

ORIGINAL ARTICLE

## A European survey on attitudes towards pain and end-of-life issues in locked-in syndrome

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### Abstract

**Objectives:** Patients with locked-in syndrome often self-report a higher quality of life than generally expected. This study reports third-person attitudes towards several salient issues on locked-in syndrome.

**Methods:** Close-ended survey among conference attendees from 33 European countries. Analysis included chi-square tests and logistic regressions.

**Results:** From the 3332 respondents (33% physicians, 18% other clinicians, 49% other professions; 47% religious), 90% agreed that patients with locked-in syndrome can feel pain. The majority (75%) disagreed with treatment withdrawal, but 56% did not wish to be kept alive if they imagined themselves in this condition ( $p < 0.001$ ). Religious and southern Europeans opposed to treatment withdrawal more often than non-religious ( $p < 0.001$ ) and participants from the North ( $p = 0.001$ ). When the locked-in syndrome was compared to disorders of consciousness, more respondents endorsed that being in a chronic locked-in syndrome was worse than being in a vegetative state or minimally conscious state for patients (59%) than they thought for families (40%,  $p < 0.001$ ).

**Conclusions:** Personal characteristics mediate opinions about locked-in syndrome. The dissociation between personal preferences and general opinions underlie the difference in perspective in disability. Ethical responses to dilemmas involving patients with locked-in syndrome should consider the diverging ethical attitudes of stakeholders.

### Keywords

Attitudes, family, locked-in syndrome, minimally conscious state, pain perception, survey, vegetative state/unresponsive wakefulness syndrome

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### Introduction

Locked-in syndrome (LIS) is a medically rare acquired state characterized by severe motor disability usually with preserved non-verbal capacity to communicate [1]. Based on patients' motor abilities, LIS can be sub-divided into *classic*, which describes tetraplegic and aphonic patients using coded communication by vertical eye movement or blinking; *incomplete*, wherein patients have remnants of more voluntary movements other than oculomotor ones; and *total* LIS, which refers to patients with complete motor immobility, including eye movements [2]. Especially for total LIS, the clinical identification of signs of awareness is not always easy and in many cases it requires the aid of para-clinical tools, such as event-related potentials [3]. This implies a marked risk of misdiagnosing these patients as unconscious [4]. For example, LIS can be misdiagnosed as a vegetative state (VS)

[5] or as recently coined 'unresponsive wakefulness syndrome' (UWS) [6] wherein patients are awake but show only reflexive movements. Another clinical entity of consciousness is the minimally conscious state (MCS). MCS refers to patients showing non-reflexive movements (e.g. visual pursuit of a mirror for 45° without loss of fixation on two occasions in any direction while the mirror moves slowly to the right and left of the vertical midline above and below the horizontal midline) [7] and/or the ability to reproducibly follow simple commands but remain incapable of functional communication [8].

As it is immediately evident, independent and physical function in LIS are severely constrained. For healthy individuals, such limitations in daily living may appear as a frightening scenario which leads to questions of whether a 'life is worth living' after severe brain injury [9]. This is mainly due to an estimated lower quality of life which is tightly linked to severe disability. Broadly speaking, quality-of-life estimations are made by comparing the patient's expectations of health with his or her experience of it [10]. When quality-of-life instruments are used to assess health and wellbeing of people with disabilities, they relate primarily to physical functioning and capability, although many

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quality-of-life scales also consider mental or emotional dimensions of experience [11]. Therefore, if quality of life is based on the perceived value of physical and mental functioning, it is possible that healthy subjects under-estimate patients with chronic disability. Indeed, studies show that, when partners or caregivers rate patients' quality of life, the scores are significantly lower than when patients do it for themselves [12–17]. In light of their severe disability, patients' higher self-ratings on quality of life measures is mostly known as the 'disability paradox' [18]. Such 'paradoxical' reports are suggested to be the result of different perspectives of perceived quality-of-life which, for patients, often equates more with social interaction rather than physical independent function [19] or even occupation and financial status [15]. Taken together, this kind of evidence contradicts the widespread opinion that patients with severe physical impairment inevitably suffer from depression and hopelessness and express wishes to shorten their lives [20].

Provided that opinions about quality of life of patients in LIS differ between clinicians and patients themselves, this study aims to identify the attitudes of different stakeholders towards several issues in LIS, namely attitudes towards pain perception, limitation of life-sustaining treatment and comparison of severity of LIS with that of patients with disorders of consciousness.

## Methods

Data were collected via a questionnaire (Online Supplementary Table I) which was designed following the rationale of previous surveys on attitudes as conducted by Jennett [21] and Zeman [22]. The questionnaire was distributed during presentations at medical and scientific conferences and meetings ( $n=59$ ) across Europe between September 2007 and October 2009, such as the congresses of the International Brain Injury Association (Lisbon 2008) and European Neurological Society (Nice 2008). Data were collected partly by participant's handwritten responses and partly on computerized paper-forms.

To ensure comparability of responses, participants were first introduced to the clinical definition of LIS and of disorders of consciousness and were then asked to provide yes/no responses to 16 questions related to these conditions. The presentations did not describe LIS and disorders of consciousness in detail, nor did they refer to rare but interesting case studies that may have influenced the respondents' beliefs regarding these states. Demographic data referring to age, gender, profession, nationality and religiosity were recorded. This study here reports the replies obtained from European physicians, other clinicians and other conference attendants to the questions: 'Do you think that patients in a LIS can feel pain?'; 'Do you think that treatment can be stopped in patients in chronic LIS?'; 'Would you like to be kept alive if you were in chronic LIS?' As LIS can be often misdiagnosed for a disorder of consciousness, the authors were also interested in how participants perceive it in comparison with these conditions. Therefore, the item 'Being in a chronic LIS is worse than being in a VS or in a MCS for the family/for the patient?' was included. The remaining

questions related to consciousness, pain and end-of-life issues in disorders of consciousness have been reported before [23–26]. Major responses on these items are summarized in Online Supplementary Table I. Nationalities were first categorized into European and non-European respondents. For European respondents, there was a further classification into three geographic regions across Europe based on previous criteria [27]: North (Belarus, Denmark, Finland, Germany, Ireland, Lithuania, Netherlands, Norway, Poland, Sweden, UK), Central (Austria, Belgium, Bosnia, Czech Republic, Hungary, Luxembourg, Romania, Serbia, Slovakia, Slovenia, Switzerland) and South (Albania, Bulgaria, Croatia, Cyprus, France, Greece, Italy, Malta, Portugal, Spain, the former Yugoslav Republic of Macedonia). Religiosity was defined as the belief in a personal God belonging to an institutionalized religion (e.g. Christianity, Islam, Judaism) independently of practicing.

Statistical analyses were performed using SPSS v.20 software package. Chi-square tests assessed differences within and between categorical variables. Multivariate logistic regressions (method: enter) were used to examine and test the associations of the odds for agreement with the questions with four predictor variables (age, gender, European region, profession and religiosity). 'Northern' Europe was set as a reference category for European region based on previous findings that withholding and withdrawing therapy in the intensive care unit (than using cardiopulmonary resuscitation) was most common in northern countries [27]. In that respect, it was interesting to see how much respondents from the other two European regions agreed with the attitudes of northern Europeans concerning treatment limitation in locked-in syndrome. Additionally, 'physicians' were selected as the reference category for professional background because physicians are critically involved in decisions about their patients (pain management, options for euthanasia). As such, the interest was in estimating the consent or deviation from medically-based opinions. The outcome variable was the dichotomy 'agreement' vs. 'disagreement'. Results were considered significant at  $p<0.05$  (two-sided). The study was approved by the ethics committee of the University of Liège. Completion of the questionnaire was voluntary, anonymous and was considered as consent for participation in the survey.

## Results

In total, 4410 records were collected. The sample was comprised of European respondents ( $n=3684$ , 84%), non-European respondents ( $n=415$ , 9%) and respondents of unknown nationality ( $n=311$ , 7%). It was decided to restrict the analysis only to the group of European respondents due to unequal group sizes between Europeans and non-Europeans (as a result of attending mainly European conferences) and because ethical issues in medicine are sufficiently distinct between Europe and other world regions. From this sample, records with missing data for age ( $n=121$ ), gender ( $n=81$ ) and profession ( $n=150$ ) were discarded. The final study sample included 3332 physicians, other clinicians and other professionals coming from 33 European countries (see Table I for demographic data).

Table I. Demographics of survey participants ( $n = 3332$ ).

Age (years), mean $\pm$ SD (range)	35 $\pm$ 16 (14–88)
Gender, $n$ (%)	
Women	1903 (57%)
Men	1429 (43%)
Profession, $n$ (%)	
Physicians <sup>1</sup>	1110 (33%)
Other clinicians <sup>2</sup>	600 (18%)
Other professionals <sup>3</sup>	1622 (49%)
Religiosity, $n$ (%)	
Religious respondents	1582 (47%)
Non-religious respondents	1585 (47%)
Missing data	165 (6%)
European geographic region	
North	590 (18%)
Central	1614 (48%)
South	1115 (33%)
Missing data	13 (1%)

<sup>1</sup>Sample mainly comprised of neurologists (35%), psychiatrists (13%), physicians who did not specify their background (37%) and physicians of other medical disciplines (15%).

<sup>2</sup>Sample mainly comprised of psychologists (28%), nurses (25%), speech therapists (14%), physical therapists (12%) and other disciplines (21%).

<sup>3</sup>Sample mainly comprised of university students (57%), school pupils (15%), researchers/scientists (5%) and others who did not specify their background (23%).

Table II. Descriptive data of responses to the questionnaire items concerning attitudes towards locked-in syndrome (LIS;  $n = 3332$ ).

Item	Response	Frequency (%)
Do you think that patients in a LIS can feel pain?	Yes	2995 (90%)
	No	292 (9%)
	Missing data	45 (1%)
Do you think that treatment can be stopped in patients in chronic LIS?	Yes	789 (24%)
	No	2473 (74%)
	Missing data	70 (2%)
Would you like to be kept alive if you were in chronic LIS?	Yes	1412 (42%)
	No	1825 (55%)
	Missing data	95 (3%)
Being in a chronic (i.e. > 1 year) in LIS is worse than being in a VS or in a MCS for the family?	Yes	1333 (40%)
	No	1875 (56%)
	Missing data	124 (4%)
Being in a chronic (i.e. > 1 year) in LIS is worse than being in a VS or in a MCS for the patient?	Yes	1963 (59%)
	No	1258 (38%)
	Missing data	111 (3%)

As a whole, the vast majority (90%) agreed that patients in LIS can feel pain (Table II). Logistic regression analysis showed that professional background and European region were the variables that best explained the data variance. More specifically, other professionals (compared to physicians; Figure 1) and respondents from Central Europe (compared to Northern European respondents) agreed less with the statement that patients in LIS feel pain (Table III). Among those who negated pain perception (9%), the majority were students and pupils ( $n = 175$ , 60%) but also physicians ( $n = 81$ , 28%) and other clinicians ( $n = 36$ , 12%).

In terms of attitudes towards end-of-life issues, the majority of respondents (74%) opposed to treatment withdrawal from patients in a chronic LIS (Table II).

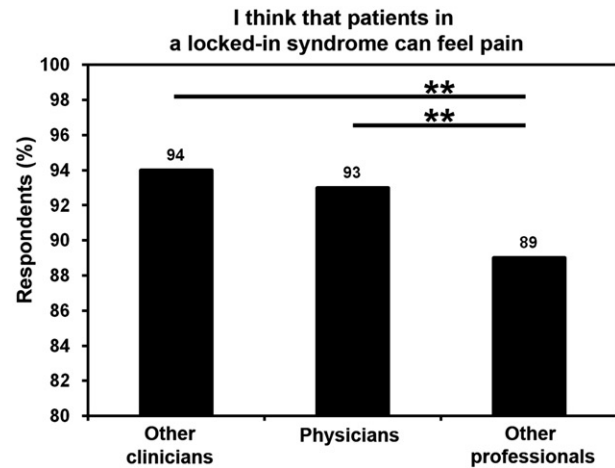


Figure 1. Professional background mediates opinions about pain perception in locked-in syndrome (LIS). Pain perception in patients in LIS was supported mostly by other clinicians (e.g. psychologists, nurses) and physicians (e.g. neurologists, psychiatrists). Fewer professionals of a background other than healthcare-related (e.g. students, engineers) recognized pain perception in patients in LIS (\*\* $p < 0.001$ ).

Southern Europeans and religious respondents disagreed more with treatment withdrawal compared to Northern and non-religious respondents, respectively (Figure 2; Table III). When the end-of-life question was addressed personally, there was dissociation between general and personal preferences: more participants wished to end their lives if they imagined themselves in a chronic LIS (Figure 3). Those who wished to die were mainly other clinicians, Central and Southern Europeans and women. On the contrary, religious respondents had higher chances to express wishes to be kept alive when compared to non-religious (Table III).

More of respondents endorsed that being in a chronic LIS was worse than VS or MCS for patients (59%) than they thought for the families (40%,  $p < 0.001$ ).

## Discussion

This study reports results of a close-ended survey of European physicians, other clinicians and other professionals on questions regarding the LIS. The aim was to describe third-person attitudes towards pain and end-of-life issues in patients in LIS and determine the underlying characteristics which mediate opinions. Initially, it was found that a vast majority (90%) considered that patients in LIS feel pain, which is in accordance with what patients self-report [15, 19, 20, 28]. Nevertheless, 9% of respondents negated pain perception in patients in LIS. Although the majority (60%) of those who did not recognize pain perception was of other professional background, 28% were physicians. For the other professionals, reduced exposure to LIS can account for their misconception of pain perception in this condition. Indeed, misunderstandings around LIS are frequent [29], possibly because the syndrome is rare. However, public information can be fraught with misconceptions even for more better known conditions, such as the VS [30]. Interestingly here, when LIS was compared to disorders of consciousness, participants considered LIS to be worse than being in a VS or MCS, but more so for the patient (59%) than for the families

Table III. Logistic regression analyses (method: enter) of agreement with the questionnaire items concerning locked-in syndrome (LIS) on participants' personal characteristics (predictor variables).

Predictor variable	I think patients in a LIS feel pain (Odds ratio, 95% CI)	I think that treatment can be stopped in patients in chronic LIS (Odds ratio, 95% CI)	I would like to be kept alive if I were in chronic LIS (Odds ratio, 95% CI)
Age <sup>1</sup>	0.99 (0.98–1.00)	1.00 (0.99–1.00)	1.00 (0.99–1.00)
Women	1.02 (0.79–1.33)	0.96 (0.80–1.15)	0.85 (0.72–0.99)*
North Europe	1	1	1
Central Europe	0.67 (0.46–0.99)*	1.12 (0.89–1.41)	0.72 (0.59–0.89)*
South Europe	0.73 (0.49–1.10)	0.65 (0.50–0.84)**	0.72 (0.58–0.90)*
Physicians	1	1	1
Other clinicians	1.08 (0.70–1.66)	1.03 (0.78–1.34)	0.79 (0.63–0.99)*
Other professionals	0.58 (0.42–0.81)**	1.30 (1.03–1.63)*	1.13 (0.93–1.36)
Religious	1.10 (0.85–1.41)	0.50 (0.42–0.60)**	1.69 (1.46–1.96)**

Predicted response: 'agreement'. An odds ratio higher than 1 signifies more agreement with the statement, whereas an odds ratio less than 1 notifies less agreement (\* $p < 0.05$ , \*\* $p < 0.001$ ).

<sup>1</sup>Continuous variable: the odds ratio equals the relative change in the odds ratio when the variable is increased by one unit. LIS, locked-in syndrome; CI, confidence interval.

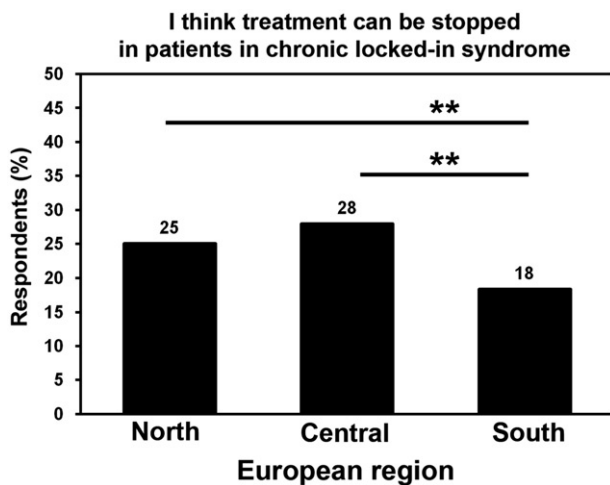


Figure 2. Geographic region mediates attitudes towards end-of-life in patients in a chronic locked-in syndrome (\*\* $p < 0.001$ ).

(40%). The inverse was identified for the VS, where participants found it worse than death mostly for families than for the patients themselves [25]. This might be due to the fact that patients in LIS are aware yet completely dependent on around-the-clock personal care, so their daily life activities are extremely restricted (e.g. they need to rely on help if they want to go somewhere, watch TV, read a book, use the toilet, etc.). Because patients in LIS are aware of their condition, in contrast to VS and MCS patients who do not reach this level of self-awareness, the situation may then be judged worse for the patients [31]. For physicians, the findings corroborate a recent survey among German neurologists, where only 86% ascribed pain perception to patients in LIS [32]. As a result, these clinicians can be expected to act according to their convictions and under-treat pain [14, 19]. In light of largely intact cognitive function in LIS [3, 33, 34], insufficient management of pain can have important medico-ethical implications, such as reduced satisfaction with quality of life on the patient's behalf [15, 20, 35]. It should be noted that, before respondents were presented with this questionnaire item, no official definition of pain was provided. Hence, it can be argued that those participants who negated pain perception

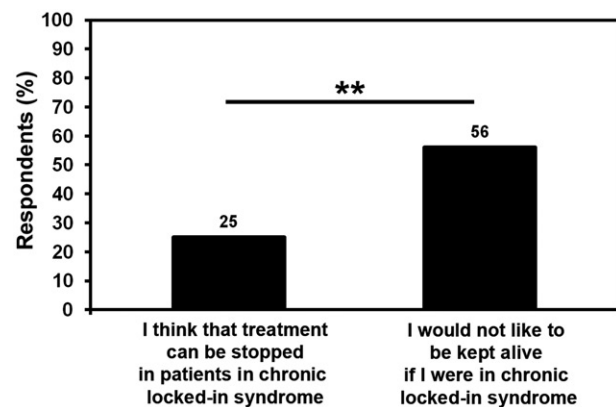


Figure 3. Dissociation in respondents' attitudes between general and personal preferences towards locked-in syndrome (LIS). Although few respondents endorsed treatment withdrawal in patients in LIS, more than half wished not to be kept alive if they were in a chronic condition of LIS (numbers are based on cumulative percentages, i.e. missing data are discarded).

in patients in LIS equated pain to nociception, namely 'the neural processes of encoding and processing noxious stimuli' [36]. However, it is thought that when participants responded to this item they considered pain as the physical discomfort that patients experience, similar to what patients themselves rate as painful, namely the unpleasant physical sensations including itchiness, stiffness, numbness and aches (i.e. the unpleasant physical sensations including itchiness, stiffness, numbness and aches [35]).

It was further found that the majority (75%) of respondents were opposed to stopping treatment in patients in LIS. Although treatment was not explicitly defined, it mainly referred to artificial nutrition and hydration and invasive ventilation, which are frequently needed in patients in LIS. To disagree with withdrawal of treatment in LIS seems reasonable, especially when one considers that these patients retain their cognitive abilities, including emotional function. Indeed, evidence from patients' self-reports holds that, although suicidal thoughts can be present in the initial stages of the syndrome, patients in LIS generally score satisfactory well-being with the passage of time [18, 37]. For instance, in a group of long-term survival, all patients wished to have

life-sustaining treatment continued [38]. Similarly, in the longest surviving cohort of patients who were studied for 11 years, 54% had never considered euthanasia [14]. More recently, in a questionnaire survey with 65 patients, the majority (72%) professed 'good' quality-of-life and only 7% expressed wishes for euthanasia [20]. Here, we also identified that participants had more chances to oppose treatment withdrawal if they held religious beliefs and were from the southern Europe. The findings corroborate a past European survey among intensivists, according to which withdrawing treatment was most commonly used in northern and central European countries and occurred more often if the physician had no religious affiliation [27]. The strength of religious faith was also found to influence attitudes towards treatment limitation among (UK) doctors. In this study, non-religious clinicians would continue deep sedation until death, would intend to hasten death and would support legalizing assisted suicide [39].

Interestingly, a quarter of the surveyed participants considered that treatment can be stopped in patients with chronic LIS. Although it might seem surprising to endorse the possibility for conscious patients to hasten death, the presence of consciousness alone does not always work in favour of patients' best interest because it jeopardizes good quality of life [31]. Indeed, in the latest survey among patients in LIS, almost half of the respondents who professed happiness did not wish to be resuscitated in case of cardiac arrest [20]. However, the support for cessation of treatment in LIS was less frequent among German neurologists: 81% were in favour of ceasing life-sustaining treatment in LIS 'under certain circumstances' (an answer option not available in this current study) and an additional 10% were willing to 'always' stop treatments [32]. Possible explanations for these different observations, in addition to the different formulation of the question, include the broader sample used in this study given the important regional differences within Europe [27, 40]. Alternatively, the respondents here could also have recognized the patients' right to autonomy and, hence, supported treatment limitation. As stated by the Belmont report [41], individuals in general should be treated as autonomous agents and persons with diminished autonomy in particular are entitled to protection. In the same line, the American Academy of Neurology recognizes that adult patients with severe and permanent paralysis have the right to make decisions regarding their own healthcare and to accept or to refuse life-sustaining therapy [42]. Because they are cognitively intact [43], patients in LIS are competent to make decisions on whether to consent to life-sustaining treatment or even ask for physician assisted death [44]. As it has also been expressed, it is ethically wrong to keep a conscious tetraplegic patient alive against his/her autonomous will [45]. Of note is that the formulation of the question used (and the use of the expression 'can be stopped') may also have legal rather than ethical connotations. As such, responses could be more likely to be variable based on local law, rather than on actual personal attitude. It would, hence, be of interest for future studies to account for ethical and legal perspectives when evaluating personal opinions.

Interestingly, a great proportion (56%) of respondents would decide differently about end-of-life if they were in LIS.

This is consistent with previous studies where physicians decide differently if they are in a professional role deciding for others than if they are in an existential role deciding for themselves [46–48]. Therefore, clinical decision-making seems to be fundamentally different when one decides for oneself or gives advice to others [49, 50]. One explanation would be that the preference not to undergo life-prolonging treatment stems from the fear of a profound identity change due to modified body image. In other words, when healthy individuals would imagine their bodies severely paralyzed in LIS, they would report a discontinuity in their personal identity after the imagined acute loss of motor control [12]. However, patients' bodies continue to live after their accidents, implying that identity in patients in LIS is primarily socially constituted [51, 52]. As such, the loss of independent function, control and mobility, which eventually may lead to social isolation [53], could also have been the reasons that the respondents refused more frequently to be kept alive in a chronic LIS. Indeed, patients in LIS profess unhappiness when they are dissatisfied with mobility in the community and with recreational activities [20]. These observations are of importance because of the occurrence of early counselling regarding withdrawal of care based on physician attitudes or due to an incorrect diagnosis of LIS [54].

## Conclusions

The present survey indicates divided attitudes on pain and end-of-life issues concerning the LIS. Although the results cannot be interpreted as simply mirroring current practices in the clinical environment or general public attitudes, they raise important questions about the attitudes embedded in the care offered for patients. Ethical responses to dilemmas involving patients in LIS should take into account diverging attitudes of stakeholders and resonate with calls for greater awareness about implicit attitudes entertained by medical professionals in the care offered to these patients [55]. Further studies should investigate how medical professionals and others involved in the healthcare of patients in LIS come to their attitudes and how these attitudes shape their decisions. Ultimately, an important feature of the LIS is that the patients are usually able to express their own preferences and communicate about them, hence doctors and relatives should use this chance to make structured efforts to understand and act in accordance with patient preference.

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### Supplementary Materials

A Supplementary Table for this article is available online.