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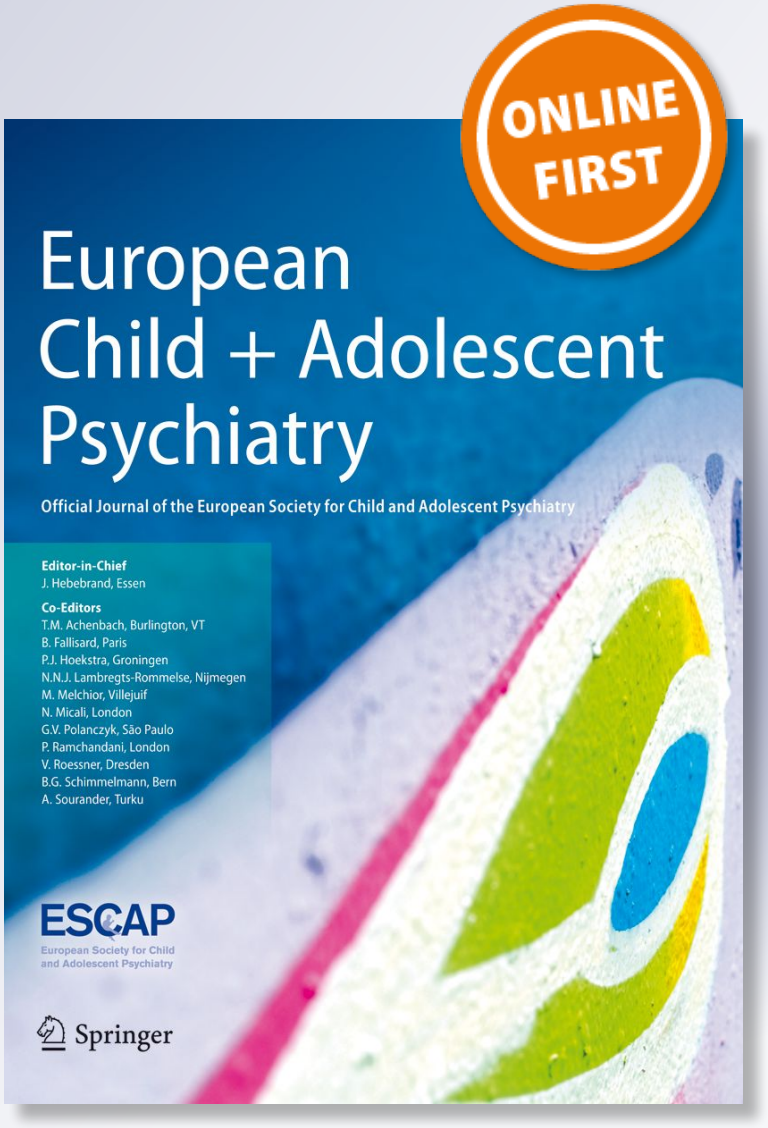

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ORIGINAL CONTRIBUTION

Quality of life and self-esteem in 7-year-old children with familial high risk of schizophrenia or bipolar disorder: the Danish High Risk and Resilience Study-VIA 7—a population-based cohort study

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Abstract

It is well established that children with familial high risk of schizophrenia (FHR-SZ) or bipolar disorder (FHR-BP) have a higher risk of developing mental disorders, however, little is known of to what degree the genetic and environmental vulnerabilities affect the quality of life and self-esteem of these children. We aimed to compare the quality of life and self-esteem between children with FHR-SZ or FHR-BP and controls. We used Danish nationwide registers to retrieve a cohort of 522 7-year-old children with FHR-SZ or FHR-BP and controls. Quality of life was assessed with the 'Health-related Quality of Life Screening Instrument', KIDSCREEN-27, and the scale 'Social Acceptance (Bullying)' from the KIDSCREEN-52. Self-esteem was assessed with the self-report scale 'I think I am'. Assessors were blind to familial risk status of the children. Children with FHR-SZ displayed lower levels of the general quality of life, as well as lower scores on the 'Psychological Well-being' scale and the 'School Environment' scale of the KIDSCREEN-27 compared with controls. Both children with FHR-SZ and FHR-BP reported more bullying victimization compared with controls. Children with FHR-SZ reported lower self-esteem on the total scale of 'I think I am', as well as on the 'Skills and talents', the 'Psychological well-being', and the 'Relationships with others' subscales compared with controls. The findings of lower quality of life and self-esteem in children with FHR-SZ together with more bullying victimization in both familial high-risk groups call for studies on low risk, early intervention strategies towards this group of vulnerable children.

Keywords Schizophrenia · Bipolar disorder · Familial high risk · Quality of life · Self-esteem

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Introduction

Schizophrenia and bipolar disorder are highly heritable illnesses [1]. However, children of parents with schizophrenia and bipolar disorder do not only have a higher risk of developing the concordant disorder of their parents, but of a wide range of psychiatric disorders both in adulthood and during childhood [1–6], as well as lower levels of general functioning [4, 7] and impaired cognition [8–10]. Furthermore, previous studies have reported that children with familial high risk of schizophrenia or bipolar disorder are less likely to live with both biological parents [11] and are more often placed out of home [12].

We have been able to corroborate many of the above-mentioned findings in our own cohort of 7-year-old children with familial high risk of schizophrenia (FHR-SZ) or bipolar disorder (FHR-BP) [13]. The children from both of the two high risk groups showed more signs of psychopathology and lower level of functioning compared with population-based controls [14], and the children with FHR-SZ had impaired motor functioning [15] and impaired cognition in various domains [16]. Additionally, the children from both familial high risk (FHR) groups were not as likely to live with both biological parents as were the controls (Table 1).

All these factors may influence the quality of life (QoL) and self-esteem of these children with familial high risk negatively. QoL and self-esteem represents important concepts because they are of immediate relevance for the children's lives. However, quantitative studies of these children's QoL and self-esteem are sparse [6, 17–24].

We aimed to compare the self-evaluated QoL and self-esteem in young children with FHR-SZ or FHR-BP with controls. Owing to the above-mentioned findings of impairments in numerous domains and disadvantageous environmental circumstances, we hypothesized that children with FHR would report lower QoL and self-esteem compared with controls. In an explorative fashion, we analyzed to what extent differences in QoL and self-esteem between the FHR groups and the controls could be explained by more psychopathology, poorer home environment, higher risk of living in a single-parent household and lower socio-economic status among the children with FHR than the controls.

Methods

The Danish High Risk and Resilience Study-VIA 7 is a cohort study of 522 7-year-old (age range 6.9–8.4 years) children of parents with schizophrenia spectrum disorders (FHR-SZ) or bipolar disorder (FHR-BP) and population-based matched controls (PBC) [13].

Participants

Children with FHR were drawn from the total population of Danish children who turned 7 years old in the study period and who had at least one parent with schizophrenia spectrum disorders or bipolar disorder (Fig. 1). Both biological parents had to be born in Denmark. The cohort was identified by combining the Danish Psychiatric Central Research Register, where inpatient and outpatient psychiatric contacts are registered with the Danish Civil Registration System. Children with at least one biological parent (the index parent) diagnosed with either schizophrenia spectrum disorders (defined as ICD 10-codes: F20, F22 and F25 or ICD 8-codes: 295, 297, 298.29, 298.39, 298.89, 298.99) or bipolar disorder (defined as ICD 10-codes F30 and F31 or ICD 8-codes: 296.19, 296.39) were identified.

Children with FHR-SZ were matched to children from the general population on gender, age and municipality. Children with FHR-BP represented an unmatched group. However, the FHR-BP group was comparable to the two other groups with respect to age and gender.

Procedures

Approval of the study was obtained from the Danish Data Protection Agency. Permission to extract data from the Danish registers to identify the cohort was granted by The Danish Ministry of Health. The Danish Committee on Health Research Ethics received the study protocol for review. However, in accordance with Danish law, the committee decided that ethical approval was not relevant as the study did not involve any intervention or collection of biological tissue samples. Adult participants received oral and written information and written informed consent was obtained. Legal guardians gave written informed consent on behalf of the children.

The questionnaires were read aloud to the children by a group of trained psychologists, medical doctors and nurses, who were blinded to the risk status of the children.

Assessment of quality of life

QoL was assessed with the 'Health-related Quality of Life Screening Instrument', KIDSCREEN-27, a self-report questionnaire which is a short version of the KIDSCREEN-52 instrument [25, 26]. The KIDSCREEN-27 consists of 27 items distributed on five scales measuring different domains of QoL. The scales are 'Physical Well-being', 'Psychological Well-being', 'Autonomy & Parent Relations', 'Social Support & Peers', and 'School Environment'. Each item is rated on a five-point Likert scale. Ten items from the KIDSCREEN-27 questionnaire

Table 1 Background characteristics of the 515 children participating with data on quality of life or self-esteem in the Danish High Risk and Resilience Study-VIA 7 and their biological parents

	FHR-SZ	FHR-BP	PBC	*p* value	FHR-SZ vs. PBC	FHR-BP vs. PBC	FHR-BP vs. FHR-SZ
Children, *N*	197	119	199	–	–	–	–
Female, *N* (%)	92 (46.7)	55 (46.2)	92 (46.2)	0.995[a]	–	–	–
Age at inclusion, mean (SD)	7.8 (0.2)	7.9 (0.2)	7.8 (0.2)	0.089[b]	–	–	–
Two ill parents, *N* (%)	8 (4.1)	< 4	–	–	–	–	–
Any current DSM-IV diagnosis[c], *N* (%) (*N* = 196/118/197)	62 (31.6)	32 (27.1)	23 (11.7)	< 0.0001	< 0.0001	< 0.001	0.398
CBCL total score, mean (SD) (*N* = 189/111/191)	27.3 (21.2)	23.4 (19.7)	17.0 (14.7)	< 0.0001[b]	< 0.0001[b]	0.004[b]	0.084[b]
CGAS score, mean (SD) (*N* = 196/118/197)	68.2 (15.5)	73.6 (14.9)	77.7 (13.5)	< 0.0001[b]	< 0.0001[b]	0.015[b]	0.002[b]
Child's home environment							
Living with both biological parents, *N* (%)	79 (40.1)	62 (52.1)	169 (84.9)	< 0.0001[a]	< 0.0001[a]	< 0.0001[a]	0.038[a]
Living out of home, *N* (%)	11 (5.6)	0	< 4	< 0.001[a]	0.003[a]	0.439[a]	0.009[a]
Living with index parent, *N* (%)	121 (61.4)	83 (69.7)	189 (95.0)	< 0.0001[a]	< 0.0001[a]	< 0.0001[a]	0.134[a]
Living with a single parent, *N* (%) (*N* = 197/119/198)	74 (37.6)	39 (32.8)	21 (10.6)	< 0.0001[a]	< 0.0001[a]	< 0.0001[a]	0.389[a]
PSP primary caregiver[d], mean (SD) (*N* = 194/118/197)	73.2 (13.9)	74.5 (14.1)	84.4 (9.1)	< 0.0001[b]	< 0.0001[b]	< 0.0001[b]	0.367[b]
[e]MC-HOME Inventory score, mean (SD) (*N* = 193/116/196)	45.0 (6.4)	46.7 (4.7)	49.0 (4.3)	< 0.0001	< 0.0001	< 0.001	0.006
Index parents, *N*	195[8]	115	203	–	–	–	–
Female, *N* (%)	107 (54.9)	63 (54.8)	115 (56.7)	0.922[a]	–	–	–
Age at child's birth, mean (SD)	30.2 (6.1)	33.1 (7.0)	32.9 (4.8)	< 0.0001[b]	< 0.0001[b]	0.702[b]	< 0.0001[b]
PSP, mean (SD) (*N* = 155/102/194)	66.2 (15.6)	68.9 (14.1)	84.3 (9.9)	< 0.0001[b]	< 0.0001[b]	< 0.0001[b]	0.109[b]
Employed or studying, *N* (%) (*N* = 183/108/200)	91 (49.7)	60 (55.6)	184 (92.0)	< 0.0001[a]	< 0.0001[a]	< 0.0001[a]	0.336[a]
Education (*N* = 174/108/196)							
Primary/lower secondary, *N* (%)	53 (30.5)	10 (9.3)	7 (3.6)	< 0.0001[f]	< 0.0001[f]	0.982[f]	< 0.0001[f]
Upper secondary, vocational, short-cycle tertiary, *N* (%)	75 (43.1)	44 (40.7)	95 (48.5)				
Bachelor's degree, equivalent or higher, *N* (%)	46 (26.4)	54 (50.0)	94 (48.0)				
Biological non-index parents, *N*	181	113	191				
Female, *N* (%)	81 (44.8)	51 (45.1)	82 (42.9)	0.911[a]	–	–	–
Age at child's birth, mean (SD)	30.9 (6.4)	33.1 (5.4)	32.9 (4.3)	< 0.001[b]	< 0.001[b]	0.829[b]	< 0.001[b]
PSP, mean (SD) (*N* = 161/94/180)	76.4 (14.3)	81.8 (13.1)	85.5 (8.4)	< 0.0001[b]	< 0.0001[b]	0.013[b]	< 0.001[b]
Employed or studying, *N* (%) (*N* = 173/108/187)	131 (75.7)	93 (86.1)	179 (95.7)	< 0.0001[a]	< 0.0001[a]	0.003[a]	0.035[a]
Education (*N* = 173/105/186)							
Primary/lower secondary, *N* (%)	31 (17.9)	5 (4.8)	10 (5.4)	0.002[f]	0.001[f]	0.329[f]	< 0.001[f]
Upper secondary, vocational, short-cycle tertiary, *N* (%)	84 (48.6)	44 (41.9)	88 (47.3)				
Bachelor's degree, equivalent or higher, *N* (%)	58 (33.5)	56 (53.3)	88 (47.3)				

Index parents refer to the biological parents with a diagnosis of schizophrenia spectrum disorder or bipolar disorder. In the population-based control group the index parents refer to the matched biological parents. In the case of siblings; parent information is only included from the first

Table 1 (continued)

included sibling

FHR-SZ children with familial high risk for schizophrenia spectrum disorders, *FHR-BP* children with familial high risk for bipolar disorder, *PBC* population-based controls, *CBCL* child behavior checklist, *CGAS* Children's Global Assessment Scale, measuring children's current level of functioning, *PSP* Personal and Social Performance Scale, measuring current level of psychosocial functioning in adults

[a]Chi square test

[b]One-way ANOVA

[c]Current diagnoses of the children were assessed with the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL)

[d]Primary caregiver: the biologic or non-biologic caregiver who spent the most time with the child

[e]HOME-MC Inventory: The Middle Childhood-Home Observation for Measurement of the Environment Inventory measuring the home environment

[f]Linear by linear association *p* value

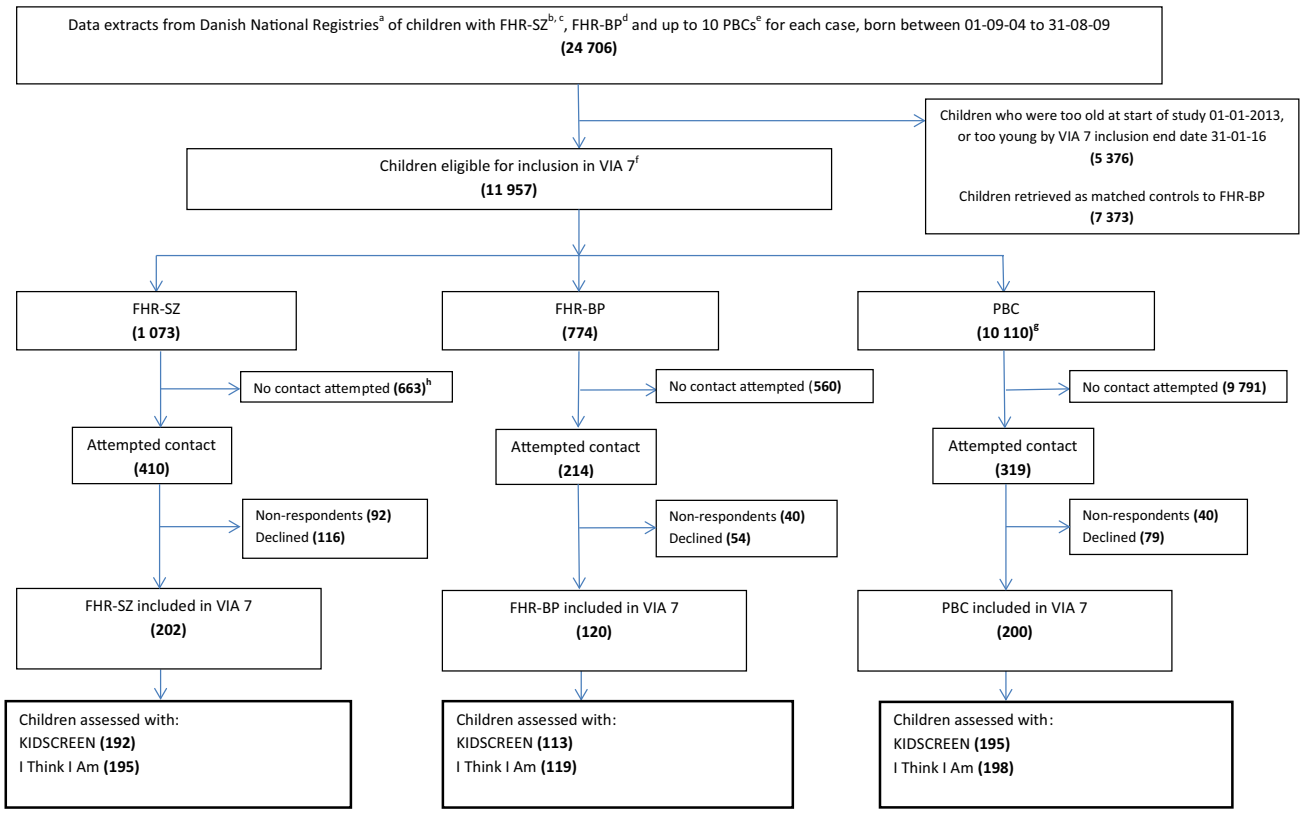

Fig. 1 Flow chart of the recruitment of 522 children in the Danish High Risk and Resilience Study-VIA 7. [a]Danish National Registries: Danish Civil Registration System and Danish Psychiatric Central Research Register. [b]FHR-SZ: children of parents with schizophrenia spectrum disorders. [c]Double diagnosed parents: Parents with diagnoses of schizophrenia and bipolar disorder were assigned to the schizophrenia high risk group as per the ICD-10 hierarchy. [d]FHR-BP: children of parents with bipolar disorder. [e]PBC: population-based control children of parents with no diagnoses of schizophrenia spectrum disorders or bipolar disorder. [f]Research protection: as of May 2011, legislation was enacted to protect individuals' phone numbers from being called for participation in scientific research. Therefore, there were eligible children who were not contacted and enrolled in VIA 7. [g]Selection of controls: up to ten controls were retrieved for each child in the schizophrenia spectrum disorder group and the bipolar disorder group. Controls were matched to cases on gender, municipality and age. The original intent was to only select control cases that were matched to children in the schizophrenia familial high risk group. However, there are 38 BP-controls among the 200 total controls. [h]Definition of contact: first through letters sent to the child's address. If the family did not respond, contact by telephone was attempted (calls and text messages), if a phone number could be found

can be combined into the KIDSCREEN-10 scale. KIDSCREEN-10 is a global QoL measure.

We included the scale 'Social Acceptance (Bullying)' from the KIDSCREEN-52 questionnaire as the KIDSCREEN-27 questionnaire does not contain a scale regarding bullying.

The raw-scores were transformed into international T-values based on Rasch person parameters as described by the KIDSCREEN Group. Higher scores reflect more favorable QoL.

Assessment of self-esteem

The children's self-esteem was assessed with the self-report scale 'I think I am' by Pirjo Ouvinen-Birgerstam [27]. The questionnaire consists of 32 statements which describe how a child sees her-/himself. The child is encouraged to decide whether these statements apply to the child's perception of her-/himself by responding 'yes' or 'no'. Each item is scored as + 1 or − 1, and, therefore, the total score ranges from − 32 to + 32. A higher score reflects a higher self-esteem.

The items are distributed on five scales representing different domains of self-esteem. The scale 'Physical appearance' mainly tells about the child's perception of her/his body both with respect to appearance and physical abilities. 'Skills and talents' informs of the perception of own abilities within e.g. reading, math and artistic skills. 'Psychological well-being' e.g. informs about what emotions the child often feels, e.g. happy, sad or angry. 'Relationships with family' reflects how the child experience the relationship with her/his parents and family, e.g. if the parents have enough time with the child, how the parents feel towards the child and if the family members in general have fun together or argue a lot. 'Relationships with others' mostly reflects how the child perceives her/his relationships with peers, e.g. if the child is being bullied or if the child has many friends. Together the five scales make up a total self-esteem scale.

The Danish version of the 'I think I am' manual provides Danish norms for grouping children in 'low', 'medium' and 'high' self-esteem based on stanine scores of the total scale. However, given the large size and narrow age range of our control group we calculated our own stanine scores based on the control group. Children with stanine scores ≤ 3 (≤ 23% percentile) were classified in the 'low self-esteem' group. Children with stanine scores from 4 to 6 (> 23% percentile to ≤ 77% percentile) were classified in the 'medium self-esteem' group, while children with stanine scores > 6 (> 77% percentile) were classified in the 'high self-esteem' group.

Other measures

Current DSM-IV psychiatric diagnoses of the children were assessed with the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) [28]. The semi-structured interview the Middle Childhood-Home Observation for Measurement of the Environment Inventory (MC-HOME Inventory) [29] was used to assess the quality of the children's home environment. Interviews with the MC-HOME Inventory were carried out in the children's homes. Parental education and employment status were used as an equivalent of socio-economic status. Parental employment was defined as being either in employment (including temporary leave) or following an acknowledged educational program for at least 15 h weekly.

Statistical analyses

Differences between the three groups on socioeconomic, clinical, and home environment characteristics were analyzed with one-way analysis of variance (ANOVA) or chi-square test, as appropriate.

Differences in scores on QoL and self-esteem among the groups were analyzed with separate ANOVA tests followed by Tukey post-hoc pairwise comparisons. The odds ratios (OR) of being in the 'lower self-esteem' group based on the total scale of the 'I think I am' were calculated with logistic regressions. Gender was added as a covariate in all models. In explorative analyses, current DSM-IV diagnosis of the children, home environment, living in a single caregiver household, and parental education and employment status were added as covariates in the models. Differences in missing values of the covariates limits the comparability of p values and estimated mean differences of the various models. Because of the high number of missing values on variables on socio-economic status, we analyzed the effect of socio-economic status separately in a subsample only including children for whom we have information on socio-economic status. Specifically, data from the 'Social acceptance (Bullying)' scale of the KIDSCREEN did not follow a normal distribution, since a large proportion of children had the highest possible score. This is a known problem of the scale. The authors of the KIDSCREEN instrument have reported a ceiling effect of 49.1% on the 'Social Acceptance (Bullying)' scale in a large sample of children from various European countries [26]. Therefore, we conducted a binary sensitivity analysis. Additionally, the subscales of 'I think I am' had very little variation in scores and data showed left-skewed distributions. To display the distributions, medians and ranges are presented in the tables together with means and standard deviations.

Analyses of background data on socio-economic, clinical, and home environment characteristics were done with SPSS Statistics 25. Other calculations were performed in R.

Results

The final cohort consisted of 522 children from 506 different families (Fig. 1). Of the final cohort, 197 children with FHR-SZ, 119 with FHR-BP and 199 controls participated with data on either QoL or self-esteem. The three groups did not differ in terms of age and gender of the children, whereas there were marked differences in clinical and socioeconomic characteristics (Table 1).

Quality of life among the three groups

Children with FHR-SZ (mean 49.6, SD 8.9, $p=0.030$) reported significantly lower QoL on the KIDSCREEN-10 global QoL scale compared with controls (mean 52.2, SD 10.2) whereas children with FHR-BP (mean 51.4, SD 11.1, $p=0.769$) were comparable to controls (Table 2). Children with FHR-SZ also had significantly lower mean scores on the 'Psychological Well-being' scale and the 'School Environment' scale of the KIDSCREEN-27 compared with controls. Children with FHR-BP did not differ significantly from controls on any of the KIDSCREEN-27 scales, though the lower mean score on the 'Psychological Well-being' scale showed a trend towards significance ($p=0.101$). Both children with FHR-SZ (mean 47.5, SD 11.6, $p<0.0001$) and FHR-BP (mean 49.4, SD 10.2, $p=0.004$) had significantly lower mean scores on the 'Social Acceptance (Bullying)' scale from the KIDSCREEN-52 compared with controls (mean 53.4, SD 8.4), meaning that the children from the FHR groups more often reported bullying victimization. Data on the 'Social Acceptance (Bullying)' scale were skewed to the left, with many children having the highest possible score (meaning they did not report to be bullied at all). Therefore, we performed a binary sensitivity analysis, by creating a binary variable stating if the child had the highest possible score or not (the latter corresponding to having endorsed any of the bullying items). Children with FHR-SZ [$N=111$ (58.7%), OR 2.9, CI 1.9–4.5, $p\leq0.0001$] and FHR-BP [$N=59$ (53.2%), OR 2.3, CI 1.4–3.8, $p\leq0.001$] had a significantly higher OR of having endorsed any of the bullying items compared to controls ($N=60$ (32.8%)).

Across all scales except from the 'Social Acceptance (Bullying)' scale, the medians of the groups were roughly comparable, indicating that the differences in means between the FHR-SZ group and controls may be explained by a subsample of children in the FHR-SZ group with very low scores.

When including current diagnosis of the child or home environment in the models, differences between controls and children with FHR-SZ in global QoL (the KIDSCREEN-10 scale), 'Psychological Well-being' and 'School Environment' were no longer significant (Table S1). In the analysis of the subsample with valid responses on socio-economic status variables (Table S2), differences between controls and children with FHR-SZ on 'Psychological Well-being' were no longer significant when parental education and employment were added to the model. Note that differences between controls and children with FHR-SZ in global QoL (the KIDSCREEN-10 scale) ($p=0.095$) and 'School Environment' ($p=0.124$) are not significant in the models only including gender as covariate in the subsample with valid responses on socio-economic status variables. However, including variables on socio-economic status substantially lowers the estimated mean differences between the two groups. Living with a single caregiver did not significantly reduce the estimated mean differences between children with FHR-SZ and controls in these domains. Differences between children with FHR and controls in the 'Social acceptance (Bullying)' scale remained significant in all models.

Self-esteem among the three groups

Children with FHR-SZ [$N=79$ (40.5%), OR 1.8, CI 1.2–2.8, $p=0.005$] had a higher OR of having scores indicating low general self-esteem based on stanine scores compared with controls [$N=54$ (27.3%)], whereas children with FHR-BP did not [$N=36$ (30.3%), OR 1.2, CI 0.7–1.9, $p=0.564$] (Fig. 2).

Children with FHR-SZ had lower mean scores on the total scale of the 'I think I am', the 'Skills and talents' subscale, the 'Psychological well-being' subscale, and the 'Relationships with others' subscale compared with controls (Table 3). However, the FHR-SZ group and the control group had equal medians on the 'Skills and talents' subscale and the 'Psychological well-being' subscale, indicating that the differences in mean scores on these subscales were explained by a subgroup of children with low scores in the FHR-SZ group.

Children with FHR-BP and controls did not differ significantly in mean scores on any of the self-esteem scales, except on 'Relationship with others' in the model including parental socio-economic status.

The differences between children with FHR-SZ and controls on the 'Total score' and 'Skills and talents' scales remained significant when covarying for current diagnosis of the child or living with single caregiver (Table S3), while the differences in total score when covarying for HOME-MC were significant for 'Skills and talents' and only trended towards significance ($p=0.052$) in the 'Total score'. Furthermore, covarying for a current diagnosis of the child or

Table 2 Comparison between children with familial high risk of schizophrenia or bipolar disorder and controls on the quality of life domains of the KIDSCREEN questionnaire

	FHR-SZ					FHR-BP					PBC					ANOVA	FHR-SZ -PBC	FHR-BP-PBC	FHR-SZ-FHR-BP
	N	Mean	SD	Median	Range	*N*	Mean	SD	Median	Range	*N*	Mean	SD	Median	Range	*p*	*p*	*p*	*p*
KIDSCREEN 10 items scale	192	49.6	8.9	49.7	27.8; 83.8	113	51.4	11.1	49.8	33.8; 83.8	195	52.2	10.2	49.8	33.8; 83.8	**0.036**	**0.030**	0.295	0.769
Physical well-being	192	49.7	10.9	49.6	12.1; 73.2	114	49.1	10.3	47.1	30.6; 73.2	196	50.2	10.1	49.6	12.1; 73.2	0.667	–	–	–
Psychological well-being	193	51.3	10.3	50.6	20.6; 73.5	113	51.8	9.6	48.5	34.3; 73.5	195	54.2	8.8	53.1	28.0; 73.5	**0.008**	**0.008**	0.101	0.868
Autonomy and parent relations	190	47.1	9.3	45.2	21.4; 74.4	112	48.4	9.7	46.5	28.6; 74.4	193	48.5	8.6	47.9	31.9; 74.4	0.292	–	–	–
Social support and peers	193	47.8	11.1	46.9	11.2; 66.3	113	49.3	10.0	46.9	19.4; 66.3	195	49.1	10.9	46.9	11.2; 66.3	0.388	–	–	–
School environment	191	53.7	10.9	51.1	23.9; 71.0	113	54.8	11.6	54.4	16.3; 71.0	195	56.8	9.8	54.4	34.8; 71.0	**0.019**	**0.015**	0.269	0.673
Social acceptance (bullying)	189	47.5	11.6	48.1	11.0; 58.8	111	49.4	10.2	48.1	22.4; 58.8	183	53.4	8.4	58.8	25.0; 58.8	**< 0.0001**	**< 0.0001**	**0.004**	0.231

p values significant at the < 0.05 level are marked in bold

Data are presented as *T*-scores. A higher score represents a higher quality of life. *p* values from ANOVA tests and Tukey post hoc pairwise comparisons with gender as covariate

FHR-SZ children with familial high risk for schizophrenia spectrum disorders, *FHR-BP* children with familial high risk for bipolar disorder, *PBC* population-based controls

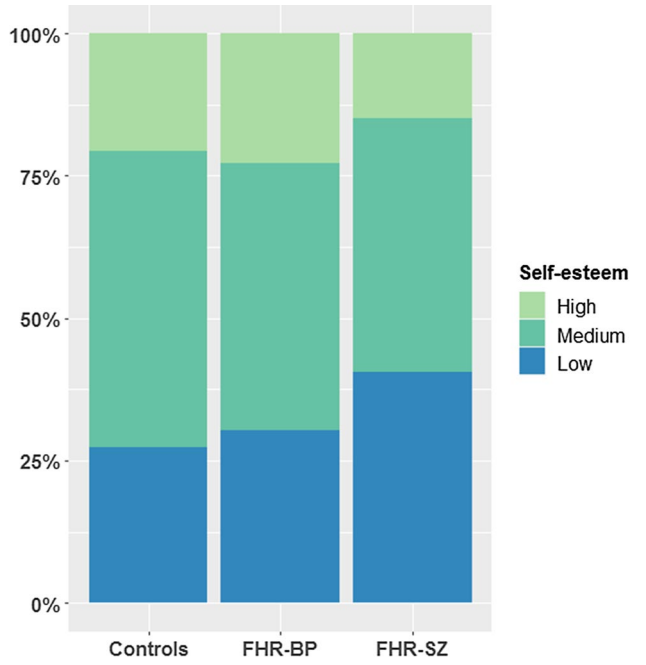

Fig. 2 Proportions of children in the three groups with low, medium or high self-esteem according to stanine scores of the total scale of the 'I think I am' questionnaire. *FHR-SZ* children with familial high risk for schizophrenia spectrum disorders, *FHR-BP* children with familial high risk for bipolar disorder, *PBC* population-based controls

home environment made differences between children with FHR-SZ and controls on the 'Psychological well-being' scale insignificant. When including covariates of parental socio-economic status (Table S4) differences between children with FHR-SZ and controls for this subsample only trended towards significance ($p = 0.087$ for 'Total Score' and $p = 0.071$ for 'Skills and Talents'). Differences between FHR-SZ and controls remained significant across all covarying factors on the 'Relationship with others' scale.

Discussion

In this nationwide cohort study, children with FHR-SZ had significantly lower self-reported QoL and self-esteem compared with controls on several domains. On the other hand, children with FHR-BP did not report significantly lower QoL or self-esteem, except from on the 'Social Acceptance (Bullying)' scale of the KIDSCREEN-52, where both high-risk groups reported significantly more bullying victimization.

Self-evaluated quality of life

In this study, children with FHR-SZ had a more negative perception of their QoL compared with controls. Explorative analysis pointed towards current DSM-IV diagnosis of the

Table 3 Comparison between children with familial high risk of schizophrenia or bipolar disorder and controls on self-esteem domains of the 'I think I am' questionnaire

	FHR-SZ					FHR-BP					PBC					ANOVA	FHR-SZ -PBC	FHR-BP-PBC	FHR-SZ-FHR-BP
	N	Mean	SD	Median	Range	*N*	Mean	SD	Median	Range	*N*	Mean	SD	Median	Range	*p*	*p*	*p*	*p*
Total	195	20.6	8.7	22	− 14; 32	119	22.8	7.5	24	− 6; 32	198	23.6	6.7	26	− 4; 32	**< 0.001**	**< 0.001**	0.640	**0.032**
Physical appearance	196	4.6	1.8	6	− 2; 6	119	4.7	1.8	6	− 2; 6	198	4.9	1.6	6	− 2; 6	0.319	–	–	–
Skills and talents	196	3.1	2.8	4	− 6; 6	119	3.9	1.9	4	− 2; 6	198	4.0	2.2	4	− 4; 6	**< 0.001**	**< 0.001**	0.982	**0.007**
Psychological well-being	197	5.2	3.3	6	− 8; 8	119	5.7	3.0	6	− 4; 8	198	5.9	2.6	6	− 4; 8	**0.041**	**0.040**	0.903	0.214
Relationships with family	196	3.7	2.4	4	− 4; 6	119	4.0	2.1	4	− 6; 6	198	3.9	1.9	4	− 4; 6	0.526	–	–	–
Relationships with others	197	3.9	2.5	4	− 6; 6	119	4.5	2.3	6	− 6; 6	198	4.9	1.8	6	− 4; 6	**< 0.0001**	**< 0.0001**	0.175	0.076

p values significant at the < 0.05 level are marked in bold

Higher scores represent a higher self-esteem. *p* values from ANOVA tests and Tukey post hoc pairwise comparisons with gender as covariate

FHR-SZ children with familial high risk for schizophrenia spectrum disorders, *FHR-BP* children with familial high risk for bipolar disorder, *PBC* population-based controls

children, home environment, and socio-economic status of the parents could be partly explanatory of the observed differences. These findings were expected as the above factors were associated with familial high-risk status in the present study. However, conclusions of causality cannot be drawn due to the cross-sectional nature of this study.

While there exists a bulk of literature on e.g. psychopathology and cognition in children with FHR, only a few quantitative studies have investigated the QoL and self-esteem from the children's own perspective.

One study on QoL in adult daughters of mothers with schizophrenia found significantly lower general QoL compared with controls [17]. Another study on children and adolescents of parents with bipolar disorder showed a reduction in a number of domains of QoL measured with KIDSCREEN-52 compared with controls [6]. Interestingly, the aforementioned study reported a significantly lower QoL in the subscales of 'Physical Well-being', 'Psychological Well-being', 'Social Support and Peers', 'Parent Relations and Home Life', and 'Self-Perception' but, in contrast to our findings, not in the 'Social Acceptance (Bullying)' subscale. These discrepancies may be attributed to the higher mean age (12.5 years, range between 6 and 17 years) of the children in the study by Goetz et al. [6], as reduced QoL may be expressed in different domains at different developmental stages or it may be attributed to cultural differences in risk of bullying or willingness to report it. In contrast, a study of children and adolescents (age range between 10 and 17 years, mean = 14.4 years) of parents with bipolar disorder, including solely offspring without a personal history of psychiatric diagnosis, reported no differences in QoL between these unaffected offspring and controls [19]. This may suggest that the finding of lower QoL in the study by Goetz et al. [6] could in part be mediated through the higher occurrence of psychiatric diagnoses in the children of parents with bipolar disorder.

Self-esteem

We found that children from the FHR-SZ group but not the FHR-BP group displayed lower self-esteem compared with controls. In the explorative analysis, current DSM-IV diagnosis of the children, home environment, and socio-economic status of the parents generally seemed to play a partly explanatory role in the observed differences.

A previous study reported poorer self-concept in adult offspring of parents with schizophrenia compared with controls [20]. Additionally, lower interviewer-rated self-esteem has been reported in preadolescent and teen offspring of parents with schizophrenia compared with controls [24]. In contrast, two studies on self-esteem in adolescents (aged between 13 and 19 years in both studies, mean age 15.9 and 16.2 years, respectively) of parents with bipolar disorder reported no such difference compared with controls [18, 23, 30]. The study by Jones et al. [23] reported less stable self-esteem in adolescents of parents with bipolar disorder compared with controls. However, this finding was not corroborated in the study by Pavlickova et al. [18] where adolescents of parents with bipolar disorder were found to have lower variability in self-esteem compared with controls. Due to sample sizes of less than 30 adolescents of parents with bipolar disorder in each of the two studies, future studies of the fluctuations of self-esteem among children of parents with bipolar disorder with larger sample sizes are warranted. In line with the above discussion of the impact of offspring psychopathology on QoL in children with FHR, a study of offspring (mean age 24.9 years) who had parents with bipolar disorder and who were themselves currently well or in clinical remission from major mood episodes, did not report differences in self-esteem compared with controls [21].

Low self-esteem in adolescents from the general population have been found to be a predictor of poor mental health, criminal behavior and worse economic prospects in adulthood [31]. Furthermore, in a longitudinal study of offspring of parents with depression, high self-esteem predicted a resilient outcome defined by the absence of psychiatric diagnosis (any mood, anxiety, or substance abuse disorder), as well as a consistently high functioning [32]. Therefore, our finding of lower self-esteem among the children with FHR-SZ compared with controls may constitute a risk factor, whereas our findings of self-esteem equal to that of controls in the FHR-BP group may constitute a resilience factor. In line with this finding, a previous study found that higher self-esteem in offspring of parents with bipolar disorder significantly decreased the risk of new onset or recurrent mood episodes in the offspring [21].

Bullying victimization

Both high-risk groups had significantly lower scores than controls on the 'Social Acceptance (Bullying)' scale of the KIDSCREEN-52, indicating that they had experienced more bullying victimization than controls. When controlling for current DSM-IV diagnosis of the children, home environment, living with a single parent, or socio-economic status of the parents, one variable at a time, the differences between the two high-risk groups and the control children on bullying remained significant. This indicates that even after controlling for other variables that might mediate the link between familial high-risk status and unfavorable outcome, the high-risk status was still associated with higher risk of children reporting being bullied.

In contrast to the above findings, only the FHR-SZ group reported lower self-esteem than controls on the 'Relationships with others' scale of the 'I think I am' even though the two scales have overlapping content. It may be because the

'Social Acceptance (Bullying)' scale of the KIDSCREEN-52 has a more narrow focus on bullying, whereas the 'Relationships with others' scale of the 'I think I am' has a broader focus. However, the discrepancies in results regarding the children with FHR-BP make it less clear if children with FHR-BP perceive to be bullied more than controls.

The finding of children with FHR experiencing more bullying deserves particular attention as bullying victimization is known to be an independent risk factor of psychopathology [33, 34]. Additionally, bullying has also been found to be associated with psychotic-like experiences [35], suicidal ideation [33, 34], and substance use

[34]. As having a familial high risk of severe mental disorders constitutes an important risk factor for developing psychopathology on its own, the finding that children with familial high-risk report more bullying victimization is of great concern as the combined risk factors may increase the risk even further. This finding suggests the need for greater efforts in prevention bullying of children with FHR.

Strengths and limitations

The use of Danish nationwide registers to identify the cohort enabled us to recruit children with FHR-SZ and FHR-BP whose parents were not necessarily in an acute phase of their illness, which might affect the current QoL and self-esteem negatively. Therefore, these results are generalizable to the QoL and self-esteem among children with FHR during every-day life and not only during the acute states of the parents' illnesses. The large sample of children with a narrow age range is also a strength. Furthermore, the inclusion of both children with FHR-SZ and FHR-BP enabled the comparison of QoL and self-esteem between those two FHR groups.

A limitation of the study is that the KIDSSCREEN questionnaires are designed for children and adolescents aged from 8 to 18 years, while the mean age of the children in this study was 7.8 years. However, we read the questions aloud to the children and explained the content, when needed. Additionally, we pilot tested the questionnaire on children within the age group of the study prior to data collection and the overall impression was that most of the children understood the questions well. Another limitation is that the FHR-BP group only consisted of 119 children, and, therefore, did not allow us to test possible differences between children with FHR-BP and controls with the same power as the comparisons between children with FHR-SZ and controls. Some of the nonsignificant differences between FHR-BP and controls might then have been significant had the sample been larger. Finally, there is an overlap between the subdomains and some of the items of the KIDSCREEN questionnaire and the 'I think I am' questionnaire. Hence, QoL and self-esteem in this report should be interpreted as overlapping domains.

Finally, an important limitation of the explorative analyses was that sample sizes differed across models due to differences in missing values among the covariates. This limits the comparability of p values and estimated mean differences in the various models.

Conclusions

The findings that children with FHR-SZ themselves report lower QoL and self-esteem already at age seven together with the result that both FHR groups report more bullying victimization are alarming. The findings that the higher occurrence of DSM-IV diagnoses in the FHR-SZ group seemed to play a partly explanatory role in the observed differences in QoL and self-esteem between children with FHR-SZ and controls highlight the importance of easy access to high-quality mental health care for children with FHR-SZ at a young age. This study did not find lower self-esteem in children with FHR-BP, but future studies should consider measuring fluctuations in self-esteem among children with FHR-BP rather than solely level of self-esteem alone.

Poor self-esteem and bullying victimization constitute risk factors for developing mental disorders, that can potentially be reduced through intervention. Future studies on the long-term impact of these risk factors for developing mental disorders in children with familial risk are needed. Furthermore, studies on developing intervention strategies targeting QoL, self-esteem and bullying victimization in children with FHR-SZ are warranted.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

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