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HEALTH PSYCHOLOGY | REVIEW ARTICLE

Predictors of distress in amyotrophic lateral sclerosis: A systematic review

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Abstract: Objective: Understanding of the factors that predict emotional distress in Amyotrophic Lateral Sclerosis (ALS) is limited. This systematic review critically appraised and synthesised the findings of longitudinal studies into baseline clinical, demographic, social, and psychological predictors of later emotional distress in people with ALS.

Methods: Medline, PsycINFO and CINAHL Plus were searched for relevant published literature from their inception until April 2018. Inclusion criteria were prospective or retrospective peer-reviewed studies, written in English, assessing baseline clinical, demographic, psychological or social predictors of emotional distress or psychological quality of life ≥ 1 month later in adults with ALS.

Results: Eight studies were included in this review. Demographic or clinical factors were investigated in seven studies, social factors in two studies, and psychological factors in three studies. There was scarce evidence that any baseline demographic or clinical factors predicted emotional distress. The only factor that consistently predicted emotional distress across multiple studies was lower social support. Mindfulness and psychological quality of life each predicted emotional distress but were only evaluated in single studies.

Conclusions: Further research is needed to investigate the mechanisms underlying emotional distress, particularly modifiable factors such as psychological factors, to reduce emotional distress in people with ALS.

Subjects: Behavioral Sciences; Psychological Science; Mental Health

ABOUT THE AUTHORS

The authors who completed this study are part of a larger group of clinical academics who aim to develop a better understanding of the psychological mechanisms that underpin emotional distress in people with physical health conditions. Presently, the research group is examining the role of metacognitive processes involved in anxiety and depression in people with cancer, cardiac conditions, and neurological conditions (amyotrophic lateral sclerosis, epilepsy and multiple sclerosis). The research group is beginning to evaluate the potential efficacy of metacognitive therapy (MCT) delivered in both individual and group based formats. The initial results of these treatment studies are very promising, and it is hoped that MCT will improve upon the effectiveness of currently available interventions.

PUBLIC INTEREST STATEMENT

People with Amyotrophic Lateral Sclerosis (ALS) often experience anxiety and depression but we do not have a good understanding of the causes of anxiety and depression. The aim of this research was to look at past research to try and find out if there are common demographic, social, or psychological factors linked to anxiety and depression in people with ALS. This review study found that only lower levels of social support was linked to anxiety and depression. It was very clear that many more studies are needed to understand the psychological factors which can be changed to help reduce anxiety and depression in people with ALS.

Keywords: Motor neurone disease; amyotrophic lateral sclerosis; psychology; distress; predictors; social; demographic; clinical

1. Introduction

Amyotrophic Lateral Sclerosis (ALS) is a progressive neurological disorder leading to muscular atrophy in limb, bulbar, and respiratory muscles (Hobson, Harwood, McDermott, & Shaw, 2016). ALS has a prevalence rate of 7 per 100,000, with an average age of onset of 65 years old (Talbot, 2009). The life expectancy for approximately 50% of people with ALS (PwALS) is three years from symptom onset (Ilse et al., 2015), although 5–10% survive for 10 years or more (Chiò et al., 2013). Effective medical treatments for ALS do not currently exist. As such, interventions tend to focus on managing symptoms and improving quality of life (QoL) (Van Den Berg et al., 2005).

One way to improve QoL in PwALS is to manage emotional distress (National Institute for Health and Care Excellence, 2016; Pagnini, Simmons, Corbo, & Molinari, 2012). Around 50% of PwALS experience clinically significant levels of emotional distress, commonly anxiety and/or depression (Ganzini, Silveira, & Johnston, 2002; Kübler, Winter, Ludolph, Hautzinger, & Birbaumer, 2005). Emotional distress in PwALS increases interest in hastened death (Ganzini, Johnston, McFarland, Tolle, & Lee, 1998), reduces QoL (Johnston et al., 1999), increases pain and fatigue (Felgoise et al., 2010), and reduces survival rates (McDonald, Wiedenfeld, Hillel, Carpenter, & Walter, 1994). However, emotional distress in PwALS remains poorly understood and there are no effective psychological or pharmacological treatments for emotional distress in this population (Gould et al., 2015).

The limited research on PwALS and emotional distress has primarily focused on quantifying its prevalence and identifying clinical correlates. However, contrary to the expectation that emotional distress will increase with disease progression, a consistent relationship between physical functioning and emotional distress does not exist (McLeod & Clarke, 2007), with growing evidence that emotional distress remains stable despite disease progression (Cupp et al., 2011; Ilse et al., 2015; Pagnini, Manzoni, Tagliaferri, & Gibbons, 2015). Cross-sectional studies have identified several psychosocial factors which are associated with emotional distress in PwALS, including lower levels of social support (Cupp et al., 2011; Matuz, Birbaumer, Hautzinger, & Kübler, 2010), social withdrawal (Gibbons et al., 2013), negative or critical illness perceptions (Miglioretti, Mazzini, Oggioni, Testa, & Monaco, 2008; Plahuta et al., 2002) and more time spent ruminating and/or worrying (Hecht et al., 2002). However, cross-sectional studies only point towards factors associated with emotional distress rather than being able to identify causal factors. For this, prospective research is needed, but prospective research identifying factors that predict emotional distress over time has not been synthesised. This systematic review therefore aims to critically appraise and synthesise the findings of longitudinal studies into baseline clinical, demographic, social, and psychological predictors of later emotional distress (distress occurring at least one month later) in PwALS.

2. Method

Methodology broadly followed the PRISMA statement for conducting and reporting systematic reviews (Moher, Liberati, Tetzlaff, & Altman, 2009). The review protocol can be found at www.crd.org.uk/prospéro (PROSPERO ID: CRD42017050036).

2.1. Search strategy

Medline, PsycINFO and CINAHL Plus were searched from their inception until November 2016 for relevant published literature. Searches combined synonyms for ALS with those for emotional distress and longitudinal studies (see Table 1). The search was limited to studies with adult participants written in English. Reference lists of included studies were examined and experts in the field were contacted to identify additional relevant studies. Searches were repeated in April 2018.

Table 1. Basic search terms

Connector	Search Terms	Search fields
	“Motor Neuron Disease” OR “Motor Neurone Disease” OR “Motor Neurone Diseases” OR “Motor Neuron Diseases” OR “Amyotrophic Lateral Sclerosis” OR “Progressive Bulbar Palsy” OR “Lou Gehrigs Disease” OR “Progressive Muscular Atrophy” OR “Primary Lateral Sclerosis”	All Fields
AND	“Depress*” OR “Anxiety” OR “Distress” OR “Worry” OR “Ruminat*” OR “Emotion*” OR “Psych*” OR “Mood” OR “Affect*” OR “Psychosocial” OR “Coping” OR “Adapt*” OR “Quality of life” OR “Adjustment” OR “Illness cognition*” OR “Fear*” OR “Belief*”	All Fields
AND NOT	“Paediatric*” OR “Child*” OR “infant*” OR “Adolescent*”	Abstract
AND NOT	“Gene*” OR “Mutation*”	Abstract
AND NOT	“Mice” OR “Mouse” OR “Rat*” OR “Animal*”	Abstract

2.2. Eligibility criteria

Studies were eligible for inclusion if they: (i) were longitudinal peer-reviewed studies which; (ii) reported data pertaining to the relationship between baseline clinical, demographic, psychological or social variables and; (iii) subsequent emotional distress or psychological QoL, assessed at least one month later using a validated measure or subscale; (iv) presented results for adults aged 18 years and over with a diagnosis of ALS; and (v) were written in English. Studies were excluded if they did not report bivariate or multivariate associations between predictor variables and dependent variables. The inclusion of only prospective studies was essential to the aims of the present study as we were interested only in clinical, demographic, psychological or social variables that had been investigated in previous studies as potential causal variables. The present study adopted the methodology previously used to investigating comparable predictive factors in cancer one year post diagnosis (Cook, Salmon, Hayes, Dunn, & Fisher, 2018).

2.3. Screening and selection

Following de-duplication, titles and abstracts of identified studies were screened according to the inclusion criteria. Studies that did not meet the eligibility criteria were excluded. Full-text copies of the remaining studies were then obtained and examined for relevance according to the same criteria. At both stages, screening was performed by RD with a random subset independently screened by a second reviewer (EB); disagreements were resolved by consensus.

2.4. Data extraction

Sample characteristics, emotional distress measures, psychosocial factors and covariates, statistical methods and results (including *r* values, beta coefficients or odds ratios and/or percentage variance explained) were extracted by RD using a standardised data extraction form and tabulated. Extracted data were cross-checked by EB and MGC; disagreements were resolved through discussion.

2.5. Risk of bias

The methodological quality of the included studies was independently assessed by RD and EB using a tool adapted from the Agency for Healthcare Research and Quality (Williams, Plassman, Burke, Holsinger, & Benjamin, 2010). This tool assesses risk of bias in nine areas, allowing studies to be compared across these dimensions. Discrepancies in reviewer ratings were resolved through discussion with a third reviewer (PF). In line with guidance from the Centre for Reviews and Dissemination (Centre for Reviews and Dissemination, 2009), no study was excluded based on the results of the risk of bias assessment; rather, risk of bias was considered when interpreting findings.

2.6. Data synthesis

A meta-analytic review was considered inappropriate due to the heterogeneity in time since diagnosis, predictors, and distress outcomes across the included studies. Therefore, data were

summarised narratively, with predictors of distress grouped into three broad categories (clinical and demographic, social, and psychological).

3. Results

The search identified 1,924 studies, leaving 1,499 studies after removing duplicates. Of these, 1,337 were excluded based on title and abstract. Full-text articles for the remaining 162 records were accessed, with 151 excluded, resulting in eight papers included in the systematic review (Bourke, Bullock, Williams, Shaw, & Gibson, 2003; Cupp et al., 2011; Goldstein, Atkins, Landau, Brown, & Leigh, 2006; Lyall et al., 2001; Matuz, Birbaumer, Hautzinger, & Kübler, 2015; Norquist, Jenkinson, Fitzpatrick, & Swash, 2003; Pagnini, Phillips, Bosma, Reece, & Langer, 2015; Roach, Averill, Segerstrom, & Kasarskis, 2009). No new studies were identified by the updated search. Figure 1 outlines the search results and article selection process (Moher et al., 2009).

Table 2 describes the characteristics of the eight included studies. Most studies ($n = 6$; 75%) were conducted in Europe, with the remaining two studies conducted in the USA. Mean sample ages ranged from 55 to 63 years; most participants were male. One study included only PwALS commencing non-invasive ventilation (NIV) with orthopnoea symptoms (Bourke et al., 2003),

Figure 1. Flow of studies through the review.

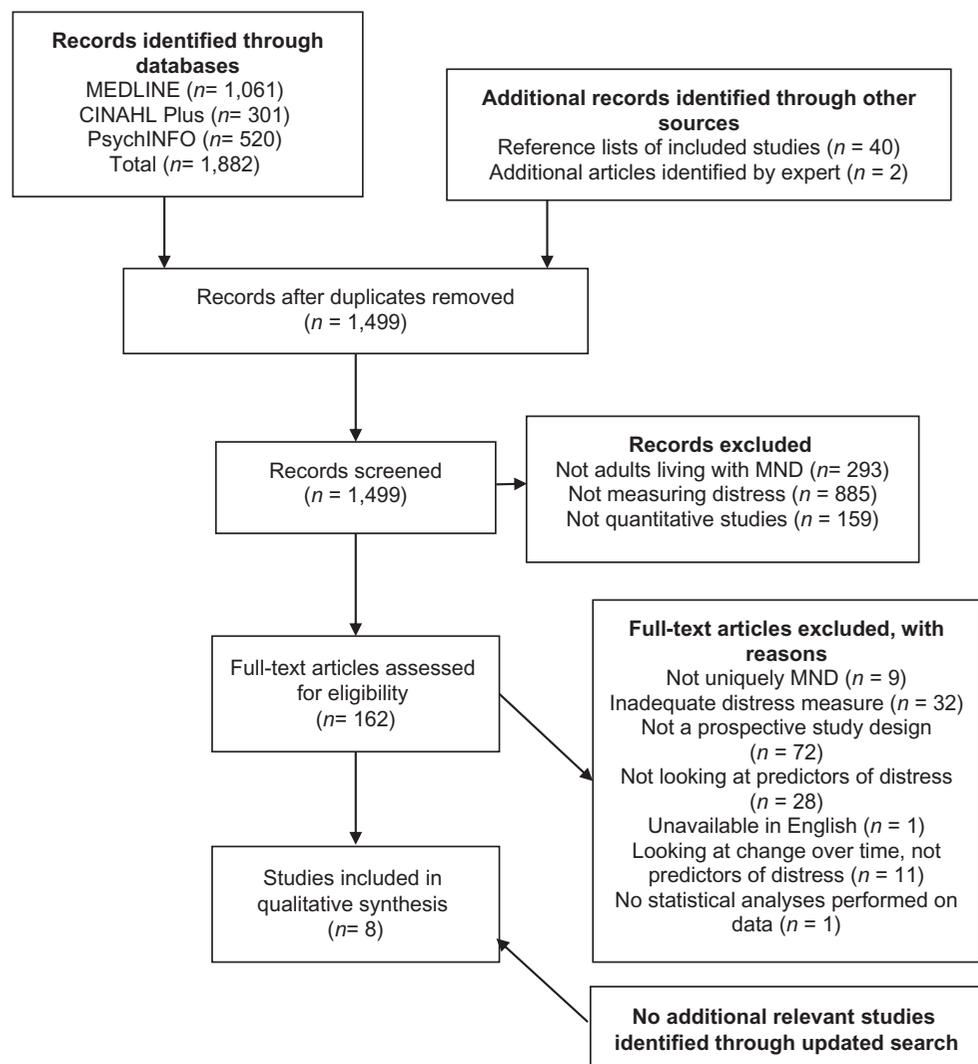


Table 2. Sample characteristics of included papers

Article	Baseline Characteristics										Attrition (%)	Country											
	Time since dx (months)	Time since onset (months)	Bulbar onset, n (%)	Female, n (%)	Age (years), mean (SD)	T1 n	T2 n	T3 n	T4 n	T5 n			T6 n	T7 n									
Bourke et al. (2003) ^a	< 3 = 15 (68.18) ^b > 3 (with RMW) = 7 (31.81) ^b	15.2 (9.9) ^b 54.0 (35.0) ^b	-	Recent dx: 5 (33.33) RMW: 2 (28.57)	57.8 (Bourke et al., 2003-74) ^c 59.3 (48-73) ^c	Time points variable according to when met criteria for NIV. Baseline = 22 T1 = 21 Met criteria = 17 Accepted trial = 15 Continued trial = 10	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	Baseline—Continuing NIV = 54.54	UK
Cupp et al., 2011	NR	37 (44) ^b	17 (23.61)	29 (40.28)	55 (Feigoise et al., 2010)	72	72	48	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	33.33	USA
Goldstein et al. (2006) ^d	9.24 (4.26) ^b	28.79 (17.21) ^b	14 (28.00)	9 (18.00)	63.14 (10.33)	50	32	26	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	48.00	UK
Lyal et al. (2001)	NR	NR	NR	NIV = 1 (6.25) C = 2 (18.18)	NIV = 61.3 (6.8) C = 61.2 (7.6)	16 11	16 11	10 6	7 4	4 4	3 NA	2 NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NIV = 87.5 C = 100	UK
Matuz et al. (2015)	NR	NR	2 (7.41)	12 (44.44)	55.3 (11.1)	27	22	19	16	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	40.75	Germany
Norquist et al. (2003)	1.29 years (1.77) ^b	NR	NR	387 (42.16)	59.97 (11.54)	918	439	123	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	86.66	Multi-country
Pagnini et al. (2015)	1-8 = 78 (40.1); 9-16 = 47 (24.1); 17-28 = 48 (24.6); ≥29 = 23 (11.7) ^e	NR	NR	81 (41.1)	58 (9.9)	197	102	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	48.22	Italy
Roach et al. (2009)	0.98 (0.68) ^f	NR	NR	20 (36.36)	58.4 (11.5)	55	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	USA

C = control group; Dx = diagnosis; NIV = non-invasive ventilation; NR = not reported; RMW = respiratory muscular weakness; SD = standard deviation; T1 = time 1; UK = United Kingdom; USA = United States of America; ^a = analysed othopnea group only; ^b = mean (standard deviation); ^c = median (range); ^d = diagnosed < 15 months ago in order to be eligible for study. Dx = diagnosis; ^e = n (%); ^f = years

while another study included only PwALS who has been diagnosed less than 15 months (Goldstein et al., 2006).

Several measures assessed emotional distress across the included studies. Five studies assessed psychological QoL using psychological subscales of existing QoL measures (Bourke et al., 2003; Cupp et al., 2011; Lyall et al., 2001; Norquist et al., 2003) (Roach et al., 2009), whilst two studies reported depression severity (Matuz et al., 2015; Pagnini et al., 2015). Two studies used emotional distress measures designed for PwALS (Cupp et al., 2011; Roach et al., 2009). Global emotional distress was the primary outcome in one study (Goldstein et al., 2006). Only one study reported the severity of anxiety and depression (Pagnini et al., 2015). No studies reported on anxiety alone. Table 3 illustrates the range of measures used to assess emotional distress.

Self-report measures were primarily used to assess clinical, demographic, social and psychological predictors. Clinical factors were also assessed using objective physical measurements, including forced vital capacity and muscle scores. Most studies analysed data using multiple regression, although there was considerable variation in the method and order of entry of predictors into models. One study used multi-level modelling (Roach et al., 2009), and another study utilised mixed-effects modelling (Pagnini et al., 2015) to analyse data.

3.1. Risk of bias

Risk of bias is presented in Table 4. Most studies selected participants appropriately, however, two studies lacked detail about how participants were recruited (Lyall et al., 2001; Roach et al., 2009). Many studies did not adequately describe the self-report questionnaires used, and measured emotional distress using subscales from QoL questionnaires rather than validated questionnaires of emotional distress. Similarly, physical functioning was not consistently assessed using validated questionnaires or clinician report, with studies often instead using individual items or subgroups of items from larger scales considering overall physical functioning. None of the studies justified sample size. One study (Roach et al., 2009) did not report attrition rates or number of participants at each time point, and only two studies (Bourke et al., 2003; Pagnini et al., 2015) adjusted for missing data. In five of the eight studies, follow-up periods were shorter than Williams et al.'s suggested 12-month period. Only four studies (Bourke et al., 2003; Norquist et al., 2003; Pagnini et al., 2015; Roach et al., 2009) controlled for potential confounding variables in the analyses, although each variable was reported in the descriptive statistics.

3.2. Demographic and clinical predictors

Table 5 displays predictors of outcome grouped by measure of emotional distress. As shown in Table 5, only one of the eight included studies did not report clinical or demographic predictors of emotional distress (Matuz et al., 2015).

Table 3. Glossary of distress measures (DVs) used in included papers

Measure	Abbreviation	Outcome assessed
ALS Depression Inventory	ADI-12	Depression
ALS Specific Quality of Life Instrument-Revised	ALSQoL-R	Quality of life, Negative emotion scale (NES)
Hospital Anxiety and Depression Scale	HADS	Depression (HADS-D, Anxiety (HADS-A), Distress (HADS-T)
Short Form-36	SF-36	Quality of life (Mental Health (MH), Mental component summary score (MCS)
The McGill Quality of Life Questionnaire	MQoL	Quality of life, psychological wellbeing domain (PWB)

Table 4. Risk of bias assessment of included papers using adapted tool from William et al. (2010)

Article	Unbiased selection of the cohort?	Sample size calculated?	Adequate description of the cohort?	Validated method for ascertaining distress?	Validated method for ascertaining other predictors?	Adequate follow-up period?	Missing data?	Analysis controls for confounders?	Analytic methods appropriate?
Goldstein et al., (2006)	Partially	Unclear	Partially	Partially	Partially	Partially	Yes	Yes	Unclear
Cupp et al., 2011	Yes	Unclear	Partially	Partially	Partially	Partially	Partially	Partially	Yes
Goldstein et al., (2006)	Partially	Unclear	Yes	Partially	Partially	Yes	Partially	Partially	Yes
Lyall et al. (2001)	Unclear	Unclear	Partially	Partially	Partially	Partially	Partially	Partially	Yes
Matuz et al. (2015)	Yes	Unclear	Yes	Yes	Partially	Yes	Partially	Partially	Yes
Norquist et al. (2003)	Yes	Unclear	Yes	Partially	Partially	No	No	Yes	Yes
Pagnini et al. (2015)	Partially	Unclear	Partially	Partially	Partially	No	Yes	Yes	Yes
Roach et al. (2009)	Unclear	Unclear	Partially	Yes	Yes	Yes	Yes	Yes	Yes

Table 5. Summary of study findings from included papers grouped by outcome (DV)

Article	Analyses	Follow-up duration (months)	RMW group only	Time since diagnosis controlled for	Dependent Variable (DV)	Multivariate analyses				Significant predictors ($p < .05$)
						Clinical/ demographic predictors	Social predictors	Psychological predictors		
DV—ANXIETY/DEPRESSION										
Matuz et al. (2015)	Multiple regression	3-6	N	N	ADI-12	-	BSSS (Perceived social support)	Cognitive appraisal (coping potential) MNDCS (emotion management coping, problem management coping, emotional avoidance coping)	$R^2 = 55\%$ Perceived social support ($\beta = -0.44$) Appraisal of coping potential ($\beta = -0.57$)	
Pagnini et al. (2015)	Mixed-effects models	4	N	N	HADS-A HADS-D	Age, gender, years of education, time since diagnosis	-	Mindfulness, MQoL	Mindfulness ($b = -0.12, t (187) = -6.83$) ^a Age ($b = -0.73, t (187) = -3.21$) ^a Mindfulness ($b = -0.14, t (187) = -8.20$) ^a	
DV—PSYCHOLOGICAL QUALITY OF LIFE										
Bourke et al. (2003)	Multiple regression	1	Y	N	SF-36 (MCS)	NIV, age, gender, NIV compliance, physical functioning (P ₁ max, P ₆ CO ₂ , limb and axial muscle scores, bulbar score)	-	-	NIV compliance (only p value reported)	

(Continued)

Table 5. (Continued)

Article	Analyses	Follow-up duration (months)	RMW group only	Time since diagnosis controlled for	Dependent Variable (DV)	Multivariate analyses					Significant predictors ($p < .05$)
						Clinical/ demographic predictors	Social predictors	Psychological predictors			
Cupp et al., 2011	Linear regression	3 (T2), 6 (T3)	N	N	ALSOQ-R (NES) fraction of baseline	Visit number, PEG antidepressant use, NIV, time between intervention and scoring, age, site of onset (NB/BU)	-	-	-	Antidepressant use, PEG (only p values reported)	
Lyall et al. (2001)	Repeated Measures ANOVA	1 wk, 1, 6, 9, 12, 15	B	N	SF-36 (MH)	NIV use	-	-	-	NS differences between groups; NIV use significantly increased psychological QoL from baseline to T2	
Norquist et al. (2003)	Stepwise regression	4 (T2), 8 (T3)	N	N	SF-36 (MCS)	Baseline physical functioning scores, age, gender, time since onset, time since diagnosis, baseline functional performance	-	SF-36 MCS baseline	-	T2 $R^2 = 49.8\%$, Age ($\beta = -.133$), MCS baseline ($\beta = 0.682$) T3 $R^2 = 53.6\%$, MCS baseline ($\beta = 0.735$)	

(Continued)

Table 5. (Continued)

Article	Analyses	Follow-up duration (months)	RMW group only	Time since diagnosis controlled for	Dependent Variable (DV)	Multivariate analyses					Significant predictors ($p < .05$)
						Clinical/demographic predictors	Social predictors	Psychological predictors			
Roach et al. (2009)	Multi-level modelling	6-30	N	Y	MQoL (PWB)	Time since diagnosis, gender, age	-	-	-	-	Gender (male) Y = -1.04 F (Hobson et al., 2016,61) = 3.99 $\eta = 0.06$
DV—EMOTIONAL DISTRESS											
Goldstein et al. (2006)	Linear regression	6 (T2), 12 (T3)	N	Y <15m	HADS-T	NR	Perceived social support	NR			T2: T1 negative social support ($R^2 = 13\%$, $t = 2.07$) T3: T1 negative social support ($R^2 = 27\%$, $t = 2.91$)

Note. ADI = ALS Depression Inventory; ALSQoL-R = ALS Specific Quality of Life Instrument-Revised; ANOVA = Analysis of Variance; B = Both; BU = bulbar onset; BSSS = Berlin Social Support Scales; DV = dependent variable; HADS-A = Hospital Anxiety and Depression Scale—anxiety subscale; HADS-D = Hospital Anxiety and Depression Scale—depression subscale; MCS = Mental Component Summary; MNDCS = Motor Neurone Disease coping scale; MQoL = McGill Quality of Life Questionnaire; N = no; NB = Non-bulbar onset; NES = Negative Emotion Scale; NIV = non-invasive ventilation; NR = not reported; NS = non-significant; P₁ max = maximum static inspiratory pressure; P_aCO₂ = partial pressure of carbon dioxide in arterial blood; PEG = percutaneous endoscopic gastrostomy; PWB = positive well-being subscale; SF-36 = Short Form—36 questionnaire; T1 = time 1; T2 = time 2; T3 = time 3; wk = week; Y = yes; ^a data extracted from random-effects models comparing quartiles; continuous data also reported with no differences with regards to significant predictors. See Table 3 for details of measures.

3.2.1. Age, gender, and education level

There was limited evidence that demographic or clinical variables predicted emotional distress. Age only predicted distress in two out of six studies, with younger age predicting more severe anxiety (Pagnini et al., 2015) and lower psychological QoL (Norquist et al., 2003) at 4 months, but not 8 months (Norquist et al., 2003). Gender seldom predicted emotional distress, with only one study finding that males had better psychological QoL over a three year period than females (Roach et al., 2009). One study included education as a predictor and found that it did not predict depression, anxiety or psychological QoL (Pagnini et al., 2015).

3.2.2. Clinical characteristics

There was limited evidence that any of the clinical variables assessed in the included studies predicted emotional distress. Baseline bulbar functioning did not predict either global emotional distress (Goldstein et al., 2006) or psychological QoL (Bourke et al., 2003). Spinal functioning did not predict global emotional distress (Goldstein et al., 2006); and muscular scores, partial pressure of carbon dioxide, or maximum inspiratory pressure did not predict psychological QoL (Goldstein et al., 2006). Time since diagnosis was evaluated in three studies (Norquist et al., 2003; Pagnini et al., 2015; Roach et al., 2009), but predicted psychological QoL in only one (Pagnini et al., 2015). Neither time since onset of symptoms (Norquist et al., 2003) nor site of symptom onset (Cupp et al., 2011) predicted later psychological QoL.

3.2.3. Treatments

Three studies considered treatments as predictors of emotional distress (Bourke et al., 2003; Cupp et al., 2011; Lyall et al., 2001). Use of NIV significantly predicted psychological QoL one week later (Lyall et al., 2001) but not when assessed 3 or 6 months later (Cupp et al., 2011). However, compliance with NIV treatment did predict improvement in psychological QoL 1 month later (Bourke et al., 2003). One paper assessed the provision of nutrition via percutaneous endoscopic gastrostomy (PEG), finding that PEG predicted psychological QoL 3 and 6 months' later (Cupp et al., 2011). Antidepressant use predicted an improvement in psychological QoL at 3 and 6 months (Cupp et al., 2011).

3.3. Social predictors

Social factors were evaluated in two of the eight studies (Goldstein et al., 2006; Matuz et al., 2015). Lower levels of perceived social support predicted more severe global emotional distress at 6 and 12 months (Goldstein et al., 2006) and greater depression severity at 3 to 6 months (Matuz et al., 2015). However, psychosocial illness-related disability, pre-illness marital intimacy and present marital intimacy did not predict emotional distress at 6 and 12 months (Goldstein et al., 2006).

3.4. Psychological predictors

Several psychological factors were examined in three studies, yet most were not predictors of subsequent emotional distress. Cognitive appraisals of coping potential predicted depression severity at both 3 and 6 months (Matuz et al., 2015). Lower trait mindfulness predicted more severe anxiety and depression at the 4 month assessment point (Pagnini et al., 2015). Coping strategies (emotion management, emotion avoidance and problem management) did not predict depression at 3 or 6 months (Matuz et al., 2015).

4. Discussion

This systematic review examined predictors of emotional distress in PwALS. There was scarce consistent evidence that any baseline demographic factors reliably predicted distress after a diagnosis of ALS. This fits with previous findings suggesting that gender and age in PwALS are not associated with emotional distress (Goldstein & Leigh, 1999; Hogg, Goldstein, & Leigh, 1994).

There was also little evidence that any clinical factor predicted distress. Consistent with a previous review (McLeod & Clarke, 2007), there was no evidence that overall physical functioning or bulbar functioning predicted emotional distress. This highlights a need to consider more specific symptoms

that may be associated with emotional distress, or perhaps to focus on the cognitive appraisals associated with clinical factors which have demonstrated utility in other health conditions (Dempster et al., 2012). There was minimal evidence that NIV improved psychological QoL, with both null and significant findings across a small number of studies. More studies with longer follow-up periods are required to consider conflicting findings. In a single study, PEG and antidepressant use each predicted distress (Cupp et al., 2011). Further detailed investigation of these factors is required to clarify their causal roles.

The only social factor that consistently predicted distress was lower social support. Two studies found that lower social support predicted later emotional distress and depression (Goldstein et al., 2006) (Pagnini et al., 2015). The subjective experience and quality of social support appears to act as a buffer to emotional distress, fitting with longstanding views about the value of social support for PwALS (Hogg et al., 1994; Rabkin, Wagner, & Del Bene, 2000). This is consistent with the protective role of social support against emotional distress in other neurological conditions (Elliott, Charyton, Sprangers, Lu, & Moore, 2011; Simpson, Haines, Lekwuwa, Wardle, & Crawford, 2006). This finding also fits with cross-sectional studies of PwALS, finding that increased social support was associated with better mental health (Chiò et al., 2004). The remaining social factors—psychosocial illness-related disability, pre-illness marital intimacy and present marital intimacy—were assessed only in single studies and did not predict emotional distress. Given the limited number of studies, research to further evaluate the role of social and relational factors would help to clarify their role in distress for PwALS.

There was limited research into psychological predictors of emotional distress over time. Despite this, there were some significant predictors identified by single studies, with mindfulness and cognitive appraisals of potential to cope each predicting later emotional distress (Matuz et al., 2015; Pagnini et al., 2015). This is consistent with cross-sectional research relating a variety of cognitive appraisals to emotional distress in PwALS (Matuz et al., 2010; Miglioretti et al., 2008). However, it is impossible to draw conclusions from single studies; further investigation of psychological predictors and underlying mechanisms required to understand their role in emotional distress for PwALS.

4.1. Strengths and limitations

Despite a comprehensive search strategy, it is possible that relevant research studies were not included in the review. Publication bias should also be considered, with significant results more likely to be published than non-significant findings. Despite these limitations, the conclusions drawn from several studies, rather than those based upon individual studies, are likely to be robust. This review highlights the importance of further investigation to understand distress in ALS, to replicate preliminary findings from single studies, and to examine contradictory findings.

A strength of the review is that it focused solely on prospective studies so that the field could begin to move beyond factors that are associated with distress in PwALS and begin to examine causal mechanisms in PwALS who experience emotional distress. This is a vital clinical step as there is often a need for early intervention given the often rapid progression of the illness. Furthermore, it is readily apparent substantially more well conducted prospective studies in distress and ALS are required to advance treatment possibilities. There were 1499 potential papers identified after duplicates were removed and only 162 that were potentially suitable. However, most of these studies did not use prospective designs or psychometrically validated measures of distress in PwALS.

4.2. Implications for Future Research

Future research should focus on increasing understanding of predictors of emotional distress. To do so, adequately powered studies with large sample sizes are needed. More longitudinal studies are required, despite the challenges in this population, to infer causality between baseline level of various predictors and subsequent emotional distress. It would also be useful to separate PwALS

into groups based upon the time since diagnosis and consider differences based upon the severity of symptoms or rate of progression. This will provide greater insight into the role of physical factors in emotional distress. As emotional distress measures can be influenced by physical functioning, adapted ALS-specific measures of emotional distress should be utilised (Pagnini et al., 2015).

A focus on understanding modifiable factors such as psychological predictors should be prioritised in future research. Further research should be theory-driven and focus on exploring and testing the specific mechanisms underlying psychological predictors. This would inform the development of appropriate psychological interventions for PwALS. Evaluation of the effectiveness of these interventions would allow health services to direct resources into evidence-based therapies to support PwALS to manage distress and therefore improve QoL.

5. Conclusions

With the exception of social support, this review found little evidence that any baseline clinical, demographic, social, and psychological factor consistently predicts later emotional distress in PwALS. Furthermore, methodological limitations associated with most included studies have implications for the conclusions that can be drawn from them. Further prospective research is needed to investigate the mechanisms underlying emotional distress, particularly modifiable psychological factors. This will help to guide the development of evidence-based, ALS-specific psychological interventions designed to reduce emotional distress and improve QoL.

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