

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	From first symptoms to diagnosis of Amyotrophic Lateral Sclerosis – perspectives of an Irish informal caregiver cohort: a thematic analysis
<b>AUTHORS</b>	Galvin, Miriam; Gaffney, Rebecca; Corr, Bernie; Mays, Iain; Hardiman, Orla

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Oechsle, Karin University Medical Center Hamburg-Eppendorf, Germany
<b>REVIEW RETURNED</b>	07-Nov-2016

<b>GENERAL COMMENTS</b>	<p>The authors present a qualitative analysis on the experiences of informal caregivers of ALS patients from the first onset of symptoms to multiprofessional specialist diagnosis. This analysis concern on a highly interesting issue as these experiences of the patients and their family caregivers are often sustainable and can influence the whole course of further disease and treatment.</p> <p>The manuscript is written in an interesting way and presents comprehensive data on methods, results and previous literature. In my opinion, the manuscript is suitable for publication in BMJ Open after some minimal revisions.</p> <p>Figure 1: the presentation suggests that this time data have been assessed quantitatively. I think it would be better to point out that these data are also assessed semi-qualitatively and are based on the caregivers memories.</p> <p>I think a short part on limitations should be added at the end of the discussion that underlines the explorative character of the study and the fact that this manuscript only presents one small part of a total study.</p>
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<b>REVIEWER</b>	Dr Tan Seng Beng Associate Professor and Consultant in Palliative Medicine Palliative Care Unit Department of Medicine Faculty of Medicine University of Malaya Medical Centre 50603 Kuala Lumpur Malaysia
<b>REVIEW RETURNED</b>	12-Nov-2016

<b>GENERAL COMMENTS</b>	Question 1: In introduction section, the gap is not explained prior to the formulation of the research question. Are there any reports on the experiences of caregivers pre-diagnosis journey for ALS? Is the
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	<p>objective of the study to explore the experiences to understand the problems of delay in diagnosis or the caregivers needs at the pre-diagnosis stage, or both. The semi-structured questions use to explore the research question depends on the clearly-defined objective.</p> <p>Question 2: the results section of the abstract needs to be clarified. Please refer to comments on question 6. In strengths and limitations, what were the new findings? what were the limitations?</p> <p>Question 4: the sampling method was not described - convenience sampling, purposive sampling, theoretical sampling, inclusion exclusion criteria; data collection method was not described. (audio, video, notes). Transcription? Translation? The steps of data analysis were not clearly defined. Coding definition?</p> <p>Question 6, 9 and 10: Data saturation was not mentioned, including how the assessment of data saturation was performed. Multiple coders were involved but inter-rater reliability was not reported for validation. Too much focused on demographics (The table is self-explanatory). Table 1: time from symptoms to diagnosis - choose mean or median depending on normality. Figure 1 is unnecessary for qualitative report. What are the other semi-structured questions in the interview? Were these questions exploring the journey as intended in the research question? How were these questions formulated? How were the themes and subthemes linked with the Title of pre-diagnosis journey? Figure 2 (most important) - the pre-diagnosis journey of informal caregivers was not clearly represented in the figure. The figure did not clearly capture the meaning of "journey". How did these themes appeared from the analysis? Why were these themes do not flow like in a journey? Why is "noticing" an important aspect of the journey, or is it part of reaction (reaction of noticing the changes)? What is the difference between reaction and response?</p> <p>Question 11 and 12: The discussion of the results was inadequate. What were the findings that add to the literature? What were the impacts? Limitations were not discussed. Future research recommendations were not discussed.</p>
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<b>REVIEWER</b>	Andrea Calvo 'Rita Levi Montalcini' Department of Neuroscience, University of Torino, Torino, Italy
<b>REVIEW RETURNED</b>	17-Nov-2016

<b>GENERAL COMMENTS</b>	<p>This study is a semi-qualitative survey focused on caregiver's perception in amyotrophic lateral sclerosis. Even if the results are more or less descriptive, the role of this type of papers are fundamental, in particular to improve the management of ALS patients and their caregivers. I have no comments, and I confirm that the discussion and conclusions represent the real situation of ALS setting.</p> <p>I suggest to add and discuss this reference: ALS patients and caregivers communication preferences and information seeking behaviour.</p> <p>Chiò A, Montuschi A, Cammarosano S, De Mercanti S, Cavallo E, Ilardi A, Ghiglione P, Mutani R, Calvo A. Eur J Neurol. 2008 Jan;15(1):55-60.</p>
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## VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Oechsle

Institution and Country: University Medical Center Hamburg-Eppendorf, Germany Please state any competing interests: No competing interests

Please leave your comments for the authors below

The authors present a qualitative analysis on the experiences of informal caregivers of ALS patients from the first onset of symptoms to multiprofessional specialist diagnosis. This analysis concern on a highly interesting issue as these experiences of the patients and their family caregivers are often sustainable and can influence the whole course of further disease and treatment.

The manuscript is written in an interesting way and presents comprehensive data on methods, results and previous literature. In my opinion, the manuscript is suitable for publication in BMJ Open after some minimal revisions.

Thank you for your comments

Figure 1: the presentation suggests that this time data have been assessed quantitatively. I think it would be better to point out that these data are also assessed semi-qualitatively and are based on the caregivers memories.

The data included in Figure 1: Time (months) from first symptoms to diagnosis and site of onset, were taken from the National ALS/MND Register, and are not based on caregivers' memories. We have added text to clarify this, highlighted in red and included below:

Using data from the National ALS/MND Patient Register, the time in months from first symptoms to diagnosis for each patient in ascending order, and the site of onset is illustrated in Figure 1.

I think a short part on limitations should be added at the end of the discussion that underlines the explorative character of the study and the fact that this manuscript only presents one small part of a total study.

Thank you for this comment. We have added text to the Discussion Section underlining the explorative nature of this qualitative sub-study which is part of a larger longitudinal primarily quantitative study.

Revision highlighted in text and included below:

This exploratory qualitative sub-study is part of a larger longitudinal primarily quantitative study. The caregiver descriptions were provided in response to one open ended interview question, with limited opportunity to expand on their experiences. It will be important to explore the time before diagnosis and the quality of their experiences through in-depth interviews with caregivers.

Reviewer: 2

Reviewer Name: Dr Tan Seng Beng

Institution and Country: Associate Professor and Consultant in Palliative Medicine, Palliative Care

Unit Department of Medicine, Faculty of Medicine, University of Malaya Medical Centre, 50603 Kuala Lumpur Malaysia Please state any competing interests: None declared

Please leave your comments for the authors below

Question 1: In introduction section, the gap is not explained prior to the formulation of the research question. Are there any reports on the experiences of caregivers pre-diagnosis journey for ALS? Is the objective of the study to explore the experiences to understand the problems of delay in diagnosis or the caregivers needs at the pre-diagnosis stage, or both. The semi-structured questions use to explore the research question depends on the clearly-defined objective.

Lack of public awareness of MND, recognition of symptoms, misattribution to other causes, and delays in seeking medical attention among patients and caregivers have been reported [13,14].

The objective of this sub-study was to facilitate caregivers to describe their experiences from when the patient first started having problems to ALS/MND diagnosis. And as such they were not asked specifically to describe delays to diagnosis or their own needs during this time.

This study reports on the responses to one open-ended question "Thinking of the time when [ ] first started having problems up to his/her diagnosis with MND, what was that time like for you?" The responses given were free ranging and it was left up to the caregivers to describe that time for them.

Question 2: the results section of the abstract needs to be clarified. Please refer to comments on question 6. In strengths and limitations, what were the new findings? what were the limitations?

Added text to abstract for clarification, and included below:

This was a largely female and spousal cohort of caregivers, living with the patient for whom they provided informal care. The majority of patients were male and were spinal onset. Caregivers described the time from first symptoms to diagnosis. Using a primarily inductive approach, the coding was data driven and the codes and themes derived from the content of these descriptions. Two main themes were identified (1) problem signs and symptoms (a) noticing and (b) reaction; (2) interaction with the health services.

We have revised the Strengths and Limitations Section.

Question 4: the sampling method was not described - convenience sampling, purposive sampling, theoretical sampling, inclusion exclusion criteria; data collection method was not described. (audio, video, notes). Transcription? Translation? The steps of data analysis were not clearly defined. Coding definition?

The participants were caregivers of patients participating in a large longitudinal study – consecutive sample of patients, and thus caregivers.

Sampling:

Revision highlighted in text and included below:

Participants were consecutively recruited as primary informal caregivers of patients taking part in a longitudinal study of the patient and caregiver journey through ALS/MND, attending the specialist multidisciplinary National ALS/MND Centre at Beaumont Hospital, Dublin. Caregiver participants were identified by the person with ALS as his/her primary informal caregiver, providing unpaid care and

assistance to them.

Data collection method:

Revision highlighted in text and included below:

The face-to-face interviews lasted approximately one hour and were conducted in the caregiver's own home by a male assistant psychologist (IM) or a female health services researcher (MG) both members of the research team. Responses to the open ended questions were noted in written format by the interviewer.

Steps of data analysis and coding definition:

As outlined in the Data Analysis Section the thematic analysis was a multi-phase process including initial coding, theme development, theme review and definition. Due to word count limitations we did not report on each step but referred readers to a publication where they are outlined in detail (Braun and Clarke, 2006).

We used a primarily inductive approach to this analysis and the coding was 'data driven'.

Thus the codes and themes derive from the content of the data themselves.

Question 6, 9 and 10: Data saturation was not mentioned, including how the assessment of data saturation was performed.

Participants were consecutively recruited as primary informal caregivers of patients taking part in a longitudinal study of the patient and caregiver journey through ALS/MND, attending the specialist multidisciplinary National ALS/MND Centre at Beaumont Hospital, Dublin.

We collected response data from all 74 caregivers who responded to the open ended question before beginning thematic analysis via coding. The caregiver responses to the open ended question were analysed thematically, two main themes and subthemes are presented in this paper.

Multiple coders were involved but inter-rater reliability was not reported for validation.

Inter-rater reliability was not reported for validation, we did not quantify the analysis of open-ended question material, the approach we took was of consensual validation, to assure the coding and themes produced were credible.

The use of multiple coding, with researchers from different disciplinary backgrounds allowed for reliability to be assessed qualitatively in terms of consistency of meaning. Credibility of findings were established based on clinical experience (BC).

Too much focused on demographics (The table is self-explanatory).

We respectfully disagree with the reviewer. We submit that it is appropriate to explain some of the tabular data for people unfamiliar with the heterogeneity of ALS/MND.

Table 1: time from symptoms to diagnosis - choose mean or median depending on normality.

Mean and Median values are useful for interpretation of the data

Figure 1 is unnecessary for qualitative report.

We respectfully submit that this Figure is important in the context of this paper, as it graphically illustrates the different durations from symptom onset to diagnosis for the cohort of patients from data recorded in the National ALS/MND Register. Disease heterogeneity, and non-uniform access to specialist services are important aspects of ALS /MND that require further analysis.

What are the other semi-structured questions in the interview?

The other semi-structured questions collected information on a range of demographic and socio-economic factors, with standardised psychometric and quality of life measures. In open-ended questions, caregivers were asked about their experiences from the time of symptom onset to diagnosis, impact of ALS/MND diagnosis on the caregiver's life, and aspects of caregiver burden. The responses to these other questions are not the focus of this paper and will be reported elsewhere.

Were these questions exploring the journey as intended in the research question? How were these questions formulated? How were the themes and subthemes linked with the Title of pre-diagnosis journey?

ALS/MND is a progressive disease and symptom onset precedes diagnosis, the term Journey is used to loosely capture this temporal sequence (in addition to its use as a concept to frame caregivers' experiences, see below). The open ended questions were formulated through group discussions with senior and experienced members of the clinical staff working as part of the multidisciplinary service for patients with ALS/MND.

Revision highlighted in text and included below:

In an open-ended question, caregivers were asked about their experiences from the time of symptom onset to diagnosis. This question was formulated through group discussions with senior and experienced members of the clinical staff working as part of the multidisciplinary service for patients with ALS/MND.

The theme Problems and Symptoms precedes Reaction to these symptoms and Responding to them - both psycho-emotional and problem focussed reactions and responses. Interaction with the Health Services follows on from Noticing and Reaction and Response to symptoms, and takes place before confirmed ALS diagnosis.

The Title of the paper has been revised.

Figure 2 (most important) - the pre-diagnosis journey of informal caregivers was not clearly represented in the figure. The figure did not clearly capture the meaning of "journey". How did these themes appeared from the analysis?

Figure 2 represents the themes and subthemes derived from the thematic analysis.

Why were these themes do not flow like in a journey? Why is "noticing" an important aspect of the journey, or is it part of reaction (reaction of noticing the changes)? What is the difference between reaction and response?

The term Journey is used in both a temporal and conceptual sense in this paper. We believe that the caregivers needed to 'notice' or have their attention drawn by others to problems and symptoms in advance of reacting or responding to them. Engagement with health services followed as part of the response to noticing problems and symptoms.

Reaction and response are similar and represent a subtheme within the Problems and Symptoms

Theme.

Question 11 and 12: The discussion of the results was inadequate. What were the findings that add to the literature? What were the impacts? Limitations were not discussed. Future research recommendations were not discussed.

Limitations discussed and future research recommended - revised Strengths and Limitations, and in text added to Discussion Section.

Thank you for your comments

Reviewer: 3

Reviewer Name: Andrea Calvo

Institution and Country: 'Rita Levi Montalcini' Department of Neuroscience, University of Torino, Torino, Italy Please state any competing interests: No conflict of interest

Please leave your comments for the authors below

This study is a semi-qualitative survey focused on caregiver's perception in amyotrophic lateral sclerosis. Even if the results are more or less descriptive, the role of this type of papers are fundamental, in particular to improve the management of ALS patients and their caregivers. I have no comments, and I confirm that the discussion and conclusions represent the real situation of ALS setting.

I suggest to add and discuss this reference: ALS patients and caregivers communication preferences and information seeking behaviour.

Chio A, Montuschi A, Cammarosano S, De Mercanti S, Cavallo E, Ilardi A, Ghiglione P, Mutani R, Calvo A.

Eur J Neurol. 2008 Jan;15(1):55-60.

Thank you for these comments.

This reference was an omission from the original submission.

We have now included it and added text to the Discussion Section, highlighted in red and included below:

Responding to problems and symptoms and how they were interpreted included suspicion, denial, avoidance, fear, confusion, worry and help-seeking. While many caregivers noticed and may not have understood what was happening, others denied any observations. Emotional and avoidance-focused coping are generally considered to be maladaptive [17]. Avoidance-based coping may be beneficial and act as a protective factor in some situations, however it becomes a problem when applied continuously [18]. Patients and caregivers seek more information following communication of ALS diagnosis (Chio et al 2008). The internet, family, friends and media were used as sources for information, from outside the health care system, during the pre-diagnosis phase.

Previous research points to communication difficulties with HCPs with respect to obtaining information about diagnosis and health status, and a lack of empathy and an absence of compassion conveyed by medical professionals [4, 14,(Chio et al 2008).]. Guidelines are available to assist in communication practices and educational programmes can be accessed to improve communication skills [22, 8, 14, 23].

## VERSION 2 – REVIEW

<b>REVIEWER</b>	Oechsle, Karin Germany
<b>REVIEW RETURNED</b>	27-Dec-2016

<b>GENERAL COMMENTS</b>	After Revision, this manuscript has improved and seems to be now suitable for publication.
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<b>REVIEWER</b>	Tan Seng Beng University Malaya, Malaysia
<b>REVIEW RETURNED</b>	31-Dec-2016

<b>GENERAL COMMENTS</b>	The revised manuscript is very good.
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