

ORIGINAL ARTICLE

Internalizing disorders and quality of life in adolescence: evidence for independent associations

Giovanni A. Salum,^{1,2,3} Diogo A. DeSousa,² Vera L. Bosa,⁴ Ilaine Schuch,⁴ Marcelo Goldani,⁴ Luciano R. Isolan,^{1,2} Stefania P. Teche,² Marcelo P. Fleck,¹ Luis A. Rohde,^{1,3} Gisele G. Manfro^{1,2,3}

¹Graduate Program in Medical Sciences: Psychiatry, Universidade Federal do Rio Grande do Sul (UFRGS), Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre, RS, Brazil. ²Anxiety Disorders Outpatient Program for Child and Adolescent Psychiatry, HCPA, Porto Alegre, RS, Brazil. ³National Science and Technology Institute for Child and Adolescent Psychiatry (INPD), HCPA, Porto Alegre, RS, Brazil. ⁴Center for Child and Adolescent Health Studies (NESCA), HCPA, Porto Alegre, RS, Brazil.

Objective: To investigate whether internalizing disorders are associated with quality of life (QoL) in adolescents, even after accounting for shared risk factors.

Methods: The sample comprised 102 adolescents from a community cross-sectional study with an oversampling of anxious subjects. Risk factors previously associated with QoL were assessed and divided into five blocks organized hierarchically from proximal to distal sets of risk factors.

Results: Multiple regression analysis yielded a hierarchical model accounting for 72% of QoL variance. All blocks were consistently associated with QoL ($p < 0.05$), accounting for the following percentages of variance: 12% for demographics; 5.2% for family environment; 37.8% for stressful events; 10% for nutritional and health habits; and 64.2% for dimensional psychopathological symptoms or 22.8% for psychiatric diagnoses (dichotomous). Although most of the QoL variance attributed to internalizing symptoms was explained by the four proximal blocks in the hierarchical model (43.2%), about 21% of the variance was independently associated with internalizing symptoms/diagnoses.

Conclusions: QoL is associated with several aspects of adolescent life that were largely predicted by our hierarchical model. Our findings reinforce the hypothesis that internalizing disorders and internalizing symptoms in adolescents have a high impact on QoL and deserve proper clinical attention.

Keywords: Quality of life; anxiety; depression; adolescents

Introduction

The investigation of quality of life (QoL) has been considered a main outcome in psychiatric research among the growing set of patient-report outcomes.¹ These can be used to estimate the cost-effectiveness of treatments in health economics and can help clinicians better integrate the perspectives of adolescents into their individual care, thus playing an important role in clinical decision making.²

Several factors have been previously associated with QoL in adolescence. For instance, demographic factors, such as gender, skin color, maternal education, and socioeconomic status, were found to be associated with QoL in early adolescence in a birth cohort study.³ In addition, associations have been found between overweight and lower QoL in adolescence⁴ and between health behavior and life satisfaction among young adults.⁵ Furthermore, the presence of stressful life events during childhood and the family environment have been associated with significant impact in QoL,⁶ with effects persisting into adulthood.⁷ Finally, it is widely

acknowledged that mental disorders affect QoL in childhood and adolescence.⁸

Anxiety disorders have been associated with QoL in adulthood,⁹⁻¹¹ however, few studies have explored this association in adolescence,¹² and even fewer have investigated independent associations of different conditions that affect both anxiety disorders and QoL, such as childhood maltreatment and psychosocial distress in the family environment.^{6,13} Therefore, it is unclear whether anxiety symptoms influence QoL independently or whether they influence other proximal variables that are associated with QoL in adolescents.

The aim of this study was to investigate associations between QoL and internalizing disorders in a community sample of adolescents with a high frequency of anxiety symptoms. We used hierarchical regression to measure dependent and independent associations of both internalizing symptoms and internalizing disorders.

Methods

Participants and procedures

Six public schools in the city of Porto Alegre, state of Rio Grande do Sul, Brazil, participated in this cross-sectional investigation. The population of these six schools comprised 2,754 adolescents. The Screen for Child

Correspondence: Giovanni Abrahão Salum, Hospital de Clínicas de Porto Alegre (HCPA), Rua Ramiro Barcelos, 2350, sala 2201A, CEP 90035-003, Porto Alegre, RS, Brazil.

E-mail: gsalumjr@gmail.com

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Anxiety Related Emotional Disorders (SCARED)¹⁴ was administered to 2,457 adolescents, aged 10 to 19 years, to screen for symptoms of anxiety. The remaining 297 (11.1%) were not covered by the survey due to school dropout or transfer to another school (n=217, 7.9%) or refusal to participate (n=80, 3.2%). More detailed information about the study design and sample selection is provided elsewhere.¹⁵

The range of the SCARED scores in the sample was divided into quartiles. All participants in the upper quartile and a 10% random sample of the participants in each of the three other quartiles were invited to undergo an extensive clinical assessment, which comprised a nutritional and body composition evaluation and an investigation of family environment, parental psychopathology and temperament, child psychopathology, and QoL. The analytical sample of this study comprised the 102 adolescents who agreed to participate in the clinical assessment and completed the study protocol (64 adolescents from the upper quartile and 38 from the other three quartiles). This oversampling of anxious participants was carried out to ensure adequate power to investigate the associations between anxiety symptoms and disorders and QoL. The invited subsamples that attended and did not attend the clinical assessment were fairly similar, with no difference regarding gender (OR = 0.79; p = 0.151), although those who attended were more likely to be older (M = 12.8, SD = 2.38 vs. M = 13.9, SD = 2.51; p < 0.001). No other significant differences were found regarding anxiety symptoms or risk factors evaluated between subjects who attended and those who did not. The study design was reviewed and approved by the Hospital de Clínicas de Porto Alegre Ethics Committee. School approval, assent from adolescents, and written informed consent from parents were obtained before participation.

A total of 102 adolescents (70.6% female; n=72) underwent clinical evaluation and participated in this study. The mean age of the sample was 13.47 years (SD = 0.70). Regarding psychiatric diagnoses, 44 (43.1%) of the adolescents had generalized anxiety disorder (GAD); 37 (36.3%) had specific phobias (SP); 23 (22.5%) had attention deficit/hyperactivity disorder (ADHD); 23 (22.5%) had social anxiety disorder (SoAD); 15 (14.7%) had separation anxiety disorder (SeAD); 11 (10.8%) had oppositional defiant disorder (ODD); and eight (7.8%) had major depression (MD). The clinical characterization of the sample reflects the oversampling of anxious adolescents.

Instruments and measures

Demographics and early environment assessment

Demographic evaluation was performed using a semi-structured interview. Variables used to evaluate the proximal environment were measured considering Rutter's adversity index.¹⁶

Psychiatric diagnosis

The Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime

(K-SADS-PL)¹⁷ is a semi-structured interview used for the diagnosis of childhood psychiatric disorders based on the DSM-IV criteria, comprising the following areas: 1) disruptive behavioral disorders; 2) anxiety disorders; 3) affective disorders; 4) psychotic disorders; and 5) substance abuse, tic disorders, eating disorders, and elimination disorders. Interviewers who performed the diagnosis for this study were required to have clinical experience, and all had received extensive training in the K-SADS-PL before the start of the project, under the supervision of a senior psychiatrist. Final diagnoses were discussed in a clinical committee. Only current diagnoses with a prevalence greater than 3% were considered for analysis.

Self-assessment instruments

Parents completed the Brazilian-Portuguese versions of the Family Environmental Scale (FES)¹⁸ and the Novelty Seeking and Harm Avoidance subscales of the Temperament and Character Inventory (TCI).¹⁹ The FES is a 53-item self-report of family environment that investigates family cohesion, conflict, expressiveness, achievement orientation, organization, and control. The TCI is a self-report measure of temperamental traits in adulthood. The Novelty Seeking subscale measures a tendency to exploratory activity and intense excitement in response to novel stimuli, and the Harm Avoidance subscale measures a tendency to intense responses to aversive stimuli and inhibition of behavior in response to signals of punishment and frustrative non-reward.

Children answered the SCARED,^{14,20} the Childhood Trauma Questionnaire (CTQ),²¹ the Children's Depression Inventory (CDI),²² the Strengths and Difficulties Questionnaire (SDQ),²³ and questions about bullying/victimization.²⁴ The SCARED is a 41-item self-report measure of pediatric anxiety symptoms, divided into five subscales: GAD (nine items); SeAD (eight items); SoAD (seven items); panic/somatic (13 items); and school phobia (four items). The CDI is a 27-item self-report measure of pediatric depressive symptoms. The CTQ is a 38-item self-report measure of childhood trauma, divided into five subscales investigated on a retrospective basis: emotional abuse; physical abuse; sexual abuse; emotional neglect; and physical neglect. The SDQ is a 25-item self-report screening questionnaire for youth mental health, divided into five subscales: emotional symptoms; conduct problems; hyperactivity-inattention; peer problems; and prosocial behavior. Bullying and victimization were assessed on a two-item (bullying and victimization), five-point scale after presenting a definition of bullying followed by examples of behaviors regarded as bullying. In all of the aforementioned measures, higher scores reflect higher severity levels.

Nutritional and health habits assessment

All anthropometric variables were measured twice through the use of standard techniques and calibrated equipment.²⁵ Body weight was measured using portable digital electronic scales (Marte®) (Marte, SR Sapucaí, MG, Brazil), and height was measured using a portable

sliding stadiometer (Altuxata, Belo Horizonte, MG, Brazil). Arm and waist circumferences were measured using a tape measure (Sanny, São Bernardo do Campo, SP, Brazil). Subscapular and triceps skinfolds were measured using a caliper (Cescorf, Porto Alegre, RS, Brazil). The sexual maturation stage was self-assessed according to Tanner's criteria.²⁶

Body composition was measured through bioelectrical impedance analysis (BIA) (Biodynamics-450, Seattle, WA, USA).²⁷ Physical activity was assessed using a self-report 3-day physical activity record (PAR24h).²⁸ The levels of regular physical activity were determined through estimation of energy and time spent on different activities in these 3 days. Food intake was assessed using a 24-hour food record and the 94-item Adolescent Food Frequency Questionnaire (AFFQ).²⁹ The intake of macro- and micronutrients was calculated using the NutriBase® software (NB7 Network; Phoenix, AZ, USA).

QoL outcome measure

The Youth Quality of Life Instrument-Research version (YQOL-R) is a 41-item self-report measure of QoL in adolescence, carefully developed using grounded theory concepts and methods to guide data collection and analysis.³⁰ The YQOL-R can be divided into four subscales: self QoL (14 items), relationship QoL (14 items), environmental QoL (10 items), and general QoL (three items). Psychometric investigations of the YQOL-R have demonstrated acceptable internal consistency and intraclass correlation coefficients (i.e., evidence of reliability); expected associations with other constructs (evidence of construct validity); and ability to distinguish between known groups (evidence of discriminant validity).^{30,31} Furthermore, we conducted a pilot investigation with a subsample of 419 students randomly selected from the six schools covered by this study to evaluate the factor structure and evidence of validity of the YQOL-R in our population (main results described elsewhere).³¹ We also conducted a single-factor principal component analysis to test whether the four YQOL-R subscales could be interpreted altogether as an overall QoL score. The single factor (eigenvalue = 2.99) accounted for 74.8% of QoL variance in the data, supporting the use of an overall YQOL-R perceptual score.

Data analysis

We followed a three-step plan of analysis to avoid multiple testing and to find a parsimonious model explaining the most variance in QoL scores. In the first step, we conducted univariate analyses to investigate the associations between each of the 51 predictor variables measured – divided into five conceptual blocks – and the QoL outcome. A description of the blocks follows:

- Block 1, demographics and early environment: (a) age in years; (b) gender; (c) socioeconomic status; (d) school; (e) parental contact with the child during early childhood; (f) social support during early childhood; (g) maternal stress during pregnancy.

- Block 2, family environment: (a) maternal temperament – novelty seeking and harm avoidance; (b) family functioning.
- Block 3, stressful events perceived by the adolescents: (a) peer victimization; (b) bullying behavior; (c) abuse and neglect.
- Block 4, nutritional and health habits: (a) percent of calories from fat; (b) percent of calories from carbohydrates; (c) percent of calories from protein; (d) total calorie intake; (e) body mass index; (f) body fat percentage; (g) sexual maturation stage; (h) hours of physical inactivity.
- Block 5a, dimensional psychiatric symptoms: (a) severity level of general psychiatric symptoms (SDQ total score); (b) severity level of anxiety symptoms (SCARED scores); (c) severity level of depression symptoms (CDI scores).
- Block 5b, psychiatric diagnoses: (a) GAD; (b) SP; (c) ADHD; (d) SoAD; (e) SeAD; (f) ODD; (g) MD.

In the second step, all predictor variables associated with total QoL scores at a significance level (p -value) of 0.20 or lower were investigated in linear model analyses. Forward stepwise regressions were run independently for each block (four variables in block 1; five variables in block 2; six variables in block 3; three variables in block 4; nine variables in block 5a and two variables in block 5b). Again, variables that showed associations at a significance level of 0.20 or lower were carried forward to the third step of the plan of analysis – a hierarchical model.

Finally, in the third step, we conducted a hierarchical model analysis to investigate possible cumulative associations. At this step, no removal criteria were used, i.e., all variables that met the criteria in the two previous steps were included in the hierarchical model. The hierarchical strategy was based on theoretical chronological assumptions. This means the order of the blocks reflects that demographics and early environment factors (block 1) are more chronologically distal to QoL than family environment (block 2), which is more distal than stressful life events perceived by the adolescents (block 3), and so on. This approach is subject to overfitting and insensitive to filtering the associations of the distal blocks with the last blocks (blocks of interest) included in the models. However, as our objective is specifically to test the independence of the last blocks, we decided to use a more comprehensive model that could investigate this research question properly. Two independent analyses were conducted: one including the four initial blocks and the 5a block and the other including the four initial blocks and the 5b block.

We checked graphically for final model fit using residual analysis. All assumptions for multiple linear regressions were met completely. The variance inflation factor showed no evidence of multicollinearity in each of the investigated models. All p -values are based on $\alpha = 5\%$.

Results

Of the 51 predictor variables investigated, 27 were significantly associated with QoL scores at $p \leq 0.20$ (step 1; data not shown – available on request to

Table 1 Linear models investigating associations of several predictor variables with quality of life in adolescence

Block	Univariate analysis of variables associated with QoL at $p < 0.20$				Coefficients adjusted in each block (forward selection within each block)				Hierarchical analysis (block entry procedure)				r^2 Change	p-value F-change						
	B	SE	Beta	p-value	B	SE	Beta	p-value	B	SE	Beta	p-value			r^2	r^2_{adj}	p-value			
1 - Demographics																				
Age (years)	-1.83	0.59	-0.29	0.003	-1.68	0.59	-0.27	0.006	-1.68	0.59	-0.27	0.006	0.120	0.093	0.003	0.120	0.002			
School	1.73	1.09	0.15	0.118																
Gender (female)	-6.34	3.13	-0.19	0.046	-5.05	3.06	-0.15	0.102	-5.05	3.06	-0.15	0.102								
Support from others	6.63	4.47	0.14	0.141																
2 - Family environment																				
Maternal NS	-0.34	0.022	-0.14	0.140									0.052	0.043	0.021	0.158	0.132	0.001	0.038	0.039
Maternal HA	-0.37	0.20	-0.17	0.080																
Family cohesion	1.68	0.71	0.22	0.021	1.68	0.71	0.22	0.021	1.68	0.69	0.20	0.034								
Family conflict	-1.11	0.69	-0.15	0.115																
Family organization	1.40	0.65	0.20	0.036									0.378	0.366	< 0.001	0.457	0.429	< 0.001	0.299	< 0.001
3 - Stressful events																				
Victimization	-4.51	3.40	-0.13	0.189																
Bullying	-6.10	3.61	-0.16	0.095																
Emotional abuse	-1.80	0.29	-0.51	< 0.001	-1.04	0.32	-0.30	0.002	-1.04	0.32	-0.26	0.006								
Physical abuse	-1.37	0.51	-0.25	0.009																
Emotional neglect	-2.10	0.30	-0.56	< 0.001	-1.49	0.34	-0.40	< 0.001	-1.49	0.34	-0.40	< 0.001								
Physical neglect	-1.69	0.58	-0.27	0.005																
4 - Nutritional and health habits																				
Body fat %	-0.37	0.19	-0.18	0.067	-0.30	0.19	-0.15	0.119	-0.30	0.19	-0.15	0.119	0.100	0.082	0.006	0.509	0.472	< 0.001	0.051	0.010
Puberty	-2.98	2.00	-0.14	0.141																
Physical inactivity (hours)	-1.57	0.53	-0.27	0.004	-1.44	0.53	-0.26	0.008	-1.44	0.53	-0.26	0.008								
5A - Psychiatric symptoms																				
Emotional	-2.63	0.56	-0.41	< 0.001	-0.68	0.45	-0.10	0.134	-0.68	0.45	-0.10	0.134	0.642	0.627	< 0.001	0.721	0.685	< 0.001	0.210	< 0.001
Conduct	-2.70	0.59	-0.41	< 0.001																
Hyperactivity	-1.73	0.67	-0.25	0.011																
Peer relationship	-3.67	0.72	-0.45	< 0.001																
Prosocial behavior	2.66	0.82	0.30	0.002	1.11	0.56	0.12	0.053	1.11	0.56	0.12	0.053								
Depressive	-2.14	0.18	-0.77	< 0.001	-1.79	0.19	-0.64	< 0.001	-1.79	0.19	-0.64	< 0.001								
Panic	-1.28	0.28	-0.40	< 0.001																
GAD	-1.83	0.36	-0.45	< 0.001	-0.59	0.28	-0.14	0.040	-0.59	0.28	-0.14	0.040								
School phobia	-2.05	0.90	-0.22	0.026																
5B - Psychiatric diagnosis																				
GAD	-10.94	2.73	-0.37	< 0.001	-10.58	2.59	-0.36	< 0.001	-10.58	2.59	-0.36	< 0.001	0.228	0.213	< 0.001	0.560	0.516	< 0.001	0.051	0.007
MD	-17.04	5.14	-0.31	0.001	-16.24	4.78	-0.30	0.001	-16.24	4.78	-0.30	0.001								

QoL = quality of life; GAD = generalized anxiety disorder; MD = major depression; NS = novelty seeking (temperament); HA = harm avoidance (temperament).

corresponding author). These 27 were therefore considered for the block analyses. Table 1 presents the associations between these variables and the QoL scores in each block independently (step 2) and in the hierarchical model (step 3). All associations were in the hypothesized directions (e.g., anxious and depressive symptoms were negatively associated with QoL). Figure 1 depicts the regression-predicted values vs. the observed YQOL-R total scores.

After controlling for proximal risk factors in the hierarchical model, all blocks still significantly accounted for the QoL variance: stressful events (29.9%), dimensional psychopathology (21%), demographics (12%), nutritional and health habits (5.1%), and family environment (3.8%). In the alternative model, psychiatric diagnoses (GAD and MD) also significantly accounted for 5.1% of the QoL variance independently. Table 1 presents the r^2 independent contributions of each block in the hierarchical model (r^2 change).

As our study design oversampled anxious adolescents (from the upper quartile of the SCARED scores), we conducted an exploratory stratified analysis for the final model, splitting the dataset into lower vs. upper quartiles, to investigate whether there were design effects in the estimates of effect size of each block. The r^2 estimates of each block within the subsample from the three lower quartiles were, respectively: $r^2 = 0.122$, $p = 0.124$; $r^2 = 0.155$, $p = 0.150$; $r^2 = 0.567$, $p < 0.001$; $r^2 = 0.579$, $p < 0.001$; and $r^2 = 0.735$, $p < 0.001$. Within the subsample from the upper quartile, the r^2 estimates of each block were, respectively: $r^2 = 0.163$, $p = 0.005$; $r^2 = 0.183$, $p = 0.007$; $r^2 = 0.281$, $p = 0.001$; $r^2 = 0.335$, $p < 0.001$; and $r^2 = 0.698$, $p < 0.001$.

Finally, we investigated the associations of the final model in each of the YQOL subscales. Table 2 presents the results of this analysis, showing higher r^2 estimates for general QoL and relationship QoL in the final model.

Discussion

We found that, although proximal blocks in the hierarchical model explained most of the QoL variance attributed to internalizing symptoms, about 21% of the variance was independently associated with internalizing symptoms. In addition, we found that QoL variance was explained by the following: 12% for demographics; 5.2% for family environment; 37.8% for stressful events; 10% for nutritional and health habits; and 64.2% for dimensional psychopathological symptoms or 22.8% for psychiatric diagnoses. As expected, all variables related to suffering and distress in adolescence were negatively associated with QoL scores, whereas variables theoretically related to better life satisfaction and support were positively associated with QoL scores.

The hierarchical model results support the hypothesis that predictor variables that are more chronologically distal account for less of the QoL variability in adolescents as compared to more proximal ones.³² In a previous study investigating the contributions of mental and nutritional aspects to global QoL in adolescence,

Sawatsky et al.³³ found that 42% of the variance of global QoL scores was explained by satisfaction with self; 30% by mental health; 20% by satisfaction with family environment; 4% by satisfaction with living environment; 3% by physical health; and 0% by satisfaction with friendship. Although our theoretical and analytical approaches are somewhat different from those of the Sawatsky et al. study,³³ on one hand, our results are in agreement with their findings about mental health and satisfaction with self as the variables that most account for variance in global QoL scores. On the other hand, our results suggested that peer relationships are an important factor for adolescent QoL. This discrepancy might be related to an indirect effect of emotional and behavioral symptoms, which thus led this variable to account for less of the QoL variance in final models.

Our data demonstrated that GAD and MD diagnoses were significantly associated with QoL. Studies have consistently shown an independent association of both conditions with QoL in adulthood^{34,35}; however, little evidence for independent negative effects of GAD and MD on QoL in adolescence are available in the literature. A previous study¹² showed a mediation role of some proximal variables, such as demographics, in the association between anxiety and adolescent QoL, also demonstrating independent significant associations. However, to the best of our knowledge, the present study is the first to demonstrate that anxiety and depression are strongly associated with QoL independently of other proximal variables, such as childhood abuse/neglect and family dysfunction (both of which are strong predictors of childhood anxiety).³⁶

One could argue that psychiatric symptoms or stressful life events perceived by the child are strongly associated with QoL only because they are redundant constructs, i.e., different measures of the same latent construct.³⁷ The fact that several dimensions (not only depressive or emotional symptoms) have significant impacts on QoL provides further evidence of the validity of the separation between these constructs in the literature. As there are significant indirect associations of several factors with these two constructs, our hierarchical analysis provides interesting inputs for this discussion. For example, the whole dimensional symptoms block accounted for 63% of the QoL variance itself. The model with the first four blocks accounted for 51% of the variance of QoL; however, when the dimensional symptoms block was added, the variance of QoL rose to 72%. Therefore, 21% of the variance (72% from the final model minus 51% from the cumulative explanation of hierarchical blocks before the inclusion of the dimensional symptoms block) could still be explained by dimensional symptoms, whereas the remaining variance may be explained by an association with proximal hierarchical variables. Regarding GAD and MD as diagnostic entities, they explained 23% of QoL variability as a block and 5.1% was significantly independent from proximal risk factors.

We also were able to show that not only did psychiatric disorders impair QoL, but the number and severity of

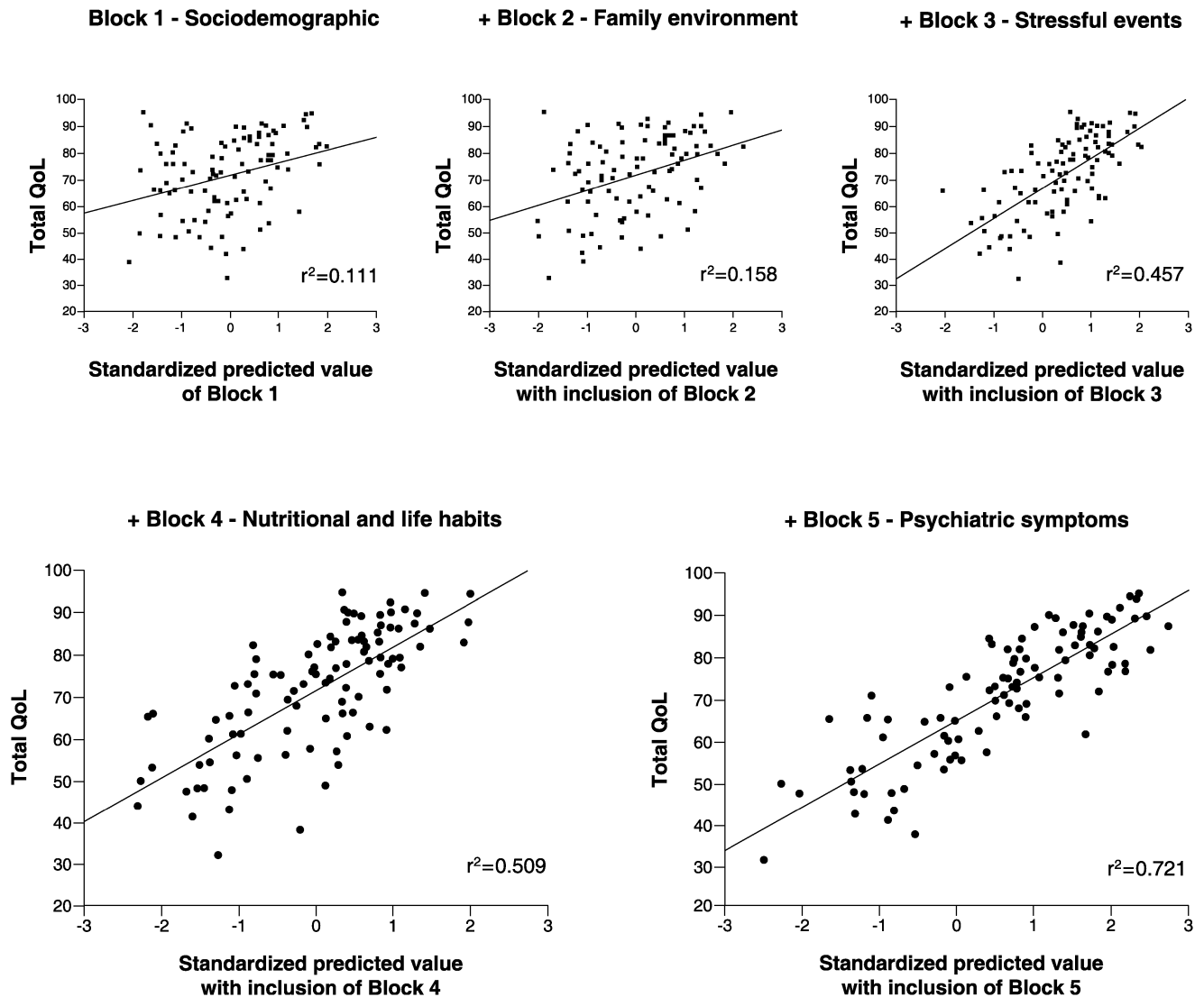


Figure 1 Standardized linear regression-predicted values vs. total QoL scores. QoL = quality of life.

symptoms of psychiatric disorders were also linearly associated with QoL scores, explaining more than the diagnosis itself (72 vs. 56%). Some studies have also found that, even in patients without current, recent, or past psychiatric disorders, health-related QoL is affected by an increase in the severity of psychiatric symptoms.³⁸ This is consistent with a dimensional view of psychiatric

disorders, in which the effects of symptoms are continuous and thresholds are arbitrary.³⁹ Furthermore, it raises the need for attention to sub-threshold symptoms and at-risk children in child mental health.⁴⁰

The present study has some limitations that need to be taken into consideration. First, our small sample size might have influenced the fact that some minor predictors

Table 2 Regression estimates of each block in the YQOL-R subscores

	Block 1	Block 2	Block 3	Block 4	Block 5a	Block 5b
General QoL	r ² = 0.169 p < 0.001	r ² = 0.194 p < 0.001	r ² = 0.340 p < 0.001	r ² = 0.359 p < 0.001	r ² = 0.608 p < 0.001	r ² = 0.439 p < 0.001
Self QoL	r ² = 0.083 p = 0.016	r ² = 0.128 p = 0.005	r ² = 0.209 p < 0.001	r ² = 0.254 p < 0.001	r ² = 0.481 p < 0.001	r ² = 0.346 p < 0.001
Relationship QoL	r ² = 0.117 p = 0.003	r ² = 0.154 p = -0.001	r ² = 0.379 p < 0.001	r ² = 0.414 p < 0.001	r ² = 0.603 p < 0.001	r ² = 0.452 p < 0.001
Environmental QoL	r ² = 0.052 p = 0.078	r ² = 0.074 p = 0.063	r ² = 0.167 p = 0.002	r ² = 0.203 p = 0.002	r ² = 0.497 p < 0.001	r ² = 0.271 p < 0.001

QoL = quality of life; YQOL-R = Youth Quality of Life Instrument-Research version.

of QoL did not reach statistical significance in the model. Second, this study was mainly designed to investigate mental disorders; therefore, some physical symptoms and other non-predicted variables that may impact QoL were not assessed. Nevertheless, our comprehensive model was able to account for a large proportion of QoL variance. Third, the design choice to oversample anxious children may limit our external validity, as some psychiatric symptoms and disorders that occur at lower frequencies in this population cannot reach statistical significance. However, when comparing the associations in the hierarchical model within the subsample consisting of the three lower quartiles and the higher-quartile subsample separately, no major differences were found. Fourth, stepwise regression models are known for overfitting, and the final variance explained by the model is very likely overestimated. However, our hypothesis was designed specifically to test whether internalizing disorders would have independent associations with QoL after accounting for proximal risk factors; therefore, we adopted this strategy as a conservative bias to our main hypothesis, as overfitting would reduce the odds of the final blocks of a hierarchical regression reaching significance. Fifth, the model is insensitive to moderation and assumes that no interactions among predictors are taking place. Finally, due to similarities between items in the mental health and QoL instruments, "item overlap" should be taken into account. Nonetheless, the general QoL subscale, which includes only general QoL items (e.g., "satisfied with life"; "enjoy life"; "life is worthwhile"), was also largely explained by our model (61% of the variance of this QoL subscale score).

In conclusion, QoL in adolescence is influenced by several factors. Although the association of anxiety and depression symptoms/disorders with QoL is largely related to proximal risk factors, such as abuse and neglect, there are also strong independent associations of these psychopathological features with QoL in adolescents. However, the chain of events leading to worse QoL and the specific associations between predictors, on one hand, and mediators, moderators, proxy and overlapping variables on the other hand are still unknown. Further longitudinal and developmental studies should focus on investigating these associations to shed light on causal chains in QoL research.

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Disclosure

LAR was on the speakers bureau and/or acted as consultant for Eli Lilly, Janssen-Cilag, Novartis, and Shire in the last 3 years (earning less than US\$ 10,000 per year and reflecting less than 5% of his gross income per year). He also received travel support (airfare and lodgings) for attending two Child Psychiatry Meetings (Novartis and Janssen-Cilag) in 2010. The ADHD and Juvenile Bipolar Disorder Outpatient Programs chaired by him received unrestricted educational and research support from the following pharmaceutical companies in the last 3 years: Abbott, Bristol-Myers Squibb, Eli Lilly, Janssen-Cilag, Novartis, and Shire. The other authors report no conflicts of interest.

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