Identifying Clinical Outcome Assessments (COAs), with a particular Focus on Mental-Health Related COAs, Mapped to the EQ-5D to Establish Comparable Utility Values for Quality-Adjusted Life Year (QALY) Evaluation

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Objective:

- Health technology assessment (HTA) bodies such as the National Institute for Health and Care Excellence (NICE) widely recommend using the **EQ-5D** in cost-effectiveness analysis, e.g., in evaluating **quality-adjusted life years (QALY)**, yet the EQ-5D is not always appropriate for the population of interest (Kennedy-Martin et al., 2020; NICE, 2023)
- The need for clinical outcome assessments (COAs) with a **mapping algorithm to the EQ-5D** can arise when there is little or no **content validity** evidence (NICE, 2023), **implementation** challenges, or lack of **sensitivity**, notably for areas such as mental health (Gnanasakthy and DeMuro, 2024; Brazier et al., 2019)
- This study aimed to **identify COAs with an EQ-5D mapping algorithm**, with a particular focus on **mental health-related COAs**

Main Outcomes:

- **131 COAs** mapped to the EQ-5D were identified in the **HERC mapping database**, including **1 COA** qualified by the **FDA COA Qualification Program** (Kansas City Cardiomyopathy Questionnaire (KCCQ)) (FDA, 2020)
- The 3 therapeutic areas covering the greatest number of COAs were: **signs and symptoms** (n=30 COAs), **musculoskeletal diseases**, and **nervous system diseases** (n=19 COAs respectively)
- There remains a **lack of mapping algorithms** for COAs in mental health with **27** COAs related to **mental health** compared to **117** COAs related to **physical health***
- The **majority** of COAs for the top 3 therapeutic areas as well as the 3 **mental health-related** therapeutic areas were **PROs** (**75%** and **74%** respectively)
- There has been a **five-fold increase** in the number of EQ-5D **COA mapping algorithms** since **2010**, corresponding to NICE's 2008 **guidance on using mapping techniques** when it is not possible/appropriate to use the EQ-5D (NICE, 2023), the growing interest and importance of HTA over the past two decades (Belfiore, 2023), as well as the publication of the International Society for Pharmacoeconomics and Outcomes Research's Best Practices for Mapping in 2017 (Wailoo, 2017)
- The more recent publication **of mental health-related** COAs **mapping algorithms** suggests **growing interest** in mapping mental health-related COAs

Note: There is cross-over between 13 COAs classified as mental health-related and physical health-related as they were developed in a population with multiple therapeutic areas

Future Direction:

- **Ongoing research** is required about how appropriate the EQ-5D is for certain **mental health conditions**
- When the EQ-5D is not appropriate, the **HERC database is a valuable tool** to identify **COAs with existing mapping algorithms** across a **range of therapeutic areas**, including **mental health-related conditions**

Methods

1. Searched (March 2024) for COAs with an identifiable development paper in The Health Economics Research Centre's (HERC) **database of mapping studies**** (Dakin et al., 2013, 2018, 2023)

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2. COAs were classified by **therapeutic indication/area** according to the Medical Subject Headings (MeSH) and **type of COA**

3. The **therapeutic areas** for all COAs were **ranked** based on the count of COAs per area

4. Therapeutic areas related to **mental health** were identified using the MeSH (n=3 areas), to enable comparisons to be drawn between **all therapeutic areas** and mental health related therapeutic areas

5. The **date** of every **mapping paper** in which a non-mental health related COA was mapped to the EQ-5D was **recorded and plotted over time**. This was then performed **separately** for all mental-health related COAs.

6. The **difference in publication dates** between the therapeutic areas was compared.

****SOURCES:**
- Medline (via PubMed)
- EuropQoL Reference Search
- ScHARRHUD
- Centre for Reviews and Dissemination
- Health Economists' Study Group

Results

Top 3 Therapeutic Areas for All COAs[+]

Pathological Conditions, Signs and Symptoms (n=30 COAs)			Musculoskeletal Diseases (n=19 COAs)			Nervous System Diseases (n=19 COAs)		
COA Full name	COA Acronym	Type of COA	COA Full name	COA Acronym	Type of COA	COA Full name	COA Acronym	Type of COA
Canadian Classification Society Angina Grading System	CCS Angina Grading System	ClinRO	American College of Rheumatology 20/50/70 Response Criteria	ACR20/50/70	Composite (PRO & ClinRO & Biomarker)	Amyotrophic Lateral Sclerosis Functional Rating Scale - Revised version	ALSFRS-R	ClinRO
Chronic Headache Quality of Life Questionnaire	CHQLQ	PRO	Ankylosing Spondylitis Disease Activity Score-C-reactive protein	ASDAS-CRP	Composite (PRO & Biomarker)	Glasgow Outcome Scale	GOS	ClinRO
Clinical COPD Questionnaire	CCQ	PRO	Clinical Disease Activity in psoriatic arthritis without C-reactive protein	cDAPSA	Composite (ClinRO & PRO)	Unified Parkinson's Disease Rating Scale	UPDRS	Composite (PRO & ClinRO)
Cystic Fibrosis Questionnaire-Revised	CFQ-R	PRO|ObsRO	Disease Activity Index in Psoriatic Arthritis	DAPSA	Composite (PRO, ClinRO & Biomarker)	Acromegaly Quality of Life questionnaire	AcroQoL	PRO
Epworth Sleepiness Scale	ESS	PRO	Acromegaly Quality of Life questionnaire	AcroQoL	PRO	Cervical Radiculopathy Impact Scale	CRIS	PRO
Fatigue Severity Scale	FSS	PRO	Oxford Hip Score	OHS	PRO	Multiple Sclerosis Walking Scale	MSWS-12	PRO
MacNew Heart Disease Health-related Quality of Life Questionnaire	MacNew	PRO	Oxford Knee Score	OKS	PRO	Parkinson's Disease Questionnaire - 39	PDQ-39	PRO
Overactive Bladder Questionnaire 5-Dimensional Health Classification System	OAB-5D	PRO	Oxford Shoulder Score	OSS	PRO	Parkinson's Disease Questionnaire - 8	PDQ-8	PRO
Patient Assessment of Constipation Quality of Life questionnaire	PAC-QOL	PRO	Refined Scoliosis Research Society 22-item	SRS-22r	PRO	Quality of Life in Epilepsy Inventory-31	QOLIE-31	PRO
St George's Respiratory Questionnaire	SGRQ	PRO	Western Ontario and McMaster Universities Arthritis Index	WOMAC*	PRO	Revised Fibromyalgia Impact Questionnaire	FIQR	PRO

3 Therapeutic Areas for Mental Health-Related COAs

Mental Disorders (n=12 COAs)			Behavior and Behavior Mechanisms (n=11 COAs)			Psychological Phenomena (n=4 COAs)		
COA Full name	COA Acronym	Type of COA	COA Full name	COA Acronym	Type of COA	COA Full name	COA Acronym	Type of COA
Calgary Depression Scale for Schizophrenia	CDSS	ClinRO	Beck Depression Inventory*-Second Edition	BDI*-II	PRO	Older People's Utility Scale	OPUS	ClinRO
Positive and Negative Syndrome Scale for Schizophrenia	PANSS	ClinRO	Clinical Outcomes in Routine Evaluation - 10	CORE-10	PRO	Brief Pain Inventory	BPI	PRO
Treatment Outcomes Profile	TOP	PRO	Clinical Outcomes in Routine Evaluation - Outcome Measure	CORE-OM	PRO	Chronic Pain Acceptance Questionnaire - Revised	CPAQ-R	PRO
Insomnia Severity Index	ISI	ClinRO | ObsRO | PRO	General Health Questionnaire	GHQ	PRO	Headache Impact Test*	HIT-6*	PRO
Quality of Life in Alzheimer's Disease	QOL-AD	ObsRO | PRO	Hospital Anxiety and Depression Scale	HADS	PRO			
Basic Nordic Sleep Questionnaire	BNSQ	PRO	Kessler 10 Psychological Distress Scale	K10	PRO			
Depression Anxiety Stress Scales Short Form	DASS-21	PRO	Long-Term Conditions Questionnaire	LTCQ-8	PRO			
Functional Assessment of Anorexia/Cachexia Treatment	FAACT	PRO	Pain Anxiety Symptoms Scale Short Form 20	PASS-20	PRO			
Alzheimer's Disease Cooperative Study - Activities of Daily Living	ADCS-ADL	ObsRO	Patient Health Questionnaire-8 items	PHQ-8	PRO			
Leeds Dependence Questionnaire	LDQ	PRO	The Zung Self-rating Depression Scale	SDS	PRO			

+Note: 22 COAs were developed in non-disease specific populations and so were not included in the top 3 therapeutic areas

Acronym List:
ClinRO: Clinician-Reported Outcome
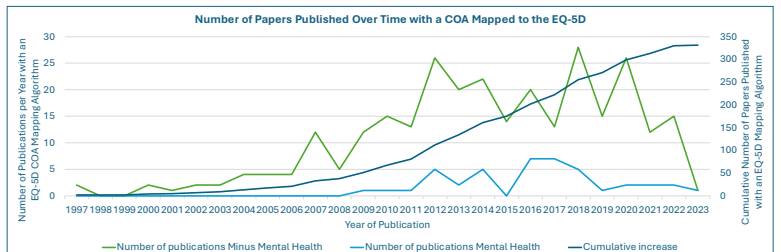*ObsRO: Observer-Reported Outcome*
PRO: Patient-Reported Outcome

Ten COAs were selected randomly to represent the array of COAs per therapeutic area. COAs are ranked by COA type and then alphabetically within the table. Please contact Tilly Stott if you would like to access the full list of COAs.

Key Takeaways: Top 3 Therapeutic Areas

- **27** of the 30 COAs developed in therapeutic indications related to **signs and symptoms** were **PROs**. → This is largely explained by many of these PROs **covering symptoms** alone, thus only known to the patient, e.g., pain, headaches, fatigue, and urinary frequency.
- **Six** of the 19 COAs for **musculoskeletal diseases** were **composite** measures. There was only **1 other composite** measure for any of the **other therapeutic areas** (mental health-related areas included).
- All but 1 of these 6 composite measures **included a biomarker** and all were developed for a form of **arthritis** (rheumatoid or psoriatic) except the ASDAS-CRP developed for ankylosing spondylitis. → All these composites measured **disease activity** which is perhaps unsurprising since disease activity indices are intended to measure **various** aspects of disease to establish a comprehensive disease activity assessment (Lukas, 2009)
- There was greater **variety of assessment** type for **nervous system disorders** with ClinROs, ObsROs, mixed COAs, in addition to PROs. → This can be understood due to the nature of the therapeutic area, as ClinROs and ObsROs can be more feasible and reliable in some cases depending on disease progression (Moessinger, 2022).

Key Takeaways: Mental Health-Related

- Four of the 12 COAs for **mental disorders** were available as a **ClinRO**. → Two of these 4 ClinROs were developed in a population with **schizophrenia** for which there is a history of ClinRO use in trials due to the nature of the disease (Siani, 2016; Citrome, 2023). One ClinRO was also developed with a population experiencing substance abuse and the final ClinRO was available as different COA types (PRO & ObsRO) as it was for insomnia and accounted for spouse perspectives.
- **All COAs for behavior and behavior mechanisms** as well as for **psychological phenomena** were **PRO**. → This fits with the trend to **prioritize patient perspectives** within mental health measurement, and not measure clinical symptoms alone (Ryland, 2020).

Key Findings: Mapping Algorithm Publication Date

- First COA mapped to the EQ-5D in **1997**
- There has been a **five-fold increase** in the number of EQ-5D **COA mapping algorithms** since **2010**
- Mapping algorithms for **mental health-related** COAs have been **published more recently** (first published in 2009)

Number of Papers Published Over Time with a COA Mapped to the EQ-5D

Legend: Number of publications Minus Mental Health — Number of publications Mental Health — Cumulative increase

X-axis: Year of Publication (1997–2023)
Left Y-axis: Number of Publications per Year with an EQ-5D COA Mapping Algorithm
Right Y-axis: Cumulative Number of Papers Published with an EQ-5D Mapping Algorithm

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