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## Predictive factors of anxiety and depression symptoms in patients with breast cancer undergoing chemotherapy. An explorative study based on metacognitions

### Summary

#### Objectives

*Chemotherapy is a treatment associated with a decrease in the patient's quality of life. Negative emotions as depressive and anxiety symptoms are common during treatment for non-metastatic breast cancer. Many studies have found a link between dysfunctional metacognitive beliefs and psychopathology. However this relationship remains unclear in patients with breast cancer during chemotherapy. Aim of the study was to explore how metacognitions predict anxiety and depression in breast cancer patients undergoing chemotherapy.*

#### Materials and Methods

*A convenience sample of 80 breast cancer patients undergoing chemotherapy in an outpatient clinic completed a demographic questionnaire, the Metacognitions Questionnaire 30 (MCQ-30), and the Hospital and Anxiety Depression Scale (HADS). Medical information about the stage of disease and the history of treatment was provided. A correlational analysis was performed to explore relationships between metacognitions and psychological symptoms. To examine the independent role of metacognitions to predict anxiety, depression, and overall distress (anxiety and depression), three hierarchical regression analyses were conducted.*

#### Results

*Results of correlational analysis has shown that negative beliefs were highly correlated with anxiety and depression. Cognitive confidence and positive beliefs factors did not show significant correlation coefficients with anxiety and depression. Moreover, need to control thoughts were moderately correlated with anxiety and depression. Finally, cognitive self-consciousness had a low correlation coefficients with anxiety but not with depression. Results of regression analysis has shown that negative beliefs were a significant predictor of anxiety. The final model predicted the 64% of variance for anxiety. Regarding depression, the final model was not significant. However, negative beliefs were a significant predictor of depression. Finally, negative beliefs were a significant predictor of overall distress. The final model explained the 46% of variance for overall distress.*

#### Conclusions

*There are specific correlations between metacognitions and anxiety and depression in breast cancer undergoing chemotherapy. Moreover, negative beliefs is the strongest predictor for anxiety, depression, and overall distress. The metacognitive approach could have positive effects on breast cancer undergoing chemotherapy.*

#### Key words

Breast Cancer • Anxiety • Depression • Metacognition • Chemotherapy

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### Introduction

Cancer patients during chemotherapy often have to deal with numerous side effects and psychological distress<sup>1</sup>. In fact, chemotherapy is a treatment associated with a decrease in the patient's quality of life<sup>2</sup>. Cancer and chemotherapy side effects concern daily activities, employment and sexual life of patients<sup>3</sup>. Physical problems as fatigue, memory and concentration problems, are associated with demoralization<sup>4</sup>. Furthermore,

one in four cancer patients is depressed with more high percentage for brain tumours and thyroid cancer <sup>5</sup>.

Regarding breast cancer, negative emotions as depressive symptoms are common during treatment for non-metastatic breast cancer <sup>6</sup>. Patients with *in situ* cancer presented an increased incidence of stress-related disorders during the first 6 months after diagnosis <sup>7</sup>. Anxiety and depression symptoms improved over the time even if a significant percentage of patients had elevated anxiety and depression at the follow-up after 18 months diagnosis <sup>8</sup>. However, initial cancer severity and the type of treatment used were not associated with Major Depressive Disorder (MDD) or Generalized Anxiety Disorder (GAD) seven months after diagnosis <sup>9</sup>.

On the other hand, breast cancer with personality disorders are at higher risk for GAD and MDD at the end of treatment. Pre-treatment patient characteristics were predictive of reduced quality of life <sup>10</sup>. Specifically, young patients with breast cancer can be considered a target to psychological support to improve their quality of life after side effects of treatments <sup>11</sup>. Difficulty in emotional processing and defense mechanisms might be potential targets of psychological intervention for patients with breast cancer for improvement psychological adjustment <sup>12</sup>.

At this regard, Wells and Matthews <sup>13</sup> have argued for the central role of metacognition to development anxiety and depression. Hence, dysfunctional metacognitive beliefs are the basis for the development and maintenance of psychological disorders <sup>14</sup>. There is a link between metacognitive processes and psychopathology also in childhood <sup>15</sup>. Metacognition is defined as "the aspect of information processing that monitors, interprets, evaluates and regulates the contents and processes of its organization" <sup>16</sup>. Vulnerability and maintenance of emotional disorders are associated with a non-specific style of thinking called the Cognitive-Attentional Syndrome (CAS) <sup>17</sup>. The CAS consists of repetitive negative thinking in the process of worry and rumination that is driven by positive and negative beliefs about worry, concerning uncontrollability and danger, and limitations on executive controls. On these basis Wells constructed a metacognitive theory for emotional disorders and also developed self-report instruments for assessing dysfunctional metacognitive beliefs as MCQ-30 <sup>18-19</sup>.

Many studies have found that metacognitive beliefs are involved in a wide array of conditions, such as anxiety disorder <sup>20</sup>, obsessive-compulsive symptoms <sup>21</sup>, schizophrenic disorders <sup>22-23</sup>, anorexia nervosa <sup>24</sup>, alcohol abuse <sup>25</sup>, eating disorders <sup>26</sup>, and Amyotrophic Lateral Sclerosis (ALS) patients' caregivers <sup>27</sup>. Moreover, in the last decade empirical research has explored the role of metacognitions in non-clinical sample. In this perspective, a recent research has found a relationships

between metacognitions and coping strategies in palliative home care workers <sup>28</sup>.

Metacognitive beliefs has a crucial role also for cancer patients during chemotherapy <sup>1</sup>. In fact, negative beliefs explained the 61% variance for anxiety. On the other hand, age, negative beliefs and cognitive self-consciousness explained the 39% variance for depression. However, there are no study that had examined the role of some medical aspects of cancer as the types of tumor. This study is the first attempt to examine the relationships between metacognitions and anxiety and depression in breast cancer patients undergoing chemotherapy. A clinical group of breast cancer patients undergoing chemotherapy participated in this study and two hypotheses were examined.

The first was to examine the relationships between metacognitive beliefs, anxiety, and depression in breast cancer patients during chemotherapy. We hypothesized significant and positive correlations between metacognitive factors, anxiety, and depression. More specifically we hypothesized that negative beliefs about worry concerning uncontrollability and danger were strongly correlated with both anxiety and depression.

The second was to explore the role of metacognitions in predicting anxiety and depression. If metacognitive beliefs can be considered as relatively stable traits that pre-exist emotional disorders <sup>18 29</sup>, it is likely that they can explain variance in symptoms of anxiety and depression in cancer patients that are undergoing chemotherapy. We hypothesized that negative beliefs about worry concerning uncontrollability and danger and cognitive self-consciousness were the strongest predictors for both anxiety and depression.

## Methods

### Participants

A convenience sample of 80 breast cancer patients undergoing chemotherapy in an oncological department of a university hospital in southern Italy participated in this study. Patients were recruited on a voluntary basis and were informed about the aim of the study before to sign an informed consent sheet.

All patients were native Italian speakers and Italian nationals. Sociodemographics and medical characteristics of the sample are presented in Table I. The mean age was 56.09 years (SD = 13.00; range = 27-82), and the level of education in years was 11.88 (SD = 4.12; mode = 13; median = 13). Eighty-five percent were married, and in terms of occupation, 69% were unemployed.

With respect to medical status, the majority of the patients (80%) had cancer in stage I. All patients were previously treated with surgical therapy and then admit-

**TABLE I.** Demographic and medical characteristics of the sample.

Demographic and medical characteristics	%	Mean (SD)
Age		56.09 (13.00)
Status		
Single (or separated/widowed)	85	
Married	15	
Level of education (years)		11.88 (4.12)
Employment status		
Employed	31	
Unemployed	69	
Stage		
I	80	
II and III	20	
Months undergoing chemotherapy		10.94 (12.77)

ted at the outpatient clinic. All patients were treated with chemotherapy and the mean of treatment was 10.94 months (SD = 12.77). Exclusion criteria included pre-existing psychopathology or neurological disorders that would interfere with the completion of the measures.

An a priori power analysis, conducted using G\*Power<sup>30</sup> – version 2, ensured that the sample sizes were sufficient to yield adequate statistical power for the procedures conducted in our study. More specifically, to detect a significant finding with 7 predictors (at the .05 level) at a desired power level of .8, a minimum of 49 participants were required.

### Instruments

*Sociodemographic information* included age, gender, educational degree, nationality, marital status.

*Medical information* included data on the stage of the disease and the history of treatment.

*Metacognitions Questionnaire-30*<sup>18 19</sup>. This is a 30 item self-report questionnaire, which measures a range of metacognitive beliefs and processes relevant to vulnerability and maintenance of emotional disorders. The items are rated on a 4-point Likert scale from 1 (*do not agree*) to 4 (*completely agree*). The items are grouped into five subscales, as in the original version<sup>29</sup>. Factorial analysis has shown the presence of five factors: cognitive confidence, which measures confidence in attention and memory (*Cognitive confidence, CC*); cognitive self-consciousness, which measures the tendency to monitor one's own thoughts and focus attention inward (*Cognitive self-consciousness, CSC*); positive beliefs about worry, which measures the extent to which a person thinks that perseverative thinking is useful (*Positive beliefs about worry, POS*); negative beliefs about worry concerning

uncontrollability and danger, which assess the extent to which a person thinks that perseverative thinking is uncontrollable and dangerous (*Negative beliefs about uncontrollability and danger, NEG*); beliefs about the need to control thoughts, which assesses the extent to which a person believes that certain types of thoughts need to be suppressed (*Need to control thoughts, NC*). A high score on each factor is considered dysfunctional. The MCQ-30 is a brief, reliable and valid self-report measure of metacognitions<sup>29 31</sup>. In this study, a validated Italian version of the MCQ-30 was used to assess metacognitive beliefs<sup>18</sup>. Results of the Italian version of MCQ-30 indicated, as in the original version, direct correlations between metacognitive factors (except for CSC) and state and trait anxiety, pathological worry, and obsessive-compulsive symptoms. Reliability of all five factors in the present clinical group was acceptable to good, with Cronbach's  $\alpha$  ranging between .70 and .87 for the different scales.

*Hospital Anxiety and Depression Scale*<sup>32 33</sup>. This is a 14 item self-report scale that is divided into two dimensions, each composed of 7 items. The two subscales provide a measure of anxiety (HADS-A) and depression (HADS-D). The HADS is specifically designed for assessing physically ill patients and is used with medical outpatients. Respondents choose one from four responses to each item. Their responses are then summed within dimensions and a total score for each dimension, as well as both dimensions, are obtained. Scores can range from 0 to 21 for each subscale; high scores indicating higher levels of anxiety and depression. According to the authors of the HADS, scores for the anxiety dimension and the depression dimension can be categorized as follows: 0-7, normal; 8-10, mild; 11-14, moderate; 15-21, severe. Moreover, scores for the entire scale assess overall emotional distress and range from 0-42, with higher scores indicating more distress. The HADS has been employed among a wide range of clinical groups. Results of an Italian study with a sample of breast cancer patients indicated a total score for both dimensions of 10 points, 10 being the cut-off score for psychological distress<sup>34</sup>. Reliability of the two factors in this present sample was good, with Cronbach's  $\alpha$  of .77 for depression scale and .85 for anxiety scale.

### Statistical analyses

Data obtained from this research was checked and subsequently analyzed by descriptive statistical analysis and modeling. Descriptive statistics were calculated for MCQ-30, HADS, and for sociodemographic and medical information. Pearson correlation coefficients were calculated to examine the bivariate associations among study variables. To examine the independent role of metacognitions to predict negative emotions, the hierarchical regression analyses is conducted. In the

**TABLE II.** Descriptive statistics (mean with standard deviations in parentheses) and zero-order correlations for all the variable observed.

Variable	M (SD)	1	2	3	4	5	6	7	8
1. HADS Anxiety	7.43 (4.34)								
2. HADS Depression	5.86 (3.63)	.57**							
3. HADS Total score	12.79 (7.40)	.91**	.87**						
4. MCQ-30 Positive beliefs	9.91 (4.44)	.19	-.08	.08					
5. MCQ-30 Negative beliefs	13.13 (4.63)	.76**	.54**	.68**	.02				
6. MCQ-30 Cognitive confidence	10.89 (4.36)	.21	.20	.26*	-.08	.19			
7. MCQ- 30 Need to control thoughts	14.16 (3.44)	.35*	.31**	.38**	.07	.44**	.10		
8. MCQ-30 Cognitive self-consciousness	18.41 (2.89)	.30**	.06	.26*	.33**	.27*	.06	.47**	
9. MCQ-30 total score	66.50 (11.47)	.64**	.37**	.59**	.47**	.68**	.47**	.66**	.65**

HADS: Hospital anxiety and depression scale; MCQ-30: short version of the Metacognitions Questionnaire. \*  $p < .05$ . \*\*  $p < .01$ .

first step we insert the age as demographic variable, in second step the “duration of chemotherapy”, then stepwise entry of the metacognitive factors. So the latter were controlled on step 1 and 2.

In stepwise multiple regression the independent variables are entered according to their statistical contribution in explaining the variance in the dependent variable. The procedure is designed to find the most parsimonious set of predictors that are most effective in predicting the dependent variable, so it excludes variables that do not contribute to explaining differences in the dependent variable.

To validate the three stepwise regression models, the data set was randomly split into a 75% training sample and a 25% validation sample. The training sample was used to develop the model, test its effectiveness on the validation sample and test the applicability of the model to cases not used to develop it. For the models presented in Table III, the shrinkage ( $R^2$  for the training sample 75% -  $R^2$  for the validation sample 25%) was not more than 3% (results not shown).

## Results

Table II shows the mean scores, and zero-order correlations for all the observed variables. Examination of the metacognitive factors the results showed that negative beliefs had the strongest correlation both with anxiety ( $r = .76$ ;  $p < .01$ ) and depression ( $r = .54$ ;  $p < .01$ ). Cognitive confidence did not show significant correlation coefficients with anxiety and depression. However, cognitive confidence showed a low correlation coefficient with overall distress ( $r = .26$ ;  $p < .05$ ). Regarding positive beliefs, there were not significant correlation coefficients with anxiety, depression, or overall distress. Need to control thoughts were weekly and positively correlated with

anxiety ( $r = .35$ ;  $p < .01$ ), depression ( $r = .31$ ;  $p < .01$ ), and overall distress ( $r = .38$ ;  $p < .01$ ). Cognitive self-consciousness had a low correlation coefficients with anxiety ( $r = .30$ ;  $p < .01$ ) and overall distress ( $r = .26$ ;  $p < .01$ ), but not with depression. The total score of MCQ was positively related with all the other observed variables.

Table III shows a summary of the regression analyses. A series of stepwise multiple-regression equations were constructed to examine the role of the metacognitive factors in predicting negative emotions of patients in chemotherapy. Before stepwise entry of the metacognitive factors, age and duration of chemotherapy were controlled on step 1 and 2.

The first regression equation examined the effect of metacognitive factors in predicting anxiety. In the first step, age was not a significant predictor ( $p < .05$ ). In the second step, age and the duration of chemotherapy were not a significant predictor of anxiety in breast cancer undergoing chemotherapy ( $p < .05$ ). In the third step, only negative beliefs were a significant predictors ( $p < .05$ ). the model predicted a good portion of variance for anxiety (64 per cent considering the adjusted  $R^2$  to correct for the number of predictors).

The second regression equation examined the role of metacognitive factors to predict depression during chemotherapy. As for anxiety, age at the first step and duration of chemotherapy were not a significant predictors ( $p < .05$ ). At the third step, only negative beliefs were a significant predictor ( $p < .05$ ) of depression in breast cancer patients undergoing chemotherapy. However, the final model was not significant to explain depression in breast cancer undergoing chemotherapy.

The third equation examined the role of the metacognitive factors to predict both anxiety and depression, considering emotional distress as an overall presence during chemotherapy. As for anxiety and depression,

**TABLE III.** Predictors of anxiety, depression and overall distress.

	<b>b</b>	<b>T</b>	<b>P</b>	<b>R<sup>2</sup></b>	<b>Adj R<sup>2</sup></b>	<b>F</b>	<b>P</b>
<b>I – Anxiety</b>							
Step 1				0.01	0.02	0.22	.64
Age	0.08	0.47	.64				
Step 2				0.06	0.00	1.01	.38
Age	0.09	0.51	.61				
Months undergoing chemotherapy	0.23	1.34	.19				
Step 3				0.71	0.64	9.47	.00
Age	0.01	0.12	.90				
Months undergoing chemotherapy	0.02	0.22	.83				
MCQ-30 Positive beliefs	0.11	0.96	.34				
MCQ-30 Negative beliefs	0.83	6.71	.00				
MCQ-30 Cognitive confidence	-0.05	-0.40	.69				
MCQ-30 Need to control thoughts	-0.09	-0.64	.53				
MCQ-30 Cognitive self-consciousness	0.13	1.06	.30				
<b>II - Depression</b>							
Step 1				0.02	0.02	0.59	.45
Age	0.13	0.77	.45				
Step 2				0.07	0.01	1.10	.34
Age	0.13	0.80	.43				
Months undergoing chemotherapy	0.22	1.27	.21				
Step 3				0.32	0.14	1.78	.13
Age	0.09	0.50	.62				
Months undergoing chemotherapy	0.08	0.48	.63				
MCQ-30 Positive beliefs	0.04	0.20	.84				
MCQ-30 Negative beliefs	0.51	2.71	.01				
MCQ-30 Cognitive confidence	-0.13	-0.76	.45				
MCQ-30 Need to control thoughts	0.11	0.49	.63				
MCQ-30 Cognitive self-consciousness	-0.20	-1.04	.31				
<b>III – Overall distress</b>							
Step 1				0.01	-0.02	0.21	.65
Age	0.08	0.46	.65				
Step 2				0.70	0.14	1.25	.30
Age	0.09	0.51	.61				
Months undergoing chemotherapy	0.25	1.51	.14				
Step 3				0.57	0.46	5.29	.00
Age	0.01	0.08	.93				
Months undergoing chemotherapy	0.07	0.55	.58				
MCQ-30 Positive beliefs	0.11	0.83	.41				
MCQ-30 Negative beliefs	0.72	4.89	.00				
MCQ-30 Cognitive confidence	-0.09	-0.67	.51				
MCQ-30 Need to control thoughts	-0.07	-0.04	.97				
MCQ-30 Cognitive self-consciousness	0.04	0.29	.77				

The table shows the standardized regression coefficients ( $\beta$ ), the t test on individual coefficients (T), the p values of T (Sig of T); the R<sup>2</sup> and the adjustment R<sup>2</sup> to correct for the number of predictor, and the F change statistic for each step, the p values of F change statistic (Sig of F change).



gender and the duration of chemotherapy were not a significant predictors ( $p < .05$ ) of emotional distress. At the third step, negative beliefs were a significant predictor of emotional distress in breast cancer during chemotherapy. Considering the adjusted  $R^2$  correct for the number of predictors, the final model explained the 46 per cent of variance for emotional distress.

## Discussion

In this study, our goal was to examine the relationships between metacognitions and emotional distress (anxiety and depression) in breast cancer patients undergoing chemotherapy. We tested two hypotheses and two main results emerged from our study.

The first aim was to explore the association between metacognitions and emotional distress. Consistent with a recent study on metacognitions and emotional distress in cancer patients<sup>1</sup>, dysfunctional metacognitive beliefs were positively associated with both anxiety and depression. Negative beliefs about worry concerning uncontrollability and danger showed a strong correlation with anxiety. Negative beliefs were also correlated with depression, but to a lesser degree. Hence, the extent to which a breast cancer patient during chemotherapy thinks that perseverative thinking is uncontrollable and dangerous is strongly related to the presence of anxiety and depression.

Furthermore, results had shown two specific relationships for breast cancer patients. Need to control thoughts, was positively related both to anxiety and depression but only weakly. In addition, cognitive confidence and positive beliefs were not related with anxiety and depression. Hence, the extent to which a breast cancer believes that certain types of thoughts need to be suppressed is related with anxiety and depression. On the other hand, confidence in attention and memory has a marginal role for anxiety and depression in breast cancer.

Another metacognitive factor, cognitive self-consciousness, was weakly related with anxiety but not with depression. Therefore, the tendency to monitor one's own thoughts and focus attention inwards has only for anxiety. Finally, positive beliefs was not related with both anxiety and depression.

The second aim of this study was to explore the independent role of metacognitions while controlling for age and duration of chemotherapy.

Past studies have shown that metacognitive factors are relatively stable traits that exist before the onset of emotional disorders<sup>18</sup> and can explain symptoms of emotional distress during chemotherapy<sup>1</sup>. To test whether metacognitive factors could independently predict anxiety, depression, and overall distress in breast cancer patients during chemotherapy, three regression analyses were conducted. Results highlighted that negative

beliefs was important predictor for negative anxiety, depression, and overall distress.

Specifically, the first equation showed that negative beliefs about worry concerning uncontrollability and danger explained a high portion of variance for anxiety (64% considering the adjusted  $R^2$ ). No other metacognitive factors have shown a significant role in predicting anxiety level in breast cancer undergoing chemotherapy. In addition, results of this research showed that both age and months undergoing chemotherapy did not have an impact on anxiety levels of patients.

Results of the second equation showed that the negative beliefs was a significant predictor of depression. However, the model was not significant for explained depression scores of breast cancer patients undergoing chemotherapy. Differently from a recent study with patients undergoing chemotherapy<sup>1</sup>, cognitive self-consciousness did not show a role to predict depression in breast cancer. Furthermore, age and duration of chemotherapy did not have an impact on depression scores.

Finally, the third regression analysis examined the role of metacognitive factors to predict overall distress (anxiety and depression) in breast cancer patients undergoing chemotherapy. The final model was statistically significant and explained the 46% of variance for emotional distress. On the other hand, only negative beliefs was a significant predictor. As for anxiety and depression, the other metacognitive factors and age and duration of chemotherapy did not show a significant role in the model.

This study aims to examine the role of metacognitions in breast cancer patients undergoing chemotherapy. Past studies have shown the role of metacognitions as vulnerability factors to predicting development of psychological symptoms. Moreover, a recent study has explored this relationship in cancer patients undergoing chemotherapy<sup>1</sup>. In this perspective, the present research was aimed to explore the relationships between metacognitions and psychological symptoms in breast cancer.

However there are a number of limitations that should be addressed by future research. A major limitation was the small size of the sample. Moreover, future research should be take account the role of medical aspects, such as the time elapsed after diagnosis.

If confirmed by future research, results of this study would have important implications in clinical practice. In fact, metacognitive approach<sup>17</sup> could have positive effects on breast cancer patients undergoing chemotherapy. At this regard, a time-limited group therapy can be efficacy for MS patients<sup>35</sup>.

## Conflict of interest

None to declare.

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