

Editorial

“A healthy mind in a healthy body”: The challenges of physical health in first episode psychosis.

ARTICLE HISTORY: Received 4 March 2026 / Published Online 8 Jun 2026

Cite this article as: Ntouros E, Dimitrakopoulos S, Mavreas V, Bozikas V-P. “A healthy mind in a healthy body”: The challenges of physical health in first episode psychosis. *Psychiatriki* 2026, 37:1-2
<https://doi.org/10.22365/jpsych.2026.001>

Individuals suffering from psychotic disorders have increased comorbidity with chronic organic disorders and reduced life expectancy compared to their healthy peers. Particularly, individuals diagnosed with schizophrenia have a life expectancy 10–20 years shorter than average.¹ The main factor contributing to this increased comorbidity and mortality from natural causes is cardiovascular diseases resulting from higher rates of metabolic syndrome (MetS), obesity, diabetes mellitus, sedentary lifestyle, poor diet, and smoking.² MetS, specifically, is defined by the coexistence of a combination of risk factors such as high blood pressure, high blood glucose levels, excessive fat around the waist, high levels of triglycerides, and low levels of high-density lipoprotein (HDL).

These aggravating factors occur more frequently in individuals with psychosis than in control groups from the very onset of symptoms. For example, the prevalence of MetS was found to be 13.2% higher than in the general population in patients who had never taken antipsychotic drugs and presented with first episode psychosis (FEP).³ Similarly, blood pressure, waist circumference, and fasting glucose have been reported to be slightly higher in antipsychotic-naïve ultra high risk (UHR) individuals, while lower HDL levels have been demonstrated in FEP adolescents who have never taken medication.⁴

Moreover, initiating treatment with second-generation antipsychotics is associated with rapid and significant weight gain, depending on the specific drug, within the first three months of treatment.⁵ This indicates that between 33% and 61% of individuals with FEP experience clinically significant weight gain, defined as an increase of $\geq 7\%$ of initial body weight within the first 12 weeks of treatment, and certain parameters of MetS progressively deteriorate over the first year of treatment.^{6,7}

The above findings have prompted the implementation of various interventions, both pharmaceutical and non-pharmaceutical, in individuals with FEP, aiming at reducing the burden associated with antipsychotic use, which remains the therapeutic standard despite its side-effect profile. These interventions are extended beyond medication-related adverse effects and target other parameters that increase cardiometabolic risk, such as poor diet, lack of physical activity, tobacco and alcohol use, and inadequate physical care.⁸ The effectiveness of these interventions varies, but combining them and implementing them in an organized framework with a holistic approach appears to be the optimal choice. In Greece, this type of comprehensive care is delivered through Early Intervention Services (EIP), where the physical health of patients with FEP is prioritized as a core treatment objective. This is achieved through detailed and systematic recording of medical data, monitoring the key parameters in accordance with international guidelines, and collaborating with primary care services.

International guidelines suggest best practices for recording and treating MetS, and attempts are now underway to estimate the likelihood of MetS emerging from the early stages of psychosis.⁹ One example of such best practice guidelines is the “Lester positive cardiometabolic resource” algorithm, which is the version used in the UK by the iphys initiative, summarizing key indicators and target values for young individuals with psychosis.¹⁰ Tables of the algorithm list the parameters for lifestyle habits (smoking, diet, activity), obesity (weight, BMI, waist circumference), hypertension, glucose levels, and lipid markers. Baseline measurements for each parameter are categorized into three levels: high risk, medium risk, and a target range to be achieved. In this way and with guidance on recommended monitoring frequency (i.e., blood pressure measured at baseline and every three months thereafter), the tool constitutes a practical resource for assessing physical health problems and planning appropriate interventions.

Enhancing the physical health of individuals with FEP requires adopting best practices and providing information and cooperation with primary health care providers within the framework of EIP, as well as with all mental health professionals involved in patient care. Coordinated practice is essential, as physical health outcomes substantially influence both the course of the illness and patients' functional recovery.

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Research article

Assessment of psychosocial well-being, psychological distress, and financial burden in patients with chronic and recurrent dermatophytosis.

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ARTICLE HISTORY: Received 15 October 2024 / Revised 23 January 2025 / Published Online 5 August 2025

Cite this article as: Imthiaz NF, Hegde SP, Sathyanath S, Shenoy MM, Pinto M, Razak A. Assessment of psychosocial well-being, psychological distress, and financial burden in patients with chronic and recurrent dermatophytosis, *Psychiatriki* 2026, 37:3-9
<https://doi.org/10.22365/jpsych.2025.015>

ABSTRACT

Chronic dermatophytosis, a persistent fungal infection lasting over six months, is a significant public health concern. The study examines the psychosocial well-being, psychological distress, and financial burden experienced by patients with chronic and recurrent dermatophytosis. A hospital-based cross-sectional design was employed, enrolling 316 patients from a tertiary care dermatology outpatient department in South India over six months. Participants completed questionnaires of quality of life (Dermatology Life Quality Index, DLQI), financial burden (Financial Burden and Worry questionnaire, FBW), and psychological distress (Hospital Anxiety and Depression Scale, HADS). Findings revealed a substantial impact on the quality of life, with 71.6% of participants reporting a very large effect as per DLQI scores. Factors such as itching, embarrassment, and daily routine disturbances were significantly associated with higher DLQI scores. Financial challenges were prominent, with 56.6% of participants delaying treatment due to financial constraints and 30.7% reducing overall expenses. The economic burden was further evident as 26.2% used savings, 12.9% borrowed money, and 16.1% reduced essential healthcare spending for other family members. Psychological distress was significant, with 31.6% and 29.7% of participants showing abnormal anxiety and depression scores, respectively, on HADS. A strong positive correlation was observed between DLQI scores, anxiety, and depression, highlighting the interdependence between disease severity and mental health. This study underscores the need for a holistic approach to managing chronic dermatophytosis that addresses not only medical but also psychosocial and financial aspects. Integrating affordable treatment options, public health awareness campaigns, and psychological counselling can significantly alleviate the burden on affected individuals. These findings provide critical insights for clinicians and policymakers to design comprehensive care strategies to improve patient outcomes and quality of life.

KEYWORDS: Chronic dermatophytosis, dermatology life quality, financial burden, psychological distress, anxiety, depression.

Introduction

Chronic dermatophytosis, which is the fungal infection caused by dermatophytes lasting for more than 6 months, has emerged as one of the most arduous and cumbersome diseases prevalent in our current Indian clinical scenario. Misinformation, lack of awareness, wrong medications, trivialization by patients, and low socioeconomic status are some of the most common causative factors for the same. Due to the obvious visi-

bility of these lesions, it has a deep-seated repercussion on the self-perception and social interactions of the individual, severely impacting their emotional, physical, and social well-being. With the rampant spread of dermatophytosis within the community, more upscale drugs with longer duration have become the mainstay of treatment, which is imposing a hefty financial burden on our patients. Along with the physical discomfort and pruritus, patients often feel depressed, anxious, and

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stigmatized, especially in their social and sexual relationships.¹ The incidence of this disease has increased enormously in our country in these years.² The incidence of dermatophytosis is not easy to estimate due to a dearth of community-based surveys, which resulted in a wide range of prevalence of 6.09% in South India to 61.5% in North India.³ Several studies have examined individual aspects of the burden associated with dermatophytosis. For example, Das et al. (2022) conducted a cross-sectional study assessing psychological morbidity and found that approximately 30% of chronic dermatophytosis patients suffered from anxiety and depression, with impaired quality of life.⁴ Similarly, Narang et al. (2019) reported high rates of psychological morbidity in patients with superficial cutaneous dermatophytosis, emphasizing the link between disease visibility, stigma, and emotional distress.⁵ Patel et al. (2020) explored both psychosocial and financial impacts in a smaller sample, noting that a significant proportion of patients delayed or interrupted treatment due to financial constraints.¹ Furthermore, Varshney et al. (2020) highlighted that chronic dermatophytosis considerably affects patients' daily activities, social interactions, and emotional stability, while Salari et al. (2022), in a meta-analysis, confirmed elevated rates of anxiety and depression among patients with skin diseases, including dermatophytosis.^{6,7}

However, while prior studies have individually explored psychological morbidity, quality of life impairment, or financial stress among dermatophytosis patients, few have comprehensively assessed these domains together in a single study population. Moreover, very limited data exist from South India, where socio-economic and healthcare access conditions may differ significantly. Previous studies either lacked a structured evaluation of financial burden using standardized instruments or focused on a narrower set of psychosocial variables. There is also a lack of detailed analysis correlating disease severity (body surface area involved) with psychological distress, financial strain, and quality of life outcomes.

Therefore, the present study addresses these critical gaps by systematically assessing psychosocial well-being (anxiety, depression), quality of life, and financial burden in patients with chronic and recurrent dermatophytosis attending a tertiary care center in South India. By analyzing the interrelationships between clinical severity, psychological distress, and financial hardship, this study aims to provide a more integrated and holistic understanding of the full impact of chronic dermatophytosis on affected individuals. The findings are intended to inform not only clinical practice, but also healthcare policy and public health interventions aimed at comprehensive patient-centered care. The aims of our study were: 1) To examine the overall impact of chronic and recurrent dermatophytosis on patients, including its effects on quality of life, financial burden, and psychological distress. 2) To examine the associations of quality of life, financial burden, and psychological distress with the demographic and clinical characteristics of patients with chronic and recurrent dermatophytosis. 3) To examine the associations of financial burden and psycho-

logical distress with quality of life.

Materials and methods

Participants and Procedures

A hospital-based cross-sectional study was conducted at the outpatient department of Dermatology, Venereology, and Leprosy in a tertiary care center in South India. The study was conducted after obtaining ethical clearance from the Ethics Committee of the hospital and according to the Declaration of Helsinki (1995) as revised in Edinburgh (2000) for a period of 6 months from April 2022 to September 2022. Three hundred and sixteen patients were enrolled in the study. All patients of both genders above 18 years, diagnosed to have chronic dermatophytosis (presence of glabrous tinea for six months or longer, continuous, or recurrent, with or without treatment) or recurrent dermatophytosis (recurrence of the glabrous tinea after 4 weeks of stopping treatment following clinical cure) were included. Patients with other concomitant skin disorders, on medication for other illnesses, pregnant and lactating females, patients with any major illness in the preceding 3 months, and any pre-existing psychiatric illnesses were excluded. Written informed consent was taken from all the study subjects. A demographic history of the patient was obtained, including age, sex, total family members, monthly family income, educational status, and occupation, after obtaining informed consent. A clinical history including the onset, duration of disease, area of involvement (body surface assessment, BSA, was calculated), and family history of similar complaints was taken. An extensive treatment history, including topical, over-the-counter medications, herbal/home remedies, etc., was taken. Patients were asked to fill out three questionnaires in the language of their choice (English/ Kannada/ Malayalam). In case the patient was unable to comprehend the questionnaires, the interview method was used.

Instruments

The Dermatology Life Quality Index (DLQI) questionnaire was used to measure the impact of skin diseases on the quality of life of an affected person.⁸ After obtaining necessary permissions, the Kannada and Malayalam translated versions were created according to the ISPOR guidelines.⁹ It consists of 10 questions, such as symptoms, embarrassment, shopping, home care, clothes, social and leisure, sport, work or study, close relationships, sex, and treatment. These questions evaluated the skin problems that had affected life over the previous week. Scoring of each question is from 0 to 3. The higher the score, the more quality of life is impaired: 0-1, no effect on the patient's life; 2-5, small effect; 6-10, moderate effect; 11-20, very large effect; 21-30, extremely large effect.

The Financial Burden and Worry questionnaire (FBW) consists of 9 questions that assess how chronic or recurrent dermatophytosis or its treatment is affecting their finances.^{1,10} After obtaining necessary permissions, the Kannada and Malayalam translated versions were created according to the ISPOR guidelines.⁹ The financial burden was calculated as the sum of selected responses. Financial worry was self-reported by the patient on

a scale of 1 to 5, with 1 being "some worry" and 5 being "very much worried."

The Hospital Anxiety and Depression Scale (HADS) is a self-assessment questionnaire for detecting states of anxiety and depression in the setting of a hospital outpatient department.¹¹ After obtaining necessary permissions, the Kannada and Malayalam translated versions were created according to the ISPOR guidelines.⁹ It has seven items, each for depression and anxiety subscales. The scores for each aspect range from zero to three, with three denoting the highest anxiety or depression level. A total score of >8 points out of a possible 21 indicates clinically significant symptoms of anxiety or depression, and the anchor points of each subscale are: 0-7, normal; 8-10, borderline abnormal; 11-21, abnormal.

Statistical Analysis

Comparisons between categorical variables (e.g., gender, education level, income group, support status) and DLQI severity groups were performed using Pearson's Chi-square test. When expected cell counts were less than five, Fisher's Exact test was used instead. Associations between continuous or ordinal variables (e.g., DLQI scores, financial burden scores, worry scores, anxiety scores, depression scores) were analyzed using Spearman's rho correlation coefficient, given the non-parametric nature of the data. Comparisons of mean financial burden scores across demographic subgroups (e.g., age groups, family size, income levels, education levels, body surface area involvement) were conducted using Welch's t-test (for two groups) and Welch-adjusted one-way ANOVA (for more than two groups), as Levene's test indicated unequal variances across groups, making the use of standard Student's t-test inappropriate. A p-value of <0.05 was considered statistically significant in all analyses. Data were analyzed using SPSS version 28.

Results

Table 1 denotes the demographic data of study participants. Males outnumbered females, and a majority of the participants were in the age group of 18 to 40 years. Participants who were dependent and self-dependent were comparable. About 36.1% of the participants were educated up to high school, and about 34.8% of the participants were educated beyond high school. About 63.3% of participants had a family size of up to 9 members, and about 62.7% were earning less than INR 15,000. The BSA (in %) of less than or equal to 10 was observed among 84.2% of participants. In addition, 45.6% of participants had been suffering from the diseases for the last 1 to 2 years, respectively.

Table 2 shows the impact of dermatophytosis on the quality of life. A total of 90 (28.4%) participants reported some effect on quality of life based on DLQI scores, while 226 (71.6%) participants experienced a very large effect, as expected from the method of group classification. Dermatophytosis thus had a considerable impact on the quality of life for the majority of participants. Since the DLQI groups were defined based on cumulative scores across individual domains, higher levels of symptoms such as itching, embarrassment, difficulty in

socialization, and impacts on social and leisure activities and daily routine were inherently more frequent among participants with a very large effect. Therefore, these differences reflect the criteria used for classification rather than independent associations.

Table 3 shows the effect of dermatophytosis on financial burden and psychological stress. Around 56% of participants had to delay their treatment due to financial problems, about 30.7% of the participants had to cut down their expenses, and another 26.2% used all their savings. In addition, 16.1% of participants ended up cutting down expenses on healthcare for their family members. Furthermore, 12.9% of participants had to take a loan and/or borrow money for their treatment. About 31.4% of participants worried about their illness. About 15.9% of participants had abnormally high anxiety scores, and 13.9% of participants were categorized as having borderline abnormal depression, and 70.3% had normal scores. About 21.2% of participants had abnormally high depression scores, and 10.4% of participants were categorized as borderline abnormal, and 68.4% had normal scores.

Table 4 shows the correlation between quality of life, financial burden, and psychological stress. There was a high positive correlation between total DLQI scores and anxiety and between anxiety and depression scores, respectively. In addition, a moderate positive correlation existed between financial burden and worry and between DLQI score and depression score. Furthermore, there was a low positive correlation between financial burden and anxiety and depression scores.

Table 5 shows the associations of DLQI with HADS and FBW. It was found that among those with a very large effect on quality of life, 43.4% of participants had higher anxiety scores compared to 2.2% of participants who had some statistically significant effect. In addition, among those with a very large effect, 37.6% of participants had higher depression scores compared to 10% of participants who had some statistically significant effect. In addition, the financial burden was statistically significantly higher among participants who had a very large effect on quality of life.

Discussion

In the present study, the financial and psycho-social burden of patients suffering from chronic and recurrent dermatophytosis is established. Most chronic diseases will have an impact on the quality of life (QOL) of the person. Skin diseases being visible will have direct consequences on the self-consciousness of the person, their feeling of looking not attractive, and thereby social withdrawal, which may add to psychological and emotional stress.¹²

DLQI is a simple, feasible, and valid tool employed to assess the QOL of a person suffering from any dermatological disorder. Chronic and recurrent dermatophytosis is a rapidly spreading disease; thus, it requires a more elaborate study. Estimating the impact of disease on QOL and the psychological status of the person may be especially useful to understand the disease burden. The impact of dermatophytosis on the DLQI score varied among the present study population, with a mean score

Table 1. Distribution of study participants according to sociodemographic details.

Sociodemographic details		Frequency (n=316)	Percentage (%)
Gender	Male	162	51.3
	Female	154	48.7
Age group (in years)	18-30	114	36.1
	31-40	100	31.6
	41-50	62	19.6
	51-60	34	10.8
	>60	6	1.8
Support	Dependent	156	49.4
	Self-supportive	160	50.6
Educational level	Illiterate	14	4.4
	Primary and higher primary	78	24.7
	Up to 10 th standard	114	36.1
	10 th std and above	110	34.8
Family size	1-4	94	29.7
	5-9	200	63.3
	≥10	22	7.0
Monthly income (In Rs)	<15,000	198	62.7
	15,000-30,000	84	26.6
	>30,000	34	10.8
BSA (%)	≤10	266	84.2
	11-30	48	15.2
	>30	2	0.6
Duration of disease	6 months - 1 year	102	32.3
	1 to 2 years	144	45.6
	More than 2 years	70	22.2

Table 2. Distribution of study participants according to DLQI score and its impact on individual quality of life (only with impact).

Quality of life component	Some effect N = 90 (Scores 0 to 10) N (%)	Very large N = 226 (Score ≥ 11) N (%)	χ^2	p
Itching	67 (74.4)	226 (100)	62.2	<0.001
Embarrassment	47 (52.2)	218 (96.5)	93.07	<0.001
Daily routine	15 (16.7)	183 (81)	113.7	<0.001
Choice of clothing	8 (8.9)	140 (61.9)	72.77	<0.001
Social and leisure activity	6 (6.7)	174 (77)	129.8	<0.001
Sports	6 (6.7)	69 (30.8)	20.5	<0.001
Loss of work or study	2 (2.2)	111 (49.1)	61.6	<0.001
Socialization	15 (16.7)	180 (79.6)	108.04	<0.001
Sexual life	5 (5.6)	143 (63.6)	86.8	<0.001
Time spent on treatment	4 (4.4)	130 (57.5)	74.2	<0.001

Table 3. Distribution of study participants according to financial burden and worry, and HADS score.

Financial burden		Frequency (n=316)	Percentage
Use savings		83	26.2
Borrow money or take out a loan		41	12.9
Could not make payments on other bills		30	9.5
Cut down on spending for food and clothes		36	11.4
Cut down on spending for health care for other family members		51	16.1
Cut down on recreational activities		46	14.6
Cut down on expenses in general		97	30.7
Delay/interrupt treatment due to financial problems		179	56.6
Cost was the barrier		179	56.6
Worry	1	58	18.3
	2	51	19.0
	3	60	16.5
	4	52	14.9
	5	47	31.4
HADS score			
Depression score			
Normal	0-7	22	70.3
Borderline abnormal	8-10	44	13.9
Abnormal case	11-21	50	15.8
Anxiety score			
Normal	0-7	216	68.4
Borderline abnormal	8-10	33	10.4
Abnormal case	11-21	67	21.2

Table 4. Spearman's Rank correlation coefficients between DLQI, FBW, and HADS scores.

	DLQI Total	Financial burden	Worry	Anxiety	Depression
DLQI Total	1.000	0.43*	0.47*	0.71*	0.62*
Financial burden		1.000	0.64**	0.45*	0.45*
Worry			1.000	0.50*	0.48*
Anxiety				1.000	0.86*
Depression					1.000

*p<0.05 is statistically significant.

of 11.11 ± 7.308 . The present finding correlated with the previous study conducted by Patel et al., where the mean DLQI score was 12.25.¹ The skin lesion and itching associated with dermatophytosis may have an impact on the social well-being of the affected person, thus on the quality of life.

QOL, though, is a subjective factor, has a more com-

plex understanding and expression, and may be a mixture of many attributes like the individual's self-esteem, social life, physical and mental health, and economic and psychological well-being.¹³ Embarrassment, itching, and disturbance of daily activities were reported to be more common factors affecting the QOL of patients with dermatophytosis in a previous study.¹⁴ In our study, the

Table 5. Associations of DLQI with HADS and FBW.

		Some effect N (%)	Very large effect N (%)	Total N	χ ²	p
Anxiety	Normal	88 (97.8)	128 (56.6)	216	50.3	<0.001
	Abnormal	2 (2.2)	98 (43.4)	100		
Depression	Normal	81 (90)	141 (62.4)	222	23.4	<0.001
	Abnormal	9 (10)	85 (37.6)	94		
		Mean ± SD	Mean ± SD	df	Welch t	
Financial Burden		1.19 ± 1.8	2.83 ± 2.3	206.5	44.5	<0.001

components of quality of life were found to be adversely affected by dermatophytosis. However, itching, embarrassment, and daily routine were the components that had an exceptionally large impact. Similar findings were found in a study conducted by Varshney et al., assessing the quality of life in chronic dermatophytosis, where domains of symptoms and feelings, which included embarrassment and itching, followed by the disturbance in daily activities.⁶ In an earlier Eastern Indian study on the QOL of patients suffering from tinea corporis, the QOL was adversely affected by the disease.¹⁵ In our study, female participants had a larger effect on DLQI compared to male participants, which was also corroborated in another study.¹⁶

Added financial burdens arising from the cost of treatment may also have an impact on the QOL of the individuals, as analyzed in previous studies. The present study is in agreement with this statement, where slightly more than half of the study population agreed that there was a delay in the treatment due to financial problems, and they also said that the cost of treatment was a barrier. More than half of the present study population had a monthly income of less than Rs 15,000/-. Meeting the other expenses and spending for this treatment was difficult because the treatment may have to be continued for a long duration. Similar findings were seen in a study where financial burden showed a notable correlation between the financial burden experienced and factors such as the estimated cost of prior treatments, concerns about financial matters, and the DLQI.¹ The financial strain experienced by participants was evident in their coping mechanisms, with 26.2% using savings, 12.9% borrowing money, and 16.1% cutting down on essential expenses such as healthcare for other family members. These findings echo those of Salari et al.,⁷ who highlighted the economic hardship faced by dermatophytosis patients in low- and middle-income countries and its detrimental effect on treatment adherence.

Moreover, financial burden was significantly correlated with psychological distress, with participants experiencing greater financial strain reporting higher levels of worry, anxiety, and depression. These findings highlight the cyclical relationship between economic hardship and emotional well-being, where financial difficulties exacerbate stress and hinder effective disease management.

The psychological burden of dermatophytosis was another key finding of this study. Anxiety and depres-

sion were highly prevalent, with 31.6% and 29.7% of participants, respectively, scoring above the threshold for clinical concern on the HADS. These rates are consistent with Narang et al.'s findings, which demonstrated that dermatophytosis patients often experience significant psychological distress due to the persistent and visible nature of the disease.⁵

The strong correlations between DLQI scores and both anxiety and depression highlight the interdependence of psychological well-being and QOL in dermatophytosis patients. This relationship underscores the need to integrate mental health support into dermatological care. Psychological counselling, as emphasized by Das et al.,⁴ has been shown to improve coping strategies and reduce stigma, thereby enhancing patients' ability to manage their condition.

These findings align with previous research studies that have also established connections between chronic dermatophytosis and its impact on various aspects of well-being.^{1,5} These included studies that have explored the relationship between disease severity and impaired quality of life, financial stress, and psychological distress. Together, these investigations emphasize that chronic dermatophytosis not only affects physical health but also exerts a substantial toll on emotional and financial well-being. Earlier studies showed that social and psychological support helped the patients to overcome the disorders, such as anxiety and depression associated with dermatophytosis, and brought improvement in their coping strategies.¹⁷

Addressing these challenges requires a holistic approach that integrates medical, psychological, and financial interventions. Early diagnosis, affordable treatment options, and psychological support should be prioritized to improve outcomes. Public health initiatives, such as awareness campaigns and subsidized treatment programs, can help reduce stigma and alleviate financial barriers.

Among several limitations of our study, the most important was that the translated versions of the study tools have not yet been psychometrically tested.

Conclusion

In conclusion, the study sheds light on the substantial psychological and financial burdens that individuals grappling with chronic dermatophytosis often face. These burdens extend beyond the physical symptoms, encompassing various aspects of their quality of life.

The intricate interplay between the disease's visible manifestations, the emotional toll of dealing with a chronic condition, and the financial strain resulting from treatment costs underscores the need for a comprehensive care approach. By closely monitoring treatment adherence, healthcare providers can optimize therapeutic outcomes and alleviate physical discomfort. However, the significance of providing psychological support should not be underestimated. By addressing the emotional challenges tied to the condition, patients can experience improved mental well-being, enhanced self-confidence, and better overall quality of life.

Acknowledging the financial implications and offering guidance on cost-effective treatment options or financial assistance programs can help alleviate the economic burden. This holistic approach recognizes that

treating chronic dermatophytosis goes beyond medical management; it involves fostering resilience, restoring confidence, and improving the overall life experience for patients.

Ultimately, the insights gleaned from this study emphasize that by addressing the psychological, emotional, and financial dimensions of chronic dermatophytosis, healthcare practitioners can make a meaningful impact on the lives of patients, enhancing their quality of life and overall well-being. It may be concluded that psychological and financial burdens were experienced by the patients of chronic dermatophytosis. Close monitoring of the patients regarding treatment adherence and psychological support may improve the QOL of these patients.

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Research article

Prevalence and severity of depression in patients with chronic viral hepatitis in Kazakhstan.

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ARTICLE HISTORY: Received 29 July 2024 / Revised 31 January 2025/ Published Online 5 August 2025

Cite this article as: Polukchi TV. Prevalence and severity of depression in patients with chronic viral hepatitis in Kazakhstan. Psychiatriki 2026, 37:10-17
<https://doi.org/10.22365/jpsych.2025.019>

ABSTRACT

Depression is a common issue among patients with chronic viral hepatitis. Living with chronic hepatitis can create chronic stress, which is a known risk factor for developing or exacerbating depression. This stress can be related to concerns about health, the effectiveness of treatment, and the social implications of the illness. Neuropsychological scales and assessments can objectively measure the severity of depression and other mental health issues in these patients. The presence of depression was studied in 233 patients with chronic viral hepatitis, who were treated in the Infectious Disease Hospital of Shymkent and the Regional Hepatology Centre of Shymkent in the period from March 2021 to January 2022. All patients were examined using the Hamilton Depression Rating Scale (HDRS) to identify the presence of depression. Of the 233 patients with chronic viral hepatitis, 38.3% had mild depressive disorder, 2.7% of patients had scores indicating moderate depressive disorder, and 2.7% of patients were found to have major depressive disorder. Multivariate analysis showed that older age, the form of chronic viral hepatitis, higher viral load, and female gender were most strongly associated with depression. Depression is a common manifestation in patients with chronic viral hepatitis and can lead to cognitive impairments such as difficulties with concentration, memory problems, and decreased executive function. In the context of chronic hepatitis, which may already affect liver function and metabolic processes, untreated depression can exacerbate these cognitive deficits.

KEYWORDS: Chronic viral hepatitis, fibrosis, cirrhosis, depression, Kazakhstan.

Introduction

Chronic viral hepatitis, particularly hepatitis B (HBV) and hepatitis C (HCV), is recognized as a systemic disease that can manifest with a variety of extrahepatic manifestations. These manifestations can affect different organ systems and develop at various times after the initial infection. Chronic viral hepatitis can lead to neurological symptoms and disorders involving the central nervous system (CNS).¹ Extrahepatic manifestations of chronic viral hepatitis can develop at different times after infection. Some may present early in the course of the disease, while others may manifest later, often in the context of advanced liver disease or as immune-mediated complications.¹ Studies have indicated that approximately 50% of individuals chronically infected with HCV may experience cognitive dysfunction.

This can range from mild cognitive impairment to more severe cognitive deficits.¹ The most common associated symptoms observed in patients with chronic viral hepatitis are anxiety and depression, chronic fatigue, mood changes, cognitive impairment, and sleep disturbances.^{2,3} Depression is a significant concern among patients with chronic viral hepatitis, particularly hepatitis B and hepatitis C. The prevalence of depression in this patient population can vary widely across studies and regions, as noted by different authors. Some studies indicate that approximately 37% to 83% of patients with chronic hepatitis C may experience symptoms of depression.² In another study, after excluding inactive HBsAg carriers, a significantly higher prevalence of depression was found among patients with HCV (35.9%) compared to patients with HBV (19.8%) and healthy participants (11.3%).⁴

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However, after excluding inactive HBsAg carriers, no differences in the prevalence of depression were observed between patients with HBV and HCV. Among patients with HCV, smoking and alcohol consumption increased the frequency of depression, whereas factors such as viral load, fibrosis stage, HCV genotype, and sex did not have a significant impact. These data suggest that depression in patients with chronic viral hepatitis may be related not only to the infection itself but also to the chronic nature of the disease, stigmatization, and perceptions of adverse outcomes.⁴ It has been found that unemployment is associated with more pronounced symptoms of depression and anxiety. However, no association was found between the duration of the disease, the mode of hepatitis C transmission, the presence of cirrhosis, and the levels of depression or anxiety.⁵

One study assessed liver fibrosis using elastography. It was found that patients with mild depression had varying degrees of liver fibrosis, including F_0 (no fibrosis), F_1 (mild fibrosis), and F_2 (moderate fibrosis). Meanwhile, all patients with moderate depression exhibited advanced fibrosis (F_3 — significant thickening of liver tissue with possible signs of cirrhosis). The F_4 stage of fibrosis, indicating cirrhosis, was also noted, representing a severe stage of the disease with irreversible tissue damage. According to the multiple regression model, the degree of liver fibrosis was a statistically significant independent predictor of depression.⁶ In another similar study, a higher prevalence of depression was also found in patients with chronic hepatitis B compared to healthy individuals who were not HBsAg carriers.⁷ Chronic hepatitis C is accompanied by a variety of extrahepatic manifestations, with the central nervous system often being involved. However, the pathophysiological mechanisms of this process are not yet fully understood.⁸ HCV infection is often associated with depression and cognitive impairments, which may be due to HCV neuroinvasion and/or chronic inflammation. Proteins have previously been identified in the brain, and it has been suggested that blood leukocytes capable of crossing the blood-brain barrier may provide the virus with access to the CNS.⁸ The results suggest that chronic hepatitis C virus infection negatively affects brain functions, with both viral replication in the mononuclear cells of peripheral blood and the state of immune activation playing an important role in this process.^{1,9}

In chronic hepatitis C infection, the innate immune system remains persistently activated, accompanied by elevated levels of proinflammatory cytokines (IL-6, TNF- α , IL-1 β) in peripheral blood.¹⁰ These mediators either cross the blood-brain barrier or transmit signals via the vagus nerve, triggering microglial activation. The resulting neuroinflammatory response within the central nervous system shifts tryptophan metabolism toward

the kynurenine pathway, leading to a decrease in serotonin levels and an increase in the concentration of the neurotoxic metabolite quinolinic acid. This biochemical shift disrupts the functioning of prefrontal-limbic networks responsible for emotional regulation and cognitive processes. Clinically, this manifests as “brain fog,” pronounced fatigue, and sleep disturbances, while the cumulative effect of these factors significantly increases the risk of depression even in the early stages of liver fibrosis. Conversely, depressive symptoms may exacerbate systemic inflammation and reduce treatment adherence, negatively impacting the course of chronic hepatitis C. This underscores the bidirectional relationship between mood disorders and chronic HCV infection.¹⁰

Studies show that depression and/or anxiety disorders associated with human immunodeficiency virus (HIV) or HBV infection may be due to common biological mechanisms. Specifically, microglial activation and cytokine release have been identified as potential pathogenetic mechanisms. Patients with HIV and depression also show an altered balance between quinolinic and kynurenic acids, indicating glutamatergic dysfunction.¹¹ The production of inflammatory cytokines and impaired regulation of the cellular immune response contribute to chronic inflammation, delayed healing, and reduced functional abilities in patients with chronic hepatitis B.¹¹ A shift in the balance of type 1 and type 2 cytokines may play a role in the immune pathogenesis associated with HBV, with depression and anxiety being considered immune-modulating factors. Cytokines also provoke hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis, which is often observed in patients with HIV/HBV suffering from depression or anxiety disorders.¹¹

In patients with chronic viral hepatitis, depression can arise from a combination of factors related to the disease itself, its physical manifestations, and the psychosocial impact it imposes.¹² Researchers have observed that patients with chronic viral hepatitis, even in the early stages with minimal liver inflammation and few comorbidities, may experience more severe symptoms of depression and fatigue compared to the general population.^{13,14} The prevalence of depression in chronic HCV infection is estimated to be 1.5 to 4.0 times higher than in patients with chronic HBV infection.¹⁵

Gender also plays a significant role in the development of mental disorders, including depression. Research consistently shows that women have a higher incidence of depression compared to men. This may be due to biological differences, sociocultural factors, and differences in stress reactions and ways of coping. It is important to consider gender specificity in the assessment and treatment of psychological problems in this category of patients.^{16,17} Patients with mental disorders,

including depression, may engage in behaviors that increase their risk of HCV infection. Individuals with depression may face challenges in adhering to treatment regimens for HCV, such as antiviral therapy. Poor adherence increases the risk of treatment failure or relapse after achieving a sustained virologic response, which can lead to reinfection.¹⁸ Research indicates that patients with chronic hepatitis B often experience a higher intensity of depression compared to healthy individuals, and this burden tends to increase as the disease progresses. Elderly patients with chronic HBV may experience the greatest severity of depression. Aging itself can bring additional challenges, such as comorbidities, social isolation, and changes in physical health, which can further exacerbate depressive symptoms.¹⁹ One study examined the relationship between maternal HBV infection and postpartum depression. In a cohort of women with no personal or family history of mental illnesses, the presence of HBV infection was not statistically significantly associated with depression compared to the absence of this infection.²⁰

It was also found that Chinese ethnicity and lack of physical activity are associated with a higher risk of depression, regardless of antiviral treatment status. At the same time, physical activity has a protective effect, especially in patients receiving such treatment. Employment was associated with a lower risk of depression among Asian Americans taking medication, while among those not taking medication, younger age and being married reduced the risk of depression. These findings highlight the importance of physical activity as a protective factor for patients with chronic hepatitis B, particularly among those receiving antiviral treatment.²¹

The persistence of significant depressive disorders in patients even during successful 12-month antiviral therapy highlights a crucial aspect of managing chronic hepatitis, particularly hepatitis B and hepatitis C. Despite achieving sustained virological response (SVR), some patients may continue to experience significant depressive symptoms. This suggests that the psychological impact of chronic hepatitis, its treatment, and associated factors may persist beyond viral suppression.²² Studies have reported a wide range of incidence rates of depression during interferon treatment, ranging from 0% to 37%.¹⁸ Nearly half of patients undergoing antiviral therapy may experience transient depression during treatment. This form of depression is directly linked to the use of interferon-based therapies, which were historically associated with neuropsychiatric side effects, including mood disturbances. Despite discontinuation of therapy, treatment-induced depression may persist beyond six months in approximately one in ten patients. Factors contributing to prolonged depression in these cases may include pre-existing mental health condi-

tions, underlying psychosocial stressors, and the residual impact of interferon treatment on the CNS.^{14,23,24,25} This study aimed to analyze the factors contributing to the development of depression in patients with chronic viral hepatitis, as well as to investigate potential relationships between depression, stages of liver fibrosis, and the treatment of chronic viral hepatitis (including interferon and other therapeutic interventions). This study provides new insights into the psychosocial aspects of chronic viral hepatitis, such as the impact of depression on treatment adherence, viral resistance, and treatment success. We also examine the duration of depression, which persists even after achieving an SVR and successful completion of antiviral therapy.

Materials and methods

Sample

The study protocol was approved by the Experimental Ethics Committee of the Kazakh Medical University of Continuing Education and Asfendiyarov Kazakh National Medical University (Protocol № 3 of 17.03.2020, Protocol № 3 of 16.03.2021) and Asfendiyarov Kazakh National Medical University (Protocol № 7 of 30.05.2022).

The study included 233 individuals with chronic viral hepatitis who were receiving inpatient treatment at the Infectious Disease Hospital in Shymkent city and visiting the Shymkent Regional Hepatology Centre during routine outpatient visits. Patients were aged over 18 years, and all participants provided written informed consent before participating in the study. The study took place between March 2021 and January 2022.

Participants in the study were aged over 18 years. The reasons for exclusion of patients from the study on chronic viral hepatitis were clearly defined and aimed at ensuring the integrity and focus of the research. Exclusion criteria based on our description: age less than 18 years, pregnancy, cancer, acute viral hepatitis, mental disorders, intoxication with psychotropic drugs, and alcoholism. These exclusion criteria are designed to enhance the study's internal validity by controlling for factors that could confound the relationship between chronic viral hepatitis and its clinical outcomes.

Tools

To assess the severity of depressive symptoms, the 17-item Hamilton Depression Rating Scale (HDRS) was used. The scale includes the following ranges for depressive severity: 0-7 points: normal (no depressive symptoms), 8-13 points: mild depressive disorder, 14-18 points: moderate depressive disorder, 19-22 points: severe depressive disorder, and more than 23 points: extremely severe depressive disorder. In the present study, we employed the Russian-language version of the Hamilton Depression Rating Scale (HDRS), which is tradition-

ally applied in clinical practice throughout Russia and other Russian-speaking CIS countries. At this time, however, no publication detailing a formal validation of this Russian-language HDRS version is available in international scientific databases. There is, nevertheless, a study that examined the HDRS in a Belarusian population and utilized a Belarusian version of the scale.²⁶ Given the linguistic and cultural proximity of Belarusian and Russian, as well as the historically shared clinical diagnostic approaches, the findings of this work can be partially extrapolated to Russian-language practice. Nevertheless, we acknowledge the need for further research aimed at formally validating the Russian-language HDRS and identifying this issue as a limitation of our study.

Statistical analysis

Data analysis was conducted using SPSS statistical software, version 22.0, developed by SPSS Inc., Chicago, IL, USA. Summary statistics, such as mean and standard deviation, were calculated for quantitative variables. This provides a concise overview of the central tendency and variability of the data. We used non-parametric tests (Kruskal-Wallis and Mann-Whitney U-test) since the preliminary analysis indicated that the data did not follow a normal distribution. A multiple regression analysis was also conducted to assess the influence of independent variables on the severity of depressive symptoms. All p-values were two-tailed, and statistical significance was defined as $p < 0.05$.

Results

Demographic data: Most participants in the study were female, comprising 52.4% (N=222) of the total sample. The average age of the participants was 47.14 years, with a standard deviation of ± 14.1 years. Types of chronic viral hepatitis: 42.1% of participants (98 individuals) had chronic hepatitis C virus, 16.7% of participants (41 individuals) had chronic HBV infection, and 17.1% of participants (40 individuals) had chronic hepatitis D virus. Liver Cirrhosis: A subset of participants had liver cirrhosis, categorized by etiology: 2.1% (5 patients) had liver cirrhosis due to HBV infection, 14.2% (33 patients) had liver cirrhosis due to HCV infection,

7.7% (18 patients) had liver cirrhosis due to co-infection with HBV and HDV. The study included 233 individuals with chronic viral hepatitis: 66 people, which accounts for 28.3% of the total participants, were residents of Shymkent city; the majority of participants, 167 people (71.6%), came from various districts within Turkestan oblast: Suzak, Sairam, Kazygurt, Arys, Saryagash, Maktaral, Tolebi, and Baudibek. Based on the age distribution of patients with chronic viral hepatitis in your study, here's the breakdown: 18-19 years: 4 patients (1.7%), 20-29 years: 25 patients (10.7%), 30-39 years: 50 patients (21.5%), 40-49 years: 52 patients (22.3%), 50-59 years: 38 patients (16.3%), 60-69 years: 59 patients (25.3%), 70-79 years: 5 patients (2.2%). Patients had varying durations of chronic viral hepatitis, ranging from 1 month to 20 years or more. The patients were divided into stages of liver fibrosis: group F_0 included 47 patients (20.2%), group F_1 - 52 patients (22.7%), group F_2 - 40 patients (17.2%), group F_3 - 38 patients (16.3%), group F_4 included 56 patients (23.6%).

Based on the results of our study involving 233 patients with chronic viral hepatitis and their Hamilton Depression Rating Scale (HDRS) scores, the breakdown of depressive disorder severity: 89 patients (38.3%) had HDRS scores indicating mild depressive disorder, 6 patients (2.7%) were found to have moderate depressive disorder, 6 patients (2.7%) had HDRS scores indicating severe depressive disorder.

The data presented shows the prevalence of depressive disorders at different stages (F_0 to F_4) in a group of patients: mild depressive disorder: stage F_0 - 10.6%, stage F_1 - 12.3%, stage F_2 - 25%, stage F_3 - 31.6%, stage F_4 - 45.5%; moderate depressive disorder: stage F_0 - 2.1%; stage F_1 - 3.5%, stage F_2 - 5%, stage F_3 - 23.7%, stage F_4 - 18.2%; severe depressive disorder: stage F_2 - 2.5%, stage F_3 - 5.3%, stage F_4 - 5.3%. These percentages indicate the proportion of patients at each stage of liver fibrosis (F_0 to F_4) who were observed to have different severity levels of depressive disorder.

The mean Hamilton Depression Rating Scale (HDRS) scores for patients at each stage of fibrosis are as follows: stage F_0 - 5.1 ± 2.1 ; stage F_1 - 6.4 ± 2.8 ; stage F_2 - 7.7 ± 3.7 ; stage F_3 - 10.3 ± 5.0 ; stage F_4 - 11.2 ± 5.4 (Table 1). These

Table 1. Prevalence of depressive disorders and mean scores on the Hamilton Depression Rating Scale (HDRS) at different stages of liver fibrosis (F_0 to F_4) among patients with chronic viral hepatitis.

Fibrosis Stage	Mild Depressive Disorder (%)	Moderate Depressive Disorder (%)	Severe Depressive Disorder (%)	N (233)	Mean HDRS Score ($\pm$ SD)	ANOVA F (df)	p (HDRS)
F_0	10.6	2.1	-	47	5.1 ± 2.1	12.35 (4, 228)	<0.001
F_1	12.3	3.5	-	53	6.4 ± 2.8		
F_2	25.0	5.0	2.5	40	7.7 ± 3.7		
F_3	31.6	23.7	5.3	38	10.3 ± 5.0		
F_4	45.5	18.2	5.3	55	11.2 ± 5.4		

scores indicate the average severity of depressive symptoms among patients at different stages of liver fibrosis. As the fibrosis stage progresses from F_0 to F_4 , there is a noticeable increase in the mean HDRS score, suggesting a higher severity of depressive symptoms associated with more advanced liver disease.

The results of the analyses indicate that several factors significantly influence the total scores of the Hamilton Depression Rating Scale (HDRS) in patients with chronic viral hepatitis. Age was found to be significantly associated with HDRS scores ($p < 0.000$). This suggests that older patients may have different levels of depressive symptoms compared to younger patients. The specific form of chronic viral hepatitis (hepatitis B and

hepatitis C) was also significantly associated with HDRS scores ($p < 0.000$). The stage of fibrosis, as categorized by F_0 to F_4 , was significantly associated with HDRS scores ($p < 0.000$). This indicates that as liver fibrosis progresses, depressive symptoms tend to increase. Gender was found to be significantly associated with HDRS scores ($p < 0.000$). This suggests that there may be differences in depressive symptomatology between male and female patients with chronic viral hepatitis. These results highlight that age, type of chronic viral hepatitis, stage of fibrosis, and gender are important factors that influence the severity of depressive symptoms in patients with chronic viral hepatitis (Table 2).

The multiple regression analysis revealed that several

Table 2. Mean Hamilton Depression Rating Scale (HDRS) scores in patients with chronic viral hepatitis.

Variable	N	Mean	HDRS		
			t / F	df (between/within)	p
Age (years)					
-18-19	4	4,0±1,2	4.402	6 / 226	0.000
-20-29	25	6,0±3,2			
-30-39	50	6,8±3,2			
-40-49	52	8,4±5,1			
-50-59	38	9,2±5,0			
-60-69	59	9,7±4,0			
-70-79	5	7,6±3,1			
Gender					
-Male	111	7,0±4,1	71.87	- / 11.42	0.000
-Female	122	9,0±4,5			
Disease					
-Chronic viral hepatitis B	44	6,4±2,8	19.61	2 / 230	0.000
-Chronic viral hepatitis C	132	7,5±4,0			
-Chronic viral hepatitis D	57	11,0±5,0			
Duration of the disease					
-Up to 1 year	28	7,4±4,3	2.154	4 / 228	0.096
-Up to 5 years	109	7,9±4,1			
-6-10 years	73	8,1±4,2			
-11-20 years	19	10,7±5,2			
-More 20 years	4	9,8±5,4			
Serum ALT levels					
-Less than 40 U/L	34	7,7±4,5	96.00	- / 19.45	0.464
-More than 40 U/L	199	8,2±4,4			
Serum AST levels					
-Less than 40 U/L	47	7,6±4,1	96.39	- / 16.30	0.391
-More than 40 U/L	186	8,3±4,4			
Viral load					
-Norm	131	7,2±3,5	55.39	- / 10.96	0.005
-Excessive	102	9,4±5,1			
Fibrosis (kPa)					
- F_0	47	5,1±2,1	20.25	4 / 228	0.000
- F_1	53	6,4±2,8			
- F_2	40	7,7±3,7			
- F_3	38	10,3±5,0			
- F_4	55	11,2±5,4			

variables are correlated with the presence of depression in patients with chronic viral hepatitis. Age ($p < 0.001$) was identified as a significant factor associated with the presence of depression. This suggests that older age may contribute to higher levels of depressive symptoms in these patients. The specific form of chronic viral hepatitis (such as hepatitis B and hepatitis C) ($p < 0.000$) was found to be significantly correlated with depression. Different forms of hepatitis may have varying impacts on mental health, potentially influencing the presence and severity of depressive symptoms. Viral load ($p < 0.000$), a measure of the amount of virus present in the blood, was also identified as a significant variable related to depression. Higher viral loads may be associated with increased likelihood or severity of depressive symptoms in patients with chronic viral hepatitis. These findings indicate that age, the type of chronic viral hepatitis, and viral load are important factors to consider when assessing and managing depression in patients with chronic viral hepatitis (Table 3).

Discussion

There have been several studies investigating depression in patients with chronic hepatitis, but most of them have assessed quality of life in conjunction with depressive disorders.^{27,28} Given the limited data available in existing literature, the objective of the present study was to conduct a cross-sectional screening for depression among patients with chronic viral hepatitis. In this prospective cohort study, the primary focus was to investigate the prevalence of depression symptoms among patients with chronic viral hepatitis who were receiving treatment at the Shymkent City Infectious Diseases Hospital and the Shymkent Regional Hepatology Center. When considering a large sample size in a study investigating depression symptoms among patients with chronic viral hepatitis, several clinical significances were identified.

The differences in the incidence of depressive symp-

toms between our study (32.6%) and the study by Li et al.²⁹ (53.1%) are attributed to several factors, including sample size and possibly other methodological differences. As noted, the study by Li et al. had a larger sample size of 1995 patients compared to our study. Differences in the characteristics of the study populations between the two studies could also contribute to variations in the reported rates of depression symptoms. The use of different assessment tools to measure depression symptoms can lead to variability in reported rates. Our study used the Hamilton Depression Rating Scale (HDRS), while Li et al. have used a different tool or criteria.²⁸

In another similar study by Jiang et al, which included 517 patients with chronic viral hepatitis, the incidence of depression in patients with chronic viral hepatitis was 58.3%, which was also related to the large number of patients included in the study.²⁷ It is likely that the differences in the final results of the study are due to the use of different tools to assess depression. The Hamilton Depression Rating Scale (HDRS), which is the most common tool for assessing depression, was used in this study.

In the study by Sarkar et al. involving 181 patients with chronic hepatitis C, the findings indicated that women were significantly affected by clinically significant depression.³⁰ In the study conducted by researchers from Greece, several significant associations were identified regarding depression in patients with chronic viral hepatitis. Similar to findings in other studies, being female was strongly associated with depression. Women may experience different psychosocial stressors, societal pressures, and hormonal influences that contribute to higher rates of depression compared to men with chronic viral hepatitis. The study found that advanced stages of liver disease were linked to higher rates of depression. Patients with more severe liver disease may also face greater uncertainty about prognosis and treatment outcomes, which can contribute to psychological distress. Elevated viral load was also identified as a sig-

Table 3. Multiple regression analysis of factors affecting depression in patients with chronic viral hepatitis at different stages of fibrosis (N=233).

Variable	β	SE	t	df	p
Age	-0.125	0.110	-1.136	224	0.001
Gender	0.451	0.121	3.727	224	0.828
Duration of the disease	0.232	0.052	4.462	224	0.835
The form of chronic viral hepatitis	0.099	0.147	0.673	224	0.000
Serum ALT levels	-0.344	0.133	-2.586	224	0.820
Serum AST levels	-0.344	0.071	-4.845	224	0.464
Viral load	-0.442	0.068	-6.500	224	0.000
Stage of fibrosis	0.366	0.068	5.382	224	0.277

nificant factor associated with depression.³¹

Depression, in addition to affecting treatment adherence, can have a significant impact on treatment response and the effectiveness of therapeutic regimens, including through neuropathological mechanisms.³² Studies show that depression can disrupt the neurochemical balance in the CNS, which, in turn, may influence the immune response and reparative processes in the body. For example, activation of inflammatory pathways and changes in neurotransmitter levels, such as serotonin, dopamine, and glutamate, can affect the perception and effectiveness of therapy. Neuropathological changes associated with chronic inflammation may impair the body's ability to respond effectively to antiviral therapy, reducing its clinical effectiveness. Furthermore, depression may contribute to increased stress levels and activation of the hypothalamic-pituitary-adrenal (HPA) axis, which, as shown in several studies, can also negatively affect treatment outcomes. Therefore, it is important to consider depression not only as a factor affecting treatment adherence but also as a potential barrier to achieving optimal therapeutic results, requiring a comprehensive approach in the treatment of patients with chronic viral infections.^{32,33}

One of the significant limitations of the present study is the lack of direct assessment of cognitive impairment in patients with chronic viral hepatitis. Although associations between the degree of liver fibrosis and the severity of depressive symptoms were identified, standardized neuropsychological tests were not employed in this study. Such tools could have revealed cognitive impairments, which are frequently associated with both depression and chronic somatic conditions. Incorporat-

ing assessment instruments such as the MoCA (Montreal Cognitive Assessment) or the MMSE (Mini-Mental State Examination) in future research would allow for a more comprehensive evaluation of patients' neuropsychological status and provide a clearer understanding of the relationship between depression and cognitive functioning in the context of chronic viral hepatitis.

Conclusion

Depression is a common manifestation among patients with chronic viral hepatitis, significantly affecting their quality of life and overall well-being. Our study highlights several factors associated with depression in patients with chronic viral hepatitis, such as advanced age, female gender, hepatitis type, and viral load. These findings underscore the importance of addressing both the physical and psychological health of patients, emphasizing the need for screening, early detection, and appropriate management of depression. It is important to recognize that while antidepressants are commonly used for treating depression in these patients, clinicians must be cautious about potential hepatotoxicity. Some antidepressants may cause liver injury, and while there is no guaranteed way to prevent this, early detection and prompt cessation of the medication can minimize the severity of the reaction. Antidepressants are not associated with an increased risk of liver cancer, and may even correlate with a reduced risk, although more robust evidence is needed. The management of chronic viral hepatitis should include a comprehensive approach that addresses both mental and physical health to improve patient outcomes.

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Research article

Borderline Personality Features Scale for Children - 11: Psychometric properties in a Greek early adolescent clinical sample from a community child and adolescent mental health service.

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ARTICLE HISTORY: Received 12 May 2025 / Revised 17 July 2025/ Published Online 20 December 2025

Cite this article as: Koullourou I, Kotsis K, Salum GA, Sharp C, Tsalamaniotis E, Karagiannopoulou E, Hyphantis T, Mantas C. Borderline Personality Features Scale for Children - 11: Psychometric properties in a Greek early adolescent clinical sample from a community child and adolescent mental health service. *Psychiatriki* 2026, 37:18-27.
<https://doi.org/10.22365/jpsych.2025.028>

ABSTRACT

Borderline personality disorder (BPD) is a severe mental health condition typically identified in adolescence. We aim to investigate the factor structure, internal consistency, item analysis, convergent validity, and diagnostic accuracy of the Greek version of the Borderline Personality Features Scale for Children-11 (BPFSC-11). A sample of 112 early adolescents aged 11 to 14 years was recruited from an outpatient community child and adolescent mental health service. Confirmatory Factor Analysis was used to explore the fit of the unidimensional model to our sample. Reliability was assessed using the omega coefficient, and regression analysis was employed to evaluate convergent validity with the dysregulation profile of psychopathology, as measured by the Youth Self Report (YSR). Item analysis was assessed via Item Response Theory, while criterion validity was evaluated against clinical evaluation using the ROC curve. We found that BPFSC-11 did not fit the data well, while a 9-item version provided a good fit (RMSEA = 0.058, CFI = 0.986, TLI = 0.982). Reliability was strong ($\omega = 0.81$). Convergent validity was demonstrated, as adolescents with high scores on the dysregulation profile of the YSR had statistically significantly higher summed scores on the BPFSC. The ROC curve analysis suggested high diagnostic accuracy (AUC=0.86). Sensitivity at the optimum cut-off point of 26 was found to be 0.88, while specificity was 0.75. Our study presents evidence for the reliability and validity of the BPFSC and provides a cut-off point for its use in outpatient clinical settings to timely identify adolescents with high borderline personality traits.

KEYWORDS: Borderline personality, community child and adolescent mental health service, early adolescence, psychometrics.

Introduction

Borderline personality disorder (BPD) is a severe mental health condition characterized by identity problems, instability of interpersonal relationships, and emotional dysregulation.¹ Recent evidence suggests that traits of

BPD (BPTs) typically start in adolescence²⁻⁴ and a noticeable proportion of adolescents evolve to present BPD in adulthood.⁵ BPD affects 2-3% of adolescents in the community and is associated with poor outcomes such as problems in school and work, difficulties in friendships

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and romantic relationships, increased service use, and high-risk behaviors. This disorder is particularly prevalent in outpatient mental health services, affecting approximately 11% - 22% of patients⁶⁻¹⁰ and in inpatient services affecting up to 33%⁶⁻⁹ of patients. Furthermore, some studies suggest the prevalence of BPD is increasing over time,^{11,12} particularly in girls.¹³ Therefore, having reliable tools to assess BPD is essential to continue to advance research for adolescents with BPTs.

One of the most used tools assessing borderline features is the Borderline Personality Features Scale for Children (BPFS-C). This tool was developed by Crick et al.¹⁴ and measures key domains such as affective instability, identity problems, negative relationships, and self-harm behaviors. The BPFS-C has shown adequate validity, reliability, and consistency, with features assessed demonstrating moderate stability over time. The authors of the original scale provided support for the construct validity, as the indicators of borderline pathology based on the developmental psychopathology model, such as emotional sensitivity and aggression, were tracked together with BPTs over a period of one year.¹⁴ In addition, Sharp et al.¹⁵ demonstrated concurrent validity of BPFS-C by providing evidence that youth with borderline features have poorer clinical and psychosocial functioning. As the only dimensional tool specifically developed for screening BPD in children aged 9 years and older, the BPFS-C serves as a valuable resource for researchers and clinicians working to identify and understand borderline personality features in this age group.

The BPFS-C original instrument consists of 24 items in a 4-factor structure. However, Sharp et al.¹⁶ found that this structure was not supported in an adolescent community sample. Using Item Response Theory, they found evidence for a shorter unidimensional version, consisting of 11 items (BPFS-11) with good reliability (Cronbach's $\alpha = 0.85$). This shorter version of BPFS-11 has been translated and validated in various languages, indicating the relevance of assessing BPTs in different countries and cultures.¹⁷⁻²³

Despite its widespread use, there are still important questions to be addressed regarding the BPFS-C 11-item factor structure and adequacy of the item pool. The Italian version²⁰ was tested in a community sample. While it demonstrated acceptable reliability overall, item 3 ('My feelings are very strong') exhibited appropriate factor loadings only in specific populations, not across all groups. Second, the Portuguese validation presented with adequate reliability but with a unidimensional structure of a 10-item, excluding item 11 ('Lots of times, my friends and I are really mean to each other:'). Third, the Turkish validation study²³ also supported a unidimensional 10-item scale, but with the exclusion of item 3. Therefore, the ideal item pool for the instrument is still a focus of important empirical examination.

Furthermore, cultural context significantly influences the experience, expression, and reporting of psychopathological symptoms.^{24,25} Evidence also suggests that cross-cultural differences affect the perceived utility of emotions and emotion regulation—both central constructs in borderline personality disorder (BPD).²⁶ Cross-cultural studies have demonstrated that adolescents from different cultural backgrounds report varying levels of anxiety and depressive symptoms.²⁷ For instance, Greek adolescents have been shown to exhibit distinct patterns of anxiety compared to their Irish counterparts.²⁸ These differences are further reflected in general psychopathology research, where relevant assessment instruments have been standardized for the Greek population.²⁹ Additionally, the diagnostic criteria for personality disorders explicitly state that such disorders involve "an enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual's culture," underscoring the critical role of cultural context in diagnosis.³⁰ This cultural dimension further underscores the importance of examining the item pool of the scale to ensure its relevance and sensitivity across diverse cultural contexts.

The present study aimed to test the factor structure, reliability (internal consistency), item analysis, and convergent validity (in relation to the dysregulation profile of psychopathology) of the BPFS-11 in an outpatient clinical sample comprised of early adolescents. Given the controversies in the literature regarding the item pool, we tested the BPFS 11-item version, as well as two different ten-item versions, one excluding item 3, and one excluding item 11, and eventually a nine-item version excluding items 3 and 11. Moreover, we aimed to establish the criterion validity by examining how well it discriminates patients with BPTs and explore its diagnostic accuracy in identifying adolescents with clinically meaningful BPTs. We hypothesized that BPFS will be a reliable tool that measures BPTs, and we expected that establishing a cut-off score will consequently help clinicians to early detect those traits, given the total gap of tools for BPTs in Greece.

Methods

Participants

All children aged 11-14 years old who sought a psychiatric assessment in a Community Child and Adolescent Mental Health Service between June 2022 and September 2024 were invited to participate in the study. Exclusion criteria were the inability to read and write in Greek and the presence of psychotic symptoms and moderate and lower levels of intellectual developmental disability. The sample was composed of 112 (out of 124 invited; participation rate: 90.3%) early adolescents aged 11 to 14 years (mean = 12.8, SD=1.16). There were 63 girls (56.3%) and 48 boys (43.7%). Adolescents were

assessed by an experienced child and adolescent psychiatrist (with 20 years of clinical experience and trained in psychodynamic psychotherapy), and they were requested to fill out the study questionnaires. Those who have presented with symptoms of borderline personality disorder were also assessed for BPD features' stability over time and across situations. In case the features from the medical history were evident in the long term, the child and adolescent psychiatrist classified those adolescents as "having high BPTs" based on the clinical assessment. To minimize potential bias, the child psychiatrist who conducted the clinical assessment was blinded to the BPFSC scores. All parents and adolescents were informed about the purpose of the study, and they gave consent in written and verbal respectively. Ethical approval was granted by the Scientific Research Committee of the University General Hospital of Ioannina [approval number 2/28-01-2021].

Instruments

Borderline Personality Features Scale – Children – 11: The instrument was developed¹⁶ to assess BPTs in the adolescent population aged 9 and older, and derived from a longer 24-item version.¹⁴ It consists of 11 items reflecting core features of BPD, such as affective instability, identity problems, and negative relationships. Items are rated on a 5-point Likert scale ranging from "not true at all" to "always true". The BPFSC-11 yields a total score (range: 11–55) measuring the overall level of borderline characteristics; the higher the BPFSC-11 total score, the greater the intensity of BPD features. Permission to use the original scale was granted by its author. We then used the Greek version, which had been translated and culturally adapted by another research team using the back-translation method.³¹

Youth Self Report – ASEBA: The Greek version of the Youth Self Report (YSR) was used.^{32,33} YSR is a 112-item questionnaire that assesses child and adolescent emotional and behavioral function, namely internalizing and externalizing behaviors. The items are rated on a three-point Likert scale and are divided into 8 subscales. For the current study, we used the Dysregulation Profile (DP), which can be computed in various ways based on the Anxious/Depressed, Attention Problems, and Aggressive Behavior syndrome scales.³⁴ The DP is defined categorically with various definitions in the literature, ranging from strict to less strict criteria^{34–43} and is based (a) on T-scores ≥ 70 on the Anxious/Depressed, Attention Problems, and Aggressive Behavior syndrome scales, (b) on a sum of T-scores ≥ 210 , (c) on a sum of T-scores ≥ 180 , and (d) on T-scores ≥ 60 on the Anxious/Depressed, Attention Problems, and Aggressive Behavior syndrome scales. Besides the above literature suggestions, we also chose participants to fit the dysregu-

lation profile if they had T-scores ≥ 65 . This cut-off was chosen to include adolescents with borderline as well as clinical scores on the YSR subscales based on the Greek norms³³. Children with a DP profile (T-scores ≥ 60) are at risk for severe psychiatric symptomatology, including cluster B personality disorders.⁴⁴ Moreover, the components of DP, such as attention problems, aggression, and anxiety/depression, are associated with BPD. For example, emotion dysregulation has been proposed as an underlying mechanism of aggression in BPD.^{45,46}

Statistical analysis

Confirmatory Factor Analysis (CFA) was performed to explore the fit of the unidimensional model to our sample, by using the Weighted Least Squares Estimator (WLSMV). Model fit was evaluated with the following fit indices: the Comparative Fit Index (CFI), the Tucker-Lewis Index (TLI), and the Root Mean Square Error of Approximation (RMSEA). The following value thresholds were used to assess the goodness of fit: RMSEA ≤ 0.06 ; TLI ≥ 0.95 , CFI ≥ 0.95 , indicating a good fit, whereas an adequate or mediocre fit is considered by values of RMSEA ≤ 0.08 (or ≤ 0.1), TLI ≥ 0.90 , CFI ≥ 0.90 .^{47–49} We should note that the sample size to free parameter ratio is 2.04, suggesting an underpowered ratio.

Regarding model testing, the literature cautions that modifications based solely on statistical indices may lead to overfitting and compromise interpretability and that all model respecifications must be justified based on prior research or theory.^{50–53} Therefore, we adopted a multi-criteria approach grounded in both psychometric principles and theoretical considerations. To guide model refinement, we relied on relevant literature from countries sharing some similarities with Greece, alongside our statistical analyses. Strong evidence of model misfit emerged from the modification index (MI) between Items 3 and 7 (MI = 16.798), which might lead to local dependency since it seems to capture overlapping content. Specifically, Item 3 ("My feelings are very strong. For instance, when I get mad, I get really really mad. When I get happy, I get really really happy") and Item 7 ("I go back and forth between different feelings, like being mad or sad or happy") appear to capture similar emotional intensity and variability. This high MI supports, beyond theoretical rationale, the statistical justification for eliminating Item 3. Additional modification indices exceeding 3.84 (yet below 10) and standardized residuals above 2.58 were observed for some items. Based on these findings, informed by the literature and grounded in theoretical relevance, we sequentially excluded item 3, then item 11, and finally both, to evaluate which model provided the best fit to our data.^{51,53}

Reliability analysis by means of internal consistency was performed using the Omega (ω) coefficient. Omega estimates the proportion of variance in the observed

total score attributable to all “modeled” sources of common variance. A value of >0.8 is considered strong, although values of 0.65 are considered acceptable. Moreover, to evaluate item characteristic curves, we used Item Response Theory. Given the polytomous nature of our items, we employed the Graded Response Model (GRM), and we used Marginal Maximum Likelihood (MML) estimation implemented via the *mirt* package in R.

For testing convergent validity, we performed a linear regression analysis of BPFS total score against the Dysregulation Profile of the YSR, hypothesizing that they would show a positive relationship. We performed four linear regressions with each one of the DP definitions, except the stricter one (T-scores on all scales ≥ 70), because only one participant filled this criterion.

To assess the diagnostic accuracy of the BPFS, a receiver operating characteristic (ROC) analysis was performed for all possible cutoff points on the BPFS against cases identified as presented with borderline features according to the clinical evaluation by the child and adolescent psychiatrist. A curve was fitted by a maximum likelihood technique to ascertain the area under the curve (AUC), which is a useful index of the diagnostic accuracy of the screening test. The optimal threshold value was chosen based on the value corresponding to the greater value of the Youden Index.

Analysis was performed using the software RStudio version 2024.12.0 and the packages *lavaan*, *psych*, *ltm*, *semTools*, *mirt*, *pROC*, and *ROCR*. The database sheet and the R code are available upon reasonable request.

Results

BPFS-11: descriptive assessment

Mean scores of the 11 items are shown in Table 1. Highest scores were observed in items 3 and 7, showing mainly affective instability, whereas the lowest score was observed in item 11, indicating that adolescents do not report seeing themselves as mean to their friends.

Confirmatory Factor Analysis

Evaluating the unidimensional model of the BPFS-11, our results (Table 2) showed a poor fit (RMSEA = 0.093 , CFI = 0.953 , TLI = 0.942). Excluding item 3 (“My feelings are very strong. For instance, when I get mad, I get really, really mad. When I get happy, I get really, really happy”) the fit was improved but still is considered suboptimal (RMSEA = 0.071 , CFI = 0.976 , TLI = 0.969). Exclusion of Item 11 only (“Lots of times, my friends and I are really mean to each other”) revealed a poor fit (RMSEA = 0.096 , CFI = 0.957 , TLI = 0.945). Exclusion of both items 3 and 11 resulted in a much-improved fit that can be considered optimal (RMSEA = 0.058 , CFI = 0.986 , TLI = 0.982). Factor loadings and fit indices for all models tested are shown in Table 2.

Reliability

Internal consistency of the scale was found to be strong, and although it was affected by item removal, (Table 2) remained good. The final solution of 9 items revealed a McDonald’s omega = 0.81 .

Item Analysis

Item analysis revealed that items provide various degrees of information to the scale. Item 8 provides very little information, while item 1 provides a lot of information (Figure 1).

Figure 2 shows the BPFS 9-item information curve that shows how well the construct is measured at all levels of the underlying construct continuum. BPFS-9 captures the BPTs well between 0.5 SD below and 2 SD above the mean.

Convergent Validity

Convergent validity was demonstrated for the total BPFS-9 score (Figure 3). Those with T-scores ≥ 60 on the YSR Anxious/Depressed, Attention Problems, and Aggressive Behavior syndrome scales had 8.59 higher summed scores in the BPFS-9 (SMD = 1.15 , $t = 4.77$, $p < 0.001$). Those with T-scores ≥ 65 had 8.56 higher summed scores in the BPFS-9 (SMD = 1.15 , $t = 2.35$, $p = 0.02$). The same results were revealed for adolescents with T-scores ≥ 210 , as they were the same 4 participants with T-scores ≥ 65 . Last, those with a sum of T-scores ≥ 180 had 7.94 higher summed scores in the BPFS-9 (SMD = 1.07 , t -value = 5.58 , $p < 0.001$).

Criterion Validity

ROC curve analysis was performed to study the cut-off point, sensitivity, and specificity of the BPFS. The ROC curve analysis (Figure 4) indicated a good diagnostic fit for the BPFS-9 with an AUC of 0.86 (95% CI [$0.76 - 0.96$]), suggesting high diagnostic accuracy. Sensitivity and specificity analysis indicated an adequate cut-off point of 26 to discriminate between early adolescents with high BPTs and adolescents without such traits. Sensitivity at the cut-off point was found to be 0.88 , while specificity was 0.75 . ROC curve analysis on the BPFS-11 showed that the difference in AUC between the two models is not statistically significant ($p = 0.75$). The cut-off point for the 11-item version was 34 (sensitivity = 0.8 , specificity = 0.85).

Discussion

The present study aimed to investigate the factor structure, reliability (internal consistency), and convergent validity of the BPFS-11 scale in a sample of Greek early adolescents. Moreover, we aimed to find the optimal cut-off score for early assessment of BPTs. Based on our literature review, no available tool was found in Greece to assess borderline features in adolescents. In

Table 1. Item descriptive statistics (N=112).

No	Item	Frequencies (N, %)					Descriptive
		Not at all true	Hardly ever true	Sometimes true	Often true	Always true	
1	I feel very lonely	31 (27.6)	31 (27.6)	35 (31.2)	9 (8.0)	6 (5.4)	2.36
2	I want to let some people know how much they've hurt me	24 (21.4)	25 (22.3)	25 (22.3)	23 (20.5)	15 (13.4)	2.82
3	My feelings are very strong. For instance, when I get mad, I get really, really mad. When I get happy, I get really, really happy	12 (10.7)	17 (15.4)	24 (20.9)	33 (29.1)	26 (23.6)	3.39
4	I feel that there is something important missing about me, but I don't know what it is	45 (40.2)	21 (18.7)	18 (16.1)	12 (10.7)	16 (14.3)	2.40
5	I'm careless with things that are important to me	35 (31.2)	23 (20.5)	21 (18.7)	25 (22.3)	8 (7.1)	2.54
6	People who were close to me have let me down	33 (29.5)	34 (30.4)	24 (21.4)	14 (12.5)	7 (6.2)	2.36
7	I go back and forth between different feelings, like being mad or sad, or happy	20 (17.9)	12 (10.7)	34 (30.4)	26 (23.2)	20 (17.9)	3.12
8	I get into trouble because I do things without thinking	40 (35.7)	29 (25.9)	21 (18.7)	11 (9.8)	11 (9.8)	2.32
9	I worry that people I care about will leave and not come back	37 (33.0)	16 (14.3)	21 (18.7)	14 (12.5)	24 (21.4)	2.75
10	How I feel about myself changes a lot	33 (29.5)	23 (20.5)	19 (17.0)	20 (17.8)	17 (15.2)	2.69
11	Lots of times, my friends and I are really mean to each other	44 (39.3)	35 (31.2)	17 (15.2)	8 (7.1)	8 (7.1)	2.12

accordance with our hypothesis, BPFS proved to be a reliable tool that measures borderline personality features as a unidimensional construct. However, the 11-item solution showed a poor fit, while the removal of two specific items, based on previous studies conducted in other countries^{17,20,23} and on statistical analysis, improved the model, without affecting its reliability and diagnostic accuracy. We also demonstrate that BPFS exhibits good convergent validity and provide a clinical cut-off point to detect early adolescents with high BPTs.

The overall fit of the 11-item scale was poor. Removing item 3 ("My emotions are very strong. For example, if I get angry, I feel really angry, and if I am happy, I feel really happy") improved the model fit, though it's still considered only mediocre. The Turkish study²³ also removed item 3 as it did not correlate with the other items of the scale. The authors concluded that item 3 was unsuitable for measuring BPTs within a single-factor structure. Indeed, the scale was not constructed to provide information useful in clinical practice on dimensions of BPD; therefore, a unidimensional scale would be more appropriate in clinical settings. Furthermore, similar to the present study, both Turkish and Italian validation studies,^{20,23} found that the mean score of item 3 was very high compared with those of the rest of the items. The high score may be explained by the fact that the intensity of emotions is a typical aspect of early adolescence. Therefore, this item may not be a feature presented exclusively in adolescents with high BPTs. The retention of item 3 and the removal of item 11 ("Lots of times, my friends and I are really mean to each other"), as in the Portuguese study,¹⁷ resulted in a poor fit. In contrast to item 3, the mean score of item 11 was low compared to the other items. This suggests that be-

ing mean to friends does not strongly characterize early adolescents with BPTs. However, removing both items resulted in a 9-item model that fit the data well. Moreover, although item 8 appears to perform poorly psychometrically, it was retained in the scale due to its conceptual relevance. The item captures impulsivity, a core feature of BPD, and there were no literature-based recommendations supporting its removal.

Reliability of the scale was good across all solutions; however, as we removed items, reliability decreased while remaining at acceptable levels. The reliability was similar to the original study and the French validation, and it was higher than the Portuguese and Italian versions.^{17,19,20}

In terms of convergent validity, results demonstrated significant correlations between the BPFS-9 and the dysregulation profile that includes Anxious/Depressed, Attention, and Aggressive problems. The findings indicate that adolescents who exhibit high BPTs tend to exhibit high levels of dysregulation as well. This result is consistent with the literature suggesting that dysregulation profile may be associated with severe psychiatric disorders such as borderline personality disorder.³⁵ The small number of adolescents (N = 4) classified within the more "severe" dysregulation profiles (T-scores ≥ 65 and summed scores > 210) may contribute to the low p-value observed, despite its statistical significance. Nonetheless, interpretation of these findings is limited and should be approached with caution—or potentially avoided—given the restricted sample size.

Our results also revealed that the BPFS has high accuracy in discriminating adolescents with high BPTs based on a clinical examination. Moreover, no differences were detected in the diagnostic accuracy between the 11-

Table 2. Confirmatory Factor Analysis parameters and reliability coefficients.

No	Item	BPFS 11	BPFS 10 (Excluding item 3)	BPFS 10 (Excluding item 11)	BPFS 9 (Excluding items 3 and 11)
		Factor loadings	Factor loadings	Factor loadings	Factor loadings
1	I feel very lonely	0.780	0.802	0.788	0.810
2	I want to let some people know how much they've hurt me	0.443	0.455	0.427	0.437
3	My feelings are very strong. For instance, when I get mad, I get really really mad. When I get happy, I get really really happy	0.455	-	0.450	-
4	I feel that there is something important missing about me, but I don't know what it is	0.629	0.643	0.644	0.658
5	I'm careless with things that are important to me	0.583	0.593	0.585	0.594
6	People who were close to me have let me down	0.677	0.691	0.668	0.681
7	I go back and forth between different feelings, like being mad or sad or happy	0.568	0.496	0.548	0.472
8	I get into trouble because I do things without thinking	0.381	0.335	0.357	0.307
9	I worry that people I care about will leave and not come back	0.672	0.677	0.684	0.690
10	How I feel about myself changes a lot	0.657	0.654	0.667	0.664
11	Lots of times, my friends and I are really mean to each other	0.397	0.390	-	-
Model Fit					
	RMSEA	0.093	0.071	0.096	0.058
	CFI	0.953	0.976	0.957	0.986
	TLI	0.942	0.969	0.945	0.982
Reliability					
	McDonald's ω	0.84	0.84	0.83	0.81

Note: RMSEA: root-mean-square error of approximation; CFI: comparative fit index; TLI: Tucker–Lewis index.

item and 9-item solutions. With a cut-off score of 26, the BPFS-9 demonstrates high sensitivity (0.88) in identifying adolescents with BPTs, which is higher than that of the BPFS-11. However, it also exhibits lower specificity (0.75) compared to the BPFS-11, resulting in a higher rate of false positives. In the context of our outpatient community service setting, prioritizing the early detection of adolescents with high BPTs, even at the cost of some false positives, may be a more clinically appropriate approach. Early identification allows for timely intervention, while subsequent clinical assessment can effectively rule out adolescents who do not exhibit true BPTs. On the other hand, consistent with the original study of Sharp et al.¹⁶ in an inpatient setting, the optimal cut-off point of BPFS-11 was 34.

Moreover, the scale captures more information for adolescents with high levels of BPTs. This finding suggests that BPFS-9 is better at capturing the higher levels of BPTs. We can argue, from a clinical point of view, that emphasis should be placed on adolescents exhibiting high levels of borderline features to facilitate timely identification and intervention.

Our study has several limitations that need to be

addressed. First, the sample size may be considered small, thus limiting the generalizability of our findings. The sample size was small for the CFA and IRT analyses; therefore, the ratio of free parameters was below standard guidelines, which may affect the precision of parameter estimates. Results should be interpreted cautiously, and replication with a larger sample is recommended. Second, the clinical outpatient population does not allow for drawing conclusions for the community and inpatient population; therefore, future studies are needed to replicate the results and validate the scale in these settings in Greece. A third limitation lies in the cross-sectional nature of the study, which inhibits test-retest reliability. Although the clinical assessment was conducted by the same child and adolescent psychiatrist, the absence of a standardized diagnostic tool for BPD remains a limitation.

Our study also has several strengths that should be emphasized. To the best of our knowledge, this is the first study exploring the psychometric properties of a scale for borderline personality features in adolescents in Greece. Therefore, represents the first study providing support for the use of BPFS in outpatient settings.

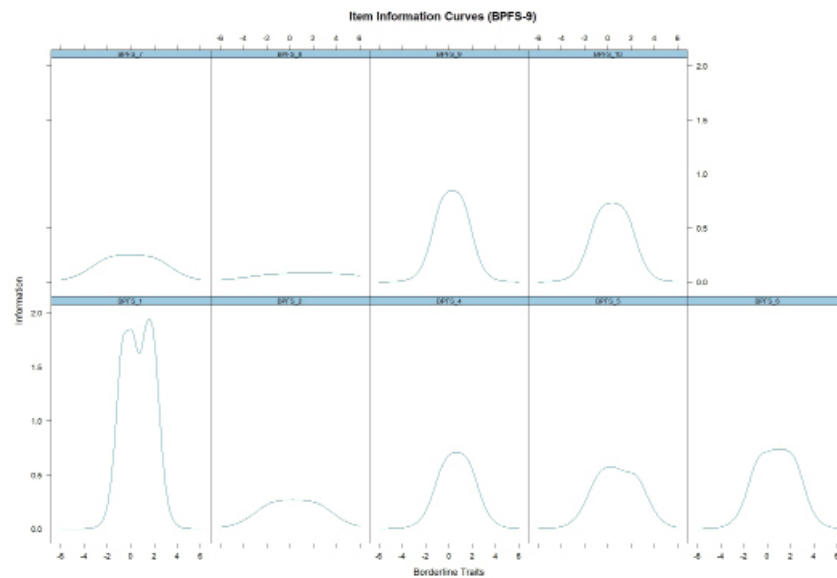


Figure 1. Item Information Curves of the Borderline Personality features Scale (9 items).

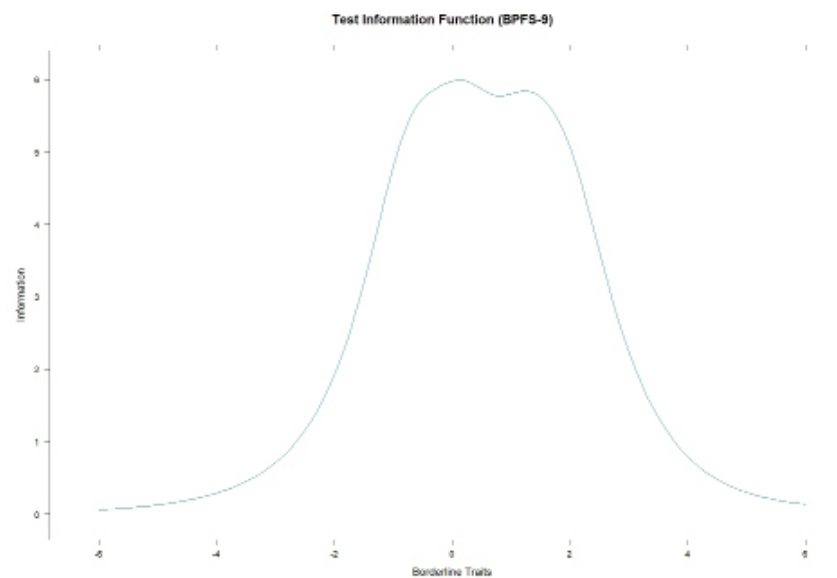


Figure 2. Test Information function of the Borderline Personality features Scale (8 items).

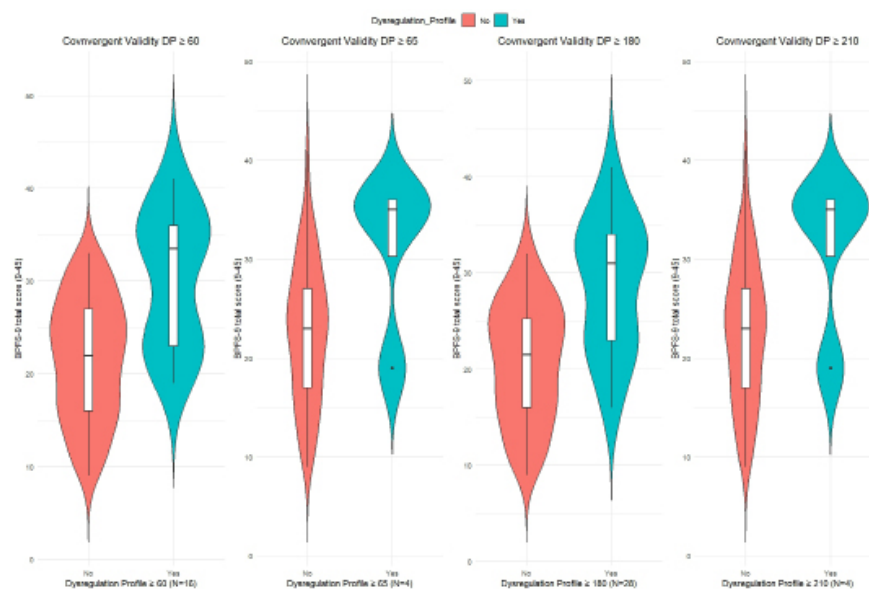


Figure 3. Convergent validity comparing BPF5-9 sum score with different definitions of Dysregulation Profile.

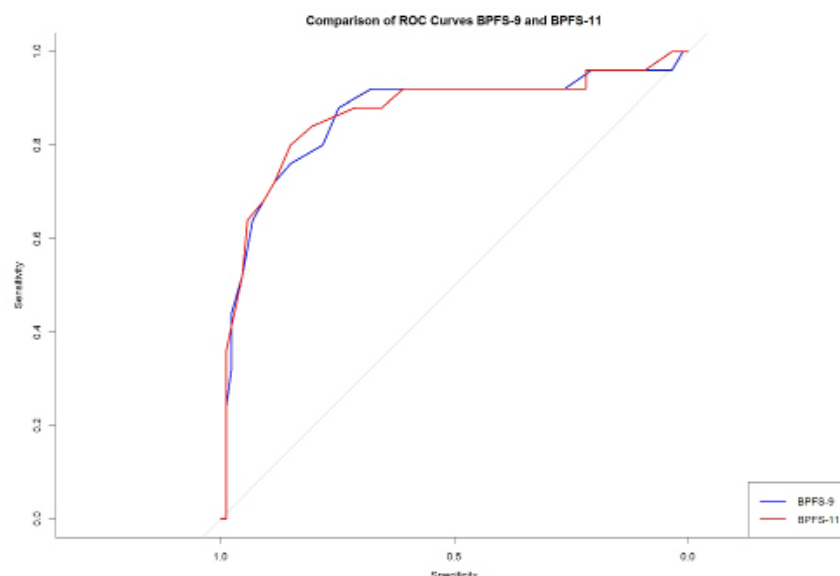


Figure 4. Receiver operating characteristic curves of the BPFS-9 and BPFS-11 in the presence or absence of the BPD at risk clinical diagnosis.

Furthermore, our sample consists of early adolescents, a group for whom early detection of BPTs is crucial for timely intervention. Finally, our study, although it did not include a structured interview for BPD as mentioned above, included a clinical assessment by an experienced child and adolescent psychiatrist.

In this study, we validated the BPFS scale, addressing a gap in tools for detecting BPTs in Greek adolescents, and provided a new insight into the item pool. Early detection of BPTs during adolescence is crucial for timely intervention. Our findings support the use of the BPFS scale for early adolescents in outpatient settings, with the unidimensional model demonstrating an adequate fit for the 9-item solution. The BPFS-9 provides a valid measure of BPTs, with a cut-off of 26, and better iden-

tifies adolescents with elevated BPTs, facilitating early detection and intervention.

Providing Greek mental health professionals with a short, feasibly administered, user-friendly, and easy-scoring scale can significantly aid the early detection of BPTs. This represents a step towards facilitating diagnosis and intervention in this crucial developmental period, but also has the potential to reduce the reluctance around the diagnosis of BPD in that age group.^{54,55} This could lessen the burden of this debilitating disorder on individuals, families, and health systems. In conclusion, our results suggest that BPFS-9 can be used in outpatient clinical settings in the early adolescent population as a brief screening tool.

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Research article

Assessment of quality and reliability of YouTube videos on cognitive-behavioral therapy including hypnosis.

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ARTICLE HISTORY: Received 13 June 2025 / Revised 24 September 2025 / Published Online 20 December 2025

Cite this article as: Abu Sabra MA, Suleiman K, AlBarmawi M, Abualruz H, Zoromba MA. Assessment of quality and reliability of YouTube videos on cognitive-behavioral therapy including hypnosis. *Psychiatriki* 2026, 37:28-36
<https://doi.org/10.22365/jpsych.2025.025>

ABSTRACT

Hypnosis combined with cognitive behavioral therapy (CBT-hypnosis) is a type of psychological treatment that focuses on how people think and behave in various mental and medical illnesses. It treats behavioral and emotional issues by tapping into the subconscious mind. Patients who are hypnotized are more open to new ideas and less prone to decline hard ones. The result is that it is simpler to adopt the healthy cognitive patterns and habits that CBT tries to promote. YouTube is a great resource for health-related education that has the power to greatly impact the choices and actions of medical professionals, patients, and their primary caregivers, because they visit the YouTube platform to investigate and obtain guidance regarding CBT-hypnosis. However, unreliable and deceptive information on YouTube could encourage undesirable habits, making patients, primary caregivers, and hypnosis practitioners avoid CBT-hypnosis. Thus, the purpose of this study was to assess the quality and reliability of YouTube videos about CBT-hypnosis as a source of supportive information for practitioners, patients, and their primary caregivers. A total of 354 YouTube videos about CBT-hypnosis were analyzed. The videos' reliability and quality were assessed using the Global Quality Scale and a modified DISCERN tool. The analysis found that the median overall GQS score was 3 (IQR: 2; min-max: 1-5), indicating that the videos had moderate quality and some important information was adequately covered. The modified DISCERN tool yielded a median total score of 3 (IQR: 1; min-max: 0-5), indicating that the videos were moderately reliable and that the information was presented in a balanced and unbiased manner. Most of the included videos came from science and technology sources (academic channels) (57.6%; n = 204). While 42.4% of videos came from non-profits and activism, people and blogs, and others lay in public. As a supportive source of information, YouTube videos about CBT-hypnosis are regarded as being of a moderate level of quality and reliability. Therefore, formal presenters should promote the distribution of good-quality content, which helps to improve the quality of information available on the YouTube platform.

KEYWORDS: Behavioral therapy, cognitive therapy, cognitive behavioral therapy, hypnosis, YouTube.

Introduction

Cognitive-behavioral therapy, including hypnosis (CBT-hypnosis), is a type of psychological treatment that combines cognitive-behavioral therapy with hypnosis to address undesirable and unhelpful thoughts, beliefs,

and attitudes, as well as to influence our language, memory, creativity, reasoning, problem-solving, and learning abilities.^{1,2} In other words, it focuses on the unconscious mind, which includes implicit thoughts, behaviors, and emotions, to generate more beneficial, healthy beliefs

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while challenging and eliminating unhealthy ones.^{3,4} CBT-hypnosis meets the criteria for an assimilative model of psychotherapy, which is thought to be an effective model of integrating psychotherapy.⁵ The literature has shown that CBT-hypnosis is utilized as an adjunctive treatment for various mental illnesses, such as anxiety, phobias, depression, PTSD, and emotional disorders, as well as to assist in managing symptoms that are difficult to alleviate.⁶⁻⁸

Integrating hypnosis and cognitive-behavioral therapy is one of the many innovative methods that mental health professionals are always looking for to improve therapeutic outcomes.^{9,10} It is simply a very powerful method of bringing about constructive change.¹¹ Hypnosis opens the subconscious mind and treats deeply ingrained problems that could be resistant to conventional therapy techniques, whereas cognitive-behavioral therapy is excellent at treating conscious patterns of thinking and behaviors.^{12,13}

According to the literature, the majority of patients who utilize CBT-hypnosis reported recovering compared to patients receiving alternative therapies^{8,14,15} Even though CBT-hypnosis is effective, its use in clinical settings, as inpatients or outpatients, remains uncommon and unique.^{10,16-18} This is because of misperceptions of CBT-hypnosis; a lack of resources, encouragement, and specialized training; or a lack of supportive information about CBT-hypnosis that can be shared with patients, primary caregivers, and practitioners.^{19,20} To overcome the aforementioned factors, patients, primary caregivers, and practitioners should seek out additional supporting sources of knowledge about CBT-hypnosis.

Modern media sources can offer a surprising wealth of information for both professionals and the lay public.²¹⁻²³ Thus, YouTube has observed a rise in the number of videos about health in recent years.^{23,24} Previous studies have proven that the media in general can be considered one of the sources of information for both professionals and the lay public, such as patients and primary caregivers, although the quality and reliability of this information are challenged and debated.²⁵⁻²⁷ For instance, in a recent study, 88% of participants watched health-related videos on YouTube, and of those viewers, 85% made decisions about their health based on what they saw and advice on whether to see a doctor or follow particular health practices.²⁸ As a result, most patients, their primary caregivers, and practitioners visit YouTube to obtain information regarding health-related issues, which can have a big influence on their treatment choices and behaviors.^{27,29,30} However, unreliable and deceptive information on YouTube could encourage undesirable habits, making patients, primary caregivers, and practitioners avoid a variety of health-related interventions, such as CBT-hypnosis.^{31,32} This has led to the

topic being an important area of research. Therefore, the main objective of this study was to assess the quality and reliability of YouTube videos about CBT-hypnosis as a source of supportive information for practitioners, patients, and their primary caregivers. The term "primary caregivers" refers to a person who is considered an essential and primary partner in sustaining healthcare outcomes for patients, most likely a family member.

Method

Search Strategy

The following search terms were used to look for videos on the YouTube website (<http://www.youtube.com>): "cognitive hypnotherapy," "cognitive hypnosis," "hypnosis," "CBT-hypnosis," "cognitive therapy," "behavioral therapy," "cognitive-behavioral therapy," "anxiety disorder," "post-traumatic stress disorder," "emotional disorders," "depression disorders," and "phobias." The Boolean operators "AND" and "OR" were used to combine different search terms to get more specific results, like this: (cognitive hypnotherapy OR cognitive hypnosis OR hypnosis OR CBT-hypnosis) AND (cognitive therapy OR behavioral therapy OR cognitive-behavioral therapy) AND (anxiety disorder OR post-traumatic stress disorder OR emotional disorders OR depression disorders OR phobias). The first YouTube search took place on January 15, 2024, and the last one was completed on March 15, 2024.

Eligibility Criteria

All videos were filtered using inclusion criteria as a guide to remove unnecessary, duplicate, irrelevant, and redundant content. Four criteria must be met for the videos to be included: (1) met the study's objective by focusing on CBT-hypnosis; (2) had clear sound and good visual quality to ensure that high-quality information is obtained; (3) were published in English; and (4) had video lengths that did not exceed 30 minutes because the video should be as concise as possible, the literature places a strong emphasis on narration, and the video's duration should be minimized, ideally not exceeding 30 minutes.^{33,34} This is because viewers would rather see a solution to their problem while still paying attention and staying focused than come across something ineffective.

Video Selection Process

Figure 1 shows the flowchart of the chosen, eligible videos. A total of 665 videos were taken from the YouTube site using the search terms used to find videos on the platform. A total of 208 videos were removed before screening due to duplication. Leaving 457 videos for titles and contents review. Two researchers, who held PhD degrees in psychiatric and mental health nursing and were certified as Clinical Nurse Specialists

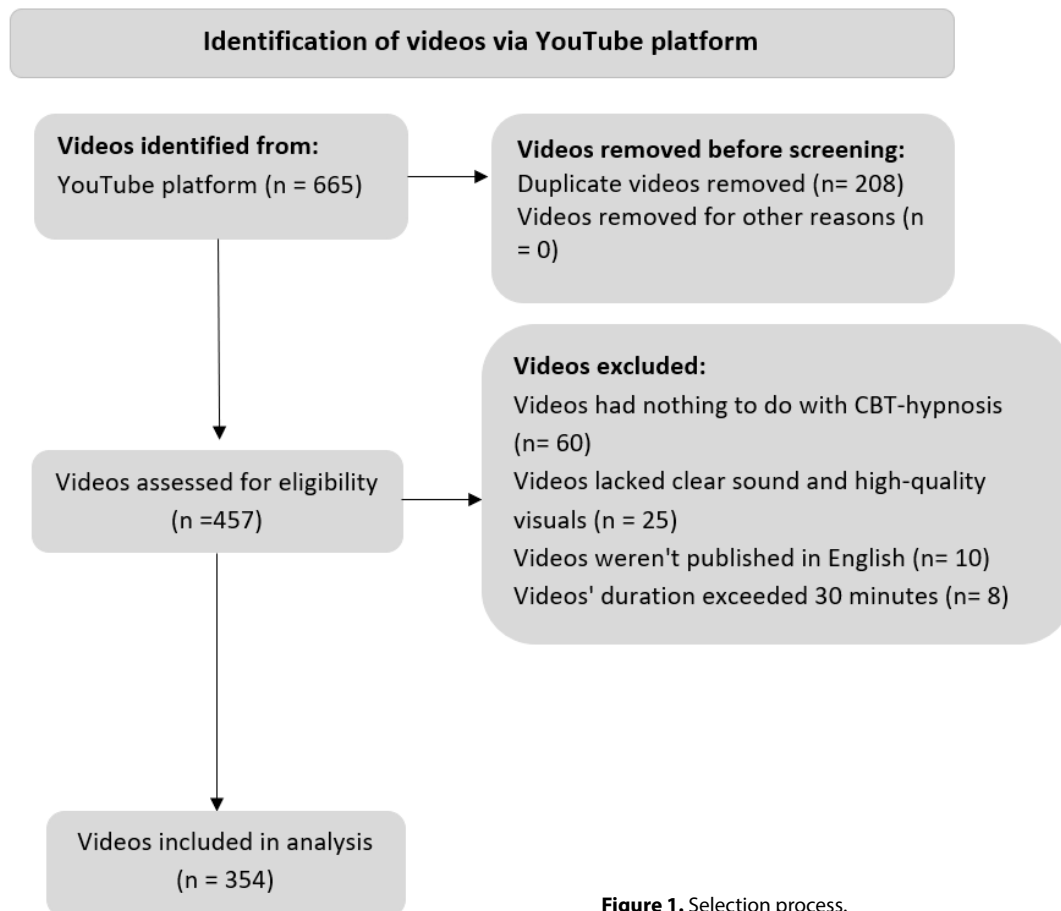


Figure 1. Selection process.

(CNS) (H.A.R. and M.A.S.), independently reviewed the titles and contents of the chosen videos. The kappa of inter-rater agreement showed that the two researchers were completely in agreement (0.81–1.00); the kappa for H.A.R. was 0.81, and the kappa for M.A.S. was 1.00. Any differences were discussed with a third researcher (K.S.). After reviewing and refining titles and content, 103 videos were eliminated: 60 because they had nothing to do with CBT-hypnosis, 25 because they lacked clear sound and high-quality visuals, 10 because they weren't published in English, and 8 because their durations exceeded 30 minutes. Ultimately, 354 videos were deemed eligible and included in the final analysis.

Instruments

Three measuring tools were used to assess the quality and reliability of the video information: the modified DISCERN tool, the Global Quality Scale (GQS), and a data sheet used to examine each video created by the authors.

The first instrument, the modified DISCERN tool, was used to examine the reliability of video content; clarity and comprehensibility, additional information in videos, bias, and objectivity are all evaluated using five questions.^{35,36} A rating system asks “yes” or “no” questions, with “1” implying yes and “0” implying no. Thus, this tool

has a maximum score of 5 points. In this rating system, videos were then classified into three reliability groups: scores of 4 or 5 indicated high reliability, scores of 3 indicated moderate reliability, and scores of 2 or 1 indicated low reliability (see Table 1).

The second tool, the Global Quality Scale (GQS), was developed to evaluate the quality of content offered in videos, including its general flow and simplicity of use³⁷. A rating system employs a 1–5 scale, where “poor quality” is represented by a “1” and “excellent quality” by a “5”. The GQS defined videos with 5 points as “Excellent quality,” videos with 4 points as “Good quality,” videos with 3 points as “Moderate quality,” videos with 2 points as “Generally poor,” and videos with 1 point as “Poor quality”. Videos with ratings of 1 or 2 were seen as low quality; those with ratings of 3 were regarded as moderate quality; and those with ratings of 4 or 5 were regarded as high quality (see Table 2). Any discrepancies in the score were explained during discussions and by a third reviewer.

In the third tool, the authors constructed a data sheet to analyze each video using the following criteria: content, information presentation methods, presenters' involvement, source, and parameters. The content of the video includes the treatment plan, mechanism of action, indications, efficacy, method of administration,

Table 1. The modified DISCERN tool.

N	Items	Yes	No	Points	Reliability
1	Are the aims clear and achieved?	1	0	1	Low
2	Are reliable sources of information used?	1	0	2	Low
3	Is the information presented balanced and unbiased?	1	0	3	Moderate
4	Are additional sources of information listed for patient reference?	1	0	4	High
5	Are areas of uncertainty mentioned?	1	0	5	High

Table 2. Video Quality Assessment.

Scoring	Classification of video quality	A global quality scale (GQS) description	N of videos	%	Video quality after analysis
1	Low quality	Poor quality, poor flow, and most information is missing, so it is not helpful for patients and their primary caregivers.	61	17.2%	Low quality (33.9%, n=120)
2	Low quality	Generally poor, with some information given but of limited use to patients and their primary caregivers.	59	16.7%	
3	Moderate quality	Moderate quality and some important information are adequately discussed	90	25.4%	Moderate quality (25.4%, n= 90)
4	High quality	Good quality, good flow, and most relevant information are covered, making it useful for patients and their primary caregivers.	87	24.6%	High quality (40.7%, n= 144)
5	High quality	Excellent quality and excellent flow, making it very useful for patients and their primary caregivers.	57	16.1%	
GQS total Score: median (IQR, Min- Max)			3 (IQR: 2; min-max: 1–5)		

contraindications, adverse effects, quality of life of the patient, and primary caregiver education. The presenters who appear in the reviewed video include formal or informal presenters. The methods of information presentation include a slide presentation, an interview, role-play, simulation and demonstration, multiple presentations, and other types of presentations. The sources of video include education, science and technology, non-profits and activism, people and blogs, and others. The video parameters include video length, number of views, likes, dislikes, subscribers, and comments.

Statistical Analysis

The data were analyzed using version 27 of the Statistical Package for the Social Sciences (SPSS).³⁸ All entered data sets were examined for outliers and missing data. The data analysis encompassed both descriptive and inferential analyses. The descriptive analysis included frequency, percentages, median, minimum, maximum, and interquartile range (IQR). The inferential analysis assessed the videos' quality and reliability. Additionally, the normality assumptions of continuous outcome variables were evaluated using the Kolmogorov-Smirnov normality test.³⁹ Since most of the outcomes violate the assumption of normality, medians and interquartile ranges (IQR) were used to report continuous variables. Moreover, the Kruskal-Wallis tests were conducted to identify any significant differences between the glob-

al quality scale, video parameters, and the modified DISCERN score. In addition, the Mann-Whitney U test was used to compare the videos' quality and reliability across two groups based on their origins: science and technology versus all the others. P-values of less than 0.05 were deemed statistically significant.

Results

Descriptive analysis

- Source of Videos

The source of 354 videos was investigated. The analysis revealed that videos from science and technology sources (academic channels) were the most frequent (57.6%; n = 204), followed by non-profits and activism (18.4%; n = 65), people and blogs (14.4%; n = 51), and other sources (9.6%; n = 34).

- Presentation Methods

An analysis was conducted on the methods of information presentation in the 354 videos. The investigation revealed that slide presentations (23.4%, n = 83) were the second most frequently utilized method, behind videos that presented content using multiple methods (26%, n = 92). The term "multiple methods" refers to the usage of various methods together in the same video, which may include speaking, role-playing, simulation and demonstration, interviews, and slide presentations. The interview methods were then categorized as the

third most frequently used (17.8%, $n = 63$). Then followed role-playing methods, which represented 11.6% ($n = 41$). On the other hand, the least used methods were speech (9.6%, $n = 34$), other types of presentations (7.9%, $n = 28$), and simulation and demonstration techniques (3.7%, $n = 13$).

- The Video Content

The content of 354 videos was analyzed for the following six criteria: (1) treatment plan; (2) indications; (3) efficacy; (4) adverse effects; (5) patient quality of life; and (6) primary caregiver support. The analysis showed that most of the videos described the indications (purpose) of using CBT-hypnosis (63.8%; $n = 225$), followed by the treatment plan of cognitive-behavioral therapy, including hypnosis (56.8%; $n = 201$), followed by the primary caregiver support (53.1%; $n = 188$), followed by the efficacy of CBT-hypnosis (41.8%; $n = 148$), and then patients' quality of life (41.0%; $n = 145$). On the other hand, the videos included the least amount of information about the adverse effects of employing CBT-hypnosis (32.8%, $n = 116$), as well as the way in which this therapy is administered (19.2%; $n = 68$), compared with other criteria analyzed. Note: the numbers and percentages are not mutually exclusive.

- The Number of Medical Patients and Presenters Who Appear in the Eligible Videos

A total of 354 videos have been analyzed for the presence of medical patients (clients) in the reviewed video as real, simulated, or no patients. The result revealed that most videos don't have medical patients (55.4%; $n = 196$), followed by 37.3% ($n = 132$) of videos that have real medical patients and 7.3% ($n = 26$) of the videos that have simulated medical patients.

On the other hand, 354 videos were assessed for the presence of presenters, whether formal or informal. According to the analysis, the qualified hypnotherapist was the most common of the formal presenters seen in the video (62.1%; $n = 210$). A "qualified hypnotherapist" is a certified professional who practices clinical hypnotherapy and hypnosis. followed by Other health team (19.4%; $n = 69$) and Psychiatric Nurses (18.4%; $n = 65$). In contrast, 40.3% ($n = 143$) of the reviewed movies show family members and friends as informal presenters. Note: the numbers and percentages are not mutually exclusive

- Video Parameters

A total of 354 video parameters were examined, including video length, the number of likes, dislikes, views, comments, and subscribers. The analysis found that the median video length was 4.0 minutes (min-max: 1-30; IQR: 5.6), the median number of views was 604.5 (min-max: 5-854838; IQR: 3545.8), the median number of likes

was 3.0 (min-max: 0-1000300; IQR: 14.0), the median number of dislikes was 5.0 (min-max: 0-505; IQR: 7.0), the median number of subscribers was 185.5 (min-max: 0-38900000; IQR: 2348.0), and the median number of comments was 2 (min-max: 0-1450; IQR: 6).

Inferential analysis

- Assessment of the Videos' Quality

In order to assess the video quality and usability of the material provided, 354 relevant videos were examined using the global quality scale (GQS). The analysis revealed that 16.1% ($n = 57$) of the videos scored a 5 out of 5, indicating that the videos were of excellent quality and excellent flow, making them very useful for patients and their primary caregivers. Then, 24.6% ($n = 87$) of the videos had a score of 4 out of 5, meaning that they had good quality, good flow, and covered most relevant information regarding CBT-hypnosis, making it useful for patients and their primary caregivers. Following that, 25.4% ($n = 90$) of the videos scored a 3 out of 5, indicating that they had moderate quality, and some important information was adequately discussed about CBT-hypnosis. After that, 16.7% ($n = 59$) of the videos had a score of 2 out of 5, meaning that they were generally poor, with some information given but of limited use to patients and their primary caregivers. Lastly, 17.2% ($n = 61$) of the videos scored a 1 out of 5, indicating that they had poor quality, poor flow, and most information was missing about CBT-hypnosis, so it is not helpful for patients and their primary caregivers (see Table 2).

Considering the results above, videos with ratings of 1 or 2 were considered as low quality; those with ratings of 3 were regarded as moderate quality; and those with ratings of 4 or 5 were regarded as high quality. Consequently, of the 120 videos, 33.9% had low quality, 25.4% had moderate quality, and 40.7% had high quality ($n = 144$). As a result, the analysis revealed that the global quality scale (GQS) total score for the evaluated videos was moderate, with a median score of 3 (IQR: 2; min-max: 1-5), indicating that the videos had moderate quality and some important information was adequately covered (See Table 2).

- Assessment of the Videos' Reliability

The information reliability of 354 eligible videos was assessed using the modified DISCERN tool. This tool is adopted to verify the information reliability of the included videos from another perspective, whereby the video's information reliability includes several aspects, such as whether the video is clear and accurate, whether reliable sources of information are used, the information presented is balanced and unbiased, additional sources of information are listed for patient reference, and areas of uncertainty are mentioned. The term "uncertainty" means the videos involve imperfect or unknown infor-

mation. The analysis revealed that 65.0% (n = 230) of videos had a clear aim and achievement, 61.6% (n = 230) of videos had trustworthy sources of information, 72.9% (n = 258) of videos mentioned imperfect or unknown information, 67.8% (n = 240) of videos had information presented in an in a balanced and unbiased manner, and 67.5% (n = 239) of videos had enough additional sources of information listed for patient reference. As a result, the analysis revealed that the modified DISCERN tool total score for the evaluated videos was moderately reliable, with a median score of 3 (IQR: 1; min-max: 0–5), indicating that the videos' information was presented balanced and unbiased (see Table 3).

- Differences between a GQS, the modified DISCERN score, and video parameters

The normality assumptions of numerical variables that were not normally distributed were assessed using the Kolmogorov-Smirnov normality test. Thus, any significant differences between a global quality scale, video parameters, and the modified DISCERN score were found using the nonparametric statistical method of the Kruskal-Wallis test. According to the analysis, there was a significant difference between the modified DISCERN scores and the global quality scale (H = 14.31; P = 0.014; effect size = 0.53; CI = 3.23 – 3.50), but not between the global quality scale and the video parameter (see Table 4).

Table 3. Video Reliability Assessment.

The Modified DISCERN Tool	N of videos	%
Are the aims clear and achieved?	230	65.0%
Are reliable sources of information used?	218	61.6%
Is the information presented balanced and unbiased?	240	67.8 %
Are additional sources of information listed for patient reference?	239	67.5 %
Are areas of uncertainty mentioned?	258	72.9 %
Modified DISCERN total Score: median (IQR, Min- Max)	3 (IQR: 1; min-max: 0–5)	

Note: The numbers and percentages are not mutually exclusive.

Table 4. Kruskal-Wallis Test for video parameter, GQS, and the modified DISCERN score.

Global Quality Scale (GQS)		H	P	Effect size	CI (Min-Max)
Video parameter	Number of views	1.91	0.386	0.15	10095.9 - 30395.94
	Number of likes	5.12	0.077	0.16	2519.4 - 8596.1
	Number of dislikes	3.95	0.139	0.17	5.3 - 12.2
	Number of subscribers	4.37	0.113	0.14	95413.5 - 928138.4
	Number of comments	1.84	0.398	0.11	9.8 - 28.7
Modified DISCERN Score		14.31	0.014*	0.53	3.23 – 3.50

Table 5. Comparison between the videos' quality and reliability based on their origins.

Variables	Source of Videos	N	Mean	Mann-Whitney U	Z	P
Videos' Reliability	Science and Technology	204	176.4	15083.5	-.236	0.814
	All the Others	150	178.9			
Videos' Quality	Science and Technology	204	179.9	14802.0	-.536	0.592
	All the Others	150	174.2			

- Comparison Between the Videos' Quality and Reliability Based on Their Origins

The Mann-Whitney U test was used to compare the videos' quality and reliability across two groups based on their origins: science and technology versus all the others. The analysis revealed that there was no significant difference in the quality of the videos between science and technology versus all the others ($Z = -.536$; $P = 0.592$). On the other hand, the analysis found that there was no significant difference in the reliability of the videos between science and technology versus all the others ($Z = -.236$; $P = 0.814$) (see Table 5).

Discussion

Seeking supporting information about CBT-hypnosis has been recognized as essential to increasing therapeutic awareness among practitioners, patients, and primary caregivers. As a result, they increase their desire and curiosity to obtain therapeutic information and search various websites and platforms such as YouTube. Consequently, patients and their primary caregivers should exercise caution while utilizing this information because a lot of users upload videos that contain medical information, but the quality and reliability of this material are still in doubt. There may be variances between these groupings. Some are seeking professional content, while others are looking for material intended for the general public. We must ensure the reliability and quality of the available information in both scenarios.

Based on the above, this topic is considered an important research area. Therefore, this study aimed to assess whether the YouTube platform provides supportive information for practitioners, patients, and their primary caregivers by analyzing the content of YouTube videos about CBT-hypnosis to investigate the quality and reliability of eligible videos.

In this study, the analysis revealed that the eligible videos that are available on the YouTube platform regarding CBT-hypnosis had moderate quality, and some important information was adequately covered. Additionally, the analysis found that the eligible videos were moderately reliable, and the information on CBT-hypnosis was provided in a balanced and unbiased manner. This implies that the information in these videos is moderately helpful to practitioners, patients, and their primary caregivers. In practice, this, in turn, increases the chances of potential risks, such as misinformation and lack of access to adequate information. This can significantly impact their treatment choices and behaviors. However, unreliable and misleading information on YouTube may encourage undesirable habits, leading patients, primary care providers, and practitioners to avoid a variety of health interventions, such as CBT-hypnosis. The primary reasons most patients, primary care pro-

viders, and practitioners visit the YouTube platform are misconceptions about CBT-hypnosis; a lack of resources, encouragement, and specialized training; or a lack of supportive information about cognitive behavioral therapy with hypnosis that can be shared with patients, primary care providers, and practitioners.

One of the most important factors contributing to the mediocre quality and reliability of videos is that the video's source may not be scientific or trustworthy. According to the analysis of this study, 57.6% of the video sources were science and technology, indicating that video sources are posted by formal presenters who are derived from scientific practical applications and uses of scientific knowledge. While 42.4% of videos came from nonprofits and activism, people and blogs, and others in the public, it seems that video sources are posted by informal presenters using non-scientific resources. As a result, the formal presenters were more likely to develop these videos than the informal presenters.

One explanation for why informal presenters create medical content, such as CBT-hypnosis, is that they create content for their followers and may have more time to create and publish online content than formal presenters. This would account for the higher levels of engagement indicated by the number of views, likes, and comments. Therefore, this study recommended continuously encouraging formal presenters to create content with good flow and cover the most relevant information about CBT-hypnosis. This, in turn, contributes to raising the quality of information offered on the YouTube platform.

The findings of this study are in harmony with those of other studies that assessed the benefits of the YouTube platform as a source for information on various medical or psychiatric conditions and therapies. For instance, Ghate et al.⁴⁰ revealed that YouTube provides a positive and useful message for individuals with trichotillomania. Another study discovered that the YouTube platform is useful for dental fear, anxiety, and phobias.⁴¹ Two studies were undertaken to analyze the quality and reliability of electroconvulsive treatment videos on YouTube, and the results showed that the information regarding ECT is considered supportive information for patients and their primary caregivers.^{25,42}

Altunsoy⁴³ found that videos on YouTube related to bipolar disorder have good flow and cover most relevant information about bipolar disorder. Zainab et al.⁴⁴ studied the "valuable" versus "misleading" information in YouTube videos about anxiety by using the global quality scale and discern tool. They reported that 137 out of 169 videos had useful information. Only 32 videos contain misleading information. Kim and colleagues⁴⁵ examined the relationship between the intention to engage in health exercise activities and the experience of

watching YouTube videos related to health exercise, as well as the mediating impact of digital health literacy and the moderating effect of parasocial interactions. They found that Increased YouTube viewing experience improved digital health literacy's cognitive, skill, and evaluative elements, all of which were important in raising the intention to engage in healthy exercise activity. In the study by Schröder et al.,⁴⁶ brief instructional YouTube health videos are useful resources for raising mental health literacy among instructors and students.

Other studies reported results that contradicted the findings of this study. For instance, Kwak et al.⁴⁷ found that YouTube videos about carpal tunnel syndrome were of low quality, meaning that they were imprecise and unreliable sources of information. They also had poor flow, and most of the information was not helpful. Another study found that the video content related to obsessive-compulsive disorder was largely inadequate.⁴⁸ The other study found that YouTube videos about Alzheimer's disease are inaccurate and incomplete.⁴⁹ Chidambaram et al.⁵⁰ investigated YouTube videos that contained misinformation on the human gut microbiota. They discovered that YouTube's content regarding the human gut microbiota is often of low reliability and quality. There are well-known issues with misinformation spreading on YouTube. A recent comprehensive review found that YouTube videos about health range in

quality from average to poor.²³ Therefore, YouTube has responded to the issue of misleading information by implementing its own solutions, such as giving preference to content created by medical professionals in search results.

This study has some limitations. First, it was limited to countries where English is spoken because only English-language videos of CBT-hypnosis were reviewed. Secondly, it only examined content on YouTube and ignored other platforms like Facebook, Instagram, TikTok, and Facebook where users could find medical information.

Conclusion

This study gives an overview of the YouTube platform and whether it is considered a source of good-quality and reliable information related to CBT-hypnosis for practitioners, patients, and their primary caregivers. According to our findings, the eligible videos that are available on the YouTube platform had moderate quality and reliability, indicating that the content is moderately objective (unbiased) and clear, and some important information is adequately discussed about CBT-hypnosis. This study may contribute to the body of knowledge and strengthen the case for adopting such media platforms as a helpful source of information.

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Review

Complications of capsulotomy in the treatment of psychiatric illness: A systematic review.

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ARTICLE HISTORY: Received 30 September 2024 / Revised 23 April 2025 / Published Online 5 August 2025

Cite this article as: Mavridis IN, Pyrgelis E-S. Complications of capsulotomy in the treatment of psychiatric illness: a Systematic Review, Psychiatriki 2026, 37:37-43.

<https://doi.org/10.22365/jpsych.2025.017>

ABSTRACT

For more than half a century, stereotactic neurosurgical procedures have been available in the treatment of patients with severe, debilitating symptoms of treatment-resistant psychiatric conditions such as obsessive-compulsive disorder (OCD). Such surgical interventions include stimulation and lesioning techniques. Capsulotomy is a lesioning procedure targeting the internal capsule. This systematic review aims to explore the safety profile of capsulotomy in the treatment of severe medically-refractory psychiatric illness, focusing on its complications. Methodologically, a literature search was conducted using the terms "psychiatric", "capsulotomy", and "complications" in the PubMed/Medline database until the end of 2022. The search retrieved 41 articles. Following screening for potential suitability, 39 articles relevant to the topic were further analyzed and finally used for this review. No specific assessment tool for risk of bias was used in this study. The vast majority of capsulotomy data in the literature comes from OCD patients, and the main modalities used for this procedure are radiofrequency (RF) ablation, Gamma Knife radiosurgery (GKRS), and magnetic resonance-guided focused ultrasound (MRgFUS). Postoperative complications are usually transient. These include neurological and psychiatric manifestations, cerebrovascular accidents, thromboembolic events, and infections (respiratory, urinary). Common complications are headache, focal edema, and frontal syndrome. Other complications include ataxia, seizures, urinary incontinence, weight gain, and fatigue. Regarding different techniques, urinary incontinence, sleep disorders, fatigue, and disorientation are frequent but transient complications of RF lesioning. Gamma capsulotomy has a risk of adverse radiation effects, such as radiation necrosis, brain edema, and cyst formation. MRgFUS seems to lack many of the inherent risks associated with more invasive treatment modalities. Capsulotomy complications, usually transient and self-limited, include neurological and psychiatric manifestations, cerebrovascular accidents, thromboembolic events, and infections. Their occurrence and nature depend on the chosen modality. The principal limitation of this study is the fact that most data come from case reports or case series. As a result, the total number of patients who underwent capsulotomy is limited. Further clinical research is mandatory to improve the safety.

KEYWORDS: Capsulotomy, complications, Gamma Knife, internal capsule, obsessive-compulsive disorder.

Introduction

For more than half a century, stereotactic neurosurgical procedures have been available in the treatment of patients with severe, debilitating symptoms of obsessive-compulsive disorder (OCD) refractory to appro-

prate pharmacological and other treatments.¹ Besides OCD, current literature suggests that specific stereotactic procedures may be efficient and relatively safe in some other treatment-resistant psychiatric conditions, such as major depression, pain, and anxiety.² Such sur-

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gical interventions include stimulation, such as deep brain stimulation (DBS), and lesioning techniques, such as anterior capsulotomy, anterior cingulotomy, subcaudate tractotomy, limbic leucotomy, and central lateral thalamotomy/anterior medial pallidotomy.³

Capsulotomy is a lesioning procedure targeting the internal capsule in the treatment of severe refractory psychiatric illness. It can be performed via stereotactic radiofrequency (RF) ablation (thermocapsulotomy, which has been used since the 1950s),^{4,5} stereotactic radiosurgery (usually Gamma Knife, gamma capsulotomy),⁵⁻⁷ and, more recently, magnetic resonance-guided focused ultrasound surgery (MRgFUS), a minimally invasive surgical method of precisely placed focal thermal lesions in the brain.⁸ The capsulotomy target involves fibers connecting the mediodorsal thalamus and prefrontal cortex.⁵ In RF ablation, which is the cheapest method, a stereotactically (frame-based) inserted electrode creates a thermal lesion at the intended target. In stereotactic radiosurgery (frameless or frame-based), the patient is inserted in the radiosurgical machinery, and focused beams of radiation create a lesion at the predefined target. It is an incisionless procedure. MRgFUS is similar to radiosurgery but uses focused beams of ultrasound instead of radiation and is less commonly available at the moment.⁴⁻⁸

In this systematic review, we aim to explore the safety profile of capsulotomy as a minimally invasive tech-

nique to treat severe medically-refractory psychiatric illness, primarily focusing on its complications. The main question to answer is: "Which are the complications of capsulotomy in the treatment of psychiatric illness?"

Methods

Methodologically, a literature search in the PubMed/Medline database was conducted using the terms "psychiatric", "capsulotomy", and "complications" until the end of 2022, which retrieved 41 articles. Following the PRISMA guidelines, the authors screened all articles for potential eligibility using relevance and English language abstracts as inclusion criteria. English language publications, including foreign language publications with abstracts in English, were included in this review. Following screening for potential suitability, 39 articles relevant to the topic (reporting capsulotomy complications) were further analyzed and finally used for this review (Figure 1). Two reviewers collected data from each report, and they worked independently. No specific assessment tool for risk of bias was used in this study.

Results

Conditions

Out of 41 publications, 39 that fulfilled the aforementioned inclusion criteria were further analyzed (Figure 1). Appropriately selected patients with major treatment-refractory psychiatric disorders can benefit

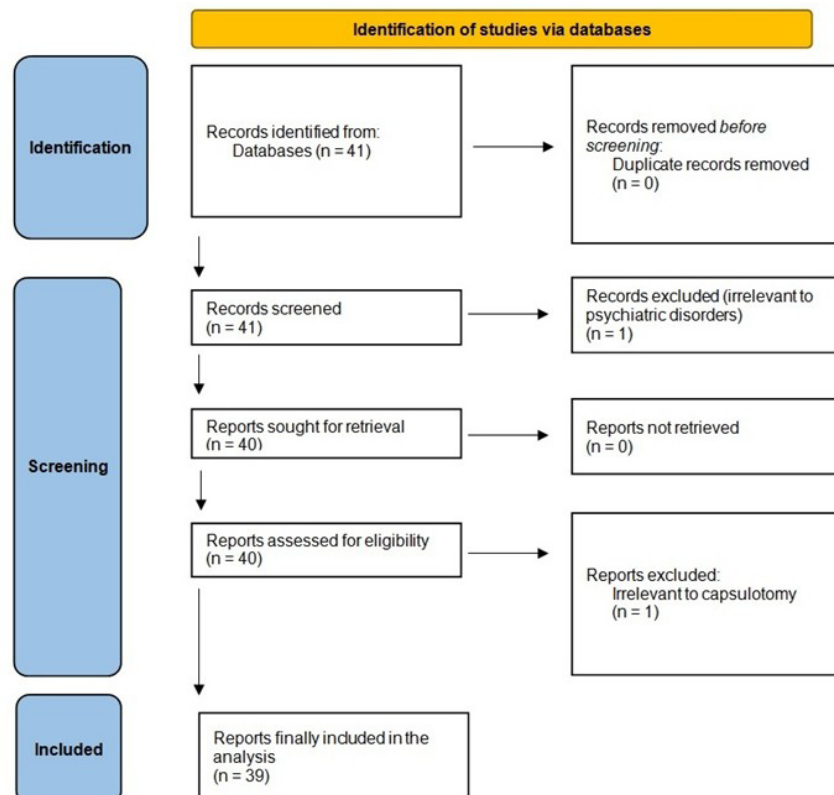


Figure 1. Article selection process of our analysis (PRISMA diagram).

from capsulotomy.⁵ Such disorders include severe refractory OCD,^{3-6,9-17} OCD with comorbid schizophrenia,⁶ bipolar affective disorder,¹⁸ anorexia nervosa,⁹ refractory depression,^{2,17,19} chronic and incapacitating anxiety disorders,^{2,10,20,21} aggressiveness²² and intractable chronic pain.^{2,10} Remarkably, the vast majority of capsulotomy

data in the literature comes from OCD patients (Table 1). The main modalities used for capsulotomy are RF ablation, Gamma Knife radiosurgery (GKRS), and, more recently, MRgFUS (Table 1). The first two methods have been used for decades, while the third is the newest one.

Table 1. Summary of clinical data regarding indication, sample, method, and complications of capsulotomy as a treatment option for psychiatric disorders.

Authors (year)	Disease	Number of patients	Lesioning method	Complications / comments
Lippitz et al. (1997) ¹³	OCD	22	RF	Lesions within the group of patients with poor outcome (n = 5) were located elsewhere, mostly further anterior in the internal capsule
Happe et al. (2001) ¹⁸	Bipolar affective disorder	1	RF	Impaired theory of mind
Ruck et al. (2006) ²¹	Anxiety	16	RF	Impairment of executive functions, apathy
Ruck et al. (2008) ⁵	OCD	25	RF or GKRS	Weight gain, executive dysfunction, apathy, disinhibition, memory problems, incontinence, seizures
Barbier et al. (2011) ⁹	Anorexia nervosa and OCD	1	RF	Transient bradycardia with accelerated junctional rhythm at rest, mild disorientation in place or time, moderate somnolence, slowed thinking, loss of concentration, apathy, emotional emptiness, mild loss of decorum
Christmas et al. (2011) ¹⁹	Major depression	20	RF	Urinary incontinence, nausea, dizziness, headache, confusion, ataxia, concentration problems, memory problems, loss of motivation, tiredness, somnolence, seizures, weight gain, subjective personality change, lack of emotional response, addiction
Jimenez et al. (2012) ²²	Aggressive behavior	10	GKRS	Disinhibition, somnolence in the immediate postoperative period, and paraparesis
D'Astous et al. (2013) ¹¹	OCD	19	Mechanical lesioning using a Bertrand leucotome	Frontal syndrome, urinary incontinence, pneumonia, urinary infection, hemiplegia due to perioperative hemorrhage, cognitive impairment
Liu et al. (2014) ²³	Schizophrenia	116	RF	Urinary incontinence (18), disorientation (4), sleep disorder (12), fatigue (10). These symptoms usually disappeared within two weeks. Long-term complications: bulimia (9), memory loss (7), personality changes (6), lazy behavior (5), hypererotism (4). One patient had slight bleeding and recovered without reoperation. One patient had a seizure and was controlled with antiepileptic medication
Batistuzzo et al. (2015) ²⁶	OCD	16	GKRS	One patient developed an asymptomatic radionecrotic cyst later during follow-up
Liu et al. (2018) ²⁹	Anorexia nervosa	74	RF	Common short-term side effects: urinary incontinence (9.5%), sleep disorders (10.8%), fatigue (8.1%). Long-term complications: disinhibition (8.1%), memory loss (4.1%), lethargy (5.4%)
Kim et al. (2018) ²⁷	OCD	11	MRgFUS	Headache and vestibular symptoms (mild and transient)
Huang et al. (2019) ³⁰	Epilepsy and severe* psychopathology	13	RF	Headache, confusion, transient memory deficits, weight gain
Gupta et al. (2019) ²⁴	OCD	40	GKRS	Mood disturbance (25%), worsening in Yale-Brown Obsessive-Compulsive Scale scores (7.5%), neurological complications (7.5%). One patient developed radiation necrosis with edema that improved with steroids.
Jung et al. (2019) ³¹	OCD	4	MRgFUS	None reported
Krámská et al. (2021) ³²	OCD	12	RF	None reported
Kasabkajian et al. (2021) ²⁵	OCD	1	GKRS	Manic episode, cognitive memory changes, visual hallucinations, confabulation, frontal lobe symptoms, hemispheric edema, small cyst

*Mainly positive psychotic symptoms, as well as aggression and excessive impulsivity, followed by anxiety, depression, and intellectual disability. GKRS: Gamma Knife radiosurgery; MRgFUS: magnetic resonance-guided focused ultrasound; OCD: Obsessive-Compulsive Disorder; RF: radiofrequency

Complications

Clinical manifestations

Postoperative complications are usually transient and self-limited within a short period. One of the most common complications is frontal syndrome.^{11,15} It can manifest as apathy, executive dysfunction, disinhibition, or increased perseverative behavior.^{5,9,14} Other usual adverse effects are local edema, often presenting with headache, which responds well to steroids,^{3,15,22} ataxia,²² paraparesis,²² and seizures, which are usually self-regressive.^{3,5,10} Impairment of sphincter control is also common, mainly presenting with urinary incontinence.^{3,10,11,19} Other complications include weight gain, somnolence, fatigue,^{3,5,10,19} disorientation, bulimia, memory loss, personality changes, lazy behavior, and hypererotism.²³

Transient postoperative confusion or delirium has also been reported.^{3,10} Other psychiatric complications such as hypomania/mania, addiction, suicidal ideation, impaired theory of mind, or negative changes of personality after capsulotomy are relatively rare.^{3,14,18-20} Permanent complications such as hemiplegia or cognitive deficits, although reported, are fortunately scarce.¹¹

Regarding cerebrovascular accidents following capsulotomy, intracranial hemorrhage is the most common. Infarcts affecting deep structures, e.g., the caudate nucleus, have been reported as well. Thromboembolic complications, such as deep vein thrombosis and air emboli,^{3,10,11} as well as cardiac complications, e.g., transient bradycardia with accelerated junctional rhythm,⁹ have also been described. Finally, there are several infections that can occur after the procedure, such as pneumonia and urinary tract infections.^{3,11} Table 1 summarizes data regarding indication, sample, method, and complications of capsulotomy in the treatment of psychiatric disorders.

Different modalities

- RF lesioning

As seen in Table 1, most of the complications mentioned above, as well as multiple adverse events in the same patient, can be observed after RF capsulotomy. The largest series (116 patients) reporting capsulotomy complications so far comes from Liu et al. (2014), who used capsulotomy to treat schizophrenic patients.²³ They reported urinary incontinence, sleep disorder, fatigue, and disorientation as frequent but transient complications. They further noticed long-term complications in their patients that included (in order of frequency) bulimia, memory loss, personality changes, lazy behavior, and hypererotism.²³

Doshi (2021)⁴ reported 107 patients who underwent RF lesioning for movement and psychiatric disorders, including 6 OCD patients who underwent anterior capsu-

lotomy/nucleus accumbens lesioning. All OCD patients were in remission. These authors reported dysarthria, confusion, hemiparesis, dyskinesia, and paresthesia as complications of RF lesioning that occurred in 12 patients (7 were transient), but these were not specific to capsulotomy.⁴

Zhan et al. (2014)³³ studied 53 medically intractable OCD patients who underwent MRI-guided bilateral anterior capsulotomy. Postoperatively, 37.9% were regarded as OCD symptom-free, 39.5% as clinically improved, and 22.6% experienced no improvement. The authors concluded that bilateral capsulotomy is a precise and relatively safe therapy for refractory OCD, which can improve patients' quality of life and restore their social function. They underlined the necessity of strict inclusion criteria for patients, considering the complications and the irreversibility of this procedure.³³

Jiménez-Ponce et al. (2011)³⁴ reported 12 patients with a primary diagnosis of aggressiveness refractory to conventional treatment, who were surgically treated with combined bilateral anterior capsulotomy and cingulotomy. Among them, 5 patients showed either mild or transitory postsurgical complications. According to the authors, the treatment successfully reduced aggressive behavior and improved clinical evaluations.³⁴

- GKRS

Gupta et al. (2019)²⁴ have reported the largest series of GKRS capsulotomy for OCD so far. They found mood disturbance as the commonest adverse event, affecting 1/4 of patients. This was followed by worsening in Yale-Brown Obsessive-Compulsive Scale scores and neurological complications, both affecting 7.5% of patients (Table 1).²⁴

Gamma capsulotomy has a particular risk of adverse radiation effects, mainly radiation necrosis or brain edema and/or cyst formation. Interestingly, a maximal dose less than 180 Gy is associated with fewer adverse effects.⁸ Radionecrotic cysts have been reported in 5% of patients at long-term follow-up.⁸ Kasabkojian et al. (2021)²⁵ underlined that GKRS capsulotomy complications can develop years after treatment, especially in cases of very high radiation doses. They also noted the consequences of severing more fibers of the anterior frontal region than intended and the importance of careful clinical and imaging follow-up.²⁵

Miguel et al. (2019)¹ reported frontal lobe edema and formation of delayed radionecrotic cysts as possible complications of GKRS capsulotomy for OCD. These adverse events, however, have become less common with modern radiation dose and targeting strategies. According to these authors, GKRS capsulotomy, and particularly its modern variant, i.e., gamma ventral capsulotomy, appears as a reliable treatment option for selected cases

of otherwise highly refractory OCD.¹ Moreover, Batusso et al. (2015) reported a double-blind, randomized controlled trial of GKRS ventral capsulotomy in 16 refractory OCD patients with no decline in cognitive or motor functioning at one-year follow-up.²⁶

Remarkably, we should note here that GKRS capsulotomy may be a viable option in patients with treatment-refractory Tourette syndrome with comorbid OCD,³⁵ as well as for other OCD-related disorders such as skin-picking disorder.³⁶

- MRgFUS

Mild and transient headache and vestibular symptoms have been reported following MRgFUS²⁷ (Table 1). Kumar et al. (2019)²⁸ reported a decision analytical model comparing MRgFUS to RF capsulotomy for OCD. Analyzing published data, they mentioned that complications occurred in 16.2% of RF cases. In 1.4% of cases, complications were considered acute/perioperative and incurred additional hospitalization costs. The adverse events, including neurological and neurobehavioral changes, did not incur further costs in the rest 14.8% of cases, although they impacted utility. Compared to RF capsulotomy, MRgFUS appeared more cost-effective. They concluded that MRgFUS lacks many of the inherent risks associated with more invasive treatment modalities for OCD.²⁸ According to other authors, MRgFUS has the advantages of less invasiveness and a real-time monitored procedure, and this modality is now growing to attempt potential applications to various brain disorders.³⁷

Discussion

Anterior capsulotomy is a generally safe, well-tolerated, and effective therapy for OCD.³⁸ The capsulotomy's surgical target includes the unilateral⁵ or bilateral anterior limb of the internal capsule (ALIC),^{5,9,11,18,19,21,27,31} occasionally combined with supragenual cingulotomy.²² GKRS capsulotomy has been performed for over 40 years in the treatment of refractory OCD. Long-term clinical response data and adverse outcomes from earlier empiric treatment parameters have resulted in shifting the target from its initial location within the midpoint of ALIC to its most ventral portion as well as the ventral striatum,⁷ where the nucleus accumbens belongs.³⁹⁻⁴¹

Remarkably, many of the early GKRS capsulotomy studies were complicated by clinically relevant radiation-induced adverse effects.⁷ More recent GKRS capsulotomy studies have demonstrated strong efficacy with diminished adverse effects with well-placed lesions created at lower radiation doses. Advances in neuroimaging technology, such as diffusion tensor imaging-based fiber tracking, may provide further insight into precisely targeting the ventral capsule/striatum, based on patient-specific variations in white matter connectivity.⁷

Pepper et al. (2015)⁴² reviewed the published literature and compared the outcome of ALIC capsulotomy and DBS of the ventral capsule/ventral striatum and nucleus accumbens in OCD. Remarkably, they found no difference in complication rates.⁴² Pepper et al. (2019) also reviewed the effectiveness and safety profile of anterior capsulotomy for OCD and found a low rate of serious complications.³⁸ More recently, Chang et al. (2021)⁸ reviewed ablative surgical techniques for OCD, including capsulotomy, and their complications.⁸ They found that adverse events following capsulotomy have been reported as transient/mild in 56.2% of patients and as permanent/serious in 21.4% of patients. These complications included apathy, incontinence, seizures, and executive dysfunction; these were also related to a very high radiation dose, multiple procedures, and larger targets. The authors importantly noticed that advancements in the capsulotomy procedure have significantly decreased its adverse events.⁸

Capsulotomy is a type of stereotactic psychiatric surgery that can be an effective and relatively safe treatment option when carried out by a specialized multidisciplinary team, aiming to treat carefully selected patients with chronic, severe, and medically-refractory psychiatric disorders. In this context only, capsulotomy can have fewer adverse effects and complications.¹⁵ New minimally invasive techniques, such as MRgFUS, have the advantage of avoiding skull opening and, thus, relevant complications, such as hemorrhage and infections, can be avoided.³ With the ongoing progress in modern neuroimaging techniques, future studies should focus on whether specific complications are associated with specific ALIC parts/tracts. This knowledge could enable safer targeting and improve the capsulotomy's safety profile.

Finally, ethics committee approval is a critical part of the design and execution of capsulotomy studies. Given that this is a last-resort procedure to manage a patient's illness that is refractory to all other treatments, appropriate institutional ethics approval is of paramount importance, along with careful study design. As with other treatment methods, explanation of potential complications and side effects to patients and their families is mandatory before making any decision to proceed.

As expected, this systematic review has several limitations. Its principal limitation is the fact that many of the included studies are case reports or case series, and data from other reviews have also been used. As a result, the total number of patients who underwent capsulotomy is restricted. Further studies, ideally multicentric, would be required in order to reach safer conclusions.

Conclusion

Capsulotomy is a lesioning procedure targeting the internal capsule in the treatment of specific severe,

treatment-resistant psychiatric disorders, mainly OCD. The modalities used for this procedure are RF ablation, GKRS, and MRgFUS. Postoperative complications are usually transient and self-regressing. These include neurological and psychiatric manifestations, cerebrovascular accidents, thromboembolic events, and infections. Urinary incontinence, sleep disorders, fatigue, and disorientation are frequent but transient complications of

RF lesioning. Its long-term complications include bulimia, memory loss, and personality changes. Gamma capsulotomy has the risk of adverse radiation effects, such as radiation necrosis, brain edema, and cyst formation. MRgFUS seems to lack many of the inherent risks associated with more invasive treatment modalities. Further clinical research is key to improving the safety of the capsulotomy.

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Review

Attachment in adolescence, intergenerational transmission, developmental outcomes and psychopathology.

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ARTICLE HISTORY: Received 12 March 2025 / Revised 18 June 2025 / Published Online 5 August 2025

Cite this article as: Salavou V, Giannakopoulos G. Attachment in adolescence, intergenerational transmission, developmental outcomes and psychopathology. *Psychiatriki* 2026, 37:44-50.
<https://doi.org/10.22365/jpsych.2025.020>

ABSTRACT

Adolescence (12 to 18 years) represents a critical period of development, wherein attachment undergoes significant changes as individuals navigate new emotional, cognitive, and social challenges and tend to create deeper connections with peers. As adolescents seek greater autonomy while simultaneously maintaining bonds with caregivers, attachment research explores how the attachment system evolves and the factors influencing it. First, we present an overview of several dimensions of attachment in adolescence, like re-organization of internal working models, peer relations, affect regulation, stability, and change of attachment. In addition, we discuss key aspects of attachment measures, self-report and interview-based instruments, reflecting upon the difficulties in capturing the attachment dynamics in this developmental phase. Second, we explore findings about the ways parental state of mind (secure, insecure, and unresolved), as well as parental reflective functioning, may influence adolescent attachment via mechanisms of intergenerational transmission. We focus especially on findings from clinical and high-risk samples. Third, we explore the impact that attachment in adolescence has on developmental outcomes and psychopathology. The review focuses on findings from Western culture cross-sectional and longitudinal studies, both on community and clinical samples over the last thirty years (1995-2025). We include studies using attachment constructs only, and exclude studies on adolescent mothers, adopted adolescents, and case studies. Finally, we reach conclusions in relation to recent developments in the field and future research directions.

KEYWORDS: Attachment in adolescence, intergenerational transmission, reflective functioning, developmental psychopathology, affect regulation.

Introduction

Bowlby^{1,2} defined attachment as an innate biological predisposition in children to seek comfort from their caregivers, particularly in situations of fear or distress. The child and caregiver form an attachment system, which serves as a haven that provides emotional safety during critical times of intense stress and as a secure base that encourages exploration of the world. The accessibility and responsiveness of the caregiver play a crucial role in the security of this attachment. Through selective processing and integration of information gathered from relational experiences, the child internal-

izes representations of the self, the caregiver, and their relationship. Over time, these representations become part of the child's internal model of self and others.³

The study of attachment has traditionally focused on infancy and childhood, yet adolescence represents a distinct developmental period marked by significant transformations in attachment dynamics. Unlike earlier stages, adolescence involves the reorganization of attachment patterns as individuals navigate autonomy while maintaining emotional bonds with caregivers.^{4,5} Models of attachment in adolescence emphasize the shifting reliance on peers as attachment figures, along-

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side ongoing negotiation of attachment needs with caregivers.⁶⁻⁹

Adolescence-specific research has grown over the last three decades, yet important gaps remain in our understanding of how caregivers' secure versus insecure states of mind, reflective functioning, affect regulation strategies, and unresolved status of loss or trauma may influence the dynamics of attachment in this developmental period. This review seeks to critically appraise key literature, including foundational contributions by researchers whose work on adolescent attachment offers significant insights.

First, we present an overview of findings regarding the specific dynamics of attachment in adolescence and key points in measuring attachment during this critical period. Second, we look into intergenerational transmission evidence, i.e., how parental state of mind (secure, insecure, and with an unresolved state of mind) and parental reflective functioning may influence attachment in adolescence, with a special interest in findings from clinical and high-risk samples. Third, we look into findings exploring the association of attachment in adolescence with developmental outcomes and psychopathology. Articles for inclusion were identified from PubMed and Science Direct databases and Google Scholar search engine over the last thirty years (1995-2025) for adolescents aged 12 to 18 years old. We included peer-reviewed studies, systematic reviews, and meta-analyses using attachment constructs only (i.e., not parental bonding) from Western culture, cross-sectional and longitudinal community and clinical samples. We excluded studies on adolescent mothers, adopted adolescents, and case studies. Finally, we reach conclusions in relation to recent developments in the field and the need for future research directions.

Attachment in Adolescence

Adolescence represents a critical period of development, wherein attachment undergoes significant changes as individuals navigate new emotional, cognitive, and social challenges. The turbulence of this period, marked by hormonal, emotional, and cognitive transformations, heightens vulnerability while simultaneously fostering increased autonomy from parents and deeper connections with peers and romantic partners.

Allen and Tan⁵ describe three primary areas of transformation in adolescence: attachment relationships with caregivers, intra-psycho processes, and peer relationships. Unlike in infancy, where attachment is primarily centered in physical proximity with the caregiver, the adolescent must balance attachment needs with the growing desire for exploration and independence, while undergoing a reappraisal of internal working models.¹⁰ Adolescents gradually shift from relying heavily on care-

givers for emotional regulation to seeking autonomy in meeting their attachment needs.

Even though maternal sensitivity has been identified as crucial for mother-infant interactions that promote security,¹¹⁻¹³ it is maternal supportiveness and attunement in adolescence, as well as de-idealization and dyadic relatedness, that significantly explain the variance in attachment security.⁶ Support from mothers, especially during conflict, is particularly influential in fostering attachment security.⁶

Current parent-adolescent interactions often have a stronger influence on attachment than past internal working models.^{6,14} However, early sensitive caregiving in childhood may have enduring effects on attachment in adolescence, even independently of the current quality of the parent-child relationship, especially for at-risk adolescents.¹⁵ Attachment security in adolescence may be as much a cause as an effect of the current caregiving environment.^{6,15,16}

Affect regulation strategies play a vital role in adolescent development, with the ability to manage emotions strongly linked to psychosocial functioning, autonomy, resilience, and long-term psychological adjustment.^{7,14,17-18} As adolescents develop metacognitive capacities to process emotions, they may increasingly seek emotional support from peers, particularly during critical moments.^{5,7,9,19} Although peers often gain importance during this phase, attachment to mothers typically remains paramount for securely attached adolescents.^{6,12,21}

In a systematic review of nineteen studies on peer attachment,⁷ adolescents with secure states of mind report emotionally close friendships, can be integrated in a larger peer group, report better abilities to resolve conflicts with friends, and are more socially accepted. Attachment with parents was found to be a mediator for intimacy in social relationships with peers. Those with insecure attachment were found to be less likely to turn to peers for support, were less likely to become intimate with peers of the opposite sex, and their long-term psychosocial adjustment was at increased risk. Severe difficulties in interpersonal functioning with peers are also reported for adolescents with disorganized attachment due to their difficulties in understanding the mental states of others.

Last but not least, there is no significant stability in attachment representation from infancy through late adolescence, both in high and low-risk samples.^{10,22-23} Potential changes in caregiver quality over time and possible measurement errors might explain this finding.¹⁰ Both ecological and gene factors seem to play a role in attachment formulation in adolescence, yet recent findings from adolescent twins suggest that genes override environmental influences.²⁴

Attachment during adolescence is not static but rather an adaptive quality that responds to changes in relationships and the broader social context. Factors such as parental availability, responsiveness, and the adolescent's evolving need for autonomy and affect regulation shape the attachment process throughout this period. The ability to balance autonomy with relatedness, as well as to navigate conflicts with parents while maintaining emotional security, is a key component of secure attachment during this developmental stage.

Measuring Attachment in Adolescence

Measuring attachment during adolescence presents unique challenges, as this developmental phase involves not only significant cognitive, emotional, and social changes but also changes in emotional needs among early, middle, and late adolescence.²⁵ For example, in middle adolescence, between 14 and 16 years, peers become significant for emotion regulation with increased autonomy from attachment figures, whereas late adolescence typically refers to the developmental period between ages 16 and 19, marked by increased cognitive maturity, identity consolidation, and preparation for adult roles.

Assessment of adolescent attachment has relied widely on the use of self-report measures and the original adaptation of adult attachment qualitative measures (e.g., the Adult Attachment Interview). Over the last twenty years, new observer-rated interviews and projective techniques have also been developed to address gaps in middle childhood and adolescence attachment research, especially given the limitations of earlier measures like SSP, focused on pre-verbal and pre-symbolic internal working models, which are more appropriate for younger children.²⁶

Developmental and clinical scientists tend to use interviews that focus on the current state of mind about early experiences and typically follow the ABCD categorical system (secure, avoidant, preoccupied, and disorganized). Social and personality scientists tend to use self-report measures that capture individuals' thoughts, feelings, and behavior in current close relationships, focusing on two dimensions, avoidance and anxiety.^{25,27}

The most recent review of attachment measures in middle childhood and adolescence found limited evidence for adequate measurement properties overall, with neither the ABCD model nor the two-factor dimensions of attachment style demonstrating strong validity in children and adolescents.²⁷ Although some self-report measures are correlated with attachment interviews, it remains unclear whether they assess the same construct. Despite employing a simpler methodology and being less time-consuming both in administering and in scoring than interviews, self-report measures are

subject to greater reporting bias. Interviews offer rich clinical material and provide more nuanced insights into how adolescents navigate emotional regulation and relational challenges, emphasizing the need for reflective functioning and mentalization as part of attachment assessments. Adolescent attachment interviews are better viewed as measuring affect regulation in the context of social interaction, rather than measuring parent-child relationships.¹⁷

Finally, there is no "gold standard" measure for attachment in adolescence so far.^{25,27} Therefore, it is recommended that researchers should define clearly the aspect of attachment they wish to investigate, using larger samples, different measures, and structural equation models to check how measures and individual items load onto latent attachment variables.²⁷ Attachment in adolescence is in a state of flux; therefore, the identity of primary attachment figures cannot be taken for granted, and various levels of specificity are required, as well as informed measurement decisions that take into account the different developmental tasks at different phases of this critical period.^{25,27}

Intergenerational transmission of attachment in adolescence and findings in clinical and high-risk samples

Intergenerational transmission refers to the process by which attachment qualities are influenced across generations, primarily through mental representations of relationships with caregivers and caregiving practices. The correspondence between adult attachment and infant attachment has been well-established.²⁸⁻³¹ Parental sensitivity has been identified as a mediator to explain transgenerational transmission in mother-infant dyads,¹¹ yet it is not enough since it still leaves 75% of the association unexplained, named "the transmission gap".^{13,31}

Although maternal sensitivity has been identified as a partial mediator of secure attachment,^{32,33} atypical frightening maternal behavior, maternal withdrawal, and role reversal, often accompanying an unresolved state of mind, have been associated with disorganized infant attachment.^{34,35} While intergenerational transmission influences attachment, it is not purely predictive. Family functioning factors (the couple relationship, support systems), neural mechanisms, socio-cognitive constructs such as reflective functioning and autonomy support, as well as differential susceptibility to parenting, have been identified as the most promising mediators to fill in the transmission gap in mother-infant dyads.³⁶⁻³⁸

The literature is vast on intergenerational effects of caregivers' states of mind on infants, and much less is known about older children and adolescents.³⁹ Stud-

ies examining the association between mother and adolescent attachment security have found a much lower correlation, with a correspondence rate of only 0.2.⁴⁰ This suggests that attachment patterns may shift during adolescence, potentially due to changes in the parent-child relationship and/or broader developmental factors, a fact consistent with Bowlby's² original environmental sensitivity hypothesis that, unlike infants, older children and adolescents may be less influenced by caregiver's state of mind.

Moreover, the intergenerational transmission of reflective functioning in parent-infant dyads has been explored for two decades,⁴¹⁻⁴³ but in the field of intergenerational transmission of reflective functioning within parent-adolescent dyads, the picture is different. To our knowledge, only two empirical studies -one cross-sectional⁴⁴ and one longitudinal-⁴⁵ have addressed this dimension, using interviews. First, in a small community sample of early adolescents (12.3-12.9 years old), maternal reflective functioning, rather than attachment security, has been shown to predict their reflective functioning.⁴⁴ Second, in the longitudinal study, the mother's state of mind concerning attachment during pregnancy could predict the firstborn adolescent's reflective functioning at age 17.⁴⁵

Concerning findings about the intergenerational transmission in clinical samples, we found one relevant cross-sectional study using interviews as a measure, with strong associations between maternal attachment and children/adolescents' attachment status with anxiety disorders as compared to a non-clinical sample (Mean=11.5, SD=2.1).⁴⁶ The sample presented strong associations with reflective functioning regarding themselves and maternal attachment preoccupation. Higher reflective functioning in the clinical group predicted a higher level of internalizing symptoms, a sign of how oversensitive children and adolescents with internalizing symptoms are to their mothers' mental state.

In another study utilizing longitudinal data from interviews and observer-rated measures, with an at-risk community cohort of mother-infant dyads, there was evidence that elevated maternal PTSD at six months increased the risk for disorganized attachment at 13 months and the lifetime risk of PTSD by adolescence, provided exposure to a life stressor.⁴⁷

Very little has been documented about the intergenerational effects of caregiver unresolved loss and trauma on adolescents in cross-sectional studies. Caregivers' unresolved trauma could predict teachers' reports of externalizing, attention, and social problems for thirteen-year-olds in a high-risk community sample, and an insecure state of mind in attachment was a moderator.³⁹ One recent review has highlighted the intergenerational association of unresolved trauma in daughters with

eating disorders and their mothers.⁴⁸ On the other hand, longitudinal studies have marked the long-term developmental psychopathology effects on offspring of maternal unresolved state of mind, including dissociative, borderline, and antisocial traits.^{49,50}

Studies on intergenerational transmission of attachment in adolescence are scarce, mainly cross-sectional, and with small sample sizes. Intergenerational transmission in adolescence is far from linear, and more studies are necessary to investigate the contributing multi-factorial dynamics. Disruptions in caregiver availability can be critical to understanding the underlying dynamics of developmental psychopathology and shouldn't be overlooked during psychiatric assessment.⁵¹

Attachment, Developmental Outcomes, and Psychopathology in Adolescence

Secure attachment has been related both to developmental and mental health outcomes in adolescence, measured with a mix of quantitative and qualitative methods. Especially, developmental outcome studies highlight the strong link between attachment representations and social competence,¹⁴ peer relationships,⁷⁻¹⁰ psychosocial adjustment,⁵²⁻⁵⁵ and resilience.^{18,26}

Studies from low to high-risk community samples suggest that insecure attachment organizations in adolescence may predict higher levels of antisocial problems and adjustment difficulties, with a distinct effect, independent of risk context, age, and gender.⁵²⁻⁵³ In a sample of 12 to 19-year-old adolescents (included since 58.3% were <15 years old), social factors mediated poor attachment and delinquent behavior, i.e., affiliation with deviant peers and parental monitoring.⁵⁶ Emotion regulation and social and relational competence seem to be mediators between secure attachment and emotional/psychosocial adjustment in adolescence.⁵⁷⁻⁵⁸ Additionally, attachment insecurity mediates the effect of parenting on changes in externalizing problems and self-esteem over time.⁵⁹ Externalizing problems, especially delinquency, in adolescence may predict maladaptive coping patterns in young adulthood.⁶⁰

Also, insecure, anxious, and avoidant attachment maternal representations have been positively associated with depressive symptoms,^{19,61,62} primarily in girls. Findings for the moderating role of maternal autonomy both on internalizing problems and risky behaviors, as well as links between paternal harsh conflict tactics and insecurity, highlight the significance of the familial context.¹⁶ Findings from attachment-based interventions in the community point to the potential for heightening affect regulation strategies in the parent-adolescent dyad and reducing avoidance and behavioral problems.⁶³⁻⁶⁴

Despite the strong link between insecure attach-

ment and both internalizing and externalizing behaviors,^{19,65-70} attachment can be understood within a vulnerability model, where both protective and risk factors shape future child and adolescent development, rather than being a direct cause of psychopathology.^{39,71} For example, in high-risk samples, vulnerability in adolescence has been associated with maternal depression, child maltreatment, and family functioning.⁷² Allen et al.⁷³ found that previously hospitalized adolescents who had experienced severe psychopathology were more likely to have insecure attachment and unresolved trauma, suggesting a link but no causal relationship between attachment organization and developmental psychopathology.

More recent studies on adolescents with borderline traits using interviews identify the mediating role of mentalizing between disorganized attachment and peer problems, as well as the mediating role of emotion dysregulation on social cognition, interpersonal difficulties, and attachment.⁷⁴⁻⁷⁶ The link between anxious attachment and emotion dysregulation has been detected in community samples as well.⁵⁶ Community girls at risk for binge-eating, with affect regulation difficulties, appeared more insecure in interview-measured attachment than not at risk peers.⁷⁷ A recent review highlights the need for developing research on mentalization and affect regulation difficulties in eating disorders.⁷⁸

Conclusions

This review highlights the significant strides made in understanding attachment theory and its role in developmental outcomes, yet it also underscores the need for continued research to fill existing gaps. One key conclusion is that attachment is not a static construct; rather, it evolves in response to ongoing relational experiences, particularly during periods of developmental transition like adolescence. Unlike adult attachment, there is no “gold standard” for measuring attachment in adolescence. The use of complementary self-report and observer-rated measures, as well as the exploration of their interrelationships and differential validity, seems to be the most useful way forward.

Concerning the first goal of this review, we established that far less is known regarding the intergenerational transmission of attachment in adolescents than in infants. Studies using interview-based measures of attachment are scarce, usually with small-sized clinical samples and generalizability issues. Since the correspondence rate of intergenerational transmission between mothers and adolescents is low, there is a strong need

for studies looking into the underlying mechanisms that affect attachment dynamics in adolescence. In addition, the transmission of unresolved trauma in parents, both in high-risk communities and clinical samples, requires further attention.

Given that emotion regulation strategies and reflective functioning capacities are involved in the context of autonomy negotiations, the field of intergenerational transmission in adolescence is underexplored. Another review in the future could focus on specific domains of adolescent attachment and explore how reflective functioning, emotion regulation, and social relatedness moderate security in parent-adolescent dyads. Secure attachment is not only a product of early childhood experiences but also ongoing interactions and relational experiences throughout development. This dynamic nature of attachment calls for a broader understanding that includes both protective and risk factors.

The second aim of this review was to explore the impact of attachment on developmental outcomes and psychopathology in adolescence. While attachment security has been linked to numerous positive outcomes, such as resilience, social competence, and psychological well-being, insecure attachment - particularly when coupled with other risk factors - can predispose individuals to a range of developmental psychopathologies, such as antisocial problems, depressive symptoms, eating pathology, and borderline traits.

Family characteristics and parental reflective functioning seem to affect attachment and need further exploration. Links between insecure attachment in parents and developmental psychopathology are evident, yet their mechanisms of interaction and their association with other risk factors need to be studied further. Emotion dysregulation seems to play a key role, not only as a sign of insecure attachment but also for its impact on interpersonal relationships. Understanding these pathways is essential for developing targeted interventions that can disrupt maladaptive cycles of attachment and promote secure relationships.

In conclusion, future research should continue to explore the nuances of this process, incorporating interdisciplinary perspectives and advanced technologies to deepen our understanding of attachment and its far-reaching impact on mental health and development. Through these efforts, we can continue to improve outcomes for children and adolescents, supporting them in forming secure, healthy relationships that foster lifelong well-being.

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Brief Communication

Similar cost-better results: the case of the hybrid Assertive Community Treatment model of care for severely mentally ill patients in rural Greece.

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ARTICLE HISTORY: Received 11 March 2025 / Revised 12 July 2025 / Published Online 5 August 2025

Cite this article as: Tsoli F, Botsari IA, Menti N, Kontoudi P, Pouliasi A, Peritogiannis V. Similar cost-better results: the case of the hybrid Assertive Community Treatment model of care for severely mentally ill patients in rural Greece. *Psychiatriki* 2026, 37:51-55.
<https://doi.org/10.22365/jpsych.2025.022>

ABSTRACT

The present study evaluated the impact of a hybrid Assertive Community Treatment (ACT) model of care on the direct medical costs of treating severe mental illness (SMI) patients in rural Greece. The study aimed to determine whether this model resulted in significant cost differences compared to usual treatment while also assessing its cost-effectiveness based on clinical improvements. A total of 23 patients with SMI and multiple hospitalizations were followed up for 16 months under the hybrid ACT model. Direct medical costs were estimated using previously published Greek data on schizophrenia treatment costs. Cost differences before and after the implementation of the hybrid ACT model were calculated, and cost-effectiveness was assessed using the Incremental Cost-Effectiveness Ratio (ICER), which reflects the cost per unit increase in Global Assessment of Functioning (GAF) scores. There was no statistically significant difference in direct medical costs between usual care (310,029€) and hybrid ACT care (313,896€), with a small cost increase of 3,867€ ($p = 0.077$). However, hybrid ACT care significantly reduced hospitalizations and length of inpatient stay, leading to an 86.9% reduction in total inpatient days. Clinical improvements were also observed, with GAF scores increasing from 40.43 to 47.26. Cost-effectiveness analysis demonstrated a particularly low ICER of 25.9€ per GAF point gained, suggesting a cost-efficient intervention. In an alternative scenario, the 2024 pricing was estimated with the use of the Consumer Price Index. In this case, the hybrid ACT care appeared to be significantly cost-saving by 25.5%. A rough estimation of indirect costs revealed further cost savings in favor of the hybrid ACT. The hybrid ACT model proved to be cost-effective due to its strong impact on reducing inpatient care and improving patient functioning. These findings align with international studies demonstrating the economic and clinical benefits of community-based mental health care. Future research should focus on larger, multicenter studies to confirm cost-effectiveness and explore the impact on indirect costs, such as caregiver burden and law enforcement involvement. The results support further investment in hybrid ACT services in rural Greece to enhance mental health care delivery in low-resourced settings.

KEYWORDS: Assertive community treatment, cost-effectiveness, functioning, rural areas, severe mental illness, treatment cost.

Introduction

Severe mental illness (SMI), such as schizophrenia-spectrum disorders and bipolar disorder, is still one of the leading causes of disability and economic bur-

den worldwide.¹ The economic burden of SMI is usually categorized as direct, indirect, and intangible costs, the latter being difficult to measure and often omitted from research.² Direct medical costs include expenditure on

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inpatient care, emergency department visits, community-based care, long-term institutional care, etc., whereas direct nonmedical costs include transportation and social services among other components. Indirect costs refer to productivity loss due to morbidity and premature mortality, such as unemployment, disability, and early retirement for patients or caregivers.²

In Greece, there is only a previous study that addressed the direct cost of the treatment of schizophrenia in a comprehensive manner,³ but research on the cost of the treatment of SMI in rural areas is lacking. In rural Greece, mental healthcare for patients with SMI is being delivered by the locally based Mobile Mental Health Units (MMHUs),^{4, 5} whereas in recent years a hybrid Assertive Community Treatment (ACT) model of care has been established, to address the needs of the most severely ill and difficult to engage patients.⁶

The objective of the present study was to estimate the changes in the cost of treatment in patients with SMI who received the comprehensive care delivered by a hybrid ACT team in a defined rural catchment area in Greece.

Materials and methods

The basic principles of the hybrid ACT model in Greek rural areas have been previously described in detail.⁶ In summary, a team of 4 mental health specialists (psychiatrist, psychologist, social worker, and nurse) delivers intensive mental health care for patients with severe mental disorders over working hours, based exclusively on regular home visits. That team is an expansion of the well-established MMHU of the area. The results of the hybrid ACT model in rural areas in the Epirus region, Northwest Greece, have been recently reported.⁷ Briefly, over a mean 16-month follow-up of 23 patients with SMI and multiple previous hospitalizations, involuntary admissions were reduced by 80.1%; voluntary admissions were reduced by 82.3%; whereas inpatient stay was reduced by 86.9%, from 52.83 to 6.91 days. Moreover, patients' functioning was significantly improved (scores in the Global Assessment of Functioning (GAF) scale from 40.43 to 47.26). The symptomatology of patients measured with the Brief Psychiatric Rating Scale (BPRS) was also significantly improved (from 42.91 to 36.68). Those data were further processed for the evaluation of cost differences concerning established treatments.

For the estimation of treatment costs in the present sample of patients, we used previously published data from Greece regarding the cost of treating patients with schizophrenia.³ According to that study, the direct annual cost of treating schizophrenia in Greece in 2005 was 10135€ for the subgroup of patients with a 100% possibility of a 50-day inpatient stay in 1 year, which corresponds to the mean 52.83-day inpatient stay of

the present sample over 16 months. The 16-month follow-up was achieved within a 3-year operation of the hybrid ACT team; accordingly, the 3-year operating cost of the hybrid ACT team was considered.

In an alternative scenario, we adjusted 2005 cost estimates to the pricing year 2024, with the use of the consumer price index (CPI) data, a methodology that has been previously used in research.⁸ According to the Hellenic Statistical Authority,⁹ the CPI in Greece in the years 2005 and 2024 was 84.75 and 117.98, respectively. Subsequently, it was hypothesized that 2024 direct treatment costs would be 1.392 times higher than 2005 costs.

A standard deviation of 10000€ was assumed based on ranges reported in similar economic evaluations of mental health interventions.¹⁰ A normal distribution of cost differences was assumed, consistent with the Central Limit Theorem and common practice in economic evaluations. This assumption allows for the use of a paired t-test to assess statistical significance in pre- and post-intervention cost comparisons, even in studies with small sample sizes.

For the performance of a cost-effectiveness analysis, the average cost-effectiveness ratio (ACER)

$$ACER = \frac{\text{The average cost of each patient}}{GAF \text{ value increase unit}}$$

and the incremental cost-effectiveness ratio (ICER)

$$ICER = \frac{(\text{Average cost with the ACT treatment} - \text{Average cost prior to ACT treatment})}{(GAF \text{ with ACT treatment} - GAF \text{ prior to ACT treatment})}$$

were used. The ICER indicates the mean additional mental healthcare costs, which must be spent to gain one additional point in the GAF scale in patients assigned to the hybrid ACT treatment.

A gross estimation of indirect treatment costs was also attempted. According to previous European data,⁸ the average proportion of indirect costs in total costs was 44%. Furthermore, previous research has shown that improvement in patients' functioning, measured by the GAF, is associated with significant cost savings.¹¹ Although previous studies have adopted a binary approach regarding the association of the GAF scores with cost savings, in this study, we considered a continuous approach. Accordingly, the previously reported increase in the GAF score of 16.9% in the present sample was assumed to result in at least a 10% decrease in indirect costs.

Results

The expected cost of care of the 23 patients before engagement with the hybrid ACT team was estimated at 310029€, according to the 2005 data. The cost of the inpatient treatment over the 16-month follow-up by

the hybrid ACT team (19071€) was added to the operating cost of the team (294825€). Table 1 shows the calculation of different costs. A paired t-test was conducted to assess whether the observed cost difference of 3867€ before and after the implementation of the hybrid ACT model was statistically significant. Given the lack of individual cost data, an assumed standard deviation of 10000€ was used for both pre- and post-treatment costs, based on similar economic evaluations. The analysis yielded a t-statistic of 1.85 and a p-value of 0.077, indicating that the cost difference was not statistically significant at the $p < 0.05$ level. The ACER and ICER values were 1998.2€ and 25.9€, respectively.

Table 2 presents the 2024 direct treatment cost projection. It appears that the operation of the hybrid ACT led to significant cost-saving (110198€ or 25.5%), alongside symptomatology and functioning improvement. In this scenario, the ACER and ICER values were negative.

Regarding indirect costs, their proportion (44%) in total costs was estimated at 7963€ in 2005 prices, or 11085€ in 2024 projected prices per patient per year. Accordingly, a further 24358€ or 33909€ cost reduction, respectively, would be expected, due to the operation of the hybrid ACT (Table 3). Figure 1 depicts the cost-effectiveness of the intervention in each cost scenario

(2005 and 2024, respectively).

Discussion

The present study addressed the impact of a hybrid ACT model of care for difficult-to-engage treatment SMI patients in rural Greece on the direct medical costs of care. Based on 2005 pricing data, there were no significant differences between the expected cost of care of patients with usual treatments and the cost of hybrid ACT care. However, the hybrid ACT model demonstrated clear clinical benefits, as reflected in the improved GAF scores and the ICER of 25.9€/GAF point, highlighting its potential value in mental health care delivery. In other words, the ICER of 25.9€/GAF point suggests that the added cost resulted in clinically meaningful improvements in patient functioning. Even more positive results were revealed with the projection of 2024 pricing data. In that case, cost savings were estimated as high as 25.5%. Furthermore, the hybrid ACT delivered care resulted in a significant reduction of patients' hospitalizations and inpatient stay, and a significant improvement in patients' symptomatology.⁷ An evaluation of a modified ACT model of care in Germany showed that the model was less costly and more effective compared with standard care in patients with SMI over 12

Table 1. Estimation of the cost difference between the previous treatment and treatment by the hybrid ACT team.

Variable	Calculation
Previously expected total direct medical cost for 16 months	$10135€^* \times 23\text{patients} \times 1.33\text{year} = 310029€$
Inpatient treatment cost over the 16-month follow-up	$6.91\text{days} \times 23\text{patients} \times 120€^{**} = 19071€$
Total operating cost of the hybrid ACT team (3 years)	294825€
Cost difference	$294825 + 19071 - 310029 = 3867€$

*Estimated annual cost per patient; **daily hospitalization cost (2005 price); ACT: Assertive Community Treatment.

Table 2. Projected estimation of the cost difference between the previous treatment and treatment by the hybrid ACT team for the year 2024.

Variable	Calculation
Previously expected total direct medical cost for 16 months	$14108€^* \times 23\text{patients} \times 1.33\text{year} = 431564€$
Inpatient treatment cost over the 16-month follow-up	$6.91\text{days} \times 23\text{patients} \times 167€^{**} = 26541€$
Total operating cost of the hybrid ACT team (3 years)	294825€
Cost difference	$294825 + 26541 - 431564 = -110198€$

*Projected estimated annual cost per patient; **daily hospitalization cost (projected price); ACT: Assertive Community Treatment

Table 3. Estimated indirect cost reduction due to the functioning improvement.

2005 pricing data	$7963€ \times 23\text{patients} \times 1.33\text{year} \times 10\% \text{ due to GAF improvement} = 24358€$
2024 projected pricing data	$11085€ \times 23\text{patients} \times 1.33\text{year} \times 10\% \text{ due to GAF improvement} = 33909€$

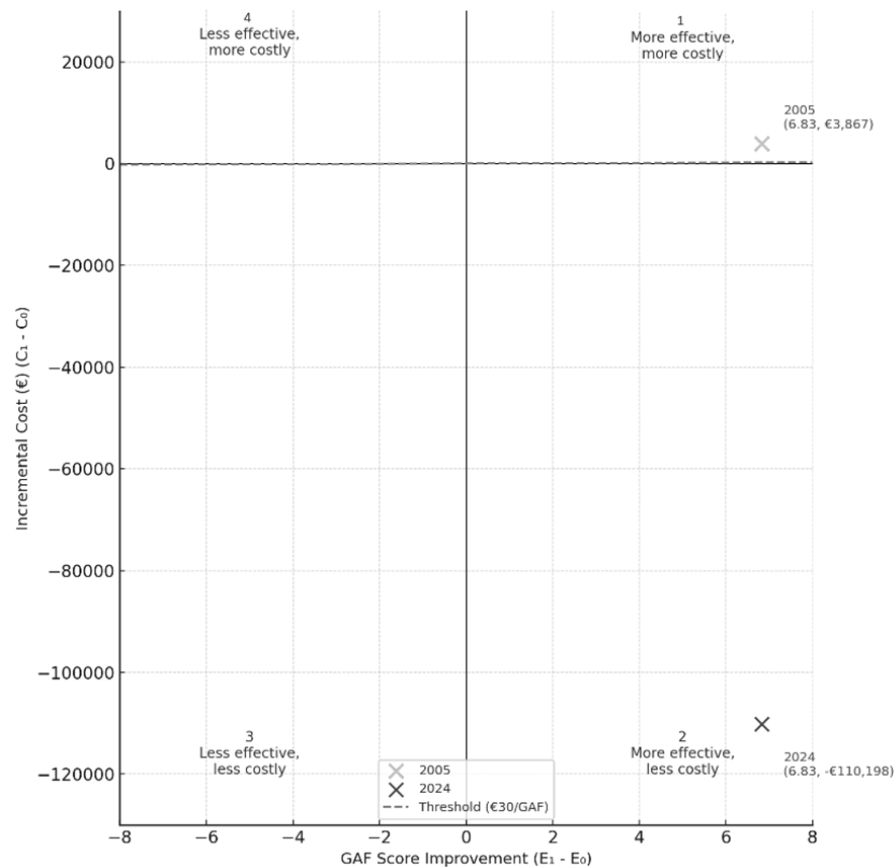


Figure 1. Cost-effectiveness plane comparing the hybrid ACT intervention in 2005 and 2024 pricing scenarios. The horizontal axis represents the change in effectiveness (GAF score improvement), and the vertical axis shows incremental cost relative to standard care. The light grey point (Quadrant I) indicates a minimal cost increase (€3867) in 2005, with improved outcomes. The dark grey point (Quadrant II) reflects the 2024 projection, showing both improved outcomes and a significant cost saving (€110198). The dashed line represents a threshold of €30 per GAF point gained.

months. The favorable effects of that care on cost were mainly attributed to the significantly reduced inpatient treatment and the improvement of patients' symptomatology and functioning,¹² as is the case in the present study. A previous study in Spain also yielded similar results, as better patients' functioning was found to be correlated with lower care costs.¹³ A recent study in Italy suggested that both symptom severity and functioning were predictors of direct treatment costs.¹⁴ Finally, a previous review on the cost of schizophrenia in Europe identified several factors, such as hospitalization, symptomatology, and adherence, that have a substantial impact on the direct healthcare costs of schizophrenia. Accordingly, the authors suggested that substantial savings could potentially be achieved by investing in the improvement of the efficiency of outpatient care, which would reduce the number of hospitalizations.¹⁵

The present study addressed the impact of hybrid ACT care on direct medical treatment costs, such as inpatient service use in SMI patients, whereas indirect costs associated with the care of schizophrenia, such as productivity loss of patients or informal care provided by caregivers for the patients, were only roughly considered. A recent study in the USA reported that the indi-

rect costs of the care of schizophrenia represent 73.4% of the total costs. Importantly, 32.7% of the costs involved caregiving, whereas a further 7.6% of the costs involved law enforcement services.¹⁶ Though the present study did not account for the latter costs, it is expected that they would be reduced due to the significant reduction in involuntary admissions and police involvement. It has been recently suggested that indirect costs of SMI are correlated with patients' symptomatology.¹⁷ Accordingly, it would be expected that indirect costs to be significantly reduced in the present sample of patients, due to the observed improvement in symptomatology and functioning,⁷ thus strengthening the case of hybrid ACT care delivery in rural areas of Greece. Indeed, the rough estimation of indirect costs in the present study, based on the improvement of patients' functioning and using European data on indirect costs of schizophrenia, revealed further cost savings. It should also be noted that the introduction of the hybrid ACT model of care may eliminate some of the direct non-medical costs associated with the care of schizophrenia, such as transportation, due to the care delivery exclusively with home visits and social work, which is integrated into the interdisciplinary team. Research on the economic evaluation

of MMHUs in rural Greece is rare. Indeed, there is only one previous study that mostly involved common mental disorders in an insular area, which suggested that the MMHU is a cost-effective treatment option in remote areas.^{18,19}

A limitation of the present study is that costs were calculated based on a previous report that used 2005 data, which represents the most comprehensive effort to calculate the cost of treatment of schizophrenia in Greece so far. Perhaps costs have changed over the last 20 years, particularly considering the economic recession in Greece in 2010 and the more recent COVID-19 pandemic. The projection of costs in 2024 pricing was based solely on the CPI, which is an acceptable method for cost adjustment, but still may not be accurate. Other limitations that may impact the generalizability of findings include the small study sample and the study of a single hybrid ACT team.

The results of the present study are relevant and highlight the positive impact of a low-cost modified

version of a highly resourced specialized service on the cost of care of severely mentally ill patients in rural areas. Along with the previously reported notion that this type of care may improve symptomatology and functioning in those patients,⁷ the findings of the present study could be relevant for mental healthcare and policy in rural and low-resourced settings.

The results reported here are encouraging and support the role of hybrid ACT care in the treatment of SMI in rural areas. It appears that a particularly small amount of further investment may result in a great reduction of inpatient treatment and significant improvements in patients' symptomatology and functioning, thus merits consideration by the Greek state. It is also possible that such positive results may result in significant cost savings. However, the present results warrant replication by multicenter studies, with the participation of large samples of patients, designed to address the cost-effectiveness of hybrid ACT care in rural settings.

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Letter to the Editor

Updating the position of fluoxetine: Editorial shift or evidence-based evolution?

ARTICLE HISTORY: Received 28 April 2025 / Published Online 5 August 2025

Cite this article as: Mikellides G, Evagorou O, Tantele M. Updating the position of fluoxetine: Editorial shift or evidence-based evolution? *Psychiatriki* 2026, 37:56-57.

<https://doi.org/10.22365/jpsych.2025.018>

To the Editors,

The Maudsley Prescribing Guidelines in Psychiatry have long been regarded as a cornerstone of psychopharmacological practice internationally. In the recently published 15th edition (2025), a notable shift in the positioning of fluoxetine is observed, particularly regarding its use during pregnancy. Fluoxetine is no longer presented as a first-line option without the inclusion of new robust evidence to justify this downgrading.^{1,2}

Historically, fluoxetine has been recognized as a first-line SSRI due to its well-established efficacy, favorable tolerability, long half-life protecting against withdrawal symptoms, and safer profile in overdose compared to older antidepressants.^{3,4} In the 15th edition, it is stated that “an association between prenatal SSRI use and congenital heart defects has been reported, with some studies suggesting a higher risk with fluoxetine and paroxetine”.¹

The only relevant citation is Reefhuis et al. (2015),⁵ which employed Bayesian analysis to reevaluate previous associations. Although a slight increase in risk for specific congenital anomalies (e.g., right ventricular outflow tract obstruction) was identified, the study concludes that the absolute risks are small and that most SSRIs, including fluoxetine, are not significantly associated with specific birth defects.

It is important to highlight that this study was already available at the time of the 14th edition (2021),² where fluoxetine continued to be considered an appropriate and safe choice during pregnancy. This raises concerns about whether the change in tone in the 15th edition reflects genuine new scientific developments or simply evolving clinical preferences.

Moreover, current NICE guidelines^{6,7} do favor sertraline due to a slightly lower observed risk in pregnancy. However, they also emphasize that women benefiting from an existing SSRI treatment should not be advised to switch medications solely because of pregnancy. Notably, fluoxetine remains the only SSRI officially approved for treating moderate to severe depression in adolescents aged 8–18 years.⁸

While adapting guidelines to evolving prescribing practices is understandable, in authoritative references such as the Maudsley Guidelines, it is crucial to clearly distinguish between evidence-based updates and pragmatic clinical trends. Failure to do so may inadvertently undermine confidence in long-standing, evidence-supported treatments like fluoxetine, ultimately affecting clinical decision-making.

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