POSTER
#PND110

SYMPTOMS, DELAYED DIAGNOSIS, AND QUALITY OF LIFE (QOL) DETERIORATION – EXPLORING THE BURDEN OF AMYOTROPHIC LATERAL SCLEROSIS (ALS)

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PURPLE SQUIRREL ECONOMICS

BACKGROUND

- Amyotrophic lateral sclerosis (ALS), also known as motor neurone disease (MND) and Lou Gehrig's Disease, is a rare degenerative neuromuscular disorder that causes progressive muscle paralysis (Brown, et al. 2017).
- ALS affects both upper and lower motor neurons, which innervate muscle (Zarei, et al. 2015; Brown, et al. 2017).
- ALS typically presents as a slight focal weakness, progressing to neuron degeneration that eventually affects the respiratory muscles, ultimately leading to death through respiratory paralysis (Brown, et al. 2017).
- Over the course of disease, patients experience a range of debilitating symptoms related to the progressive loss of muscle function and control, including impaired movement, breathing, and swallowing (Zarei, et al. 2015; Brown, et al. 2017).
- ALS can be classified as bulbar onset or limb onset (Zarei, et al. 2015; Kuhnlein, et al. 2008), yet diagnosis and classification of ALS is challenged by a lack of definitive tissue area to biopsy and high degree of diagnostic uncertainty (Al-Chalabi, et al. 2016).
- Given the range of symptoms and severe nature of disease, ALS has a high quality of life (QOL) burden on both patients and caregivers (Olsson, et al. 2011; Qutub, et al. 2014).

DISEASE ONSET 50 to 65 Years Old

2015
17,000 PATIENTS WERE DIAGNOSED WITH ALS

ESTIMATED PREVALENCE OF 5.2 PER 100,000 PERSONS

~80% OF PATIENTS DIE WITHIN 5 YEARS OF DIAGNOSIS

(Zarei, et al. 2015; Chio A, et al. 1999; Mehta, et al. 2018)

OBJECTIVE

- We conducted a systematic literature review (SLR) to comprehensively review the relevant evidence on the QOL in ALS patients to further understand the humanistic burden and to encourage future research.

SYSTEMATIC LITERATURE REVIEW

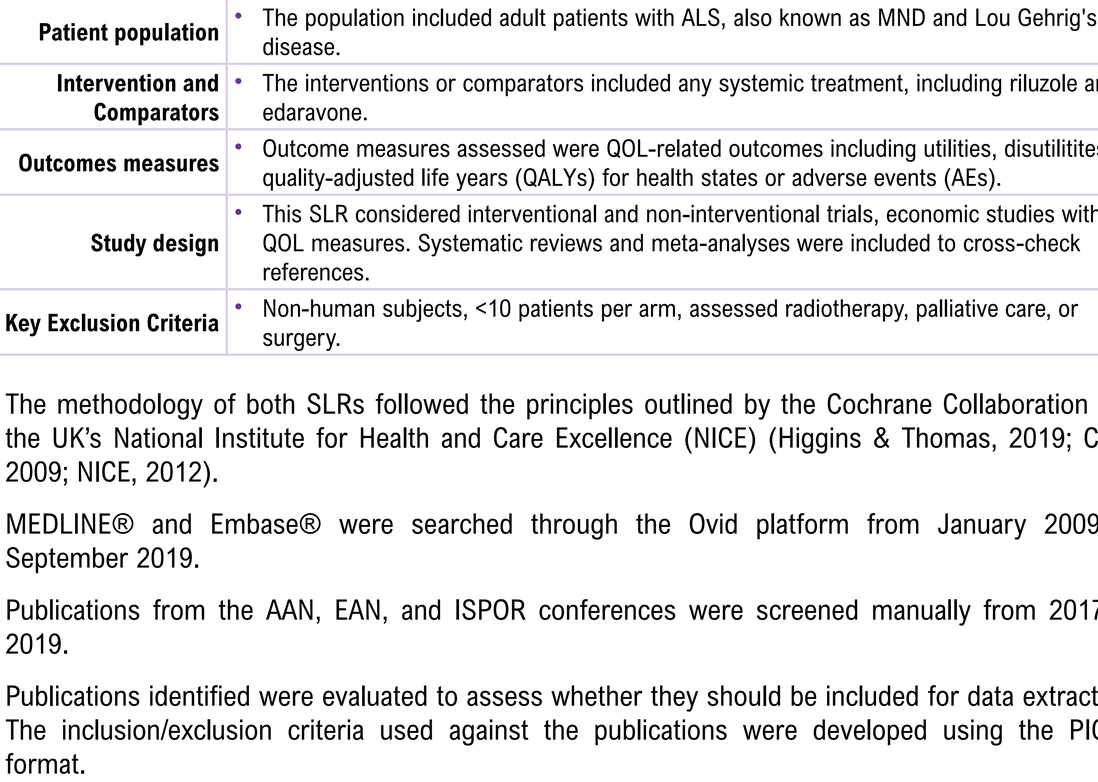
- A QOL SLR following PRISMA guidelines was conducted, with the scope defined in terms of the PICOS criteria (Population, Intervention, Comparators, Outcomes and Study Design).

Table 1: PICOS used in the selection process

PICOS	Inclusion
Patient population	• The population included adult patients with ALS, also known as MND and Lou Gehrig's disease.
Intervention and Comparators	• The interventions or comparators included any systemic treatment, including riluzole and edaravone.
Outcomes measures	• Outcome measures assessed were QOL-related outcomes including utilities, disutilitites, quality-adjusted life years (QALYs) for health states or adverse events (AEs).
Study design	• This SLR considered interventional and non-interventional trials, economic studies with QOL measures. Systematic reviews and meta-analyses were included to cross-check references.
Key Exclusion Criteria	• Non-human subjects, <10 patients per arm, assessed radiotherapy, palliative care, or surgery.

- The methodology of both SLRs followed the principles outlined by the Cochrane Collaboration and the UK's National Institute for Health and Care Excellence (NICE) (Higgins & Thomas, 2019; CRD, 2009; NICE, 2012).
- MEDLINE® and Embase® were searched through the Ovid platform from January 2009 to September 2019.
- Publications from the AAN, EAN, and ISPOR conferences were screened manually from 2017 to 2019.
- Publications identified were evaluated to assess whether they should be included for data extraction. The inclusion/exclusion criteria used against the publications were developed using the PICOS format.
- Data from included studies were extracted into an Excel-based data extraction template.

Figure 1: QOL SLR PRISMA

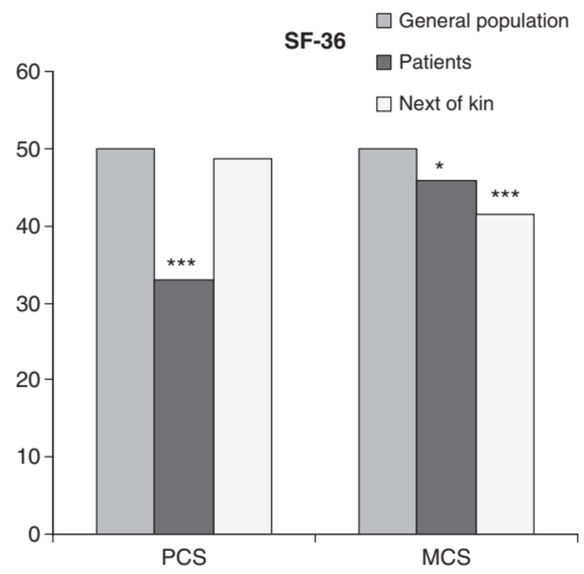


QUALITY OF LIFE RESULTS

- The most frequently reported ALS symptoms included fatigue (up to 90%) (Nicholson, et al. 2018), pain (up to 78%) (Hanisch, et al. 2015), and depression (up to 68%) (Prell, et al. 2019) with fatigue as the most prevalent, bothersome, and undertreated (Nicholson, et al. 2018).
- Other symptoms included progressive muscle weakness, loss of voluntary movement, and difficulty breathing, speaking, and swallowing (Oda, et al. 2016 [abstract]; Mohammad, et al. 2013 [abstract]).
- The average delay between symptom onset and diagnosis was 13 months (Chiò A, et al. 2013).
- ALS patients had significantly worse QOL compared to the general population on the SF-36, which was largely driven by decrements in both physical and mental function as shown in Figure 2 (Olsson Ozanne, et al. 2011; Ilse, et al. 2015).
- Over the course of disease, patients experience declining bodily function and QOL (Martinez-Campo, et al. 2017; Shamshiri, et al. 2016).
- The caregiver burden in ALS is high, with approximately half of caregivers suffering from depression and high levels of burden (48% reporting a ZBI score ≥17) (Qutub, et al. 2014; Lillo, et al. 2012; Galvin, et al. 2016; Sandstedt, et al. 2018).
- While some treatment options such as edaravone, masitinib, non-invasive ventilation, and percutaneous endoscopic gastrostomy can slow the functional and QOL decline in patients with ALS, they do not provide symptomatic or QOL improvements (Tanaka, et al. 2016 [abstract]; Lou, et al. 2010; Vandoorne, et al. 2016; Mora, et al. 2020).
- Other treatment options, such as recombinant human erythropoietin and thalidomide, offer no benefit for patients; as such, there remain limited effective treatment options for patients (Lauria, et al. 2015; Stommel, et al. 2009).

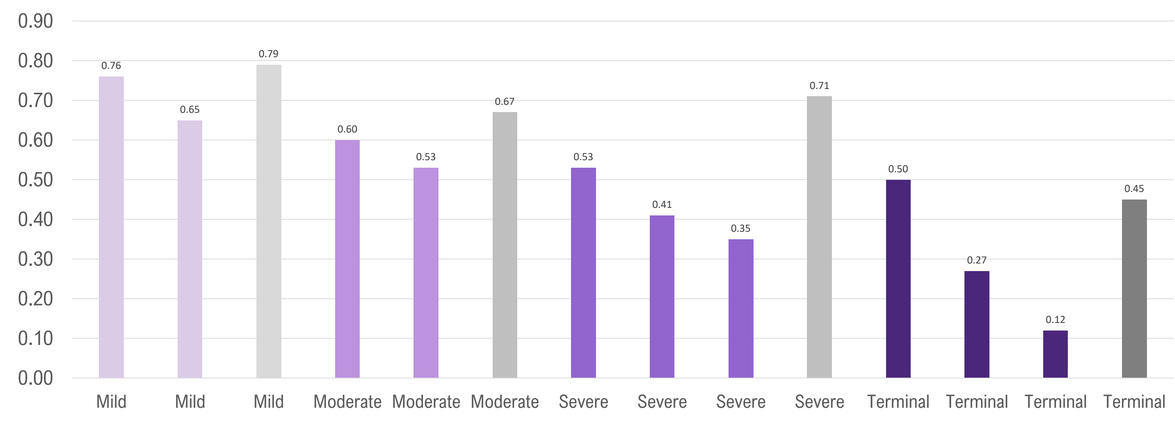
UTILITIES RESULTS

Figure 2: Mean values in the SF-36 in the general Swedish population, ALS patients, and their next of kin (Olsson, et al. 2011)



- Four studies were identified in the SLR that reported utility data stratified by disease severity using the King's staging criteria (mild, moderate, severe, and terminal) (Moore, et al. 2019; Jones, et al. 2014; Lopez-Bastida, et al. 2009; Tavakoli, et al. 2001).
- Utilities were captured with the EQ-5D and standard gamble methods and were separated into the four ALS health states.
- Utility values ranged from 0.79 to 0.65, 0.67 to 0.53, 0.71 to 0.35, and 0.50 to 0.12, across the four health states respectively, demonstrating a severe decline in health-related QOL with increasing disease severity (Figure 3).

Figure 3: Health utility values in ALS by disease severity across the four studies (Moore, et al. 2019; Jones, et al. 2014; Lopez-Bastida, et al. 2009; Tavakoli, et al. 2001)



LIMITATIONS

- One limitation included the heterogeneity of study designs across studies as they were conducted in different countries and settings, which made cross-study comparisons challenging.
- There may be a degree of heterogeneity across the ALS patient populations of different studies, such as age and proportion of females among other baseline characteristics, which could limit cross-study comparison without further adjustment.
- Another limitation is that QOL studies were not assessed for the quality of their design via validated measures.

CONCLUSIONS

- Patients with ALS experience poor QOL and loss of function that deteriorates with disease progression to higher levels of severity.
- The burden of symptoms is high; patients experience various debilitating symptoms, with fatigue, depression, and pain being the most common.
- Caregiver burden is also high, and caregivers experience depression and decrements in QOL.
- Current therapies only slow the decline in QOL and loss of function.
- Published evidence demonstrates a need for novel treatment strategies to alleviate the heavy humanistic burden in ALS.

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