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#### **DEAR COLLEAGUES!**

I am pleased to introduce another thematic issue of Consortium Psychiatricum. This time, it is dedicated to eating disorders.

First, let me take this opportunity to thank professor Oleg Skugarevsky, who kindly agreed to serve as guest editor to this issue and to share with us his expertise in the field of eating disorders.

I also want to thank all the authors, who submitted works for this thematic issue. I think that the final collection of articles selected for publication covers nearly all the important aspects of the thematic problem discussed in this issue.

The issue contains five original research articles that discuss such phenomena as the risk factors of eating disorders in girls, suicidal behavior and non-suicidal self-injuries in patients with eating disorders, the role of meta-cognition in symptoms of anorexia and bulimia, and the qualitative study on the perceptions of eating disorders by primary care practitioners.

The issue also features two reviews: one that deals with the pharmacological strategies of appetite modulation in eating disorders; and the other, with the prevalence of eating disorders in bipolar patients.

Two short papers draw our attention to the not-so-widely discussed, but still highly relevant, topics of practice: eating disorders in pregnant women and the role of nutritionist in a treatment team.

We continue to publish papers on the organization of community psychiatry, this time with a paper from Bulgaria.

Beginning with the previous issue, we have launched a new rubric that deals with the history of psychiatric hospitals and institutions. It is my hope that the topic will be of interest to our readers, because it goes beyond the scope of a particular institution to reflect on an epoch and provide a vista into the history of psychiatry, this time, in the examples of several territorial psychiatric hospitals of the Russian Empire between the 19th and 20th centuries.

Enjoy!

George Kostyuk, Editor-in-Chief, Consortium Psychiatricum



#### DEAR COLLEAGUES,

Let me applaud the very idea to dedicate an entire issue of the journal to eating disorders. The topic is particularly attractive since it seeks to bring under one rubric this group of biological disorders that develop and change in response to the psychosocial challenges the subject faces. While it primarily manifests as a "man-made" disorder, abnormal eating behavior always raises the question of the "limits of responsibility" of its psychological mediators, on the one hand, and that of the biological mechanisms underlying the predisposition and the severe biological consequences and complications, on the other.

The phenomenology of eating disorders in the paradigm of the biopsychosocial approach challenges the health care system, testing its readiness to integrate with the neurosciences. According to the clinical approach in psychiatry, abnormal eating behavior can legitimately be viewed through the lens of transdiagnostic phenomena. Both its initial and overt clinical symptoms can serve as a "gateway" to the serious mental disorders (for example, schizophrenia spectrum disorders, affective psychotic disorders), making their diagnosis difficult and thereby complicating treatment strategies, and worsening the prognosis. At the same time, since eating disorders are manifestations of a hedonistic mechanism and impulse control disruption, they increase the risk of suicide, which often affects the treatment strategy for patients suffering from these ailments.

The collection of articles in this issue brings these contexts together in a unique way. These publications expand our understanding of the phenomenology continuum of abnormal eating behavior, from its preclinical manifestations on a population scale to its clinically visible states. Particular attention, in our opinion, should be focused on the material concerning the variety of views amongst general practitioners on the phenomenology under discussion from the standpoint of the cultural characteristics of the citizens of the Kyrgyz Republic. Perinatal risks of abnormal eating behavior are discussed with a view to developing strategies for psychotherapeutic assistance.

I hope that immersion into the unique developments and discussion of the various aspects of abnormal eating behavior will enrich the real practice of specialists and contribute to their professional growth.

Professor O.A. Skugarevsky

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# The Paradoxical Moderating Effects of Metacognition in the Relationships between Self-esteem, Depressive Symptoms, and Quality of Life in Anorexia and Bulimia

Парадоксальное опосредующее влияние процессов метапознания на взаимосвязь между самооценкой, симптомами депрессии и качеством жизни у пациентов с анорексией и булимией

#### doi: 10.17816/CP6139 Original research

Cassi R Springfield<sup>1</sup>, Kelsey A Bonfils<sup>1</sup>, Nikita Chernov<sup>2</sup>, Tatyana Moiseeva<sup>2</sup>, Marta Sozinova<sup>2</sup>, Nadezhda Dmitryeva<sup>2</sup>, Paul H Lysaker<sup>3,4</sup>, Olga Karpenko<sup>2</sup>, George Kostyuk<sup>2</sup>

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#### ABSTRACT

**BACKGROUND:** Self-esteem and depressive symptoms contribute to a lower quality of life in people suffering from eating disorders. However, limited research has examined whether other factors may affect how these variables influence one another over time. Metacognition is a previously unexplored determinant that may impact the relationships between self-esteem, depressive symptoms, and quality of life in instances of eating disorders.

**AIM:** This study sought to examine metacognitive self-reflectivity and mastery as moderators of the relationships between self-esteem, depressive symptoms, and quality of life and to determine if these relationships are different in people with anorexia compared with people with bulimia.

**METHODS:** Participants with anorexia (*n*=40) and bulimia (*n*=40) were recruited from outpatient clinics. The participants were assessed on their metacognitive ability and self-reported on measures to assess their depressive symptoms, self-esteem, and quality of life.

**RESULTS:** The results indicate that metacognitive self-reflectivity moderates the relationship between self-esteem, depressive symptoms, and quality of life in people with anorexia such that when self-reflectivity is high, lower self-esteem and higher depressive symptoms are associated with a lower quality of life. These relationships did not appear to be significant when self-reflectivity was low. In contrast, in the anorexia and bulimia groups, metacognitive mastery appeared to moderate the relationships between self-esteem, depressive symptoms, and quality of life such that when mastery was low, lower self-esteem and higher depressive symptoms were associated with a lower quality of life. These relationships did not appear relationships did not appear significant when mastery was high.

**CONCLUSION:** Metacognitive self-reflectivity and mastery seem to play paradoxical moderating roles in the relationships between self-esteem, depressive symptoms, and quality of life in people with anorexia and bulimia. These findings pave the way toward further research and have important clinical implications.

#### аннотация

**ВВЕДЕНИЕ:** Уровень самооценки и наличие симптомов депрессии способствуют снижению качества жизни при расстройствах пищевого поведения. Тем не менее, лишь ограниченное число работ посвящено вопросу влияния различных факторов на динамику данной взаимосвязи. Определяющую роль во взаимосвязях самооценки, симптомов депрессии и качества жизни при расстройствах пищевого поведения могут играть ранее не исследованные процессы метапознания.

**ЦЕЛЬ:** Изучить процессы метапознания — способность к саморефлексии и мастерство — как факторы, которые могут опосредовать связь самооценки, симптомов депрессии и качества жизни, и выявить возможные различия этих процессов между группами пациентов с анорексией и с булимией.

**МЕТОДЫ:** В исследование были включены пациенты с анорексией (n=40) и булимией (n=40), получавшие лечение в амбулаторных условиях. Исследователи проводили оценку их способностей к метапознанию; также участники самостоятельно заполняли опросники, касающиеся депрессивных симптомов, самооценки и качества жизни.

**РЕЗУЛЬТАТЫ:** Результаты демонстрируют, что саморефлексия опосредует взаимосвязь между самооценкой, симптомами депрессии и качеством жизни у пациентов с анорексией: при высоком уровне способности к саморефлексии низкая самооценка и выраженные симптомы депрессии ассоциированы с ухудшением качества жизни. При низкой способности к саморефлексии данная связь не была статистически значимой. При этом мастерство в группах с анорексией и с булимией оказывает влияние на взаимосвязь самооценки, симптомов депрессии и качества жизни: низкая самооценка и выраженные симптомы депрессии были ассоциированы с ухудшением качества жизни и с булимией оказывает влияние на взаимосвязь самооценки, симптомов депрессии и качества жизни: низкая самооценка и выраженные симптомы депрессии были ассоциированы с ухудшением качества жизни при низком уровне мастерства. Данная связь не была статистически значимой при высоком уровне мастерства.

**ЗАКЛЮЧЕНИЕ:** Процессы метапознания, такие как способность к саморефлексии и мастерство, оказывают парадоксальное влияние на взаимосвязи между самооценкой, симптомами депрессии и качеством жизни у пациентов с анорексией и булимией. Эти результаты открывают перспективы для дальнейших исследований и имеют важное клиническое значение.

**Кеуwords:** eating disorders; self-reflectivity; bulimia; anorexia; metacognitive mastery **Ключевые слова:** расстройства пищевого поведения; способность к саморефлексии; булимия; анорексия; метакогнитивное мастерство

#### INTRODUCTION

Eating disorders, including anorexia nervosa and bulimia nervosa, are associated with a broad array of disruptions in psychological functioning, which, along with symptoms of eating disorder, can uniquely negatively affect quality of life across multiple domains [1, 2]. Two of the most studied psychological phenomena to date that accompany eating disorders are low self-esteem and depressive symptoms. Low self-esteem has been identified, for example, as an important risk factor in the development and persistence of eating disorders [3, 4] and is linked to poorer outcomes [5]. Depressive symptoms (e.g., low mood, loss of interest or pleasure in life activities, unjustified feelings of guilt, etc.) have similarly been linked to poorer outcomes for people with eating disorders [6, 7].

While this research has painted a richer picture of how low self-esteem and depressive symptoms are linked to poor quality of life over time in cases of eating disorders, it is less clear whether these relationships are affected by other psychological variables. As such, work is needed to search for potential determinants of these relationships in people with eating disorders in order to better understand the causal roots of poor quality of life and identify potential mechanisms which could be targeted by treatment.

One potential set of psychological processes that might affect the relationships between self-esteem, depressive symptoms, and quality of life involves metacognition. Metacognition in general refers to the process of thinking about, monitoring, and adjusting one's own thoughts, and can include attitudes about habitual thought processes, error monitoring, as well as forming an integrated sense of oneself and others [8]. As research has evolved, it has been suggested that metacognitive processes underlie not just how persons choose to take discrete actions, but also allow persons to form a larger and evolving sense of themselves and others as unique persons in the world [9]. Following this, deficits in metacognition, in particular those that manifest in difficulties forming an integrated sense of self or others, have been suggested to represent a transdiagnostic phenomenon which affect quality of life across differing forms of mental disorders, including schizophrenia, depression, bipolar disorder, posttraumatic stress disorder, and personality disorders [2,10]. This work suggests that metacognitive capacity may have a complex relationship with quality of life, allowing persons to both be aware of the realities of the challenges they face as well as potentially experiencing the devastation of loss [11-13].

Turning to eating disorders, preliminary work suggests that there are impairments in metacognition in these populations [14-17]. Notably, one study found evidence of significant metacognitive deficits which are relatively more severe in anorexia relative to bulimia [18]. The study further indicated that poorer metacognitive capacity was predictive of more severe levels of general psychopathology in bulimia (e.g., positive psychotic symptoms, negative psychotic symptoms, cognitive symptoms, and hostility) and higher levels of disordered eating behavior in anorexia. This finding raises the possibility that metacognitive abilities in eating disorders may similarly influence quality of life, as they do in other conditions, which may potentially help us in understanding how self-esteem and depressive symptoms are related to guality of life in general or, more specifically, in one particular form of eating disorders.

To explore this issue, the current study examined whether two domains of metacognition — metacognitive

self-reflectivity and metacognitive mastery — play a role in the relationships between self-esteem, depressive symptoms, and quality of life in eating disorders. The first of these domains, self-reflectivity, refers to the ability to identify and distinguish between one's own mental experiences, including thoughts and emotions, and integrate these experiences in a meaningful way to form increasingly complex ideas about oneself [19]. One way this ability could affect the relationships between low self-esteem, depressive symptoms, and quality of life is that those with higher levels of self-reflectivity might be able to perceive in clearer detail the links between their emotional distress and the general state of their lives. This is consistent with the results of work done among people with obsessive compulsive disorders showing that increased reflection upon one's cognitive processes can be associated with increased negative appraisals of intrusive thoughts and increased importance placed on these thoughts [20]. This might also be thought to parallel what has been referred to as depressive realism in persons in general or the insight paradox observed in psychosis, in which increased insight results in higher levels of distress [21].

The second metacognitive domain is mastery. Mastery refers to the ability to make sense of psychosocial challenges and then use metacognitive knowledge of oneself and others to decide how to effectively respond to them. While self-reflectivity could enable low self-esteem and depressive symptoms to result in low quality of life, mastery may have the opposite effect. With greater levels of mastery, persons are more likely to be able to make sense of and live with the pain of low self-esteem and depressive symptoms and be able to achieve a relatively higher quality of life. This conclusion has been supported in studies of psychosis indicating that symptoms are less disruptive when mastery is at relatively greater levels [22] and that mastery is related to generally higher levels of quality of life over time [23]. Additionally, both metacognitive selfreflectivity and metacognitive mastery have been identified as moderating variables in other disorders, including schizophrenia-spectrum disorders, bipolar disorders, and major depressive disorders [22, 24].

To explore these questions, we assessed self-esteem, depressive symptoms, metacognitive self-reflectivity, metacognitive mastery, and several aspects of quality of life among adults with two forms of eating disorders: anorexia and bulimia. We chose these two disorders, because while low self-esteem, depressive symptoms, and poor quality of life are prominent features in each, different risk factors and maintenance processes have been identified, and metacognition appears, at least preliminarily, to have different correlates in each disorder [18].

This study had two primary aims. First, we sought to examine whether metacognitive self-reflectivity and metacognitive mastery moderated the relationships between self-esteem and quality of life and depressive symptoms and quality of life. As described above, we had competing hypotheses regarding the role of metacognitive self-reflectivity and mastery in these relationships; thus, we aimed to examine whether self-reflectivity and mastery *strengthened* or *weakened* the negative effects of poor selfesteem/experiences of depressive symptoms with qualityof-life outcomes. Second, we aimed to explore whether these relationships would vary between diagnostic groups of anorexia and bulimia.

#### METHODS

#### Participants

Participants consisted of adults diagnosed with anorexia nervosa (*n*=40) and bulimia nervosa (*n*=40). They were recruited from the outpatient department of Mental-health clinic No. 1 named after N.A. Alexeev via referral from their treating physician. The participants were not eligible if they had ongoing alcohol or drug dependence, neurological disorders, had been hospitalized in the preceding month, or if they were unable to provide informed consent.

#### Measures

The Metacognition Assessment Scale-Abbreviated (MAS-A) [25] was used to assess metacognitive capacity. MAS-A scores were derived from transcripts of the Indiana Psychiatric Illness Interview (IPII) [26], which is a semistructured interview that asks participants to describe their life story and their understanding of their mental illnesses. The MAS-A produces a total score, as well as four subscale scores, including self-reflectivity, awareness of the minds of others, decentration, and mastery [19]. For the current study, we focused on the self-reflectivity and mastery subscales, both of which range from 0 to 9. Higher scores on the self-reflectivity subscale suggest a greater ability to think about and integrate one's own thoughts and emotions in increasingly integrated, as opposed to fragmented, ways. Higher mastery scores in parallel reflect the ability to find increasingly individualized and nuanced ways to understand and respond effectively to psychosocial

challenges. This study used a Russian language version of the IPII and the MAS-A, which has been used previously to measure metacognition in Russian samples [27].

The Rosenberg Self Esteem Scale (RSES) [28] is a 10item self-report measure that assesses global self-worth. Responses are provided on a 4-point Likert scale from strongly agree (4) to strongly disagree (1). The total score is calculated by summing all items. Higher scores indicate better self-esteem.

The Beck Depression Inventory-II (BDI-II) [29] is a 21-item self-report scale that assesses the severity of depressive symptoms. Responses to each item are on a 4-point Likert scale from 0–3, with higher scores indicating more depressive symptoms. An overall score is calculated by summing the ratings for each item (range: 0–63).

The World Health Organization Quality of Life (WHOQOL) [30] questionnaire is a 100-item self-report measure that assesses quality of life across six domains: psychological wellbeing, physical health, environment, level of independence, social relationships, and spiritual, religious, and personal beliefs. Responses to each item are on a 1–5 Likert scale, with higher values indicating better quality of life.

#### **Procedures**

Procedures were approved by the ethics committee of Mental-health clinic No. 1 named after N.A. Alexeev. After securing informed consent, diagnostic clinical interviews were conducted to confirm the diagnoses. Diagnoses were determined according to ICD-10. The IPII, RSES, BDI-II, and WHOQOL were then administered by a trained interviewer. IPII interviews were transcribed and rated by raters trained by the author of the MAS-A (PL). MAS-A raters were blind to other scores. All measures were administered in the Russian language.

#### **Statistical analysis**

First, the demographic characteristics and mean scores for each group were examined. Pearson's R correlations were then conducted to examine bivariate relationships between MAS-A self-reflectivity, MAS-A mastery, RSES, BDI, and WHOQOL domains. The PROCESS macro [31] in SPSS 29.0 was used to conduct a series of moderation models, which were run separately across the two diagnostic groups. The relevant predictor (i.e., RSES or BDI), the moderator of interest (i.e., MAS-A self-reflectivity or MAS-A mastery), and the interaction term between these variables were entered into separate regression models predicting WHOQOL Table 1. Means, standard deviations, and correlations by diagnostic group

Anorexia ( <i>n</i> =40)										
	Mean (SD)	1	2	3	4	5	6	7	8	9
RSES	25.08 (3.97)									
BDI	15.05 (10.27)	-0.21								
MAS-A self-reflectivity	3.31 (0.49)	0.04	0.03							
MAS-A mastery	2.23 (0.48)	0.09	0.02	0.29						
WHOQOL-social	35.98 (5.03)	0.51***	-0.40**	-0.22	0.06					
WHOQOL-physical	40.03 (6.73)	0.50***	-0.43**	-0.04	0.12	0.56***				
WHOQOL-independence	60.38 (10.68)	0.19	-0.14	-0.07	0.003	0.43**	0.38*			
WHOQOL-environment	96.13 (14.47)	0.70***	-0.33*	-0.16	0.20	0.57***	0.68***	0.38*		
WHOQOL-spiritual	14.13 (3.80)	0.46**	-0.34*	-0.14	0.22	0.54***	0.54***	0.13	0.61***	
WHOQOL-psychological	54.68 (11.74)	0.54***	-0.48**	0.02	-0.07	0.59***	0.70***	0.21	0.58***	0.53***
Bulimia ( <i>n</i> =40)										
	Mean (SD)	1	2	3	4	5	6	7	8	9
RSES	25.28 (6.54)									
BDI	11.75 (9.92)	-0.19								
MAS-A self-reflectivity	4.11 (0.46)	-0.22	0.13							
MAS-A mastery	3.0 (0.68)	-0.16	0.03	0.49***						
WHOQOL-social	40.60 (7.38)	0.18	-0.45**	0.03	-0.03					
WHOQOL-physical	37.15 (8.54)	0.23	-0.37*	-0.26	-0.35*	0.33*				
WHOQOL-independence	58.40 (11.06)	0.06	-0.36*	-0.14	-0.28	0.16	0.62**			
WHOQOL-environment	100.48 (10.84)	0.34*	-0.46**	-0.16	-0.13	0.39*	0.57**	0.46**		
WHOQOL-spiritual	14.65 (3.09)	0.15	-0.45**	-0.14	-0.16	0.54**	0.06	0.04	0.07	
WHOQOL-psychological	60.63 (13.98)	0.31	-0.63***	-0.13	-0.18	0.60***	0.63***	0.45**	0.63***	0.46**

*Note:* \*\*\**p* <0.001; \*\**p* <0.01; \**p* <0.05. For MAS-A self-reflectivity and MAS-A mastery, higher scores indicate better metacognition. For RSES, higher scores indicate better self-esteem. For BDI, higher scores indicate more severe depressive symptoms. For WHOQOL domains, higher scores indicate better quality of life. RSES=Rosenberg Self Esteem Scale; BDI=Beck Depression Inventory-II; MAS-A self-reflectivity=Metacognition Assessment Scale-Abbreviated — Self-Reflectivity; MAS-A mastery=Metacognition Assessment Scale-Abbreviated — Mastery; WHOQOL-social=World Health Organization Quality of Life — social relationships; WHOQOL-physical=World Health Organization Quality of Life — physical health; WHOQOL-independence=World Health Organization Quality of Life — level of independence; WHOQOL-environment=World Health Organization Quality of Life — environment; WHOQOL-spiritual=World Health Organization Quality of Life — spiritual, religious, and personal beliefs; WHOQOL-psychological=World Health Organization Quality of Life — psychological well-being.

domains (WHOQOL-psychological, WHOQOL-social, WHOQOL-physical, WHOQOL-independence, WHOQOLenvironment, and WHOQOL-spiritual). Moderation was deemed present if the interaction term was statistically significant and significantly improved the regression model. Significant interactions were visualized using the pick-a-point approach [32], and the Johnson-Neyman technique [33] was used to ascertain the value of the moderator (MAS-A self-reflectivity or MAS-A mastery) at which relationships between the RSES, BDI, and WHOQOL domains changed in significance.

#### RESULTS

All participants were female (*n*=80). The participants were an average of 24.01 years old (SD=5.22) across the sample,

and the anorexia (M=23.95; SD=4.87) and bulimia groups (M=24.08; SD=5.60) did not differ in age. Mean scores and correlations are presented in Table 1. MAS-A self-reflectivity was not significantly associated with the RSES, BDI, or WHOQOL domains across diagnostic groups. In the bulimia group, MAS-A mastery was significantly correlated with WHOQOL-physical (r=-35, p=0.03). No other correlations between MAS-A mastery, RSES, BDI, or WHOQOL domain were significant across the diagnostic groups.

#### **Moderation analyses: self-reflectivity**

The results of the moderation analyses for self-reflectivity in the anorexia group can be seen in Table 2. Significant interactions were found in moderation models examining the relationships between RSES and WHOQOL-social,

#### Table 2. Results of significant moderations by self-reflectivity in anorexia

Anorexia				
Variable	Coefficient	SE	t	p
Self-Esteem Models				
WHOQOL-social: <i>R</i> <sup>2</sup> =0.40, <i>F</i> =7.91, <i>p</i> <0.001				
Constant	84.73	27.16	3.12	0.004
Self-Esteem	-1.67	1.09	-1.53	0.135
Self-Reflectivity	-19.12	7.84	-2.44	0.020
Interaction Term: R <sup>2</sup> change=0.08	0.68	0.31	2.16	0.037
WHOQOL-physical: <i>R</i> ²=0.37, <i>F</i> =7.12, <i>p</i> <0.001				
Constant	114.45	37.15	3.08	0.004
Self-Esteem	-2.94	1.49	-1.97	0.057
Self-Reflectivity	-27.98	10.72	-2.61	0.013
Interaction Term: R <sup>2</sup> change=0.12	1.11	0.43	2.57	0.014
WHOQOL-environment: <i>R</i> ²=0.62, <i>F</i> =19.68, <i>p</i> <0.001				
Constant	233.47	62.0	3.77	<0.001
Self-Esteem	-4.90	2.49	-1.97	0.057
Self-Reflectivity	-59.04	17.89	-3.30	0.002
Interaction Term: R <sup>2</sup> change=0.10	2.18	0.72	3.04	0.004
WHOQOL-independence: <i>R</i> <sup>2</sup> =0.17, <i>F</i> =2.49, <i>p</i> =0.07				
Constant	210.10	67.64	3.11	0.004
Self-Esteem	-5.88	2.72	-2.16	0.037
Self-Reflectivity	-47.45	19.51	-2.43	0.020
Interaction Term: R <sup>2</sup> change=0.13	1.86	0.78	2.38	0.023
Depressive Symptom Models				
WHOQOL-environment: <i>R</i> <sup>2</sup> =0.21, <i>F</i> =3.24, <i>p</i> =0.03				
Constant	70.55	28.04	2.52	0.017
Depressive Symptoms	2.49	1.51	1.65	0.108
Self-Reflectivity	9.68	8.36	1.16	0.255
Interaction Term: R <sup>2</sup> change=0.08	-0.88	0.45	-1.97	0.057†
WHOQOL-spiritual: <i>R</i> <sup>2</sup> =0.23, <i>F</i> =3.58, <i>p</i> =0.02	· · · · ·			
Constant	6.22	7.28	0.85	0.399
Depressive Symptoms	0.70	0.39	1.78	0.084
Self-Reflectivity	2.93	2.17	1.35	0.185
Interaction Term: R <sup>2</sup> change=0.10	-0.25	0.12	-2.12	0.041

†Interaction term is approaching significance.

*Note:* WHOQOL-social=World Health Organization Quality of Life — social relationships; WHOQOL-physical=World Health Organization Quality of Life — physical health; WHOQOL-environment=World Health Organization Quality of Life — environment; WHOQOL-independence=World Health Organization Quality of Life — level of independence; WHOQOL-spiritual=World Health Organization Quality of Life — spiritual, religious, and personal beliefs.

WHOQOL-physical, and WHOQOL-independence. Overall, results indicated that when self-reflectivity was high, lower self-esteem was associated with poorer quality of life. At lower levels of self-reflectivity, these relationships became non-significant. Johnson-Neyman values were similar; for WHOQOL-social, scores at or above 3.06 on self-reflectivity (32.5% of the sample) exhibited a significant relationship, while for WHOQOL-physical, scores at or above 3.13 (32.5%) exhibited a significant relationship. For WHOQOL-independence, scores at or above 3.63 on selfreflectivity (25%) exhibited a significant relationship. Selfreflectivity also significantly moderated the relationship between RSES and WHOQOL-environment. At all levels of self-reflectivity, lower self-esteem was associated with poorer quality of life, but the effect was stronger when self-reflectivity was high. There were no statistically



Figure 1. Visualizations of the moderation effect of self-reflectivity on the relationships between self-esteem, depressive symptoms, and quality of life domains (WHOQOL) in the anorexia group.

significant transition points found using the Johnson-Neyman technique (see Figure 1 for graphs of these interactions). No significant interactions were found in the models examining the relationships between RSES and WHOQOL-psychological or WHOQOL-spiritual.

Regarding depressive symptoms, self-reflectivity significantly moderated the relationship between BDI and WHOQOL-spiritual for those with anorexia (Figure 1). In the model examining BDI and WHOQOL-environment, the interaction term was approaching significance (p=0.057). For both models, when self-reflectivity was high, higher BDI scores were associated with lower WHOQOL scores, while at lower levels of self-reflectivity, relationships were non-significant. For WHOQOL-environment, scores at or above 3.31 on self-reflectivity (32.5%) had a significant relationship, while for WHOQOL-spiritual, scores at or above 3.29 (32.5%)

Table 3. Results of significant moderations by mastery in anorexia and bulimia

Bulimia				
Variable	Coefficient	SE	t	p
Self-Esteem Models				
WHOQOL-physical: <i>R</i> <sup>2</sup> =0.29, <i>F</i> =4.97, <i>p</i> =0.006				
Constant	-13.72	22.50	-0.61	0.546
Self-Esteem	2.37	0.81	2.91	0.006
Mastery	15.07	7.30	2.06	0.046
Interaction Term: R <sup>2</sup> change=0.14	-0.72	0.27	-2.69	0.011
WHOQOL-psychological: <i>R</i> <sup>2</sup> =0.24, <i>F</i> =3.73, <i>p</i> =0.02	·		`	
Constant	-33.67	38.29	-0.88	0.385
Self-Esteem	3.88	1.38	2.80	0.008
Mastery	26.45	12.43	2.13	0.040
Interaction Term: R <sup>2</sup> change=0.13	-1.11	0.46	-2.43	0.020
WHOQOL-environment: <i>R</i> <sup>2</sup> =0.28, <i>F</i> =4.59, <i>p</i> =0.008	·		'	
Constant	15.51	28.90	0.54	0.595
Self-Esteem	3.36	1.04	3.21	0.003
Mastery	23.86	9.38	2.54	0.015
Interaction Term: R <sup>2</sup> change=0.15	-0.95	0.34	-2.76	0.009
Depressive Symptom Models				
WHOQOL-psychological: <i>R</i> <sup>2</sup> =0.49, <i>F</i> =11.44, <i>p</i> <0.001				
Constant	101.88	12.15	8.39	<0.001
Depressive Symptoms	-2.84	0.89	-3.20	0.003
Mastery	-10.56	4.05	-2.61	0.013
Interaction Term: R <sup>2</sup> change=0.07	0.67	0.30	2.26	0.030
Anorexia				
Variable	Coefficient	SE	t	p
Self-Esteem Models				
WHOQOL-social: <i>R</i> ²=0.36, <i>F</i> =6.89, <i>p</i> <0.001				
Constant	-21.60	17.85	-1.21	0.234
Self-Esteem	2.41	0.75	3.20	0.003
Mastery	20.99	8.81	2.38	0.023
Interaction Term: R <sup>2</sup> change=0.10	-0.88	0.37	-2.40	0.022

*Note:* WHOQOL-physical = World Health Organization Quality of Life – physical health; WHOQOL-psychological = World Health Organization Quality of Life – psychological well-being; WHOQOL-environment = World Health Organization Quality of Life – environment; WHOQOL-social = World Health Organization Quality of Life – social relationships.

exhibited a significant relationship. Interactions were not significant in the models examining the relationships between BDI and all other WHOOOL domains.

Moderation analyses were repeated for those in the bulimia group. No significant interactions were found in moderation models examining the relationships between RSES and WHOQOL-psychological, WHOQOL-social, WHOQOL-physical, WHOQOL-environment, WHOQOLindependence, or WHOQOL-spiritual. Similarly, no significant interactions were found in the models examining the relationships between BDI and all WHOQOL domains.

#### **Moderation analyses: mastery**

The results of the moderation analyses examining mastery can be seen in Table 3. In the anorexia group, mastery significantly moderated the relationship between RSES and WHOQOL-social. When mastery was low, lower RSES scores were associated with lower WHOQOL scores, while at higher levels of mastery, these relationships were nonsignificant. Johnson-Neyman values indicated that these relationships were significant when mastery scores were at or below 2.27 (75% of the sample). Interactions were not significant in the models examining the relationships



Figure 2. Visualizations of the moderation effect of mastery on the relationships between self-esteem, depressive symptoms, and quality of life domains (WHOQOL) in the bulimia group.

between RSES and all other WHOQOL domains. Similarly, no significant interactions were found in the models examining the relationships between BDI and all WHOQOL domains in the anorexia group.

Moderation analyses examining mastery were then repeated in the bulimia group. Significant interactions were found in the models examining RSES and WHOQOL-physical, WHOQOL-psychological, and WHOQOL-environment. For all models, results indicated that at lower levels of mastery, lower self-esteem was associated with poorer quality of life, but when mastery was high, the relationships were non-significant. Johnson-Neyman values were similar across models; for WHOQOL-physical, scores at or below 2.74 (22.5%) exhibited a significant relationship, while for WHOQOL-psychological, relationships were significant for scores at or below 2.93 (22.5%). For WHOQOL-environment, relationships were significant for scores at or below 3.02 (77.5%) on mastery (see Figure 2 for graphs of these interactions). No significant interactions were found in the models examining the relationships between RSES and WHOQOL-independence, WHOQOL-social, or WHOQOL-spiritual.

Regarding depressive symptoms, mastery significantly moderated the relationship between BDI and WHOQOLpsychological for those with bulimia (Figure 2). At lower levels of mastery, higher BDI scores were associated with lower WHOQOL scores, while at higher levels of mastery, the relationships were non-significant. Scores at or below 3.51 (77.50%) on mastery exhibited a significant relationship. Interactions were not significant in the models examining the relationships between BDI and all other WHOQOL domains in the bulimia group.

#### DISCUSSION

This study is the first, to our knowledge, to investigate whether metacognitive self-reflectivity and mastery have an impact on the relationships between self-esteem. depressive symptoms, and quality of life, and whether these impacts vary between people diagnosed with anorexia or bulimia. As expected, metacognitive self-reflectivity and metacognitive mastery had contrasting moderating relationships between the eating disorder groups. In the anorexia group, as expected, self-reflectivity moderated the relationship between self-esteem and guality of life. This relationship was such that at higher levels of selfreflectivity, low self-esteem was associated with poorer quality of life across several domains. However, at lower levels of self-reflectivity, relationships between self-esteem and quality of life were not significant. Similarly, selfreflectivity moderated the relationship between depressive symptoms and quality of life such that when self-reflectivity was high, stronger depressive symptoms were associated with poorer quality of life across several domains, but these relationships were not significant at lower levels of selfreflectivity. Importantly, moderations were significant for the anorexia group only; these patterns of relationships were not found in the bulimia group. When examining mastery as a moderator, opposite patterns were revealed. As expected, mastery significantly moderated the relationship between self-esteem and quality of life across both eating disorder groups. This relationship was such that at lower levels of mastery, low self-esteem was associated with poorer quality of life across several domains. However, these relationships were not significant at higher levels of mastery. Similarly, in the bulimia group, mastery moderated the relationship between depressive symptoms and quality of life such that higher depressive symptoms were significantly associated with lower quality of life, but only when mastery was low. These results suggest that metacognitive self-reflectivity and mastery have contrasting moderating effects and that these relationships differ between anorexia and bulimia.

These results are consistent with a growing body of work highlighting the importance of metacognition in eating disorders [16] and adds to recent work examining these constructs within the integrated model of metacognition [18]. Further, these findings extend work suggesting that impairments in the ability to think about oneself and others are transdiagnostic phenomena that have important relationships to outcomes [2, 10, 34]. Importantly, though metacognitive self-reflectivity and metacognitive mastery were not consistently associated at a bivariate level with selfesteem, depressive symptoms, or quality of life across the diagnostic groups, both self-reflectivity and mastery played a significant modifying role in the inter-relations among these variables. This is consistent with past work highlighting the role of self-reflectivity and mastery as moderating variables in other populations [22, 24] and furthers the idea that one's ability to notice, differentiate, interpret, and integrate internal mental states and to understand and respond effectively to psychosocial challenges may alter how one is impacted by other important psychological experiences; i.e., the framework wherein one experiences and understands internal mental states impacts how those mental states have downstream effects on outcomes and other variables. This is an important insight and suggests future work should more closely consider metacognitive abilities when determining the differential impacts of psychological variables across a population.

Consistently, participants with anorexia showed significant relationships between self-esteem, depressive symptoms, and aspects of quality of life when self-reflectivity was high, while non-significant relationships between these variables were exhibited when self-reflectivity was low. Johnson-Neyman values indicated that, in large part, these transitions in significance occurred at scores of approximately 3 on selfreflectivity. At a level of a 3 (on a scale ranging from 0 to 9), participants are able to identify and distinguish between different cognitive operations (e.g., a thought, a wish, a memory), but not necessarily between emotional states or experiences [25]. Importantly, the abilities to recognize changes in mental states over time, incorporate thoughts and emotions into narratives, and integrate internal mental experiences meaningfully into one's life narrative occur at considerably higher levels of self-reflectivity (scores 5–9), suggesting that many participants across both eating disorder samples, given the mean scores, were limited in their ability for self-reflection past acknowledgement of differing cognitive and emotional mental states.

In contrast, across both eating disorders groups, significant relationships between self-esteem, depressive symptoms, and aspects of quality of life appeared to exist when mastery was low, while at higher levels of mastery, non-significant relationships between these variables were displayed. Johnson-Neyman values indicated that these changes in significance occurred at scores of approximately 3 or lower on mastery. At a level of 3 and below on mastery, participants may be unable to identify and describe psychological distress and challenges or, if they are able to identify a psychologically distressful situation, they may be unable to respond to these challenges in a meaningful way [25]. The ability to respond to psychological challenges through behavioral inhibition, cognitive restructuring, and integration of metacognitive knowledge about themselves and others occurs at much higher levels of mastery (scores of 5–9). Like the findings for self-reflectivity, given the mean mastery scores across the sample, many of our participants proved limited in their metacognitive abilities beyond the ability to identify and describe distress.

Findings from the current study suggest that lower levels of self-reflectivity may have a protective value in anorexia, while higher levels of mastery may also possess protective value in both bulimia and anorexia. As described, the link between self-esteem, depressive symptoms, and quality of life was non-significant for those with anorexia when selfreflectivity was low. Thus, lower levels of self-reflectivity may buffer the negative impacts of low self-esteem and depressive symptoms on quality of life. Having higher self-reflectivity likely helps a person to better integrate their internal experiences, allowing them to experience the expected negative impacts of low self-esteem and depressive symptoms (i.e., poorer quality of life), while also allowing them to better access these experiences. Better awareness of and access to these experiences also opens the door to possible areas of intervention. For some, it may be beneficial to develop self-reflectivity during treatment, with monitoring and support to help navigate any potential impact on outcomes that may arise as self-reflective skills develop. While it may be protective to some extent, it is also important to note that those with lower self-reflectivity may be unable to enjoy the benefits that higher self-esteem or lower depressive symptoms can have on their quality of life. Thus, it is possible that self-reflectivity interventions may promote better quality of life outcomes when paired with interventions targeting self-esteem and depressive symptoms, though more research in this area is needed. Of note, it is possible that our findings simply reflect a lack of statistical significance. This may be related in part to our limited sample size in the moderation analyses. Further, many participants in our study had relatively low levels of self-reflectivity. Replicating this work in larger samples with a broader range of self-reflective capacity is needed to better understand these relationships.

Oppositely, higher levels of mastery may also have a protective value. Across groups, relationships between self-esteem, depressive symptoms, and quality of life were non-significant when mastery was high, suggesting that higher levels of mastery may protect against the negative impact of low self-esteem and depressive symptoms on guality of life that were observed when mastery was low. Higher levels of mastery may allow persons to better make sense of, tolerate, and respond to the distress associated with low self-esteem and depressive symptoms, resulting in a better quality of life. These results suggest that for those with eating disorders, it may be beneficial to develop metacognitive mastery skills in order to reduce the negative impact on quality of life in these groups. Of note, these moderating relationships were consistently present for those with bulimia across several quality-oflife domains; however, only one model in the anorexia group proved significant, indicating that lower self-esteem was associated with lower quality of life in the domain of social relationships. Thus, it appears that mastery may similarly affect both anorexia and bulimia. But further research is needed to investigate this.

While our results highlight metacognitive self-reflectivity and mastery as important moderating variables, they also highlight the fact that these findings are not consistent across eating disorders. Indeed, our results suggest a unique relationship with self-reflectivity in anorexia that was not present in bulimia, such that moderation was present for both self-esteem and depressive symptoms across multiple aspects of quality of life. Our results also suggest a unique relationship with mastery in bulimia that was present for both self-esteem and depressive symptoms across multiple aspects of quality of life which were not consistently observed in anorexia. There are several possible explanations for these differences between anorexia and bulimia. One possibility may be related to differences in symptomology. For example, recent work has determined that metacognition is linked to multiple forms of general psychopathology in bulimia; however, in anorexia, metacognition seems uniquely linked to disordered eating behaviors, and this group demonstrates greater impairments in metacognition [18]. Additionally, the level of insight may contribute to the differences between anorexia and bulimia. People with anorexia can experience significantly impaired insight [35, 36], which may include the inability to acknowledge their illness and symptoms. Lack of insight in anorexia has notable clinical implications, including treatment avoidance, poor treatment discipline, and assessment difficulties [37, 38]. Although we did not measure insight in this study, it is possible that self-reflectivity is related to insight in anorexia, and that both may influence the ability to acknowledge and reflect upon internal experiences such as self-esteem and depressive symptoms in a way that is unique to this population. This idea is consistent with some past work using a different model of metacognition, which found a relationship between metacognition and insight in anorexia [35]. Future work should investigate this issue.

There are several important limitations to consider. First, all of the participants in the sample identified as female, which limits the generalizability of these findings to people who identify with other genders. Additionally, the sample sizes for each diagnostic group were modest, which is important to take into account when interpreting the findings of the current study. In particular, the limited sample size in the moderation analyses may have an influence on the non-significant relationships between selfesteem, depressive symptoms, and quality of life at varying levels of self-reflectivity and mastery. Replication of this work with larger sample sizes is warranted and may further inform our understanding of the moderating relationships observed here. In the current study, we did not include a healthy control group for comparison. Further, we only focused on relationships between self-esteem, depressive symptoms, and quality of life. Deficits in interpersonal skills, social cognitive impairment, and personality traits have been implicated in eating disorders and are thought to contribute to poor outcomes [2, 39]. These relationships may also be influenced by metacognition. This is a possible avenue for future work to explore. Additionally, other variables may help to explain these relationships between metacognition, self-esteem, depressive symptoms, and quality of life. For example, neurocognitive functioning and egosyntonicity, both implicated in eating disorders [40, 41], may have an impact on the link between metacognition, self-esteem, depressive symptoms, and quality of life in this population. These variables were not assessed in this study, but future work that incorporates these variables may further inform our understanding of these relationships and have clinical implications. In addition, the current study focused on two specific domains of metacognition: self-reflectivity and mastery. Decentration and awareness of the minds of others, both additional domains within the integrated model of metacognition, should be investigated in future work. Lastly, all the data collected in the current study were done so at a single timepoint. Thus, conclusions regarding causality or how these variables may interact or change over time cannot be drawn. Further longitudinal research is needed to further examine the complexity of these relationships.

With replication, results from this study may have clinical implications for people with eating disorders. First, given the differing relationships between self-esteem, depressive symptoms, and quality of life at varying levels of self-reflectivity and mastery, metacognition should be assessed and taken into consideration in treatment planning and intervention choices. For people with anorexia, specifically, interventions targeting self-esteem or depressive symptoms may be less likely to positively affect quality of life aspects when self-reflectivity is low. Additionally, interventions focused on metacognitive ability, including Metacognitive Reflection and Insight Therapy and Metacognitive Interpersonal Therapy, could be modified for use in eating disorders. Metacognitive Reflection and Insight Therapy has been successfully adapted for use with people with psychosis across different cultures [42-45], while Metacognitive Interpersonal Therapy has been adapted for use in personality disorders [42, 46]. Either intervention could be adapted to offer improvements and improve the quality of life of people with anorexia or bulimia.

#### CONCLUSION

To our knowledge, this study is the first to explore metacognitive self-reflectivity and mastery as moderators in the relationship between self-esteem, depressive symptoms, and quality of life in eating disorders. The results suggest that these different metacognitive abilities have paradoxical relationships with these variables that differ between anorexia and bulimia. Specifically, the results indicate that self-reflectivity has an impact on the relationship between self-esteem, depressive symptoms, and guality of life such that when self-reflectivity is high, lower self-esteem and higher depressive symptoms are associated with a lower quality of life. In this study, these relationships existed only for those with anorexia. Oppositely, across both groups, mastery moderated the relationships between self-esteem, depressive symptoms, and quality of life such that lower selfesteem and higher depressive symptoms were associated with a lower quality of life only when mastery was low. Further work should continue to explore the complex role of self-reflectivity and mastery in eating disorders. A comprehensive understanding of these relationships is necessary to inform clinical interventions.

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#### RESEARCH

# Risk Factors of Disordered Eating in Adolescent Girls from a Community Sample: A Multidimensional Approach

Факторы риска нарушений пищевого поведения у девочек-подростков неклинической популяции: многомерный подход

doi: 10.17816/CP6132 Original research

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#### ABSTRACT

**BACKGROUND:** Eating disorders (ED) are severe, chronic, and complex in nature mental illnesses that are difficult to treat. One of the ways to stave off EDs is by screening among adolescents to preempt the development of clinical forms of ED in risk groups.

**AIM:** 1) to investigate the prevalence of ED risk among adolescent girls and compare subgroups at high and low risk of ED; 2) to investigate using a multidimensional approach those variables that can interact with temperament and character traits to predict ED symptomatology.

**METHODS:** The cross-sectional observational self-report study of a community sample of adolescent girls 12–17 years old (*n*=298; M=14.77±1.13) was carried out in the city of Ryazan, Russia. The Russian versions of Eating Attitudes Test and Cloninger's Temperament and Character Inventory-Revised were used. In addition, an original questionnaire (Risk Factors of Eating Disorders) was developed. Regression models (to test for significant moderation) and path analysis (to test for significant mediations) were used.

**RESULTS:** Girls at risk of developing EDs are characterized by a heightened level of concern about weight and dissatisfaction with their body, tend to suffer from low self-directedness, higher novelty seeking and tendency to higher harm avoidance, display high alexithymia, experience self-distrust, negative emotionality and are dissatisfied with family relationships. They also suffer from low self-esteem and tend to be perfectionism and engage in risk behavior. Significant moderating effects were uncovered between the following ED risk factors: (1) self-distrust/risk behavior and BMI; (2) alexithymia/negative emotionality/self-esteem and cooperativeness; and (3) negative emotionality/risk behavior and self-transcendence. Family relationship dissatisfaction mediates the association between self-directedness/ cooperativeness/self-transcendence and disordered eating.

**CONCLUSION:** There are various mutual influences between the numerous ED risk and prevention factors, which all together determine the paths between the predictors and final outcome.

#### аннотация

**ВВЕДЕНИЕ:** Расстройства пищевого поведения (РПП) являются тяжелыми, хроническими и сложными по своей природе психическими заболеваниями, трудно поддающимися лечению. Одним из направлений профилактики РПП является скрининг подростков с целью предупреждения развития клинических форм РПП в группах риска.

**ЦЕЛЬ:** 1) изучить распространенность риска РПП среди девочек-подростков и сравнить подгруппы высокого и низкого риска; 2) исследовать с помощью многомерного подхода те переменные, которые могут взаимодействовать с чертами темперамента и характера для прогнозирования симптоматики РПП.

**МЕТОДЫ:** Проведено поперечное наблюдательное исследование на основе самоотчетов неклинической выборки девочек-подростков 12–17 лет (*n*=298; M=14,77±1,13) г. Рязани. Использовались русскоязычные версии теста EAT-26 и опросник темперамента и характера Клонингера (TCI-R). Был также разработан и применен опросник «Факторы риска РПП». Для проверки значимых модераций использовались регрессионные модели, для проверки значимых медиаций — анализ путей.

**РЕЗУЛЬТАТЫ**: Девочки с риском РПП характеризуются высокой озабоченностью весом и неудовлетворенностью телом, низкой самонаправленностью, повышенным стремлением к новизне и склонностью к избеганию вреда, высокой алекситимией, неверием в свои силы, негативной эмоциональностью и неудовлетворенностью семейными отношениями, низкой самооценкой и тенденцией к повышенному перфекционизму и рискованному поведению. Значимые модерации были получены между следующими факторами риска РПП: (1) недоверие к себе/рискованное поведение и ИМТ; (2) алекситимия/отрицательная эмоциональность/самооценка и готовность к сотрудничеству; (3) негативная эмоциональность/рискованное поведение и трансцендентность «Я». Неудовлетворенность семейными отношениями опосредует связь между самонаправленностью/готовностью к сотрудничеству/ трансцендентностью «Я» и риском РПП.

**ЗАКЛЮЧЕНИЕ:** Существуют разнообразные взаимовлияния между многочисленными факторами риска и протекторами РПП, которые определяют пути между предикторами и конечным результатом.

**Кеуwords:** eating disorders; screening; adolescent girls; EAT-26; risk factors; personality; temperament and character **Ключевые слова:** расстройства пищевого поведения; скрининг; девочки-подростки; EAT-26; факторы риска; черты личности; темперамент и характер

#### INTRODUCTION

Eating disorders (ED) such as anorexia nervosa (AN) and bulimia nervosa (BN) are severe mental illnesses that are difficult to treat [1, 2]. Their prevalence has not decreased, despite the large number of studies that have looked into the prevention and treatment of these diseases [3–5]. Both diseases are chronic and complex in nature [6, 7]. Some of the main risk factors for AN and BN are female gender and adolescence or early adulthood [4, 8–10]. The next on the list of leading risk factors is body image dissatisfaction [8, 11–14]. Clinical forms of ED have a pre-existing period, usually beginning in adolescence, that is characterized by a marked concern with body shape and weight and attempts to try various diets or purge, as well as an intense focus on physical fitness to avoid weight gains [7, 8, 12, 15]. What's more, the risk of developing EDs increases as a result of social pressure from family, peers, and the media, which idealize the thinness of the female figure, instilling the idea that a beautiful figure of a woman is key to her success in life [16–18]. Recent cohort and longitudinal studies have shown that symptoms of ED that begin in adolescence, even if they do not morph into clinical ones, persist into early adulthood and lead to a greater risk of developing anxiety, depressive disorders, and obesity [19, 20].

One of the ways to prevent EDs is by conducting screening among adolescents girls especially in order to stave off the development of clinical forms of ED in risk groups [21, 22], even though, as recent studies have shown, conclusive evidence that such screening has benefits or does harm does not yet exist [4, 23]. Nevertheless, the ability to detect early disordered eating behavior which has not yet assumed pathological forms is of value not only to medical staff, but also to psychologists and teachers at secondary educational institutions. It is known that preventive programs, among them media literacy and healthy weight programs, cognitive-behavioral therapy, and cognitive dissonance interventions, can significantly reduce ED risk factors [24-26]. What we know about the trajectory of ED symptomatology development from early adolescence to adulthood allows us to conclude that ED prevention should start before puberty [27].

Despite the socio-cultural pressure that all adolescent girls, to some extent, experience, the risk of ED does not affect many of them. This has to do with the multifactorial nature of ED. Behavioral genetics research shows that there is a hereditary predisposition to develop these disorders [6, 28, 29]. Moreover, the particular environmental context can also reduce or increase the risk of ED [30]. Among those environmental factors, one of the most significant is family dynamics [31–34]. Some characteristics of one's personality may or may not predispose them to ED [35–38].

It should also be noted that biological, developmental, psychological, and socio-cultural risks and protective mechanisms form complex constellations that accompany the process of individual development [35, 39–41]. The more information we can collect on the interplay amongst many of the factors involved in an individual's development of a particular eating behavior, the better we will be at understanding the mechanisms of ED genesis [42, 43]. It is especially important to understand how the risk of ED emerges in its preclinical stages, namely during adolescence; which groups of adolescents become vulnerable to ED, and if it is possible to identify those areas of mental development and environmental context through whose leverage we can affect the risk of ED [39, 40].

Among the psychobiological factors associated with ED are the individual traits of temperament and character

[44–47]. Temperament is considered one of the predictors for developing psychopathology due to its biological background, including rather high heritability, early manifestation, and relative stability during development [48, 49]. For example, temperamental characteristics in early childhood may predict body dissatisfaction and ED symptoms in adolescence [50, 51]. Temperament is one of the early indicators that can point to the subsequent development of personality traits influenced by experience and context [49].

One of the best known is Cloninger's multidimensional psychobiological model of temperament and character, which clinical observations have led him to develop. This served as the basis for the development of the Temperament and Character Inventory (TCI) [52], which has become the go-to tool in various studies related to the substantiation of the neurobiological foundations of personality development, including neurobiological and genetic studies of psychopathology [53–55].

The adequate diagnostic and differentiating properties of TCI make it a tool that is used in the study of mental and personality disorders, as well as in person-centered therapy [56–58]. The TCI used in ED studies indicates significant differences between ED patients and healthy controls [44, 59, 60]. Using the Cloninger's seven temperament and character dimensions as indicators and applying latent profile analysis, significant differences among profiles and ED diagnoses were observed [45]. There are also indications that subclinical forms of disordered eating behavior also show an association with TCI indicators [37, 61, 62].

Not only temperament and character traits, but also a number of other personality traits show significant associations with disordered eating behavior. These include perfectionism [63, 64], alexithymia [65, 66], low self-esteem [67, 68], personal ineffectiveness [69, 70], negative emotionality [71, 72], and other features.

The multidimensional nature of ED, with many risk and protective mechanisms, encourages researchers to probe for any possible forms of interaction between these factors. By using various methods of multivariate analysis, we are able to assess the moderation and mediation effects of such interactions that offer different etiological and maintenance models of ED [41, 43, 73–76].

#### Aim of the current study

The main purpose of this research was to probe for direct and indirect relationships between Cloninger's

temperament and character traits and the risk of developing ED in a community sample of adolescent girls. We have used a multidimensional approach to investigate variables that can interact with temperament and character traits to predict ED symptomatology. In addition, we endeavored to compare subgroups at high and low risk of ED in terms of BMI, body dissatisfaction and weight preoccupation, as well as a range of personality traits and satisfaction with family relationships. We hypothesize that a multidimensional approach has the potential to spawn valid models with significant predictor potential of ED risk in adolescent girls.

#### METHODS

#### **Study design**

The cross-sectional observational self-report study of a nonclinical sample of adolescent girls (298 participants) was carried out in the city of Ryazan (Central region of the Russian Federation) from November 2009 to November 2010.

#### Sampling

Convenience sampling was adopted for the aims of this research.

#### **Participants**

*Inclusion criteria*: (1) adolescent girls aged 12 to 17 years, (2) attending Middle and High School, (3) consent of participants and their parents, and (4) absence of indications of diagnosed mental disorders (according to information received from the school administration).

*Exclusion criteria:* (1) refusal of the girl or her parents to participate in the study at any stage, (2) inappropriate responses to the validation items of the Temperament and Character Inventory, and (3) Body Mass Index (BMI) of more than 34 or less than 13.

#### Procedure

Prior to the start of the study, informed consent was obtained from the girls' parents for participation of their daughters in the study. Beforehand, the girls received information about the aims and conduct of the study. They were also informed that they could withdraw from the study at any time.

The girls were asked to fill out three paper-and-pencil questionnaires with Likert scales: (1) The Eating Attitudes Test (EAT-26), with 26 items; (2) The Risk Factors of Eating Disorders (RFED) questionnaire with 55 items (Table S1 in the Supplementary); and 3) The Cloninger Temperament and Character Inventory (TCI-R, short form), with 140 items. The questionnaires were used to gauge eating attitudes and behavior, weight and body concerns, temperament and character, some personality traits, and dynamics in the family. The girls were also asked to indicate their height and weight and make some marks in a form with eleven 100-mm vertical lines (Dembo-Rubinstein Self-esteem Scale) to rate their health, happiness, appearance, and some other features (Figure S1 in the Supplementary).

The questionnaires were filled by the group of girls in a classroom environment during two lessons of 45 minutes with a break of 10–15 minutes.

#### Measures

#### 1. Eating Attitude Test (EAT-26)

The Russian version of the Eating Attitudes Test (EAT-26) [77,78] was used to assess the risk of ED. EAT-26 is a widely used self-report questionnaire for screening for symptoms of AN and BN in adults and adolescents [79]. The questionnaire includes 26 items, for all of which the respondent can choose one of six possible answers, from "never" to "always". The answers "always", "usually", and "often" are scored as 3, 2, 1, respectively. The rest of the answers — "sometimes", "rarely", and "never" — are assigned a value of 0 points. Scoring for question 26 is reversed. The total scores on the questionnaire can vary from a minimum value of 0 points to a maximum of 78 points. Total score cutoff at or above 20 is usually used for identifying respondents with possible ED risk.

According to the factor structure proposed by the authors, EAT-26 has three subscales: (1) Dieting; (2) Bulimia and Food Preoccupation; and (3) Oral Control. However, there has been a number of studies indicating that for nonclinical populations of adolescents or students at colleges and universities, the three-factor model is not applicable [80, 81]. In the present study, we have some of the scores of the above-mentioned subscales, but also, based on the data of exploratory factor analysis (EFA), we have obtained new estimates in accordance with the 5-factor model, which more adequately describes our sample (see more details in the Statistical analysis section and in the Supplementary Table S2).

To analyze the effects of moderation and mediation, we used the EAT-26 total scores derived from the 6-point scoring system, which scored the answer "always" as 5 and answer "never" as 0 points, since EAT-26 variables have multiple outliers in the 4-point scoring system, reducing their fit to a normal distribution.

#### 2. Cloninger Temperament and Character Inventory-Revised (TCI-R, short form)

To assess the traits of temperament and character, we used Cloninger Temperament and Character Inventory-Revised (TCI-R, short form) [52]. The original version of the questionnaire and permission to use it were obtained from the lead author. The translation was done with the help of an expert, a bilingual psychologist from the U.S. A reverse translation was also done by an independent translator. Currently, TCI is considered a tool for assessing the seven dimensions of personality in terms of the comprehensive biopsychosocial model applicable not only to the assessment of psychopathology, but also to the general population [55].

In accordance with Cloninger's model, temperament involves four dimensions: Novelty Seeking (NS), Persistence (PS), Reward Dependence (RD), and Harm Avoidance (HA).

Individual differences of a higher level associated with the formation of personal characteristics relating to the relationship of a person to themselves, with society, and with the world as a whole constitute the three dimensions of character. Self-Directedness (SD) is a personality trait associated with the ability of an individual to be selfsufficient, responsible, and able to calibrate their behavior to their own goals and values; Cooperativeness (C) is associated with individual differences that explain human behavior in their interaction with others; for example, empathy, willingness to help, etc.; Self-transcendence (ST) describes individual differences in people's relationship with the world as a whole, their identification with something related to spirituality, and the desire to determine the meaning of a person's existence in the world [55].

The original questionnaire contains 240 items, the first 140 of which can be used as a short form. The authors of the questionnaire allow the use of answers in the form of "agreement-disagreement", as well as in the form of a Likert scale. We used a 3-point scoring system with the response options "true", "somewhat true", and "false". A score of 1 was assigned to "false" responses and a score of 3 to "true" responses. Thus, the evaluation of each answer was done in points ranging from 1 to 3. The reverse items were evaluated in the opposite order.

#### 3. Risk Factors of Eating Disorders (RFED) questionnaire

To assess the typical ED risk factors, we developed an original 55-item questionnaire (Risk Factors of Eating

Disorders, RFED), which included eight scales aimed at assessing some personal characteristics, body dissatisfaction, and weight concerns, as well as questions to assess family relationships. The mentioned-above 3-point scoring system was used. Total scores were measured for each scale. A brief description of the mentioned scales is given below, and the entire questionnaire is presented in Table S1 (in the Supplementary).

*Perfectionism*, 7-point scale with Cronbach's alpha 0.665 and statements such as "I love everything to be perfect", "I would like to be honors-student".

*Alexithymia*, 6-point scale with Cronbach's alpha 0.802 and statements such as "Sometimes I can't tell if I'm hungry or upset", "Sometimes I get feelings I can't define".

*Self-Distrust*, 7-point scale with Cronbach's alpha 0.771 and statements such as "I feel like I can't achieve much in life", "I don't believe in myself". This characteristic is comparable to the "ineffectiveness" of the Eating Disorder Inventory [82].

*Negative Emotionality*, 11-point scale with Cronbach's alpha 0.847 and statements such as "I am often depressed", "I always think long and hard about what is happening to me", "I often cry".

*Risk Behavior*, 4-point scale with Cronbach's alpha 0.643 and statements such as "I would like to experience the thrill even at the risk of my life (for example, skydiving)", "If I was offered a weak drug, I would risk trying".

*Body Dissatisfaction*, 4-point scale with Cronbach's alpha 0.804 and statements such as "I don't like my body", "I envy the looks of other girls".

Weight Concerns, 8-point scale with Cronbach's alpha 0.812 and statements such as "I think I can't be happy until I lose weight", "Weight affects my mood, self-esteem, wellbeing and self-confidence".

Family Relationships Dissatisfaction, 8-point scale with Cronbach's alpha 0.789 and statements such as "I think my family underestimates me", "My successes at home are scarcely encouraged", "In the family, I am often scolded for missteps and shortcomings".

# 4. Dembo-Rubinstein method of self-esteem measurement

The Dembo-Rubinstein method of self-esteem measurement [83] was used. Respondents were asked to assess their own health, mind, creativity, memory, appearance, self-belief, will, determined character, authority among peers, level of physical fitness, happiness. As an analyzed variable the level of self-esteem was used as an average value from the measurements of all characteristics obtained. This assessment tool is presented in more detail in Figure S1 (in the Supplementary).

#### **Statistical analysis**

## 1. Descriptive statistics and assessment of scale reliability

Descriptive statistics was used to extract the general characteristics of the sample: age, body mass index, and other categorical and continuous variables. Observations with missing data were removed. Because a number of variables characterizing eating behavior had a significant skewness and kurtosis, it was decided to prioritize methods of nonparametric statistics.

Cronbach's alpha was used for the assessment of the scale's reliability for questionnaires with Likert scales (EAT-26, TCI-R, RFED).

#### 2. Exploratory factor analysis (EFA)

As mentioned above, the three-factor model of EAT-26 is not applicable for adolescent nonclinical samples. In this regard, at the first stage, we decided to conduct an exploratory factor analysis to refine the model which could be adequate to our sample. We used the factor extraction method based on the method of principal component analysis of the correlation matrix with the Varimax rotation, with 3-, 4-, 5-, and 6-factor models tested according to an eigenvalue level higher than 1.0 and the scree plot. Factor loadings of less than 0.60 were discarded.

The method of principal component analysis of the correlation matrix with the Varimax rotation was also used to assess the reproducibility of the factor structure of TCI-R for the temperament and character scales separately, as well as for all seven scales. Factor models were tested in accordance with the expected number of questionnaire scales (Table S3 in the Supplementary).

# 3. Identification and comparison of contrast groups with high and zero risk of ED

In accordance with the generally accepted cut-off criterion for the EAT-26, groups of girls with high (EAT-26 $\geq$ 20) and zero (EAT-26=0) values of the total EAT-26 were identified. The 2x2 contingency table was analyzed with the Pearson's chi-square test of independence of distribution of the proportions of girls with high and zero ED risk depending on the grade (7–8 and 9–11 grades).

# 4. Comparison of eating attitudes and behavior (EAT-26) in two age groups

To account for the differences between younger and older adolescents, the entire sample was divided into 2 age groups: 12–14 years old and 15–17 years old. Since the distributions of the EAT-26 scores do not meet the criteria of normality, age differences were assessed using the Mann-Whitney test.

#### 5. Binary logistic regression analysis

The logistic regression analysis (Wald statistic) was performed to assess the effects of independent predictors — BMI, temperament, and character traits (TCI-R), personality traits, and dissatisfaction with family relationships (RFED) — on the binary dependent variable of high (EAT-26 $\geq$ 20) vs. zero (EAT-26=0) risk of ED. We used the Enter model of logistic regression analysis.

#### 6. Correlation analysis

The Spearman correlation analysis was used to estimate how EAT-26 total, BMI, TCI-R, RFED and self-esteem characteristics relate to each other.

#### 7. Moderation analysis

To identify any significant moderation of the influence of one variable on another, regression analysis with two independent variables was used, taking into account the multiplicative term between the independent variables. BMI and seven traits of temperament and character (TCI-R) were used as independent variables. The EAT-26 total score assessed on a 6-point scale was treated as a dependent variable and Self-Esteem and six personality measures (RFED — Perfectionism, Alexithymia, Self-Distrust, Negative Emotionality, Risk Behavior), as moderators.

#### 8. Mediation analysis

Path analysis using EQS 6.4 soft was utilized to identify any significant mediation of the influence of one variable on another. BMI and seven traits of temperament and character (TCI-R) were used as independent variables. The EAT-26 total score assessed on a 6-point scale was treated as a dependent variable, and Family Relationships Dissatisfaction as a mediator variable.

We used the Statsoft Statistica v10.0 software for all types of analyses, except for EFA and the moderation analysis, which were analyzed using IBM SPSS Statistics, v.23. EQS 6.4 soft was used for mediation analysis.

#### RESULTS

#### **Overall sample characteristics**

The sample was made up of students from four general secondary schools of the city of Ryazan, Russia. Two hundred and ninety-eight girls from 12.3 to 17.3 years old, students in 7–11 grades, were selected based on the inclusion-exclusion criteria. The mean age of the participants was  $14.77\pm1.13$  years. Some 90.3% of the group had already experienced menstruations. The mean age of menarche was  $12.7\pm0.9$  years. Most of the sample consisted of girls in 7–8 grades (88 and 98, accordingly, for a total of 186). The smaller part of the sample was made up of students in grades 9, 10, and 11 (28, 41, and 43 persons accordingly, for a total of 112). BMI varied from 13.49 to 33.98. Mean BMI=19.49\pm3.16.

#### **Eating attitudes and behavior characteristics**

Thirty-three girls (11.1%) with total EAT-26 scores at or above 20 (risk group for ED) were identified. The contrast group with total scores of 0 consisted of 29 girls. A comparison of the proportion of girls with a risk and no risk of ED depending on their grade (7–8 and 9–11 grades) yielded significant differences by the 2x2 contingency tables: chi-square=4.39, df=1, p=0.036 (Figure 1).

Factor analysis results confirm the impossibility of reproducing the 3-factor structure proposed by the authors of the questionnaire. Seven eigenvalues >1 were obtained. In accordance with the Kaiser criterion, up to 7 independent factors can be considered. The most realistic for our sample seems to be a 5-factor model with the exclusion of items 2,



Figure 1. The proportion of girls with high (EAT-26≥20) and low (EAT-26=0) ED risks depending on grade (7–8 and 9–11 grades).

4, 5, 10, 15, 19, 22, 24, 26, which have low factor loadings (Table S2 in the Supplementary). The remaining items, all with factor loadings of more than 0.62, form 5 factors: (1) Drive for Thinness (items 1, 11, 12, 14,  $\alpha$ =0.839); (2) Dieting (items 6, 7, 16, 17,  $\alpha$ =0.868); (3) Social Pressure to Gain Weight (items 8, 13, 20,  $\alpha$ =0.753); (4) Bulimia (items 9, 25,  $\alpha$ =0.828); and (5) Food Preoccupation (items 3, 21,  $\alpha$ =0.554).

To statistically evaluate the differences between younger and older adolescents, the entire sample was divided into two age groups: 12–14 years old and 15–17 years old. Since the distributions of the scales and the EAT-26 total score did not meet the criteria of normality, age differences were assessed using the Mann-Whitney test. A comparison of EAT-26 total and its three and five subscales demonstrated some significant differences between age groups (Table 1).

	Age group (years)								
Variables	12-14 (N=169)	15-17 (N=129)	12-14 (N=169)	15-17 (N=129)	12-14 (N=169)	15-17 (N=129)	Mann-Whitney te		
	Min/Max		Mean±SD		Mean Ran	k	U	р	
Age	12.3/14.9	15.0/17.3	13.9±0.60	15.9±0.61	85	234	0.0	0.0001	
BMI	13.5/26.6	14.3/33.9	18.75±2.55	20.46±3.60	131.8	172.7	7912.0	0.0001	
EAT-26 total	0/42	0/47	7.01±7.47	9.26±10.09	142.7	158.39	9753.5	0.119	
Three factors model (EAT-26)									
Dieting	0/25	0/33	4.03±5.24	5.88±7.12	140.7	161.05	9411.0	0.041	
Bulimia and Food Preoccupation	0/6	0/10	0.32±0.95	0.79±1.85	142.5	158.6	9724.5	0.016	
Oral Control	0/20	0/14	2.66±3.54	2.60±3.29	148.9	150.3	10793.0	0.881	
Five factors model (EAT-26)									
Drive for Thinness	0/12	0/12	2.15±3.36	3.44±4.07	137.9	164.7	8942.5	0.004	
Dieting	0/12	0/12	0.72±1.93	0.92±2.18	146.0	154.1	10305.5	0.270	
Social Pressure	0/9	0/9	1.69±2.50	1.37±2.35	153.3	144.5	10257.0	0.328	
Bulimia	0/0	0/4	0	0.05±0.39	148.5	150.8	10731.5	0.106	
Food Preoccupation	0/3	0/6	0.12±0.56	0.28±0.93	145.5	154.8	10221.0	0.051	

Table 1. Descriptive statistics of BMI and eating attitudes measured by the EAT-26 in two age groups of adolescent girls

Table 2. Temperament and Charac	cter scales characteristics
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Scales	Mean±SD	Min	Max	Skewness	Kurtosis	Cronbach's alpha
Novelty Seeking	40.53±5.75	26	56	0.127	-0.024	0.707
Harm Avoidance	40.80±6.31	25	55	0.004	-0.480	0.754
Reward Dependence	44.40±4.98	27	57	-0.483	0.178	0.584
Persistence	40.81±7.04	22	58	-0.033	0.031	0.861
Self-Directedness	45.09±6.47	25	58	-0.284	-0.157	0.789
Cooperativeness	45.98±5.33	24	59	-0.831	1.164	0.697
Self-Transcendence	31.31±5.97	16	46	0.122	-0.414	0.802



### Figure 2. Correlation heatmap between EAT-26 total, BMI, TCI-R, RFED personality and self-esteem characteristics in the total sample

*Note:* EAT-26 (4) and EAT-26 (6) – total scores of EAT-26 derived from 4-point and 6-point scoring accordingly; statistically significant coefficients at p < 0.001 are highlighted by frames.

The incidence of EAT26 values at or above 20 is higher in the 15- to 17-year-old group — 15.5% vs. 7.7% in the 12- to 14-year-old age group. Although the differences are not statistically significant, there is a trend towards significance (chi-square=3.43; p=0.064).

#### **TCI-R characteristics**

Basic statistics and the Cronbach's alpha coefficients of seven TCI-R scales in the sample (N=298) are given in Table 2. The procedure used in exploratory factor analysis and factor loadings before and after rotation are presented in Table S3 (in the Supplementary). Cross-correlations between scales are presented in Figure 2.

#### **Binary logistic regression analysis**

Variables considered as probable and independent predictors of ED risk — BMI, temperament and character traits (TCI-R), personality traits, family relationship dissatisfaction (RFED), self-esteem — were included into the logistic regression analysis. The binary dependent variable was high (EAT-26≥20) or zero (EAT-26=0) risk of ED. The Wald statistics was used (Table 3).

Based on the decrease Wald statistics principle, independent predictors of ED can be presented in decreasing order of predictive value as: (1) Weight Concerns, (2) Body Dissatisfaction, (3) Self-Directedness, (4) Self-Distrust, (5) Negative Emotionality, (6) Low Self-Esteem, (7) Family Relationships Dissatisfaction, (8) Alexithymia, (9) Novelty Seeking, and (10) BMI. Some variables with p-level <0.1 (Harm Avoidance, Perfectionism, Risk behavior) demonstrate a tendency toward significance.

#### **Correlation analysis**

Spearman correlations between EAT-26 total, BMI, TCI-R, RFED personality, and self-esteem characteristics were established (Figure 2). EAT-26 total was assessed on a 4-point scale and with the same assessment, but on a 6-point scale. The last estimation option was chosen as preferable due to the smaller number of outliers in the EAT-26 total distribution and was subsequently used to test the moderation and mediation models. It can be seen that many probable risk factors are also correlated with each other, which confirms that it is possible to detect the effects of moderation and mediation.

Table 3. Independent predictors of high risk of developing eating disorders

Independent variables (predictors)	Contrast g N	roups	Wald	p
	EAT=0	EAT≥20	statistic	
BMI	29	33	4.52	0.034
TCI (Temperament and Character Inventory)				
Novelty Seeking	29	33	5.13	0.023
Harm Avoidance	29	33	3.23	0.072
Reward Dependence	29	33	0.46	0.500
Persistence	29	33	0.21	0.643
Self-Directedness	29	33	10.65	0.001
Cooperativeness	29	33	1.27	0.260
Self-Transcendence	29	33	0.928	0.335
RFED (Risk Factors of Eating Disorders)				`
Weight Concerns	28	33	19.76	0.0001
Body Dissatisfaction	28	33	15.05	0.0001
Perfectionism	28	33	3.06	0.080
Alexithymia	28	33	5.30	0.021
Self-Distrust	28	33	10.29	0.001
Negative Emotionality	28	33	8.20	0.004
Risk Behavior	28	33	3.66	0.056
Family Relationships Dissatisfaction	28	33	5.66	0.017
Self-Esteem	26	31	5.74	0.017

Table 4. Summary	of the regression	analysis of all	l significant	moderator effects
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Parameters	В	SE B	t	р	<b>R</b> <sup>2</sup>			
Model 1. "BMI* Self-Distrust"								
Intercept	31.953	19.109	1.672	0.096	0.180			
BMI	-1.258	0.980	-1.284	0.200				
Self-Distrust	-2.493	1.618	-1.541	0.124				
BMI* Self-Distrust	0.217	0.083	2.616	0.009				
Model 2. "BMI* Risk Behavior"								
Intercept	-34.655	18.984	-1.825	0.069				
BMI	2.596	0.959	2.706	0.007	0.102			
Risk Behavior	5.888	2.711	2.172	0.031				
BMI* Risk Behavior	-0.218	0.135	-1.610	0.108				
Model 3. "Cooperativeness* Alexithymia"								
Intercept	-27.780	31.495	-0.882	0.378				
Cooperativeness	0.851	0.669	1.272	0.204	0.093			
Alexithymia	6.141	2.539	2.419	0.016				
Cooperativeness* Alexithymia	-0.106	0.054	-1.943	0.053				
Model 4. "Cooperativeness* Negative Emotionality"	·							
Intercept	-43.042	36.823	-1.169	0.243				
Cooperativeness	1.141	0.787	1.450	0.148	0.092			
Negative Emotionality	3.728	1.511	2.467	0.014				
Cooperativeness* Negative Emotionality	-0.065	0.033	-1.997	0.047				
Model 5. "Cooperativeness* Self-Esteem"			· · ·					
Intercept	177.208	52.187	3.396	0.001				
Cooperativeness	-2.874	1.135	-2.532	0.012				
Self-Esteem	-1.802	0.717	-2.511	0.013	0.075			
Cooperativeness* Self-Esteem	0.034	0.015	2.172	0.031				
Model 6. "Self-Transcendence* Negative Emotionality"								
Intercept	54.015	22.704	2.379	0.018	0.083			
Self-Transcendence	-1.455	0.739	-1.970	0.050				
Negative Emotionality	-1.337	0.947	-1.412	0.159				
Self-Transcendence* Negative Emotionality	0.067	0.030	2.241	0.026				
Model 7. "Self-Transcendence* Risk Behavior"								
Intercept	-23.853	16.830	-1.417	0.157				
Self-Transcendence	1.269	0.535	2.370	0.018	0.065			
Risk Behavior	6.476	2.485	2.606	0.010				
Self-Transcendence* Risk Behavior	-0.153	0.077	-1.981	0.048				

Table 5. Intercept (A0) and linear regression coefficients (A1) at low and high values of moderators

	Independent variables	Moderators	Levels of moderators and coefficients			
Model			Low		High	
			A0	A1	A0	A1
1	BMI	Self-Distrust	12.12	0.47	-3.87	1.86
2	BMI	Risk Behavior	-6.43	1.55	16.56	0.70
3	Cooperativeness	Alexithymia	24.48	-0.05	64.50	-0.73
4	Cooperativeness	Negative Emotionality	23.89	-0.03	63.85	-0.72
5	Cooperativeness	Self-Esteem	68.24	-0.84	25.25	-0.04
6	Self-Transcendence	Negative Emotionality	30.00	-0.25	15.66	0.47
7	Self-Transcendence	Risk Behavior	7.19	0.54	32.48	-0.06

#### **Moderation analysis**

Over all, eight variables — BMI and seven TCI measures have been considered as predictors; the EAT-26 total score assessed at a 6-point scale, as a dependent variable; and six personality measures (Perfectionism, Alexithymia, Self-Distrust, Negative Emotionality, Risk Behavior and Self-Esteem), as moderators.

To test for moderator effects, with EAT-26 total as the dependent variable, a subsequent series of linear multiple regressions were computed. Each independent variable, each moderator variable, and the product of the independent and moderator variable were entered into these regression analyses. The nature of each statistically significant interaction was examined with high and low representing the effects at 1 SD above the mean and 1 SD below the mean, respectively.

A total of 48 moderation models were analyzed, of which seven cases showed significant moderation effects (Table 4, Table 5).

There are two significant interactions between BMI as predictor of disordered eating with such RFED parameters as Self-Distrust and Risk Behavior.

Three moderation effects were also uncovered as relates to the TCI character score Cooperativeness as an independent variable and Alexithymia, Negative Emotionality, and Self-Esteem as moderators.

The next independent variable for which significant moderation effects were identified was the TCI character score Self-Transcendence. For this independent variable, two significant moderators were found: Risk Behavior and Negative Emotionality.

#### **Mediation analysis**

BMI and seven traits of temperament and character (TCI-R) were used as independent variables. The EAT-26 total score assessed on a 6-point scale was treated as the dependent variable, and Family Relationships Dissatisfaction as the mediator variable. All 8 mediation models were analyzed, of which three showed significant mediation effects. Three models with the TCI character traits SD, C, and ST as independent variables and Family relationship dissatisfaction as the mediator showed a good fit. The hypothesized relationships between three dimensions of character by the Cloninger's TCI and Family Relationships Dissatisfaction as the mediator variable were statistically significant. The effects of C and ST on eating behavior (EAT-26 total scores on a 6-point assessment)



Figure 3. Graphic depiction of mediation models with Family Relationships Dissatisfaction as a mediator variable and Self-Directedness (A), Cooperativeness (B), and Self-Transcendence (C) as independent variables. Only significant effects are presented.

*Note*: A — All path coefficients are significant. The indirect effect is significant and equal to -0.078. This model is exactly estimated, so there are no fit indices; B — Fit indices: chi-square=2.582, df=1, p=0.108, CFI=0.969, RMSEA=0.073. 90% CI (0.0001; 0.188). All regression coefficients are significant. The indirect effect is significant and equal to -0.108; C — Fit indices: chi-square=1.369, df=1, p=0.242, CFI=0.992, RMSEA=0.035, 90% CI (0.0001; 0.163). All regression coefficients are significant. The indirect effect is significant are significant. The indirect effect is a significant and equal to -0.108; C — Fit indices: chi-square=1.369, df=1, p=0.242, CFI=0.992, RMSEA=0.035, 90% CI (0.0001; 0.163). All regression coefficients are significant. The indirect effect is significant and equal to 0.072.

are fully mediated by Family Relationship Dissatisfaction without the direct effects. SD demonstrates also a direct effect on the EAT-26 level: however, the effects through the mediation are more pronounced.

The results of the mediation analysis are presented in Figure 3 (A, B, C) and in Table S4 (in the Supplementary).

#### DISCUSSION

#### Age differences in eating attitudes and behavior and prevalence of ED risk

The comparison of EAT-26 total and its three and five subscales showed some significant differences between age groups. There were no significant age differences in the total EAT-26 scores, but the Dieting scale of the traditional 3-factors model had higher scores in older girls (15–17 years old). But in the five-factor model, significant differences were observed only on the "Drive for Thinness" scale, while on the "Dieting" scale, which reflects the specifics of the eating behavior, the differences were not significant. This can be explained by the fact that the Dieting scale in the three-factor model includes items concerning both dieting and drive for thinness. It is likely that the age differences in the dieting scale scores (three-factor model) are mainly due to those items related to weight concerns and drive for thinness.

In terms of one of the research questions concerning the prevalence of ED risk in adolescent girls from the community sample, the present study demonstrates that 11.1% of girls in all samples had EAT-26 scores at or above 20, which is evidence of a risk of ED. At the same time, comparison between the age groups of 12–14 and 15–17 years olds showed that the risk of ED was noticeably higher in the older age group (15.5% vs 7.7% in the younger group). The differences are not statistically significant, but there is a trend (p=0.064). This is consistent with the results of other investigations dealing with EAT-26 screening in adolescent samples [84].

The prevalence of ED risk as measured by EAT-26 varies greatly with age, gender, and region in which the study is conducted. Most contemporary reviews and metaanalyses are based on samples of university and college students [85, 86]. In the only cross-cultural study [87] involving female students from Russia and Japan, 8.6% of the Russian respondents and 7.9% of the Japanese respondents appeared at risk. The differences are not statistically significant. The results for adolescents are lower. In many cases, the samples include not only girls, but boys as well. For example, it is reported that in a Greek sample of adolescent girls the occurrence of EAT scores that exceeded the cutoff level over the years were 24.7% (2011) [88], 19.3% (2017) [89], and 25-33% for boys and girls, depending on the BMI level (2021) [90]. For Hong Kong and Chinese adolescent girls, we can find estimates of ED risk at 6.5% (1996) [91], 26.6% (2011) [92], 27.1% (2017) [93], and 6.8% (2022) [94]. Among 15- to 19-yearold adolescent girls from the Kingdom of Saudi Arabia, disordered eating behaviors were established in 25.47% of participants in the study [95]. A systematic review and metaanalysis of child and adolescent mental health disorders in the GCC report on the pooled prevalence of disordered eating behavior tested by the EAT-26 as 31.55% [96]. The prevalence of disordered eating behavior in a Dutch cohort study on mental health and social development from preadolescence into young adulthood as reported by F.R. Smink et al. stood at 14-22% [97].

In the few community studies of adolescents' eating attitudes and behavior conducted in Russia, an average of about 8–15% adolescent girls exceeded the cutoff [98, 99]. One study highlighted the significant influence of the school type factor. The ED risk was most pronounced in students at a prestigious linguistic gymnasium (21.4%) compared with students at ordinary schools (6%) [98]. On the whole, the prevalence of ED risk arrived at in this study is in line with the existing data on Russia and is generally consistent with the results of other studies involving high school adolescent girls in the West.

## Assessment of putative predictors of ED risk

The logistic regression analysis of a sample of two subgroups with high (EAT-26≥20) and zero (EAT-26=0) risk of ED regarded as a binary-dependent variable made it possible to identify and rank some variables as putative predictors of ED risk. Among them the most potent effects were attributed to Weight Concerns and Body Dissatisfaction. The rank correlation coefficients between EAT-26 and the parameters of Weight Concerns and Body Dissatisfaction are also the biggest amongst other significant coefficients. These parameters may be considered as dominant risk factors. This fully consists with the previously reported data on the risk factors of ED [8, 11–13, 100, 101]. In a recent umbrella review of published meta-analyses, the risk factor of body dissatisfaction leading to ED was graded as suggestive [14].

At the same time, the effect of BMI on eating attitudes and behavior is much subtle and ranks last among all mentioned effects. The correlation coefficient between BMI and EAT-26 total is very low (0.18). This suggests that subjective perceptions of body image and weight in adolescent girls play a much more important role in the risk of developing ED as measured by EAT-26 than an objective indicator such as BMI. Generally, in studies of risk factors for ED among adolescents with reasonable weight, BMI shows a weak association and is not considered an important predictor of ED. However, in overweight and obese adolescents BMI becomes a more significant risk factor for ED [15,90,94,102]. It should also be noted that the relationship between BMI and ED risk should be considered in the context of the risk of developing a specific disorder: AN, BN or binge eating disorder (BED).

With regard to temperament and character traits, statistically significant effects were identified for SD (p=0.001) and NS (p=0.023). There is also a trend towards significance in HA (p=0.072). Girls at high risk of ED have higher NS and HA and lower SD. SD seems to have the biggest effect. Correlations between SD and EAT-26 total are also the strongest, but they are negative. Many previous studies regarding the comparison of Cloninger's temperament and character traits in individuals with ED and healthy controls have reported similar results [36, 37, 44, 60, 62, 103–105]. As a rule, low SD is not only characteristic of ED, but also of other psychopathologies [106, 107]. As for temperamental traits, the results of a meta-analysis show that higher NS values are typical of a BN diagnosis, only, while higher values of HA are characteristic of all types of EDs [46].

Among other personal characteristics that seem to have a significant impact, we can point to such traits as high Alexithymia (p=0.021), Self-Distrust (p=0.001), Negative Emotionality (p=0.004), and low Self-Esteem. (p=0.017). For the high Perfectionism and Risk Behavior categories, there are only tendencies towards significance (p=0.08 and p=0.056, accordingly). All of these features are among the known risk factors of ED, which has been confirmed by many studies [63–72].

Another variable that seems to have a significant weight is Family Relationships Dissatisfaction (p=0.017). Girls at risk are significantly more dissatisfied with the dynamics in their families. They believe that their parents underestimate them, treat them too harshly, often punish them for misconduct, do not notice their achievements, and so on. It is known that family factors are also considered important components in the system of risk and protection factors in the development of disordered eating behavior [31, 32, 34]. For example, adolescents diagnosed with Restrictive Eating Disorders are characterized by alexithymia, which comes with a pattern of dysfunction in family interactions, with a predominance of collusive alliances [33]. In a populationbased longitudinal study of adolescents in Australia, an association was found between low levels of parental warmth and the risk of ED. The relationship was limited to girls, and low parental warmth was associated with bulimic behavior. As for the relationship between the dynamics in the family and body dissatisfaction and drive for thinness, there was a noticeable compounding effect between low parental warmth and low monitoring [108]. In a sample of Italian adolescent boys and girls, significant gender differences were also uncovered in the association between poor family dynamics and dysfunctional eating behavior: girls perceive their families as characterized primarily by a low level of flexibility [109].

#### **Moderation and mediation models**

The correlation between the EAT-26 total score and all prediction variables, in common with the correlation between all variables, demonstrates that many of the hypothesized risk factors also correlate with each other. This suggests that there may be more complex associations between variables that only a multivariate analysis can help reveal. Among all the moderation and mediation models we tested, several models demonstrated a good fit.

There are two significant interactions between BMI as a predictor of ED risk with Self-Distrust and Risk Behavior as a moderator. Adolescent girls who score high on Self-Distrust demonstrate a faster increase in EAT-26 total scores with an increase in BMI, than those whose Self-Distrust scores are on the low end. At the same time, the level of Risk Behavior has the opposite effect on the relationship between BMI and eating attitudes. Girls with a high level of Risk Behavior attitude show a weaker increase in EAT-26 total scores, with an increase in BMI. As mentioned above, BMI is a weak predictor of ED risk, in particular for people with normal weight, but we see that, when combined with a high degree of Self-Distrust or low level of Risk Behavior, the role of the BMI factor increases.

As already mentioned, C is also considered as weakly associated with ED, but its role increases in combination with factors such as a high level of Alexithymia or Negative

Emotionality. At high levels of one or the other moderator, there is a noticeable negative relationship between C and EAT-26. The same effect was found for low Self-Esteem, another moderator. These results indicate the presence of complex relationships between psychobiological personality predictors and the risk of ED in the context of the moderation effects of other personality variables. The same goes for ST, which is also considered almost unrelated to the risk of ED. For this character trait, two moderation effects were also found for the variables Negative Emotionality and Risk Behavior. Girls with a high level of Negative Emotionality show a positive relationship between ST and EAT-26 total scores, whereas with a low level of Negative Emotionality we see an opposite consistent pattern. At a low level of Risk Behavior, there is an evident positive relationship between ST and EAT-26, while at a high level there is no relationship.

The C and ST items were also shown to be indirectly associated with ED risk through the mediation variable Family Relationships Dissatisfaction. This variable as a mediator also increases the positive association between low SD and ED risk.

The moderation and mediation models we have uncovered suggest that we are dealing with a complex system of interactions between many factors that can increase or decrease the risk of ED in adolescents. Evidence is accumulating pointing to the complex effects of riskprotection interactions in relation to the study of the genesis of adolescent ED. For example, high self-esteem appears to be a protective factor when the girls possess a high degree of perfectionism [110]; self-oriented perfectionism partially mediates the relationship between body dissatisfaction and disordered eating behavior [111]; body shame partially mediates the relationship between body dissatisfaction and eating behavior [112]; stress and attachment anxiety predict emotional eating through rumination [113]; gender significantly moderates the relationship between anxiety symptoms and EAT bulimia subscale scores, but BMI does not [114]; perceived peer support seems to have a moderation effect on the relationship between a father's psychological control and negative eating attitudes and behaviors [115]; daytime sleepiness mediates the relationship between internalizing symptoms and disordered eating [116]; emotional eating and cognitive restraint mediates the relationship between difficulties in emotion regulation and perfectionism and ED symptoms [117]; and many more. Indeed, further research into

the moderators or mediators involved in the system of risk or protective factors regarding adolescent ED risk is required.

Unfortunately, there are no similar studies on the effects of moderation and mediation of the relationship between temperament and character traits and adolescent eating behavior. However, there is some information regarding studies with adult participants. Serial mediation analyses showed that association between HA and body dissatisfaction in women with BN is fully mediated by two significant, indirect effects through low self-esteem and through depression and low self-esteem in serial [118]. It was also shown that the association of high HA and low SD with ED severity is mediated by difficulties in emotion regulation [119]. In one of the studies, it was found that temperamental traits seem to play a full mediating role in the relationship between puberty and ED severity: age of puberty increases the level of HA, which in turn increases the severity of ED [120].

In modern research, network-based methods for psychometric data are increasingly used, including in ED studies. In the network model, symptoms are conceptualized as interacting and mutually reinforcing elements in a complex network [2, 121, 122]. In one of these studies, performed in a sample of 2,302 treatment-seeking ED patients with different diagnoses, seven Cloninger's TCI-R scales were also included among of the 32 features related to ED diagnoses [123]. The authors indicated that among all the symptoms of ED in question overvigilance, excessive focus on inhibiting emotions and feelings, interoceptive awareness, and perfectionism were critical. However, it should be pointed out that with this approach, when patients with fundamentally different diagnoses such as AN and BED are mixed, information is lost as regards the specifics of a particular disorder.

#### Strengths and limitations of the study

In the present study, for the first time in Russia, a multidimensional approach was applied to the study of the risk factors of eating disorders in adolescent girls, based on the psychobiological model of temperament and character of Robert Cloninger. In addition, an original questionnaire (Risk Factors of Eating Disorders) was developed. As a result, it was possible to identify several risk factors for ED associated with psychobiological, personal, and family factors, taking into account the effects of moderation and mediation. One of the limitations of this study is its cross-sectional design, which does not allow for establishing a definitive relationship between the presence of one or the other risk factor and long-term consequences such as disordered eating. The second limitation is the absence of a standard validation procedure for some of the measuring instruments used in this study. In addition, it can be noted that all variables were obtained as a result of girls' self-reporting, which could lead to inaccuracies in the estimates. Therefore, the results obtained can only be regarded as preliminary.

One of the possible directions to continuing this study may be the introduction of other anthropometric variables (not only BMI), which can be associated with an adolescent's eating habits and reflect not only the actual values, but also the deviation of individual anthropometric measurements from their normalized values (percentiles, z-scores).

#### CONCLUSION

In general, it can be concluded that there are various interrelated influences amongst the numerous possible ED risk and prevention factors, which determines the paths between the predictor and the outcome. The better we understand these pathways, the more effectively it will be possible to plan the prevention and treatment of ED. It is of utmost importance to think about ways to stave off the risk of ED starting from childhood and adolescence.

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#### **Supplementary data**

Supplementary material related to this article can be found in the online version at doi: 10.17816/CP6132

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# Anorexia Nervosa through the Lens of Primary Health Care Practitioners in the Kyrgyz Republic

Нервная анорексия в представлении врачей первичной медицинской помощи Кыргызской Республики

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#### ABSTRACT

**BACKGROUND:** Anorexia nervosa was investigated in a large number of studies. Several of the studies in our review highlighted how important it is to factor in the opinion of health care practitioners if we want to improve the quality of the medical care provided to patients with anorexia nervosa. Additionally, the dominance of studies focused on anorexia nervosa within the Western culture raised the need for cultural diversity in such research.

**AIM:** The present study endeavored to explore how primary healthcare practitioners in Bishkek, Kyrgyz Republic, perceive anorexia nervosa and people who suffer from it.

**METHODS:** The study used the qualitative approach of Interpretative Phenomenological Analysis. Six semi-structured interviews with six primary health care practitioners from Bishkek were conducted.

**RESULTS:** The analysis of the collected data pointed towards four themes: (1) Anorexia nervosa as a reaction to distressing events in the form of loss of appetite; (2) Attributing blame for developing anorexia nervosa by a patient to family members; (3) Local versus Western socio-cultural standards in the development of anorexia nervosa and seeking treatment; and (4) Denial of mental health disorders by patients.

**CONCLUSION:** The discussion of the interpreted results led us to the conclusion that the perceptions of the health care providers in Bishkek represent the common prism through which anorexia nervosa is viewed in the larger population, which is constructed out of information received from the physical and virtual environments.

#### аннотация

**ВВЕДЕНИЕ:** Нервная анорексия исследована достаточно подробно. Многочисленные исследования указывают на то, что для повышения качества медицинской помощи пациентам с нервной анорексией, важно понимать, как воспринимают болезнь врачи. Отмечается необходимость культурного разнообразия в исследованиях.

**ЦЕЛЬ:** Цель данной работы — изучить, как врачи первичного звена здравоохранения в городе Бишкек (Кыргызская Республика), воспринимают людей, страдающих нервной анорексией, и само расстройство.

**МЕТОДЫ:** Один из качественных методов — интерпретативный феноменологический анализ — был использован при работе с шестью интервью, взятыми у врачей первичной медицинской помощи различных центров семейной медицины города Бишкек.

**РЕЗУЛЬТАТЫ:** Анализ полученных данных выявил четыре темы: (1) Нервная анорексия как реакция на тревожные события в виде потери аппетита; (2) Приписывание вины за развитие нервной анорексии у пациента членам семьи; (3) Местные и западные социокультурные стандарты в развитии нервной анорексии и обращении за медицинской помощью; (4) Отрицание пациентами наличия у них психического расстройства.

**ЗАКЛЮЧЕНИЕ:** Представления врачей первичного звена отражают общее понимание нервной анорексии жителями города Бишкек, сконструированное из мозаичной социокультуральной информационной среды.

**Keywords:** anorexia nervosa; primary healthcare; interpretative phenomenological analysis; Kyrgyz Republic Ключевые слова: нервная анорексия; первичная медико-санитарная помощь; интерпретативный феноменологический анализ; Кыргызская Республика

#### INTRODUCTION

Eating disorders (EDs), particularly anorexia nervosa (AN), represent a serious threat to public health [1–4], constituting on average a prevalence of around 1% as reported mainly by westernized countries [5], with 20–40% of new cases starting during adolescence and accompanied by significant lethality [6, 7]. They affect both males and females, irrespective of age [8]. Recent studies suggest that the health care system needs to prioritize the prevention of EDs, as more than half of the people diagnosed with EDs receive no or improper treatment [9].

Treatment of such disorders as AN is complicated by the high incidence of cases of relapse, the comorbidity with other mental disorders, along with shifts from one subtype to another, and the denialism that often accompanies AN [1, 10, 11]. The complications related to the treatment of AN also have much to do with limited knowledge among medical practitioners, who often constitute the first line of specialists patients encounter. The poor training of primary healthcare (PHC) providers on the topic of EDs leads to a poor record of identification of symptoms during clinical assessments [12, 13]. Along with that, key barriers to seeking treatment include stigmatizing beliefs and attitudes among health care practitioners [14]. The authors of the study emphasized the importance of confronting such perceptions and beliefs amongst medical workers in order to curb them. In other words, circumscribing and addressing perceptions and attitudes among healthcare workers regarding AN and developing more efficient evidence-based clinical

guidelines regarding the subject matter is crucial if we want to improve the medical care that is available to persons with AN [4, 14, 15].

Early research into EDs and AN has mainly focused on the female population of Western countries, where the concepts of EDs and AN first appeared [16]. Recent research in the field of EDs has shifted the focus from Western to other countries. Thus, such research has highlighted the importance of exploring the impact of socio-cultural factors on views about EDs as a way to better manage them in the context of, for example, the Asian culture [17].

#### The present study

Lack of research in the area of AN in the Kyrgyz Republic is in contrast with the current rising number of studies in this area in other non-western countries [16-18]. This feeds the belief that AN is present in the Kyrgyz Republic but does not receive enough attention. Taking into account the recommendations on the importance of investigating the perceptions of healthcare practitioners in order to improve the quality of medical care [14, 15, 19], this study aimed to investigate how Kyrgyz PHC practitioners perceive AN and people suffering from it. The supporting rationale for choosing PHC practitioners for our sampling was the assumption that such practitioners are supposed to be accessible to the majority of the local population, according to the current structure of the health care system [20]. People with AN can seek treatment from PHC practitioners, who may be the first line of defense in the health care infrastructure posture and, therefore, exercise considerable influence in the process of seeking and receiving medical care.

The scarcity of research related to attitudes toward AN in the Kyrgyz Republic and Central Asia in general leaves Russia as the main proxy source of literature in terms of how EDs are confronted on the closest thing to the territory of the Kyrgyz Republic. For example, one study contributed to research into cultural differences in terms of AN by investigating the dichotomous thinking about EDs in the context of cultural differences between Japanese and Russian female samples and provided an interesting angle on cultural specifics in Russia, where the political and economic upheavals of the Perestroika era prompted a need for stability and led to rigid thinking [18]. Another study conducted in Russia [21] provided insight into virtual culture as a socio-cultural phenomenon involved in the development of AN.

Along with the limited research into EDs and AN in Central Asia, representative samples of the majority of studies in European countries and America might not be reflective of the situation of patients in Central Asia and the issues related to the perception of AN in their countries. The classification of EDs within The Diagnostic and Statistical Manual of Mental Disorders [22] does not include a contextual understanding in terms of diverse cultures, which may lead to underdiagnoses [16]. Therefore, it becomes imperative to explore how healthcare practitioners view AN and perceive patients with AN in the Kyrgyz Republic.

#### **METHODS**

#### **Study design**

This study employed a qualitative approach and followed the methodology of Interpretative Phenomenological Analysis (IPA). The reason for choosing this approach was to explore a particular phenomenon from the point of view of the participants through in-depth, semi-structured interviews [23]. Therefore, IPA was chosen as the tool for investigating the perceptions of PHC practitioners who participated in this study. Additionally, the theory of social constructionism was employed in order to discuss and draw conclusions on the results of the study.

#### Setting

The interviews were conducted at Centers for Family Medicine (CFM), which are part of the primary healthcare system in Bishkek, Kyrgyz Republic [20]. The participants chose those settings because they proved convenient for them and allowed them to meet with the researcher at their place of work. Each of the participants was interviewed separately face-to-face with a researcher in auditoriums made available for the purpose. Two of the participants (Aliya and Tynara) were interviewed at CFM No. 8, three of the participants (Aikyz, Burul and Gulnaz) were interviewed at CFM No. 2, and one (Tonya) was interviewed at CFM No. 3. The interviews were audio-recorded upon consent.

#### **Participants**

Six participants aged 28–65, all females and staff at community health centers in Bishkek, Kyrgyz Republic, were recruited. Five of the participants were primary care physicians, while one was a clinical advisor (Tynara). All participants were Kyrgyz by ethnicity, Kyrgyz- and Russian-speaking, and resided in the urban communities of Bishkek. All the participants were graduates of local medical schools and completed internships in city hospitals.

#### **Procedure**

The participants were contacted directly at their place of work, and they were recruited by means of snowball sampling. The participants were informed on the matter of the study and the terms of participation, which included ethical considerations. Those who agreed to participate signed written informed consent forms. Interviews lasted from one hour to one hour and a half and took place at the participant's place of work. All of the interviews were audiorecorded and transcribed upon consent. Interviews were conducted by the lead author, in person, in the Russian language. The interviewer was a young woman aged 31 at the time of the interviews. She is of Kyrgyz ethnicity and grew up in an urban environment in Bishkek.

The study was structured around the following two research questions: "How do Primary Healthcare Practitioners in the Kyrgyz Republic perceive AN and people who have it? What public, cultural, and traditional background do they draw from when discussing patients with AN?" (Box 1).

#### **Transcription and translation**

The interviews were conducted in the Russian language, since the language was spoken by the participants and the researcher. They were transcribed verbatim and translated into English by the researcher. Only the researcher who Box 1. The semi-structured interview guide used for the study (only key questions)

- What do you know about eating disorders?
- Do you know how they differ from each other?
- What do you know about anorexia nervosa?
- Why do you think people develop it?
- How do you feel about people who have anorexia nervosa?
- Have you had patients with anorexia nervosa?
- How did you feel about that experience? What was your choice of treatment?
- What would you think/feel about/suggest to a person who has anorexia nervosa?

conducted the interviews had access to documents and data collected from the participants.

#### **Ethical approval**

The study was approved by the Institutional Review Board, American University of Central Asia (Approval Letter No. 2022031600000255).

#### **Data analysis**

The IPA approach employed in this study is widely used in psychological research [24]. The process of exploration was guided by the phenomenology, idiographic approach, and hermeneutics, in accordance with IPA guidelines [24]. The interpretation of the data depended on the existing set of knowledge the researchers held, which is known as fore-conception [25]. In order to avoid fusing with a single perspective, researchers explored the phenomenon of AN from multiple perspectives, which is known as a hermeneutic circle [26].

According to the IPA guidelines [23], the study was conducted upon collection of data by means of semistructured interviews. The interview protocol was based on information gleaned from previous research in the related field [14, 15, 19]. The steps for data analysis included verbatim transcription, careful reading and re-reading of the interviews by the research team, identification of emerging themes, classification of the themes, and their refining. All the steps were conducted in accordance with the IPA guidelines [23]. The results were discussed in the frame of social constructionism theory.

## RESULTS

Four superordinate themes were uncovered: (1) AN is perceived by physicians as a reaction to distressing events in the form of loss of appetite, (2) attribution of blame for developing AN by a patient to family members, (3) local versus western socio-cultural standards in the development of AN and the search for treatment, and (4) denial of mental health issues by AN patient.

# (1) AN is perceived by physicians as less of a psychological condition and more of a reaction to distressing events in the form of loss of appetite

Although some participants saw AN as a psychological disorder that manifests itself in the form of restrictive eating behavior, they generally described AN patients as female adolescents who want to lose weight and push things to the extreme due to a distorted perception of their bodies:

"When you start talking to a patient, not interrogating, but talking, they say that they want to be thinner. At the same time, she weighs 40 kilograms, and keeps on trying to lose weight. That's when we start to sound the alarm."

## Aliya, 50 years old

Most of the descriptions of AN provided by the participants assumed a goal of weight loss from patients as a result of overreaction to psychological distress: for example, Gulnaz highlighted how she and her colleagues could relate to patients with AN based on personal experience of losing appetite and weight at times of emotional distress or burnout. She stressed that she related to the experience of patients with AN, because she was personally experiencing the struggles of losing appetite while going through the hardships of being a medical worker during the COVID-19 pandemic. She provided the example of her experiencing the disorder, discribing it as a brief episode of changes in eating behavior due to her chaotic work schedule, which led to her feeling worn out, as she mistakenly assumed that AN was nervous exhaustion to emotional distress:

"I had it myself. During the pandemic. During the first wave all the doctors got sick, and I was left alone. There were some pediatric physicians, they were helping me. But during that time my phone was ringing constantly. I did not even have time to eat properly. I had little kids, and a husband. They were helping me, of course, but I was so exhausted." Gulnaz, 31 years old By providing the example described above, Gulnaz compares herself with AN patients, implying that people who end up developing the condition are predisposed to the disorder organically, unlike her. She views the disorder as a result of an exaggerated reaction to stress:

"Some people have a stable nervous system, for example, right? Some people have a labile one. Some are labile, they cry like that, they immediately react to something like this." **Gulnaz, 31 years old** 

The distinction between people who can overcome stressful situations and people who may suffer from the consequences of experiencing excessive emotional distress due to the specifics of their nervous system is seen across the interviews (Aliya, Burul, Gulnaz, Tynara). For example, Burul describes people who tend to react excessively to distressing events as "anxious" peoples:

"It becomes clear when a person has some kind of stress, like exams or something. Ultrasound screening is normal; gastroscopy is also ok. It's usually anxious people." **Burul, 28 years old** 

Aliya sees the risk population for AN as adolescents, as the developmental features of the nervous system characteristic of their ages makes them vulnerable to stress:

"And teenagers, they are flexible, they have hormonal imbalance. During this period, they are flexible, vulnerable and sensitive. They are vulnerable to it during these times." Aliya, 50 years old

Our participants perceive emotional distress and hormonal disbalance as interrelated conditions that lead to maladaptive behavior, such as weight loss. This assumption is incorporated in the common understanding of the development of the disorder among several participants (Aikyz, Burul, Gulnaz, and Tynara).

Another participant, Gulnaz, highlighted the importance of the longevity of the stressor; so it can be assumed that people have to experience negative emotions for a considerable period of time for the negative changes in the nervous system to appear. However, her usage of the word "apparently" points to her doubt about her knowledge on the nature of AN: "Nervous exhaustion develops when a person is under stress for a long time (thinks). Or under some kind of pressure. They start losing their resources, and they are on the brink of a breakdown. This is called nervous exhaustion, apparently, nervous anorexia."

#### Gulnaz, 31 years old

The prolonged distressing event as the reason for experiencing physiological consequences can also be lethal, according to Tynara. She links AN to nervous exhaustion caused by the disruptions in the nervous system due to stress, as well:

"Even if you eat well, you will lose weight, as it is nervous exhaustion. The whole body starting from the very nail, it's all the nervous system it is being regulated by. If a person is always in a stressful state, of course, nervous exhaustion will develop, nervous exhaustion. A person can even die from it." **Tynara, 65 years old** 

Since the consequences of experiencing distress lead to a loss of weight, it is not identified as a disorder by the participants, until it becomes noticeably severe. Burul, for example, described a patient who demonstrated apathy towards her, which led her to link the loss of weight to adverse life events; however, to her, the patient was not overly underweight to consider it a disorder:

"I had a patient recently. Not that skinny, it was not anorexia yet. She comes in, and it becomes clear by the way she talks. They speak so quietly, in sunglasses, they do not look at you. In a low mood. And then you start asking them, and it appears that they had some kind of stress, exams or something. She asked me whether stress could be the reason. Of course, it can. I asked her about her problems. She said that she could not keep up with her studies. She failed her exam." **Burul, 28 years old** 

Oftentimes, the participants directly linked cases of AN to psychological and interpersonal stressors:

"His mom made the call, as we make house calls to provide our services. And he was just lying there. She said that it's been two months. He didn't stand up, he didn't complain, didn't eat. She said that something happened at his job. Something personal. He didn't fit in with colleagues." **Tonya, 46 years old** 

# (2) Participants attributed the blame for developing AN symptoms to family members

While some respondents (Aliya and Tynara) empathized with the relatives and family of AN patients, as they carry the burden of the care providers, at the same time many (Aliya, Aikyz, Burul, Gulnaz, Tonya) saw relatives, in particular mothers, as those responsible for the development of the disorder in female adolescents. The participant Gulnaz thought that "anorexia in women does not develop due to work, it's all due to family issues" and that "someone made them suffer at home". Such attitudes may have to do with the local cultural context and gender bias. Tynara assumed that "something might be not ok at home" and that "someone is aggressive at home". A female adolescent, according to Tynara, lost a lot of weight due to emotional abuse at home. She shared that her step-mother "always screams" and "constantly criticizes" her.

Mental health issues, as seen by the participants, arise when children lose their autonomy due to parental pressure. In cases of AN, mothers are seen as controlling and demanding. Since mothers are often the prime caregivers and actively participate in their daughters' problems and treatment, they are often perceived as key figures and the source of stress for the daughters. The mothers are described as the ones who can set overly ambitious goals for their daughters, since they "didn't reach them themselves" (Aliya). Thus, daughters internalize those goals from their mothers, in the opinion of the doctors, which leads to perfectionism in their effort to reach those goals:

"I do not know what they push for, what kind of leverage they have. I think every parent needs an individual approach. For each parent and each patient. For example, [parents say] you should attend dance classes, and this is their level [of expectation], right? Why does she have to go there? To dance classes? Why would her parents want her to dance? What do they want from this girl? Why do they want that from the girl?" Aliya, 50 years old

One participant (Aikyz) described the scenes she observed during her practice, where mothers shout at their daughters: "You do not eat anything!", "You did it to yourself!" This imagery and tone for Aikyz indicate the blaming and criticizing behavior of the mothers, who confuse care with blaming and probably dosing and so push their daughters to develop EDs symptoms. Tonya linked the development of the disorder in a male patient who passed away to the pressure he experienced from his mother. He had to be a provider for the family, according to his mother. Tonya stressed the gender-based pressure in the family, primarily from the mother:

"She made him go to work because: "You're a man!" She created some kind of a bar for him: "You have to provide for us already". And maybe something broke within him. When I saw him, he was already in bed." Tonya, 46 years old

In general, all participants emphasized the role of a stressful situation at home in the development of AN symptoms, especially in female adolescents. They shared interpretations of the home environment as aggressive and hostile, or neglectful. Burul stated that "parents must pay attention to girls", but that they "do not have enough time" and "do not understand each other". They do not reward their girls by saying "well done" or "you are beautiful". Looking for the causes of the condition in adolescent patients but lacking a full understanding of the disorder, the participants saw the development of the disorder as a result of not feeling accepted enough by parents:

"Girls start to, like, especially when parents do not pay enough attention to a child, and they start to want to be like someone else... Parents do not say to them that they are good, beautiful. I think that they have associations like that, like, beauty is everything, thin waist (thinks). And they start to diet. Based on the opinions of those surrounding them, they start to react already...'So, they will love me, if I become thin, I will be beautiful' (impersonates)."

# Burul, 28 years old

In conclusion, the participants considered the negative environment at home, in particular the relationship with mothers, to be the key underpinning of distress, especially in young or adolescent patients, and as the cause behind the development of EDs symptoms. Such a perception, as a whole, suggests that there is a tendency among the participants to look for an external cause for patients' behavior and find a convenient reason to attribute the blame to. On the other hand, such a perspective contradicts the view of AN patients as people with a heightened response to common stressors.

# (3) Physicians contrast local to western sociocultural standards in the development of AN and willingness to seek treatment

Some participants (Aliya, Aikyz, Burul, Gulnaz) based their views about AN suffered by patients in the Kyrgyz Republic on the discourse about body type ideals pushed by the media on adolescents, engendering a threat that pushes young people to put an outsized importance on their bodies:

"They live in terms of those TV shows, Hollywood and there, I do not know all of those actresses, right? They have amazing bodies, right? And they think that all of this is, I do not know, happiness. Being beautiful means having it all."

#### Burul, 28 years old

Burul links the onset of AN symptoms to stressful life events, and somewhat refuses to consider it as a special psychological condition, dismissing such an approach as enabled by the media. She maintains that in "real life" people lose weight when they face adverse life events and can not handle the ensuing distress, as opposed to what is depicted in the media. The implication is that the media exaggerates the issue to the point of making it appear more severe than it is in real life:

"We saw patients like that on TV. They come to us, but they are not as scary, of course. The scary ones are only on the screen. I had a patient who lost a lot of weight, but not too much, not skin and bones. It's only in the movies, skin and bones. In real life they are skinny, but not like in the movies. They have some weight; it is just starting to become noticeable." **Burul, 28 years old** 

Aikyz is another participant who separates between AN portrayed in the media and that in real life. Her understanding of the disorder is rooted in beauty standards:

"The first thing that comes to mind, is (thinks) the models. They need to look thin, so they lose weight to the point that it becomes scary."

# Aykiz, 33 years old

The participants (Aliya, Aikyz, Burul, Gulnaz) attributed the cause to the influence of the global media, which promotes beauty ideals based on Western culture. For Aliya, the

promotion of norms of physical appearance through the access to the media young people enjoy leads to the burden of comforming to the globally celebrated beauty ideals:

"The idea of a perfect body shape is promoted via the Internet. Those who are involved in the virtual culture of Westernized beauty standards appear under pressure to look a certain way."

#### Aliya, 50 years old

Those who feel pressured to follow those beauty standards, according to Burul, seek external validation because of a lack of self-esteem. She mentioned low selfesteem as a reason for falling under the influence of the virtual environment. The process of achieving this goal involves major sacrifices; "the rush":

"For the most part, I think the reason is the pursuit of beauty, the rush, right? And low self-esteem." **Burul, 28 years old** 

The local culture in the Kyrgyz Republic has opposite norms, according to the participants (Aikyz, Burul, Gulnaz), in terms of the physical appearance of a person, especially a female. Traditionally, females are seen as the ones responsible for procreation. They have to maintain a properly functioning reproductive system, which requires a bigger body shape:

"Our mentality does not demand it. Our people love the chubby ones, so that they could give birth to normal, healthy kids." **Gulnaz, 31 years old** 

As the local beauty standards deviate from global ones, people who look noticeably underweight may even become targets of bullying. Aikyz feels relieved that she did not get bullied for being thin during her high school days, unlike one of her classmates:

"I had a girl in my class, she was very skinny. Well, I used to be skinny too, but I was not called names. Because, maybe, I was shorter than her, it was not that noticeable. She was very tall. And every time during classes they called her 'anorexic'." **Aikyz, 33 years old** 

Tynara described how the treatment of her sister was postponed because of a need to organize the traditional annual commemoration "Ash" for her deceased husband. She was afraid of being shamed by relatives if she failed to follow the tradition. She was extremely underweight by the time of her treatment. Tynara tried to hospitalize her, but the traditions were too hard to stand against:

"I said: 'Come here' [to Bishkek], but she said: 'My husband is dead, I have to organize Ash'. It is usually like that among us, Kyrgyz people. Relatives would say: 'Oh, she went off to Bishkek', they would get offended."

# Tynara, 65 years old

While most of the participants (Aliya, Aikyz, Burul, Gulnaz) talked about the burden of following the socially accepted norms for females in the form of external appearance, Tonya provided insight into local gender stereotypes as relates to the male population. She stated that males are pressured to hide their emotions, which leads to such reactions to emotional distress as a loss of appetite:

"Girls overcome it faster. They overcome it somehow, they socialize more maybe. And boys close down, it is more difficult for them. He has this [belief] that he is a man, that he has to do it, to provide for his girlfriend, mother, sister." **Tonya, 46 years old** 

Overall, socio-cultural specifics are perceived as the influencing factors in the development of conditions seen as AN by the participants, as they see how significant the environment, whether virtual or physical, can be in terms of impact on mental health and worldview in general.

# (4) Denial of mental health issues

The participants (Aliya, Aikyz, Tynara, Gulnaz, Tonya, Burul) described such patients as being unaware of the psychological roots of their physiological concerns. Thus, Tonya sees the cases of denial as unresolvable, as she does not know how to provide care in such situations. Since she assumes that AN develops in young adults because their nervous system is "not yet developed", she describes them as "impulsive, with barriers" (Tonya). Those barriers do not let them admit to themselves that they need the help of a mental health specialist.

"At the same time, he will deny everything, thinking he is healthy and cheerful, that he is doing everything right, and that he does not need help from a physician. He just came to do some tests. For example, a blood test, because he feels a little bit tired. That's all. We can't say anything directly, and questions alluding to a mental health issue will be rebuffed by him."

# Tonya, 46 years old

Such patients come to seek help for their physiological concerns, rather than psychological help. Burul chalks such a situation up to a lack of self-awareness or escapism. The denial may morph into a refusal of treatment, when patients admit it to themselves but hide from that awareness due to the shame associated with being called "crazy" (Burul):

"But they come for other reasons, of course, they feel nauseous, for example or they have stomach ache. I think they, I do not know, maybe realize it, but they do not want to see. Maybe they do realize it."

# Burul, 28 years old

As Aliya is the only one who confidently described the disorder as a result of a patient's goal-oriented restrictive eating behavior with values linked to perfectionism due to societal pressure, she sees denial in adolescents as an explanatory outcome. They are doing what they think they have to do; therefore, there is nothing they are doing wrong:

"Because if a girl does not reconsider her thinking, nothing will help, medication will not help. I tried just to talk to her, but the girl said: 'I want it this way'." Aliya, 50 years old

For Aikyz, seeking treatment is impossible without the acknowledgement of having a disorder. Only people with self-reflection can seek help for themselves. However, common situations include cases of denial, where people would not admit to themselves that they have a problem. Along with denial, patients try to avoid stigmatization, as they do not want to be perceived as "psychos" (Aikyz):

"She [a psychotherapist at CFM] told me that if he [patient] has the capacity to self-criticize, it is possible [to treat him]. And if he refuses, there is nothing we can do." **Aikyz, 33 years old** 

All the participants suggested an empathetic approach towards patients in denial. For example, Gulnaz sees

young people as the ones at risk of developing AN, as well as those who may resist treatment due to their rebellious temperament. She highlights the fact that the resistance may occur in the case where they feel "judged", which is why they require a subtle approach:

"We have to talk to them gently. Young people behave this way nowadays. If you start arguing with them, they will have a reverse reaction. Without judgment. We have to find a common language for everyone."

# Gulnaz, 31 years old

Interestingly, although in the majority of cases the participants (Gulnaz, Burul, Tynara, Tonya) had difficulty seeing the symptoms of AN as a psychological disorder proper, connecting it to life stressors and the underlying psychological conditions, they expressed an often vague but passionate need for mental health practitioners to participate in the process of diagnosis and treatment:

"I want the number of them [psychotherapists] to increase. We need them a lot. The salaries need to go up, I do not know how it will be done, but the attention of the young trainees must be brought to it, so that they would study to become psychotherapists. It would be great, yes."

# Gulnaz, 31 years old

As mentioned in the citation above, the need for the support of specialists in mental health seems rather vague and expressed only in the number of psychiatric interns. Here and in other interviews (Aikyz, Burul, Gulnaz, Tonya, Tynara), the respondents did not describe using any current resources related to mental health in their work with AN patients. It seems that the participants positioned themselves outside of the system of psychological support:

"I refer to her [psychiatrist] only if a patient needs it. She is a psychiatrist, so she treats mainly those with severe disorders. Like schizophrenia, intellectual retardation, or very severe disorders. So, if a person has light insomnia, or, I do not know."

#### Gulnaz, 31 years old

From the above citation, understanding of what kind of a mental health specialist is needed and for which cases is vague. It seems that only severe cases require referrals to psychiatrists. In cases where a patient experiences seemingly mild distress symptoms, referrals to mental health specialists are not discussed by the participants.

#### DISCUSSION

The PHC practitioners in this study perceive AN patients as people who have lost appetite as a result of emotional distress which is influenced by their external environment, where family members play a significant role. On a larger scale, they attribute the development of AN to sociocultural pressures in the global and local contexts, discussing discourses available in the media. AN patients, according to the participants, are in denial of the fact that there are underlying psychological reasons behind their physiological concerns. However, our interviews lacked references to working with mental health care professionals and encouraging patients to seek psychological support or treatment.

It was crucial for us to let the participants steer the dialogue towards them, as was suggested in the IPA guidelines [27]. Therefore, the participants freely moved away from the topic of AN into discussing other psychological causes of weight loss, framing it into the discourse related to AN. Hopping from talking about intentional loss of weight to losing weight due to stress may be identified as confusion between these two phenomena or folding of one into another. Either way, both confusion and folding are linked to a lack of knowledge about AN. Overall, AN patients are perceived by the participants as those who lose weight as a result of stress, mainly. AN is a primarily psychological condition which leads to physiological consequences, according to them. This explanation is similar to the description of AN within previous diagnostic criteria, where EDs were described as psychophysiological gastrointestinal reactions, where negative emotions lead to physiological gastrointestinal symptomatology [28]. The majority of PHC physicians see AN as a consequence, or one of the symptoms of experiencing emotional distress, rather than a separate disorder. Discussions of the influence of the media on the desire to lose weight due to beauty standards proved distant from real life cases. The participants were hesitant to answer the question about the symptomatology of AN and mainly referred to the disorder as "nervous exhaustion". It can be concluded that they are unaware of the current clinical symptomatology of AN, as was highlighted by previous studies [15, 28]. However, one of the participants demonstrated knowledge of AN symptomatology related to body image concerns. After all, lack of knowledge among PHC practitioners in Bishkek may not be widespread.

The physical appearance and behavior of an average AN patient was constructed from the words "skinny", "pale", "passive", "apathetic", pointing to the depiction of a person in psychological distress. The imagery of an abstract AN patient is built from the media representation of AN, along with the clinical practice of the participants. Not all of the participants viewed an AN patient as an adolescent female, with some of them describing cases of AN in males, adults, and elderly people. However, the participants who did not attribute AN to a particular age or gender viewed it as a case of nervous exhaustion. So, it cannot be stated definitively that AN is not gender- or age-specific from the point of view of the participants.

The role of family members was highlighted by all of participants, with the focus on the mother-daughter relationship. The existing literature also focuses on the role of primary caregivers within EDs and AN [29-31]. The controlling and pressuring nature of parenting leads the participants to perceive parents of AN patients as responsible for the development of the disorder in their children. However, the controlling style of parenting is what makes seeking help possible for unwilling patients. So, responsibilities and blame end up in a circle. Previous research [30] explored family dynamics, as it plays a significant role at every stage of AN, and focused on maternal caregivers making sense of their daughters' experiences of having the disorder. Thus, mentioning the role of maternal caregivers within AN is important, which was covered by the participants of this study.

The participants linked body image concerns to the global media, which spreads the ideas of a socially accepted physical appearance. However, there is a point of intersection where the global social standards meet the local social environment. Local body type ideals differ from westernized ones. This is linked to the role females fulfill in the local society, where they are responsible for reproduction, which is thought to require a thicker body shape to be performed safely. The authors of a previous study on the subject [16] mentioned that their participants held up thicker body type preferences in terms of Asian culture. Thus, there is often a gap between the dominant Westernized view of body shape and local ones. The result of present-studies regarding geographical differences in the socio-cultural factors influencing perceptions of physical appearance [32] and the global spread of information

through virtual communities is consistent with previous research in the field [18, 21].

Development of AN was also linked to low self-esteem and refusal to accept one's body. The refusal to accept oneself pushes a person to seek validation from others. Previous studies have also suggested that low self-esteem leads to the development of disordered eating [1, 33].

AN patients are reluctant to accept treatment for the psychological causes of their condition. Our participants see AN patients as those who are unaware of, do not want to be aware of, or deny the psychological causes of their physiological concerns. Their thinking can be described as rigid. This can be an illustration of a case of dichotomous thinking in terms of disordered eating described in a study on the subject matter [18]. According to our participants, the perfect body shape is a value for patients who intentionally lose weight. Consistently, recovery is understood as targeting these values and reformulating them. This is in line with the preventative program described in previous research [9].

Denial of mental health issues by patients makes physicians feel helpless. According to our participants, treatment can be effective in the case of early mental health interventions, but it is often postponed until it is too late to reverse the process. This perspective is similar to that of Nordic healthcare specialists, who held negative expectations towards the outcome of AN treatment [14]. Denial and resistance to treatment was also discussed in previous studies [34–36].

The overall perceptions of local PHC practitioners as relates to AN and people with AN can be fitted in the frames of the social constructionism theory. According to it, meaning creation and categorization emerge concurrently during interactions between people [37]. The perception constructs through language, the cultural and historical context, as well as through sets of meanings [37]. AN has been discussed in other research efforts [38] in the framework of the social construction of psychopathology, which is a collectively constructed set of understandings of suffering grafted to a particular, constantly changing social context [38]. Therefore, the social construct of AN among local healthcare specialists in the Kyrgyz Republic is shaped by the local context and represents locally held socio-cultural perceptions of psychopathology.

#### Implications for future research and practice

This study is a step in further research that attempts to explore manifestations of AN in the Kyrgyz Republic; the experiences of PHC practitioners and socio-cultural factors in the framework of AN. There is a potential for this study to be applied in healthcare practice targeted at the improvement of quality in medical care for AN in the form of providing information for the development of training programs for medical workers and reducing stigmatization.

#### **Strengths and limitations**

This study has tried to advance research on the topic of AN in the context of diverse cultures, as it reflects the socio-cultural factors influencing perceptions regarding AN and can be applied in medical practice.

However, there are limitations to the study, which are related to the subjectivity of interpretations. It must be brought to attention that the results hereby are predominantly influenced by the researchers' perspectives.

### CONCLUSION

The PHC practitioners in the study construct a perception of AN and patients with AN using consideration drawn from the global and local contexts. Most of the topics discussed by the participants are present in the extant literature, making the views expressed by Kyrgyz PHC practitioners reflective of common understanding of AN by means of information emanating from local and virtual social media sources.

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# Factors Associated with Lifetime History of Eating Disorder in Non-psychotic Patients with Suicidal Ideation

Факторы, ассоциированные с расстройством пищевого поведения в течение жизни у пациентов с непсихотическими психическими расстройствами и суицидальной идеацией

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# ABSTRACT

**BACKGROUND:** Data on the sociodemographic, biographical, and clinical factors associated with a lifetime diagnosis of eating disorders (ED) in patients with non-psychotic mental disorders (NPMD) and suicidal ideation (SI) are scarce.

**METHODS:** A cohort study was conducted at the Moscow Research and Clinical Center for Neuropsychiatry. The sample consisted of consecutive patients with non-psychotic mental disorders and SI, aged 18–45 years. Participants with a lifetime diagnosis of anorexia and/or bulimia (then in remission or recovery) were compared with those without ED in terms of their sociodemographic profile, clinical characteristics, lifetime traumatic events, and some behavioral patterns. All participants underwent the Russian version of the Self-Injurious Thoughts and Behaviors Interview and completed the Brief Reasons for Living Inventory, the State and Trait Anxiety Inventory, and the Beck Depression Inventory.

**RESULTS:** A total of 892 patients with non-psychotic mental disorders and SI were included in the study. The mean age was 25.7 years, and 84% were assigned female at birth. Same-sex experience was more common in the ED group. Patients with an ED were more likely to have a history of physical and sexual abuse and to have witnessed domestic violence. The proportion of participants with piercings, tattoos, or severe body modifications was significantly higher in the ED group. Patients with a lifetime ED were more likely to engage in nonsuicidal self-injurious behaviors and to have a history of suicide attempts.

**CONCLUSION:** Lifetime ED in NPMD patients with SI is associated with younger age, being assigned female at birth, having an alternative gender identity, having same-sex experience, having more than one psychiatric diagnosis, having been diagnosed with bipolar disorder, experiencing severe depression and anxiety, being exposed to multiple traumatic experiences, having various body modifications, practicing NSSI, and having a lifetime story of suicide attempts.

### аннотация

**ВВЕДЕНИЕ:** На сегодняшний день имеется недостаточно данных о социально-демографических, биографических и клинических факторах, связанных с наличием диагноза расстройство пищевого поведения (РПП) у пациентов с непсихотическими психическими расстройствами и суицидальными мыслями.

**МЕТОДЫ:** Когортное исследование проведено на базе ГБУЗ «Научно-практический психоневрологический центр имени З.П. Соловьева» ДЗМ. Выборка состояла из последовательно отобранных пациентов с непсихотическими психическими расстройствами и суицидальными мыслями в возрасте 18–45 лет. Участников с диагностированной в течение жизни анорексией и/или булимией (и находящихся сейчас в стадии ремиссии или выздоровления) сравнивали с участниками без РПП по социально-демографическому профилю, клиническим характеристикам, наличию психотравмирующих событий в течение жизни, а также по некоторым поведенческим паттернам. Все участники прошли русскоязычную версию интервью об аутоагрессивных мыслях и поведении (SITBI), а также заполнили краткий опросник причин жизни (bRFL), опросник ситуативной и личностной тревожности (STAI) и опросник депрессии Бека (BDI).

**РЕЗУЛЬТАТЫ:** В исследование было включено 892 пациента с непсихотическими психическими расстройствами и суицидальными мыслями. Средний возраст составлял 25,7 года, и у 84% участников при рождении был определен женский пол. Однополый опыт был более распространен в группе РПП. Пациенты с РПП чаще имели историю физического или сексуального насилия и были свидетелями домашнего насилия. Доля участников с пирсингом, татуировками или серьезными модификациями тела была значительно выше в группе РПП. Пациенты в группе РПП были более склонны к несуицидальному самоповреждающему поведению (НССП) и совершению суицидальных попыток.

ЗАКЛЮЧЕНИЕ: РПП в истории жизни у пациентов, проходящих стационарное лечение по поводу неспихотического психического расстройства с суицидальной идеацией, ассоциировано со следующими параметрами: более молодой возраст; женский пол при рождении; альтернативная гендерная идентичность, опыт сексуальных отношений с лицами своего биологического пола, два и более психиатрических диагноза, диагноз биполярное расстройство, большая тяжесть депрессии и тревоги; множественные психотравмирующие события в анамнезе; различные модификации тела; нанесение НССП и попытки суицида.

# Keywords: suicide; nonsuicidal self-injury; anorexia; bulimia; resilience Ключевые слова: суицид; несуицидальное самоповреждение; анорексия; булимия; устойчивость

#### INTRODUCTION

Mental disorders are associated not only with a reduced quality of life [1], but also with reduced life expectancy. A meta-analysis by Walker et al. (2015) found that the mortality rate of people with mental disorders is more than double that of the general population [2]. One of the causes of this high mortality rate is suicide [3]. According to some studies, approximately 60% of people who die by suicide meet the diagnostic criteria for a depressive disorder [4]. The Netherlands Study of Depression and Anxiety (NESDA) confirmed the high prevalence of suicidal ideation (SI) and suicide attempts (SA) in patients with comorbid anxiety and depression [5]. Follow-back studies have found that suicide occurs in up to 10% of cases of borderline personality disorder (BPD) [6]. Despite a considerable body of research, most suicidologists agree that suicide prevention at the individual level remains woefully ineffective [7]. This difficulty may be explained by a lack of knowledge about the factors involved in the transition from SI to SA. In this regard, further research focusing on less studied parameters is important to identify the high-risk groups for the transition from thoughts to attempts. Recent studies report that variables such as previous mental disorder (currently inactive due to recovery or remission) may still be risk factors for adverse outcomes, including death by suicide [8, 9].

Anorexia and bulimia nervosa are major public health problems with lifetime prevalence rates of 0.1–4.6% and the typical age of onset in adolescence [10]. Most people with eating disorders (EDs) never achieve complete remission.

Approximately 60% of people with anorexia nervosa (AN) do not remit even after 20 years of illness, experiencing multiple relapses and descending into a chronic course of the disorder [11]. It is therefore understandable that those who suffer from such severe and enduring forms of EDs are exposed to many negative consequences. Interestingly, not only current ED, but also a lifetime diagnosis of ED is associated with a poor prognosis [12]. In fact, ED has one of the highest rates of premature mortality among mental disorders [13]. In addition to the adverse somatic consequences of ED, some authors suggest that an increased risk of SA may also explain the high mortality rates. According to a meta-analysis by Arcelus et al. (2011), one in five people with a diagnosis of AN who died committed suicide [14]. Zerwas et al. (2015), who analyzed Danish registries from 1989 to 2006, showed that SA and death by suicide were five times more common in women and men with ED compared to their healthy counterparts [15]. The significant risk of SA and mortality in patients with a lifetime history of ED was further reported by Yao et al. (2016) [16].

To date, the factors associated with a lifetime history of ED diagnoses in patients with non-psychotic mental disorders (NPMD) and SI remain understudied. We hypothesized that the sociodemographic, biographical, and clinical profiles of patients currently suffering from NPMD and SI with a history of ED would differ from those who have never had an ED.

The aim of this study is to investigate the biographical, sociodemographic, and clinical factors associated with a lifetime diagnosis of ED in patients with NPMD and SI.

#### **METHODS**

#### Design

A retrospective cohort study was conducted at the Moscow Research and Clinical Center for Neuropsychiatry between January 2021 and January 2023.

The study protocol was approved by the local ethics committee of the Moscow Research and Clinical Center for Neuropsychiatry. Written informed consent was obtained from all patients enrolled in the study by trained psychiatrists before all study procedures.

#### **Participants**

In the present study, we enrolled consecutive adult inpatients (18 years and older) with non-psychotic mental disorders and SI. All the patients were screened for self-injurious thoughts and behaviors prior to admission as part of the Center's routine admission protocol. The exclusion criteria were past/present psychotic disorders with delirium, organic disorders, schizophrenia, and delusional disorders; severe neurological and somatic disorders; ongoing substance use disorder; and cognitive deficit below the level of understanding of the investigator's questions and the items of the self-report instruments. All participants were assessed by an experienced psychiatrist, who provided an ICD-10 mental disorder diagnosis. Assessment of ED history was based on a direct clinical interview according to ICD-10 criteria.

Those who met the criteria for lifetime anorexia nervosa (AN), bulimia nervosa (BN), or both, were included in the ED group, similar to the Micali et al. (2016) study [17]. We limited the age of participants to 45 years to reduce potential recall bias and the effect of menopause on participants' current status. All patients meeting criteria for ongoing ED were also excluded, so only those in remission or recovery from ED were included in the final analysis. To achieve the aim of the study, we compared parameters between patients who had experienced ED in the past (ED+) and those who had not (ED-).

#### Measures

The relevant sections of the Self-Injurious Thoughts and Behaviors Interview (SITBI) were used to assess SI, SA, and nonsuicidal self-injurious (NSSI) behavior. The SITBI is a structured interview that assesses the presence, frequency, and characteristics of suicidal and NSSI thoughts and behavior [18]. The Russian-language version was developed using the standard forward-backward translation procedure. The final version of the tool has already been used successfully in both clinical and research settings [19, 20].

Demographic and clinical variables were recorded on an ad hoc case record form. All participants underwent the SITBI and completed the Russian versions of the Beck Depression Inventory (BDI), the State-Trait Anxiety Inventory (STAI), and the Brief Reasons for Living Inventory (bRFL).

The last of the above tools has been developed to assess suicide resilience factors. The bRFL is a self-report instrument that assesses such suicide-resilience factors as survival and coping beliefs, responsibility to family, childrelated concerns, fear of suicide, fear of social disapproval, and moral objections [21, 22]. The psychometric properties of the Russian language version of the bRFL [23] were similar to those of the original English [24] and German language [25] versions of the inventory. To date, no work has been done to normalize its scores.

The BDI was used to measure the level of depression in the study participants [26]. The BDI is a self-report, 21item, multiple-choice inventory with a total score ranging from 20 to 80 (higher scores indicate deeper levels of depression). Cut-off scores for the BDI are as follows: 0–9 for minimal depression, 10–18 for mild depression, 19–29 for moderate depression, and 30–63 for severe depression. The Russian version of the BDI has shown good psychometric properties and is widely used in clinical and research settings [27].

The STAI was used to measure anxiety levels. The STAI is a self-report measure consisting of 40 items, with 20 items each in the State Anxiety (STAI-S) and Trait Anxiety (STAI-T) subscales [28]. Items are answered on a 4-point Likert scale ranging from 1 (not at all) to 4 (very much), and the total score ranges from 20 to 80, with higher scores indicating greater severity of anxiety symptoms. A cut-off score of 40 is commonly used to define likely clinical levels of anxiety. The Russian version was validated by Khanin (1983) and has shown good psychometric properties [29].

#### **Statistical analysis**

Categorical variables are presented as frequencies (%) and continuous variables as means (standard deviation (SD)). The Student's t-test was used to compare quantitative variables and the Pearson's chi-squared test for categorical variables. The Benjamini-Hochberg correction was used to correct for multiple comparisons of mental disorder diagnoses in this analysis [30, 31]. All statistical tests were performed at a two-tailed significance level of p <0.05. Data analysis was performed using Jamovi software v1.6.2.

# RESULTS

#### **Sample characteristics**

A total of 892 patients with NPMD and SI were included in the study. The mean age was 25.72 (7.42; 18–45) years. Seven hundred and forty-eight (84%) patients were female. However, 58 (6.5%) of them had an alternative gender identity (the majority of which were non-binary gender identities).

Most patients were diagnosed with mood disorders (unipolar depressive disorder — 267 (29.9%); bipolar disorder — 201 (22.5%) and personality disorders (218 (24.4%)). Sixty-six patients (7.4%) had more than one

psychiatric diagnosis. The mean age at first contact with mental health services was 22.49 (6.96) years.

We assessed participants only for lifetime fulfillment of the criteria for anorexia or bulimia, but not for other EDs. A lifetime history of ED was established in 305 (34.2%) patients. Sixty-nine (7.7%) patients had anorexia; 110 (12.3%) — bulimia; and 126 (14.1%) — "mixed" type (at different stages of life, meeting the criteria for both disorders). The mean age of onset of ED was 16.80 (5.10) years.

The clinical and demographic variables of the sample are presented in Table 1.

#### **Factors associated with EDs**

Compared with the controls, patients with EDs were significantly younger (23.49 (5.74) vs. 26.89 (7.66), p <0.001), had been assigned a female sex at birth (293 (96.7%) vs. 455 (77.5%), p <0.001), and had an alternative gender identity (30 (9.8%) vs. 28 (4.8%), p=0.004). As shown in Table 1, significantly more patients with ED had incomplete higher education and were students (0.05). There were no differences in marital status between the groups.

Patients with ED had their first contact with mental health services at a significantly younger age (20.60 (5.42) vs. 23.47 (7.45), p < 0.001). Bipolar disorder was significantly more common in the ED group (93 (30.5%) vs. 108 (18.4%), p < 0.001), while anxiety disorders were more common in the control group (19 (6.2%) vs. 116 (19.8%), p < 0.001). There were no differences in the prevalence of other mental disorder diagnoses between the groups. Patients with ED were more likely to have more than one additional mental disorder diagnosis (34 (11.1%) vs. 32 (5.5%), p=0.002).

Patients with ED had significantly higher scores on the BDI (32.03 (10.09) vs. 29.32 (9.84), p < 0.001, Cohen's d=0.272, indicating a moderate difference between the two groups) and the STAI-S (62.59 (9.71) vs. 61.03 (10.39), p=0.047, Cohen's d=0.155, indicating a small effect size). However, the groups did not differ on the STAI-T scores.

Participants with ED were more likely to have been exposed to physical (206 (67.5%) vs. 313 (53.3%), p <0.001) and sexual (114 (37.4%) vs. 142 (24.2%), p <0.001) abuse and to have witnessed domestic violence (143 (46.9%) vs. 216 (36.8%), p=0.004). Same-sex experience was more common in the ED group (118 (38.7%) vs. 146 (24.9%), p <0.001). Significantly more patients with ED had piercings (134 (43.9%) vs. 156 (26.6%), p <0.001), tattoos (162 (53.1%) vs. 198 (33.7%), p <0.001), tattoos covering scars (39 (13.8%)

Table 1. Demographic and clinical characteristics of the total sample, cases, and controls

Variable	Level	ED+ ( <i>n</i> =305)	ED- ( <i>n</i> =587)	Total ( <i>n</i> =892)	Statistical test	
Age, mean (SD)ª		23.49 (5.74)	26.89 (7.66)	25.72 (7.24)	t=-6.81 <sup>b</sup> , <i>p</i> <0.001	
Cay agains and at hirth a (0()h	Male	10 (3.3%)	132 (22.5%)	142 (16.0%)	χ²=56.86, df=1,	
Sex assigned at birth, $n$ (%) <sup>b</sup>	Female	293 (96.7%)	455 (77.5%)	748 (84.0%)	<i>p</i> <0.001	
	Cisgender	275 (90.2%)	559 (95.2%)	834 (93.5%)	··· <sup>2</sup> 0 47 -15 13 -= 0 004	
Gender identity, <i>n</i> (%) <sup>b</sup>	Alternative gender identity	30 (9.8%)	28 (4.8%)	58 (6.5%)	χ <sup>2</sup> =8.47, df=1 <sup>a</sup> , <i>p</i> =0.004	
	Elementary/Middle school	15 (4.9%)	25 (4.9%)	40 (4.5%)		
	High school	55 (18.0%)	84 (14.3%)	139 (15.6%)		
Level of education, <i>n</i> (%) <sup>b</sup>	Vocational education	42 (13.8%)	84 (14.3%)	126 (14.1%)	χ²=14.55, df=4, <i>p</i> =0.00	
	Incomplete higher education	114 (37.4%)	172 (29.3%)	286 (32.1%)		
	Completed higher education	79 (25.9%)	222 (37.8%)	301 (33.7%)		
	Employed	110 (36.1%)	237 (40.4%)	347 (38.9%)		
	Student	100 (32.1%)	156 (26.6%)	256 (28.7%)		
Employment, <i>n</i> (%) <sup>b</sup>	Retired	4 (1.3%)	24 (4.1%)	28 (3.1%)	χ <sup>2</sup> =8.64, df=3, <i>p</i> =0.034	
	Unemployed	91 (29.8%)	170 (29.1%)	261 (29.3%)		
	Single	159 (52.1%)	312 (53.2%)	471 (52.8%)		
M '	Married	89 (29.2%)	172 (29.3%)	261 (29.3%)		
Marital status, <i>n</i> (%) <sup>b</sup>	Other type of relationship	57 (18.7%)	103 (17.5%)	160 (17.9%)		
	Same sex experience	118 (38.7%)	146 (24.9%)	264 (29.6%)		
Age at first contact with mental health services (in years), mean (SD)ª		20.60 (5.42)	23.47 (7.45)	22.49 (6.96)	t=-5.97, <i>p</i> <0.001	
	Schizotypal disorder	43 (14.1%)	57 (9.7%)	100 (11.2%)	χ <sup>2</sup> =3.88, df=1, <i>p</i> =0.049	
	Bipolar disorder	93 (30.5%)	108 (18.4%)	201 (22.5%)	χ²=16.82, df=1, <i>p</i> <0.00	
	Depressive disorder	82 (26.9%)	185 (31.5%)	267 (29.9%)	χ²=2.05, df=1, <i>p</i> =0.152	
Mental disorders diagnosis, <i>n</i> (%) <sup>b</sup>	Anxiety disorders	19 (6.2%)	116 (19.8%)	135 (15.1%)	χ²=28.62, df=1, <i>p</i> <0.00	
	Obsessive-compulsive disorder	2 (0.7%)	12 (2.0%)	14 (1.6%)	χ²=2.50, df=1, <i>p</i> =0.113	
	Personality disorders	79 (28.9%)	139 (23.7%)	218 (24.4%)	χ²=0.54, df=1, <i>p</i> =0.464	
Multiple psychiatric diagnoses, <i>n</i> (%) <sup>b</sup>	Yes	34 (11.1%)	32 (5.5%)	66 (7.4%)	χ²=9.50, df=1, <i>p</i> =0.002	
BDI score, mean (SD)ª		32.03 (10.09)	29.32 (9.84)	30.27 (10.01)	t=3.56, <i>p</i> <0.001	
STAI-S score, mean (SD)ª		62.59 (9.71)	61.03 (10.39)	61.57 (10.18)	t=1.99, <i>p</i> =0.047	
STAI-T score, mean (SD)ª		62.64 (9.35)	61.63 (10.21)	61.98 (9.93)	t=1.33, <i>p</i> =0.185	
Physical violence history, <i>n</i> (%) <sup>ь</sup>	Yes	206 (67.5%)	313 (53.3%)	519 (58.2%)	χ <sup>2</sup> =16.68, df=1, <i>p</i> <0.00	
Domestic violence witnessing, <i>n</i> (%) <sup>b</sup>	Yes	143 (46.9%)	216 (36.8%)	359 (40.2%)	χ²=8.49, df=1, <i>p</i> =0.004	
School bullying, <i>n</i> (%)	Yes	215 (70.5%)	391 (66.6%)	606 (67.9%)	χ <sup>2</sup> =1.39, df=1, <i>p</i> =0.239	
Sexual abuse history, <i>n</i> (%) <sup>ь</sup>	Yes	114 (37.4%)	142 (24.2%)	256 (28.7%)	χ²=17.05, df=1, <i>p</i> <0.00	
Lifetime drug use experience, <i>n</i> (%) <sup>ь</sup>	Yes	157 (51.5%)	262 (44.6%)	419 (47.0%)	χ²=3.77, df=1, <i>p</i> =0.052	
Body Piercing, <i>n</i> (%) <sup>ь</sup>	Yes	134 (43.9%)	156 (26.6%)	290 (32.5%)	χ²=27.56, df=1, <i>p</i> <0.00	
Tattoos, <i>n</i> (%) <sup>ь</sup>	Yes	162 (53.1%)	198 (33.7%)	360 (40.4%)	χ²=31.33, df=1, <i>p</i> <0.00	
Severe body modifications, <i>n</i> (%) <sup>b</sup>	Yes	36 (11.8%)	29 (4.9%)	65 (7.3%)	χ²=3.88, df=1, <i>p</i> <0.007	
Lifetime SA, <i>n</i> (%) <sup>ь</sup>	Yes	159 (52.1%)	208 (35.4%)	367 (41.1%)	χ²=23.11, df=1, <i>p</i> <0.00	
Lifetime NSSI, <i>n</i> (%) <sup>ь</sup>	Yes	262 (85.9%)	361 (61.5%)	623 (69.8%)	χ²=56.75, df=1, <i>p</i> <0.00	

*Note:* <sup>a</sup> Student's t-test, <sup>b</sup> Chi-squared test; # — significant after Benjamini-Hochberg correction; SA=suicide attempt; NSSI=nonsuicidal self-injury; ED=eating disorders; STAI-S=State anxiety; STAI-T=Trait anxiety; BDI=Beck's depression inventory.

vs. 32 (5.5%), *p* <0.001), and severe body modifications (36 (11.8%) vs. 29 (4.9%), *p* <0.001).

Significantly more patients with ED had a lifetime history of SA (159 (52.1%) vs. 208 (35.4%); *p* <0.001) and NSSI (262 (85.9%) vs. 361 (61.5%); *p* <0.001).

As shown in Table 2, patients with ED had significantly lower scores on the bRFL subscales such as survival and coping beliefs (4.00 (1.51) vs 4.22 (1.42), p=0.032), responsibility to family (3.65 (1.55) vs 4.02 (1.62), p=0.001), child-related concerns, and moral objection (1.85 (1.31) vs 2.44 (1.64), p <0.001). Total bRFL mean scores were also significantly lower in the main group (2.87 (0.93) vs 3.25 (1.14), p <0.001). There were no differences between the groups on factors such as fear of suicide and fear of social disapproval.

#### DISCUSSION

The age of the sample was limited to 45 years in order to reduce the effect of menopause on the current status of participants and to minimize potential recall bias. The age of the participants in our study was relatively low (25.7 years), which is in line with previous studies reporting an earlier onset of various mental disorders in people with ED [32]. The age characteristics of the sample may also partly explain the higher than expected prevalence of NSSI and nonfatal SA among the participants.

The majority of patients in our sample were female, which is consistent with the literature on the higher prevalence of anxiety, depression [33, 34], SI, and non-lethal SA [35] in women, and the greater number of women among those seeking psychiatric help [36].

The significant number of people with incomplete and completed higher education in our sample is due to the specifics of the Russian population and is consistent with data from the Organization for Economic Cooperation and Development (OECD) on the high percentage of people with higher education among citizens of the Russian Federation aged 25–64. According to this indicator, the Russian Federation ranks second out of 35 OECD member countries [37].

When comparing the groups of patients with and without a lifetime diagnosis of ED, a significant number of differences in clinical and socio-demographic parameters were found. In the group of persons with ED, there was a significantly higher proportion of people who were assigned female at birth, which is consistent with the higher prevalence of ED in women [38]. There was also a significant difference in gender: those with ED were more likely to have an alternative gender identity, identifying as bigender, gender-fluid, or agender. All participants with an alternative gender identity were assigned female at birth. The association found between alternative gender identity and ED is consistent with the results of previous studies. In a study of 289,000 US college students, transgender people were 4.6 times more likely than cisgender women to self-report an ED in the preceding year [39]. Another study reported that non-binary individuals were three times more likely to self-report a history of AN or BN than transgender men and women [40]. Lifetime same-sex experience was also more common among patients with ED, which is also consistent with the literature on a higher prevalence of ED among bisexual and homosexual individuals [41].

Patients with ED were significantly younger, which explains the greater number of people with incomplete higher education and student status in this group. The usual age of onset for many EDs is between 14 and 19 years [42], and sometimes even earlier [43], which is lower than for other non-psychotic disorders [44]. This may explain the

	Mean (SD)		Student's t-test			
	ED+ ( <i>n</i> =305)	ED- ( <i>n</i> =587)	(df=890)	Cohen's d		
Survival and coping beliefs <sup>a</sup>	4.00 (1.51)	4.22 (1.42)	t=-2.14, <i>p</i> =0.032	0.150 <sup>b</sup>		
Responsibility to family <sup>a</sup>	3.65 (1.55)	4.02 (1.62)	t=-3.24, <i>p</i> =0.001	0.233 <sup>b</sup>		
Child-related concerns <sup>a</sup>	2.84 (1.83)	3.53 (1.99)	t=-5.00, <i>p</i> <0.001	0.356 <sup>c</sup>		
Fear of suicide <sup>a</sup>	3.35 (1.56)	3.53 (1.71)	t=-1.63, <i>p</i> =0.103	0.108 <sup>b</sup>		
Fear of social disapproval <sup>a</sup>	2.43 (1.56)	2.65 (1.66)	t=-1.88, <i>p</i> =0.060	0.135⁵		
Moral objection <sup>a</sup>	1.85 (1.31)	2.44 (1.64)	t=-5.30, <i>p</i> <0.001	0.384 <sup>c</sup>		
Total mean	2.87 (0.93)	3.25 (1.14)	t=-4.88, <i>p</i> <0.001	0.354 <sup>c</sup>		

#### Table 2. Brief Reasons for Living Inventory scores

*Note:* <sup>a</sup> Absolute range — 1–6; ED=eating disorders; <sup>b</sup> small effect size; <sup>c</sup> medium effect size.

younger age of first contact with mental health services in people with ED.

The high comorbidity between ED and other psychiatric disorders has been widely reported. The lifetime prevalence of at least one DSM-IV comorbidity varies from 45% to 97%, depending on the source [45, 46]. This is confirmed by the significant number of people with ED (34.2%) in our consecutively recruited sample of patients with NPMD and SI. The study groups differed in the frequency of diagnoses of BD (more common in patients with ED) and anxiety disorders (more common in the group without ED). This is consistent with the meta-analysis by Fornaro et al. (2020), which found an association between EDs and BD. Thus, BN occurred in 7.4% (95%CI=6-10%) of individuals with BD, while 6.7% (95%CI=12-29.2%) of individuals with BN had a diagnosis of BD. AN occurred in 3.8% (95%CI=2-6%) of individuals with BD; 2% (95%CI=1-2%) of individuals with BD had a diagnosis of AN [47]. It is noteworthy that despite the lower frequency of anxiety disorder diagnoses in the ED group, the severity of state anxiety was actually higher in this group. ED was also associated with higher depression scores on the BDI. In addition, participants in the ED group were more likely to have more than one psychiatric diagnosis, again reflecting the greater severity of psychiatric disorders in this group.

The present study uncovered a high prevalence of traumatic experiences (childhood physical abuse and witnessing domestic violence) among patients with ED. Similar data have been reported in other studies [48]. The prevalence of adverse childhood experiences in our study is higher than previously reported [49], which may be explained by the fact that these adversities predict not only ED, but also suicidality (inclusion criteria of our study).

A higher number of patients exposed to sexual trauma among participants with ED is also consistent with the literature data showing that sexual trauma precedes and contributes to the development of ED: particularly bulimia [50].

Tattoos, piercings, and body modifications have been found to be more common in patients with ED in several studies, including studies of ED without comorbid psychiatric disorders [51]. Previous studies have found these variables to be more prevalent in young people and in those with indirect and direct self-injurious behaviors [52] — variables that are prevalent in our study population.

In our study, the prevalence of NSSI was high in both groups, which could be explained by the higher prevalence

of NSSI in people with SI. We found that an ED in patients with SI was associated with involvement in NSSI practices. On the one hand, the higher prevalence of NSSI could be explained by the younger age of the participants and the predominance of women in the ED group [53]. On the other hand, a meta-analysis by Cucchi et al. (2016) reported odds ratios for NSSI according to the ED subtype (ranging from 20 to 32.7%) [54] and a bidirectional relationship between NSSI and ED was proposed [55]. A recent study in the Russian Federation [52] found that the prevalence of ED in psychiatric inpatients with NSSI and SI stood at 51%, and that the odds ratio for having NSSI in participants with both SI and ED was 4.9. The exclusion of people aged 45 years and over in our study may explain the difference in the prevalence of NSSI between this study and ours.

Suicide is one of the leading causes of excess mortality in patients with ED, according to recent studies [56]. Previous studies have examined the relationship between SA and ED [57], but there is still no consensus as to whether there is a difference in the degree of risk of SA depending on the subtype of ED: some authors have suggested that there is no difference between subtypes of ED [58], while others have reported a significant increase in risk in patients with AN [59]. However, the existence of an association between the presence of an ED and the risk of SA has been confirmed in a large number of studies, including this one [60, 61]. At the same time, our findings should be interpreted with caution, as many of the factors associated with lifetime ED diagnoses have previously been identified as risk factors for SA. For example, a recent study from Moscow found a strong association between NSSI and suicidality in people with epilepsy [62]. Further research is needed to identify the possible common biological and psychological underpinnings of these often co-occurring factors [63, 64].

According to the ideation to action research framework, the transition from suicidal ideation to suicide attempt may have to do with the tension between the pro-suicidal drive and resilience factors. To test whether the patients who had shown a proclivity to develop ED during their lifetime also had lower resistance to suicide, we measured the number of beliefs that could potentially be important as reasons not to commit suicide in both groups. We did not find any studies that used the Reasons for Living Inventory in people with ED prior to our study. We found that participants with ED had a lower total score on the bRFL, as well as lower scores on several suicide-resilience factors such as "survival and coping beliefs", "responsibility to family", "child-related concerns", and "moral objections".

We believe that many of the characteristics we have identified in patients with ED are similar to those previously reported in patients with BPD. At the same time, no difference was found between the groups in terms of personality disorder diagnosis after Benjamini-Hochberg correction. The fact that borderline BPD is often underdiagnosed in people with other psychiatric conditions [65] may explain this discrepancy. In our study the diagnosis of mental disorder was based on expert opinion. Further studies using a diagnosis based on the results of structured psychiatric interviews are needed to assess whether BPD is more common in non-psychotic patients with SI and lifetime ED.

#### Strengths and limitations of the study

Our study has both strengths and limitations. We used consecutive sampling to avoid selection bias. To the best of our knowledge, our study is the first attempt to assess reasons for living in patients with ED and SI, the group at high risk of suicide.

Age differed significantly between the groups in our study. This may be a limitation of the study if we consider it as a simple covariate. However, it is possible that age simply reflects generational differences between people who grew up in different environments. Long-term prospective cohort studies are needed to answer the question of whether parameters such as ED and NSSI decrease with age or whether they remain stable in intrinsic value across generations.

The main shortcoming of our study is that EDs were diagnosed retrospectively. Many of the participants recovered from an ED in early adulthood; so, recall bias can't be completely ruled out. Another limitation is our approach to psychiatric diagnosis, which was based on expert opinion, only. The potential impact of this on the frequency of personality disorder diagnoses has been discussed above. Patients with psychotic disorders and those older than 45 years were not included in our study, so our results should not be extrapolated to these populations.

# CONCLUSION

Lifetime ED in NPMD patients with SI is associated with younger age, being assigned female at birth, having an alternative gender identity, having had a same-sex experience, having more than one psychiatric diagnosis, having a diagnosis of bipolar disorder, experiencing more severe depression and anxiety, having been exposed to multiple traumatic experiences, having various body modifications, practicing NSSI, and having a lifetime history of SA. Patients with ED are vulnerable to the development of suicidal behavior because of their low resilience to the transition from SI to SA.

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# Non-suicidal Self-injuries and Suicide Risk in Adolescent Girls with Eating Disorders: Associations with Weight Control, Body Mass Index, and Interpersonal Sensitivity

Несуицидальные самоповреждения и суицидальный риск у девочек-подростков с расстройствами пищевого поведения: связи с контролем веса, индексом массы тела и межличностной чувствительностью

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# ABSTRACT

**BACKGROUND:** Eating disorders (EDs) are associated with a risk of premature death, as well as suicidal and selfinjurious behavior. A low or high body mass index (BMI) and weight control behavior can also have an impact on selfinjurious and suicidal behavior. While some studies show that interpersonal sensitivity is a risk factor for EDs, affective disorders, and self-injurious behavior, in-depth studies of these issues have not been done.

**AIM:** The present study investigates how self-injurious and suicidal behavior relate to weight control behavior, BMI, and interpersonal sensitivity in adolescent girls from a clinical population with diagnosed EDs compared with adolescent girls from the general population.

**METHODS:** The main group was comprised of 31 girls with a diagnosis of ED (as the main diagnosis or co-occurring with affective disorders, M=15±1.13 years), being treated in in the Eating Disorder Clinic of the Scientific and Practical Center for Mental Health of Children and Adolescents named after G.E. Sukhareva. The comparison group consisted of 27 adolescent girls recruited from Proton Educational Center (M=15.51±1.09 years). The measures included a qualitative

survey that yielded data on weight control behavior, and self-injurious behavior, a Blitz questionnaire probing the suicide risk (used only in the main group), and the Interpersonal Sensitivity Measure. Height and weight data were also recorded for BMI calculation.

**RESULTS:** The qualitative analysis of weight control behavior yielded the following results: purging behavior, restrictive behavior, and corrective behavior. Participants in the main group used purging and restrictive behavior more often, whereas participants in the comparison group used strategies associated with a healthy lifestyle. The main group and participants who practiced purging and restrictive weight control in the overall sample had the smallest BMI. Self-injurious behavior was approximately evenly distributed both amongst the main and comparison groups. Self-cutting was the most prevalent type of self-injury. In the main group, self-injury was associated with a smaller BMI, while in the comparison group it was associated with an increase in the fear of rejection and overall interpersonal sensitivity. Based on the assessment of the suicide risk, six participants in the main group were deemed high-risk; they also displayed increased fear of rejection, dependence on the assessments of others, and overall interpersonal sensitivity. All girls in the suicide risk subgroup had non-suicidal self-injuries.

**CONCLUSION:** The results of our study broaden our understanding of the risk factors of suicidal and self-injurious behavior in adolescent girls with EDs and reveal the characteristics of the type of weight control behavior used by this group in comparison with adolescent girls in the general population. Girls with EDs who were considered at the risk of committing suicide demonstrated high interpersonal sensitivity, which provides a rationale for further studying the general interpersonal mechanisms that underlie the pathogenesis of EDs, as well as that of self-injurious and suicidal behavior.

# аннотация

**ВВЕДЕНИЕ:** Расстройства пищевого поведения (РПП) связаны с риском преждевременной смерти, суицидальным и самоповреждающим поведением. Слишком низкий или высокий индекс массы тела (ИМТ) и способы контроля веса также могут вносить вклад в самоповреждающее и суицидальное поведение. В отдельных исследованиях было выявлено, что фактором риска для РПП и самоповреждающего поведения может также быть такой показатель, как межличностная чувствительность, однако комплексного исследования этих проблем еще не проводилось.

**ЦЕЛЬ:** Исследовать связи самоповреждающего и суицидального поведения со способами контроля веса, ИМТ и межличностной чувствительностью у девочек-подростков клинической выборки с диагнозом РПП и в популяции.

**МЕТОДЫ:** В основную группу вошли девочки-подростки с РПП (как основным диагнозом или сопутствующим в случаях сочетания с аффективными расстройствами, M=15±1.13), проходящие лечение на базе Клиники расстройств пищевого поведения ГБУЗ «Научно-практический центр психического здоровья детей и подростков им. Г.Е. Сухаревой ДЗМ» (N=31). Группу сравнения составили девочки-подростки (N=27) из образовательного центра «Протон» (M=15.51±1.09). Использовалась анкета, направленная на сбор качественных данных о проявлениях контроля за весом и самоповреждающем поведении, блиц-опросник суицидального риска (только в клинической выборке) и опросник межличностной чувствительности. На основе данных о росте и весе высчитывался ИМТ.

**РЕЗУЛЬТАТЫ:** Качественный анализ позволил выделить темы, связанные с контролем веса: очистительное, ограничительное и корректирующее поведение. В основной группе чаще использовались очистительные и ограничительные стратегии контроля веса, а в группе сравнения — корректирующие стратегии, связанные с поддержанием здорового образа жизни. Наиболее низкий ИМТ (дефицит массы тела) оказался в клинической выборке и у девочек с ограничительным и очистительным поведением в совокупной выборке.

Самоповреждающее поведение примерно в равном соотношении оказалось распространено как в основной группе, так и в группе сравнения. Наиболее распространенный метод самоповреждения — порезы. В основной группе самоповреждающее поведение было связано с меньшим ИМТ, а в группе сравнения — с повышением страха отвержения и общим показателем межличностной чувствительности.

Суицидальный риск был выявлен у 6 девочек из основной группы и оказался связан со страхом отвержения, зависимостью от оценок окружающих и общим показателем межличностной чувствительности. Все девочки из подгруппы суицидального риска указали и на несуицидальные самоповреждения.

ЗАКЛЮЧЕНИЕ: Результаты исследования позволяют расширить представления о факторах риска суицидального и самоповреждающего поведения у девочек с РПП и о способах контроля веса, предпринимаемых ими, по сравнению с девочками из общей популяции. Высокая межличностная чувствительность, выявленная у девочек-подростков из подгруппы суицидального риска, свидетельствует о важности изучения межличностных механизмов, лежащих в основе суицидального и самоповреждающего поведения.

# **Keywords:** adolescent girls; eating disorders; body mass index; suicide risk; non-suicidal self-injuries; interpersonal sensitivity; fear of rejection

**Ключевые слова:** девочки-подростки; расстройства пищевого поведения; индекс массы тела; суицидальный риск; несуицидальные самоповреждения; межличностная чувствительность; страх отвержения

#### INTRODUCTION

Eating disorders (EDs) cause serious health issues and affect a significant part of the population, especially young women [1]. This issue is rather relevant due to its high mortality rate, the predominance of adolescent girls among those diagnosed with EDs, and its negative impact on mental health and fertility in adulthood. Up to 44% of adolescent girls exhibit subclinical forms of EDs [2], and up to 2.58% of women and 1.89% of men in Western countries are diagnosed with ED [3], primarily anorexia nervosa (0.1–2%) and bulimia nervosa (0.37–2.98%) [4]. According to the latest data, 5.5% to 17.9% of girls and 0.6% to 2.4% of boys would develop EDs by the time they mature [5].

Mortality rates amongst people suffering from EDs are 5–7 times higher than the predicted rate in corresponding age-sex cohorts [6], especially among individuals with anorexia nervosa [7]. Up to 24.9% of patients with anorexia nervosa and 31.4% of patients with bulimia nervosa have attempted suicide [8]. Extreme methods of weight control (taking diet pills, inducing vomiting, taking laxatives and diuretics), even in the absence of diagnosed EDs, are a predictor of suicidal thoughts and suicide attempts among women [9].

An equally serious problem that potentially reduces the life expectancy of people with EDs is intentional, non-suicidal actions aimed at damaging their own body [10]. Non-suicidal self-injury is also associated with an increased risk of suicidal behavior and death from suicide in adolescence and early adulthood [11, 12]. Self-injurious behavior is widespread among patients with EDs: 40.8% of adolescents diagnosed with EDs have harmed themselves at least once [13]. According to some data, self-injurious behavior can also be an indicator of a more complex ED [14], predicting more severe ED manifestations in the future [15]. Among patients with EDs and concomitant self-injurious behavior, a significant majority are diagnosed with bulimia nervosa, have had an ED for a longer time, display symptoms of binge eating, purging behavior, co-occurring affective disorders, and they are often substance abusers or victims of violence [13]. It is reported that 78% of those who have engaged in non-suicidal self-injury report suffering from EDs, including binge eating (57.6%), fasting (57.6%), excessive exercise (33.9%), inducing vomit (25.4%), and using diuretics and laxatives (15.3%) [16]. The probability of self-injurious behavior among persons with EDs is significantly higher for people with a history of suicide attempts [17].

Another widely discussed issue is the contribution of the body mass index (BMI) to the suicide risk. Some studies have linked a low BMI to the suicide risk, while others have not. A prospective study on a female sample (n=1,200,000) has shown that BMI <20 is associated with a suicide attempt and completed suicide; low weight in adolescence and youth also turned out to be significant factors [18]. In another large study on a population sample

of adolescents aged 12–15 years (*n*=104,907) from 45 lowand middle-income countries, a high, rather than low, BMI and obesity were significant predictors of suicidal ideation and suicide attempts [19].

Interpersonal functioning deficits are considered one of the transdiagnostic risk factors across the ED spectrum [20]. These deficits are caused, on the one hand, by interpersonal stressors [21], and, on the other, by personal attitudes that affect social functioning and determine vulnerability to interpersonal interaction, in particular, interpersonal sensitivity [22, 23]. Interpersonal sensitivity is considered a dimension of psychological distress [24] and an inherent trait in people with a high susceptibility to the behavior and emotions of others, especially to perceived or real criticism or rejection [25]. There are relatively few studies that look at interpersonal sensitivity as a personality trait [22, 23, 25–27], and all of them, except one [23], involve participants beyond adolescence.

Our recent study of online communities focused on appearance and body found that members of pro-anorexia groups (focused on the normalization of anorexia) have higher levels of body dissatisfaction and sensitivity to rejection due to their appearance, compared with members of body-positive communities [26]. According to our other study, the fear of rejection appears to be a predictor of selfinjurious behavior in adolescents and young adults [27]. The only clinical study we found of adolescents aged 12-18 years with a diagnosed ED demonstrated that a heightened interpersonal awareness (one of the components of interpersonal sensitivity) contributes to ED symptoms. Cognitive distortion (negative interpretation of social cues) was proved to act as a mediator of this association. However, due to its methodological limitations, the study failed to consider interpersonal sensitivity in a broader sense or some of its other aspects (since the other scales of the questionnaire showed insufficient internal consistency, and the authors did not include them in the analysis) [23].

Thus, the few available studies of interpersonal sensitivity (as a personality trait) are freighted by limitations associated with either sampling or study methodology. In addition, the various aspects of interpersonal sensitivity were investigated in these studies in relation with either the ED symptoms [23, 26] or non-suicidal self-injuries [27], while the repeatedly confirmed association between EDs and self-injurious and suicidal behavior necessitates a comprehensive study. The goal of this study was to probe for an association between self-injurious or suicidal behavior and weight mangement, BMI and interpersonal sensitivity in adolescent girls with EDs treated in an inpatient or outpatient setting. To compare the results, we used data from a population sample of adolescent girls from a general education school.

#### METHODS

#### Setting

The study was conducted in the form of an individual survey of adolescent girls who have an ED included in section F50 of the International Classification of Diseases and Related Health Problems (10th revision) as the primary or co-occurring diagnosis. The study was conducted in February-April 2023 at the Clinicfor Eating Disorders of the State Budgetary Institution of Healthcare "Scientific and Practical Center for the Mental Health of Children and Adolescents named after G.E. Sukhareva of the Moscow Department of Health" (SBHI "SPC MHCA named after G.E. Sukhareva of the Moscow Department of Health"). And was approved by the Local Ethics Committee of the institution (Minutes No. 1–23 datedJanuary 18, 2023).

#### Participants

A total of 31 patients participated in the study (M=15±1.13 years). Twenty girls had an ED (F50) as their primary diagnosis: anorexia nervosa or bulimia nervosa. The ED in 11 patients persisted as a co-occurring disorder while they had the depressive syndrome within the affective disorders (F30–F39) or mixed disorders of behavior and emotions (F92) as their primary disorder at the time of the examination.

Fourteen of the girls were being hospitalized for the first time; 11 girls were being re-hospitalized; and 6 girls were in outpatient treatment mode.

Inclusion criteria: female; aged 13–17; diagnosed ED. Exclusion criteria: male; age under 13; thought disorders; cognitive impairment.

To compare the participants in terms of self-injurious behavior, weight control, BMI, and interpersonal sensitivity, we interviewed 27 adolescent girls, aged 13–17 (M=15.51±1.09 years), without ED diagnosis, at the Proton Educational Center, a state budgetary educational institution in Moscow.

Participation in the study was voluntary, based on the informed consent of adolescents and their parents.

#### Measures

All study participants completed a General Questionnaire, a Suicide Risk Blitz Questionnaire, and an Interpersonal Sensitivity Questionnaire. In addition, weight and height were measured to calculate the body mass index.

The General Questionnaire for this study was designed to collect socio-demographic data (sex, age, education, and place of residence) and obtain information about weight control and self-inflicted physical harm:

- Do you control your weight?
- How old were you when you started controlling your weight?
- Indicate what methods of weight control you have used in the last 6 months.
- Have you ever intentionally hurt yourself physically?
- How exactly did you hurt yourself physically?

The Suicide Risk Blitz Questionnaire (developed at the SBHI "SPC MHCA named after G.E. Sukhareva of the Moscow Department of Health") contains 6 questions about suicidal thoughts, plans and attempts, as well as self-injurious behavior. It was used only in a clinical sample. A yes/no dichotomous scale is used in the responses. The KR-20 reliability coefficient [28] was used to calculate the reliability of the questionnaire (0.66 in the current sample; 0.70 in the adaptation sample). At the time of the study, this questionnaire had undergone clinical testing, including testing of psychometric characteristics; an article based on the results of testing is being prepared.

Interpersonal Sensitivity Questionnaire [25, 29]. In the Russian version, the questionnaire includes 22 items, with a choice of responses on a 5-point scale. It includes three scales: dependence on the assessments of others (Cronbach's alpha  $\alpha$ =0.93 in the general sample,  $\alpha$ =0.94 in the main group), fear of rejection ( $\alpha$ =0.88/0.87), anxiety in interpersonal relationships ( $\alpha$ =0.84/0.82), and total interpersonal sensitivity score ( $\alpha$ =0.95/0.94).

BMI was calculated using the formula: BMI= $m/h^2$ , where m is body weight in kilograms and h is height in meters. BMI was assessed according to age and sex, based on WHO recommendations for assessing anthropometric parameters in children [30].

#### **Statistical analysis**

Quantitative data were analyzed using the statistical package SPSS ver. 23. The analysis included frequencies, descriptive statistics, contingency tables (Pearson's  $\chi^2$  test for comparing categorical variables), correlation

analysis (Spearman's coefficient), and non-parametric tests (Mann-Whitney, Kruskal-Wallis tests). Qualitative data were analyzed by content analysis (the number of the most frequently occurring words in descriptions of weight control and self-injurious behavior was counted) and content analysis (basic weight control strategies were summarized).

#### RESULTS

The sociodemographic characteristics of the sample are presented in Table 1.

#### Weight control and body mass index

According to the results of the survey, the age at which weight control started ranges from 8 to 15 years. The bulk of the responses was in the range of 11–14 years, the average age when weight control started was 12.4, SD=1.6.

As part of the content analysis of responses about the weight control methods used in the main group, the most frequently used words (out of 194 used) were the following: fasting (12 mentions); sports/physical activity (10 mentions); vomiting and laxative (8 mentions each); and calorie counting (7 mentions).

In the control group of 27 girls, 17 indicated that they do watch their weight. In this subgroup, the most frequently used words (out of 87 used) when describing the weight control methods used were the following: sport (14 mentions); food/nutrition (9 mentions); weight/weighing (4 mentions); and fasting (3 mentions). Words such as health, diet, gym, calories, body, laxative, and sweet were used not more than once.

Based on a content analysis of the data in both groups, seven categories were identified (purging routines, food restriction, calorie counting, fasting, body measurements, weighing, exercise, and proper nutrition) and summarized into three key patterns that characterize the weight control strategies used by girls both from the main group and from the control group:

- Purging behavior: artificial induction of vomiting; taking diuretics and laxatives;
- 2. Restrictive behavior: counting calories; diets and other food restrictions; fasting;
- Corrective behavior: behavior focused on managing external attractiveness like body measurements; weighing; physical activity, including sports; different types of physical activity combined with a healthy diet (Table 2).

Table 1. Sociodemographic and clinic	al characteristics of the sample
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Sociodemogr	aphic and clinical characteristics	Main group (N=31)	Control group (N=27)
Sociotechiogi		%, n	%, n
Age		M=15.00±1.13	M=15.51±1.09
Sex	Female	100% ( <i>n</i> =31)	100% ( <i>n</i> =27)
	Currently in school	87.0% ( <i>n</i> =27)	100% ( <i>n</i> =27)
Education	Currently in college	9.7% ( <i>n</i> =3)	-
	Does not study anywhere	3.3% ( <i>n</i> =1)	-
	With parents or one of the parents	96.7% ( <i>n</i> =30)	96.3% ( <i>n</i> =26)
Residence	With other relatives	3.3% ( <i>n</i> =1)	-
	Family Education Assistance Center	-	3.7% ( <i>n</i> =1)
	Anorexia nervosa (F50.0)	41.93% ( <i>n</i> =13)	-
	Atypical anorexia nervosa (F50.1)	19.35% ( <i>n</i> =6)	-
	Atypical bulimia nervosa (F50.3)	3.22% ( <i>n</i> =1)	-
	Major depressive disorder, single episode, moderate (F32.1). Anorexia nervosa (F50.0)	9.7% ( <i>n</i> =3)	-
	Major depressive disorder, single episode, moderate (F32.1). Bulimia nervosa (F50.2)	9.7% ( <i>n</i> =3)	-
Diagnosis	Bipolar disorder, current episode mixed (F31.6). Bulimia nervosa (F50.2)	3.22% ( <i>n</i> =1)	-
	Other persistent mood [affective] disorders (F34.8). Bulimia nervosa (F50.2)	3.22% ( <i>n</i> =1)	-
	Other mixed disorders of conduct and emotions (F92.8). Eating disorder, unspecified (F50.9)	3.22% ( <i>n</i> =1)	-
	Other mixed disorders of conduct and emotions (F92.8). Atypical anorexia nervosa (F50.1)	3.22% ( <i>n</i> =1)	-
	Other mixed disorders of conduct and emotions (F92.8). Bulimia nervosa (F50.2)	3.22% ( <i>n</i> =1)	-

# Table 2. Weight control strategies: findings from the content analysis

Weight control methods	Catagorias	Weight control		
Main group	Control group	Categories	strategies	
Vomit (8); laxatives (8); diuretics (1)	Laxatives (1)	Purging procedures	Purging behavior	
Diets (5); small portions (3); food restrictions (4); throwing away food (2)	Diets (3); food restrictions (4); throwing away food (1)	Diets and other food restrictions		
Calorie counting (7)	ounting (7) Calorie counting (1)		Restrictive behavior	
Fasting (12)	Fasting (3)	Fasting		
Wrist circumference with fingers, measurement of arms, legs with a measuring tape (2)	-	Body measurements		
Weighing (9)	Weighing (4) Weighi		Corrective behavior (appearance control)	
Sports/physical activity/exercise (10)	Sports/physical activity/exercise (14)	Physical exercise		
-	Proper/healthy nutrition (5); meal plan (1)	Proper nutrition		

*Note:* The values in the brackets are the number of weight control behavior mentions in study groups.

The main group had no descriptions that could be associated with a healthy diet, while the control group did not have such specific methods of weight control as measuring the thinness of one's arms and legs. The control group gave responses that could generally be associated with a healthy lifestyle, and weight control in some cases was described as an attempt to regulate it, rather than reduce it. For example, "swimming, dancing, walking long distances", "going to the gym, avoiding eating sweets", "sports, proper nutrition", and "eating the amount of food that the body requires", whereas the focus of the responses in the main group was squarely on weight loss. Therefore, relatively more words related to weight loss were used (fasting, vomiting, laxatives, diuretics, etc.) and sports were described as "exhausting physical activity", and, in most cases, physical exercises were combined with fasting, inducing vomiting, and counting calories. Thus, girls from the main group significantly more often mentioned purging and restrictive behavior, while girls from the control group indicated corrective behavior related to controlling their looks: x<sup>2</sup> (2)=22.19; p <0.001.

The distribution of the sample by BMI is presented in Table 3.

In the main group, patients with anorexia nervosa were underweight, while eight out of eleven girls with depressive syndrome and EDs had normal body weight, with a tendency to the lower limit of the normal (in the range from 17.06 to 22.84). There were more underweight patients among those hospitalized for the first time than among those re-hospitalized or receiving outpatient treatment:  $\chi^2$  (2)=11.67, p <0.01. The BMI of girls from the main group was significantly lower than that of the control group:  $\chi^2$  (2)=21.12, p <0.001.

In the pooled sample of underweight girls, the majority used restrictive means or purging to control their weight, while the normal-weight or overweight girls mostly used appearance control strategies:  $\chi^2$  (2)=12.15, *p* <0.05.

#### Non-suicidal self-injuries and suicide risk

The suicide risk was assessed only in the main group, while the question about intentionally causing physical harm to oneself and the methods used was asked in both groups.

In the clinical sample (N=31), 51.7% of the girls answered the question about self-injuries in the affirmative; the distribution of answers in the main and control groups is approximately the same: 16 "yes" and 15 "no" in the main group, 13 "yes" and 14 "no" in the control group (N=27). The most common way of inflicting self-injuries was self-cutting: 12 instances in the main group and 11 in the control group. In most cases, several different types of self-injuries were indicated.

As part of the content analysis in the clinical subgroup of girls who confirmed self-injuries (N=16), out of 117 words used, the most frequent were cut (13 mentions), beat/hit (5 mentions), scratch/claw (5 mentions), cauterize/ burn (4 mentions), and bite/nibble (2 mentions). Tear out, strangle, cool, and overheat were mentioned once each. Also, one response was related to a suicide attempt: "Pills in large quantities (suicide)", and one was related to physical activity: "Exhausting workouts". In three responses, food restrictions were defined by patients as a type of selfharm: "I wrote on my leg with a pen to eat less", "all EDs are also harmful", and "food restrictions". In the control group (N=13), the most frequently mentioned words out of the 101 words used were cut (11 mentions); beat/hit (8 mentions); bite, scratch, press (2 mentions each); prick, claw, and burn (2 mentions each).

When comparing between patients who confirmed and those who denied engaging in self-injurious behavior, significant differences (Mann-Whitney test) were found only in BMI: girls with self-injuries turned out to have a lower BMI (U=204.00, p <0.001). As for the control group, significant differences between those who confirmed self-injuring and those who denied doing so were found

		BMI				
Group	Diagnosis	underweight	normal-weight	overweight	Total	
	Eating disorders (F50.0; F50.1; F50.2)	19	1	0	20	
Main group (N=31)	Affective disorders (F32.1; F34.8; F31.6) and other mixed disorders of conduct and emotions. (F92.8). Eating disorders (F50.0; F50.1; F50.2; F50.9)	2	9	0	11	
Control group (N=27)	-	3	20	4	27	

#### Table 3. BMI distribution in the main and control groups

in relation to fear of rejection and overall interpersonal sensitivity, but not BMI (Table 4).

The suicide risk was assessed only in the main group as it was the most vulnerable to suicidal behavior, and also due to the fact that the questionnaire that was used for this purpose was only being clinically tested at the time of its use. The distribution of responses is presented in Table 5.

The suicide risk score was calculated based on the sum of affirmative answers. The suicide risk group included those who scored 3 points or more. In this group, three girls scored 3 points, two scored 4, and one scored 6. When comparing the subgroups in terms of suicide risk, patients who scored three or more on the Blitz Questionnaire had higher dependence on the assessments of others, fear of rejection, and overall interpersonal sensitivity (Table 6).

The suicide risk subgroup included girls with depression and EDs who engaged in purging or restrictive behaviors to control their weight.

# Association of suicide risk with interpersonal sensitivity and BMI

The link between suicide risk and BMI and psychological characteristics was tested using the Spearman's coefficient. Significant associations are presented in Table 7.

Table 4. Significan	t differences in	n self-injurious	behavior in	the control group
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Scales	Self-injurious behavior: Yes/No	N	Average rank	Median	U Mann- Whitney test	p
Fear of rejection	Yes	13	19.01	30.00	166.50	0.000
	No	14	8.61	20.00		
Overall interpersonal sensitivity score	Yes	13	18.12	68.00	144.50	0.008
	No	14	10.18	45.00		

Table 5. Distribution of responses in the main group to the suicide risk Blitz Questionnaire

No	Questions	Yes		No	
No.	Questions	N	%	N	%
1	Have you thought about wanting to die in the past three months?	13	41.9	18	58.1
2	Have you come up with a plan for how you want to die in the past three months?	7	22.6	24	77.4
3	Have you tried to implement this plan in the past three months?	2	6.5	29	93.5
4	During your lifetime, have you ever hurt yourself, hitting, cutting, burning yourself, or injuring yourself in any other way?	16	51.6	15	48.4
5	Have you ever tried to die?	3	9.7	28	90.3
6	Are you thinking about dying right now?	1	3.2	30	96.8

#### Table 6. Significant differences in the suicide risk factor in the main group

Scales	Suicide risk according to the Blitz Questionnaire	N	Average rank	Median	U Mann- Whitney test	p
Dependence on the	Yes	6	23.83	32.5	28.00	0.017
assessments of others	No	25	14.12	25.00	28.00	
Foor of rejection	Yes	6	24.42	19.00	24.50	0.000
Fear of rejection	No	25	13.98	12.00	24.50	0.009
Overall interpersonal	Yes	6	24.08	72.00		
sensitivity score	No	25	14.06	55.00	26.50	0.012

Table 7. Association of suicide risk with BMI and inter	rpersonal sensitivity (Spearman's r.)
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Scales	Suicide Risk Blitz Questionnaire
Dependence on the assessments of others	0.55**
Fear of rejection	0.67***
Anxiety in interpersonal relationships	0.55**
Overall interpersonal sensitivity score	0.62***
Body mass index	0.47*

*Note:* \**p* <0.05, \*\**p* <0.01, \*\*\**p* <0.001.

As can be seen from Table 7, an increase in suicide risk is significantly associated with higher interpersonal sensitivity scores. There is also a significant association between increased BMI and suicide risk.

#### DISCUSSION

According to the results of our study, weight control can start quite early, as early as eight years old, but more often it starts at the beginning of adolescence (12–13 years).

Based on the content analysis, three weight control strategies were identified: (1) purging behavior (vomiting, and using laxatives and diuretics); (2) restrictive behavior (dieting, fasting); and (3) corrective behavior focused on controlling and changing one's appearance (body measurements, weighing, physical activity, including sports, as well as combining various types of physical activity with a healthy diet). Corrective behavior is more focused on creating a socially attractive image, while purging and restrictive behaviors are aimed at reducing body mass that is subjectively perceived as too large, regardless of objective indicators. Corrective behavior was characteristic of girls from both the main group and the control group, but it qualitatively differed in terms of the weight correction methods used. Girls from the main group reported using measurements to check the thinness of their arms or legs, constant weighing, excessive and exhausting physical exertion. In the comparison group, the responses of the girls mainly reflected their desire for a balance of nutrition and physical activity; i.e., a healthy lifestyle.

The lowest BMI, as expected, was found in the main group in girls hospitalized for the first time and diagnosed with anorexia nervosa (F50.0), as well as (in the total sample) in girls with restrictive and purging behavior.

Non-suicidal self-injuries were approximately equally distributed both in the main group and in the overall population, which confirms the high prevalence of selfinjurious behavior in adolescence in both the clinical and non-clinical samples. In the pooled sample, just over 50% confirmed that they had intentionally harmed themselves and cutting was the most common type of self-injury.

Interestingly, girls from the main group interpreted physical harm to themselves more broadly than girls from the control group. While the girls from the control group described types of non-suicidal self-injury (cutting, hitting, and scratching the skin), the description of self-injurues in the main group was more consistent with deliberate selfharm and included, in addition to non-suicidal self-injuries, self-destructive actions, such as extreme weight control practices, overdose on pills, and exhausting workouts. Girls with self-injuries in the main group had the lowest BMI, and girls with self-injuries in the control group had the greatest fear of rejection and overall interpersonal sensitivity.

In the clinical sample, a suicide risk subgroup was identified based on the Blitz Questionnaire, which included girls with depressive syndrome and EDs who practiced purging or restrictive behavior. The girls from this subgroup scored the highest on the Interpersonal Sensitivity Questionnaire (dependence on the assessments of others, fear of rejection, and overall interpersonal sensitivity), while all of them confirmed self-injurious behavior.

The significant association between the suicide risk and interpersonal sensitivity demonstrates the importance of interpersonal vulnerability in attitudes to suicide: the more pronounced the interpersonal sensitivity is, the higher the suicide risk. It is also interesting to note the positive association between BMI and suicide risk in our study, which is explained by the specifics of the sample: girls with a BMI close to the norm at the time of participation in the study had a concomitant diagnosis of anorexia nervosa or bulimia nervosa but were treated for depression, in which suicide risk is known to increase.

The limitations of the study include a small sample size and the cross-sectional nature of the study, which limit
the margin for interpreting the results and extrapolating conclusions when building predictive models. However, the advantage of this study is that a group of similarage adolescent girls studying in a comprehensive school was included for comparison. A qualitative-quantitative approach was also used both in data collection and in their analysis and interpretation, which allowed us to more fully describe the phenomenology of weight control and selfinjuries in adolescent girls in a comparative context, as well as to investigate the association of these parameters with suicidal behavior, BMI, and interpersonal sensitivity.

The presented data are consistent with the results of other studies. The fixation of girls from the clinical sample on monitoring their weight and measuring their body parts, in contrast to the increased interest in diets and healthy eating habits in the control group, illustrates body image disconnect such as bias towards certain body parts with overestimation or underestimation of their size [31]. Measuring body parts is part of the concept of body checking, which consists in scrutinizing one's own body and appearance in search of flaws. This behavior is closely associated with EDs [32]. According to neurophysiological studies, adolescent girls with anorexia nervosa have a heightened emotional perception of body parts, and a distorted perception of their size and shape [33].

The differences in self-injurious behavior found in our study between the main group and the control group are consistent with the results of our previous study performed using an older sample. In that study, we also noted that superficial self-harm may be associated with the use of more severe self-harm methods that have a destructive impact on the body as a whole (e.g. risky behavior, deprivation of needs, fasting, substance abuse). The fear of rejection (a factor of interpersonal sensitivity) is one of the predictors of both superficial self-harm and more severe self-destructive behavior [27].

The combination of superficial self-harm with extreme weight loss practices common to girls in the clinical sample backs up the notion that behavioral symptoms of EDs can be classified as indirect self-injurious behavior, and that fasting or purging behavior can be used as a way to inflict physical harm on oneself, both in the short and in the long term [34].

The identified suicide risk in girls with depressive syndrome, co-occurring anorexia/bulimia nervosa, and restrictive and purging behavior, as well as the highest rates of interpersonal sensitivity (especially fear of rejection), in this subgroup are consistent with the results of other studies. According to a retrospective analysis of medical records, depression is one of the psychopathological markers of suicide risk in young people diagnosed with anorexia nervosa and bulimia nervosa [35], and the use of extreme methods of weight control (purging and restriction) in anorexia nervosa is also a significant factor affecting suicide risk [36, 37]. High interpersonal sensitivity, considered in clinical studies primarily as a psychopathological symptom (feeling of the fragility of one's own Self, especially intensely experienced in relationships with others) also indicates an unfavorable prognosis. It has been found that individuals engaged in intense physical exercise have higher interpersonal sensitivity, and its influence increases as compulsive traits increase [38]. In addition, high interpersonal sensitivity among adolescents with anorexia nervosa indicates a risk of re-hospitalization after a year [39]. Therefore, the assessment of interpersonal sensitivity may be useful in predicting the course of the disease.

It should be noted that the association between BMI and suicide risk found in our study is not an exception; it reflects the complexity and nonlinearity of the association between body weight and suicidal behavior, which requires further study. Despite the current view that being underweight is associated with an increased risk of completed suicide [40], the presented data show that both low and high BMI are risk factors for suicide in women with depressive symptoms [41], and that deviation from normative BMI (too low or too high) during childhood is more closely associated with adult suicidal ideation/attempts than actual BMI [42].

There are plans to expand the clinical sample in the future to look into the personal and psychopathological factors of suicide risk in adolescent girls with different types of EDs and concomitant self-injurious behavior. Conducting longitudinal studies starting from primary school age seems promising, given that girls at that age can already be inclined to control their body weight.

#### CONCLUSION

This study is the first conducted on a Russian-speaking sample which examines the association of eating behaviors (weight control methods) and body mass index with non-suicidal self-injuries, suicide risk, and interpersonal sensitivity in adolescent girls with EDs, compared with adolescent girls in the general population. The highest vulnerability in terms of suicide risk was shown in adolescent girls with depressive syndrome and concomitant anorexia/ bulimia nervosa who used extreme methods of weight control (purging and restrictive behavior), engaged in nonsuicidal self-injuries, and scored high on interpersonal sensitivity. A hallmark of the self-injurious behavior in adolescent girls with EDs was the combination of nonsuicidal self-injuries with specific dietary restriction and weight loss practices (excessive exercising, fasting) that are aimed at causing physical harm to oneself rather than conforming to social standards of attractive looks.

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# Pharmacological Strategies for Appetite Modulation in Eating Disorders: A Narrative Review

Фармакологические стратегии модуляции аппетита при расстройствах пищевого поведения: нарративный обзор литературы

doi: 10.17816/CP6150 Review

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# ABSTRACT

**BACKGROUND:** A substantial increase in the prevalence of eating disorders has been noticed over the past decades. Priority in the treatment of eating disorders is justifiably given to psychosocial interventions. However, it is also well known that centrally acting drugs can significantly affect appetite and food consumption.

**AIM:** To narratively review the available neurobiological data on the mechanisms of central regulation of eating behavior as a rationale to summarize pharmacological strategies for appetite modulation in eating disorders.

**METHODS:** The authors have carried out a narrative review of scientific papers published from January 2013 to March 2023 in the PubMed and Web of Science electronic databases. Studies were considered eligible if they included data on the neurobiological mechanisms of appetite regulation or the results of clinical trials of centrally acting drugs in eating disorders. Relevant studies were included regardless of their design. Descriptive analysis was used to summarize the obtained data.

**RESULTS:** The review included 51 studies. The available neurobiological and clinical data allowed us to identify the following pharmacological strategies for appetite modulation in eating disorders: serotonergic, catecholaminergic, amino acidergic and peptidergic. However, implementation of these data into clinical practice difficult due to an insufficient number of good-quality studies, which is particularly relevant for adolescents as there is a research gap in this population.

**CONCLUSION:** The progress in neurobiological understanding of the mechanisms of central regulation of appetite opens opportunities for new pharmacotherapeutic approaches aimed at changing the patterns of eating behavior. Obviously, treatment of eating disorders is a much broader problem and cannot be reduced to the correction of eating patterns. Nevertheless, at certain stages of treatment, drug-induced modulation of appetite can play an important role among multi-targeted biological and psychosocial interventions. Translation of neurobiological data into clinical practice requires a large number of clinical studies to confirm the long-term efficacy and safety of pharmacotherapeutic approaches and to develop personalized algorithms for the treatment of various forms of eating disorders in different age groups.

#### аннотация

**ВВЕДЕНИЕ:** На протяжении последних десятилетий наблюдается значительный рост частоты расстройств пищевого поведения. При лечении расстройств пищевого поведения приоритет обоснованно отдается психосоциальным интервенциям. Вместе с тем хорошо известно, что лекарственные препараты центрального действия способны оказывать существенное влияние на аппетит и потребление пищи.

**ЦЕЛЬ:** Проанализировать и обобщить имеющиеся нейробиологические данные о механизмах центральной регуляции пищевого поведения для обоснования фармакологических стратегий модуляции аппетита при расстройствах пищевого поведения.

**МЕТОДЫ:** Авторами выполнен нарративный обзор научной литературы, опубликованной за период с января 2013 г. по март 2023 г. в электронных базах данных PubMed и Web of Science. Исследования считались приемлемыми, если они включали данные о нейробиологических механизмах регуляции аппетита, а также результаты клинических исследований препаратов центрального действия при расстройствах пищевого поведения. Релевантные исследования включались в обзор независимо от их дизайна. Для обобщения полученной информации использовался описательный анализ.

**РЕЗУЛЬТАТЫ:** В обзор включено 51 исследование. Анализ имеющихся нейробиологических и клинических данных позволил обосновать следующие фармакологические стратегии модуляции аппетита при расстройствах пищевого поведения: серотонинергическая, катехоламинергическая, аминокислотергическая и пептидергическая. Однако недостаточное количество клинических исследований с высоким уровнем доказательности затрудняет внедрение полученных данных в клиническую практику, что особенно актуально для подросткового возраста ввиду практически полного отсутствия рандомизированных контролируемых исследований в этой возрастной популяции.

ЗАКЛЮЧЕНИЕ: Прогресс в нейробиологическом понимании механизмов центральной регуляции аппетита открывает перспективу разработки новых фармакотерапевтических подходов, направленных на изменение паттернов пищевого поведения. Лечение расстройств пищевого поведения, безусловно, представляет собой гораздо более широкую проблему, не сводимую исключительно к коррекции объема потребляемой пищи. Тем не менее на определенных этапах лечения фармакогенная модуляция аппетита может играть важную роль в ряду комплексных биологических и психосоциальных интервенций. Трансляция нейробиологических данных в клиническую практику требует проведения большого числа клинических исследований для подтверждения долгосрочной эффективности и безопасности фармакотерапевтических подходов и разработки персонализированных алгоритмов лечения различных вариантов расстройств пищевого поведения в разных возрастных популяциях.

**Keywords:** eating disorders; anorexia nervosa; bulimia nervosa; binge-eating disorder; appetite regulation; pharmacotherapy; adolescence

**Ключевые слова:** расстройства пищевого поведения; нервная анорексия; нервная булимия; компульсивное переедание; регуляция аппетита; фармакотерапия; подростковый возраст

# INTRODUCTION

Eating disorders (EDs) are increasingly becoming the focus of the attention of researchers due to their growing prevalence in different age groups and significant contribution to the global disease burden [1]. There are three main types of EDs: anorexia nervosa, bulimia nervosa, and binge eating disorder; there are also various atypical and unspecified forms [2].

Anorexia nervosa is characterized by severe weight loss, accompanied by an intense fear of gaining weight, a strict

and restrictive diet, and purging behavior (self-induced vomiting, laxative abuse, use of diuretics, etc.) [3]. This type of ED is associated with the highest mortality rate among mental disorders [2]. Bulimia nervosa is characterized by recurring episodes of binge eating; each episode is followed by actions that aim to reverse the excess food intake and suppress the eventual weight gain (vomiting, taking laxatives, dieting for a long time, excessive exercise) [3]. Binge eating disorder is characterized by repeated episodes of eating large amounts of food, combined with a feeling of loss of control over this urge [3]. These episodes are often followed by feelings of shame, disgust, or depressive thoughts, but, unlike bulimia nervosa, no action is usually taken to prevent weight gain [3].

Psychosocial interventions have traditionally been the primary method used to treat EDs, while pharmacotherapy has usually played a secondary role [4, 5]. Meanwhile, many exogenous substances are known to significantly alter appetite and affect the amount of food consumed, either decreasing or increasing it [6, 7]. These substances include both medicinal products and psychoactive substances (legal and prohibited) [8-12]. For example, some substances with addictive potential, in particular nicotine and psychostimulants, reduce appetite [8, 9]. This effect has been the reason for the use of amphetamine derivatives as anorectics in the treatment of obesity for several decades [10]. Many antipsychotics, on the contrary, increase appetite and cause weight gain [11]. An increase in appetite is also caused by certain psychoactive substances, such as cannabis [12].

Despite the fact that there are plenty of pharmacological substances that have the potential to affect appetite and eating behavior, there remains a clear shortage of drugs officially approved for the treatment of EDs. In the Russian Federation only one drug, the antidepressant fluoxetine, is approved for use in EDs, namely in bulimia nervosa<sup>1</sup>. In the United States, another drug is authorized for EDs treatment: lisdexamfetamine [13]. This psychostimulant, which is used in the treatment of attention deficit hyperactivity disorder, has recently been approved by the United States Food and Drug Administration, FDA, for use in binge eating disorder [13]. In addition to these two compounds, there are a number of drugs on the pharmaceutical market that are approved for the treatment of excess weight and obesity [14]. Presumably, these drugs may have therapeutic potential in EDs.

There is currently no consensus on pharmacotherapeutic algorithms for various types of EDs. Existing national guidelines and recommendations are not always consistent across the board [4, 5, 15]. In practice, psychotropic drugs in EDs are often prescribed to treat concomitant psychiatric symptoms (anxiety, depression, obsessions), as well as to address body image distortions and delusional thinking [15, 16]. The possibility of using drugs to directly influence the endogenous mechanisms of appetite regulation are often ignored. In our opinion, historical skepticism towards pharmacotherapeutic interventions is probably partly due to a lack of understanding of the neurobiological basis of EDs. Lately, the body of data from experimental and neurophysiological studies has significantly expanded our understanding of the neurobiological mechanisms that underlie eating behavior regulation.

The aim of this paper is to narratively review the available neurobiological data on the mechanisms of central regulation of eating behavior as a rationale to summarize pharmacological strategies for appetite modulation in EDs.

#### METHODS

The authors conducted a narrative review of scientific literature on the subject published from January 2013 to March 2023 in the electronic databases PubMed and Web of Science. This time interval was chosen because of the surge in scientific research in the field of neurobiology and treatment of EDs that has taken place over the past decade, including innovative pharmacotherapeutic approaches based on promising pharmacological strategies. The search terms included the keywords "eating disorders", "anorexia nervosa", "bulimia nervosa", "binge eating disorder", "appetite", "eating behavior", "obesity", "neurobiology", "pharmacotherapy", "pharmacological strategies" and "drug treatment", "antidepressants", "antipsychotics", and "psychostimulants". The keywords used for the search combined two interconnected terms; for example: "eating disorders" AND "pharmacotherapy".

Studies were considered eligible if they included data on the neurobiological mechanisms of appetite regulation and eating behavior, as well as the results of clinical

<sup>1</sup> State Register of Medicines. Instruction for the medical use of fluoxetine [Electronic resource]. URL: http://grls.rosminzdrav.ru/Grls\_View\_v2.aspx?routingGuid=d3561b67-fc74-4378-a169-f1913e60459b.

studies of drugs for various types of EDs. Relevant studies were included regardless of their design. Since a number of relevant studies had been published before 2013, their results were also included in the review if they were deemed important. References from more recent publications included in the review were used to search for such studies. Descriptive analysis was used to summarize the obtained data.

# RESULTS

A total of 51 studies were included. Of those, 40 papers were published from January 2013 to March 2023, and the remaining 11 were published earlier.

In this section we will delve into the neurobiological mechanisms of central regulation of eating behavior relevant to the known pharmacodynamic effects of drugs. Next, we will outline pharmacological strategies based on the targeted effect of drugs on the neurochemical mechanisms involved in appetite regulation. Each strategy will be supported by the results of clinical studies of the respective drugs in EDs. In conclusion, data will be presented on alternative, promising neurochemical targets for innovative approaches to EDs pharmacotherapy.

# The neurobiological mechanisms of eating behavior regulation

Eating behavior regulation is a complex and multifactorial process. The endocrine system (hypothalamic-pituitarythyroid axis, hypothalamic-pituitary-adrenal axis, sex hormones), conditioned reflex mechanisms (the type and smell of food), gastric interoception (a full stomach), changes in biochemical homeostasis (decrease in blood glucose), etc. all play an important role [17]. A detailed discussion of appetite and eating behavior regulation is beyond the scope of this review. Only those of the neurobiological mechanisms that are relevant to the pharmacodynamics of centrally acting drugs will be presented below.

Eating, in addition to replenishing energy, is associated with reward and reinforcement. The main neuroanatomical structures responsible for appetite and motivation to eat are the hypothalamus and the endogenous reward system. An increase or decrease in food intake is regulated by peptidergic neurons located in the arcuate nucleus of the hypothalamus [18]. There are two types of these neurons that have opposite effects on appetite.

Neurons of the first type (POMC neurons) produce polypeptide pro-opiomelanocortin (POMC) and are

anorexigenic (appetite-suppressive). Post-translational changes in POMC create two active peptides:  $\beta$ -endorphin and  $\alpha$ -Melanocyte-stimulating hormone ( $\alpha$ -MSH). The former is a ligand for opioid receptors, and the latter is a ligand for type 4 melanocortin receptors (MC4Rs) [19]. MC4Rs are actively expressed in the neurons of the paraventricular nucleus of the hypothalamus, which are part of the central anorexigenic pathway [20].

Neurons of the second type (NPY/AgRP neurons) synthesize neuropeptide Y (NPY) and agouti-related peptide (AgRP), which have orexigenic (appetite-stimulating) effects [18]. Also, these neurons produce gamma-aminobutyric acid (GABA) [18]. GABA-mediated mechanisms can also play an important role in the orexigenic activity of NPY/AgRP neurons: many "anorexigenic" structures, including nearby POMC neurons, receive inhibitory GABAergic signaling from NPY/AgRP neurons [19].

Both types of peptidergic neurons of the hypothalamus receive afferent signals from different areas of the CNS, as well as from the periphery (from the stomach, intestines, pancreas, and adipose tissue) [21, 22]. The activity of these neurons is regulated by many neurotransmitters (monoamines, endogenous opioids, glutamate, and GABA), neuropeptides, and hormones (cholecystokinin, leptin, ghrelin, and others). For example, leptin synthesized by adipocytes stimulates POMC neurons and inhibits NPY/AgRP neurons, thereby reducing food intake [19]. Most endogenous modulators of eating behavior affect not only appetite and food intake, but many other physiological processes as well [21, 23]. Specifically, centrally synthesized orexins, besides to modulating eating behavior, play an important role in the regulation of the sleep/wake cycle. Orexinergic neurons are located in the hypothalamic nuclei and innervate various parts of the brain, mainly those areas where monoaminergic neurons are located [24].

Monoaminergic signaling is of crucial importance in the regulation of the orexigenic and anorexigenic activity of hypothalamic neurons [23]. An increase in serotonergic tone (an increase in the concentration of serotonin released from the axonal terminals of serotonergic neurons of the raphe nuclei) shifts the balance towards appetite suppression [25]. This effect is probably mediated by the stimulation of postsynaptic 5HT2C receptors on POMC neurons, which increases the anorexigenic activity of the latter [18, 23]. This subtype of serotonin receptors is actively expressed in the hypothalamus [26]. Knockout

of this receptor causes obesity in laboratory animals [27]. 5HT2C receptors blockade (especially in combination with H1-histamine receptors blockade, which is shared by a number of antipsychotics and some antidepressants) has been noted to induce weight gain [28]. Along with serotonin, the catecholaminergic mechanisms of appetite and food intake regulation are also important [29]. These mechanisms are complex and multidirectional, but to put it simply, an increase in catecholaminergic signaling leads to an increase in the anorexigenic pathway activity, which is confirmed by the known clinical effects of psychostimulants [13, 30].

Orexigenic and anorexigenic hypothalamic neurons are connected with the ventral tegmental area, and POMC neurons inhibit dopamine neurons located there [31]. The latter one innervate the ventral striatum (nucleus accumbens) and the amygdala. These dopaminergic projections are part of the mesolimbic pathway that plays a central role in the endogenous reward system [32]. It is assumed that the level of dopamine released in the nucleus accumbens is associated with the feeling of pleasure from various types of "pleasant" activities, including tasty food. Ingestion of palatable food activates the reward system, triggering the release of dopamine in the nucleus accumbens and amygdala, thus reinforcing the behavior that leads to overeating and "food addiction" [33].

Eating tasty food also affects the opioid system, inducing the release of endogenous opioid peptides [34]. Administration of an opioid receptor antagonist (GSK1521498) for 28 days to subjects with obesity comorbid with binge eating disorder has been shown to reduce palatable food intake [35]. It has been also demonstrated that opioid receptor antagonists increase the anorexigenic activity of the arcuate nucleus [19].

The functional activity of the reward system is controlled by the glutamatergic neurons of the prefrontal cortex, probably through an activating effect on GABAergic interneurons [36]. It is assumed that dopaminergic and glutamatergic dysfunctions might lead to dysregulation of the reward/reinforcement processes associated with food intake and/or to a lack of inhibitory control, constituting an important neurobiological mechanism for developing EDs [37].

Overall, the central regulation of appetite and eating behavior is mediated by a number of neurobiological mechanisms. The hypothalamus plays a key role. The activity of orexigenic and anorexigenic hypothalamic neurons is modulated by a variety of neurotransmitters, peptides, co-transmitters, and hormones. Dysregulation of the functioning of the endogenous reward system may also play an important role in the development of eating behavior patterns in EDs.

# Pharmacological strategies for appetite modulation

The described neurobiological mechanisms of appetite regulation give us a rationale for a number of pharmacological strategies based on altering the functional activity of neurotransmission to target the central orexigenic and anorexigenic processes. In principle, four main strategies can be outlined: serotonergic, catecholaminergic, amino acidergic (glutamatergic), and peptidergic (opioid).

#### Serotonergic strategy

As noted above, increased serotonin concentration in synapses formed by the axons of serotonergic neurons extending from the raphe nuclei and hypothalamic peptidergic neurons leads to appetite suppression, probably due to a stimulation of 5HT2C receptors on POMC neurons of the arcuate nucleus of the hypothalamus, which leads to an increase in the activity of central anorexigenic structures [18, 23]. 5HT2C receptors can be pharmacologically stimulated in two ways: through indirect and direct agonism.

Fenfluramine, a drug that blocks serotonin reuptake, is an indirect agonist of serotonergic neurotransmission [38]. Fenfluramine was previously widely used for the treatment of obesity, then it was withdrawn from the market due to cardiac and pulmonary toxicity, and was recently approved for use in a number of countries for another indication: as an anticonvulsant in children with Dravet syndrome (but not in the Russian Federation) [38]. Almost all antidepressants are also indirect agonists of serotonin receptors [39-43]. Their antibulimic activity is well known and has been repeatedly confirmed with data from randomized controlled trials (RCTs) [39-43]. In the earliest studies on the topic, tricyclic antidepressants and monoamine oxidase inhibitors were found to be effective in reducing binge eating and subsequent purging behavior [39]. However, the severity of the side effects of these drugs limits their use in EDs [39]. Selective serotonin reuptake inhibitors (SSRIs) are preferred because of their more favorable safety profile. An 8-week, double-blind RCT in patients with bulimia nervosa (n=387) demonstrated that fluoxetine at a dose of 60 mg/ day was superior to placebo in reducing the frequency of

binge eating and vomiting, as well as reducing symptoms of depression, carbohydrate cravings, and abnormal eating habits; at a dose of 20 mg/day, it had no significant effect [40]. In respondents fluoxetine demonstrated efficacy in preventing relapse in a 52-week follow-up study [41]. Fluvoxamine was also studied and demonstrated efficacy in preventing a bulimia nervosa relapse compared to placebo in a 15-week double-blind RCT (n=72) [42]. There is evidence of the efficacy of duloxetine in the treatment of binge eating disorder in patients with depressive disorder: a 12-week double-blind RCT (n=40) demonstrated its superiority over placebo in reducing the frequency of binge episodes, the body weight, and the severity of psychopathological symptoms [43]. It should be noted that not all antidepressants have been evaluated in RCTs in patients with EDs. In general, despite the reduction in the frequency of binge episodes, antidepressants (with rare exceptions) do not lead to a significant change in the body weight [39-43]. We should also note that not all of the studied antidepressants have a selective effect on serotonergic neurotransmission. Non-selective drugs also enhance the activity of catecholaminergic neurotransmission; so, considering them within serotonergic strategy is not entirely correct.

The second way to stimulate 5HT2C receptors in the hypothalamus is direct agonism. A selective 5HT2C serotonin receptor agonist, lorcaserin, is available in many countries (but not in the Russian Federation) [44]. It reduces appetite and suppresses hunger, helping to reduce the food intake. Lorcaserin is approved for the treatment of obesity, and it may have therapeutic potential for EDs associated with overeating [44].

Conversely, the 5HT2C receptor antagonism should have the opposite effects: increased appetite and increased food intake. This is confirmed by the known side effects of antipsychotic drugs, e.g. clozapine and olanzapine both are potent blockers of 5HT2C receptor and cause the most pronounced weight gain among antipsychotics [45]. Atypical antipsychotics have been repeatedly considered as potential treatments for anorexia nervosa. A meta-analysis of seven RCTs demonstrated a moderate effect on weight recovery in patients with anorexia nervosa for olanzapine and no effect for risperidone and quetiapine [46]. Another meta-analysis confirmed the efficacy of olanzapine in the treatment of anorexia nervosa, namely in increasing body mass index [47]. It should be noted that although we consider the effect of antipsychotics on appetite and eating behavior to be part of the serotonergic strategy, other neurochemical mechanisms are likely to be also involved (for example, blockade of histamine receptors). For some drugs, the neuroendocrine effects associated with hyperprolactinemia (due to dopamine receptors blockade in pituitary lactotrophs) may come to the fore. Other effects of antipsychotics, including peripheral ones (effects on the liver, pancreatic  $\beta$ -cells, adipose tissue, and skeletal muscles), can also play a significant role in changing eating behavior and increasing body weight [45].

In addition, the role of the 5HT2C serotonin receptor in the regulation of appetite, eating behavior, and body weight is not that clear. The only drug approved for the treatment of bulimia nervosa, fluoxetine, is known to block (similarly to clozapine and olanzapine) 5HT2C receptors [48].

#### **Catecholaminergic strategy**

The efficacy of psychostimulants in reducing body weight has long been known. The main pharmacodynamic effect of these drugs is an increase of the synaptic concentration of catecholamines (dopamine and norepinephrine) [49]. As noted above, an increase in catecholaminergic afferentation (as well as serotonergic one) shifts the balance between the orexigenic and anorexigenic activity of hypothalamic neurons towards appetite suppression. It is likely that some other mechanisms, including peripheral ones, are also involved in weight loss induced by psychostimulants [29, 50].

Given the efficacy of psychostimulants in the treatment of obesity, they have been studied as therapeutic agents for EDs. Lisdexamfetamine is currently on the market in a number of countries (not in the Russian Federation) for the treatment of binge eating disorder [13]. The results of an 11-week double-blind RCT in patients with binge eating disorder (*n*=255) demonstrated that lisdexamfetamine was superior to placebo in reducing binge days [51]. Analysis of secondary efficacy parameters confirmed its superiority over placebo in reducing compulsive overeating and the severity of obsessive-compulsive symptoms [52]. Another double-blind RCT confirmed the safety and efficacy of lisdexamfetamine in patients with binge eating disorder (*n*=418) and provided evidence that its continued use for six months was superior to placebo in preventing relapse [53].

The amphetamine derivative sibutramine is used to treat obesity and could theoretically be useful in the treatment of EDs. A multicenter 24-week RCT of sibutramine efficacy in binge eating disorder (n=304) confirmed its efficacy in reducing binge episodes, weight, and associated symptoms such as cognitive restraint, disinhibition, and hunger [54]. It should be noted that sibutramine increases the functional activity of both catecholaminergic and serotonergic neurotransmission [55], thereby exploiting (similarly to nonselective antidepressants) both monoaminergic strategies. Another sympathomimetic, phentermine, has been approved (in combination with topiramate, which is discussed below, as part of an amino acidergic strategy) for the treatment of obesity in a number of countries (not in the Russian Federation) [30].

Bupropion (not approved in the Russian Federation) is an antidepressant with similar pharmacodynamic effects to those of psychostimulants. It blocks norepinephrine and dopamine reuptake but, unlike psychostimulants, does not have an addictive potential [56]. Atomoxetine, a norepinephrine reuptake inhibitor, used to treat attentiondeficit hyperactivity disorder in children, adolescents, and adults, has also a similar mechanism of action [57]. Bupropion as monotherapy is contraindicated in subjects with ED due to a high risk of seizures [58]. Bupropion in combination with naltrexone is approved in several countries for the treatment of obesity [59] and hypothetically might be useful in EDs. Atomoxetine, according to a small, single-center, 10-week RCT (n=40), can reduce binge eating frequency and body weight in binge eating disorder compared with placebo [60].

The opposite effect on the catecholaminergic neurotransmission (specifically, dopamine receptors blockade), as noted above, may contribute to the weight gain observed during the use of antipsychotics. This is confirmed by the fact that partial agonists of dopamine receptors (aripiprazole, cariprazine, and brexpiprazole) cause less weight gain of compared to antagonists [28].

In addition, it should be emphasized once again that eating behavior patterns are determined not only by the hypothalamic mechanisms of appetite regulation; the endogenous reward system also plays an important role. The functional activity of this system can be modulated by centrally acting drugs, in particular those drugs that affect the functional activity of the catecholaminergic neurotransmission [61, 62]. Specifically, antipsychotics suppress the reward system by blocking dopamine receptors in the mesolimbic dopaminergic pathway [62]. Therefore, the direction and severity of the pharmacological effect of catecholaminergic drugs on eating behavior will be largely determined by the sum of complex and multidirectional effects on the orexigenic/anorexigenic structures of the hypothalamus and on the reward system [62].

#### Amino acidergic (glutamatergic) strategy

Among the drugs with therapeutic potential in EDs, topiramate and zonisamide can be considered within the framework of the amino acidergic strategy. The exact mechanism how these drugs influence eating behavior and body weight has not been established. It is assumed that by altering the activity of voltage-gated ion channels, these drugs change the balance between the excitatory glutamatergic and inhibitory GABAergic signaling received by hypothalamic peptidergic neurons that regulate appetite [30]. Open-label clinical studies confirm that zonisamide can reduce binge eating and body weight in the short term (12 weeks) and at the 1-year follow-up, but is poorly tolerated, resulting in frequent patient withdrawal [63, 64]. Clinical studies of topiramate confirm its positive effect in reducing the frequency of binge episodes and body weight. A meta-analysis of three RCTs confirms the efficacy of topiramate in the treatment of binge eating disorder [65]. The combination of topiramate with the psychostimulant phentermine is used to treat excess weight, including in pediatric patients [66]. With this combination, the dose of phentermine may be reduced, which minimizes the risk of addiction and cardiovascular side effects [67].

Therapeutic use of ketamine, a dissociative anesthetic the effects of which are mainly mediated by its NMDA receptor antagonism, can be also considered within the amino acidergic (glutamatergic) strategy [68]. Due to its rapid clinical effect in depression [69], ketamine is extensively studied for other psychiatric indications, including EDs [70]. Preliminary clinical data on the efficacy and safety of ketamine in EDs suggest its therapeutic potential, but this should be confirmed in RCTs [70]. An interesting hypothesis regarding the possible augmentation of ketamine effect in anorexia nervosa by the addition of dietary supplements containing zinc also requires clinical confirmation. Zinc is known to be an allosteric modulator of the NMDA receptor, and is deficient in individuals with anorexia nervosa [71].

# Peptidergic (opioid) strategy

The competitive  $\mu$ -opioid receptor antagonist naltrexone has been approved (in combination with bupropion) in a number of countries (not in the Russian Federation) for the treatment of obesity [59]. Naltrexone itself only slightly reduces body weight but has synergism with the pharmacodynamic effects of bupropion [59]. Blockade of  $\mu$ -opioid receptors, on the one hand, activates the anorexigenic neurons of the hypothalamus (probably due to the elimination of negative feedback mediated by  $\beta$ -endorphin) and, on the other hand, blocks the reinforcement/reward [19]. Given the efficacy of the naltrexone and bupropion combination in obesity, it might have a therapeutic potential in EDs. The effect of this combination in binge eating disorder was evaluated in a 12-week placebo-controlled RCT (*n*=22), which demonstrated no significant superiority over placebo [72]. According to the authors, this was due to the insufficient statistical power of the study, therefore larger-scale RCTs are required [72].

#### **Novel neurochemical targets**

Within the framework of the discussed pharmacological strategies, in addition to the neurochemical targets that are addressed by existing drugs, some other targets that are promising for the development of innovative approaches to the pharmacotherapy of EDs can be identified.

Specifically, these novel targets include endocannabinoid receptors. Endocannabinoids, by means of retrograde neurotransmission, regulate the release of dopamine in the neuroanatomical structures related to the reward system [73]. Blocking endocannabinoid receptors may help reduce binge eating disorder symptoms and body weight [74]. In a multicenter RCT (*n*=289), the endocannabinoid receptor antagonist rimonabant caused significantly greater weight loss in the treatment of patients with binge eating disorder compared to placebo [74].

Psychedelics (that bind to serotonin receptors and change the activity of serotonergic processes) are now increasingly being considered as potential therapeutic agents for EDs [75, 76]. A preliminary study on the effects of ayahuasca, a psychedelic brew used for rituals in South America, demonstrated a reduction in ED symptoms as assessed by the patients themselves (*n*=13) [75]. A substance with psychedelic activity, psilocybin, is being considered as potential treatment for depressive and anxiety disorders, and it is also being studied for possible beneficial effects in patients with anorexia nervosa [76].

Given the effect of orexin neurotransmission on a number of physiological functions, including food intake, orexin receptor antagonists are viewed as agents with therapeutic potential in various neuropsychiatric disorders, including EDs [77]. Another promising neurochemical target is related to trace amines, which are increasingly being considered in the context of psychiatric disorders [78]. In particular, the trace amine-associated receptor 1 (TAAR1) has recently been studied as a dopaminergic and glutamatergic neurotransmission modulator, making it a promising therapeutic target in EDs [79]. Interestingly, TAAR1 is also stimulated by amphetamine, the active metabolite of lisdexamfetamine [79]. The agonism of lisdexamfetamine at TAAR1 may mediate its ability to restore neurochemical dysfunction in the prefrontal cortex by compensating for impaired inhibitory control mechanisms.

# DISCUSSION

Our review of the literature identifies four pharmacological strategies for modulating appetite and food intake in EDs: serotonergic, catecholaminergic, amino acidergic (glutamatergic), and peptidergic (opioid). Each strategy is substantiated in terms of the neurotransmitter mechanisms of central regulation of eating behavior. The clinical prospects of these strategies are supported by the results of clinical studies of various classes of centrally acting drugs in different types of EDs. The two drugs with the highest quality of evidence to date are fluoxetine for bulimia nervosa [40, 41] and lisdexamfetamine for binge eating disorder [51, 53]. No single drug has a sufficiently strong evidence for anorexia nervosa, although meta-analyses suggest a possible moderate efficacy for olanzapine [46, 47]. It should also be noted that the majority of clinical studies in EDs have been short-term (8 to 15 weeks) [40, 42, 43, 51, 60, 63, 72], with the longest study lasting 52 weeks [41]. Given the propensity of EDs to relapse [2, 3], the long-term efficacy and tolerability of drugs cannot be assessed based on the available data.

### **Strengths and limitations**

The strength of this narrative review is in its summary of the current neurobiological and clinical data supporting the possibility of pharmacological modulation of appetite and eating behavior. To our knowledge, this is the first publication to describe precise pharmacological strategies for appetite modulation in EDs based on the neurobiological mechanisms of regulation of eating behavior, on the one hand, and the results of clinical studies, on the other. A limitation of this review is that a number of relevant studies on this topic may have been missed, since a systematic search strategy was not used for the purposes of the review. In addition, the methodological quality of the data obtained was not sufficiently high in some cases; many of the included studies had methodological shortcomings. The high heterogeneity of the endpoints and results of the studies made it very difficult to generalize the data obtained and prevented us from formulating practical conclusions regarding the pharmacotherapy of EDs.

## Implications for future research and practice

This review of the literature demonstrates that the efficacy of centrally acting drugs in EDs associated with overeating (bulimia nervosa and binge eating disorder) has much stronger evidence than in anorexia nervosa. However, such dichotomy of eating habits based on the opposite changes in appetite and the amount of food consumed is not entirely correct. Within the same ED, a patient may have a combination of various patterns of eating behavior, manifested by both an increase and a decrease in food intake, which significantly limits the therapeutic potential of the pharmacological correction of ED. In addition, treating EDs is a much broader issue not limited to changes in appetite and food intake. However, at certain stages of treatment, pharmacological modulation of appetite may play an important role in a number of multi-targeted biological and psychosocial interventions aimed at ED correction. The neurobiological and clinical data collected in recent years inspire cautious optimism in this regard. Unfortunately, today, given the complexity of EDs treatment and the lack of high-quality clinical studies, it seems premature to talk about implementing the available data into clinical practice (especially in anorexia nervosa). Developing evidence-based guidelines and recommendations requires a large number of further studies.

One of the most important areas for future research is to evaluate the efficacy and safety of drug treatment for various types of EDs in adolescence. Despite a high prevalence of EDs among adolescents [1,2], there are virtually no RCTs of drug treatment in the adolescent population [80]. Meanwhile, the age factor undoubtedly makes a significant contribution to the efficacy and safety of pharmacotherapy. Adolescence presents particular challenges, and not only because of the high prevalence of EDs and their transnosological nature. Adolescence is characterized by active processes of neurobiological maturation of the CNS associated with significant structural and functional changes [81]. On the one hand, these changes may be associated with an absence or distortion of the expected drug-induced effects. On the other hand, it cannot be ruled out that the use of centrally acting drugs in adolescence, a critical period in CNS development, can change the neurodevelopmental trajectories of the brain structures targeted by these drugs, and the structures connected with them [82]. Large-scale long-term studies are needed to comprehensively assess the possible negative (including long-term) consequences of EDs pharmacotherapy in adolescence.

#### CONCLUSION

EDs are a global health problem that affects different age groups and requires the development of effective treatment. Over the past decade, great effort has been poured into the pharmacological treatment of EDs. Yet the pharmacotherapy options for these disorders remain limited. At the same time, the progress made in our neurobiological understanding of the mechanisms of appetite and eating behavior regulation opens up vast prospects in developing new therapeutic approaches that could alter patterns of eating behavior. The translation of neurobiological data into clinical practice requires a large number of clinical studies to confirm the long-term efficacy and safety of various pharmacotherapeutic approaches and develop personalized treatment algorithms for various types of EDs, specifically in adolescents.

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# REVIEW

# Prevalence of Eating Disorders in Patients with Bipolar Disorder: A Scoping Review of the Literature

Распространенность расстройств пищевого поведения у пациентов с биполярным расстройством: обзор предметного поля doi: 10.17816/CP6338

Review

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#### ABSTRACT

**BACKGROUND:** Eating disorder (ED) and bipolar disorder (BD) exhibit certain phenomenological similarities rooted in eating behavior and emotional regulation. However, despite the growing body of research on the comorbidity of ED and BD, scientific data on the concurrent course of these disorders has remained poorly systematized.

**AIM:** To conduct a scoping review of published data on the prevalence of various types of ED among patients with BD types I and II in the context of the sex and clinical features of the concurrent course of these disorders.

**METHODS:** The analysis was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews. The search was conducted in the MEDLINE electronic database. Studies were included if they were focused samples of patients diagnosed with BD and ED, and the Diagnostic and Statistical Manual of Mental Disorders, fourth and fifth editions (DSM-IV, DSM-5), or International Statistical Classification of Diseases and Related Health Problems, tenth Revision (ICD-10), were used for the verification of the ED and BD diagnoses. The descriptive analysis method was used to summarize the review findings.

**RESULTS:** A total of 41 studies were selected for the review. Lifetime ED in patients with BD ranged from 2.2% to 31.1%, and the prevalence rates of BD among patients with ED varied from 11.3% to 68.1%. ED nominally had a higher prevalence among individuals with BD type II and females. Additionally, the presence of ED in patients with BD was associated with earlier onset of mood disorder, a higher number of depressive episodes, higher levels of atypical depressive symptoms, suicide attempts, as well as a higher frequency of comorbid obsessive-compulsive and anxiety disorders, addictions, and various metabolic disorders.

**CONCLUSION:** Despite the high degree of volatility in the results, the prevalence rates of a concurrent course of ED and BD are rather high. For this reason, screening for ED in patients with BD and vice versa holds significant value in the accurate diagnosis and selection of the most effective therapy. The patterns of comorbidity among different types of ED and BD, depending on gender, need further exploration in future research.

#### аннотация

**ВВЕДЕНИЕ:** У расстройств пищевого поведения (РПП) и биполярного аффективного расстройства (БАР) отмечаются определенные феноменологические сходства, связанные с пищевым поведением и эмоциональной регуляцией. Однако, несмотря на планомерный рост исследований коморбидности РПП и БАР, научные данные о совместном течении этих расстройств остаются недостаточно систематизированными.

**ЦЕЛЬ:** Провести обзор предметного поля опубликованных данных по распространенности различных видов РПП среди пациентов с БАР I и II типов с учетом пола, а также анализ клинических особенностей совместного течения данных расстройств.

**МЕТОДЫ:** Анализ представлен в соответствии с рекомендациями PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) для обзора предметного поля. Поиск проводился в электронной базе данных MEDLINE. В обзор включались оригинальные исследования с выборками пациентов с диагнозами БАР и РПП, соответствующими критериям DSM-IV, DSM-V (диагностического и статистического руководства по психическим расстройствам 4 и 5 издания) или МКБ-10 (Международной классификации болезней10-й редакции). Для обобщения результатов обзора использовался описательный анализ.

**РЕЗУЛЬТАТЫ:** Всего для обзора было отобрано 41 исследование. Были обнаружены достаточно разнородные показатели распространенности РПП в течение жизни у пациентов с БАР — от 2,2% до 31,1%, а также показатели распространенности БАР среди пациентов с РПП — от 11,3% до 68,1%. РПП номинально имели более высокую распространённость среди лиц с БАР II типа и женщин. Кроме того, наличие РПП у пациентов с БАР было ассоциировано с более ранним манифестом расстройства настроения, большим количеством депрессивных эпизодов, более высоким уровнем атипичных симптомов депрессии, суицидными попытками, а также с более высокой частотой коморбидных обсессивно-компульсивных и тревожных расстройств, аддикций и различных метаболических нарушений.

ЗАКЛЮЧЕНИЕ: Несмотря на высокую вариативность результатов, показатели распространённости совместного течения РПП и БАР являются достаточно высокими. По этой причине скрининг на РПП у пациентов с БАР и, наоборот, скрининг БАР у пациентов с РПП имеет важное значение в точной диагностике и подборе наиболее эффективной терапии. В будущих исследованиях ещё только предстоит более детально изучить паттерны коморбидности различных видов РПП в зависимости от типа БАР и пола.

**Keywords:** eating disorders; bipolar disorder; anorexia nervosa; bulimia nervosa; prevalence **Ключевые слова:** расстройства пищевого поведения; биполярное расстройство; нервная анорексия; нервная булимия; распространённость

#### INTRODUCTION

Bipolar disorder (BD) is characterized by frequent comorbidity with other mental disorders [1]. The most common mental disorders that co-occur with BD include eating disorders (ED), obsessive-compulsive disorders (OCD), anxiety spectrum disorders, and substance use disorders [2]. Comorbid conditions in patients with BD often develop years before the onset of the first affective episodes. It is important to consider this fact in the process of diagnosis, therapy, and prognosis of the further course of the disease [2].

Comorbidity of BD with ED, such as anorexia nervosa (AN), bulimia nervosa (BN) and binge eating disorder (BED) deserves special attention. That is because these disorders exhibit certain similarities in their clinical presentations that are associated with eating behavior and emotional regulation. For instance, depression within the context of BD is characterized by a high frequency of atypical symptoms, such as increased appetite, overeating (hyperphagia), and weight gain [3]. These symptoms are also common for BN and BED, as patients often experience a feeling of guilt and symptoms of hypothymia after overeating [3]. Conversely, depression characterized by melancholic features and hypo-/ manic episodes is associated with decreased appetite and weight loss, although some patients with AN may experience improved mood or even euphoria during weight reduction [4–6]. Several clinical features distinguish the comorbid course of BD and ED, including a higher prevalence among females, an earlier age of the onset of mood disorder, a more severe course, a higher frequency of associated

disorders, and a higher rate of suicide attempts [7, 8]. An important aspect is the association between comorbid BD and ED with weight gain, obesity, metabolic syndrome, and type 2 diabetes, which cannot be fully explained by the influence of psychotropic medication [9, 10].

The high comorbidity of ED and BD can be explained by their shared biological mechanisms of development. In particular, it has been suggested that ED and BD share similar genomic regions which are involved in the processes of neurodevelopment and neuroprotection [8,11,12]. Also, certain neuroendocrine changes common to ED and BD for example, in the system of peptide hormones such as leptin and ghrelin — were found to be associated with changes in appetite and body weight, increasing the risk of obesity [13, 14].

Despite the observed acceleration in research on the comorbidity of ED and BD, scientific data on the comorbidity of these disorders remain poorly systematized. This is associated with the heterogeneity of the research methods used and the changes that have occurred in the classifications of mental disorders: in particular, the division of BD into types I and II, as well as the identification of BED as a new diagnostic category. Furthermore, one of the most significant developments in psychiatry involves the examining of the manifestations of comorbidity between ED and BD among males, as ED cannot be considered as a "purely female illness" and has also been found in males.

Thus, the aim of this study was to conduct a scoping review of published data on the prevalence of various types of EDs among patients with BD types I and II, in the context of the sex and clinical features of the concurrent course of these disorders.

#### **METHODS**

#### Search strategy

The review was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews (PRISMA-ScR) [15, 16]. The MEDLINE electronic database was searched between January 1994 and September 2022 using the following keywords: ("Bipolar disorder" OR "bipolar affective disorder" OR "bipolar depression" OR "mania" OR "hypomania") AND ("eating disorders" OR "anorexia nervosa" OR "bulimia nervosa" OR "binge eating disorders") AND ("prevalence" OR "frequency" OR "comorbidity" OR "clinical features"). The indicated timeframe was chosen because the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV), was released in 1994, describing BD type II and BED for the first time.

#### **Eligibility criteria**

The inclusion criteria were as follows: (1) original studies that included samples of patients diagnosed with BD or BD type I or II; (2) original studies that included samples of patients diagnosed with AN, BN, BED, and unspecified ED; and (3) the DSM-IV, DSM-5 or ICD-10 diagnostic criteria were used to diagnose ED and BD.

Studies were not eligible if they included participants diagnosed with major depressive disorder, depressive episodes, dysthymia, and schizophrenia spectrum disorders. Studies that pre-selected patients with BD and comorbid ED were also excluded due to the risk of inflated results.

#### **Review strategy**

The following data was extracted from the included articles: title, authors, year of publication, country, type of study, diagnostic tools, absolute and relative frequencies of ED prevalence in patients with BD and BD prevalence in ED patients stratified by sex and previously described types of these disorders. Data extracted independently by one author (YYV) and validated by the other two review authors (KED and MGE).

#### **Data synthesis**

The analytical technique used for this review involved a descriptive analysis of the included studies. Firstly, we selected the absolute and relative frequencies of various ED in patients with BD (types I and II) and vice versa. Secondly, we extracted the absolute and relative frequencies of ED and BD in males and females. The relative frequencies (%) were calculated based on the total number of patients if the original articles provided only absolute frequencies. Additionally, the relative frequencies were calculated for the following groups of participants: "any BD" including patients with BD types I and II and "any ED" including at least AN and BN or all three previously described forms of ED. Based on the obtained data, we assessed the lifetime prevalence and current prevalence. Lifetime prevalence refers to the prevalence of a disorder over the course of a lifetime. Current prevalence refers to the prevalence of a disorder at the present moment. The statistical significance of the differences was not analyzed when comparing the prevalence among different groups. Therefore, the results only represent nominal differences in relative frequencies.

## RESULTS

Out of the 514 publications obtained through the database searches, 49 met the inclusion criteria. After reading the full-text articles, the final qualitative analysis included 41 original studies [7,8,17–59]. Firstly, the results of a systematic review and meta-analysis will be analyzed. This will be followed by the analysis of original studies included in the review.

#### Systematic reviews and meta-analyses

A systematic review and meta-analysis by Fornaro M. et al. included 36 studies, involving 15,084 patients diagnosed with BD and 11 studies, involving 15,146 patients diagnosed with different types of ED [17]. The results of the metaanalysis showed that the prevalence of AN stood at 3.8% (95% CI=2-6%), BN - 7.4% (95% CI=6-10%), and BED - 12.5% (95% CI=9.4–16.6%) among patients with BD as a primary diagnosis [17]. At the same time, the prevalence of BD stood at 2% (95% CI=1-2%), BN - 6.7% (95% CI=12-29.2%), and BED — 9.1% (95% CI=3.3-22.6%) across patients primarily diagnosed with AN. It was suggested that patients with BD type II were more likely to have any comorbid ED [17]. Although the same trend was observed for AN and BED, it was not reported for BN, which was more often detected in patients with BD type I [17]. Comorbid BD and AN were more often encountered among females and patients of younger age [17]. Patients with comorbid BD and BN/BED were also more likely to be female and more often suffered from obesity [17]. The authors also noted that the higher the proportion of patients with BD taking antidepressants, the lower the comorbidity with BN was [17].

According to a systematic review by Álvarez Ruiz EM. et al. in 2015, which included 93 studies, the prevalence rates of ED among patients diagnosed with BD ranged from 5.3% to 31% [18]. Comorbid ED in patients with BD was associated with an earlier onset of mood disorder (especially in the case of AN), more severe symptoms, a higher number of affective episodes (particularly depressive episodes), an increased risk of suicide, as well as an increased number of comorbid conditions (especially substance use disorders and anxiety disorders) and obesity compared to noncomorbid BD [18]. In addition, a negative correlation was found between the prevalence of ED and the male sex and participants with a partner [18].

According to another systematic review (McDonald CE. et al., 2019), including 39 studies and involving patients with BD, the prevalence of any ED among patients diagnosed with BD ranged from 1.9% to 33.3% [19]. Lifetime prevalence and current prevalence of AN in patients with BD ranged from 0.2% to 15.5%, BN — from 0.01% to 15% and BED from 2.6% to 30.0% [19]. In four out of six studies, alcohol use disorder and mood instability were more common among patients with comorbid BD and ED compared to patients diagnosed with BD alone [19]. Five out of nine studies reported significantly higher rates of suicide attempts in patients with comorbid BD and ED compared with patients diagnosed with BD alone, which may indicate increased hidden impulsivity and emotional dysfunction [19]. The sub-group analysis results, including that of five studies, indicate that the frequency of comorbid ED is comparable between BD types I and II [19].

Data from another systematic review by Thiebaut S. et al. in 2019, including 79 studies (six studies included the general population, 34 studies included patients with BD and 39 studies included patients with ED), showed that from 0.6% to 33.3% of patients primarily diagnosed with BD had concomitant ED [20]. Conversely, up to 35.8% of patients primarily diagnosed with ED had concomitant BD [20]. More commonly, patients with BD had a bingeeating/purging type of AN, BN, and BED [20]. The association with BD was less significant in restrictive AN compared to other EDs [20]. While the age of BD manifestation was lower in the case of comorbid ED, the age of ED manifestation appeared to be independent of the presence of comorbid BD [20]. In addition, the prevalence of ED did not depend on the type of BD [20].

# Original studies on the comorbidity of ED and BD

Out of 41 original studies included in the current review, 33 aimed to determine the prevalence of ED in patients with BD and eight studies focused on the prevalence of BD in patients with ED (see Table 1 and Table 2). The studies presented were heterogeneous in terms of the adopted methods, including the type of prevalence (current or lifetime) and diagnostic tools. Out of the 33 studies, 25 presented a lifetime ED prevalence. The lowest lifetime prevalence of any ED among BD patients was reported by Berkol TD. et al. and accounted for 2.2% [27], and the highest value was reported in the study by Fornaro M. et al. and accounted for 31.1% [41]. The highest current prevalence of ED among patients with BD was slightly lower, reaching 26.6% [26]. The lifetime prevalence of AN among patients with BD ranged from 0.6% to 15.5%; BN, from 1.8% to 19.5%; and BED, from 2.3% to 28.8%. The prevalence of comorbid AN and BN among patients with BD was presented in one study by Balzafiore D.R. et al. and amounted to 13% [23].

The influence of sex on the prevalence of ED among patients diagnosed with BD was studied in 10 studies. The lifetime prevalence of any type of ED was nominally higher among females than it was among males with BD (see Table 1). In 10 studies, the lifetime prevalence of ED stratified by sex was examined among patients with BD. The overall lifetime prevalence of any type of ED was nominally higher among females than it was among males with BD (see Table 1). In eight studies, the lifetime prevalence of ED was studied as dependent on the types of BD. In particular, seven studies reported nominally higher rates of ED throughout life among patients with BD type II compared to patients with BD type I [23, 25, 29, 31, 40, 43, 49]. In eight studies, the lifetime prevalence of ED was examined based on the BD subtypes. Among them, seven studies reported nominally higher rates of lifetime ED among patients with BD type II compared to those with BD type I [23, 25, 29, 31, 40, 43, 49].

	Country	Type of study	Diagnostic methods	Type of prevalence	Type of	Prevalence of	Prevalence of ED			
Reference					ED	Total	by BD type (I/II)	by sex (female/male)		
			DIGS, DSM-IV	Lifetime	Any ED	10.3% ( <i>n</i> =14)	NA	NA		
Lee Y et al., 2022 [21]	South Korea	Cross-sectional			AN	1.5% ( <i>n</i> =2)	NA	NA		
2022 [21]	Nored				BN	8.8% ( <i>n</i> =12)	NA	NA		
Karanti A et al.,	Sweden	Cross sastional	MINI, DSM-IV	NA		2.10((n-1.96))	1.2% ( <i>n</i> =57)	NA		
2019 [22]	Sweden	Cross-sectional			Any ED	2.1% ( <i>n</i> =186)	3.3% ( <i>n</i> =129)	NA .		
					Any ED	15.1% ( <i>n</i> =76)	14% ( <i>n</i> =34)	22.5% ( <i>n</i> =66)		
					AnyED	13.1% (//-/0)	16% ( <i>n</i> =42)	4.7% ( <i>n</i> =10)		
Balzafiore DR	USA	Prospective	SCID-IV,	Lifetime	AN	3.3% ( <i>n</i> =17)	NA	NA		
et al., 2017 [23]	034	FIOSPECTIVE	MINI, DSM-IV	Liteunie	BN	6.5% ( <i>n</i> =33)	NA	NA		
					AN+BN	13% ( <i>n</i> =10)	NA	NA		
					ED NOS	21% ( <i>n</i> =16)	NA	NA		
Bobo WV et al.,	USA	Cross-sectional	SCID, DSM-IV	Lifetime	BN	14.3% ( <i>n</i> =210)	NA	NA		
2018 [24]	034	CI033-Sectional	300, 03101-10		BED	20.5% ( <i>n</i> =301)	NA	NA		
Boulanger H.	France	Cross-sectional	SCID, DSM-	Lifetime	BED	18.6% ( <i>n</i> =27)	15.1% ( <i>n</i> =13)	24.3% ( <i>n</i> =20)		
et al., 2017 [25]	Trance	CI033-Sectional	IV, BES	Liteume	BLD	18.0% (11-27)	23% ( <i>n</i> =14)	11.1% ( <i>n</i> =7)		
	USA	Cross-sectional	SCID, EDDS, DSM-IV, DSM-5	Current	Any ED	26.6%, ( <i>n</i> =291)	24.7% ( <i>n</i> =173)	31.5% ( <i>n</i> =214)		
							30% ( <i>n</i> =118)	18.5% ( <i>n</i> =77)		
					AN BN	0.2% (n=2) 14.7% (n=160)	0% ( <i>n</i> =0)	0.3% ( <i>n</i> =2)		
McElroy SL							0.5% ( <i>n</i> =2)	0% ( <i>n</i> =0)		
et al., 2016 [26]							14% ( <i>n</i> =98)	17.5% ( <i>n</i> =119)		
							15.7% ( <i>n</i> =62)	9.9% ( <i>n</i> =41)		
					BED	11.8% ( <i>n</i> =129)	10.7% ( <i>n</i> =75)	13.7% ( <i>n</i> =93)		
							13.7% ( <i>n</i> =54)	8.6% ( <i>n</i> =36)		
Berkol TD et al., 2016 [27]	Turkey	Cross-sectional	SCID, DSM-IV	Lifetime	Any ED	2.2% ( <i>n</i> =5)	NA	NA		
Holtzman JN				Lifetime		15 10/ (= 76)		22.5% ( <i>n</i> =66)		
et al., 2016 [28]	USA	Cross-sectional	SCID, DSM-IV	Lifetime	Any ED	15.1% ( <i>n</i> =76)	NA	4.8% ( <i>n</i> =10)		
Goffin KC et al.,	USA		SCID, DSM-IV	Lifetime	Any ED	15.40((n-76))	14,2% ( <i>n</i> =34)	NA		
2016 [29]	USA	Cross-sectional	300, 03101-10	Lifetime	AnyED	15.4% ( <i>n</i> =76)	16,5% ( <i>n</i> =42)	/vA		
Woldeyohannes HO et al., 2015 [30]	Canada	Cross-sectional	MINI, DSM-5	Current	BED	25.4% ( <i>n</i> =78)	NA	NA		
			DIGS, DSM-IV	Current/NA	Any ED	8.4% ( <i>n</i> =184)	NA	12.3% ( <i>n</i> =158) 2.9% ( <i>n</i> =26)		
Liu X et al., 2015 [8]	USA	Cross-sectional			AN	3% ( <i>n</i> =66)	NA	NA		
2013[0]					BN	5% ( <i>n</i> =109)	NA	NA		
					ED NOS	0.4% ( <i>n</i> =9)	NA	NA		

Table 1 The provalence of EF	among patients with PD	according to sex and type of BD
Table 1. The prevalence of EL	among datients with DD	

	Country	ry Type of study	Diagnostic methods	Type of prevalence	Type of ED	Prevalence of ED			
Reference						Total	by BD type (I/II)	by sex (female/male)	
				Lifetime	Any ED	704 (n=20)	6.3% ( <i>n</i> =14)	9% ( <i>n</i> =25)	
					AllyED	7% ( <i>n</i> =29)	7.7% ( <i>n</i> =15)	2.9% ( <i>n</i> =4)	
Baek JH et al.,	South	Cross-sectional	SCID, DIGS,		AN	1% ( <i>n</i> =4)	0.9% ( <i>n</i> =2)	1.4% ( <i>n</i> =4)	
2014 [31]	Korea	CI033-Sectional	DSM-IV	Liteunie		170 (77-4)	1% ( <i>n</i> =2)	0% ( <i>n</i> =0)	
					BN	6% ( <i>n</i> =25)	5.4% ( <i>n</i> =12)	7.5% ( <i>n</i> =21)	
						070(11-23)	6.7% ( <i>n</i> =13)	2.9% ( <i>n</i> =4)	
				Lifetime	Any ED	9.5% ( <i>n</i> =46)	NA	NA	
Nery FG., et al	Brazil	Cross-sectional	SCID, DSM-IV		AN	2.5% ( <i>n</i> =12)	NA	NA	
2014 [32]	DI dZII	Closs-sectional	500, 0510110	Lifetime	BN	4.8% ( <i>n</i> =23)	NA	NA	
					BED	2.3% ( <i>n</i> =11)	NA	NA	
McElroy SL et al., 2013 [33]	USA	Cross-sectional	SCID, DSM-IV	Current	BED	9.5% ( <i>n</i> =68)	NA	NA	
						4.5% (= 0)	4.5% ( <i>n</i> =9)	A/A	
Perugi G et al.,				<i>c</i> ,	Any ED	4.5% ( <i>n</i> =9)	NA	NA	
2013 [34]	Italy	Cross-sectional	MINI, DSM-IV	Current	AN	1.5% ( <i>n</i> =3)	NA	NA	
					BN	3% ( <i>n</i> =6)	NA	NA	
					A	10.20( (= 200)	18.3% ( <i>n</i> =200)	28.9% ( <i>n</i> =182)	
		Cross-sectional			Any ED	18.3% ( <i>n</i> =200)	NA	3.9% ( <i>n</i> =18)	
Azorin JM et al.,	France					4.70( (		7.3% ( <i>n</i> =46)	
2013 [35]			SCID, DSM-IV	Lifetime	AN	4.7% ( <i>n</i> =51)	NA	1.1% ( <i>n</i> =5)	
						13.7% ( <i>n</i> =149)		21.7% ( <i>n</i> =136)	
					BN		NA	2.8% ( <i>n</i> =13)	
					Any ED	10.8% ( <i>n</i> =18)	NA	NA	
Gao K et al., 2013 [36]	USA	Cross-sectional	MINI-STEP- BD, DSM-IV	Lifetime	AN	0.6% ( <i>n</i> =1)	NA	NA	
2013 [30]					BN	10.2% ( <i>n</i> =17)	NA	NA	
	Brazil					5.3% ( <i>n</i> =19) 2.2% ( <i>n</i> =8)	NA NA	7.2% ( <i>n</i> =18)	
					Any ED			0.9% ( <i>n</i> =1)	
Seixas C et al.,				Lifetime				3.2% ( <i>n</i> =8)	
2012 [37]		Cross-sectional	SCID, DSM-IV		AN			0% ( <i>n</i> =0)	
					BN	3% ( <i>n</i> =11)	NA	4% ( <i>n</i> =10)	
								0.9% ( <i>n</i> =1)	
						44.20( (	14.4% ( <i>n</i> =102)	21% ( <i>n</i> =104)	
					Any ED	14.3% ( <i>n</i> =125)	13.7% ( <i>n</i> =23)	5.5% ( <i>n</i> =21)	
						2 4 9 ( / 27)	2.8% ( <i>n</i> =20)	4.5% ( <i>n</i> =27)	
McElroy SL					AN	N 3.1% ( <i>n</i> =27)	3.1% ( <i>n</i> =7)	0% ( <i>n</i> =0)	
et al., 2011 [7]	USA	Cross-sectional	SCID, DSM-IV	Lifetime	DN		4.7% ( <i>n</i> =33)	7.5% ( <i>n</i> =37)	
					BN	4.8% ( <i>n</i> =42)	5.4% ( <i>n</i> =9)	1.3% ( <i>n</i> =5)	
						0.00( (	8.9% ( <i>n</i> =63)	12.3% ( <i>n</i> =61)	
					BED	8.8% ( <i>n</i> =77)	8.9% ( <i>n</i> =14)	4.2% ( <i>n</i> =16)	
Schoofs N et al.								28.8% ( <i>n</i> =15)	
2011 [38]	Germany	Prospective	DSM-IV	Lifetime	BED	28.8% ( <i>n</i> =15)	NA	0% ( <i>n</i> =0)	
						44.000	14.6% ( <i>n</i> =20)	14.6% ( <i>n</i> =20)	
					Any ED	ED 14.6% ( <i>n</i> =20)	NA	NA	
Brietzke E et al.,	Brazil	Cross-sectional	SCID, DSM-IV	Lifetime	AN	2.9% ( <i>n</i> =4)	NA	NA	
2011 [39]					BN	2.9% ( <i>n</i> =4)	NA	NA	
					BED	8.7% ( <i>n</i> =12)	NA	NA	
Baek JH et al.,	South						8.7% ( <i>n</i> =6)		
2010 [40]	Korea	Cross-sectional	DIGS, DSM-IV	Lifetime	Any ED	14.3% ( <i>n</i> =15)	27.3% ( <i>n</i> =9)	NA	

	Country	y Type of study		Type of prevalence	Type of ED	Prevalence of ED			
Reference						Total	by BD type (I/II)	by sex (female/male)	
						21.10(n-46)		31.1% ( <i>n</i> =46)	
					Any ED	31.1% ( <i>n</i> =46)	NA	NA	
Fornaro M					AN	15.5% ( <i>n</i> =23)	NA	NA	
et al., 2009 [41]	Italy	Cross-sectional	SCID, DSM-IV	Lifetime	BN	5.4% ( <i>n</i> =8)	NA	NA	
					AN+BN	2% ( <i>n</i> =3)	NA	NA	
					BED	14.2% ( <i>n</i> =21)	NA	NA	
								24.5% ( <i>n</i> =13)	
					Any ED	21% ( <i>n</i> =17)	NA	14.3% ( <i>n</i> =4)	
								11.3% ( <i>n</i> =6)	
					AN	7.4% ( <i>n</i> =6)	NA	0% ( <i>n</i> =0)	
Wildes JE et al.,								9.4% ( <i>n</i> =5)	
2008 [42]	USA	Cross-sectional	DSM-IV	Lifetime	BN	8.6% ( <i>n</i> =7)	NA	7.1% ( <i>n</i> =2)	
								3.8% ( <i>n</i> =2)	
					AN+BN	2.5% ( <i>n</i> =2)	NA	0% ( <i>n</i> =0)	
								13.2% ( <i>n</i> =7)	
					BED	11.1% ( <i>n</i> =9)	NA	7.1% ( <i>n</i> =2)	
Perugi G et al.,			SCID, DSM-				0% ( <i>n</i> =0)		
2006 [43]	Italy Cross-sectional IV, DSM III-R Lifetime BN 19.5% (n=16	19.5% ( <i>n</i> =16)	19.8 % ( <i>n</i> =16)	NA					
	Israel	Cross-sectional	SCID, DSM-IV	Lifetime	Any ED	14.3% ( <i>n</i> =8)	NA	NA	
Pashinian A					AN	1.8% ( <i>n</i> =1)	NA	NA	
et al., 2006 [44]					BN	1.8% ( <i>n</i> =1)	NA	NA	
					BED	10.7% ( <i>n</i> =6)	NA	NA	
	Italy		SCID, DSM-IV	Lifetime	BN	9.8% ( <i>n</i> =5)	NA	22.7% ( <i>n</i> =5)	
Ramacciotti CE								0% ( <i>n</i> =0)	
et al., 2005 [45]		Cross-sectional			BED	17.7% ( <i>n</i> =9)	NA	13.6% ( <i>n</i> =3)	
								20.7% ( <i>n</i> =6)	
Baldassano CF							5.7% ( <i>n</i> =21)	11.6% ( <i>n</i> =33)	
et al., 2005 [46]	USA	Cross-sectional	MINI, DSM-IV	Current	BN	7.5% ( <i>n</i> =36)	13.1% ( <i>n</i> =15)	1.5% ( <i>n</i> =3)	
					Any ED	18.1% ( <i>n</i> =25)	NA	NA	
MacQueen GM	Canada			Current	AN	2.9% ( <i>n</i> =4)	NA	NA	
et al., 2003 [47]		nada Prospective	SCID, DSM-IV		BN	6.5% ( <i>n</i> =9)	NA	NA	
					BED	8.7% ( <i>n</i> =12)	NA	NA	
Vieta E et al.,			SCID, DSM		525		2.3% (n=3)	NA	
2001 [48]	Spain	Cross-sectional	III-R	Lifetime	BN	2.3% ( <i>n</i> =3)	NA		
				Lifetime		ED 5.9% ( <i>n</i> =17) 2.1% ( <i>n</i> =6)	4.6% ( <i>n</i> =11)		
					Any ED		12.2% ( <i>n</i> =6)	NA	
							1.7% ( <i>n</i> =4)		
McElroy SL et al., 2001 [49]	USA	Cross-sectional	SCID, DSM-IV		AN		4.1% ( <i>n</i> =2)	NA	
						N 3.8% ( <i>n</i> =11)	3.3% ( <i>n</i> =8)		
					BN		6.1% ( <i>n</i> =3)	NA	
					Any ED	6.4% ( <i>n</i> =8)	NA	NA	
Pini S et al.,	Italy	Cross-sectional	SCID, DSM- III-R	Lifetime	AN	2.4% ( <i>n</i> =3)	NA	NA	
1999 [50]	licity	ly Cross-sectional			BN	4% ( <i>n</i> =5)	NA	NA	
Edmonds LK	New								
et al., 1998 [51]	Zealand	Cross-sectional	DIGS, DSM-IV	Lifetime	Any ED	7.2% ( <i>n</i> =4)	NA	NA	

*Note: NA* — not available, BES — Binge Eating Scale, DIGS — Diagnostic Interview for Genetic Studies, DSM — Diagnostic and Statistical Manual of mental disorders, EDDS — Eating Disorder Diagnostic Scale, MINI — Mini International Neuropsychiatric Interview, MINI-STEP-BD — Mini International Neuropsychiatric Interview Systematic Treatment Enhancement Program for Bipolar Disorder version 5.0.0, SCID — Structured Clinical Interview for DSM.

A separate analysis was conducted to examine the prevalence of BD among patients with ED (Table 2). The lowest lifetime prevalence of BD among patients with ED was reported by Radon L et al. and amounted to 11.3% [52], whereas the highest rate was reported in the study by Campos R.N. et al. and accounted for 68.1% [58]. In three out of five studies that additionally analyzed the type of BD in patients with ED, a nominally higher prevalence of BD type II in patients with ED was revealed compared to patients without ED. The prevalence of BD type I among patients with AN ranged from 0.7% to 7.7%; among patients with BN, from 1.9% to 7.7%; and among patients

with BED, from 1.1% to 6%. In turn, the prevalence of BD type II among patients with AN ranged from 1% to 2.6%; among patients with BN, from 1.1% to 9.3%; and among patients with BED, from 0.7% to 7%. The only study that attempted to determine the current prevalence of BD in patients with ED showed paradoxically high rates amounting to 41.4% for any BD, 17.2% for BD type I, and 24.2% for BD type II [54]. The paradox is that current prevalence rates are usually lower than lifetime prevalence, which again highlights the issue of heterogeneity in research methodology. The stratification by sex was conducted only in two studies and showed contradictory results [54, 55].

		Type of study	Diagnostic methods	Type of prevalence	Type of BD	Prevalence of BD		
Reference	Country					Total	by ED type (AN/BN/ ED/ BED/ NOS)	by sex (female/ male)
Radon L et al., 2022 [52]	France	Cross-sectional	Short-CIDI, DSM-5	Lifetime	Any BD	11.3% ( <i>n</i> =20)	NA	NA
							3.5% ( <i>n</i> =9)	11 = 0((n-20))
					Any BD	11.5%	4.2% ( <i>n</i> =11)	11.5% ( <i>n</i> =30)
					ANY BD	( <i>n</i> =30)	1.9% ( <i>n</i> =5)	NA
							1,9% ( <i>n</i> =5)	IVA
							0.7% ( <i>n</i> =2)	4.60(n=12)
Thiebaut S	Franco	Creas costional	Medical records, MINI, DSM-5	Lifetime	BD l type	4.6% ( <i>n</i> =12)	1.9% ( <i>n</i> =5)	4.6% ( <i>n</i> =12)
et al., 2019 [53]	France	Cross-sectional		Lifetime			1.1% ( <i>n</i> =3)	NA
							0.7% ( <i>n</i> =2)	
					BD ll type	6.9% ( <i>n</i> =18)	2.6% ( <i>n</i> =7)	6.9% ( <i>n</i> =18)
							2.3% ( <i>n</i> =6)	
							0.7% ( <i>n</i> =2)	
							1.1% ( <i>n</i> =3)	
					Any BD	41.4% ( <i>n</i> =94)	4% ( <i>n</i> =9)	65.4% ( <i>n</i> =77)
							18% ( <i>n</i> =41)	
							14.5% ( <i>n</i> =33)	
							4.8% ( <i>n</i> =11)	
						type 17.2% ( <i>n</i> =39)	2.2% ( <i>n</i> =5)	NA
Tseng MM	China	Cross-sectional	SCID, MINI,	Current	<b>DD</b> I trune		7% ( <i>n</i> =16)	
et al., 2017 [54]	China		DSM-5		BD l type		6.1% ( <i>n</i> =14)	
							1.7% ( <i>n</i> =4)	
							1.8% ( <i>n</i> =4)	
						l type 24.2% ( <i>n</i> =55)	11% ( <i>n</i> =25)	N/A
					BD II type		8.4% ( <i>n</i> =19)	NA
							3.1% ( <i>n</i> =7)	

		y Type of study	Diagnostic methods			Prevalence of	of BD	
Reference	Country			Type of prevalence	Type of BD	Total	by ED type (AN/BN/ ED/ BED/ NOS)	by sex (female/ male)
							3.1% ( <i>n</i> =9)	81.5% ( <i>n</i> =84)
					Apy BD	35.7%	15.6% ( <i>n</i> =45)	
					Any BD	( <i>n</i> =103)	12.9% ( <i>n</i> =37)	10 50/ (* 10)
							4,2% ( <i>n</i> =12)	18.5% ( <i>n</i> =19)
							2% ( <i>n</i> =6)	
Tseng MM	Taiwan	Cross-sectional	SCID, DSM-IV	Lifetime	BD l type	16% ( <i>n</i> =46)	6.2% ( <i>n</i> =18)	NA
et al., 2016 [55]	raiwan	cross-sectional		Lifetime	bbitype	1070 (77-40)	6% ( <i>n</i> =17)	
							1.7% ( <i>n</i> =5)	
							1% ( <i>n</i> =3)	
					BD II type	19.7%	9.3% ( <i>n</i> =27)	NA
					выптурс	( <i>n</i> =57)	7% ( <i>n</i> =20)	NA
							2.4% ( <i>n</i> =7)	
		len Prospective		Lifetime	Any BD	4.1% ( <i>n</i> =35)	NA	NA
Welch E et al.,	Sweden		DSM-IV				NA	
2016 [56]	Sweden						4.1% ( <i>n</i> =35)	
							NA	
					Any BD	18% (n=49)	9.2% ( <i>n</i> =25)	<ul> <li>18% (n=49)</li> <li>NA</li> <li>15.5% (n=42)</li> <li>NA</li> </ul>
	France						8.8% ( <i>n</i> =24)	
							NA	
							NA	
					BD l type	15.5% ( <i>n</i> =42)	7.7% ( <i>n</i> =21)	
Godart N et al.,		Cross-sectional	MINI, DSM-IV	Lifetime			7.7% ( <i>n</i> =21)	
2015 [57]							NA	
							NA	
						2.5% (n=7)	1.4% ( <i>n</i> =4)	2.5% ( <i>n</i> =7)
							1.1% ( <i>n</i> =3)	
					BD II type		NA	NA
							NA	
					Any BD	68.1% ( <i>n=</i> 47)	NA	68.1% ( <i>n</i> =47)
			SCID, DSM-IV,			68.1% ( <i>n</i> =4/)		NA
Campos RN	Brazil	Cross-sectional	Zurich criteria for bipolar	Lifetime	BD I type	26% (n=18)	NA	26% ( <i>n</i> =18)
et al., 2013 [58]	Diazii	cross-sectional	spectrum	Lictime	bortype	e 26% ( <i>n</i> =18)		NA
			disorders		BD II type	D ll type 8.7% ( <i>n</i> =6)	NA	8.7% ( <i>n</i> =6)
					во п сурс			NA
		SA Cross-sectional	SCID, DSM-IV	Lifetime			NA	3.2% ( <i>n</i> =1)
Lilenfeld LR	USA				Any BD	3.2% ( <i>n</i> =1)	NA	5.2.70 (17-1)
et al., 2008 [59]	USA						3.2% (n=1)	NA
							NA	, ., .

*Note: NA* — not available, Short-CIDI — Composite International Diagnostic Interview Short, DSM — Diagnostic and Statistical Manual of mental disorders, MINI — Mini International Neuropsychiatric Interview, SCID — Structured Clinical Interview for DSM.

Table 3 summarizes the main clinical features and outcomes of the comorbid course of ED and BD, taking into account concomitant mental and somatic disorders and various complications. It is noteworthy that the presence of ED in patients with BD was associated with indicators of a more severe clinical course of the disease, suicidal attempts, and a higher frequency of comorbid mental disorders (in particular, OCD and anxiety disorders). In addition, patients with comorbid ED and BD were more likely to exhibit symptoms of atypical depression, such as mood reactivity and increased appetite and interpersonal sensitivity, which commonly manifest themselves during the course of bipolar depression [63].

Features	Trait	Reference			
	Mood instability	Boulanger H et al., 2018 [25]			
	Increased appetite	Perugi G et al., 2006 [43]			
	Mood reactivity	Perugi G et al., 2006 [43]; Boulanger H et al., 2018 [25]			
Clinical symptoms	Impulsivity	Boulanger H et al., 2018 [25]; Berkol TD et al., 2016 [27] Tseng MM et al., 2017 [54]; Tseng MM et al., 2016 [55]			
	Social isolation	Perugi G et al., 2006 [43]			
	Interpersonal sensitivity	Perugi G et al., 2006 [43]			
	OCD	Liu X et al., 2016 [8]; Radon L et al., 2022 [52] Tseng MM et al., 2016 [55]; Woldeyohannes HO et al., 2016 [30]			
Comparised disconderer	Addictions	Liu X et al., 2016 [8]; Balzafiore DR et al., 2017 [23] Boulanger H et al., 2018 [25]; Brietzke E et al., 2011 [39] Tseng MM et al., 2017 [54]; Tseng MM et al., 2016 [55] Thiebaut S et al., 2019 [53]; Woldeyohannes HO et al., 2016 [30]			
Comorbid disorders	Alcohol/Substance Abuse	Boulanger H et al., 2018 [25]; Tseng MM et al., 2017 [54]			
	PTSD	Woldeyohannes HO et al., 2016 [30]			
	Hyperlipidemia	McAulay C et al., 2021 [60]			
	Type 2 diabetes	McAulay C et al., 2021 [60]			
	Early onset of mood disorder	Anna V et al., 2009 [78]; McElroy SL et al., 2011 [7] Liu X et al., 2016 [8]; Balzafiore DR et al., 2017 [23] McElroy SL et al., 2001 [49]; Brietzke E et al., 2011 [39]			
Course	Large number of depressive episodes	Anna V et al., 2009 [78]; Wildes JE et al., 2007 [12] Brietzke E et al., 2011 [39]			
	Fast cycling	McElroy SL et al., 2011 [7]; Fornaro M et al., 2010 [41] Liu X et al., 2016 [8]; Balzafiore DR et al., 2017 [23] McElroy SL et al., 2001 [49]; Seixas C et al., 2012 [37]			
	Suicidal attempts	McElroy SL et al., 2011 [7]; McElroy SL et al., 2016 [26]; McElroy SL et al., 2013 [33]; Liu X et al., 2016 [8] Balzafiore DR et al., 2017 [23]; Berkol TD et al., 2016 [27] Brietzke E et al., 2011 [39]; Thiebaut S et al., 2019 [53] Tseng MM et al., 2017 [54]; Tseng MM et al., 2016 [55] Seixas C et al., 2012 [37]; Goffin KC et al., 2016 [29] Woldeyohannes HO et al., 2016 [30]			
Complications	Increased weight/High BMI	McElroy SL et al., 2016 [26]; Fornaro M et al., 2010 [41] Perugi G et al., 2006 [43]; McElroy SL et al., 2011 [7] Wildes JE et al., 2007 [12]; Tseng MM et al., 2017 [54] Tseng MM et al., 2016 [55]; McAulay C et al., 2021 [60] Wildes JE et al., 2008 [42]			
	Obesity	McElroy SL et al., 2016 [26]; McElroy SL et al., 2011 [7] Wildes JE et al., 2007 [12]; McElroy SL et al., 2013 [33] McAulay C et al., 2021 [60]; Wildes JE et al., 2008 [42]			

#### Table 3. Clinical features of the comorbid course of ED and BD

Note: OCD — obsessive compulsive disorder, PTSD — post-traumatic stress disorders, BMI — Body Mass Index.

### DISCUSSION

#### **Main results**

In this scoping review, an analysis of four systematic reviews and 41 original studies was conducted, focusing on the prevalence of various types of EDs among patients with BD types I and II under the prism of sex and the clinical features of the concurrent course of these disorders. Based on the study findings, it emerged that the prevalence rates of ED among individuals diagnosed with BD reached a substantial 60%. The concurrent course of BD and ED was associated with a poorer prognosis, higher rates of suicidal ideation and attempts, a burden of comorbid disorders, higher body mass index (BMI), obesity, and metabolic dysfunctions.

#### Strengths and limitations of the study

The strengths of this review include the examination of the prevalence of ED in different types of BD and vice versa. We also paid special attention to the prevalence of these disorders based on sex. Studying the diagnostic instruments used in the original studies allowed us to clarify the type of prevalence and diagnostic features of BD and ED.

The limitations of this review are related to the broad inclusion criteria, resulting in heterogeneity in the considered clinical forms of ED and BD. Firstly, not all studies have specified types of ED and BD, even though associations between different types of these disorders can vary widely. Secondly, data on the lifetime prevalence of ED and BD remains limited due to inconsistencies in diagnostic criteria and studied symptoms, making it difficult to provide definitive conclusions. Third, the original studies included in the current scoping review and the studies included in the systematic reviews may overlap. Finally, the presence of therapy could have influenced the current prevalence rates, which could have influenced the results of the current review.

#### **Comparison with the existing literature**

Despite the high volatility in the results, the prevalence rates of the co-occurrence of ED and BD were found to be quite high (up to 60%) and significantly exceeded the prevalence of these disorders in the general population, which aligns with the findings of earlier systematic reviews [17-20]. Although data on the ED frequency among patients with BD types I and II showed conflicting results, in the study by Fornaro M. et al., the prevalence of ED was slightly higher in patients with BD II compared to BD I [17]. This finding may be explained by sex disparities in the prevalence of BD itself: BD type I is equally prevalent in males and females, while the prevalence of BD type II among females. is almost twice as high as that among males [61]. In our scoping review, a higher prevalence of ED was found in females with BD compared to males. However, the prevalence rates of ED in males with BD followed the same trajectory as that among females and were higher than those in the general population [62], indicating a greater vulnerability of patients with BD to developing comorbid ED. Furthermore, no study has examined the patterns of comorbidity between different types of ED and BD stratified by sex, which might have to do with the issue of multiple comparisons with small sample sizes. The association between ED and BD is also explained by their similarities in phenomenology: both disorders are characterized by distortions in eating behavior and emotional regulation [64]. These similarities will be discussed below in the light of the existing findings.

To start with, patients with ED and BD have high rates of suicidality and self-harm [65, 66]. In particular, AN is associated with a higher level of suicides and BN is associated with a large number of suicidal thoughts and suicide attempts [65, 66]. Another important predictor of a complicated course of comorbid ED and BD is BMI. Patients with comorbid BD and BED frequently suffer from obesity [9, 67, 68]. It is known that a common characteristic of both ED and BD is dysregulated eating, which is significantly associated with episodes of binge eating [64]. It is interesting to note that many patients with ED report binge eating in an attempt to improve their mood, as binge eating can temporarily reduce anxiety and depressive symptoms [69]. Patients with BD type II often try to improve their low mood with food, alcohol, drugs, exercise, and sexual activity [69]. However, nutritional dysregulation is a characteristic not only of the depressive phases of BD, but also of hypomania [70]. Thus, patients with hypomanic symptoms demonstrate more chaotic and irregular eating patterns, which correlate with the severity of hypomanic symptoms [70].

According to the systematic review by Yuhan Karida Liu at al., the prevalence of overall obesity among patients with BD (BMI  $\geq$  30 kg/m<sup>2</sup>) was 29.0% (95% CI=22.8–35.6%), which is significantly higher than that in the healthy control group [71]. In addition, patients with BD have a higher level of obesity (41.4%) compared with patients without this disorder (27.1%), as well as significantly higher triglyceride levels and lower high-density lipoprotein [72]. There are studies showing that the risk of obesity in patients with BD precedes medication intake, which raises doubts about the influence of a medication alone on the weight gain. Furthermore, initial episodes of binge eating predict weight gain associated with medication intake [73].

In addition to clinical studies, there is a small number of family and genetic research studies examining the relationship between ED and BD. For instance, several studies have found a positive family history of mood disorders among patients with ED [74, 75]. It was also found that the prevalence of mood disorders among first-degree relatives in probands with AN and/or BN was higher than in probands with schizophrenia and borderline personality disorder but similar to the prevalence of affective disorders in patients with BD [76]. Some genetic studies also confirm the relationship between ED and BD: a genome-wide association study revealed a single nucleotide polymorphism within the SOX2-OT genes (rs4854912) with a secondary peak in the adjacent FXR1 gene (rs1805576) on chromosome 3q26.33 [8]. In another experimental study, strong associations between ED and BD were found while genotype and phenotype associations were analyzed based on the data from genome-wide association studies [77]. Therefore, it can be assumed that ED and BD have a common, albeit still poorly understood, pathophysiological basis.

Furthermore, the comorbidity of ED and BD complicates the selection of therapy, since the treatment of one disorder can worsen the symptoms of the other [78]. For example, in a patient with undiagnosed BD undergoing antidepressant therapy (including fluoxetine), a phase of inversion can occur, leading to the development of a mixed or hypo/ manic episode. Moreover, a number of mood stabilizers and antipsychotics are associated with an increase in body weight, which, in turn, can exacerbate the severity of eating disorders. In this context, it is important to ensure that neither of the syndromes worsens due to the chosen treatment, either directly or through side effects. The optimal treatment option may include pharmacological agents that will benefit both disorders by stabilizing the mood disorder and not adversely affecting eating behavior [79].

There are several studies that successfully used normothymic therapy for the treatment of ED [18, 80, 81]. In addition, some studies have observed that lithium supplementation in patients with affective disorder, mood instability, or impulsivity alleviated the symptoms of ED through more regular eating and the ability to diet [70, 82]. Thus, screening for ED is important in the context of BD (and vice versa), especially in the early stages of the disease, as it helps to determine further treatment tactics and improve clinical outcomes.

#### Implications for future research and practice

Particular attention in future studies should be given to the stratification of participants by age, since EDs usually manifest themselves earlier than mood disorders, which may increase the number of false-negative results in the diagnosis of BD. This, in turn, indicates that there is very little information in the literature about the chronological relationship between these disorders. Adopting a longitudinal design in studies exploring the comorbid course of ED and BD is also required in future research in order to identify patterns over the period of time.

#### CONCLUSION

According to the results of this scoping review, the prevalence rate of comorbid ED and BD amounts to 60%, which is significantly higher than the prevalence of these disorders in the general population. The comorbid course of BD and ED is associated with a poorer prognosis, higher rates of suicidal thoughts and attempts, a burden of comorbid disorders, higher BMI, obesity, and metabolic disruptions. Family and genetic research data confirm the association between these disorders. However, these results should be taken with caution due to the broad inclusion criteria used for this review, leading to heterogeneity in the considered clinical forms of ED and BD. Further research may need to determine the patterns of comorbidity between different types of ED and BD stratified by sex. Screening for ED in patients with BD, and vice versa, is important in designing appropriate treatment strategies and improving clinical outcomes.

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# OPINION

# Possible Role of Nutritionists in Multidisciplinary Teams Managing Patients with Eating Disorders in the Russian Federation

Перспектива включения нутрициолога в полипрофессиональную команду при работе с людьми с расстройствами пищевого поведения в Российской Федерации

doi: 10.17816/CP6136 Opinion

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# ABSTRACT

The goal of this publication was to weigh the benefits of including a nutritionist in a team of specialists managing patients with eating disorders (EDs). The article describes the professional status of nutritionists as of the first half of 2023, as well as their field of competence and limitations. The nutritionist is intended to play an auxiliary role in the team, primarily assisting the patient in following the recommendations of the attending physician(s). A nutritionist can also take preventive action by educating the population on the importance of good nutrition.

# аннотация

Цель публикации — показать возможные варианты включения нутрициолога в команду специалистов, которая работает с людьми с расстройствами пищевого поведения (РПП). В статье описывается статус профессии «нутрициолог» по состоянию на первую половину 2023 г., также обозначаются границы компетенции и ограничения специальности. Предполагаемая роль нутрициолога в команде будет вспомогательной, выражающейся в основном в помощи больному в выполнении рекомендаций лечащего врача/врачей. Также нутрициолог может осуществлять профилактическую деятельность, заключающуюся в информировании населения о важности полноценного питания.

# **Keywords:** eating disorders; nutritional science; nutritionist **Ключевые слова:** расстройства пищевого поведения; нутрициология; нутрициолог

No professional standards currently exist in the Russian Federation for nutritionists. At the same time, there are already specialists, and even professional organizations, who have chosen nutrition as their primary professional activity. The employees of the "Scientific Research Institute of Nutrition", representatives of the Russian Union of Nutritionists, Dietitians and Food Industry Specialists (RoSNDSPI), and members of the public association "Nutritionists of Russia" are actively working on a draft professional standard. Nutritional science studies food, nutrients, and other food ingredients, their actions and interactions, and their role in maintaining health or causing disease. This field of knowledge is actively developing; it includes the study of consumption, assimilation, transfer, utilization, and excretion of nutrients from the body. Nutritional science also studies people's motives for choosing food and how this choice affects their health<sup>1</sup>.

Nutritionists are specialists who help their clients adhere to the principles of rational nutrition. They can also engage in public education or scientific research and collaborate with other specialists: dietitians, gastroenterologists, endocrinologists, psychiatrists, psychologists, coaches, food technologists, etc.

Until the professional standard is adopted, nutritionists in their work rely on Federal Law No. 323-FZ of November 21, 2011 "On Public Health Protection in the Russian Federation" (Federal Law No. 323-FZ)<sup>2</sup>. This federal law defines what is considered medical service or intervention and what is not. Understanding this distinction is important, because a nutritionist is not a medical specialist. Therefore, nutritionists have no right to perform medical activities.

Nutritionists can rely on the Code of Professional Ethics of a Nutritionist of the Russian Federation, adopted by the Public Association "Nutritionists of Russia" (Code) <sup>3</sup>. This Code consists of nine articles and includes a preamble; knowledge of professional ethics; limitation of professional competence; limitation of the means used; professional development; respect for the client; maintaining confidentiality; scope of professional activity of a nutritionist; and issues not within the professional competence of a nutritionist, and Code violation.

According to the Code, nutritionists:

- introduce clients to the rules of healthy eating;
- inform their clients about the impact of a lack or excess of nutrients on their health;
- inform them about food groups that should be included in the daily diet;

- teach them how to analyze the information displayed by manufacturers on food products;
- analyze nutrition and perform anthropometric measurements;
- provide an example menu to their clients, while the clients choose specific products themselves;
- help them implement the recommendations of their attending physician, if any, in everyday life.<sup>3</sup>

Nutritionists must:

- work within their field of competence, based on their education and experience;
- increase their professional competence and awareness in the field of nutritional science and nutrition;
- respect their clients regardless of their social status, nationality, religion, affiliation, race, gender, age, sexual orientation, etc.;
- respect the principle of confidentiality.<sup>3</sup>

Nutritionists are not specialists in alternative medicine and cannot recommend dietary supplement regimens or "nutrition protocols" for the treatment of diseases, detoxification programs, fasting — including intermittent fasting — or exclusion of food groups. Nutritionists do not prescribe laboratory tests and do not interpret the results, nor do they prescribe or stop medications for their clients. Such actions would be not only a gross violation of the Code, but also a violation of the federal law.

In the Russian Federation there is a shortage of dietitians, with the number of doctors not covering the needs of the country's population. There is one doctor per 247,000 people, while the standard is one specialist per 25,000 citizens<sup>4</sup>. At the 17<sup>th</sup> All-Russian Congress of Dietitians and Nutritionists with international participation, Alla Pogozheva, deputy chief external dietitian of the Ministry of Health of Russia, voiced the need to increase their staff levels<sup>5</sup>.

The shortage of dietitians in the Russian Federation may lead to an increase in the prevalence of diet-induced

<sup>1</sup> Martinchik AN Maev IV, Yanushevich OO. General Nutritionology: A textbook. Moscow: MEDpress-inform; 2005. 392 p. Russian.

<sup>2</sup> Federal Law No. 323-FZ of November 21, 2011 "On Public Health Protection in the Russian Federation". Article 2. The basic concepts used in this Federal Law. Russian.

<sup>3</sup> The Code of Professional Ethics of the NGO "Nutritionists of Russia" of December 28, 2021. [Internet]. Forum of nutritionists of Russia. [cited 2023 May 15]. Available from: https://nutritiologists.ru/code-of-ethics. Russian.

<sup>4</sup> Russia's facing a dearth of dietologists [Internet]. Practical dietetics; 2011. [cited 2023 May 15]. Available from: https://www.praktik-dietolog.ru/ news/15.html. Russian.

<sup>5</sup> Belova I. [Lack of dietologists is still an issue in Russia]. Rossiiskaya gazeta [Internet]. 2018 Oct 29 [cited 2023 May 15]. Available from: https://rg.ru/2018/10/29/reg-cfo/v-rossii-poka-ne-udalos-ustranit-nehvatku-dietologov.html. Russian.

diseases and to a lack of proper understanding of rational nutrition by the population. The latter, in turn, may raise interest in "popular" diets and increase the total number of patients with eating disorders (EDs). In 2018, the Federal Statistics Service conducted a random survey of Russians' diet. According to published data, 48.8% of people aged 14 years and over reported one or more diseases (conditions) associated with nutrition<sup>6</sup>.

Order of the Ministry of Health of the Russian Federation No. 920n of November 15, 2012<sup>7</sup>, does not regulate the time for one patient appointment. According to the Regulation on the Organization of the Activities of a Dietitian (approved by Order of the Ministry of Health of the Russian Federation No. 330 of August 5, 2003, the duties of a dietitian, in addition to advising patients on therapeutic and rational nutrition, include:

- organizing therapeutic nutrition in healthcare institutions;
- monitoring catering departments, including preparing the necessary documents, ensuring the proper storage of food;
- · advising doctors on therapeutic nutrition;
- analyzing of therapeutic nutrition effectiveness;
- determining the list and size of food portions for patients in healthcare institutions;
- organizing advanced training of catering personnel on therapeutic nutrition;
- conducting sanitary and educational work on therapeutic and rational nutrition for employees of healthcare institutions, etc.<sup>8</sup>

Due to the limited time of any appointment, it may be difficult to discuss any strategy for introducing certain dietary habits and lifestyle modifications with the patient. This is where nutritionists intervene, working with clients to implement the doctor's prescriptions. The dietitian and nutritionist can work effectively in tandem, staying in touch and sharing information about the process and consultation summaries. For example, at the Fomin Clinic (KDF-Zapad LLC), a private health care center in Moscow, joint management of patients by the gastroenterologist-nutritionist tandem has already been established.

Due to the above-mentioned shortage of dietitians and their primary field of competence, nutritionists ought to focus on helping patients with EDs, in which a healthy diet plays a special role in therapy. According to the Code, if clients have a disease, they can only be managed with the permission of the attending physician (Article 2.4)<sup>3</sup>. Nutritionists help clients follow the principles of a rational, balanced diet and the recommendations of the attending physician in everyday life (Article 7.11)<sup>3</sup>. It is forbidden for persons without psychological training to offer advice on issues related to EDs (Article 8.6)<sup>3</sup>.

Thus, nutritionists are not authorized to work with clients with EDs if these clients are not receiving medical care. Nutritionists must be aware of the limits of their competence and stay within these limits. It can be assumed that their role when working in tandem with a doctor or as part of a multi-disciplinary team will be auxiliary.

The functions of a nutritionist may include:

- diversifying the client's diet;
- introducing new cooking methods, proposing various recipes;
- helping clients implement the recommendations of the attending physician;
- training in organizing nutrition and grocery shopping;
- meal planning;
- debunking food myths, including chemophobic beliefs;
- helping monitor physical activity and sleep;
- helping clients recognize the return of symptoms as soon as possible to prevent a relapse.

If a relapse is suspected, the nutritionist is supposed to refer the client to a doctor.

In anorexia nervosa, a dietitian or gastroenterologist determines the patient's individual energy and nutrient needs and creates a meal plan meeting those needs. A nutritionist may play an auxiliary role after a client with anorexia nervosa has regained weight.

<sup>6</sup> Sample observation of the diet of the population [Internet]. Federal State Statistics Service; c2018 [cited 2023 May 15]. Available from: https://www.gks.ru/free\_doc/new\_site/food18/index.html. Russian.

<sup>7</sup> Order of the Ministry of Health of the Russian Federation No. 330 of August 5, 2003 "On measures to improve therapeutic nutrition in medical institutions of the Russian Federation". Russian.

<sup>8</sup> Order of the Ministry of Health of the Russian Federation No. 330 of August 5, 2003 "On measures to improve therapeutic nutrition in medical institutions of the Russian Federation". Russian.

If a client has been diagnosed with bulimia nervosa, a nutritionist can assist in maintaining positive eating habits after eliminating compensatory behaviors:

- eating with utensils, not with hands;
- warming food before eating it;
- planning meals in advance;
- allowing a normal amount of fat in food;
- including all food groups in the diet;

• having 1–3 snacks per day in addition to main meals. In binge eating, a nutritionist can play an auxiliary role after a significant reduction in binge episodes and help maintain changes:

- help the client recognize hunger and satiety;
- provide support with meal planning;
- remind the client of the importance of healthy eating and the dangers of fasting.

One of the important tasks of a nutritionist can be preventing EDs through education of the population. To achieve this, the specialist does the following:

- explains the effects of fasting and purging;
- speaks of the need for macro- and micronutrients, sufficient energy value of nutrition;
- teaches the client the basics of a balanced diet;
- encourages a varied and enjoyable diet, including products from all groups;
- debunks myths about nutrition;
- gives advice to clients with inadequate weight loss expectations;
- refers clients with suspected EDs to a psychiatrist.

Thus, in the future, a nutritionist may become part of a multi-specialist team that manages patients with EDs. Implementation of this initiative certainly requires a professional standard. Nutritionists must operate strictly within their field of competence and be aware of the limitations of the means they use. Their work would primarily consist of preventive measures, and they may interact with patients with EDs only as part of a multidsicplinary team.

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# Pregorexia: A Psychotherapy Strategy for Eating Disorders in Pregnant Women

Прегорексия: стратегия психотерапии при расстройстве пищевого поведения у беременных женщин

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# ABSTRACT

Pregorexia refers to an eating disorder observed in pregnant women characterized by the adoption of extreme dieting and workout regime during pregnancy meant to ward off weight gain and keep body shape under control. Psychological factors such as a distortion of how one perceives their own body, concerns about visible signs of pregnancy, and fear of gaining weight have been identified as some of the underlying causes of pregorexia. This condition may have detrimental effects, such as stunted fetal growth, spontaneous miscarriage, and development of anemia by the pregnant woman.

# аннотация

Прегорексия — расстройство пищевого поведения у беременных женщин, проявляющееся в ограничениях в питании и увеличении физических нагрузок в период беременности для контроля веса и объемов тела. В качестве психологических причин прегорексии отмечаются нарушения образа тела, беспокойство по поводу внешних признаков беременности и страх набора веса. Негативные последствия прегорексии могут проявляться в задержках внутриутробного развития плода, спонтанных самопроизвольных абортах, развитии анемии у женщины.

Keywords: pregorexia; eating disorders; pregnancy; body image Ключевые слова: прегорексия; расстройства пищевого поведения; беременность; образ тела

# INTRODUCTION

Pregorexia is an eating disorder that emerges in women during pregnancy and the postpartum period. It is characterized by dietary restrictions, compensatory behaviors (such as self-induced vomiting, use of diuretics or laxatives), and excessive exercising before and after the birth of the child, all aimed at controlling weight and body shape [1]. Despite being a serious condition with longterm consequences for both the mother and her child, pregorexia poses several challenges regarding diagnosis and effective psychotherapy strategies [2]. In the ICD-11 and DSM-5, pregorexia is classified as "Unspecified feeding and eating disorder/Other feeding or eating disorder" [3].

There is no consensus on the prevalence of pregorexia, ranging from 0.6% to 27.8% according to different studies [4]. Incorrect and delayed diagnosis of pregorexia can have adverse effects on a pregnancy, leading to impaired fetal growth and physical health deterioration in pregnant women. Dehydration and

1 International Classification of Diseases 11<sup>th</sup> Revision. The global standard for diagnostic health information. Available from: https://icd.who.int/browse11/l-m/ru.

cardiovascular dysfunction are among the risks faced by pregnant women with pregorexia. Additionally, the consequences of pregorexia include placental insufficiency resulting in missed abortion and miscarriages, premature birth, small-for-gestational-age baby, as well as infant conditions, such as omphalocele and gastroschisis, neural tube defects, including anencephaly [5].

# PLACE OF PREGOREXIA AMONG EATING DISORDERS

Due to the limited number of epidemiological studies on pregorexia, it is challenging to accurately determine its incidence. However, it has been observed that approximately 25% of pregnant women exhibit some signs of eating disorders, with their prevalence rate ranging from 5% to 7.5% among them [6].

Several risk factors increase the likelihood of developing pregorexia during the pre- and postnatal periods [7]. These include:

- a history of previous episodes of eating disorders;
- other current psychiatric disorders such as depressive episodes, anxiety disorder, or obsessive-compulsive disorder;
- experience of sexual or physical abuse in the past;
- obsession with body image (body dysmorphic disorders);
- unintended pregnancy;
- addictions; and
- lack of community support during pregnancy.

Apart from individual psychological and physiological risk factors, it is crucial to acknowledge the impact the environment can have on pregnant women. The immediate and extended environments, along with what is offered in the media, convey the idea that one needs to constantly watch one's body weight and shape, as well as distrust their own internal sensations and experiences. The images in the media put relentless pressure on women to try to look "physically attractive" and conform to set beauty standards. In the postnatal period, pregorexia can be triggered by societal pressure on women to swiftly return to their "pre-pregnancy" body shape, while simultaneously breastfeeding and prioritizing the needs of their infant. The conflicting expectations of being the perfect mother and the perfect woman contribute to chronic emotional stress, which pushes some women to resort to dietary restrictions, cleansing practices, and compulsive exercising as means to selfregulate their emotions.

# **PSYCHOTHERAPY APPROACHES TO PREGOREXIA**

Given the limited research on the specific psychotherapeutic approaches to pregorexia as a distinct eating disorder, the American Psychiatric Association Practice Guideline for the Treatment of Patients with Eating Disorders recommends to employ cognitive-behavioral therapy (CBT-AN, CBT-E). Additionally, in our practice, my colleagues and I also use acceptance and commitment therapy (ACT), dialectical behavior therapy (DBT), expressive therapy (art therapy), and family/partner counseling [8].

Based on personal experiences and those of my colleagues in the psychotherapy of patients with pregorexia, the following therapeutic targets have been identified:

- Body image, which includes addressing interoceptive awareness, emotional, cognitive, and behavioral aspects, as well as the perception of one's body in space. The rapid and often unpredictable changes in body image during pregnancy and the postpartum period can cause significant emotional distress [9,10]. This distress may push women to resort to dietary restrictions, compensatory behaviors, and excessive exercising;
- Gestational dominance: particularly relevant in cases of hypogestognostic or anxiety-depressive types [11];
- Dysfunctional attitudes toward lifestyle during pregnancy and the postnatal period;
- Eating behavior parameters encompassing aspects such as food restriction, compulsive body-checking behaviors, compensatory behaviors (such as selfinduced vomiting, use of diuretics or laxatives, and excessive exercising aimed at "burning of" every calorie they intake);
- The influence of social connections and emotional factors in interpersonal relations, including relationships with the healthcare professionals involved in the care of women during and after pregnancy.

To facilitate the diagnosis of eating disorders in pregnant women and in the postnatal period, the following questionnaires may be utilized: Body Image Questionnaire, EAT-26 (Eating Attitudes Test-26), Eating Behavior Rating Scale [12, 13, 14].

Considering time constraints and the health risks involved for both the pregnant woman and the fetus, it is advisable to establish goals and objectives for psychotherapy that prioritize behavioral changes (renouncing dietary restrictions, cleansing practices, calorie counting, and expanding the variety and quantity of food consumed).

At the beginning of psychotherapy, it is recommended [15] to maintain a food diary with a focus on capturing the emotional state before and after eating, monitoring sensations of hunger and satiety, documenting episodes of cleansing behaviors and compulsive weighing, and analyzing triggers that evoke negative emotions. Keeping a food diary helps clients enhance their awareness of eating disorders and the events that trigger them. It also helps to identify and categorize eating-related situations as challenging or manageable. Additional tools used in the psychotherapy of pregorexia include training in bodily relaxation techniques and mindfulness practices to reduce anxiety and prevent episodes of eating disorders. These interventions are commonly employed in the psychotherapy of other eating disorders and are deemed suitable for pregorexia psychotherapy [16-20].

Alongside the focus on behavioral changes, acceptance and commitment therapy incorporates work on the value system [21, 22].

Target values are identified, such as physical health and motherhood, and, subsequently, goals and objectives are established based on these values. This approach aims to increase value-oriented and motivation-driven patterns of behavior.

# **CONCLUSIONS AND RECOMMENDATIONS**

- Psychoprophylactic measures are needed in pregnant women with a history of eating disorders and related episodes.
- Effective management of patients with pregorexia requires collaboration between psychologists, nutritionists, and gynecologists.
- In cases where eating disorders are suspected during pregnancy and/or the postnatal period, a comprehensive assessment of the woman's condition is crucial. This assessment should encompass factors such as the history of weight and height fluctuations, patterns of eating behavior (e.g., food and calorie restriction, skipping of meals, compulsive overeating, chewing and spitting, regurgitation), compensatory behaviors, and other weight management strategies (e.g., excessive exercising, cleansing behaviors like self-induced vomiting, misuse of diuretics and laxatives, use of weight loss medications). Additionally, it is also

necessary to assess the significance placed on nutrition, weight, and body shape, the presence or absence of a history of eating disorders and response to previous psychotherapy, as well as the presence of any secondary socio-psychological disorders linked to eating behavior and appearance.

 It is crucial to acknowledge that women with pregorexia may deliberately conceal their symptoms or may not be fully aware of the severity of the disorder and the potential harm it poses to their own health, as well as the health of their fetus.

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# The Mental Health System in Bulgaria: Socialist Heritage and Prospects

Организация психиатрической помощи в Болгарии: социалистическое наследие и дальнейшие перспективы

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# ABSTRACT

The article overviews the current system of psychiatric care in Bulgaria based on statistical data for the country. We attempted to look at the reality of the psychiatric care system in Bulgaria as regards its structural parts, the relationships between them, their resource provision, as well as its financing. Attention is focused on some practices and policies that seem inadequate to the needs of patients, their successful treatment, and successful social rehabilitation and integration. It can be said that in recent years the Bulgarian mental health care system has not changed much and that it has a long way to go. There are socio-economic difficulties in the country, and the system needs to evolve to improve the level of care provided to patients. More importantly, Bulgaria must invest in mental health education, in preventive psychiatry, and in developing a culture of clinical management and organization.

# аннотация

В настоящей статье представлен общий обзор системы психиатрической помощи в Болгарии на основании статистических данных по стране. Предпринята попытка рассмотреть структурные подразделения действующей системы, взаимоотношения между ними, их ресурсное обеспечение и финансирование. Особое внимание уделяется некоторым практическим подходам и принципам, которые, как представляется, в недостаточной мере учитывают потребности пациентов и не способствуют их успешному лечению, социальной реабилитации и интеграции. Можно утверждать, что в последние годы болгарская система психиатрической помощи не претерпела значимых изменений, и требуется еще много усилий по ее развитию. На фоне стоящих перед страной социально-экономических трудностей систему необходимо совершенствовать, с тем чтобы повысить качество предоставляемой пациентам помощи. Более того, государству следует увеличить инвестиции в образование, касающееся психического здоровья, в профилактическую психиатрию, а также в развитие культуры управления и организации в сфере здравоохранения.

**Кеуwords:** mental health; policies; health system; psychiatric care; Bulgaria **Ключевые слова:** психическое здоровье; государственное управление; система здравоохранения; психиатрическая помощь; Болгария

# INTRODUCTION

Bulgaria has around 7 million inhabitants that include a small Turk (8.4%) and Roma (4.4%) populations. Residents in cities (78%) predominate over those in rural areas (22%) in a territory of over 110,879 km<sup>2</sup>. Bulgaria joined the European Union (EU) in 2007 and ranks 71<sup>st</sup> in the world in per capita GDP (gross domestic product). The Health Act

was introduced in 2005 for the first time, although some efforts in that direction had been made prior.

The dispensary health care system during state socialism<sup>1</sup> in Bulgaria covered multiple aspects: "continuous, close monitoring of patients and the study of their (and their families') needs and lifestyles", "efforts towards the fullest possible satisfaction of patients' needs in specialized psychiatric treatment, social support, employment and rehabilitation, legal aid", expert and prophylactic care aimed at creating a healthier environment, health education, as well as early detection of illness and relapse. The entry point into the system was via so-called dispensary registration. Dispensarization, in its most basic form, was provided for by the Public Health Act of 1973, while the particular ordinance concerning the dispensarization of persons with mental health conditions was issued as late as 1987 [1].

The mental health infrastructure in Bulgaria, by common consensus among the Ministry of Health (MH), the Bulgarian Psychiatric Association, medical, nursing, and other staff, patients, and families, is wanting, and there is a pressing need for reform. Attempts at such reform have stalled so far due to the complexity of arranging funding and a lack of consensus among the stakeholders [2].

# **HISTORICAL ACCOUNT**

Mental health care was never a priority in the health system of Bulgaria: there were very few treatment facilities for the mentally ill before the *coup d'état* of September 9, 1944. The new regime also failed to recognize it as a priority; mental health care was conspicuously absent in the first program of the Fatherland Front, the communistdominated coalition that came to power after the coup. From the early 1950s onwards, the new and major undertaking became to develop an outpatient system which was epitomized by the dispensary approach. As the embodiment of social psychiatry with its "prophylactic orientation", the dispensarization project had to cover many aspects and fulfill the high hopes of the Bulgarian psychiatric community for "bringing psychiatry closer to society" [3].

Dispensarization was meant to be an expression of "the prophylactic trend in socialist healthcare", to quote Petar Kolarov, which was presented as the latter's basic principle [4]. Complete dispensarization sought to create — in the words of Todor Zhivkov — "such an environment and responsibility that every citizen in our country, from cradle

to the grave, would have a personal file and be monitored and cared for". Consistently with this attention to creating a healthier environment, including a healthier social environment, the dispensary approach was conceptualized as the embodiment of social psychiatry. The latter was usually presented as follows: social psychiatry means "bringing psychiatric care as close to the social community as possible". Precisely social psychiatry had "raised the authority of psychiatry and brought it up to par with a number of leading medical disciplines" [5]. This was in keeping with the Soviet model of dispensarization, which was adopted by Bulgarian psychiatry.

The dispensary system in the period of state socialism in Bulgaria included multiple activities: "continuous, close monitoring of patients and studying their (and their families') needs and lifestyles", "fullest possible satisfaction of patients' needs in specialized psychiatric treatment, social support, employment and rehabilitation, legal aid", expert and prophylactic activities aimed at creating a healthier environment, health education, early detection of the disease, and relapse [6]. Entry into this system was via so-called dispensary registration. Dispensarization — in its most basic form — was enshrined in the Public Health Act of 1973, while the specific legal framework concerning the dispensarization of persons with mental health conditions was issued as late as 1987 [7].

Both before and immediately after 1917, the view that better mental health was the natural result of improved social conditions was particularly popular among the Russian psychiatric community. This model received further ideological justification after the October Revolution of 1917, and this put a trump card in the hands of psychiatrists who wanted to reorganize the system in a prophylactic spirit. The most outstanding among them was Lev Rozenshtein, who became the "father" of the dispensary model directed and financed by the state — in the Soviet Union. His idea of "neuropsychiatric dispensaries" originated specifically in his interest in alcoholism, but he was in fact the first to turn the dispensary into a form of "consolidated institutional care for alcoholic and nervously ill patients" [8].

# **CURRENT STATUS**

The main aspects of the current situation are characterized by a deep fragmentation of outpatient mental health care, which is not properly integrated with other services in

<sup>1</sup> It is taken by implication as Soviet state socialism, as other forms of socialist health care, such as the Scandinavian model, are outside the scope of this paper.

health care delivery, or with other tangential aspects of the public sector such as social services, education, and justice, among others. Legitimate patient organizations are not adequately represented on the level of health policy in psychiatry. These shortcomings have to do with the lack of a holistic approach to psychiatric care.

Data from an epidemiological study conducted in 2011 shows that all respondents with a common mental disorder in the 12-month period that had preceded the interview had received help (20.69%). For 19.7% of them, the help assumed the form of medication: 16.85% saw a general practitioner, while 5.58% were examined by a psychiatrist. Interestingly, 3.75% of those without a medical condition aligned with the criteria of the study also sought medical care for related mental health problems. People with panic disorder — 59.34%, followed by those with dysthymia — 43.44%, and those with a depressive episode — 32.33%, and those with post-traumatic stress disorder — 31.74%, received medical treatment most frequently. Two to three times less frequently people with generalized anxiety (17.73%) and phobias (14.32%) received treatment. People with substance use disorders in the 12 months preceding the interview received care in only 3.95% of the cases (2.35% by a psychiatrist). People with panic disorder saw a psychiatrist most often (20.47%), followed by those with generalized anxiety disorder (11.78%) and recurrent depressive disorder (11.52%). Non-medical services came into play relatively infrequently, at 0.99%. Most of the people with posttraumatic stress disorder (PTSD) represented 7.44%. A telling fact about recognition of this diagnosis in Bulgaria is that of the same group of people only 3.75% received qualified psychiatric care [9]. A second epidemiological study was conducted in Bulgaria, EPIBUL-2, in 2017 [10], but the results have not been published.

# **HUMAN RESOURCES**

There is a shortage of medical specialists in all fields throughout Bulgaria. Psychiatry is among the most affected fields in terms of staff insufficiency. There is also a problem with several lines of funding for the various psychiatric structures, which leads to an uneven distribution of doctors in them. In the field of mental health in Bulgaria, medical doctors can specialize in three areas: psychiatry, forensic psychiatry, and child psychiatry. These are independent medical fields, which means that it is not necessary to first acquire a specialty in psychiatry in order to train in forensic or pediatric. A minimum of 11 years pass from the beginning of training to graduation in the "psychiatry" field in Bulgaria.



Figure 1. Number of psychiatrists for the period covering 1960–2016 according to official statistics.

Published data in health reference books (Figure 1) demonstrates a clear decrease in the number of psychiatrists, from 987 in 1996 to 759 in 2016. Unfortunately, this tendency has witnessed a regrettable acceleration in the past 7 years, with a non-recoverable dropout rate of approximately 100 doctors every two years. A possible explanation of this process could be rooted in the poor workplace conditions, including the organizational and psychological climate, which tend to lead to burnout [11, 12].

According to the National Statistical Institute, in 2022 there were 675 psychiatrists in Bulgaria, or 2.28% of all doctors<sup>2</sup>.

On the other hand, the Bulgarian Medical Association reports that 569 psychiatrists are active members<sup>3</sup>. Membership in the association is mandatory; therefore, it is a more legitimate source of information. The discrepancy

<sup>2</sup> The National Statistical Institute [Internet]. Doctors by specialties in medical and health care institutions on 31.12.2022 by statistical regions and districts. [cited 2023 June 8]. Available from: https://www.nsi.bg. Bulgarian.

<sup>3</sup> The Bulgarian Medical Association. National Register of doctors affiliated to the union by gender, age, specialty and place of practice [cited 2023 June 8]. Available from: https://blsbg.eu/en.



Figure 2. The number of psychiatrists under contract with the National Health Insurance Fund (NHIF), presumably working in the field of community care<sup>4</sup>.



Figure 3. Psychiatrists per 100,000 people in the EU<sup>5</sup>.

5 Eurostat data for 2015.

<sup>4</sup> The National Health Insurance Fund. Available from: https://nhif.bg/.

with the Statistical Institute data is due to the fact that many individuals (real persons) are reported twice as employees. Job positions may be held in terms of two or more contracts per individual employee.

It is evident that the distribution is unequal, with certain areas suffering limited coverage (Figure 2). Besides, the average reported age of psychiatrists in the country is currently estimated at 58 years, with an expected rise to 63 years in 2028.

Compared with other countries in the European region, Bulgaria has an extremely diminished pool of human resources active in psychiatric practice (Figure 3).

Data for other staff providing mental health services collected by the MH are from 2014. These are medical workers who practice only in inpatient psychiatric care settings. Due to the small numbers in some of the categories, we will present them in whole numbers rather than per population. Doctors assistants – 84; nurses – 1151; social workers – 56; psychologists – 134; and hospital attendants – 830<sup>6</sup>.

# **LEGISLATION ISSUES**

Discussion about Bulgarian legislation in the field of mental health started in 2001, along with the process of accession to the EU. One of the key requirements to join the EU concerned Bulgaria's procedure for involuntary treatment. It was debated whether to have a separate law on mental health or not. The country has never had a separate law regulating mental health, and issues such as mandatory treatment, guardianship, and legal capacity were regulated in the People's Health Act, which was in force until 2005, when it was replaced by the new Health Act. While some experts were of the opinion that a separate law would be a form of discrimination against persons with mental disorders, others insisted that clear regulations in this field of care were necessary. In fact, the legislative system lacked the capacity to elaborate a separate law at that time and the decision was made to have a specific chapter in the new Health Act relating to mental health. The Health Act has been in force since January 1, 2005, and it governs many of the public health issues that were not covered by other recently adopted Acts, on medical facilities, and health insurance. Mental health is regulated in Chapter 5 of the Act, which has two sections, one on the protection of mental health and one on involuntary commitment and treatment [13].

#### **ORGANIZATIONAL DISTORTION**

The Health Reform in Bulgaria in 2000 launched a new phase in relationships in the system and introduced market elements in patient care, albeit largely mediated through the new health insurance institution. In psychiatry, the new conditions benefited mainly those involved in outpatient care, where the processes of services provision regulated by market forces and decentralization took place, as happened in most other medical disciplines. However, psychiatry, in its hospital unit aspect, remained outside of these processes and, thus, largely retained its institutional character. The lack of funding and managerial will to implement the objectives set out in a number of strategic documents has led to deep distortions and disproportions in the provision of mental health services. As a result, the principles of continuity of care, complexity in service, and supportive therapy have been compromised.

The paradox in the development of the psychiatric system in our country is that during the totalitarian healthcare system some form of bio-psycho-social approach was expressed through the complexes of hospitals, dispensaries, and the developed occupational therapy, although it remained firmly tethered to the practice of isolation and stigmatization of people with mental disorders. In the 1990s, this infrastructure was allowed to fall into disrepair and was largely plundered due to the lack of a wellarticulated concept of reform, along with the resistance to change that came from the different stakeholders. As a result, the provision of mental health services has become chaotic, plagued by poor quality, inefficiencies, and is noncompatible to the requirements of modern psychiatric care. The few examples of good practice at some individual facilities that boast a developed rehabilitation and occupational therapy base cannot ensure a guaranteed sustainability but are rather the result of a tenuous combination of individual efforts and favorable local conditions.

New ways of treating mental disorders go far beyond pure medical intervention, which in psychiatry is largely encumbered with drug therapy and some non-medical methods — transcranial magnetic electrostimulation and electroconvulsive therapy. Such methods involve coordinated action by different groups of specialists doctors, nurses, psychologists, and social workers — as well as the introduction of new jobs and even professions

<sup>6</sup> The Ministry of Health Republic of Bulgaria. Internal report from the 28 regional health inspectorates. Not published.

such as case manager. The lack of a comprehensive reform concept also leads to uncoordinated actions in sectors that, by definition, have to cooperate. To effect improvement, there is a need for a change in the legal framework, secure funding, and training. For now, there is still a lack of clear political will for change despite the series of strategic documents, programs, and action plans that have been adopted.

The provision of mental health services in Bulgaria relies on a combination of psychiatric hospitals, psychiatric dispensaries, and private outpatient psychiatric ambulatories.

There are 12 state psychiatric hospitals in the country, 12 Mental Health Centers (ex-psychiatric dispensaries), 5 psychiatric hospitals (in University clinics), and 17 psychiatric departments in general hospitals. The total number of beds in 2017 stood at 4,105, which is 5.8/100,000 population and represents 8.4% of all beds in the country.

Psychiatric hospitals are of an institutional type. The territorial distribution of these facilities is uneven across the country and does not take into account the migratory processes that have occurred over the last decade, as well as the transformations in socio-economic relations. Most of the hospitals are built on the basis of the isolation principle typical of the middle of the last century. The location of these institutions outside settlements does not take into account the administrative divisions of the country and does not conform to the naturally created health service territorial divisions. As a result, the patients taken in and treated in these settings are often at a significant distance from their homes, which complicates the relationship with their relatives and stands in the way of their reintroduction into society. Hospitals serve several areas simultaneously, making it difficult to manage and finance them effectively.

The 12 psychiatric dispensaries in the country are structured in a way to ensure a transition from institutional to outpatient care. Until the end of the last century, their activity was limited to the distribution of communityborne illnesses to the institution, the maintenance of an information base of patients from certain regions that are housed at the institution, and the provision of outpatient care. The psychiatric dispensaries were part of a dispensary-hospital complex housed in a basic structural unit of the institutional model. The healthcare reform has lend legal status to the healthcare institutions in the country, different forms of ownership and financing, all of which has led to the dismantling of the dispensary-hospital model. After the decentralization of outpatient care, a large part of the outpatient functions of the dispensaries was taken up by private psychiatric ambulatories, along with the documentation for patients. Many of these ambulatories signed contracts with the NHIF, and so outpatient care for insured citizens with mental disorders has continued for the most part. For a number of reasons, psychiatric dispensaries did not enter into contracts with the NHIF at the same time, and municipalities remained funded through the approved budgets of the municipalities. Instead of the former dispensaries, today Mental Health Centers have been transformed into hospitals, with a number of beds that has jumped from 25% out of the total number of beds in the country in 1989 to almost 50%.

In addition, there are small psychiatric departments in general hospitals funded by the MH through special allocations as part of a complex, mixed funding system which struggles to meet the actual needs of the population.

A large proportion of outpatient care is provided by private psychiatrists, who are funded through the national health insurance. Outpatient psychiatric care in Bulgaria is structured primarily around psychiatric individual and group practices that work independently or within another health care facility.

Across the health care provision landscape, pharmacotherapeutic opportunities have been considerably improved in recent years thanks to the availability and use of new medicaments, especially second-generation antipsychotics and contemporary antidepressants.

Contrary to the practices in Western European countries, psychiatric treatment of severe mental diseases in Bulgaria almost entirely boils down to the application of medications, whereas other forms of treatment<sup>7</sup> exist only in rudimentary form, where the following weaknesses have been identified as the most significant:

- there is no systematic assertive patient engagement or fieldwork;
- integration of and cooperation between parts of the medical and social services infrastructure exist in

<sup>7</sup> Such as mobile psychiatric care, telemedicine, transcranial magnetic stimulation, some forms of occupational and art therapy. Even traditional forms such as electroconvulsive therapy are complicated.

individual cases, but with no broader or systematic application;

- methods of psychosocial rehabilitation are represented partially and unevenly;
- there are no teams or sectors for intervention in early psychosis, which could be dealing systematically with secondary prevention;
- there is no clear demarcation between services according to the hierarchy of healthcare provision.

It has been universally recognized that the consequence of such tendencies is a gradual increase in the number of forensic patients.

Mental disorders are traditionally linked with rejection by society, fear, and stigma. Stigmatization of persons with mental health issues constitutes a serious problem, the consequences of which are numerous and manifest both in the experience of one's own illness and in the diminished motivation to seek professional assistance. The stigma that comes with mental disorders is so strong that it creates a wall of silence in relation to the problem, worsens the underlying disease, and makes it even more unbearable and difficult.

Bulgaria is not an exception in this general tendency of stigmatization of individuals with mental health problems. Mental disease is still a taboo topic in Bulgarian society, not only at the individual level and the level of the families of the deceased, but also in the broader social context. Both in the local community and globally, there are attempts to debate the issue, campaigns, and other forms of de-stigmatization, but the media still devotes insufficient attention to this issue, or do it inappropriately. There are episodic manifestations to combat stigma and discrimination, on a project basis, but this is not a sustainable state policy<sup>8</sup>.

One of the major problems is the fragmentary nature and lack of continuity of both care and therapy and information about patients. After discharge from a psychiatric hospital, the patient is not routinely referred for follow-up, maintenance therapy, or any psychosocial interventions with a view to their recovery and reintegration into the community. Such activities are undertaken chaotically, depending on the particular circumstances of the patient, initiatives from their carers and family, or the local availability of services.

The complex systems that exist make it very challenging for patients to secure and continue to use treatment. For example, in order to use the services funded by the NHIF, the patient is required to visit a general practitioner, get a referral to a specialist, visit that specialist, certify the medication protocol and in the case of costly medications it must be approved by a special committee, and only after go back to the general practitioner before they can visit a pharmacy to obtain the medicines. This is likely too complicated as a setup for many patients to successfully navigate, let alone when they suffer impaired insight or cognitive functioning, or poor motivation and drive resulting from their mental disorder. Drugs for schizophrenia and bipolar affective disorder are reimbursed, but no more than at three per patient<sup>9</sup>. Anti-depressants are only partially reimbursed after one provides evidence of a depressive disorder.

One of the major challenges in psychiatric care is currently the fragmentary nature and lack of continuity of both care and therapy, as well as information about individual patients. After discharge from a psychiatric hospital, the patient is left with no regulation to follow for guidance as to follow-up, maintenance therapy, or any psychosocial interventions with a view to re-inserting them into their community. Efforts in this direction are often chaotic and depend on the condition and status of the patient, coming from a relevant outpatient service or the initiative of relatives. This state of affairs is perpetuated by the fact that a large proportion of patients that enter psychiatric hospitals are self-directed.

Social services in Bulgaria are regulated by and codified under the Social Assistance Act. There are about 6,000 beds for people with chronic disabilities in social care homes, and a small number of day care centers and shelter homes that are funded by the Ministry of Labor and Social Policy.

The existing types of social services institutions for the psychosocial rehabilitation of people with mental disabilities are Day Care Centers for Disabled Adults, Protected Homes, Social Assistance, and Home Care. The processes of deinstitutionalization in the social context, where the responsibility of the Agency for Social Assistance (ASA) begins, are still being put in place, with

<sup>8</sup> National Center for Public Health and analysis. Project "Improved mental health services". Available from: https://bgmental.ncpha.government. bg/en/node/35.

<sup>9</sup> The NHIF has drug reimbursement rules that do not allow more than three drugs to be paid for an illness. It is necessary that these indications for the prescription of medicines be explicitly stated in the summary of product characteristics.

the European integration process of Bulgaria. As a result of these efforts, day care centers for people with mental disabilities have been opened in different areas across the country. But they work independently, unrelated to the larger medical service infrastructure, and, in smaller settlements, are confined to the immediate neighborhood. This also applies to shelter housing, access to which is not provided through the medical service apparatus, but through an order specified by the ASA. As of December 31, 2014, there are 13 shelter-like institution homes for adults with mental disorders with a capacity of 1,036 people.

# **FINANCIAL MANAGEMENT**

The financing of health care and the system of health care reforms in Bulgaria up to this moment have been a study in transition from a Soviet model (the Semashko model<sup>10</sup>) to one that is more flexible and responsive. In the previous model, universal insurance coverage was achieved through a state-funded national health system. Doctors and other health workers we remunerated as civil servants, hospitals were allocated global budgets, and private practice and private insurance were forbidden.

Over time, Bulgaria has made progress towards a more pluralistic healthcare system based on a social health insurance model. The NHIF was established in 1999 and has become the single largest purchaser of health care services in the country. In principle, the NHIF proves to be quite comparable to many "social (or mandatory) sickness insurance funds" in the EU. In principle, the entire population is covered through compulsory and autonomous public health insurance funds. Employees (and their employers) pay into social security contributions based on their income, while the poor, the unemployed, the children, pensioners, the disabled, and other socially vulnerable or priority population groups are exempt from contributions and are covered by the state. The only existing national state fund combines health risks for the entire population and buys services both from state and private providers. The reforms also separated the purchase of services, with the idea that money follows patients, rather than funding existing healthcare facilities regardless of their activity and usage. The mechanisms

for paying suppliers have been reformed; the private provision of health services and private health insurance was allowed; outpatient assistance was privatized; and hospitals became legally independent entities. The MH has retained its responsibility for public health, emergency aid, tuberculosis, HIV/AIDS, mental health, and some additional services, and its role has evolved more towards managing the system, which remains extremely financially inadequate with respect to actual needs.

Under the Health Insurance Act, insured persons are entitled to "medical assistance within the basic package of healthcare services guaranteed by the budget of the National Health Insurance Fund". Ordinances issued by the MH — and not by the NHIF — specify the basic benefits package. The benefits package includes primary and specialized outpatient medical and dental care, medicines, diagnostics, inpatient hospital care, and some highly specialized medical services (e.g. oncology treatment, emergency aid, mental health, renal dialysis, in vitro fertilization and organ transplantation are covered by the MH). The cost-sharing requirements are different for different types of services, and insurance coverage for services is ultimately capped by the NHIF budget approved by parliament for a year.

NHIF uses a wide range of payment methods that differ for different types of providers. In general, hospitals are paid by the NHIF based on a fee in a service payment package for about 300 clinical pathways and are also subject to annual budget caps. Psychiatric care remains outside the scope of NHIF, which has no commitment to inpatient care and covers only long-term antipsychotics costs for outpatient care in psychiatry.

In summary, over the past 20 years, reform of the mental health care system has taken outpatient services from their innate function of community-based care to *de facto* inpatient services, with outpatient care remaining outside the scope of the overall national health insurance funding model.

# **PROSPECTS FOR THE FUTURE**

Following an official evaluation and recommendations by the European Psychiatric Association in 2018<sup>11</sup>,

<sup>10</sup> Soviet model of Nikolay A. Semashko, a centralized budget-funded and regulated system, which claimed to guarantee "free access to health services for the entire population".

<sup>11</sup> European Psychiatric Association Report on Bulgarian Mental Health care and Reform Process 2018. Available from: https://www.europsy.net/ app/uploads/2019/01/EPA-Bulgaria-Report-2018-Final.pdf.

a National Strategy for Mental Health was adopted by an act of the Council of Ministers in 2021<sup>12</sup>. The National Council was established in 2022 to guide and steer the process of its implementation. The Strategy envisages a major paradigm shift towards community-based care and seeks the appropriate funding for multidisciplinary case management in psychiatry<sup>13</sup>.

The main aims of the Strategy are briefly summarized below<sup>14</sup>:

- reducing morbidity and mortality from mental disorders by integrating psychiatric services into general medical care (deinstitutionalization);
- creating a network of integrated services for people with severe mental illnesses, in close proximity to their place of residence, centers for the treatment of disorders, and eating disorders;
- reducing alcohol and drug use and reducing manifestations of aggression and self-aggression;
- developing child and adolescent psychiatry, old-age psychiatry, and Forensic psychiatry;
- a special focus on child mental health, in line with the Convention on the Rights of the Child to ensure special protection of children's rights, including the right to health and access to health and medical care;
- introduce a system to collect statistical information by region, type of mental illness among children, age and their analysis, including conducting targeted surveys on mental illness among children, disaggregated by age;
- develop specific measures and incentives to attract and retain specialists in child and adolescent psychiatry, forensic psychiatry, and psychiatry of advanced age;
- restore the balance between individual psychiatric professionals, social worker's psychologists, nurses, and orderlies with the development of appropriate incentives to attract professionals;
- respect human rights and combat stigma and discrimination.

Currently the National Strategy is under implementation and monitoring.

# CONCLUSION

In conclusion, it can be said that in recent years the Bulgarian mental health care system has not changed much and still has a long way to go. Despite the socioeconomic difficulties in the country, the system needs to evolve to improve the level of care provided to patients. Bulgaria should take active part in as many international projects as possible aimed at introducing better treatment practices in the community for patients with mental disorders. More importantly, Bulgaria must invest in mental health education, in preventive psychiatry, and in developing a culture of clinical management and organization. It is necessary to encourage Bulgarian society to play an active role through education and information in the fight against the stigma of mental disease.

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<sup>12</sup> https://www.mh.government.bg/media/filer\_public/2021/11/02/21rh388.pdf.

<sup>13</sup> Case management is the coordination of community-based services by a professional or team to provide quality mental health care customized accordingly to individual patients' setbacks or persistent challenges and lead them to recovery. Case management seeks to reduce hospitalizations and support individual recovery through an approach that considers each person's overall biopsychosocial needs without incurring crippling economic costs. As a result, care coordination includes traditional mental health services but may also encompass primary healthcare, housing, transportation, employment, social relationships, and community participation. It is the link between the client and care delivery system.

<sup>14</sup> National strategy for mental health of the citizens of the Republic of Bulgaria 2021 – 2030. Available from: https://www.mh.government.bg/ media/filer\_public/2021/11/02/21rh388pr1.pdf.

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# The History of Territorial Psychiatric Hospitals in Russia

История окружных психиатрических больниц в России

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# ABSTRACT

The deployment of territorial psychiatric hospitals throughout the Russian Empire in the second half of the 19<sup>th</sup> – early 20<sup>th</sup> century represented one of the most important stages in the development of psychiatry in Russia. In essence, it was the first practical attempt at designing and constructing psychiatric hospitals that were large, specialized autonomous units aimed not only at ensuring the isolation of patients, but also at treating their condition. The project was unique not only because of the sheer complexity of the idea of an integrated approach to the treatment and care of patients, but also because of its geographic scope. Hospitals under this project were built throughout the Russian state, from its western borders to Siberia. The leading mental health professionals of the day were recruited into the project, and the hospitals established by virtue of their efforts yielded a large body of empirical material that could be taped for the study of mental disorders and approaches to their treatment. This article discusses what led to the creation of the project, the main milestones in its implementation, as well as the contribution made by the thus-established territorial psychiatric hospitals to the development of psychiatry in Russia.

# аннотация

Учреждение окружных психиатрических больниц на территории Российской империи во второй половине XIX–начале XX века — один из самых важных этапов в развитии отечественной психиатрии. Фактически это первый опыт проектирования и строительства психиатрических лечебниц как крупных специализированных автономных комплексов, нацеленных не только на изоляцию пациентов, но и на терапию их состояния. Проект уникален не только сложностью замысла и комплексным подходом к лечению и содержанию пациентов, но и широтой географии. Больницы по данному проекту строились в самых разных частях российского государства: от западных рубежей до Сибири. В разработке проекта принимали участие ведущие психиатры своего времени, а учрежденные благодаря их усилиям больницы дали огромный практический материал для изучения психических расстройств и подходов к лечению. В статье рассматриваются предпосылки создания проекта, главные вехи его реализации, а также вклад создававшихся окружных психиатрических лечебниц в развитие российской психиатрии.

**Keywords:** *history of Russian psychiatry; territorial psychiatric hospitals; coercive treatment; care of mentally ill patients; occupational therapy* 

**Ключевые слова:** история российской психиатрии; окружные психиатрические больницы; принудительное лечение; призрение душевнобольных; трудотерапия

# BACKGROUND

It's not without reason that the idea of establishing territorial psychiatric hospitals appeared in Russia. By the time of its emergence, there had already been a fairly rooted culture of care for the mentally ill around the second half of the 19th century. The year 1762 can be taken as grand zero, when Emperor Peter III of Russia responded to the proposal of the Senate to send the mentally ill Kozlovsky princes to a monastery with the following order: "Send insane folks not to monasteries, but rather build a purposeful house for that, as is the custom in foreign countries, where lunatic asylums are established" [1]. In 1775, a decree was issued whereby the Welfare boards (Prikazy) were ordered to arrange asylums for the insane in each governorate. These were seen primarily as places of isolation — rather than treatment — of patients. Nevertheless, the decree emphasized that the patients should be treated "humanely", and that the warden be "kind-hearted and gentle" [1]. Since then, the number of asylums for the mentally unstable has steadily increased. For example, in 1810 there were 14 specialized institutions in the Russian Empire, whereas by 1860 their number had grown to 43, of which 34 were independent and 9, departments at governorate hospitals. As the Russian psychiatrist Rote A.I. noted: "This step brought invaluable benefits, but still it was only the first practical attempt, these were lunatic asylums actually established by the state, which, however, did not yet constitute houses of care, much less for the treatment of mentally ill persons" [2]. The main challenge was finding enough qualified personnel: there were few specialists in Russia, doctors visited patients in such facilities only on certain days, and the mentally ill were supervised by personnel without appropriate training (most commonly, retired soldiers worked in lunatic asylums).

In 1842, the Ministry of Internal Affairs initiated an inspection of governorate asylums for the mentally ills. Based on the ensuing reports, it became obvious that the then-existing asylums for the mentally ills could not cope with the flow of patients and were not set up in the best way possible. Two years later, a special committee was set up under the Ministry of Internal Affairs that included government officials and doctors. The Committee held as follows: seeing that it was economically unprofitable to maintain facilities for the mentally ills in each separate governorate, and that it was practically impossible to staff each facility with qualified personnel, instead, one large institution ad to built to serve several governorates [1]. While December 30, 1844, can be considered the birthday of the project of territorial psychiatric hospitals, it took another 18 years for subsequent revision and approvals. The project was supported by governorate authorities, but after each detailed review, it often became clear that the real costs of building the hospitals would be much higher than the amount initially budgeted. In 1856, a commission convened to revise the project. The outcome of its activities was an updated project: it involved the construction of a number of central institutions, and "as an experiment" it was recommended to start with the construction of a hospital in Kazan [1]. It should be noted that out of the 8 hospitals provisioned by the project, only 7 were built and that virtually no information has been uncovered about the very last hospital, built in Grodno.

# KAZAN, THE PLACE WHERE IT ALL BEGAN

In the spring of 1861, the design of the Kazan territorial asylum for the insane was approved by Emperor Alexander II [2]. The choice of the location was driven by the fact that the Welfare boards in the Kazan governorate had the funds needed to build the hospital, and that there was a University in Kazan which could train future medical personnel. At Kazan University, the teaching of psychiatry, albeit in all but theory, began in 1866, a year before psychiatry became a compulsory medical course in all higher educational institutions of the Russian Empire. This shows that the medical community felt the need to build up psychiatric knowledge and train the relevant professionals. The Kazan hospital opened in 1869. However, the experience of its operation in the first years turned out to be so controversial that it put into risk the very implementation of the remaining stages of the project.

The first territorial hospital for the insane in Russia was built on a project by the architect Zhukovsky P.T. Professor Balinsky Ivan Mikhailovich, who can arguably be referred to as the inspiration behind psychiatric facility construction in Russia, took the most active part in the effort, as he designed quite a number of mental health hospitals, as did doctor of medicine Frese Aleksandr Ustinovich, who became the first director of the facility. Frese A.U. stood at the origins of psychiatric science in Russia and, to boot, had the necessary experience: in 1862 he traveled to Europe to study the construction and operation of European psychiatric hospitals. The territory hospital was purposebuilt for the accommodation of mentally ill patients, and was strikingly different from the governorate and local (zemstvo) asylums for the insane. Here is a 1879 report on the state of affairs in a zemstvo asylum in Kazan: "If the status of a person who went insane is difficult in general. then it must be unbearable in such a building as a zemstvo asylum for the insane. The aged, badly ventilated building with dark narrow corridors, and low ceiling and damp individual cells affected the mood". And here is the report of the Poltava zemstvo (local administration) commission: "Wardens treat patients like a herd of animals, rule by the power of the fist; and howls are often heard in the house: 'Give me something to eat!'" [3]. The Kazan territorial hospital, built outside the city limits combining three spacious buildings and surrounded by extensive gardens, represented a striking contrast compared with such facilities (Figure 1). The multiple-buildings system made it possible to segregate patients by gender, by the nature of their condition, and even by social status, as it boasted firstand second-class blocks. Broad expanses lined with turf adjoined the blocks for restless patients, "to give some fresh air to patients who, by dint of their state of anxiety, cannot take walks in the gardens" [4]. Each department was equipped with canteens, buffets, a cloakroom, a water closet and a warden's room. For entertainment and leisure, a carpentry workbench, a lathe, billiards, checkers, books, and even a piano were available.

Restrain and other measures of physical coercion on patients were strictly prohibited at the hospital: violent

patients were not tied up, but rather placed in special rooms with walls upholstered with soft material to avoid self-inflicted harm [5]. The Kazan hospital had steam heating, artificial ventilation and a water supply line. Frese A.U. brilliantly hence set forth the basic principle of the organization of his institution: "A lunatic asylum is not a prison, nor is an insane a criminal. The task of the lunatic asylum is to convince the patient of the truth of this situation by creating an objective environment" [6]. Moreover, a comfortable environment, good nutrition, outdoor walks, variety of leisure activities, according to Dr. Frese, were "important aids to the successful treatment of insanity". The condition of patients was monitored by the director-physician, four residents, two male paramedics, and two female paramedics. The wardens and their pair of assistants kept order in the men's and women's quarters. Doctors and employees actually resided at the hospital and, thus, patients received "continuous and comprehensive care" [6].

Yet, the Kazan territorial hospital all but jeopardized the entire project of the construction of territorial hospitals. The matter was that Frese A.U. was of the opinion that his institution was meant primarily for the mentally ill with a chance at recovery. For incurable patients he allotted only a tenth of the total number of beds. Assessing the operation of his hospital from 1869 to 1879, Dr. Aleksandr Frese noted that 30% of the patients admitted were discharged after having fully recovered. The chances of



Figure 1. The Territorial hospital for the mentally ill in Kazan.

recovery were especially high for those admitted to the hospital for the first time, provided that the duration of their condition at that point in time did not exceed six months. If after a year in the hospital there was no improvement. the patients were transferred to zemstvo asylums for the insane or returned to the care of relatives [4]. This approach resulted in many unoccupied beds in the hospital. Even though the Kazan territorial hospital had been envisioned to serve the seven nearest governorates, in reality it admitted patients from all over the empire. However, Frese A.U. throughout his life remained convinced that it was more economically sound for the state to cure a mentally disturbed person and return him/her to his/her everyday life, and, therefore, to active life, than to spend resources on care for incurable patients. He considered that the unoccupied beds in his hospital were due to a lack of public awareness about its operation and the conditions of the custody of patients [6]. Dr. Frese even published a pamphlet describing his institution and toured neighboring governorates in search of patients who fit the criterion of curability. This state of affairs continued until his death in 1884.

Ragozin Lev Fedorovich, who was not only an outstanding Russian psychiatrist, but also a gifted administrator, was appointed as the next director of the hospital. He took over the leadership of the institution at a very challenging time for the institution. Here is how professor Ostankov A.P. described the state of things: "The experience of the Kazan district hospital in the opinion of the ministry was considered so unsuccessful that even petitions initiated by the zemstvo requesting the construction of territorial hospitals were unsuccessful; the topic of central hospitals could at the time have been regarded as doomed had it not been for the energetic and fruitful activity of Ragozin L.F. and if further existence of the Kazan territorial hospital under his leadership had not radically changed the views of the government about territorial hospitals" [7]. Lev Ragozin, with the help of Ostovsky A.Ye., an engineer, expanded and partially rebuilt the hospital, introduced a boarding house system, which led to more money flowing into the coffers, which allowed him to, finally, take in all the patients of the zemstvo asylum for the insane, the zemstvo asylum was closed thereafter. Thus, Ragozin L.F. improved the living conditions of chronic patients and, at the same time, reduced costs for their care. But, most importantly, he regained the government's confidence in the project of territorial hospitals.

In 1888, Lev Ragozin assumed the post of director of the Medical Department of the Ministry of Internal Affairs, and, with his most active participation, six more territorial psychiatric hospitals were built, as had been provided for by the project of 1856, in cities such as Warsaw, Vinnitsa, Vilna (later Vilnius), Tomsk, Moscow, and Grodno [3]. Thus, the geographical spread of the project covered areas ranging from the western borders of the Russian Empire to Siberia.

# AT THE TURN OF THE CENTURIES

In 1891, the Warsaw territorial psychiatric hospital opened its doors in Tworky (later the territory of Poland). Obviously, by the time of its planning and establishment, the inertia of the past was still a reality: the hospital was built according to the pavilion system, which was considered as the best for sorting patients into groups, since Ragozin L.F. and colleagues had failed to prove that the hull model of hospital-building was much more practical and economical than the pavilion type. The largest amount of space was allotted to patients with hope of recovery, but the hospital also accepted incurable patients, persons sentenced to remain under medical supervision by the state, and people whose mental abilities were in doubt and needed to be tested [8]. In all other respects, the management of the Warsaw hospital was based on the principles tested at the Kazan territorial hospital: a picturesque countryside; doctors, paramedics, and caretakers living on the premises; and a ban on physical methods of restraint [8]. Ablebodied patients were recruited to work in the fields or in workshops, which was beneficial both for their condition and for replenishing the medical benefits fund. The hospital accepted patients from all ten governorates of the Kingdom of Poland and, as contemporaries noted, remained overcrowded even after its expansion in 1895.

For the care of the mentally ill patients in the southwestern region of the Russian Empire in 1896, a territorial psychiatric hospital was built about six kilometers from Vinnitsa (in Western Ukraine). The project was created with the active participation of Ragozin L.F. and Ostovsky A.Ye., who had been previously involved in the expansion of the Kazan hospital. Later on, work on the project was continued by civil engineer Krivtsov Ya.V. [1]. It was he who took the idea of building territorial hospitals to its logical conclusion, as he later became involved in the construction of the Vilna, Moscow, and Tomsk hospitals, making the necessary changes and improving the approach to construction.



Figure 2. The project of the Vinnitsa territorial hospital.

Looking back, it is remarkable that, from an architectural point of view, the Vinnitsa hospital marks the transition from a pavilion-style hospital to a hull model. As was noted by Professor Ostankov P.A., the pavilions of the Vinnitsa hospital "directly open into one another without intermediate corridors and warm galleries" [9]. This suggests that, through trial and error, Russian psychiatry arrived at an ideal solution: patients were fanned out to different departments and did not mix with one another. However, all departments remained under the same roof. Owing to such a topology, it became easier to keep an eye on the movements and occupations of patients and to make the rounds. In addition, heating and providing water to one large building proved cheaper than arranging for similar amenities in several, separate pavilions (Figure 2). In terms of amenities, the hospital was even ahead of its time: for instance, it had its own power plant, whereas a municipal power plant was built in Vinnitsa only in 1911. The construction of the territorial psychiatric hospital even influenced the infrastructure of the district: a highway was laid and paved from Vinnitsa to the hospital. The Vinnitsa hospital served the Kyiv, Volyn, and Podolsk governorates.

In 1903, the grand opening of the Vilna (in Lithuania) territorial psychiatric hospital took place. At the time, it was the largest psychiatric hospital in the Russian Empire, designed for a capacity of one thousand beds. Two hundred patients were treated at the expense of the state, while the remainder of the bed space was fee-based so that maintenance of the hospital could pay for itself. All the principles of arranging for territorial hospitals were strictly followed here: constraint and isolation of patients was limited, compliant patients were allowed to venture even outside the territory, while games and concerts were organized at the hospital. A huge park and vegetable gardens adjoined the building, work in which was used as one of the options for occupational therapy for patients (Figure 3). It must be said that the first director of the Vilna hospital, Krainsky Nikolai Vasilievich, not only reasonably managed the hospital, but also actively championed the idea of large-scale psychiatric institutions. Speaking at the IX Pirogov Congress in 1904, he said the following: "Largescale psychiatric hospitals in scientific and organizational terms have a significant advantage over small ones, better conditions for sorting various groups of patients: it is easier to find the benefits necessary for scientific psychiatry in them, and it is easy to achieve mutual exchange of opinions and information" [10].



Figure 3. Vilna territorial hospital.

# **TO SIBERIA**

In the first decade of the 20<sup>th</sup> century, there was much concern over the issue of care of the mentally ill not only in the European part of the Russian Empire, but also in Siberia. For instance, the note by a medical inspector addressed to the Tomsk governorate administration stated that in the psychiatric department of one of the hospitals designed for a sixty-bed capacity, there were one hundred and twenty patients, because of which "we are compelled to deny assistance to a mass of people in need of treatment". The inspector concluded his message with a request "not to refuse a message about the time of the opening of the Tomsk territorial psychiatric hospital". The relevance of the project was also illustrated by the fact that the City Duma (Council) allowed the Construction Committee to use any building materials located within the municipal boundary free of charge and promised to build an access road from the city to the hospital at its expense.

The point was not only that vast Siberia was in need of an institution for the isolation and treatment of people who, due to the state of their mind, could not live in society. At that time, Siberia was also a place of exile for criminals, among whom there was a considerable percentage of people with mental disorders. In that context, the purpose of the psychiatric hospital was broadened, which included housing of the mentally ill who had committed crimes, assessment of the mental abilities of persons in respect to whom the court was in two minds, imprisonment of mentally ill prisoners and isolation of incurable patients and patients deemed to be a danger to the public. Given all these categories, the Tomsk hospital became one of the largest in the Russian Empire; it accommodated 1,050 patients<sup>2</sup> (Figure 4).

The hospital in Tomsk was built according to the same layout as the Vinnitsa and Moscow hospitals. By that time, "psychiatric facility construction" had accumulated some experience in the operation of buildings, so that the chief engineer of the project, Krivtsov Ya.V., could correct the shortcomings: for instance, too-long corridors were recognized as a drawback of the Vinnitsa hospital, and they were eschewed in the layout of the Tomsk hospital. Basically, the new clinic repeated the principles of rationality and harmony tested in other territorial hospitals: a vast area on the river bank, a three-story main building with reception rooms, board, library, and church (Figure 5).



Figure 4. Front view of the Tomsk territorial hospital.



Figure 5. The main staircase of the Tomsk territorial hospital.

<sup>1</sup> Archive of the Regional State Autonomous Healthcare Institution "Tomsk clinical psychiatric hospital".

<sup>2</sup> Historical reference. Regional State Autonomous Healthcare Institution "Tomsk clinical psychiatric hospital".

The protruding parts of the building accommodated apartments for the director and doctors. The wards for patients were located in the sideward and rearward buildings. The plan of the hospital consisted of connecting T-shaped and H-shaped structures, such that a system of closed courtyards for patients emerged. Comfortable wooden cottages were built for the caretaking personnel on the premises of the hospital.

The Tomsk psychiatric hospital welcomed its first contingent of patients in the autumn of 1908. From then on, it served not only the four Siberian governorates, but also the Semipalatinsk, Akmola, and Transbaikal regions<sup>3</sup> (Figure 6).

Toporkov Nikolai Nikolaevich, who until 1907 headed the Vilna territorial hospital, was appointed director of the Tomsk hospital. Notwithstanding the fact that professor Toporkov N.N. had experience in managing a large-scale institution, he had to solve many problems literally from the ground up (Figure 7). Since the Tomsk hospital served a vast territory, many of its patients after having covered guite a long distance reached it extremely exhausted and in need not only of psychiatric help, but also of general somatic treatment. It came as a no surprise that the mortality rate of patients in the first year of operation of the hospital was quite high, reaching up to 13.5%. The second problem was the influx of criminal patients. Toporkov N.N. and other doctors at the hospital launched an extensive labor therapy: shoe, tailor, bookbinding, basketry, weaving, pottery, and rope workshops were set up (Figure 8). The area of more than 400 hectares was used to grow crops and keep domestic animals. In the subsidiary farm there were even stables for breeding pedigree horses. Interestingly, in 1910, the hospital took part in the governorate exhibition of gardening and horticulture and its products were awarded a bronze medal<sup>4</sup>. Occupational therapy not only had a positive effect on the state of the mentally ill, but also opened up new perspectives for patients, as with the learning of a new craft, they gave themselves a chance to better adapt in society. Literacy teaching was practiced quite widely in the hospital. In addition, Toporkov N.N. paid attention to the organization of leisure time: holidays and dances were organized for patients, and employees of the hospital



Figure 6. Arrival of patients at the Tomsk territorial hospital.



Figure 7. Toporkov N.N., the first director of the Tomsk territorial hospital, surrounded by colleagues.



Figure 8. Patients of the Tomsk territorial hospital busy weaving fishing nets.

<sup>3</sup> Certificate of execution of the Highest approved opinion of the State Council on the construction of a district hospital for the mentally ill in Tomsk. Archive of the Regional State Autonomous Healthcare Institution "Tomsk clinical psychiatric hospital".

<sup>4</sup> Historical reference. Regional State Autonomous Healthcare Institution "Tomsk clinical psychiatric pospital".

played in the wind and balalaika bands at these events (Figure 9). Despite the long odds, the Tomsk territorial hospital could find pride in its achievements as early as in the first years of its inception. For instance, in 1909 it presented its album and diagrams at the III Congress of Psychiatrists. In 1911, it took part in the International Hygienic Exhibition in Dresden, and in 1913 it showcased its achievements at the All-Russian Hygienic Exhibition in St. Petersburg, where it was awarded a small gold medal.

# **CRIME AND TREATMENT**

An important stage in the project was Moscow territorial hospital for the mentally disturbed (today, Psychiatric Clinical Hospital No. 5 of the Moscow Healthcare Department), which opened in the autumn of 1907. It was built on the same principle as the previous buildings of the project: numerous buildings were located in one common hull connected with each other through corridors (Figure 10). Initially, Moscow hospital was planned as a specialized institution; i.e., for the incarceration of patients who have committed crimes. The regulation of the hospital of 1907 stated its purpose as follows: "...for the maintenance and care of the mentally ill, especially dangerous criminals, both convicted and under investigation; to test the mental faculties of persons assigned by court ruling; as well as for the care and use of persons mentally ill, incurable, and constituting a danger to society" [11].

Time itself called for the establishment of a psychiatric hospital of such type. By 1907, the medical institutions of the Russian Empire had begun increasingly admitting patients convicted of various criminal offenses, and zemstvo hospitals had been instructed to admit them unconditionally. As a result, beds for other patients became scarce. A commission including the prominent psychiatrists Merzheevsky I.P., Bekhterev V.M., and Krainsky N.V. came to the conclusion that care of the mentally disturbed needed to be differentiated. Acute mentally disturbed patients and those constituting no threat to the public with chronic diseases remained under the care of the zemstvo, while a decision was made to move patients awaiting testing, prisoners, and patients constituting a public danger with chronic diseases into territorial hospitals. Therefore, the Moscow and Tomsk hospitals were built with account of the need of the state to sequester people who were deemed to be a threat to society and could not be placed in ordinary prisons due to their mental condition.



Figure 9. Participants in amateur performances after the show.

The need to build a territorial psychiatric hospital near Moscow becomes particularly obvious if one turns to the testimonies of contemporaries. One of the petitions to the government at the time stated that the mentally ill were brought to Moscow from almost all over Russia and abandoned to their fate on the streets or at railway stations. The dangerous acts they committed caused escalation of public tension. It was obvious that such patients were in need of special care and treatment. To solve the problem, the Tsar's government decided to purchase the territory of the former estate of the Obolensky princes in the village of Troitskoye, Molodinskaya volost, Podolsky district, and build a prison-type territorial psychiatric hospital. Despite the stated purpose of the establishment, the building was kept in the original spirit of the project: a picturesque area with beautiful groves, ponds, and a river; a completely autonomous farmstead; living conditions for doctors and the caretaking personnel right on the premises; and division into buildings, of which only four departments were intended for "criminal" patients. The small gardens



Figure 10. Moscow territorial hospital, 1910.

adjoining these structures were surrounded by brick walls. There was no common fence that could be seen around the hospital, now in the first years of its operation (Figure 11). As early as at the construction stage, the hospital provided jobs to the residents of the village of Troitskoye, which by that time was in decline and, one might say, was being deserted. Throughout its history and until now, the hospital has remained a "city-forming enterprise" for the village.

It should be noted that, although the Moscow territorial hospital was built at the subsequent stages of the project, it was the first example of a prison-type hospital. It is, therefore, not surprising that the audit carried out by the Ministry of Internal Affairs before the official opening of the hospital uncovered some shortcomings [12]. In his report, Yesaulov N.N., the inspector of the Moscow Medical Department, called the enormous floor area of the building with many passages and descents into a dark tunnel an unfixable flaw of the design. All that, along with the dense thickets around the hospital, played in favor of escapes. To reduce the likelihood of such incidents, screens were installed in the windows of some wards, locks appeared in isolation rooms, and ordinary window panes were replaced with durable sheet glass. In addition, control frames were installed in the doors, and metal bars were installed in the windows of the tunnel. Wide clearings were cut through the dense thickets surrounding the hospital, so that any unauthorized movement would immediately come into the view of the hospital personnel. Numerous construction shortcomings were also identified, in spite of which the hospital nevertheless opened, and in the first years of its operation it not only performed its immediate tasks, but its construction was also finally completed.

Kolotinsky Sergei Diomidovich, the first director of the Moscow Territorial Psychiatric Hospital, actually assumed the management of the entire hospital campus (Figure 12). The perimeter of the main building alone, consisting of seventeen buildings, stretched four kilometers. The two adjoining three-story buildings accommodated apartments for doctors and the so-called supervisory building with apartments for paramedical personnel. Nurses, servants, and workers resided in the basement. Heating in the hospital was provided by calorific stoves, and a narrowgauge railroad was laid underground, used for delivering fuel to the stoves. Hot air was supplied through ducts in the walls and heated the vast areas of the hospital. Water was supplied to the hospital from a pumping station through a six-story water tower. In 1908, a school was opened on the second floor of this tower for the children of the hospital personnel. This was because at the beginning, a significant part of the hospital personnel were employees of the Vinnitsa hospital who had followed the director, along with their families. Since there were not enough room in the zemstvo school, a school was established for the children of doctors and residents right on the premises of the hospital. Adjacent to the tower was a household utility building with a kitchen, a bakery, a canteen for employees, a bathhouse, a laundry, a sewing workshop, and disinfection rooms. Like other territorial hospitals, the Moscow hospital had its own power plant. Owing to that plant, not only the entire hospital town, but also part of the road to the station was illuminated.



Figure 11. Moscow territorial hospital. Patients taking a walk, 1910.



Figure 12. Moscow territorial hospital. Chief physician's office.

"The extraordinary splendor, cleanliness, spaciousness, convenience" — such was the feedback about the Moscow territorial psychiatric hospital left by Leo Tolstoy, the great Russian writer. He visited the hospital in 1910, and, later, his impressions of the visit became the basis for his article "On Insanity" (Figure 13).

In 1911, Moscow territorial hospital for the mentally ill took part in the International Hygiene Exhibition in Dresden and was awarded a bronze medal, which was a clear acknowledgement of how far Russian psychiatry had come. The exposition of the hospital at the exhibition included a model of the buildings and other visual materials: reports, albums, official forms, sample documents, instructions for hospital personnel on the care and supervision of patients, as well as drawings and crafts by the mentally ill. Today, all this constitutes a significant part of the collection of the hospital's museum (Figure 14).

The First World War came as a serious shock for the territorial psychiatric hospitals. In 1914–1915, the Moscow territorial hospital admitted patients and employees from the territorial hospitals in Warsaw and Vilna. One can imagine what selfless labor and administrative talent it took to accommodate so many people. But the personnel of the Moscow hospital rose to the occasion. Local doctors even managed to stop the outbreak of cholera brought to the Moscow region along with the evacuated patients.

Since the beginning of the 20<sup>th</sup> century, Moscow territorial hospital has become an example of sound care and treatment of the mentally ill. Today, Psychiatric Clinical Hospital No. 5 of the Moscow Healthcare Department is the largest hospital in Russia providing coercive treatment. It is designed for 1,630 patients. The hospital has 27 departments: 12 general and 15 specialized. Among

the above: 3 women's departments, one department for HIV-infected patients, and one department for patients with a combined tuberculosis pathology. The hospital employs 120 doctors and 932 nurses. The main goal of the medical institution is a complete rehabilitation and resocialization of the mentally disturbed, as well as the prevention of recidivism on the part of discharged patients deemed a danger to the public. Therefore, the medical practice utilizes not only the most advanced psychopharmacological drug products, but a lot of rehabilitation activities work is also carried out, such as psychotherapy, art therapy, cultural therapy, occupational therapy in medical, and labor workshops.

Despite the length of stay in the hospital during the phase of coercive measures, preparation for discharge begins from the time of admission, for which purpose the rehabilitation potential is determined and, based on objective data, an individual medical and social rehabilitation program is prepared. A training classroom has been arranged on the premises of the Department of Medical and Social Rehabilitation (DMSR), which can accommodate up to 12 patients (learners). The classroom is equipped with Internet access and involves various forms of vocational training (both full-time and part-time). These conditions also allow for the training of both adult patients and persons under legal age using video conferencing and remote technology.

At the site of the DMSR, three sewing workshops were launched, with a total of 50 stations, which makes it possible for a large number of patients to immerse in occupational therapy. Many of them underwent professional training during their treatment and thereby gave themselves the opportunity for further employment.



Figure 13. Tolstoy L.N. visits the Moscow hospital.



Figure 14. Moscow territorial hospital. Duty doctor's room.

As part of a need for consistency as regards coercive treatment and the effort to prevent recidivism, joint meetings are held with specialists from neuropsychiatric dispensaries who are charged with direct supervision of the patient after his/her discharge. As part of these activities, doctors tasked with carrying out compulsory outpatient monitoring and treatment after discharge get acquainted with patients and learn from the attending physicians and other hospital specialists (psychologists, social workers) all the details of the patient's clinical pattern, treatment, social status, and occupational therapy potential.

The following is worth mentioning as a separate point: several dynasties of doctors have served in the hospital, and this has contributed to the continuity of traditions and the transfer of experience from generation to generation.

In 2021, Psychiatric Clinical Hospital No. 5 of the Moscow Healthcare Department was awarded the Golden Butterfly award and a diploma of the winner of the 16<sup>th</sup> All-Russian competition "For devotion in the field of mental health" named after academician Dmitrieva T.B. in the nomination "Best Institution of the Year".

# CONCLUSION

The 19<sup>th</sup> century — the era of urbanization and rapid technological progress — brought society face to face with the problem of how best to provide care to and treat the mentally ill. Russia's response to that challenge was to develop a set of principles of structure in psychiatric care, create legislation, and to implement a project to pepper the country with a series of territorial psychiatric hospitals: the first medical establishments in its history designed on the basis of a detailed analysis of the need for and types of inpatient psychiatric care and a comprehensive discussion of the issue with leading professionals in the field and government officials.

There is little doubt that the project of territorial psychiatric hospitals took psychiatry in Russia to a whole new level, as its implementation coincided with the introduction of psychiatry into the curriculum of medical universities, and the first territorial hospitals were set up in the proximity of university cities. Subsequently, the activities of territorial hospitals provided extensive clinical material for the departments of psychiatry, and universities, in turn, communicated the latest achievements in medical science and contributed to their introduction into medical practice. At the same time, the project of territorial psychiatric hospitals became the first experience of a new "psychiatric facility construction". It advanced not only medical science, but also civilian architecture. Through trial and error, a balance was struck between scale and soundness. As practice shows, the principles used in the planning and management of territorial hospitals have withstood the test of time and retained their relevance today.

Finally, the project of territorial psychiatric hospitals was instrumental in shifting the emphasis in care for the mentally disturbed from isolation to treatment, in encouraging a more humane attitude towards the mentally ill and, at the same time, making care more efficient. Territorial hospitals played a decisive role in popularizing psychiatry among the general public: psychiatric hospitals began to be perceived not as frightening "lunatic asylums", but as institutions where the mentally ill patients were given assistance and which promoted their recovery.

The fate of the territorial hospitals, which were part of the 19<sup>th</sup> century project, was different. Some of them did not survive the wars and revolutions of the 20<sup>th</sup> century and lost their original purpose, while others, despite suffering extensive damage during the Second World War, managed to recover and resume activities, albeit by then in the territories of other states. Today the Kazan, Moscow, and Tomsk hospitals continue to operate within the borders of Russia. It is worth noting that a century and a half later, they continue to advance the cause of psychiatry, honor the clinical traditions established by their first directors, and offer highly qualified comprehensive care to those who need it.

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