

Comparison of modelling approaches for network meta-analysis of time-to-event outcomes to aid decision making

Suzanne Freeman^{1,2}, Nicola Cooper^{1,2}, Alex Sutton^{1,2}, Neil Hawkins^{2,3}

Cochrane Colloquium, 17th September 2018

suzanne.freeman@leicester.ac.uk

¹ Biostatistics Research Group, Department of Health Sciences, University of Leicester, UK, ² NIHR Complex Reviews Support Unit ³ Health Economics & Health Technology Assessment, University of Glasgow



Conflicts of Interest

I have no actual or potential conflicts of interest in relation to this presentation.

Funding

The Complex Reviews Support Unit (CRSU) is funded by the National Institute for Health Research (project number 14/178/29).

The views and opinions expressed herein are those of the authors and do not necessarily reflect those of NIHR, NHS or the Department of Health.



Background

- Time-to-event data is often summarised as a single hazard ratio (HR)
- HRs are then synthesised in pairwise or NMA
- Estimated HRs represent an 'average' of the HR over the study duration
- A constant HR may not be appropriate if the treatment effect varies over time
 - May be confounded by differences in study duration



Cervical Cancer Network

 Overall survival data from 5922 patients from 37 RCTs



RT = radiotherapy, CTRT = chemoradiation, CT+RT = chemotherapy and radiotherapy, CT+S = chemotherapy and surgery





Naïve comparison averages down the column

Indirect comparison estimates and synthesises relative treatment effects across the rows











Royston-Parmar



RT = radiotherapy, CTRT = chemoradiation, CT+RT = chemotherapy and radiotherapy, CT+S = chemotherapy and surgery, KM = Kaplan-Meier



Generalised Gamma



RT = radiotherapy, CTRT = chemoradiation, CT+RT = chemotherapy and radiotherapy, CT+S = chemotherapy and surgery, KM = Kaplan-Meier



Other approaches

- Piecewise Exponential
- Fractional Polynomial
- Other parametric approaches:
 - Log-logistic
 - Weibull



Considerations for choosing between models

- Risk of over fitting (e.g. is the model highly parameterised?)
- Are user-defined parameters required? (e.g. time intervals, number of knots)
- Reliability of estimation (e.g. is model sensitive to starting values?)
- Reliability of extrapolation (e.g. what happens when number of events is small?)
- Interpretability of parameters
- Ease of comparison back to individual trials



Acknowledgements

The authors would like to thank the Chemoradiotherapy for Cervical Cancer Meta-analysis Collaboration (CCC-MAC) and the Neoadjuvant Chemotherapy for Cervical Cancer Meta-analysis Collaboration (NAC-CCMAC) who brought together the individual participant data for the meta-analyses used in the case studies, and the groups that contributed to these meta-analyses for permission to use data from their trials for this research. The contents of this presentation and the methods used are, however, the sole responsibility of the authors and do not necessarily represent the views of the meta-analyses collaborative groups or the trial groups listed. CCCMAC: Gynecologic Oncology Group, USA; Yale University School of Medicine; Cross Cancer Institute and University of Alberta, Canada; Instituto de Radiologa y Centro de Lucha Contra el Cancer, Uruguay; University Medical Center Groningen and University of Groningen, Netherlands; Institute for Oncology and Radiology of Serbia; Toronto Sunnybrook Cancer Center, Canada; First Teaching Hospital, China; Acybadem Oncology and Neurological Science Hospital, Turkey; Sanjay Gandhi Postgraduate Institute of Medical Sciences, India; Chiang Mai University, Thailand; University of Yamanashi, Japan. NACCCMAC: MRC Clinical Trials Unit, UK MRC CECA; Libera Universita "Campus Bio-Medico" di Roma, Italy; Buenos Aires University, Argentina; Royal Marsden Hospital, UK; Centro Estatal de Cancerologia, Mexico; Chang Gung Memorial Hospital, Taiwan; Istituto Nazionale per la Ricerca sul Cancro, Italy; Institut Bergonie, France; Derbyshire Royal Infirmary, UK; Tottori University School of Medicine, Japan; All India Institute of Medical Sciences, India, Hospital Pereira Rossell, Uruguay; City Hospital Birmingham, UK; Hopital General de Montreal, Canada; The Norwegian Radium Hospital, Norway; Leicester Royal Infirmary, UK; University of Sydney, Australia.

