Handout

Measuring Patient- and Carer-Reported Outcomes Following Genome Sequencing for Rare Disease Diagnosis: A Psychometric Assessment of Outcome Measurement Instruments

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Introduction

- Rare diseases (RDs) – such as Angelman syndrome and myotonic dystrophy type 1 – are individually rare yet **collectively affect 6-8% of the general population**
- Obtaining a RD **diagnosis can take several years** and require many costly investigations
- Genome sequencing (GS) is an advanced technology that can sequence most of a person's genome, and is **increasing RD diagnostic yield and speed**
- The **information uncovered by GS can be complex**, and can have positive and negative impacts on patients and families
- Outcomes can be grouped into five domains[1-5]

Clinical 5 sub-domains

Emotional 2 sub-domains

Cognitive 4 sub-domains

Behavioural 7 sub-domains

Social Domain 9 sub-domains

- However, these **outcomes may not be captured** by generic health economics outcome measurement instruments[6]
- Specific concerns surround the **content validity, construct validity, and responsiveness** of these instruments
- **Comprehensive and accurate measurement** of outcomes is important for assessing the **cost-effectiveness** of GS for RD diagnosis

Aim: To determine the patient- and caregiver-reported outcome measurement instruments best suited to measuring outcomes from GS for RD diagnosis

Methods

Phase 1 — **Systematic Literature Review:** Identifying the instruments used to measure patient and caregiver outcomes from GS unrestricted by context, testing purpose, disease, or instrument validation status

Phase 2 — **Critical Appraisal:** Assessing the psychometric properties of validated instruments identified in P1 using COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) methodology

Phase 3 — **Cohort Study:** Evaluating the psychometric properties of a sub-set of P2 instruments via a prospective mixed methods cohort study of UK Genomic Medicine Service patients and caregivers – instruments were selected for their relevance, comprehensiveness, and feasibility

Results: Critical Appraisal

- Only 3 studies intended to develop and/or validate an instrument for measuring outcomes from GS
- The quality of psychometric evidence available was highly variable

Quality of the summarised evidence per measurement property

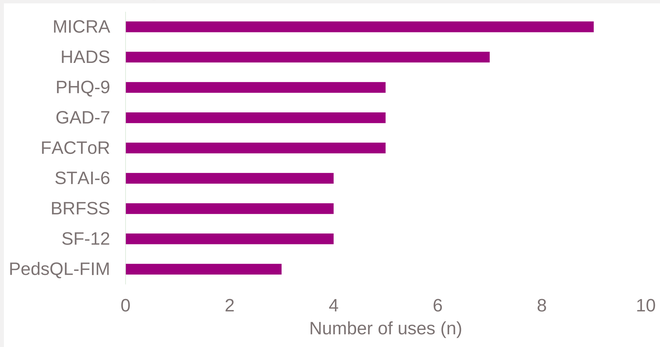
Psychometric property		PrU	P-PrU	FACToR	GAD-7	MHI-5	PHQ-9	VR-12
Content validity	Relevance	L	L	L	VL	VL	VL	VL
	Comprehensiveness	L	L	L	VL	VL	VL	VL
	Comprehensibility	NA	NA	L	NA	NA	NA	NA
	Overall	L	L	L	VL	VL	VL	VL
Structural validity		M	M	NA	NA	NA	NA	NA
Internal consistency		H	H	H	H	H	H	H
Cross-cultural validity		NA	NA	NA	NA	NA	NA	NA
Reliability		NA	NA	VL	NA	NA	NA	NA
Measurement error		NA	NA	NA	NA	NA	NA	NA
Criterion validity		NA	NA	NA	NA	NA	NA	NA
Hypotheses testing for construct validity		H	VL	M	H	H	H	H
Responsiveness		NA	NA	NA	NA	NA	NA	NA

H = high, M = medium, L = low, VL = very low, NA = not applicable

Results: Systematic Review

- 29 included studies used 63 eligible instruments (49 validated)
- 5 were generic health economics instruments, and 5 were validated GS specific instruments

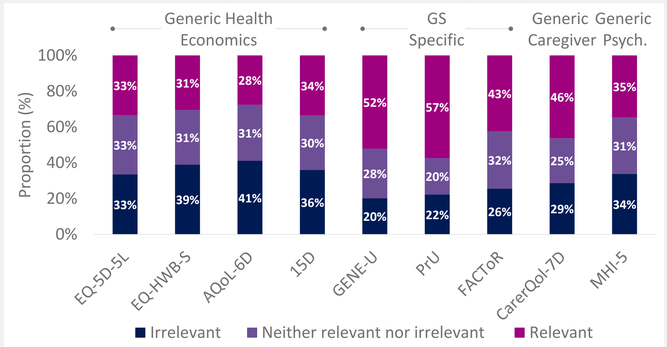
Most commonly used included instruments



Results: Cohort Study

- 2,267 invitations have been distributed (recruitment is ongoing)
- 117 caregivers of a child, 108 adults, and 5 proxies for an adult have completed the baseline survey (230 total, 10.15% recruitment)

Instrument relevance (summarized Likert categories)



Discussion

- Previous approaches to measuring outcomes from GS for RD diagnosis have been variable with **limited psychometric data** to support instrument selection
- Preliminary results suggest that generic instruments **may lack key domains** for capturing patient and caregiver outcomes from GS for RD diagnosis
- The results of this study will help to address this by enabling:
  - Improved **instrument selection** decisions
  - Improved **understanding** of where generic health economics instruments may fall short
  - Improved **interpretation** of evidence generated using generic health economics instruments

Next Steps

- Distribute 6- and 12- month follow-up surveys
- Conduct 20-30 qualitative interviews
- Facilitate a recommendations workshop with leading researchers and policy-makers (Phase 4)

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Glossary: 15D: Quality of Life Questionnaire 15 Dimensions, AQoL-6D: Assessment of Quality of Life 6 Dimensions, BRFSS: Behavioral Risk Factor Surveillance System Questionnaire, CarerQol-7D: Care-related Quality of Life Instrument, EQ-5D-5L: European Quality of Life 5 Dimensions 5 Level Version, EQ-HWB-S: European Quality of Life Health and Wellbeing Instrument Short, FACToR: Feelings About genomiC Testing Results Questionnaire, GAD-7: Generalized Anxiety Disorder Questionnaire 7-Item, GENE-U: GENEtic Utility Scale, HADS: Hospital Anxiety and Depression Scale, MHI-5: Mental Health Inventory 5-Item, MICRA: Multidimensional Impact of Cancer Risk Assessment, PedsQL-FIM: Pediatric Quality of Life Inventory Family Impact Module, PHQ-9: Patient Health Questionnaire 9-Item, PrU: Personal Utility Scale, P-PrU: Personal Utility Scale SF-12: 12-Item Short Form Survey, STAI-6: State-Trait Anxiety Inventory Short Form

Key references:
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