Hybrid Matching Methods for Treatment Program Evaluation: A Case Study

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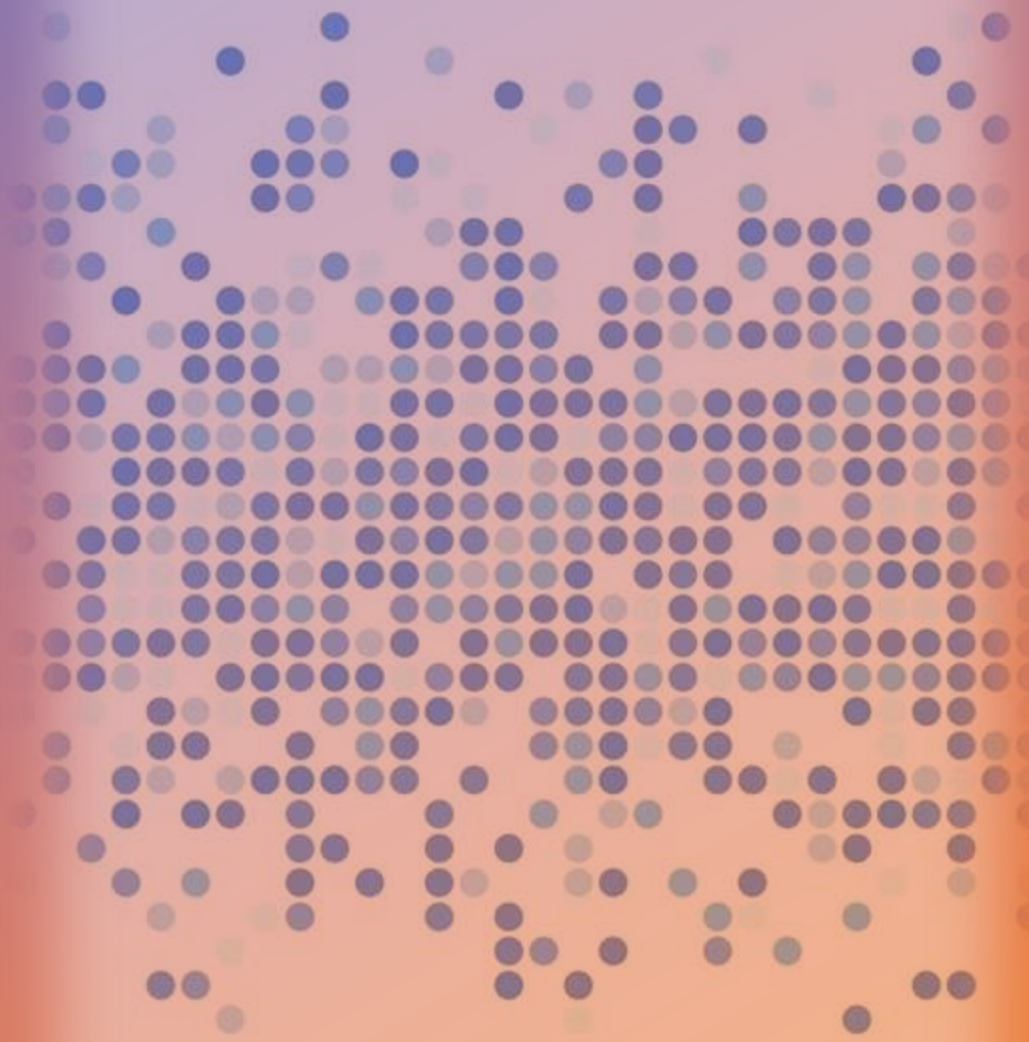

Overview

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Introduction

- Type-2 Diabetes (T2D) - one of the most prevalent chronic conditions
  - Affecting over 462 Million people worldwide
- Web-based Health Management Program (HMP)
  - Preventing the onset of T2D
  - Offered by several health payers (HP)
- HPs are highly interested in measuring the associated impact of HMPs on patient outcome
  - Golden standard is Randomized Control Trials (RCT) – expensive and time consuming
  - Analysis of data from observational studies (EHR, Claims, Lab and Biometrics etc.) – less costly and easily available
- We evaluated effectiveness of a particular HMP provided by a midsize regional HP based on two outcomes
  - T2D onset
  - Acute Care usage (In-patient visit or ER visit)

Challenges

- T2D has slow onset
  - Determining success of T2D prevention/diagnosis becomes challenging
- Use of observational data
  - Contains selection bias and influence of confounders
  - RCTs automatically handles them through randomization
- Covid-19 pandemic
  - Significant shifts in healthcare usage patterns

Background

Causal Inference

- Causal inference determines independent, actual effect of an Event A on an Event B
- Determine whether T affects Y
  - X affects both T and Y
  - Control for X, so that the measured effect on Y is only because of T, and not X
- Most popular method to control for the effect of confounders (X) is matching

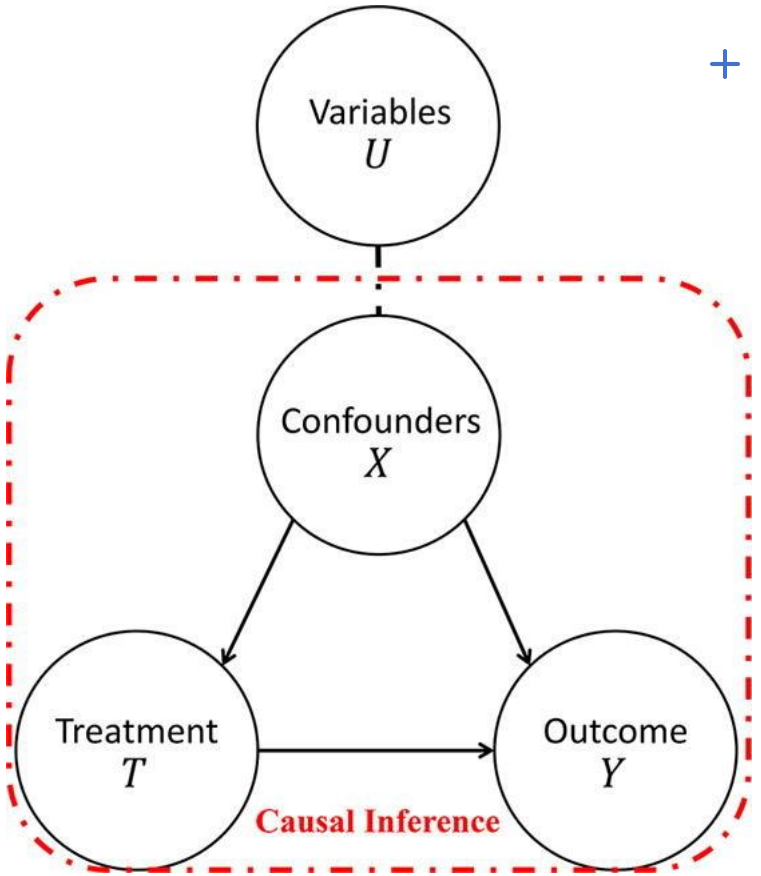


Fig: Causal Inference [1]

[1] Kuang K, Li L, Geng Z, Xu L, Zhang K, Liao B, Huang H, Ding P, Miao W, Jiang Z. Causal inference. Engineering. 2020 Mar 1;6(3):253-63.

Matching Algorithms

- Choose nearest neighbor for each treated sample from all the controls
  - Based on propensity score (PSM) [1]
  - Based on all the features (NNM)
- Matching balances the distributional differences between treated and control

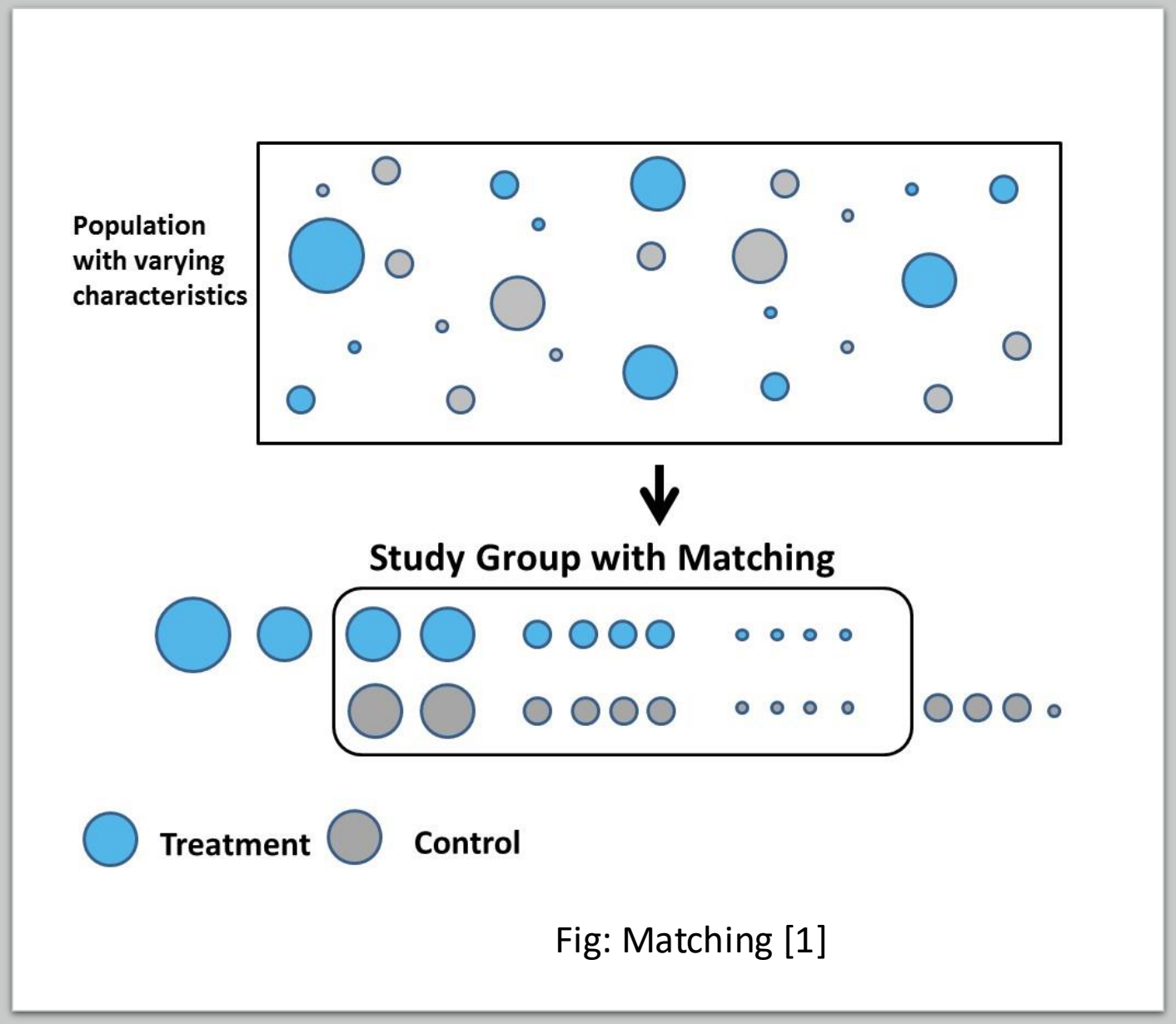


Fig: Matching [1]

[1] https://www.summitllc.us/propensity-score-matching

Survival Analysis

We are interested in the time to event (T2D onset or Acute Care) usage from the index or registration date, which is called the survival time

- Kaplan-Meier Survival Plots
  - represents probability that an event has not occurred after the index date at a respective time interval
- Logrank tests
  - evaluates the hypothesis that there is no difference between the populations in terms of survival times
- Cox's Regression
  - quantifies the effect of several covariates on the survival time
- Restricted Mean Survival Time (RMST)
  - quantifies the postponement of the outcomes during a specified (restricted) interval

Contribution

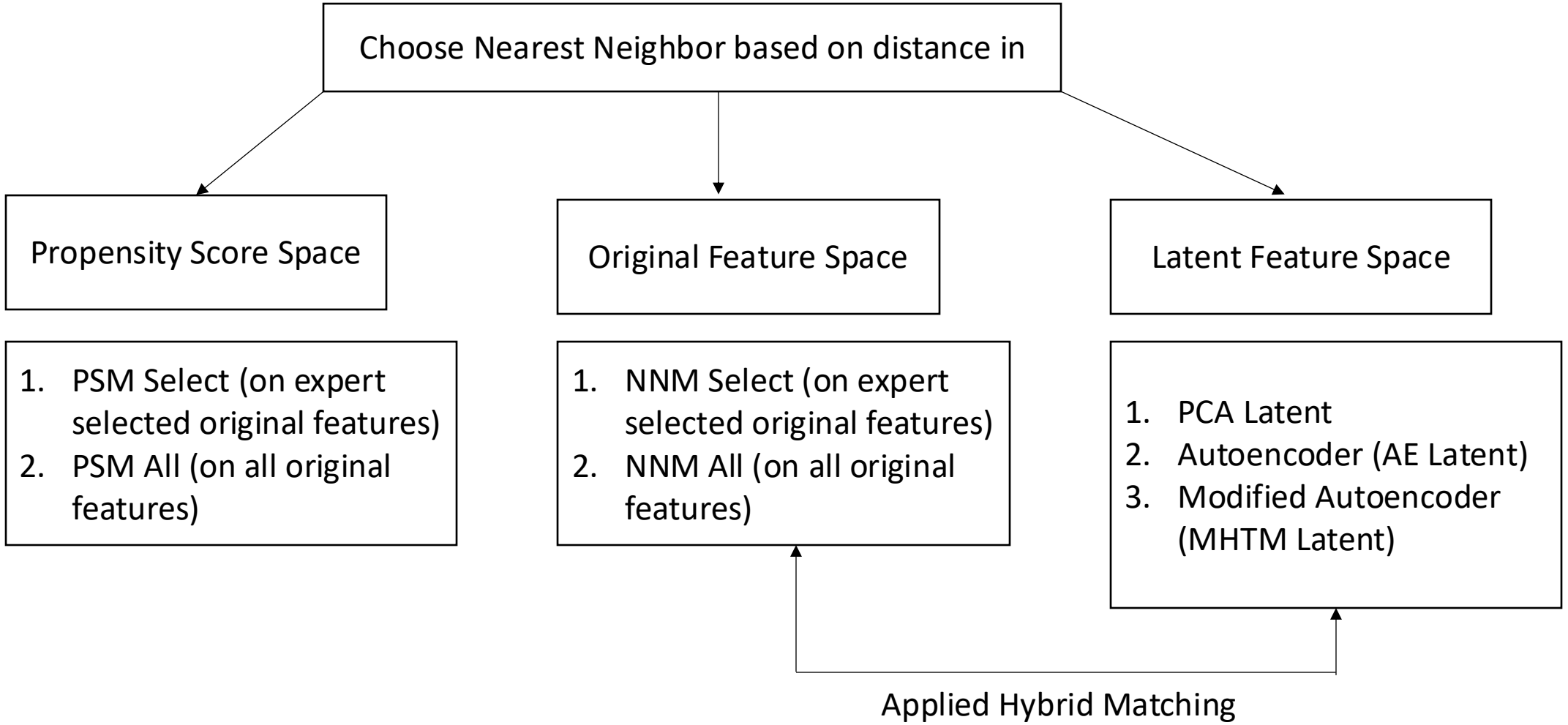
- Proposed a novel hybrid matching procedure for balancing distributional differences
- Deployed a suite of matching methods for causal analysis
  - From most popular propensity score matching to deep learning based state-of-the-art approaches – to ensures robustness
  - Used varying number of features (selected using several methods) to control for confounding
- Evaluated the HMP based on multiple outcomes
- Utilized survival analysis techniques to capture the evolving nature of T2D and account for the right censoring of data

Methodology

Data

- More than 9 million de-identified patient records from Nov 2017-April 2021
- Each patient data (77 features) is a time series of records
  - 69 Diagnosis/Summary codes, 3 cost related features, rest are demographic and insurance related information
- Patients were only chosen –
  - if no diabetes diagnosis on index/registration date
  - has at least 6 months of history before their index/registration date

Matching Methods



Hybrid Matching Method

- Deployed as an additional pre-filtering step for all non-propensity score-based methods
- Combines K-nearest neighbors, exact matching and coarsened exact matching

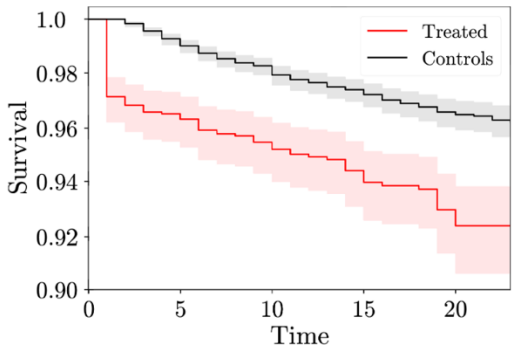
Algorithm 1: Hybrid NNM Matching of treated and control subjects.

Input: : $X_t, X_c, K, X_{ex}, X_{int}, X_{nn}, H$
Output: Matched controls X_{mc}
$X_{mc} = \{\}$;
for *patient* i *in* X_t *with registration time* t_i **do**
  X_{c1}: filter X_c to extract controls only with time t_i;
  X_{c2}: $\forall X_c^i \in X_{c1}$, filter X_{c1} s.t $X_t^i(X_{ex}) = X_c^i(X_{ex})$;
  X_{c3}: $\forall X_c^i \in X_{c2}, \forall X_{int^j} \in X_{int}$, filter X_{c2} s.t $X_t^i(X_{int^j}) \in [X_c^i(X_{int^j}) \pm h_j]$;
  X_{mc}^i: find the K nearest neighbors of X_t^i from X_{c3} based on the Euclidean distance of X_{nn} features;
  $X_{mc} = \{X_{mc}; X_{mc}^i\}$;
end

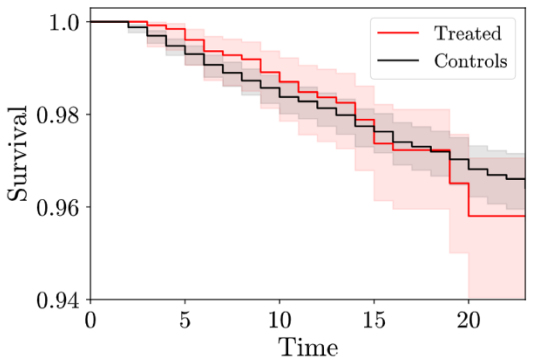
Results and Discussions

Kaplan-Meier Curves and Logrank Test

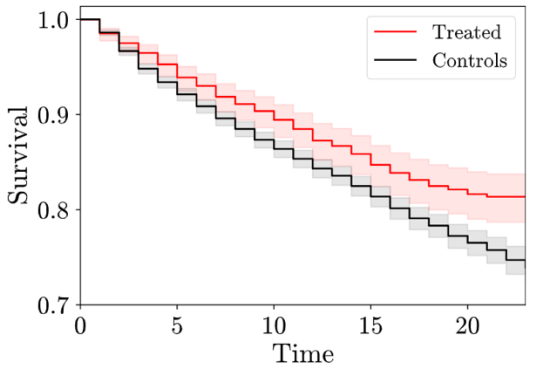
- Curves are from NNM Select
- 1(a) shows HMP patients have a higher and faster rate to get a T2D Diagnosis than controls
- 1(b) shows HMP and control patients are similar after removing patients who has T2D diagnosis in first 2 months
- 1(c) shows HMP patients have a lower rate of acute care utilization than controls



(a) T2D from idx date (p<0.05)



(b) T2D from idx date+2 months (p=0.96)



(c) Acute Care from idx date (p<0.05)

Method	T2D	T2D+2	Acute
NNM Select	**	0.96	**
PSM Select	**	0.71	**
NNM All	**	0.65	0.10
PSM All	**	0.78	**
PCA Latent	**	0.94	**
MHTM Latent	**	0.39	**
AE Latent	**	0.37	0.05

(d) Logrank p-values. ** means p < 0.05

RMST Analysis and Cox's Regression Coefficient

- RMST difference values measured every 6-month up to 18 months
- Negative value indicates that the treated has an event sooner than controls
- NNM Select and PSM Select benefits from domain knowledge, produces similar trends, and is the best estimate
- Latent Space methods produce results similar to the best estimate
- Values monotonically increase across months showing patient (HMP vs Control) trajectory diverges
- Treatment coefficient -0.271 in Cox's Regression indicates reduced acute care usage of HMP patients

Table 1: RMST Analysis for T2D and Acute Care after Index Date

	Diabetes Diagnosis			Acute Care		
	6 Months	12 Months	18 Months	6 Months	12 Months	18 Months
NNM Select	-0.147	-0.315	-0.497	0.069	0.241	0.441
PSM Select	-0.148	-0.319	-0.506	0.060	0.222	0.428
NNM All	-0.140	-0.297	-0.469	0.028	0.135	0.257
PSM All	-0.144	-0.312	-0.496	0.094	0.396	0.791
PCA Latent	-0.141	-0.291	-0.469	0.054	0.191	0.356
MHTM Latent	-0.148	-0.325	-0.518	0.048	0.176	0.379
AE Latent	-0.148	-0.331	-0.536	0.047	0.158	0.301

Matching Quality Comparison

Table 2: Comparison of Treated and Control Means (*p<0.05) for All Methods.

	Treated	Matched Controls							All Controls
Features		NNM Select	PSM Select	NNM All	PSM All	PCA Latent	MHTM Latent	AE Latent	
Age	50.74	50.82	49.71*	50.80	50.81	50.77	50.78	50.79	52.64*
Total Cost	712.1	641.0	634.8	589.3*	708.0	765.6	749.3	827.0	899.38
Gender	0.21	0.21	0.22	0.21	0.27*	0.21	0.21	0.21	0.43*
Tobacco	0.06	0.05	0.06	0.07	0.10*	0.09*	0.10*	0.09*	0.11*
Pressure	0.00	0.00	0.01	0.00	0.01*	0.00	0.00	0.00	0.02*
Obesity	0.50	0.49	0.50	0.50	0.32*	0.30*	0.29*	0.29*	0.30*
Hypertension	0.34	0.33	0.32	0.35	0.32	0.25*	0.25*	0.25*	0.38*
Hypothyroid	0.10	0.08	0.08*	0.09	0.09	0.09	0.09	0.08*	0.09
Disease Count	2.91	2.87	2.66*	2.73*	2.82	2.42*	2.40*	2.38*	3.36*
Acute Care (Prior 2 Mon.)	0.04	0.03	0.02*	0.03	0.03	0.03	0.03	0.03	0.06*
Acute Care (Prior 6 Mon.)	0.12	0.11	0.08*	0.11	0.11	0.11	0.11	0.11	0.17*
Inpatient (Prior 6 Mon.)	0.03	0.03	0.02	0.03	0.03	0.03	0.03	0.03	0.06*
ER Visits (Prior 6 Mon.)	0.09	0.09	0.06*	0.09	0.08	0.09	0.09	0.09	0.12*
Business Line	0.96	0.96	0.90*	0.96	0.82*	0.96	0.96	0.96	0.82*

Conclusion

- Illustrated the practical challenges of evaluating the effectiveness of HMPs using observational studies based on EHRs
- Got robust and consistent conclusions about the observed outcomes by comparing results from 7 different matching methods
- HMP increased T2D diagnosis in the first two months, but no significant differences after that
- HMP patients were less likely to utilize acute care