study of Medicare beneficiaries aged 66-75 years diagnosed with LIPCa, we quantified the prognostic influence of multilevel factors on transition from AS to RT to inform AS persistence optimization decision-making.
- RT transition was most strongly influenced by physician specialty (radiation oncology vs urology), more recent AS initiation period (2016-2018), and comorbid AMI, highlighting the combined influence of provider- and patient-level factors on AS persistence.
- Our findings underscore the need for standardized, multidisciplinary care coordination, and refined surveillance protocols to strengthen consistent, individualized, and evidence-based AS management when clinically appropriate.¹⁻³
- Our study results may be limited by unmeasured confounding (e.g., actual reasons for RT transition), potential misclassification of AS initiators, and generalizability to Medicare FFS beneficiaries aged 66 to 75 years with LIPCa from 2007 to 2020.

Key Takeaways & Conclusions

- Among elderly Medicare beneficiaries diagnosed with LIPCa who initiated AS, RT transition was influenced by multilevel factors, with physician specialty, recency of AS initiation, comorbidity burden – particularly a history of AMI - being the strongest prognostic factors.
- Further studies should investigate the causal mechanisms linking these factors and RT transitions.

References

- Eastham JA, Aufferberg GB, Barocas DA, et al. Clinically Localized Prostate Cancer: AUA / ASTRO Guideline 2022 Endorsed by SUO GUIDELINE STATEMENTS Principles of Active Surveillance. Published online 2022:1-43.
- Cooperberg MR, Meeks W, Fang R, Gaylis FD, Catalona WJ, Makarov D V. Time Trends and Variation in the Use of Active Surveillance for Management of Low-risk Prostate Cancer in the US. 2023;6(3):1-9. doi:10.1001/jamanetworkopen.2023.1439
- SEER-Medicare: Available Files by Year. Accessed April 25, 2022. <https://healthcaredelivery.cancer.gov/seermedicare/medicare/table.html>
- Fu Y, Whitfield S, Nix T. PolicyMap: Mapping Social Determinants of Health. <http://dx.doi.org/10.1080/02763869.2017.1332191>.
- Modi PK, Kaufman SR, Qi J, et al. National Trends in Active Surveillance for Prostate Cancer: Validation of Medicare Claims-based Algorithms. doi:10.1016/j.urology.2018.06.03
- Fan Q, Nogueira L, Yabroff KR, Hussaini SMQ, Pollack CE. Housing and Cancer Care and Outcomes: A Systematic Review. J Natl Cancer Inst. 2022;114(12):1601-1618. doi:10.1093/jnci/djac173

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