METHODS: This exploratory analysis suggests that use of a broader range of metrics to assess and benchmark value across tumor types may be needed to appropriately inform decision-makers looking to maximize clinical benefit to patients while managing constrained resources.

SAMPLE SIZE ESTIMATION FOR PROSPECTIVE OBSERVATIONAL STUDIES

OBJECTIVES: Unlike randomized clinical trials (RCTs), prospective observational studies typically address objectives rather than test specific hypotheses. Nevertheless, a minimum sample size is required to allow for adequate exploration of the objectives, and estimation of sample size is an important part of the planning process for these studies. Sample size estimation for observational studies is more complex than sample size calculation for RCTs; subgroup analyses and modeling are required to acquire more assumptions and larger sample sizes. At the same time, sample sizes are to be expected in observational studies, and these analysis methods may require more complex algorithms and cost calculations.

RESULTS AND CONCLUSIONS: These methods illustrate the difference between sample size estimation in prospective observational studies and sample size calculation in randomized clinical trials.

THE IMPACT OF CENTRE SELECTION ON THE GENERALISABILITY OF ECONOMIC EVALUATION RESULTS FROM MULTI-CENTRE RANDOMISED CONTROLLED TRIALS

METHODS: The working hypothesis is that transparent centre selection is a crucial step in assessing the generalisability of EE results from RCTs. Two questions arise: 1) What criteria underpin the current practice of selecting centres for RCT-based EEs? 2) Can a valid quantitative method be formulated to assist the centre selection process at the trial design stage? RESULTS: First, the use of modelling-based methods addressing generalisability has to be supported by evidence that centres are representative for the jurisdiction under scrutiny. There is, thus, a need to assess the current practice of selecting centres for RCT-based EEs. Second, a quantitative methodology for purposefully selecting centres for RCTs conducted with EEs has to be devised in order to underpin an objective centre selection process. The proposed operational measure is a generalisability index (GIx) which aggregates relevant generic and intervention-specific covariates and can be formulated at both jurisdiction and centre-level. The GIx can be validated against centre-level cost-effectiveness estimates. CONCLUSIONS: A successfully validated GIx will provide evidence towards the legitimate use of existing generalisability techniques. The GIx will allow an objective generalisability assessment for centres that did not participate in the RCT. Describing the rationale for centre selection must become a standalone item in reporting checklists for RCTs and EEs. Furthermore, such a methodology will bridge policy and research by correlating jurisdictional interests with RCT design.

MULTIPLE CHOICES - HOW TO MAKE RATIONAL DECISIONS ACROSS SEVERAL INTERVENTIONS WHEN FACED WITH DIFFERENT OUTCOMES AND PERSPECTIVES?

OBJECTIVES: In any assessment to facilitate decision making to allocate limited funding across multiple innovations, the relative value of clinical outcomes or cost-containment depends upon preferences. In the case of allocating funds across a portfolio of interventions, one could maximize cases-, hospitalizations-, or deaths-avoided and/or minimize costs from a health care payer or societal perspective.

METHODS: The optimal mix of innovations to reach the preferred target can be investigated by applying operational research modelling. However, a composite outcome is required in order to maximize multiple endpoints consecutively depending upon preferences. RESULTS: A comprehensive method was developed in Microsoft Excel® using the solver function to evaluate the optimal mix of vaccines to implement within a portfolio, in order to avoid specific clinical outcomes (e.g., deaths, hospitalizations, or deaths) or maximize QALYs gained within specific subgroups including budget. A composite endpoint was developed to take into account different endpoints, clinical and cost, weighted according to preferences defined by the assessor. The composite endpoint was used as the objective function. RESULTS: Depending upon the preference weights defined when determining the composite endpoint, the allocation of resources across a portfolio of several vaccines resulted in different recommendations. If death-avoided was weighted highest then the model would optimize on elderly influenza vaccination, adolescent HIV and infant pneumococcal vaccines. If cases-avoided was the highest preference then varicella, rotavirus and pertussis vaccines were recommended. If costs-avoided from a payer perspective were maximized, the model would be to first implement adolescent HIV, elderly influenza and rotavirus vaccination.

The combination of preferences to avoid mortality and/or morbidity and/or maximize cost offsets resulted in the recommendation to implement different vaccines from the portfolio. CONCLUSIONS: The use of a composite measure and operational research modelling provides a tool to facilitate resource allocation across a portfolio of interventions depending upon decision-maker preferences.

THE ROLE OF THE INSTRUMENT DEVELOPER IN THE TRANSLATION OF PATIENT REPORTED OUTCOME MEASURES

PRM66

OBJECTIVES: Developers of patient reported outcome (PRO) measures are often involved in the translation of their measures into other languages, and they provide valuable guidance by reviewing concept elaboration and back translation re-performed in different recommendations. If death-avoided was weighted highest then the model would optimize on elderly influenza vaccination, adolescent HIV and infant pneumococcal vaccines. If cases-avoided was the highest preference then varicella, rotavirus and pertussis vaccines were recommended. If costs-avoided from a payer perspective were maximized, the model would be to first implement adolescent HIV, elderly influenza and rotavirus vaccination.

METHODS: These exam-
and communication they enable. We will also look at the practicalities of each method, and their relative merits and drawbacks and how these can be addressed to make their usefulness in refining and improving the translation.

**CONCLUSIONS:** We will argue that both methods are beneficial in particular circumstances, and will explore the situations in which each one would be the most appropriate.

**PRM67**

*WHAT PRO MODALITY IS APPROPRIATE FOR YOUR STUDY?*

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**OBJECTIVES:** To help clarify which ePRO modality (IVR, IVR, Handheld) is appropriate for specific situations through providing three examples of diary requirements and appropriate modalities. Emphasize making this decision early in the planning process. **METHODS:** Examples for three scenarios requiring patients to record their PRO data electronically were drawn up based on experience how making approaches through providing three examples of diary requirements and appropriate modalities. Emphasize making this decision early in the planning process.

**RESULTS:** Scenario One – 10,000 patient global vaccine study. Scenario Two – 500 patient global study, daily diary having 40 questions with more than 5 response options. Scenario Three – 50 Gi patients to record their PRO data episodically using a VAS scale daily for over a year. **RESULTS:** Scenario One – Appropriate Choice – IVR. It is expensive and logistically challenging for Sponsors to deploy 10,000 PDAs. Using the IVR platform in place would reduce cost and logistics for the Sponsor and sites. Scenario Two – Appropriate Choice – IVR. When patients are provided more than 5 response options in a lengthy questionnaire, an IVR would be better since responses options are visual. IVR would be better than FDA given the sample size and logistics. Scenario Three- Appropriate Choice = FDA: A FDA would be most convenient for the patient since they are providing data daily for over a year. FDA is best for VAS scales since the size of the screen can be controlled. **CONCLUSIONS:** There is overlap in deciding which ePRO modality to use for a particular clinical study. It is critical to decide on the modality early when assembling the protocol, so all points can be considered. Looking at the diary requirements (frequency, length, access) for the study will help the Sponsor to decide which modality is best. Reducing patient and site burden will allow for greater compliance.

**PRM68**

*OUTCOME MEASURES HIERARCHY FOR ATTENTION-DEFICIT HYPERACTIVITY DISORDER*

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**OBJECTIVES:** Attaining good patient health outcomes is the underlying purpose of any health care intervention, including drug therapy. **METHODS:** The outcome measure is the basis for evaluating the quality of health services, and a key element in determining the value of health interventions since the value of health care is defined as outcomes relative to cost. According to Porter (2010), value improvement starts with defining and measuring the total set of outcomes for a medical condition and determining the major risk factors. Porter has provided a challenging framework for identifying the full set of outcomes for any medical condition: the outcome measures hierarchy (OMH). **RESULTS:** According to the OMH the full set of outcomes for any medical condition, and its treatment, can be conveyed in a threedimensional hierarchy. Each tier of the hierarchy contains two broad levels, each of which involves specific outcomes or direct outcome dimensions. Each medical condition should have its own outcome measures. Measurement efforts should begin with at least one outcome dimension at each tier, and ideally at each level. Possible outcome dimensions for Attention-Deficit Hyperactivity Disorder (ADHD) are explored and discussed according to Porter’s OMH. ADHD is a frequent neuropsychological disorder that is characterised by inattention, hyperactivity and impulsivity. ADHD is associated with considerable social, family, behavioural and cognitive dysfunction, and is comorbid to depression, bipolar disorder, anxiety, and drug use. Specific dimensions proposed are aimed at capturing particular aspects of patients affected by ADHD. For each dimension, success is measured with several clinical and patient reported metrics. The OMH is the patient’s health status achieved or retained after a health intervention (clinical or drug therapy). **CONCLUSIONS:** Tier 2 regards the process of recovery and the eventual disutility of the treatment process. Tier 3 concerns the sustainability of health.

**PRM69**

*MEASURING RELATIVE EFFECTIVENESS IN EUROPE: AS IN THE USA, HERE TOO, IT IS TIME TO TURN THE QALY PAGE*

Prieto L

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**OBJECTIVES:** The recently enacted Patient Protection and Affordable Care Act in the United States of America (USA) has created a Patient-Centered Outcomes Research Initiative for all medical conditions. healthcare, and a key element in determining the value of health interventions since the value of health care is defined as outcomes relative to cost. According to Porter (2010), value improvement starts with defining and measuring the total set of outcomes for a medical condition and determining the major risk factors. Porter has provided a challenging framework for identifying the full set of outcomes for any medical condition: the outcome measures hierarchy (OMH). **RESULTS:** According to the OMH the full set of outcomes for any medical condition, and its treatment, can be conveyed in a threedimensional hierarchy. Each tier of the hierarchy contains two broad levels, each of which involves specific outcomes or direct outcome dimensions. Each medical condition should have its own outcome measures. Measurement efforts should begin with at least one outcome dimension at each tier, and ideally at each level. Possible outcome dimensions for Attention-Deficit Hyperactivity Disorder (ADHD) are explored and discussed according to Porter’s OMH. ADHD is a frequent neuropsychological disorder that is characterised by inattention, hyperactivity and impulsivity. ADHD is associated with considerable social, family, behavioural and cognitive dysfunction, and is comorbid to depression, bipolar disorder, anxiety, and drug use. Specific dimensions proposed are aimed at capturing particular aspects of patients affected by ADHD. For each dimension, success is measured with several clinical and patient reported metrics. Tier 1 of the OMH is the patient’s health status achieved or retained after a health intervention (clinical or drug therapy). **CONCLUSIONS:** Tier 2 regards the process of recovery and the eventual disutility of the treatment process. Tier 3 concerns the sustainability of health.

**PCN1**

*BURDEN OF HOSPITALIZATION IN PATIENTS WITH ADVANCED LUNG CANCER IN FRANCE AND GERMANY*

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**OBJECTIVES:** To assess the burden of hospitalization in advanced lung cancer patients in France and Germany. **RESULTS:** Rehospitalized were identified in a random sample of patients (N=40) actively involved in management of Non small cell lung cancer (NSCLC) in France and Germany were invited to participate in a lung cancer disease specific program. Each consenting physician was asked to complete patient record forms for the next 10 advanced (stage IIIb/IV) lung cancer patients seen in their practice. The study period extended from July to October 2010. Data on hospitalization over the past year was provided by the physicians using the patient chart records. The primary reason of hospitalization and the length of stay (LOS) were reported. **RESULTS:** Majority of the patients (N=1213) were male (68%), Caucasian (92%), Stage IV (85%), currently on first line therapy (51%) with an average age of 63 years. Hospitalization records were obtained for 93% (n=1133) of the patients among which 30% (n=341) of the patients had one or more hospitalization events in the previous year with an average (SD) LOS of 10 (6) days. The primary cause reported for the hospitalization was disease symptoms (39%) or drug related side effects (20%) and therapy side effects (17%). The LOS for surgery related hospitalization (n=89) ranged from 1-20 days (mean: 8 days). Among patients hospitalized for disease symptoms (n=197) the most frequently reported primary causes were dyspnea (23%), cough (10%) and pain (11%) with average LOS of 13, 12 and 8 days respectively. Among patients hospitalized for side effects (n=75), anemia (24%), febrile neutropenia (8%), febrile aplasia (8%) were most frequently reported with average LOS of 4 days. **CONCLUSIONS:** Burden of hospitalization due to disease symptoms and treatment related side effects is significant in France and Germany. Innovative therapies effective in alleviating symptoms and side effects could help significantly in decreasing hospitalization costs.

**PCN2**

*A RETROSPECTIVE LONGITUDINAL STUDY OF TREATMENT PATTERNS AND OUTCOMES AMONG PATIENTS WITH UNRESECTABLE STAGE III/IV MELANOMA IN CANADA (MELODY)*

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**OBJECTIVES:** Unresectable melanoma patients (stages III/IV) have a poor prognosis. Recent improvements in survival have been attributed in part to earlier detection and investigational therapies, however melanoma is considered incurable if it becomes metastatic. No information about treatment patterns for unresectable melanoma in Canada has been published. Objectives of this study were to describe disease characteristics, treatment patterns, health outcomes, and resource utilization for Canadian unresectable melanoma patients treated outside randomized clinical trials (RCT). **METHODS:** Charts of melanoma patients at seven Canadian sites were selected for eligibility. Unresectable melanoma cases were then selected consecutively in reverse chronological order from January 2009 until target number (n=250) exceeded. Data on patient and disease characteristics, treatments (across three lines), adverse event management, health outcomes and resource utilization were then extracted from charts of patients with at least two months of follow-up, from diagnosis until censoring (June 2010 or death). **RESULTS:** Of 1426 melanoma patient charts reviewed, 262 (18%) were for unresectable melanoma patients, 16% (43/262) of which were first diagnosed in an advanced stage. Overall, 10% (26/262) participated in an RCT during the follow-up period and 60% (156/262) received systemic therapy outside an RCT. In the latter group, responsive- ness to therapy was low; only 20% (26/132) on first-line and 16% (9/58) on second-line therapy experienced complete or partial response. On first-line therapy, 40% (53/132) experienced adverse events requiring medical management and 18% (24/ 132) were hospitalized during treatment; corresponding figures for second-line were 38% (22/58) and 24% (14/58) respectively. **CONCLUSIONS:** This study characterizes treatment patterns and provides quantitative estimates of resource utilization for unresectable melanoma patients across Canada. Extant systemic treatment associated with poor response and considerable resource utilization. This study quantifies the grim prognosis faced by advanced melanoma patients in Canada receiving currently available treatments.

**PCN3**

*CETUXIMAB FOR THE FIRST-LINE TREATMENT OF METASTATIC COLORECTAL CANCER* 

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**OBJECTIVES:** To evaluate the efficacy and safety of cetuximab in combination chemotherapy vs. chemotherapy alone for the first-line treatment of metastatic colorectal cancer (mCRC), in patients with KRAS wild-type tumours. 

**METHODS:**