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9  **Anxiety and depression among caregivers of patients with eating disorders and their change over**

10  **one year**

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29 **Abstract**

30 *Purpose.* Limited data are available on the difficulties experienced over time by caregivers of patients

31 eating disorders (CPED). The aim of this study was to describe changes in anxiety and depression among

32 such caregivers over one year and to identify factors predicting any changes in both.

33 *Methods.* At recruitment, 145 ED patients and their 246 caregivers completed sociodemographic and

34 clinical instruments, including the Hospital Anxiety and Depression Scale (HADS) , and the Short-Form

35 12 (SF-12). Patients also completed the Eating Attitudes Test-26 (EAT-26), and their psychiatrists

36 assessed clinical variables. Patients and caregivers completed the same instruments one year later.

37 *Results.* At baseline, prevalence of anxiety and depression among caregivers was 56% and 32%,

38 respectively. Scores were essentially the same one year later. Factors associated with changes in anxiety

39 were higher anxiety level at baseline and caring for a patient with a restrictive ED. Factors associated

40 with changes in depression included higher depression at baseline and caring for a patient with a

41 restrictive ED. Neither health-related quality of life among patients and caregivers, or patients' eating

42 attitudes were related to caregivers anxiety or depression.

43 *Conclusions.* These findings confirm the presence of substantial and continuing emotional distress among

44 caregivers of patients with ED, highlighting the importance of offering them more extended follow up

45 and treatment.

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48 **Keywords:** caregivers, eating disorder, anxiety, depression, follow-up

49 **Introduction**

50 Patients with eating disorders (ED) require ongoing medical care and psychosocial support, much of

51 which comes from family members. This can be a challenge, given that average duration of an episode of

52 anorexia nervosa is six years, patients may have repeated hospital admissions during this time, many

53 patients deny the seriousness of their illness, and are often ambivalent about or resistant to treatment [15,

54 26].

55 Although fraught with the potential for conflict, family members generally report that they lack

56 skills and resources to provide adequate care, and find the task of caregiving very stressful. Thus, it is not

57 surprising that ED has a considerable impact on the lives of affected family members [23, 24].

58 To date, research on the burden borne by family caregivers has focused mainly on schizophrenia,

59 affective disorders, and Alzheimer's disease- Other illnesses have remained relatively unexplored [3, 32].

60 Only a handful of cross-sectional studies have focused on the needs and difficulties experienced by family

61 members providing care to individuals suffering from EDs: most of them have come within the last

62 decade [11, 26, 32]. Not surprisingly, these studies demonstrated poorer quality of life among ED family

63 members than in the general population. This lower quality of life was associated with a high subjective

64 burden of care, anxiety, depression, loss of behavioural or emotional control, and low psychological well-

65 being [6, 18]. For example, Kyriacou [15] found that 52% of the ED caregivers scored above the cut-off

66 of 11 for anxiety as measured by the Hospital and Depression Scale (HADS), and 13% were above the

67 cut-off for depression. Some studies have shown higher rates of distress among ED caregivers than

68 among caregivers for patients with psychosis and in Alzheimer's disease [15, 26, 29, 32].

69 Anxiety, depression, and other problems can make in harder to provide quality care for an ED

70 patient [23, 24]. They are also associated with more physical and organic problems than observed in the

71 general population, such as cardiovascular diseases or musculoskeletal pain [3].

72 Identifying caregiver and patient factors that may be related to caregiver anxiety and depression

73 would be a step toward developing interventions to reduce ED caregivers' distress. This could improve

74 integrated health care strategies for this type of problem [29]. To our knowledge, no longitudinal studies

75 have focused on the assessment of anxiety and depression among ED caregivers. Thus, we evaluated ED

76    caregivers' anxiety and depression at the time of assessment and one year laterin an effort to identify

77    caregiver and patient factors that influence changes in ED caregivers' depression and anxiety after one

78    year, adjusting by baseline score.

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**Material and Methods**

Recruitment of participants

This was a prospective cohort study of ED patients and their caregivers with one year follow up. All patients were attending the psychiatric services at Galdakao-Usansolo hospital and the Ortuella Mental Health Center in Bizkaia, which is in the Basque Country (Spain). Both are part of the network of public health care centers of the Basque Health Service, which provide unlimited free care to nearly 100% of the population.

*Patients.* We recruited patients diagnosed with either anorexia nervosa (restrictive or purgative), bulimia nervosa (not purgative or purgative), or an eating disorder not otherwise specified (restrictive or purgative or binge) according to the Diagnostic and Statistical Manual of Mental Disorders IV[1]. Patients between the ages of 16 and 65 years were asked to participate in the study. Patients were excluded from the study if they had malignant or severe organic or psychiatric diseases that made it impossible to complete the study questionnaires, if there was a language barrier, or if they did not provide inform consent. The study was approved by the ethics committees of both institutions.

*Caregivers.* Each patient was asked to identify her or his primary caregivers. We recruited those caregivers who met the definition of family caregiver stablished by Perlick et al. [20]. They defined a primary caregiver as a person who fulfils three or more of the following criteria: 1) a parent, partner, or other relative; 2) maintains frequent contact with the patient; 3) provides significant financial support to the patient; 4) is the person who is most often present with the patient during consultation or treatment and who is aware of the severity of the illness (accompanies the patient to medical appointments, participates in consultations and therapy, supervises eating behaviour at home, etc.); and 5) is the person the therapy team contacts in the event of an emergency. As part of our unit's standard protocol for ED patients, all ED caregivers receive professional counselling from clinicians to deal with their relatives' ED. The usual procedure with the caregivers was to attend them in a session with the aim to provide some not standardized instructions about how manage with the patient at home and to give them some psychoeducative material such as the Janet Treasure's manual tittled "Skills-based Learning for Caring for a Loved One with an Eating Disorder: The New Maudsley Method". The exclusion criteria were the same as for the patients.

111      Data collection started in 2007. Patients and caregivers were informed of the study goals. When

112      both the patient and the caregiver gave their informed consent to participate, the patients' psychiatrist

113      completed the clinical protocol and a coauthor (JM) mailed the study instruments separately, to the

114      patient and caregiver. Patients and caregivers who did not return the materials within 20 days were sent a

115      reminder letter. One year later, the same study instruments were mailed, with the same follow-up for non-

116      responders.

117

118      Measures

119      *Caregivers* were asked to provide sociodemographic information including gender, age,

120      relationship with the patient (mother, father, etc.), educational level, whether he or she lived with the

121      patient, number of contact hours per week with the patient, and clinical information, including whether

122      the caregiver had sought help from a mental health professional for his/her problems. Caregivers were

123      also asked to complete two questionnaires:

124      The *Hospital Anxiety and Depression Scale (HADS)* was specially designed for identifying and

125      quantifying anxiety and depression in physically ill patients [33]. It is a 14-item measure—7 for

126      evaluating depression (the HADS-D subscale) and 7 for evaluating anxiety (the HADS-A subscale).

127      Scores for each item range from 0 to 3. A subscale score of 0-7 indicates the absence of anxiety or

128      depression; a score of 8-10 indicates a possible case of anxiety or depression; and a score of 11 or higher

129      indicates the presence of anxiety or depression. The instrument's validity and reliability have been

130      confirmed [4], and it has been adapted and validated in a Spanish population [22].

131      *The Short-Form 12 (SF-12)* is a 12-item instrument designed to measure general health-related

132      quality of life (HRQoL) [28]. Answers provide two summary scores, the mental component scale (MCS)

133      and physical component scale (PCS), which reflect the individual's perceived mental and physical health.

134      Scores range from 0 to 100 for each component scale. A score of 50 or more indicates a positive

135      perception of health, whereas a score below 50 indicates a negative perception. We used a version

136      validated in Spanish [8].

137    *ED patients* were asked to provide basic demographic data, including gender and age. They were

138    also asked to complete the HADS, the SF-12 and the *Eating Attitudes Test (EAT-26)* [9]. This test

139    measures the symptoms and characteristics of eating disorders. It is subdivided into three subscales diet,

140    bulimia, and oral control. The total EAT-26 score can range from 0 to 76. A score of 20 or higher is used

141    to determine ED cases. The EAT-26 has been validated in a Spanish population [5].

142    Each *patient's psychiatrist* assessed the patients' clinical variables, such as type of compensating

143    behaviour (restrictive or purgative), suicidal intentions, and psychiatric co-morbidities such as drug

144    addictions, anxiety disorder, or psychosis. The length of time (in months) the patient had been receiving

145    clinical treatment and the length of time (in months) the patients had been in the specific ED programme

146    were also recorded.

147

148    Statistical analysis

149    Demographic variables are described using means and standard deviations (SDs), and frequencies and

150    percentages. Chi-Square and Fisher's exact tests for categorical variables and Student's T-test and

151    ANOVA (or the Wilcoxon and Kruskal-Wallis tests when the data did not fit a normal distribution) for

152    continuous variables were used to test differences at baseline between patients and caregivers who agreed

153    to participate and those who declined to participate.

154    The main outcomes in this study were caregiver anxiety and depression (as measured by the

155    HADS questionnaire) at baseline and their respective mean changes after one year. The mean change in

156    the HADS-A and HADS-D were defined as the difference between the scores at baseline and one year

157    later. A positive mean change value reflects a decrease anxiety or depression. Among participant

158    caregivers and patients, the non parametric sign test was used to assess whether the mean changes of the

159    outcomes were significant.

160    To identify variables associated with caregiver's emotional status at baseline and one year follow

161    up, we conducted a series of univariate analyses. The following variables were examined as possible

162    predictors: a) caregivers' sociodemographic and clinic characteristics, HADS scores and SF-12 scores;

163    and b) patients' clinical characteristics assessed by the psychiatrist and EAT-26 questionnaire at baseline.

164  The Wilcoxon and Kruskall-Wallis tests were used to evaluate the performance among caregiver

165  variables. For the assessment of the relationship of the caregivers' age with the studied outcomes,

166  Pearson's correlation coefficient was calculated. Due to the study design (a patient could have more than

167  one caregiver), hierarchical linear mixed models were used for the assessment of significant differences

168  of patients' variables in the studied outcomes.

169       Only those variables identified with a p<0.20 [27] in the univariate analysis and those identified

170  as clinically significant were entered into  the hierarchical multivariable linear models in order to

171  determine which combination of factors best accounted for the caregivers' emotional status at baseline

172  and its mean change after one year. Finally, the intraclass correlation coefficient (ICC) was calculated for

173  the obtained models to assess the correlation among observations within a cluster. It was estimated by

174  dividing patient variance by the total sample variance. A small coefficient would indicate that patients

175  and caregivers must be independent. All data analyses were computed using SAS System version 9.2 for

176  Windows.

177    **Results**

178    <u>Patient and caregiver characteristics</u>

179    During the study period, 169 ED patients and their respective 309 caregivers were recruited. Of these, 145

180    patients and 246 caregivers fulfilled the criteria and completed all the questionnaires at baseline: 84

181    patients (58%) and 143 caregivers (58%) completed the questionnaires after one year. The

182    sociodemographic and clinic characteristics of the caregivers and patients with an ED are shown in Table

183    1.

184    ---------------------------------------------------Table 1---------------------------------------------------

185    When comparing patients and caregivers who agreed to participate and those who declined to

186    participate, the participant caregivers differed from nonparticipants only in age (participants were an

187    average of 4 years older, $p = 0.01$), and in having sought help from a mental health specialist (30% of

188    participants and 17% of nonparticipants, $p = 0.02$). Among the patients, participants differed from

189    nonparticipants only in the EAT-26 total score, with participants faring worse (32.99) than

190    nonparticipants (25.34, p = 0.02). All other variables were equally distributed between the groups.

191    As measured by HADS scores, at baseline 24.82% of caregivers had possible case of anxiety

192    (HADS-A score of 8-10) and 31.21% had clinical anxiety (HADS-A score $\geq$ 11), 19.86% had possible

193    depression (HADS-D score of 8-10) and 12.06% had clinical depression (HADS-D score $\geq$ 11). After one

194    year, 17.02% of the caregivers had possible anxiety and 21.28% had clinical anxiety, while 21.99% had

195    possible depression and 8.51% had clinical depression.

196    HRQoL of patients and caregivers (measured by the two dimensions of the SF-12) and eating

197    attitudes of the patients (based on the EAT-26) were not associated caregivers' anxiety and depression.

198    *Caregivers'* variables (Table 2) showing a *p*<0.20 significance with caregivers' *anxiety levels at*

199    *baseline* included the caregiver's relationship with the ED patient, having sought help from a mental

200    health professional, and the depression level at baseline. For *depression at baseline,* variables included

201    the relationship with the patient, the educational level, contact hours, having sought help from a mental

202    health professional, and anxiety level at baseline. *Caregiver* variables showing a *p*<0.20 significance with

203 *changes* in caregivers' *anxiety* levels after one year  included age, contact hours and anxiety levels at

204 baseline; for *changes* in *depression* variables included relationship with the patient, the educational level

205 and depression level at baseline.

206 ---------------------------------------------Table 2------------------------------------------------------

207      *Patient* variables (Table 3) showing a *p*<0.20 significance with *caregivers anxiety at baseline*

208 included suicidal intention, drug addiction, psychosis co-morbidity and depression level at baseline; for

209 *depression* they included suicidal intention, drug addiction, time in clinical treatment, and time in a

210 specific ED programme. Patient variables showing a *p*<0.20 significance with *changes* in *caregivers'*

211 *anxiety* included suicidal intention, depression level at baseline, time in clinical treatment, time in the

212 specific ED programme and types of compensating behaviour;  for *depression* they included having

213 depression at baseline. We also included the type of compensating behaviour (*p*=0.24) as a clinically

214 important factor associated with changes in caregivers' depression level.

215 ---------------------------------------------Table 3------------------------------------------------------

216 *Caregivers' anxiety at baseline* (Table 4). Being a father of the index patient was associated with a

217 significantly lower level of caregiver anxiety than being mother (which was the reference group). Having

218 a possible case of depression or clinical depression at baseline was significantly associated with higher

219 levels of anxiety (caregivers' without depression were the reference group). Caregivers of patients with

220 drug addictions had higher baseline anxiety than caregivers of patients without that comorbidity. ICC

221 value 0.04.

222 *Caregivers' depression at baseline* (Table 4). Being a sibling or child of the index patient and having

223 achieve university studies were associated with lower levels of caregivers' depression at baseline

224 compared with being mother of the index patient or with having achieved at most primary studies (which

225 were respectively the reference groups). Having possible or clinical anxiety at baseline was significantly

226 associated with a higher level of depression than non having anxiety at baseline (the reference group).

227 Caring for a patient who had expressed suicidal intentions was significantly related to higher levels of

228 depression. ICC value 0.22.

229 ---------------------------------------------Table 4------------------------------------------------------

230         *Changes in caregivers' anxiety* (Table 5). Caregivers' with possible or clinical anxiety at

231   baseline and those whose relative had a restrictive ED improved more than caregivers who did not have

232   anxiety at baseline or whose relative had a purgative ED (the respective reference groups). ICC value

233   0.15.

234         *Changes in caregivers' depression* (Table 5). Caregivers with possible or a clinical depression at

235   baseline improved more than those without depression at baseline. Less improvement in caregivers'

236   depression after one year was observed among those who had attained at least a secondary school

237   education as those with less education. Caregivers of patients with a restrictive ED and with a score

238   between 8 and 10 in the HADS-D at baseline had greater improvements in depression after one year than

239   caregivers of purgative ED patients who scored ≤7. ICC value 0.20.

240   -------------------------------------------------Table 5--------------------------------------------------------

241

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243

244     **Discusion**

245     The aim of this prospective study was to examine possible factors that might contribute to anxiety and

246     depression among caregivers of ED patients over time. Identifying modifiable, easily measured factors in

247     a caregiver's or patient's profile could help alleviate anxiety or depression and improve both the care

248     given to the ED patient and the caregiving experience.

249     In this study caregiver of ED patients presented with considerable distress, which was

250     maintained nearly without change after one year. Factors associated with improvement in caregiver

251     anxiety after one year included high caregiver anxiety at baseline and taking care of a patient with

252     restrictive (rather than purgative) ED. Factors associated with improvement in depression included a high

253     caregiver depression at baseline, caring for a patient with a HADS-D score between 8-10, and caring for a

254     patient with restrictive (rather than purgative) ED. Finally, a higher educational level of the caregiver is a

255     factor associated with worsening in caregiver depression at follow up.

256     The finding of considerable distress in caregivers is consistent with observations from previous

257     studies. In our population, approximately 56% of caregivers had HADS scores exceeding the cut-off for

258     anxiety and almost 32% exceeded the cut-off for depression. Earlier studies which used the HADS [3, 15]

259     reported rates of 67-70% for anxiety and 34-40% for depression. These levels of caregivers' anxiety and

260     depression are significantly higher than the rates observed in the general community: 16.6% for anxiety

261     and 6% for depression [7]. In Spain, also in the general community, depression rates of 2.9-4.8% have

262     been observed in men and 7.8-10.4% in women, while anxiety rates of 3.8 have been observed in men

263     and 8.7 in women [2].

264     In terms of psychological distress (as measured by the HADS), levels among caregivers of ED

265     patients are at least as high as that experienced by caregivers of patients requiring palliative care, or those

266     with Alzheimer's disease, or invasive ovarian cancer [10, 17, 21]. Livingston et al. [17], for example,

267     found that among caregivers of people with Alzheimer's the prevalence of anxiety was 45% and

268     depression was 26%. In a study by Gough and Hudson [10] of 106 primary family caregivers of patients

269     requiring palliative care, 55.7% had anxiety and 28.2% were depressed. Among caregivers of patients

270     with cancer, Price et al. [21] observed anxiety rates of 42% and depression rates of 19%. In Spain, Soto et

271     al (2003) [25] found that the 44% of the caregivers of hospitalized cancer patients had clinically relevant

272 symptoms of anxiety and 23% had symptoms of depression. Our findings offer additional evidence of the

273 considerable psychological morbidity experienced by caregivers in ED, and suggest that some or all

274 would benefit from evaluation and treatment.

275       Our multivariate analysis suggests that the relationship between caregiver and patient is one

276 predictor of caregiver anxiety and depression *at baseline*. Mothers had significantly higher baseline levels

277 of anxiety than did fathers, and higher levels of depression than siblings or children. These findings are

278 consistent with the literature [15]. Our data also confirm the well established symptomatology overlap

279 between anxiety and depression [16], finding that high levels of anxiety were associated with high levels

280 of depression and vice versa. We also observed that education was a predictor of both anxiety and

281 depression, which also confirms other reports [13, 30]. In general, individuals with less education were

282 more depressed than those with higher education. Regarding patient factors, only drug addiction was

283 associated with caregiver, while only suicidal intention was associated with caregiver depression.

284 Altogether, these results highlight the importance in providing special attention to caregivers' of ED

285 patients, and the importance of assessing caregiver's mental health independent of the patient.

286       Longitudinal analysis showed a small decline in caregivers' anxiety (mean change in HADS-A

287 score=1.40) at one year, and even smaller decline in caregiver's depression (mean change in HADS-D

288 score=0.37); both results were statistically significant. Despite the improvement, the rates of anxiety and

289 depression remained higher than in the general population (38% and 31%, respectively). This is

290 consistent with findings from Parabiaghi et al. [19], who demonstrated a significant improvement in

291 caregiving burden, emotional distress, and coping among caregivers of patients with schizophrenia.

292       In our study, predictive factors for change in caregiver anxiety were having anxiety at baseline

293 and caring for and ED patient with a restrictive diagnosis. For change in caregiver depression, predictive

294 factors were having depression at baseline, caring for a patient with a possible case of depression at

295 baseline (HADS-D score of 8-10), and caring for a patient with a restrictive ED. These results may reflect

296 the finding that the use of multiple purging methods is associated with greater disease severity over time

297 [12]. Finally, according to the literature lower educational level predicted worse depression over time. We

298 found that a higher educational level (having a secondary school education compared with primary

299  schooling or no education) was associated with higher depression overtime. Nevertheless, the difference

300  was just 1.12 point by the HADS-D and the p value was in the significance limit with a $p=0.05$.

301       In regard to the relationship between caregivers' anxiety and/or depression and their HRQoL, the

302  literature suggests that anxiety and depression are suitable predictors of global satisfaction with life [6,

303  14, 18]. Our study, however, did not replicate those results-HRQoL as measured by SF-12 was not a

304  predictor of anxiety or depression.

305       In a cross-sectional study by Winn et al. [31] more weekly contact hours with an ED patient

306  predicted a negative caregiving experience. In our study, this variable did not predict caregiver  anxiety or

307  depression or changes in them. This is consistent with cross-sectional finding from Whitney et al.[29] and

308  Parabiaghi et al. [19], neither of which found that contact hours are associated with caregiver distress.

309       Our study has several strengths and advantages compared to previous studies. We used variables

310  that are usually and easily collected in the course of routine clinical work. Measuring anxiety and

311  depression with the HADS is simple and straightforward. We evaluated both caregiver and patient

312  factors. The hierarchical model we used helped control for clustering of observations and can thus

313  improve the efficiency of estimated impacts. Other strengths included the longitudinal nature of the study

314  and the relatively large sample of patients.

315       Several limitations must also be noted. As in any prospective cohort study, some participants

316  were lost during follow up. However, the caregivers who continued to participate at one year did not

317  differ in most variables from those who did not respond at one year.  One difference was that a higher

318  percentage of caregivers participating at one year reported that they had sought treatment from a mental

319  health professional than did caregivers who chose not to participate in the study. However, there were no

320  differences in psychopathology or quality of life between the two groups. Another limitation of the study

321  it is that it focused exclusively on outpatients who presented for care in a hospital setting, being this

322  probably the reason why the sample is slightly skewed towards older participants with a severe form of

323  illness. Thus, the results will not necessarily generalize to other settings, such as inpatients or patients

324  treated as part of primary care.

325       In summary, the findings of this study confirm the presence of substantial anxiety and depression

326  in caregivers of ED patients. This emotional distress is independent of almost all patient characteristics. It

327   also appears to change little over the course of one year. These findings have clinical implications,

328   highlighting the importance of providing adequate assessment and support to caregivers of patients with

329   ED, independent of the patient, and offering them more extended follow up and treatment. Because our

330   data reflect only one-year follow-up, it would be useful to conduct a longer study to assess whether there

331   are more changes in caregivers' emotional status over time and to identify variables that may be influence

332   those changes.

333

334 **Acknowledgments**

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343 **Reference List**
344

345 1. APA (2000) Diagnostic and Statistical manual of mental disorders (DSM-IV-TR). American
346 Psychiatric Association, Washington, DC.

347 2. Ayuso JL, Artal J, Vázquez-Barquero JL (2007) Epidemiología de la enfermedad mental en la
348 comunidad. In: Vázquez-Barquero JL ed. Psiquiatría en atención primaria. Biblioteca Aula
349 Médica, Madrid, pp. 21-40

350 3. Berbel E, Sepulveda AR, Graell M, Andres P, Carrobles JA, Morandé G (2010) Valoración del
351 estado de salud y psicopatología de los familiares en el trastorno del comportamiento alimentario:
352 diferencias entre cuidadores principales y secundarios. Revista de Psicopatología y Psicología
353 Clínica 15:179-192

354 4. Bjelland I, Dahl AA, Haugh TT, Neckelmann D (2002) The validity of the Hospital Anxiety and
355 Depression Scale. An updated literature review. Journal of Psychosomatic Research 52:69-77

356 5. Castro J, Toro J, Salamero M, Guimera E (1991) The Eating Attitudes Test: validation of the
357 Spanish version. Psychological Assessment 7:175-189

358 6. De la Rie S, Van Furth EF, De Koning A, Noordenbos G, Dorker M (2005) The quality of life of
359 family caregivers of eating disorder patients. The Journal of Treatment and Prevention 13:345-351

360 7. Fleury MJ, Grenier G, Bamvita JM, Perreault M, Caron J (2011) Typology of adults diagnosed
361 with mental disorders based on socio-demographics and clinical and service use characteristics.
362 BMC Psychiatry 11:67

363 8. Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, Bullinger M, Kaasa S,
364 Leplege A, Prieto L, Sullivan M (1998) Cross-validation of item selection and scoring for the SF-
365 12 Health Survey in nine countries: results from the IQOLA Project. Journal of clinical
366 Epidemiology 51:1171-1178

367 9. Garner DM, Olmsted MP, Bohr Y, Garfinkel PE (1982) The Eating attitudes Test: psychometric
368 features and clinical correlates. Psychological Medicine 12:871-878

369 10. Gough K, Hudson P (2009) Psychometric properties of the Hospital Anxiety and Depression Scale
370 in family caregivers of palliative care patients. Journal of Pain and Symptom Management 37:797-
371 806

372 11. Graap H, Bleich S, Herbst F, Scherzinger C, Trostmann Y, Wancata J, De Zwaan M (2008) The
373 needs of carers: a comparison between eating disorders and schizophrenia. Social Psychiatry and
374 Psychiatric Epidemiology 43:800-807

375 12. Haedt A, Edler C, Heatherton T, Keel P (2006) Importance of Multiple PUrging Methods in the
376 Classification of Eating Disorder Subtypes. International Journal of Eating Disorders 39:648-654

377 13. Haro JM, Palacín C, Vilagur G, Martínez M, Bernal M, Luque I, Codony M, Dolz M, Alonso J,
378 Grupo ESEMeD-España (2006) Prevalencia de los trastornos mentales y factores asociados:
379 resultados del estudio ESEMeD España

380 14. Huppert JD, Smith TE (2001) Longitudinal analysisi of subjective quality of life in schizophrenia:
381 anxiety as the best symptom predictor. The Journal of Nervous and Mental Disease 189:669-675

382 15. Kyriacou O, Treasure J, Schmidt U (2008) Expressed emotion in eating disorders assessed via self-
383 report: an examination of factors associated with expressed emotion in carers of people with

384    anorexia nervosa in comparison to control families. International Journal of Eating Disorders
385    41:37-46

386  16.  Lamers F, Van Oppen P, Comijs HC, Smit JH, Spinhoven P, Van Balkom AJ, Nolen WA, Zitman
387    FG, Beekman AT, Pennix BW, e. (2011) Comorbidity patterns of anxiety and depressive disorders
388    in a large cohort study: the Netherlands Study of Depression and Anxiety (NESDA). Journal of
389    Clinical Psychiatry 72:341-348

390  17.  Livingston G, Mahoney R, Regan C, Katona C (2005) The caregivers for Alzheimer's Disease
391    Problems Scale (CAPS): development of a new scale within the LASER-AD study. Age and Aging
392    34:287-290

393  18.  Martín J, Padierna A, Aguirre U, Quintana JM, Las Hayas C, Muñoz P (2011) Quality of life
394    among caregivers of patients with eating disorders. Quality of Life Research Epub ahead of print:

395  19.  Parabiaghi A, Lasalvia A, Bonetto C, Cristofalo D, Marrella G, Tansella M, Ruggeri M (2007)
396    Predictors of changes in caregiving burden in people with schizophrenia: a 3-year follow-up study
397    in a community mental health service. Acta Psychiatrica Scandinavica 116:66-76

398  20.  Perlick DA, Hohenstein JM, Clarkin JF, Kaczynski R, Rosenheck RA (2005) Use of mental health
399    and primary care services by caregivers of patients with bipolar disorder: a preliminay study.
400    Bipolar Disorders 7:126-135

401  21.  Price MA, Butow PN, Costa DSJ, King MT, Albridge LJ, Fardell JE, DeFazio A, Webb PM,
402    Australian Ovarian Cancer Study Group, Australian Ovarian Cancer Study Group Quality of LIfe
403    Study Investigators (2010) Prevalence and predictors of anxiety and depression in women with
404    invasive ovarian cancer and their caregivers. The Medical Journal of Australia 193:S52-S57

405  22.  Quintana JM, Padierna A, Esteban C, Arostegui I, Bilbao A, Ruiz I (2003) Evaluation of the
406    psychometric characteristics of the Spanish version of the Hospital anxiety and depression Scale.
407    Acta Psychiatrica Scandinavica 107:216-221

408  23.  Sepulveda AR, Kyriacou O, Treasure J (2009) Development and validation of the Accommodation
409    and Enabling Scale for Eating Disorders (AESED) for caregivers in eating disorders. BMC Health
410    Services Research 9:171-184

411  24.  Sepulveda AR, López C, Todd G, Whitaker W, Treasure J (2008) An examination of the impact of
412    "the Maudsley eating disorder collaborative care skills workshops" on the well being of carers.
413    Social Psychiatry and Psychiatric Epidemiology 43:584-591

414  25.  Soto J, Planes M, Gras ME (2003) Symptoms of anxiety and depression in relatives and close
415    friends of hospitalized cancer patients. Revista de Psicología Universitas Tarraconensis 25:109-116

416  26.  Treasure J, Murphy T, Szmukler G, Todd G, Gavan K, Joyc (2001) The experience of caregiving
417    for severe mental illness: a comparison between anorexia nervosa and psychosis. Social Psychiatry
418    and Psychiatric Epidemiology 36:343-347

419  27.  Vittinghoff E, Glidden DV, Shiboski SC, McCulloch CE (2004) Regression Methods in
420    Biostatistics. Linear, Losgistic, Survival, and Repeated Measures Models. Springer-Verlag, Inc,

421  28.  Ware J, Kosinski M, Keller SD (1996) A 12-item Short-Form Health survey: construction of scales
422    and preliminary test of reliability and validity. Medical Care 34:220-233

423  29.  Whitney J, Haigh R, Weinman J, Treasure J (2007) Caring of people with eating disorders: factors
424    associated with psychological distress and negative caregiving appraisals in carers of people with
425    eating disorders. British Journal of Clinical Psychology 46:413-428

426    30. WHO International Consortium in Psychiatric Epidemiology (2011) Cross-national comparisons of
427         the prevalences and correlates of mental disorders. Bull World Health Organization 78:413-426

428    31. Winn S, Perkins SP, lwyn R, hmidt U, isler ITJ, relowitz M, dge L, rost SJM, hnson E, eville S, M,
429         phy R, Robinson P, Yi I (2007) Predictors of mental health problems and negative caregiving
430         experiences in carers of adolescents with bulimia nervosa. International Journal of Eating
431         Disorders 40:171-178

432    32. Zabala MJ, Macdonald P, Treasure J (2009) Appraisal of caregiving burden, expressed emotion
433         and psychological distress in families of people with eating disorders: a systematic review.
434         European Eating Disorders Review 17:338-349

435    33. Zigmond AS, Snaith RP (1983) The hospital anxiety and depression scale. Acta Psychiatrica
436         Scandinavica 67:361-370
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440**Table 1**. Sociodemographic and clinical data of caregivers (n=143) and patients (n=84)

| CAREGIVER VARIABLES | N (%) |
|---|---|
| Female | 78 (55) |
| **Age** Mean (SD) | 49.92 (11.21) |
| **Relationship with the patient** | |
| Mother | 68 (48) |
| Father | 45 (31) |
| Partner | 16 (11) |
| Other (sibling and child) | 14 (10) |
| **Educational level** | |
| Uneducated/primary school | 60 (40) |
| Secondary school | 31 (22) |
| University studies | 51 (36) |
| **Live with the patient** | |
| No | 19 (13) |
| Yes | 122 (87) |
| **Contact hours (weekly)** | |
| <32 | 70 (51) |
| ≥32 | 68 (49) |
| **Sought help from a mental health professional** | |
| No | 100 (70) |
| Yes | 43 (30) |
| **Baseline HADS-A** Mean (SD) | 8.75 (4.33) |
| **Baseline HADS-D** Mean (SD) | 6.03 (3.21) |
| **Mean change in HADS-A** Mean (SD)* | 1.40 (4.07) |
| **Mean change in HADS-D** Mean (SD)* | 0.37 (2.54) |
| PATIENT VARIABLES | |
| Female | 84 (100) |
| **Age** Mean (SD) | 26.46 (9.50) |
| **Type of compensating behaviour** | |
| Restrictive | 39 (47) |
| Purgative | 44 (53) |
| **Suicidal intention** | |
| Yes | 16 (19) |
| No | 68 (81) |
| **Drug addiction** | |
| Yes | 2 (2) |
| No | 82 (98) |
| **Anxiety disorder** | |
| Yes | 14 (17) |
| No | 70 (83) |
| **Psychosis** | |
| Yes | 1 (1) |
| No | 83 (99) |
| **Time in clinical treatment (months)** [Median (IQR)] | 36 (11.5-84) |
| **Time in the specific ED programme (months)** [Median (IQR)] | 18 (8-48) |
| **Baseline HADS-A** [Mean (SD)] | 11.71 (4.40) |
| **Baseline HADS-D** [Mean (SD)] | 8.43 (5.07) |
| **Mean change in HADS-A** [Mean (SD)]* | -1.42 (3.57) |
| **Mean change in HADS-D** [Mean (SD)]** | -1.16 (3.98) |

441**N (%)**: frequencies (percentage). **Mean [Lamers et al. 2011]**: Mean (standard deviation).
442**HADS-A:** Hospital Anxiety and Depression Scale, anxiety subscale; **HADS-D:** Hospital Anxiety and
443Depression Scale, depression subscale.
444**Mean change:** positive mean value means an improvement

445[*] $p < 0.001$ for the comparison between the baseline and one year follow-up of caregivers' HADS-A/D and
446patients' HADS- A score values . Non parametric sign test was used.

447[**] $p = 0.02$ for the comparison between the baseline and one year follow-up of patients' HADS-D score values.
448Non parametric sign test was used.

449**Restrictive**: anorexia nervosa-restrictive + bulimia nervosa-not purgative + eating disorder not otherwise
450specified (EDNOS)-restrictive.

451**Purgative**: anorexia nervosa-purgative + bulimia nervosa-purgative + eating disorder not otherwise specified
452(EDNOS)-purgative and binge.

**Table 2**. Univariate analysis of the influence of *caregiver variables at baseline and one year follow-up*.

| | Baseline scales | | | | Mean change scales after one year follow-up | | | |
| | HADS-A | | HADS-D | | HADS-A | | HADS-D | |
| | Mean (SD) | p-value | Mean (SD) | p-value | Mean (SD) | p-value | Mean (SD) | p-value |
|---|---|---|---|---|---|---|---|---|
| **Age of caregiver**[*] | -0.09 | 0.26 | 0.07 | 0.40 | -0.14 | 0.10 | 0.06 | 0.51 |
| **Relationship of caregiver to ED patient** | | < 0.001 | | < 0.001 | | 0.75 | | 0.18 |
| Mother | 10.07 (4.18) | | 7.28 (4.21) | | 1.69 (3.20) | | 0.86 (2.48) | |
| Father | 6.32 (3.26) | | 4.26 (2.66) | | 0.77 (2.79) | | 0.19 (2.72) | |
| Partner | 8.25 (4.16) | | 6.19 (4.35) | | 1.44 (2.83) | | 0.19 (2.37) | |
| Others (sibling and child) | 11 (4.64) | | 5.77 (4.82) | | 2.08 (4.82) | | 0.08 (2.10) | |
| **Educational level** | | 0.27 | | 0.15 | | 0.91 | | 0.16 |
| Uneducated/primary school | 9.28 (4.74) | | 6.52 (4.29) | | 1.57 (3.58) | | 0.57 (3.58) | |
| Secondary school | 9.07 (3.65) | | 6.36 (3.81) | | 0.99 (2.78) | | -0.27 (2.44) | |
| University studies | 7.88 (4.17) | | 5.16 (3.89) | | 1.35 (2.99) | | 0.43 (2.31) | |
| **Contact hours** | | 0.40 | | 0.08 | | 0.13 | | 0.52 |
| ≤ 32 | 8.29 (4.25) | | 5.29 (3.64) | | 1.79 (3.47) | | 0.46 (2.39) | |
| > 32 | 8.96 (4.31) | | 6.55 (4.29) | | 0.98 (2.94) | | 0.11 (2.52) | |
| **Sought help from a mental health professional** | | 0.0005 | | 0.001 | | 0.53 | | 0.65 |
| No | 7.87 (3.67) | | 5.28 (0.29) | | 1.29 (2.87) | | 0.29 (2.52) | |
| Yes | 10.86 (5.04) | | 7.85 (0.58) | | 1.66 (3.94) | | 0.58 (2.58) | |
| **Baseline HADS-A** | | | | < 0.001 | | < 0.001 | | |
| ≤7: no anxiety | - | | 3.46 (2.36) | | 0.20 (1.70) | | - | |
| 8-10: possible case of anxiety | - | | 6.58 (3.08) | | 1.70 (3.28) | | - | |
| ≥ 11: presence of clinical anxiety | - | | 9.30 (4.15) | | 2.87 (3.69) | | - | |
| **Baseline HADS-D** | | < 0.001 | | | | | | 0.004 |
| ≤7: no depression | 6.85 (3.16) | | - | | - | | -0.13 (2.52) | |
| 8-10: possible case of depression | 11.55 (2.91) | | - | | - | | 1.56 (2.36) | |
| ≥ 11: presence of clinical depression | 14.88 (3.62) | | - | | - | | 1.29 (2.05) | |

**ED**: Eating Disorder. **HADS-A:** Hospital Anxiety Depression Scale questionnaire, Anxiety subscale. **HADS-D:** Hospital Anxiety Depression Scale questionnaire, Depression subscale. **Mean (SD):** Mean (standard deviation).

[*]Pearson's correlation coefficient.

A positive value in the mean change of HADS-A,/D scale is considered as a decrease in the respective scale.

**Table 3**. Univariate analysis of the influence of *patient variables at baseline and one year follow-up*.

| | *Baseline scales* | | | | *Mean change scales after one year follow-up* | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| | HADS-A | | HADS-D | | HADS-A | | HADS-D | |
| | Beta (s.e.) | p-value | Beta (s.e.) | p-value | Beta (s.e.) | p-value | Beta (s.e.) | p-value |
| **Suicidal intention** | | | | | | | | |
| Yes | 1.83 (1.02) | 0.08 | 2.85 (0.99) | 0.005 | -1.23 (0.55) | 0.16 | 0.59 (0.68) | 0.39 |
| No | Reference | | Reference | | Reference | | Reference | |
| **Drug addiction** | | | | | | | | |
| Yes | 5.96 (3.12) | 0.06 | 6.99 (2.94) | 0.02 | 2.20 (2.34) | 0.35 | 1.32 (1.85) | 0.48 |
| No | Reference | | Reference | | Reference | | Reference | |
| **Psychosis** | | | | | | | | |
| Yes | 4.63 (3.28) | 0.16 | 1.88 (3.42) | 0.58 | 0.36 (2.54) | 0.89 | 0.29 (2.01) | 0.88 |
| No | Reference | | Reference | | Reference | | Reference | |
| **Baseline HADS-D** | | | | | | | | |
| ≤7: no depression | Reference | | NA | | Reference | | Reference | |
| 8-10: possible case of depression | 1.33 (0.98) | 0.18 | NA | | 1.17 (0.84) | 0.17 | 1.42 (0.65) | 0.03 |
| ≥ 11: presence of clinical depression | 1.38 (0.91) | 0.14 | NA | | -0.31 (0.77) | 0.69 | -0.41 (0.59) | 0.49 |
| **Time in clinical treatment (months)**[*] | 0.004 (0.006) | 0.55 | -0.01 (0.006) | 0.10 | -0.008 (0.005) | 0.11 | 0.002 (0.004) | 0.65 |
| **Time in the specific ED programme (months)**[*] | 0.007 (0.01) | 0.47 | 0.02 (0.01) | 0.08 | -0.01 (0.008) | 0.20 | -0.0001 (0.006) | 0.99 |
| **Type of compensating behaviour** | | | | | | | | |
| Restrictive | -0.62 (0.78) | 0.43 | -0.92 (0.79) | 0.25 | 1.07 (0.67) | 0.12 | 0.62 (0.53) | 0.24 |
| Purgative | Reference | | Reference | | Reference | | Reference | |

**ED**: Eating Disorder. **HADS-A:** Hospital Anxiety Depression Scale questionnaire, Anxiety subscale. **HADS-D:** Hospital Anxiety Depression Scale questionnaire, Depression subscale. **Restrictive**: anorexia nervosa-restrictive + bulimia nervosa-not purgative + eating disorder not otherwise specified (EDNOS)-restrictive. **Purgative**: anorexia nervosa-purgative + bulimia nervosa-purgative + eating disorder not otherwise specified (EDNOS)-purgative and binge. **NA:** not available. **Reference**:  Reference group.
**Beta (s.e.):** Beta and standard error estimates obtained in the univariate models.

[*]For a 1-month increment in the variable.

A positive value in the mean change of HADS-A,/D scale is considered as a decrease in the respective scale. Hierarchical models have been used for the performance of these univariate analyses.

**Table 4**. _Multivariable analysis_ of patient and caregiver variables that affect _caregivers baseline HADS anxiety and depression scales_

| | HADS-A | | HADS-D | |
|---|---|---|---|---|
| | **Beta (s.e.)** | **p-value** | **Beta (s.e.)** | **p-value** |
| **Intercept** | 7.26 (0.52) | < 0.001 | 4.72 (0.67) | < 0.001 |
| _Caregiver variables_ | | | | |
| **Relationship of caregiver to ED patient** | | | | |
| Mother | Reference | | Reference | |
| Father | -1.72 (0.67) | 0.01 | -0.66 (0.65) | 0.32 |
| Partner | -1.54 (0.84) | 0.07 | -0.55 (0.89) | 0.54 |
| Others (sibling and child) | 1.15 (0.85) | 0.18 | -1.99 (0.81) | 0.02 |
| **Educational level** | | | | |
| Uneducated/primary school | - | | Reference | |
| Secondary school | - | | 0.28 (0.73) | 0.70 |
| University studies | - | | -1.41 (0.65) | 0.03 |
| **Baseline HADS-A** | | | | |
| ≤7: no anxiety | - | | Reference | |
| 8-10: possible case of anxiety | - | | 2.01 (0.74) | 0.01 |
| ≥ 11: presence of clinical anxiety | - | | 4.67 (0.68) | < 0.001 |
| **Baseline HADS-D** | | | | |
| ≤7: no depression | Reference | | - | |
| 8-10: possible case of depression | 5.08 (0.72) | < 0.001 | - | |
| ≥11: presence of clinical depression | 6.62 (0.83) | < 0.001 | - | |
| _Patient variables_ | | | | |
| **Suicidal intention** | | | | |
| Yes | - | | 2.65 (0.82) | 0.002 |
| No | - | | Reference | |
| **Drug addiction** | | | | |
| Yes | 4.71 (2.29) | 0.04 | - | |
| No | Reference | | - | |
| **ICC** | 0.04 | | 0.22 | |

Hierarchical models have been used for the performance of the multivariate analyses, where father as caregivers, without pharmacological treatment, baseline HADS-A or HADS-D ≤7 and whose patients without addiction to alcohol and drugs and without suicidal intents.

**Beta (s.e.):** Beta and standard error estimates obtained in the multivariable models. **Reference**: Reference group. **-** : not entered in the final multivariable model. **ICC**: Intraclass correlation coefficient. It was estimated by dividing patient variance by the total sample (patients + caregivers variance). A small coefficient would indicate that patients and caregivers must be independent. **HADS-A:** Hospital Anxiety Depression Scale questionnaire, Anxiety subscale. **HADS-D:** Hospital Anxiety Depression Scale questionnaire, Depression subscale.

Table 5. *Multivariable analysis* of patient and caregiver variables that affect the *mean change in caregivers HADS anxiety and depression scales after one year follow-up*.

| | Mean change HADS-A | | Mean change HADS-D | |
|---|---|---|---|---|
| | Beta (s.e.) | p-value | Beta (s.e.) | p-value |
| **Intercept** | -0.743 (0.58) | 0.20 | -1.29 (0563) | 0.02 |
| *Caregiver variables* | | | | |
| **Baseline HADS-A** | | | | |
| ≤7: no anxiety | Reference | | - | |
| 8-10: possible case of anxiety | 1.66 (0.75) | 0.03 | - | |
| ≥ 11: presence of clinical anxiety | 2.97 (0.64) | < 0.001 | - | |
| **Baseline HADS-D** | | | | |
| ≤7: no depression | - | | Reference | |
| 8-10: possible case of depression | - | | 2.30 (0.53) | <0.001 |
| ≥11: presence of clinical depression | - | | 1.75 (0.63) | 0.01 |
| **Educational level** | | | | |
| Uneducated/primary school | - | | Reference | |
| Secondary school | - | | -1.12 (0.56) | 0.05 |
| University studies | - | | 0.13 (0.49) | 0.79 |
| *Patient variables* | | | | |
| **Baseline HADS-D** | | | | |
| ≤7: no depression | - | | Reference | |
| 8-10: possible case of depression | - | | 1.77 (0.63) | 0.008 |
| ≥ 11: presence of clinical depression | - | | -0.30 (0.55) | 0.58 |
| **Type of compensating behaviour** | | | | |
| Restrictive | 1.25 (0.61) | 0.048 | 1.09 | 0.03 |
| Purgative | Reference | | Reference | |
| **ICC** | 0.15 | | 0.20 | |

Hierarchical models have been used for the performance of the multivariate analyses, where caregivers with baseline HADS-A or HADS-D ≤7, and whose patients without anxiety disorder and drugs and purgative clinical diagnosis.

A positive value in the mean change of HADS-A,/D scale is considered as a decrease in the respective scale.

**Beta (s.e.):** Beta and standard error estimates obtained in the multivariable models. Reference: **Reference group**. **-**: not entered in the final multivariable model. **ICC**: Intraclass correlation coefficient. It was estimated by dividing patient variance by the total sample (patients + caregivers variance). A small coefficient would indicate that patients and caregivers must be independent.

**HADS-A:** Hospital Anxiety Depression Scale questionnaire, Anxiety subscale. **HADS-D:** Hospital Anxiety Depression Scale questionnaire, Depression subscale.

**Restrictive**: anorexia nervosa-restrictive + bulimia nervosa-not purgative + eating disorder not otherwise specified (EDNOS)-restrictive.

**Purgative**: anorexia nervosa-purgative + bulimia nervosa-purgative + eating disorder not otherwise specified (EDNOS)-purgative and binge.