Time to Event Analysis of Arthroplasty Registry Data

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ABSTRACT

Background: Arthroplasty registry data are traditionally analysed using standard survival methods, that is, Kaplan-Meier survival curves and the Cox proportional hazards model. The outcome of interest is usually the time from the primary procedure until occurrence of a single event – revision of the prosthesis. Other outcomes may also be of interest, for example, time to death, time to receiving another arthroplasty and the association between covariates and these events. The rise in life expectancy of the population combined with an increasing number of joint replacements being performed has resulted in many patients experiencing several joint replacement procedures during their lifetime. The analyses of registry data such as these require the use of more sophisticated statistical methods. Application and evaluation of statistical methods to analyse registry data containing complex arthroplasty histories are lacking.

Aim: The aim of this thesis was to investigate the use of statistical methods in the analysis of multiple event data contained in arthroplasty registries. Within this broad aim the objectives were to investigate the use of competing risks methods in estimating the risk and rate of revision, investigate methods for handling covariates with time-varying effect, investigate the use of multi-state modelling techniques in providing a more comprehensive analysis and description of complex arthroplasty histories than traditional survival methods and to develop a notation system to facilitate the description and analysis of arthroplasty event history data.

Methods: Data were obtained from the Australian Orthopaedic Association National Joint Replacement Registry and the Norwegian Arthroplasty Register. Estimates of revision from the Kaplan-Meier method were compared to estimates from the cumulative incidence function which accounts for the competing risk of death. Effects of covariates on the rate and risk of revision were estimated with competing risk regression and compared to estimates from the Cox proportional hazards model.

Multi-state models were set up and applied to the data. The Summary Notation for Arthroplasty Histories (SNAH) was developed in order to help manage and analyse this type of data.

Results: The Kaplan-Meier method substantially overestimated the risk of revision compared to estimates using competing risks methods when the incidence of the competing risk of death was high. The influence of some covariates on the hazard rate was different to the influence on the actual probability of occurrence of the event as this was modulated by their relationship with the competing event. Multi-state models, in combination with SNAH codes, were well suited to the management and analysis of arthroplasty registry data on patients who had multiple joint procedures over time. Multi-state modelling techniques proved useful in the investigation of the progression of end-stage osteoarthritis in data from two national arthroplasty registries.

Conclusion: In the presence of competing risks, the Kaplan-Meier method may lead to biased estimates of the risk of revision, and hazard ratios obtained from the Cox proportional hazards model and competing risks regression models need to be interpreted with care. Multi-state models provide a useful tool to analyse data containing complex arthroplasty histories.

Declaration

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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Manuscripts Contributing to this Thesis

Gillam MH, Ryan P, Graves SE, Miller LN, de Steiger RN, Salter A. Competing risks survival analysis applied to data from the Australian Orthopaedic Association National Joint Replacement Registry. *Acta Orthopaedica* 2010;81(5):548-55.
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Gillam MH, Salter A, Ryan P, Graves SE. Different competing risks models applied to data from the Australian Orthopaedic Association National Joint Replacement Registry. *Acta Orthopaedica* 2011;82(5):513-20.
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Gillam MH, Lie SA, Salter A, Furnes O, Graves SE, Havelin LI, Ryan P. The progression of end-stage osteoarthritis: analysis of data from the Australian and Norwegian joint replacement registries using a multi-state model. *Osteoarthritis and Cartilage* (2012). First published online 26. December 2012. http://dx.doi.org/10.1016/j.joca.2012.12.008

Presentations Arising from this Thesis

Gillam MH. Competing Risks Survival Analysis Applied to Data from the Australian Orthopaedic Association National Joint Replacement Registry. Australasian Faculty of Public Health Medicine (AFPHM) annual meeting. Adelaide, November 2012.

Gillam MH, Lie SA, Salter A, Furnes O, Graves SE, Havelin LI, Ryan P. Investigation of the progression of end-stage osteoarthritis using data from the Australian and Norwegian joint replacement registries. Population Health Congress. "Population Health in a Changing World". Adelaide, 9-12 September 2012.

Gillam MH. Investigation of the progression of end stage osteoarthritis using data from the Australian and Norwegian joint replacement registries. School of Population Health Seminar Series. Adelaide, August 2012.

Gillam MH. Multi-state models and arthroplasty histories. AFPHM annual meeting. Adelaide, November 2011.

Gillam MH. Competing Risks Survival Analysis applied to data from the Australian Orthopaedic Association National Joint Replacement Registry. (Invited seminar) http://www.med.uio.no/imb/english/research/news-and-events/events/guest-lectures-seminars/2011/bmms-gillam.html. Seminar at Institute of Basic Medical Sciences, Faculty of Medicine, University of Oslo. Norway, October 2011.

Gillam MH, Lie SA, Salter A, Furnes O, Graves SE, Havelin LI, Ryan P. Studie av progresjon av coxartrose og gonartrose på data fra de australske og norske leddproteseregistrene (Study of progression of hip and knee osteoarthritis on data from the Australian and Norwegian joint replacment registries). Norwegian Orthopaedic Congress 2011. Oslo, Norway, 26-28 October 2011.

Gillam MH, Salter A, Ryan P, Graves SE. Regression Models for Competing Risks Applied to Data on Patients with Fractured Neck of Femur from the Australian

Orthopaedic Association National Joint Replacement Registry (AOA NJRR). Faculty of Health Sciences 2011 Postgraduate Research Conference. Adelaide, August 2011.

Gillam MH. Multi-state models and arthroplasty histories. School of Population Health and Clinical Practice Seminar Series. Adelaide, August 2011.

Gillam MH, Ryan P, Graves SE, Miller LN, de Steiger RN, Salter A. Competing Risks Survival Analysis applied to data from the AOA National Joint Replacement Registry. The 70th Annual Scientific Meeting of the Australian Orthopaedic Association. Adelaide, 10-14 October 2010.

Gillam MH, Ryan P, Graves SE, Miller LN, de Steiger RN, Salter A. Competing Risks Analysis Applied to Joint Replacement Registry Data. Faculty of Health Sciences 2010 Postgraduate Research Conference. Adelaide, September 2010.

Gillam MH. Competing risks survival analysis applied to data from the AOA National Joint Replacement Registry. School of Population Health and Clinical Practice Seminar Series. Adelaide, August 2010.

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Abbreviations

AOANJRR:	Australian Orthopaedic Association National Joint Replacement Registry
CIF:	Cumulative Incidence Function
Cox PH:	Cox Proportional Hazards
CPR:	Cumulative Percent Revision
FNOF:	Fractured Neck of Femur
HR:	Hazard Ratio
KM:	Kaplan-Meier
NAR:	Norwegian Arthroplasty Register
OA:	Osteoarthritis
RD:	Relative Differences
SNAH:	Summary Notation for Arthroplasty Histories
SubHR:	Subdistribution Hazard
THA:	Total Hip Arthroplasty
TKA:	Total Knee Arthroplasty