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HEDS NEWSLETTER Winter 2011

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WELCOME FROM THE NEW DIRECTOR

As ever, there is a lot to say about the work that we are doing within HEDS, but first I must say a big 'thank you' to Alan Brennan who stepped down as Director of HEDS in August after seven successful years in charge. During his time at the helm, HEDS has grown in size and influence, contributed to an excellent Research Assessment Exercise for ScHARR, developed two Masters Programmes and much, much, more.

So what else is new? We have been able to recruit some excellent new members of staff to boost our capabilities in network meta-analysis, modelling, and health economics. This is in response to several new research grants and a growth in our consultancy activity.

Our pharmaceutical consultancy is of particular note. This programme of work has been increasing steadily this year and, rather than seeing it as separate from our academic research grants, we are determined to integrate it into our other research programmes, thereby grounding our 'research' in contemporary problems and our 'consultancy' in cutting-edge methods. Our methodological knowledge – much of which has found its way into the NICE Decision Support Unit (DSU)'s Technical Support Documents – sets us apart from other units and organisations undertaking consultancy work. This methodological expertise will be developed further as the DSU starts to revise NICE's Guide to the Methods of Technology Appraisal this autumn.

In terms of landmark research topics, we are completing our first NICE Diagnostics Appraisal Programme topic - gene expression profiling (GEP) to guide selection of chemotherapy regimes in breast cancer management. Based on methods developed and tested by HEDS, this work programme is expected to become increasingly important with the growth in near-patient testing, genetic testing, and other developments. This work will have a profound effect on market access for new products (that will continue to be evaluated outside of Value Based Pricing).

In addition, the Department of Health's Policy Research Unit in Economic Evaluation of Health and Care Interventions (EPRU) has just held its first Advisory Board meeting, to discuss work to date and guide future work priorities. One part of the Unit's current work programme is the development of a framework for incorporating into VBP societal weights for burden of illness and therapeutic improvement. Professor John Brazier presented the framework and basic design for the empirical work that it is hoped will inform the weights used by the Department.

Exciting times ahead! Keep up to date with HEDS and the Health Economics environment all year round by visiting the HEDS blog at <http://scharrheds.blogspot.com/>



Professor Simon Dixon

HEDS LEADS IN CONSULTANCY



With over seventeen years' experience in this arena, researchers in HEDS have a proven track record of providing support for high quality Health Technology Assessment submissions to the National Institute for Health and Clinical Excellence (NICE), the Scottish Medicines Consortium, and similar policy decision-making bodies worldwide. With numerous members of staff serving on the NICE committees and contributing to the reference case for submissions, we are well equipped to identify and define the specific requirements needed to support the clinical development and economic value of products. We provide a broad range of services specifically tailored and customised to our clients' needs, and our reputation is built on the wide range of expertise we can draw from.

Our researchers design and build *de novo* decision analytic models, and also adapt, review, and critique existing models. We conduct projects to inform model parameters such as: costing studies exploring resource use, systematic reviews of clinical effectiveness evidence, and both Classical and Bayesian methods of evidence synthesis including network meta-analyses. As internationally recognised experts in the field of

health related quality of life, we review the appropriateness of existing generic instruments, develop new preference-based measures and use state of the art mapping techniques to obtain cross-walks to predict preference-based health state utility values suitable for generating quality adjusted life years. Inside are several case studies giving a flavour of the range and depth of support we can provide.

HEDS leads in consultancy

Case study 1: Cost-effectiveness evaluation in a chronic progressive condition

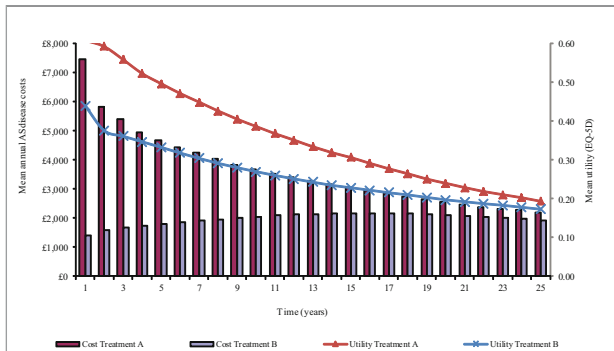


Figure 1: Changes over time in the mean annual AS disease costs and utilities (3)

Ankylosing spondylitis (AS) is a chronic progressive inflammatory condition that causes irreversible skeletal damage. Effective pharmaceutical interventions are scarce and there is a clear unmet need for medical interventions in this patient group. We designed and built a *de novo* decision-analytic model to explore the cost-effectiveness of a pharmaceutical treatment for AS. The results were used to support a submission to the National Institute for Health and Clinical Excellence (NICE). Relationships between the condition specific clinical variables (BASDAI and BASFI) and both AS specific costs and health related quality of life (EQ-5D) were constructed to estimate changes over time in the decision-analytic model (Figure 1). We provided continued support to our client throughout the appraisal process, with the result that the intervention was recommended for patients with severe AS in England and Wales.

References

1. Ara RM, Packham JC, Haywood KL The direct healthcare costs associated with ankylosing spondylitis patients attending a UK secondary care rheumatology unit. *Rheumatology (Oxford)* **47**(1):68-71 2008
2. Ara R, Reynolds AV, Conway P. A treatment option for patients with severe active ankylosing spondylitis: The costs and benefits associated with etanercept. *Clin Exp Rheumatol* **26**(4):740-740 2008
3. Ara RM, Reynolds AV, Conway P. The cost-effectiveness of etanercept in patients with severe ankylosing spondylitis in the UK. *Rheumatology (Oxford)* **46**(8):1338-1344 2007

Case study 2: Deriving a preference-based measure for cancer using the EORTC QLQ-C30

Although the EORTC QLQ-C30 is one of the most commonly used measures in cancer, it cannot be used directly to generate quality adjusted life years in decision-analytic models as it does not incorporate preferences. We therefore estimated a preference-based measure for cancer from the QLQ-C30. A dataset of 655 patients with multiple myeloma enrolled in a clinical trial was used to derive a health state classification system amenable to valuation using Rasch analysis and other psychometric analyses.

A valuation study involving 350 members of the UK general population was conducted using time trade-off techniques. Preference weights for the classification system were obtained using multivariate regressions for both mean and individual level data. The health state classification system has 8 dimensions (physical functioning, role functioning, social functioning, emotional functioning, pain, fatigue and sleep disturbance, nausea, constipation and diarrhoea) with 4 or 5 levels each. Regression models have few (0 to 2) inconsistencies in estimated preference weights and small mean absolute error ranges (0.046 to 0.054). The preference-based weights for the EORTC QLQ-C30 can be used to generate quality adjusted life years in decision-analytic models.

Reference

Rowen D, Brazier JE, Young TA, Gaugris S, Craig BM, King MT, Velikova, G. (2011) Deriving a preference-based measure for cancer using the EORTC QLQ-C30. *Value in Health*, forthcoming, available online <http://www.sheffield.ac.uk/scharr/sections/heds/dps-2010>

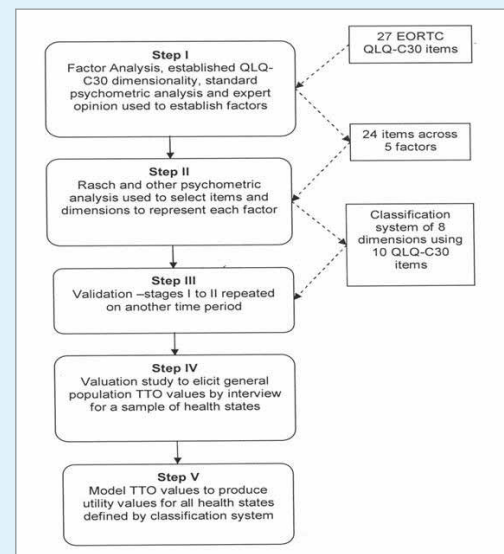


Figure 2: Flow diagram of the process used to derive the EORTC-8D from the EORTC QLQ-C30

Case study 3: Systematic review of the epidemiology of advanced melanoma in the U.K.

Cutaneous malignant melanoma (CMM) is an aggressive form of skin cancer. Prognosis in advanced stages is poor, and current treatment options in this patient group are limited. While there is a substantial epidemiological evidence base for other skin cancers, the evidence for advanced (inoperable stage III and stage IV) CMM incidence rates is more limited. We were commissioned to conduct a systematic literature review to inform a UK marketing strategy for an intervention in this patient group.

Our systematic literature search of published (involving more than 10 healthcare and clinical databases) and grey literature identified only three UK-based studies. While heterogeneity of the studies hindered synthesis of the data, between 1971 and 2003 an estimated 2% of all melanoma patients had some degree of advanced melanoma at the time of diagnosis, whereas between 1991 and 2004 the number of stage IV patients decreased from 0.42 to 0.13 cases per 100,000 population per year. Our review highlighted the dearth of evidence in this area and the need for more detailed evidence on this particular subset of patients. The results of the review are to be published in conference proceedings and a peer-reviewed journal.

HEDS leads in consultancy

Case study 4: Cost-effectiveness evaluation in Chronic myeloid leukaemia (CML)

Chronic myeloid leukaemia is a cancer of myeloid blood cells. It is a rare condition affecting around 560 people in the UK each year. Chronic phase CML may be asymptomatic and typically lasts for several years. Patients then progress to accelerated phase, lasting around 12-18 months, with worsening symptoms including bruising, bleeding and infections, and then to blast-crisis phase which is typically fatal within 3–6 months. Allogeneic stem cell transplant (SCT) offers a potential cure, but lack of suitable donors precludes this option for the majority of people with CML. However, effective pharmaceutical interventions developed over the last few years have offered great improvements in survival for those ineligible for SCT. We designed and built a *de novo* state transition model (Figure 4) to explore the cost-effectiveness of a pharmaceutical treatment for CML. Key modelling issues related to the extrapolation of relatively short term outcomes for progression and treatment discontinuations to provide robust long term predictions.

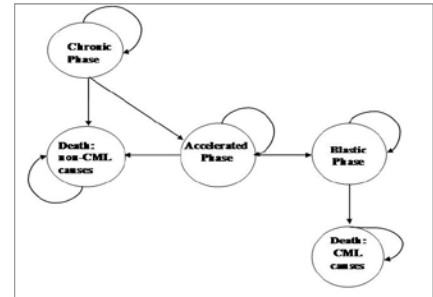


Figure 4 : Model structure for CML

The cost effectiveness modelling results formed the basis of successful submissions to both the Scottish Medical Consortium and NICE.

Case study 5: Health care costs relating to Psoriatic Arthritis

Psoriasis arthritis (PsA) is a chronic, systemic inflammatory arthritis, usually seronegative, associated with psoriasis. It is a debilitating disease and, while there are effective treatment options that may improve disease severity, these treatments are expensive. Evidence describing how the shift in disease severity could translate into a shift in health care resource use is scarce.

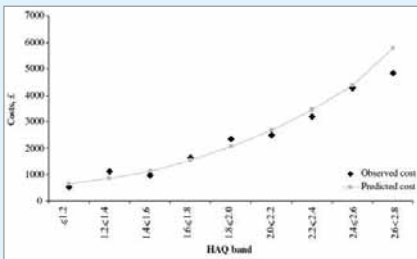


Figure 5: Plot of the mean observed and mean predicted annual costs by HAQ band

We examined the relationship of treatment costs in the UK with respect to disease severity from the National Health Service perspective. The relationship between disease severity (HAQ) and health care costs was examined using a Generalised Linear model using age as a covariate; this showed that an improvement in disease severity was associated with a reduction in direct health care costs. Figure 5 provides the mean observed and mean predicted annual cost by Health Assessment Questionnaire (HAQ) band. The results of this study were used to support a manufacturer's submission to the NICE, which led to a positive recommendation.

References

Poole CD, Lebmeier M, Ara R, Rafia R, Currie CJ. Estimation of health care costs as a function of disease severity in people with psoriatic arthritis in the UK. *Rheumatology (Oxford)* 49(10):1 949-1956 2010.

Rafia R; Ara R; Lebmeier M. The cost effectiveness of etanercept in patients with psoriatic arthritis in the UK. *Annual Meeting of the British Society Rheumatology England* April 2010

Case study 6: Network meta-analysis

Diabetes mellitus type 2 is a metabolic disorder characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency. Its management primarily involves lifestyle interventions and maintaining blood glucose levels. Metformin is generally recommended as first line treatment, followed by treatments in other classes (i.e. sulfonylureas, nonsulfonylurea secretagogues, alpha glucosidase inhibitors, and thiazolidinediones) either in combination with metformin or as monotherapy.

We performed a network meta-analysis to synthesise evidence about six treatments relative to a standard treatment (Figure 6). Outcome measures included HbA1c, TC, HDL and LDL. The results of the network meta-analysis provided valuable information required for marketing decision-making.

NOTE: The nodes represent the treatments and the numbers indicate the number of times that pairs of treatments were compared.

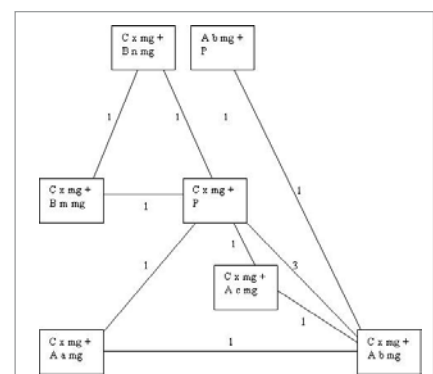


Figure 6: Network meta-analysis of treatments for Type 2 diabetes

Feedback

HEDS would appreciate your feedback on this newsletter. Please email: heds.newsletter@shef.ac.uk
We look forward to hearing from you.



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Newsletter HEDS Teaching & Training

HEDS MSC COURSES

Applications for HEDS post-graduate courses are currently welcomed. For information on all courses, visit http://www.sheffield.ac.uk/scharr/prospective_students

MSc International Health Technology Assessment, Pricing & Reimbursement

This MSc is the only graduate programme offering the entire range of knowledge and skills needed by those developing health technologies for market or involved in commissioning or evaluating health technologies. Those working in the pharmaceutical, medical devices, or diagnostics industries will gain a comprehensive understanding of the processes and contexts of markets, pricing, and customers needed for new product development in multiple jurisdictions. The course also meets the needs of those involved in health technology policy formulation, management and evidence-based commissioning and purchasing of health technologies for governments or health services.

The course is delivered entirely online by distance learning, using the most current methods. This format was created to suit people with busy work commitments in this field, and is also highly accessible to an international audience as there are no travel, residential or visa requirements.

For further information, visit http://www.shef.ac.uk/scharr/prospective_students/masters/ihtapr/index



MSc Health Economics and Decision Modelling

This MSc is the only Masters programme in the UK dedicated to the practical application of mathematical modelling to inform healthcare decision making. It is a truly bespoke course, bridging the gap between the underlying theory and application of mathematical modelling for decision making and more traditional health economics. The course is ideal for students wishing to pursue a career as a professional health economist/modeller. For more information, or if you represent a commercial organisation that would consider undertaking sponsorship of a student on the proposed MSc in Health Economics and Decision Modelling, please go to our website http://www.sheffield.ac.uk/scharr/prospective_students/masters/hedm

MSc Economics & Health Economics

This MSc programme is run jointly with the Department of Economics at the University of Sheffield. It is aimed at students who wish to pursue careers as applied economists in the health sector or who wish to continue with academic research.

The programme emphasises the development of the advanced analytical and technical capabilities required for applied economics, and demonstrates how these skills can be used to address the important issues and problems involved in allocating resources in the health sector. This emphasis is achieved through first semester economics modules, followed in the second semester by the development and application of those skills.

MSc Economics and Health Economics receives studentship funding from the National Institute for Health Research. The studentship is for full-time UK students, and covers the fees and a standard research council stipend. For more information on this course, visit http://www.sheffield.ac.uk/scharr/prospective_students/masters/ehe

TWO DAY SHORT COURSE

Utility Data for Health Technology Assessment, 15-16 March 2012

This course examines in detail the requirements for utility data in health technology assessment for agencies such as NICE. The course covers both how to measure and use utility to meet the current requirements of NICE and recent research including EQ-5D-5L valuation and use of social value weightings, for example in Value Based Pricing. The course is for academics, Government agencies, pharmacoeconomics and outcomes experts in industry, and consultancies with an interest in the use of health state utility data. The course will consist of a mixture of presentations, group work, discussions, and individual exercises.

The course is an updated version of a course run four times over the last three years, and attended by delegates from all around the world. The course team consists of John Brazier, Ben van Hout, Tracey Young, Roberta Ara, Donna Rowen, and Anju Keetharuth from HEDS.

Further details and booking information can be found on our website: <http://www.shef.ac.uk/scharr/sections/heds/shortcourses>