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ABSTRACTS

ISPOR 17TH ANNUAL EUROPEAN CONGRESS RESEARCH ABSTRACTS

RESEARCH PODIUM PRESENTATIONS – SESSION I

CANCER OUTCOMES RESEARCH STUDIES

CN1
LONG-TERM IMPACT OF THE DUTCH COLORECTAL CANCER SCREENING PROGRAMME ON CANCER INCIDENCE: EXPLORATION OF THE SERRATED PATHWAY

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OBJECTIVES: The Netherlands has recently started with the stepwise implementation of biennial faecal immunochemical testing for colorectal cancer (CRC). We evaluated the impact of the transition to, and the fully implemented screening programme on the long-term CRC incidence and colonoscopy demand. **METHODS:** The previously reported and calibrated ASCCA model was set up to simulate the Dutch CRC screening programme between 2014 and 2044. We adopted an open-model approach by simulating multiple birth cohorts and combining the results while accounting for the ageing of the population. Besides a no screening scenario, we evaluated the impact of screening under three sets of natural history assumptions which differed in the contribution of the serrated pathway to the CRC incidence (0%, 15% and 30%). Model-predicted outcomes were CRC incidence and colonoscopy demand per year. **RESULTS:** Due to ageing, the model-predicted CRC incidence in the no screening scenario increased from 77/100,000 in 2014 to 109/100,000 in 2044. Under screening, the predicted CRC incidence in 2014 was between 105/100,000 (assuming all CRCs originate from adenomas) and 109/100,000 (assuming that 30% of CRCs arises from serrated lesions) due to the detection of asymptomatic, prevalent tumours. After this peak, the predicted incidence gradually decreased until in 2039 a new equilibrium was reached, ranging between 65/100,000 and 71/100,000 assuming that 100% versus 70% of CRCs originate from adenomas, respectively. Due to the stepwise implementation, the predicted number of colonoscopies required for the screening programme increased gradually over time from 38,000 (752,199 invitees) in 2014 to 117,000 (2,154,875 invitees) in 2044. **CONCLUSIONS:** The Dutch screening programme will markedly decrease CRC incidence in the next 25 years. The conclusions about the impact of screening were robust to key natural history assumptions. With the results of this study, decision-makers can anticipate the expected change in CRC-related health care use and colonoscopy demand.

CN2
PRIMARY TREATMENTS FOR INTERMEDIATE-RISK PROSTATE CANCER: A COST-EFFECTIVENESS AND VALUE-OF-INFORMATION ANALYSIS

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OBJECTIVES: Intermediate-risk prostate cancer patients are recommended primary treatment with either radical prostatectomy (RP), external beam radiotherapy (EBRT), brachytherapy (BT), or EBRT plus high-dose rate BT boost (EBRT + HDR-BT); or expectant management with active surveillance (AS). The costs of these treatments differ considerably, whilst the amount and quality of evidence for their comparative effectiveness in terms of disease progression, adverse events and health-related quality of life is unbalanced and inconclusive. Therefore, we undertook a cost-effectiveness analysis of RP, EBRT, BT, EBRT + HDR-BT and AS, and performed a value-of-information analysis to direct future research. **METHODS:** We developed a probabilistic Markov model estimating the expected incremental cost/(Quality Adjusted) Life Years from a UK-NHS perspective, with a time horizon of 10 years. Input data were obtained from the best available literature. We explored the uncertainty around the model outcomes by identifying the most influential parameters and estimating the expected value of perfect (parameter) information. **RESULTS:** AS is most likely to be cost-effective at a cost/QALY threshold (λ) < £3,000/QALY, BT for λ £3,000 to £12,000/QALY and RP for λ >£12,000/QALY. One-way sensitivity analysis shows that utilities and probabilities of adverse events are main effect drivers and initial treatment costs are main cost drivers. Large decision uncertainty exists around λ £11,000 with a population EVPI of nearly £100 million. The EVPPI suggests that eliminating uncertainty around costs and utilities is most worthwhile. **CONCLUSIONS:** With current information AS and BT are cost-effective treatments for intermediate-risk prostate cancer at relatively low cost/QALY thresholds, and RP is expected to be the most cost-effective of available treatments at the prevailing range of cost/QALY thresholds (i.e. £20,000-£30,000) . However, large decision uncertainty exists and acquiring further information is likely cost-effective. Future research on costs and utilities associated with treatment outcome and adverse events is expected to be most valuable.

CN3
EARLY STAGE COST-EFFECTIVENESS ANALYSIS OF A BRCA1-LIKE TEST TO DETECT TRIPLE NEGATIVE BREAST CANCERS RESPONSIVE TO HIGH DOSE ALKYLATING CHEMOTHERAPY

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OBJECTIVES: Triple negative breast cancers (TNBC) with a BRCA1-like profile may benefit from high dose alkylating chemotherapy (HDAC). This study examines whether treating TNBC with personalized HDAC based on BRCA1-like testing can be more cost-effective than current clinical practice. Additionally we estimated the minimum required prevalence of BRCA1-likeness and the required positive predictive value (PPV) for a BRCA1-like test to render this strategy cost-effective. **METHODS:** Our markov model compared the outcomes of treating TNBC women with personalized HDAC based on BRCA1-like testing vs. current clinical practice from a societal Dutch perspective and a 20-year time horizon. From our base-case model we assessed: 1) the incremental number of respondents; 2) the incremental number of Quality Adjusted Life Years, 3) the incremental costs, and 4) the incremental cost-effectiveness ratio (ICER). We performed one-way sensitivity analysis (SA) of all model parameters, and two-way SA of prevalence and PPV. Data were obtained from a current trial (NCT01057069), published literature and expert opinions where necessary. **RESULTS:** Based on our base-case analysis with 68% BRCA1-like prevalence, 100% PPV, and costs of € 164 / test, treating TNBC according to BRCA1-like testing would be cost-effective (€16.192/QALY). One-way SA on the prevalence and PPV demonstrated that only the PPV drives the ICER changes. In two-way SA, the lower bound for the two parameters was: prevalence 39.6% and PPV 46.4%. Regardless of prevalence, at PPVs > 46.4% BRCA1-like testing was always cost-effective. **CONCLUSIONS:** Treating TNBC with personalized HDAC based on BRCA1-like testing is expected to be cost-effective at a minimum PPV of 46%. This information can help test developers in decisions on further research and development.

CN4
THE COST OF COSTING TREATMENTS INCORRECTLY: ERRORS IN THE APPLICATION OF DRUG PRICES IN ECONOMIC MODELS DUE TO DIFFERING PATIENT WEIGHTS

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OBJECTIVES: Drug costs are generally a key driver of the results of economic models. We tested the impact on drug cost estimates for the following common approaches: using mean patient weight, individual patient weights or fitting a distribution to the observed patient weights. **METHODS:** For the analysis, we utilised patient weight and height data from trial CA184-024 (517 patients) in metastatic melanoma. Based on this dataset, costs of a single administration of drug therapy were calculated using UK list prices. Costs were calculated for four recently licensed treatments with different posologies: ipilimumab (mg/kg, with 2 vial sizes), cabazitaxel (mg/m^2), ustekinumab (doubled dosage over 100kg patient weight) and romiplostim (µg/kg, with a large, single vial size). **RESULTS:** Cost estimates using the mean patient weight were £18,750, £3,696, £2,147 and £482 per administration of ipilimumab, cabazitaxel, ustekinumab and romiplostim, respectively. These results increased by 4.9%, 2.3%, 10.3% and 36.6% when costing individual patient weights, and by 5.2%, 2.3%, 11.8% and 36.9% when fitting a distribution to the patient weights. The use of only mean patient weight consistently underestimated costs compared to methods that incorporated the distribution of weight data. Sampling from the observed patient weight distribution provides a more accurate estimation of costs; however, it is subject to over- or under-estimation, depending on enrolment in a trial programme, particularly amongst patients who are substantially over- or under-weight. **CONCLUSIONS:** Accurate estimation of drug costs requires an understanding of the distribution of patient weights. Failing to take this into account can result in cost estimates that are substantially lower than will be seen in practice, which could (in turn) impact treatment (implementation) decisions. These errors would be further compounded should drug wastage not be adequately captured. Modellers should be mindful of these issues when costing therapies or conducting health technology assessment submissions.

CONCEPTUAL PAPERS

CP1
THE EVALUATION OF ECONOMIC METHODS TO ASSESS THE SOCIAL VALUE OF MEDICAL INTERVENTIONS FOR ULTRA-RARE DISORDERS (URDS)

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OBJECTIVES: To develop a set of criteria to critically appraise the strengths and weaknesses of health economic methods for the systematic valuation of interventions for ultra-rare disorders (URDs). **METHODS:** An international group of clinical and health economic experts met in conjunction with the Annual European ISPOR Congresses in Berlin/Germany and Dublin/Ireland, November 2012 and 2013, to deliberate and agree on a set of criteria to assess the potential of the various methods, which have been used or proposed to estimate the social value of medical interventions for URDs. **RESULTS:** The group identified a broad set of potential criteria, which may be grouped according to the following dimensions: theoretical foundations (normative premises, i.e., links to moral and economic theories, including - but not limited to – nonutilitarian consequentialist and deontological reasoning, definition and treatment of core concepts of economic thinking such as opportunity costs and efficiency), empirical underpinnings (social preferences related to attributes of the health condition or of the person afflicted with it), and pragmatic aspects (feasibility of implementation and potential for bias and misuse). For each of the dimensions, a set of criteria has been agreed upon, which in turn will need further scrutiny and justification. **CONCLUSIONS:** Previously, a need had been identified for modifications or alternatives to the conventional logic of cost effectiveness applying benchmarks for the maximum allowable cost per quality-adjusted life year (QALY). We propose a framework for the systematic assessment how well different evaluation approaches reflect prevalent social norms and value judgments. As a next step, the framework shall be applied on multi-criteria decision analysis methods and social cost value analysis, either using the person trade-off (PTO) or the relative social willingness-to-pay (RS-WTP) instrument.

CP2
VALUE IN THE MAKING: HARVESTING THE VALUE OF COMPLEX MEDICAL INNOVATIONS IN PRACTICE

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Rapid development of medical innovations in the face of rising health care costs have been calling for a more value-conscious adoption and diffusions of innovations. This conceptual paper departs from swift adoption of the da Vinci surgical robot in the Netherlands. It describes three challenges facing health care systems to evaluate promising, yet complex and often expensive medical innovations. Firstly, they are often adopted and diffused prior to their evidence-based superiority being proven. Secondly, formal evaluation frameworks are somehow detached from the dynamics of and incentives for adoption and diffusion of these innovations. Third, the real risks and benefits of these innovations are not easily amenable to an experimental inquiry. Unlike pharmaceuticals, whose impact is intrinsic to its biochemical components and thus can be subject to experiment, the value of complex surgical devices, imaging equipments, or targeted therapy interventions are inseparable from actual patterns of human practices and clinical pathways that utilize them. Multi-stakeholder (early) deliberation has often been proposed to better align value requirements with the adoption and diffusion processes. This article examines the importance of developing a shared value perspective on the implementation of complex innovations through early deliberation. Product developers, (potential) adopters (providers or patients), purchasers, and policy makers may engage in an upfront iterative deliberation on all the particularities and (pre)conditions that account for delivering value of a certain innovation during early adoption in a given care delivery setting. Such deliberation offers a cumulative learning as to how to reduce true-to-life uncertainties and risks 'along the way', thereby serving for value 'fulfillment' in practice. Implication of such situated deliberative platforms for technology (outcome) assessment and for the role of authorities is discussed. A concrete framework for multi-stakeholder deliberation applied to the case of the da Vinci surgical robot in the Netherlands is also proposed.

CP3
EVALUATING THE QUALITY OF EVIDENCE FROM A NETWORK META-ANALYSIS

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Systematic reviews that collate data about the relative effects of multiple interventions via network meta-analysis are highly informative for decision-making purposes. A network meta-analysis provides two types of findings for a specific outcome: the relative treatment effect for all pairwise comparisons, and a ranking of the treatments. It is important to consider the confidence with which these two types of results can enable clinicians, policy makers and patients to make informed decisions. We propose an approach to determining confidence in the output of a network meta-analysis, based on methodology developed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group for pairwise meta-analyses. The suggested framework for evaluating a network meta-analysis acknowledges (i) the key role of indirect comparisons (ii) the contributions of each piece of direct evidence to the network meta-analysis estimates of effect size; (iii) the importance of the transitivity assumption to the validity of network meta-analysis; and (iv) the possibility of disagreement between direct evidence and indirect evidence. We illustrate the framework using a network meta-analysis of topical antibiotics without steroids for chronically discharging ears with underlying eardrum perforations.

CP4
AMENDING THE GUIDE TO METHODS OF TECHNOLOGY APPRAISAL AT NICE TO INCORPORATE TWO NEW VALUE ELEMENTS: BURDEN OF ILLNESS AND WIDER SOCIETAL IMPACT

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BACKGROUND: In July 2013 the Department of Health referred terms of reference for value based assessment of health technologies to NICE. **OBJECTIVE:** We present the approach taken over the past 11 months to amending the Guide to Methods of Technology Appraisal to incorporate burden of illness and wider societal impact. **METHODS:** Given the time frame available, NICE built on prior work undertaken by the Department of Health (in the context of value based pricing) on the concepts of burden of illness and wider societal benefits by commissioning the NICE Decision Support Unit to review and critique this existing work. NICE reconvened the working party from the Guide to the Methods of Technology Appraisal review which took place in 2012, which included standing membership drawn from the stakeholder communities such as patient and professional organisations, academia and pharmaceutical industry. The working party considered the prior work undertaken by the Department of Health and the Decision Support Unit's critique for burden of illness and wider societal benefit, and provided advice on the incorporation of the 2 new value elements into NICE's current methods at 4 meetings. A consultation paper describing NICE's proposals and draft of the amended sections of the methods guide was published in March 2014, and consultation ran for 12 weeks. It is anticipated that the final amendment of the methods guide will be considered by the NICE Board in advance of the ISPOR conference. **RESULTS:** Key points drawn from the discussion at the working party and consultation responses regarding burden of illness and wider societal impact, will be discussed. **DISCUSSION:** Considering NICE's 'position' in the world of health technology assessment and appraisal, the conclusions from this latest amendment of the Guide to Methods of Technology Appraisal to incorporate value based assessment will be (highly) anticipated.

DIAGNOSTIC RESEARCH STUDIES

DI1
COST-EFFECTIVENESS (CE) OF IMAGING-GUIDED STRATEGIES FOR THE DIAGNOSIS OF CORONARY ARTERY DISEASE (CAD): RESULTS FROM THE EVINCI STUDY

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OBJECTIVES: To evaluate the cost-effectiveness (CE) of imaging-guided strategies for the diagnosis of significant coronary artery disease (CAD) in patients with intermediate pre-test likelihood. **METHODS:** Significant CAD was defined at invasive coronary angiography (ICA) as >50% stenosis in the left main or >70% stenosis in a major coronary vessel or 30-70% stenosis with fractional flow reserve ≤0.8.Nine diagnostic strategies were compared using a CE analysis. Strategies included the use of one single or two combined non-invasive imaging tests (CTCA as first line test and then stress ECHO, CMR, PET or SPECT) followed by ICA in the case of positivity of the single test or both non-invasive examinations in the case of combinations. ICERs were obtained using per-patient data collected throughout the EVINCI multicentre European study. Strategy costs were calculated using examination country-specific reimbursements, while effectiveness was defined as the percentage of correct diagnosis. All costs were converted to Euro 2012 and adjusted using PPP. A propensity-score adjustment was used in the analysis and 95%CI were obtained with non-parametric bootstrap. **RESULTS:** Among the strategies analysed only three resulted cost-effective for the diagnosis of significant CAD. These included stress ECHO and CTCA as single non-invasive test, CTCA first then ECHO, CTCA first and then stress PET, all followed by ICA when required. Stress ECHO approach was the least costly but also the least effective, while CTCA alone [ICER: 2345 (2287-2400)] or in combination with PET [ICER: 5227(5161-5296)] had increasingly higher effectiveness for a willingness to pay (WTP) exceeding 2,000 Euro and 5,000 Euro, respectively. **CONCLUSIONS:** Results from the health-economic analysis of the EVINCI study showed that stress ECHO guided diagnostic strategy could be cost-effective when the WTP is low. Strategies involving CTCA alone or as first line exam followed by stress PET could allow a more accurate diagnostic workflow for higher WTP.

DI2
THE VALUE OF RISK-STRATIFIED INFORMATION IN THE NATIONAL LUNG CANCER SCREENING TRIAL

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OBJECTIVES: Clinical guideline recommendations are generally informed by population-based evidence. However, interventions that are (cost-)effective on average may not be (cost-)effective for many (even for most) patients meeting trial inclusion criteria. This study aims to investigate the value of risk-stratified recommendations for lung cancer screening among current or former smokers between the ages of 55 and 74 years compared to a screen-all policy. **METHODS:** Using data from the National Lung Cancer Screening Trial (NLST), we calculated the costs and QALYs for low-dose computed tomography (CT) versus chest radiography (X-ray) from empirically observed health states and 6 years life expectancy. Based on Kovalchik's risk of lung cancer death prediction model, we stratified 53,454 NLST trial patients into quintiles. The expected value of individualized care (EVIC) was calculated to