

# Psychological Distress Prior to Surgery Is Related to Symptom Burden and Health Status in Lung Cancer Survivors.

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## Research Article

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# Abstract

## Purpose

Patients with lung cancer experience a variety of distressing symptoms which could adversely quality of life. The aim of this study was to determine whether psychological distress prior to surgery is associated with health status and symptom burden in lung cancer survivors.

## Methods

A longitudinal observational study with one-year follow-up was carried out. Health status was measured by the WHO Disability Assessment Scale (WHO-DAS 2.0), the Euroqol-5 dimensions (EQ-5D) and the Pittsburgh Sleep Quality Index (PSQI). Symptoms severity included dyspnoea (Multidimensional Profile of Dyspnoea); pain (Brief Pain Inventory); fatigue (Fatigue Severity Scale) and cough (Leicester Cough Questionnaire).

## Results

174 lung cancer patients were included. Patients in the group with psychological distress presented a worse self-perceived health status, functionality and sleep quality. The group with psychological distress also presented higher dyspnea, fatigue and pain.

## Conclusion

Patients with psychological distress prior surgery present a greater symptom burden and a poorer self-perceived health status, lower functionality and sleep quality, than patients without distress one year after the lung resection.

## Introduction

Lung cancer (LC) is the leading cause of cancer-related mortality worldwide [1], accounting for 27% of cancer deaths in 2014 [2]. Improvements in the diagnosis and treatment of LC have resulted in increased opportunities for long-term survival [3, 4]. Curative lung resection is the preferred treatment for early-stage lung cancer, significantly improving 5-years survival rates in this population [5]. This has led to a growing interest in addressing issues faced by these long-term survivors [6], identifying the physical and psychosocial factors affecting their well-being [7].

LC patients present various symptoms, such as pain, coughing, fatigue and shortness of breath in the early stages after surgery or even a long time after surgery [8, 9, 10]. Moreover, patients with lung cancer experience a variety of distressing symptoms, many of which begin prior to diagnosis and continue

throughout the course of the disease and its treatments, adversely affecting functional status and quality of life (QOL) [11, 12, 13].

Psychological distress has been defined by the National Comprehensive Cancer Network as “an unpleasant experience of an emotional, psychological, social, or spiritual nature that interferes with the ability to cope with cancer treatment” [14]. It includes a wide continuum of psychological feelings relating to worry, anxiety, depression, fear, and sadness and extends on a continuum from common normal feelings of vulnerability to problems that are disabling, such as true depression [15, 16].

Psychological distress prevalence rates in patients with cancer range from 22 to 58% [17, 18], with a higher prevalence among lung cancer patients when compared to patients with other cancers [19, 20]. Higher psychosocial distress can result from late diagnosis, smoking, multiple symptoms, financial problems and health-related stigma [21, 22, 23, 24], and could exacerbate disease-related symptoms contributing to poorer QOL outcomes well into survivorship [25]. This is consistent with theories such as the somatic perception hypothesis [26, 27] and somatosensory amplification [28], which posit that psychological factors, such as negative effects, can influence the perception and appraisal of somatic sensations or symptoms through their effects on higher cognitive processing patterns.

The clinical importance of assessing and treating psychological distress and mood disorder has received much attention from patient advocacy groups and health care providers, including consideration of distress as the sixth vital sign in cancer care [29]. However, despite being one of the most frequent cancers worldwide, little research has been done with regard to the influence of psychological distress on symptom burden and health status in lung cancer survivors at long term [30]. So, the aim of this study was to determine whether psychological distress prior to surgery is associated with health status and symptom burden in lung cancer survivors.

## Methods

A longitudinal observational study with one-year follow-up was carried out. We recruited patients above 18 years of age diagnosed with lung cancer and undergoing pulmonary resection, from the Thoracic Surgery Service of the “Virgen de las Nieves” Hospital Complex in Granada (Spain) between October 2018 and January 2020. All patients were informed about the purpose of the study and signed an informed consent form prior to their inclusion. Patients were excluded if they had one of these conditions: cognitive impairment or mental instability, physical disabilities that prevented their evaluation, inability to communicate, contraindication to physical exercise and presence of other respiratory pathologies. Ethical approval for this study was obtained from the Biomedical Research Ethics Committee of Granada.

Data collection was performed at admission and one-year after hospitalization, by the same researchers, who had been previously trained. The evaluation was performed in the “Virgen de las Nieves Hospital Complex, at admission; and in the Health Sciences Faculty of the University of Granada, one-year after hospitalization.

Patients' medical history was verified to confirm that they met the inclusion criteria. Data collected from the medical history included anthropometric data, comorbidities, and lung resection characteristics, including type and duration of the surgery. Comorbidities were assessed by the Charlson index, one of the most widely used scoring systems for assessing comorbidities and has been validated in several disorders [31].

## Group assignment

Patients were divided into two groups based on the presence of psychological distress at hospital admission, assessed by the Hospital Anxiety and Depression Scale (HADS). The HADS is a questionnaire that has been previously used as a screening tool for psychological distress [32]. The questionnaire consists of 14 items, scored in scale of 0–3. It is divided in turn into two subscales, one for anxiety (consisting of 7 items) and another for depression (consisting of 7 items), the higher score in each subscale greater anxiety or depression, respectively [33]. The cut-off point used was 11, based on previous studies with cancer patients [32].

## Outcome measures

Health status and symptoms severity were included as main outcomes. Health status was measured by the WHO Disability Assessment Scale (WHO-DAS 2.0), the Euroqol-5 dimensions (EQ-5D) and the Pittsburgh Sleep Quality Index (PSQI). Symptoms severity included dyspnoea, assessed by the Multidimensional Profile of Dyspnoea (MDP); pain, evaluated by the Brief Pain Inventory (BPI); fatigue, with the Fatigue Severity Scale; and cough, measured by the Leicester Cough Questionnaire (LCQ).

WHO-DAS 2.0 is a generic tool for measuring health and disability in clinical practice, measuring changes in performance and their levels of difficulty in performing and performing their activities. The scale consists of 36 items, divided into 6 domains, which are scored from 1 (slight) to 5 (extreme/unable to do so). The minimum score is 36 and the maximum is 180. This means that the greater the number, the greater the disability [34]. This test has high reliability and good validity [35, 36].

EQ-5D is a validated tool to measure the self-perceived health status. It has been validated in Spanish [37]. It is divided into two sections, the first of which contains five items about mobility, self-care, usual activities, pain/discomfort and anxiety/depression. These questions were scored between 1 and 3, where 1 represents “no problems” and 3 refers to “extreme problems.” The second section is a VAS that measures patients’ self-evaluated health status from 0 to 100 (0 represents “the worst imaginable health” and 100 indicates “the best imaginable health”).

The PSQI is a self-rated questionnaire which assesses sleep quality and disturbances over a 1-month time interval [38], with strong reliability and validity [39]. It is formed by seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction.

The symptom severity assessments included dyspnoea, pain, fatigue and cough.

Dyspnoea was assessed with MDP that punctuates the general discomfort of the breath and the sensory and affective decreases of the dyspnoea [40, 41]. It also evaluates the dyspnoea at specific moment or activity and is valid and reliable for measuring these sensations in patients with respiratory problems [40]. It consists of 11 items, which the higher the score, the greater the dyspnoea perceived by the patient.

Pain was assessed with BPI, a questionnaire developed by Daut in 1983 and validated in Spanish by Badia et al. in cancer patients in 2002 [42]. BPI is a multidimensional pain assessment tool that provides information on the intensity of pain and its interference in patients' daily activities. The version used is that of 9 questions, the higher the score, the greater pain perceived by the patient [42], that has shown excellent reliability and validity in terms of psychometric evidence[43].

Fatigue was assessed with FSS, a self-administered questionnaire with 9 elements that assess the severity of fatigue in different situations [44]. The rating of each element varies from 1 to 7, where 1 indicates a strong disagreement and 7 strongly agree, and the final rating represents the average value of the 9 elements. The maximum score is the sum of all items, which would be 63, and the minimum 9. The higher the score the more fatigue perceived by the patient (Valko PO et al., 2008), this scale shown good reliability and validity in terms of psychometric evidence.

Cough was assessed with LCQ [45], a questionnaire translated and validated into Spanish [46]. It is a short and easy to administer chronic cough questionnaire consisting of nineteen items with scores on a Likert scale ranging from 1 to 7. It is divided into three subscales: physical, psychological and social. The minimum and maximum score are 3 and 21 respectively, where a lower LCQ score means presence of higher cough.

## Statistical analysis

A priori power analysis with G\*Power 3.1.9.2 software was performed based on a pilot study (unpublished) of fifteen subjects (effect size of 0.50) obtaining a statistical power of 95% and a sample size of 176 (88 per group). However, 97 participants per group were recruited to allow for a dropout rate of 10%.

Statistical Package SPSS version 20.0 (International Business Machines, Armonk, NY) was used to analyse the data obtained. Prior to statistical analysis, the Kolmogorov-Smirnov test was performed to assess the normality of the variables. Descriptive statistics (i.e. mean  $\pm$  standard deviation) were carried out to describe sample baseline characteristics. A between group comparison was performed after subjects were grouped by psychological distress, using the t Student's test. Statistical significance was accepted at a p value of 0.05.

## Results

Of 198 potential patients, a final sample size of 174 was selected and divided into two groups depending on the presence of psychological distress. The distribution of patients is shown in Fig. 1.

Sociodemographic variables of the sample, duration of the intervention and length of hospital stay are presented in Table 1.

Table 1

Sociodemographic variables of the sample, duration of the intervention and length of hospital stay.

|                                                                                                                                                                                                          | <b>Patients without psychological distress</b><br><b>(n = 112)</b> | <b>Patients with psychological distress</b><br><b>(n = 62)</b> | <b>p</b> |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|----------------------------------------------------------------|----------|
| Age (years)                                                                                                                                                                                              | 56.60 ± 15.23                                                      | 62.22 ± 11.11                                                  | 0.095    |
| Length of hospital stay (days)                                                                                                                                                                           | 6.68 ± 1.84                                                        | 7.44 ± 2.08                                                    | 0.102    |
| Duration of intervention (minutes)                                                                                                                                                                       | 200.17 ± 71.53                                                     | 203.89 ± 47.54                                                 | 0.846    |
| BMI (kg/m <sup>2</sup> )                                                                                                                                                                                 | 27.12 ± 5.12                                                       | 26.74 ± 3.60                                                   | 0.732    |
| MNA (Total)                                                                                                                                                                                              | 26.04 ± 3.11                                                       | 25.73 ± 2.63                                                   | 0.667    |
| Sex (% men)                                                                                                                                                                                              | 48.1                                                               | 66                                                             | 0.127    |
| Charlson Index                                                                                                                                                                                           | 4.44 ± 2.42                                                        | 4.37 ± 2.48                                                    | 0.896    |
| <i>Data are expressed as mean ± SD or Percentage (%); BMI: Body Mass Index; SD: standard deviation; FEV1%: forced expiratory volume in the first second in percentage; *p &lt; 0.05, **p &lt; 0.001.</i> |                                                                    |                                                                |          |

As shown in Table 1, significant differences were found in sex, with a higher percentage of women in the group with psychological distress ( $p < .001$ ). Nevertheless, no significant differences were found between groups in the other baseline characteristics such as age ( $p = .095$ ), BMI ( $p = .732$ ), comorbidities ( $p = 0.896$ ) or MNA ( $p = .667$ ). Length of hospital stay and duration of intervention were also similar in both groups, however, the group with psychological distress had a longer hospital stay and intervention.

The differences between preoperative and postoperative health status values, one year after hospitalization, are shown in Table 2.

Table 2

Differences between preoperative and postoperative health status values, one year after hospitalization.

|                                        | Patients without psychological distress (n = 112) | Patients with psychological distress (n = 62) | p        |
|----------------------------------------|---------------------------------------------------|-----------------------------------------------|----------|
| <b>WHO-DAS 2.0</b>                     |                                                   |                                               |          |
| WHO-DAS 2.0 cognition                  | 7.55 ± 1.71                                       | 8.81 ± 4.39                                   | 0.005*   |
| WHO-DAS 2.0 mobility                   | 5.96 ± 1.63                                       | 6.25 ± 1.96                                   | 0.293    |
| WHO-DAS 2.0 self-care                  | 4.30 ± 0.62                                       | 4.41 ± 0.75                                   | 0.281    |
| WHO-DAS 2.0 relations                  | 5.75 ± 0.99                                       | 6.64 ± 2.26                                   | < .001** |
| WHO-DAS 2.0 housework                  | 5.36 ± 1.75                                       | 6.23 ± 2.34                                   | 0.006*   |
| WHO-DAS 2.0 work and school activities | 3.44 ± 3.73                                       | 3.96 ± 4.28                                   | 0.404    |
| WHO-DAS 2.0 participation              | 10.09 ± 2.58                                      | 11.23 ± 4.32                                  | 0.031*   |
| WHO-DAS 2.0 (total)                    | 42.42 ± 7.39                                      | 47.58 ± 13.83                                 | 0.002*   |
| <b>EQ-5D</b>                           |                                                   |                                               |          |
| EQ-5D VAS                              | 80.35 ± 16.98                                     | 64.50 ± 20.57                                 | 0.002*   |
| EQ-5D mobility                         | 1.15 ± 0.36                                       | 1.30 ± 0.47                                   | 0.177    |
| EQ-5D self-care                        | 1.05 ± 0.22                                       | 1.30 ± 0.47                                   | 0.007*   |
| EQ-5D usual activities                 | 1.20 ± 0.40                                       | 1.40 ± 0.50                                   | 0.102    |
| EQ-5D pain                             | 1.10 ± 0.30                                       | 1.70 ± 0.47                                   | < .001** |
| EQ-5D anxiety/depression               | 1.30 ± 0.46                                       | 1.80 ± 0.76                                   | 0.003*   |
| <b>Pittsburgh Sleep Quality Index</b>  |                                                   |                                               |          |
| Sleep disturbances                     | 0.8 ± 0.39                                        | 1 ± 0                                         | 0.193    |
| Use of sleeping medications            | 0.33 ± 0.78                                       | 1.2 ± 1.55                                    | 0.104    |
| Daytime dysfunction                    | 0.5 ± 0.80                                        | 0.4 ± 0.52                                    | 0.737    |
| Subjective sleep quality               | 0 ± 0                                             | 0.6 ± 0.84                                    | 0.022*   |
| Sleep latency                          | 0.5 ± 0.52                                        | 0.4 ± 0.84                                    | 0.737    |

Data are expressed as mean ± SD or Percentage (%); WHO-DAS 2.0: WHO Disability Assessment Scale, EQ-5D: EuroQol-5D Health Questionnaire; EQ-5D VAS: EuroQol-5D Visual Analogue Scale Health Questionnaire \*p < 0.05, \*\*p < 0.001.

|                                                                                                                                                                                                                                                | Patients without psychological distress (n = 112) | Patients with psychological distress (n = 62) | p      |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|-----------------------------------------------|--------|
| Sleep duration                                                                                                                                                                                                                                 | 0.5 ± 0.80                                        | 1 ± 1.33                                      | 0.289  |
| Sleep efficiency                                                                                                                                                                                                                               | 0.33 ± 0.78                                       | 1 ± 1.33                                      | 0.159  |
| Total                                                                                                                                                                                                                                          | 3 ± 1.47                                          | 5.6 ± 3.8                                     | 0.041* |
| <i>Data are expressed as mean ± SD or Percentage (%); WHO-DAS 2.0: WHO Disability Assessment Scale, EQ-5D: EuroQol-5D Health Questionnaire; EQ-5D VAS: EuroQol-5D Visual Analogue Scale Health Questionnaire *p &lt; 0.05, **p &lt; 0.001.</i> |                                                   |                                               |        |

With regard to the self-perceived health status of the patients, one year after hospitalization, the group who presented psychological distress had worse scores in self-care (p = .007), pain (p < .001), anxiety / depression (p = .003) and VAS (p = .002).

The patients with psychological distress also presented worse scores in most of the WHO-DAS 2.0 domains (cognition (p = .005), relations (p < .001), housework (p = .006), participation (p = .031)) and total score (p = .002).

Regarding the quality of sleep, the group with psychological distress had worse scores in most of the subscales, being statistically significant in subjective sleep quality (p = .022) and the total score (p = .041).

The differences between preoperative and postoperative symptoms, one year after hospitalization, are shown in Table 3.

Table 3

Differences between preoperative and postoperative symptoms, one year after hospitalization.

|                                                                                                                                                                                                                                                                                                                                                                                            | Patients without psychological distress (n = 112) | Patients with psychological distress (n = 62) | p        |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|-----------------------------------------------|----------|
| FSS                                                                                                                                                                                                                                                                                                                                                                                        | 20.55 ± 13.98                                     | 30.40 ± 18.69                                 | 0.025*   |
| <b>Multidimensional Dyspnea Profile</b>                                                                                                                                                                                                                                                                                                                                                    |                                                   |                                               |          |
| MDP E total                                                                                                                                                                                                                                                                                                                                                                                | 3.75 ± 5.58                                       | 17 ± 13,79                                    | < .001** |
| MDP SQ                                                                                                                                                                                                                                                                                                                                                                                     | 3.30 ± 6.48                                       | 11.30 ± 12.43                                 | 0.002*   |
| <b>Brief Pain Inventory</b>                                                                                                                                                                                                                                                                                                                                                                |                                                   |                                               |          |
| Severity score                                                                                                                                                                                                                                                                                                                                                                             | 1.6 ± 4.63                                        | 10.60 ± 11.16                                 | < .001** |
| Interference score                                                                                                                                                                                                                                                                                                                                                                         | 5.4 ± 13.26                                       | 7 ± 14.17                                     | 0.668    |
| Total                                                                                                                                                                                                                                                                                                                                                                                      | 7 ± 17.39                                         | 17.6 ± 21.08                                  | 0.043*   |
| <b>Leicester Cough Questionnaire</b>                                                                                                                                                                                                                                                                                                                                                       |                                                   |                                               |          |
| Physical                                                                                                                                                                                                                                                                                                                                                                                   | 6.95 ± 0.1                                        | 6.17 ± 1.74                                   | 0.133    |
| Psychological                                                                                                                                                                                                                                                                                                                                                                              | 7 ± 0                                             | 6.8 ± 0.42                                    | 0.114    |
| Social                                                                                                                                                                                                                                                                                                                                                                                     | 7 ± 0                                             | 7 ± 0                                         | 1        |
| Total                                                                                                                                                                                                                                                                                                                                                                                      | 20.95 ± 0.1                                       | 19.97 ± 2.16                                  | 0.129    |
| <i>Data are expressed as mean ± SD. FSS: Fatigue Severity Scale; MDP E: Multidimensional Profile of Dyspnea Affective Scale; MDP SQ: Multidimensional Profile of Dyspnea Sensory Qualities Choice; General MDP: Multidimensional Profile of General Dyspnea; BPI-SP: short questionnaire for the evaluation of pain; LCQ: Leicester Cough Questionnaire; *p &lt; 0.05, **p &lt; 0.001.</i> |                                                   |                                               |          |

Statistically significant and clinical differences were found between groups in symptoms. The group with psychological distress presented higher dyspnoea ( $p < .001$ ), fatigue ( $p = .025$ ) and pain ( $p = .043$ ) than the group without psychological distress, one year after hospitalization. The cough did not present differences between both groups.

## Discussion

The aim of this study was to determine whether psychological distress prior to surgery is associated with health status and symptom burden in lung cancer survivors at long-term. Our study show that, patients who present psychological distress before lung resection, present a poorer health status and more symptomatology one year after the intervention.

The sample of subjects included in this study was representative of the general population of patients with lung cancer, with a similar age range and surgery characteristics [47, 48, 49].

To the best of our knowledge, this is the first attempt to study psychological distress in LC survivors. Our results report that LC survivors who presented psychological distress prior surgery present a greater symptom burden than patients without distress, with more dyspnea, pain, fatigue and cough. This is supported by research linking elevated psychological distress with poor physical, functional, and psychosocial outcomes for patients with lung and other cancers [50, 51, 52, 53]. Laird et al. [54] analysed a sample of 654 patients with advanced cancer and cachexia, reporting an important relationship between depression and the presence of pain and fatigue. In the same line, Fitzgerald et al. [55] analysed a group of 487 patients with cancer also reporting a significant relationship between depression, fatigue and pain. However, both studies did not focus on a specific type of cancer and they analysed the relationship between variables at a single time. Tishelman et al. [56] also noted that breathing, pain, and fatigue were associated with the most distressed subjects in a sample of 400 patients with lung cancer. A recent study [23] also studied the presence of psychological distress in a sample of 2205 newly diagnosed patients with non-small lung cancer (NSLC). Their results showed that emotional problems were related to symptom burden, similar to our results; however, they did not follow the impact of psychological distress at long-term.

A decreased health status, in LC survivors who presented psychological distress prior surgery, was found in our study, with a poor functionality, self-perceived health status and sleep quality. Arrieta et al. [57] analysed a sample of 82 patients with NSLC and found an association between HADS score, quality of life and prognosis, even 6 month after treatment. However, they did not included the symptoms or other factors which could affect quality of life. González-Saenz de Tejada et al. [58] carried out a similar study in patients with colorectal cancer. They explored the association of psychological status before surgery with changes in quality of life outcomes at 1-year post-intervention. Their results reported that patients with cancer and absence of psychological distress before surgery presented better results in quality of life outcomes at 1 year after surgery, similar to our study.

According to our results, PSQI scores has been associated to psychological distress. This correspond with the literature where the patients' levels of anxiety and depression have been associated with poor sleep quality [59, 60]. In the same line, Chang et al. [61] reported that the hypothalamic-pituitary-adrenal axis activation caused by an increased psychological stress have a pronounced effect on sleep quality of lung cancer patients. Our study also show a reduced functionality one year after surgery in LC survivors with psychological distress. Similar results were found in the study of Lin et al. [51] where 145 lung cancer patients were analysed, and psychological distress was associated to a lower functional status and worse quality of life. Cheville et al. [62] studied a sample of 2405 patients with lung cancer and showed similar results, relating psychological distress to functionality. These authors reported that psychological distress could even predicts survival and functional status five years after diagnosis.

We should recognise potential limitations to this study. First, the severity of psychological distress was not evaluated over time so, the temporal relationship between change in these problems, quality of life, and symptom burden is unknown. However, our study design has based on previous studies where psychological distress was only evaluated once [32, 60]. Second, the lack of a structured psychiatric

clinical interview to assess depression and anxiety. Nevertheless, previous studies have used the HADS to evaluate the presence of psychological distress [63, 11].

Our findings demonstrate that psychological distress is an important consideration in the care of patients with lung cancer, and that a brief screening of these problems prior to surgery can predict the evolution of symptoms and health status at long term. A better understanding of the impact of psychological distress on cancer survivors could raise awareness, promote the development of better treatment strategies, and improve the quality of life of these patients. So, future studies, which develop interventions that approach these disorders, may be useful to improve the recovery and prognosis of these patients.

## **Conclusion**

Psychological distress is an important factor to take into account in lung cancer survivors. Patients with psychological distress prior surgery present a greater symptom burden, with more dyspnoea, cough, fatigue and pain. Regards to health status, LC survivors with psychological distress prior surgery presented a poorer self-perceived health status, lower functionality and sleep quality, than patients without distress one year after the lung resection.

## **Declarations**

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### **Conflicts of interest/Competing interests**

Nothing to declare.

### **Availability of data and material**

Not applicable.

### **Code availability**

Not applicable.

### **Authors' contributions**

Marta Linares-Moya: conceptualization, methodology, supervision.

Janet Rodríguez-Torres: methodology, data curation, writing-original draft.

Alejandro Heredia-Ciuró: supervision. methodology.

María Granados-Santiago: data curation, visualization.

Laura López-López: methodology, data curation.

Florencio Quero-Valenzuela: data curation, supervision.

Marie C Valenza: conceptualization, methodology, formal analysis.

## **Ethics approval**

The study protocol was reviewed and approved by the University of Granada Ethics Committee (Granada, Spain). This study was performed in accordance with the Declaration of Helsinki (General Assembly of the World Medical Association, 2014).

## **Consent to participate**

All participants signed the informed consent previous to the inclusion in the study.

## **Consent for publication**

All authors give their consent for publication.

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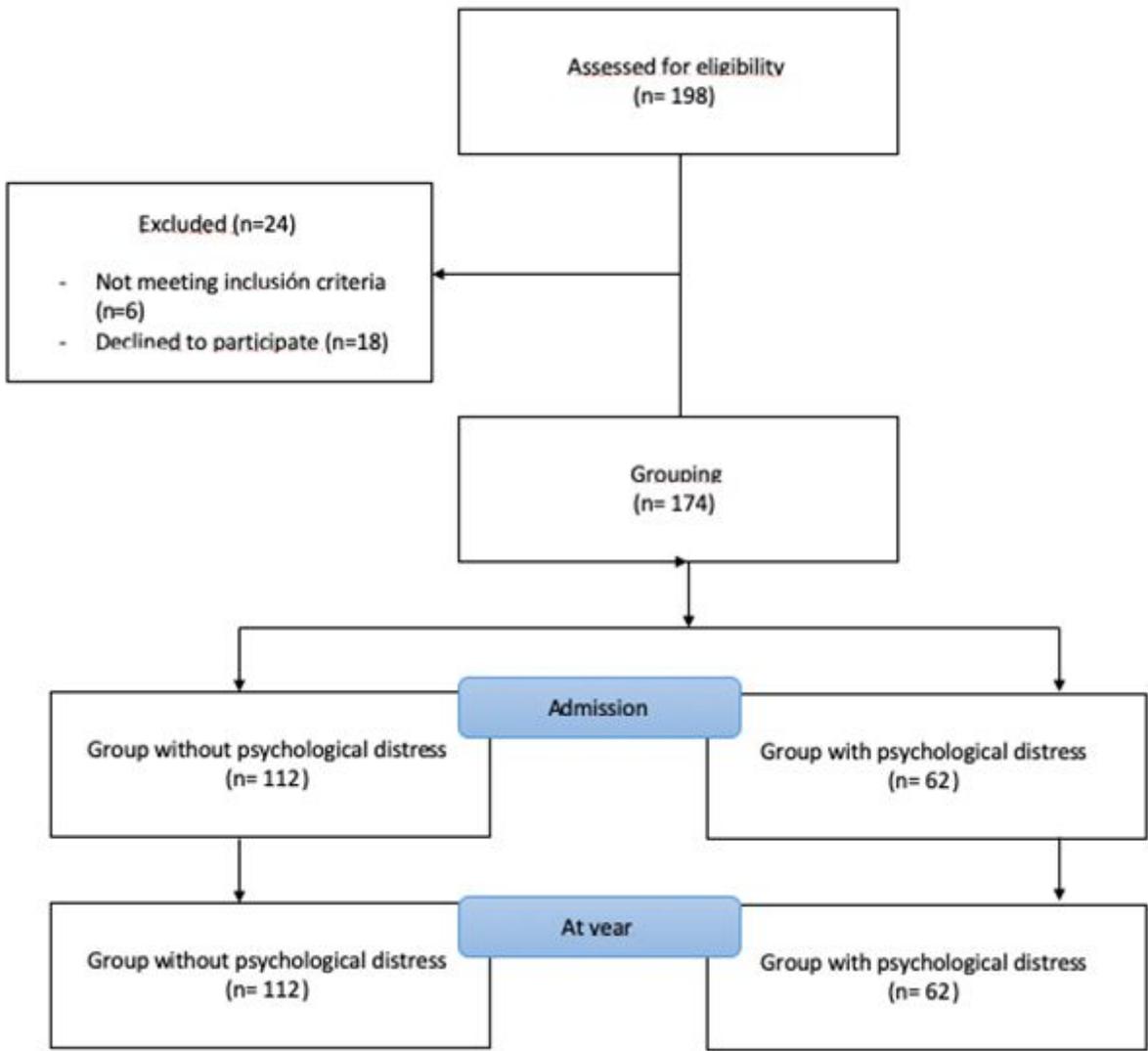
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## Figures



**Figure 1**

Flow diagram of participants.