

HG4

THE VALUE OF HETEROGENEITY FOR COST-EFFECTIVENESS SUBGROUP

ANALYSIS: THEORETICAL FRAMEWORK AND APPLICATION

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OBJECTIVES: Decisions about the use of new medical technologies based on estimates of the average cost-effectiveness across a potentially heterogeneous population runs the risk of foregoing net health benefits (NHB) for sub-groups of the population. We propose a general framework within which to assess between-patient heterogeneity and its role in cost-effectiveness subgroup analysis (CESA), complementing this with a practical application. **METHODS:** We first describe how to extend methods for cost-effectiveness analysis (based on current information) to address issues such as estimation of NHB, sources of heterogeneity, definition and selection of subgroups. Next, we define the role of uncertainty in CESA, extending the concept of Value of Information (VoI) to include the notion of a static and dynamic Value of Heterogeneity (VoH). The application of the proposed theoretical framework is illustrated using a cost-effectiveness model developed for the analysis of a multicentre-trial (RITA-3), which assessed the efficacy of an early arteriography with revascularisation versus standard management in patients with acute coronary-syndrome. Using this model we conducted a re-analysis investigating alternative subgroup specifications, varying between one and five subgroups, with a view to produce an efficiency frontier for subgroup analysis relating to this decision problem. We assessed the static and dynamic VoH under each specification. **RESULTS:** The population expected NHB when considering five subgroups was 105,500 QALYs greater than decision based on estimates for the average population (static-VoH). Although, identifying 5 subgroups reduced in the Expected Value of Perfect Information (EVPI) (920 QALYs, at a threshold of £30,000/QALY), the potential NHB from resolving uncertainty was greater after heterogeneity has been identified (dynamic-VoH). **CONCLUSIONS:** Our initial findings support the argument that explicit consideration of heterogeneity in CEA leads to a positive static and dynamic VoH. In addition, heterogeneity not only may increase the EVPI but can also reduce its magnitude. The VoH framework offers a useful guidance for a more systematic CESA.

PODIUM SESSION III:

TOWARDS A BETTER UNDERSTANDING OF REIMBURSEMENT DECISIONS BASED ON HTA ARGUMENTS

HT1

EFFECTIVENESS, EFFICIENCY AND BUDGET IMPACT AFFECT THE BELGIAN DRUG REIMBURSEMENT DECISION (DRD)

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OBJECTIVES: The European Transparency Directive 89/105 (TD) imposes the use of objective and verifiable criteria in national pharmaceutical reimbursement decisions: for pharmaceuticals claiming added therapeutic value (ATV), the Belgian DRD uses 5 criteria comparing the product to its alternatives: effectiveness, efficiency, price, budget impact and therapeutic need. The study aim was to analyze the effect significance and size on the (yes/no) DRD of a set of parameters including: added therapeutic value ATV (yes/no), trial end-points (clinical or surrogate), level of evidence (RCT yes or no), availability of alternatives (yes/no), ICER and budget impact (in K Euro) in order to estimate the percentage of variability in DRD that could be explained by these explicit factors. **METHODS:** The National Health Insurance administrative database was used for extracting all publicly available DRDs on products claiming ATV submitted between 2002 and 2007. Data retrieval was substantially extended compared to previous work. ICERs expressed per QALY or per LYG were pooled. Logistic regression was performed using SPSS 15.0. The significance level was set at 0.05. **RESULTS:** A total of 110 submissions were retrieved: 40% had complete records. The regression analysis yielded a significant model ($p < 0.01$) with 58% of the variance explained and only 3 significant factors: ATV ($p < 0.001$), budget impact estimate ($p < 0.05$) and the computed ICER ($p < 0.05$). Higher estimates of budget impact and ICER decreased the probability of a positive DRD. No significant interactions were observed ($p > 0.10$). **CONCLUSIONS:** Multivariate analyses identified granting of ATV, pharmaceutical budget impact and the economic ICER to significantly affect the DRD. These 3 factors are among the 5 criteria on which the DRD should be based. Because of missing data some caution is needed on these inferences. Systematic public reporting of key submitted data would increase the feasibility of powerful analyses enhancing transparency.

HT2

VALUE BASED PRICING: ONE THRESHOLD TOO FAR FOR THE UNITED KINGDOM

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ISSUE: The budget for the NHS in England is declining in real terms by around 2% per year. Despite productivity having fallen in recent years, the NHS expected to make efficiency savings of between £15 and 20bn over the next 3 years. Will the proposed implementation of value based pricing (VBP) help or hinder the pursuit of a more efficient NHS. **OVERVIEW:** The objectives for implementing VBP and replacing the PPRS in the UK are to encourage innovation where there is unmet need, improve outcomes and ensuring value for money to the NHS with better access to effective medicines. Different willingness to pay thresholds are suggested as a way to incorporate these societal benefits when setting the price of a new pharmaceutical. Using this mechanism to incentivise pharma could be profitable for the industry with the unintended outcome of decreasing efficiency in the health service

at a time when it is not affordable. Let's consider two 'innovative' products (A and B) and assume a WTP of £40,000/QALY is acceptable. It would not be unreasonable to expect the price to be set to this level. Now let's take the price of the new drug out of the equation. Drug A has a cost/QALY of £15K and drug B £25k. The innovation of drug A comes at a higher price than drug B. An alternative would be to fix the innovative component at an additional £20k for example, up to a set maximum threshold. Drug A plus innovation mark-up would be allowed to price to £35k and drug B limited to the £40k maximum threshold. **CONCLUSION:** The efficiency of the UK NHS will be compromised if, as proposed, multiple willingness to pay (WTP) thresholds are implemented in the value based pricing (VBP) scheme for pharmaceuticals.

HT3

UNDERSTANDING THE COMPLEXITY OF HTA NETWORKS

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OBJECTIVES: In recent years Health Technology Assessments (HTA) are increasingly applied to healthcare decisions, involving a complex constellation of stakeholders. Effective collaboration and communication with the HTA stakeholder community requires a holistic understanding of this ecosystem. To better understand multi-stakeholder influence dynamics across the HTA ecosystem, social network analysis techniques were employed. **METHODS:** Information on 74 HTA agencies was collected from various sources. Four data categories were included: agencies, institutions, people (members) and technologies. For each category a number of attributes were included (location, affiliations, memberships, type of technology, decision on technology, etc.). The connections and types of connections between the datasets were added. The Ni3 software was applied to this data to conduct the analysis and visualize HTA networks. **RESULTS:** The analysis enabled us to establish directions of influence (sources vs. absorbers: e.g., NICE vs. AHTAPol) within a network, correlation between the level of connectivity and the influence on market access, and also to observe HTA impact on the level of a drug or therapeutic area. The tool enabled mapping of relationship links that represent direction and weight of influence, overlaying displayed stakeholders with visual charts summarizing sets of quantitative values (such as number of employees or budget) for visual pattern matching and comparison, and geographic analysis. **CONCLUSIONS:** The application of social network analysis allowed visualization of the complex multi-stakeholder dynamics across HTA ecosystems to answer questions such as who are key influencers when it comes to coverage and reimbursement decisions. Understanding the complexity of healthcare networks is key to answering today's business-relevant questions. Although this research was explorative in nature, it warrants further refinement by combining HTA expert networks with commonly available KOL networks, to further explore the connectivity within the New Health ecosystem.

HT4

WHAT DETERMINES THE RECOMMENDATIONS ISSUED BY POLISH HEALTH TECHNOLOGY AGENCY (AHTAPOL)?

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OBJECTIVES: AHTAPol operates in Poland since 2005. Recommendations issued by Consultative Council of AHTAPol are closely tracked as they support reimbursement decision making. We aimed at evaluating of predictors for positive (supporting covering of costs from public budget) and negative recommendations of AHTAPol. In particular we wanted to see whether a threshold value for ICER (cost per QALY) can be identified to drive AHTAPol decisions. **METHODS:** As only recommendations texts, neither HTA reports nor critical appraisals, are publicly available on the official website, two independent analysts have reviewed all recommendations issued before January 28, 2011. Each recommendation was evaluated using predefined criteria on decision rationales, i.e. whether negative or positive recommendations were supported by arguments on clinical efficacy (with special interest on hard endpoints defined according to Polish HTA guidelines), safety, cost-effectiveness, budget impact and others. PPV, NPV, LR- and LR+ were calculated for each criteria. Although the content of recommendations is structured, not all could be assessed based on each of the predefined criteria. Prediction model was developed for positive and negative recommendations. **RESULTS:** Two hundred eighty-five recommendations were identified including 177 positive and 108 negative ones, which were generally more elaborated. Clinical efficacy motivates recommendations most often, but positive impact on hard endpoints was explicitly reported in 15 negative recommendations and lack of such proven efficacy in 38 positive recommendations. Safety and cost-effectiveness were more often recalled in negative than positive recommendations. Budget impact of novel technology was a weak predictor of recommendation. No threshold value of QALY cost can be specified based on recommendations. **CONCLUSIONS:** Decision making by Consultative Council of AHTAPol is multi-dimensional and can be hardly predicted. Apart from efficacy, negative recommendations are mainly driven by unfavorable safety and cost-effectiveness.

PODIUM SESSION III:

FINDING CROSSWALKS BETWEEN QALY INSTRUMENTS AND DISEASE-SPECIFIC PROS

MA1

MAPPING THE EQ-5D INDEX FROM I-QOL IN IDIOPATHIC AND NEUROGENIC OAB PATIENTS: RESULTS FROM A CROSS-SECTIONAL STUDY IN THE UNITED STATES AND FOUR EUROPEAN COUNTRIES

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