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Many methods are currently available to estimate treatment effects with observational data. We conducted simulations evaluating some well-established methods (regression, propensity weighting, stratification or matching on propensity) as well as some newer ideas (tree based methods, local control, entropy balancing, prognostic scoring) under several different scenarios including homogeneous and heterogeneous treatment effects. Mean square error, bias, coverage probability for the overall treatment effect, and prediction accuracy of personalized treatment contrast (for scenarios with heterogeneous treatment effect) were assessed. We will present some guidelines for estimating treatment effects with observational data and strategies that are appropriate with respect to (i) tree-structured treatment models (ii) polynomial outcome model with interactions (iii) presence of noise covariates.

PRM245

HEALTH TECHNOLOGY ASSESSMENT AND ENVIRONMENTAL COSTS: TIME FOR HEALTH CARE TO CATCH UP?

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OBJECTIVES: The United Nations recently published its most definitive report, calling for greater action on climate change. Historically, however, health technology assessment (HTA) has had a more narrow focus with emphasis on the health of patients and health inequalities. Recently some health care decision makers have extended the focus to include the environment, e.g. the Swedish Government is considering a Green Premium for generic drugs, and the UK NHS has CO2 emissions targets. We consider the case for incorporating environmental impacts into HTA, and the associated methodological challenges. **METHODS:** We reviewed health care decisions where environmental impacts were considered - a summary will be provided in the paper. We then convened a workshop with key opinion leaders. **RESULTS:** There are two lines of reasoning for incorporating environmental impacts into HTA: 1) Direct impact: changes in the environment could affect the health of individuals; and 2) Health decision makers' objectives are broader and are informed by other policy goals, such as the CO2 targets adopted by the NHS in the UK. We also identified two types of methodological challenges for implementation. First, the nascent evidence base is insufficient to support the accurate comparison of the environmental impact of technologies. Second, uncertainty about how best to incorporate evidence into HTA. The cost-utility analysis approach favoured by many HTA agencies could capture some of the value of environmental impacts – in particular, those that generate health impacts. Both cost-benefit analysis and multi-criteria decision analysis have potential, having both previously been applied to evaluate both health and environmental interventions, though are less familiar to health care decision makers. **CONCLUSION:** Further work is needed to track decision makers' demand for evidence on environmental impacts. Robust methods also are needed for capturing and incorporating environmental data as part of HTA as more decision makers begin incorporating environmental impacts.

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MULTIPLE DECISION CRITERIA FOR ASSESSING AN INCREMENTAL COST-EFFECTIVENESS RATIO OF EXPENSIVE HEALTH TECHNOLOGIES

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OBJECTIVES: To develop a new method that naturally extends the UK NICE way of single-threshold for incremental cost-effectiveness ratio (ICER). It aims to provide multiple decision criteria for assessing an ICER of expensive health technologies such as molecular-targeted cancer drugs and regenerative medicine products. **METHODS:** We took a theoretical approach, provided that the cost (C) -effectiveness (E) function, C = f (E), is known regarding the treatment alternatives for a disease area, given two points P_b and P_s plotted with a pair of C and E on the C-E plane, where P_b represents the best comparator, and P_s as the second best for a new technology X located at the point. P_x (e_x (effectiveness; known), c_x (cost; assumed)). At first, given a single threshold of ICER, the "expensiveness" in the C-E function was defined using a tangent/derivative method (poster presentation PRM119 by Kamae I, et. al. in ISPOR Montreal 2014). Second, we estimated three benchmarks based on the C-E function: 1) the ICER of P_b to P_s, 2) the tangent at P_b, 3) the tangent at the point on the C-E curve which intersects with the vertical line at the point: (E, C) = (e_x, 0). Then the magnitude relationship was examined between the three benchmarks and the ICER of the technology X defined by the slope of the line connecting P_x with P_b. **RESULTS:** Multiple decision criteria at six levels were identified and formulated as for acceptance of the "expensive" cost-effectiveness of a new health technology: 1) unconditional acceptance (simple dominance), 2) preferred (extended dominance), 3) less preferred, 4) minimally preferred, 5) not preferred, but negotiable, and 6) cannot accept. Example calculations clarified how the theory works in practical setting. **CONCLUSIONS:** Our approach offers multiple decision criteria to assess expensive health technologies as a natural extension beyond the NICE way of single-threshold assessment.

PRM247

EFFICACY, EFFECTIVENESS AND THE "EFFICACY-TO-EFFECTIVENESS GAP": REVIEW OF THE CURRENT STATE OF PLAY AND PERSPECTIVES. FIRST RESULTS FROM THE IMI GETREAL CONSORTIUM

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BACKGROUND: The concept of "efficacy-effectiveness gap" (EEG) has gained awareness in the scientific community and started to erode the confidence in decisions taken on drugs: authorization, appraisal, and medical choice between alternatives. The Innovative Medication Initiative was launched the GetReal project to tackle this issue. It gathers representatives of more than 14 pharmaceutical companies, public institutions such as EMA, HAS, ZIN, NICE and Academic research teams and aims at (1) better understanding how evidence of efficacy and effectiveness should be considered and reconciled and (2) proposing operational solutions. **OBJECTIVE AND METHOD:** We conducted a focused literature review to gain clarity and perspective on the concept of EEG: on which historical background it emerged, how it is understood and which solutions have been suggested to narrow it. **RESULTS:** A disconnect between outcomes from clinical trials and information needed for clinical practice has been identified in the process of standardization of drugs assessment (Schwartz, 1967), evidence-based medicine (Feinstein, 1997), and knowledge dissemination (Lehman, 1995), and called the EEG. Several factors have been identified to explain it, including characteristics of real-life health care settings (physician and patient behaviours) and the weak generalizability of clinical trials due to their design. The need for a more systematic assessment of effectiveness is now widely acknowledged. Adaptive licencing was recently proposed to account of the sequential evidence generation on drugs outcome (Eichler, 2011). The EEG can be conceptualized as the interaction of drug effect and "real-life" contextual factors (Unutzer, 1999). **CONCLUSIONS:** Although the literature on the EEG is extensive, the contextual factors that *actually* impact drug's outcome in real-life are still to be identified. Innovative and integrative study methods and designs are required to enable the EEG to be addressed adequately early on in the drug development process: this is the next step in the GetReal project.

PRM248

HEALTH TECHNOLOGY ASSESSMENTS FOR PERSONALISED MEDICINES: ARE CURRENT METHODOLOGIES SUITABLE FOR THE ASSESSMENT OF PERSONALISED THERAPIES?

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OBJECTIVE: An increased drive towards personalised healthcare and medicine by policy-makers, alongside technological advances in medicines and diagnostics, is leading to more personalised medicines coming to market. Given that personalised medicines differ from traditional medicines in their development, use and cost, previously published articles have stated that current health technology assessments (HTA) methodologies are not designed to appropriately evaluate these technologies. This research was conducted to provide insights on methods for evaluating personalised medicines and what modifications to current HTA processes would be needed to ensure robust and timely assessment. **METHODS:** Qualitative interviews were conducted with five experts in personalised medicine and market access across the UK, US and Germany to discuss the movement towards and benefits of personalised medicines as well as the key metrics on which they should be evaluated. These insights, supported with secondary research, were used to provide suggestions on the structure and methodology of personalised medicine assessments and how current assessment processes would need to be altered to accommodate these unique technologies. **RESULTS:** The key areas where personalised medicines would need special consideration in HTAs identified were: - Study design: population size, geography, ethnicity - Companion diagnostics: cost, logistics - Unmet need: individualised view of perceived benefit - Cost effectiveness: costs and outcomes of therapy and companion diagnostic, reduction in overall health care costs **CONCULSION:** The key areas identified are discussed in further detail, specifically, as to how they could be incorporated into current HTA models to effectively assess personalised medicines and how they would influence the decision-making process.

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CHALLENGES IN MEETING EVIDENCE NEEDS OF PAYER, PHYSICIAN, PATIENT AND INDUSTRY STAKEHOLDERS FOR NOVEL THERAPEUTICS

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OBJECTIVES: Evidence development programs for novel therapeutics must simultaneously demonstrate safety, efficacy, clinical significance, economic value and effectiveness to meet diverse stakeholder requirements. This is further complicated by variable evidence needs across global markets and resource limitations. Understanding how to address all stakeholder perspectives for treatments in ophthalmology was accomplished through primary research. **METHODS:** Conducting primary research through in-depth phone interviews and advisory board meetings with patient, payer and clinical stakeholders in three ophthalmic conditions: chronic, non-infectious posterior uveitis, wet age-related macular degeneration and glaucoma provided important insights. Patient research questions focused on identifying patient burden and unmet needs. Further research with physicians and payers was accomplished through evaluating diverse criteria applied to assessing clinical and economic evidence plans. **RESULTS:** When therapeutic areas lack universally accepted clinical guidelines that can be relied upon to guide treatment decisions, payers rely heavily on clinicians to understand current standard of care and accepted endpoints. Clinician leaders, interestingly, were not in universal agreement. Moreover, physicians and payers differed on use of economic endpoints and appropriate therapeutic comparators. Physicians differed on the endpoints that would be most relevant for demonstrating treatment response and how to address the patient burden. Overall, clinicians were more willing to consider clinical trial endpoints that differed from those endpoints found in published data. Payers preferred to have consistent endpoints to facilitate indirect comparisons between treatments. **CONCLUSIONS:** The differing needs of payer and clinician stakeholders create additional barriers for development planning for novel therapeutics, particularly when published treatment guidelines are not available. Manufacturers must consider multi-stakeholder insights across global markets in clinical trial design development. [1]Santen Pharmaceuticals, Emeryville, CA, USA. [2]GfK Market Access, Wayland, MA, USA.