

Background

- Patient-reported outcomes (PROs) are "A measurement based on a report that comes directly from the patient (i.e., study subject) about the status of a patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else"¹
- PROs include Quality of life (QoL), symptom measures, and functional outcomes of disease²
- The use of PROs in randomized controlled trials (RCTs) has increased over time, in addition to the efficacy and safety measures and endpoints²
 - 2004 to 2007: 14% of RCTs included PROs
 - 2007 to 2013: 27% of RCTs included PROs
- Regulators also have actively started looking for changes in QoL after an intervention, in addition to the routinely collected disease-related measures.
- We were interested to measure the extent to which RCTs in India conducted on the nervous system and mental health disorders collect and report PRO information

Objective

- To evaluate the current status of patient-reported outcomes (PROs) captured in randomized controlled trials (RCTs) performed on any nervous system and mental health disorders, in India

Methodology

Eligibility Criteria

Facet	Inclusion	Exclusion/ Not of interest (NOI)
Population	<ul style="list-style-type: none"> • Humans suffering from any nervous system and mental health disorder • Any age • Residing only in India 	<ul style="list-style-type: none"> • No human subjects • Healthy human volunteers • Subjects residing in any country out of India • Multi-country studies
Intervention	<ul style="list-style-type: none"> • Any intervention 	<ul style="list-style-type: none"> • No restriction
Comparator	<ul style="list-style-type: none"> • Any comparator 	<ul style="list-style-type: none"> • No restriction
Outcome	<ul style="list-style-type: none"> • PROs: quality of life, patient satisfaction, all other PROs 	<ul style="list-style-type: none"> • All other outcomes
Study design	<ul style="list-style-type: none"> • Randomized controlled trials 	<ul style="list-style-type: none"> • All other types of papers
Databases	<ul style="list-style-type: none"> • PubMed, Embase, Google Scholar, WoS 	<ul style="list-style-type: none"> • -----

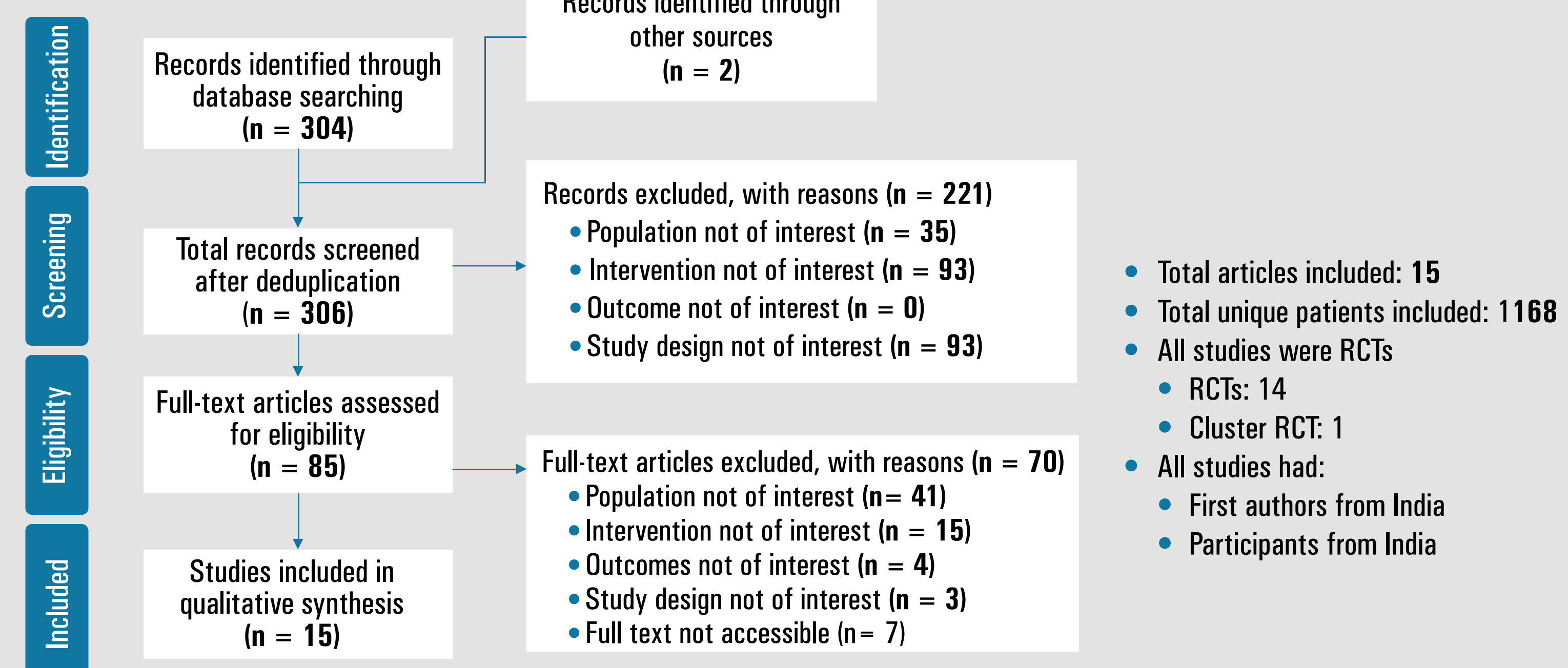
PubMed Search Strategy

From inception till 31st March 2022

No.	Terms	Hits	Facet
#1	"quality of life"[MeSH Terms] OR "quality of life"[All Fields] OR "Life Quality"[All Fields] OR "QoL"[All Fields] OR "health related quality of life"[All Fields] OR "health related quality of life"[All Fields] OR "HRQoL"[All Fields]	4,06,170	All QoL studies
#2	"Patient Reported Outcome Measures"[MeSH Terms] OR "Patient Reported Outcome Measure"[All Fields] OR "patient reported outcome"[All Fields] OR "patient reported outcome"[All Fields] OR "PROs"[All Fields] OR "PROM"[All Fields] OR "Satisfaction"[All Fields] OR "Experience"[All Fields] OR "Questionnaire"[All Fields]	14,14,321	All PRO studies
#3	#1 OR #2	16,93,284	All studies about QoL/ other PROs
#4	"Randomized Controlled Trials as Topic"[MeSH Terms] OR "Randomized Controlled Trial"[Publication Type] OR "Randomized Controlled Trial"[All Fields] OR "RCT"[All Fields] OR "randomized clinical trial"[All Fields] OR "randomized controlled clinical trial"[All Fields]	7,74,704	All RCTs
#5	"Nervous System Diseases"[Mesh] OR "Mental Disorders"[Mesh]	36,48,420	All studies about nervous system diseases or mental disorders
#6	#3 AND #4 AND #5	24,323	All RCTs about nervous system diseases/ mental health disorders containing QoL/ other PROs
#7	India	7,00,489	All studies containing the word 'India'
#8	#6 AND #7	304	All RCTs about nervous system diseases/ mental health disorders from India containing QoL/ other PROs

Note: Restrictions were not imposed on the search strategy; ineligible articles were manually screened out

Results



Population: Demographics

Sample size <ul style="list-style-type: none"> • Overall: 1168 • Range: 10-260 	Age <ul style="list-style-type: none"> • Mean ± SD: 6.6 ± 3.9 to 50.0 ± 1.73 years (9 studies) • Mean (95% CI): 51.7 (49.0-54.3) to 54.3 (51.6-57.1) years (1 study) • Median (range): 23 (13-49) to 24 (12-50) years (1 study) • 4 studies did not report
Age group <ul style="list-style-type: none"> • Adult population only: 8 studies • Pediatric population only: 5 studies • Both adult and pediatric population: 2 studies 	Sex <ul style="list-style-type: none"> • Males: 576 (49.34%) • Females: 592 (50.66%)

Population: Nervous System/ Mental Health Disorder

Disorder	Number of Studies	Subtypes
Epilepsy	5 studies	Focal seizures, Intractable Epilepsy, Sleep problems in epileptic children, 2 studies did not report subtype
Depression	3 studies	Recurrent depressive disorder, Depression in T2DM patients, 1 study did not report subtype
Migraine	3 studies	Acute migraine, Pediatric migraine, 1 study did not report subtype
Others	4 studies	Alcohol withdrawal syndrome, Hyperkinetic disorder, Minimal Hepatic Encephalopathy, Schizophrenia

Intervention/ Comparator Details

Intervention	Comparator
14 different interventions in 15 studies	One comparator: 14 studies
1. Amitriptyline 2. Antiepileptic Drugs - Phenytoin therapy 3. Baclofen 4. Botulinum toxin type A 5. Carbamazepine 6. Clonidine 7. Phenobarbital 8. Prochlorperazine 9. Rifaximin 10. Sertraline + Antiepileptic drugs 11. Topiramate 12. Enhanced care 13. Valproate + Mestizem (2 studies) 14. Viazodene	Three comparators: 1 study 8 studies: Placebo 8 studies: active comparators 1. Antiepileptic drugs 2. Antiepileptic Drugs 3. Chlorzazepoxide 4. Olanzapine 5. Oxcarbazepine 6. Phenytoin 7. Sertraline 8. Usual care 2 placebos, 1 active comparator (ergotamine + caffeine)

PRO Information

- | Number of PROs evaluated per study | PRO changes over time |
|---|---|
| <ul style="list-style-type: none"> • Most studies evaluated 1 or 2 PROs • Number of PROs evaluated: <ul style="list-style-type: none"> • 1 PRO: 8 studies • 2 PROs: 6 studies • 3 PROs: 1 study • Total evaluations: 23 PROs in 15 studies | <ul style="list-style-type: none"> • All studies measured PRO changes over time • Measurement time ranged from 2 hours to 2 years |

PRO Information: Types of PROs

- A total of 7 different PROs were evaluated by the 15 included studies
 - Symptoms: 9 studies
 - QoL: 8 studies
 - Behavior: 2 studies
 - Adherence, Satisfaction, Sexual function, Sleep: 1 study each
 - Total evaluations: 23 PROs in 15 studies
- A total of 27 different PRO scales were used to measure the 7 PROs
 - Symptoms: 12 scales
 - QoL: 8 scales
 - Behavior: 3 scales
 - Adherence, Satisfaction, Sexual function, Sleep: 1 scale each
 - 10 scales had subscales
 - 3 scales had 10+ subscales
 - One scale (QoLCE) had 16 subscales

PROs: Scales and Subscales

No.	Name of PRO	Scales used	Subscales
1	Symptoms	Hamilton Depression Rating Scale (HDRS)	NA
		National Hospital Seizure Severity Scale (NHS3)	NA
		Parent Symptom Questionnaire	Conduct; Impulsive hyperactive; Total score
		Clinical Global Impression (CGI)	NA
		Generic 4 -point scale	NA
		Brief Psychiatric Rating Scale (BPRS) score	NA
		Scale for Assessment of Positive Symptoms (SAPS)	NA
		Scale for Assessment of Negative Symptoms (SANS)	NA
		Patient Health Questionnaire-9 (PHQ-9)	NA
		Generic 4-point scale	Grade 0-1; 2-3
2	Quality of Life (QoL)	10-point Visual Analog Scale (VAS)	NA
		Clinical Institute Withdrawal Assessment for Alcohol Revised scale (CIWA-Ar) score	Nausea and vomiting; Tremors score; Paroxysmal sweats; Anxiety score; Agitation score; Tactile disturbance; Auditory disturbance; Visual disturbance; Headache score; Orientation and clouding; Total CIWA Ar score
		Quality of Life in Epilepsy Inventory (QOLIE-31)	Seizure worry; Overall QoL; Emotional; Energy/fatigue; Cognitive; Medication effect; Social function; Final score
		WHO QoL (Brev) scale	Physical; Psychological; Environmental; Social
		QoL in Childhood Epilepsy (QOLCE) questionnaire	Anxiety; Attention/concentration; Behavior; Control/helplessness; Depression; Energy/fatigue; General health; Language; Memory; Other cognitive processes; Physical restrictions; QoL; Self-esteem;
		Sickness impact profile (SIP) questionnaire	Social activities; Social interactions; Stigma 5 Independent scales (Eating, Home management, Recreation and past times, Sleep/rest, Work); 3 Physical scales (Ambulation, Body care and movements, Mobility); 4 Psychosocial scales (Alertness, Communication, Emotional behavior, Social interactions); Total Sickness impact profile score
		PedMIDAS	NA
		31-item QoL questionnaire (QOLIE-31) (version 1.0)	NA
		WHO wellbeing score (WHO-5)	NA
		Hartiemer and Santanello QoL questionnaire	Work functioning; Social interactions; Migraine symptoms; Energy/Vitality; Feelings and Concerns
3	Behavior	Hillside Behaviour Rating Scale	Gross-motor activity; Distractibility and concentration; Frustration tolerance; Cooperation; Interest in task; Impulsivity; Distractibility and concentration
		Conners parent rating scale (CPRS-48)	NA
		Behaviour screening questionnaire (BSQ)	NA
4	Adherence	Morisky Medication Adherence Scale (MMAS-4)	NA
5	Satisfaction	Visual Analog Scale (VAS)	NA
6	Sexual function	Arizona Sexual Experience Scale (ASEX)	NA
7	Sleep	Sleep Behavior Questionnaire	Total sleep score; Sleep fragmentation score; Parasomnias score; Daytime drowsiness score

Note: PedMIDAS: Pediatric Migraine Disability Assessment Scale

Discussion

- Only 15/306 (4.9%) RCTs on nervous system/ mental health disorders in India reported PROs
- Diverse disorders; lack of uniformity in the definitions used to describe the conditions and subtypes.
- Symptoms (9 studies) and QoL (8 studies) were the most frequently measured PROs
- WHO PRO scales were used for measuring QoL in 2 studies
- Large amount of variation in the measurement of PROs: 27 different scales for measuring 23 PROs in 15 studies
- Many generic scales were used to measure PROs; none were India-specific

Limitations

- Search was limited to PubMed; databases like Embase were not searched
- Search was restricted to publication in English language only

Conclusion

- Recording and analyzing PROs in RCTs on nervous system/ mental health disorders in India is inadequate and has a large amount of variation

References

1. Caldwell, Brittany. Value and Use of Patient-Reported Outcomes (PROs) in Assessing Effects of Medical Devices. 2016; Available from: <https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/default.htm>
2. Mercieca-Berber R, King MT, Calvert MJ, Stockler MR, Friedlander M. The importance of patient-reported outcomes in clinical trials and strategies for future optimization. Patient Relat Outcome Meas. 2018 Nov;Volume 9:353-67.