Economic analysis of health services: developing methods to identify, investigate, and disseminate best clinical practice

Authors: Jonathan Karnon, Clarabelle Pham, Orla Caffrey, Paul Hakendorf, David Ben-Tovim, Maria Crotty

Email: jonathan.karnon@adelaide.edu.au

Abstract

The growing availability of linked routinely collected data provides opportunities to observe use of health care services by individuals over time. In the hospital setting, such data can be used to compare services delivered for specific diagnoses by different hospitals.

This paper describes a novel methodology for the risk adjusted cost-effectiveness (RAC-E) analysis of alternative forms of service delivery for specific conditions. A decision analytic framework is used to estimate lifetime costs and survival for individual patients, which are then analysed to generate per patient estimates of expected lifetime costs and survival. Differences between observed and expected costs and survival inform estimates of the net benefits of services provided at different hospitals for similarly diagnosed patients.

The methodology is illustrated using a case study analysis of services for patients presenting at hospital with chest pain. Comparing services provided by four public hospitals in South Australia, significant differences in risk adjusted costs and life years were estimated. Such results require careful interpretation, but may provide a basis for more detailed investigation of the potential causes of such differences, and lead to dissemination of best practice within jurisdictions.

1. Introduction

Comparative analysis of hospital performance has generally focused on comparisons between hospitals at an aggregate level, i.e. comparing inputs and outputs across the whole of the hospital.(AHRQ, 2008; Hollingsworth, 2008) Hollingsworth is moderately optimistic regarding the ability of such analyses to identify inefficient hospitals, particularly if multiple techniques identify the same inefficient organizations.(Hollingsworth, 2008) Such efficiency studies may identify managerial variables that impact on efficiency, for example, the percentage of outpatient services, and hospitals' debt–equity ratio.(Chen et al, 2005) The results of these analyses may be used for public reporting and/or pay-for-performance, which may provide sufficient incentives to identify and act upon potential causes of inefficiency.

However, different hospitals are likely to have different areas of expertise and inefficiencies in one area may not be reflected in another.(Mukamel et al, 2002) If, for example, outpatient services are negatively associated with efficiency, an across the board reduction in outpatient services is unlikely to be the optimal response. Targeted responses are likely to be more cost-effective.

Linked routinely collected data provide a valuable data source to inform comparative cost-effectiveness analyses of the delivery and organisation of hospital services for specific diagnostic groups. Such analyses may identify best practice hospitals with respect to specific diagnoses, leading to investigation and dissemination of care pathways at these hospitals. To usefully inform such analyses, linked data sources must include linkages between hospital records and population mortality records, but until recently such data have been available in only a few geographical locations.(Brook, 2009)

The use of routinely collected data to evaluate applied models of care requires methods of analysis that can adequately extrapolate the likely costs and outcomes of the individual subjects, whilst controlling for differences in relevant patient level risk factors to ensure that one hospital does not appear superior to another simply on the basis of their treating subjects with differing casemix. This paper describes a general methodology for using linked routinely collected data to analyse the risk adjusted cost-effectiveness (RAC-E) of the delivery and organization of hospital services for specific diagnoses. To illustrate the application of the framework, the methodology is described with reference to a case study evaluation of services for patients presenting at hospital with chest pain.

1. The framework

The general approach uses a decision analytic framework to extrapolate observed costs and intermediate endpoints to estimate lifetime costs and survival for individual patients presenting with a specific diagnosis within a defined time period. These lifetime estimates are analysed to predict expected lifetime costs and survival, which are compared to the extrapolated lifetime costs and survival to inform estimates of the net benefits of services provided for specific conditions at different hospitals. The following methods sections describe available data in South Australia and the linkage process; the identification of diagnostic areas for investigation; the decision analytic framework; the estimation of the input parameters; and the baseline and sensitivity analyses of the full model.

2.1 The data

The following sets of routinely collected data were obtained to inform RAC-E analyses:

- 4,072,341 records from the Integrated South Australian Activity Collection (ISAAC), which contains information on all hospital separations (public and private) in SA from July 2001 to June 2008. These data describe patient, admission, and inpatient stay characteristics, as well as providing ICD-10 categorised data on principle and additional diagnoses and procedures.

- 1,530,634 cost estimates submitted to SA Health describing separation-specific costs for all separations at the four largest SA hospitals from July 2001 to June 2008. For each separation, resource use in 17 categories has been recorded, to which unit costs were attached to estimate total costs for each separation.

- 92,288 deaths from the South Australian Register for Births, Deaths, and Marriages between July 2001 and December 2008.

Multiple separations for individual patients were linked within the ISAAC dataset using common patient identifiers (i.e. a deterministic linkage process). The cost data contained identifiers that matched directly to specific inpatient separations, and so no linkage was required. Linkage of the ISAAC data to the Register for mortality data was undertaken by staff within the State Department of Health, using probabilistic linkage combined with clerical review.

2.2 Identifying areas for investigation

As in the provision of health technologies, there is a need to prioritise research efforts. To identify areas of hospital activity with potentially important and identifiable differences in service provision between

hospitals, the assembled dataset was analysed to identify Australian Refined Diagnosis Related Groups (AR-DRGs) with the greatest:

- variation in numbers of separations over time (indicating changes in practice),
- variation in contemporary separation costs and length of stay between hospitals (indicating variation in practice), and/or
- aggregate annual costs (indicating importance of the diagnostic group with respect to potential gains in efficiency).

The reported case studies were chosen primarily on the basis of the data presented in Table I. Chest pain patients represent patients who were admitted to hospital with chest pain, but for whom no definitive diagnosis was established. Identification of this group is informed by a combination of relevant AR-DRG and ICD-10 codes (see Table I for definitions). The data shows a large increase in admission rates (+75%). The total costs expended are significant, and the mean costs of the most costly hospitals were approximately double the costs of the least costly hospital. Local clinicians advised that variation in SDO was a likely explanation of the observed cost differences.

Table I Summary analysis of separation cost data for patients with stroke and chest pain diagnoses at the four main public hospitals in South Australia in 2005/6

Diagnostic code*	No. seps (2002/3)	No. seps (2006/7)	% increase separations	Mean cost (2006/7)†	Total patient cost (2006/7)	Minimum mean cost (2006/7)‡	Maximum mean cost (2006/7)‡	% Difference (Max – Min)
Chest pain patients (using AR-DRG and ICD-10 codes)								
F74Z & R07	2,324	4,259	83%	$1,176	$5,008,584	$780	$1,424	83%
F42B & R07	497	674	36%	$2,584	$1,741,616	$2,319	$5,037	117%
Total	2,821	4,933	75%	$1,369	$6,753,277	$870	$1,599	84%

*F74Z (AR-DRG) – chest pain; F42B (AR-DRG) – Circulatory Disorders W/O AMI W Invasive Cardiac Inves Proc W/O Complex DX/Pr; R07 (ICD-10) – chest pain
† across all hospitals
‡based on mean costs at each included hospital

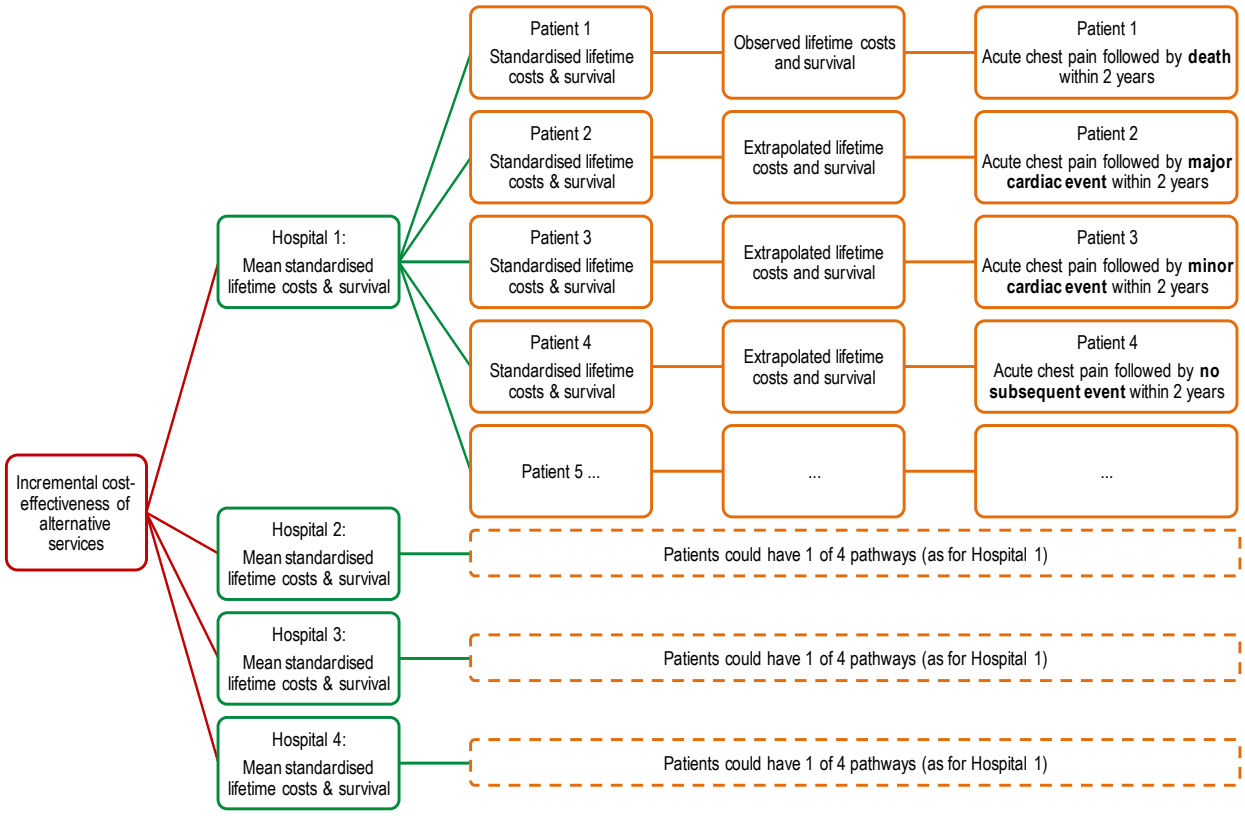
2.3 Defining the decision analytic framework

A decision analytic framework facilitates extrapolation of observed costs and health effects according to the status of each patient at the end of a defined observation period beyond the separation of interest (e.g. a stroke separation). A relatively simple model structure was defined, whereby lifetime costs and survival are estimated directly from the defined intermediate endpoints (accounting for differences in

patient and event characteristics). Figures 1 illustrates the models used in the chest pain analyses. The intermediate endpoints differentiated between hospital admissions for major and non-major non-fatal cardiac diagnoses. Alternatively, patients may die prior to experiencing any of the defined intermediate endpoints, or remain alive without subsequent related hospital admissions. The choice of intermediate endpoints was informed by published decision analytic models,(Karnon et al, 2005 & 2007) and discussions with local stroke and cardiac clinicians.

The definition of major and non-major cardiac diagnoses was based on a survey of local clinicians, as well as analyses of the linked dataset – looking at mortality rates following different cardiac events, as defined by AR-DRG and ICD-10 codes.

Figure 1 Decision analytic model structure



A longer observation period provides a more accurate assessment of the impact of service delivery on intermediate endpoints at different hospitals, and may facilitate the population of a more complex model structure, for example representing the occurrence of multiple relevant health events. The trade-

off is that as the observation period lengthens, the relevance of the comparative analyses to contemporary services declines.

The length of the observation period should consider the characteristics of the condition being evaluated, for example, is there a recognised post-acute interval over which patients are at increased risk of related events? For vascular conditions, published models have differentiated between risks in the first year post-event, and subsequent years.(Karnon et al, 2005 & 2007).

Additional factors that may affect the defined duration of the observation period are time points at which significant structural changes to services occurred. If the comparative analysis is limited to a small number of hospitals, it may be possible to consult with the individual hospitals to identify particular dates at which changes occurred (e.g. the introduction of a specialized services or wards for patients with the diagnosis of interest).

In chest pain analyses, an observation period of 2 years was chosen – the eligible patient groups comprised patients with the respective principal diagnoses admitted in the year to July 2006. The sensitivity of the results to the defined observation period can be analysed by changing the follow-up period, for example, analyses of patient admitted in the year to July 2006 with follow-up shortened to July 2007, and of patients admitted in the year to July 2007 (with follow-up to July 2008) could be undertaken.

2.4 Parameter estimation

The parameter estimation stage involves two broad tasks. Firstly, estimates of costs incurred, and life years gained, beyond each of the defined intermediate endpoints are required for each patient. Secondly, having estimated lifetime costs and survival, regression models are fitted to predict expected lifetime costs and survival for each patient.

Extrapolated costs and survival

Extrapolated costs and survival may be estimated using an external data source, for example, data describing costs and outcomes in patients experiencing the different intermediate endpoints who were treated at a separate set of hospitals to those included in the analysis. If available, the relevance of patient-level data from jurisdictions other than that of interest to the RAC-E analysis needs to be considered.

Alternatively, existing prognostic models that predict costs and outcomes following the intermediate endpoints may be used. In addition to issues regarding relevance of data external to the jurisdiction of interest, the value of such models is dependent on the availability of data to populate the models, i.e. if one or more of the prognostic model parameters are not recorded routinely in the jurisdiction of interest then it may not be possible to generate predictions from the prognostic models.

In the absence of relevant external data, routinely collected data from the hospitals included in the RAC-E analysis were used to inform extrapolated costs and survival. In the South Australian analysis, data from an extended time period were available (i.e. July 2001 to June 2008). Patients with a hospital admission in the Major Diagnostic Category: Diseases and Disorders of the Circulatory System, in the year prior to a chest pain admission were excluded in order to focus on chest pain that was unlikely to be related to recently treated heart disease. The 45,019 eligible patients presenting between July 1, 2002 and June 30, 2008 were categorized according to the defined intermediate endpoints (minor cardiac event, major cardiac event, no subsequent event, or dead within 2 years of chest pain admission).

Regression models were fitted to each dataset to predict subsequent survival and associated costs. Parametric survival analyses informed survival functions for each of the three groups, using spline functions to represent multiple points of inflexion.(Royston, 2001; Royston and Parmar, 2002) A comprehensive model selection process was undertaken, testing covariates describing:

- socio-demographics (age, sex, and a range of postcode defined socioeconomic variables),
- type of cardiac (intermediate) event, and
- 44 ICD-10-based co-morbidity variables.(Duckett et al, 2008)

The hospital separations data were formatted to represent the costs incurred by patients in each full year alive beyond the date of their intermediate endpoint. These data were initially analysed to identify significant cost differences in sequential years following each intermediate endpoint. On this basis, separate cost models were estimated for the first year, and for subsequent years following the cardiac endpoints.

Annual cost estimates were informed by a two-stage modeling process. Firstly, logistic regression models estimated the probability of patients incurring a positive cost (i.e. experiencing a cardiac-related hospital admission). Secondly, generalized linear models (GLMs) estimated the cost magnitude, given a

positive cost incurred. The GLM models tested the appropriateness of the four main distribution families (Gaussian, Poisson, Gamma, Inverse Gaussian) and different link functions ranging from -1 to +1.(Doshi and Glick, 2009)

Annual survival probabilities for each patient were derived from the estimated survival functions, to which annual cost estimates and a relevant discount rate were applied. The discounted annual costs and survival probabilities were summed over patient-specific time horizons, equal to 100 years minus patient age at the time of their initial chest pain admission, and added to the costs incurred and life years gained up to and including each patient's intermediate endpoint.

Standardising costs and survival

The extrapolated lifetime costs and survival for each eligible patient were standardised by comparing the extrapolated parameters for each patient with the lifetime costs and survival that would be expected at the time of the initial chest pain admission, based on relevant patient characteristics.

A GLM was fitted to estimate expected lifetime costs. The distribution of lifetime survival included a flat region around the end of the two year observation period, meaning that parametric survival models could not adequately represent the data. A two-phase modelling approach was applied, using a logistic model to estimate the probability that patients survived the first three years post-event, followed by two separate GLM models that estimated survival times within the initial three years, and beyond the initial three years. Explanatory variables were observable at the time of the initial chest pain admission, including a vector of dummy variables for the four hospitals included in the analysis.

A potential issue with the use of extrapolation datasets that include patients and hospitals to whom the extrapolated parameter values will be applied, is that the analysis of expected values for certain patient sub-groups may be overly influenced by individual hospitals. As an example, if one hospital treats a high proportion of the most severe cases, then the expected costs and survival for those patients will reflect services provided at that hospital, and so will be artificially similar to the extrapolated costs and survival of that hospital.

The likelihood of this being a significant issue can be assessed by analyzing the distribution of the model covariates between the hospitals, with Chi squared tests presented to identify significant differences. The sensitivity of the results to the omission of data from particular hospitals can also be addressed in the presented analyses, as discussed below.

In analyses with access to patient data from a larger number of hospitals (compared to the 4 used in the current analysis), it may be advisable to use hierarchical modeling techniques that control for non-modifiable hospital level factors that may influence costs and/or outcomes, such as hospital teaching status and hospital size.

2.5 Analysis

The main analysis compares the mean estimates of extrapolated and expected lifetime costs and survival for each patient. Subtracting expected values from the extrapolated estimates for each patient, and analyzing with respect to hospital attended, identifies hospitals that incur more or less costs, and whose patients gain more or less life years, than would be expected given the mix of patients attending each hospital. Differences in the 'observed minus expected' cost and survival estimates between hospitals can be interpreted as risk adjusted differences in costs and survival: if costs incurred by patients at hospital A are $300 more than expected, whilst costs incurred by patients at hospital B are $200 less than expected, then the risk adjusted difference in per patient costs between hospitals A and B is $500.

Tables II presents the mean results from the chest pain analysis. Ordered in increasing magnitude of observed over expected effects, incremental cost-effectiveness ratios (ICERs) can be estimated between the analysed hospitals. The results show that two hospitals are dominated, with hospital 4 gaining life years at an additional cost of $2,909 compared to hospital 2.

Table 2 Reference case results

		Observed minus Expected		
Hospital	Separation costs*	Costs	Life years	ICER
3	$1,474	$290	-0.04594	Dominated
2	$1,233	-$489	-0.04588	
4	$732	$17	-0.03038	Dominated
1	$1,589	-$65	0.10012	$2,909

* unadjusted separation costs

Two main forms of sensitivity analysis are undertaken. Firstly, a deterministic analysis of the impact of individual hospitals on the results can be undertaken. This process involves multiple re-fitting of the cost and survival extrapolation models, excluding data from one of the included hospitals in sequence. For each set of re-estimated extrapolation models, the expected costs and survival models are re-fitted and

the final analysis of the observed minus expected costs and survival for each hospital is undertaken. These analyses assess the extent to which data from individual hospitals influence the results (and have not been undertaken yet).

The second form of sensitivity analysis is equivalent to a probabilistic sensitivity analysis, based on bootstrapping at each stage of the analysis (sampling with replacement a dataset of equal size to the original dataset). Each of the three datasets informing the extrapolation models are bootstrapped, and the cost and survival models are refitted. Similarly, the resulting dataset of lifetime costs and survival for patients presenting in the eligible time period (e.g. 2005/6 for the stroke and chest pain analyses) is bootstrapped. The summed estimates of observed minus expected costs and survival for each hospital are recorded for each set of bootstrapped analyses, which can then be analysed to estimate credible intervals around the ICERs and incremental net benefits between the hospitals, as well as to plot cost-effectiveness acceptability frontiers and pairwise acceptability curves.

Figure 2a present the acceptability curves for all four hospitals, which shows that Hospital 4 has the largest expected net benefits (ENBs) and over a 90% probability of being cost-effective at a life year value of $50,000 (the threshold used by the Pharmaceuticals Benefits Advisory Committee in Australia). Other than Hospital 4, Hospital 2 has the highest expected net benefits at all other life year dollar values, and so Figure 2b presents 'two hospital preferred' acceptability curves, with comparison restricted to Hospitals 2 and 4. On this basis, Hospital 4 has a 95% probability of being the most cost-effective hospital at a threshold value of $50,000.

Figure 2a Cost-effectiveness acceptability frontier for chest pain analysis

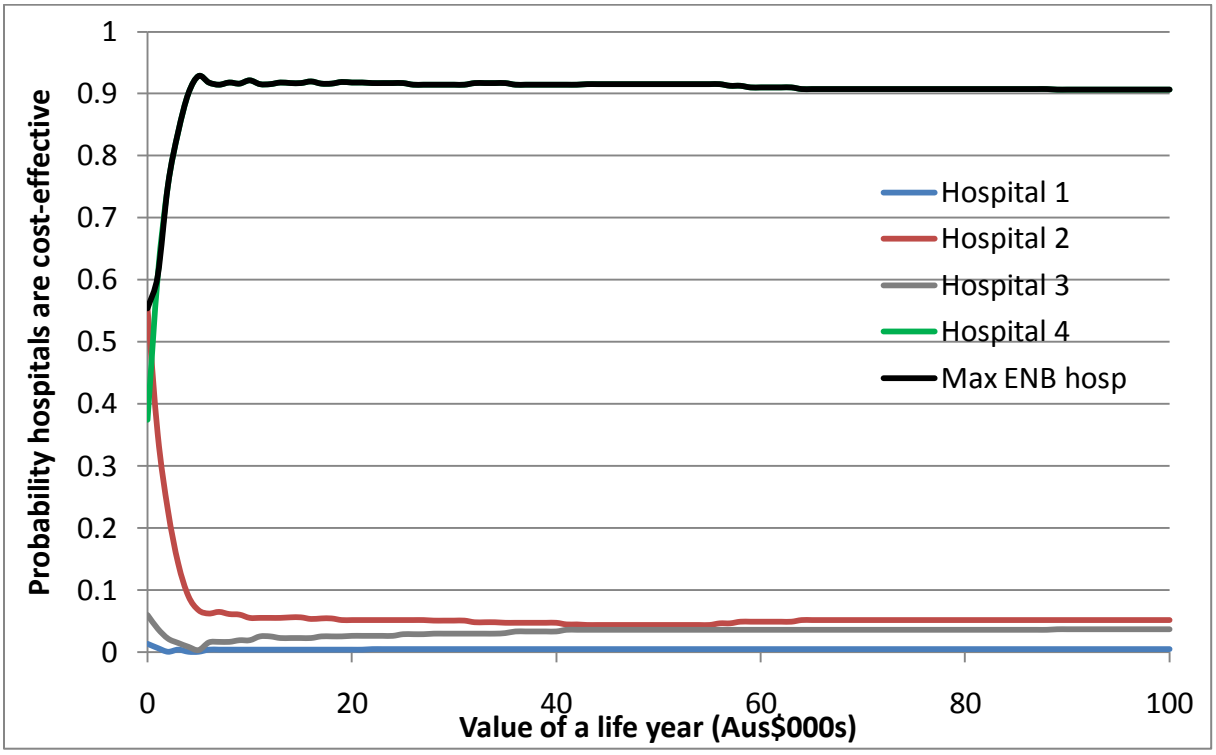
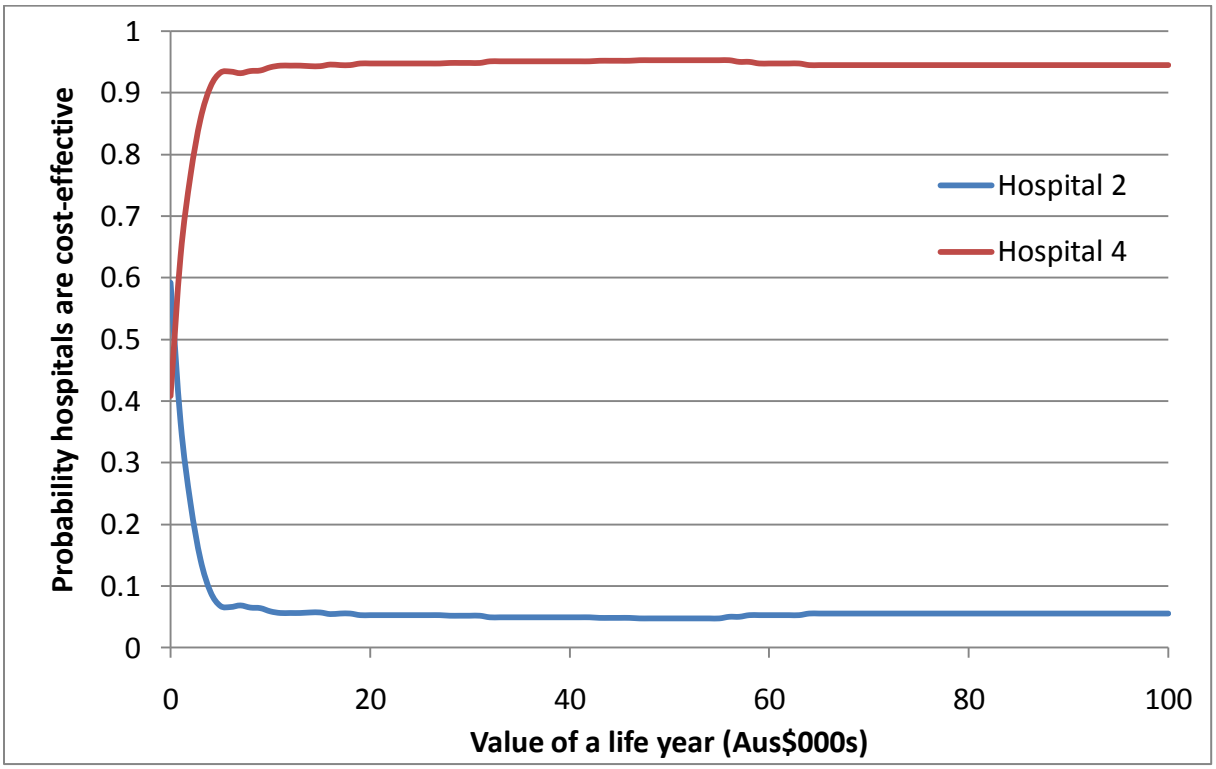


Figure 2b C-E acceptability curves for two hospital chest pain comparison



3 Discussion

This paper has described a new method for comparing hospital performance at a diagnostic condition level that produces long-term estimates of the differences in costs and effects associated with services delivered at alternative hospitals. Within an eligible population, defined with respect to diagnosis and date of hospital admission, costs incurred and outcomes are observed over a relatively short time horizon, from which point a decision analytic framework is used to extrapolate costs and outcomes to a lifetime horizon. The outputs control for differences in the risk profile or characteristics of patients treated at different hospitals, hence the term risk-adjusted cost-effectiveness (RAC-E) analysis.

RAC-E analyses provide a good indication of differences in the cost and quality of services delivered at different hospitals, but uncertainty around the estimated ICERs is inevitable. The presented sensitivity analyses may provide some assurance around the robustness of the mean ICERs, but the RAC-E analyses should be viewed as a first hurdle to the conduct of further, more detailed investigations of SDO at different hospitals. We envisage that the results of a RAC-E analysis would be discussed by relevant clinicians and policy makers, in the context of the limitations of the data, and potential determinants of differences in costs and quality, to inform a decision about whether the estimated differences in RAC-E warrant further investigation. If no further action is warranted, the analysts move onto the next case study. If investigation is required, what form might such investigations take?

Investigations are likely to be qualitative in nature, assessing differences in applied clinical pathways between hospitals, covering issues such as clinical management, clinical and non-clinical resource management, clinical audit, and financial management within relevant Departments. Process mapping provides a useful tool that describes the patient journey as an end-to-end sequence of all the steps required to provide clinical care for a patient, which can be developed as a group documenting the patient journey step by step, or by a series of interviews.(Victorian Quality Council, 2007) Such approaches have been applied in similar circumstances, including work around Redesigning Care to improve patient flows.(Ben-Tovim et al, 2008a & 2008b) It may also be important to consider out-of-hospital services that are available to some or all of the patient cohorts attending different hospitals, and so it may be necessary to undertake similar mapping processes to describe patient pathways post-discharge.

We are currently undertaking a critical pathway analysis of chest pain patients presenting at two fo the four analysed hospitals in South Australia.

What's wrong with guidelines?

Critics might argue that such evaluation and investigation is not necessary because clinical guidelines already provide sets of recommendations regarding sequential steps in the process of diagnosing, treating, and monitoring conditions. Where clinical guidelines are available, hospitals should simply implement the guidelines.

Evidence underpinning clinical guidelines is generally variable, for example, breast cancer guidelines have high level evidence around the use of systemic therapies, but poor evidence around processes for diagnostic staging and monitoring.(NICE, 2009) It is also the case that guidelines evaluate actions at different stages of the patient journey in isolation. Studies evaluating the effects of published guidelines have essentially assessed the combined effects of guideline content and an associated implementation or dissemination strategy, and few of these studies have assessed the effect of guidelines on patient outcomes.(Lugtenberg et al, 2009) Controlled evaluation of alternative sets of procedures along a care pathway is generally infeasible due to the complexity of the pathways.

In clinical areas with guidelines based on high level evidence, and with high levels of guideline utilization, the following factors may still contribute to differential costs and outcomes:

- Service delivery and organization issues that are not covered by guidelines, for example, specific content of rehabilitation processes and discharge advice, dietary intake and nutrition monitoring, etc.

- Differences in the application of services recommended by guidelines due to, for example, differences in surgical expertise, timeliness of clinical review, etc.

However, studies have shown great variability in the uptake of clinical guidelines,(Grol et al, 2003; Grimshaw et al, 2004) which is related to a host of factors around the development, content, and implementation of guidelines, as well as contextual, organisational and cultural factors.(Lugtenberg et al, 2009; Quaglini, 2008)

The RAC-E analytic process described in this paper provides valuable information across all of the above scenarios. In areas of high level evidence and utilization, RAC-E analyses may provide some validation of the guidelines if no significant differences between hospitals are estimated, or they may lead to the identification of differential effects factors that have not been adequately captured by existing

guidelines. If investigation of observed differences in RAC-E identify that hospitals with better guideline utilization are performing more efficiently, such data again validates the guidelines and may provide impetus to implement guidelines.

In other clinical areas, guidelines may not exist and RAC-E analyses provide an opportunity to assess the extent and impact of variation in practice, which may indicate a need for guideline development. It may be difficult or infeasible to develop guidelines in some areas due to a lack of high level evidence, and so condition-specific RAC-E analyses and investigations provide an alternative process for identifying best practice.

Limitations

The RAC-E methodology is subject to some limitations, which are a consequence of using routinely collected data. There are potential data quality issues around the use of such data, for example, the South Australian hospital separations data is extracted from patient records by teams of data extractors based at each hospital. The quality of the extracted data may vary with respect to the characteristics of the doctors who record information in the records, as well as with the experience of the coders, though these errors may be assumed to be randomly distributed. However, there are also some incentives related to the coding process, which informs a significant proportion of each hospitals budget, and this may result in some non-random variation in coding. Audits provide some assurance of coding quality, but uncertainty around data quality remains. However, as linked data becomes more widely used and valued, greater emphasis will be placed on improving quality, hopefully leading a 'good-natured circle' of increased analysis of routine data and improvements in data quality.

The case study applications described in this paper relied on imperfect data linkage processes, and the data only went up to July 2008, which may reduce the relevance of the results to current practice. At a local level, in South Australia and the Northern Territory, the SA-NT Data Linkage Consortium is an operational body that has secured access to hospital separations and emergency department data, and population-based mortality records. Such bodies have the resources to apply state of the art linkage techniques, and provide more rapid access to contemporary data, which will improve the validity of RAC-E analyses in the future.

The analysis to date includes only inpatient health care data, which may mean the analysis is omitting important aspects of outpatient and/or out-of-hospital health care that may explain some of the estimated differences in long-term costs and outcomes. The quantitative analysis would be stronger

using a wider range of routinely collected health care data, but in their absence the described analytic framework can still provide a useful indication of differences in the costs and outcomes associated with services for specific conditions provided at alternative hospitals. As proposed, a secondary process of qualitative investigation would identify any relevant omitted factors, which may inform re-analyses of RAC-E, e.g. inserting costs associated with specific out-of-hospital programs. This is also an area for methodological development, and the use of instrumental variables may also improve the analytic framework.(Bascle, 2008)

Conclusions

The RAC-E methodology presented in this paper should be viewed as a complement to conventional efficiency analyses, which measure efficiency at an aggregate hospital level. The RAC-E method is designed to be applied at a condition level. By estimating differences between hospitals with respect to long-term incremental costs and benefits, decisions around dissemination of best practice can be made using the same metrics as decisions around the funding of new health technologies (incremental cost-effectiveness).

Pragmatic interpretation of the results of RAC-E analyses is required, accounting for uncertainties around data quality, and costs and effects not captured by the available data. However, such issues should diminish as linked routinely collected data becomes more widely available. Moreover, the described methodology provides a means of extracting some of the significant benefits that arise from the use of data that represents real life activity on a large scale and overcomes traditional data issues such as self selection bias.(Stanley and Meslin, 2007)

References

Agency for Healthcare Research and Quality. 2008. *Health Care Efficiency Measures: Identification, Categorization, and Evaluation*. Publication No. 08-0030, Rockville, MD. http://www.ahrq.gov/qual/efficiency/ (accessed 7 September 2010)

Hollingsworth B. 2008. The measurement of efficiency and productivity of health care delivery, *Health Economics*; 17:1107–1128

Chen A, Hwang Y, Shao B. 2005. Measurement and sources of overall and input inefficiencies: Evidences and implications in hospital services, *European Journal of Operational Research*; 161:447–468

Mukamel D, Zwanziger J, Bamezai A. 2002. Hospital competition, resource allocation and quality of care. *BMC Health Services Research;* 2(1): 10–18.

Brook E, *The Lonely Planet Guide for Data Linkage*, http://www.health.sa.gov.au/Default.aspx?tabid=406 (accessed 7 September 2010)

Karnon J, Brennan A, Pandor A, Fowkes G, Lee A, Gray D, et al. 2005. Modelling the long term cost effectiveness of clopidogrel for the secondary prevention of occlusive vascular events in the UK, *Current Medical Research and Opinion*; 21(1):101-12

Karnon J, Goyder E, Tappenden P, McPhie S, Towers I, Brazier J, Madan J. 2007. A review and critique of modelling in prioritising and designing screening programmes, *Health Technology Assessment*;11(52)

Royston P. 2001. Flexible parametric alternatives to the Cox model. *Stata Journal*; 1(1): 1–28.

Royston P, Parmar MKB. 2002. Flexible parametric-hazards and proportional odds models for censored survival data, with application to prognostic modelling and estimation of treatment effects. *Statistics in Medicine*; 21:2175–2197

Duckett S, Coory M, Kamp M, Collins J, Sketcher-Baker K, Walker K. 2008. *VLADs for Dummies (Queensland Health Edition)*, Wiley Publishing Australia Pty Ltd

Doshi J, Glick H. 2009. *Applications of Statistical Considerations in Health Economic Evaluations*, http://www.uphs.upenn.edu/dgimhsr/ispor09.pmsc.htm (accessed 7 September 2010)

Victorian Quality Council, Process mapping. 2007. *A guide for health service staff*, http://www.health.vic.gov.au/qualitycouncil/downloads/process_mapping.pdf

Ben-Tovim DI, Bassham JE, Bennett DM, Dougherty ML, Martin MA, O'Neill SJ, Sincock JL, Szwarcbord MG. 2008a. Redesigning care at the Flinders Medical Centre: clinical process redesign using "lean thinking", *Medical Journal of Australia*; 188 (6 Suppl): S27-S31

Ben-Tovim DI, Dougherty ML, O'Connell TJ, McGrath KM. 2008b. Patient journeys: the process of clinical redesign, *Medical Journal of Australia*; 188 (6 Suppl): S14-S17

National Institute for Clinical Excellence. 2009. Early and locally advanced breast cancer. Diagnosis and treatment, *NICE clinical guideline 80*, February 2009

Lugtenberg M, Burgers JS, Westert GP. 2009. Effects of evidence-based clinical practice guidelines on quality of care: a systematic review, *Qual Saf Health Care* 2009;18:385-392

Grol R, Grimshaw J. 2003. From best evidence to best practice: effective implementation of change in

patients' care. *Lancet*; 362(9391):1225-1230

Grimshaw JM, Thomas RE, MacLennan G, Fraser C, Ramsay CR, Vale L, et al. 2004. Effectiveness and efficiency of guideline dissemination and implementation strategies, *Health Technol Assess*; 8(6)

Quaglini S. 2008. Compliance with Clinical Guidelines, in *Computer-Based Medical Guidelines and Protocols: A Primer and Current Trends* (eds. ten Teije A, Miksch S, Lucas P), IOS Press

Bascle G. 2008. Controlling for endogeneity with instrumental variables in strategic management research, *Strategic Organization*; 6(3): 285-327

Stanley FJ, Meslin EM. 2007. Australia needs a better system for health care evaluation, *Medical Journal of Australia*; 186(5):220-1