### PRM250

**PATHWAYS OF IMPLEMENTATION OF MULTI-CRITERIA DECISION ANALYSIS INTO ORPHAN DRUG APPROVAL PROCEDURE FOR DRUG SUPPLY PROGRAMS IN RUSSIAN FEDERATION**

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**BACKGROUND:** While the orphan drug supply program is in progress, development of decision-making rules for approving orphan drug for supply programs of Russian Federation becomes very actual. Real world data provides evidence, that routine approaches for approving such kind of drugs, e.g. pharmacoeconomic conclusions, are not applicable. Than the need in more appropriate approaches is existed. Multi-criteria decision analysis is one such approaches (MCDA). **OBJECTIVE:** To evaluate prospective of implementation of MCDA in health care system of Russian Federation and to develop road map of MCDA in Russia. **METHODS:** Literature review and interviewing experts. **RESULTS:** There are different potential perspectives (qualitative) to implement MCDA is to test various MCDA methods to find out optimal one for Russian Federation: it is expected to select the most relevant criteria from the wide range of them. First of all, MCDA is considered to be the instrument to improve the transparency, to underline different points of view and unmet needs. On the second stage it may be possible to use quantity MCDA assessment as a rule to approve orphan drugs for drug supply programs. Local recommendations for MCDA in Russian Federation has been published. **CONCLUSION:** Implementation of MCDA as assisting instrument for orphan drug approving for drug supply programs is likely to be a valuable approach, that may improve the quality, transparency of decision-making process and to provide social equity for accepting decisions.

### PRM251

**PROBABILITY SCORE MATCHING AND SUBCLASSIFICATION WITH MULTIPLE-LEVEL TREATMENTS**

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There is extensive literature on methods, such as propensity scoring, for estimating causal effects from observational data. Much less work has been done for the more general setting with three or more treatments. Whereas the literature has suggested that these propensity-based methods do not naturally extend to the multi-level treatment case, we show, using the concept of weak unconfoundedness, that adjusting for or matching on a scalar function of the covariates removes biases associated with observed covariates. We focused on subclassification and matching approaches as these have found to be effective for two treatments and are among the most popular methods in that setting. We apply the proposed methods to an analysis of the effectiveness of treatments for fibromyalgia from a prospective observational study. We also carried out a simulation study to assess the performance of these methods relative to such approaches like: pairwise propensity score matching; matching on the Mahalanobis distance of all covariates; matching on the set of propensity scores (with the number of scores equal to the number of distinct treatment levels minus one) that are obtained from the published literature, analyses of database information, and/or interviews with experts in the field. Steady state solutions of the model equations estimating the causal effects and period prevalence. This approach is particularly useful to account for inter-treatment stromal tumors and multiple myeloma. Resulting estimates are important for budget impact analysis and health care services planning by reducing uncertainty associated with identifying the patient numbers that might be treated.

### PRM252

**GETTING TO REIMBURSEMENT FASTER: COMBINING RANDOMISED, FRAGMATIC, AND OBSERVATIONAL CLINICAL TRIAL DATA**

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Reimbursement authorities often require pharmaceutical companies to provide them with more than just placebo-controlled data from RCTs. Instead, they typically seek data from a wider “real-world” setting, where the focus is on generating evidence of comparative effectiveness. The natural temptation for many pharmaceutical companies is to provide this evidence from separate, post-market approval studies. However, this approach can be expensive and undoubtedly leads to delays in reimbursement. We propose that both the additional costs of evidence gathering and the delays between regulatory and reimbursement approvals could be reduced by combining the main design elements of randomised, pragmatic and observational studies into a single, integrated Phase 3/4 study. This single study approach would typically begin with a standard RCT phase where, for example, an initial cohort of patients would be randomised to receive either the investigational therapy or placebo. Either in parallel or following this phase, a second patient cohort would be randomised under pragmatic clinical conditions with the aim of comparing the investigational therapy with placebo and a limited number of active comparator treatments. Lastly, a third (observational) cohort would be enrolled and allocated to a wider range of therapies for patients in clinical practice. Data from the RCT cohort would be used to obtain limited regulatory approval. Following this, data from the pragmatic cohort, once available, would then be formally combined using standard statistical techniques with data from the RCT cohort in order to obtain a wider regulatory approval and possibly some form of conditional reimbursement. The pragmatic and observational cohorts would then provide the comparative effectiveness data to allow for reimbursement across different patient groups. We outline the strengths and weaknesses of this approach, and discuss its operational considerations.

### PRM253

**AN EPIDEMIOLOGIC MODEL APPLICATION TO PHARMACOECONOMICS FOR IMPROVED HEALTH CARE PLANNING**


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Epidemiologic and pharmacoeconomic models differ in terms of populations considered, methodological techniques used, and questions addressed. A typical pharmacoeconomic model assesses chronic or acute conditions, uses Markov techniques, and considers a closed patient group receiving a defined therapy to assess incremental costs needed to achieve gains in quality adjusted life years. A typical epidemiologic model assesses vaccination or public health interventions for infectious disease using differential equations and considers open population representing community in terms of disease occurrence or numbers of disease cases over time. The manner of conducting sensitivity analyses also differs. In oncology, in which multiple lines of treatment are available, the epidemiologic approach has application to estimating the potential impact of new treatments. Epidemiologic modeling permits a framework to estimate disease prevalence that is little used in pharmacoeconomics.

### PRM254

**NON-INTERVENTIONAL RESEARCH ETHICAL REQUIREMENTS IN ENGLAND AND FRANCE: SHARED EXPERIENCE FROM A BINATIONAL RESEARCH PROJECT**

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**BACKGROUND:** Ethical review for non-interventional research is progressively becoming part of research standards. This evolution ensures that participants in research are respectfully considered. In practice, information on ethical requirements for non-interventional research seems insufficient. Increasing and legitimate expectations from peer-reviewed journals regarding reviews by ethics committees sometimes challenge the capacity of ethics review panels to respect ethical requirements for conducting a questionnaire-based research on physicians in France and England. **METHODS:** This investigation consisted of a documentary analysis, including official guidance documents on ethical requirements, communications with institutions and publications reviews. Documents were identified using an ad hoc search on official websites. Publications were identified on PubMed and Google. **FINDINGS:** In England, the service of the National Research Ethics Service (NRES) serves as the ethics reviewer. It offers an informal preliminary review of the study protocol and ethics requirements. The NRES supplies an email which can be used as a justification for peer-reviewed journals. In France, structures to support ethical reviews for non-interventional research are the result of an on-going reform of the law 89-494 of May 3, 2004. **CONCLUSION:** This experience showed that the role of ethical review panels is necessary to ensure compliance with ethical requirements in non-interventional research. It is a domain in constant movement which calls for innovative approaches to compile and disseminate information regarding ethical requirements for non-interventional research across Europe and the world, especially regarding cross-national research projects.