

**Anxiety and depression in women with breast cancer: social and clinical determinants and influence of the social network and social support (DAMA Cohort)**

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## ABSTRACT

Background: Anxiety and depression are the most prevalent mental health pathologies among women with breast cancer. Social, clinical and contextual variables may influence emotional stress among women with breast cancer.

The aim of this work is to study anxiety and depression in a cohort of women diagnosed with breast cancer between 2003 and 2013 in Barcelona. We evaluate social and clinical determinants.

Methods: We performed a mixed cohort study (prospective and retrospective) using a convenience sample of women diagnosed with breast cancer. The information sources were the Hospital Anxiety and Depression questionnaire and hospital medical records. Dependent variables were anxiety and depression; independent variables were social class, age, employment status, tumour stage at diagnosis, time since diagnosis, social network and social support. We performed a descriptive analysis, a bivariate analysis, and a multivariate logistic regression analysis.

Results: A total of 1086 (48.6%) women had some degree of anxiety-related problem. As for depression. In the case of depression, 225 (15%) women had some degree of depression-related problem. Low emotional support and social isolation were clear risk factors for having more anxiety and depression. Low social class was also a risk factor, and age also played a role.

Discussion: Our results show that women long period of cancer survival have high prevalences of anxiety than depression, and this prevalence of anxiety is higher than the general population. In addition, we found inequalities between social classes and the isolation and social support are worse too in low social class.

**KEYWORDS:** anxiety disorder, depression, mental disorders, breast cancer, long term survivors, social network, social support, social determinants, clinical determinants.

## 76 BACKGROUND

77 Emotional distress in cancer patients reduces quality of life, has a negative impact on  
78 compliance with medical treatment and carries elevated risk of mortality<sup>1</sup>. For most people,  
79 the word "cancer" is associated with a serious illness that is usually very aggressive and  
80 requires very invasive treatments. Thus, since the event is considered or evaluated as a threat,  
81 an anxious emotional reaction arises. Likewise, perceiving it as a significant loss (loss of  
82 health, psychological well-being, life expectancy, etc.) will tend to result in sadness, which can  
83 trigger depression<sup>2</sup>. The first challenge for this study is to assess the prevalence of anxiety and  
84 depression in women with breast cancer, which can be complex due to the diversity of  
85 diagnostic criteria, the fact that not all diagnostic cut-offs have been empirically validated,  
86 and because prevalence rates are often assessed at different time points during the disease<sup>1</sup>.  
87 Some authors estimate that 30% of individuals diagnosed with cancer experience significant  
88 levels of distress at some time during of the course of the disease<sup>3</sup>.

89 Emotional distress is not a static situation. Women who survive breast cancer go through  
90 many different stages, which may influence their emotional welfare and mental health. Nearly  
91 30% of breast cancer survivors experience chronic pain five years after treatment. Pain and  
92 depression are common symptoms in many serious diseases and carry a risk of self-perceived  
93 poor health, poor quality of life, premature mortality<sup>4</sup>, anxiety and depression<sup>5</sup>. Patient's age  
94 is also an important variable, with younger women generally feeling worse, for several  
95 reasons<sup>6</sup>. On the other hand, the presence of problems related to deficiencies in basic needs,  
96 the chemotherapeutic treatment with doxorubicin, which causes more intense symptoms, a  
97 greater meddling of the disease, passive coping and perceiving a lesser sense of meaning and  
98 peace at the beginning of the study are related to depressive symptoms<sup>7</sup>.

99 Some women with advanced cancer face relapse<sup>8</sup>, highlighting the need for a broader  
100 perspective when studying emotional disorders. In this sense, a longitudinal study used  
101 growth mixture modelling to examine longitudinal changes in depressive symptoms from  
102 before the start of adjuvant treatment for breast cancer to six months after completion. The  
103 authors identified 3 groups, Class 1, 2 and 3. People in Class 1 reported clinically significant  
104 symptoms of depression before treatment, which declined only slightly over time and  
105 remained at a clinically significant level 6 month after completing treatment. People in class 2  
106 reported subclinical depressive symptoms before treatment, which declined significantly over  
107 time until overall symptomatology reached a minimum. People in class 3 reported minimal  
108 depression symptoms before treatment, which declined significantly even to a lower level, six  
109 months after completing treatment<sup>9</sup>.

110 The level of social support a woman has, and her social network are key determinants in the  
111 risk of suffering emotional distress. While social support may play a protective role at the time  
112 of diagnosis, previous studies suggest that support tends to decrease over time, and that  
113 women with a greater decrease in social support have worse psychosocial outcomes<sup>10</sup>. Also,  
114 social isolation is usually associated with decreased long-term survival in several types of  
115 cancer, including breast cancer<sup>11</sup> and decreased quality of life<sup>12</sup>.

116 Several mechanisms have been proposed as drivers of the relationship between social support  
117 and mental health outcomes. The literature suggests that social support promotes QOL by  
118 enhancing mood and sense of identity, reducing the burden associated with instrumental  
119 daily-life activities, and offering information and a positive assessment of coping resources.  
120 Most studies have investigated the relationship between mental health and clinical-type risk  
121 factors (comorbidities, higher histological grade, positive lymph node status and

chemotherapy)<sup>13</sup>; Conversely, studies that demonstrate the influence of cognitive and social variables in cancer survivors in different periods of time (from less than 5 years to more than 10 years) are scarce.

After reviewing the literature, this study aims to analyse the relationship between social determinants of health related to the social network and clinical aspects, and mental health in terms of anxiety and depression, in a cohort of women diagnosed with breast cancer between 2003 and 2013 in the main hospitals of Barcelona (Parc Salut Mar, Hospital Vall d'Hebron, Hospital Clínic and Hospital Santa Creu i Sant Pau).

## **METHODS**

### **Design**

We performed a mixed cohort study (prospective and retrospective)<sup>14</sup> using a convenience sample of women who had been diagnosed with breast cancer. In this article, we present the results of the initial cross-sectional study, including 2235 women in different stages of their breast cancer.

Population of study<sup>15</sup>, included all women aged  $\geq 18$  years who were diagnosed with and/or treated for breast cancer at one of the four main hospitals in the Barcelona Public Hospital Network (Hospital Clínic, Hospital Vall d'Hebron, Hospital de Sant Pau, Parc de Salut Mar) between January 1, 2003 and December 31, 2013. Subjects were identified from the Minimum Basic Data Set (MBDS) and selected for participation if, according to the 9th revision of the International Classification of Diseases (ICD-9), they had received any code between 174.0 and 174.9 at the time of admission to the hospital.

Exclusion criteria were as follows: a) having died from any cause before the onset of the study, b) having a previous diagnosis of another type of cancer before breast, and c) living outside Catalonia, due to difficulties in the follow-up process. 9771 women meet the study criteria and were identified and contacted by their pertinent hospital. All of them were informed about the study and invited to participate. Those who accepted were asked to sign a written informed consent (IC). In the end, a total of 2235 women were included in the study.

### **Sources of information**

We obtained information from the women themselves and their medical records. We collected data at three time points: 1) A first telephone contact welcome call, a "Welcome Survey", was made in which we thank the women for their participation in the study and we performed a short survey to register both their sociodemographic and economical characteristics; 2) Afterwards, a study survey was sent in which we asked for several different aspects of women's health, including specific questionnaires for mental health and social support; and 3) clinical variables were obtained from the Medical Records at the hospital. This entire process to obtain information, was carried out from mid-2015 to December 2016.

All the women signed an Informed Consent. The study passed an Ethical Committee which register number is 2015/6499/I.

### **Study variables**

Mental health was studied using the Hospital Anxiety and Depression (HAD) questionnaire which includes a set of questions that ultimately classifies people into the following categories: A) no anxiety, doubtful anxiety and probable anxiety; D) no depression, doubtful depression and probable depression. Therefore, dependent variables were anxiety and depression classified within the three categories mentioned above.

The independent variables were as follows: 1) age, grouped as <50 years, 50-65 years or >65 years; 2) social class, according to the national occupational classification, and grouped into upper class (I-II), middle class (III) or lower class (IV-V)<sup>16</sup>; 3) employment status, classified in four main categories: active worker, disabled, not working, and retired; 4) Social network, measured by the Berkman-Syme Network Index (SNI), distinguishes between socially-isolated (people with a less than 2 people network or who don't belong to associationism of any kind), and those with several degrees of social connection; 5) Social support was studied using the MOS-SS questionnaire that classifies individuals into low social support or medium-high. 6) Co-habitation at home, according to whether the woman lives alone or accompanied. Clinical variables were: 7) tumour stage at diagnosis (*in situ*, early-stage, locally advanced or metastatic); 8) time *since* diagnosis (<5 years, 5-10 years; or >10 years); 6) social network (social isolation or different degrees of social connection); 9) occurrence of relapses.

## Statistical Analysis

We performed a descriptive analysis of each variable, followed by a bivariate analysis of explanatory and dependent variables using the Chi square test. A correlation analysis was carried out between the different variables studied. We fit multivariate logistic regression models using the following reference values: absence of pathology versus doubtful presence of pathology, and absence of pathology versus probable presence of pathology (either anxiety or depression). Statistical significance was set at <0.05 in all calculations. All analyses were performed using SPSS 18.0 statistical package.

## RESULTS

The Dama cohort includes 2,235 women, 314 (14%) of whom had probable anxiety and 772 (34.5%) had doubtful anxiety. This means that 1086 women (48.6%) suffered some degree of anxiety-related problems. Regarding depression, 129 women (5.8%) had probable depression, and 206 (9.2%) had doubtful depression. Thus, a total of 335 women (15%) suffered from depression-related problems (shown in **Table 1**). Table 1 also shows the distributions of the main characteristics of women in the Dama cohort: 44.6% belonged to the upper social class (I+II); 14.4% are aged ≤50 years; 22.7% live alone, and the rest do so with 1 person or more; 35.3% are currently employed. Regarding the main clinical indicators, 7.9% of breast cancers were diagnosed *in situ*, 38.6% were in the initial phase, 39.8% in a locally advanced stage, and 1.1% were metastatic. 9.4% of women suffered a relapse, and 42.5% of women were diagnosed between 5 and 10 years before the study started. The social situation described by women in the Dama cohort showed that 21.5% of them were socially isolated and 15.5% of them had low social support.

The results of the bivariate analysis between the dependent variables (anxiety and depression) and the independent variables are shown in **Table 2**. We observed significant differences in anxiety and depression between social classes, with women in the lower social class having more anxiety and depression. By employment status, the worst situation is for the disabled women with significant differences too. Suffering relapses, living in social isolation and having low social support are also significantly associated with risk of depression

and anxiety. Living alone is significantly associated with anxiety, but not depression; women who live alone suffer less anxiety. Age is also important, with younger women showing more anxiety than older ones. We found no significant association between tumour stage at diagnosis and time since diagnosis.

We observed significant differences in anxiety, especially probable anxiety, as a function of age, social class and relapse (**Table 3**). Older women (>65 years) had lower risk of probable anxiety than the younger ones [OR=0.42 (0.23-0.75), *p* 0.004]. Women from the lower and medium social classes had higher risk than those in the highest class [OR=1.76 (1.21-2.55), *p* 0.003; and OR=1.43 (1.01-2.02), *p* 0.042, respectively]. Women who had had a relapse were at greater risk of having symptoms [OR=1.63 (1.02-2.62), *p* 0.043]. In terms of social support, the women with low social support present more risk for both doubtful and probable anxiety [OR=2.18 (1.59-2.99), *p* 0.000] and [OR=4.79 (3.31-6.95), *p* 0.000], respectively. Women who lived alone had a lower risk of doubtful anxiety and probable anxiety than those who lived with somebody else [OR=0.66 (0.51-0.86), *p* 0.002; and OR=0.68 (0.46-0.97), *p* 0.03, respectively]. In terms of employment status, women with disability had the highest risk of both doubtful and probable anxiety. We found no significant differences in either doubtful or probable anxiety according to tumour stage at diagnosis, time since diagnosis and social network.

**Table 4** shows the results for depression in relation to the different variables. Employment status was found to be particularly important: women who were not working had a higher risk of depression than those who were, and women with disability had the highest risk [OR=4.67 (2.27-9.59), *p* 0.000] for probable depression; and [OR=2.58 (1.49-4.5), *p* 0.001] for probable depression [OR=4.67 (2.27-9.59), *p* 0.000]. We observed that women with low social support have a higher risk of both doubtful depression [OR=5.08 (3.18-8.11)] and of probable depression [OR=2.35 (1.49-3.69)] than those with medium or high social support. We also observed social class inequalities in probable depression with women from lower social classes (IV + V) being more than twice as likely to have depression than those in high social classes (I + II) [OR=2.22 (1.29-3.82), *p* 0.004]. In terms of cohabitation, women living alone were less likely to have doubtful depression than those who lived with other people. Women in social isolation had higher risk of probable depression than those who had different levels of social connection [OR=2.35 (1.49-3.69), *p* 0.000]. We found no significant differences in either doubtful anxiety or probable anxiety according to age, tumour stage at diagnosis, time since diagnosis, and relapse.

## DISCUSSION

We found that 5.8% of the women in our study had probable depression, which is similar to that described for women in the general population (5.6% prevalence/year). In contrast, the prevalence of probable anxiety among women in the Dama Cohort was 14%, while the corresponding prevalence/year among women in the general population was 1.18 %<sup>17</sup>. If we also include women who have been classified as having possible depression, we can see that the detected prevalence of both pathologies is remarkably high. In addition, our results showed that depression and anxiety are more common among women of low social status, those who were not working, irrespective of the reason, those who had suffered relapse or metastasis, those with a weak social network, and those in a situation of social isolation and low social support.

We found that younger women suffer more anxiety. In contrast, the rate of depression is lower in younger women (<50 years), while the prevalence was very similar in the other age groups among them. Other studies among newly diagnosed women have reported similar

prevalence and age-related distributions of anxiety, but somewhat different results for depression, namely the so-called U-effect, with the lowest prevalence of depression among middle-aged women<sup>18</sup>. A systematic review and meta-analysis focused on long-term survivors found similar prevalence data to those obtained in our study<sup>19</sup>. This review is interesting because it highlights the growing problem of some studies that focus on women with newly diagnosed diseases, regardless of the effects on long-term survival, despite the increase in women in this group. This entails a first challenge which is to define what "long-term survival" means. To an oncologist, long-term survivors are women who are still alive 5 years after diagnosis. Both the US Center for Disease Control and the National Coalition for Cancer Survivorship define a cancer survivor as any person living with cancer from the time of diagnosis to the time of death. In any case, the systematic review mentioned above showed that the risk of depression decreases with time from diagnosis, while that of anxiety increases, reaching a prevalence of approximately 17%. These results clearly follow the same pattern as those observed in our work with women in the Dama cohort.

Social class is another element with significant influence. We observed a greater proportion of women with probable anxiety and depression in the middle and lower social classes (IV + V), especially after the follow-up of the disease had been carried out for some time. This is probably because women with fewer economic resources have less access to the different resources that could help meet their health needs. Likewise, the socioeconomic conditions of these groups are linked to a precarization of social connections, reducing the elements of social support for women<sup>20</sup>. In addition, health outcomes are also influenced by the level of deprivation of the neighbourhood, observing worse health outcomes in those who live in more depressed environments. On the other hand, these patients were also less likely to be married and live alone, which has turned out to be a risk factor. Contrary to the hypothesis that social support mediates the relationship between social class and mental health, some studies have shown that this is not the case, and that the socioeconomic level, and specifically the income level, can directly influence the levels of social support, stress of a woman and, consequently, her risk of anxiety and depression<sup>19</sup>.

Regarding relapse, there is little previous evidence on the relationship between relapse and anxiety and depression in long-term breast cancer survivors. On the other hand, there is some literature on the effect of fear of relapse, regardless of the stage of the tumour at the time of diagnosis<sup>21</sup>. In many cases, relapse is a difficult issue to address, and affected women often hide the severity of their illness or prognosis from close family and friends. Most experience shock, isolation and a feeling of loss of control, due to significant changes in their daily lives, among which are the inability to work and an increase in medical appointments that cause emotional distress<sup>22</sup>. In fact, long-term survivors can sometimes have a greater need for psychological support, depending on the duration of the treatment period and, above all, the onset of relapse<sup>23</sup>.

Emotional support is an important determinant of the mental well-being of cancer survivors. In our study, low emotional support was found to be a clear risk factor for anxiety and depression. A follow-up study carried out in Sweden showed similar results, and fatigue was also found to be relevant<sup>24</sup>. There are several mechanisms that may be mediating the relationship between social support and mental health. Some authors suggest that social support promotes QoL by enhancing of mood and sense of identity, decreasing the burden associated with the activities of daily living, and providing a positive appraisal of coping resources and information<sup>7</sup>. It is also known that the different dimensions of emotional support – tangible, emotional, affective and social interaction – influence self-efficacy in decision-making related to treatment and in the process of self-care and disease management<sup>25</sup>. The concepts of social network and social isolation are closely linked to

emotional support, measured by the number of people one relates with and the frequency of such relationships. Some survival studies in women with breast cancer have demonstrated a relationship between social network and mortality, with higher mortality rates in women with a poorer social network<sup>26</sup>. Several studies support the hypothesis that processes (implicit and explicit) that regulate emotions are consequently related to how the CM is confronted. Consequently, the links the CM may have with depression and anxiety and the effects it may have on the disease depend, among other factors, on the loneliness of the women affected. Women who were highly connected and had a rich social network were thus able to cope with cancer by expressing their emotions and had fewer mental health symptoms than women with fewer emotional outlets<sup>27</sup>. However, women who live as a family seem to be more likely to have symptoms of anxiety and depression. In the qualitative interviews that were carried out to better understand the results obtained in the quantitative work, women with children or older parents reported more suffering; especially in those cases with small children. In these, many fears arise since if they die their children will be left alone. A woman tells us: "My husband loves me very much, but he is an adult and over time he can find someone else, but my son, what will he do? A mother does not have a replacement, she is unique."

#### Limitations

The use of a convenience sample, which means that it may not be representative of all women with breast cancer in the city of Barcelona. The absence of a city-wide tumour register also prevents us from drawing comparisons with all women with breast cancer. Nevertheless, data obtained from other registries<sup>28</sup> have shown that the DAMA Cohort is representative in terms of age, and in terms of the distribution of tumour stage at diagnosis, except for women diagnosed with metastases, which are underrepresented in this Cohort. Since this was a self-reported survey, memory bias was also likely to be an issue. However, note that we used data from the 4 most important hospitals in Barcelona's public network, which attend the highest proportion of cases (approximately 85% of all diagnoses), and we obtained a high response rate (23%).

#### Clinical implications

The study provides relevant information on women in different stages of survival, which is relevant given that most of the studies focus on the period of diagnosis and treatment. Thus, we were able to evaluate information about women's unmet needs over the years, which enabled us to confirm the persistence of such needs, although they may change over time. In addition to helping to determine the factors that influence mental well-being, our findings provide useful information to advance our understanding of the determinants of mental health in patients with breast cancer and generate a framework in which to design and implement interventions for support the most vulnerable groups. In addition, it highlights the importance of including mental health care in the follow-up of women with breast cancer from the very first moment after their diagnosis and during subsequent years<sup>29</sup>. Concluding, the main finding of the study is the fact that women continue to have mental health problems in the years after active treatment and that these are influenced by social factors rather than clinical. This puts us on the path to continue directing efforts in the design of future interventions.

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346    **Conflicts of interest**

347    The authors have no conflicts of interest to declare

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Table 1. Description of the different explanatory and dependent variables to study: anxiety and depression.

| VARIABLE                               | n= 2235 women | %    |
|--|---------------|------|
| <b>SOCIAL CLASS</b>                    |               |      |
| High class (I+II)                      | 996           | 44.6 |
| Medium III                             | 682           | 30.6 |
| Lower class (IV-V)                     | 509           | 22.7 |
| Missing                                | 48            | 2.1  |
| <b>AGE</b>                             |               |      |
| Less than 50 years old                 | 321           | 14.4 |
| Between 50 and 65 years old            | 1017          | 45.5 |
| More than 65 years old                 | 896           | 40.1 |
| <b>COHABITATION</b>                    |               |      |
| Alone                                  | 507           | 22.7 |
| With 1 person                          | 968           | 43.3 |
| With more than 1 person                | 751           | 33.6 |
| Missing                                | 9             | 0.4  |
| <b>EMPLOYMENT STATUS</b>               |               |      |
| Active worker                          | 788           | 35.3 |
| Not working                            | 452           | 20.2 |
| Disabled                               | 190           | 8.5  |
| Retired                                | 766           | 34.3 |
| <b>STAGE AT MOMENT OF DIAGNOSIS</b>    |               |      |
| In situ                                | 177           | 7.9  |
| Initial phase                          | 863           | 38.6 |
| Locally advanced                       | 889           | 39.8 |
| Metastatic                             | 24            | 1.1  |
| Missing                                | 282           | 12.6 |
| <b>RELAPSE</b>                         |               |      |
| Yes                                    | 210           | 9.4  |
| No                                     | 1878          | 84.0 |
| Missing                                | 147           | 6.6  |
| <b>TIME SINCE DIAGNOSIS</b>            |               |      |
| 5 years or less                        | 842           | 37.7 |
| Between 5 and 10 years                 | 949           | 42.5 |
| More than 10 years                     | 425           | 19.0 |
| Missing                                | 19            | 0.9  |
| <b>SOCIAL SUPPORT</b>                  |               |      |
| Low                                    | 346           | 15.5 |
| Medium-high                            | 1889          | 84.5 |
| <b>SOCIAL NETWORK</b>                  |               |      |
| Social isolation                       | 480           | 21.5 |
| Different degrees of social connection | 1664          | 74.5 |
| Missing                                | 91            | 4.1  |
| <b>ANXIETY</b>                         |               |      |
| No anxiety                             | 1149          | 51.4 |
| Doubtful anxiety                       | 772           | 34.5 |
| Probable anxiety                       | 314           | 14.0 |
| <b>DEPRESSION</b>                      |               |      |
| No depression                          | 1900          | 85.0 |
| Doubtful depression                    | 206           | 9.2  |
| Probable depression                    | 129           | 5.8  |

Table 2: Bivariate analysis of the different independent variables and their significances.

|                              | ANXIETY    |      |                  |      |                  |      |       | DEPRESSION    |      |                  |      |                  |      |       |
|------------------------------|------------|------|------------------|------|------------------|------|-------|---------------|------|------------------|------|------------------|------|-------|
|                              | No anxiety |      | Doubtful (n=772) |      | Probable (n=314) |      |       | No depression |      | Doubtful (n=206) |      | Probable (n=129) |      |       |
|                              | n          | %    | n                | %    | n                | %    | p     | n             | %    | n                | %    | n                | %    | P     |
| SOCIAL CLASS                 |            |      |                  |      |                  |      |       |               |      |                  |      |                  |      |       |
| High class (I+II)            | 546        | 54.8 | 336              | 33.7 | 114              | 11.4 | 0.003 | 882           | 88.6 | 81               | 8.1  | 33               | 3.3  | 0.000 |
| Medium III                   | 340        | 49.1 | 255              | 36.8 | 97               | 14   |       | 586           | 84.7 | 68               | 9.8  | 38               | 5.5  |       |
| Lower class IV+V             | 244        | 47.9 | 173              | 33.4 | 92               | 18.1 |       | 403           | 79.2 | 55               | 10.8 | 51               | 10.0 |       |
| AGE                          |            |      |                  |      |                  |      |       |               |      |                  |      |                  |      |       |
| <= 50 years                  | 155        | 48.3 | 118              | 36.8 | 48               | 15   | 0.002 | 286           | 89.1 | 18               | 5.6  | 17               | 5.3  | 0.134 |
| 50-65 years                  | 494        | 48.6 | 356              | 35.0 | 167              | 16.4 |       | 857           | 84.3 | 104              | 10.2 | 56               | 5.5  |       |
| >65 years                    | 500        | 55.8 | 297              | 33.1 | 99               | 11   |       | 756           | 84.4 | 84               | 9.4  | 56               | 6.3  |       |
| EMPLOYMENT STATUS            |            |      |                  |      |                  |      |       |               |      |                  |      |                  |      |       |
| Active worker                | 408        | 51.8 | 277              | 35.2 | 103              | 13.1 | 0.000 | 713           | 90.5 | 54               | 6.9  | 21               | 2.7  | 0.000 |
| Not working                  | 224        | 49.6 | 150              | 33.2 | 78               | 17.3 |       | 368           | 81.4 | 49               | 10.8 | 35               | 7.7  |       |
| Disabled                     | 72         | 37.9 | 74               | 38.9 | 44               | 23.2 |       | 133           | 70.0 | 29               | 15.3 | 28               | 14.7 |       |
| Retired                      | 427        | 55.7 | 253              | 33.0 | 86               | 11.2 |       | 649           | 84.7 | 74               | 9.7  | 43               | 5.6  |       |
| COHABITATION                 |            |      |                  |      |                  |      |       |               |      |                  |      |                  |      |       |
| Alone                        | 286        | 56.4 | 155              | 30.6 | 66               | 13   | 0.011 | 429           | 84.6 | 42               | 8.3  | 36               | 7.1  | 0.156 |
| With 1 person                | 509        | 52.6 | 323              | 33.4 | 136              | 14   |       | 809           | 83.6 | 101              | 10.4 | 58               | 6.0  |       |
| With more than 1 person      | 350        | 46.6 | 768              | 38.6 | 111              | 14.8 |       | 654           | 87.1 | 62               | 8.3  | 35               | 4.7  |       |
| STAGE AT MOMENT OF DIAGNOSIS |            |      |                  |      |                  |      |       |               |      |                  |      |                  |      |       |
| In situ                      | 96         | 54.2 | 54               | 30.5 | 27               | 15.3 | 0.895 | 151           | 85.3 | 11               | 6.2  | 15               | 8.5  | 0.075 |
| Initial phase                | 463        | 53.7 | 276              | 32.0 | 124              | 14.4 |       | 740           | 85.7 | 84               | 9.7  | 39               | 4.5  |       |
| Locally advanced             | 450        | 50.6 | 305              | 34.3 | 134              | 15.1 |       | 731           | 82.2 | 94               | 10.6 | 64               | 7.2  |       |
| Metastatic                   | 13         | 54.2 | 8                | 33.3 | 3                | 12.5 |       | 21            | 87.5 | 1                | 4.2  | 2                | 8.3  |       |
| TIME OVER DIAGNOSES          |            |      |                  |      |                  |      |       |               |      |                  |      |                  |      |       |
| 5 years or less              | 511        | 52.3 | 336              | 34.4 | 130              | 13.3 | 0.833 | 836           | 85.6 | 85               | 8.7  | 56               | 5.7  | 0.745 |
| Between 5 and 10 years       | 449        | 50.3 | 314              | 35.2 | 129              | 14.5 |       | 760           | 85.2 | 80               | 9.0  | 52               | 5.8  |       |
| More than 10 years           | 181        | 51.7 | 116              | 33.1 | 53               | 15.1 |       | 291           | 83.1 | 39               | 11.1 | 20               | 5.7  |       |
| RELAPSE                      |            |      |                  |      |                  |      |       |               |      |                  |      |                  |      |       |
| Yes                          | 97         | 46.4 | 71               | 34.0 | 41               | 19.6 | 0.000 | 166           | 79.4 | 25               | 12.0 | 18               | 8.6  | 0.023 |
| No                           | 1002       | 53.3 | 618              | 32.9 | 259              | 13.8 |       | 1596          | 84.9 | 176              | 9.4  | 107              | 5.7  |       |
| SOCIAL NETWORK               |            |      |                  |      |                  |      |       |               |      |                  |      |                  |      |       |
| Social isolation             | 221        | 19.6 | 154              | 21.8 | 105              | 33.9 | 0.000 | 356           | 19.6 | 65               | 32.3 | 59               | 48.0 | 0.000 |
| Social connection            | 908        | 80.4 | 551              | 78.2 | 205              | 66.1 |       | 1464          | 80.4 | 136              | 67.7 | 64               | 52.0 |       |
| SOCIAL SUPPORT               |            |      |                  |      |                  |      |       |               |      |                  |      |                  |      |       |
| Low Social Support           | 108        | 31.2 | 124              | 35.8 | 114              | 32.9 | 0.000 | 214           | 61.8 | 69               | 19.9 | 63               | 18.2 | 0.000 |
| Medium-high Support          | 1041       | 55.1 | 648              | 34.3 | 200              | 10.6 |       | 1686          | 89.3 | 137              | 7.3  | 66               | 3.5  |       |

Table 3. Anxiety: multivariate logistic regression

|  | DOUBTFUL ANXIETY*<br>(reference value No anxiety)<br>N*= 772 (34.5%) |          |          |              | PROBABLE ANXIETY<br>(reference value No anxiety)<br>N*=314 (14.6%) |          |          |              |
|--|--|----------|----------|--------------|--|----------|----------|--------------|
| SOCIAL AND CLINICAL DETERMINANTS       | IC at 95%  |          |          |              | IC at 95%  |          |          |              |
|  | OR   | Inferior | Superior | p value      | OR   | Inferior | Superior | p value      |
| <b>AGE</b>                             |  |          |          |              |  |          |          |              |
| Less than 50 years old                 | Reference  |          |          |              | Reference  |          |          |              |
| Between 50 and 65 years                | 0.85   | 0.615    | 1.18     | 0.34         | 0.797  | 0.510    | 1.244    | 0.318        |
| More than 65 years                     | 0.74   | 0.438    | 1.127    | 0.161        | 0.419  | 0.233    | 0.754    | <b>0.004</b> |
| <b>SOCIAL CLASS</b>                    |  |          |          |              |  |          |          |              |
| Lower (IV+V)                           | 1.108  | 0.841    | 1.46     | 0.466        | 1.76   | 1.214    | 2.55     | <b>0.003</b> |
| Medium III                             | 1.104  | 0.866    | 1.408    | 0.424        | 1.43   | 1.013    | 2.02     | <b>0.042</b> |
| High (I+II)                            | Reference  |          |          |              | Reference  |          |          |              |
| <b>COHABITATION</b>                    |  |          |          |              |  |          |          |              |
| Alone                                  | 0.662  | 0.510    | 0.859    | <b>0.002</b> | 0.68   | 0.46     | 0.97     | <b>0.03</b>  |
| With other people                      | Reference  |          |          |              | Reference  |          |          |              |
| <b>EMPLOYMENT STATUS</b>               |  |          |          |              |  |          |          |              |
| Retired                                | 1.054  | 0.748    | 1.486    | 0.764        | 1.08   | 0.67     | 1.75     | 0.74         |
| Not working                            | 1.097  | 0.797    | 1.510    | 0.569        | 1.39   | 0.91     | 2.14     | 0.12         |
| Disabled                               | 1.597  | 1.052    | 2.425    | <b>0.028</b> | 1.93   | 1.18     | 3.36     | <b>0.010</b> |
| Active worker                          | Reference  |          |          |              | Reference  |          |          |              |
| <b>STAGE AT MOMENT OF DIAGNOSIS</b>    |  |          |          |              |  |          |          |              |
| In situ                                | Reference  |          |          |              | Reference  |          |          |              |
| Initial phase                          | 1.223  | 0.828    | 1.807    | 0.311        | 0.97   | 0.58     | 1.64     | 0.93         |
| Locally advanced                       | 1.347  | 0.913    | 1.988    | 0.134        | 1.025  | 0.612    | 1.72     | 0.92         |
| Metastatic                             | 1.272  | 0.474    | 3.411    | 0.633        | 0.61   | 0.122    | 3.06     | 0.548        |
| <b>TIME SINCE DIAGNOSIS</b>            |  |          |          |              |  |          |          |              |
| 5 years or less                        | 0.951  | 0.698    | 1.295    | 0.748        | 0.77   | 0.51     | 1.18     | 0.24         |
| Between 5 and 10 years                 | 0.955  | 0.710    | 1.285    | 0.761        | 0.78   | 0.52     | 1.16     | 0.22         |
| More than 10 years                     | Reference  |          |          |              | Reference  |          |          |              |
| <b>RELAPSE</b>                         |  |          |          |              |  |          |          |              |
| Yes                                    | 1.05   | 0.72     | 1.52     | 0.79         | 1.63   | 1.02     | 2.62     | <b>0.043</b> |
| No                                     | Reference  |          |          |              | Reference  |          |          |              |
| <b>SOCIAL NETWORK</b>                  |  |          |          |              |  |          |          |              |
| Social isolation                       | 0.913  | 0.700    | 1.191    | 0.503        | 1.025  | 0.72     | 1.45     | 0.89         |
| Different degrees of social connection | Reference  |          |          |              | Reference  |          |          |              |
| <b>SOCIAL SUPPORT</b>                  |  |          |          |              |  |          |          |              |
| Low                                    | 2.184  | 1.595    | 2.989    | <b>0.000</b> | 4.79   | 3.31     | 6.95     | <b>0.000</b> |
| Medium-High                            | Reference  |          |          |              | Reference  |          |          |              |

\* where the total N values differs from the sum of partial records, this is due to missing values

Table 4. Depression: multivariate logistic regression.

|  | DOUBTFUL DEPRESSION<br>(reference No depression)<br>N*= 206 (9.2%) |          |          |              | PROBABLE DEPRESSION*<br>(reference value No depression)<br>N*= 129 (5.8%) |          |         |              |
|--|--|----------|----------|--------------|---|----------|---------|--------------|
| SOCIAL AND CLINICAL DETERMINANTS       | IC at 95%  |          |          |              | IC at 95%   |          |         |              |
|  | OR   | Inferior | Superior | p value      | OR  | Inferior | Suprior | p value      |
| <b>AGE</b>                             |  |          |          |              |   |          |         |              |
| Less than 50 years old                 | Reference  |          |          |              | Reference   |          |         |              |
| Between 50 and 65 years                | 1.53   | 0.86     | 2.71     | 0.14         | 0.79  | 0.396    | 1.574   | 0.50         |
| More than 65 years                     | 1.14   | 0.57     | 2.29     | 0.71         | 0.55  | 0.238    | 1.296   | 0.174        |
| <b>SOCIAL CLASS</b>                    |  |          |          |              |   |          |         |              |
| Lower (IV+V)                           | 1.27   | 0.84     | 1.91     | 0.25         | 2.22  | 1.29     | 3.82    | <b>0.004</b> |
| Medium III                             | 1.03   | 0.71     | 1.51     | 0.87         | 1.29  | 0.751    | 2.249   | 0.349        |
| High (I+II)                            | Reference  |          |          |              | Reference   |          |         |              |
| <b>COHABITATION</b>                    |  |          |          |              |   |          |         |              |
| Alone                                  | 0.62   | 0.41     | 0.94     | <b>0.027</b> | 1.01  | 0.604    | 1.688   | 0.97         |
| With other people                      | Reference  |          |          |              | Reference   |          |         |              |
| <b>EMPLOYMENT STATUS</b>               |  |          |          |              |   |          |         |              |
| Retired                                | 1.594  | 0.939    | 2.714    | 0.084        | 2.21  | 1.01     | 4.38    | <b>0.047</b> |
| Not working                            | 1.619  | 0.997    | 2.629    | 0.052        | 2.38  | 1.21     | 4.67    | <b>0.012</b> |
| Disabled                               | 2.589  | 1.489    | 4.502    | <b>0.001</b> | 4.67  | 2.27     | 9.59    | <b>0.000</b> |
| Active worker in active employment     | Reference  |          |          |              | Reference   |          |         |              |
| <b>STAGE AT MOMENT OF DIAGNOSIS</b>    |  |          |          |              |   |          |         |              |
| In situ                                | Reference  |          |          |              | Reference   |          |         |              |
| Initial phase                          | 1.82   | 0.91     | 3.67     | 0.095        | 0.623   | 0.296    | 1.311   | 0.212        |
| Locally advanced                       | 2.00   | 0.996    | 4.04     | 0.051        | 1.038   | 0.510    | 2.113   | 0.918        |
| Metastatic                             | 0.78   | 0.092    | 6.63     | 0.822        | 0.756   | 0.087    | 6.604   | 0.800        |
| <b>TIME DIAGNOSIS</b>                  |  |          |          |              |   |          |         |              |
| 5 years or less                        | 1.15   | 0.73     | 1.82     | 0.55         | 1.20  | 0.63     | 2.29    | 0.58         |
| Between 5 and 10 years                 | 0.91   | 0.581    | 1.41     | 0.66         | 1.32  | 0.72     | 2.42    | 0.36         |
| More than 10 years                     | Reference  |          |          |              | Reference   |          |         |              |
| <b>RELAPSE</b>                         |  |          |          |              |   |          |         |              |
| Yes                                    | 1.64   | 0.996    | 2.705    | 0.052        | 1.12  | 0.55     | 2.27    | 0.75         |
| No                                     | Reference  |          |          |              | Reference   |          |         |              |
| <b>SOCIAL NETWORK</b>                  |  |          |          |              |   |          |         |              |
| Social isolation                       | 1.296  | 0.892    | 1.883    | 0.174        | 2.35  | 1.49     | 3.69    | <b>0.000</b> |
| Different degrees of social connection | Reference  |          |          |              | Reference   |          |         |              |
| <b>SOCIAL SUPPORT</b>                  |  |          |          |              |   |          |         |              |
| Low                                    | 3.61   | 2.48     | 5.24     | <b>0.000</b> | 5.08  | 3.18     | 8.11    | <b>0.000</b> |
| Medium-High                            | Reference  |          |          |              | Reference   |          |         |              |

\* where the total N values differs from the sum of partial records, this is due to missing value

