

# Psychopathology, psychosocial factors and obesity

## *Psicopatologia, fattori psicosociali e obesità*

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**SUMMARY. Aims.** The aims of this study were to evaluate the association between obesity and socio-demographic and psychopathological variables in a clinical sample of patients referred to a center for the diagnosis and treatment of obesity, compared with a homogeneous sample of normal-weight subjects. **Methods.** In the context of a research project regarding obesity and psychopathology, a multivariate logistic regression analysis was used to examine the association between obesity and the demographic and clinical variables, on the basis of the data set of a consecutive sample of 293 obese patients (48 males, 245 females, mean age:  $45.41 \pm 13.55$ , mean body mass index [BMI]  $35.6 \pm 6.2$ ) compared with a control group of 293 non-obese subjects (48 males, 245 females, mean age  $45.66 \pm 13.86$ , mean BMI  $21.8 \pm 2.06$ ). All subjects were assessed by structured clinical interview, the Structured Clinical Interview for Diagnosis for axis I DSM-IV (SCID-I) and for axis II DSM-IV (SCID-II). **Results.** Multivariate statistical analysis showed that the status of housewife and the presence of lifetime axis I and II psychiatric diagnosis in general, and of depressive, anxiety, eating and some personality disorders in particular, significantly increased the likelihood of being overweight/obese. The likelihood for different combinations of risk factors increased from a value of 32.3% for an individual not exposed to any risk factor, to a value of 86.7% for those exposed to all risk factors considered. **Conclusions.** The presence of an axis I and/or II diagnosis and housewife status are both independently associated with an increased likelihood of being overweight/obese. The interaction of these factors increases this likelihood. Even taking into account the limits of the study, in particular of its cross-sectional nature, these findings may have important implications in both prevention and treatment of obesity.

**KEY WORDS:** obesity, overweight, mental disorders, depression, anxiety, eating disorders, personality disorders, comorbidity, psychosocial factors.

**RIASSUNTO. Scopi.** Gli obiettivi di questo studio sono stati la valutazione dell'associazione tra obesità, variabili socio-demografiche e psicopatologiche in un campione clinico di pazienti afferenti a un centro per la diagnosi e il trattamento dell'obesità, confrontati con un campione omogeneo di controllo costituito da soggetti di peso normale. **Metodi.** Nel contesto di un progetto di ricerca riguardante obesità e psicopatologia, è stata applicata una regressione logistica multivariata per esaminare l'associazione tra obesità e variabili demografiche e cliniche relative a un campione consecutivo di 293 pazienti obesi (48 maschi, 245 femmine, età media:  $45,41 \pm 13,55$ , indice di massa corporea [BMI]  $35,6 \pm 6,2$ ), confrontato con un gruppo di controllo omogeneo appaiato di 293 soggetti non obesi (48 maschi, 245 femmine, età media  $45,66 \pm 13,86$ , BMI medio  $21,8 \pm 2,06$ ). Tutti i soggetti sono stati valutati mediante un'intervista clinica strutturata, la Structured Clinical Interview per la diagnosi di asse I del DSM-IV (SCID-I) e per l'asse II DSM-IV (SCID-II). **Risultati.** L'analisi statistica multivariata ha dimostrato che lo status di casalinga e la presenza "lifetime" di disturbi di asse I e II e in generale della presenza di una qualsiasi diagnosi psichiatrica, e, in particolare, delle diagnosi di disturbo depressivo, d'ansia, del comportamento alimentare e di alcuni disturbi di personalità, sono associate in modo significativo a una maggiore probabilità di essere in sovrappeso oppure obesi. Le probabilità di essere sovrappeso/obesi si modificano in rapporto alle diverse combinazioni di fattori di rischio, aumentando da un valore di 32,3% per un individuo non esposto ad alcun fattore di rischio, a un valore di 86,7% per i soggetti esposti a tutti i fattori di rischio considerati. **Conclusioni.** La presenza di una diagnosi di asse I e/o II e lo stato di casalinga è indipendentemente associata a un maggiore rischio di sovrappeso/obesità. L'interazione di questi fattori aumenta questo rischio. Pur tenendo conto dei limiti dovuti alla natura trasversale dello studio, questi risultati sono collegati a implicazioni importanti sia ai fini della prevenzione sia del trattamento dell'obesità.

**PAROLE CHIAVE:** obesità, sovrappeso, disturbi mentali, depressione, ansia, disturbi alimentari, disturbi di personalità, comorbilità, fattori psicosociali.

## INTRODUCTION

Overweight and obesity are a public health problem featuring a constant upwards trend<sup>1,2</sup> and represent a relevant

risk factor for a number of other medical conditions associated with increased rates of morbidity and mortality<sup>1-4</sup>. The multifactorial etiology of obesity involves complex interactions between genetic, hormonal and social-environmental

factors, including sedentary lifestyle and poor eating habits<sup>1,2</sup>.

Several other factors, including age, gender, socio-cultural, economic and marital status and job categories have been associated with the development of overweight/obesity<sup>5-7</sup>. Psychosocial factors occurring in childhood, such as episodes of violence and abuse, poor parental support and academic difficulties, appear to produce a significant impact in determining the development of overweight/obesity in adolescence and adulthood<sup>8,9</sup>. Moreover, a relevant number of cross-sectional studies, the majority of which focused on depression, have revealed a significant association of psychopathology with overweight/obesity. Indeed, a meta-analysis of 17 cross-sectional population studies has shown that depression is associated with an increased risk of becoming obese, an association found in women but not in men<sup>10</sup>. Moreover, an association between obesity and anxiety disorders emerged from a recent review and meta-analysis of population-based studies, largely based upon a cross-sectional design<sup>11</sup>. Most of the studies show a positive relationship with panic disorder, mainly in women, and with specific phobia and social phobia, although the role of subtypes of anxiety disorders and obesity severity remains to be fully clarified<sup>12</sup>. Similarly, a strong association is reported in literature between eating disorders (ED), particularly binge eating disorder (BED) and obesity<sup>13</sup>. Finally, data currently available derived from cross-sectional studies show a high overall prevalence of personality disorders in obese subjects<sup>14-17</sup>. As cross-sectional studies do not allow any inference to be made as to the direction of causality (i.e. mental disorder may be the cause or consequence of obesity), more information is provided by longitudinal studies, again prevalently focused on depression. Indeed, the presence of depressive symptoms during childhood and adolescence has been revealed as one of the most frequently identified risk factors in relation to the development of obesity in adulthood, particularly among women<sup>8,10,18</sup>. However, a review and meta-analysis of longitudinal studies has demonstrated a reciprocal relationship between obesity and depression, with important implications in terms of prevention, early diagnosis and treatment<sup>19</sup>. Indeed, a condition of overweight/obesity was found to increase the risk of depression, whilst on the other hand depression was found to be predictive of later development of obesity, with a 58% increased risk of becoming obese<sup>19</sup>. With regard to anxiety, a recent prospective cohort study showed that symptoms of anxiety, on a par with symptoms of depression, were associated with a greater change in weight and increased incidence of obesity in both men and women<sup>20</sup>. Several longitudinal studies have demonstrated binge eating as a risk factor for overweight/obesity<sup>21-26</sup>, although a study of adolescent girls failed to identify this association<sup>27</sup>. Pertaining to personality psychopathology, a longitudinal study showed that aggressive personality traits and sociopathy were positively associated with the development of overweight<sup>23</sup>, with another study revealing a positive relationship between some specific personality disorders in early adulthood and an increased risk of problems related to eating habits and weight in later life<sup>28</sup>. Overall, a large body of literature, including large community studies<sup>10,11,17,29,30</sup> has reported a significant association between specific psychopathological conditions, mainly depression, and overweight/obesity, with a bi-directionality of causal relationship. Starting from these premises and con-

sidering the relative paucity of studies of clinical populations of obese patients conducted to verify diagnosis by means of structured psychiatric interviews, a study program on obesity and psychopathology was set up several years ago, the results of which have been previously reported elsewhere<sup>31-35</sup>. In a first cross-sectional study of 150 consecutive obese patients attending a university center for the diagnosis and treatment of obesity we demonstrated a very high lifetime prevalence of axis I (58%) and axis II (28%) disorders according to DSM-IV-TR<sup>31</sup>. Prevalence rates were significantly higher than those found in the corresponding general population across all principal classes of common mental disorders (mood and anxiety disorders) and among ED, with depressive disorders (DD) (26%) and BED (16%) being the single most widely represented diagnoses. In a subsequent case-controlled study<sup>32</sup>, the principal aim of which was to investigate quality of life in relation to psychopathology, a larger sample of obese patients (n=293) was studied and compared to a sample of normal controls (n=293) matched according to gender, age, marital status and education; in this study a significantly higher odds of both axis I and II disorders was detected among obese subjects, in particular anxiety and mood disorders, with particular reference to major depression (MD), and BED<sup>32</sup>. In the present paper we report the results of a further analysis of the data set obtained in the latter study, for the purpose of examining, by means of multivariate analysis, the association between obesity and psychiatric disorders, taking into account social variables, potential confounding effects and the interaction of factors.

## MATERIALS AND METHODS

### Sample

An unselected sample of consecutive patients referred to a University Center for the diagnosis and treatment of obesity that treats approx. 450 subjects a year was assessed. The center provides a comprehensive medical and psychological evaluation with a multidisciplinary approach, including drug treatment, dietary and psycho-educational interventions tailored to individual needs. When necessary, psychological support or psychiatric intervention was made available. Of the 298 subjects contacted over a 9-month period, only five refused to take part in the study. The final study group was made up of 293 subjects. As a control group of normal-weight subjects, we used a convenience sample of university students and their families made up of 293 individuals, matched as much as possible for sex, age, marital status and education. Sample and controls were prevalently constituted by females (48 males, 245 females, both in cases and controls), married (respectively 199, 67.9% and 198, 67.6%), with a high level of education (high school or graduates were respectively 155, 52.9% and 156, 53.2%), without any difference from a statistical point of view; as far as occupation was concerned, a higher number of employed was found among controls (167, 57% vs 127, 43.4% of cases) and of housewives among cases (92, 31.4% vs 64, 21.8% of controls) ( $p < .001$ ). As expected, mean BMI (cases=35.60 $\pm$ 6.20, controls=21.83 $\pm$ 2.06) and average waist circumference (cases=112.17 $\pm$ 13.94 cm, controls=78.38 $\pm$ 9.58 cm) were both significantly higher among cases than controls (respectively,  $t=36.047$ ,  $df=584$ ,  $p < 0.001$ ,  $t=34.173$ ,  $df=584$ ,  $p < 0.001$ ). Among cases approx. 16.8% (n=50) of subjects were overweight; obese subjects were distributed in classes as follows: class I 33.2% (n=97); class II 29.1% (n=85), class III 20.9% (n=292).

## Methods

Socio-demographic data, medical history and clinical data were collected by means of a structured interview purpose-developed for the study.

After signing an informed consent form, all patients and controls underwent a comprehensive psychiatric evaluation using the Structured Clinical Interview for Diagnosis for axis I DSM-IV (SCID-I Research Version)<sup>36</sup>, and the interview for the Structured Clinical Diagnosis of axis II of DSM-IV (SCID-II)<sup>37</sup>.

Interviews were conducted by residents in psychiatry trained in the use of the instrument by a trained specialist (FP), the inter-rater reliability, assessed using Cohen's K before starting the study, was not less than 0.80.

Anthropometric measurements were taken using standard calibrated instruments. Height (m) was measured using a wall-mounted stadiometer; weight (kg) using electronic scales with an upper weight limit of 300 kg. Body Mass Index (BMI) was calculated as Weight/Height<sup>2</sup>.

## Statistical analysis

Differences between continuous variables were calculated by means Student's t test for unpaired data; comparison of categorical variables was performed by means of chi square test. Basing upon data of preliminary univariate analyses previously published in another paper of our group<sup>32</sup>, in order to assess the combined effects of different variables on the risk of obesity, a multivariate logistic regression was performed, considering obesity vs normal weight status as dependent variables, while sociodemographic variables and the presence of an axis I or axis II diagnosis were considered as independent variables. The dependent variable was analyzed as a function of each independent variable and their second order interactions. The backward-stepwise method was adopted, in which all variables and interactions were initially inserted in the model based on the available clinical and epidemiological knowledge; subsequently, non-significant interactions ( $p > 0.20$ ) and variables ( $p > 0.05$ ) were consecutively eliminated by means of a step by step procedure starting from the saturated model applied to perform logistic regression. The association of each independent variable with the dependent variable was expressed by means of OR and its 95% confidence interval. The probability of being obese as a function of the different combinations of risk factors identified was calculated using the parameters obtained with the logistic model. A further logistic regression was used to identify the specific diagnosis of axis I and axis II associated with obesity. This second analysis considered the status of being overweight vs. normal weight as dependent variable and a number of diagnoses (bipolar disorder, major depressive disorder or other unipolar disorders, anxiety disorders, eating disorders, substance use disorders, psychotic disorders, avoidant personality disorder, obsessive compulsive personality disorder, passive aggressive personality disorder, depressive personality disorder, paranoid personality disorder, schizoid personality disorder, histrionic personality disorder, narcissistic personality disorder, borderline personality disorder, antisocial personality disorder, personality disorder not otherwise specified [NOS]), as independent variables, in addition to professional status.

## RESULTS

Univariate analyses demonstrated that obesity was associated with a significant lifetime major risk both for axis I

(OR=3.47,  $p=0.000$ ) and axis II disorders (OR=2.27,  $p=0.000$ )<sup>32</sup>.

No statistically significant difference was found in distribution of subjects according to overweight/obesity classes and psychiatric diagnosis (any axis I, any axis II disorders or any specific disorder); with only two exceptions: MD and obsessive compulsive disorder (OCD). Indeed, patients affected by MD ( $n=59$ ) included a significantly higher proportion of overweight (20.3%), class I (35.6%) and II (37.3%) obese subjects and a lower proportion of class III (6.8%) subjects compared to patients affected by any other disorder ( $n=234$ ), who were diagnosed as follows: overweight=15.9%, class I=32.6%, class II=27%, class III=24.5% (chi square test=9.430,  $gl=3$ ,  $p=0.024$ ). Patients affected by OCD ( $n=4$ ) were characterized by a significantly different distribution, with all 4 subjects classified as obesity class I (100%), compared to patients affected by any other disorder ( $n=288$ ) who were classified as follows: overweight=17%, class I=32.3%, class II=29.5%, class III=21.2% (chi square test=8.153,  $gl=3$ ,  $p=0.043$ ).

Multivariate logistic regression showed a significant effect of professional status (housewife) and both axis I and axis II diagnosis (Table 1). The final model indicated that individuals with a diagnosis of axis I run a 2.7 times greater likelihood of obesity compared with subjects without axis I disorders (95% CI 1.20 to 2.63). Individuals with an axis II diagnosis are at a 2.80 times greater likelihood of obesity compared with subjects with no axis II diagnosis. Housewives showed an approx. 1.8 times greater likelihood of obesity than other professional statuses considered. The model showed no significant interactions, so that the likelihood of obesity in presence of more than one risk factor is the product of the individual odds ratios. The likelihood of being obese for different combinations of risk factors increased from a value of 32.3% for an individual not exposed to any risk factor, to a value of 86.7% for those exposed to all risk factors considered (Table 2).

Table 1. Multivariate Logistic Regression analysis: significant associations between obesity (dependent variable) and clinical/psychosocial variables (independent variables)

	p	OR	CI 95%
Housewife	0.004	1.77	1.20-2.63
Lifetime axis I diagnosis	0.0000001	2.75	1.89-3.98
Axis II diagnosis	0.0001	2.80	1.70-4.62

Table 2. Likelihood of being obese for different combinations of risk factors

Risk factors	Likelihood of being obese
No risk factor	32.3%
Housewife	45.8%
Lifetime axis I diagnosis	56.7%
Axis II diagnosis	57.2%
Housewife+axis I diagnosis	69.9%
Housewife+axis II diagnosis	70.3%
Axis I+axis II diagnosis	78.6%
Housewife+axis I+axis II diagnosis	86.7%



When logistic regression was used to identify the specific axis I and axis II diagnoses associated with obesity, a higher likelihood associated with the status of housewife was again confirmed, together with being affected by major depression (OR=2.17), anxiety disorder (OR=2.35), eating disorder (OR=12.92), avoidant disorder (OR=10.07), paranoid disorder (OR=11.43), personality disorder NOS (OR=1.96) (Table 3).

## DISCUSSION

Before discussion data from this study, it should be underlined that findings should be considered in the light of several major limitations. First, the sample investigated comprised individuals seeking weight loss treatment and should therefore not be considered representative of obese subjects living in the community or of obese people contacting other clinical settings for reasons other than their overweight; second, the sample examined was largely made up of females, a finding consistent with other studies investigating clinical samples<sup>40,41</sup>, likely reflecting a more pronounced propensity of women to seek assistance for weight related problems; third, mental disorders were evaluated only by means of structured clinical interviews, without using self-reported instruments; fourth, the cross-sectional nature of this study prevents the drawing of any conclusion as to the direction of causality in the association between mental disorders and obesity.

Data available in the literature show consistently higher prevalence rates of mental disorders in clinical<sup>38-43</sup> samples of obese patients. The association of mental health and obesity may be related to an interplay of a wide range of individual (such as gender and age) and contextual factors (such race, ethnicity and culture)<sup>44,45</sup>. Moreover, several biological factors have been proposed to explain the relationship between mental disorders and obesity with significant implications for the treatment<sup>46</sup>.

Preliminary results of this study project, based upon univariate analyses<sup>32</sup>, showed a significantly increased odds of any lifetime axis I and axis II disorders, axis II disorders or their comorbidity to be associated with obesity; in particular, among axis I disorders, mood disorders (including MD, BD), anxiety disorders, ED were strongly associated with over-

weight. Basing on these previous findings, in this paper we re-examined the association between obesity and psychiatric disorders by means of multivariate analyses, taking into account psychosocial variables and the potential confounding effects and interaction of factors.

In particular, multivariate analysis revealed how being an housewife was the only socio-demographic condition associated to an increased likelihood of overweight/obesity. This finding is congruent with the limited data present in literature showing a higher prevalence of obesity among housewives compared to other workers<sup>7,47</sup>. Numerous factors have been hypothesized as underlying these findings, including low socio-economic and/or cultural status, unhealthy dietary habits and insufficient physical activity, given that family and domestic duties may represent a limitation with respect to a commitment to regular physical activity<sup>7</sup>. However, the fact that physical activity alone has not proved to be sufficient to obtain and maintain a substantial weight loss should be considered<sup>47</sup>.

Multivariate analysis confirmed that being affected by a lifetime axis I diagnosis, in particular MD disorder or other unipolar mood disorders, anxiety disorders and eating disorders (BED) is associated with an increased likelihood of overweight/obesity. Likewise, being affected by an axis II personality disorder, in particular avoidant, paranoid, and not otherwise specified disorder, is also correlated with an increased odds of overweight/obesity. These results are largely in accordance with data currently available in the literature with regard to the association of psychopathology and overweight/obesity. Accordingly, the findings reported in longitudinal studies have demonstrated that depressive symptoms during childhood and adolescence are associated with an increased risk of development of obesity in adulthood<sup>8,19,48</sup>. Several putative reasons have been put forward to explain this increased risk of overweight/obesity among depressed subjects. Unhealthy lifestyles, both in terms of insufficient physical activity and eating habits have been implicated, particularly in atypical depression, frequently associated with binge eating and overeating<sup>19,49-51</sup>. Antidepressant treatments may lead to a weight gain in subjects affected by depression or other mental disorders<sup>19</sup>. Dysfunction of biological systems implicated in both depression and obesity, such as the hypothalamic-pituitary-adrenal (HPA) axis, the central monoaminergic systems, leptin, the immune systems and glucose and lipid metabolism may interact, thus contributing towards explaining such a frequent association between depression and overweight/obesity<sup>52-56</sup>. In agreement with our results, literature data emphasizing the association between obesity and anxiety disorders reveal an overall positive relationship<sup>11,12</sup>. Data from a prospective study showed an association between anxiety disorders in childhood and adolescence and an excess of weight in subsequent years, although at a statistically significant level only for females<sup>57</sup>. A recent longitudinal population study demonstrated that both male and female subjects who received a diagnosis of anxiety disorder during infancy featured a higher BMI than controls in the following years<sup>48</sup>. The risk of weight gain related to an anxiety disorder has itself been attributed to different factors such as a possible dysregulation of the HPA axis, dysfunctional eating habits due to symptoms such as increased appetite and/or craving for sweet or fat foods, the presence a comorbid chronic condition (e.g., asthma) with a significant

Table 3. Multivariate Logistic Regression analysis: significant associations between obesity (dependent variable) and categories of mental disorders (independent variables)

	p	OR	CI 95%
Housewife	0.003	1.83	1.23-2.73
Major depressive disorder or other unipolar disorders	0.001	2.17	1.35-3.50
Anxiety disorders	0.0003	2.35	1.48-3.73
Eating disorders	0.00003	12.92	3.88-42.97
Avoidant personality disorder	0.03	10.07	1.18-85.72
Paranoid personality disorder	0.02	11.43	1.37-95.37
Personality disorder NOS	0.03	1.96	1.06-3.62

impact on functioning, resulting in decline in physical activity and excess weight<sup>11</sup>. In addition, anxiety disorders may indirectly be related to an increased odds of overweight/obesity though genetic and hormonal factors, traumatic events in childhood, personality dysfunctional traits, comorbidity with other psychiatric and somatic conditions<sup>11</sup>. In our study binge eating disorder was seen to be strongly associated with an increased likelihood of overweight/obesity, a result in agreement with the findings obtained in the majority of longitudinal studies, showing a positive association between binge eating and subsequent weight gain<sup>21-26</sup>. However, it should be underlined that even a study reporting a negative association has been published<sup>27</sup>. Uncontrolled overeating is viewed as one of the main explanations for the weight gain frequently observed among patients affected by BED; moreover, a common genetic factor shared by patients affected by obesity and binge eating disorder was hypothesized<sup>58,59</sup>. Our data lend further support to the hypothesis that some personality disorders may contribute towards the development of weight problems, as shown by previous cross-sectional studies showing a higher BMI in subjects with a cluster A or B personality disorders<sup>60,61</sup>, higher percentages of cluster A, B, and C personality disorders in subjects with severe obesity<sup>60</sup>, an increased odds of avoidant and antisocial personality disorder in obese women with extreme obesity<sup>17</sup>, and a positive association between overweight/obesity and paranoid, antisocial and avoidant personality disorders among female patients<sup>15</sup>. Moreover, a longitudinal community study has demonstrated an association between several personality disorders, namely schizoid, schizotypal and antisocial disorders in early adulthood, and a major risk of weight problems or obesity in later life<sup>28</sup>. The reason for this association is unknown, although some behavioral factors may partly explain these findings, such as a tendency towards marked social avoidance and the consequent development of a sedentary lifestyle in individuals affected by avoidant and paranoid personalities, while impulsiveness and the related tendency to loss of control over eating habits could be taken into account for individuals with antisocial and borderline personality disorders<sup>15</sup>.

Some authors have claimed that the frequent association between cluster A personality disorders and obesity may be due to a common dopaminergic dysfunction, although this hypothesis fails to explain the gender differences observed in the association between obesity and these personality disorders reported in some studies<sup>15,17</sup>. One of the main findings of the present study is the apparent interactive role of social and psychopathological factors in increasing the odds of obesity. Indeed, the probability of being overweight/obese rises approx. to 46% for a housewife and to approx 57% for a person affected by an axis I or II disorder; this probability increases to approx. 70% for a housewife affected by an axis I or II disorder, becoming extremely high for subjects affected by an axis I and II disorder (approx. 79%) and for housewives featuring comorbidity with an axis I and II disorder (approx. 87%). In other words, our study demonstrates how the presence of an axis I and II disorder according to DSM-IV-TR, and being a housewife are independently associated to a higher odds of being obese, highlighting how the interaction of these factors further increases this probability. Therefore, the evidence provided by this study appears to be of interest not only from a theoretical, but also from a prac-

tical point of view, particularly in view of the potential use in identifying subjects at risk of developing obesity. Although our data are congruent with those deriving from longitudinal studies, supporting the possible role of several psychiatric conditions in conjunction with psychosocial variables in developing obesity, as previously acknowledged, the cross-sectional nature of our study prevents the drawing of any conclusion in terms of direction of causality in the association between mental disorders and obesity. Indeed, psychopathology may be not only the cause but even a consequence of obesity, at least as regard to depression<sup>19</sup>, a hypothesis further supported by studies regarding remission of depression after surgical treatment of bariatric patients<sup>62</sup>. However, irrespective of the nature of the relationship between obesity and mental disorders (whichever is the prevalent disorder), the data obtained demonstrate that more than half of obese patients seeking treatment for their overweight or obesity are affected by psychiatric comorbidity, a finding which justifies the need for careful psychiatric evaluation and treatment in the context of a multidisciplinary approach.

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