experienced and high-quality source for post-approval studies. Elaborated management processes in multi-country panels guarantee a constant quality of the panel over geographies.

PRM18
CLASSIFICATION OF COGNITIVE DYSFUNCTION AND COGNITIVE NORMAL USING SCORES FROM FOUR COGNITIVE ASSESSMENTS IN PATIENTS WITH DEPRESSIVE DISORDER

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OBJECTIVES: Cognitive functioning is a multidimensional attribute comprising various domains including attention, memory, executive function, and psychomotor speed. The number of impacted domains and magnitude of deficits that equate to a classification of cognitive dysfunction (CD) are unclear. This analysis examined criteria used for CD classification in an observational study of depressed patients. **METHODS:** A large US health plan was used to identify depressed patients with a newly prescribed antidepressant. Consenting, eligible patients were interviewed by telephone and completed a structured assessment of cognitive function measuring 4 domains: verbal episodic memory (Hopkins Verbal Learning Test-Revised), attention (Digit Span Forward), working memory (Digit Span Backward), and executive function (D-KEFS-Letter Fluency Test). Patients were classified in 2 groups based on test scores relative to normative data. "CD" was defined as patients with ≥ 2 scores that were ≥ 1.5 standard deviations (SD) below the normative mean (criterion 1) or patients with ≥ 3 scores that were ≥ 1.0 SD below the normative mean (criterion 2). Patients not meeting either of these were classified as "cognitive normal (CN)." T-tests compared differences between the groups across cognitive domains. **RESULTS:** Of 564 eligible patients who completed the study, 45% met criteria for CD. Among these, 63% met both criteria for classification of CD, 19% met only criterion 1, and 18% met only criterion 2. The percentage of patients with scores ≥ 1.0 SD below the mean and ≥ 1.5 SD below the mean were significantly higher in the CD group compared to the CN for all 4 tests. Mean scores on all domains were significantly lower (P < 0.001) in the CD group compared to the CN group. **CONCLUSIONS:** Among patients with depression, those with cognitive dysfunction had significantly worse functioning across all domains. This suggests that the criteria appropriately identified a subset of patients with impaired cognitive functioning.

RESEARCH ON METHODS – Cost Methods

PRM19
TIME DEPENDENT RESOURCE USE AND COSTS ASSOCIATED WITH DIFFERENT STATES OF DISEASE IN PATIENTS DIAGNOSED WITH HER-2 POSITIVE METASTATIC BREAST CANCER

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OBJECTIVES: Adequate reflection of disease progression and costs over time is essential in cost-effectiveness analyses (CEAs) based on health state transition models. However costing studies normally investigate the burden of metastatic breast cancer (MBC) without explicitly examining impact of specific disease states on health care costs over time. The objective of this study was to assess time-dependent costs of different health states of human epidermal receptor 2 (HER-2) positive MBC and the factors contributing to these costs. **METHODS:** In The Netherlands, HER-2 positive MBC patients were identified in three different hospitals. Resource use was collected during 24 months, which was linked to unit costs and related to time with respect to date of MBC diagnosis, disease progression and death for each individual patient. Subsequently, monthly costs for different health states were calculated. Finally, a nonlinear mixed effect modelling approach was used to provide a quantitative description of the time course of cumulative progression costs. **RESULTS:** Costs during stable disease were constant over time with a mean of €3,236. In contrast, monthly costs for progressive disease demonstrated a change over time with the largest costs in the first two months after diagnosis (p<0.005). The developed mixed effect model adequately described cumulative cost time course and associated variability. During the last months of life, costs varied over time, with the last month of life as the most expensive one with a mean of €4,522 per patient per month. **CONCLUSIONS:** To reflect costs of HER-2 positive MBC accurately in Markov models, costs stable disease can be defined time-independent, however, costs of progressive disease should be defined time dependent, and costs related to the final months of life should be modeled as such. The mixed effect model we have developed could now be considered for adequate description of the time-dependent cost of progressive disease.

PRM20
ASSESSING THE FUTURE BURDEN OF RENAL REPLACEMENT THERAPY IN THE UNITED KINGDOM

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OBJECTIVES: The UK has an ageing and growing population and the prevalence of renal replacement therapy (RRT) has grown by 5.0% annually since 2000. RRT accounts for over 2% of the current NHS expenditure. Transplantation increases survival, improves quality of life and maintenance costs are less than dialysis. Despite increasing rates of transplantation, an estimated 7,000 patients remain on the waiting list. The objective of this study was to quantify the relationship between graft survival time, total estimated cost and the number of projected patients on the transplant waiting list. **METHODS:** We utilized a population based simulation model with published disease progression, incidence and prevalence parameters specific to the UK. We evaluated the number of years of functioning

graft required for transplantation to remain cost saving compared to dialysis; the number of future transplants or improvement in graft survival required to avoid the transplant waiting list increasing. The study utilises UK costs and future costs and benefits were discounted at 3.5% **RESULTS:** Over a 10-year projected time horizon the total per-patient cost saving associated with remaining on dialysis compared to transplant was £276,330; however, a cost saving was conditional upon achieving at least 3-years of functioning graft. In order to maintain the transplant waiting list at approximately 7,000, the number of annual transplants conducted would need to increase from 2,645 in 2010 to 3,640 by 2022 (a 37.6 % increase). At current activity levels the transplant waiting list is projected to increase by approximately 1,983; improvement in graft survival could potentially reduce this by 941. **CONCLUSIONS:** For kidney transplantation to be cost saving recipients must maintain at least 3 years of functioning graft. As early graft failure also impacts on future transplant waiting time, management strategies that maximize graft survival will reduce costs and improve service delivery targets.

PRM21
COMPARISON OF ALTERNATIVE METHODS OF RESOURCE-USE DATA COLLECTION FOR THE ECONOMIC EVALUATION OF HEALTH CARE INTERVENTIONS: A CASE STUDY IN FRAIL OLDER PEOPLE

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OBJECTIVES: Economic evaluations require patient-level resource-use to estimate patient costs. The National Programme for IT (2002) prompted UK health and social care to record patient-level resource-use using Electronic Administration Records (EAR's). Retrieving EAR's is labour intensive, but may provide better information than self-report methods, such as the Client Service Receipt Inventory (CSRI), particularly in cognitively impaired people. Study objectives are to examine agreement, and associated cost estimates, between resource-use obtained from EAR's or CSRI in frail older (≥ 70) participants. **METHODS:** Health and social care data for 247 patients (193 cognitively impaired) were sought retrospectively six months post-index hospital admission. Resource-use data were collected using a self/proxy-reported modified CSRI, and EAR systems for primary (PC), secondary (SC), and social (SoC) care. Lin's coefficient (ρc) assessed agreement between methods, where <0.4 = poor agreement. **RESULTS:** Agreement between EAR and CSRI 'per contact' resource-use was: good, primary care (ρc = 0.60); fair, outpatient care (ρc = 0.53). Agreement was incomparable for social care due to different resource-use recording formats; CSRI's inpatient care question was removed due to the preferred detailed information available in EAR's. EAR data provided detailed patient care information, such as diagnosis and procedure type, allowing improved allocation of unit costs. Difference in mean cost per patient between methods varied by service (CSRI/EAR (£): PC = 61/433; SC = 7281/7833; SoC = 252/886); CSRI inpatient costs were simulated assuming perfect agreement with EAR, but using level of information outlined within the CSRI. **CONCLUSIONS:** EAR's provided more complete patient costs. Using EAR's reduces burden upon participants, which is important for frail and cognitively impaired people. Although the CSRI can be modified and simple to administer, poor recall and inadequate detail about patient care contacts prevented accurate patient-level cost estimation. Gaining access to EAR's is labour intensive, but recommended in cognitively impaired participants.

PRM22
CARBON COST-EFFECTIVENESS OF COCOONING IMMUNIZATION AGAINST PERTUSSIS IN ENGLAND AND WALES: AN ECOLOGICAL PERSPECTIVE

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OBJECTIVES: The cost-effectiveness of pertussis vaccination has been demonstrated for various vaccination strategies. However, beyond financial cost expressed in monetary terms vaccines also incur environmental cost expressed in CO_2 equivalent (CO_2e) emission. By preventing disease, this cost might be offset by avoided events such as doctors' visits, hospital bed stays, medication, amongst other items. In this exercise we examine the CO_2e savings of a pertussis (dTpa) booster dose for cocooning in England and Wales. We propose a complementary measure to the classical Incremental Cost-Effectiveness Ratio that includes environmental cost instead of monetary cost. **METHODS:** The cradle to gate carbon footprint (from raw material extraction, to manufacturing, to disposal) for a typical dTpa vaccine dose was assessed to estimate the total amount of CO_2e emitted ("carbon cost"). A previously published static epidemiological model was used to account for the reduction in incidence of pertussis. Two scenarios were compared: the current pertussis vaccination schedule and the same schedule with additionally a cocooning strategy. **RESULTS:** For each dose of a dTpa vaccine manufactured, results show approximately 1kg of CO_2e was emitted. The model shows cocooning immunization against pertussis is projected to reduce the reported incidence of pertussis in young infants. Results also show that due to the reduction in emitted CO_2e after the introduction of a cocooning strategy, vaccination is an acceptable alternative to the current strategy to control pertussis infection. **CONCLUSIONS:** The method presented demonstrates how traditional economic models can be utilized to model environment features. Assessment of the cradle to gate carbon footprint of a vaccine provides a preliminary view of both the impact on the environmental in general and on the environment profile of health care in the UK.

PRM23
MODELLING THE COST-EFFECTIVENESS OF FIRST-LINE BIOLOGICS FOR RHEUMATOID ARTHRITIS IN ENGLAND AND WALES

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OBJECTIVES: In 2012, NICE initiated a multiple treatment assessment reviewing all licensed biologics for the treatment of rheumatoid arthritis (RA) previously treated

with conventional DMARDs only. The sequence of treatments used after the failure of first biologic treatment was to be included as part of the cost-effectiveness modelling. We therefore built a model to match the treatment pathway for first-line biologics and beyond. **METHODS:** We researched the treatment pathway and existing cost-effectiveness models in order to create an appropriate model. We rebuilt the model used by the technology assessment group in TA195, which considered second-line biologics and beyond. We adapted this model to reflect the current treatment pathway and consider first line biologics. **RESULTS:** We created a patient simulation model, which generated a cohort of virtual patients and tracked their costs and QALYs over the pathway. Patients began treatment with a biologic, and could discontinue at month 6 due to an adverse event (AE), in which case they switched to a different biologic, with first-line efficacy. Patients who did not have an AE discontinued at month 6 if their DAS 28 improvement was insufficient. After discontinuation at month 6, or later, patients next received rituximab, unless contraindicated. If rituximab was contraindicated, or the patient had an AE by month 6, they moved onto another biologic treatment, after which they received a DMARD treatment sequence (including palliative care). Patients who had insufficient DAS28 response on rituximab at month 6 switched to tocilizumab (unless received previously), after which they received the DMARD sequence. Patients who had sufficient DAS28 improvement with rituximab remained on rituximab long-term, until they received the DMARD treatment sequence. Patients could exit the model at any point if they died. **CONCLUSIONS:** We used robust methodology and clinical rationale to assess the cost-effectiveness of licenced treatments reflected across NICE's recommended treatment pathway for RA.

PRM24
MODELLING THE COST-EFFECTIVENESS OF FIRST LINE BIOLOGICS FOR RHEUMATOID ARTHRITIS IN IRELAND
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OBJECTIVES: In 2013, NCPE assessed the cost-effectiveness of subcutaneous (SC) abatacept as a first line biologic for the treatment of rheumatoid arthritis (RA), compared to existing biologics. It was necessary to consider the treatment pathway beyond first line biologics. We therefore built a model to match the treatment pathway for first line biologics and beyond. **METHODS:** We used our individual patient sampling model for England and Wales as a starting point to create a model which considers biologic cycling, to match the treatment pathway in Ireland. We differentiated between the efficacy of a biologic at first line, and at second line or later. **RESULTS:** We created a model which could be used to calculate the cost-effectiveness of biologics for the treatment of RA in Ireland. Patients first received treatment with SC abatacept, intravenous abatacept, adalimumab, etanercept, infliximab, certolizumab pegol or golimumab. If they experienced an adverse event (AE) on that treatment within 6 months, they switched to another biologic at first line efficacy. If not, their response to treatment was tested using the DAS28: if this improved by 1.2 or more, their time on treatment was sampled from a Weibull distribution, otherwise they discontinued at month 6. The patient then moved onto a randomly sampled second line biologic, which was either one of the first line biologics or rituximab. The time on second line biologic was sampled from a Weibull distribution, and then the patient moved onto a third line biologics (second line biologics and tocilizumab). The patient cycled through the biologics until they died, or had received all 8 treatments. After 8 biologics, remaining patients received leflunomide, cyclosporin, azathioprine and palliative care. **CONCLUSIONS:** We used robust methodology and clinical rationale to model the treatment pathway of biologics for RA in Ireland and facilitated cost-effectiveness comparison between first line biologics.

PRM25
A SYSTEMATIC REVIEW OF ECONOMIC EVIDENCE IN HEPATITIS C: METHODS USED IN RECENT ECONOMIC EVALUATIONS
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OBJECTIVES: To perform a systematic literature review of economic evidence for genotype 1 hepatitis C virus (HCV) treatments and to summarise and assess the methods used in recent economic evaluations. **METHODS:** Multiple databases were searched to identify economic evaluations in patients with genotype 1 HCV. Detailed review methods are presented elsewhere. **RESULTS:** 53 economic analyses and 17 Health Technology Assessment (HTA) documents were identified. Most economic analyses were performed using lifetime horizon Markov models, all for interferon-containing regimens. Most were performed in the United Kingdom (UK) (n = 13), United States (n = 13), or Germany (n = 7). Two recent National Institute for Health and Care Excellence (NICE) submissions were included: telaprevir triple therapy (with peginterferon plus ribavirin) and boceprevir triple therapy, for previously treated and untreated patients. The models used were different; however their structures and some inputs were based on previous NICE appraisals for peginterferon plus ribavirin. There were a number of limitations found in the included economic evaluations, which may have affected the cost-effectiveness outcomes: 1) The models did not adequately capture all health benefits and costs in their quality-adjusted life-year calculations; 2) The models did not account for the possibility of benefits caused by reduced transmission of HCV; 3) The models did not incorporate patient factors that may influence disease progression; 4) Modelling of subgroups may have been insufficient, particularly as the understanding of patient and viral factors that predict treatment response grows; and 5) Some made generalisations for the compensated cirrhosis population that were not comparable with the UK population. **CONCLUSIONS:** Recent economic models have generally adhered to previous iterations of HCV models and have not evolved with our knowledge of the disease. In light of upcoming treatment alternatives, model refinement may be necessary to capture the increasingly complex treatment decisions that will be required.

PRM26
IMPACT OF USING EITHER MULTIPLICATIVE OR ADDITIVE UTILITY DECREMENTS IN DECISION MODELS
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OBJECTIVES: In cost-utility analyses (CUAs) it is common to estimate the utility of patients while on treatment or when experiencing comorbidities by adjusting their baseline utility with the treatment/comorbidity-related utility decrement. This study assessed the impact of adjusting patients' baseline utility with additive versus multiplicative utility decrements on the lifetime quality-adjusted life years (QALYs) in CUAs for two chronic illnesses. **METHODS:** Two Markov models were developed. In the first model, utility during treatment was obtained by adjusting the baseline utility with the treatment-related utility decrement; treatment was given for one year. In the second model, utilities with comorbidities were obtained from external sources and were combined with the health state utilities by considering the lowest value. In both models, the response of the multiplicative, additive and the combined approach was investigated by comparing the number of QALYs gained over a lifetime. **RESULTS:** In the first model, as treatment was only given during the first year, the impact on the number of QALYs gained over a lifetime was minimal. Thus, a similar incremental cost-effectiveness ratio per QALY (ICER/QALY) was obtained with all the approaches. In contrast, for the second model, the number of QALYs gained over a lifetime between the approaches was significantly different. This is because comorbidities were experienced during a longer period of time. Consequently, the difference in ICER/QALY was also substantial. **CONCLUSIONS:** When developing CUA, either a multiplicative or combined, rather than additive, approach should be used to calculate the utility of patients during treatment or with comorbidities, using utility decrements, if considerable uncertainty is present in the baseline utility. However, if QALYs gained with treatment or with comorbidities represent only a small fraction of the overall QALYs gained, the difference between the approaches is not expected to have a significant impact on the results.

PRM27
UNCHARTERED TERRITORY – ANALYSIS OF CROSS-BORDER SERVICE PROVISION WITHIN PUBLIC HEALTH SYSTEMS
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OBJECTIVES: The European Union's (EU) 2011 Directive on cross-border health care establishes the right of EU citizens to receive treatment abroad and be reimbursed in their home country. While the focus has been on patient mobility and access, it may also facilitate international outsourcing of services between countries. This research examines the methodological challenges in evaluating the costs and consequences of cross-border service provision. **METHODS:** Using the example of deep brain stimulation (DBS) treatment in Ireland, we conducted an economic analysis of the provision of cross-border services from the perspective of the public health system. This included an analysis of clinical and cost-effectiveness, ethical and societal implications and the challenges of integrating care between separate health systems. **RESULTS:** Accurate modelling of the provision of a new or expanded service serves as the basis for evaluating costs, impact on patients and potential gaps in continuity of care. Cost minimisation analysis may be appropriate under some circumstances, with due regard to the importance of patient selection and follow up. Cross-border services may have significant implications for equity of access, with potential negative consequences for those most in need of treatment. Results of the economic analysis indicate that a national DBS service in Ireland would cost an additional €20,900 per patient over 10 years. The potential for anomalies within health systems with a mixture of private and public funders is highlighted, with the difference being reduced to €4,100 per patient in a single payer scenario. **CONCLUSIONS:** Health care funding structures can impact significantly on the cost-effectiveness of cross-border services, even when differences in the actual cost of care are minimal. Given the externalities involved, analysis from the payer perspective may be too narrow for the economic evaluation of routine cross-border provision of elective services.

PRM28
EMPIRICAL EVIDENCE FOR THE VALIDITY AND RELIABILITY OF RESOURCE-USE MEASURES BASED ON PATIENT RECALL: A SYSTEMATIC REVIEW
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OBJECTIVES: Accurate measurement of resource use is required for economic evaluations alongside clinical trials. Patient-completed questionnaires are commonly employed as a means of collecting data; however, concerns over data quality persist, and there is little certainty about best practice. This review collates the evidence concerning the validity and reliability of resource-use measures based on patient recall with the aim of aiding health economists in developing better measures. **METHODS:** A search strategy incorporating terms covering health care resources, utilisation, patient-reported measures and validation/reliability concepts was applied to the MEDLINE, EMBASE and PsycINFO bibliographic databases. Studies were included if they reported original research to inform costing studies, and were about patient or proxy self-reports of direct health care-related resource use in which a comparator (to assess validity or reliability) was specified. Studies were excluded if they were not in English or if they assessed general population surveys. Reference and citation lists of included studies were hand searched to identify additional studies. Data on study and population characteristics, type of instrument, recall period and sample size were extracted. Results and conclusions concerning the validity and reliability of reports of types of resource use consumed (e.g. medication, inpatient stays) were also extracted. **RESULTS:** A total of 13,367 abstracts were identified as potentially relevant through the database searches. Following abstract and full-text screening, 60 articles were deemed relevant, with a further 9 identified through hand searching. The majority focused on adults (60/69),