



Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en



Hot topic in geriatric medicine

Italian intersociety consensus on prevention, diagnosis, and treatment of delirium in hospitalized older persons[☆]

G. Bellelli^{a,*}, A. Morandi^a, M. Trabucchi^a, G. Caironi^b, D. Coen^b, C. Fraticelli^b, C. Paolillo^b, C. Prevaldi^b, A. Riccardi^b, G. Cervellin^b, C. Carabellese^c, S. Putignano^c, A. Cherubini^d, P. Gnerre^e, A. Fontanella^e, N. Latronico^f, C. Tommasino^f, A. Corcione^f, G. Ricevuti^g, N. Ferrara^g, F. De Filippi^h, A. Ferrari^h, M. Guarinoⁱ, M.P. Ruggieriⁱ, P.A. Modesti^j, F. Perticone^j, C. Locatelli^k, P. Hrelia^k, M.O. Toscano^l, E. Bondi^l, A. Tarasconi^m, L. Ansaloni^m, S. Maggi^d

^aAIP (Associazione Italiana di Psicogeriatrica), Brescia, Italy

^bAcEMC (Academy of Emergency Medicine and Care), Pavia, Italy

^cAGE (Associazione Geriatri Extraospedalieri), Pavia, Italy

^dEUGMS (European Union Geriatric Medicine Society), Italy

^eFADOI (Federazione delle Associazioni dei Dirigenti Ospedalieri Internisti), Roma, Italy

^fSIAARTI (Società Italiana di Anestesia, Analgesia Rianimazione e Terapia Intensiva), Roma, Italy

^gSIGG (Società Italiana di Geriatria e Gerontologia), Firenze, Italy

^hSIGOT (Società Italiana di Geriatria Ospedale e Territorio), Roma, Italy

ⁱSIMEU (Società Italiana di Medicina di Emergenza e Urgenza), Milano, Italy

^jSIMI (Società Italiana di Medicina Interna), Roma, Italy

^kSITOX (Società Italiana di Tossicologia), Pavia, Italy

^lCNI-SPDC (Coordinamento Nazionale Servizi Psichiatrici di Diagnosi e Cura), Garbagnate Milanese, Italy

^mWSES (World Society of Emergency Surgery), Bologna, Italy

ARTICLE INFO

Article history:

Received 25 June 2017

Accepted 26 June 2017

Available online xxx

Keywords:

Clinical management

Consensus

Delirium

Cognitive decline

ABSTRACT

Delirium is a severe neuropsychiatric syndrome characterized by inattention and global cognitive dysfunction in the setting of an acute medical illness, medical complication, drug intoxication or drug withdrawal. The most important risk factors are advanced age and dementia whereas pain, dehydration, infections, stroke, metabolic disturbances, and surgery are the most common triggering factors. Although delirium is a common clinical syndrome in different setting of care (acute care hospitals, inpatient rehabilitation facilities, nursing homes, and hospices) it often remains under-recognised, poorly understood and not adequately managed then there exists a clear need for improved understanding to overcome cultural stereotypes and for the development and dissemination of a comprehensive model of implementation of general good practice points. A network of Italian national scientific societies was thus convened (1) to develop a collaborative multidisciplinary initiative report on delirium in the elderly hospitalized patients, (2) to focus the attention of health care personnel on prevention, diagnosis and therapy of patients suffering from delirium, and (3) to make the health services research community and policy-makers more aware of the potential risks of this condition providing a reference for training activities and data collection.

© 2017 Elsevier Masson SAS and European Union Geriatric Medicine Society. All rights reserved.

1. Introduction

In the elderly delirium has often the connotation of a syndrome with multifactorial aetiology, characterized by an acute behavioural decompensation with fluctuating attention in the context of a pre-existing vulnerability [1–3]. According to recent reports delirium is very common in the hospital setting. The overall prevalence of delirium at the community level is about 1–2%,

[☆] This article is being published jointly in *Internal and Emergency Medicine* and *European Geriatric Medicine*.

* Corresponding author at: School of medicine and surgery, university of Milano-Bicocca, via Cadore 48, 20900 Monza, Italy.

E-mail address: giuseppe.bellelli@unimib.it (G. Bellelli).

whereas it increases to 14–24% in the hospital setting and particularly in the emergency, surgical or medical ward, where up to one in five patients may present delirium [4–7]. High prevalence was also observed in nursing homes and long-term care facilities [6,8]. The two most important risk factors for delirium are advanced age and dementia, two-thirds of all cases of delirium in the elderly occurring in patients with dementia [9]. Pain, dehydration, infections, stroke, metabolic disturbances, and surgery are other common triggering factors. Due to the progressive aging of the population, an increase of both prevalence and incidence of delirium can thus be expected in the next future.

Delirium can have serious consequences, including postoperative complications, prolonged hospital stay, falls, and immobilization, inducing functional decline, institutionalization, and mortality [5,10,11]. Delirium significantly impacts on the emotional status of affected patients, enhancing the stress experienced by families, caregivers, and supporting staff. On these bases, annual costs of delirium were estimated to be between \$38 billion and \$151 billion in the United States [12].

Finally, there is a considerable body of evidence on the possibility to both predict the onset of delirium, about one third of cases can be prevented, and to successfully treat most of the affected patients [13,14].

These data, taken together, constitute the rationale for this position paper and support the idea that a correct approach to patients with delirium should be one of the objectives (and quality assessment criteria) of hospitals in the twenty-first century care.

2. Method of work

A network of Italian national scientific societies developed present consensus statement. Task force members were identified by the president and/or the boards of each relevant scientific society, as appropriate. Published guidelines of national and international scientific societies were reviewed [15–23]. Thereafter, a writing group has produced a first draft of the document. To obtain a widespread consensus, draft was distributed to the scientific societies for local evaluation and revision by as many experts as possible. The ensuing final draft was finally approved by scientific societies. It was finally decided not to assign levels of evidence to the recommendations that are proposed, whereas the literature review has been extended.

3. General principles

Although delirium is a clinical condition known since a very long time (since the days of the Latins), it received an autonomous connotation in nosography only in 1980, with DSM III 20. Unfortunately in the health care setting the correct use of the term delirium as well as the knowledge of the diagnostic criteria is still

limited. Terms such as “acute confusional state”, “toxic-metabolic encephalopathy”, or “psychomotor agitation”, which do not represent specific disease entities, are still currently used as delirium synonyms. A review of the literature, in this regard, has shown that only in half of the cases, the term “delirium” has been used properly in accordance with the reference diagnostic criteria; acute alterations of the cognitive function were described using more than fifteen different terminologies [24]. In accordance with international classifications, the term “delirium” is to be used as a single term gathering in a single model symptoms and signs of a syndrome due to various cause [1]. An effective education of health care personnel to appropriately use the term “delirium” in clinical practice is now needed (Box 1).

It is now recognized that the delirium is not always a transient condition as it was believed once, but is able to persist and produce complications both in the medium and the long term [5,25]. It is therefore essential to successfully communicate the presence of this condition (and the cognitive status of the patient) in the hospital discharge report, especially for patients who are assigned to post-acute care wards, rehabilitation, or long-term nursing care. In particular, the term “delirium” is to be used in the letter of resignation as a clinical diagnosis, to facilitate follow-up by general practitioner or the specific treatment of the cognitive disorder in specialist outpatient facilities.

Two recent Italian studies showed that delirium is inadequately recognized at both admission and hospital discharge and that the methods of diagnosis and management in the health care setting are often inadequate [24,26]. Despite being a very common clinical condition, the level of competence and awareness of delirium and its complications is very low among both health personnel. The diffusion of knowledge of delirium among health personnel is crucial to improve level of competence and awareness of delirium and its complications in order to achieve a final improvement in the standard of care of patients.

The course of patients with delirium is often complicated by the anxiety symptoms. Furthermore, the emotion of caregivers and staff, who are often unskilled, are today still largely unmet needs well documented by available reports [27]. The ability of staff members to understand that delirium is a dramatic and heart-breaking condition can help to break the cycle and to limit the possibility of considering the affected patient as a “nuisance” to be transferred to other wards [28]. To change the attitude of health personnel and caregivers toward delirium is a crucial step in the path to improve the quality of care as indicated by a systematic review of Yanamadala and colleagues [29]. Problem can be mitigated or eliminated by providing instruction that enables staff personnel and caregivers to gain new knowledge, acquire new skills and learn how to use methods for the detection of delirium. Active involvement of participants may induce a transitional change, whereas training courses generally geared to increase knowledge on the subject do not seem to be equally effective [29].

The involvement of associations of patients and family members in training events can be another potential mechanism to trigger attitudinal change. In this regard this position paper wants to encourage academics and doctors to include in educational themes also stories related to the emotional feedback of patients who experienced delirium, such as those available free of charge on the website of the European Delirium Association [30]. Informative and educational videos and brochures [31] may increase the awareness of the general population.

4. Prevention

The possibility that elderly or frail patients may develop delirium in hospital because of inappropriate interventions is high (Box 2). Delirium is often related with the use of drugs with high

Box 1. General principles.

- Use the term “delirium” in a systematic way. The use of generic and non-specific terms should be avoided to favour dissemination and to prevent argument trivialization. The definition of delirium and the diagnostic criteria are to become widespread heritage of health professionals.
- Mention delirium as a clinical diagnosis in the hospital discharge report.
- Raise awareness among operators that delirium may be associated with both serious medical complications and stressful emotional experiences for patients and caregivers.
- Raise awareness among operators regarding clinical long-term consequences of delirium

Box 2. Prevention.

- In all frail patients, particularly in the presence of risk factors for delirium, multi-component prevention interventions have to be implemented such as: time-space reorientation, limited use of psychoactive drugs, early mobilization, sleep hygiene, maintenance of proper hydration and nutrition, and provision of visual and auditory prosthesis (if used).
- At the time of access to the hospital or other health institution, elderly or frail patients should be evaluated for the presence of risk factors for delirium. In addition to the general risk factors, risk factors specific to the care setting should be specifically searched and considered.
- Avoid transfer between hospital wards of patients at risk for delirium unless necessary to provide specifically demanded treatment.
- Prevention programs of delirium should be specifically considered by the general direction of hospitals in view of the documented benefits for patients and the potential cost savings.

anticholinergic activity and application of medical devices, such as catheters or restraints [2]. Therefore, the prevention of delirium during hospitalization is a fundamental aspect of care.

The first step in this process is the identification of patients at increased risk of developing delirium. It is important to remember that in addition to the general risk factors, there are specific risk factors for each setting of care (e.g. depth of general anaesthesia, intensity of postoperative pain in patients who have undergone surgery, age-specific problems), which must be considered [32–36].

Environmental changes, such as a shift from one room to another or from one department to another, may adversely affect personal and space-time orientation of patients at risk of delirium [15]. The need to minimize the changes of room and ward is also supported by the fact that frequent department displacements interferes with the continuity of care and requires continuous system adjustments. For example, care plan reformulation at each ward change leads to inevitable lengthened in decision-making and fragments assistance [37]. As part of intensive care, two randomized clinical trials have shown that early mobilization may reduce the duration of delirium [38,39].

The Hospital Elder Life Program (HELP) is a multi-component prevention program including non-pharmacological interventions for temporal-spatial reorientation, limited use of psychoactive drugs, early mobilization, sleep hygiene, adequate hydration and maintenance nutrition and supply of visual and hearing aids (if used by the patient) [40]. The program requires an experienced interdisciplinary team, in close collaboration with a nursing team educated on the topic of delirium and, possibly, with volunteers. The HELP program has been proven effective by more than a dozen studies with follow-up, completed in more than 200 hospitals around the world, with a calculated savings of about \$9000 per patient/year [40]. In addition, a correct approach to patients with delirium also allows obtaining clinical results for outcomes apparently independent of delirium, such as falls and pressure ulcers. More precisely, according to a recent meta-analysis the implementation of non-pharmacological multifactorial interventions aimed at preventing delirium reduces the rate of falls in elderly patients by up to 64% [41]. Such interventions are effective in the prevention of delirium, both in patients with medical and surgical problems [13,42]. Cost-effectiveness analysis of prevention programs in the hospital setting in Italy is also required.

For these reasons, we propose that delirium prevention programs receive a strong attention by directorate general of

health services to have specific programs implemented in clinical practice.

The proactive advice by a geriatric team is another approach that was proved to be effective in reducing the negative impact of postoperative delirium in elderly patients with femoral fractures [43,44]. For this reason, we hope that ortho-geriatric models, characterized by structured collaboration between orthopaedic and geriatricians or internists with high skills on elderly patients, can spread more and more in Italy. Similarly, the implementation of models in which clinical experts of delirium are involved in the peri-operative management of surgical patients and patients with high clinical complexity is to be pursued.

5. Prompt recognition and diagnosis

Prompt recognition of delirium is crucial. Delirium may present with three different clinical types:

- hyperkinetic or overactive; characterized by psychomotor agitation, and, sometimes, illusions and hallucinations;
- hypokinetic or underactive; characterized by psychomotor slowing, drowsiness, reduced response to external stimuli and apathy;
- mixed; characterized by an alternation of phases of hyperkinetic and hypokinetic type.

The hyperkinetic variant is the most easy to recognize, but it is also the least frequent [37] (Box 3). The hypokinetic variant is conversely the most common clinical presentation, especially among the elderly, but it is more difficult to recognize and is related to a worse prognosis [45]. The symptoms of hypokinetic delirium may in fact be mistakenly attributed to dementia, depression, or sedative drugs, being often considered as a “normal” state in view of age and biological complexity of the patient.

The use of validated screening tools, among which the most widespread is the Confusion Assessment Method (CAM) [46–48] and its variant for intensive therapy CAM-ICU5, can be of great help for this purpose, making easy the recognition of delirium. When using screening tools, recognition and diagnosis of delirium is almost total. On the contrary, when these instruments are not utilized the rate of recognition is low [3,49,50]. However, CAM requires a specific training of personnel. When training is absent the reliability of CAM in the diagnosis of delirium is impaired [46,48,49]. The “4AT” is an instrument of delirium screening that can be used in various settings of care, including units of geriatrics and internal medicine, surgery, first aid facilities/emergency departments and rehabilitation [51]. This tool is objective because based on fixed scores, and is very rapid requiring no more than two minutes to run. It also allows the evaluation of patients who are unable to complete the more detailed cognitive tests because drowsy or, conversely, agitated. Most importantly, it does not require a specific training. We therefore propose that the 4AT is included among the assessment tools for admission of elderly hospitalized patients, being, if possible, incorporated in the nursing routine along with other tools as experienced in some Dutch hospitals [43,52].

However, even when delirium is recognized and correctly identified, some health professionals might not consider this diagnosis as a medical emergency. Therefore, patients who are suffering from timely access may be excluded from effective treatments. Instead, delirium may represent a real medical emergency as demonstrated by the recent consensus conference on sepsis and septic shock [53]. Sepsis is defined as the development of organ failure in the presence of an infection. The presence of central nervous system alterations (for example, a patient disoriented in time or in space) can be marked by at least

Box 3. Diagnosis.

- Elderly or frail patients, especially those with risk factors, should be systematically evaluated for the presence of signs or symptoms of delirium on their arrival at the hospital. A reassessment at regular intervals, especially on the occasion of new therapies or clinical events, must be part of the care plan.
- Health care providers who treat patients at high risk for delirium should know and use screening tools such as 4AT scale.
- At the first signs or symptoms of delirium is necessary to search possible causes (infection, hypoglycaemia, stroke, dehydration, adverse effects of medications, use of psychotropic substances, withdrawal syndromes, pain is not adequately treated, acute retention of urine, constipation). The diagnosis of delirium may highlight sepsis that would otherwise be misunderstood.

1 point reduction in the Glasgow Coma Scale. Delirium is an acute cerebral dysfunction and may then determine the first presentation of sepsis, a condition in which the early diagnosis and prompt initiation of antibiotic treatment may reduce mortality. The trivialization of delirium in only a benign clinical condition somehow “disturbing for the team”, represents a major obstacle to improve the quality of care provided to these patients in the hospital.

The health of the individual with delirium may thus be affected by different intra and extra-hospital complications, including death [54]. Delirium should always be seen as a medical emergency.

6. Principles of treatment

All patients with delirium should receive a specific treatment plan with proper consideration of health and care needs including an active search for underlying acute diseases and other clinical conditions that underlie the reorientation of space and time (Box 4). Rationalization of drug therapy, early mobilization, promotion of sleep, maintenance of an adequate nutrition and hydration and the provision of visual aids and auditory, should be specifically

Box 4. Treatment.

- All patients with delirium should receive a treatment plan with proper consideration of health and care needs.
- Non-pharmacological aspects of care are paramount and include an active search for acute diseases and clinical conditions that underlie the onset of delirium, the reorientation of space and time, early mobilization, promoting sleep, maintaining adequate nutrition and hydration, providing visual and hearing aids, if used, minimizing invasiveness (bladder catheterization, nasogastric tube, intravenous access), as well as the rationalization of drug therapy already in progress.
- Drug treatment of delirium should be used only when the patient is a danger to himself or when symptoms are particularly important and/or threaten the ability to undertake essential therapies.
- Benzodiazepines are not indicated for the treatment of delirium. In selected patients and minimally effective doses, haloperidol or atypical antipsychotics are currently the preferred treatment, even if efficacy studies have not produced unequivocal results.

implemented as recommended by the National Institute for Health and Care Excellence (NICE) [15].

The application of these measures requires a multidisciplinary and coordinated approach, declined on the needs of the individual. It is also important to recognize the important potential role of including family and caregivers in the support to patients. Flexibility of hours of visits to the ward as well as the compilation of investigative tools of the needs and preferences of the patient, should be encouraged as proposed by the Royal College of Nursing and the Alzheimer Society in the UK for family members of patients with Alzheimer’s disease [55]. There are also numerous acronyms to remember the possible causes of delirium, such as the one proposed by Flaherty [56].

The pharmacological treatment of delirium should instead be used only when the patient is a danger to himself, when the symptoms are particularly important, and or when the clinical conditions may be an obstacle to undertake essential therapies [51]. Benzodiazepines are not recommended for the treatment of delirium being proved capable of precipitating episodes of delirium [57]. Conversely, their use remains accepted in particular situations, such as abstinence from alcohol or from benzodiazepine themselves [58,59]. Haloperidol has the most documented efficacy in the treatment of delirium. Quetiapine has been used in two randomized controlled trials [60,61], demonstrating the ability to reduce the duration of delirium, although the number of enrolled patients is considered to be insufficient to support its use. Olanzapine, risperidone and ziprasidone have been used in other small trials but again with unsatisfactory results and or limited number of patients [62,63]. Other atypical antipsychotics are potentially useful, but few data is available [62,64–68]. Finally, there are studies on specific populations of patients (patients admitted to intensive care or hospice care) that do not document any benefit (and suggest possible disadvantages) from addition of these drugs to an appropriate non-pharmacological interventions [69–72]. Likewise, there are no adequate studies regarding the treatment of hypokinetic delirium with antipsychotic drugs, despite these drugs are frequently adopted in clinical practice.

7. Communication between doctors, patients and family members

Ineffective communications among health care professionals, as well as a poor communication of health care professionals with patients and their families, have a negative impact on the quality of care provided to patients with delirium within the hospital (Box 5). The absence of a reference health records with family or caregivers not properly informed on pre-existing health conditions of the patient may cause an incomplete collection of anamnestic information in the hospital, with a resultant delay of diagnosis [71]. Furthermore, the difficulty to interact with patients suffering from delirium may be exacerbated by an inappropriate approach of health personnel. Finally, a poor quality of discharge communication may have a negative impact on the quality of care provided at home to patients with delirium.

Teaching techniques of communication with both the patient suffering from delirium, and his family, should therefore become a specific subject of university curricula. Specific interaction

Box 5. Communication strategy.

- Effective communication must be part of the quality standard of care in the hospital.
- Communication methods and techniques should be a specific subject of university curricula.

techniques with individuals with cognitive impairment can be replicated in simulated environments and may become enriching learning experiences and a source of reflections for students [73].

The fluctuating nature of delirium makes essential an effective communication among health care professionals. Because cognitive and motor performance of patients with delirium can vary greatly within a few hours or days it is important that all staff members (physicians and nurses) receive precise information on behavioural problems and variations of the patient's cognitive status or needs at shift change. Bedside shift reports were found to improve communication between nurses, as well as nurses' communication with patients and their families or caregivers who are in a privileged position to capture variations. If not actively involved, these operators may not provide useful information believing that this is not part of their duties, or feeling intimidated by the presence of other team members. The inter-professional training, in this context, has been shown to improve clinical outcomes and to facilitate the development of a good working climate within the team [74].

8. Conclusions

Delirium is a common clinical condition at least in part preventable and treatable. In this perspective, the delirium can be considered a valuable indicator of the patient's health and of the quality of services provided in hospitals and other care facilities. The principles of care outlined in this position paper propose an effective treatment model based on evidence. Central to this process is the need to rethink the delirium in the medical and surgical staff and to promote interdisciplinary training interventions aimed at involving all team members. In this perspective the quality of care of delirium could be a good indicator of the in-hospital quality of care [41].

Ethical statement

Compliance with ethical standards.

Statement of human and animal rights. This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent. None.

Disclosure of interest

The authors declare that they have no competing interest.

References

- [1] American Psychiatric Association. Task force on DSM-5 diagnostic and statistical manual of mental disorders: DSM-5, 5th ed, Washington, DC: The American Psychiatric Association; 2013.
- [2] Inouye SK, Studenski S, Tinetti ME, Kuchel GA. Geriatric syndromes: clinical, research, and policy implications of a core geriatric concept. *J Am Geriatr Soc* 2007;55:780–91. <http://dx.doi.org/10.1111/j.1532-5415.2007.01156.x>.
- [3] Hall RJ, Meagher DJ, MacLulich AM. Delirium detection and monitoring outside the ICU. *Best Pract Res Clin Anaesthesiol* 2012;26:367–83. <http://dx.doi.org/10.1016/j.bpa.2012.07.002>.
- [4] Hsieh SJ, Ely EW, Gong MN. Can intensive care unit delirium be prevented and reduced? Lessons learned and future directions. *Ann Am Thorac Soc* 2013;10:648–56. <http://dx.doi.org/10.1513/AnnalsATS.201307-232FR>.
- [5] Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. *Lancet* 2014;383:911–22. [http://dx.doi.org/10.1016/S0140-6736\(13\)60688-1](http://dx.doi.org/10.1016/S0140-6736(13)60688-1).
- [6] Bellelli G, Morandi A, Di Santo SG, Mazzone A, Cherubini A, Mossello E, et al. "Delirium Day": a nationwide point prevalence study of delirium in older hospitalized patients using an easy standardized diagnostic tool. *BMC Medicine* 2016;14. <http://dx.doi.org/10.1186/S12916-016-0649-8>.
- [7] Han JH, Wilson A, Ely EW. Delirium in the older emergency department patient: a quiet epidemic. *Emerg Med Clin North Am* 2010;28:611–31. <http://dx.doi.org/10.1016/j.emc.2010.03.005>.
- [8] Eeles E, Rockwood K. Delirium in the long-term care setting: clinical and research challenges. *J Am Med Dir Assoc* 2008;9:157–61. <http://dx.doi.org/10.1016/j.jamda.2007.12.001>.
- [9] Fick DM, Agostini JV, Inouye SK. Delirium superimposed on dementia: a systematic review. *J Am Geriatr Soc* 2002;50:1723–32.
- [10] Han JH, Shintani A, Eden S, Morandi A, Solberg LM, Schnelle J, et al. Delirium in the emergency department: an independent predictor of death within 6 months. *Ann Emerg Med* 2010;56:244e241–52e241. <http://dx.doi.org/10.1016/j.annemergmed.2010.03.003>.
- [11] Witlox J, Eurelings LS, de Jonghe JF, Kalisvaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis. *JAMA* 2010;304:443–51. <http://dx.doi.org/10.1001/jama.2010.1013>.
- [12] Leslie DL, Marcantonio ER, Zhang Y, Leo-Summers L, Inouye SK. One-year health care costs associated with delirium in the elderly population. *Arch Intern Med* 2008;168:27–32. <http://dx.doi.org/10.1001/archinternmed.2007.4>.
- [13] Abbara I, Trotta F, Rimland JM, Cruz-Jentoft A, Lozano-Montoya I, Soiza RL, et al. Efficacy of non-pharmacological interventions to prevent and treat delirium in older patients: a systematic overview. The SENATOR project ONTOP Series. *PLoS One* 2015;10:e0123090. <http://dx.doi.org/10.1371/journal.pone.0123090>.
- [14] Martinez F, Tobar C, Hill N. Preventing delirium: should non-pharmacological, multicomponent interventions be used? A systematic review and meta-analysis of the literature. *Age and Ageing* 2015;44:196–204. <http://dx.doi.org/10.1093/ageing/afu173>.
- [15] National Institute for Health, Care Excellence. Delirium: diagnosis, prevention and management. NICE clinical guideline 103; 2010 [Available from: <http://www.nice.org.uk/nicemedia/live/13060/49909/49909.pdf>].
- [16] The Clinical Epidemiology, Health Service Unit, Melbourne Health, in collaboration with the Delirium Clinical Guideline Expert Working Group. Clinical practice guidelines for the management of delirium in older people; 2006 [Available from: <http://www.health.gov.au/internet/main/publishing.nsf/Content/delirium-guidelines.htm>].
- [17] Canadian Coalition for Seniors' Mental Health. National guidelines for seniors' mental health – the assessment and treatment of delirium; 2006 [Available from: <http://www.ccsmh.ca/en/default.cfm>].
- [18] Registered Nurses' Association of Ontario. Screening for delirium, depression and dementia in older adults; 2006 [Available from: <http://www.rnao.org/Page.asp?PageID=924&ContentID=818>].
- [19] National Institute for Health, Care Excellence. Alcohol-use disorders: diagnosis and clinical management of physical alcohol-related complications. NICE clinical guideline CG100; 2010 [Available from: <http://www.guidance.nice.org.uk/CG100>].
- [20] New York State Department of Health. Cognitive disorders and HIV/AIDS: HIV-associated dementia and delirium; 2007 [Available from: <http://www.hivguidelines.org/clinical-guidelines/hiv-and-mental-health/cognitivedisorders-and-hiv-aids/>].
- [21] Tasmania Department of Health, Human Services. Palliative care management guidelines – delirium; 2009 [Available from: <http://www.clinicalguidelines.gov.au/browse.php?treePath=&pageType=2&fldglrID=167&>].
- [22] American Medical Directors Association. Delirium and acute problematic behavior in the long-term care setting; 2008 [Available from: <http://www.ama.com/tools/guidelines.cfm>].
- [23] British Society of Geriatrics. Guidelines for the prevention, diagnosis and management of delirium in older people in hospital; 2005 [Available from: <http://www.bgs.org.uk/index.php/clinicalguides/170-clinguidedeliriumtreatment>].
- [24] Bellelli G, Nobili A, Annoni G, Morandi A, Djade CD, Meagher DJ, et al. Under-detection of delirium and impact of neurocognitive deficits on in-hospital mortality among acute geriatric and medical wards. *Eur J Intern Med* 2015;26:696–704. <http://dx.doi.org/10.1016/j.ejim.2015.08.006>.
- [25] Davis DHJ, Terrera GM, Keage H, Rahkonen T, Oinas M, Matthews FE, et al. Delirium is a strong risk factor for dementia in the oldest-old: a population-based cohort study. *Brain* 2012;135:2809–16. <http://dx.doi.org/10.1093/brain/aww190>.
- [26] Bellelli G, Morandi A, Zanetti E, Bozzini M, Lucchi E, Terrasi M, et al. Recognition and management of delirium among doctors, nurses, physiotherapists, and psychologists: an Italian survey. *Int Psychogeriatr* 2014;26:2093–102. <http://dx.doi.org/10.1017/S1041610214001653>.
- [27] Langan C, Sarode DP, Russ TC, Shenkin SD, Carson A, MacLulich AM. Psychiatric symptomatology after delirium: a systematic review. *Psychogeriatrics* 2017. <http://dx.doi.org/10.1111/psyg.12240>.
- [28] Teodorczuk A, Mukaetova-Ladinska E, Corbett S, Welfare M. Reconceptualizing models of delirium education: findings of a Grounded Theory study. *Int Psychogeriatr* 2013;25:645–55. <http://dx.doi.org/10.1017/S1041610212002074>.
- [29] Yanamadala M, Wieland D, Heflin MT. Educational interventions to improve recognition of delirium: a systematic review. *J Am Geriatr Soc* 2013;61:1983–93. <http://dx.doi.org/10.1111/jgs.12522>.
- [30] <http://www.europeandeliriumassociation.com/patient-video.html>.
- [31] <https://www.youtube.com/watch?v=w3B0DDQgJaA>; <https://www.youtube.com/watch?v=Aw8FwFhqpGg>.
- [32] Dubois MJ, Bergeron N, Dumont M, Dial S, Skrobik Y. Delirium in an intensive care unit: a study of risk factors. *Intensive Care Med* 2001;27:1297–304.
- [33] Ansaloni L, Catena F, Chattat R, Fortuna D, Franceschi C, Mascitti P, et al. Risk factors and incidence of postoperative delirium in elderly patients after elective and emergency surgery. *Br J Surg* 2010;97:273–80. <http://dx.doi.org/10.1002/bjs.6843>.

- [34] Hatherill S, Flisher AJ. Delirium in children and adolescents: a systematic review of the literature. *J Psychosom Res* 2010;68:337–44. <http://dx.doi.org/10.1016/j.jpsychores.2009.10.011>.
- [35] Aldecoa C, Bettelli G, Bilotta F, Sanders RD, Audisio R, Borozdina A, et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. *Eur J Anaesthesiol* 2017;34:192–214. <http://dx.doi.org/10.1097/EJA.0000000000000594>.
- [36] Freter S, Koller K, Dunbar M, MacKnight C, Rockwood K. Translating delirium prevention strategies for elderly adults with hip fracture into routine clinical care: a pragmatic clinical trial. *J Am Geriatr Soc* 2017;65:567–73. <http://dx.doi.org/10.1111/jgs.146568>.
- [37] Teodorczuk A, Mukaetova-Ladinska E, Corbett S, Welfare M. Deconstructing dementia and delirium hospital practice: using cultural historical activity theory to inform education approaches. *Adv Health Sci Educ* 2015;20:745–64. <http://dx.doi.org/10.1007/s10459-014-9562-0>.
- [38] Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 2009;373:1874–82. [http://dx.doi.org/10.1016/S0140-6736\(09\)60658-9](http://dx.doi.org/10.1016/S0140-6736(09)60658-9).
- [39] Schaller SJ, Anstey M, Blobner M, Edrich T, Grabitz SD, Gradwohl-Matis I, et al. Early, goal-directed mobilisation in the surgical intensive care unit: a randomised controlled trial. *Lancet* 2016;388:1377–88. [http://dx.doi.org/10.1016/S0140-6736\(16\)31637-3](http://dx.doi.org/10.1016/S0140-6736(16)31637-3).
- [40] Inouye SK, Baker DI, Fugal P, Bradley EH, Project HD. Dissemination of the hospital elder life program: implementation, adaptation, and successes. *J Am Geriatr Soc* 2006;54:1492–9. <http://dx.doi.org/10.1111/j.1532-5415.2006.00869.x>.
- [41] Hsieh TT, Yue J, Oh E, Puelle M, Dowal S, Travisson T, et al. Effectiveness of multicomponent nonpharmacological delirium interventions: a meta-analysis. *JAMA Intern Med* 2015;175:512–20. <http://dx.doi.org/10.1001/jamainternmed.2014.7779>.
- [42] Abrahma I, Rimland JM, Trotta F, Pierini V, Cruz-Jentoft A, Soiza R, et al. Non-pharmacological interventions to prevent or treat delirium in older patients: clinical practice recommendations of the SENATOR-ONTOP series. *J Nutr Health Aging* 2016;20:927–36. <http://dx.doi.org/10.1007/s12603-016-0719-9>.
- [43] Marcantonio ER, Flacker JM, Wright RJ, Resnick NM. Reducing delirium after hip fracture: a randomized trial. *J Am Geriatr Soc* 2001;49:516–22.
- [44] Scholtens RM, van Munster BC, Adamis D, de Jonghe A, Meagher DJ, de Rooij SE. Variability of delirium motor subtype scale-defined delirium motor subtypes in elderly adults with hip fracture: a longitudinal study. *J Am Geriatr Soc* 2017;65:e45–50. <http://dx.doi.org/10.1111/jgs.14582>.
- [45] Bellelli G, Speciale S, Barisione E, Trabucchi M. Delirium subtypes and 1-year mortality among elderly patients discharged from a post-acute rehabilitation facility. *J Gerontol A Biol Sci Med Sci* 2007;62:1182–3.
- [46] Inouye SK. *The Confusion Assessment Method (CAM): training manual and coding guide*. New Haven: Yale University School of Medicine; 2003.
- [47] Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegel AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med* 1990;113:941–8.
- [48] Wei LA, Fearing MA, Sternberg EJ, Inouye SK. The Confusion Assessment Method: a systematic review of current usage. *J Am Geriatr Soc* 2008;56:823–30. <http://dx.doi.org/10.1111/j.1532-5415.2008.01674.x>.
- [49] Inouye SK, Foreman MD, Mion LC, Katz KH, Cooney Jr LM. Nurses' recognition of delirium and its symptoms: comparison of nurse and researcher ratings. *Arch Intern Med* 2001;161:2467–73.
- [50] Fick DM, Hodo DM, Lawrence F. Recognizing delirium superimposed on dementia – Assessing nurses' knowledge using case vignettes. *J Gerontol Nurs* 2007;33:40–7.
- [51] Bellelli G, Morandi A, Davis DH, Mazzola P, Turco R, Gentile S, et al. Validation of the 4AT, a new instrument for rapid delirium screening: a study in 234 hospitalised older people. *Age Ageing* 2014;43:496–502. <http://dx.doi.org/10.1093/ageing/afu021>.
- [52] Leentjens AF, Molag ML, Van Munster BC, De Rooij SE, Luijckendijk HJ, Vochteloo AJ, et al. Changing perspectives on delirium care: the new Dutch guideline on delirium. *J Psychosom Res* 2014;77:240–1. <http://dx.doi.org/10.1016/j.jpsychores.2014.07.014>.
- [53] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* 2016;315:801–10. <http://dx.doi.org/10.1001/jama.2016.0287>.
- [54] Kakuma R, du Fort GG, Arsenaull L, Perrault A, Platt RW, Monette J, et al. Delirium in older emergency department patients discharged home: effect on survival. *J Am Geriatr Soc* 2003;51:443–50. http://www.dignityincare.org.uk/_library/Resources/This_is_me.pdf.
- [55] http://www.dignityincare.org.uk/_library/Resources/This_is_me.pdf.
- [56] Flaherty JH, Tariq SH, Raghavan S, Bakshi S, Moinuddin A, Morley JE. A model for managing delirious older inpatients. *J Am Geriatr Soc* 2003;51:1031–5.
- [57] Pandharipande P, Shintani A, Peterson J, Pun BT, Wilkinson GR, Dittus RS, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. *Anesthesiology* 2006;104:21–6. <http://dx.doi.org/10.1097/0000542-200601000-00005>.
- [58] Mayo-Smith MF, Beecher LH, Fischer TL, Gorelick DA, Guillaume JL, Hill A, et al. Management of alcohol withdrawal delirium. An evidence-based practice guideline. *Arch Intern Med* 2004;164:1405–12. <http://dx.doi.org/10.1001/archinte.164.13.1405>.
- [59] Lonergan E, Luxenberg J, Areosa Sastre A, Wyller TB. Benzodiazepines for delirium. *Cochrane Database Syst Rev* 2009;1:CD006379. <http://dx.doi.org/10.1002/14651858.CD006379.pub2>.
- [60] Tahir TA, Eeles E, Karapreddy V, Muthuvelu P, Chapple S, Phillips B, et al. A randomized controlled trial of quetiapine versus placebo in the treatment of delirium. *J Psychosom Res* 2010;69(5):485–90. <http://dx.doi.org/10.1016/j.jpsychores.2010.05.006>.
- [61] Maneeton B, Maneeton N, Srisurapanont M, Chittawatanarat K. Quetiapine versus haloperidol in the treatment of delirium: a double-blind, randomized, controlled trial. *Drug Des Devel Ther* 2013;7:657–67. <http://dx.doi.org/10.2147/dddt.s45575>.
- [62] Skrobik YK, Bergeron N, Dumont M, Gottfried SB. Olanzapine vs haloperidol: treating delirium in a critical care setting. *Intensive Care Med* 2004;30:444–9. <http://dx.doi.org/10.1007/s00134-003-2117-0>.
- [63] Hirota T, Kishi T. Prophylactic antipsychotic use for postoperative delirium: a systematic review and meta-analysis. *J Clin Psychiatry* 2013;74:e1136–44. <http://dx.doi.org/10.4088/JCP.13r08512>.
- [64] Lacasse H, Perreault MM, Williamson DR. Systematic review of antipsychotics for the treatment of hospital-associated delirium in medically or surgically ill patients. *Ann Pharmacother* 2006;40:1966–73. <http://dx.doi.org/10.1345/aph.1H241>.
- [65] Lonergan E, Britton AM, Luxenberg J, Wyller T. Antipsychotics for delirium. *Cochrane Database Syst Rev* 2007;2:CD005594. <http://dx.doi.org/10.1002/14651858.CD005594.pub2>.
- [66] Girard TD, Pandharipande PP, Carson SS, Schmidt GA, Wright PE, Canonico AE, et al. Feasibility, efficacy, and safety of antipsychotics for intensive care unit delirium: the MIND randomized, placebo-controlled trial. *Crit Care Med* 2010;38:428–37.
- [67] Kim SW, Yoo JA, Lee SY, Kim SY, Bae KY, Yang SJ, et al. Risperidone versus olanzapine for the treatment of delirium. *Hum Psychopharmacol* 2010;25:298–302. <http://dx.doi.org/10.1002/hup.1117>.
- [68] Larsen KA, Kelly SE, Stern TA, Bode Jr RH, Price LL, Hunter DJ, et al. Administration of olanzapine to prevent postoperative delirium in elderly joint-replacement patients: a randomized, controlled trial. *Psychosomatics* 2010;51:409–18. <http://dx.doi.org/10.1176/appi.psy.51.5.409>.
- [69] van Eijk MMJ, Roes KCB, Honing MLH, Kuiper MA, Karakus A, van der Jagt M, et al. Effect of rivastigmine as an adjunct to usual care with haloperidol on duration of delirium and mortality in critically ill patients: a multicentre, double-blind, placebo-controlled randomised trial. *Lancet* 2010;376:1829–37. [http://dx.doi.org/10.1016/S0140-6736\(10\)61855-7](http://dx.doi.org/10.1016/S0140-6736(10)61855-7).
- [70] Page VJ, Ely EW, Gates S, Zhao XB, Alce T, Shintani A, et al. Effect of intravenous haloperidol on the duration of delirium and coma in critically ill patients (Hope-ICU): a randomised, double-blind, placebo-controlled trial. *Lancet Respir Med* 2013;1:515–23. [http://dx.doi.org/10.1016/S2213-2600\(13\)70166-8](http://dx.doi.org/10.1016/S2213-2600(13)70166-8).
- [71] Fisher JM. 'The poor historian': heart sink? Or time for a re-think? *Age Ageing* 2016;45:11–3. <http://dx.doi.org/10.1093/ageing/afv169>.
- [72] Agar MR, Lawlor PG, Quinn S, Draper B, Caplan GA, Rowett D, et al. Efficacy of oral risperidone, haloperidol, or placebo for symptoms of delirium among patients in palliative care: a randomized clinical trial. *JAMA Intern Med* 2017;177:34–42. <http://dx.doi.org/10.1001/jamainternmed.2016.7491>.
- [73] Fisher JM, Walker RW. A new age approach to an age old problem: using simulation to teach geriatric medicine to medical students. *Age Ageing* 2014;43:424–8. <http://dx.doi.org/10.1093/ageing/afv200>.
- [74] Sockalingam S, Tan A, Hawa R, Pollex H, Abbey S, Hodges BD. Interprofessional education for delirium care: a systematic review. *J Interprof Care* 2014;28:345–51. <http://dx.doi.org/10.3109/13561820.2014.891979>.