Systematic Review of Global Functioning and Quality of Life in People with Psychotic Disorders

Running head: Global Functioning and QoL in People with Psychosis

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Aims. People with psychotic disorders face impairments in their global functioning and their quality of life (QoL). The relationship between the two outcomes has not been systematically investigated. Through a systematic review we aim to explore the presence and extent of associations between global functioning and QoL and establish whether associations depend on the instruments employed.

Methods. In May 2016, 10 electronic databases were searched using a two-phase process to identify articles in which associations between global functioning and QoL were assessed. Basic descriptive data and correlation coefficients between global functioning and QoL instruments were extracted, with strength of the correlation assessed according to the specifications of Cohen 1988. Results were reported with reference to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines and PRISMA standards. A narrative synthesis was performed due to heterogeneity in methodological approaches.

Results. Of an initial 15,183 non-duplicate articles identified, 756 were deemed potentially relevant, with 40 studies encompassing 42 articles included. 14 instruments for measuring global functioning and 22 instruments for measuring QoL were used. 29 articles reported linear associations while 19 assessed QoL predictors. Correlations between overall scores varied in strength, primarily dependent on the QoL instrument employed, and whether QoL was objectively or subjectively assessed. Correlations observed for objective QoL measures were consistently larger than those observed for subjective measures, as were correlations for interviewer than self-assessed QoL. When correlations were assessed by domains of QoL, the highest correlations were found for social domains of QoL, for which most correlations were moderate or higher. Global functioning consistently predicted overall QoL as did depressive and negative symptoms.

Conclusions. This review is the first to explore the extent of associations between global functioning and QoL in people with psychotic disorders. We consistently found a positive

association between global functioning and QoL. The strength of the association was dependent on the QoL instrument employed. QoL domains strongly associated with global functioning were highlighted. The review illustrates the extensive array of instruments used for the assessment of QoL and to a lesser extent global functioning in people with psychotic disorders, and provides a framework to understand the different findings reported in the literature. The findings can also inform the future choice of instruments by researchers and/or clinicians. The observed associations reassure that interventions for improving global functioning will have a positive impact on the QoL of people living with a psychotic disorder.

Key words: Schizophrenia, Psychosis, Functioning, Quality of life.

Introduction

Psychotic disorders are of special interest due to the severity of their symptoms, the surrounding stigma and the consequences of dysfunction, discrimination and costs. The importance of functioning to psychotic disorders was reaffirmed when psychosis was described as an imprecise group of symptoms, of sufficient severity to disrupt everyday functioning (Petho & Ban, 1988).

According to the International Classification of Functioning, Disability and Health (World Health Organization, 2001), functioning denotes the positive features of the relationship between a health condition and the environmental and personal context of the individual, while disability indicates negative features of that relationship. Thus, functioning is concerned with the ability of an individual to perform their roles and participate in life (Bowling, 2005). Global functioning should encompass the measurement of several types of functioning (Aas, 2010). Since 1962, a number of instruments have been created to measure global functioning, as well as specific dimensions (or types) of functioning e.g., social functioning, executive functioning, etc. (see Fig. 1).

Almost parallel to the development of instruments to assess functioning, and shortly after quality of life (QoL) in health care was raised by Elkinton, when he asked: “What is the harmony within a man, and between a man and his world –the quality of life– to which the patient, the physician, and society aspires?” (Elkinton, 1966), interest in QoL as an outcome of people with psychosis began to emerge (Fig. 1). This interest occurred alongside the implementation of community support programmes after deinstitutionalization (Baker & Intagliata, 1982, Lehman, 1988). QoL has been defined as “an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” (World Health Organization, 1997). Despite this, there is no agreement on what aspects and how QoL should be assessed.

More than 50 QoL instruments have been used in patients with mental disorders (Prigent *et al.*, 2014).

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Functioning and more recently QoL have thus been identified as important outcomes in people with psychosis. Reviews focused on the assessment of global functioning and QoL in people with psychotic disorders are scarce (Awad *et al.*, 1997, Pinikahana *et al.*, 2002) and the relationship between them has not been systematically assessed. As impairment in global functioning of people with psychosis is expected, it is important to understand the impact of this impairment on QoL. Establishing the relationship between global functioning and QoL measures would support the future choice of instruments for the assessment of these outcomes and, in turn, identify strategies to diminish the societal burden of psychotic disorders.

The aim of the present study is to explore the presence and extent of associations between global functioning and QoL in people with psychotic disorders and establish whether this relationship is dependent on the instruments employed.

Methods

Selection criteria

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher *et al.*, 2009). Studies included for data extraction were full text articles with a cross-sectional design or a follow-up design that provided required information at baseline. Baseline information only was sought, as changes in the functioning of people with psychosis over time is well documented (Ascher-Svanum, 2013, Harvey, 2014, Harvey & Davidson, 2002). Articles could be written in English or Spanish (given native English and Spanish speakers within the authorship team). The sample

needed to comprise people with schizophrenia and schizophrenia spectrum disorders with or without people with mood disorders with psychotic symptoms (bipolar disorder type I, major or severe depressive disorder with psychotic symptoms) assessed according to the Ninth/Tenth Revision of the International Classification of Diseases (ICD 9/10) or the Diagnostic and Statistical Manual of Mental Disorders Fourth/Fifth Edition (DSM-IV/5), and aged between 18 and 64 years, in which associations between global functioning and QoL were assessed. There were no time-period restrictions.

Due to the lack of a universal definition of global functioning, instruments that assessed several dimensions of functioning as an inclusive outcome were deemed a global functioning instrument. Likewise, given the absence of a universally accepted definition of QoL, instruments reporting on a group of outcomes that contribute to an individual's satisfaction with life and/or overall health (Fayers & Machin, 2016) were accepted for inclusion in the review.

Intervention studies, reviews and meta-analyses were excluded as well as studies based on populations with organic or induced psychosis, psychosis due to other mental disorders or other medical conditions and populations at high risk of psychosis but not yet diagnosed. Intervention studies were excluded as functioning levels differ in artificial environments such as clinical trials (Ascher-Svanum, 2013, Bellack *et al.*, 2007, Patterson *et al.*, 2001).

Search strategy

In May 2016 Annual Reviews, Cochrane Library, CINAHL, EconLit, Embase, Medline, PsycARTICLES, PsycINFO, PubMed and ScienceDirect were searched using a two-phase identification process. Search terms were introduced with corresponding MeSH Terms,

synonyms and stem words, as well as appropriate filters and use of Boolean operators. The detailed search strategy is available as Supplementary material.

Searches were divided into phases in order to identify potential publication bias. This approach was adopted because of concern that only strong associations would be reported in title and abstract. In Phase A, all keyword terms were searched in title and abstract. In Phase B, all keyword terms except functioning were searched in title and abstract, with stem "function" then searched for in the main text.

Study selection

Two independent reviewers (ANF and AN) assessed studies for inclusion, with inconsistences and disagreements resolved by consensus. After deletion of duplicates, Phase A records were screened for inclusion criteria in their titles and abstracts. Full-text articles of included studies were obtained and assessed in full for eligibility. A similar process was used for Phase B records, except that screening for inclusion included a search for functioning in the main text. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (von Elm *et al.*, 2007) was used to assess whether analytical observational studies reported STROBE elements determined *a priori* as essential. These items were 3, 7, 12, 16 and 18 (i.e., objectives, variables, statistical methods, main and key results).

Data extraction

Data extracted from each article encompassed basic descriptive data and correlation coefficients between global functioning and QoL instruments. Extraction was undertaken by ANF under the guidance of AN. After extraction, socio-demographic variables were coded for summarization in frequency tables.

The correlation coefficients between global functioning and QoL extracted were; correlations between global functioning and other variables; and correlations between QoL and other variables comprising the domains and items covered for each instrument. This analysis reports on the strength of the correlation between global functioning and QoL and between global functioning and individual domains of QoL. Strength of correlation was assessed according to the specifications of Cohen 1988 (Cohen, 1988) established as $0.10 \leq r < 0.3$ small effect, $0.3 \leq r < 0.5$ medium effect and $0.50 \leq r$ large effect.

A narrative synthesis was performed given heterogeneity in methodological approaches, including instruments employed in the assessment of global functioning and QoL, and statistical analyses employed. QoL instruments were defined as objective, if comprised of objective items only (usually intended for interviewer-assessment), subjective if comprised of subjective items only (usually intended for self-assessment), or subjective and objective. Results were reported with reference to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines (Stroup *et al.*, 2000) and PRISMA standards.

Results

Search results

Across Phases A and B 15,183 records were initially identified, of which 8,673 were duplicates and excluded from further review. In Phase A, upon screening of title and abstract, 637 articles were then assessed as requiring full text review for eligibility, with 34 articles assessed as eligible. In Phase B upon screening of title and abstract, 2,601 articles were assessed as requiring full-text screening for functioning, with 119 then identified as requiring full-text review for eligibility. Eight additional articles were identified as eligible for inclusion (see Fig. 2). Thus 42 articles were included in this review as listed in Table 1.

<Please insert Figure 2 around here>

The articles

Articles were published between 1997 and 2016, all met the required STROBE criteria for inclusion. Three-fifths (25 articles) were from Europe. Four articles related to the European Psychiatric Services: Inputs Linked to Outcome Domains and Needs (EPSILON) study: Gaite *et al.* (2002) and Becker *et al.* (2005) reported on the entire sample while Meijer *et al.* (2002) reported on the Amsterdam participants at baseline, and at 18 months follow up (2009), as part of a broader Netherlands' study. Each of these articles undertook different analyses of the data and as there was no pooling of results, the results for each are reported to maximise the comprehensiveness of the narrative synthesis. Four more articles (Brissos *et al.*, 2011, Holloway & Carson, 1999, Hunter & Barry, 2012, Kusel *et al.*, 2007) were published as part of larger studies. The systematic review thus comprised articles from 40 independent studies.

Data extracted overview

The median number of participants across all studies was 135, with the range 36 to 971. Schizophrenia was the single diagnosis in 26 articles (62%), only four articles (Greenley *et al.*, 1997, Holloway & Carson, 1999, Lasebikan & Owoaje, 2015, Stubbs *et al.*, 2015) (10%) included participants with bipolar disorder or depressive disorder with psychotic symptoms. Over half of the articles (57%) utilized one instrument for measuring functioning and one for measuring QoL. Six articles, employed two functioning instruments, 11 articles two QoL instruments and one article (Reine *et al.*, 2005) three QoL instruments. Fujino *et al.* (2016) utilized two instruments, which together assessed global functioning.

Within the included studies we identified 14 instruments for measuring global functioning and 22 for QoL. The Global Assessment of Functioning (GAF) was the most utilized functioning instrument (29 articles) and the WHO Quality of Life abbreviated version

(WHOQOL-BREF) together with its Portuguese version the most utilized QoL instrument (12 articles) (see Supplementary material).

Of the 42 articles, 29 (69%) reported linear associations between global functioning and QoL overall scores and/or domain scores and presented correlation coefficients, four articles (10%) assessed associations between global functioning and QoL using alternate statistical methods; and 19 articles (45%) assessed predictors of QoL (Table 2). Outcomes for each are examined below.

Linear associations between global functioning and QoL (overall scores)

20 articles (48%) provided correlations between overall scores of global functioning and QoL instruments. Two of these articles (Bai *et al.*, 2014, Mas-Exposito *et al.*, 2011) also provided correlations between global functioning with QoL domains and among global functioning and QoL domains (Table 2).

Correlations between overall scores ranged in strength from strong to weak with nearly half of the correlations reported as moderate (r=0.34 to 0.49). Most moderate correlations involved the GAF which is consistent with the frequent use of the instrument. The two largest correlations assessed QoL using the Quality of Life Scale (QLS), the largest assessed functioning with the Personal and Social Performance (PSP) (r=0.84), the second largest with the GAF (r=0.83). The smallest correlation reported as significant were for the GAF and the Quality of Life Questionnaire (QLQ) and the GAF and Manchester Short Assessment of Quality of Life (MANSA) (r=0.16 for each) (Fig. 3).

<Please insert Figure 3 around here>

Amongst the QoL instruments, nearly one-third of the correlations were assessed in relation to the QLS primarily the complete 21-item version, with the 7-item and 5-item versions also assessed in Ritsner *et al.* (2005). Half the correlations were large, including that

for the 7-item version. One-quarter of correlations were assessed in relation to the self-assessed WHOQOL-BREF. Correlations were reported for four domain scores and two separate scored items that assessed the individual's overall perception of QoL and health (University of Washington, 2011, World Health Organization, 1998) in Galuppi *et al.* (2010), and just for overall QoL in three articles (Bai *et al.*, 2014, Chino *et al.*, 2009, Ito *et al.*, 2015). Some articles reported correlations for the four domains and a total score (Bai *et al.*, 2014, Mas-Exposito *et al.*, 2011, Miclutia *et al.*, 2008). Ito *et al.* (2015) reported non-significant associations for the overall score in insidious onset and acute onset (r=-0.24, -0.21) respectively. Correlations observed for objective QoL measures such as QLS, were consistently larger (r=0.20 to 0.84) than those observed for subjective measures such as WHOQOL-BREF (r=-0.21 to 0.58). Interviewer-assessment was also associated with larger correlations than self-assessment as reflected in Riedel *et al.* (2011).

Linear association between overall scores of global functioning and QoL domains

Thirteen articles (31%) provided correlations between global functioning and QoL domains, as listed in Table 3. Global functioning was measured with GAF in over half of the articles (62%), and with the exception of Bai *et al.* (2014) which employed the self-reported version of the graphic PSP (SRG-PSP), the interviewer undertook all assessments of functioning. The most utilized QoL instrument was the WHOQOL-BREF, followed by the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). Assessments of QoL were self-assessed, with four exceptions (Meijer *et al.*, 2002, Reine *et al.*, 2005, Riedel *et al.*, 2011, Rocca *et al.*, 2014).

In total we recorded 100 correlation coefficients across 39 domains within included QoL instruments. Strength of correlations varied widely and were primarily weak (48%). Just over one-quarter of correlations were presented in a single article (Reine *et al.*, 2005), with

the GAF compared to three different QoL instruments, the SF-36, Schizophrenia Quality of Life (S-QoL) and Lehman's Quality of Life Interview brief version (QoLI brief) (subjective items). All associations reported in this study were weak, and in some instances lower than for other comparable assessments.

The largest correlation coefficient (r=0.72) was between functioning assessed with GAF and "subjective wellbeing" assessed by the interviewer with the Riedel-Spellmann-Musil-Scale (RSM-Scale) (Riedel *et al.*, 2011). The next four highest correlations were also assessed between these instruments (r=0.61 to 0.65) (Riedel *et al.*, 2011). The smallest significant correlation (r=0.10) was between functioning assessed with GAF and interviewer-assessed "mental and physical health" of the QoLI brief, subjective items only (Reine *et al.*, 2005).

Most correlations between global functioning and QoL domains were positive. Exceptions were for Mas-Exposito *et al.* (2011), which employed the WHO Short Disability Assessment Schedule (WHO DAS-S) for evaluating functioning, and Fujino *et al.* (2016) and Kuo *et al.* (2009), which employed the Schizophrenia Quality of Life Scale Japanese version (JSQLS) and Revision 4 Chinese version (SQLS-R4) to assess QoL respectively. For each of these three instruments lower scores signify better outcomes.

Correlations for the WHOQOL-BREF tended to be larger than those for the SF-36. The WHOQOL-BREF gave rise to correlations that were primarily moderate in strength for each of the four domains of the instrument, although large correlations were also reported for the physical (Galuppi *et al.*, 2010) and psychological domains (Miclutia *et al.*, 2008). In regard to the SF-36, of the 24 correlations all were small except for four correlations from two of three articles: one correlation for the physical domain (Dima *et al.*, 2015), one for the mental health domain (Meijer *et al.*, 2002) and two for the social domain (Dima *et al.*, 2015, Meijer *et al.*, 2002).

The three most frequently assessed domains of quality of life were the physical, psychological and social components. The vast majority of correlations for the physical component were small (70%), half were small for the psychological component and 45% small for the social component. Around a third of these small correlations were assessed in Reine *et al.* (2005) which reported just over a quarter of all correlations. Over half (56%) of the correlations reported for occupational and environmental issues, as well as for components related to treatment and satisfaction with life in general were small.

When correlations were limited to broad domains (i.e., included several items), over half of the correlations were moderate for the environmental, psychological and social components, and small for over half the correlations for physical components.

Over two thirds of the total correlations between global functioning and QoL domains were self-assessed and nearly half were small (r=-0.03 to 0.29). The remaining 29 correlations were interviewer-assessed and over half were small (r=0.10 to 0.21).

Associations resulting from alternate statistical approaches

In the four articles assessing associations between global functioning and QoL using alternate statistical methods four separate approaches were used. Mubarak (2005) which compared means of dysfunction with a dichotomisation of QoL found that people with high dysfunction (low functioning) had low QoL. Pitkanen *et al.* (2012) which compared medians of QoL with a dichotomisation of functioning reported that lower functioning indicated poorer QoL. Becker *et al.* (2005) which compared means of QoL across three levels of functioning showed an increase in mean of QoL across levels of functioning from low to high. Medeiros-Ferreira *et al.* (2013) which compared means of HRQoL and functioning in subgroups of people with or without metabolic syndrome reported no association.

Functioning as predictor of QoL

19 articles (45%) assessed predictors of QoL. Of these, Fujino *et al.* (2016) and Rocca *et al.* (2014) did not include global functioning as an initial predictor, 13 modelled global functioning as a predictor in their final models and four (Adewuya & Makanjuola, 2009, Gaite *et al.*, 2002, Kuo *et al.*, 2009, Razali & Wahid, 2012) did not include it in the final models (Table 2).

Of the 13 articles that modelled global functioning as a predictor of QoL, nine considered QoL overall and three specific domains of QoL. Woon *et al.* (2010) tested both. Global functioning predicted QoL overall in most analyses (Alessandrini *et al.*, 2016, Kusel *et al.*, 2007, Lasebikan & Owoaje, 2015, Meijer *et al.*, 2009, Norman *et al.*, 2000, Rocca *et al.*, 2016, Roe *et al.*, 2011, Woon *et al.*, 2010). Exceptions were Stubbs *et al.* (2015) and Prince (2007).

Discussion

This systematic review is the first to explore the presence and extent of associations between global functioning and QoL in people with psychotic disorders. The appraisal proved difficult given a lack of similarities between studies, and differences in methodological approaches including instruments employed, and inconsistencies in results for given instruments. Despite these difficulties, we found that most of the included articles reported positive associations between higher global functioning and better QoL, and through a narrative review we were able to clarify the extent of these associations alongside important explanatory factors.

Our results showed that the strength of the association was primarily dependent on the QoL instrument used and whether QoL was being objectively or subjectively assessed. The largest correlations were given by objective QoL instruments completed by an interviewer, the RSM-Scale in particular. The RSM-Scale covers social, occupational and psychological

functioning and includes physical functioning and subjective well-being (Riedel *et al.*, 2011). The other objective QoL instrument, the QLS, covers social (interpersonal relations), occupational (instrumental role) and psychological domains (intrapsychic foundations) as well as common objects and activities (Heinrichs *et al.*, 1984). Thus, domains covered by both objective QoL instruments, overlap with domains encompassed by measures of global functioning, which account for the strong associations observed. Furthermore both, objective QoL instruments and measures of global functioning were assessed by the one interviewer leading to further consistency in assessment. In contrast, subjective QoL instruments are intended to be completed through self-assessment and given that the patient's perspective can differ from an evaluator's (Atkinson *et al.*, 1997, Bengtsson-Tops *et al.*, 2005, Sainfort *et al.*, 1996), the resulting differences will affect the strength of the correlation.

Even with the application of the same instruments, correlation coefficients will vary as a result of sampling variation. This was evident for studies that used the GAF and MANSA (Kusel *et al.*, 2007, Roe *et al.*, 2011). A smaller correlation was found when participants were all living in a psychiatric rehabilitation residential facility in Israel (Roe *et al.*, 2011), than recruited from inpatient and outpatient settings in the United Kingdom (Kusel *et al.*, 2007). Likewise, the importance of country and in turn differences in cultural and possibly health system structure and functioning is arguably reflected in Hosseini and Yousefi (2011). Two thirds of participants in this study lived in an Iranian institution, and while QoL was measured with an objective QoL instrument (QLS), a small correlation was assessed. In comparison strong to moderate associations were assessed in other studies using the QLS from Europe (Hunter & Barry, 2012, Karadayi *et al.*, 2011, Kusel *et al.*, 2007, Nafees *et al.*, 2012), Canada (Norman *et al.*, 2000) and Israel (Ritsner *et al.*, 2005).

Variation in QoL of people living with psychosis based on sociodemographic characteristics is well documented (Browne, 1996, Caron *et al.*, 2005, Chan *et al.*, 2003).

Ethnicity has also been acknowledged as a contributor to the QoL of people with psychosis within a given cultural setting (Ben-Zur *et al.*, 2014, Lehman, 1995), which may in part be due to the impact of racism and discrimination on an individual's expectations (Lehman, 1995, Prince, 2007). Religious beliefs and spirituality may also contribute directly to a better QoL (Caqueo-Urízar *et al.*, 2016, Cohen *et al.*, 2010, Grover *et al.*, 2014). It is thus evident that social and demographic issues will affect associations between global functioning and QoL of people living with psychosis.

Our results support respondent burden as a potential confounder in the assessment of associations between functioning and QoL (Fricker *et al.*, Ulrich *et al.*, 2005). We observed small correlations only when three QoL instruments were employed (Reine *et al.*, 2005), as predominantly small correlations when two QoL instruments were employed (Dima *et al.*, 2015, Meijer *et al.*, 2002).

We also observed that some authors (Bai *et al.*, 2014, Mas-Exposito *et al.*, 2011, Miclutia *et al.*, 2008) reported a total score for the WHOQOL-BREF when there is no such approved score for this instrument. The WHOQOL-BREF generates four domain scores and two separately scored items (overall perception of QoL and health) (University of Washington, 2011, World Health Organization, 1998). As the appropriate use of an instrument is essential for a valid outcome, all results pertaining to the WHOQOL-BREF total score are not considered reliable. In another study (Medeiros-Ferreira *et al.*, 2013), standard scoring techniques for the EQ-5D were not applied. Reine *et al.* (2005) reported the physical and mental composite scores of the SF-36, and while assessed (Ware Jr *et al.*, 1995), it has been suggested they provide an imprecise summary of profile scores (Taft *et al.*, 2001). For these reasons, results of these studies were not considered reliable, reinforcing the importance of the proper use of an instrument, and the necessity of adhering to standardised scoring protocols.

Another important finding was that the domains covered by an instrument are key to the associations obtained. Further, the items included within an instrument will lead to differences in correlations as reflected in the results for the three variations of the QLS (the complete 21 items and abbreviated 7 and 5 items). We consider that in the assessment of QoL of people with psychosis it is important to include items that broadly encompass the mental or psychological domain, otherwise the outcome will not fully reflect the potential experiences of this population. Thus, the assessment of mental health in the EQ-5D is considered problematic given that the dimension is comprised of a single item regarding the presence of anxiety and/or depression. In turn, while moderate correlations were obtained between the EQ-5D and global functioning, correlations themselves should not be considered sufficient in determining a reliable and valid QoL instrument.

Findings regarding the strength of the associations between global functioning and QoL domains highlighted social components. These had the highest correlations, with more than half moderate or higher even when subjectively assessed. However, the breadth of domains also impacted correlations, and were smaller for narrow domains. As with comparisons between overall scores, the QoL instrument was the primary determinant of the strength of the correlations between global functioning and QoL domains.

Our systematic review has highlighted the extensive array of instruments for the assessment of QoL, and to a lesser extent global functioning in people living with a psychotic disorder. Further, given that both outcomes are commonly used, our systematic review provides the framework to understand the different findings reported in the literature, and inform the future choice of instruments by researchers and/or clinicians.

We found no patterns in the use of instruments in regard to either year, country where studies were conducted, diagnostic criteria or other characteristics. This variability could be in part due to the absence of a universal definition of global functioning and QoL. However,

the diversity is likely at least in part driven by cultural issues leading to modification of available instruments. Also limiting study findings was the need to undertake a narrative review given the heterogeneity of study findings. We did not include articles published in other than English or Spanish. All articles identified employed English, although over three-quarters were from non-English speaking countries. Therefore it is considered that this limitation will have minimal impact if any on our findings. We did not register our protocol with PROSPERO: International prospective registered systematic reviews (University of York, 2011) as we considered our review fell under stated exclusion criteria: “looking at the reporting of and/or use of outcomes in research would not be included”.

We believe that clearer and precise definitions of global functioning and QoL are required so these outcomes can be concisely and uniformly measured, and we can identify the domains of life that need to be targeted for improving these outcomes. Further, only by having standard/homogeneous instruments, can we consistently assess the impact of interventions aimed at improving these outcomes, and thereby contribute to the ongoing development and implementation of strategies for improving global functioning and QoL in people living with psychotic disorders.

Overall, most articles identified reported moderate and positive associations between global functioning and QoL. The strength of correlation was dependent upon the instruments employed and the respondent (e.g., a clinician or the individual living with psychosis). However, the moderate associations between global functioning and QoL reassure that interventions that improve functioning in people with a psychotic disorder will have a positive impact on their QoL. Policy makers and clinicians should make improvement of QoL of people with psychosis a priority alongside symptom remission. Happiness and satisfaction, fulfilment of goals and expectations, are essential to people living with psychotic illness.

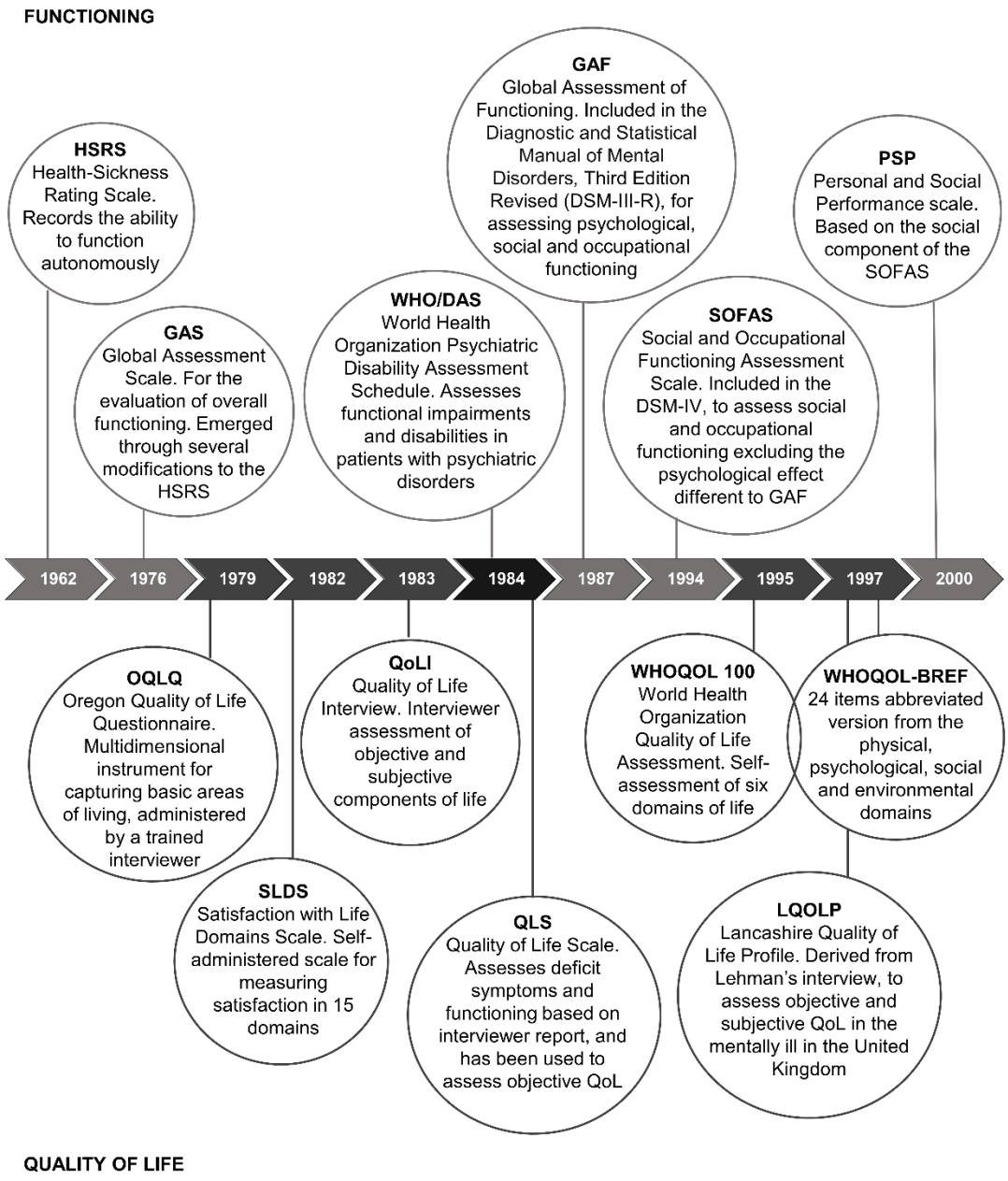

Fig. 1. Timeline of functioning and quality of life instruments development.

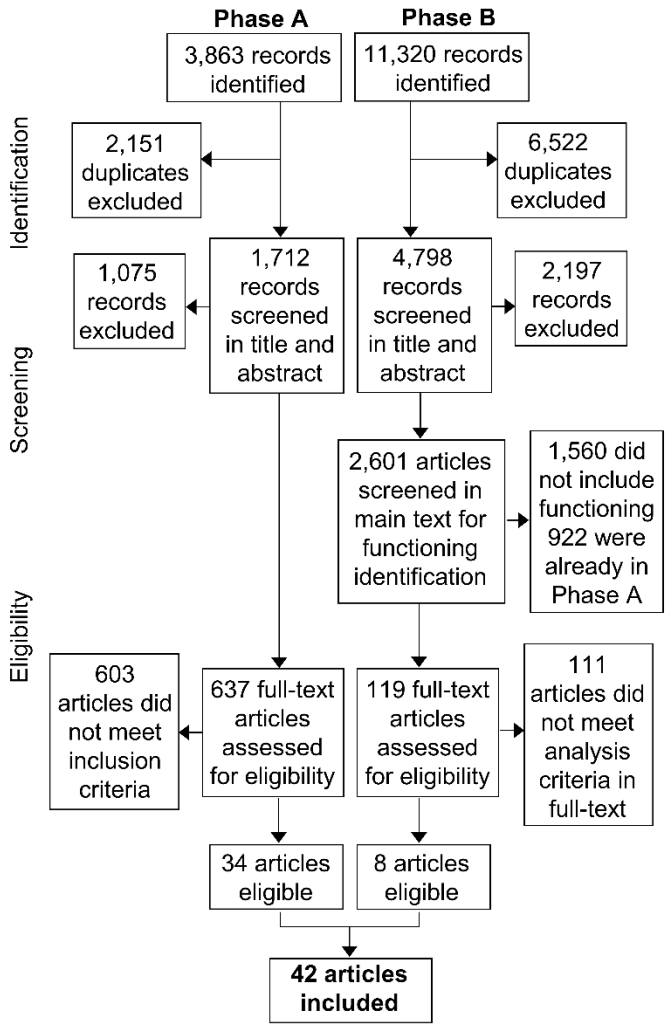

Fig. 2. PRISMA flow diagram of Phase A and Phase B search.

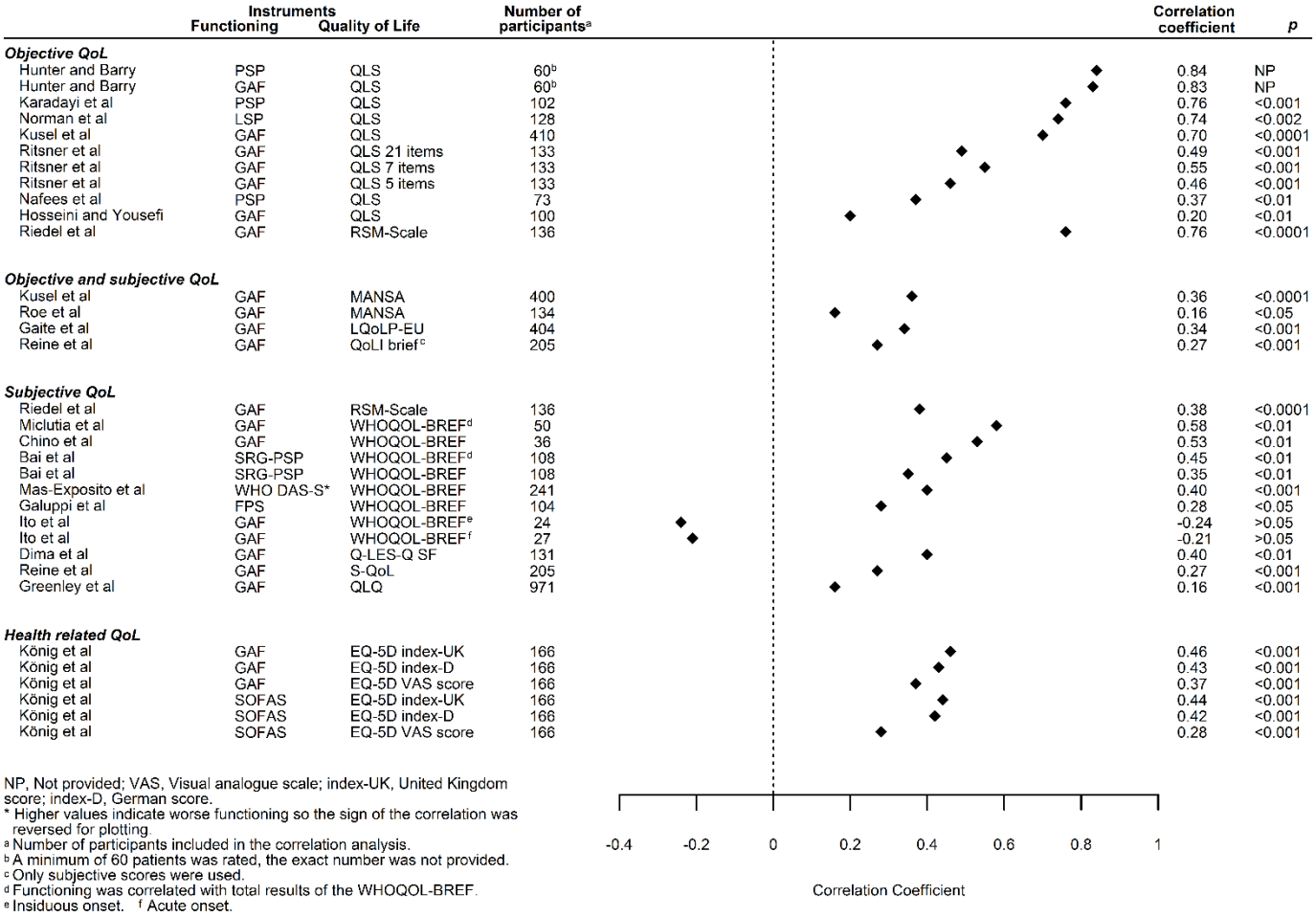

Fig. 3. Correlations between global functioning and quality of life.

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Conflict of Interest

None.

Availability of Data and Materials

Data supporting our findings can be available under request.

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Table 1. *Main characteristics of included studies*

Study	Conducted	Country of publication	Participants N	Participants Age range	Participants Dx[a] (%)	Instruments Functioning	Instruments Quality of Life
Greenley *et al.* (1997)	NA	USA	971	NA	NS	GAF	QLQ
ELCCT: Holloway & Carson (1999)	NA	England	70	NA	NS	WHO/DAS	LQOLP; LEC
Norman *et al.* (2000)	1989-1993	Canada	128	17-57	100	LSP	QLS; GWB
EPSILON: Gaite *et al.* (2002) Becker *et al.* (2005)	1997-1998	Denmark; England; Italy; Spain; The Netherlands	404	18-65	NS	GAF	LQoLP-EU (European version)
Meijer *et al.* (2009, 2002)	1997-1998	The Netherlands[b]	143	18-65	100	GAF	SF-36; LQoLP Dutch version
Mubarak (2005)	NA	Malaysia	258	NA	100	WHO/DAS	QoLI
Reine *et al.* (2005)	2000	France	205	18-70	100	GAF	SF-36; QoLI brief version; S-QoL
Ritsner *et al.* (2005)	NA	Israel	133	18-60	100	GAF	QLS; Q-LES-Q
König *et al.* (2007)	2003-2004	Germany	166	21-80	72	GAF; SOFAS	EQ-5D; WHOQOL-BREF
UK-SCAP: Kusel *et al.* (2007)	1999-2000	United Kingdom	442	NA	NS	GAF	QLS; MANSA
Prince (2007)	1994-1996	USA	264	17-65	NS	GAS	QoLI
Miclutia *et al.* (2008)	NA	Romania	50	18-55	100	GAF	WHOQOL-BREF
Adewuya & Makanjuola (2009)	2006	Nigeria	99	NA	100	GAF	WHOQOL-BREF
Chino *et al.* (2009)	NA	Japan	36	NA	100	GAF	WHOQOL-BREF
Kuo *et al.* (2009)	NA	Taiwan	100	18-65	100	GAF	SQLS-R4; LQOLP Taiwanese
Galuppi *et al.* (2010)	2008	Italy	104	NA	100	FPS	WHOQOL-BREF
Woon *et al.* (2010)	NA	Singapore	83	NA	100	GAF	WHOQOL-BREF
PSP Portuguese validation study: Brissos *et al.* (2011)	2009-2010	Portugal	76	18-65	100	PSP Portuguese version	WHOQOL-BREF Portuguese version
Hosseini &Yousefi (2011)	1999-2000	Iran	100	21-60[c]	100	GAF	QLS
Karadayi *et al.* (2011)	NA	Turkey	102	18-65	100	PSP	QLS
Mas-Exposito *et al.* (2011)	2006-2008	Spain	241	NA	100	GAF; WHO DAS-S	WHOQOL-BREF

Study	Conducted	Country of publication	Participants			Instruments	
			N	Age range	Dx[a] (%)	Functioning	Quality of Life
Riedel *et al.* (2011)	2007	Germany	136	18-65	78	GAF	QLS; RSM-Scale
Roe *et al.* (2011)	2007-2008	Israel	159	19-66	NS	GAF	MANSA
Guilera *et al.* (2012)	2007-2009	Spain	352	18-55	88	WHODAS II; SOFAS	EQ-5D
EGOFORS: Hunter & Barry (2012)	NA	Belgium; France; Germany; Israel; Italy; Spain; Sweden; Turkey; United Kingdom	295	NA	100	GAF; PSP	QLS
Nafees *et al.* (2012)	NA	United Kingdom	73	18-65	100	PSP; GAF	QLS
Pitkanen *et al.* (2012)	2005-2006	Finland	311	18-65	41	GAF	EQ-5D; Q-LES-Q short form
Razali & Wahid (2012)	NA	Malaysia	206	18-60	100	PSP	QoLI brief version
Medeiros-Ferreira *et al.* (2013)	2008-2009	Spain	76	NA	NS	GAF	EQ-5D
Akinsulore *et al.* (2014)	2010	Nigeria	100	NA	100	GAF	WHOQOL-BREF
Bai *et al.* (2014)	NA	Taiwan	108	20-60	100	PSP; SRG-PSP	WHOQOL-BREF
Rocca *et al.* (2014)	2009-2011	Italy	92	18-65	100	PSP	QLS
Zendijidjian *et al.* (2014)	NA	France	91	NA	100	GAF	SF-36
Dima *et al.* (2015)	2009-2010	Romania	131	18-65	NS	GAF	SF-36; Q-LES-Q short form
Ito *et al.* (2015)	2008-2011	Japan	168	16-55	NS	GAF	WHOQOL-BREF
Lasebikan & Owoaje (2015)	2008	Nigeria	652	NA	56	GAF	WHOQOL-BREF
Stubbs *et al.* (2015)	2010-2012	United Kingdom	438	NA	NS	GAF	EQ-5D 3 levels
Alessandrini *et al.* (2016)	2010-2014	France	271	NA	100	FROGS	S-QoL 18
Fujino *et al.* (2016)	NA	Japan	93	NA	100	UPSA-B; SFS	JSQLS
Rocca *et al.* (2016)	2008-2011	Italy	323	18-65	100	GAF	QLS

NA, not available; NS, not specified; USA, United States of America; ELCCT, East Lambeth Continuing Care Team study; EPSILON, European Psychiatric Services: Inputs Linked to Outcome Domains and Needs study; UK-SCAP, United Kingdom Schizophrenia Care and Assessment Programme; EGOFORS, European Group on Functional Outcomes and Remission in Schizophrenia study; GAF, Global Assessment of Functioning; WHO/DAS, World Health

Organization Disability Assessment Schedule; LSP, Life Skills Profile; SOFAS, Social and Occupational Functioning Assessment Scale; GAS, Global Assessment Scale; FPS, Personal and Social Functioning Scale; PSP, Personal and Social Performance scale; WHO DAS-S, World Health Organization Short Disability Assessment Schedule; SRG-PSP, Self-reported version of the graphic PSP; FROGS, Functional Remission Of General Schizophrenia; UPSA-B, University of California, San Diego (UCSD) Performance-based Skills Assessment-Brief version; SFS, Social Functioning Scale; QLQ, Quality of Life Questionnaire; LQOLP, Lancashire Quality of Life Profile; LEC, Life Experiences Checklist; QLS, Quality of Life Scale; GWB, General Well-Being Scale; SF-36, Medical Outcomes Study (MOS) 36-Item Short-Form Health Survey; QoLI, Lehman's Quality of Life Interview; S-QoL, Schizophrenia Quality of Life; Q-LES-Q, Quality of Life Enjoyment and Satisfaction Questionnaire; EQ-5D, EuroQol five dimensions questionnaire; WHOQOL-BREF, World Health Organization Quality of Life abbreviated version; MANSA, Manchester Short Assessment of Quality of Life; SQLS-R4, Schizophrenia Quality of Life Scale Revision 4 Chinese version; RSM-Scale, Riedel-Spellmann-Musil-Scale; JSQLS, Schizophrenia Quality of Life Scale Japanese version.

[a] Percentage of schizophrenia diagnosis.

[b] Including EPSILON's participants from Amsterdam and other participants from The Netherlands.

[c] Lower – Upper age of participants included in the study.

Table 2. *Summary of associations provided by article*

Articles (total 42)	N	%	References
Correlations			
Overall global functioning– Overall quality of life (QoL)	20	48	Karadayi *et al.* (2011), Mas-Exposito *et al.* (2011), Riedel *et al.* (2011), Hosseini& Yousefi (2011), Roe *et al.* (2011), Hunter& Barry (2012), Nafees *et al.* (2012), Gaite *et al.* (2002), Reine *et al.* (2005), König *et al.* (2007), Kusel *et al.* (2007), Miclutia *et al.* (2008), Galuppi *et al.* (2010), Dima *et al.* (2015), Chino *et al.* (2009), Greenley *et al.* (1997), Ritsner *et al.* (2005), Norman *et al.* (2000), Bai *et al.* (2014), Ito *et al.* (2015).
Overall global functioning – Domains of QoL	13	31	Mas-Exposito *et al.* (2011), Riedel *et al.* (2011), Meijer *et al.* (2002), Reine *et al.* (2005), Miclutia *et al.* (2008), Galuppi *et al.* (2010), Rocca *et al.* (2014), Dima *et al.* (2015), Kuo *et al.* (2009), Woon *et al.* (2010), Akinsulore *et al.* (2014), Bai *et al.* (2014), Fujino *et al.* (2016).
Domains of global functioning – Overall QoL	5	12	Mas-Exposito *et al.* (2011), Guilera *et al.* (2012), Holloway& Carson (1999), Chino *et al.* (2009), Bai *et al.* (2014).
Domains of global functioning– Domains of QoL	5	12	Mas-Exposito *et al.* (2011), Rocca *et al.* (2014), Alessandrini *et al.* (2016), Bai *et al.* (2014), Fujino *et al.* (2016).
Alternate statistical methods	4	10	Mubarak (2005), Pitkanen *et al.* (2012), Becker *et al.* (2005), Medeiros-Ferreira *et al.* (2013).
Associations estimated by multivariate analysis			
Global functioning – Overall QoL	10	24	Roe *et al.* (2011), Meijer *et al.* (2009), Kusel *et al.* (2007), Stubbs *et al.* (2015) Alessandrini *et al.* (2016), Rocca *et al.* (2016), Norman *et al.* (2000), Woon *et al.* (2010), Prince (2007), Lasebikan& Owoaje (2015).
Global functioning – Domains of QoL	4	10	Brissos *et al.* (2011), Zendjidjian *et al.* (2014), Woon *et al.* (2010), Akinsulore *et al.* (2014).

Table 3. *Correlations between overall scores of global functioning and domains scores of quality of life*

Components	*QoL instrument construct*	**Subjective**									**Both**		**Objective**	
	Articles	Woon *et al.* (2010)	Akinsulore *et al.* (2014)	Miclutia *et al.* (2008)	Mas-Exposito *et al.* (2011)	Galuppi *et al* (2010)	Bai *et al.* (2014)	Fujino *et al.* (2016)	Kuo *et al.* (2009)	Dima *et al.* (2015)	Reine *et al* (2005)	Meijer *et al.* (2002)	Riedel *et al.* (2011)	Rocca *et al.* (2014)
	Instruments	GAF	GAF	GAF	WHODAS-S	FPS	SRG-PSP	UPSA-B	GAF	GAF	GAF	GAF	GAF	PSP
	QoL domains (number of items)	WHOQOL-BREF						JSQLS	SQLS-R4	SF-36[a] Q-LES-Q SF	SF-36[a] QoLI[b] S-QoL[c]	SF-36[a] LQoLP Dutch	RSM-Scale[d]	QLS
Environmental	Environment (8)	0.34♦	0.19	0.42**	-0.36♦	0.43♦	0.39**							
	Living conditions (11) (RSM Sub_3)												0.26♦ 0.47♦[e]	
	Living situation (4)											0.04		
	Residence (3)										0.07[b]			
	Finances (4)											0.11		
	Disposable income (3)										-0.05[b]			
	Personal security (3)										0.10[b]			
	Safety (2)											0.08		
Life in general	Subjective wellbeing (16) (RSM Sub_1)												0.36♦ 0.72♦[e]	
	Life satisfaction (1)									0.23*				
	Goals (Fulfilment) (13)											0.21**		
	Framework (10)											0.14		
	Symptoms/Side Effects (8)							-0.34**						
	Satisfaction with treatment (1)									0.23*				
Occupational	Occupational functioning (8)												0.34♦ 0.59♦[e]	
	Instrumental role (4)													0.44♦
	Job satisfaction (3)										-0.10[b]			
	Common Objects and activities (2)													0.17
	Leisure activities (4)										0.12[b]			

Components	*QoL instrument construct*	**Subjective**									**Both**		**Objective**	
	Articles	Woon *et al.* (2010)	Akinsulore *et al.* (2014)	Miclutia *et al.* (2008)	Mas-Exposito *et al.* (2011)	Galuppi *et al* (2010)	Bai *et al.* (2014)	Fujino *et al.* (2016)	Kuo *et al.* (2009)	Dima *et al.* (2015)	Reine *et al* (2005)	Meijer *et al.* (2002)	Riedel *et al.* (2011)	Rocca *et al.* (2014)
	Instruments	GAF	GAF	GAF	WHODAS-S	FPS	SRG-PSP	UPSA-B	GAF	GAF	GAF	GAF	GAF	PSP
	QoL domains (number of items)	WHOQOL-BREF						JSQLS	SQLS-R4	SF-36[a] Q-LES-Q SF	SF-36[a] QoLI[b] S-QoL[c]	SF-36[a] LQoLP Dutch	RSM-Scale[d]	QLS
Psychological	Psychological (6)	0.31♦	0.42**	0.58**	-0.31♦	0.34*	0.39**							
	Psychological wellbeing (10)										0.26[c]♦			
	Mental health (5)									0.28[a]**	0.24[a]♦	0.38[a]**		
	Composite Mental score										0.21[a]**			
	Resilience (5)										0.26[c]♦			
	Emotional functioning (10)												0.35♦ 0.65♦[e]	
	Role Emotional (3)									0.12[a]*	0.17[a]*	0.25[a]**		
	Self-esteem (6)										0.24[c]♦			
	Negative esteem (5)											0.35**		
	Positive esteem (5)											0.21*		
	Psychosocial (15)							-0.17	-0.03					
Physical	Health (7)											0.33**		
	Health (1)					0.30*								
	General Health Perceptions (5)										0.15[a]*	0.20[a]*		
	Physical Health (7)	0.29**	0.42**	0.29**	-0.30♦	0.57♦	0.44**							
	Physical functioning (10)									0.40[a]**	0.14[a]	0.28[a]**		
	Physical functioning (7)												0.22♦ 0.41♦[e]	
	Physical well-being (4)										0.21[c]♦			
	Role physical (4)									0.20[a]**	0.18[a]*	0.26[a]**		
	Composite physical score										0.14[a]			
	Cognition (4)												0.28♦ 0.61♦[e]	

Components	*QoL instrument construct*	**Subjective**									**Both**		**Objective**	
	Articles	Woon *et al.* (2010)	Akinsulore *et al.* (2014)	Miclutia *et al.* (2008)	Mas-Exposito *et al.* (2011)	Galuppi *et al* (2010)	Bai *et al.* (2014)	Fujino *et al.* (2016)	Kuo *et al.* (2009)	Dima *et al.* (2015)	Reine *et al* (2005)	Meijer *et al.* (2002)	Riedel *et al.* (2011)	Rocca *et al.* (2014)
	Instruments	GAF	GAF	GAF	WHODAS-S	FPS	SRG-PSP	UPSA-B	GAF	GAF	GAF	GAF	GAF	PSP
	QoL domains (number of items)	WHOQOL-BREF						JSQLS	SQLS-R4	SF-36[a] Q-LES-Q SF	SF-36[a] QoLI[b] S-QoL[c]	SF-36[a] LQoLP Dutch	RSM-Scale[d]	QLS
Social	Autonomy (4)										0.28[c]♦			
	Energy/Fatigue (4)									0.21[a]**	0.24[a]♦	0.17[a]*		
	Motivation energy (7)							-0.16	-0.11					
	Bodily Pain (2)										0.15[a]*	0.19[a]**		
	Mental and physical health (3)										0.10[b]**			
	Interpersonal relationships (8)													0.56♦
	Social relationships (3)	NP	0.21*	0.47**	-0.31♦	0.37*	0.37**							
	Social relations (3)										0.20[b]**			
	Functioning in social roles (9) (RSM Sub_2)												0.35♦ 0.65♦[e]	
	Social functioning (7)												0.38♦ 0.65♦[e]	
	Social functioning (2)									0.32[a]**	0.18[a]*	0.37[a]**		
	Sentimental life (2)										0.23[c]♦			
	Leisure and social (6)											0.18*		
	Friends relationships (5)										0.16[c]*			
	Family relationships (5)										0.09[c]			
	Family relations (2)											0.12		
	Family relations (2)										-0.05[b]			

*p<0.05, **p<0.01, ⁼p<0.005, ♦p<0.001

Note: Quality of life domains were extracted from each of the QoL instruments. The number of items for the assessment of every domain are within parenthesis.

NP, not provided.

[b] QoLI brief. Only subjective items were used.

[d] RSM-scale allocates their 36 items into five-dimensions model, it also assigns the items to three sub scores: Items 1-16 (Sub_1), items 17-20, 23, 32-35 (Sub_2), items 21-22, 24-31, 36 (Sub_3).
[e] Interviewer-assessment.