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MAJOR REVIEW (ORIG)

Patient-Reported Outcome Measures in Clinical High Risk for Psychosis: A Systematic Review

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A key issue in both research and clinical work with youth at clinical high risk (CHR) of psychosis is that there are clearly heterogenous clinical outcomes in addition to the development of psychosis. Thus, it is important to capture the psychopathologic outcomes of the CHR group and develop a core outcomes assessment set that may help in dissecting the heterogeneity and aid progress toward new treatments. In assessing psychopathology and often poor social and role functioning, we may be missing the important perspectives of the CHR individuals themselves. It is important to consider the perspectives of youth at CHR by using patient-reported outcome measures (PROMs). This systematic review of PROMs in CHR was conducted based on a comprehensive search of several databases and followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. Sixty-four publications were included in the review examining PROMs for symptoms, functioning, quality of life, self-perceptions, stress, and resilience. Typically, PROMs were not the primary focus of the studies reviewed. The PROMs summarized here fit with results published elsewhere in the literature based on interviewer measures. However, very few of the measures used were validated for CHR or for youth. There are several recommendations for determining a core set of PROMs for use with CHR.

Key words: psychosis/self-report/clinical assessments/ultra high risk

Introduction

A key issue that has recently become a major focus in both research and clinical work with youth at clinical high risk (CHR) of psychosis is that there are heterogenous clinical outcomes, in addition to the development of psychosis. That is, even though CHR individuals may not develop a full-blown psychotic illness, they do not necessarily make a full recovery.[1] A recent special issue of Schizophrenia Research was dedicated to the notion that "embracing heterogeneity creates new opportunities for understanding and treating those at clinical high risk for psychosis." Indeed, it is vital to capture the psychopathologic outcomes of the CHR group and, as Woods et al.[2] suggest, to develop a core outcomes assessment set (COS) that may help in dissecting the heterogeneity and aid progress toward new treatments.

However, in assessing psychopathology and often poor social and role functioning, we may be missing the important perspectives of the CHR individuals themselves. In a response to Woods et al.[2] and Petros et al.,[3] point out that the assessment of CHR individuals has typically focused on vulnerability and illness with an emphasis on the transition to psychosis, and that few studies have investigated favorable or good outcomes including the protective or resilience factors that might actually contribute to such outcomes. This group has developed tools to determine good outcomes that would include not just clinician perspectives, but also the perspectives of the young people who may be at risk of developing psychosis.[4] These tools showcase the importance of considering the perspectives of youth at CHR.

Thus, there may be the need to develop, as part of a COS, a core set of patient-reported outcomes (PRO) that could be used across different outcome studies. In fact, the US Food and Drug Administration made a commitment to advancing patient-focused drug development including use of patient experience data in regulatory decision-making. Some of the rational behind this is that patient experience data often provide

supporting information in cases where the condition may not be that well defined or may be useful in conjunction with biomarkers of symptom or health improvement.[5] This is in line with the current Accelerating Medicines Partnership® Schizophrenia (AMP® SCZ) program that aims to develop algorithms of clinical and biomarker data to determine outcomes of CHR youth which in turn can advance the testing of new pharmacological treatments.[6] PRO may be very useful in such clinical trials, yet little is known about their use in CHR research.

Reininghaus and Priebe (2012) reviewed the use of patient-reported outcome measures (PROMs) in individuals with established psychosis.[7] This review focused on treatment satisfaction, subjective quality of life, need for care, and the quality of the therapeutic relationship. Conclusions from this review were that, first, despite the increased use of PROMs in research studies, the evidence of their methodological quality remains limited; and second, there was a great deal of overlap across the measures, conceptually, operationally, and empirically. A second recent review of adults undergoing pharmacological and non-pharmacological interventions in mental health care found that PRO and clinician-reported outcomes supplemented each other and usually provided matching study conclusions.[8]

In both research and clinical settings, the use of PROMs with CHR youth has been limited due to the focus on clinician-reported outcomes. To the best of our knowledge, no systematic review has been conducted to summarize the use of PROMs in CHR youth. The first goal of this systematic review is to systematically search and identify how many studies used PROMs that assessed key outcomes such as symptoms, functioning, quality of life, resilience, stress levels, and self-perception amongst individuals at CHR for psychosis. There are many possible domains to address. However, we selected a limited number of domains based on the work of Petros et al.[3,4] who identified functioning, symptoms, distress and suicidality, and subjective well-being as domains that were deemed important by both clinicians and patients and on the known outcomes that are typically reported in CHR studies. Our domains, therefore, included clinical symptoms, functioning, quality of life, resilience which fits with subjective well-being, stress level as this is an important factor in possibly increasing attenuated symptoms, and self-perception which included self-esteem, self-schemas, self-perception, and defeatist beliefs. Our second goal was to determine whether the PROMs used were specifically validated for the CHR population.

Methods

The study protocol for this systematic review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) database (CRD42021261500) and conducted in accordance with the PRISMA.[9]

Search Strategy

A comprehensive search of the following online databases was conducted: MEDLINE, CINAHL, EBM reviews, Embase, and PsycINFO. In addition, google scholar was manually searched (using keywords from the PubMed search strategy) for gray literature that would have been missed by the online database search. The search was executed on April 28, 2021, with no other date or geographic restrictions applied. Only literature published in English was included. The search strategy is outlined in supplementary material.

Inclusion/Exclusion Criteria

The following Population, Intervention, Comparison and Outcomes (PICOS) inclusion criteria were applied: (1) study population consisted of CHR, ultrahigh risk or otherwise at risk for psychosis individuals, (2) any or no intervention/control group, (3) one or more of the PROMs of interest: Quality of life, clinical symptoms, functioning, levels of stress, self-perception (including self-esteem, self-schemas, and defeatist beliefs), and resilience, and (4) one of the following study designs: Observational studies (retrospective cohort, prospective cohort, case–control, and cross-sectional) or intervention studies (randomized controlled trial, single-arm intervention trial).

The following exclusion criteria were applied: (1) formal assessments conducted by raters or clinicians to assess PRO of interest, or (2) studies with the following designs: Case studies, reviews, protocols, conference proceedings (not peer-reviewed), or validity studies.

Procedures

After the search was executed, all citations were screened based on their titles and abstracts in duplicate. However, since some of the articles of interest may not have reported PROMs in the abstract, the full PICOS criteria were not applied at the title/abstract stage. Then, of those with a positive screen at the title/abstract phase, the full-text articles were retrieved and assessed for full eligibility, also in duplicate. Any discrepancies were resolved by a third reviewer.

Relevant systematic reviews were recursively searched for any studies that may have been missed by the online database search.

A pilot data extraction test was undertaken on a sample of included studies prior to starting full data extraction. After completion of the pilot test, for studies that met the inclusion criteria, data were extracted in duplicate including study characteristics, patient characteristics, and PROMs and results. All conflicts were resolved by a third reviewer. Study mapping was then conducted to determine if any overlapping study populations were identified. Occasionally there were several publications reporting on the same study population. For studies that generated more than one publication, the publication that

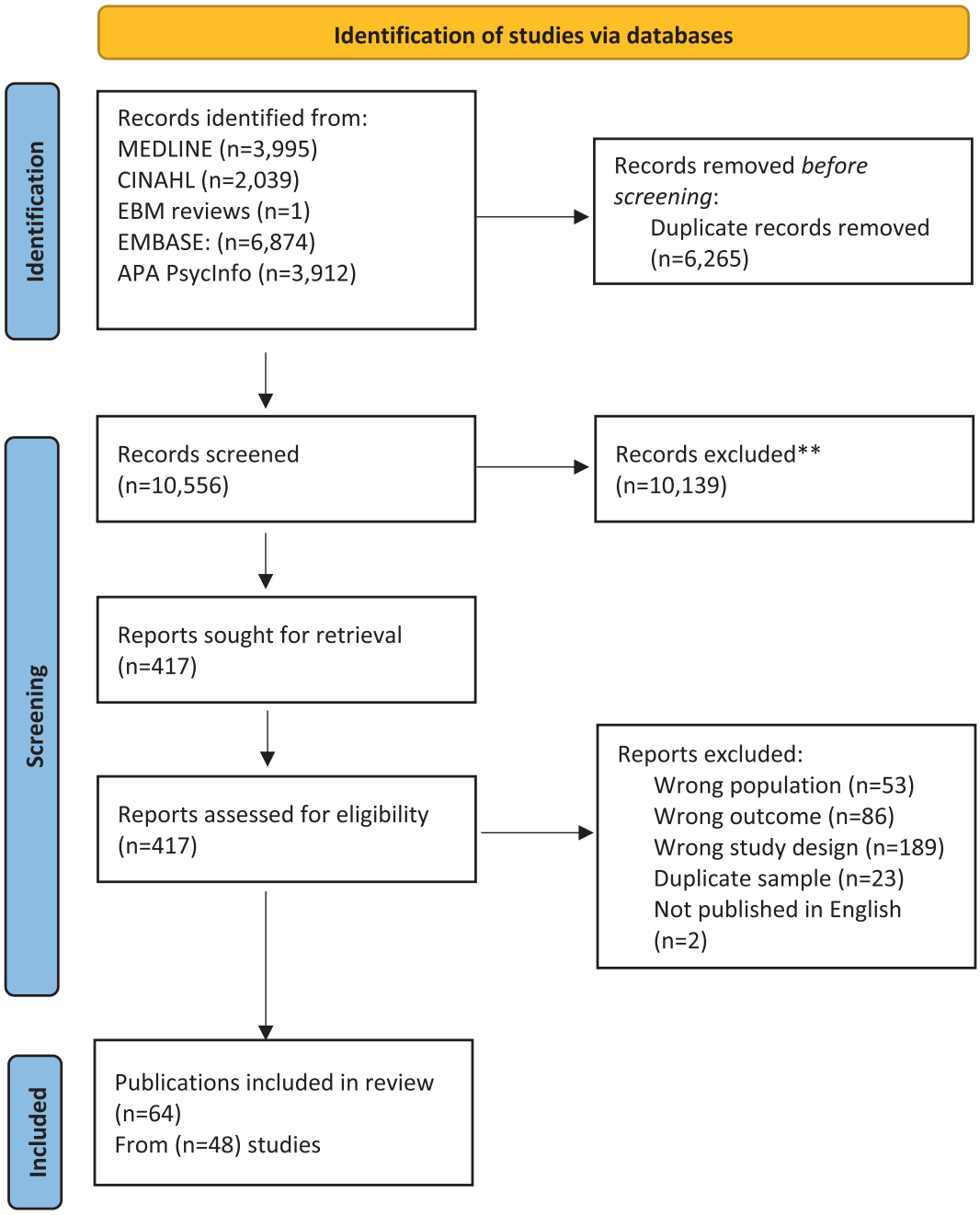

Fig. 1. PRISMA flow diagram.

addressed the highest number of participants completing a given PROM from the study was selected and then any publications from the study that included other unique PROMs of interest were also included. Publications from studies that did not offer data on unique PROMs of interest were excluded.

Qualitative Synthesis

After completion of data extraction, since this was to be the first broad descriptive of the use of PROMs in CHR youth, a qualitative synthesis was conducted.

A quality assessment of the included studies was conducted using a modified checklist similar to a previously published review.[10] The categories scored in the quality assessment checklist were: (1) role of the funding source in data interpretation and analysis, (2) sample size, (3) clearly reported inclusion criteria, (4) exclusion criteria, (5) reported sex distribution, (6) reported race/ethnic origin distribution, (7) reported IQ, educational level, and (8) reported dropout rate. Each item in the checklist was assigned a score of 0–2, with 0 being the lowest quality and 2 being the highest quality. In cases

where the information was partially reported, a score of one was assigned. See supplementary material 2 for the quality assessment scoring checklist.

Evaluation of Validation

To determine if the included studies used validated PROMs, the included publications were assessed to determine if the publication reported any validation of the measures being used in the study or if any relevant validation was referenced. Since many of the measures were designed for adult populations or populations with serious mental illness, such as schizophrenia, the aim was to determine if the PROMs had been validated with or developed for CHR populations or even with or for youth populations.

First, all the included papers were checked to determine if the authors reported on psychometrics for the specific PROMs used. Secondly, if a reference for psychometric properties of the PROM was provided that was reviewed. Thirdly, a search was done to determine if any information in the literature could be obtained on the PROM.

Results

Search Results

The search ascertained 16 821 citations, and after duplicates were removed, 10 556 were screened at the title/abstract phase. Of those, 417 were then assessed for eligibility to meet the PICOS criteria and ultimately, 64 publications met criteria coming from 48 unique studies (figure 1). Since participants in the included studies may be referred to as CHR, Ultra-High Risk, or At Risk For Mental State, in this paper and the tables we will use the term CHR to refer to all study participants.

Study Characteristics and Outcomes

Supplementary material 3 summarizes the study characteristics of the 48 different studies included in this systematic review. Overall, 21 studies were conducted in Europe, 10 in North America, 9 in Asia, 3 in Australia, 3 in multiple continents, 1 in Israel, and 1 in Kenya. The range in CHR sample size, mean age and female distribution were 7–765 participants, 13.9–34.72 years, and 8.3%–84%, respectively. The most reported PROM amongst the included studies was clinical symptoms (n = 31), followed by self-perception (n = 17) and then quality of life (n = 13). See figure 2.

Quality Assessment

The quality of the included studies was assessed and reported in figure 3. Almost all studies reported the source of their study funding, inclusion/exclusion criteria, and at least some demographic characteristics that were of interest. However, most studies were observational, therefore overall dropout rate assessments were of low quality. Sample sizes were also on the smaller end with 75% of studies reporting CHR sample sizes of 100 or less.

Quality of Life

There were 13 studies that reported quality of life as a PROM.[11–23] See table 1. The only quality of life tool used in more than one study was a variation of the World Health Organization Quality of Life questionnaire.[11–16] Among the studies that compared CHR individuals and healthy controls, quality of life was consistently lower in CHR. Furthermore, among studies that reported quality of life over time, improvements were observed across most studies from baseline measurements, except for 2 of the treatment studies where there were no significant

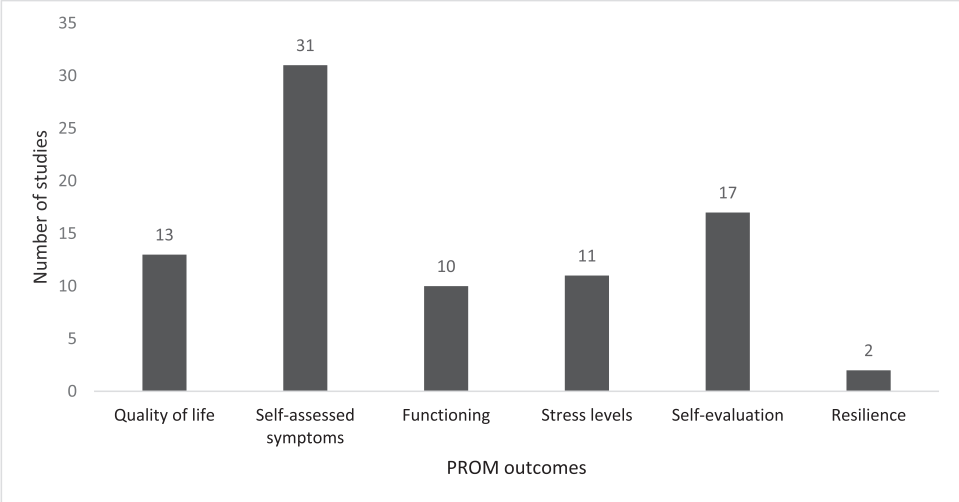

Fig. 2. Number of studies reporting PROMs in CHR. Note: Counts are not mutually exclusive.

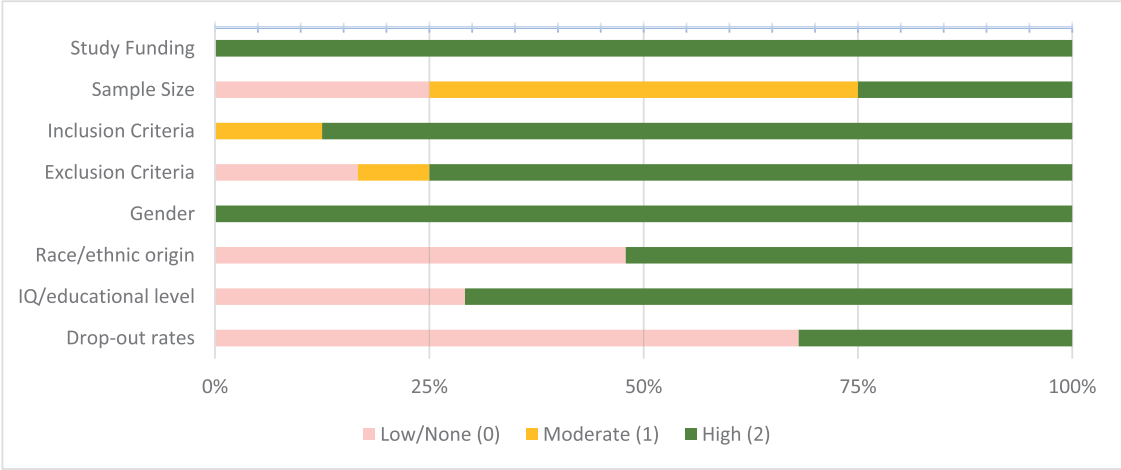

Fig. 3. Quality assessment of included studies.

Table 1. Studies Using Quality of Life Measures

First Author, Year	Questionnaire/Scale	Results
Glenthoj, 2020[17]	QoL-8D	CHR reported significantly poorer QoL than healthy controls. There were no significant differences in QoL between baseline and 12 months.
Ortega, 2019[22]	EQ-5D-3L	CHR reported significantly poorer QoL than healthy controls.
Nitka, 2016[19]	KIDSCREEN-27 Health-Related Quality of Life Questionnaire for Children and Adolescents	CHR reported significantly poorer physical well-being, psychological well-being, and school environment, than healthy controls.
Morrison, 2012[23]	MANSA	There were no significant treatment effects for QoL between CBT plus monitoring group versus monitoring only group at 6, 12, and 24 months.
Chang, 2020[20]	SF-12	Those with comorbid diagnoses reported significantly poorer ratings on SF-12 mental and physical health domains compared to those with no comorbidity.
Kobayashi, 2009[21]	SWNS	Subjective well-being significantly improved between baseline and 4 weeks. There were no significant differences between baseline and 8 weeks.
Tsujino, 2013[18]	Subjective Well-being Under Neuroleptics - Short version	There were no significant differences in subjective well-being after 26 weeks of follow up.
Domínguez-Martínez, 2015[11]	WHOQoL-BREF	Poorer quality of life was associated with more severe symptoms and increased functional impairment.
Heinze, 2018[12]	BREF	CHR reported significantly poorer QoL than help seeking controls at baseline, and 3, 6, and 12 months.
Matsumoto, 2019[13]	BREF	CHR reported significantly improved QoL between baseline and 6 and 12 months.
Ohmuro, 2017[14]	BREF	CHR reported significantly poorer QoL than FEP except in domains of social relationships and environments.
Pelizza, 2021[15]	BREF	Poorer QOL was associated with increased levels of anhedonia.
Tsai, 2021[16]	BREF–Taiwan Version	Overall QoL and the psychological aspect of QoL significantly improved for the HASL program experimental group at post-test (1 week), and 6-, and 12-month follow-up.

Note: CHR, clinical high risk; QoL, Quality of Life; FEP, first episode psychosis; HASL, Health-Awareness-Strengthening Lifestyle; AQoL-8D, Assessment of Quality of Life; EQ-5D-3L, Euro Quality of Life 5-dimensions Questionnaire – 3-level version; MANSA, Manchester short assessment of quality of life; SF-12, Short Form-12 Health Survey; SWNS, Subjective Well-being Under Neuroleptics, Short version; WHOQoL-BREF, World Health Organization Quality of Life-Brief Version.

differences between baseline and 12 months of follow-up[17] and 26 weeks of follow-up.[18]

Clinical Symptoms

Table 2 presents the 31 studies that reported self-reported symptoms amongst CHR individuals.

Nineteen studies had self-reported anxiety outcomes. Seven studies used the Social Interaction Anxiety Scale,[23–29] 5 used the Beck Anxiety Inventory,[30–34] 3 used the Social Anxiety Scale,[26,27,35] 3 studies used the State-Trait Anxiety Inventory form,[13,16,36] and the remaining studies used other types of assessments.[12,37–39] Overall, it was found that generally, CHR participants reported more anxiety and social anxiety symptoms than healthy controls and non-CHR. Over time, anxiety improved in CHR when compared to baseline measurements.[13,26,35]

Sixteen studies self-reported depression symptoms, fifteen of them using the Beck Depression Inventory. Across studies, it was consistently found that CHR reported more depressive symptoms than non-CHR participants.[14,15,25,30–34,36,40,41] Similar to anxiety symptoms, depressive symptoms seemed to improve longitudinally.[13,42] One study found that depressive symptoms were more prevalent in female CHR participants.[29] Seven studies reported on general symptom scales typically including both anxiety and depression,[38,39,43–47] where CHR participants usually presented with increased symptoms, relative to healthy controls with the one exception being on the Depression, Anxiety and Stress Scale.[39]

Psychotic-like experiences were self-reported in 2 studies,[24,28] while only one study reported self-measured negative symptoms.[24] Of the studies investigating positive and negative symptoms, only one measure was used in more than one study, the Community Assessment of Psychic Experiences.[24,28] Overall, CHR participants had more positive and negative symptoms than non-CHR participants.

Finally, 2 studies reported on the general health questionnaire[26,48] on which CHR had poorer ratings than healthy controls. One study used the Kessler Psychological Distress Scale,[12] on which CHR presented with increased psychological distress relative to non-CHR.

Functioning

Functioning was self-reported in 10 studies as presented in table 3. Four studies used the Social Adjustment Scale,[37,40,49,50] 2 used the Social Functioning Scale,[51,52] while the rest used 4 separate measures namely measures of adaptive functioning, social responsiveness, social adaptation, and the Sheehan Disability scale.[17,22,33,53] Overall, those in the CHR group generally scored lower in functioning and social adjustment and higher in social impairment in comparison to healthy controls and non-CHR.[17,22,33,37,40,49,50] Among CHR, premorbid functioning was shown to be related to poorer social functioning.[52] One longitudinal study found no significant changes in social impairment when measuring CHR from baseline to a 12-month follow-up,[17] nor was any change observed posttreatment.[51]

Stress Levels

Table 4 summarizes 11 studies that reported on self-rated stress or stress levels, and of those, 6 studies used the Perceived Stress Scale,[22,34,54–57] and all other studies used unique stress assessment tools.[58–62] Although the stress assessment tools varied across studies, CHR individuals consistently had higher stress levels relative to healthy controls, and no differences in stress between CHR, first episode of psychosis, or multiple episode psychosis individuals were observed.

Self-Perception

Seventeen studies reported self-perception outcomes that included measures of self-esteem, self-schemas, self-perception, and defeatist beliefs, presented in table 5. Six studies measured self-esteem, 3 used the Rosenberg Self-Esteem Scale,[30,63,64] 2 studies used the Self-Esteem Rating Scale[62] (one used the short-form version[65]) and one study used the Self-Perception Profile for Adults.[66] Across several studies, CHR individuals were found to have lower self-esteem relative to healthy controls,[30,62,64,66] and a longitudinal study reported that self-esteem in CHR did not significantly improve over time.[65]

Six studies reported on self-schemas or self-perception: Four used the Brief Core Schema Scale,[31,67–69] one used the Self-Perception Scale,[70] and one used the Personal Qualities Questionnaire.[48] Among studies comparing CHR and healthy controls, CHR reported increased negative schemas and decreased positive schemas about themselves and others.[31,48,67,68,70] It was also found that CHR had greater negative self-perception when compared to a healthy control group.[70] Negative schemas/beliefs were found to be correlated with non-bizarre thoughts and perceptual abnormalities severity subscales as rated on the CAARMS[69] and attenuated psychotic positive symptoms rated on the Scale of Psychosis-risk Symptoms.[67]

For defeatist beliefs, 7 studies reported outcomes: Two studies used the Personal Beliefs About Experience Questionnaire,[71,72] one study used the Dysfunctional Attitudes Questionnaire,[48] one study used the Defeatist Performance Beliefs Questionnaire,[73] one used the Self-Efficacy Scale,[65] one used the Locus of Control Ratings Scale,[43] and one used Social Entrapment and Defeat Scales.[39] CHR individuals endorsed more defeatist performance beliefs,[73] and social defeat[39] relative to healthy controls. A study examining self-efficacy longitudinally found that it did not improve over time in individuals at

Table 2. Studies Using Measures of Clinical Symptoms

First Author, Year	Questionnaire/Scale	Results
DeVylder, 2013[34]	BAI BDI	CHR reported significantly more severe anxiety and depression than healthy controls.
Olvet, 2015[33]	BAI BDI CDI	CHR reported significantly more severe anxiety and depression than healthy controls.
Atkinson, 2017[30]	BDI-II	CHR reported significantly more severe anxiety and depression than healthy controls.
Cowan, 2019[31]	BAI BDI-II	CHR reported significantly more severe anxiety and depression than healthy controls.
Lederman, 2017[32]	BAI BDI-II	CHR reported significantly more severe depression compared to healthy controls and FEP.
Popovic, 2020[41]	BDI	CHR reported significantly more severe depression scores than healthy controls.
Salokangas, 2019[42]	BDI	Among CHR, depression symptoms decreased significantly from baseline to follow-up.
Choi, 2017[40]	BDI-II	CHR reported significantly more severe depression symptoms than healthy controls.
Matsumoto, 2019[13]	BDI-II STAI	CHR clinical measures significantly improved from baseline to 6 and 12 months.
Ohmuro, 2017[14]	BDI-II	CHR reported significantly more severe depressive symptoms than FEP.
Pelizza, 2021[15]	BDI-II BOL	CHR reported significantly more severe depressive symptoms than FEP and non-CHR.
Appiah-Kusi, 2017[36]	BDI-II STAI	CHR reported significantly more depression and anxiety than healthy controls.
Izon, 2021[23]	BDI-II SIAS	Depression but not anxiety in CHR was associated with high expressed emotion in the CHR family.
Rietdijk, 2013[29]	BDI-II SIAS	Among CHR, women reported significantly more severe depression and anxiety symptoms than men.
Morrison, 2012[23]	BDI-PC Social Interaction Anxiety Scale	CHR treatment effects were nonsignificant on reported depression and anxiety symptoms.
Blessing, 2017[43]	BSI-18	CHR reported significantly less severe symptoms on the BSI-18 after communication of diagnosis.
Tsai, 2021[16]	CMSTAI-Y	After CHR participated in the HASL program, the experimental CHR group reported significantly less severe state and trait anxiety than the nonexperimental CHR group.
Veling, 2016[28]	CAPE GPTS SIAS	CHR and psychosis patients reported significantly more severe levels of all symptoms in comparison to healthy controls.
Geraets, 2018[24]	CAPE SIAS	CHR reported significantly more severe positive, negative, depressive, and social anxiety symptoms than healthy controls.
González-Rodríguez, 2014[44]	FCQ	Reports of basic symptoms on the FCQ were not significantly different between CHR and FEP.
Barkus, 2010[47]	GHQ	CHR reported higher scores on the GHQ than healthy controls. CHR reported significantly more severe psychiatric symptoms on the GHQ than healthy controls.
Morrison, 2006[48]	GHQ	CHR reported significantly more severe psychiatric symptoms on the GHQ than the healthy controls.
Marshall, 2012[26]	GHQ SAS SIAS	CHR reported significant improvements in symptoms reported on the GHQ at each follow-up assessment compared with baseline; CHR reported significant improvements in anxiety symptoms over time at each assessment, relative to baseline.
Heinze, 2018[12]	K-10 OASIS	CHR reported significantly more severe levels of depressive symptoms and psychological distress relative to non-CHR; there were no significant differences in reported anxiety compared to non-UHR.
Koren, 2016[38]	MASQ	Participants with APS reported significantly more severe symptoms (subscales: mixed, anxiety, depression, arousal, anhedonia) than non-APS.
Lincoln, 2018[35]	SAS	CHR reported significant improvements in anxiety symptoms over time compared to baseline.
McAusland, 2017[27]	SAS SIAS	CHR reported significantly more severe anxiety symptoms than healthy controls; female participants reported more severe anxiety symptoms than males.

Table 2. Continued

First Author, Year	Questionnaire/Scale	Results
Cressman, 2015[37]	SAS-A	CHR reported significantly more severe social anxiety symptoms and social adjustment than healthy controls.
Valmaggia, 2015[39]	SSPS	CHR reported significantly more severe paranoid appraisals than healthy controls; CHR status was not significantly associated with depression or anxiety.
	DASS	
Langbein, 2018[45]	SCL-90-R	CHR, FEP and healthy controls reported significant differences in the global severity index and on all symptom subscales.
Manninen, 2014[46]	YSR	CHR met the clinical range significantly more often for anxious/depressed, withdrawn/depressed and thought problem symptoms than non-CHR.

Note: CHR, clinical high risk; FEP, first episode psychosis; HASL, Health-Awareness-Strengthening Lifestyle; APS, attenuated psychosis syndrome; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; CDI, Children's Depression Inventory; BDI-II, Beck Depression Inventory II; STAI, state-trait anxiety inventory; SIAS, Social Interaction Anxiety Scale; BOL, Brief O-Life Questionnaire; BDI-PC, Beck Depression Inventory for Primary Care; BSI-18, Brief Symptom Inventory-18; CMSTAI-Y, Chinese Mandarin State and Trait Anxiety Inventory Form Y; CAPE, Community Assessment of Psychic Experiences; GPTS, Green Paranoid Thoughts Scale; FCQ, Frankfurt Complaint Questionnaire; GHQ, Goldberg Health Questionnaire; SAS, Social Anxiety Scale; K-10, Kessler Psychological Distress Scale; OASIS, Overall Anxiety Severity and Impairment Scale; MASQ, Mood and Anxiety Symptom Questionnaire; SAS-A, Social Anxiety Scale for Adolescents; SSPS, State Social Paranoia Scale; DASS, The Depression, Anxiety and Stress Scale; SCL-90-R, Symptom Checklist 1990 Revised; YSR, Youth self-report.

Table 3. Studies Using Measures of Functioning

First Author, Year	Questionnaire/Scale	Results
De Wit, 2014[53]	Adaptative Functioning Scale "Friends" on the ASEBA-ASR	There were no significant differences in social functioning between those who did and did not remit from CHR status.
Olvet, 2015[33]	SDS	CHR reported significantly poorer SDS percentage scores than healthy controls.
Ortega, 2018[22]	SASS	CHR reported significantly poorer social adaptation than healthy controls.
Cressman, 2015[37]	SAS-SR	CHR reported significantly more severe social anxiety and poorer social adjustment than healthy controls.
Choi, 2017[40]	SAS-SR	CHR reported significantly more severe anxiety, depression, and poorer social functioning than healthy controls.
Corcoran, 2011[49]	SAS-SR	CHR reported significantly more severe anxiety, depression, and poorer social functioning than healthy controls.
Lincoln, 2014[50]	SAS-SR	CHR reported significantly more severe social impairment than healthy controls.
Addington, 2011[51]	SFS	There were no significant differences in social functioning between the CBT and supportive therapy intervention groups at baseline, 6,12, or 18 months.
Lyngberg, 2015[52]	SFS	There was a significant correlation between good social functioning and good premorbid functioning during early and late adolescence.
Glenthoj, 2020[17]	SRS-A	There were no significant differences in functioning between baseline and 12-month follow-up. CHR reported significantly more severe social impairment than healthy controls.

Note: Abbreviations are explained in the first footnote to table 1. ASEBA-ASR, Achenbach System of Empirically Based Assessment – Adult Self-Report; SDS, Sheehan Disability Scale; SASS, Social Adaptation Self-evaluation Scale; SAS-SR, Social Adjustment Scale Self-Report; SFS, Social Functioning Scale; SRS-A, Social Responsiveness Scale, Adult Version;

CHR.[65] Although another study found that after communication of a diagnosis, internal locus of control ratings increased.[43]

Resilience

Two studies reported resilience as a PROM.[74,75] One study measured resilience using the Connor-Davidson Resilience Scale,[74] while the other study used the Child and Youth Resilience Measure.[75] Both studies found that CHR individuals were less resilient than healthy controls and those CHR individuals who transitioned to psychosis or had persistent symptoms were less resilient than those who did not make the transition or had remitted at follow-up assessments.

Table 4. Studies Reporting Stress Levels

First Author, Year	Questionnaire/ Scale	Results
Bentley, 2016[58]	BASC-2	CHR reported a significant relation between parent–child relationships and social stress; significant negative association between positive parent–child relationships and lower social stress in CHR.
Cullen, 2020[59]	DSI	CHR reported significantly more severe daily stress relative to healthy controls and remitted CHR; symptomatic, progressed and converted groups also reported significantly more daily stressor exposures relative to remitted CHR.
Appiah-Kusi, 2020[57]	PSS	CHR reported significantly more severe stress than healthy controls.
DeVylder, 2013[34]	PSS	CHR reported perceived stress at baseline which was associated with impaired stress tolerance assessed with SOPS.
Nordholm, 2016[54]	PSS	CHR experienced significantly more severe perceived stress than healthy controls.
Phillips, 2012[55]	PSS	CHR reported significantly more severe stress than healthy controls.
Ortega, 2018[22]	PSS HRSRS	CHR reported significantly more severe perceived stress and more severe stressful life events, relative to healthy controls.
Studerus, 2021[56]	PSS-10	CHR reported significantly more severe overall stress than healthy controls.
Kommescher, 2017[60]	SCQ	CHR, first episode or multiple episode psychosis individuals had no significant differences in any of the subscales except for devaluation.
Pruessner, 2011[62]	TICS	CHR reported significantly more severe perceived stress in the past month and past year, relative to healthy controls.
Mamah, 2020[61]	WERC	For CHR, stress and high harm avoidance, low self-directedness, low cooperativeness, and high self-transcendence were significantly related.

Note: Abbreviation is explained in the first footnote to table 1. SOPS, Scale of Psychosis-Risk Symptoms; BASC-2, Behavior Assessment System for Children Second Edition; DSI, Daily Stress Inventory; PSS, Perceived Stress Scale; HRSRS, Holmes-Rahe Social Readjustment Scale; PSS-10, Perceived Stress Scale - 10-item version; SCQ, Stress Coping Questionnaire; TICS, Trier Inventory for Chronic Stress; WERC, Washington Early Recognition Center Stress Screen.

Validation

In total, 8 of the 84 PROMs included had been reportedly validated in varying degrees in CHR populations, with an additional 19 that had been developed or validated for youth. A total list of all PROMs noting those that had been validated for youth and/or CHR can be found in supplementary material 4. Table 6 reports on the psychometrics of the 8 measures that have some validation for CHR populations. Detailed description of the sources of this information is presented in supplementary material 5.

Discussion

This review presented a variety of PROMs examined among CHR individuals. We identified 64 publications from 48 unique CHR study populations measuring the PROMs of interest. The most common PROs reported in the included studies were symptoms (mainly anxiety and depression), followed by self-perception measures, and then stress levels. In general, outcomes of the different PROMS suggested that CHR participants tended to present with more symptoms, poorer self-perception, increased stress, poorer functioning, and quality of life than healthy controls. Furthermore, over time symptoms, but not functioning, tended to improve. All of these outcomes are, for the most part, supported in the CHR literature with the use of interviewer measures.[76]

To the best of our knowledge, this is the first systematic review to synthesize the reporting of a wide range of PROMs used with CHR populations, and therefore, provides an overview of the current state of the field highlighting the need for further research in this area. A strength of this review was the inclusion of 64 publications representing 48 unique study populations of CHR individuals. We searched numerous online databases, screened, and extracted publications in duplicate, published our protocol *a* priori, and followed PRISMA guidelines for systematic review conduct, thus making this review the most comprehensive systematic review reporting the PROMs of interest in CHR to date.

However, this study had several limitations that need to be acknowledged. We made an informed decision to explore specific domains of PROs. This meant that certain

Table 5. Studies Reporting Measures of Self-perceptions

First Author, Year	Questionnaire/ Scale	Results
Cowan, 2019[31]	BCSS	CHR reported significantly more negative beliefs about self and others and significantly fewer positive beliefs about self and other, relative to health controls.
Stowkowy, 2012[67]	BCSS	CHR reported significantly more negative schemas about the self and others.
Stowkowy, 2016[68]	BCSS	CHR reported significantly more severe negative schemas about the self and about other people compared to healthy controls.
Taylor, 2014[69]	BCSS	CHR had no significant differences in negative or positive beliefs about the self, relative to FEP.
Clay, 2020[73]	DPB	CHR reported significantly more severe DPBs than healthy controls.
Morrison, 2006[48]	DAS PQQ	CHR reported significantly more severe beliefs about rejection and criticism from others, and significant discrepancies in self-perception, and general mental distress.
Blessing, 2017[43]	LCS	CHR reported significantly increased internal locus of control ratings after communication of diagnosis.
Pyle, 2015[71]	PBEQ	Internalized stigma was significantly related to depression, social anxiety, distress due to unusual psychological experiences, and suicidal thinking in CHR.
Stowkowy, 2015[72]	PBEQ	CHR who transitioned to psychosis agreed more to statements concerning lack of control over experiences; all sub-scores were significantly related to the CDSS and to SOPS negative symptoms with the exception of self as experiences, which was unrelated to negative symptoms.
Atkinson, 2017[30]	RSES	CHR participants reported significantly poorer self-esteem than healthy controls.
Jhung, 2016[63]	RSES	In CHR, no significant correlations of noncurrent or current emotional experiences (anhedonia and SAM scales) were found with self-esteem.
Shi, 2017[64]	RSES	CHR reported significantly poorer self-esteem relative to healthy controls; in CHR, poorer self-esteem was significantly associated with more severe positive, negative, and depressive symptoms. In CHR, higher self-esteem was significantly and positively correlated with GAF; Self-esteem significantly improved in CHR after treatment (6 months).
Pruessner, 2011[62]	SERS	CHR reported significantly poorer protective factors (self-esteem, social support, and active coping), relative to healthy controls; more severe stress in the past month was significantly related to lower self-esteem.
Alvarez-Jimenez, 2018[65]	SERS-SF SES	No significant improvement in self-esteem or self-efficacy between baseline and follow-up were found.
Seo, 2018[70]	SPS	CHR reported significantly poorer self-perception than healthy controls.
Benavides, 2018[66]	SPPA	CHR and SCZ had significantly poorer GSE compared to healthy controls, but no significant differences between CHR and SCZ.
Valmaggia, 2015[39]	Social Entrapment and Defeat Scales	CHR reported significantly more severe levels of social defeat than healthy controls.

Note: Abbreviations are explained in the first footnote to table 1. CDSS, Calgary Depression Scale for Schizophrenia; SOPS, Scale of Psychosis-Risk Symptoms; SAM, Self-Assessment Manikin; GAF, Global Assessment of Functioning; SCZ, Schizophrenia; GSE, Global Self-Esteem; BCSS, Brief Core Schema Scale; DPB, Defeatist Performance Beliefs Questionnaire; DAS, Dysfunctional Attitudes Scale; PQQ, Personal Qualities Questionnaire; LCS, Locus of Control Scale; PBEQ, Personal Beliefs about Experiences Questionnaire; RSES, Rosenberg Self-Esteem Scale; SERS, Self-Esteem Rating Scale; SERS-SF, Self-Esteem Rating Scale Short Form; SES, Self-Efficacy Scale; SPS, Self-Perception Scale; SPPA, Self-Perception Profile for Adults.

domains were missing. We did not include any concepts in the cognitive domain such as metacognitions. There is a wide literature on metacognitions in CHR where much of the literature does not particularly focus on outcome but rather on whether this could be a difficulty that could be considered as a predictor of psychosis.[77] We did not include domains such as social support or coping styles that may be useful as correlates of different outcomes.

Secondly, there were limited treatment studies (particularly randomized controlled trials),[78] that used the PROMs of interest in this review, more often these studies used clinician-reported measures to assess the main outcome. Many of the treatment studies made use of PROMs, such as perceived self-support, coping skills, appraisal of the therapeutic relationship, and treatment satisfaction that were not under review in this paper.

Table 6. Psychometric Properties of PROMs Validated for CHR

Measure	Test–Retest Reliability	Internal Consistency	Construct Validity	Convergent Validity	Discriminative Validity	Criterion Validity	Group Differences	Responsiveness to Change
BDI	NR	√	√	√	√	√	√	√
BASC-2	NR	NR	NR	√	NR	√	√	NR
CAPE	√[a]	√	NR	√	LIMITED	√	√	NR
FCQ	NR	√	NR	NO	NR	NO	NR	NR
LSHS-R	NR	√	NR	√	√	√	√	NR
SFS	NR	√	NR	√	√	NR	√	NR
WERCAP	√	√	NR	NR	√	√	√	√
BCSS	NR	√	NR	√	√	√	NR	NR

Note: BDI, Beck Depression Inventory; BASC-2, Behaviour Assessment System for Children Second Edition; CAPE, Community Assessment of Psychic Experiences; FCQ, Frankfurt Complaint Questionnaire; LSHS-R, Launay-Slade Hallucinations Scale; SFS, Social Functioning Scale; WERCAP, Washington Early Recognition Center Affectivity and Psychosis Screen; BCSS, Brief Core Schema Scale, NR, not reported; NO, tested but did not meet that criteria; PROMs, patient-reported outcome measures; CHR, cilinical high risk.
[a]Just for positive symptoms.

These measures would be of value in treatment studies, yet the use of these PROMs is limited in the literature. Of note, one useful method to capture PRO that was not addressed in this review is the use of experience sampling methods, for example, the work of van der Steen et al.[79] and Gerritsen et al.[80]

Secondly, although PROMs provide observations of experiences from the participant's perspective, self-reported outcomes can be subject to social desirability bias or recall error that may lead to misclassification of these outcomes. Careful assessment and focus on participant experience through standardized/validated measures would help to mitigate these concerns.

Thirdly, in most of the included studies, the PROMs were not the primary focus of the study's aims. Thus, sample sizes of CHR individuals may have not been powered to appropriately assess the PROMs, and therefore, future studies focusing on these outcomes in larger samples would be of interest. Next, none of the papers offered comparisons between the PROMs and interviewer-administered measures as was done in a previously published PROM review.[8]

Finally, there was limited evidence as to whether many of these PROMs were validated for CHR or even youth. We reported that less than 10% of the reported PROMs had been validated for CHR and one-third with youth populations. We searched for reports on psychometrics for these PROMs to the best of our ability but are aware that there may be more recent papers or papers that were missed that might have been added to our reported psychometrics. Regardless it was still a small proportion that had been validated. A recent publication by Buck et al.[81] advocated strongly for psychometrically sound instruments to track and evaluate clinical outcome. In their comprehensive review of PROMs for treatment outcome in schizophrenia they reported on 12 PROMs. Their findings demonstrated that most measures showed strengths in internal consistency and test–retest reliability with several of the 12 having evidence of convergent or criterion validity.

Future Directions

Thus, in order to include PROMs in a core outcomes assessment certain criteria should be considered. The first recommendation is to use PROMs that are validated for CHR and/or youth that have demonstrated psychometric strengths. This may mean that the choice of measures will be limited to a few in each of the different clinical domains to ensure having PROMs with good psychometrics vs. the wide range that has been reported in this review. Other important methodological criteria to consider would be, in addition to validity, sensitivity, reliability, generalizability, and feasibility. The measure should have relevance for a youth population, something that might be achieved by obtaining the individual perspectives and involvement of CHR individuals in developing PROMs. For example, Petros et al.[4] determined what PROs, in particular good outcomes, were meaningful to CHR youth who were service users. Furthermore, the measure should be brief and the use of several PROMs should be avoided unless they address clearly distinct domains.[7] Finally, PROMs should be matched to the aims of the specific study in that the participant perspective is being considered as a healthcare outcome.[82] For clinical and functional outcomes, it might mean selecting measures that match the interviewer-rated domains to determine how the participant sees the clinical change. For both clinical and observational studies an aim might be to understand the participants' sense of subjective well-being.

There have been efforts to identify, evaluate and recommend validated PROMs through various national guidelines. Most notable was the collaboration in the US between the National Institute of Health and several outcome scientists to develop the patient-reported outcomes

measurement information system.[83,84] Thus, one option might be to work through the patient-reported outcomes measurement information system (www.healthmeasures.net) to find relevant measures or learning from patient-reported outcome measurement information system how to adapt and validate the most relevant measures for CHR youth.

Thus, in summary, determining a core set of well-validated PROMs, specifically for CHR individuals, would allow for a more robust understanding of CHR individuals to aid in determining future treatments and improved care.

Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin Open* online.

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