A Methodological Comparison of Three Landmarking Approaches for Time-to-Event Prediction: Predicting Diagnosed Cannabis Use Disorder Among Medical Marijuana Cardholders in Arkansas

MSR105

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BACKGROUND

- Landmarking, where follow up time is broken into discrete time intervals or "landmark times", enables dynamic time-to-event prediction, with pooled approaches incorporating time-varying predictors generally outperforming single-landmark models.[1]
- Prediction interval length may influence performance and is often treated as a tunable design parameter, as its optimal value may depend on outcome incidence, follow-up duration, and the frequency with which predictors are updated.[1, 2]
- Although landmarking is increasingly used for dynamic time-to-event prediction, there is limited guidance on how alternative landmarking strategies and prediction horizon length jointly affect model performance in large, real-world healthcare datasets.

Objective: Using prediction of cannabis use disorder (CUD) among Arkansas medical cannabis (MC) cardholders, this study compared landmark supermodeling, strict landmarking, and cumulative landmarking across multiple prediction horizons (90,180, and 360 days).

METHODS

Data Source

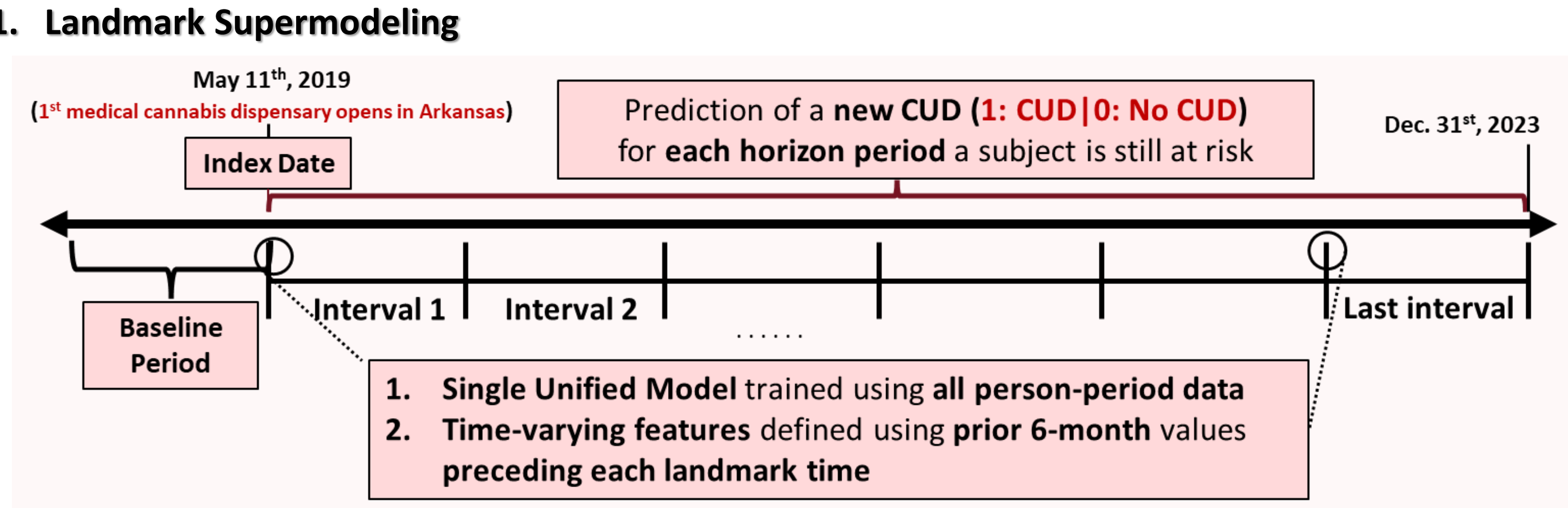
- Time-to-event datasets were constructed using statewide health insurance claims data between November 2018 – December 2023 from the **Arkansas All-Payer Claims Database (AR-APCD).**[3]

Study Sample

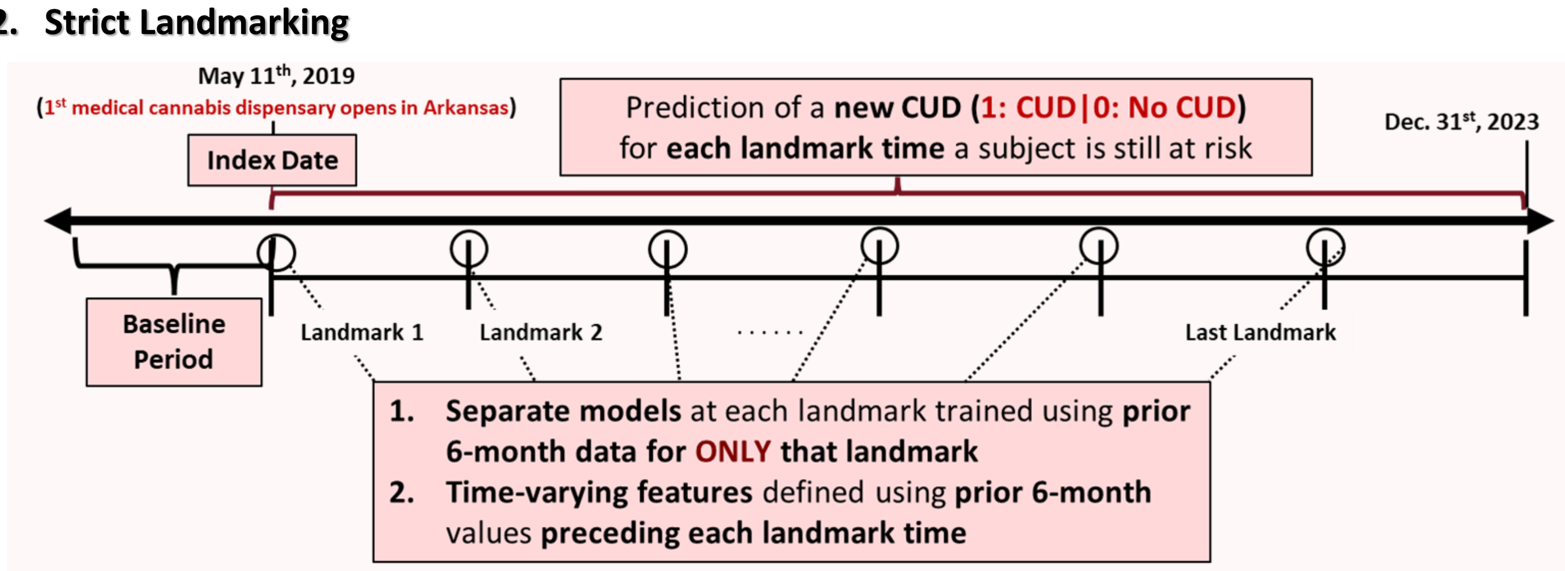
- **Subjects:** Insured (medical + pharmacy benefits), adult (≥ 18 years old) Arkansas MMJ Cardholders w/o recent history of CUD in the past 6 months.
- **Index Date:** May 11th, 2019 (opening date of 1st Arkansas MMJ dispensary) or receipt date of MMJ eligibility card, whichever came last
- **Follow-up**: Index date until 1st occurrence of one of the following: 1) New CUD diagnosis, 2) study end date (Dec. 31st , 2023), 3) health plan disenrollment, 4) death from any cause

Landmarking Approaches

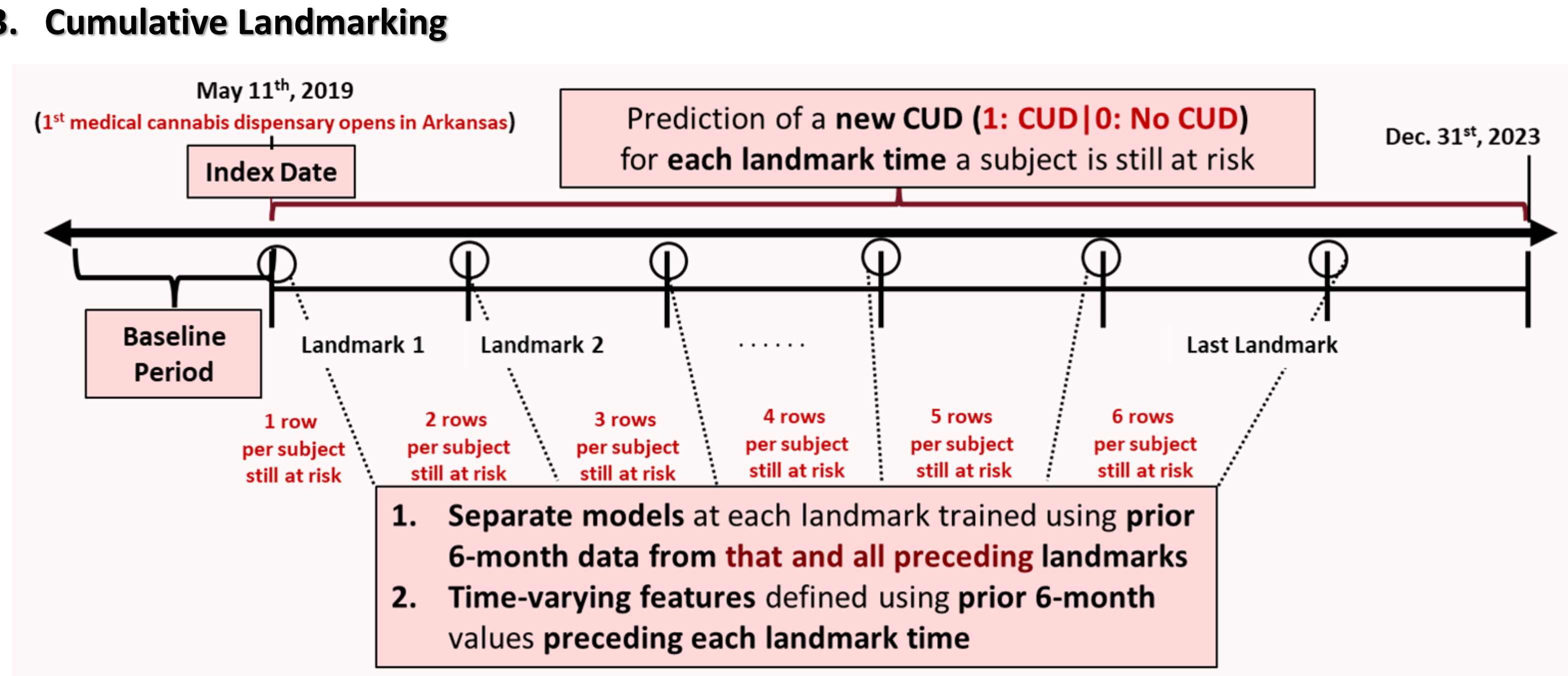
1. **Landmark Supermodeling**



2. **Strict Landmarking**



3. **Cumulative Landmarking**



METHODS

Data Structure

- **Discrete-time framework:** person-period dataset with one row per N-day at-risk interval, with follow-up represented as sequential time intervals (e.g., **1, 2, 3**)

Example of Discrete-Time Data Transformation Across Horizons

Person-level Data

ID	Follow-up Time	Event
1	256 days	1
2	370 days	0

Discrete-time Transformation

90-day Horizon

Person-period Data

ID	90-day Interval	Event
1	1	0
1	2	0
1	3	1
2	1	0
2	2	0
2	3	0
2	4	0
2	5	0

180-day Horizon

Person-period Data

ID	180-day Interval	Event
1	1	0
1	2	1
2	1	0
2	2	0
2	3	0

360-day Horizon

Person-period Data

ID	360-day Interval	Event
1	1	1
2	1	0
2	2	0

- **Secondary analysis (landmark supermodels only):** compared **discrete-time** vs. **discrete-time-daily,** with the latter recording follow-up time on a daily scale (e.g., **90, 180, 256**) while maintaining interval-based prediction updates.

Engineered Features [n=175]

- Included **demographics**, **acute + chronic comorbidities**, **prescription characteristics**, and **healthcare utilization characteristics.**

Model Training/Testing

- **Train/test split:** Randomized 70:30 split at person level
- **Data balancing:** 1:25 random undersampling (RUS) of the majority class
- **Hyperparameter tuning:** 90 iterations with 5-fold cross validation
- **Classifiers:** Random Survival Forest (RSF), Support Vector Machine Survival (SVMS), Cox Proportional Hazards (CPH), Random Forest (RF), Logistic Regression (LR)

Performance Metrics & Evaluation

- **Model discrimination:** cumulative sensitivity/dynamic specificity AUC (**C/D AUC**)
- **Model calibration:** horizon-aligned Inverse probability of censor weighting (**IPCW**) Brier scores (**BS**)
  - **Horizon-alignment:** Calculated at common calendar endpoints (u = 360, 720, 1080, 1440 days) for fair comparison across horizons (Δ); evaluated at landmark times $t = u - \Delta$.

1. **Landmark Supermodeling**: Evaluated on the full held-out test set with all person-period observations stacked across landmarks.
2. **Strict Landmarking:** Evaluated at each landmark, selecting the best classifier per interval, with overall metrics computed as weighted averages based on subjects at risk at each time point.
3. **Cumulative Landmarking:** Evaluated at each cumulative iteration, selecting the best classifier per iteration, with overall metrics computed as weighted averages based on cumulative follow-up time at each iteration.

Computing Resources

- This work was supported with computing resource allocations (MED230043) awarded through the Advanced Cyberinfrastructure Coordination Ecosystem: Services & Support (ACCESS) program.[4]

RESULTS

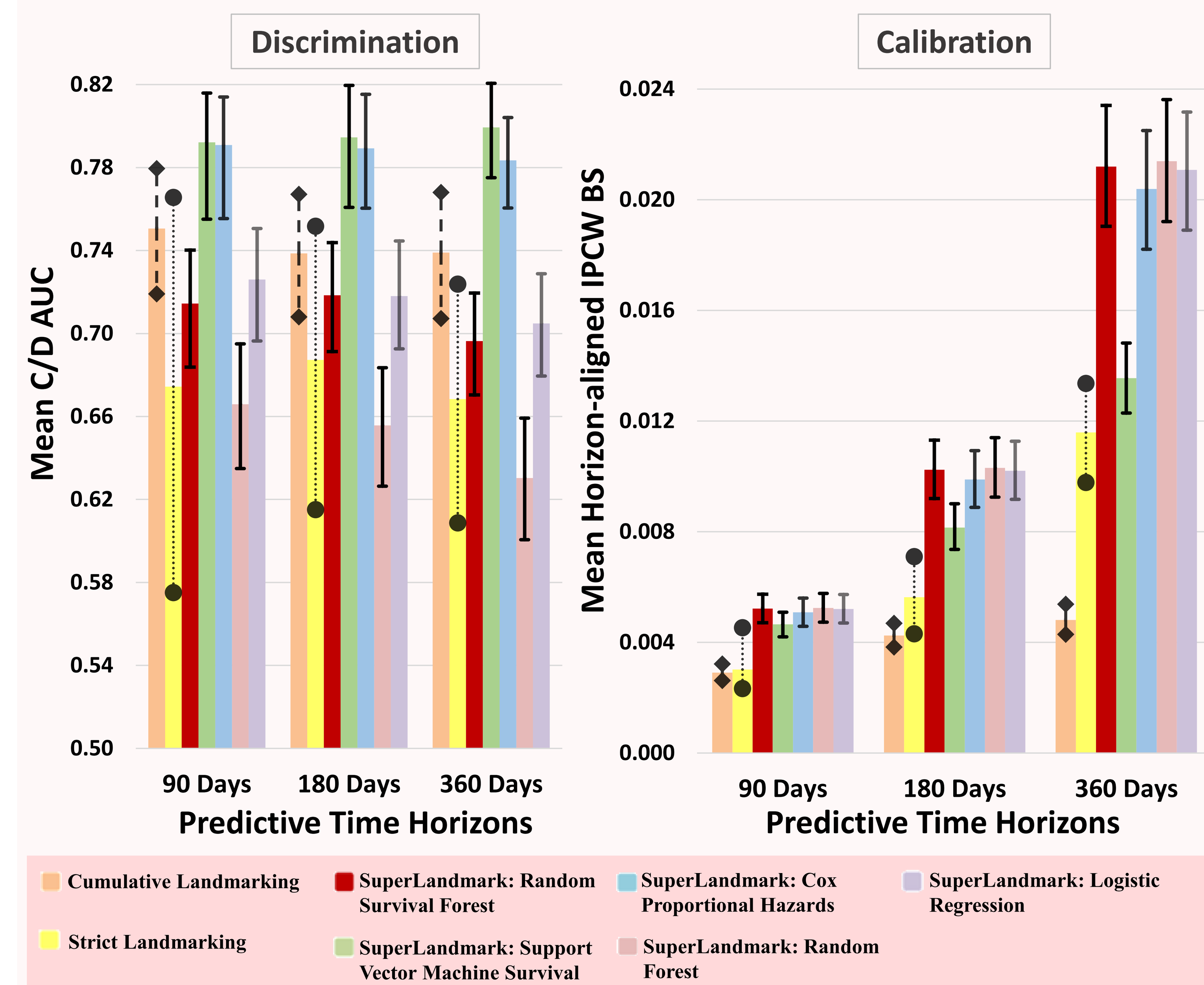
A total of **54,758 Arkansas medical cannabis cardholders** met eligibility criteria, of which **857 (1.57%)** received a new CUD diagnosis during the follow-up period.

Highest Discrimination: 360-day SVMS landmark supermodel (**mean C/D AUC = 0.7993**)

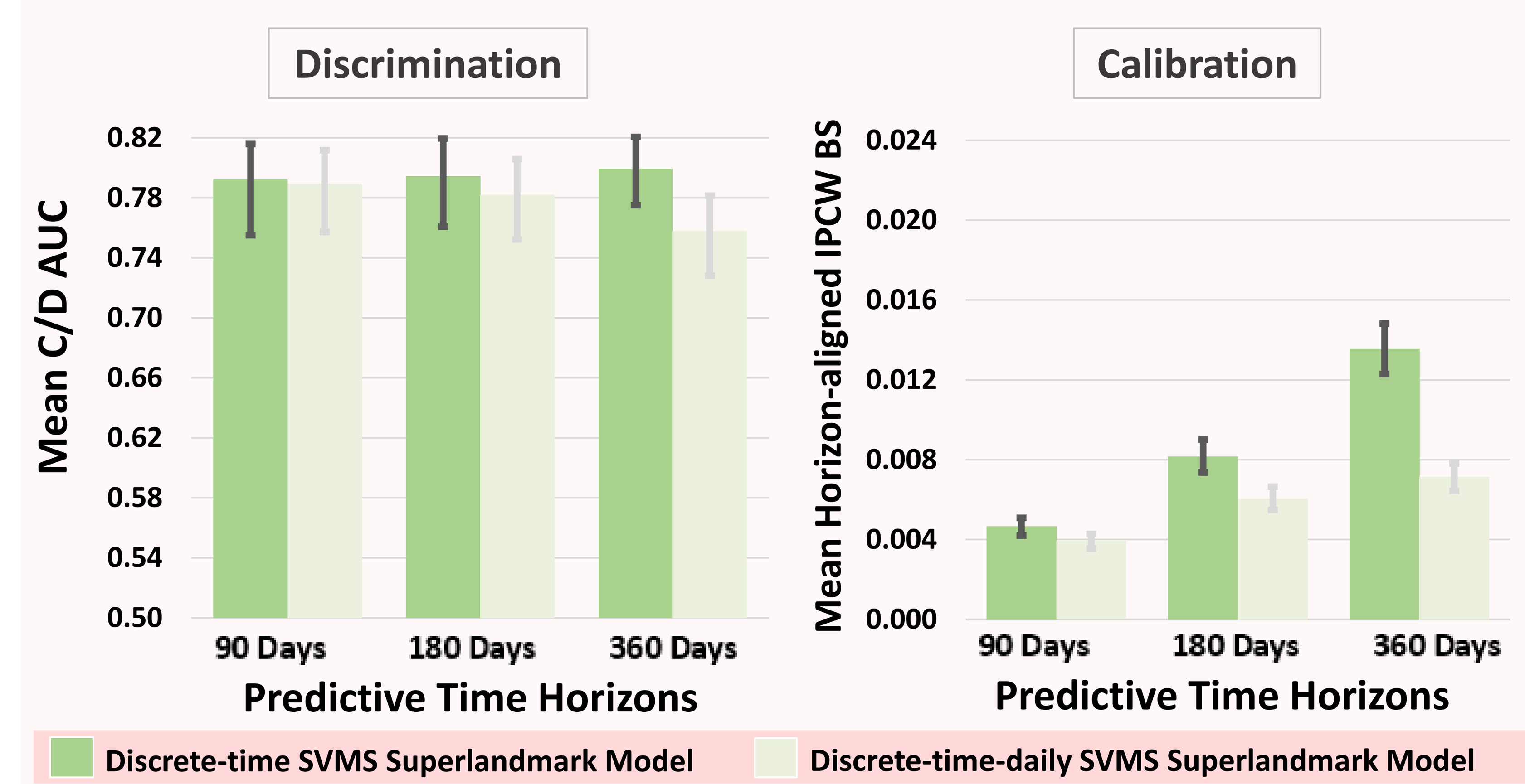
Lowest Calibration Error: 90-day cumulative landmark model (**mean horizon-aligned IPCW BS = 0.00291**)

RESULTS

Model Performance Across All 90, 180, and 360-day Prediction Horizons



Discrete-Time versus Discrete-time Daily Performance Comparison



CONCLUSION

- ✓ Landmark supermodeling consistently achieved the strongest discriminative performance across prediction horizons while maintaining calibration comparable to that of alternative landmarking strategies.
- ✓ Performance differences across interval lengths and temporal specifications were modest, reinforcing prior work emphasizing practical considerations (data availability, hardware limitations, clinical plausibility) in selecting interval lengths.

References

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