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Title

The psychological impact of prolonged disorders of consciousness on caregivers: a systematic review of quantitative studies.

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Key words: disorder of consciousness, families, caregivers, wellbeing.

Abstract

Objective: Systematic review of the nature, frequency and severity of psychological experiences of people who have a close relationship with a person with a prolonged disorder of consciousness.

Data sources: Cochrane Library, Web of Science, PsycINFO, PubMed, Embase®, MEDLINE®, Allied & Complementary Medicine™, were searched from inceptions until December 2016 with additional hand searching of reference lists of included articles.

Review methods: Studies were included that used quantitative methodologies and psychological measures to investigate experiences. The PRISMA statement was followed with inclusion criteria set a priori. A data synthesis summarised psychological constructs studied.

Results: A total of 18 studies (ranging between n=16 – 487 participants) met the inclusion criteria with 15 of 18 studies focused on the primary caregiver. A total of 23 standardized psychological measures were identified to assess four primary psychological constructs: Loss and grief, psychological wellbeing changes, burden and use of coping strategies.

Conclusions: Small sample sizes, limited variables and reliance on observational methods affected quality. Caregivers do find ways to manage independently, but some exhibit clinically significant psychological distress that does not change over time alone and may get worse.

Introduction

The Vegetative State and the Minimally Conscious State are disorders of consciousness, and can be life long conditions (1). Caregivers are faced with a unique situation of a distinct *lack* of intentional behaviour, or behaviours, that cannot be interpreted as always meaningful from the injured person. Caregivers are challenged by having to understand the condition and information about treatment options (2) whilst making decisions in the face of much uncertainty about the diagnosis and prognosis (3). Caregivers concerns include the possible suffering of the injured person and their own ability to cope (4).

Caregivers have been described as having psychological reactions such as sadness, pain, loneliness, loss and grief (5). This complex and ambiguous loss (6) of experiencing of profound loss and grief at the same time the person is still alive and present (5, 7-9) has been described by some caregivers as a state of being “present, but absent”(7) and by others as “living, but dead” (10).

Attempts have been made to understand the experience of families coping with specific roles and tasks such as; advocacy roles (11), aspects of day to day care, end of life care (12, 13) and the agreement to novel treatments (14). Family decision making has been shown to rely on their unique knowledge of the persons pre-injury self (15), their own beliefs that continuation of treatment is necessary even when this not seen by the professionals as being beneficial to the person (16) or misinterpretations of the aims of interventions (12).

The psychological responses of caregivers in disorders of consciousness have largely been studied in theoretical and descriptive terms (see 7, 16-18). Duff (19) observed that in addition to negotiating and navigating the health system, families have to learn to negotiate with each other and differences in reactions across the family may be a factor in psychological distress (16). Caregivers may suspend their own lives, and feel that they are the only people able to understand and respond to the injured persons needs (19) with psychological reactions including guilt and blame (18) noted.

Caregivers can maintain high hope for significant recovery and that responses observed in the person with the disorder of consciousness are meaningful, despite the opposite view of the assessing professionals (16). Understandably, caregivers have been observed to hold onto hope that the injured person is aware that they are present (20) and that a means of communication can be established (21).

It is important to consider what the psychological needs of caregivers (1) who have strong emotional connections with the person with a disorder of consciousness are, especially as caregivers are key contributors in assessment, clinical decision making processes and providers of care. The present study therefore seeks to (i) present the first systematic review of the literature to investigate the range of psychological constructs studied and the standardized tools used with people closely connected to a person with a disorder of consciousness and (ii) establish the psychological impact of having a close relationship with a person with a prolonged disorder of consciousness, which may assist clinicians in improving support services and outcomes for caregivers.

Methods

Search strategy

A systematic search of a range of databases: Cochrane Library, Web of Science, PsycINFO, PubMed, Embase®, MEDLINE®, Allied & Complementary Medicine™ was conducted from their inception until 01 December 2016.

The term Disorders of Consciousness is used within the United Kingdom encompassing both the Vegetative and Minimally Conscious States (1), however the search was widened to include terms that have been used both historically and internationally (such as; Apallic Syndrome, Unresponsive Wakefulness Syndrome, Persistent Vegetative State, Minimally Conscious State, Minimally Responsive State and the Low Awareness State -see supplementary material online Appendix A for details). The search was restricted to peer reviewed journal articles, published in English, on humans. A manual search of the reference list of included articles to find articles that may have been missed in the electronic search strategy was conducted.

Inclusion / exclusion criteria

No limits were placed on design methodology in the search process. Duplicates were removed, and titles and abstracts were screened by one author (SS) in order to determine if the inclusion criteria were fulfilled.

Articles were included if: (1) The participant had a close pre-injury relationship with a person with a prolonged disorder of consciousness (2) the non-injured caregiver was

(the participant) the focus of the research (3) the psychological variables and experiences of the participant were directly studied and reported on in the article (4) the article was not focused on the experiences of proxy clinical decision making for the injured person or end of life care as it was not possible to determine if the psychological findings were primary or secondary in the study to these specific decisions (5) the methodology employed psychological self-report measures to identify the range of psychological experiences of the non-injured family member (6) the focus was on understanding and directly assessing the participants psychological experience (7) the article was published in a journal that uses peer review (8) the article was published in English.

If an abstract appeared relevant, the full text was sourced. Author 1, a Consultant Clinical Psychologist completed full text screening on 61 articles to determine if the inclusion criteria were met, as well as reviewing the reference lists of included articles. Whilst a number of historical observational, descriptive opinion and discussion papers were identified about the psychological experience of families, these were excluded in relation to the lack of use of standardized psychological assessment tools (part 5 of the inclusion criteria). At this point, qualitative study methodologies were also excluded.

Data extraction was conducted and included: (a) study characteristics (author, year, country) (b) details of study design, (c) participant/sample characteristics (gender, size, diagnosis of injured family member), (d) psychological construct / variable being studied (e) information about the nature of standardized assessment outcome measures, with (f) results and conclusions recorded.

Results

Figure 1 details the articles included at each stage of the process and illustrates the PRISMA flowchart outlining each stage. A total of 3310 articles were originally identified, after duplicates were excluded, 1632 titles remained. The review of titles and abstracts removed 1571. Full text articles were retrieved for 61 titles to assess against the inclusion criteria. This yielded the 18 articles included in this review.

INSERT FIGURE 1 HERE

Study characteristics

The included 18 studies detailed the experiences of caregivers in Southern Europe (the majority from Italy $n = 16$, and $n=2$ from Spain) with the earliest published in 2001. The majority of participants were the primary relative/caregiver ($n=15$ of 18). Although sample sizes ranged from 16 – 487 across the studies, typically studies had 53 or fewer participants. Most ($n= 12$ of 18) were multicentre designs. Recruitment and data collection periods were not specified in 10 of the studies (9,22-29) whilst in nine of 19 the range was one month (4) to 135 months (30). It appeared several papers were related studies and might have reported on the same data set (for example 23, 31-33). It was therefore not possible to submit studies identified to an effect size analysis and instead a descriptive data synthesis of the results was performed.

INSERT TABLE 1 HERE

Included studies employed 22 different standardized psychological self report measures which enabled comparison with the normative population and 1 structured clinical interview technique in order to investigate 13 psychological variables experienced by the caregivers. These variables were then grouped and abstracted to the higher order psychological construct that they assess: (i) loss and grief (ii) psychological wellbeing changes (encompassing depression, anxiety, anger, trauma, hopelessness and perceived quality of life) (iii) experience of burden and (iv) employment of coping strategies (including social support, coping styles, perceived caregiver needs, attachment style, health status).

INSERT TABLE 2 HERE

Experience of Loss and Grief. Grief was directly investigated in 9/18 studies (see 4,9, 22,25,29,30,31,34,35), and all studies operationalized this using the measure; Prolonged Grief-12 previously known as the Inventory of Complicated Grief (27). The range for participants who met the criteria for prolonged grief disorder was from 15% (31) to 60% (32). Prolonged grief disorder was observed to be a distinct condition to depression with different risk factors (9). The presence of syndromal level grief, did not appear to change over time (23) or be related to the diagnosis (31) of the injured person.

Characteristics of caregivers with Prolonged Grief Disorder were linked to typically being younger themselves and supporting a person who was injured at a younger age (9). The use of active and problem focused coping styles was associated with fewer

grief symptoms, whilst denial and self blame were associated with more (34). Findings on gender were mixed. In one study, women were twice as likely as men to meet the criteria for Prolonged Grief Disorder (26) whilst another study found no difference in gender (23).

Changes in psychological wellbeing. Of the 14 of 18 studies that directly examined depressive symptoms (4,9,22-28,30-34) using three different measures, all found participants in their sample who had clinically significant levels of depressive symptoms relative to the normative data. Four studies found high levels of depressive symptoms recorded in around a third of participants (23,26,32,34) whilst higher levels of depressive symptoms in over half of the participants were found in two studies (27,31).

The diagnosis of the injured person was not found to contribute to the experience of depression in two of the studies (4,36). However, a shorter time since injury was associated with higher depressive symptoms in caregivers of people with Vegetative State in one study (9). No connections between age and the development of depressive symptoms were identified in one study (9).

Coping strategies that employed denial, were associated with depressive symptoms (26) with women experiencing significantly higher depressive symptoms than men (24,28) whilst another study found women to be less depressed (28). The presence of depressive symptoms was the strongest predictor of lower perceived quality of life (8). Levels of psychological distress remained constant over time (36) whilst others have found it increased (28) without any specific intervention.

Anxiety levels were investigated in 13 out of 18 studies using three different measures. Some studies have found the experience of anxiety symptoms in the majority of participants to be at normative levels (such as Cipolletta et al. 25 and Cruzado et al. 26). Those without significant anxiety symptoms were more likely to use acceptance style coping strategies (26). However clinically significant levels of anxiety have been noted (such as 26,27,28,31), with one study reporting significantly higher levels of anxiety symptoms in female caregivers (24) and limited change over time (37).

Only one study investigated the caregivers experience of anger which was in line with the general population (34) and one investigated a sense of hopelessness which was greater than the general population (38).

In terms of quality of life, three of 18 studies investigated this using two measures. Poorer quality of life was predicted by the presence of depressive symptoms (34) and were observed to get worse over time (22).

Burden. The experience of physical, financial and psychosocial dimensions of burden associated with caregiving for a family member with a disorder of consciousness, was investigated in nine of 18 studies, employing 4 different measures. Less than half of a sample of 48 participants were in paid employment with 30.6% of 48 participants experiencing financial problems over a two year period (33) and 38% in another study reported financial difficulties (31).

Two studies found high levels of emotional burden amongst caregivers occurred irrespective of the setting that the person with a disorder of consciousness was cared in (27,32). In a longitudinal study emotional burden was noted to increase over time (22, 35, 37), as did reports of caregiver strain (22). Others did not find any association in the levels of burden and the length of time they had been providing care (34, 38). Of the total variability in burden in 49% of 19 participants, was predicted by a preoccupied attachment style and hopelessness (28).

Caregivers who experienced higher levels of psychosocial burden reported needing the most information from professionals (23) and the author hypothesized this related to support needs rather than an actual need for information. One study identified the need for help and support to be higher when caring for a person with a diagnosis of Minimally Conscious State (36) whilst another found no difference of diagnosis on burden (32). Greater perceived burden was reported in those family members who spent more than 3 hours per day with the injured person (32).

Coping. Of 18 studies, 13 investigated caregiver coping employing nine different measures. Caregivers reported that over time their levels of social support decreased (28,32). Those using positive attitude, social support and problem-orientated approaches have been identified as having less anxiety, depression, prolonged grief and family strain whereas the opposite effect was seen in those employing avoidance strategies (25). Employment of active and problem focused coping strategies has been the most frequently used approaches for caregivers but a number also employ emotion

focused and avoidance strategies such as self distraction (32.1% of 53) and denial (39.6% of 53) (26).

Discussion

The key finding is that caregivers of people with disorders of consciousness have been identified in this review as having clinically significant levels of grief, burden, wellbeing changes and challenges coping.

This is the first systematic review of the psychological impact of having a close relationship with a person with a prolonged disorder of consciousness. Despite current and historical descriptors of the condition being used to enable to the widest possible search of relevant literature and databases searched from inception, appropriate studies were only located from 2001 onwards. This reflects the lack of empirical research in this area. Although a limitation of this review is that the papers were selected by a single author, the findings are consistent with many of the descriptive and observational opinion papers that have predominated on caregiver experiences (2,3,16,17,18).

This review goes some way to collating the range of variables and constructs investigated to date, the nature of assessment measures employed and the findings. This inevitably leads to the question; are the right variables being studied? Qualitative researchers have found alongside psychological reactions of sadness, pain, loneliness and grief that families also report a focus on love, commitment and loyalty to the

injured person (5). These are constructs that have not been investigated in the studies identified in this review.

Importantly, the qualitative literature is pointing towards a unique and complex form of loss, an ambiguous loss, where the injured person is physically present but psychologically absent to the caregiver (5,6,39,40,41). However, all the studies operationalized loss similarly and used the same measure (PG-12). This may assess to a different loss phenomenon particularly as caregivers losses are enduring and they remain emotionally and materially in the injured persons life (31). Future research in this area should include exploration of this form of loss.

Kitzinger et al. (42) encouraged clinicians to respect the variety of ways caregivers may cope with the injury and see these as normal responses to an abnormal and deeply distressing situation. How best understand this unique experience and how to support families to find a way to live with this, is an area of research requiring urgent attention. It may require a paradigm shift in understanding of loss where caregivers are actively engaged in meaning making about their situation (43) finding new ways to redefine and continue their bonds with the injured person (44) and move between coping with their loss and being engaged in restorative activity (45). Time alone does not appear to help, so as families are involved in a long-term coping process, so too should be the availability of specialist psychological support (22).

The life changing event of a severe brain injury has an impact on the whole family and they can be very severely distressed and need support themselves (1). Investigation

into the exact nature of this support is needed, but research to date indicates that assessment and intervention for anxiety, depression and psychological wellbeing is important (4). This review indicates that it is also important to support families to help to control the perceived level of burden and gain social support.

The vast majority of the literature has investigated the experience of the primary and main caregiver who typically spends the most time with the injured person, little is known about the wider family network who are able to visit less often and perhaps have less exposure to the reality of the condition and access to information from the professionals.

Research in this area is challenged with balancing relatively small numbers of people with disorders of consciousness with the need to recruit sufficient research participants in a similar setting, who are themselves often distressed and focused on the care of the injured person not on themselves. Small sample sizes are an issue across the included studies and limit generalization. Further, all the research identified reflects the experience of caregivers in southern Europe particularly Italy where a national population research programme is in place. Further investigation is required to determine if this is reflective of the broader international experience.

The use of observational and cross sectional methodologies limits causal conclusions and means little is therefore known of the longitudinal experience of these caregivers, indeed in other areas of severe brain injury few studies investigate caregiver experiences past 5 years post injury (46).

Future research would benefit from a wider selection of variables, longitudinal design and comparisons of participants responses not only with the normative sample for the measure, but also with comparison groups that may have clinical parallels for example, profound neuro-disability but with a reliable yes/no communication method. This should help to identify the specific group and timing of those who need targeted support from professionals (22,47). Given this review has highlighted there are caregivers experiencing high levels of distress, further research is need to establish how best to support their psychological needs.

Clinical Messages

- Some caregivers of people with a prolonged disorder of consciousness will cope alone. Others suffer clinically significant changes in psychological well being, grief, burden and the ability to cope.
- Prolonged disorders of consciousness create a unique form of loss that must be taken into account to understand caregiver's distress

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Conflict of interest

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Figure 1: Included articles.

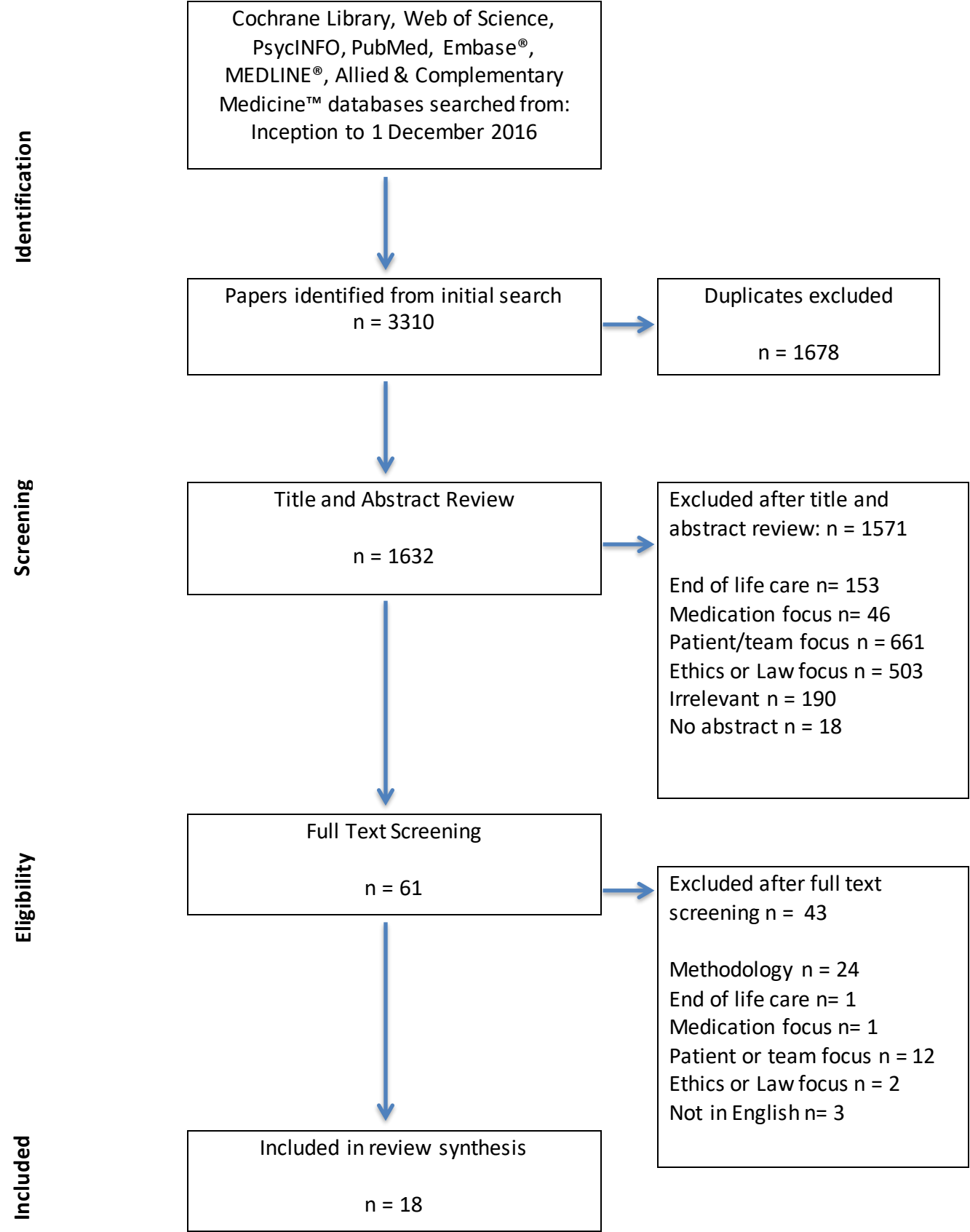


Table 1. Summary of included studies methodological designs and features.

Study (Reference list item)	Country	VS/ MCS	n	Gender		Primary caregiver	Study Design	Multi centre	Recruit time (months)	Variables studied	Measures used	% prolonged grief
				M	F							
Bastianelli et al (22)	Italy	VS	52 BL 27 F/UP	22 13	30 14	Yes Yes	L	Yes	U	Grief&Loss Depression Anxiety Burden QoL	PG-12 AD FSQ-SF CQOL	38.5% of 52
Covelli et al (33)	Italy	MCS or VS*	487 BL 216 F/UP	77	129	Yes	L	Yes	10	Health Burden Depression Coping	SF-12 FSQ BDI-II COPE	
Corallo et al (4)	Italy	VS or MCS	48	18	30	Yes	L	No	1	Grief&Loss Depression Anxiety Caregiving needs Health	PG-12 BDI-II STAI-Y CNA SF-36	NR
Romaniello et al (38)	Italy	MCS or VS	19	4	15	No	C	No	5	Hopelessness Burden Attachment	BHS CBI ASQ	
Giovannetti et al (34)	Italy	MCS or VS	129	41	88	Yes	O	No	28	Grief&Loss Depression Anxiety Anger	PG-12 BDI-II STAXI- 2 STAI-Y	20.9% of 129

										QoL Social Support Coping	WHOQOL-Bref MOS-SSS COPE	
Corallo et al (36)	Italy	MCS or VS	50	24	26	Yes	O	No	27	Burden Health	FSQ SCL-90R	
Pagani et al (23)	Italy	MCS or VS	487	131	266	Yes	O & C	Yes	U	Depression Anxiety Burden Caregiving needs	BDI-II STAI-Y FSQ CNA	
Pagani et al (24)	Italy	MCS or VS	418	124	296	Yes	C	Yes	U	Depression Anxiety	BDI-II STAI-Y	
Moretta et al (35)	Italy	MCS or VS	24 18 F/U	19	15	Yes	P&L	No	23	Grief&Loss Anxiety	PG-12 STAI-Y	32% of 24
Cipolletta et al (25)	Italy	VS	61	23	38	No	O	Yes	U	Grief&Loss Anxiety Depression Burden Coping	PG-12 AD FSQ COPE	37.7% of 61
Giovanetti et al (32)	Italy	VS or MCS	487	139	337	Yes	C	Yes	15	Depression Anxiety Burden Coping Caregiving needs	BDI-II STAI-Y FSQ COPE CNA	
Cruzado et al (26)	Spain	VS or MCS	53	20	23	No	C	No	U	Depression Anxiety Coping	BDI-II BAI Brief COPE-28	

Elvira dela Morena et al (29)	Spain	VS or MCS	53	12	41	Yes	C	No	U	Grief&Loss Coping	PG-12 Brief COPE-28	60.4% of 53
Leonardi et al (31)	Italy	VS	487	139	337	Yes	O	Yes	10	Grief&Loss Depression Anxiety Burden Coping Caregiving needs	PG-12 BDI-II STAI-Y FSQ COPE CNA	27.6% of 487
Giovannetti et al (27)	Italy	VS or MCS	35	5	30	Yes	O	Yes	U	Depression Anxiety Coping	BDI-II STAI-Y COPE	
Guarnerio et al (30)	Italy	VS or MCS	40	9	31	Yes	O&C	Yes	135	Grief&Loss Depression Trauma	PG-12 QD SCID 1 DTS	15% of 40
Chiambretto et al (9)	Italy	VS or MCS	45	16	29	Yes	O&C	Yes	U	Grief&Loss Depression	PG-12 QD	35.6% of 45
Chiambretto et al (28)	Italy	VS	16	6	10	Yes	E&O	Yes	U	Depression Anxiety Burden Personality Coping	QD STAI-Y FSQ2 CISS EPQ	

AD: Anxiety and Depression Short Scale, ASQ: The Attachment Style Questionnaire, BAI: Beck Anxiety Inventory, BL: Baseline, BDI-II: Beck Depression Inventory II, BHS: Beck Hopelessness Scale, Brief COPE-28: Brief Coping Orientation of Problems Experienced-28, C: Cross sectional, COPE: Coping Orientations to Problem Experiences, CBI:

Caregiver Burden Inventory, CISS: Coping Inventory for stressful situations, CQOL: Caregiver Quality of Life, CNA: Caregiver Needs Assessment, DTS: Davidson Trauma Scale, E: Exploratory, EPQ: Eysenck Personality Questionnaire, F/U: Follow-up, FSQ: Family Strain Questionnaire, L: Longitudinal, O: Observational, P: Prospective, PG-12: Prolonged Grief Disorder Questionnaire, QD: The Depression Questionnaire, MCS: Minimally Conscious State, MOS-SSS: Medical Outcome Study Social Support Survey, NR: not reported, R: Retrospective, SCL-90R: Symptom Checklist-90R, SF-36: Short Form Health Survey, SCID 1: Structured Clinical Interview for DSM-IV Axis 1, STAI-Y: State Trait Anxiety Inventory-Y, STAXI-2: State Trait Anger Expression Inventory – 2, WHOQOL-BREF: World Health Organization Quality of Life-Bref, VS: Vegetative State, U: Unspecified, *(and severe disability).

Table 2: Frequency of constructs and measures

Construct	Measure	Study Ref	Frequency of use
Loss and Grief n=9 studies	PG-12	4,9,22,25,29,30,31,34,35	9
Psychological Wellbeing n=15 studies	BDI-II	4,23,24,26,27,31,32,33,34	9
	QD	9,28,30	3
	AD	22,25	2
	STAI-Y	4,23,24,27,28,31,32,34,35	9
	BAI	26	1
	STAXI-2	34	1
	SCID1	30	1
	DTS	30	1
	BHS	38	1
	WHO-QOL-Bref	34	1
	CQOL	22	1
Burden n=9 studies	CBI	38	1
	FSQ	23, 25, 31, 32, 33, 36	6
	FSQ-SF	22	1
	FSQ-2	28	1
Coping n=13 studies	COPE	25, 27, 31, 32, 33, 34	6
	Brief COPE28	26,29	2
	CISS	28	1
	EPQ	28	1
	CNA	20,21,22,39	4
	SF12	33	1
	SF36	4	1
	SCL-90R	36	1
	ASQ	38	1

AD: Anxiety and Depression Short Scale, ASQ: The Attachment Style Questionnaire, BAI: Beck Anxiety Inventory, BDI-II: Beck Depression Inventory II, BHS: Beck Hopelessness Scale, Brief COPE-28: Brief Coping Orientation of Problems Experienced-28, COPE: Coping Orientations to Problem Experiences, CBI: Caregiver Burden Inventory, CISS: Coping Inventory for stressful situations, CQOL: Caregiver Quality of Life, CNA: Caregiver Needs Assessment, DTS: Davidson Trauma Scale, EPQ: Eysneck Personality Questionnaire, F/U: Follow-up, FSQ: Family Strain Questionnaire, PG-12: Prolonged Grief Disorder Questionnaire, QD: The Depression Questionnaire, MOS-SSS: Medical Outcome Study Social Support Survey, SCL-90R: Symptom Checklist-90R, SF-36: Short Form Health Survey, SCID 1: Structured Clinical Interview for DSM-IV Axis 1, STAI-Y: State Trait Anxiety Inventory-Y, STAXI-2: State Trait Anger Expression Inventory – 2, WHOQOL-BREF: World Health Organization Quality of Life-Bref, FSQ-2: Family Strain Questionnaire-2; SF-12: Short Form-12.

APPENDICES

Appendix 1: Search terms used

Databases: Allied & Complementary Medicine™, Embase®, MEDLINE®, Cochrane Library, Web of Science, PsychINFO, PubMed

The following search terms with Boolean operators for breadth and efficiency of the historical and international range of definitions were used:

Search Strategy

- 1.Famil*
- 2.Caregiver*
- 3.Spouse*
- 4.Relative*

5.“Disorder* of consciousness”

- 6.Low Awareness State*
- 7.Post coma unawareness
- 8.Unawareness state
- 9.Apallic
- 10.Vegetative State*
- 11.Minimally conscious state*

12. 1 AND 5
13. 1 AND 6
14. 1 AND 7
15. 1 AND 8
16. 1 AND 9
17. 1 AND 10
18. 1 AND 11

19. 2 AND 5
20. 2 AND 6
21. 2 AND 7
22. 2 AND 8
23. 2 AND 9
24. 2 AND 10
25. 2 AND 11

26. 3 AND 5
27. 3 AND 6
28. 3 AND 7
29. 3 AND 8
30. 3 AND 9
31. 3 AND 10
32. 3 AND 11

33. 4 AND 5

- 34. 4 AND 6
- 35. 4 AND 7
- 36. 4 AND 8
- 37. 4 AND 9
- 38. 4 AND 10
- 39. 4 AND 11