



End-of-life practices in traumatic brain injury patients: Report of a questionnaire from the CENTER-TBI study



Ernest van Veen^{a,b,c}, Mathieu van der Jagt^a, Giuseppe Citerio^{d,e}, Nino Stocchetti^{f,g}, Jelle L. Epker^a, Diederik Gommers^a, Lex Burdorf^b, David K. Menon^h, Andrew I.R. Maasⁱ, Hester F. Lingsma^b, Erwin J.O. Kompanje^{a,c,*}, the CENTER-TBI investigators and participants

^a Department of Intensive Care, Erasmus University Medical Center, Rotterdam, the Netherlands

^b Department of Public Health, Erasmus University Medical Center, Rotterdam, the Netherlands

^c Department of Medical Ethics and Philosophy of Medicine, Erasmus University Medical Center, Rotterdam, the Netherlands

^d School of Medicine and Surgery, University of Milan-Bicocca, Milan, Italy

^e San Gerardo Hospital, ASST-Monza, Italy

^f Department of Physiopathology and Transplantation, Milan University, Milan, Italy

^g Neuro ICU Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico Milano, Milan, Italy

^h Department of Anaesthesia, University of Cambridge, Cambridge, United Kingdom

ⁱ Department of Neurosurgery, Antwerp University Hospital and University of Antwerp, Edegem, Belgium

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ABSTRACT

Purpose: We aimed to study variation regarding specific end-of-life (EoL) practices in the intensive care unit (ICU) in traumatic brain injury (TBI) patients.

Materials and methods: Respondents from 67 hospitals participating in The Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) study completed several questionnaires on management of TBI patients.

Results: In 60% of the centers, ≤50% of all patients with severe neurological damage dying in the ICU, die after withdrawal of life-sustaining measures (LSM). The decision to withhold/withdraw LSM was made following multidisciplinary consensus in every center. Legal representatives/relatives played a role in the decision-making process in 81% of the centers. In 82% of the centers, age played a role in the decision to withhold/withdraw LSM. Furthermore, palliative therapy was initiated in 79% of the centers after the decision to withdraw LSM was made. Last, withholding/withdrawing LSM was, generally, more often considered after more time had passed, in a patient with TBI, who remained in a very poor prognostic condition.

Conclusion: We found variation regarding EoL practices in TBI patients. These results provide insight into variability regarding important issues pertaining to EoL practices in TBI, which can be useful to stimulate discussions on EoL practices, comparative effectiveness research, and, ultimately, development of recommendations.

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Abbreviations: ICU, intensive care unit; EoL, end-of-life; TBI, traumatic brain injury; LSM, life-sustaining measures; CENTER-TBI, Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury; CT, computed tomography; IQR, interquartile range; UK, United Kingdom; GCS, Glasgow Coma Scale; ICP, intracranial pressure; CER, Comparative effectiveness research.

* Corresponding author at: Department of Intensive Care Medicine, Erasmus University Medical Center, P.O. Box 2040, Rotterdam, 3000 CA, the Netherlands.

E-mail addresses: e.vanveen.1@erasmusmc.nl (E. van Veen), m.vanderjagt@erasmusmc.nl (M. van der Jagt), giuseppe.citerio@unimib.it (G. Citerio), nino.stocchetti@policlinico.mi.it (N. Stocchetti), j.epker@erasmusmc.nl (J.L. Epker), d.gommers@erasmusmc.nl (D. Gommers), a.burdurf@erasmusmc.nl (L. Burdorf), dkm13@cam.ac.uk (D.K. Menon), andrew.Maas@uza.be (A.I.R. Maas), h.lingsma@erasmusmc.nl (H.F. Lingsma), e.j.o.kompanje@erasmusmc.nl (E.J.O. Kompanje).

1. Introduction

Life-sustaining measures (LSM), such as mechanical ventilation, have allowed physicians to prolong the life of patients. However, these LSM may sometimes be considered as disproportionate when they postpone unavoidable death and, as a consequence, may only result in prolonged suffering of patients and their relatives. Therefore, in many countries, it is seen as good medical practice to withhold or withdraw LSM in these situations and allow the patient to die when further treatment is judged as disproportionate [1,2].

A systematic review reported variation in the prevalence of withdrawing/withholding LSM [3] resulting from institutional factors [4–10], physician factors [10–14], and religion/geographic factors [14–16]. Recent studies have advised to also study variation pertaining to specific

end-of-life (EoL) practices [3,17]. A degree of variation in specific EoL practices is understandable, given the complexities of EoL care. However, if considerable variation negatively influences patient care, this variation may not be acceptable. One driving issue here is that withdrawal of LSM may be inappropriately instituted in individuals who have a chance of good quality survival. Furthermore, important issues may be that symptom control during withdrawal is suboptimal, interactions with families may be compromised, ethical issues may not be appropriately addressed, and organ donation may be affected. Studying variation may provide insight into these issues in patients with traumatic brain injury (TBI) on the intensive care unit (ICU), which can be useful to stimulate discussions regarding EoL best practices, and, ultimately, development of recommendations [3,17]. Furthermore, variation may inform comparative effectiveness research (CER), which entails studying the impact of differences in patient management on outcomes to inform best practices.

Therefore, we aimed to study variation regarding specific EoL practices in TBI patients. We investigated the occurrence of withdrawing LSM, how the decision to withhold/withdraw LSM was made, the role of legal representatives/relatives, if age influenced the decision-making process, the initiation of palliative therapy, and the timing and execution of withholding/withdrawing LSM.

2. Methods

2.1. CENTER-TBI and study sample

The Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI, www.center-tbi.eu) study is a prospective observational study on traumatic brain injury (TBI) [18,19]. For this, data on patient characteristics, management and outcomes were collected in centers from 20 countries across Europe and Israel (Fig. 1). Further, respondents from all participating centers in the CENTER-TBI study were asked to complete questionnaires which were used to create “provider profiles” of participating neurotrauma centers [20].

2.2. Questionnaire development and administration

The topics investigated for this provider profile study, are summarized in Table 1. In the questionnaires, we explicitly asked respondents to provide their understanding of the “general policy” for their institution. We defined this as the local standards used in more than 75% of patients, recognizing that there might be exceptions. Most questions used categorical answers. For some questions, the respondents had the option to fill in “other” and provide a free text response.

In an earlier publication from Cnossen et al. [20], detailed information about the development, administration, and content of the questionnaires is available.

2.3. Analyses

We calculated frequencies and percentages for all questions. The sample total of question two and six could exceed 100% because the respondents had the option to provide more than one response. For question six, we made a new response category. The result of this response category is the sum of centers that filled in all response categories for that question. Furthermore, for question seven, respondents could answer “never”, “sometimes”, “often”, or “always”. For the analyses we considered “never” and “sometimes” as “no general policy”, and “often” and “always” as “general policy”. Question five had six answers, of which four had a similar meaning. We combined these four answers to define one response category (Table 1).

We examined potential variation between and within seven regions based on the United Nations geo-scheme: Baltic States (Latvia, and Lithuania), Eastern Europe (Bosnia and Herzegovina, Hungary,

Romania, and Serbia), Israel, Northern Europe (Denmark, Finland, Norway, and Sweden), Southern Europe (Italy, and Spain), the United Kingdom, and Western Europe (Austria, Belgium, France, Germany, the Netherlands, and Switzerland).

3. Results

3.1. Center characteristics

Of the 68 centers, 67 filled in the questionnaires and were included in the analysis. Between questions the response rate varied from 96 to 99%. Most participating centers were academic centers ($N = 61$, 91%), designated as a level I or II trauma center ($N = 49$, 73%). The average number of beds was 1187 of which on average 39 were ICU beds. In 2013, the median annual number of TBI patients was 92 (interquartile range (IQR) 53–159). The questionnaire about ethical aspects of the ICU was mostly completed by intensivists, neurosurgeons, and neurologists.

Of all patients with severe neurological damage who die in the ICU, approximately, how many die after withdrawal of life-sustaining measures?

In 60% of the centers, $\leq 50\%$ of all patients with severe neurological damage who die in the ICU, died after withdrawal of LSM. In 40% of the centers, this was $>50\%$. In 56% of the centers from Northern Europe, $>75\%$ of the patients with severe neurological damage who die in the ICU, died after withdrawing LSM. Contrary, in most centers from the Baltic States, Israel, and Southern Europe (80%, 100%, and 75% respectively), this was $<25\%$ (Fig. 2).

How is the decision reached to withhold/withdraw life-sustaining measures (e.g. mechanical ventilation, vasoactive medication, renal replacement therapy, intravenous fluid administration)?

In 67% of the centers, multidisciplinary discussion following consensus among all participating physicians was preferred. This was also preferred in most centers in Southern Europe, the United Kingdom (UK) and Western Europe (75%, 75%, and 84% respectively). In Northern European centers, however, this was preferred in 33% of the centers (Table 2).

Does the age of the patient influence your decision making about withholding and withdrawing life-sustaining treatment?

In 81% of the centers, age influenced the decision-making process, together with other criteria. This was also the case in all centers in Southern Europe. However, in the Baltic States and Eastern Europe, age did not play a role in 60%, and 50% of the centers respectively (Table 2).

To what extent do opinions of legal representatives/relatives play a role in decision-making about withdrawal/withholding of life-sustaining measures?

In 19% of the centers, legal representatives/relatives played no role in the decision-making process before withholding/withdrawing LSM. This was the case in 67% of the centers in Northern Europe. Contrary, in all centers in Israel, and in 60% of the centers in Western Europe, legal representatives/relatives played a role in the decision-making process to some or to a great extent (Fig. 3).

If the decision is made to withdraw life-sustaining measures and before actual withdrawal, do you initiate palliative therapy in anticipation of distressing symptoms (such as pain, terminal restlessness, death rattle, stridor, dyspnoea)?

In 79% of the centers, palliative therapy in anticipation of distressing symptoms after the decision to withhold/withdraw LSM was initiated. In Northern Europe, Southern Europe, and Western Europe this was the case in 78%, 92%, and 96% respectively. Contrary, in 60% of the centers from the Baltic States, palliative therapy was not initiated (Fig. 4).

If the decision is made to withdraw life-sustaining measures in a comatose severely injured TBI patient, which life-sustaining measures do you stop?

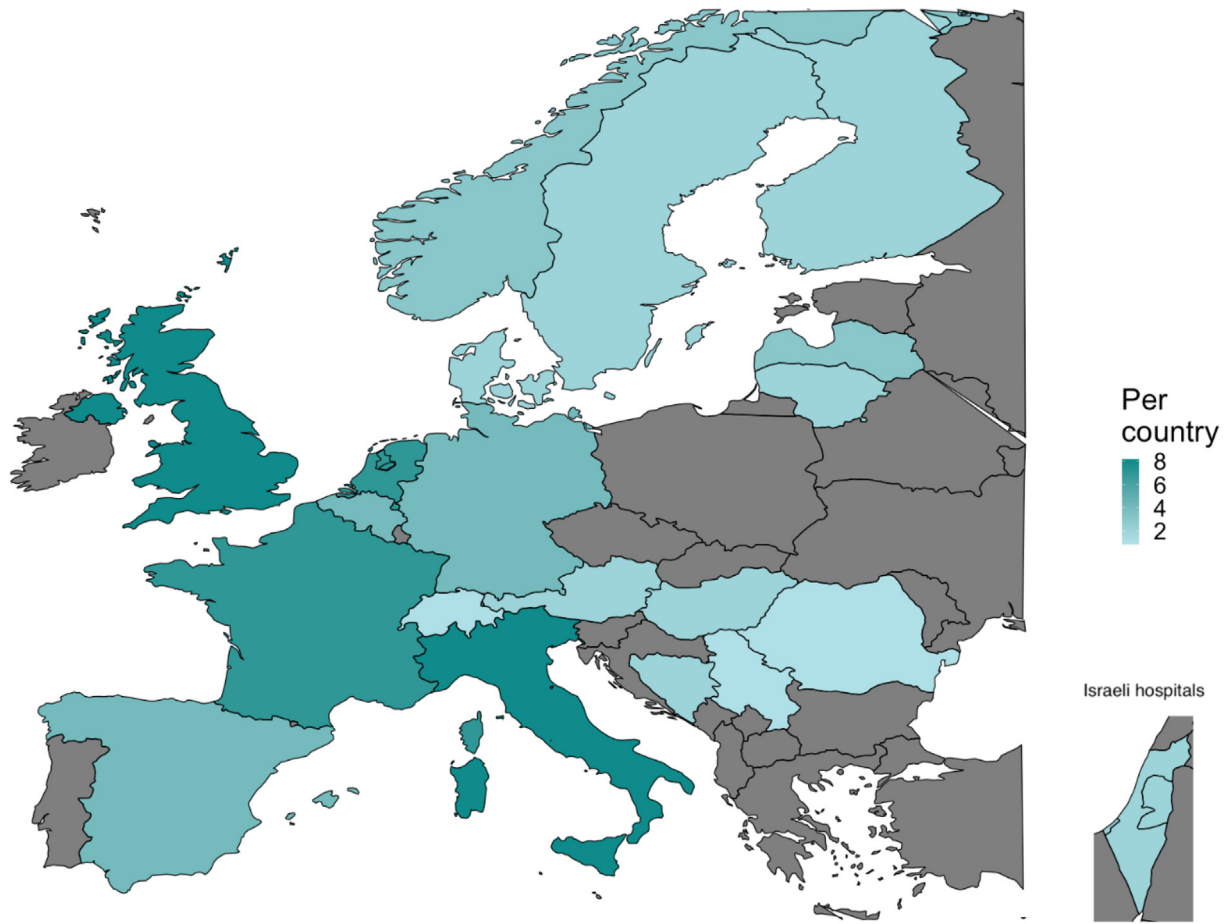


Fig. 1. Number of hospitals.

Table 1

Topics covered in this study, and the related questions to each topic.

Occurrence of withdrawing LSM
1. Of all patients with severe neurological damage who die in the ICU, approximately, how many die after withdrawal of life-sustaining measures?
Practices around the decision-making process
2. How is the decision reached to withhold/withdraw life-sustaining measures (e.g. mechanical ventilation, vasoactive medication, renal replacement therapy, intravenous fluid administration)?
3. To what extent do opinions of legal representatives/relatives play a role in decision-making about withdrawal/withholding of life-sustaining measures?
4. Does the age of the patient influence your decision making about withholding and withdrawing life sustaining treatment?
Practices before withholding/withdrawing LSM
5. If the decision is made to withdraw life-sustaining measures and before actual withdrawal, do you initiate palliative therapy in anticipation of distressing symptoms (such as pain, terminal restlessness, death rattle, stridor, dyspnoea)?
Timing and execution of withholding/withdrawing LSM
6. If the decision is made to withdraw life-sustaining measures in a comatose severely injured TBI patient, which life-sustaining measures do you stop?
7. At what time after injury would you consider to withdraw life support in a patient with TBI, who is in a very poor prognostic condition (based on CT scan, GCS, clinic, ICP etc), but not brain dead?

Abbreviations: CT: Computed Tomography, GCS: Glasgow Coma Scale, ICP: Intracranial Pressure, ICU: Intensive Care Unit, LSM: Life-sustaining measures, TBI: Traumatic brain injury.

In a comatose severely injured TBI patient, mechanical ventilation would be stopped in 63% of the centers, the administration of vasoactive medication would be stopped in 93% of the centers, renal replacement therapy would be stopped in 81% of the centers, the administration of intravenous fluids would be stopped in 34% of the centers, and nasogastric feeding would be stopped in 58% of the centers. In 25% of the centers, all of these LSM would be stopped after the decision to withdraw LSM (Table 3).

At what time after injury would you consider to withdraw life support in a patient with TBI, who is in a very poor prognostic condition (based on CT scan, GCS, clinic, ICP etc), but not brain dead?

In general, there was an increase in considering withholding/withdrawing LSM after more time had passed (ranging from 24 h to >2 weeks), in a patient with TBI, who was in a very poor prognostic condition but not brain dead. In 25% of the centers from Southern Europe, and in 16% of the centers from Western Europe, withholding/withdrawing LSM would be considered after 24 h. In 40% of the centers from the Baltic States, and in 25% of the centers from the UK this was considered after >2 weeks (Table 3).

4. Discussion

We aimed to study the variation regarding specific end-of-life (EoL) practices in critically ill traumatic brain injury (TBI) patients, using questionnaires filled in by experts in participating neurotrauma centers. We found variation in the occurrence of withdrawing LSM, how the decision to withhold/withdraw LSM was made, the role of legal representatives/relatives, the influence of age in the decision-making process, the initiation of palliative therapy, and the timing and execution of

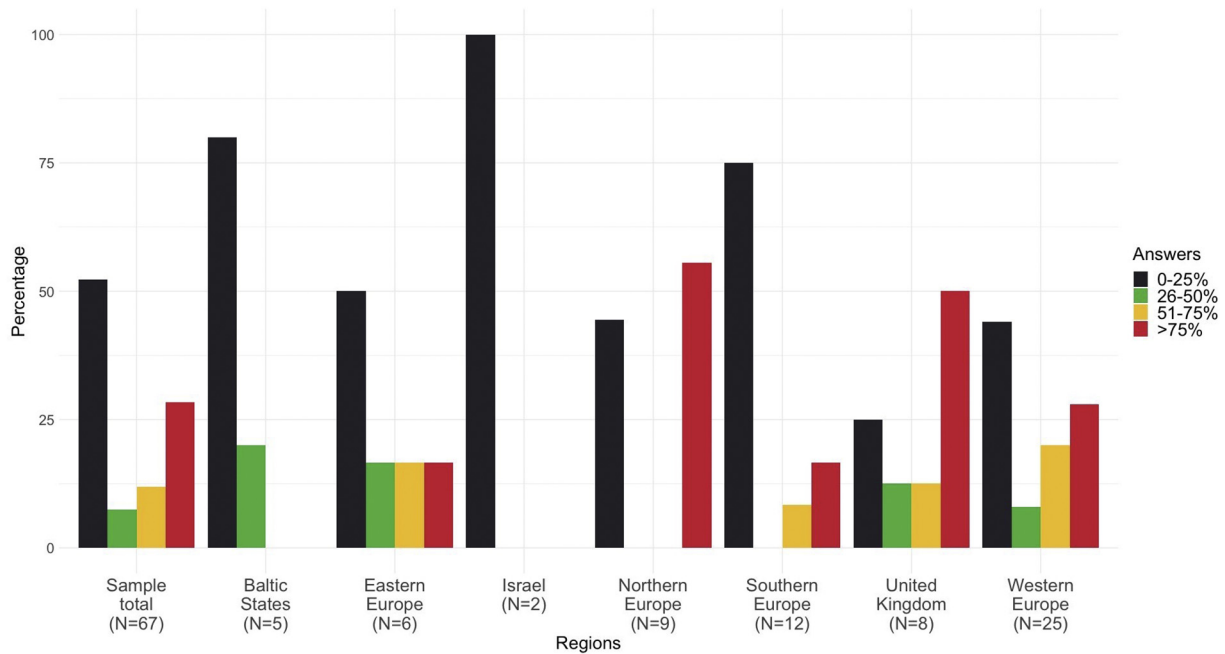


Fig. 2. Of all patients with severe neurological damage who die on the intensive care unit, approximately, how many die after withdrawal of life-sustaining measures?

withholding/withdrawing LSM. The results indicate important practice variation regarding EoL practices in TBI, which can be useful to stimulate discussions on EoL practices, comparative effectiveness research (CER), and recommendations.

First, we found variation in the occurrence of withdrawing LSM. This is in line with previous literature [3], showing not only variation within countries [4–6,10,21–27], but also within departments [12].

Second, we found variation regarding the decision-making process. All centers responded that they preferred multidisciplinary discussion before withdrawing/withholding LSM. This is in line with recommendations in previous literature [28–30]. However, the way this multidisciplinary discussion was implemented varied across centers. We also found variation regarding the extent of the role of legal representatives/relatives in this decision-making process. Previous literature

stressed the importance of legal representatives/relatives in the decision-making process [29–31]. A Canadian questionnaire study showed that 39% of surrogate decision-makers wanted to share responsibility for the decision [32]. However, Wendler and Rid found that at least one third of the surrogate decision-makers could be emotionally burdened after making treatment decisions for incapacitated loved ones [33]. Healthcare providers should contemplate on whether or not they wish to communicate the uncertainty involved in EoL decision-making (when such prognostic uncertainty is indeed present), because it might have unpredictable impact on this emotional burden of legal representatives/relatives. Reasons to communicate about uncertainty have already been raised by Smith et al. and Lazaridis [34,35]. Smith et al. proposed a framework that should be adapted to the core values of the patient [34]. By following this framework, legal representatives/

Table 2
Practices around the decision-making process regarding withholding/withdrawing LSM.

	Sample total (N = 67)	Baltic States (N = 5)	Eastern Europe (N = 6)	Israel (N = 2)	Northern Europe (N = 9)	Southern Europe (N = 12)	United Kingdom (N = 8)	Western Europe (N = 25)
How is the decision reached to withhold/withdraw life-sustaining measures (e.g. mechanical ventilation, vasoactive medication, renal replacement therapy, intravenous fluid administration)?								
One physician (e.g. the most senior person) decides following multidisciplinary discussion	10 (15%)	1 (20%)	0(0%)	2 (100%)	3(33%)	0(0%)	2(25%)	2(8%)
During multidisciplinary discussion in which the majority (more than 50%) has to agree	14 (21%)	1 (20%)	2(33%)	1(50%)	3(33%)	3(25%)	0(0%)	4(16%)
During multidisciplinary discussion in which there has to be unanimous consensus among all participating doctors	45 (67%)	2(40%)	4(67%)	0(0%)	3(33%)	9(75%)	6(75%)	21(84%)
One physician decides (along with objective medical criteria) without multidisciplinary discussion (veto)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Other ^a	2(3%)	1(20%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	1(4%)
Does the age of the patient influence your decision making about withholding and withdrawing treatment?								
Yes, always, independent of other criteria	1(1%)	0(0%)	0(0%)	1(50%)	0(0%)	0(0%)	0(0%)	0(0%)
Yes, but only in combination with other criteria as CT scan, GCS, depth of coma	54(82%)	2(40%)	3(50%)	1(50%)	7(78%)	12(100%)	6(75%)	23(92%)
No, I only decide on the severity of the injury and anticipated prognosis	12(18%)	3(60%)	3(50%)	0(0%)	2(22%)	0(0%)	2(25%)	2(8%)

Abbreviations: CT: Computed Tomography, GCS: Glasgow Coma Scale, LSM: Life-sustaining measures.

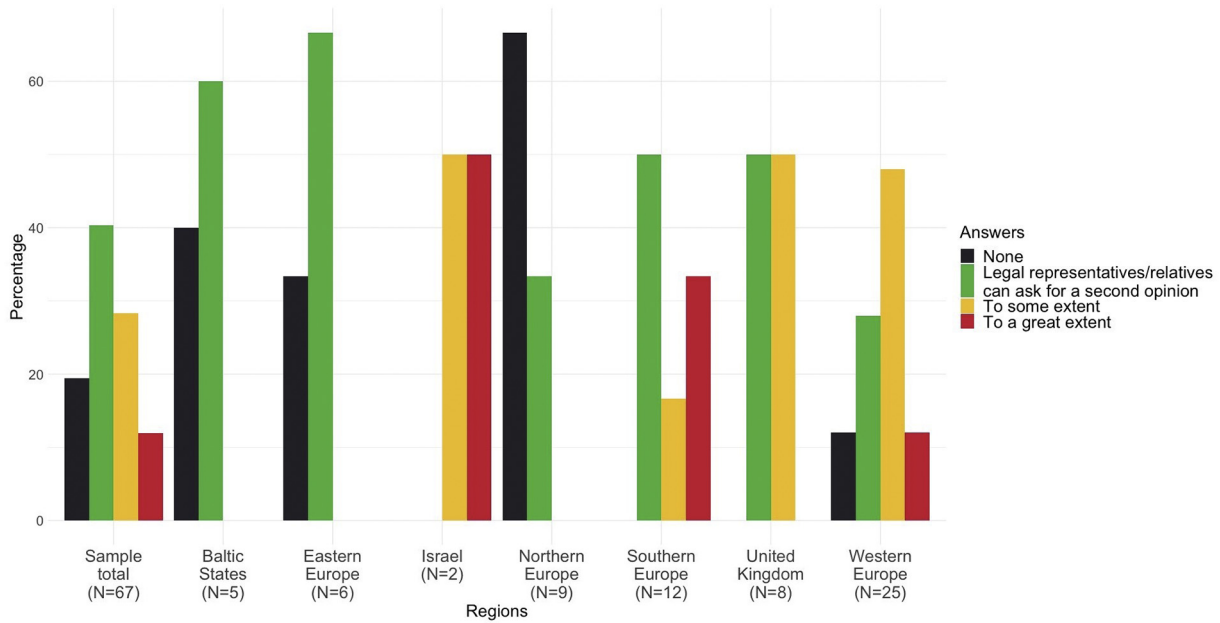


Fig. 3. To what extent do opinions of legal representatives/relatives play a role in decision-making about withdrawal/withholding of life-sustaining measures?

relatives might experience more support when they are involved in EoL decisions. A multisociety statement recommended that the medical profession should lead public engagement efforts and advocate policies and legislation about the use of life-prolonging technologies [36]. These policies and legislation could be informative for the decision to involve legal representatives/relatives in the decision-making process.

Third, we found variation in practices before withholding/withdrawing LSM. Decisions regarding palliative therapy were not formalized in a protocol in the majority of centers. Despite this, palliative therapy was initiated in most centers after the decision to withhold/withdraw LSM. Where such care was not reported, the response might have been influenced by the wording of our questionnaire, which may have been construed as starting such therapy in advance

of, rather than at the time of, withdrawing LSM. Palliative therapy might be common practice in general, but not in anticipation of distressing symptoms. Past recommendations stressed the importance of good palliative care [29,30,37]. Previous literature described that there should be no maximum dosage of narcotics or sedatives [30,37]. The right amount of drugs should be adapted to the need of the individual patient. Furthermore, Hawryluck et al. described, that pre-emptive dosing in anticipation of pain and suffering should be considered as good palliative care if the intent of the physician is clear and well documented [37].

Fourth, we found variation regarding which LSM to stop after the decision to withhold/withdraw LSM was made. In a quarter of centers, all LSM were stopped after the decision to withhold/withdraw LSM.

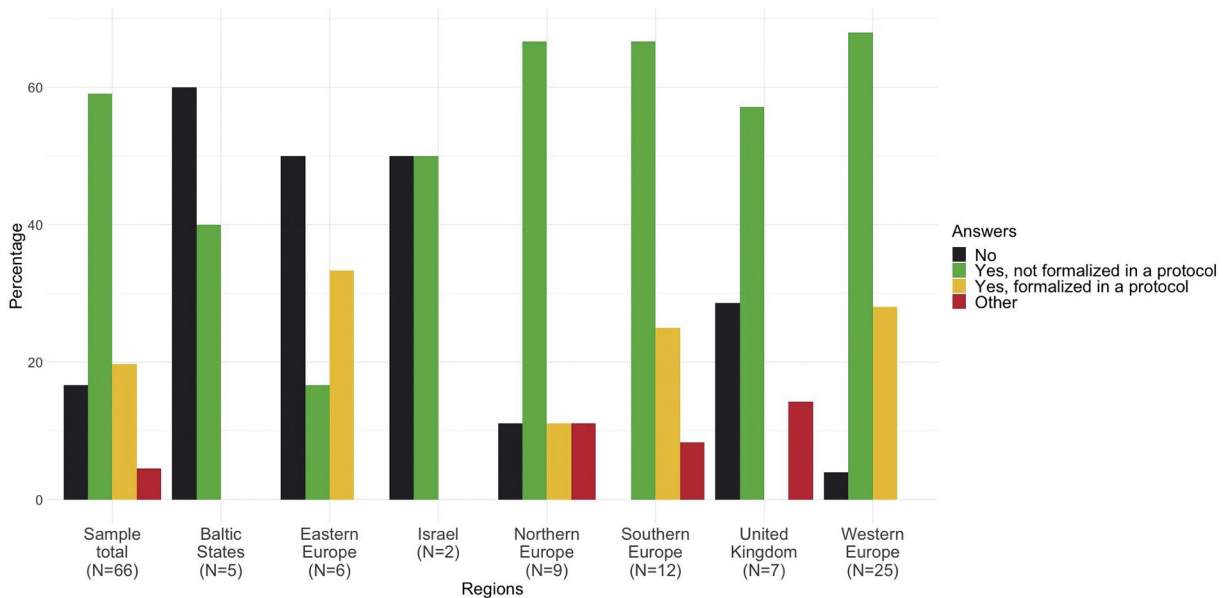


Fig. 4. If the decision is made to withdraw life-sustaining measures and before actual withdrawal, do you initiate palliative therapy in anticipation of distressing symptoms (such as pain, terminal restlessness, death rattle, stridor, dyspnoea)?

Table 3
Timing and execution of withholding/withdrawing life-sustaining measures (LSM).

	Sample total (N = 67)	Baltic States (N = 5)	Eastern Europe (N = 6)	Israel (N = 2)	Northern Europe (N = 9)	Southern Europe (N = 12)	United Kingdom (N = 8)	Western Europe (N = 25)
If the decision is made to withdraw life-sustaining measures in a comatose severely injured TBI patient, which life-sustaining measures do you stop?								
We stop mechanical ventilation	42 (63%)	4 (80%)	1 (17%)	0 (0%)	8 (89%)	3 (25%)	8 (100%)	18 (72%)
We stop administration of vasoactive medication	62 (93%)	5 (100%)	4 (67%)	2 (100%)	8 (89%)	10 (83%)	8 (100%)	25 (100%)
We stop renal replacement therapy	54 (81%)	4 (80%)	1 (17%)	2 (100%)	8 (89%)	9 (75%)	7 (88%)	23 (92%)
We stop administration of intravenous fluids	23 (34%)	3 (60%)	1 (17%)	1 (50%)	4 (44%)	1 (8%)	2 (25%)	11 (44%)
We stop nasogastric feeding	39 (58%)	3 (60%)	2 (33%)	1 (50%)	8 (89%)	5 (42%)	3 (38%)	17 (68%)
Number of centers that indicated to stop all of the above life-sustaining measures	17 (25%)	3 (60%)	0 (0%)	0 (0%)	4 (44%)	0 (0%)	1 (13%)	9 (36%)
At what time after injury would you consider to withdraw life support in a patient with TBI, who is in a very poor prognostic condition (based on CT scan, GCS, clinic, ICP etc) but not brain dead? ^a								
24 h	7 (10%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (25%)	0 (0%)	4 (16%)
2–4 days	13 (19%)	0 (0%)	0 (0%)	0 (0%)	2 (22%)	4 (33%)	1 (13%)	6 (24%)
4–7 days	18 (27%)	0 (0%)	1 (17%)	0 (0%)	4 (44%)	5 (42%)	2 (25%)	6 (24%)
>1 week	25 (37%)	0 (0%)	0 (0%)	1 (50%)	5 (56%)	7 (58%)	1 (13%)	11 (44%)
>2 weeks	30 (45%)	2 (40%)	0 (0%)	1 (50%)	5 (56%)	5 (42%)	2 (25%)	15 (60%)

Abbreviations: CT: Computed Tomography, GCS: Glasgow Coma Scale, ICP: Intracranial Pressure, LSM: Life-sustaining measures, TBI: Traumatic brain injury.

Previous literature suggested to critically evaluate all LSM that provide no comfort to dying patients, for whom the chances for meaningful recovery are absent. [28,30]. Asch et al. reported that blood products and hemodialysis, were among the LSM most preferably withdrawn by physicians, while tube feeding and intravenous fluids were least preferred to be withdrawn [38]. This is in line with our results. One reason for the reluctance to withdraw tube feeding and intravenous fluids could be that physicians believe that this could be perceived as starving the patient. On the other hand, continuing feeding and fluids might also prolong suffering at the end-of-life because the patient may live longer due to this “active” treatment.

Last, we found variation in when withdrawal of LSM was considered, and how often age influenced the decision-making process of withdrawing LSM. A previous study found that brain injury was an important trigger for withdrawing LSM [39]. Our results show that withdrawing LSM in a patient with very poor prognostic conditions but who is not brain dead was considered after 4–7 days in more than a quarter of the centers, and that age was a criterion for the decision to withdraw life-sustaining measures in many centers. Obviously, there is a general tendency to practice the “benefit of the doubt” in poor grade patients early in the course. The use of “considered” in our question meant that we could not be sure of the frequency with which such consideration actually led to the withdrawal of LSM. Consequently, caution is needed in interpreting the responses to this question. In general, physicians should exercise extreme caution regarding early prognostication and withdrawal of LSM following severe traumatic brain injury in spite of the existence of validated prognostic models [40,41]. Based on our results, in Northern European centers, patients in the intensive care unit (ICU) with severe neurological damage may have died more frequently because of withdrawal of LSM compared to other regions. This finding could lead to one of two diametrically opposing inferences. On one hand, the practice in Northern Europe may be appropriate, and ensure that patients who have no prospect of an acceptable functional outcome have withdrawal of LSM, thus minimizing the burden of suffering to the patient and family, and optimizing the use of limited health care resources. On the other hand, given that

there was less unanimous consensus needed for the decision to withdraw LSM in Northern European countries, this practice could indicate a potential for self-fulfilling prophecies [42]. Self-fulfilling prophecies may exist in TBI too [43]. Early withholding/withdrawing of LSM, and withholding of treatment of patients that are “too old”, could lead to those self-fulfilling prophecies. On the Durban World Congress, ethics experts concluded that age should not be the sole criterion upon which to decide to withhold/withdraw LSM [44]. Although age is an important factor in prognostic models in TBI [40,41], and even though increasing age has been found to be independently associated with the decision to withdraw LSM [6,45], clinicians should be cautious taking age as a dominant criterion to withdraw LSM. Regarding the timing of withdrawing LSM, in a position statement from the Neurocritical Care Society, the recommendation was to wait at least 72 h before withdrawing LSM in patients with devastating brain injury [29]. “Early” withdrawal of LSM might be unwise due to too much uncertainty of the prognosis. On the other hand, “late” withdrawal of LSM would not always be in the best interest of the patient because of the potential for prolonged suffering. Finding the balance between resolving prognostic uncertainty and preventing harm and suffering in individual patients remains a difficult and incompletely resolved clinical problem.

Our study has limitations that should be considered when interpreting the results. First, our results are based on the perceptions of practices reported by respondents rather than actual clinical practice data. However, even if this is the case, the fact that respondents’ answers vary between centers, already provides insight in variation across European and Israeli neurotrauma centers. Second, some of our questions were open to ambiguity and may not have been interpreted correctly by the respondents. For example, in the questionnaire, we made no distinction between withholding and withdrawing life-sustaining measures. Because clinical choices could be different between the two, this may have influenced the results. In any case, a questionnaire cannot capture all the nuances that underpin clinical practice, which involves many complex potential alternative options that cannot be captured by questionnaires. Third, our results should invoke discussions rather than be considered as definitive, given the nature and room for

interpretations of our survey questions. Fourth, the data obtained may not be representative for all neurotrauma centers within the geographical areas studied, because the participating neurotrauma centers represent a select group. Fifth, the results come from data obtained in 2013. Last, it is possible that a more favorable picture or individual preferences may have been presented (even unwittingly), instead of the general policy in a center.

Medical practices are affected by the cultural climate of the society in which they exist [46]. Therefore, culture may explain some of the observed variation, such as the lack of influence of legal representatives/relatives in the decision-making process. Other variation, such as the possibility to withdraw LSM may have a more legal basis. For example, in Israel withdrawing mechanical ventilation is against the law [47]. However, most variation found in our study also appears to be within regions, and even within the countries in those regions. Thus, on the basis of our results, we cannot clearly attribute the variation to specific region or country characteristics such as most prevalent religion.

Our data comes from diverse sources, representing many cultural, religious and legal backgrounds. Our intent is not to change the daily practices of clinicians but to provide insight into systems used in other countries with a view to establishing common ground. Furthermore, withdrawing LSM should not preempt the availability and affordability of palliative care. Future research should study reasons for the found variation (e.g. cultural differences, and differences pertaining to legislation). Moreover, future research should evaluate the effect of the variation of specific EoL practices on clinically relevant outcomes using comparative effectiveness research. Such research should incorporate both mortality and long-term functional outcome to be able to interpret the outcome data. The complexity of some of the drivers of reported practice makes the case for mixed methods approaches to this problem, with a potentially substantive role for qualitative research methods. These strategies are important in order to inform preferred approaches to improve the quality of care for patients and relatives, and to prevent self-fulfilling prophecies.

Some variation between regions might always remain because of differences in patients, physician preferences and experience, and institutional factors. A recent study showed that this variation is primarily caused by differences between providers [48]. However, the WELPICUS study, published in 2014 [49] showed that theoretical consensus regarding EoL practices can be established. In order to put this theoretical consensus into practice, recommendations for specific EoL practices should be developed. The development of such recommendations can be facilitated through insight regarding important variations in practice, further discussion, and CER. Where possible, multidisciplinary and (inter)national groups should be involved in this development, as should patient representatives, as this may promote acceptance of recommendations on a broader scale.

5. Conclusion

We found variation regarding EoL practices in critically ill TBI patients, using questionnaires filled in by experts in European and Israeli neurotrauma centers. Specific issues that vary and need to be considered in discussions on EoL practices, CER, and recommendations, are the influence of legal representatives/relatives, the role of age in the decision-making process, what LSM to withdraw/withhold, and the timing of withdrawing/withholding LSM. Our results may give impetus to the design of (prospective) studies on EoL practices, exploring the role of self-fulfilling prophecies, further updating prediction models on prognosis and optimizing palliative care.

CENTER-TBI investigators and participants

Cecilia Åkerlund¹, Krisztina Amrein², Nada Andelic³, Lasse Andreassen⁴, Audny Anke⁵, Anna Antoni⁶, Gérard Audibert⁷, Philippe Azouvi⁸, Maria Luisa Azzolini⁹, Ronald Bartels¹⁰, Pál Barzó¹¹, Romuald

Beauvais¹², Ronny Beer¹³, Bo-Michael Bellander¹⁴, Antonio Belli¹⁵, Habib Benali¹⁶, Maurizio Berardino¹⁷, Luigi Beretta⁹, Morten Blaabjerg¹⁸, Peter Bragge¹⁹, Alexandra Brazinova²⁰, Vibeke Brinck²¹, Joanne Brooker²², Camilla Brorsson²³, Andras Buki²⁴, Monika Bullinger²⁵, Manuel Cabeleira²⁶, Alessio Caccioppola²⁷, Emiliana Calappi²⁷, Maria Rosa Calvi⁹, Peter Cameron²⁸, Guillermo Carbayo Lozano²⁹, Marco Carbonara²⁷, Giorgio Chevallard³⁰, Arturo Chiericato³⁰, Giuseppe Citerio^{31, 32}, Maryse Clossen³³, Mark Coburn³⁴, Jonathan Coles³⁵, Jamie D. Cooper³⁶, Marta Correia³⁷, Amra Čović³⁸, Nicola Curry³⁹, Endre Czeiter²⁴, Marek Czosnyka²⁶, Claire Dahyot-Fizelier⁴⁰, Helen Dawes⁴¹, Véronique De Keyser⁴², Vincent Degos¹⁶, Francesco Della Corte⁴³, Hugo den Boogert¹⁰, Bart Depreitere⁴⁴, Đula Đilvesi⁴⁵, Abhishek Dixit⁴⁶, Emma Donoghue²², Jens Dreier⁴⁷, Guy-Loup Dulière⁴⁸, Ari Ercole⁴⁶, Patrick Esser⁴¹, Erzsébet Ezer⁴⁹, Martin Fabricius⁵⁰, Valery L. Feigin⁵¹, Kelly Foks⁵², Shirin Frisvold⁵³, Alex Furmanov⁵⁴, Pablo Gagliardo⁵⁵, Damien Galanaud¹⁶, Dashiell Gantner²⁸, Guoyi Gao⁵⁶, Pradeep George⁵⁷, Alexandre Guhuysen⁵⁸, Lelde Giga⁵⁹, Ben Glocker⁶⁰, Jagoš Golubovic⁴⁵, Pedro A. Gomez⁶¹, Johannes Gratz⁶², Benjamin Gravesteijn³³, Francesca Grossi⁴³, Russell L. Gruen⁶³, Deepak Gupta⁶⁴, Juanita A. Haagsma³³, Iain Haitsma⁶⁵, Raimund Helbok¹³, Eirik Helseth⁶⁶, Lindsay Horton⁶⁷, Jilke Huijben³³, Peter J. Hutchinson⁶⁸, Bram Jacobs⁶⁹, Stefan Jankowski⁷⁰, Mike Jarrett²¹, Ji-yao Jiang⁵⁶, Kelly Jones⁵¹, Mladen Karan⁴⁷, Angelos G. Koliakos⁶⁸, Erwin Kompanje⁷¹, Daniel Kondziella⁵⁰, Evgenios Koraropoulos⁴⁶, Lars-Owe Koskinen⁷², Nóemi Kovács⁷³, Alfonso Lagares⁶¹, Linda Lanyon⁵⁷, Steven Laureys⁷⁴, Fiona Lecky⁷⁵, Rolf Lefering⁷⁶, Valerie Legrand⁷⁷, Aurelie Lejeune⁷⁸, Leon Levi⁷⁹, Roger Lightfoot⁸⁰, Hester Lingsma³³, Andrew I.R. Maas⁴², Ana M. Castaño-León⁶¹, Marc Maegele⁸¹, Marek Majdan²⁰, Alex Manara⁸², Geoffrey Manley⁸³, Costanza Martino⁸⁴, Hugues Maréchal⁴⁸, Julia Mattern⁸⁵, Catherine McMahon⁸⁶, Béla Melegh⁸⁷, David Menon⁴⁶, Tomas Menovsky⁴², Davide Mulazzi²⁷, Visakh Muraleedharan⁵⁷, Lynnette Murray²⁸, Nandesh Nair⁴², Ancuta Negru⁸⁸, David Nelson¹, Virginia Newcombe⁴⁶, Daan Nieboer³³, Quentin Noirhomme⁷⁴, József Nyírádi², Otesile Olubukola⁷⁵, Matej Oresic⁸⁹, Fabrizio Ortolano²⁷, Aarno Palotie^{90, 91, 92}, Paul M. Parizel⁹³, Jean-François Payen⁹⁴, Natascha Perera¹², Vincent Perlbarg¹⁶, Paolo Persona⁹⁵, Wilco Peul⁹⁶, Anna Piippo-Karjalainen⁹⁷, Matti Pirinen⁹⁰, Horia Ples⁸⁸, Suzanne Polinder³³, Inigo Pomposo²⁹, Jussi P. Posti⁹⁸, Louis Puybasset⁹⁹, Andreea Radoi¹⁰⁰, Arminas Ragauskas¹⁰¹, Rahul Raj⁹⁷, Malinka Rambadagalla¹⁰², Ruben Real³⁸, Jonathan Rhodes¹⁰³, Sylvia Richardson¹⁰⁴, Sophie Richter⁴⁶, Samuli Ripatti⁹⁰, Saulius Rocka¹⁰¹, Cecilie Roe¹⁰⁵, Olav Roise¹⁰⁶, Jonathan Rosand¹⁰⁷, Jeffrey V. Rosenfeld¹⁰⁸, Christina Rosenlund¹⁰⁹, Guy Rosenthal⁵⁴, Rolf Rossaint³⁴, Sandra Rossi⁹⁵, Daniel Rueckert⁶⁰, Martin Rusnák¹¹⁰, Juan Sahuquillo¹⁰⁰, Oliver Sakowitz^{85, 111}, Renan Sanchez-Porras¹¹¹, Janos Sandor¹¹², Nadine Schäfer⁷⁶, Silke Schmidt¹¹³, Herbert Schoechl¹¹⁴, Guus Schoonman¹¹⁵, Rico Frederik Schou¹¹⁶, Elisabeth Schwendenwein⁶, Charlie Sewalt³³, Toril Skandsen^{117, 118}, Peter Smielewski²⁶, Abayomi Sorinola¹¹⁹, Emmanuel Stamatakis⁴⁶, Simon Stanworth³⁹, Ana Stevanovic³⁴, Robert Stevens¹²⁰, William Stewart¹²¹, Ewout W. Steyerberg^{33, 122}, Nino Stocchetti¹²³, Nina Sundström¹²⁴, Anneliese Synnot^{22, 125}, Riikka Takala¹²⁶, Viktória Tamás¹¹⁹, Tomas Tamosiutis¹²⁷, Mark Steven Taylor²⁰, Braden Te Ao⁵¹, Olli Tenovuori⁹⁸, Alice Theadom⁵¹, Matt Thomas⁸², Dick Tibboel¹²⁸, Marjolein Timmers⁷¹, Christos Toliass¹²⁹, Tony Trapani²⁸, Cristina Maria Tudora⁸⁸, Peter Vajkoczy¹³⁰, Shirley Vallance²⁸, Egils Valeinis⁵⁹, Zoltán Vámos⁴⁹, Gregory Van der Steen⁴², Joukje van der Naalt⁶⁹, Jeroen T.J.M. van Dijk⁹⁶, Thomas A. van Essen⁹⁶, Wim Van Hecke¹³¹, Caroline van Heugten¹³², Dominique Van Praag¹³³, Thijs Vande Vyvere¹³¹, Audrey Vanhauudenhuysse^{16, 74}, Roel P. J. van Wijk⁹⁷, Alessia Vargiolu³², Emmanuel Vega⁷⁹, Kimberley Velt³³, Jan Verheyden¹³¹, Paul M. Vespa¹³⁴, Anne Vik^{117, 135}, Rimantas Vilcinis¹²⁷, Victor Volovic⁶⁵, Nicole von Steinbüchel³⁸, Daphne Voormolen³³, Petar Vulekovic⁴⁵, Kevin K.W. Wang¹³⁶, Eveline Wieggers³³, Guy Williams⁴⁶, Lindsay Wilson⁶⁷, Stefan Winzeck⁴⁶, Stefan Wolf¹³⁷, Zhihui Yang¹³⁶, Peter Ylén¹³⁸, Alexander Younsi⁸⁵, Frederik A. Zeiler^{46, 139}, Veronika Zelikova²⁰, Agate Ziverte⁵⁹, Tommaso Zoerle²⁷

- ¹ Department of Physiology and Pharmacology, Section of Perioperative Medicine and Intensive Care, Karolinska Institutet, Stockholm, Sweden
- ² János Szentágothai Research Centre, University of Pécs, Pécs, Hungary
- ³ Division of Surgery and Clinical Neuroscience, Department of Physical Medicine and Rehabilitation, Oslo University Hospital and University of Oslo, Oslo, Norway
- ⁴ Department of Neurosurgery, University Hospital Northern Norway, Tromsø, Norway
- ⁵ Department of Physical Medicine and Rehabilitation, University Hospital Northern Norway, Tromsø, Norway
- ⁶ Trauma Surgery, Medical University Vienna, Vienna, Austria
- ⁷ Department of Anesthesiology & Intensive Care, University Hospital Nancy, Nancy, France
- ⁸ Raymond Poincaré hospital, Assistance Publique – Hôpitaux de Paris, Paris, France
- ⁹ Department of Anesthesiology & Intensive Care, S Raffaele University Hospital, Milan, Italy
- ¹⁰ Department of Neurosurgery, Radboud University Medical Center, Nijmegen, The Netherlands
- ¹¹ Department of Neurosurgery, University of Szeged, Szeged, Hungary
- ¹² International Projects Management, ARTTIC, München, Germany
- ¹³ Department of Neurology, Neurological Intensive Care Unit, Medical University of Innsbruck, Innsbruck, Austria
- ¹⁴ Department of Neurosurgery & Anesthesia & intensive care medicine, Karolinska University Hospital, Stockholm, Sweden
- ¹⁵ NIHR Surgical Reconstruction and Microbiology Research Centre, Birmingham, UK
- ¹⁶ Anesthésie-Réanimation, Assistance Publique – Hôpitaux de Paris, Paris, France
- ¹⁷ Department of Anesthesia & ICU, AOU Città della Salute e della Scienza di Torino - Orthopedic and Trauma Center, Torino, Italy
- ¹⁸ Department of Neurology, Odense University Hospital, Odense, Denmark
- ¹⁹ BehaviourWorks Australia, Monash Sustainability Institute, Monash University, Victoria, Australia
- ²⁰ Department of Public Health, Faculty of Health Sciences and Social Work, Trnava University, Trnava, Slovakia
- ²¹ Quesgen Systems Inc., Burlingame, California, USA
- ²² Australian & New Zealand Intensive Care Research Centre, Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia
- ²³ Department of Surgery and Perioperative Science, Umeå University, Umeå, Sweden
- ²⁴ Department of Neurosurgery, Medical School, University of Pécs, Hungary and Neurotrauma Research Group, János Szentágothai Research Centre, University of Pécs, Hungary
- ²⁵ Department of Medical Psychology, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany
- ²⁶ Brain Physics Lab, Division of Neurosurgery, Dept of Clinical Neurosciences, University of Cambridge, Addenbrooke's Hospital, Cambridge, UK
- ²⁷ Neuro ICU, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy
- ²⁸ ANZIC Research Centre, Monash University, Department of Epidemiology and Preventive Medicine, Melbourne, Victoria, Australia
- ²⁹ Department of Neurosurgery, Hospital of Cruces, Bilbao, Spain
- ³⁰ NeuroIntensive Care, Niguarda Hospital, Milan, Italy
- ³¹ School of Medicine and Surgery, Università Milano Bicocca, Milano, Italy
- ³² NeuroIntensive Care, ASST di Monza, Monza, Italy
- ³³ Department of Public Health, Erasmus Medical Center-University Medical Center, Rotterdam, The Netherlands
- ³⁴ Department of Anaesthesiology, University Hospital of Aachen, Aachen, Germany
- ³⁵ Department of Anesthesia & Neurointensive Care, Cambridge University Hospital NHS Foundation Trust, Cambridge, UK
- ³⁶ School of Public Health & PM, Monash University and The Alfred Hospital, Melbourne, Victoria, Australia
- ³⁷ Radiology/MRI department, MRC Cognition and Brain Sciences Unit, Cambridge, UK
- ³⁸ Institute of Medical Psychology and Medical Sociology, Universitätsmedizin Göttingen, Göttingen, Germany
- ³⁹ Oxford University Hospitals NHS Trust, Oxford, UK
- ⁴⁰ Intensive Care Unit, CHU Poitiers, Poitiers, France
- ⁴¹ Movement Science Group, Faculty of Health and Life Sciences, Oxford Brookes University, Oxford, UK
- ⁴² Department of Neurosurgery, Antwerp University Hospital and University of Antwerp, Edegem, Belgium
- ⁴³ Department of Anesthesia & Intensive Care, Maggiore Della Carità Hospital, Novara, Italy
- ⁴⁴ Department of Neurosurgery, University Hospitals Leuven, Leuven, Belgium
- ⁴⁵ Department of Neurosurgery, Clinical centre of Vojvodina, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia
- ⁴⁶ Division of Anaesthesia, University of Cambridge, Addenbrooke's Hospital, Cambridge, UK
- ⁴⁷ Center for Stroke Research Berlin, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany
- ⁴⁸ Intensive Care Unit, CHR Citadelle, Liège, Belgium
- ⁴⁹ Department of Anaesthesiology and Intensive Therapy, University of Pécs, Pécs, Hungary
- ⁵⁰ Departments of Neurology, Clinical Neurophysiology and Neuroanesthesiology, Region Hovedstaden Rigshospitalet, Copenhagen, Denmark
- ⁵¹ National Institute for Stroke and Applied Neurosciences, Faculty of Health and Environmental Studies, Auckland University of Technology, Auckland, New Zealand
- ⁵² Department of Neurology, Erasmus MC, Rotterdam, the Netherlands
- ⁵³ Department of Anesthesiology and Intensive care, University Hospital Northern Norway, Tromsø, Norway
- ⁵⁴ Department of Neurosurgery, Hadassah-hebrew University Medical center, Jerusalem, Israel
- ⁵⁵ Fundación Instituto Valenciano de Neurorehabilitación (FIVAN), Valencia, Spain
- ⁵⁶ Department of Neurosurgery, Shanghai Renji hospital, Shanghai Jiaotong University/school of medicine, Shanghai, China
- ⁵⁷ Karolinska Institutet, INCF International Neuroinformatics Coordinating Facility, Stockholm, Sweden
- ⁵⁸ Emergency Department, CHU, Liège, Belgium
- ⁵⁹ Neurosurgery clinic, Pauls Stradins Clinical University Hospital, Riga, Latvia
- ⁶⁰ Department of Computing, Imperial College London, London, UK
- ⁶¹ Department of Neurosurgery, Hospital Universitario 12 de Octubre, Madrid, Spain
- ⁶² Department of Anesthesia, Critical Care and Pain Medicine, Medical University of Vienna, Austria
- ⁶³ College of Health and Medicine, Australian National University, Canberra, Australia
- ⁶⁴ Department of Neurosurgery, Neurosciences Centre & JPN Apex trauma centre, All India Institute of Medical Sciences, New Delhi-110029, India
- ⁶⁵ Department of Neurosurgery, Erasmus MC, Rotterdam, the Netherlands
- ⁶⁶ Department of Neurosurgery, Oslo University Hospital, Oslo, Norway
- ⁶⁷ Division of Psychology, University of Stirling, Stirling, UK

- ⁶⁸ Division of Neurosurgery, Department of Clinical Neurosciences, Addenbrooke's Hospital & University of Cambridge, Cambridge, UK
- ⁶⁹ Department of Neurology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands
- ⁷⁰ Neurointensive Care, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK
- ⁷¹ Department of Intensive Care and Department of Ethics and Philosophy of Medicine, Erasmus Medical Center, Rotterdam, The Netherlands
- ⁷² Department of Clinical Neuroscience, Neurosurgery, Umeå University, Umeå, Sweden
- ⁷³ Hungarian Brain Research Program - Grant No. KTI/A_13_NAP-A-II/8, University of Pécs, Pécs, Hungary
- ⁷⁴ Cyclotron Research Center, University of Liège, Liège, Belgium
- ⁷⁵ Emergency Medicine Research in Sheffield, Health Services Research Section, School of Health and Related Research (ScHARR), University of Sheffield, Sheffield, UK
- ⁷⁶ Institute of Research in Operative Medicine (IFOM), Witten/Herdecke University, Cologne, Germany
- ⁷⁷ VP Global Project Management CNS, ICON, Paris, France
- ⁷⁸ Department of Anesthesiology-Intensive Care, Lille University Hospital, Lille, France
- ⁷⁹ Department of Neurosurgery, Rambam Medical Center, Haifa, Israel
- ⁸⁰ Department of Anesthesiology & Intensive Care, University Hospitals Southampton NHS Trust, Southampton, UK
- ⁸¹ Cologne-Merheim Medical Center (CMMC), Department of Traumatology, Orthopedic Surgery and Sportmedicine, Witten/Herdecke University, Cologne, Germany
- ⁸² Intensive Care Unit, Southmead Hospital, Bristol, Bristol, UK
- ⁸³ Department of Neurological Surgery, University of California, San Francisco, California, USA
- ⁸⁴ Department of Anesthesia & Intensive Care, M. Bufalini Hospital, Cesena, Italy
- ⁸⁵ Department of Neurosurgery, University Hospital Heidelberg, Heidelberg, Germany
- ⁸⁶ Department of Neurosurgery, The Walton centre NHS Foundation Trust, Liverpool, UK
- ⁸⁷ Department of Medical Genetics, University of Pécs, Pécs, Hungary
- ⁸⁸ Department of Neurosurgery, Emergency County Hospital Timisoara, Timisoara, Romania
- ⁸⁹ School of Medical Sciences, Örebro University, Örebro, Sweden
- ⁹⁰ Institute for Molecular Medicine Finland, University of Helsinki, Helsinki, Finland
- ⁹¹ Analytic and Translational Genetics Unit, Department of Medicine; Psychiatric & Neurodevelopmental Genetics Unit, Department of Psychiatry; Department of Neurology, Massachusetts General Hospital, Boston, MA, USA
- ⁹² Program in Medical and Population Genetics; The Stanley Center for Psychiatric Research, The Broad Institute of MIT and Harvard, Cambridge, MA, USA
- ⁹³ Department of Radiology, Antwerp University Hospital and University of Antwerp, Edegem, Belgium
- ⁹⁴ Department of Anesthesiology & Intensive Care, University Hospital of Grenoble, Grenoble, France
- ⁹⁵ Department of Anesthesia & Intensive Care, Azienda Ospedaliera Università di Padova, Padova, Italy
- ⁹⁶ Dept. of Neurosurgery, Leiden University Medical Center, Leiden, The Netherlands and Dept. of Neurosurgery, Medical Center Haaglanden, The Hague, The Netherlands
- ⁹⁷ Department of Neurosurgery, Helsinki University Central Hospital
- ⁹⁸ Division of Clinical Neurosciences, Department of Neurosurgery and Turku Brain Injury Centre, Turku University Hospital and University of Turku, Turku, Finland
- ⁹⁹ Department of Anesthesiology and Critical Care, Pitié-Salpêtrière Teaching Hospital, Assistance Publique, Hôpitaux de Paris and University Pierre et Marie Curie, Paris, France
- ¹⁰⁰ Neurotraumatology and Neurosurgery Research Unit (UNINN), Vall d'Hebron Research Institute, Barcelona, Spain
- ¹⁰¹ Department of Neurosurgery, Kaunas University of Technology and Vilnius University, Vilnius, Lithuania
- ¹⁰² Department of Neurosurgery, Rezekne Hospital, Latvia
- ¹⁰³ Department of Anaesthesia, Critical Care & Pain Medicine NHS Lothian & University of Edinburgh, Edinburgh, UK
- ¹⁰⁴ Director, MRC Biostatistics Unit, Cambridge Institute of Public Health, Cambridge, UK
- ¹⁰⁵ Department of Physical Medicine and Rehabilitation, Oslo University Hospital/University of Oslo, Oslo, Norway
- ¹⁰⁶ Division of Surgery and Clinical Neuroscience, Oslo University Hospital, Oslo, Norway
- ¹⁰⁷ Broad Institute, Cambridge MA Harvard Medical School, Boston MA, Massachusetts General Hospital, Boston MA, USA
- ¹⁰⁸ National Trauma Research Institute, The Alfred Hospital, Monash University, Melbourne, Victoria, Australia
- ¹⁰⁹ Department of Neurosurgery, Odense University Hospital, Odense, Denmark
- ¹¹⁰ International Neurotrauma Research Organisation, Vienna, Austria
- ¹¹¹ Klinik für Neurochirurgie, Klinikum Ludwigsburg, Ludwigsburg, Germany
- ¹¹² Division of Biostatistics and Epidemiology, Department of Preventive Medicine, University of Debrecen, Debrecen, Hungary
- ¹¹³ Department Health and Prevention, University Greifswald, Greifswald, Germany
- ¹¹⁴ Department of Anaesthesiology and Intensive Care, AUVA Trauma Hospital, Salzburg, Austria
- ¹¹⁵ Department of Neurology, Elisabeth-TweeSteden Ziekenhuis, Tilburg, the Netherlands
- ¹¹⁶ Department of Neuroanesthesia and Neurointensive Care, Odense University Hospital, Odense, Denmark
- ¹¹⁷ Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology, NTNU, Trondheim, Norway
- ¹¹⁸ Department of Physical Medicine and Rehabilitation, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway
- ¹¹⁹ Department of Neurosurgery, University of Pécs, Pécs, Hungary
- ¹²⁰ Division of Neuroscience Critical Care, John Hopkins University School of Medicine, Baltimore, USA
- ¹²¹ Department of Neuropathology, Queen Elizabeth University Hospital and University of Glasgow, Glasgow, UK
- ¹²² Dept. of Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, The Netherlands
- ¹²³ Department of Pathophysiology and Transplantation, Milan University, and Neuroscience ICU, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milano, Italy
- ¹²⁴ Department of Radiation Sciences, Biomedical Engineering, Umeå University, Umeå, Sweden
- ¹²⁵ Cochrane Consumers and Communication Review Group, Centre for Health Communication and Participation, School of Psychology and Public Health, La Trobe University, Melbourne, Australia
- ¹²⁶ Perioperative Services, Intensive Care Medicine and Pain Management, Turku University Hospital and University of Turku, Turku, Finland
- ¹²⁷ Department of Neurosurgery, Kaunas University of Health Sciences, Kaunas, Lithuania
- ¹²⁸ Intensive Care and Department of Pediatric Surgery, Erasmus Medical Center, Sophia Children's Hospital, Rotterdam, The Netherlands
- ¹²⁹ Department of Neurosurgery, Kings college London, London, UK
- ¹³⁰ Neurologie, Neurochirurgie und Psychiatrie, Charité – Universitätsmedizin Berlin, Berlin, Germany
- ¹³¹ icoMetrix NV, Leuven, Belgium
- ¹³² Movement Science Group, Faculty of Health and Life Sciences, Oxford Brookes University, Oxford, UK

¹³³ Psychology Department, Antwerp University Hospital, Edegem, Belgium

¹³⁴ Director of Neurocritical Care, University of California, Los Angeles, USA

¹³⁵ Department of Neurosurgery, St.Olavs Hospital, Trondheim University Hospital, Trondheim, Norway

¹³⁶ Department of Emergency Medicine, University of Florida, Gainesville, Florida, USA

¹³⁷ Department of Neurosurgery, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany

¹³⁸ VTT Technical Research Centre, Tampere, Finland

¹³⁹ Section of Neurosurgery, Department of Surgery, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, MB, Canada

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Authors' contributions

EvV analyzed the data and drafted the manuscript, and the supplementary tables and figures. All coauthors gave feedback on the manuscript. EJK supervised the project. All coauthors gave feedback on (and approved) the final version of the manuscript.

Appendix A. Supplementary data

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