UNIVERSITY of WASHINGTON

Using Latent Class Probability Estimation and Residual Inclusion to Address Confounding in Medication Adherence Modeling

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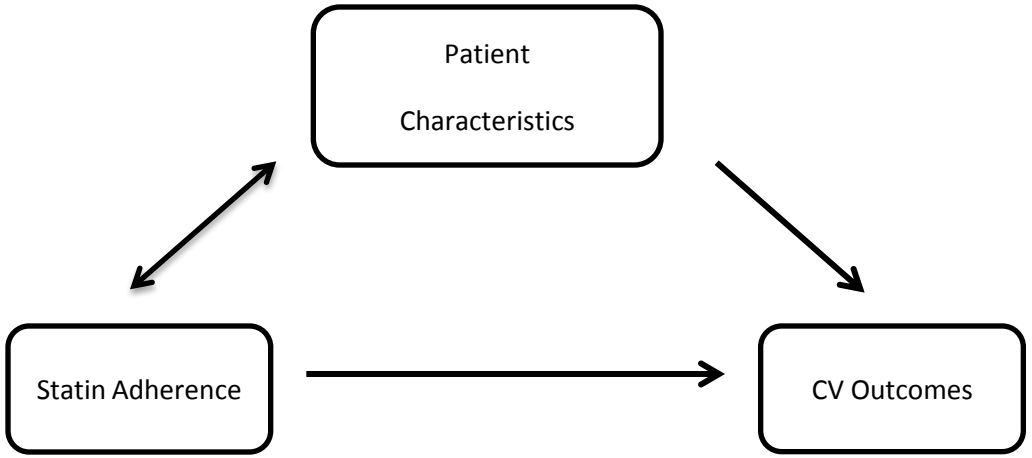
Background: Medication Adherence

- Often suboptimal and variable in chronic disease settings.
- Using claims data, we find some patient characteristics are associated with adherence.
- Patterns of adherence may also be associated with characteristics that we cannot observe.

Challenge



- Difficult to estimate the association between adherence and outcomes, partly due to potential confounding by unobserved patient characteristics.

Objectives

- To characterize variation and predictors of medication adherence.
- To improve the ability to explain the effect of adherence on outcomes by adjusting for unobserved confounders.

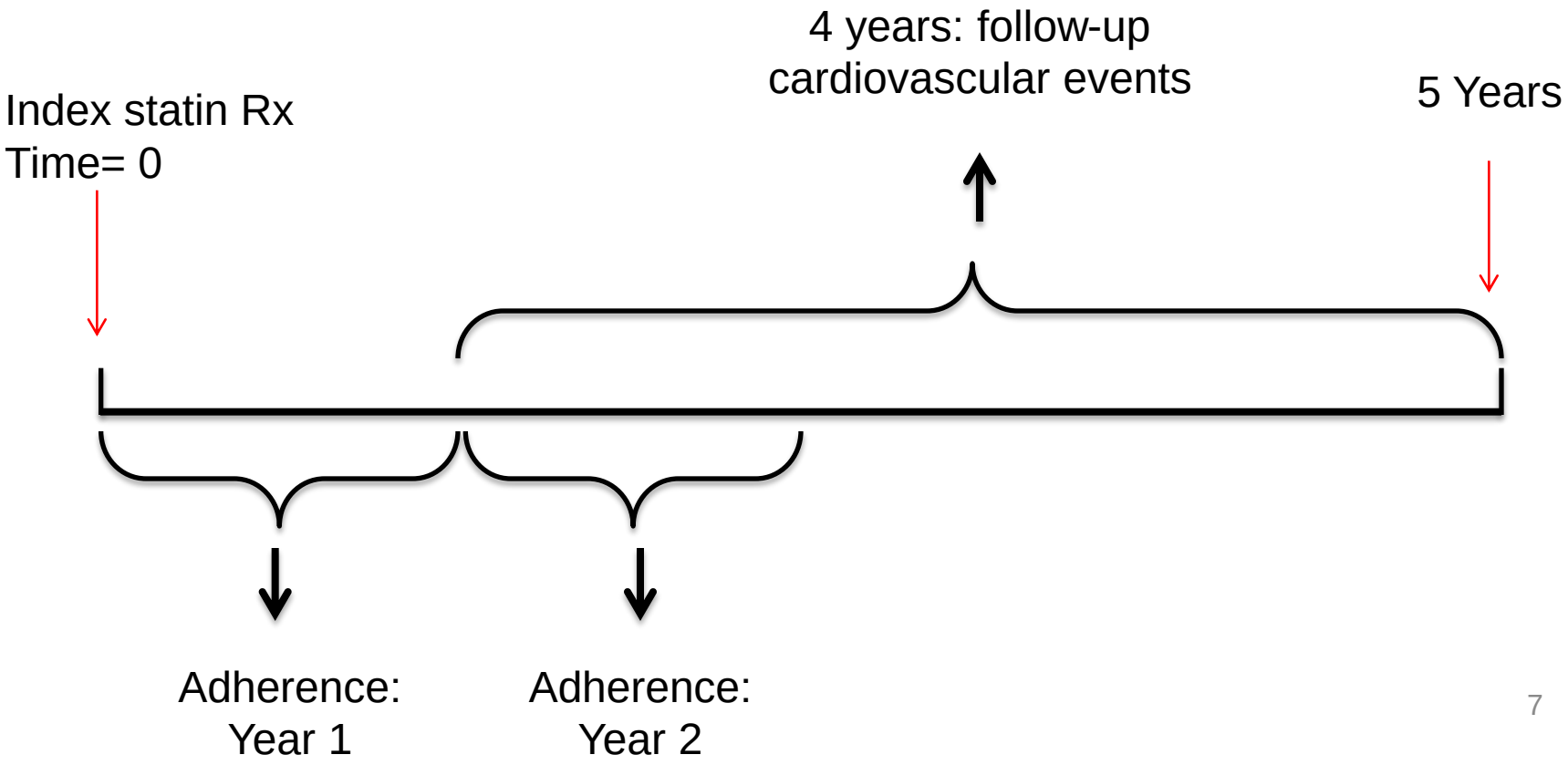
Methods

- Cohort definition, adherence estimation
- Three-part analysis:
  1. Characterize adherence variation
  2. Estimate probability of adherence
  3. Associate adherence and outcomes

"Real-World" Adherence

- 10% random sample of the IMS LifeLink Integrated Patient-Centric Claims (5.6 million), 1997- 2008
- Adult new statin users for primary prevention
  - In prior 12 months, no cardiovascular diagnoses or statin use (n=20,858)
- Minimum two-year follow-up
- Adherence measured as yearly Proportion of Days Covered (PDC)

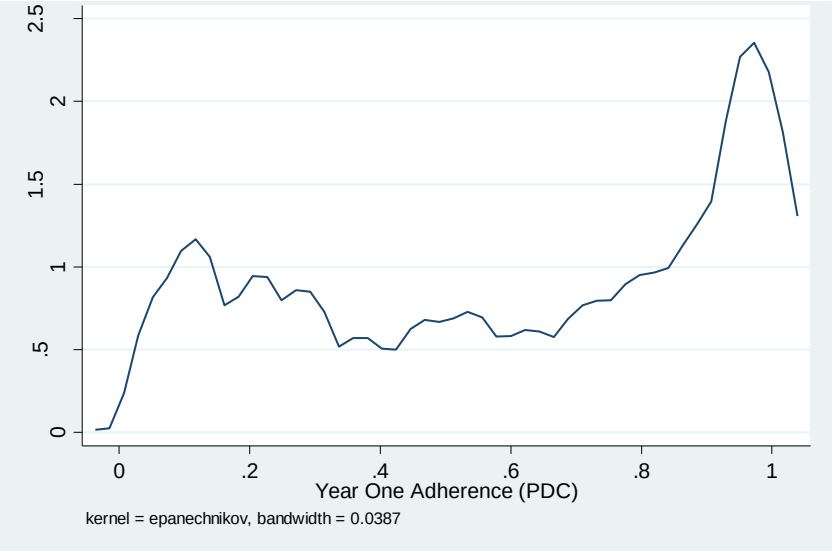
Adherence and CV risk

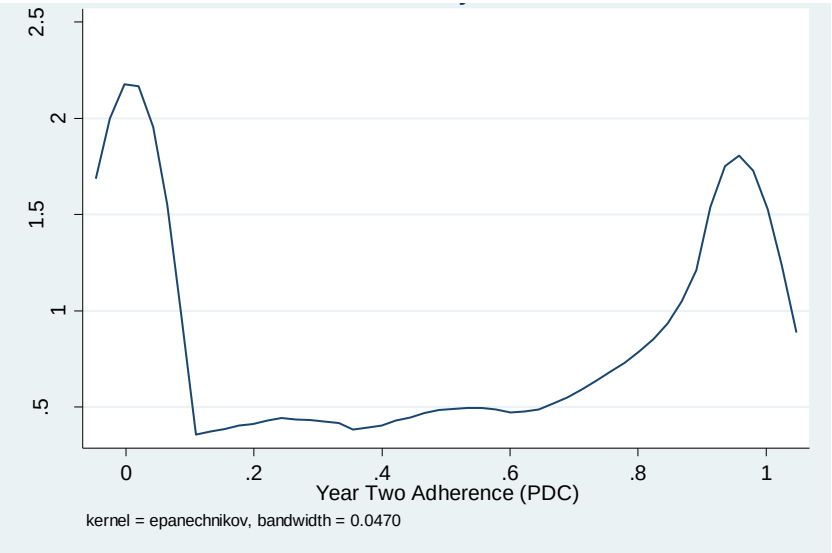


Cohort Characteristics

Characteristic	Study Cohort
Total	N = 20,858
Male n (%)	10,382 (49.77%)
Mean age in years (SD)	55.18 (10.6) (Range: 18-96)
No healthy behaviors n (%) **(e.g., flu shot, physical, etc.)**	11,853 (56.83%)
Chronic disease indicator score (SD) **(measure of comorbidity using Rx claims)**	4.79 (2.92) (Range: 1-23)
Generic statin (vs. brand) n (%)	2,215 (10.62%)
CV Event (MI, stroke) n (%)	1,522 7.30%

Distribution of Adherence: Years 1 & 2





- Appears that high- and low-adherers exist.
- Variation in adherence behavior.

Finite Mixture Model

- Model scenario where >1 distributions exist.
- Allows one to identify and estimate the parameters of interest for each sub-population in the data, not just of the overall mixed population
- Provides a natural representation of unobserved heterogeneity in a finite number of latent classes

Year 2 adherence = $\alpha + \beta_1 male + \beta_2 age + \beta_3 generic\ statin + \beta_4 healthy\ behavior + \beta_5 chronic\ disease\ indicator + \varepsilon$

Part 1: FMM Results

N=20,858	Change in year 2 adherence	P>z	[95%Conf.	Interval]
Class 1				
Male	0.032	<0.001	0.020	0.044
Age	0.003	<0.001	0.003	0.004
No healthy behaviors	-0.065	<0.001	-0.077	-0.053
CDI	0.000	0.898	-0.002	0.002
Generic	-0.017	0.077	-0.036	0.002
Constant	0.201	0.000	0.169	0.233
Probability	67.41%	0.000	66.39%	68.41%
Class 2				
Male	0.001	0.654	-0.002	0.003
Age	0.001	<0.001	0.001	0.001
No healthy behaviors	-0.008	<0.001	-0.010	-0.005
CDI	0.001	0.006	0.000	0.001
Generic	-0.001	0.670	-0.005	0.003
Constant	0.911	<0.001	0.901	0.920
Probability	32.59%		31.59%	33.61%

Who is in each component?

Classification of subjects based on most likely latent class membership.

N=20,858	Frequency	Percent	Mean Adherence
Class 1 "Low"	13,632	65.37	32.73%
Class 2 "High"	7,224	34.63	95.46%

Determinants of Posterior Probability

- Ordinary least squares regression

Class 2 posterior probability = $\alpha + \beta_1 male + \beta_2 age + \beta_3 generic\ statin + \beta_4 healthy\ behavior + \beta_5 chronic\ disease\ indicator + \varepsilon$

Part 2: Results

Determinants of Class 2 posterior probability.

N=20,858	Coef.	P>t	[95% Conf.	Interval]
Male	0.045	<0.001	0.033	0.057
Age	0.005	<0.001	0.005	0.006
No healthy behaviors	-0.051	<0.001	-0.062	-0.039
CDI	0.000	0.951	-0.002	0.002
Generic	0.003	0.716	-0.015	0.022
_cons	0.045	0.007	0.012	0.079

Modeling Adherence and CV risk

- Cox proportional hazards model
- Up to 5-year risk of vascular events (MI, Stroke)
  - Follow-up: mean 42 months (range 24-119)
- Excluded patients with Year 1 CV events.

$$\log h_i CVEvent(t) = \beta_1 Year\ 2\ Adherence + \beta_2 male + \beta_3 age + \beta_4 CDI + \varepsilon$$

$$\log h_i CVEvent(t) = \beta_1 Year\ 2\ Adherence + \beta_2 male + \beta_3 age + \beta_4 CDI + \beta_4 Part\ 2\ residual + \varepsilon$$

Part 3: Cox Proportional Hazards Results

N=20,858	Hazard Ratio	P>z	[95%Conf.	Interval]
Model 1				
Adherence	0.676	<0.001	0.594	0.769
Male	1.238	<0.001	1.117	1.373
Age	1.055	<0.001	1.051	1.060
CDI	1.190	<0.001	1.174	1.206
Model 2				
Adherence	0.530	<0.001	0.427	0.658
Male	1.251	<0.001	1.128	1.387
Age	1.057	<0.001	1.052	1.062
CDI	1.190	<0.001	1.174	1.207
Residual (covariate)	1.328	0.006	1.086	1.624

Limitations

- Using pharmacy claims for adherence estimation.
- Patient censoring.
- Structural uncertainty.

Conclusions

- FMM allows analysis of heterogeneity in statin adherence.
- Patient characteristics are associated with likelihood of adherence.
- Unobserved determinants can be captured and used to investigate true effect of adherence on outcomes.

Future Work

- Model structure.
- Validation data set to investigate residuals.

Questions

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