panel hearings. In two recent highly publicised Food and Drug Administration advisory panel recommendations for orkambi (cystic fibrosis; Vertex Pharmaceuticals) and flibanserin (hypoactive sexual desire disorder; Sprout Pharmaceuticals), testimonials from patients involved in the trials appeared to play an important role in influencing positive recommendations. Feedback from patients participating in clinical trials can provide important information on the potential benefits of a drug beyond the clinical endpoints measured in a trial. However, critics suggest that the purposively selected patient testimonials used within these regulatory interactions are not sufficiently robust sources of data. The authors argue that patient testimonials which influence regulatory decision making should be considered as qualitative data and therefore appraised in-line with other qualitative data submitted as part of a new drug application e.g., qualitative data supporting content validity of patient-reported outcome measures. Testimonials are unlikely to be considered either credible or rigorous in their current format, particularly as samples are often heavily biased towards patients who have experienced positive outcomes whilst on the product. Patient interviews planned a priori can provide valuable insights on the efficacy of a new medication and other important factors such as tolerability and adherence. The authors propose a structured framework to eliciting and analysing these data through qualitative interviews 'nested' within clinical trials. The authors present a procedural checklist for ensuring that credible and robust data are collected. This includes ensuring representative sampling (e.g., patients on both treatment arms and with varying socio-demographic and clinical profiles), utilising trained qualitative interviewers experienced in qualitative data collection and analysis, and timing of interviews (e.g., during and/or after the clinical study).

PRM252
A PRACTICAL GUIDE TO ADDING PATIENT HETEROGENEITY INTO PHASE III TRIALS: RESULTS FROM IMI GETREAL WP2
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OBJECTIVES: Phase III trials typically exclude patients with certain baseline characteristics, such as older age or co-morbidities, and thereby hamper learning of new drugs' effectiveness in real-life. A simulation study was conducted to support implementation of new inclusion criteria for Phase 3 trials in schizophrenia without increasing sample size nor compromising detection of the new drug effect. **METHODS:** A simulation study was performed examining the impact of re-introducing through stratifying by each of the following excluded patients population: age > 65 years, duration of illness < 3 years, patients with previous suicide attempts, patients with history of alcohol or substance abuse, and patients treated in private practices. Patients with these characteristics were multiplied in a synthetic trial population until their real-life proportion in schizophrenia was reached. The simulation used data subsets from the 10,281-patient observational SOHO cohort study. A "base case RCT" was created by applying typical Phase 3 exclusion criteria. A series of "synthetic RCTs" were defined by replacing patients with SOHO patients that were initially excluded. The real-life drug effect was predicted from each synthetic RCT through regression models and compared with the real-life effect in SOHO. **RESULTS:** Perhaps surprisingly, effects of all 3 investigated drugs were found to be larger in real-life than in the base case RCT. Synthetic RCTs were created by replacing patients of the base RCT with patients with a given baseline characteristic. Prediction of real-life effects improved with increasing replacement in terms of mean squared prediction errors and coverage of confidence interval. However, the impact of introducing these "real-life" populations was not equal among factors. For instance, introducing older patients minimally improved prediction of real-life effects, while allowing inclusion of just 5% of patients with past suicide attempts (who make up 25% of the real-life schizophrenia population) significantly improved effectiveness predictions.

PRM253
RAPID AND AUTOMATED TEST FOR CONNECTEDNESS OF EVIDENCE NETWORKS IN NETWORK META ANALYSIS
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OBJECTIVES: Develop a method to quickly test whether a network meta-analysis evidence network is connected. BACKGROUND Network meta-analysis, or mixed treatment comparisons, is a method to combine evidence on multiple treatments that have been compared in randomised controlled trials that form a connected network of treatment comparisons. Evidence networks consist of nodes, representing treatments, and edges, representing clinical trials comparing two treatments. If nodes corresponding to treatments are not connected, they cannot be compared. Connectedness is typically tested by visual inspection, however this is time consuming when there are many separate networks representing different outcomes, subgroups, and scenarios, and also prone to error, especially in large networks . Path finding algorithms can be used to automate testing for connectedness, but these are slow and inefficient. We present a fast and simple approach to test connectedness. **METHODS:** Our method constructs a symmetric square matrix, called the direct connection matrix, with the number of rows and columns equal to the number of treatments in the network. We fill this matrix with ones where treatments of the corresponding row and column have been compared in a trial, and zeros otherwise. The diagonal is filled with ones. Exponentiation of the matrix to the number of treatments, minus one, gives the indirect connection matrix. Non-zero entries of this final matrix represent treatment combinations that can be compared using available evidence, and vice versa. This test is easy to implement in software and can be conducted rapidly. We prove the validity of the method mathematically and illustrate with application to a network of anticoagulants for the prevention of stroke in atrial fibrillation. **CONCLUSIONS:** We have developed a simple and rapid test of connectedness of networks that is easy to automate and can be applied to any network meta-analysis.

PRM254
THE NEED TO REVISE DISCOUNT RATES IN BELGIUM, THE NETHERLANDS, POLAND AND THE UK
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OBJECTIVES: To demonstrate the need to revise discount rates in the cost-effectiveness analysis (CEA) methods guidelines in Belgium, the Netherlands, Poland and the UK. **METHODS:** We identify what discount rates are recommended in the CEA guidelines of the countries above and examine what rationale has been provided in each case. We assess the recommended guidelines in the context of the current theory and empirical evidence on discounting. **RESULTS:** The UK requires discounting of 3.5% for cost and effects in its basecase guidance, but also recommends 1.5% for public health interventions and for specific life-saving interventions. No adequate justification has been provided for this disparity. Applying different discount rates for the same goal of achieving health gain from the same pool of resources is illogical and yields inefficient outcomes. Belgium, the Netherlands and Poland all recommend differential discounting of costs and effects. The discounting guidance in these countries pre-dates recent work that further clarifies the basis for differential discounting. This is significant, as this recent work shows how, under certain assumptions, the differential between costs and effects can be linked to growth in threshold. In turn, this may imply that the differential employed in these countries may be too great. Finally, assuming that the discount rate applied to costs should approximate government borrowing costs, it is likely that the cost discount rate is too high in the base case of all of the countries considered here. **CONCLUSIONS:** The choice of discount rates is important as they are highly influential on the cost-effectiveness of many interventions. Applying different discount rates to different interventions is not justified. Similarly, the rates applied in countries recommending differential discounting lack firm justification. Resource allocation in all the countries considered would likely be improved by the application of a lower common discount rate.

PRM255
ESTABLSHING THE COST-EFFECTIVENESS OF GENOMIC-BASED DIAGNOSTIC TESTS: ARE CURRENT METHODS SUFFICIENT AND APPROPRIATE?
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OBJECTIVES: The clinical value of genomic tests is not always apparent, and very few have demonstrated cost-effectiveness. The objective of this conceptual paper is to understand whether the principles and methods of cost-effectiveness analysis (CEA) are appropriate for the evaluation of genomic-based diagnostic tests, such as whole genome sequencing. **METHODS:** Literature on CEA methods to evaluate genomic tests was systematically searched using 'pearl growing' methods. Data were extracted to identify challenges and solutions to conducting CEA in this context. The key characteristics of genomic tests from an economic perspective were summarized and used to distinguish further challenges. **RESULTS:** Our review highlights two main differences between CEA of genomic tests and that of other technologies: the complexities of evaluating tests for multiple disorders and the potential for genomic information to have consequences for future generations requiring infinite time horizons. Another common feature, not unique to genomic-based diagnostic tests but commonly identified in the literature, was the valuation of non-health benefits. Alternatives to evaluate the diagnosis of multiple disorders are discussed: an iterative approach assessing each diagnosis independently; an aggregate approach combining the cost and benefits from all disorders into a single evaluation; a pragmatic approach that identifies the most important disorders combined with a qualitative assessment of the direction of bias for disorders not included in the full analysis. Consideration of the potential for infinite time horizons suggests CEA should focus on systems that could store, and share, genomic information between generations. **CONCLUSIONS:** The challenges shared with other health technologies, particularly diagnostic tests, suggest that the general principles and methods of CEA are appropriate for genomic tests. Further methodological research would be valuable on approaches for assessing the value of sharing genomic information across generations, approaches to evaluate tests for multiple disorders and trading-off health and non-health benefits.

PRM256
THE CHALLENGES IN EVALUATING THE COST-EFFECTIVENESS OF COMPLEX INTERVENTIONS
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Standard cost-effectiveness methods and critical appraisal toolkits may not be adequate for complex interventions. We systematically reviewed and quality assessed cost-effectiveness studies of a complex intervention, propose a series of new questions to inform their critical appraisal and discuss how future research should be targeted to improve the methods. Reablement was used as an example of a complex intervention. Reablement is a multidisciplinary and multifactorial intervention to support people to relearn activities of daily living. The systematic review identified 12 cost-effectiveness studies on reablement, out of 3,311 unique records. The 12 included studies were data extracted and quality evaluated using a standard checklist. No study provided enough information to inform the decision on whether reablement is cost-effective and should be reimbursed by the payer. The issues included: (i) the use of a perspective not relevant for the decision-maker, (ii) lack of consideration for inter-sectoral effects, (iii) short time horizon, (iv) poor descriptive detail on the interventions, (v) limited comparators, (vi) poor quality evidence on effectiveness, (vii) limited evaluation of uncertainty and (viii) no consideration of the