

Effect of Prednisone Dosing on Mineralocorticoid Related Side Effects with Abiraterone in Prostate Cancer

Purpose:

- To characterize the incidence and timing of mineralocorticoid excess syndrome (MES) in Abiraterone treated patients by prednisone dose level.

Background:

- Abiraterone is an integral treatment modality in advanced prostate cancer but causes MES.
- Clinical trials have utilized both 5 mg and 10 mg prednisone dosing to minimize MES and the side effects of prednisone (1, 2).
- Limited real-world data to compare the side effects of different dosing levels of prednisone (3).
- Unclear metabolic risk of prednisone treatment in prostate cancer patients.

Study Methodology:

- 1,410 prostate cancer patients were identified from Health Data Compass, an enterprise data warehouse partnering with UCHHealth and Children's Hospital Colorado. After applying exclusions, 1062 patients who received abiraterone from August 2011 to database lock on September 2022 were further analyzed.
- Data was recorded from both ICD diagnostic coding and also direct clinical measurements of Hypertension, Hypokalemia, Hyperglycemia.
- Incidence of these events over the 24 weeks following abiraterone initiation were analyzed via time to event frailty cox-proportional hazard models.

Results:

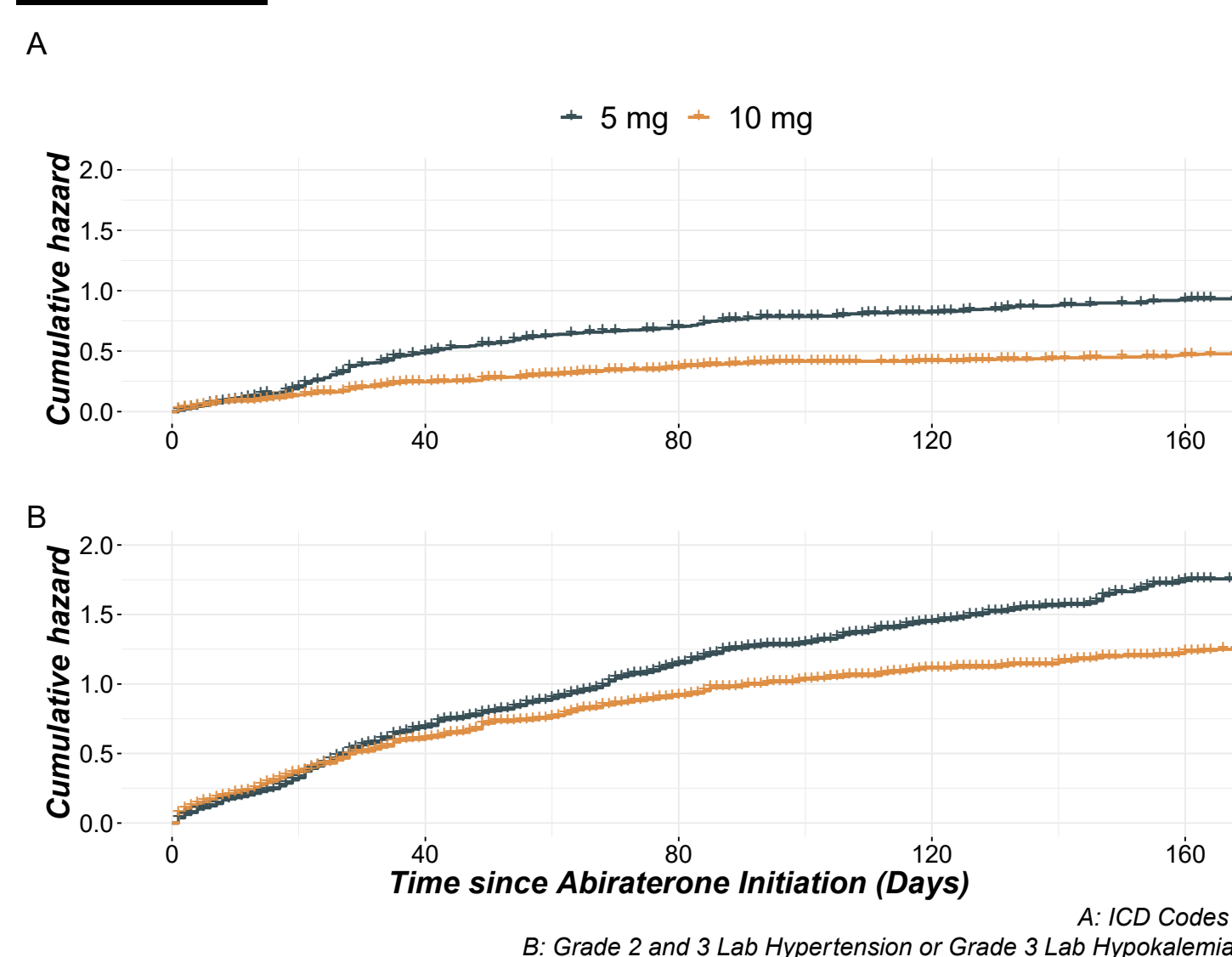


Figure 1: Combined analysis of hypertension and hypokalemia. Figure 1A shows analysis via ICD10 codes of hypertension and hypokalemia demonstrating increased cumulative risk of experiencing at least one mineralocorticoid adverse event in the 5 mg cohort (HR 0.5, CI 0.41 – 0.61, P < 0.001). Figure 1B: A similar trend was shown with analysis done via direct grade 2 and 3 blood pressure measurements and grade 3 serum potassium in the 5 mg cohort (HR 0.79, CI 0.68 – 0.91, P = 0.002).

Abiraterone treated prostate cancer patients receiving 5 mg of prednisone daily as compared to 10 mg showed a statistically significant increased cumulative risk of experiencing at least one mineralocorticoid adverse event

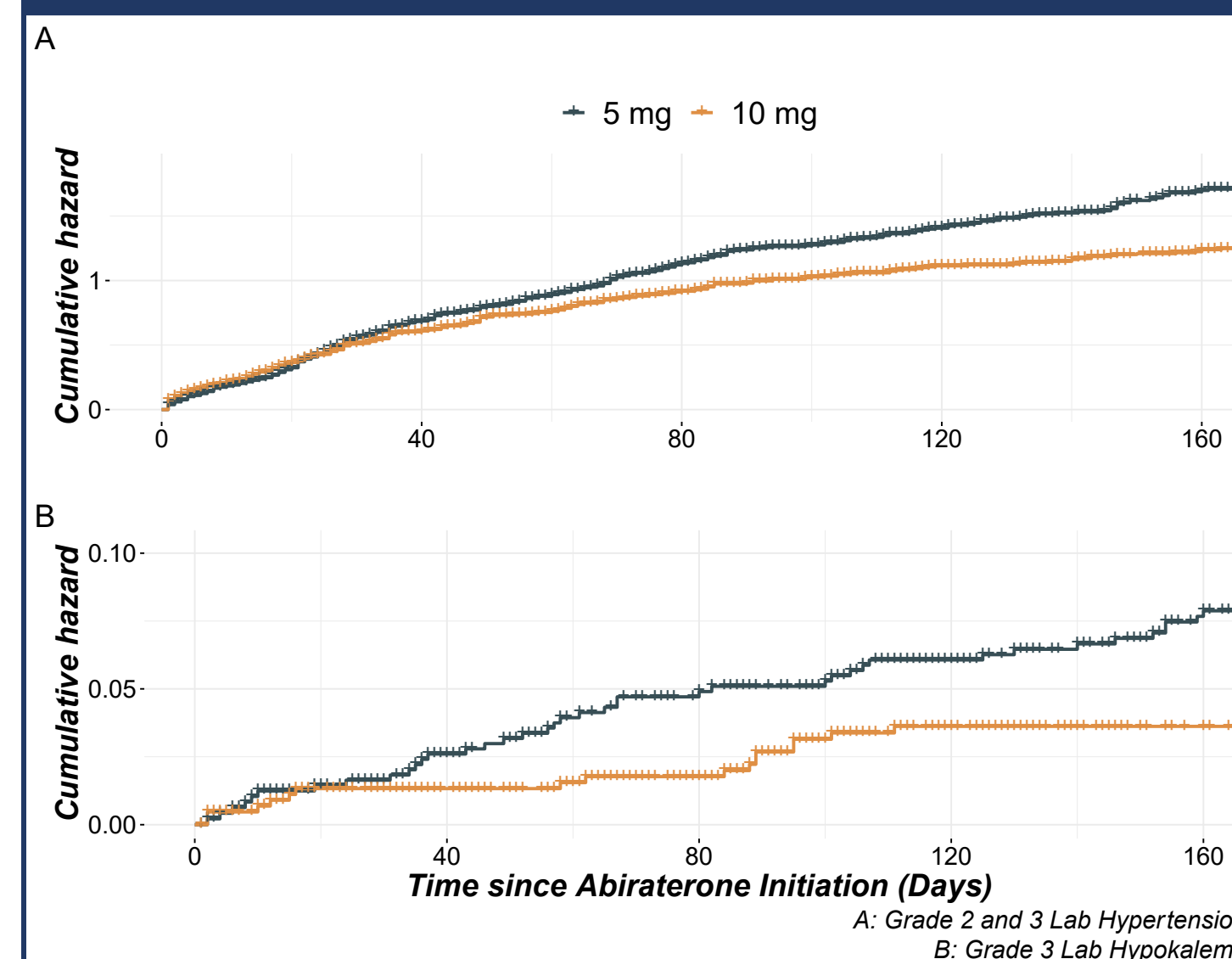


Figure 2: Analysis of grade 2 and 3 hypertension via direct clinical value (2A) and analysis of grade 3 hypokalemia via clinical laboratory value (2B) showed a statistically significant increased in cumulative risk of experiencing at least one event in the 5 mg cohort (HR 0.81, CI 0.7 – 0.93, P = 0.004) and (HR 0.46, CI 0.26 – 0.82, P = 0.008) respectively

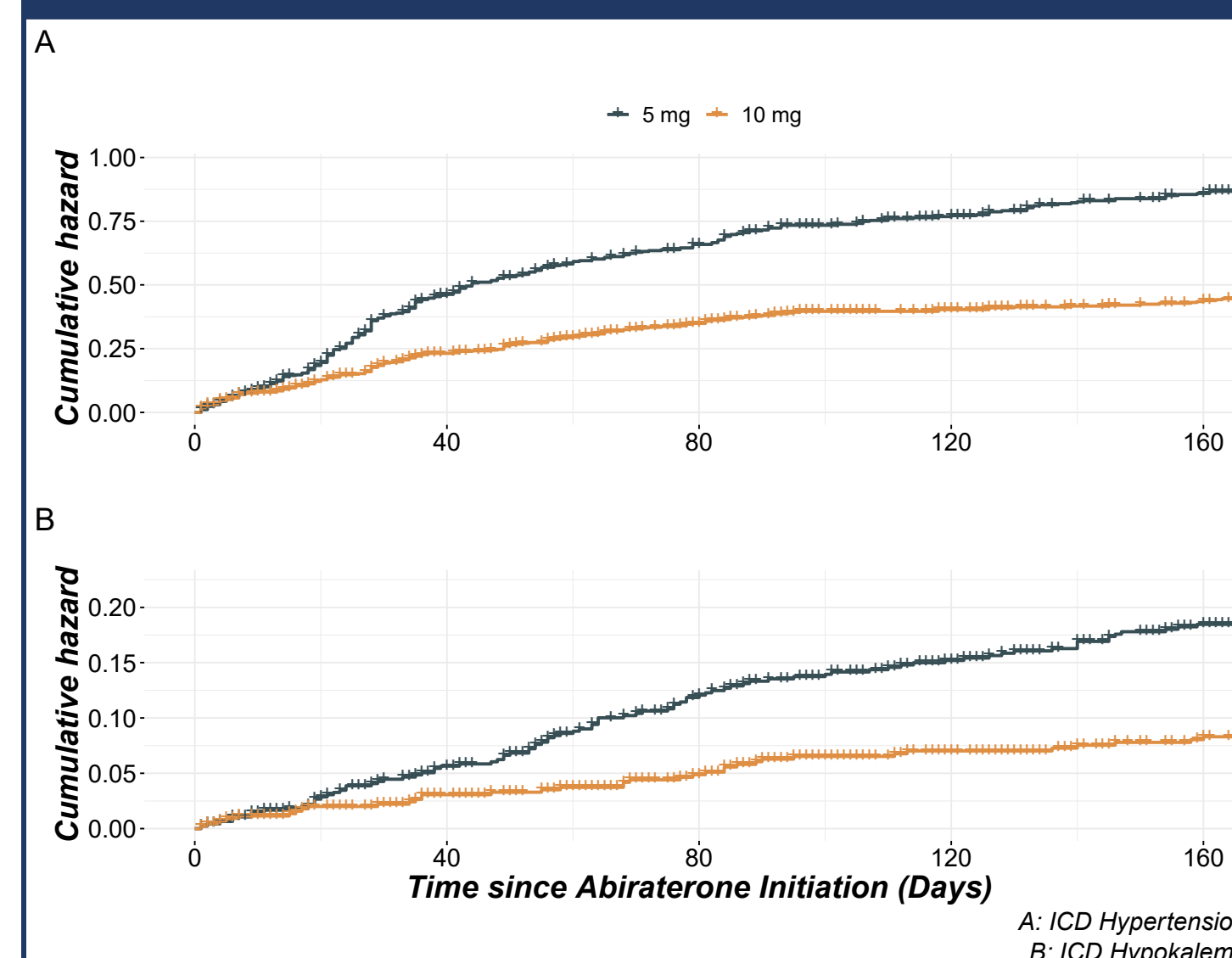


Figure 3: Analysis of hypertension via ICD10 code (3A) and analysis of hypokalemia via ICD10 code (3B) showed a statistically significant increased in cumulative risk of experiencing at least one event in the 5 mg cohort (HR 0.52, CI 0.43 – 0.62, P < 0.001) and (HR 0.45, CI 0.3 – 0.66, P < 0.001) respectively

Acknowledgements: The Finlon-Glode educational fund, supported by the Health data Compass Data Warehouse project (healthdatacompass.org), and the University of Colorado Cancer Center for their support in data analysis

Results Continued:

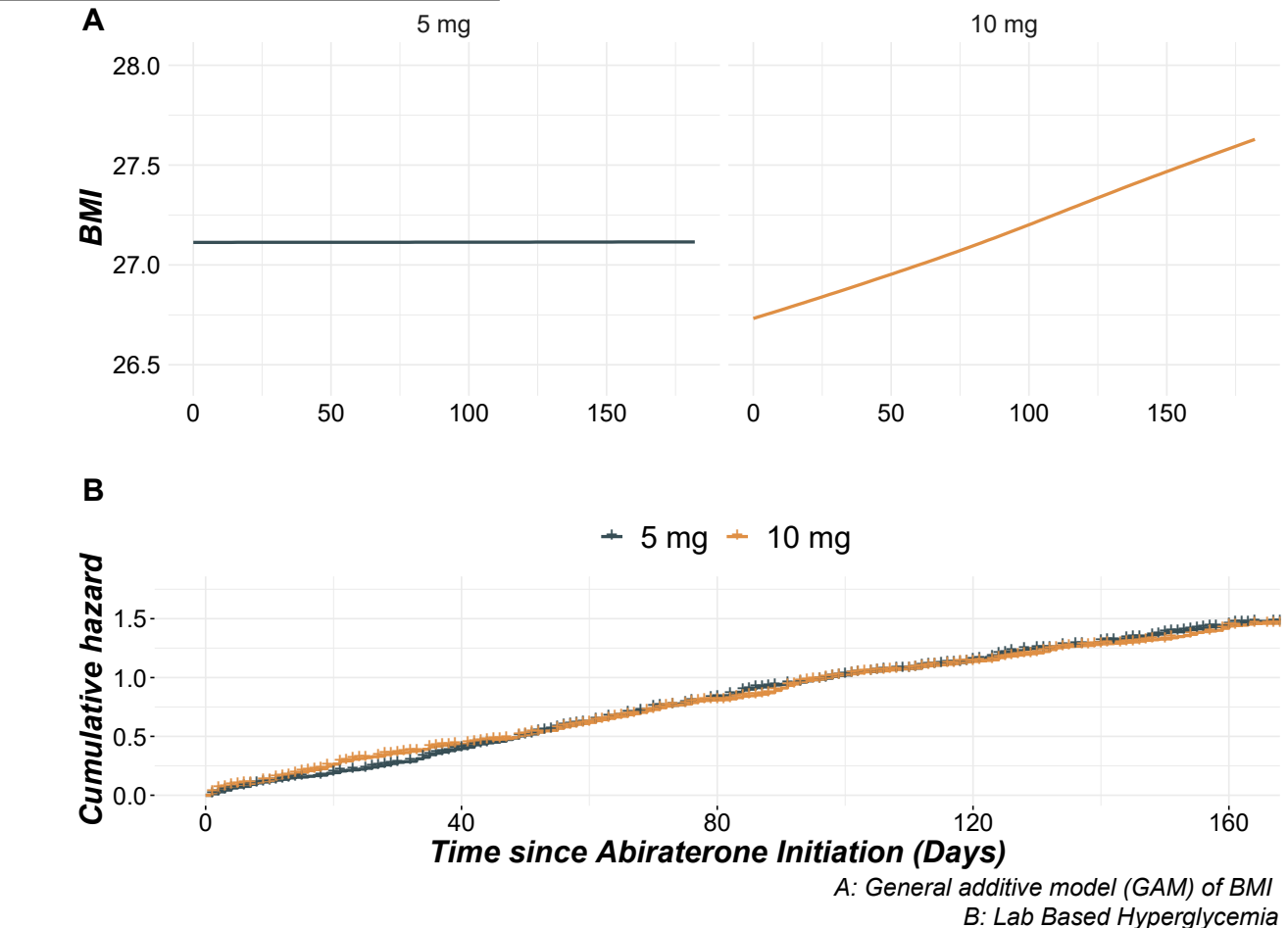


Figure 4: Metabolic impact of prednisone use. 4A. BMI analysis showed a non-clinically significant decrease over the first 6 months in the group that started on 10 mg of prednisone from a BMI of 26.73 to 27.63 and an increase from 27.11 to 27.12 in the 5 mg group. There was no difference in the cumulative hazard rate of hyperglycemia (4B) (HR 0.99, CI 0.75 – 1.3, P = 0.916).

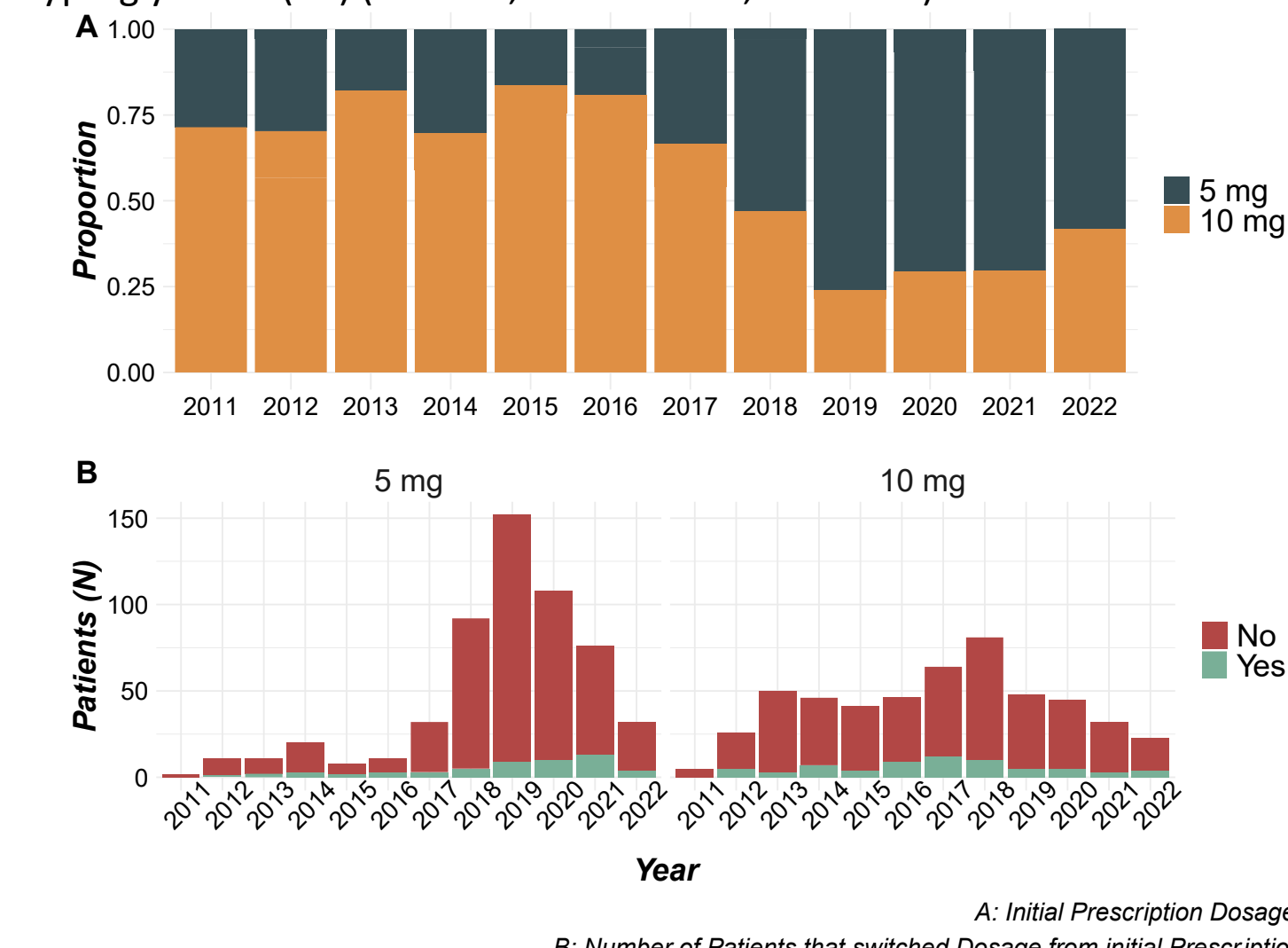


Figure 5: Prednisone dosing trends over time. Figure 5A quantifies the number of 5mg and 10mg prednisone treated patients each year. Figure 5B quantifies the number of patients switching doses by calendar year. Dose reduction was more likely over time (HR 1.4, CI 1-2, P = 0.048).

Conclusion:

- Patients on 5 mg of prednisone had an increased cumulative risk of experiencing at least one MES adverse event
- In this retrospective assessment there were similar findings in using ICD diagnostic coding and direct clinical assessments of hypokalemia and hypertension

Future Directions for Research:

- To better understand the impact of variable prednisone dosage regimens on other prostate cancer disease outcomes

References

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