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Reliability and Validity of Using EQ-5D-5L among Healthy and Adolescents with Major Mental Health Disorders in Ethiopia

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Authors' contributions

AG, GBG, and YB conceived the idea; AG, ES, CM and YB designed the study, acquired the funding, and provided detailed information regarding data collection processes in Ethiopia. AG and GBG performed data quality control. AG and MK prepared the draft manuscript. All authors reviewed the analysis, interpretation of the results, and the final manuscript.

Declaration of Interest

Elly Stolk is a member of the EuroQol Research Foundation. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Ethical considerations

Ethical approval was secured from Ethics Review Committee of School of Pharmacy, Addis Ababa University, Ethiopia and prior permission was sought from Demographic Health Surveillance site of Butajira Rural Health Project (BRHP) office, Ethiopia. Written Informed consent was obtained from all study participants to confirm their willingness for participation after explaining the purpose of study.

Abstract

Background: The EQ-5D is a validated and widely used generic measure of health-related quality of life (HRQoL) in both healthy individuals and those with various medical conditions. The objective of this study was to test whether EQ-5D-5L is reliable and valid for use among school sample adolescents and those with major mental health disorders in Ethiopia.

Methods Participants were recruited from ten sub-districts comprising the Butajira Rural Health Programme (BRHP) and Butajira major mental health disorders center. Data were collected using an Amharic (Ethiopia) EQ-5D-5L self-complete -paper and the questionnaire was administered 10 days after the first completion for test-retest procedures. Two-way mixed-effects models absolute intraclass correlation coefficient (ICC) was used to test reliability of the instrument while Kruskal-Wallis rank test with pairwise comparison was used to assess the known group validity of the instrument.

Results: There were 501 (201 school sample and 300 adolescents with major mental health disorders) participants recruited and 497 were included in the sample for analysis. The ICC was high (ICC > 0.7, $p < 0.001$) for all EQ-5D-5L dimensions, EQ-5D-5L utility index and EQ-VAS scores. The findings revealed that the Amharic EQ-5D-5L has significant known group validity as shown by the difference in scores among various disease group (depression, schizophrenia, and bipolar) and experience of chronic illness.

Conclusions: The results shows that the Amharic EQ-5D-5L is reliable and valid instrument for the measurement of HRQoL among adolescent populations in Ethiopia.

Keywords: Adolescent, EQ-5D-5L, Ethiopia, HRQoL, Mental health, Quality of Life

Introduction

The prevalence of childhood and adolescent emotional and behavioral disorders in Ethiopia is approximately 17% (1). Several strategies have been established to address this disease burden, with one of the strategic priorities being to ensure the affordability and accessibility of psychotropic drugs (2–4). In order to adequately understand the burden of mental health conditions, and evaluate the effectiveness and cost-effectiveness of treatments, it is important to measure health outcomes in a valid and reliable way. The health of the population cannot be well characterized from the analysis of mortality and morbidity statistics alone. There is also a need to characterize health in terms of broader dimensions such as symptoms, function, and overall well-being (5). This broader conceptualization of health has led to increasing development and use of instruments designed to measure health-related quality of life (HRQoL). HRQoL is a multi-dimensional concept which focuses on the effect of disease or a health condition and its treatment on a person's daily life (6,7). HRQoL measures can be preference-based, based on the valuation of health outcomes, or psychometric, based on domain specific symptom and function scores. Preference-based measures generate a health utility value on a scale anchored at 0 (dead) and 1 (full health), with some measures having values that are less than 0. These utility values can be combined with length of life to generate quality-adjusted life years (QALYs) estimates for cost-utility assessment (8,9).

One of the most commonly used generic preference-based measures of utility in adults is the EQ-5D which was developed by a multi-disciplinary group of researchers in European countries, but has now been translated into more than 130 languages with various modes of administration. The EQ-5D has a visual analogue scale (EQ-VAS) on a 100 (best imaginable health) to 0 (worst imaginable health) scale and five question related to mobility, self-care, usual activities,

pain/discomfort and anxiety/depression which can be scored using utility values that represent population preferences. The five questions initially included 3-level (EQ-5D-3L) response options (no problems, some/moderate problems, extreme problems/unable to/confined to bed). Subsequently, the EuroQol Group established the five-level (EQ-5D-5L) response option version in 2009 to improve the instrument's sensitivity and eliminate ceiling effects (10). The EQ-5D-5L has been used to evaluate general health, long-term disability, medical conditions and psychosocial treatment. This input is of particular value in resource allocation decision making (11,12). The EQ-5D-5L has been translated to Amharic (the official language of Ethiopia), using the standardized approach recommended by the EuroQol group (13). A value set has also been developed for the EQ-5D-5L from the Ethiopian general population using the EQ-PVT software of EQ-5D-5L valuation study (14), demonstrating that it is feasible and culturally acceptable to measure preferences for health outcomes in Ethiopia.

The HRQoL of children and adolescents is attracting more attention within health care systems. One measure of this is the increasing number of published studies evaluating the feasibility, reliability, and validity of different health status measurement tools in children and adolescents (13,15,16). The EQ-5D-3L and EQ-5D-5L were originally developed for use with adults. A child and adolescent version were developed in 2009 – the EQ-5D-Y (Youth, 3 levels of severity), using age-appropriate modification of questions, for example, anxiety/depression is expressed as feeling worried, sad or unhappy (17,18). The EQ-5D-Y has been shown to be valid for use in children and adolescents in several countries including Germany, Italy, South Africa, Spain, and Sweden (15,16) and is recommended for use for those aged 8 to 15 years (10). Although different countries use the EQ-5D-Y in children and adolescents for measuring health outcomes in clinical and general population settings, the EQ-5D-Y user guide suggests that either the EQ-5D-Y or adult EQ-5D versions can be

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used for individuals aged 12-15 years (17). The use of the EQ-5D-3L was also found to be adequate in those aged 12 to 18 years although concerns about the content validity prompted the development of the EQ-5D-Y(19). Neither EQ-5D nor EQ-5D-Y have been applied in an adolescent population in the Ethiopian setting. However, before using the tool in a low-income country like Ethiopia, it should be evaluated as differences in communication style, language, culture and values may be associated with differences in the conceptualization of health. EQ-5D-Y does not yet have utility values that can be used in economic evaluation but the EQ-5D-5L Amharic version has utility values (range: -0.718 to 1) (14). Therefore, this study aims to investigate the measurement properties, reliability and validity of the adult version of EQ-5D-5L in a school sample adolescent population as well as adolescents with mental health conditions.

Methods

Study design

A repeated cross-sectional study design in the same population was used to recruit participants from schools and hospitals using a face-to-face administration of the Amharic (Ethiopia) EQ-5D-5L self complete- paper. After ten days, participants were asked to complete the measure again.

Study setting

This study was conducted in one urban and nine rural kebeles of Butajira District, which is part of the Butajira Demographic Surveillance Site (DSS), located in Gurage Zone, in the Southern Nations, Nationalities and Peoples Regional State of Ethiopia. These study areas were selected because they reflect the urban and rural localities of the country. The populations of the areas covered are mixed in terms of ethnicity and culture. The country has successfully implemented its policy of expanding and re-establishing primary health care facilities over the last 25 years. As a result, 16,440 health posts, 3,547 health centers, and 311 hospitals have been established (HSDP-IV, 2014/2015).

Sampling method and study population

A cluster sampling strategy was used to select 201 study participants from all of the ten sub-districts in south-central Ethiopia covered by the Butajira Rural Health Programme (BRHP). Each sub-district includes one elementary and one high school. For each school (n=20), a supervisor selected one class from both elementary and high schools using simple random sampling techniques. Within each class (n=40-60), 20 students between the age of 12 and 17 were randomly selected and were invited to complete the Amharic EQ-5D-5L and EQ-VAS by trained data collectors. For the major mental health disorders (schizophrenia, bipolar disorder and depressive disorder) participants were identified by psychiatry nurses at the Butajira hospital, a major mental health disorder center. Patients who had a scheduled follow-up visit at the center and who were not experiencing an acute worsening of their condition were identified consecutively until 100 patients had been identified for each disorder (n= 300 respondents).

Data Collection and Fieldwork

Data collection was undertaken in the selected schools and the hospital. Trained data collectors (n=4) explained the objective of the study and what the questionnaire was before handing out a paper-based version of the questionnaire to participants for them to self-complete. The psychiatry nurses acted as data collectors in the hospital. Prior to data collection, parents were informed of the methodology and objectives of the study by means of an official letter written by the researchers that included an informed consent form. Participants were provided the consent form signed by their parents.

The questionnaire included demographic and health items, and health measurement using the EQ-5D-5L, and the EQ-VAS scaled from 0 (the worst health you can imagine) to 100 (the best health

you can imagine). All study participants received the questionnaire again 10 days after the first completion for the test-retest procedures to investigate reliability of the instrument.

Quality Control (QC)

Data collectors were trained on the concept of HRQoL, and the use of the EQ-5D-5L as a generic questionnaire to value health states. The supervisors and data collectors checked the completeness of responses, especially for the second interview.

Ethical approval

Ethical approval was secured from Ethics Review Committee of School of Pharmacy, Addis Ababa University, Ethiopia and prior permission was sought from Demographic Health Surveillance site of Butajira Rural Health Project (BRHP) office, Ethiopia.

Data Analysis

Descriptive statistics including mean, standard deviation (SD), percentage and percentage scoring at the floor and the ceiling were used to assess data characteristics of participants' sociodemographic data and the five separate domains of EQ-5D-5L. Ceiling effects are measured by the proportion of respondents getting the highest score, while floor effects are measured using the proportion of respondents reporting the lowest possible score.

The ability of the EQ-5D-5L to produce a consistent result at two different times (the first completion, and 10 days thereafter) was evaluated using test-retest reliability. The procedure consisted of applying the same measurement at two different times where change is assumed to not have occurred (20). We attributed change in scores over this period to random error (21,22). A two-way mixed-effects model, absolute ICC (23) was used to estimate the stability of the EQ-5D-5L and

EQ-VAS scores. This approach considers measurement errors which other correlation coefficients, such as Pearson or Spearman do not consider. An ICC > 0.7 was considered acceptable (23).

The ability of the EQ-5D-5L and EQ-VAS score to discriminate between subgroup with and without major mental health disorder, and other sociodemographic characteristics were assessed by known group or discriminant validity. The known group validity was examined in terms of several known relationships hypotheses that are found in other population-based validation studies. The first hypothesis was that the school sample and those with mental health conditions would have similar missing responses/ambiguous answers. The second hypothesis was that there would be more variation in the pain and discomfort, as well as the anxiety and depression dimensions. The third hypothesis was that participants with significant health problems (in our case adolescents with major mental health disorders) would report poorer health status than those without known mental health problems in terms of utility values and EQ-VAS scores. We compared: (a) adolescents with major mental health disorders and adolescents with no known mental health disorder; (b) females and males; (c) those with and without experience of chronic illness; and (d) adolescents with lower and higher educational status.

Patient's utility score were computed using the disutility weights of Ethiopian general population (14). Microsoft Office Excel 2016 was used to calculate the tariff EQ-5D-5L utility using the following formula: *Utility value = 1- (mo2 * (0.0337)+ mo3 * (0.0644)+ mo4 * (0.2276)+ mo5 * (0.3598)+ sc2 * (0.0235)+ sc3 * (0.0395)+ sc4 * (0.1419)+ sc5 * (0.2223)+ ua2 * (0.0323)+ ua3 * (0.0483)+ ua4 * (0.1574)+ ua5 * (0.2721)+ pd2 * (0.0361)+ pd3 * (0.0516)+ pd4 * (0.2703)+ pd5 * (0.4064)+ ad2 * (0.0259)+ ad3 * (0.0848)+ ad4 * (0.2987)+ ad5 * (0.4578)).*

mo=mobility, sc=self-care, ua=usual activity, Pd=pain and discomfort, ad=Anxiety and depression

Comparisons and correlation between health state utility index and EQ-VAS scores of school samples and adolescents with major mental health disorder were assessed using non-parametric Kruskal-Wallis rank test with a pair-wise comparison for both utility index and VAS scores to determine the validity of the instrument. The statistical significance level was set at $p < 0.05$.

Results

Respondent Characteristics

There were 501 participants who completed the questionnaire. There were four missing responses in the EQ-5D-5L or EQ-VAS. A total of 497 formed the sample for analysis. About two-thirds of patients with major mental health disorders (59.22%) were males. The mean (SD) age was 15.57 (1.35) years and 41.80 % of the school sample adolescents had experience of chronic illness within their life time, either from their own experience, from illness in the family, or through caring for others (Table 1).

Self-Reported Health Problems

Table 2. shows the proportion of respondents reporting problems on EQ-5D-5L dimensions by disease type. In all disease types, the highest proportions of health problems were reported in the anxiety/depression and pain/discomfort dimensions. The lowest proportion of health problems was in the self-care dimension for school sample adolescents and in the mobility dimension for participants with mental health disorders. The mean self-reported EQ-VAS score was 92.37 (SD=11.81), 72.12 (SD=19.15), 67.55 (SD=19.55), and 68.81 (SD=16.05) for the school sample adolescent, bipolar, schizophrenia, and depression patients, respectively. In general, the proportion of respondents reporting any problem was highest in schizophrenia and depression patients. School

sample adolescent respondents reported fewer problems compared to respondents with major mental health disorders.

Floor and ceiling effects

Floor effects were uncommon, but the proportion scoring the maximum of perfect health was high in all scales except for the anxiety/depression dimension and the pain/discomfort dimension (Table 2).

Test-Retest Reliability of EQ-5D-5L utility index

The two-way mixed-effects model, ICC was high for all EQ-5D-5L dimensions and EQ-5D index scores, which lies within the strong agreement range across all respondents (ICC > 0.7, $p < 0.001$) (Table 3).

Test-Retest Reliability of EQ-VAS Scores

The two-way mixed-effects model, ICC for all groups for EQ-VAS was found to be 0.828 (95% CI = 0.775 - 0.866), which indicated good agreement between the two sets of EQ-VAS scores (Table 3).

Known Group Validity

Respondents with mental health disorders, and those who had experience of chronic illness reported statistically significantly more problems on the EQ-5D-5L dimensions of self-care, doing usual activities, having pain or discomfort, feeling anxiety or depression, and EQ-VAS score and utility index than those who have no known mental health disorder, and have no experience of chronic illness (Table 4). There was no significant difference between the mental health disorder patient

group and school sample adolescents in the mobility dimension ($\chi^2 = 6.655$, $p = 0.084$), but having

experience of chronic illness was associated with a difference in scores ($\chi^2 = 23.81$, $p < 0.001$).

There were statistically significant differences in EQ-5D-5L utility index scores and EQ-VAS scores

between individuals with no known mental health condition (school samples) and those with mental

health disorders ($\chi^2 = 207.21$, $p < 0.001$, $\chi^2 = 133.24$, $p < 0.001$), and experience of chronic illness

($\chi^2 = 60.71$, $p < 0.001$). Similar results were observed in all dimensions of EQ-5D-5L, except the

mobility dimension (Table 4). The discriminant validity shows individuals with major mental health

disorders (schizophrenia, bipolar and depression group reported) significantly more problems with

anxiety/depression dimension than the adolescents with no known mental health condition.

There was a significant difference in EQ-VAS score and EQ-5D-5L utility index between school

sample and individuals with mental health disorder (depression, schizophrenia, and bipolar) ($p < 0.001$) (Figures 2 and 8), and EQ-5D-5L utility index between individuals with depression and

bipolar mental disorder ($p = 0.045$) (Fig 8). There was a significant difference in EQ-VAS score and

EQ-5D-5L utility index between different experience of chronic illness like in self and no experience

of chronic illness ($p = <0.001$), in self and the family (p= <0.001), and in self and caring for others

($p = <0.001$) (Figure 4 and 6).

Discussion

This study aimed to investigate the psychometric properties of the EQ-5D-5L among adolescent

population in Ethiopia by evaluating the reliability and validity of this instrument among adolescents

with school samples and adolescents with major mental health disorders. The result shows that the Amharic EQ-5D-5L is easy to fill in and the overall small proportion of missing or inappropriate responses demonstrated the feasibility of administering EQ-5D-5L in an adolescent population group. Low prevalence of severe problems with ceiling effects was observed in the different dimensions of the EQ-5D-5L, which is typical for school sample adolescents. The highest proportion of problems was reported on the 'having pain or discomfort' and 'feeling anxiety/depression' dimensions for both adolescents with no known mental health disorder and with major mental health disorders. These findings are consistent with other EQ-5D-Y studies (17).

Good levels of reliability were observed in EQ-5D-5L dimensions and utility values as well as the EQ-VAS in both school sample adolescents and those with major mental health disorder respondents which is similar with the previous EQ-5D-Y studies (15,17). These values were somewhat lower on pain/discomfort dimension compared to others dimensions. Participants may not have fully understood the aspects which are covered by pain/discomfort dimension in EQ-5D-5L. On the other hand, it is reasonable to expect that reporting of pain might vary over a few weeks, and a lack of correlation does not necessarily mean that the instrument is not reliable.

In general, the observed ability of the EQ-5D-5L to discriminate between the compared group supports the validity of instruments in all dimensions, except with mobility dimension. This may be due to the large ceiling effects on mobility dimension which does not show a significant difference between the compared group. This is not unexpected given that it was not anticipated that mobility would be a particular problem in a school sample or in participants with a mental health condition.

Known group validity was also observed in this study based on differences between EQ-5D-5L scores of patients with major mental health disorders and healthy adolescents. The difference was particularly more marked in patients with schizophrenia and depression. Patient with schizophrenia and depression experience mental, social and physical impairment which can be associated with the nature and severity of the disease or positive and negative symptoms of the conditions (24). Previous studies of EQ-5D-3L and EQ-5D-5L in adults have shown mixed evidence on the validity in populations with mental health conditions. The validity of the EQ-5D-5L has been demonstrated in patients with anxiety and depression including the ability to discriminate across severity groups and reflect changes in health (25–27). However, neither the EQ-5D-3L or the EQ-5D-5L were able to reflect changes in depression symptoms in individuals who had Type 2 Diabetes who were screened for these symptoms (28). There was limited evidence on EQ-5D-5L for patients with schizophrenia and bipolar although the EQ-5D-5L has been found to be reliable and valid in an adolescent and young adult population with post-traumatic stress disorder (29). Mulhern et al (30) found that EQ-5D-3L was able to discriminate across severity groups in those with depression and anxiety as well as in those with schizophrenia although a latter review (31) cast doubt on the utility of generic health measures like the EQ-5D-3L in patients with schizophrenia. Our study indicates that EQ-5D-5L can discriminate between those with and without schizophrenia and bipolar but further evidence is required.

This study has some limitations. The adult measure and disutility weights were applied to drive utilities for adolescents as an Amharic version was available, EQ-5D-Y may have better content validity for this group. There was no cognitive debriefing so the suitability of the dimensions and

comprehensibility was not tested nor did we examine the responsiveness of the instrument to change as there was no intervention. Therefore, further research is recommended to investigate acceptability and suitability of the EQ-5D-5L compared to the EQ-5D-Y as well as the responsiveness of the measure in this population. The use of different interviewers for the school sample adolescent and the patients with major mental health disorders may also have affected the results. Despite these limitations, this study adds to the knowledgebase of the validity of the Amharic EQ-5D-5L in adolescents. The use of the Amharic EQ-5D-5L in adolescents would offer a cost-effective option compared to developing a new value set for the EQ-5D-Y in this low-resource setting.

Conclusions

This first psychometric study among school samples and adolescents with major mental health disorders in Ethiopia reveals that the Amharic EQ-5D-5L is reliable and valid instrument for the measurement of HRQoL.

References

1.   WHO/EMOH. Mental Health System in Ethiopia. 2006;

2.   Burstr K. EQ-5D-Y as a health-related quality of life measure in children and
      adolescents with functional disability in Sweden : testing feasibility and validity.
      2014;426–35.

3.   Vieta E, Bobes J, Ballesteros J, Pinto AG-, Luque A, N. Ibarra. Validity and
      reliability of the Spanish versions of the Bech-Rafaelsen Õ s mania and melancholia
      scales for bipolar disorders. Acta Psychiatr Scand. 2008;117(3):207–15.

4.   Bergfors S, Åström M, Burström K, Egmar A-C. Measuring health-related quality of
      life with EQ-5D-Y instrument in children with asthma. Acta Paediatr.
      2015;104(2):167–73.

5.   Brauer CA, Rosen AB, Greenberg D, Neumann PJ. Trends in the Measurement of
      Health Utilities in Published Cost-Utility Analyses. Value Heal. 2006;9(4):213–8.

6.   Litwin MS. Health-Related Quality of Life. Humana Press. 2006;237–51.

7.   Karimi M, Brazier J. Health , Health-Related Quality of Life , and Quality of Life :
      What is the Difference ? Pharmacoeconomics. 2016;34(7):645-9.

8.   Whitehead SJ, Ali S. Health outcomes in economic evaluation : the QALY and
      utilities. Br Med Bull. 2010;96(1):5–21.

9.   Kularatna S, Whitty JA, Johnson NW, Uk F, Scuffham PA, Arts P. Health State
      Valuation in Low- and Middle-Income Countries : A Systematic Review of the

Literature. Value Heal. 2013;16(6):1091–9.

10.   Janssen B. EQ-5D-5L User Guide. 2015;(April).

11.   Johansson KA, Strand KB, Fekadu A, Chisholm D. Health Gains and Financial
       Protection Provided by the Ethiopian Mental Health Strategy : an Extended Cost-
       Effectiveness Analysis. Health Policy Plan. 2016;1–8.

12.   Oppe, M., & van Hout B. EuroQol Working Paper Series experimental design of the
       EQ-VT. EuroQol Res Found. 2017;1–17.

13.   Ravens-sieberer U, Erhart M, Wille N, Wetzel R, Nickel J, Bullinger M. Generic
       Health-Related Quality-of-Life Assessment in Children and Adolescents
       Methodological Considerations. Pharmacoeconomics. 2006;24(12):1199–220.

14.   Welie AG, Gebretekle GB, Stolk E, Mukuria C, Krahn MD, Enquoselassie F, et al.
       Valuing Health State: An EQ-5D-5L Value Set for Ethiopians. Value Heal Reg
       Issues. 2019;22:7–14.

15.   Scott D, Ferguson GD, Jelsma J. The use of the EQ-5D-Y health related quality of
       life outcome measure in children in the Western Cape , South Africa : psychometric
       properties , feasibility and usefulness - a longitudinal , analytical study. Health Qual
       Life Outcomes [Internet]. 2017;1–14. Available from:
       http://dx.doi.org/10.1186/s12955-017-0590-3

16.   Ravens-Sieberer U, Wille N, Badia X, Bonsel G, Burström K, Cavrini G, et al.
       Feasibility, reliability, and validity of the EQ-5D-Y: results from a multinational

study. Qual Life Res [Internet]. 2010/04/17. 2010 Aug;19(6):887–97. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20401552

17.   Wille N, Badia X, Bonsel G, Burstro K, Ravens-sieberer LSU. Development of the EQ-5D-Y : a child-friendly version of the EQ-5D. 2010;875–86.

18.   Goñi JMR, Oppe M, Stolk E, Shah K, Kreimeier S, Rivero O, et al. International Valuation Protocol for the EQ - 5D - Y - 3L. Pharmacoeconomics [Internet]. 2020;(0123456789). Available from: https://doi.org/10.1007/s40273-020-00909-3

19.   van Reenen M, Janssen B. EQ-5D-5L User Guide basic information on how to use the EQ-5D-5L instrument. Rotterdam: EuroQol Res Found. 2015;1–25.

20.   Vet HCW De, Terwee CB, Knol DL, Bouter LM. When to use agreement versus reliability measures. J Clin Epidemiol. 2006;59(10):1033–9.

21.   Liu H, Feurer ID, Dwyer K, Speroff T, Shaffer D, Pinson CW. The effects of gender and age on health-related quality of life following kidney transplantation. J Clin Nurs. 2008;17(1):82–9.

22.   Brazier J, N J, Kind P. Testing the validity of the Euroqol and comparing it with the SF-36 health survey questionnaire. Qual Life Res. 1993;2(3):169–80.

23.   Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. J Chiropr Med. 2015;

24.   Bassett AS, Collins EJ, Nuttall SE, Honer WG. Positive and negative symptoms in families with schizophrenia. Schizophr Res. 1993;11(1):9–19.

25. Feng YS, Kohlmann T, Janssen MF, Buchholz I. Psychometric properties of the EQ - 5D - 5L : a systematic review of the literature. Qual Life Res [Internet]. 2021;30(3):647–73. Available from: https://doi.org/10.1007/s11136-020-02688-y

26. Franklin M, Enrique A, Palacios J, Richards D, Franklin M. Psychometric assessment of EQ - 5D - 5L and ReQoL measures in patients with anxiety and depression : construct validity and responsiveness. Qual Life Res [Internet]. 2021;30(9):2633–47. Available from: https://doi.org/10.1007/s11136-021-02833-1

27. Bilbao A, Martín-fernández J, García-pérez L, Ignacio J, Arrasate M, Candela R, et al. Psychometric properties of the EQ-5D-5L in patients with major depression : factor analysis and Rasch analysis. J Ment Heal [Internet]. 2021;0(0):1–11. Available from: https://doi.org/10.1080/09638237.2021.1875422

28. Crick K, Al F, Arto S, Jeffrey O. Responsiveness of the anxiety / depression dimension of the 3- and 5-level versions of the EQ-5D in assessing mental health. Qual Life Res [Internet]. 2018;27(6):1625–33. Available from: http://dx.doi.org/10.1007/s11136-018-1828-1

29. Dams J, Rimane E, Steil R, Renneberg B, Rosner R. Reliability , Validity and Responsiveness of the EQ-5D-5L in Assessing and Valuing Health Status in Adolescents and Young Adults with Posttraumatic Stress Disorder : a Randomized Controlled Trail. Psychiatr Q. 2021;459–71.

30. Mulhern B, Mukuria C, Barkham M, Knapp M, Byford S, Soeteman D, et al. Using

generic preference-based measures in mental health : psychometric validity of the EQ-5D and SF-6D Using generic preference-based measures in mental health : psychometric validity of the EQ-5D and SF-6D. Br J Psychiatry. 2014;22(03):236–43.

31. Peasgood, T., Brazier, J. and Papaioannou D. A systematic review of the validity and responsiveness of EQ-5D and SF-6D for depression and anxiety. HEDS Discuss Pap 12/15. 2012;1–62.

List of Tables

Table 1. Background characteristics of the respondents

Characteristics	Study sample n (%)
Age (mean, SD)	15.57 (1.3)
Gender	
Female	188 (37.8)
Male	306 (62.2)
Type of disease	
Healthy	201 (40.4)
Bipolar	99 (19.9)
Schizophrenia	100 (20.1)
Depression	97 (19.5)
Education	
No formal education	95 (19.1)
Primary school	228 (35.0)
Secondary school	174 (25.3)
Experience of serious illness	
In self	226 (45.5)
In family	78 (15.7)
In self and in family	15 (3.0)
In caring for others	21 (4.2)
No	157 (31.6)
Religion	
Christian	273 (54.9)
Muslim	224 (45.1)

Table 2. Percentages of reported problems in the EQ-5D-5L in adolescent population

	No known mental health disorders (n = 201)		Bipolar disorder (n = 99)		Schizophrenia (n = 100)		Depression (n= 97)	
	n	%	n	%	n	%	n	%
Mobility								
No problems	190	94.50	96	97.00	91	91.00	86	88.70
Slight problems	9	4.50	2	2.00	6	6.00	8	8.25
Moderate problems	0	0.00	1	1.00	2	2.00	3	3.10
Severe problems	1	0.50	0	0.00	1	1.00	0	0.00
Unable/extreme problems	1	0.50	0	0.00	0	0.00	0	0.00
Total								
Self-care								
No problems	193	96.02	54	54.54	52	52.00	60	61.86
Slight problems	6	3.00	21	21.21	16	16.00	22	22.68
Moderate problems	1	0.50	14	14.14	20	20.00	12	12.37
Severe problems	1	0.50	9	9.09	9	9.00	3	3.09
Extreme problems	0	0.00	1	1.01	3	3.00	0	0.00
Total								
Usual activities								
No problems	166	82.58	39	39.04	26	26.00	34	35.05
Slight problems	29	14.43	13	13.13	25	25.00	23	23.71
Moderate problems	6	2.99	27	27.27	26	26.00	27	27.84
Severe problems	0	0.00	19	19.19	18	18.00	13	13.40
Extreme problems	0	0.00	1	1.01	5	5.00	0	0.00
Total								
Pain/Discomfort								
No problems	153	76.12	51	51.51	43	43.00	34	35.05
Slight problems	41	20.40	22	22.22	34	34.00	39	40.21
Moderate problems	3	1.50	23	23.23	12	12.00	19	19.59
Severe problems	2	0.99	2	2.02	8	8.00	5	5.15
Extreme problems	1	0.49	1	1.01	3	3.00	0	0.00
Total								

Anxiety/Depression								
No problems	130	64.68	30	30.30	20	20.00	6	6.19
Slight problems	52	25.87	36	36.36	41	41.00	30	30.93
Moderate problems	16	8.00	26	26.26	21	21.00	36	37.11
Severe problems	2	0.99	6	6.06	13	13.00	24	24.74
Extreme problems	1	0.49	1	1.01	5	5.00	1	1.03
Total								
EQ-VAS score (mean, SD)	92.37 (11.81)		72.12 (19.15)		67.55 (19.55)		68.81 (16.05)	
EQ-5D-5L Utility score (mean, SD)	0.96 (0.094)		0.83 (0.21)		0.75 (0.32)		0.78 (0.20)	
Minimum EQ-5D-5L Utility score	0.27		-0.42		-0.43		0.20	
Maximum EQ-5D-5L Utility score	1.00		1.00		1.00		1.00	

Table 3. Agreement between first and second EQ-5D-5L dimension scores

EQ-5D-5L scale	ICC	ICC range	P-value
Mobility	0.777	0.739 - 0.809	< 0.001
Self-care	0.836	0.800 - 0.865	< 0.001
Usual activity	0.790	0.724 - 0.838	< 0.001
Pain/discomfort	0.720	0.672 - 0.762	< 0.001
Anxiety/depression	0.754	0.706 - 0.794	< 0.001
EQ-5D index score	0.823	0.788- 0.852	< 0.001
EQ-VAS score	0.828	0.775- 0.866	< 0.001

ICC: Intraclass correlation coefficient

EQ-5D-5L: EuroQol five-dimensional three/five-level

EQ-VAS: European Quality Visual Analogue Scale

Statistical analysis: A two-way mixed-effects model, absolute intraclass correlation coefficient ICC

Table 4. Known group validity on EQ-5D-5L dimension and EQ-VAS scores by health, gender and educational status

Dimensions / Mobility	Disease condition				Chronic illness history					Sex		Educational status		
	No	Bipolar	Schizophrenia	Depression	No	In self	In family	Both	In caring others	Male	Female	Informal	Primary	Secondary
n	201	99	100	97	157	226	78	15	21	309	188	95	228	174
Mean rank	49357	23716	25447	25235	42135	54439	18340	3480	5360	75379	48374	23032	56866	43856
Chi-square	6.655				23.811					5.288		1.455		
p-value	0.0837				< 0.001					0.0215		0.4831		
n	201	99	100	97	157	226	78	15	21	309	188	95	228	174
Mean rank	38023	29062	30421	2624	36765	63061	16721	3215	3992	75459	48294	27824	53956	41974
Chi-square	99.022				33.063					1.470		17.851		
p-value	< 0.001				< 0.001					0.2254		< 0.001		
n	201	99	100	97	157	226	78	15	21	309	188	95	228	174
Mean rank	33474	29341	32451	28488	35027	66378	15720	2950	3681	75196	48557	29031	52662	42061
Chi-square	136.414				51.490					1.510		22.468		
p-value	< 0.001				< 0.001					0.2191		< 0.001		
n	201	99	100	97	157	226	78	15	21	309	188	95	228	174
Mean rank	38701	26598	28644	29314	38291	60563	16848	3693	3863	73766	49491	26899	51360	44997
Chi-square	65.367				14.240					4.791		14.930		
P-value	< 0.001				0.0066					0.0286		0.0006		
n	201	99	100	97	157	226	78	15	21	309	188	95	228	174
Mean rank	33735	25947	29610	34463	36176	64611	16227	3786	2955	74553	49201	28891	50618	44245
Chi-square	142.246				39.541					2.611		24.585		
P-value	< 0.001				< 0.001					0.1061		< 0.001		

EQ-VAS mean score	92.4	72.1	67.5	68.8	81.4	72.8	85.3	86.0	93.9	80.1	76.6	69.4	81.8	79.9
n	201	99	100	97	157	226	78	15	21	309	188	95	228	174
Mean rank	72339	19146	16467	15802	42343	45187	23700	4666	7859	78959	44795	17761	62387	43605
Chi-square	207.213					60.709					1.719		24.894	
P-value	0.0001					0.0001					0.1899		< 0.001	
Utility mean score	0.96	0.84	0.76	0.78	0.85	0.83	0.92	.88	0.96	0.87	0.83	0.80	0.88	0.85
n	201	99	100	97	157	226	78	15	21	309	188	95	228	174
Mean rank	186	219	186	165	267	209	296	278	344	259	233	193	282	237
Chi-square	133.243					39.50					3.906		28.4362	
p-value	< 0.001					< 0.001					0.048		< 0.001	

Statistical analysis: Non-parametric Kruskal-Wallis rank test

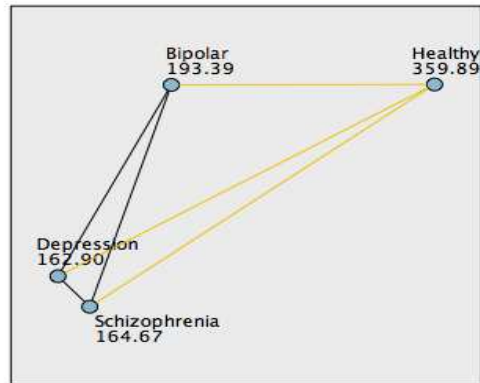**Figure 1. Shows the distribution of EQ-VAS scores between disease group.**
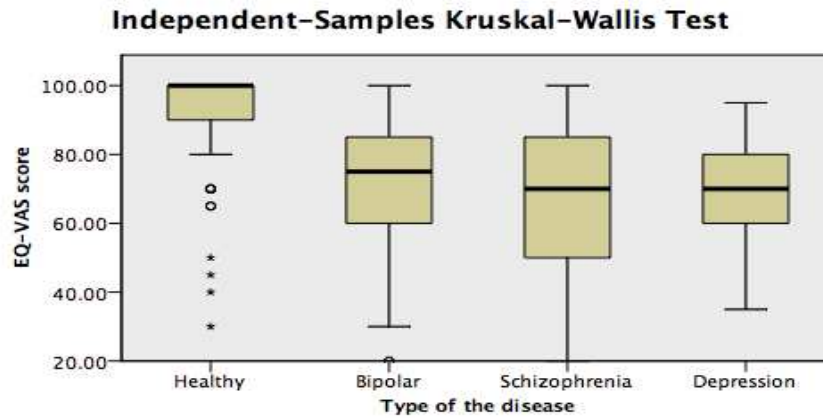
Total N	497
Test Statistic	207.213
Degrees of Freedom	3
Asymptotic Sig. (2-sided test)	.000

1. The test statistic is adjusted for ties.

Figure 2. The pairwise comparison of EQ-VAS scores within the type of disease.
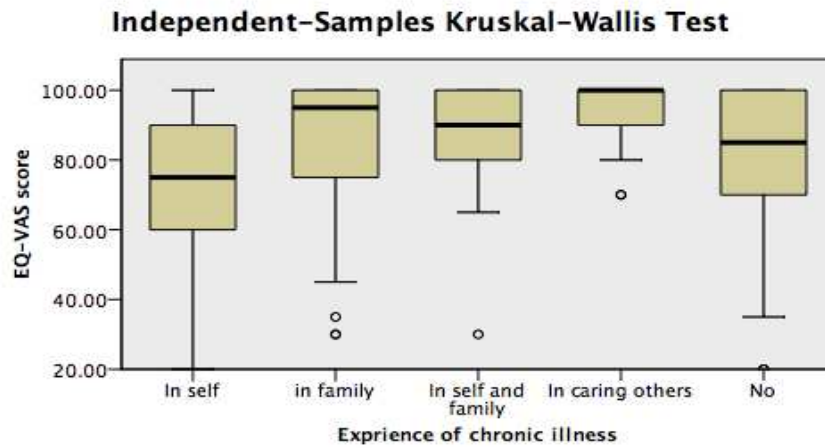

Pairwise Comparisons of Type of the disease

Each node shows the sample average rank of Type of the disease.

Sample1–Sample2	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj.Sig.
Depression–Schizophrenia	1.768	20.309	.087	.931	1.000
Depression–Bipolar	30.492	20.359	1.498	.134	.805
Depression–Healthy	196.991	17.618	11.181	.000	.000
Schizophrenia–Bipolar	28.724	20.204	1.422	.155	.931
Schizophrenia–Healthy	195.223	17.439	11.195	.000	.000
Bipolar–Healthy	166.499	17.498	9.516	.000	.000

Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same.
Asymptotic significances (2–sided tests) are displayed. The significance level is .05.

Figure 3. Shows the distribution of EQ-VAS scores between different experience of chronic illness.
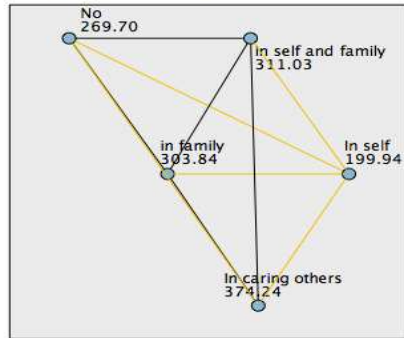
Independent–Samples Kruskal–Wallis Test

Total N	497
Test Statistic	60.709
Degrees of Freedom	4
Asymptotic Sig. (2–sided test)	.000

1. The test statistic is adjusted for ties.

Figure 4. Shows the pairwise comparison of EQ-VAS scores within the different in.
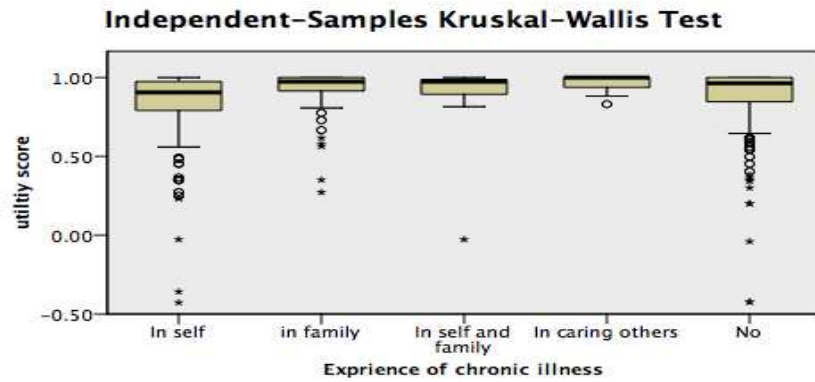

Pairwise Comparisons of Exprience of chronic illness

Each node shows the sample average rank of Exprience of chronic illness.

Sample1–Sample2	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj.Sig.
In self–No	–69.757	14.806	–4.712	.000	.000
In self–in family	–103.899	18.714	–5.552	.000	.000
In self–In self and family	–111.093	37.996	–2.924	.003	.035
In self–In caring others	–174.298	32.510	–5.361	.000	.000
No–in family	34.142	19.741	1.730	.084	.837
No–In self and family	41.336	38.512	1.073	.283	1.000
No–In caring others	104.541	33.112	3.157	.002	.016
in family–In self and family	–7.194	40.177	–.179	.858	1.000
in family–In caring others	–70.398	35.034	–2.009	.044	.445
In self and family–In caring others	–63.205	48.176	–1.312	.190	1.000

Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same.
Asymptotic significances (2–sided tests) are displayed. The significance level is .05.

**Figure 5. Shows the distribution of utility scores between different experience of chronic illness.**

Independent–Samples Kruskal–Wallis Test

Total N	497
Test Statistic	39.500
Degrees of Freedom	4
Asymptotic Sig. (2–sided test)	.000

1. The test statistic is adjusted for ties.

Figure 6. Shows the pairwise comparison of utility scores within the different experience of chronic illness.
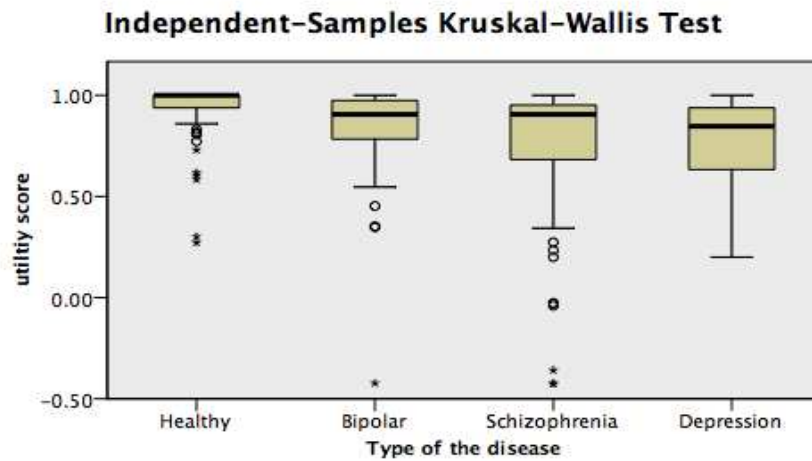

Pairwise Comparisons of Exprience of chronic illness
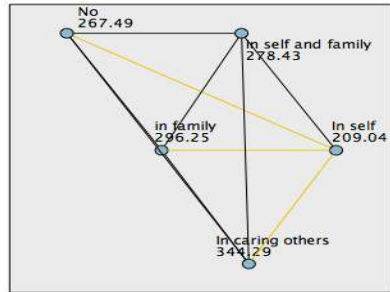
Each node shows the sample average rank of Exprience of chronic illness.

Sample1-Sample2	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj.Sig.
In self-No	−58.445	14.714	−3.972	.000	.001
In self-In self and family	−69.391	37.762	−1.838	.066	.661
In self-in family	−87.208	18.599	−4.689	.000	.000
In self-In caring others	−135.244	32.310	−4.186	.000	.000
No-In self and family	10.946	38.275	.286	.775	1.000
No-in family	28.763	19.619	1.466	.143	1.000
No-In caring others	76.798	32.908	2.334	.020	.196
In self and family-in family	17.817	39.930	.446	.655	1.000
In self and family-In caring others	−65.852	47.879	−1.375	.169	1.000
in family-In caring others	−48.036	34.818	−1.380	.168	1.000

Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same.
Asymptotic significances (2-sided tests) are displayed. The significance level is .05.

**Figure 7. Shows the distribution of utility scores between type of diseases.**

Independent-Samples Kruskal-Wallis Test

Total N	497
Test Statistic	133.243
Degrees of Freedom	3
Asymptotic Sig. (2-sided test)	.000

1. The test statistic is adjusted for ties.

Figure 8. Shows the pairwise comparison of utility scores within the disease types.

Pairwise Comparisons of Type of the disease
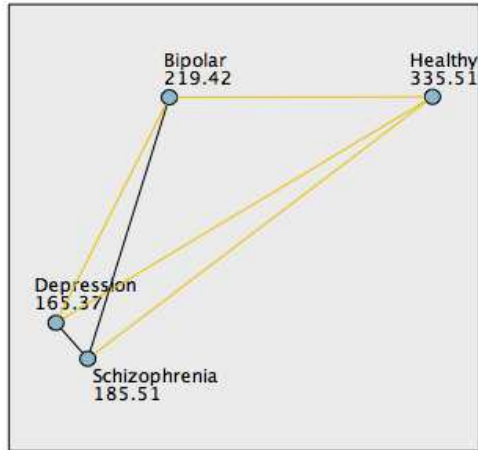
Each node shows the sample average rank of Type of the disease.

Sample1-Sample2	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj.Sig.
Depression-Schizophrenia	20.144	20.183	.998	.318	1.000
Depression-Bipolar	54.058	20.234	2.672	.008	.045
Depression-Healthy	170.149	17.509	9.718	.000	.000
Schizophrenia-Bipolar	33.914	20.080	1.689	.091	.547
Schizophrenia-Healthy	150.005	17.331	8.655	.000	.000
Bipolar-Healthy	116.091	17.390	6.676	.000	.000

Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same.
Asymptotic significances (2-sided tests) are displayed. The significance level is .05.