Estimating the Value of Whole Exome Sequencing for Parents of Children with Rare Genetic Diseases

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OBJECTIVES: Patients with rare genetic diseases often experience a diagnostic odyssey; no diagnosis available in obtaining a diagnosis, due to lengthy diagnostic work-ups. Whole-exome sequencing (WES) can rapidly identify the mutation(s) responsible for rare, single-gene diseases. Before incorporating this new technology into clinical practice, we must understand the value of diagnostic information. We aimed to identify key attributes surrounding the value of a diagnosis to parents and to select the discrete choice experiment (DCE) survey to estimate the value of WES diagnostic information to parents of children with rare diseases.

METHODS: We used a multi-phased approach to identify attributes and constructs in the literature, developed a DCE survey to identify an extensive list of candidate attributes. We used results from focus groups with parents of children (n=15) and adults (n=8) with rare diseases to identify additional attributes. Candidate attributes were refined by a research team including medical geneticists. The DCE survey was pre-tested in a sample of parents of children with rare diseases (n=5) and attributes were further refined.

RESULTS: The DCE included six attributes, each with four levels: type of diagnostic (genomic sequencing, other genetic testing, operative procedures, series of tests and procedures), chance of a diagnosis (5/10, 4/10, 6/10, 9/10); negative impact of diagnostic test results (lifestyle restrictions, victim of discrimination, labeled by others, no impact); positive impact of diagnostic test results (increased reassurance, out-of-pocket costs, $10,000); time to obtain a diagnosis (6 months, 3 years, 5 years, 10 years).

CONCLUSIONS: The survey will be administered to n=300 parents of children with rare diseases (diagnosed and not diagnosed) to evaluate willingness-to-pay for WES, a diagnosis, and a faster diagnosis.

Patient-Reported Outcome Measures for Multiple Sclerosis Phase IV Clinical Trials: A Systematic Review

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OBJECTIVES: To identify and appraise the reporting on psychometric properties of selected outcome reported measures (ORMs) used in multiple sclerosis (MS) trials, and to identify ORM features potentially suitable for Phase IV use.

METHODS: We systematically searched PubMed, ClinicalTrials.gov, and MS conferences from 2009 onwards to identify ORM studies in MS Phase IV trials. For further assessment, we selected ORM studies on concepts: health-related quality of life (HRQoL), fatigue, depression, and cognition. These ORM studies were appraised in the context of the U.S. Food and Drug Administration guidance for work reporting on psychometric properties of a selected patient reported outcome measures (PROs) used in multiple sclerosis (MS) trials. This included literature review, medical expert and direct patient interviews.

RESULTS: A total of 24 PROs on the selected concepts were identified from 30 studies. PROs were MS-specific for 7 of 13 HRQoL, 1 of 7 mood/depression, and 1 of 4 fatigue measures. No study reported on the full set of HRQoL concepts.

CONCLUSIONS: We identified HRQoL, mood, and fatigue PROs with properties (validity, reliability, and responsiveness). The selection of concepts was guided by PROs identified for Phase IV trials, and to identify PROs potentially suitable for Phase IV use.

Understanding the Suitability of Cystic Fibrosis-Specific Clinical Outcome Assessments for Clinical Trials and to Support Medical Product Labeling

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OBJECTIVES: To identify and review the suitability of cystic fibrosis (CF)-specific clinical outcome assessments (COAs) for clinical trial assessment of novel CF therapies and to support product labeling.

METHODS: CF-specific COAs were identified from literature searches and clinical trials, as well as via clinical trials. COAs were assessed for their clinical relevance and alignment with the functional impact of sIBM described in the literature. Expert review and identified as relevant and important to sIBM patients.

The draft conceptual framework includes items related to upper extremity, lower extremity, general function and swallowing. Cognitive testing of paper and ePRO versions support the use of this tool in a broad functional range of sIBM patients. The sIFA is the first content valid tool developed specifically for use in the functional assessment of treatment benefit in sIBM patients aligned with the FDA PRO Guidance. Psychometric evaluation is underway.

Patient-Reported Outcome Measures for Multiple Sclerosis Phase IV Clinical Trials: A Systematic Review

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The PARKINSON'S DISEASE QUESTIONNAIRE (PDQ-39) - EVALUATING THE PSYCHOMETRIC PROPERTIES OF AN ELECTRONIC VERSION

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OBJECTIVES: The 39-item PARKINSON’S Disease Questionnaire (PDQ-39) is the most thoroughly developed and extensively validated self-report measure for the assessment of health-related quality of life in people with Parkinson’s (PwP). The measure has been shown to possess sound psychometric properties and its use is widely recommended as an outcome measure in clinical trials and for FDA Drug Development Tool qualification by FDA. The respiratory symptom score has excellent psychometric properties; impact items are yet to be validated.

CONCLUSIONS: Since 9 CF-specific COAs were identified in this study, only the COA-R measures in CF clinical trials and previous success in supporting the PDQ-39 for FDA label claims for respiratory symptoms. Limitations include the acceptability of a 2-week recall period and inconsistencies in concepts measured across pediatric and adult populations. CFQ-R appears potentially suitable for assessment of CF-related symptoms and impact in CF clinical trials. Further data relating to content validity of CFQ-R may be required to support future labeling approvals.

A NOVEL MEASURE TO ASSESS SELF-REPORTED PHYSICAL FUNCTIONING IN PATIENTS WITH SPORADIC INCLUSION BODY MYOSITIS (sIBM)

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OBJECTIVES: sIBM is a progressive idiopathic inflammatory muscleopathy characterized by atrophy and weakness of proximal and distal muscle groups with the knee extensors and wrist/finger flexors frequently involved as well as dysphagic processes. Progressive weakness results in a loss of independence and the need for assistive devices and supportive care. While no pharmacological treatments for sIBM are currently available, the few clinical trials that have been undertaken have not shown benefit of new therapies and track clinical progression, a patient-reported measure (PROM) of physical function, the sIBM Physical Functioning Assessment (sIFA), was developed. The sIFA was rigorously developed in accordance with FDA PRO Guidance. This included literature review, medical expert and direct patient input. A single-visit, observational study involving sequential concept elicitation and cognitive debriefing interviews was conducted. Standard qualitative analytical methods were used for analysis of the interviews. sIFA items were mapped to patient-centered concepts identified from clinical trials and to the functional impact of sIBM described in the literature. Expert review and identified as relevant and important to sIBM patients.

The draft conceptual framework includes items related to upper extremity, lower extremity, general function and swallowing. Cognitive testing of paper and ePRO versions support the use of this tool in a broad functional range of sIBM patients. The sIFA is the first content valid tool developed specifically for use in the functional assessment of treatment benefit in sIBM patients aligned with the FDA PRO Guidance. Psychometric evaluation is underway.

SIX DIFFERENCES IN OVER-THE-COUNTER SLEEP AID USE IN OLDER ADULTS

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OBJECTIVES: Over-the-counter (OTC) sleep aids are widely self-administered and are generally safe, but their primary ingredients (diphenhydramine and doxylamine) are considered old and should be replaced by the new generation of sleep aids. This study examined the prevalence of OTC sleep aids in the 151 US National Health and Wellness Survey (USNHS), a cross-sectional, internet-based, IRB-approved annual survey of adults (N=75,000). Stratified sampling was used to represent the demographic make-up of the general population in age, sex, and ethnicity. Weights were applied using age, sex, ethnicity, and education to reflect the US population. Respondents reporting regular use of OTC sleep aids were compared with self-reports of sleep problems outside of their label recommendations. This analysis characterizes the use of DPFH/DOX for sleep disturbances by age and sex in older American adults.

METHODS: Baseline data were collected from the 2013 IHS National Health and Wellness Survey (USNHS), a cross-sectional, internet-based, IRB-approved annual survey of adults (N=75,000). Stratified sampling was used to represent the demographic make-up of the general population in age, sex, and ethnicity. Weights were applied using age, sex, ethnicity, and education to reflect the US population. Respondents reporting regular use of OTC sleep aids were compared with self-reports of sleep problems outside of their label recommendations. This analysis characterizes the use of DPFH/DOX for sleep disturbances by age and sex in older American adults.

RESULTS: Of the projected 41.3 M (n=16,500) adults age ≥65, 15% (3.8 M age 65-74; 2.6 M age 75+) reported studied scored on a 0 (no difficulty) to 10 (unable to do) numerical rating scale. sIFA items are aligned with the functional impact of sIBM described in the literature. Expert review and identified as relevant and important to sIBM patients. The draft conceptual framework includes items related to upper extremity, lower extremity, general function and swallowing. Cognitive testing of paper and ePRO versions support the use of this tool in a broad functional range of sIBM patients. The sIFA is the first content valid tool developed specifically for use in the functional assessment of treatment benefit in sIBM patients aligned with the FDA PRO Guidance. Psychometric evaluation is underway.