Recent statistical methodology publications using NACC UDS Database

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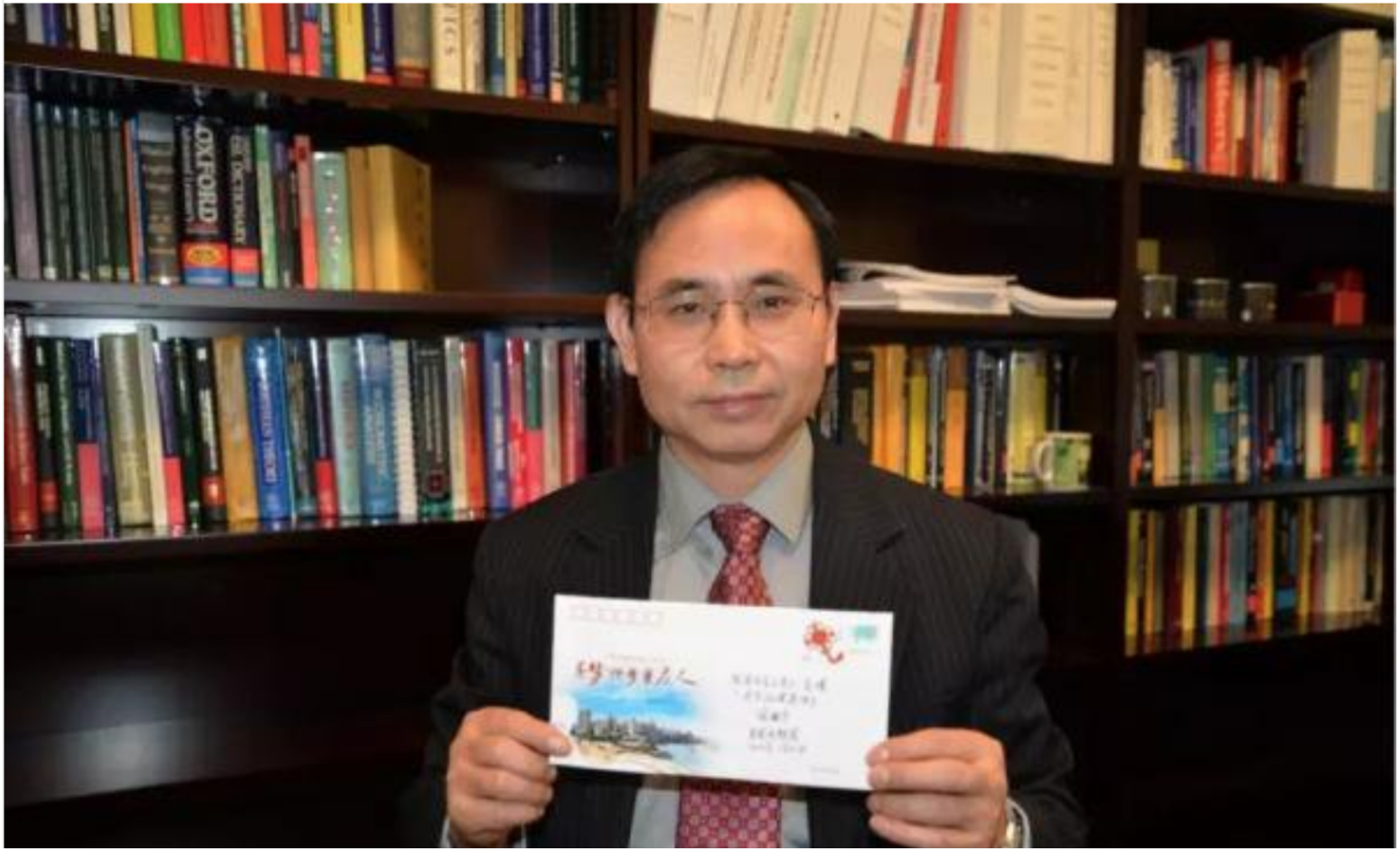
Personnel change

People's Daily,China
@PDChina · 5 months

Renowned biostatistics scientist Zhou Xiaohua quit his post at the University of Washington (@UW) to work as a full-time professor at Peking University(@PKU1898)'s Beijing International Center for Mathematical Research, marking the latest scientist to return to teach in China



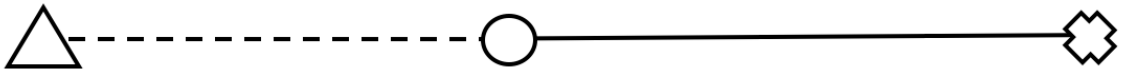
Recent Statistical methodology publications

- Survivors' duration bias
  - Chiou SH, Austin MD, Qian J, Betensky RA. Transformation model estimation of survival under dependent truncation and independent censoring. Stat. Methods Med. Res, Revision 2018.
- Verification bias
  - Yu W, Kim J, Park T. Estimation of Area Under the ROC Curve under nonignorable verication bias. Statistica Sinica, In press 2018.
  - Cho H, Harel O, Mattews GJ. Confidence intervals for the area under the receiver operating characteristic curve in the presence of ignorable missing data. Int Stat Rev, In press 2018.

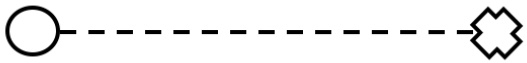
Survivors' duration bias

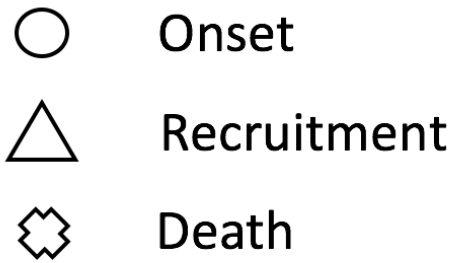
- Incident cohort: Normal cognition at initial visit, cognitive decline started later.

- Prevalent cohort: Onset of cognitive decline before entering NACC cohort.

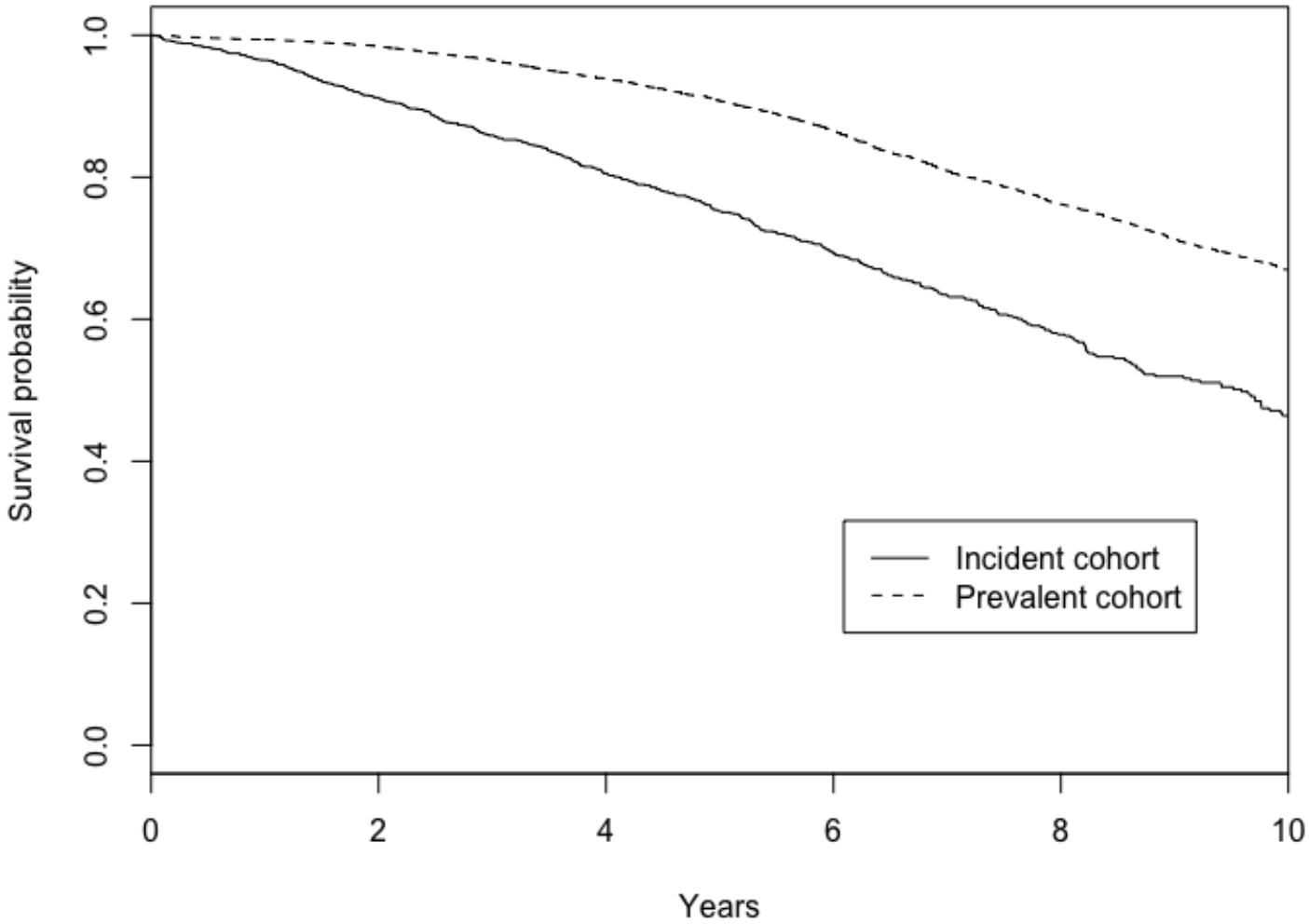


- Unobserved (truncated) individuals: Began cognitive decline but died before entering the cohort.

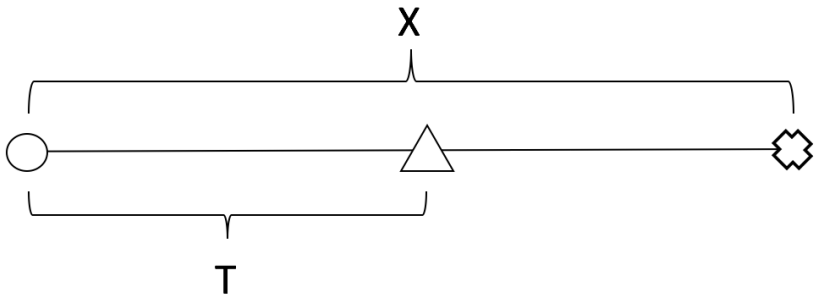




Kaplan-Meier plots using NACC data



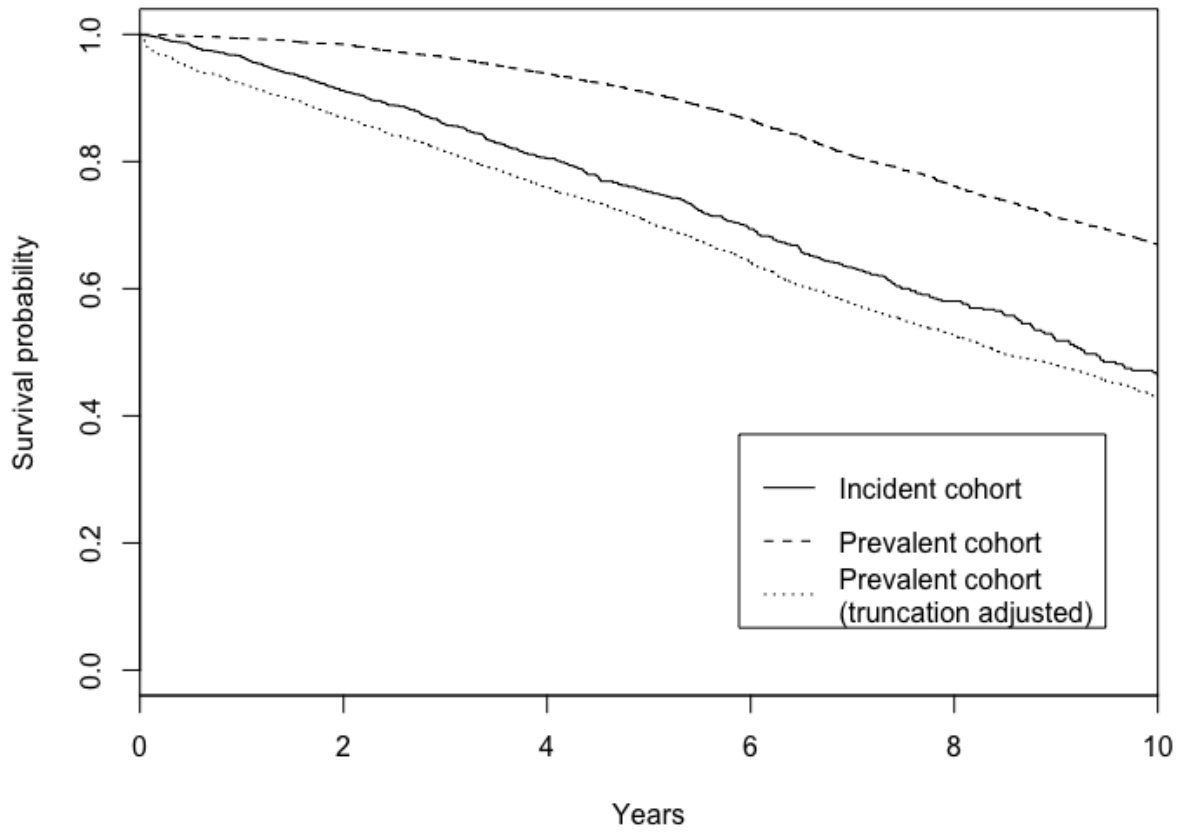
A left truncation formulation



- T: time from onset of cognitive decline to initial NACC visit.
- X: time from onset of cognitive decline to death.
- Censoring may be due to loss to follow-up, or administrative censoring (end of follow-up period).
- In a prevalent cohort, the condition $X \geq T$ is always satisfied, this is known as left truncation.

Truncation Kaplan-Meier estimator

- Kaplan-Meier estimator (for right censored data) can be modified to handle left truncation under uninformative truncation assumption.

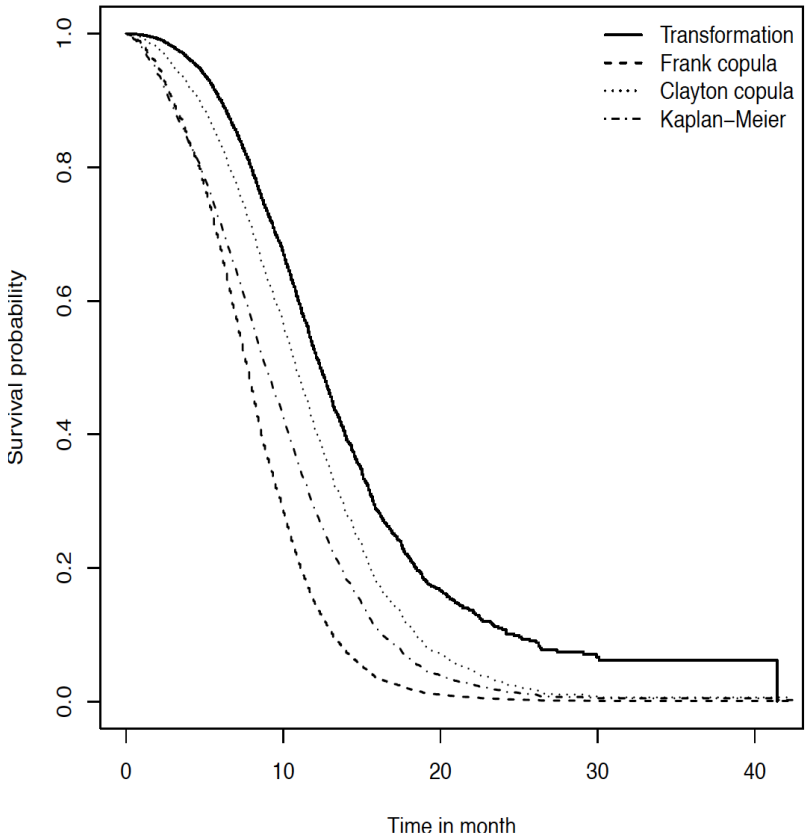


Violation of uninformative truncation

- The joint distribution of (X, T) are independent in the observable region $(X \geq T)$.
- This condition is testable, for instance, by the conditional Kendall's Tau test (Tsai, 1990; Martin and Betensky, 2005)
- For NACC data, $p > 0.05$.
- Chiou et al. (2018) considered a transformation model for dependent truncation, and applied to a subset of NACC data such that $p < 0.001$.

Dependent truncation

(d) Estimated survival curves.



Chiou et al. (2018).

Verification Bias in Diagnostic Testing

- When one is interested inassessing the accuracy of neurological tests in detecting Alzheimer's disease (AD), we ought to know the true AD status of a subject.
- The current gold standard for diagnosing the AD is by neuropathological brain autopsy.
- For many subjects, we may not have their true disease statuses either because they were still alive or that autopsy was not performed.
- When only verified sujects are used in estimation of the accuracy of diagnostic tests, the estimated accuracy of the tests may be biased. This type of bias is called verification bias.

Assumptions of Verification Process

- Missing at random (ignorable missingness): the probability of disease verification depends on test results and other observed covariates, but not on the possibly unknown disease status.
- Missing not at random (nonignorable missingness): the probability of disease verification depends on the true disease status.
- Living people may have better health status and less likely to have AD, missingness is probably non-ignorable.
- Require more stringent modeling assumptions (sometimes cannot be checked from data)

AUC estimation under nonignorable verification

- Receiver operator characteristic (ROC) plots true positive rate (sensitivity) vs. false positive rate (1-specificity) of a diagnostic test with different cut-off values.
- Area under the curve (AUC) is a summary measure of diagnostic accuracy.
- Cho et al. (2018) proposed a method for statistical inference of AUC, through parametric modeling of the validation subset. Assumptions can be checked more easily than models on the full sample (which contains the missing observations).

Other ongoing methodology work / thoughts

- Longitudinal modeling cognitive decline using different versions of neuropsychological test batteries.
- Change-point detection prior to clinical diagnosis.
- Prediction of future disease burden from neuropathology data.
- Disease progression modeling with longitudinal biomarker.
- Image biomarker analysis.

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