

Early advance care planning in amyotrophic lateral sclerosis patients: results of a systematic intervention by a palliative care team in a multidisciplinary management programme – a 4-year cohort study

Sukockienė Eglė^{a*}, Iancu-Ferfoglia Ruxandra^{a*}, Boegli Monique^b, Lefranc-Barranco Catherine^b, Truffert André^a, Héritier-Barras Anne-Chantal^a, Genton Laurence^c, Leuchter Igor^d, Adler Dan^e, Janssens Jean-Paul^{e**}, Escher Monica^{fg**}

^a Division of Neurology, Department of Clinical Neurosciences, Geneva University Hospitals, Switzerland

^b Pain Consultation, Division of Clinical Pharmacology and Toxicology, Department of Acute Medicine, Geneva University Hospitals, Switzerland

^c Division of Nutrition, Department of Medical Specialties, Geneva University Hospitals, Switzerland

^d Division of ENT, Department of Clinical Neurosciences, Geneva University Hospitals, Switzerland

^e Division of Pulmonary Diseases, Department of Medicine, Geneva University Hospitals, Switzerland

^f Palliative Care Consultation, Division of Palliative Medicine, Department of Rehabilitation and Geriatrics, Geneva University Hospitals, Switzerland

^g Unit for Development and Research in Medical Education (UDREM), Faculty of Medicine, University of Geneva, Switzerland

Summary

INTRODUCTION: Although recommended, the implementation of early advance care planning is suboptimal in amyotrophic lateral sclerosis (ALS) patients. Barriers to advance care planning include healthcare professionals' and patients' reluctance, and uncertainty about the right time to initiate a discussion.

AIM OF THE STUDY: To determine how often advance care planning was initiated, and the content of the discussion in a first routine palliative care consultation integrated within a multidisciplinary management programme.

METHODS: Between June 2012 and September 2016, a prospective cohort study was conducted in Geneva University Hospitals. Sixty-eight patients were seen every 3 months for a 1-day clinical evaluation in a day care centre.

RESULTS: The patients' mean \pm standard deviation age was 68.6 ± 11.9 years, 50% were women. Four patients were excluded because of dementia. Advance care planning was initiated with 49 (77%) patients in the first palliative care consultation. Interventions most often addressed were cardiopulmonary resuscitation (49%), intubation and tracheostomy (47%) and palliative sedation (36.7%). Assisted suicide was discussed with 16 patients (36.6%). Functional disability was the only factor associated with initiation of advance care planning. Nearly half of the patients wrote advance directives (45%) or designated a healthcare surrogate (41%). Bulbar onset, functional disability and noninvasive ventilation were not associated with the completion of advance directives.

CONCLUSION: Early initiation of advance care planning is feasible in most ALS patients during a routine consultation, and relevant treatment issues can be discussed. All ALS patients should be offered the opportunity to write advance directives as completion was not associated with disease severity. (Registered at clinicaltrials.gov: No. NCT03536962.)

Introduction

Amyotrophic lateral sclerosis (ALS) is a severe neurodegenerative disease, usually fatal within 2 to 4 years. The early initiation of advance care planning is important in order to provide care consistent with patients' values and preferences [1]. Interventions such as noninvasive or invasive ventilation, or cardiopulmonary resuscitation have the potential to prolong survival, but they have little influence on the course of the disease and, in the case of an acute event, full recovery to the previous state of health is uncertain. Thus their pros and cons should be discussed with patients [2]. However, in a European survey, these issues were addressed on a regular basis in only 55% of ALS centres [3]. Contrary to European guidelines, early discussions about end-of-life decisions with ALS patients were found to be infrequent [4]. Barriers to advance care planning include healthcare professionals' and patients' reluctance to discuss end-of-life matters [5–7], and uncertainty about the right time to initiate a discussion [8]. The systematic integration of a palliative care consultation in a multidisciplinary management programme for ALS patients has the potential to overcome these barriers [9, 10].

* Equally contributing first authors

** Equally contributing last authors

Correspondence:

PD Dr Monica Escher, MER, Division of Palliative Medicine, Geneva University Hospitals, 4-6 Rue Gabrielle-Perret-Gentil, CH-1211 Geneva 14, [monica.escher\[at\]hcuge.ch](mailto:monica.escher[at]hcuge.ch)

The main aim of this study was to determine the rate and content of advance care planning in a first palliative care consultation. Secondary objectives were to determine the rate of completion of advance directives and/or designation of a healthcare surrogate, and whether factors indicative of disease severity (noninvasive ventilation, bulbar-onset ALS, Revised Amyotrophic Lateral Sclerosis Functional Rating Scale [ALSFRS-R] score) were associated with the writing of advance directives.

Materials and methods

Between June 2012 and September 2016, a longitudinal observational study of ALS patients followed by the Geneva multidisciplinary management programme was conducted. All the patients provided written informed consent. The trial was registered at clinicaltrials.gov (trial N° NCT03536962). It was approved by the Geneva Research Ethics Committee (CER 09-160R NAC 09-056R).

Patients' demographic and clinical data were collected on their inclusion in the study (e.g., age, gender, ALSFRS-R score, time from first symptoms). The other parameters, such as the date of noninvasive ventilation initiation, gastrostomy tube (percutaneous endoscopic gastrostomy; PEG) insertion, the date of death, the date and content of the first palliative care consultation and the designation of a healthcare surrogate, were recorded during follow-up.

Details of the multidisciplinary management structure have been previously reported [11]. Briefly, patients are seen every 3 months for a 1-day clinical evaluation in an outpatient day-care centre. The evaluation includes the systematic interventions of a coordinated team with experience in motor neurone disease care, including a neurologist, a pulmonologist, a medical nutritionist and a dietitian, an ENT specialist, a speech therapist, a palliative care nurse and physician, an occupational therapist, and a physiotherapist. Other team members, such as a psychiatrist or a social worker, can be solicited if needed. Multidisciplinary care is organised according to the guidelines of EFNS [12]: this model of care has been shown to benefit patients with motor neurone disease [13, 14].

Specialised palliative care has been part of the structure from its very beginning. Members of the palliative care team include a senior physician and four part-time nurses. The physician is certified in internal medicine, clinical pharmacology and palliative care. The nurses are certified in palliative care. Two of them make home visits for the ALS patients followed up in the multidisciplinary management programme in addition to their regular work within the ALS clinic. Both nurses and physician have extensive clinical experience in palliative care.

All the patients referred to the multidisciplinary management programme have a palliative care consultation. The consultation is planned in the schedule patients receive at home. The patient's assessment day begins with the neurologist and, after pulmonary functional testing, the patient is seen by the pulmonologist. The nutritionist's evaluation includes a targeted history and measurement of body weight and composition. In addition to standard clinical examination, the patient is observed during lunch by the speech therapist. The afternoon is divided between the physical therapist, the occupational therapist and the pal-

liative care consultation, which is scheduled last in the day. The neurologist then summarises the results of the various evaluations and the therapeutic propositions to the patient, and plans the date for the next assessment in the ALS clinic.

Diagnosis of definite, probable or possible ALS is established by an experienced neurologist according to the revised El Escorial criteria; the revised ALS Functional Rating Score (ALSFRS-R) is used to determine progression of disability. Based on initial symptoms, patients are classified as "bulbar" or "non-bulbar". Initiation of noninvasive ventilation or PEG tube insertion are performed electively, on an outpatient basis or during a short hospital stay. The decision to start noninvasive ventilation is based on symptoms and functional parameters. When weight loss exceeds 10% or glottic dysfunction and/or recurrent aspiration occurs, PEG is systematically suggested.

At the first encounter, the palliative care specialist – either the physician or the nurse – introduces herself and explains to the patient what palliative care is, and what the goals of the consultation are. The consultation lasts between 30 and 60 minutes, depending on the patient's needs. To account for patient fatigue at the end of the day, the discussion starts with the patient's currently most important difficulty or concern. Advance care planning can be the first topic addressed, but it can also be the last. To target her intervention, the palliative care specialist also uses the specialised evaluations made earlier in the day, which are all documented in the patient's electronic medical file. It avoids unnecessary repetitions in history taking (e.g., difficulties in eating) and it allows potentially sensitive issues to be addressed and explored in a straightforward manner (e.g., low sniff nasal-inspiratory pressure and preferences about noninvasive and mechanical ventilation).

The goals of the palliative care consultation are: (1) symptom assessment and management; (2) exploration of social and familial issues, and identification of organisational needs; (3) initiation of advance care planning, and support in the writing of advance directives. The general concept of our multidisciplinary management team regarding invasive life support and tracheostomy was detailed in a previous publication [15]. Assisted suicide is discussed according to patients' needs and request.

Statistics

Study data were collected in SecuTrial®, a GCP-compliant Electronic Data Capture System.

Patients' characteristics were described as frequency and percentage for qualitative data and as mean \pm standard deviation (SD) for quantitative data, or median (interquartile range [IQR]) according to the distribution of the data. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 22.0 (Armonk, NY: IBM Corporation). Mean parameters were compared using the Student *t*- and Mann-Whitney tests. The χ^2 (chi-square) test was used for nominal variables. Statistical significance was established at $p < 0.05$.

Results

Sixty-eight patients were included. Mean age was 68.6 ± 11.9 years and half the patients were female. Median ALS-

FRS-R score at the first multidisciplinary management visit was 39 (IQR 32–42). Four patients suffered from dementia and were excluded, leaving 64 patients for analysis. The median time between initial symptoms and the first multidisciplinary management visit was 11.1 months (IQR 8–18). The median number of visits was 4 (IQR 2–6), and the median number of palliative care consultations was 3 (IQR 2–4). At the time of the first palliative care consultation, 12 (19%) patients were under noninvasive ventilation, and 4 (6%) patients had a gastrostomy tube.

Overall, 13 patients were diagnosed with bulbar onset ALS. Most (98%) patients lived at home and the main caregiver was the spouse (78%). During follow-up, noninvasive ventilation was initiated in 27 patients (41%) and a gastrostomy tube was inserted in 14 patients (21%). Thirty (44%) patients died, among whom six (20%) received palliative sedation. Causes of death were cardiac and/or respiratory in 24 (80%) patients; 4 (13%) patients died through assisted suicide. Deaths occurred at home ($n = 13$, 43%), on a palliative care ward ($n = 6$, 20%), on a hospital ward ($n = 4$, 13%) or in a long-term care institution ($n = 3$, 10%). Location of death was not available for four patients.

Advance care planning was initiated with 49 (77%) patients in the first palliative care consultation. These patients had a higher ALSFRS-R score compared with the other patients (37 ± 8.7 vs 30.3 ± 10 points; $p = 0.003$), but they were no more likely to have a bulbar-onset disease. The proportion of patients who had early advance care planning did not differ between patients under noninvasive ventilation (10/12, 83%) and those without noninvasive ventilation (39/52, 75%; $p = 0.5$). Advance directives and the designation of a healthcare surrogate were discussed with 38/64 (59%) patients. The main medical interventions addressed were intubation and tracheostomy ($n = 23$, 47%), cardiopulmonary resuscitation ($n = 24$, 49%) and palliative sedation ($n = 18$, 36.7%) (table 1). Assisted suicide was discussed with about a third of patients ($n = 16$, 36.6%). Among them, three considered it was an option, and three considered it was not. Most patients talked about assisted suicide not as a definite option, but as a possibility offering a sense of control. The main reasons for which advance care planning was not initiated can be divided into two categories: (1) the patient was not interested, and (2) the patient was too anxious, or was shocked that negative clinical outcomes could be considered. Patient's lack of interest was sometimes related to a coping strategy ("live day by day") or to a feeling that an extensive discussion was premature.

During follow-up, advance directives were written by 29 (45%) patients and 26 (41%) designated a healthcare sur-

rogate. The proportion of patients who wrote advance directives did not differ between patients with bulbar (6/13, 43%) vs non-bulbar onset (23/51, 45%; $p = 0.96$), or between patients under noninvasive ventilation (8/27, 30%) vs without non-invasive ventilation (21/37, 57%; $p = 0.18$). Mean ALSFRS-R scores at first multidisciplinary management visit were similar between patients who wrote advance directives and patients who did not (34.9 ± 8.6 vs 37.1 ± 8.6 ; $p = 0.43$). At the end of the follow-up period, 14 patients out of 29 who completed advance directives had died.

Discussion

This study shows that early advance care planning is feasible in ALS patients, since it was initiated for most patients during the first encounter with the palliative care team. It contrasts with the assumption that patients are reluctant to discuss end-of-life care [5, 7]. Relevant end-of-life issues and medical interventions were addressed with half the patients at the first consultation. A third of patients felt free to address as sensitive an issue as assisted suicide. Thoughts about suicide are reported by ALS patients, although they rarely discuss them with a physician [16, 17]. Assisting an individual in committing suicide is not punished in Swiss law when there is no selfish motive for the help given. Contrary to palliative sedation, assisted suicide is not considered a therapeutic intervention [18] and it is not discussed as such during palliative care consultations. Discussing patient's thoughts about assisted suicide is, however, part of the process of advance care planning. In our cohort, 13% of deceased ALS patients resorted to assisted suicide. In a Dutch study, 22% of 102 ALS patients died as a result of euthanasia or physician-assisted suicide [16]. Ten percent died under palliative sedation compared with 20% in our study. The use of deep sedation until death for the alleviation of symptoms has increased over the years in Switzerland [19]. It concerned 24.5% of deceased patients in 2013, a proportion similar to the ALS patients in our cohort.

Not all patients in our cohort were able or willing to engage in advance care planning at the first consultation. Patients need to adjust and communication about future care must be respectful and timely. In the course of the disease, titration of medical information and support according to deteriorating abilities allows the health professional to stay close to the patient's perception of his or her situation and related needs [10].

Although less than half of the patients completed advance directives or formally designated a healthcare surrogate,

Table 1: Medical interventions discussed on the first palliative care consultation with 49 ALS patients. These patients had a significantly higher ALSFRS-R score (37 ± 8.7 vs 30.3 ± 10 points; $p = 0.003$).

Intervention	Addressed n (%)	Accepted n	Refused n	Not sure / did not want to discuss n
Oro-tracheal intubation and/or tracheostomy	23(47)	4	12	7
Cardiopulmonary resuscitation	24 (49)	5	15	4
Palliative sedation	18 (36.7)	13	1	4
Admission to the intensive care unit	13 (26.5)	5	5	3
Noninvasive ventilation	7 (18)*	1	1	5
Gastrostomy tube	14 (30)†	1	7	6

* Proportion calculated for 39 patients, as 10 patients were under noninvasive ventilation at the time of the consultation † Proportion calculated for 47 patients, as 2 patients had a gastrostomy tube (percutaneous endoscopic gastrostomy) at the time of the consultation

this proportion is higher than reported in other European centres [3]. Cultural and social background can explain some of the differences seen between countries. In a single-centre retrospective Hong Kong study, 16 out of 51 (38.1%) motor neurone disease patients had advance directives [20]. In contrast, high rates of advance directives were reported in the United States, where there are financial incentives to support completion of advance directives [6, 21]. Notwithstanding the absence of advance directives, patients' care preferences expressed during advance care planning are known to be valuable. They were associated with less intensive treatments, such as admission to intensive care [22, 23]. The Swiss law provides a list of health-care surrogates [1] – first the spouse, then the children – if a patient has not designated any [24]. Patients were informed of this disposition during the advance care planning discussion, which probably decreased the perceived need to formally designate a surrogate.

Factors indicative of disease severity were not associated with the completion of advance directives. As recommended, advance directives should be discussed with all ALS patients, with respect to their personal values and background [12]. The completion of advance directives is a valuable goal, but it is just one component of advance care planning. Even more important is the process itself. Discussing values and preferences with patients helps them define what matters most to them, and enables them to set priorities and treatment goals [1]. Advance care planning requires skills and expertise. Our study adds support to the integration of routine palliative care consultations into ALS multidisciplinary care since it offers patients early access to specialists trained in advance care planning.

The strengths of the study are the inclusion of all the patients with ALS in our area and the prospective collection of data. However, this study has limitations. The sample size was modest, there was no control group as our aim was to provide a detailed observational study of a cohort of ALS patients cared for in a multidisciplinary management programme. Data on the impact of advance care planning on clinical outcomes were not collected. We did not explore patients' and caregivers' perspectives to determine how useful they found advance care planning.

Early advance care planning was feasible in most ALS patient, and relevant end-of-life issues and treatment options could be discussed during a first encounter already. No factor of disease severity was associated with advance directive completion and it should be offered to all the patients. Future studies addressing the impact of advance care planning on clinical outcomes in ALS patients, and the benefits and burdens of advance care planning that patients with progressive neurological disorders and their families might experience are needed.

Acknowledgments

The authors are grateful to Antoine Poncet and Ninon Horie for systematic data collection and providing datasets for statistical analysis.

Financial disclosure

The study was supported financially by the Ligue Pulmonaire Genevoise, a non-profit association involved in home care for patients with respiratory disorders. The Ligue Pulmonaire Genevoise did not contribute to the design of the study, to the collection, analysis, and interpretation of data, or to the writing of the manuscript.

Potential competing interests

The authors declare no conflict of interest.

References

- Sudore RL, Lum HD, You JJ, Hanson LC, Meier DE, Pantilat SZ, et al. Defining Advance Care Planning for Adults: A Consensus Definition From a Multidisciplinary Delphi Panel. *J Pain Symptom Manage*. 2017;53(5):821–832.e1. doi: <http://dx.doi.org/10.1016/j.jpainsymman.2016.12.331>. PubMed.
- Rietjens JAC, Sudore RL, Connolly M, van Delden JJ, Drickamer MA, Droger M, et al.; European Association for Palliative Care. Definition and recommendations for advance care planning: an international consensus supported by the European Association for Palliative Care. *Lancet Oncol*. 2017;18(9):e543–51. doi: [http://dx.doi.org/10.1016/S1470-2045\(17\)30582-X](http://dx.doi.org/10.1016/S1470-2045(17)30582-X). PubMed.
- Borasio GD, Shaw PJ, Hardiman O, Ludolph AC, Sales Luis ML, Silani V; European ALS Study Group. Standards of palliative care for patients with amyotrophic lateral sclerosis: results of a European survey. *Amyotroph Lateral Scler Other Motor Neuron Disord*. 2001;2(3):159–64. doi: <http://dx.doi.org/10.1080/146608201753275517>. PubMed.
- Marin B, Beghi E, Vial C, Bernard E, Lautrette G, Clavelou P, et al.; EURECAL consortium. Evaluation of the application of the European guidelines for the diagnosis and clinical care of amyotrophic lateral sclerosis (ALS) patients in six French ALS centres. *Eur J Neurol*. 2016;23(4):787–95. doi: <http://dx.doi.org/10.1111/ene.12941>. PubMed.
- Hiscock A, Barclay S. 'It's a hard conversation to have'. Healthcare professionals' views concerning advance care discussions with young people affected by life-limiting neuromuscular diseases: an interview study. *BMJ Support Palliat Care*. 2019;9(1):e9. doi: <http://dx.doi.org/10.1136/bmjspcare-2017-001369>. PubMed.
- Murray L, Butow PN. Advance care planning in motor neuron disease: A systematic review. *Palliat Support Care*. 2016;14(4):411–32. doi: <http://dx.doi.org/10.1017/S1478951515001066>. PubMed.
- You JJ, Downar J, Fowler RA, Lamontagne F, Ma IW, Jayaraman D, et al.; Canadian Researchers at the End of Life Network. Barriers to goals of care discussions with seriously ill hospitalized patients and their families: a multicenter survey of clinicians. *JAMA Intern Med*. 2015;175(4):549–56. doi: <http://dx.doi.org/10.1001/jamainternmed.2014.7732>. PubMed.
- Billings JA, Bernacki R. Strategic targeting of advance care planning interventions: the Goldilocks phenomenon. *JAMA Intern Med*. 2014;174(4):620–4. doi: <http://dx.doi.org/10.1001/jamainternmed.2013.14384>. PubMed.
- Brizzi K, Paganoni S, Zehm A, De Marchi F, Berry JD. Integration of a palliative care specialist in an amyotrophic lateral sclerosis clinic: Observations from one center. *Muscle Nerve*. 2019;60(2):137–40. doi: <http://dx.doi.org/10.1002/mus.26607>. PubMed.
- Seeber AA, Pols AJ, Hijdra A, Grupstra HF, Willems DL, de Visser M. Advance care planning in progressive neurological diseases: lessons from ALS. *BMC Palliat Care*. 2019;18(1):50. doi: <http://dx.doi.org/10.1186/s12904-019-0433-6>. PubMed.
- Sukockienė E, Iancu Ferfoglă R, Truffert A, Héritier Barras AC, Genton L, Viatte V, et al. Multidisciplinary care in amyotrophic lateral sclerosis: a 4-year longitudinal observational study. *Swiss Med Wkly*. 2020;150:w20258. PubMed.
- Andersen PM, Abrahams S, Borasio GD, de Carvalho M, Chio A, Van Damme P, et al.; EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS)—revised report of an EFNS task force. *Eur J Neurol*. 2012;19(3):360–75. doi: <http://dx.doi.org/10.1111/j.1468-1331.2011.03501.x>. PubMed.
- Cheng HWB, Chan KY, Chung YKJ, Choi CW, Chan CH, Cheng SC, et al. Supportive & palliative interventions in motor neurone disease: what we know from current literature? *Ann Palliat Med*. 2018;7(3):320–31. doi: <http://dx.doi.org/10.21037/apm.2017.10.01>. PubMed.
- Oliver DJ. Palliative care in motor neurone disease: where are we now? *Palliat Care*. 2019;12:1178224218813914. doi: <http://dx.doi.org/10.1177/1178224218813914>. PubMed.
- Héritier Barras AC, Adler D, Iancu Ferfoglă R, Ricou B, Gasche Y, Leuchter I, et al., CeSLA group. Is tracheostomy still an option in amyotrophic lateral sclerosis? Reflections of a multidisciplinary work group. *Swiss Med Wkly*. 2013;143:w13830. doi: <http://dx.doi.org/10.4414/smw.2013.13830>. PubMed.
- Maessen M, Veldink JH, Onwuteaka-Philipsen BD, Hendricks HT, Schelhaas HJ, Grupstra HF, et al. Euthanasia and physician-assisted suicide in amyotrophic lateral sclerosis: a prospective study. *J Neurol*. 2014;261(10):1894–901. doi: <http://dx.doi.org/10.1007/s00415-014-7424-6>. PubMed.

- 17 Stutzki R, Weber M, Reiter-Theil S, Simmen U, Borasio GD, Jox RJ. Attitudes towards hastened death in ALS: a prospective study of patients and family caregivers. *Amyotroph Lateral Scler Frontotemporal Degen-er.* 2014;15(1-2):68–76. doi: <http://dx.doi.org/10.3109/21678421.2013.837928>. PubMed.
- 18 ASSM [Internet]. Berne: Académie Suisse des Sciences Médicales. Attitude face à la fin de vie et à la mort. Directive médico-éthique. Available from: <https://www.samw.ch/fr/Publications/Directives.html>.
- 19 Ziegler S, Schmid M, Bopp M, Bosshard G, Puhan MA. Continuous Deep Sedation Until Death-a Swiss Death Certificate Study. *J Gen Intern Med.* 2018;33(7):1052–9. doi: <http://dx.doi.org/10.1007/s11606-018-4401-2>. PubMed.
- 20 Cheng HWB, Chan OMI, Chan CHR, Chan WH, Fung KS, Wong KY. End-of-life Characteristics and Palliative Care Provision for Patients With Motor Neuron Disease. *Am J Hosp Palliat Care.* 2018;35(6):847–51. doi: <http://dx.doi.org/10.1177/1049909117735832>. PubMed.
- 21 Auriemma CL, Chen L, Olorunnisola M, Delman A, Nguyen CA, Cooney E, et al. Public Opinion Regarding Financial Incentives to Engage in Advance Care Planning and Complete Advance Directives. *Am J Hosp Palliat Care.* 2017;34(8):721–8. doi: <http://dx.doi.org/10.1177/1049909116652608>. PubMed.
- 22 Khandelwal N, Kross EK, Engelberg RA, Coe NB, Long AC, Curtis JR. Estimating the effect of palliative care interventions and advance care planning on ICU utilization: a systematic review. *Crit Care Med.* 2015;43(5):1102–11. doi: <http://dx.doi.org/10.1097/CCM.0000000000000852>. PubMed.
- 23 Apostol CC, Waldfogel JM, Pfoh ER, List D, Billing LS, Nesbit SA, et al. Association of goals of care meetings for hospitalized cancer patients at risk for critical care with patient outcomes. *Palliat Med.* 2015;29(4):386–90. doi: <http://dx.doi.org/10.1177/0269216314560800>. PubMed.
- 24 Confédération Suisse Fedlex. The publication platform for federal law [Internet]. [updated 2020 January 1, cited 2020 April 6]. Swiss Civil Code of 10 December 1907. Available from: <https://www.admin.ch/opc/fr/classified-compilation/19070042/index.html>