

MI-CRE Methods Group journal club: Prevalent new-user cohort design

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1 July 2021

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Talk outline

- Paper background
- Prevalent new-user cohort method in detail
- Adjusting for informative censoring
- Results
- What does the PNUC method estimate?
- Loose ends

Introduction

- Question: Are PPIs efficacious in idiopathic pulmonary fibrosis?
- Contention: Effects seen in earlier studies are due to bias
- Data: UK linked GP and hospital data (CPRD-GOLD/HES/ONS), $n = 2944$
- Outcomes: All-cause mortality, respiratory death, hospitalisation
- Covariates: Demographics, comorbidity, medicines (all time-varying)

Idiopathic Pulmonary Fibrosis (IPF)

- Progressive scarring of the lungs, cause unknown
- Average life expectancy after diagnosis about four years
- Pirfenidone (2008) and nintedanib (2014) slow progression
- Proton pump inhibitors also guideline recommended (weak evidence)

Review: Active comparator new-user cohort design

- Confounding by indication (inactive comparator)
- Healthy adherer bias (prevalent users)

Why *prevalent* new-user?

- *i.e.* Compare those staying on old tx with switchers to new
- Increase sample size if few treatment-naïve patients
- Better external validity e.g. disease progression
- Key feature: conditioning on length of exposure

Prevalent new-user cohort design step by step

- 1 Defining the base cohort
- 2 Forming exposure sets
- 3 Estimating the propensity score
- 4 Matching and forming the analysis cohort
- 5 Estimating the causal effect

Defining exposure sets and estimating the propensity score

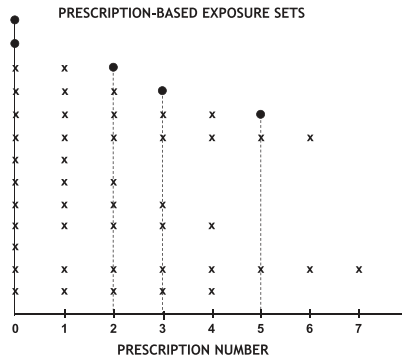


Figure 3. Depiction of a base cohort formed of 13 subjects with prescription-based exposure sets defined by the number of comparator drug prescriptions (x) before the first study drug prescription (•) was given

Suissa et al. (2017)

Matching

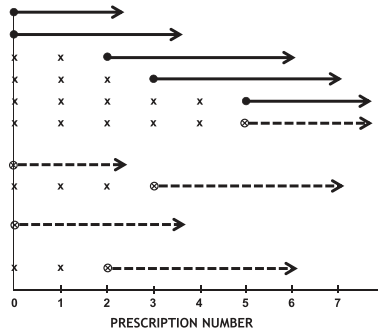


Figure 4. Depiction of the final prevalent new-user comparative cohort with comparator drug subjects matched to study drug subjects on the number of comparator drug prescriptions (x) before the first study drug prescription (●) was given, with the arrows indicating the follow-up period for outcomes

Suissa et al. (2017)

Informative censoring

- In this study, “prevalent user” = IPF patient *not* treated with PPI
- Follow-up of prevalent users is censored if PPI treatment starts
- Starting PPI = patient is still alive (but sicker?)

Adjusting for informative censoring

- Option 1: Restriction
 - exclude PPI ever users from prevalent cohort
- Option 2: Weighting
 - use inverse probability of censoring weights (IPCW)
 - estimate from logistic regression model (*à la* propensity)

Results 1

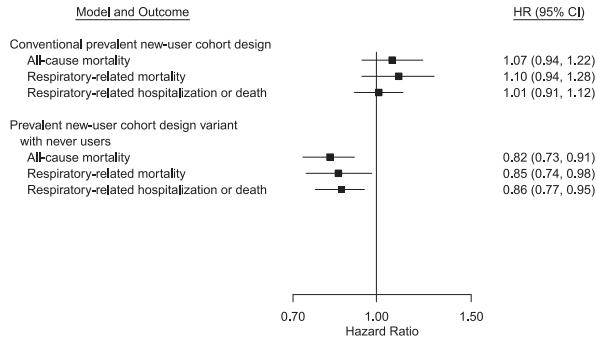


Figure 3. Hazard ratios (HRs) for respiratory-disease-related hospitalization and mortality associated with proton pump inhibitor use (compared with no use) obtained using 3 different study designs in a cohort of patients with idiopathic pulmonary fibrosis, United Kingdom, 2003–2016. Bars, 95% confidence intervals (CIs).

Marginal Structural Cox Model

- All patients followed from IPF diagnosis
- Exposure and covariates assessed in each person-month
- Inverse probability of treatment weights (IPTW)
- Inverse probability of censoring weights (IPCW)
- Estimation with weighted time-dependent Cox model

Results 2

936 Tran and Suissa

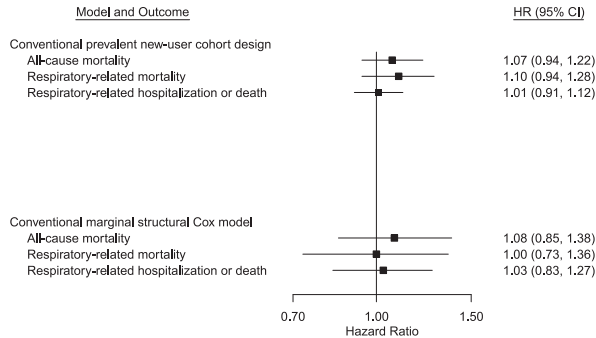
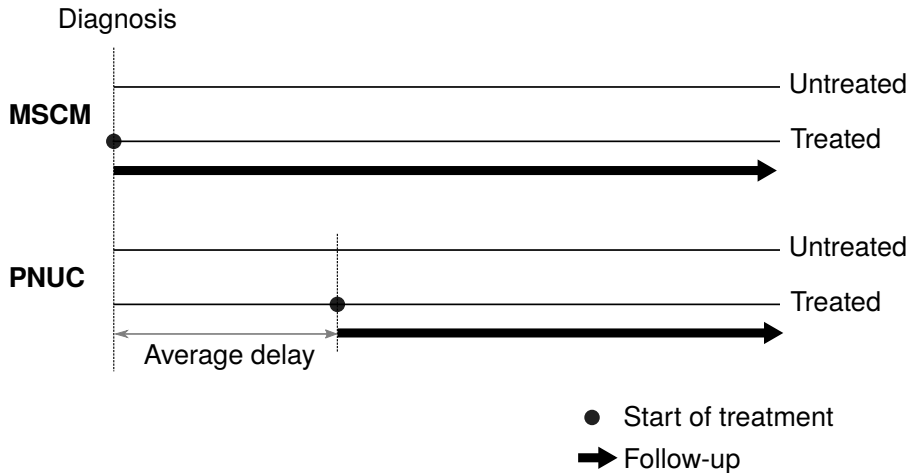


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Estimands



PNUC sub-cohorts

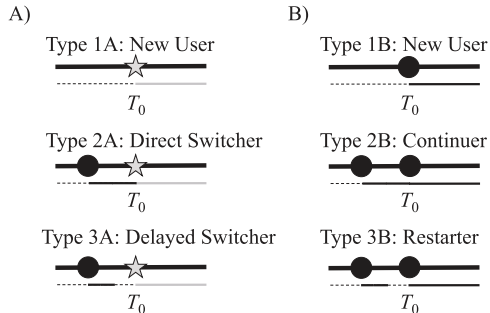


Figure 1. Infographic showing treatment histories of various types of initiators of treatment A and users of B. Panel A includes the initiators of treatment A (types 1A–3A) and panel B includes the 3 corresponding individuals taking treatment B that would be “ideal” counterfactual contrasts for types 1A–3A. Gray stars represent prescriptions for A, while black circles represent prescriptions for B. Below each set of prescriptions is a secondary timeline showing time with no treatment (dashed black), time treated with A (gray), and time treated with B (solid black).

Webster-Clark et al. (2020)

Loose ends

- Sampling with/without replacement
- Conditioning on length of exposure vs entire history
- Positivity and matching
- Estimating the propensity score
- See also: https://pharmacoepi.unc.edu/wp-content/uploads/sites/6788/2020/12/Webster-Clark_Michael_PNU.pdf

Discussion

- Have you used the prevalent new-user cohort design or the marginal structural Cox model approach? If so, please tell us about it.
- Would you use either of these methods for your current research interests? What do you see as the barriers to using them?

Other business

- Suggestions for articles or topics to discuss
- Volunteers to present
- Comments on format, timing, frequency and audience for the journal club

References

- S. Suissa, E. E. M. Moodie, and S. Dell’Aniello. Prevalent new-user cohort designs for comparative drug effect studies by time-conditional propensity scores. *Pharmacoepidemiology and Drug Safety*, 26(4):459–468, 2017. doi: 10.1002/pds.4107. URL <https://onlinelibrary.wiley.com/doi/abs/10.1002/pds.4107>.
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- M. Webster-Clark, R. K. Ross, and J. L. Lund. Initiator Types and the Causal Question of the Prevalent New-User Design: A Simulation Study. *American Journal of Epidemiology*, page kwaa283, Dec. 2020. doi: 10.1093/aje/kwaa283. URL <https://academic.oup.com/aje/advance-article/doi/10.1093/aje/kwaa283/6043913>.