



FACULDADE DE MEDICINA
UNIVERSIDADE DO PORTO

MESTRADO INTEGRADO EM MEDICINA

2014/2015

Teresa Isabel Fernandes Sá
Management and Treatment of Anorexia
Nervosa: a retrospective cohort study

março, 2015

FMUP



FACULDADE DE MEDICINA
UNIVERSIDADE DO PORTO

Teresa Isabel Fernandes Sá
Management and Treatment of Anorexia
Nervosa: a retrospective cohort study

Mestrado Integrado em Medicina

Área: PSQUIATRIA E SAÚDE MENTAL

Trabalho efetuado sob a Orientação de:

Dr^a Isabel Brandão

Trabalho organizado de acordo com as normas da revista:

Eating and Weight Disorders - Studies on Anorexia,

Bulimia and Obesity

março, 2015

FMUP

Eu, Teresa Isabel Fernandes Sá, abaixo assinado, nº mecanográfico 200904816, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro ter atuado com absoluta integridade na elaboração deste projeto de opção.

Neste sentido, confirmo que **NÃO** incorri em plágio (ato pelo qual um indivíduo, mesmo por omissão, assume a autoria de um determinado trabalho intelectual, ou partes dele). Mais declaro que todas as frases que retirei de trabalhos anteriores pertencentes a outros autores, foram referenciadas, ou redigidas com novas palavras, tendo colocado, neste caso, a citação da fonte bibliográfica.

Faculdade de Medicina da Universidade do Porto, 23/ 03/ 2015

Assinatura conforme cartão de identificação:

Teresa Isabel Fernandes Sá

NOME

Teresa Isabel Fernandes Sá

CARTÃO DE CIDADÃO

E-MAIL

TELEFONE OU TELEMÓVEL

12526053

Mimed09272@med.up.pt

964535366

NÚMERO DE ESTUDANTE

DATA DE CONCLUSÃO

200904816

março 2015

DESIGNAÇÃO DA ÁREA DO PROJECTO

Psiquiatria e Saúde Mental

TÍTULO DISSERTAÇÃO

Management and Treatment of Anorexia Nervosa: a retrospective cohort study

ORIENTADOR

Dr.ª Isabel Brandão

COORIENTADOR (se aplicável)

É autorizada a reprodução integral desta Dissertação para efeitos de investigação e de divulgação pedagógica, em programas e projectos coordenados pela FMUP.

Faculdade de Medicina da Universidade do Porto, 23/ 03/ 2015

Assinatura conforme cartão de identificação: Teresa Isabel Fernandes Sá

*À meu pai,
a quem devo o meu gosto pela leitura e a procura inesgotável pelo saber.*

*À minha mãe, irmã e irmão,
por tudo.*

À minha avó, Palmira.

Original article

Management and Treatment of Anorexia Nervosa: a retrospective cohort study

Teresa Sá¹, Isabel Brandão², Patrícia Nunes³, Filipa Soares³, Joana Rebelo³, António Roma-Torres³

¹*Faculty of Medicine, University of Porto, Portugal*

²*Department of Psychiatry and Mental Health of São João Hospital Center, Faculty of Medicine, University of Porto, Portugal*

³*Department of Psychiatry and Mental Health of São João Hospital Center, Porto, Portugal*

Corresponding author:

Teresa Sá

Faculdade de Medicina da Universidade do Porto,
Departamento de Psiquiatria e Saúde Mental,
Alameda Professor Doutor Hernâni Monteiro,
4200-319 Porto, Portugal

e-mail: teresa.isabel.sa@gmail.com

Abstract

Purpose: The main aims of the present study were to present an Anorexia Nervosa (AN) treatment program offered in a major university hospital in Portugal, and to determine the influence of body mass index (BMI) at admission, on outcome. Our hypothesis is that patients with higher severity, based on current BMI, may have worst prognosis with poorest outcome.

Methods: The sample included data from case records of 121 patients seen consecutively for the first time at our center, between 2008 and 2012. So we performed a retrospective cohort study which included data collected at admission and at 2 follow-up years.

Results: From the initially selected patients, 54.6% completed treatment and follow-up, 0.8% died from medical complications and 44.6% dropout. After 2 years of follow-up, those admitted at severe/extreme level had an insignificant higher BMI than those in the mild/moderate level. Outcomes between groups were similar and no differences in relation to the other possible prognostic factors were seen.

Conclusions: This paper presents a particular model of care for AN patients that in general leads to relevant weight gains and decrease psychopathology. According to our research, BMI at the start of an outpatient treatment does not seem to be an important consideration in outcome or prognostic features. Future research must be done to evaluate how different factors may influence the treatment outcome.

Keywords: anorexia nervosa; treatment outcome; BMI; level of severity

Introduction

Eating disorders (EDs) are severe and complex psychiatric pathologies [1,2] which are often chronic and most frequently affect young people [2]. They usually cause physical, behavioral, emotional and cognitive symptoms [1] with high health risk to patients and a challenge to professionals care for [3].

The richness and complexity that Anorexia Nervosa (AN) displays as psychopathological model such as the increased incidence in recent years justifies the interest of the scientific community. Epidemiological data in Portugal are quite scarce, but a recent study suggests similar data to other western countries [4] with the mean prevalence rate of 0.3% in young female [5], and a 10:1 female to male ratio [6]. AN is characterized by persistent restriction of energy intake to maintain a normal body weight for age and height, a pathological fear of gaining weight or becoming fat, and disturbance in self-perception of weight or body shape [6]. Patients with AN may restrict total food intake and extensively exercising matching the restricting subtype (AN-R), or binge/purge typically by self-inducing vomiting using laxatives or diuretics, in binge/purging type (AN-BP) [7]. Adolescence or young adulthood are the most common periods of onset, which is often associated with a stressful life event [6]. The course and outcome of AN are highly variable and comorbid disorders are common [6].

There is no strong evidence-based treatment for AN therefore it is expected that there will be disagreement about what the most appropriate program [8]. It is a complex process partly reflected by the often long and severe course of the disorder, with a large group of patients with long-lasting problems, recurrent treatment attempts, dropouts and a chronic course [9]. However, there seems to be a common treatment basis which typically involves a multidisciplinary approach [10,11]. The São João Hospital Center (CHSJ) is a university hospital which is a reference place for EDs treatment, including patients from all over the north of Portugal. Our therapeutic program is guided by understanding the importance of promoting autonomy and self-initiative of patients. It consists of several phases shaping a global design with the ultimate goal of promoting a gradual change in eating behavior and subjective experience of patients (Roma Torres, 1986). In general, evidence on treatment approaches is very limited, so that more knowledge about predictors of treatment response and resistance are needed [9]. Several studies have argued that premature identification of prognostic features has significant implications in therapeutic strategy and treatment outcome, which could lead to more targeted and effective interventions [12,13,1]. There are also conflicting reports about the role played by body mass index (BMI) at the start of either outpatient or inpatient treatment as a predictor of outcome [14].

The main aims of the present study were to introduce and explore the CHSJ AN program and to determine the influence of BMI at admission, on the outcome. Our hypothesis is that patients with higher severity level, which can be based on current BMI

[9], extreme ($\text{BMI} < 15 \text{ Kg/m}^2$) and severe ($\text{BMI} 15\text{-}15.99 \text{ Kg/m}^2$), may have worst prognosis with poorest outcome, higher dropout rates, inpatient treatment and comorbidities, than the moderate ($\text{BMI} 16\text{-}16.99 \text{ Kg/m}^2$) or mild ($\text{BMI} \geq 17 \text{ Kg/m}^2$) level.

Material and methods

Participants

The sample included 121 patients (114 female, 7 male) seen consecutively for the first time at CHSJ in Oporto and evaluated by clinical psychiatric interview, done by 2 experienced senior psychiatrists. The newest edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) includes significant changes within EDs section [6,10]. This revised diagnostic criteria resulted in significant changes on EDs prevalence, particularly an increase in AN diagnosis, because of the exclusion of the amenorrhea criterion [15]. Accordingly, all diagnoses were reviewed and patients who met the latest AN criteria, at the time of his first appointment, were admitted. Participants were referred to our unit by general practitioners or psychiatrists. Some of them came by themselves or following family advice. Eleven patients were directly transferred from the emergency room to the psychiatric ward, 7 of them were immediately admitted to inpatient care due to severe electrolyte imbalance, physiological instability, very low BMI ($<13 \text{ Kg/m}^2$) or suicide risk. For study inclusion, participants were required to be at least 13 years old and met full DSM-5 criteria for AN. Exclusion criteria were pregnancy or lactation patients.

This study was approved by the ethics committee of CHSJ.

Data collection

Data were collected from the case records of patients admitted from January 2008 until December 2012. Patients were followed at least for 2 years. So we performed a retrospective cohort study which included demographic variables (gender, marital status, occupation), anthropometric variables (weight and BMI), illness duration, family history of EDs or psychiatric disturb, psychiatric comorbidity, inpatient treatment, suicide attempts/ideation, psychopharmacological treatment and treatment outcome.

Although not a decisive marker for healthy weight in adolescents, BMI was used as a general measure of health [16]. For the study, we considered weight measured at the time of interview and 2 years later. For adolescents, BMI-for-age percentile was determined using the Centers for Disease Control and Prevention (CDC) BMI percentile calculator. The CDC has applied a BMI-for-age below the 5th percentile suggesting underweight for children and teenagers. Nevertheless a BMI above this reference may be considered to be significantly underweight, due to the disability to maintain their expected growth rate [6]. At our sample, 7 patients are on 5-10th percentile and 2 on the 10-25th, with all other adolescents below the 5th percentile. Defining whether weight is less than that minimally expected we considered individual body shape, weight and growth history.

Treatment program

All patients were treated following the regular practice on Department of Psychiatry and Mental Health of CHSJ, which has been developing his own model of care (Roma Torres, 1986). The guiding principle of our treatment is the consideration of AN as

a self-autonomy conflict with three aspects that should be emphasized: motivation to change focused on respect for autonomy and responsibility, eating is not a choice, it is a mandatory requirement of nature; nutritional rehabilitation, with minimal diet establishment notably concentrated on control health rather than disease; family approach involving the relatives but leaving the patient in charge of feeding behavior learned throughout the treatment.

Our program is guided by an interdisciplinary team with psychological, medical, nutritional and nursing care. Psychiatric appointments were regularly done. Psychotherapy is established once refeeding process begins and should last for all stages of treatment. It must be centered primarily on eating behavior and weight gain, without neglecting emotions. The cognitive behavioral approach aims to change behavior in the first place, respecting the individual, its own autonomy, emotion and thought. Attempts to promote weight gain might create tension and anxiety therefore we offer a non hypercaloric diet (1700 Kcal/day into 6 meals) to obtain a minimum weight compatible with health. We do not want to stop patient from being thin but simply accept his own option without endangering his health. Our intervention emphasizes nutritional reeducation instead of total weight recovery, admitting temporary persistence of low weight since there are clear improvements in other health indicators. Finally, the importance of family involvement in patient's recovery is well recognized [17] but sometimes family structure can operate in an invasive way, restricting the individual's autonomy and independence [18]. From the beginning of therapy, feeding is something that is in charge of patient, obviously according to his current age, without family interference and with medical support when difficulties persist. This ensures the principle of autonomy, encouraging the patient to take an active role in therapy and reassuring the fear of losing control over food, which is a characteristic psychological mechanism of anorexic behavior.

Inpatient care is justified when fatal outcome is to be feared and it is a decision that has to be taken according to medical, psychopathological and family reasons. It consists in a therapeutic plan with patient and family which may imply the complete absence of any visits or contact with relatives, restarted by the therapist's decision, depending on the progress made, according to previous contingent steps scheduled.

The use of pharmacotherapy has been disappointing therefore it is not considered in the treatment strategy however, it may be helpful especially because of comorbid disorders.

Outcome of patients

There is no agreement on what is considered a positive or negative outcome. In this study we considered the following treatment outcome: good outcome (full remission or partial remission), poor outcome, death or dropout. Our definition of remission is according to the DSM-5 criteria for AN [6]. Full remission was considered as total absence of AN symptoms, that had been previously met. Patients were defined in partial

remission if they no longer filled the criterion of low body weight but, either intense resistance to weight gain and/or disturbances in self-perception criteria, were still met. Poor outcome consists on the persistence of all DSM-5 clinical manifestations of AN despite the treatment. Defining dropout is another important issue. We considered that had left treatment or follow-up on its own initiative, earlier than 2 years, meet the requirements. We also distinguished early from later dropout, when patients left during the first month or only attended to three sessions or less.

Statistical analysis

Descriptive statistics were used to characterize the sample. Continuous variables were expressed as mean \pm standard deviation (SD) and categorical variables as frequency and percentages. Since not all data were normally distributed, both parametric (Student's t-test for independent and paired samples) and non-parametric (Mann-Whitney) tests were used for continuous data, and Chi square test for categorical data. All tests were two tailed and $p < 0.05$ was established. All statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows, version 22.0(Chicago, IL).

Results

Overall sample description

This study's population included 121 patients (114 female, 7 male) with a mean age of 21.4 ± 7.3 years and a mean BMI of 15.77 ± 1.64 Kg/m², at admission. Most participants are single (88.4%) and living with both parents (82.6%). More than a half were students (66.9%), 51 (42.1%) of them were attending high school and 47 (38.8%) were graduating or had already completed a college degree. Some patients (12.4%) had family history of psychiatric disorders, mainly depressive disorders (6.6%) and 9.1% had close relatives (mother, sister, aunt or grandmother) diagnosed with AN.

At admission, participants had median illness duration of 2.0 years (mean 3.63 ± 4.94 years, range 0.5–25 years) and the mean age of onset was 17.67 ± 4.72 years. Forty seven (38.8%) never tried to find medical advice whereas 28 (23.1%) had attended to psychiatric appointment before. A comorbid psychiatric diagnosis was present in 65 (53.7%) of them, most commonly a mood disorder/dysthymia (25.6%, n=31), or anxiety disorder (9.9%, n=12). Two or more comorbid psychiatric diagnosis were present in 8 (6.6%). There were 57 patients (54.7%) taking psychopharmacological medications such as antidepressants (14.9%, n=18), anxiolytics (4.1%, n=5) or even multiple medications concurrently (25.6%, n=31).

Clinical characteristics considering AN subtypes

Within the sample, 41.3% of patients had the AN-BP subtype and 58.7% had the AN-R subtype. Cross-over between subtypes is common [19], however only 8 subjects (6.6%) had their diagnosis changed throughout our study, which may be due to the relative short follow-up period. Three AN-R subtype patients developed AN-BP and 5 with AN turn into bulimia nervosa (BN). Table 1 presents the patient's characteristics at admission according to AN subtype. AN-R participants are more frequently single and still studying. The mean illness duration was significantly higher for AN-BP 4.6 ± 5.4 years, than for AN-R 2.9 ± 4.5 years. An evaluation between subtypes did not show any difference on gender, educational status or BMI at admission. However, considering severity based on BMI groups [6] (mild/moderate ≥ 16 and severe/extreme < 16), in AN-R subtype there were significantly more cases of severe/extreme illness and in AN-BP predominate mild/moderate disease ($p=0.027$). Comorbidities are much more frequent in AN-BP ($p=0.012$) with significantly more personality disorders than in the AN-R group (12% vs. 2.8%) and at least once in their lifetime, 22% of AN-BP patients had tried or thought in suicide versus 1.4% of AN-R patients ($p<0.001$). At the end of follow-up there were no significant differences in BMI, remission or dropout rates among AN subtypes. Comorbidities were still more frequent in AN-BP group (69% vs 34.2%, $p=0.051$), such as pharmacotherapy (75.9% AN-BP vs 34.2% AN-R, $p=0.01$).

At the end of follow-up

From the 121 patients, 66 (54.6%) completed treatment and follow-up, 1 (0.8%) died exactly at the end of follow-up from medical complications of the disease, and 54 were lost at 2-year follow-up, which means a 44.6% dropout rate. The rate of early dropout was 9.1% corresponding to 11 patients. Analysis of treatment results revealed that 36 patients (29.8%) achieved good outcomes, 15 of them (12.4%) met partial remission criteria and 21 (17.4%) reached full remission, while 30 (24.8%) had poor outcome. Thirty six individuals (29.8%) had received inpatient treatment, and lifetime suicidal ideation/attempt was reported by 9.9% of cases. The mean BMI values for patients who remained in the study had significantly risen from $15.73 \pm 1.60 \text{ Kg/m}^2$ to $18.16 \pm 3.88 \text{ Kg/m}^2$ ($p < 0.001$), as well as the weight (41.6 Kg to 48.0 Kg, $p < 0.001$), with 4 subjects meeting overweight World Health Organization (WHO) criteria ($\text{BMI} \geq 25$) and 1 meeting obesity class I ($\text{BMI} 30.0\text{--}34.9$).

Follow-up data between level of severity groups (DSM-5)

Table 2 summarizes results of follow-up according to illness level of severity. After 2 years, those admitted at $\text{BMI} < 16$ (severe/extreme level, $14.53 \pm 1.08 \text{ Kg/m}^2$) had an insignificant higher BMI than those in the $\text{BMI} \geq 16$ (mild/moderate level, $17.18 \pm 0.64 \text{ Kg/m}^2$), with $18.31 \pm 4.84 \text{ Kg/m}^2$ vs $18.00 \pm 2.36 \text{ Kg/m}^2$, $p = 0.750$, respectively. Outcomes between groups were similar, with 44.4% of subjects at severe/extreme level achieved remission (partial or full) compared to 46.7% of those who met mild/moderate level ($p = 1.000$), while 55.6% and 53.3% remained under treatment with poor outcome, for each group respectively. Dropout rate reached 39.3% ($n = 24$) in patients admitted at $\text{BMI} < 16$ and 50% ($n = 30$) of those admitted at $\text{BMI} \geq 16$, however differences did not fulfill statistical significance ($p = 0.275$). Likewise, there was no difference in comorbid psychiatric diagnosis ($p = 0.840$), neither nonspecific pharmacotherapy ($p = 1.000$) between both groups, at the end of study. Finally, inpatient treatment admissions in severe/extreme patients had significantly higher rate (41% vs 18.3%, $p = 0.009$), as well as effective number of admissions 0.62 ± 0.86 vs 0.27 ± 0.63 , $p = 0.006$, than mild/moderate cohort.

Discussion

The primary aim of the current research was to present the AN treatment program offered in a major university hospital in Portugal. The goal of CHSJ program is not only to achieve a healthy weight but specially to provide skills to promote a full sustained recovery. The main innovative feature of our therapeutic strategy is to ensure the principle of autonomy while working in three essential aspects: motivation to change, nutritional education with non hypercaloric diet and family therapy encouraging the patient to take an active role on its own treatment. Accordingly, and in line with previous guidelines [17,20], we believe that outpatient programs should be privileged, allowing individuals to maintain their routines and social life, applying the newly learned skills in their usual environment [21].

The problem of very high rate of treatment dropout has been long recognized [21]. Data from standard clinical practice reveal that dropout rates have remained so over the course of time, regardless of country or treatment modality, reaching 50% or more for both outpatient and inpatient samples [11,22]. In our program we had 44.6% dropout rate, 9.9% of which matching early dropouts, a favorable value compared to previous estimates among outpatient eating disorder services of 13–32% [23]. We do not know exactly the major reasons for premature treatment termination of our patients but resistance to treatment and reluctance to recovery have been long recognized as key-problems in the treatment, as well as illness duration, treatment type and family variables [11].

The discussion of outcome findings between studies was limited by the lack of consistent definitions of outcome criteria [24]. After 2 years, 29.8% of our initial patients had good outcomes, 17.4% of them had recovered no longer fulfilling any of diagnostic criteria of AN and 12.4% achieved partial remission, having a normal body weight but maintaining some psychological symptoms, which is compatible with literature remission rates that ranged from 13.2% to 40.5%, depending on the definition used [25]. This wide range rates could be explained, not only by the absence of commonly accepted outcome criteria, but also by different study methodologies or DSM diagnostic criteria along the years [24]. On the other hand, reports on long-term course of AN in adults suggested that recovery increased with longer follow-up periods [26] reaching almost half of the surviving patients, while about 20% remained chronically ill [13], so that we considered 2 years a short term follow-up to achieve conclusive and successful global AN outcome. Nevertheless, our treatment proved to be effective in increasing BMI from $15.73 \pm 1.60 \text{ Kg/m}^2$ to $18.16 \pm 3.88 \text{ Kg/m}^2$. It also led to relevant weight gains, from initial $41.6 \pm 5.8 \text{ Kg}$ to final $48.0 \pm 11.0 \text{ Kg}$ which means an increment of about 6.5 Kg. Both high final SD were probably due to outliers as result of overweight patients at the end of study.

There are many factors which have been frequently associated with poor short and long-term outcome for AN [12]. One of the most reported prognostic indicators in

literature is body weight at the start of treatment [12-14]. Therefore, an additional purpose of the present study was to explore the impact of BMI at referral to our unit, on outcome and patient prognosis. Contrary to previous findings that have related a lower BMI on admission to outpatient treatment with a lower rate [14] or even a higher rate of treatment completion [13,14], there were no significant differences in dropout rates among the current study groups. The findings of our research do not also suggest a direct relationship between initial BMI and outpatient treatment outcome. However, the two groups apparently responded differently to treatment, with a much higher increment on BMI reached by the severe/extreme group (initial $14.53 \pm 1.08 \text{ Kg/m}^2$ vs final $18.31 \pm 4.84 \text{ Kg/m}^2$, $p < 0.001$) comparing to the mild/moderate group (initial $17.18 \pm 0.64 \text{ Kg/m}^2$ vs final $18.00 \pm 2.36 \text{ Kg/m}^2$, $p = 0.056$). So low body weight at the start of treatment is one factor that has been suggested to strongly influence treatment outcome [14,27] but according to our study it does not seem to clearly affect outpatient approaches. As in another studies, our patients presented different psychiatric comorbidities remaining unclear if these are secondary to the AN or if they simply shared etiological framework [21]. Again, by the end of follow-up, no differences with respect to comorbidity or suicide attempts/ideation rates along the study were noted between severity groups, which seem to be more related to the type of AN present. On the other hand and as expected, there was a significantly higher rate of hospitalizations in the severe/extreme group, with almost a half of the patients to be hospitalized at least once.

According to our research, BMI at the start of an outpatient treatment does not seem to be an important consideration in outcome or prognostic features. These findings oppose other studies that had considered that BMI at admission to inpatient units seems to select severe patients who are less compliant with treatment, which leads to dropout and contributes to poor prognosis [27,28].

The present study has several limitations that should be considered. It was a retrospective medical chart review whereby the information collected was dependent exclusively on case records. Since standardized measures were not used, our data are mainly clinical which limits the generalizability of our findings. On the other hand, the recruitment of subjects from a single center with a large catchment area, treated by the same experienced therapists, can be considered a strength of this study. For future research, it could be useful to examine data on the long-term outcome of patients and readmission rates over the course of a longer follow-up period.

In conclusion, this paper presents a particular model of care for AN patients based on outpatient treatment that in general leads to relevant weight gains and decrease psychopathology during the therapeutic approach and up to 2 years of follow-up. The lack of consensual definition of remission creates difficulties when comparing outcome data from treatment modalities and centers, so we emphasize the need for uniform adoption of remission definitions [25]. Furthermore, the high incidence of dropout as in the case of the majority of literature [29,11], largely decreases the power and generalization of the results.

Clearly, many factors are related to the recovery process of whatever treatment and BMI should only be a guide. In order to fully understand it, future research must be done to evaluate how differences in areas like motivation to change, therapeutic alliance or treatment acceptance, considered the biggest challenges in the management of patients with AN [30], may influence the treatment outcome.

Conflict of Interest

All authors report no conflict of interest.

Table 1 Sample characteristics at admission according to type of anorexia nervosa

	AN-R	AN-BP	p-value
	n = 71	n = 50	
Demographic %			
Gender			
Female	91.5	98.0	0.237
Male	8.5	2.0	
Marital status			
Single	94.4	80.0	0.042*
Married	4.2	18.0	
Common law marriage	1.4	2.0	
Educational status			
University	36.6	43.8	0.336
High school	46.5	37.5	
Junior high school (9th grade)	15.5	14.6	
Preparatory education (6th grade)	1.4	0.0	
Primary education (4th grade)	0.0	4.2	
Occupation			
Employee	15.5	24.0	0.007*
Unemployed	7.0	24.0	
Student	77.5	52.0	
Clinical History			
Age at onset	16.9 ± 4.3	18.8 ± 5.1	0.044*
Age at first appointment	19.8 ± 5.9	23.6 ± 8.4	0.001*
Illness duration	2.9 ± 4.5	4.6 ± 5.4	0.021*
BMI at admission	15.50 ± 1.7	16.08 ± 1.5	0.051
Severity based on BMI (DSM-5)%			
Mild/Moderate	40.8	60.0	0.027*
Severe/Extreme	59.2	38.0	
Comorbidities at admission %			
No	59.2	28.0	0.010*
Yes	40.8	72.0	
Substance abuse	0.0	2.0	
Mood disorder or dysthymia	19.7	34.0	
Anxiety disorder	7.0	14.0	
Obsessive compulsive disorder	5.6	2.0	
Personality disorder	2.8	12.0	
2 or more	5.6	8.0	
Pharmacotherapy at admission %			
No	66.2	34.0	0.010*
Yes	33.8	66.0	
Anxiolytics	2.8	6.0	
Antidepressants	12.7	18.0	
Hypnotics	1.4	0.0	
Antipsychotics	1.4	2.0	
2 or more	15.5	40.0	
Inpatient admissions %			
Yes	25.4	36.0	0.230
No	74.6	64.0	

* Significant at $p < 0.05$

Data are present as mean ± standard deviations or percentages and are based on available data only (i.e. missing or unknown data were excluded)

Table 2 Follow-up data according to illness level of severity

	Mild/moderate (BMI \geq 16)	Severe/extreme (BMI<16)	p-value
Clinical History at 2 years of follow-up			
	n= 30	n= 37	
BMI	18.00 \pm 2.36	18.31 \pm 4.84	0.736
Comorbidities %			
No	53.3	48.6	0.840
Yes	46.7	51.4	
Mood disorder/dysthymia	16.7	21.6	
Anxiety disorder	6.7	8.1	
Personality disorder	10.0	2.7	
2 or more	13.3	18.9	
Pharmacotherapy %			
No	46.7	48.6	1.000
Yes	53.3	51.4	
Antidepressants	16.7	10.8	
2 or more	36.7	40.5	
Remission			
Good outcome (Partial/Full)	46.7	44.4	1.000
Poor outcome	53.3	55.6	
Other possible prognostic factors			
	n= 60	n= 61	
Inpatient admissions %			
No	81.7	59.0	0.009*
Yes	18.3	41.0	
Number of inpatient admissions	0.27 \pm 0.63	0.62 \pm 0.86	0.006*
Suicide attempts/ideation %			
No	86.7	93.4	0.240
Yes	13.3	6.6	
Outcomes %			
	n= 60	n= 61	
Full remission	16.7	19.7	
Partial remission	6.7	6.6	
Poor outcome	26.7	32.8	
Death	0.0	1.6	
Dropout	38.3	32.8	
Early dropout	11.7	6.6	
Dropout			
Yes	50.0	39.3	0.275
No	50.0	60.7	

* Significant at p< 0.05

Data are present as mean \pm standard deviations or percentages and are based on available data only (i.e. missing or unknown data were excluded)

References

1. Segura-Garcia C, Chiodo D, Sinopoli F, De Fazio P (2013) Temperamental factors predict long-term modifications of eating disorders after treatment. *BMC psychiatry* 13:288. doi:10.1186/1471-244X-13-288
2. Soler J, Soriano J, Ferraz L, Grasa E, Carmona C, Portella MJ, Seto V, Alvarez E, Perez V (2013) Direct experience and the course of eating disorders in patients on partial hospitalization: a pilot study. *European eating disorders review : the journal of the Eating Disorders Association* 21 (5):399-404. doi:10.1002/erv.2224
3. Goldstein M, Peters L, Baillie A, McVeagh P, Minshall G, Fitzjames D (2011) The effectiveness of a day program for the treatment of adolescent anorexia nervosa. *The International journal of eating disorders* 44 (1):29-38. doi:10.1002/eat.20789
4. Machado PP (2003) Eating Disorders in Portugal: Contribution of possible cultural correlates. *Eating Disorders in Mediterranean area: An exploration in transcultural psychology*:111-119
5. Hoek HW, van Hoeken D (2003) Review of the prevalence and incidence of eating disorders. *International Journal of Eating Disorders*
6. American Psychiatric Association (APA) (2013) *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition*. APA Press 329-354, Washington, DC
7. Jackson CW, Cates M, Lorenz R (2010) Pharmacotherapy of eating disorders. *Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition* 25 (2):143-159. doi:10.1177/0884533610362239
8. Lask B (2009) A comprehensive treatment service must include developmental, systemic and collaborative components. *World psychiatry : official journal of the World Psychiatric Association* 8 (3):158-159
9. Mander J, Teufel M, Keifenheim K, Zipfel S, Giel KE (2013) Stages of change, treatment outcome and therapeutic alliance in adult inpatients with chronic anorexia nervosa. *BMC psychiatry* 13:111. doi:10.1186/1471-244X-13-111
10. Berg KC, Wonderlich SA (2013) Emerging psychological treatments in the field of eating disorders. *Current psychiatry reports* 15 (11):407. doi:10.1007/s11920-013-0407-y
11. Rodriguez-Cano T, Beato-Fernandez L, Moreno LR, Vaz Leal FJ (2012) Influence of attitudes towards change and self-directedness on dropout in eating disorders: a 2-year follow-up study. *European eating disorders review : the journal of the Eating Disorders Association* 20 (3):e123-128. doi:10.1002/erv.2157
12. Howard WT, Evans KK, Quintero-Howard CV, Bowers WA, Andersen AE (1999) Predictors of success or failure of transition to day hospital treatment for inpatients with anorexia nervosa. *The American journal of psychiatry* 156 (11):1697-1702. doi:10.1176/ajp.156.11.1697
13. Mewes R, Tagay S, Senf W (2008) Weight curves as predictors of short-term outcome in anorexia nervosa inpatients. *European eating disorders review : the journal of the Eating Disorders Association* 16 (1):37-43. doi:10.1002/erv.807
14. Sly R, Bamford B (2011) Why are we waiting? The relationship between low admission weight and end of treatment weight outcomes. *European eating disorders*

review : the journal of the Eating Disorders Association 19 (5):407-410.
doi:10.1002/erv.1061

15. Keel PK, Brown TA, Holm-Denoma J, Bodell LP (2011) Comparison of DSM-IV versus proposed DSM-5 diagnostic criteria for eating disorders: reduction of eating disorder not otherwise specified and validity. *The International journal of eating disorders* 44 (6):553-560. doi:10.1002/eat.20892

16. Turrell SL, Peterson-Badali M, Katzman DK (2011) Consent to treatment in adolescents with anorexia nervosa. *The International journal of eating disorders* 44 (8):703-707. doi:10.1002/eat.20870

17. National Institute for Clinical Excellence (NICE) (2004) *Eating disorders - Core interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders*. London

18. Espindola CR, Blay SL (2013) Long term remission of anorexia nervosa: factors involved in the outcome of female patients. *PloS one* 8 (2):e56275. doi:10.1371/journal.pone.0056275

19. Trent SA, Moreira ME, Colwell CB, Mehler PS (2013) ED management of patients with eating disorders. *The American journal of emergency medicine* 31 (5):859-865. doi:10.1016/j.ajem.2013.02.035

20. Wilson GT, Shafran R (2005) Eating disorders guidelines from NICE. *Lancet* 365 (9453):79-81. doi:10.1016/S0140-6736(04)17669-1

21. Garcia-Garcia E, Rocha-Velis I, Vazquez-Velazquez V, Kaufer-Horwitz M, Reynoso R, Mendez JP (2013) Experience of an eating disorders out-patient program in an internal medicine hospital. *Eating and weight disorders : EWD* 18 (4):429-435. doi:10.1007/s40519-013-0073-4

22. Sly R, Morgan JF, Mountford VA, Lacey JH (2013) Predicting premature termination of hospitalised treatment for anorexia nervosa: the roles of therapeutic alliance, motivation, and behaviour change. *Eating behaviors* 14 (2):119-123. doi:10.1016/j.eatbeh.2013.01.007

23. Watson HJ, Fursland A, Byrne S (2013) Treatment engagement in eating disorders: who exits before treatment? *The International journal of eating disorders* 46 (6):553-559. doi:10.1002/eat.22085

24. Larranaga A, Fluiters E, Docet MF, Fernandez Sastre JL, Garcia-Mayor RV (2013) Comparative study of cognitive-behavioral psychotherapy and nutritional support in patients with different types of eating disorders. *Medicina clinica*. doi:10.1016/j.medcli.2013.05.042

25. Ackard DM, Richter SA, Egan AM, Cronmeyer CL (2014) What does remission tell us about women with eating disorders? Investigating applications of various remission definitions and their associations with quality of life. *Journal of psychosomatic research* 76 (1):12-18. doi:10.1016/j.jpsychores.2013.10.002

26. Salbach-Andrae H, Schneider N, Seifert K, Pfeiffer E, Lenz K, Lehmkuhl U, Korte A (2009) Short-term outcome of anorexia nervosa in adolescents after inpatient treatment: a prospective study. *European child & adolescent psychiatry* 18 (11):701-704. doi:10.1007/s00787-009-0024-9

27. Huas C, Godart N, Foulon C, Pham-Scottez A, Divac S, Fedorowicz V, Peyracque E, Dardennes R, Falissard B, Rouillon F (2011) Predictors of dropout from inpatient treatment for anorexia nervosa: data from a large French sample. *Psychiatry research* 185 (3):421-426. doi:10.1016/j.psychres.2009.12.004
28. Halmi KA, Agras WS, Crow S, Mitchell J, Wilson GT, Bryson SW, Kraemer HC (2005) Predictors of treatment acceptance and completion in anorexia nervosa: implications for future study designs. *Archives of general psychiatry* 62 (7):776-781. doi:10.1001/archpsyc.62.7.776
29. Dejong H, Broadbent H, Schmidt U (2012) A systematic review of dropout from treatment in outpatients with anorexia nervosa. *The International journal of eating disorders* 45 (5):635-647. doi:10.1002/eat.20956
30. Zipfel S, Wild B, Groß G, Friederich H-C, Teufel M, Schellberg D, Giel KE, de Zwaan M, Dinkel A, Herpertz S, Burgmer M, Löwe B, Tagay S, von Wietersheim J, Zeeck A, Schade-Brittinger C, Schauenburg H, Herzog W (2014) Focal psychodynamic therapy, cognitive behaviour therapy, and optimised treatment as usual in outpatients with anorexia nervosa (ANTOP study): randomised controlled trial. *The Lancet* 383 (9912):127-137. doi:10.1016/s0140-6736(13)61746-8

ANEXOS

Eating and Weight Disorders - Studies on Anorexia, Bulimia and Obesity

Editor-in-Chief: Massimo **Cuzzolaro**

Co-Editor: Lorenzo Maria **Donini**

ISSN: 1590-1262 (electronic version)

Instructions for Authors

TYPES OF PAPERS

- **Review Articles**

Overview papers on selected topics. Review articles are in general invited by the editors but suggestions by interested individuals may also be considered. Prospective authors should submit a formal and detailed proposal to the Editor, indicating the title and a brief outline of the content.

Manuscripts should provide an up-to-date and authoritative review and synthesis of existing literature. Review Articles should not exceed 7.500 words including an abstract of no more than 250 words, references, tables and figures. Keywords are requested.
- **Original Articles**

Accounts of research or clinical practice that should be based on original rather than confirmatory data. Typically, Original Articles will present new data derived from a sizable series of subjects or patients. Original Articles should not exceed 5.000 words including an abstract of no more than 250 words, references, tables and figures. Keywords are requested.
- **Brief Reports**

Short papers including data from preliminary studies, new approaches to clinical practice, replication studies that are primarily based on negative or confirmatory data. Brief Reports should not exceed 2.000 words, 1-2 illustrations and up to 3 references are permitted. Brief Reports should not have an abstract nor keywords.
- **Case Reports**

Short papers that illustrate either a previously unrecognized disorder or a new aspect of a known condition. Ethical and legal considerations require the protection of a patient's anonymity. Case Reports should not exceed 2.000 words including 3 references, 1-2 tables and figures. Case Reports should not have an abstract nor keywords.
- **Correspondence**

Brief letters (maximum of 500 words including references; no tables or figures, no abstract, no keywords) providing pertinent comments on published articles will be considered and the authors concerned will be given a right to reply. Letters raising problems of general interest will also be considered.
- **Letter to the Editor**

Letters to the editors are published in the Correspondence section. They must not exceed 1000 words, 3 references and 3 authors. They should not have an abstract. They should be addressed to the Editor-in-Chief. Submitted letters will be subject to shortening and editorial revision.
- **Editorial**

The journal publishes also Editorials. Authors who wish to submit an editorial should first consult the journal's Editor-in-Chief.
- **Clinical Symposia** from invited contributors are published occasionally.

MANUSCRIPT SUBMISSION

Manuscript Submission

Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

Permissions

Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Any material received without such evidence will be assumed to originate from the authors.

Online Submission

Authors should submit their manuscripts online. Electronic submission substantially reduces the editorial processing and reviewing times and shortens overall publication times. Please follow the hyperlink “Submit online” on the right and upload all of your manuscript files following the instructions given on the screen.

LANGUAGE

Manuscripts that are accepted for publication will be checked by our copyeditors for spelling and formal style. This may not be sufficient if English is not your native language and substantial editing would be required. In that case, you may want to ask a native speaker to help you or arrange for your manuscript to be checked by a professional language editor prior to submission. A clear and concise language will help editors and reviewers concentrate on the scientific content of your paper and thus smooth the peer review process.

The following editing service provides language editing for scientific articles in medicine, biomedical and life sciences, chemistry, physics, engineering, business/economics, and humanities

- Edanz Editing Global

Please contact the editing service directly to make arrangements for editing and payment.

Use of an editing service is neither a requirement nor a guarantee of acceptance for publication.

TITLE PAGE

Title Page

The title page should include:

- The name(s) of the author(s)
- A concise and informative title
- The affiliation(s) and address(es) of the author(s)
- The e-mail address, telephone and fax numbers of the corresponding author

Abstract

Please provide a structured abstract of 150 to 250 words which should be divided into the following sections:

- Purpose (stating the main purposes and research question)
- Methods
- Results

- Conclusions

Keywords

Please provide 4 to 6 keywords which can be used for indexing purposes.

TEXT

Text Formatting

Manuscripts should be submitted in Word.

- Use a normal, plain font (e.g., 10-point Times Roman) for text.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.
- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Manuscripts with mathematical content can also be submitted in LaTeX.

LaTeX macro package (zip, 182 kB)

Headings

Please use no more than three levels of displayed headings.

Abbreviations

Abbreviations should be defined at first mention and used consistently thereafter.

Footnotes

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

Acknowledgments

Acknowledgments of people, grants, funds, etc. should be placed in a separate section before the reference list. The names of funding organizations should be written in full.

REFERENCES

Citation

Reference citations in the text should be identified by numbers in square brackets. Some examples:

1. Negotiation research spans many disciplines [3].

2. This result was later contradicted by Becker and Seligman [5].

3. This effect has been widely studied [1-3, 7].

Reference list

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text. Do not use footnotes or endnotes as a substitute for a reference list.

The entries in the list should be numbered consecutively.

- Journal article

Gamelin FX, Baquet G, Berthoin S, Thevenet D, Nourry C, Nottin S, Bosquet L (2009) Effect of high intensity intermittent training on heart rate variability in prepubescent children. *Eur J Appl Physiol* 105:731-738. doi: 10.1007/s00421-008-0955-8

Ideally, the names of all authors should be provided, but the usage of “et al” in long author lists will also be accepted:

Smith J, Jones M Jr, Houghton L et al (1999) Future of health insurance. *N Engl J Med* 965:325–329

- Article by DOI

Slifka MK, Whitton JL (2000) Clinical implications of dysregulated cytokine production. *J Mol Med.* doi:10.1007/s001090000086

- Book

South J, Blass B (2001) *The future of modern genomics*. Blackwell, London

- Book chapter

Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) *The rise of modern genomics*, 3rd edn. Wiley, New York, pp 230-257

- Online document

Cartwright J (2007) Big stars have weather too. IOP Publishing PhysicsWeb. <http://physicsweb.org/articles/news/11/6/16/1>. Accessed 26 June 2007

- Dissertation

Trent JW (1975) *Experimental acute renal failure*. Dissertation, University of California

Always use the standard abbreviation of a journal’s name according to the ISSN List of Title Word Abbreviations, see

- ISSN.org LTWA

If you are unsure, please use the full journal title.

For authors using EndNote, Springer provides an output style that supports the formatting of in-text citations and reference list.

- EndNote style (zip, 2 kB)

Authors preparing their manuscript in LaTeX can use the bibtex file `spbasic.bst` which is included in Springer’s LaTeX macro package.

TABLES

- All tables are to be numbered using Arabic numerals.

- Tables should always be cited in text in consecutive numerical order.

- For each table, please supply a table caption (title) explaining the components of the table.

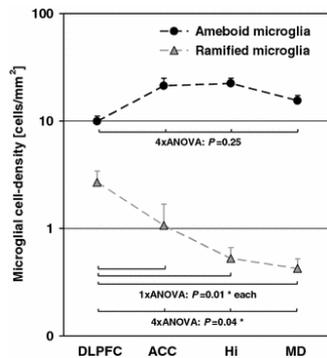
- Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.
- Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

ARTWORK AND ILLUSTRATIONS GUIDELINES

Electronic Figure Submission

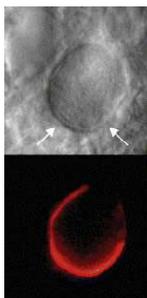
- Supply all figures electronically.
- Indicate what graphics program was used to create the artwork.
- For vector graphics, the preferred format is EPS; for halftones, please use TIFF format. MSOffice files are also acceptable.
- Vector graphics containing fonts must have the fonts embedded in the files.
- Name your figure files with "Fig" and the figure number, e.g., Fig1.eps.

Line Art



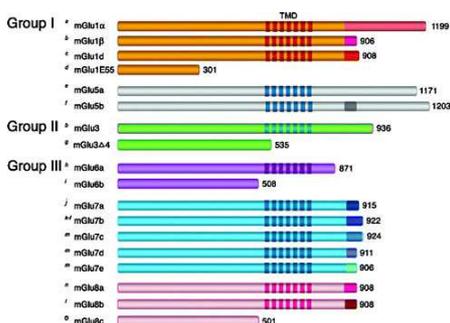
- Definition: Black and white graphic with no shading.
- Do not use faint lines and/or lettering and check that all lines and lettering within the figures are legible at final size.
- All lines should be at least 0.1 mm (0.3 pt) wide.
- Scanned line drawings and line drawings in bitmap format should have a minimum resolution of 1200 dpi.
- Vector graphics containing fonts must have the fonts embedded in the files.

Halftone Art



- Definition: Photographs, drawings, or paintings with fine shading, etc.
- If any magnification is used in the photographs, indicate this by using scale bars within the figures themselves.
- Halftones should have a minimum resolution of 300 dpi.

Combination Art



- Definition: a combination of halftone and line art, e.g., halftones containing line drawing, extensive lettering, color diagrams, etc.
- Combination artwork should have a minimum resolution of 600 dpi.

Color Art

- Color art is free of charge for online publication.
- If black and white will be shown in the print version, make sure that the main information will still be visible. Many colors are not distinguishable from one another when converted to black and white. A simple way to check this is to make a xerographic copy to see if the necessary distinctions between the different colors are still apparent.
- If the figures will be printed in black and white, do not refer to color in the captions.
- Color illustrations should be submitted as RGB (8 bits per channel).

Figure Lettering

- To add lettering, it is best to use Helvetica or Arial (sans serif fonts).
- Keep lettering consistently sized throughout your final-sized artwork, usually about 2–3 mm (8–12 pt).
- Variance of type size within an illustration should be minimal, e.g., do not use 8-pt type on an axis and 20-pt type for the axis label.
- Avoid effects such as shading, outline letters, etc.
- Do not include titles or captions within your illustrations.

Figure Numbering

- All figures are to be numbered using Arabic numerals.
- Figures should always be cited in text in consecutive numerical order.
- Figure parts should be denoted by lowercase letters (a, b, c, etc.).
- If an appendix appears in your article and it contains one or more figures, continue the consecutive numbering of the main text. Do not number the appendix figures, "A1, A2, A3, etc." Figures in online appendices (Electronic Supplementary Material) should, however, be numbered separately.

Figure Captions

- Each figure should have a concise caption describing accurately what the figure depicts. Include the captions in the text file of the manuscript, not in the figure file.
- Figure captions begin with the term **Fig.** in bold type, followed by the figure number, also in bold type.
- No punctuation is to be included after the number, nor is any punctuation to be placed at the end of the caption.
- Identify all elements found in the figure in the figure caption; and use boxes, circles, etc., as coordinate points in graphs.
- Identify previously published material by giving the original source in the form of a reference citation at the end of the figure caption.

Figure Placement and Size

- When preparing your figures, size figures to fit in the column width.
- For most journals the figures should be 39 mm, 84 mm, 129 mm, or 174 mm wide and not higher than 234 mm.
- For books and book-sized journals, the figures should be 80 mm or 122 mm wide and not higher than 198 mm.

Permissions

If you include figures that have already been published elsewhere, you must obtain permission from the copyright owner(s) for both the print and online format. Please be aware that some publishers do not grant electronic rights for free and that Springer will not be able to refund any costs that may have occurred to receive these permissions. In such cases, material from other sources should be used.

Accessibility

In order to give people of all abilities and disabilities access to the content of your figures, please make sure that

- All figures have descriptive captions (blind users could then use a text-to-speech software or a text-to-Braille hardware)
- Patterns are used instead of or in addition to colors for conveying information (colorblind users would then be able to distinguish the visual elements)
- Any figure lettering has a contrast ratio of at least 4.5:1

ELECTRONIC SUPPLEMENTARY MATERIAL

Springer accepts electronic multimedia files (animations, movies, audio, etc.) and other supplementary files to be published online along with an article or a book chapter. This feature can add dimension to the author's article, as certain information cannot be printed or is more convenient in electronic form.

Submission

- Supply all supplementary material in standard file formats.
- Please include in each file the following information: article title, journal name, author names; affiliation and e-mail address of the corresponding author.
- To accommodate user downloads, please keep in mind that larger-sized files may require very long download times and that some users may experience other problems during downloading.

Audio, Video, and Animations

- Always use MPEG-1 (.mpg) format.

Text and Presentations

- Submit your material in PDF format; .doc or .ppt files are not suitable for long-term viability.
- A collection of figures may also be combined in a PDF file.

Spreadsheets

- Spreadsheets should be converted to PDF if no interaction with the data is intended.
- If the readers should be encouraged to make their own calculations, spreadsheets should be submitted as .xls files (MS Excel).

Specialized Formats

- Specialized format such as .pdb (chemical), .vrl (VRML), .nb (Mathematica notebook), and .tex can also be supplied.

Collecting Multiple Files

- It is possible to collect multiple files in a .zip or .gz file.

Numbering

- If supplying any supplementary material, the text must make specific mention of the material as a citation, similar to that of figures and tables.
- Refer to the supplementary files as "Online Resource", e.g., "... as shown in the animation (Online Resource 3)", "... additional data are given in Online Resource 4".
- Name the files consecutively, e.g. "ESM_3.mpg", "ESM_4.pdf".

Captions

- For each supplementary material, please supply a concise caption describing the content of the file.

Processing of supplementary files

- Electronic supplementary material will be published as received from the author without any conversion, editing, or reformatting.

Accessibility

In order to give people of all abilities and disabilities access to the content of your supplementary files, please make sure that

- The manuscript contains a descriptive caption for each supplementary material
- Video files do not contain anything that flashes more than three times per second (so that users prone to seizures caused by such effects are not put at risk)

AFTER ACCEPTANCE

Upon acceptance of your article you will receive a link to the special Author Query Application at Springer's web page where you can sign the Copyright Transfer Statement online and indicate whether you wish to order OpenChoice, offprints, or printing of figures in color.

Once the Author Query Application has been completed, your article will be processed and you will receive the proofs.

Open Choice

In addition to the normal publication process (whereby an article is submitted to the journal and access to that article is granted to customers who have purchased a subscription), Springer provides an alternative publishing option: Springer Open Choice. A Springer Open Choice article receives all the benefits of a regular subscription-based article, but in addition is made available publicly through Springer's online platform SpringerLink.

- Springer Open Choice

Copyright transfer

Authors will be asked to transfer copyright of the article to the Publisher (or grant the Publisher exclusive publication and dissemination rights). This will ensure the widest possible protection and dissemination of information under copyright laws.

Open Choice articles do not require transfer of copyright as the copyright remains with the author. In opting for open access, the author(s) agree to publish the article under the Creative Commons Attribution License.

Offprints

Offprints can be ordered by the corresponding author.

Color illustrations

Online publication of color illustrations is free of charge. For color in the print version, authors will be expected to make a contribution towards the extra costs.

Proof reading

The purpose of the proof is to check for typesetting or conversion errors and the completeness and accuracy of the text, tables and figures. Substantial changes in content, e.g., new results, corrected values, title and authorship, are not allowed without the approval of the Editor.

After online publication, further changes can only be made in the form of an Erratum, which will be hyperlinked to the article.

Online First

The article will be published online after receipt of the corrected proofs. This is the official first publication citable with the DOI. After release of the printed version, the paper can also be cited by issue and page numbers.

INTEGRITY OF RESEARCH AND REPORTING

Springer's statements on human and animal rights, conflict of interest and informed consent can be found at:

- [Statement on Human and Animal Rights](#)
- [Conflict of Interest](#)
- [Informed Consent](#)