

Press release

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Basic information

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Department of: Public Health

Main supervisor: Erik Thorlund Parner

Title of dissertation: Time-to-event analysis under time trends or dependent censoring

Date for defence: May 5th, 2017 at (time of day): 13:00 Place: Bygning 1262 (Samfundsmedicinsk auditorium)

Press release (Danish)

Analyse af ventetidsdata under tidstrends eller afhængig censurering

Hvor stor en del af stigningen i autisme incidens kan forklares af ændringer i administrative faktorer? Hvordan analyseres registerbaserede ventetidsdata hvis udfaldet udviser en trend over kalendertid? Hvordan sikrer man sig valide resultater fra en regressionsanalyse baseret på pseudoobservationer? Disse er blot nogle af de problemstillinger et nyt ph.d.-projekt fra Aarhus Universitet, Health, forsøger at belyse. Projektet er gennemført af Stefan Nygaard Hansen, der forsvare sin ph.d. den 5. Maj, 2017.

Autisme spektrum forstyrrelser er en børnepsykiatrisk lidelse, hvori man har set en betydelig stigning i antallet af diagnoser gennem årene. Denne tendens ligger til grund for mange interessante forskningsspørgsmål – blandt andet i hvilken grad ændringer i administrative faktorer, eksempelvis diagnosekriterier, kan forklare denne stigning. Dette spørgsmål undersøges nærmere ved brug af ventetidsdata fra danske registre.

Register-baserede studier beror sig ofte på data genereret ved at rekruttere individer over kalendertid og efterfølgende monitorere dem indtil et fast sluttidspunkt. Det viser sig, at denne type af design vil føre til en afhængig censureringsmekanisme, hvis risikoen for hændelsen har ændret sig betydeligt over tid. Specielt vil antagelsen, der er nødvendig for at sikre brugen af populære estimatorer som eksempelvis Kaplan–Meier estimatoren, ikke være opfyldt. Alternative fremgangsmåder vil blive diskuteret – blandt andet en metode der baserer sig på proportionale rater samt en der baserer sig på stratifikation. Et alternativt mål for sygdomsrisikoen indenfor studieperioden bliver også foreslået.

Regressionsanalyse for ventetidsdata har primært fokuseret på modeller for hazard raten. En forholdsvis ny metode benytter sig af de såkaldte pseudoobservationer og muliggør regression af mange interessante størrelser så som overlevelsfunctioen og den årsagsspecifikke kumulative incidens. Egenskaber for estimatorer i regressionsanalyse baseret på pseudoobservationer i små stikprøver undersøges i et simulationsstudie. Baseret på disse simulationer gives retningslinjer for det nødvendige antal af hændelser per parameter i regressionsmodellen for at undgå "overfitting". For regressionsanalyse baseret på pseudoobservationer har man brug for en antagelse om totalt uafhængig censurering for at opnå estimatorer der er middelværdirette. Denne antagelse er dog i visse praktiske situationer urealistisk. En alternativ tilgang som kun behøver totalt uafhængig censurering indenfor visse strata præsenteres derfor.

Forsvaret af ph.d.-projektet er offentligt og finder sted den 5. maj kl. 13:00 i Samfundsmedicinsk auditorium (Bygn. 1262), Aarhus Universitet, Bartholins Allé 2, 8000 Aarhus C. Titlen på projektet er "Time-to-event analysis under time trends or dependent censoring". Yderligere oplysninger: Ph.d.-studerende Stefan Nygaard Hansen, e-mail: stefanh@ph.au.dk, tlf. 87168039.

Press release (English)

Time-to-event analysis under time trends or dependent censoring

How much of the increase in autism incidence can be explained by changes in administrative factors? How do you analyze register-based time-to-event data if the outcome exhibits a trend over calendar time? How do you ensure valid results from regression analysis using pseudo-observations? These are just some of the topics discussed in a PhD project carried out by Stefan Nygaard Hansen at Aarhus University, Health. The dissertation is defended May 5th, 2017.

Autism spectrum disorder is a childhood psychiatric disorder that has seen a substantial rise in the number of diagnoses over time. This tendency has spawned many interesting research questions – one of them being to what extent administrative factors, such as a change in diagnostic criteria, may explain this rise. This question is investigated in greater detail using register-based time-to-event data.

A feature common for many register-based studies is the use of data obtained by recruiting individuals over calendar time and following them until a fixed end of follow-up date. It is shown that this type of design will be subject to dependent censoring if the event risk has changed considerably over time. In particular, the assumption needed to warrant the use of popular total sample estimators, such as the Kaplan–Meier estimator, is violated. Alternative approaches are discussed, including an analysis based on proportional hazards and one based on stratification. Finally, an alternative summary measure of the disease risk within the study period is proposed.

Regression analysis for time-to-event data has mainly focused on modelling the hazard rate. A newer approach using the so-called pseudo-observations allows, however, for regression of other interesting quantities such as the survival function and cause-specific cumulative incidence. Small sample properties of estimates obtained by pseudo-observation regression are investigated in a simulation study. Guidelines for the number of events needed per parameter in pseudo-observation regression to avoid overfitting are presented.

In general, an assumption of completely independent censoring is required for the pseudo-observation method to yield unbiased estimates. This assumption may, however, in some settings be unrealistic. An alternative approach that only require completely independent censoring within some strata is discussed.

The defence is public and takes place on May 5th at 13:00 in Building 1262 (Samfundsmedicinsk auditorium), Aarhus University, Bartholins Allé 2, 8000 Aarhus C. The title of the project is "Time-to-event analysis under time trends or dependent censoring". For more information, please contact PhD student Stefan Nygaard Hansen, email: stefanh@ph.au.dk, Phone +45 8716 8039.

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