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The wish to die and hastening death in amyotrophic lateral sclerosis: A scoping review

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ABSTRACT

Background Amyotrophic lateral sclerosis (ALS) develops into a life-threatening condition 2 to 4 years after the onset of symptoms. Although many people with the disease decide in favour of life-sustaining measures, thoughts about hastening death are not uncommon.

Objectives Our aim was to examine the scope of literature on the wish to die in ALS and provide an insight into determinants and motives for different end-of-life options.

Methods We searched eight databases for English and German publications on death wishes in ALS for the period from 2008 to 2018 and updated the search up to May 2020. After the screening process, 213 full texts were included for the final analysis. We analysed the texts in MAXQDA, using deductively and inductively generated codes.

Results We identified end-of-life considerations, ranging from wishes to die without hastening death, to options with the possibility or intention of hastening death. Besides physical impairment, especially psychosocial factors, socio-demographic status and socio-cultural context have a great impact on decisions for life-shortening options. There is huge variation in the motives and determinants for end-of-life considerations between individuals, different societies, healthcare and legal systems.

Conclusions For a variety of reasons, the information and counselling provided on different options for sustaining life or hastening death is often incomplete and insufficient. Since the motives and determinants for the wish to hasten death are extremely diverse, healthcare professionals should investigate the reasons, meaning and strength of the desire to die to detect unmet needs and examine which interventions are appropriate in each individual case.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is the most common non-oncological disease in

palliative care.¹ This incurable neurodegenerative disorder leads to progressive weakness and muscle spasticity, problems with mobility, swallowing, speaking and breathing. On average, people with ALS (PALS) die due to respiratory failure 2 to 4 years after the onset of symptoms. However, 5% to 10% of patients live for a decade or longer.² According to different studies, 5% to 50% of PALS develop cognitive dysfunction, ranging from language deficits to frontotemporal dementia with behavioural and functional impairment.^{2–4} Nonetheless, many PALS are able to make decisions until their final days of life. Although there is no curative therapy, PALS have several options for sustaining life, alleviating symptoms, but also for hastening death. This raises various ethical issues, emphasising the need for further research to develop guidelines and training programmes.⁵

The wish to hasten death (WTHD) in people with incurable diseases is challenging for all parties concerned. It has gained increasing attention in publications on palliative care. Nevertheless, Monforte-Royo *et al* demonstrated that there is no consistent definition of the WTHD. The “wish” or “desire to die” and “to hasten death” are used synonymously, general “thoughts of dying” are not differentiated from “a genuine wish to die”, or hastening death, or more specific terms, such as assisted suicide or euthanasia.^{6–8} These differentiations are of practical importance to understanding the diversity of situations these terms relate to and their different clinical, ethical, legal and social implications. Furthermore, clear definitions are crucial to operationalising the WTHD, standardising measuring methods and for the comparability of research, as well as for the development and implementation of interventions in the field of palliative care.^{6,8}



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Balaguer and Monforte-Royo *et al* suggested an international consensus definition of the WTHD in 2016, according to which “[t]he WTHD is a reaction to suffering, in the context of a life-threatening condition, from which the patient can see no way out other than to accelerate his or her death. This wish may be expressed spontaneously or after being asked about it, but it must be distinguished from the acceptance of impending death or from a wish to die naturally, although preferably soon.” They emphasise the multifactorial nature of the WTHD and draw attention to possible key factors: “The WTHD may arise in response to one or more factors, including physical symptoms (either present or foreseen), psychological distress (e.g. depression, hopelessness, fears, etc.), existential suffering (e.g. loss of meaning in life), or social aspects (e.g. feeling that one is a burden).”⁸

While most research on the WTHD has been conducted in patients with cancer,⁶ Ohnsorge *et al* highlight the requirement for more research in non-cancer patients.^{9 10} Our team conducted a scoping review to prepare an empirical research project on preferences and needs of PALS in relation to counselling and provision of information concerning life-sustaining and life-shortening options. To this end, we examined the literature to identify the scope of literature on our subject and existing gaps in knowledge. In this publication we present the results on two selected research questions: What are the main determinants and motives for the WTHD among PALS, and what possible solutions do they consider?

METHODS

Protocol and eligibility criteria

We developed a review protocol, but did not publish it.

Inclusion criteria

- a. Content-related criteria
 - Publications on death wishes and life-shortening measures in ALS (discontinuation of therapy, volun-

tary stopping of eating and drinking, suicide, assisted suicide, euthanasia, palliative sedation).

- b. Sources
 - Original studies, reviews, guidelines, conference abstracts and posters, case reports and comments, editorials, grey literature, newspaper and magazine articles.
- c. Languages
 - German and English.
- d. Year of publication
 - Initially 1998 to May 2018, then changed to 2008 until May 2020.
- e. Origin of publications
 - Worldwide.

We included texts from different countries and cover a 12-year period; approaches toward end-of-life issues may therefore vary over time, between healthcare systems and due to different legal options.

Information sources and search strategy

In order to achieve a comprehensive overview on our topic, we also searched for reviews, guidelines, conference abstracts and posters, case reports and comments, editorials, grey literature, newspaper and magazine articles, in addition to research articles. We selected the following eight databases with adapted algorithms to cover the perspectives of multiple disciplines: PubMed, LIVIVO, Cochrane Library, PsycINFO, CINAHL, CareLit (nursing), BELIT (bioethics) and ProQuest Social Sciences (table 1).

Screening

Excluding duplicates reduced the number of records from 1306 to 1091. Two researchers independently screened the abstracts of a 10% randomised sample to assess the eligibility and

Table 1 Search strategy

Databases	Algorithm	Records 1998 to 2018+2018 to 2020
PubMed PsycINFO	((“amyotrophic lateral sclerosis” (Title/Abstract) OR “motor neuron disease” (Title/Abstract) OR “motor neurone disease” (Title/Abstract) OR “ALS” (Title/Abstract) OR “MND” (Title/Abstract)) AND (“hasten death” OR “hastening death” OR withhold* OR withdraw* OR euthanasia OR suicide OR (“decision-making” AND “end of life”) OR (“palliative care” AND ethics) OR (“mechanical ventilation” AND ethics) OR “advance care planning” OR “advance directives”)) NOT (placebo OR mouse OR rat OR “animal model”))	854+187
LIVIVO – The Search Portal for Life Sciences Cochrane Library CINAHL ProQuest Social Sciences	((“amyotrophic lateral sclerosis” OR “motor neuron disease” OR “motor neurone disease” OR “ALS” OR “MND”) AND (“hasten death” OR “hastening death” OR withhold* OR withdraw* OR euthanasia OR suicide OR (“decision-making” AND “end of life”) OR (“palliative care” AND ethics) OR (“mechanical ventilation” AND ethics) OR “advance care planning” OR “advance directives”)) NOT (placebo OR mouse OR rat OR “animal model”))	314+86
BELIT	(“amyotrophic lateral sclerosis” OR “motor neuron disease” OR “motor neurone disease” OR “MND”)	121+4
CareLit	“Amyotrophe Lateralsklerose” OR “Motoneuronkrankung”	17+18
Total		1306+295 =1601

discussed the differences in their assessments. The full abstract screening process resulted in 722 titles being excluded, with 369 texts remaining.

During the screening process, we noted that palliative care and medical options for PALS have changed considerably over recent years, as have the legal situations in several countries and the ethical debates. As our interest focusses on the current situation, we decided to exclude articles published before 2008 and included the remaining 197 publications for full-text screening.

Data extraction and eligibility assessment

We imported 197 full texts and linked bibliographical data into MAXQDA 2018. Relevant text passages were labelled with codes that we generated deductively and inductively. Thirty-nine texts provided no relevant information and were excluded. After full-text screening, 158 studies remained. In addition, we hand-searched reference lists in reviews and guidelines for further relevant articles, including 15 additional publications. In total, 173 texts were analysed. A search update in

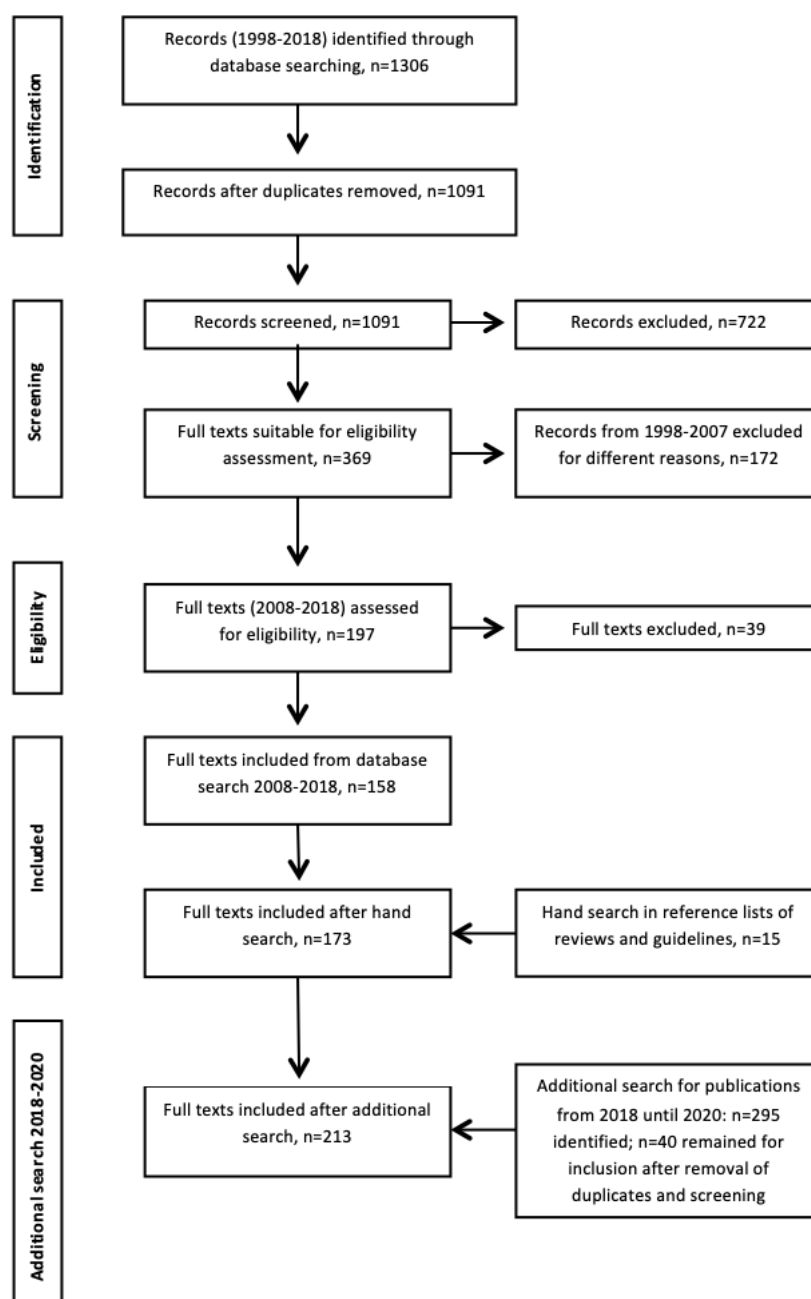


Figure 1 Review process.

Table 2 Overview of text types and study designs included

Text type/study design	Number of articles
Quantitative studies	56
Qualitative studies	39
Mixed methods	9
Reviews	43
Case studies	16
Commented cases	9
Personal experience and case reports	29
Guidelines and guidance	6
Editorials	6
Total	213

May 2020 resulted in 40 additional publications, summing up to 213 texts in total (figure 1 and table 2).

RESULTS

Considerations on end-of-life options in PALS

We identified different wishes and end-of-life considerations in PALS: Wishes to die without hastening death, thoughts on or requests for options with the possibility of hastening death, and options with the intention of hastening death (figure 2).

Wishes to die with and without hastening death

Qualitative studies suggest that the wish to die in PALS is not necessarily linked to the WTHD. The diagnosis can be perceived as a “death sentence”, associated with feelings of being “denied a future”. This can be related to the wish to be dead or “just to disappear”.¹¹ When life is perceived as suffering and enduring, inevitable death can be longed for as relief.^{12–14} A “quick death”

from another cause like a heart attack is sometimes hoped for.^{13 15} The wish to die can coexist with wishes to live and fear of death.^{16 17}

However, most studies do not differentiate between a wish to die and a WTHD, or use these terms interchangeably with suicidal ideation. In a US study, using a modified Patient Health Questionnaire with differentiated items on death wishes, PALS who had “thoughts that [they] would be better off dead” or “thoughts of ending [their] life” were combined, accounting for 19% (n=62) with a wish to die or WTHD.¹⁸ In a smaller Swiss-German study, the participants were surveyed about their current wish “to ask others for assistance” in ending their lives prematurely; the 14% (n=9) PALS who reported such a wish are referred to as participants with an actual WTHD.¹⁹ In a French study using the Columbia Suicide Severity Rating Scale, 18 PALS (25%) had passive suicidal ideation—also referred to as wish to die—and 10 (14%) had suicidal ideation ranging from non-specific thoughts, to suicidal thoughts without intent to act or some intent to act, but without plan.¹⁶

While these studies report a similar prevalence of death wishes, a German study identified only a low average score on the Schedule of Attitudes towards Hastened Death. Although none of the participants had a clinically relevant desire to hasten death, one-third sought information on how to shorten life. Furthermore, two-thirds opined that euthanasia should be allowed.²⁰ Whereas the WTHD remained stable over 13 months in the Swiss-German study,¹⁹ the WTHD decreased over 1 year in the German study, even though study participants faced further physical decline.²⁰ Another study from Poland shows

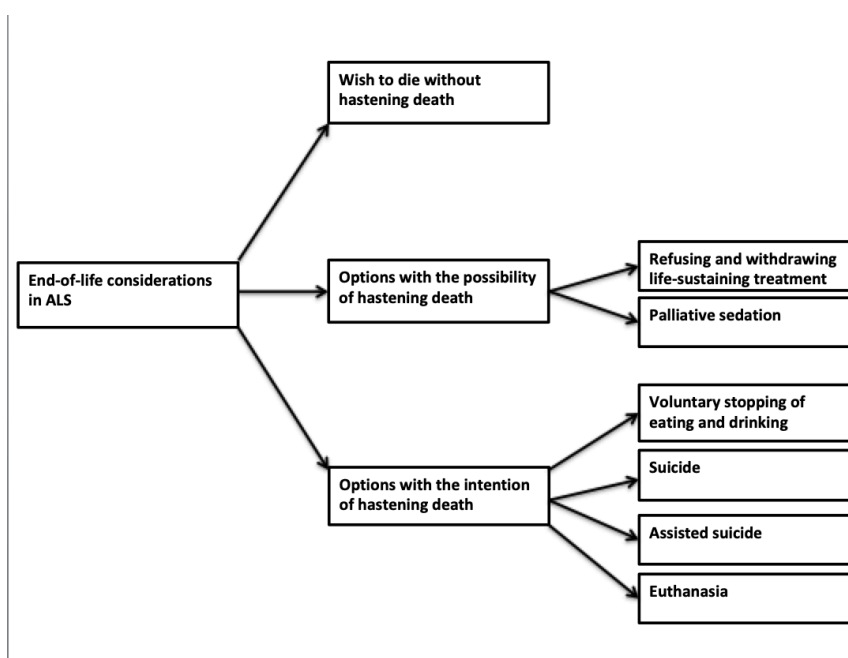


Figure 2 End-of-life considerations in amyotrophic lateral sclerosis (ALS).

similar results: in a sample of 19 PALS, the mean score on the Schedule of Attitudes towards Hastened Death was 4.5, indicating a low desire to hasten death. Only two patients had a clinically relevant WTHD in this sample.^{21 22}

Options with the possibility of hastening death

Although there is no curative therapy for ALS, there are several options for improving quality of life and prolonging life, such as percutaneous endoscopic gastrostomy (PEG), non-invasive ventilation (NIV), or tracheostomy and invasive ventilation (IV). The options of refusing these treatments, requesting their withdrawal, as well as palliative sedation, harbour the potential of hastening death. However, they do not necessarily lead to immediate death and death might not be intended.

Refusing and withdrawing life-sustaining treatment

According to several quantitative studies, PALS are more likely to refuse invasive treatments, like PEG and tracheostomy, than non-invasive treatments, like ventilation via a mask.^{19 23–25} In a Swiss-German study, 75% of PALS considered using NIV in the future, 55% a PEG and only 27% IV. While attitudes in this study remained stable over 13 months,¹⁹ other studies report a change in attitudes in favour of invasive treatments. This has been explained by a “wait-and-see” strategy and a process of adaptation and adjustment of preferences over the course of the disease.²⁰ According to a Japanese study, decisions in favour of treatment resulted from supportive consultations with healthcare professionals, families providing encouragement and an adequate healthcare system.²⁶ However, in a comparative study on Germany, Poland and Sweden, PEG was the most frequent therapy in Sweden, whereas German study participants most commonly chose NIV. Swedish participants had the most positive attitudes towards beginning and ending PEG, NIV and IV, while Polish participants were the most undecided and least likely to consider withdrawal of these measures.²⁷

Decisions to discontinue NIV may evolve over time, but often arise in the context of clinical deterioration, either when infections occur or when progression of gradual functional decline results in an unacceptable life situation.^{28 29} Those who only use NIV overnight or for several hours a day might simply not put the mask on again once they no longer perceive it as advantageous.³⁰ However, when NIV is used as permanent treatment, discontinuation becomes a complex decision.^{11 28}

According to recent guidelines, NIV has become a standard treatment in ALS.^{31 32} In a qualitative Canadian study, PALS saw NIV as an aid to relieving symptoms like dyspnoea, whereas they perceived the decision concerning IV as choice between life and

death.³³ The European Federation of Neurological Societies (EFNS)² now also gives recommendations for the initiation of IV. Nevertheless, the numbers using it vary over time and between countries due to cultural influences, different healthcare systems and legal frameworks: 0% in the UK, 1.4% to 14% in the USA, 3% in Germany, 2% to 5% in France, 10.6% in Northern Italy and 27% to 45% in Japan.^{34 35} An increase in IV has been reported in some regions, for example, 8% in Berlin/Germany and 32% in West Denmark.^{36 37} In France and Switzerland, healthcare professionals tend to discourage tracheotomy.³⁵

It is noteworthy that IV is not always the result of an informed choice.³⁸ There is evidence that IV is performed as an emergency measure³¹ when the decision is still pending,^{26 35 39–41} or even carried out against the declared wishes of the patient, without informing the patient about palliative alternatives.^{42 43} In the context of Advanced Care Planning and do-not-resuscitate orders, there are also several accounts of healthcare professionals disregarding the wish to forgo resuscitation.^{13 44–46}

While the desire to discontinue NIV is often voiced once it is insufficient and IV or palliative care would be the alternatives, decisions to withdraw from IV are highly individual. These often develop over several months or years, but may also appear only few days after starting ventilation.^{36 47} A number of authors have pointed out a need for systematic research and guidance on the process of withdrawing ventilation.^{48–52} They describe emotional, practical and also ethical challenges,^{53–56} especially in distinguishing euthanasia^{11 30 31 57–60} from a termination of ventilation as “letting die”.⁶¹ This can result in not respecting the patient’s wish for discontinuation.⁶² Some practitioners have published their experiences on ventilator-withdrawal,^{36 37 47 49 50 52 56 57} and standards have been established in national contexts in recent years, for example, in the UK and Ireland.^{28 56 63} However, ventilator-withdrawal is not an option for all PALS, since it is regarded as illegal, for example, in Japan and Poland.^{26 27 39}

Palliative sedation

Palliative sedation is recommended as a last resort, with the intention of alleviating symptoms but not hastening death.⁶⁴ Sedation is also used for symptom control in patients who request withdrawal from long-term ventilation, but guidance on this procedure in ALS is still scarce.^{4 36 37 47 50} However, reported cases show that patients perceive palliative sedation as a legal alternative to euthanasia and ask to be put asleep to avoid the experience of further decline.^{64–67}

In a Dutch cohort survey, continuous deep sedation was defined as the intention to sedate without hastening death and differentiated from “intensified alleviation of symptoms”, in which hastening of death

might be accepted. From 2000 to 2005, it was used in 14.8% (n=31) of PALS. However, continuous deep sedation was often combined with intensified alleviation of symptoms or withholding medical treatment, such as nutrition and fluids.⁶⁸ According to a follow-up study, continuous deep sedation is not used as a substitute for euthanasia or assisted suicide in the Netherlands.⁶⁹

Options with the intention of hastening death

Whereas the options described above include the possibility of hastening death, those below involve the intention of causing death.

Voluntary stopping of eating and drinking

Voluntary stopping of eating and drinking is mentioned as one option in assisted dying³⁴ or end-of-life decision-making⁷⁰ for PALS, but not discussed comprehensively in the research literature. Nevertheless, one reported case and a newspaper article demonstrate how patients seek information about voluntary stopping of eating and drinking from experts.^{71 72} It is also presented as an alternative to assisted suicide or euthanasia,⁷³ or as a form of natural death.⁷⁴

Suicide

Although reviews refer to suicide as a rare cause of death in ALS,^{34 75} national surveys have reported a higher risk for PALS compared with people without neurological diseases: a retrospective Danish cohort study on suicide rates from 1980 to 2016 revealed an adjusted incident rate ratio of 4.9 in ALS.⁷⁶ Earlier studies showed a fivefold risk of attempted suicide in PALS in Denmark,⁷⁷ an almost sixfold risk of suicide in Sweden⁷⁸ and a sevenfold risk in Taiwan.⁷⁹ The relative risk of suicide seems higher among younger PALS and during the first year after diagnosis.^{76–79} Qualitative accounts illustrate how the time after diagnosis is perceived as a period of shock, where suicidal thoughts occur.^{13 15 46 80–82} Furthermore, some family caregivers of deceased PALS in a German study reported suicidal thoughts at critical points over the course of the disease.⁸³

Tsai *et al* stress the urgency of suicide prevention right from the time following diagnosis.⁷⁹ An early introduction of palliative care can also lead to a less traumatic disease experience and help with adjusting to loss and feelings of uncertainty.¹⁵ Furthermore health-care professionals should be aware of the psychological distress PALS experience.⁷⁸

PALS describe the timing of suicide as critical in newspaper articles and personal accounts. On the one hand, it is about determining one's own limits in relation to the extent to which life with the disease can be tolerated^{84–86} or appreciated.¹⁷ On the other hand, the option of suicide is no longer available to PALS when paralysis and swallowing difficulties have progressed too far. As with assisted suicide,

where the lethal drug has to be self-administered, there is a risk that PALS decide to commit suicide prematurely to avoid missing the time window for this option.^{17 86–89}

Assisted suicide

In the US states of Oregon⁹⁰ and Washington,⁹¹ PALS are the second most frequent group requesting assisted suicide after patients with cancer. Under the Oregon Death with Dignity Act, 991 people died of assisted suicide between 1998 and 2015, and PALS accounted for 8% (n=79).^{73 90} Finally, PALS take the prescribed lethal substances more often (77.1% compared with 66%).⁹¹

Even if assisted suicide is not legal under national law, its availability and related considerations are not fully excluded. Qualitative studies and reported cases demonstrate how PALS weigh up the reasons for and against assisted suicide at some point in their illness trajectory,^{92–94} or think about travelling abroad to receive suicide assistance.^{55 65 84 86 95 96} Numbers from different Swiss right-to-die organisations indicate that suicide tourism is not uncommon among people with neurological diseases such as ALS.⁹⁷

Euthanasia

The Netherlands are one of the countries where euthanasia and assisted suicide are legal: about 20% of PALS die this way.^{68 69} Compared with other diseases, the proportion of euthanasia and assisted suicide is highest in PALS.⁹⁸ The administration of a lethal drug by a physician (euthanasia) is preferred to assisted suicide, and the likelihood that PALS will seek medical assistance in dying is 10 times higher in the Netherlands than in Oregon.⁷³

End-of-life options and organ donation

According to some case reports and discussions, there are individual patient requests to combine end-of-life options with organ donation, either after withdrawal of life-sustaining treatments or euthanasia.^{59 60 99–101} From the patients' perspective this might be perceived as a meaningful option. However, it must be ensured that the donation is a voluntary act, and the decision to die does not depend on the donation. Discussing the legal and ethical complexity of this issue, van Dijk *et al* also suggest that patients with ALS, multiple sclerosis or Huntington's disease should be informed about the option by patient advocacy organisations.¹⁰¹

Determinants and motives for the WTHD

Concerning the different end-of-life options mentioned above, we identified four main categories representing the determinants and motives for a wish to die or considerations to hasten death in ALS (figure 3): physical impairment, psychosocial factors, socio-demographic status and socio-cultural context.

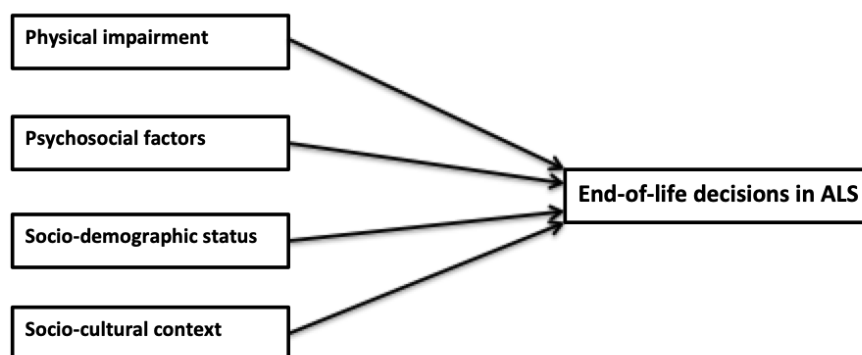


Figure 3 Factors determining end-of-life decisions in amyotrophic lateral sclerosis (ALS).

Physical impairment

Among different physical impairments, the *loss of the ability to communicate* is a strong trigger for the wish to withdraw from therapeutic measures or requests for euthanasia.^{13 15 29 33 49 102} Ophthalmoparesis, which leads to total locked-in syndrome, represents a particular turning point in the course of the disease and sometimes triggers the termination of IV.^{36 37} The *loss of other physical abilities*, such as *moving*,^{26 33} *breathing*^{17 103 104} or *eating*,^{33 100 105} are also relevant factors in the decision-making process. Correlations with higher *pain* scores and *insomnia* were found in cases where a wish for assisted suicide occurred in the last month of life.⁷⁴

Psychosocial factors

According to various authors, psychosocial factors have a greater impact on decisions about life-prolonging or life-shortening options than physical symptoms.^{19 29 74 106} Table 3 gives an overview of psychosocial factors.

Mental health

Cognitive impairment, as such, is not associated with the decision to terminate life-prolonging treatment.²³ Yet, it is often assumed that *depression* is associated with a WTHD.^{29 55 107 108} However, studies yield different, partly contradictory results, as shown in table 4. While there may be a connection between depression and the

Table 3 Psychosocial factors

Psychosocial factors	Authors
<i>Mental health</i>	
Cognitive impairment	23
Depression	16 18–20 24 29 55 57 69 98 100 107–109 140 141
<i>Dependency and loss of control</i>	
Being a burden to family	13 15 29 33 34 88 91 107 110
Dependency	98 111
Autonomy/control	15 75 90 107 112–115
<i>Existential suffering</i>	
Dignity	68 106 114 119
Loss of self	119
Meaning of life	12 32 106 108 109
Suffering	17 101 107 114 115 120
Anxiety	11 13 17–19 24 29 33 55 68 69 71 83 88 98 104 106–108 112 114 115 119 124 135 140
Hopelessness	35 75 107 121
Fatigue	68
Desperation	66
Loneliness, social isolation	19 29 69 75 107
Anger	55
<i>Quality of life</i>	
Quality of life	19 20 24 36 51 69 73 75 90 91 93 94 116 119 122 123
<i>Influences from significant others</i>	
Influences from healthcare professionals	4 26 31 92 119 124–126
Influences from family and friends	24 26 31 106 109 124 127 128
<i>Coping with the disease and experiences with therapy</i>	
Coping style	16 25 129
Experiences with therapy	26 129 130

Table 4 Studies on depression and the WTHD in amyotrophic lateral sclerosis (ALS)

Authors	N *	Depression assessment scale	Assessment scale for the wish to hasten death (WTHD)	Findings
Ganzini L, Goy ER, Dobscha SK 2008	58 (ALS 7)	Hospital Anxiety and Depression Scale Participants reported the influence of depression as a reason for the desire to die on a scale: 1="depression not at all important in the decision to request a lethal prescription" and 5="depression very important in the decision to request a lethal prescription."	The participants estimated their desire to die in the last 2 weeks on a 11-point scale: 0="I desire to live as long as possible" and 10="I have a strong desire to die soon."	Three-quarters of the people who received a lethal drug were not depressed. Six out of 18 who received a lethal drug felt influenced in their decision by depression.
Gourie-Devi M, Gupta R, Sharma V, <i>et al</i> 2017	20	Beck's Depression Inventory	The Scale of Suicidal Ideation and Wish-to-Die Questionnaire	Of five patients who expressed a wish to die, only two had mild-to-moderate depression that did not require treatment.
LeBon B, Fisher S 2011	1	Not specified	Not specified	In this individual case study, the patient who was non-clinically depressed wanted his ventilator to be switched off.
Lulé D, Nonnenmacher S, Sorg S, <i>et al</i> 2014	93	Allgemeine Depressionsskala (German version of the Center for Epidemiologic Studies Depression Scale) range 0–60	Schedule of attitudes towards hastened death range 0–20, with 10 indicating a clinically significant desire for hastened death. A 120-item questionnaire on the status of decision, treatment and determinants of decisions regarding NIV, IV and PEG; including the questions "Did you seek information how to shorten life?" and "Should euthanasia be allowed?" (options: "yes" or "no").	About one-third of the patients (n=35) sought information on how to shorten life and more than two-thirds (n=63) were of the opinion that euthanasia should be allowed. Nonetheless, the desire for hastened death was low and decreased over the 6-month study period, despite declining physical functions. Depression was not a significant predictor of WTHD.
Maessen M, Veldink JH, van den Berg LH, <i>et al</i> 2010	51	Nurses' Observation Scale for Geriatric Patients	Data from the Support and Consultation in Euthanasia in The Netherlands evaluation study plus additional questions answered by the treating physicians on the patients, including depressive symptoms at the time of consultation.	None of the patients who wanted to die were depressed.
Maessen M, Veldink JH, Onwuteaka-Philipsen BD, <i>et al</i> 2014	102	Hospital Anxiety and Depression Scale	Physicians were asked about their end-of-life practices, using descriptive terms from medical practice and avoiding terms like "euthanasia", "physician-assisted suicide" and "sedation". Whereas "intensified alleviation of pain or symptoms while taking into account the possible hastening of death" was subsumed under end-of-life practices, continuous deep sedation was not, because the intention was palliation of otherwise untreatable symptoms and not to hasten death.	No difference in depressive symptoms in the group of patients who explicitly demanded euthanasia and assisted suicide and those who did not.
Rabkin JG, Goetz R, Factor-Litvak P, <i>et al</i> 2015	329	Patient Health Questionnaire	The item on the wish to die was modified into: "thoughts that you'd be better off dead/thoughts about ending your life" and the frequency in the last 4 weeks was measured with four possible answers: "not at all; several days, more than half the days; and nearly every day."	Patients who did not express the wish to die had significantly lower depression values.

Continued

Table 4 Continued

Authors	N *	Depression assessment scale	Assessment scale for the wish to hasten death (WTHD)	Findings
Smith TJ, Vota S, Patel S, <i>et al</i> 2012	2	Not specified	Two ALS patients who requested the withdrawal of life-support measures and organ donation after cardiac death.	Requests for withdrawal and organ donation were not associated with clinical depression.
Stutzki R, Schneider U, Reiter-Theil S, <i>et al</i> 2012	33	Hospital Anxiety and Depression Scale	Numeric rating scale (0–10) regarding the actual WTHD: "How strong is your current desire to ask others for help to end your life prematurely?"; "How distressing or how helpful was it for you to speak about such issues?" Questions regarding life-prolonging measures: "What is your attitude toward the following life-prolonging measures? (a) Tracheotomy; (b) NIV; (c) PEG." Respondents were given four possible answers: "(a) I am not sure; (b) I am absolutely in favour of it; (c) I am in favour of it under certain circumstances; (d) I am against it". Questions regarding hastening death: Two possible answers (yes/no) were given for the questions: "Have you ever thought about committing suicide after receiving your diagnosis?", "Can you imagine a future scenario in which a physician prescribes a fatal drug which you administer yourself?", "Can you imagine a future scenario in which a physician prescribes and administers to you a fatal drug?", "Have you ever discussed suicide with others?", "Would you like to discuss suicide with a physician?".	The Hospital Anxiety and Depression Scale score is a predictor of the desire to discuss suicide with a physician.
Stutzki R, Weber M, Reiter-Theil S, <i>et al</i> 2014	66	Hospital Anxiety and Depression Scale	Numeric rating scale (0–10) regarding the actual WTHD: "How strong is your current wish to ask others for assistance to end your life prematurely?" Questions regarding life-prolonging measures: Participants' attitudes on tracheostomy, NIV and PEG were assessed using four possible answers ("disfavour, favour under certain circumstances, favour generally, uncertain"). Questions regarding hastening death: Two possible answers (yes/no) were given for the questions: "Have you ever thought about committing suicide?", "Can you imagine asking a physician for a prescription to commit suicide?", "Can you imagine asking a physician to administer a lethal medication?", "Have you been under treatment for depression since your ALS diagnosis?", "With whom did you talk about the option to hasten death?", "Have you ever talked about (sic!) someone about the option to hasten death?", "Would you like to talk with a physician about the option to hasten death?".	The WTHD can be predicted based on the degree of depression
Veldink J, Maessen M, Onwuteaka-Philipsen B, <i>et al</i> 2012	/	Not specified	Not specified	No significant difference between ALS patients who requested euthanasia or assisted suicide and patients who did not.

Continued

Table 4 Continued

Authors	N *	Depression assessment scale	Assessment scale for the wish to hasten death (WTHD)	Findings
Verschueren A, Kianimehr G <i>et al</i> 2019	71	Beck's Depression Inventory	Columbia Suicide Severity Rating Scale and Reasons for Living inventory	Patients with suicidal ideation were more likely to be depressed and have greater physical disability. Physical disability and depression were correlated.

ALS, amyotrophic lateral sclerosis; IV, invasive ventilation; NIV, non-invasive ventilation; PEG, percutaneous endoscopic gastrostomy; WTHD, wish to hasten death.

desire to die in individual cases,^{69 109} the majority of studies show that depression does not determine the WTHD.

Dependency and loss of control

Among other psychosocial factors, various authors have mentioned the notion of *being a burden to relatives*,^{13 15 29 33 34 88 91 107 110} *being completely dependent*^{98 111} and *losing autonomy and control over one's own life*^{15 75 90 107 112–115} as relevant factors in decision-making on future therapeutic options. Perceiving one's existence as a burden to family or society can push patients into believing that they have the “honourable” duty” of requesting assisted suicide.⁵⁵ However, Lemoignan and Ells (2008) revealed that positive emotions like love and the will to protect others influenced the decision against hastening death.³³ Some authors indicate that considering assisted suicide is a strategy for retaining control over one's life.^{15 17 34 88} Therefore, PALS should be informed about all options for maintaining control, including withdrawal of life-sustaining options and palliative care. Conversations about death and dying, Advance Care Planning, and advance directives can also facilitate the feeling of being in control.^{15 32 34 116–118} Control over the circumstances of death (place of death, period of calm, privacy and intimacy, pain control) offers a more positive experience of dying.^{11 17}

Existential suffering

Maintaining *dignity*^{68 106 114 119} and *self*¹¹⁹ as well as *meaning and significance in one's life*^{12 32 106 108 109} are further variables that influence the decision for or against therapeutic options. PALS also fear a condition of intolerable *suffering*.^{17 101 107 114 115 120} This suffering presents as strong emotions, especially

anxiety,^{17–19 24 29 33 55 69 83 98 114 115} *hopelessness*,^{35 75 107 121} *fatigue*,⁶⁸ *desperation*,⁶⁶ *loneliness*^{19 69 75 107} and *anger*.⁵⁵

Table 5 specifies various aspects of anxiety.

Quality of life

In a number of studies, *quality of life* is presented as a significant criterion for end-of-life decisions in ALS,^{19 24} but the theoretical constructs of quality of life referred to different indicators. Some authors reported physical factors, such as mobility,^{69 119} the ability to breathe independently⁹⁴ or a general loss of function,³⁶ as relevant to quality of life; others described the difficulty of everyday activities,¹⁰³ or the loss of enjoyable activities,^{73 90 91} as relevant motives. Emotions,⁶⁹ as well as life satisfaction or subjective well-being,²⁰ are further indicators used to assess quality of life. The results on the association between quality of life and the WTHD are therefore ambiguous and depend on how quality of life is defined and measured. However, a subjectively reported poor quality of life seems to be an important factor, which is reflected in numerous publications.^{51 75 93 94 116 122 123}

Influences from significant others

The influence exerted by *healthcare professionals* is also relevant to decisions taken by PALS.^{4 26 31 124 125} Physicians' attitudes towards medical measures and end-of-life practices may influence the information given and their application. For instance, Thurn *et al* (2019) showed that physicians are more likely to inform about foregoing artificial nutrition, hydration and continuous deep sedation, as well as performing euthanasia and continuous deep sedation, when the patient has a short-term prognosis. By contrast, existential suffering was associated negatively with performing continuous deep sedation, but positively

Table 5 Aspects of anxiety in amyotrophic lateral sclerosis (ALS)

Aspects of anxiety	Authors
Anxiety, not specified, as predictor or reason for the wish to die	18 19 24 69 83 98
Fear of choking and suffocation	29 33 55 68 71 98 106 108 115 135 140
Fear of dying	11 33 104 106 113 124
Fear of an uncertain future with probably unbearable suffering and disability	13 17 74 88 107 112 114 115
Fear of life-prolonging interventions, for example, non-invasive ventilation	119

with ventilator withdrawal. Religious physicians were more reluctant towards palliative end-of-life practices and physician-assisted dying, while palliative care physicians were more receptive towards palliative end-of-life practices. Most physicians had a reactive rather than proactive attitude towards end-of-life decisions, which may result in a delayed discussion of relevant issues.¹²⁶ Maessen *et al* (2014) stated that, apart from individual cases, patients who desired assisted suicide were not less satisfied with their healthcare than those who did not.⁶⁹ However, a Japanese study reports that decision-making for or against IV depends on factors including the information, attitude and influence of healthcare professionals.²⁶ A qualitative study from the UK illustrates how a patient felt restricted in his autonomy by the ongoing attempts of hospital staff to convince him to accept NIV; instead, he simply wanted to be left alone.¹¹⁹ A qualitative study by Foley *et al* (2014) also reveals a lack of respect for patient autonomy. This patient complained that physicians started PEG-feeding and NIV before he had been given enough time to think about it.⁹²

Relatives and friends also contribute significantly towards decisions taken at the end of life.^{26 31 125} While the social support provided by family and friends can have protective effects with regard to a possible WTHD, their absence can have opposite effects.¹⁰⁹ For some patients, the family represents a personal value worth living for.^{124 127} The status of *parenthood* seems to have a protective influence on decision-making: some patients with children are more willing to take life-prolonging measures,¹²⁸ are less able to accept their own deaths and want to limit the effects of the disease on their children.¹¹ The probability that they wish to discuss suicide with a physician apparently decreases with the number of children.²⁴ Awareness of the importance of children, even if life otherwise appears meaningless, can be a strong motivator to carry on living.¹⁰⁶

Coping with the disease and experiences with therapy

Another psychosocial factor is an adaptive, flexible *coping style*, which is related to a desire for life,¹²⁹ and can function as a protective factor.¹⁶ Nonetheless, Martin *et al* (2014) report that PALS (n=78) who refused PEG or NIV take a more active approach to their disease management; they are more likely to seek information and less likely to accept recommendations from healthcare professionals unquestioned.²⁵

Negative experiences with therapy can lead to its discontinuation. In particular, some patients tolerate NIV poorly. The mask is experienced as alien; some patients feel trapped or more ill than they are. The “claustrophobic nature” of the mask creates fear¹³⁰ and insecurity.¹²⁹ Resistance to IV can also result in discontinuation of therapy.²⁶

Socio-demographic status

With regard to socio-demographic status, only education, age and gender are of importance. PALS with a higher educational level are more likely to actively make end-of-life decisions: Martin *et al* (2014) report that well-educated patients are more likely to decide in favour of NIV or PEG.²⁵ Moreover, long-term ventilation and assisted suicide also tend to be chosen by well-educated patients.^{68 91 131 132}

There are gender-specific differences in requests for assisted suicide. Men are more likely to consider or choose assisted suicide,^{83 91} but are also more likely to undergo tracheotomy and invasive ventilation.³¹ Invasive ventilation is chosen more often by married patients.³¹ However, gender seems to have no influence on the probability of withdrawing from therapy.³⁶

The significance of age is ambiguous. On the one hand, Fang *et al* (2008) revealed that patients who committed suicide after diagnosis were younger than those who did not. Younger patients have more years to lose which seems to cause greater distress.⁷⁸ On the other hand, people who chose IV were younger than those who refused ventilation.^{11 31} Older patients are more likely to accept their death.¹¹

Socio-cultural context

Regarding the socio-cultural context, we identified the following factors: *religiosity*, *spirituality*, the *values* of those affected, *the public debate* and *media coverage*, specific characteristics of *the national context* as *state legislation* and *the financial coverage of costs by the healthcare system*.

Religious patients tend to make less use of life-sustaining measures. Death is accepted as inevitable and understood as God's will.^{109 133} Patients with a higher degree of spirituality have more hopes and less worries about their own death¹²¹ and religious patients are less likely to choose (assisted) suicide or euthanasia as a way to limit their suffering.^{19 24 27 34 68 91 109 121 132} Conservatism has an equivalent effect, representing traditional values like conformity, self-restriction, orderliness and reluctance to change.²⁷

Reports on other cultural factors are relatively rare. Some authors mention variation in the use of ventilation within different states, cultures and ethnic groups.^{4 34 63} Cheng *et al* (2019) emphasise the cultural influence in end-of-life discussions, for example, on Advance Care Planning and the role of the family in decision-making processes in view of Chinese culture.¹³⁴ Some authors argue that *media reports* produce a distorted, rather negative picture of quality of life in late-stage ALS, which can provoke, for example, patients' fear of suffocation.^{135 136} The “cruelty” and “unworthiness” of the condition of PALS is used as an argument for euthanasia and “dignified” dying is presented as desirable.¹²⁴ The euphemistic terms “physician-assisted” and “death with dignity” used in *public debate*

generate implicit, possibly misleading assumptions that are intended to legitimise such practices.⁸⁸

Depending on the *national context*, the legal and the healthcare systems are also relevant factors when deciding for or against life-prolonging options. Some authors caution against liberal legislation on assisted suicide and euthanasia as for example in the Netherlands,^{68 69} because it might strengthen prejudice on a presumed low quality of life in the future or misconceptions and fears about the future.^{88 125} However, Maessen *et al* (2014) found no association between the quality of life and requests for assisted suicide or euthanasia.⁶⁹ In Japan, where it is illegal to discontinue IV once started, neurologists assume that this is a reason for refusing it.^{31 39}

Concerning the financial coverage by the healthcare system in different societies, the extremely cost-intensive care, particularly of ventilated patients is not, or insufficiently, financed in some countries.^{31 63 123 137} A nursing shortage, lack of a family caregiver and associated financial aspects may lead to the decision to withdraw from IV or to forego ventilation in the first place.^{71 138 139} Studies from Washington and Oregon show, however, that personal financial considerations were less common reasons for the WTHD.⁹¹

DISCUSSION

Distinctions between different wishes to die are required

Our review provides an overview of different end-of-life considerations in PALS and their motivations and determinants, which are relevant to end-of-life decision-making. Although some qualitative studies indicate that there are a variety of wishes to die, most studies make no clear distinction between an actual or hypothetical wish to die with or without hastening death. This is consistent with the findings of the non-disease specific review on the WTHD conducted by Monforte-Royo *et al*.⁶ The authors describe the WTHD as a reactive phenomenon to suffering that may be of fluctuating or ambivalent in nature,⁸ and vary over time.⁷ A request to hasten death does not necessarily correspond to a genuine wish to die, as it can coexist with a desire to live, for example, when life is favoured, but not in its present form.⁷ Ohnsorge *et al* confirmed that the wish to die can exist simultaneously with wishes to live.^{9 10} Our findings corroborate that the WTHD or the need for information about options with the possibility of hastening death, for example, voluntary stopping of eating and drinking and palliative sedation, are a reactive phenomenon to (anticipated) suffering. A few studies reported conflicting results on the stability of the WTHD in PALS.^{19 20} Although there is evidence in the literature on PALS that the availability of the option of assisted dying is a means to maintain control, none of the studies elaborated on whether the WTHD or the wish to die coexists with wishes to live.

Most studies we examined were conducted before the international consensus definition of the WTHD was published by Balaguer *et al* in 2016. For future research, a uniform definition of the WTHD would be important for a differentiated understanding of various end-of-life options and the comparability of research.

Uniform assessment tools are needed for research

Concerning the determinants and motives of the WTHD, we identified physical impairment, psychosocial factors, socio-demographic status of patients and their socio-cultural context as significant influences. These factors vary greatly between individuals, different social contexts and healthcare or legal systems. Since not all factors we identified were investigated in a single study, our review provides only limited information on the most frequent motives of PALS for the WTHD. This shortcoming has been reported in quantitative studies on the WTHD in general, because the phenomenon in question is reduced to only a few preselected variables as factors for determinants and motives.⁷ Only few authors compare different factors and measure the strengths of their impact on the decision-making process. For example, Stutzki *et al* (2014) identified loneliness, anxiety, the feeling of being a burden to others, depression and a low quality of life as significant predictors for a current WTHD. Furthermore, PALS with low levels of religiosity were more likely to consider assisted suicide or euthanasia.¹⁹ Maessen *et al* (2010) identified, in comparison to patients with cancer, predictors of unbearable suffering and an associated desire for euthanasia or assisted suicide as (1) fear of suffocation, (2) dependency and (3) limited communication.⁹⁸ Although the results from the two studies seem different, there are clear content-related interconnections. A limited ability to communicate increases the risk of loneliness, the feeling of dependency can create a feeling of being a burden to others and the fear of suffocation is one aspect of anxiety. Therefore, we can assume that these factors are very important for the WTHD or the desire to withdraw from therapy. The extent to which depression is a significant factor remains unclear, because results are contradictory. For a more accurate assessment of the relationship between depression and the WTHD, the conduct of a transnational study is recommended, with a larger sample size, uniform assessments and the same data collection points over the course of the disease. Because there is also a lack of research concerning the determinants and motives for or against a WTHD in different cultures and ethnic groups, further studies on these topics are required.

Impact of psychosocial factors and the broader socio-cultural context

The international consensus definition of the WTHD⁸ focusses on physical symptoms, psychological distress, existential suffering and on social aspects in the sense of

feelings of being a burden to others. This corresponds well with our results, in that psychosocial factors, in particular, have a great impact on decisions in favour of life-shortening measures. However, according to our findings, the broader socio-cultural context and socio-demographic status are also of importance. In particular, the immense variation in use of IV between countries^{4 34 35} suggests differences, not only on an individual level. On the one hand, positive attitudes and a decision in favour of IV are related to an adequate healthcare system, support and information provided by healthcare professionals and supporting attitudes of families.^{26 34} On the other hand, an inadequate healthcare system or lack of financial coverage, as well as the absence of legal options to discontinue treatment, seem to influence decisions.^{39 63 123 137} Media reports are referred to as distributing negative images of ventilation;¹²⁴ and cultural or social values also seem to play a role, although these aspects remain rather vague in the studies we examined.^{4 63 134} Furthermore, negative attitudes of healthcare professionals towards certain therapies are reported to influence the way information is provided,^{63 124 127} thus indirectly undermining patient autonomy.

Ethical issues

From an ethical perspective, this reveals a highly problematic aspect: PALS are not always provided with sufficient or adequately presented information and counselling about treatment options and the possibility of discontinuing treatment. This is partly due to attitudes, but also prejudices, of healthcare professionals^{124 126 127} and to social and legal conditions. For example, Matuz revealed that some physicians in Germany avoid communication about IV, because they assume a negative quality of life, and fear ethical conflicts or legal consequences if patients request withdrawal from IV.¹²⁴ This underlines the fact that healthcare professionals must be aware of their personal judgements and reactions to patient requests, especially in end-of-life discussions.⁸⁹ Mattulat refers to another German study from 2003, which showed that 81% of invasively ventilated patients had not been informed about the pros and cons of mechanical ventilation before they were tracheotomised, and only 29% were given the opportunity of discussing the end-of-life phase with their physicians.¹¹⁶ Therefore, at least sometimes, PALS are not given the basic information needed to make an informed decision about end-of-life issues, resulting in a disrespect of their autonomy and a lack of required support.

LIMITATIONS

This scoping review is limited to English and German publications. We may have therefore missed relevant literature in other languages. As we started the period of analysis in 2008, our results are based on the current situation; we cannot trace what impact

changes in the legal situation, ethical debates in some countries, the publication of guidelines and changes in palliative care, and medical options might have had. Furthermore, for a comprehensive overview of our topic, we also included non-scientific sources. Therefore, the fact that the publications differ regarding their evidence level must be considered.

CONCLUSIONS

The existing research suggests that the WTHD in ALS occurs in the early illness trajectory and at crucial points over the course of the disease, when certain functions and abilities are lost. While some studies report a stable WTHD, others show that the WTHD diminishes during the coping process. Suicide, assisted suicide and euthanasia are options many PALS at least consider and seek information about at some point. For a variety of reasons, counselling on these options is incomprehensive and insufficient. Therefore, suicide prevention and assistance in the coping process should be provided, in particular during the first year after diagnosis, but must also be available thereafter during decision-making about treatment options. The motives and determinants of PALS for the WTHD are extremely diverse in terms of their content, their regional or cultural background and their occurrence during the disease trajectory. Hence, healthcare professionals should investigate the reasons, meaning and strength of the desire to die to detect unmet needs and examine which alternatives or offers of interventions and counselling are appropriate in each individual case.

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