submissions, in 53% of cases a high ICER was reported in the summary of guidance as a reason for rejection. In about 30% of these cases, the high drug cost was specified as the driver of the high ICER. The lack of a robust economic case was mentioned in 45% of rejections. Limited evidence of clinical benefit was shown in 43% of cases. Other reasons included inadequate type or quality of clinical data (21%) and non-acceptance of clinical positioning (11%). In 45% of cases the rejections were largely due to economic reasons; 6% of cases were not accepted due primarily to clinical reasons and in 49% of rejections the criticisms related to both the economic and clinical evidence. Uncertainty in the evidence was reported as a problem in most negative recommendations. **CONCLUSIONS:** Only slightly over half of the orphan drug HTA submissions to these agencies are explicitly rejected primarily on the basis of a high ICER. Most HTA rejections are due to a combined lack of robust economic and clinical evidence. This suggests that collecting the right kind of data and presenting a solid case that accounts adequately for any uncertainty is at least as important as meeting trial endpoints and choosing an optimal price.

PHP101

EVALUATION OF ACCEPTANCE AND REJECTION RATES OF ORPHAN DRUGS ACROSS SIX HTA BODIES

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OBJECTIVES: Orphan drugs (ODs) face numerous difficulties in demonstrating their value through rigorous HTA processes. HTA bodies may therefore choose to take into consideration the special circumstances of treatments for orphan indications, either formally or informally. The objective of this study was to examine the decisions made on ODs by six English-speaking HTA bodies, and assess potential trends between agencies. **METHODS:** AWMSG, CEDAC, NCPE, NICE, PBAC and SMC HTA websites were searched for completed OD assessments (identified via Orphanet website) as of April 2010, and data extracted on the recommendations. Recommendations with restrictions were categorised as approvals. Comparisons were made to published approval rates for drug submissions as a whole. **RESULTS:** Of the 71 ODs selected, 55 were assessed by at least one HTA body. The proportion of positive recommendations for orphan treatments was lower than published approval rates for general (orphan and non-orphan) HTA drug submissions in most bodies. NICE approved 67% completed OD submissions, versus approximately 87% of drugs overall. However, PBAC recommended 60% of ODs compared to 54% of drugs as a whole. Decisions also varied substantially between agencies. CEDAC had the highest proportion of rejections (73%), compared to NICE, which rejected 33%. There was also variation in decisions made on specific treatments. Sutent, for example, with an orphan designation for renal cell carcinoma, was accepted by AWMSG, CEDAC and SMC, while it received a negative recommendation from NCPE, NICE and PBAC. **CONCLUSIONS:** The willingness to assess ODs varies widely by agency and drug, as do resultant approval rates. HTA agencies are far more likely to reject OD submissions than non-orphan drugs as a whole. However given the differences in their remit to assess ODs, direct comparisons should be interpreted with caution. Further research is needed to explore the reasons behind these differences in HTA agency decisions.

PHP102

A SURVEY OF HTA RESEARCH METHODS AND TRENDS IN EUROPE

ISPOR HTA SIG Research Methods/Principles Working Group

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OBJECTIVES: To describe research methods and key issues in the HTA process in Europe. **METHODS:** Representatives from HTA bodies globally were recruited by members of the ISPOR HTA SIG Research Methods/Principles Working Group to complete a 45-minute on-line survey consisting of 48 items within 4 topics related to 1) organizational information and process; 2) primary HTA methodologies and importance of attributes; 3) HTA application and dissemination; and 4) quality of HTA including key issues. Data were reported for Europe. **RESULTS:** The survey was completed by 11 European countries including Austria, Denmark, France, Germany, Hungary, Italy, The Netherlands, Portugal, Spain, Sweden, and Switzerland. Top reasons technologies were evaluated included perceived impact on patient outcomes, potential cost, and prevalence of the condition. The most common methodologies used were cost/economic analyses, systematic reviews & meta-analyses, clinical trials, modeling, and comparative analyses. The most important attributes (in order) were effectiveness, efficacy, safety, cost-effectiveness, and budget impact. While quality of life was frequently assessed by >74% of European respondents, it was not listed as an attribute of top importance. Only 24% repeat/update the assessment at regular intervals. For 82% a different organization makes the final decision on coverage, only partially relying on the report. The most common educational background for decision makers was physician-specialist. Stakeholders are allowed to review the report and are involved in assessments >50% of the time, and in the final decisions ~35% of the time. Key issues/trends included early assessment of technologies with mechanism for conditional coverage, increasing regional interest in HTA, reassessment/horizon scanning, and link between theory and practice in HTA. **CONCLUSIONS:** This survey of representatives within HTA and reimbursement bodies provides current insight into the state of HTA research methods in Europe. Future research could expand the results to specifically address Eastern European countries, Asia, and other emerging markets.

PHP103

NICE GUIDANCE: AN ANALYSIS OF LEVELS OF RESTRICTION BY DISEASE AREA

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OBJECTIVES: To assess the outcomes of NICE's guidance in totality and different disease areas. **METHODS:** A list of NICE Guidance published between 2007 to the end of 2009 was identified using HTAinSite™. We classified these recommendations into; 'recommended', 'restricted' and 'not recommended', and calculated the percentages. We then analyzed these recommendations according to disease areas; 'cardiovascular/metabolics', 'mental health', 'infectious diseases', muscoskeletal conditions', 'oncology', and 'others'. **RESULTS:** In 2007, NICE assessed 25 drugs, 31 in 2008 and 18 in 2009. Of these, in 2007 NICE recommended 8 drugs (31%) for all eligible patients, restricted 13 (53%), and did not recommend 4 (16%). In 2008, 3 (10%) were recommended, 21 (68%) were restricted, and 7 (22%) were not recommended. Finally, in 2009, 2 (11%) treatments were recommended, while 11 (61%) received restricted recommendations and 5 (28%) were not recommended. Between 2007 and 2009 NICE completed 7 appraisals in 'cardiovascular/metabolics' of which 4 received a full recommendation, while in 'mental health' 2 out of 2 were fully recommended. In contrast, in 'infectious diseases', 1 out of 5 was fully recommended. In 'muscoskeletal conditions' only 1 out of 21 were recommended (17 restricted and 3 not recommended) while in 'oncology' only 1 out of 23 received a full recommendation (13 restricted, 9 not recommended). In the 'others' group, 4 out of 12 received a recommendation (6 restricted, 2 not recommended). If manufacturers had not proposed Patient Access Schemes (PAS) the proportion of guidance not recommended in 2009 would be 44%. **CONCLUSIONS:** Appraisal outcomes have become more restrictive over time. Furthermore, low cost primary care therapeutics are more likely to receive a positive NICE recommendation than high cost speciality care interventions.

PHP104

DESIGNING EUROPEAN GUIDELINES FOR HEALTH OUTCOMES AND COST-EFFECTIVENESS ASSESSMENTS: THE ECHOUTCOME EUROPEAN COMMISSION PROJECT

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OBJECTIVES: Over the last decade the National Institute of Clinical Excellence in the UK has published guidelines for health technology assessments (HTA) that includes recommendations on health outcomes and cost-effectiveness assessments. In Europe, this has opened the opportunity for countries to either propose their own guidelines or use the British ones. The ECHOUTCOME project is an interdisciplinary European research platform funded by the seventh Framework Program of the European Commission with the aim of designing new European guidelines in Health Outcomes and Cost-Effectiveness assessments. **METHODS:** This three years project is structured in three phases. Phase 1 aims to conduct a pan-European survey of HTA organizations and health outcomes use in the 27 European countries. Multiple correspondence and cluster analyses will be carried out to study the potential similarities and divergences across Europe. The objective of Phase 2 is to test the robustness and underlying assumptions such as reproducibility, neutrality to risk, constancy of time-trade-off rate, utility independence, etc. on QALYs, DALYs and HYEs measures. This testing will be conducted in the general population (n = 300 per country) in Belgium, France, Italy and UK. Phase 3 aims to propose new approaches in Health Outcomes and Cost-Effectiveness analyses. **RESULTS:** The main deliverable of the ECHOUTCOME project will be new European Guidelines for assessing Health Outcomes and conducting Cost-Effectiveness assessments. Of particular interest will be the recommendations on the practical usefulness of QALYs, DALYs and HYEs based on the experimental validation of their underlying assumptions. **CONCLUSIONS:** The ECHOUTCOME project is the first European validation study of health outcomes measures. This work will produce guidelines for public health decision-making in the 27 European countries. The ECHOUTCOME outcomes will enhance the debate and increase the understanding that will improve the knowledge of existing Health Outcomes and Cost-Effectiveness techniques and will promote new approaches for decision-making.

PHP105

HOW CAN THE USE OF PREDICTIVE BIOMARKERS LEAD TO POSITIVE HTA RECOMMENDATIONS?

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OBJECTIVES: The popularity and availability of biomarkers has rapidly increased in recent years, thanks to innovative advances in pharmacogenomics. Predictive biomarkers have high potential value in HTA as they may increase the observed efficacy and cost-effectiveness of treatments. This study reviews, in selected major markets worldwide, the impact of currently available predictive biomarkers on HTA in the context of the agency's evidence requirements. **METHODS:** A broad review of biomarker tests used in HTA submissions in Europe, Australia, Canada, and the US was conducted; the