Risk assessment and prevention of delirium

Vreeswijk, Ralph

2022

document version
Publisher's PDF, also known as Version of record

RISK ASSESSMENT

AND

PREVENTION OF DELIRIUM

Ralph Vreeswijk

These studies presented in this book are performed at the Medical Center Alkmaar in Alkmaar and at the Spaarne Gasthuis in Haarlem

Cover: Chihuly glass art Tacoma USA
Photo: Ralph Vreeswijk

Sponsoring:
Spaarne Gasthuis Academie
Vakgroep Geriatrie Spaarne Gasthuis

Paranimfen:
Coby Heij
Anne Fons

Vreeswijk Ralph
Risk assessment en prevention of delirium
Amsterdam: Vrije Universiteit, faculteit der Geneeskunde
Thesis Vrije Universiteit, With references, with summery in Dutch
ISBN: 978-90-832797-4-9 (printed version)
ISBN: 978-90-832797-5-6 (electronic version)

Printed by: Proefschriftspecialist.nl - Zaandam

VRIJE UNIVERSITEIT

RISK ASSESSMENT AND PREVENTION OF DELIRIUM

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. J.J.G. Geurts,
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de Faculteit der Geneeskunde
op woensdag 21 december 2022 om 15.45 uur
in een bijeenkomst van de universiteit,
De Boelelaan 1105

door

Ralph Vreeswijk

geboren te Amsterdam

promotor:	prof.dr. A.B. Maier
copromotor:	dr. C.J. Kalisvaart
promotiecommissie:	prof. dr. K.D.P.W.B. Nanayakkara prof.dr. B. Van Meijel prof.dr. J.V. Laurila dr. G.G.M. Scholten-Peeters prof.dr. J.J. Meij

Contents

“Great things are not done by impulse,
but by a series of small things brought together.”
Vincent van Gogh

Chapter 1

INTRODUCTION

Delirium is an acute brain dysfunction in the hospitalized older patient. It is a serious and potentially preventable mental condition. Characterized by disturbances of consciousness, attention, cognition, psychomotor behavior and emotions [1,2], it affects 10 to 60% of all patients treated in medical, surgical, medical-surgical mixed or general wards [3,4,5], and up to 80% of those treated in intensive care units (ICUs).[3,6-10]
Any sudden change in the mental or psychological functioning of a patient may indicate delirium. Therefore, delirium should rank highest in the differential diagnosis at all times. The reasons for this are clear. In most cases delirium is caused by a somatic condition or illness. The sudden onset of fluctuating behavioural symptoms represents the psychological or mental manifestation of that underlying illness. Timely intervention and treatment of the primary causal event or agents may lead to full recovery of the patient and to complete disappearance of the mental symptoms. Not recognizing delirium, itself or patients that are at risk for delirium can have detrimental consequences for the well-being of the patient. Delirium is associated with high morbidity and mortality, longer hospital stays and a high rate of institutionalization following discharge.[11] Another study, showed that patients who develop delirium had a 62% increased risk of mortality and lost an average of 13% of a year of life compared to patients without delirium.[12]

From an economic perspective, delirium is strongly associated with additional healthcare costs.[13] In the United States (US), annual additional delirium-related healthcare costs are estimated to range from 6.6 to 20.4 billion USD (mean: 9014 USD per case) in ICU patients[14] and 38 to 152 billion USD per year in non-ICU patients aged 70 years and older (range: 16,303 to 64,421 USD per case).[15] Weinrebe et al. calculated personnel and material costs, including costs affecting the hospitalization period and concluded that a hyperactive delirium patient costs approximately 1200 € more than a non-delirious patient.[16] They concluded that early routine detection of delirium can be achieved through training and this approach leads to a shortening of the hospitalization period and lower costs. In a recent study they compared patients without delirium and delirious patients' ≥ 65 year, whom had a significantly higher mortality rate and longer ICU and hospital LOS and had worse outcomes with significantly greater costs[17]. In addition, delirium prevention based on multicomponent interventions has been demonstrated to be cost-effective. The Hospital Elder Life Program (HELP) saved an average of $831 per intervention patient for acute hospital costs[18] and $9,446 per patient per year in long-term nursing home costs.[19] A follow-up study involving 7,000 patients per year on 6 hospital units resulted in annual savings of $6.9 million ($7.4 million less $440K for costs of program).[20] For the Netherlands, no cost figures (per hospital) for delirium are known.

Among healthcare workers there is a lack of attention, knowledge, use of screening tools and use of preventive interventions protocols for delirium, which is of great concern, given that the problem is common and associated with serious complications. Delirium is increasing in magnitude with aging and it is potentially preventable.[22-24] Despite these studies, advances in the field are hampered by insufficient recognition of the seriousness and impact of the problem of delirium on a national scale. A negative attitude of healthcare workers and an

inadequate reaction towards behavior of the patient with a delirium and/or his or her family can result in a high stress level even leading to post traumatic stress syndrome.[39,40]

A systematic review and meta-analysis showed that multicomponent interventions are effective in preventing incident delirium among older inpatients and that effects seemed to be stable among different settings.[21] Considering that effective delirium prevention is possible, the knowledge of associated costs and the consequences that delirium has for patients, can help healthcare providers to justify prevention strategies and finally give better care for older patients.

Delirium stages. (Fig 1)
An older patient who has experienced delirium would have gone through a number of stages during his/her hospitalization. Each stage has its specific actions.

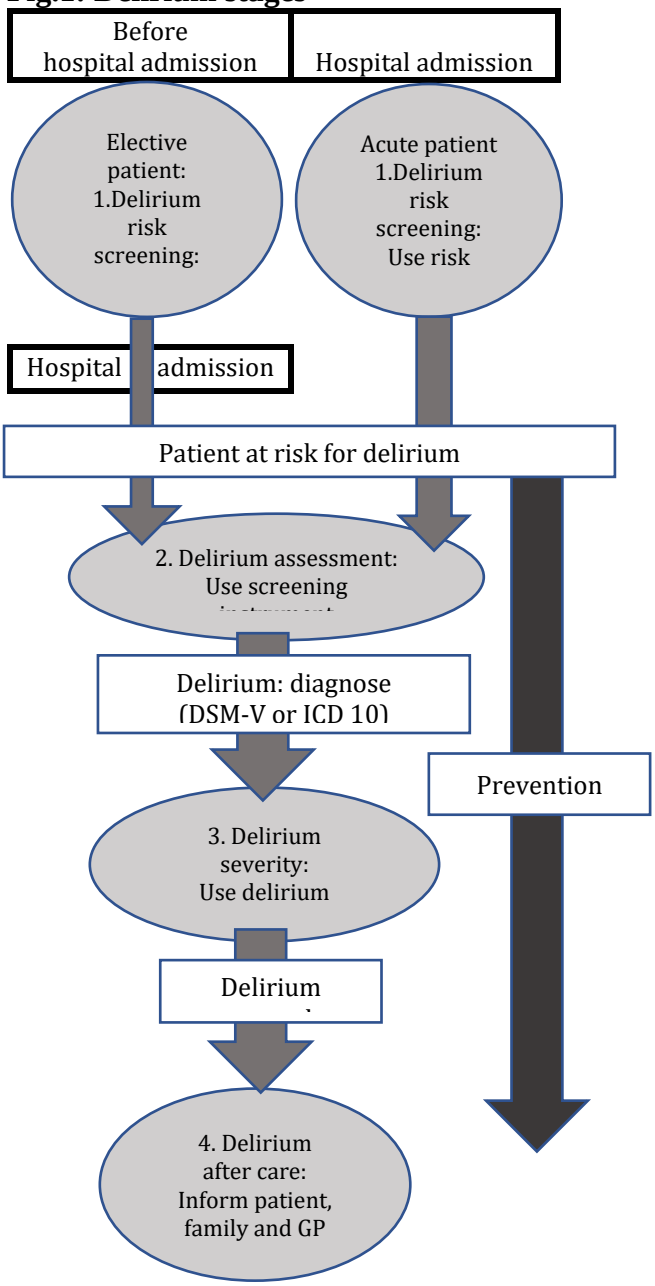
Stage 1. Delirium risk assessment.
Various delirium risk models are available to determine whether the patient has an increased risk of developing delirium.

Stage 2. Assessment for developing delirium and preventive interventions.
After establishing increased risk of delirium, delirium screening scales can be used to establish a developing delirium and primary preventive interventions can be applied.

Stage 3. Delirium severity determination.
After diagnosing delirium, it is advisable to use a severity scale for delirium in order to be able to adequately anticipate the delirium symptoms. In this stage preventive interventions can be applied to prevent worsening of the delirium.

Stage 4. Post delirium.
Patients are often fully aware that they have gone through a delirium episode, raising questions and giving anxiety. Since, there are serious consequences in prognosis it seems prudent to explain everything in full and follow-up these patients in time.

Fig.1: Delirium stages



The two first stages are especially important when it comes to prevention of delirium.

Risk assessment of delirium: The approach towards theories on the aetiology of delirium has led to the understanding that delirium is a multifactorial syndrome, involving the inverse relationship between patient vulnerability, *predisposing factors*, on admission, and the severity of noxious insults and aggravating or, *precipitating factors*, during hospitalization. Any number of predisposing factors may also contribute to the composite state of

vulnerability or frailty. There is a relation between frailty and delirium.[25] Many predisposing and precipitating risk factors have been identified.

Predisposing Factors: Seven groups: Demographic and social factors, Sensory disorders, Care processes, Cognitive and psychiatric comorbidity, Functional disorders, Nutrition and Medical comorbidity. [26]

Precipitating factors: Nine groups: Medication, Severe acute disease, Infections, Hypoperfusion states and pulmonary compromise, Metabolic abnormalities, Urine and faeces retention, Environmental/psychological aspects, Anesthesia and other procedures, Neurological disease. [26]

Many authors have identified risk factors for specific groups. Some of these risk factors were combined to make predictive models for delirium.

A recent study of Lindroth (2017) found 23 prediction models for delirium for different patient populations.[27] However, over 31 can be found for different populations and with different predisposing and/or precipitating variables.[28-34]

Screening for delirium

Screening for delirium is not simple.
Delirium is a syndromal diagnosis. No specific diagnostic test for delirium exists, and the diagnosis is made based on its key features. The main challenge in diagnosing delirium is to detect the great variety of fluctuating signs and symptoms of the syndrome and to organize them into a definable set that spans an entire spectrum of manifestations. The challenge of recognizing delirium is an important one, if only because there are many phenotypes of delirium, from extreme lethargy to agitation resembling mania, and these features may also fluctuate. Some delirium symptoms are already visible in de prodromal phase. Frequently observed symptoms before diagnosing delirium were disorientation: 50% – 83% compared with 23% in comparison patients, difficulty concentrating: 60% – 83% compared with 43%, short-term memory impairment: 50% – 83% compared with 34%, long-term memory impairment:67% – 83% compared with 53%, and an underlying somatic illness: 40% – 76% compared to 17% in patients without delirium.[48]

The variety of delirium definitions does not make things easier. Synonymous to delirium are concepts like ICU psychosis or syndrome, postoperative delirium after surgery, terminal delirium, drug-induced delirium, and hepatic encephalopathy in the context of hepatic failure. Two influential diagnostic classification systems exist. The Diagnostic and Statistical Manual for Mental Disorders (DSM) criteria of the American Psychiatric Association, with revised versions over the last decade (DSM-III, DSM-III-R, DSM-IV, DSM-IV-TR and DSM-V) and The International Classification of Diseases (ICD) versions 9, 10 and 11.[44] Although the differences between the systems appear to be small, some have pointed out that these differences can lead to diverging results on the recognition and diagnosis of delirium. Work by Laurila in Finland evaluating different classification systems showed that using the ICD-10 criteria 10.1 % of the patients with delirium were recognized, 19.5 % of the patients with the DSM-III(R) and 24.9 % with the use of the DSM- IV criteria.[45]

The differentiation between dementia, depression and delirium can also cause problems. The Ontario Psychogeriatric Association (OPGA) provides a good description of the differences

between delirium, dementia and depression in a table.[38] Failure to recognize the significance of such symptoms and differences between dementia, delirium and depression may lead to labelling a patient as uncooperative or difficult or to respond unkindly, thereby exacerbating the situation.
Some real good tests have been developed in spite of all these difficulties.

Prevention of delirium
In principle many risk factors for delirium are potentially preventable or avoidable. This is a combination of extra attention from geriatricians, nurses and attention for patients at risk for delirium.

Based on knowledge on predisposing and precipitating risk factors for delirium, interventions have been proposed to influence the detrimental effect of these factors and thus prevent delirium (primary prevention) or to reduce its duration and severity (secondary prevention). Recent reviews show that delirium is preventable with a multicomponent intervention strategy.[46,47] Relatively few interventions have been evaluated and supported by good quality clinical trials. Studies are small, non-randomized, and do not have blinded outcome measures. Zhang found only 2 randomized clinical trials. Outcome measures differ greatly between studies.[46] But overall the conclusion of Martinez with 7 found studies was that multicomponent interventions are effective in preventing incident delirium among older inpatients and the effects seemed to be stable among different settings.[47]
Further work is needed to determine how best to implement multicomponent preventive strategies in every day clinical practice. But it is also important that doctors and nurses see the necessity that delirium prevention is possible.
Despite all the work on understanding the risk factors for delirium, the prediction models developed and assessment of delirium, it is not common use to screen for patient at risk, the use of screening and severity tools and preventive interventions in daily practice. Delirium is still underrecognized.[35-37]
Assessment of cognitive functioning is non-existent outside geriatrics, neurology or psychiatry wards. So, even if a patient is noted to have cognitive impairment, confusion is a commonly employed catchall diagnosis, and little attempt may be made to determine the extent to which there is a reversible component as in delirium. Indeed, doctors and nurses spend less time with confused than with non-confused patients.[41,42] Even when a diagnosis of delirium is made, it is still very difficult to control delirium due to knowledge, attitude toward older patients, changing nursing staff over the day and interrater differences in the interpretation of the fluctuating symptoms, both in course and severity. More staff education and more assessment scales for nurses are needed.[43] Only then will it also be possible to focus attention on even more subtle signs like those present in the prodromal phase of delirium.

There is a need to examine the role of risk assessment for delirium on admission and of more specific (including pharmacological), additional interventions in the prevention of delirium. This will be facilitated by use of standardized assessment instruments to diagnose delirium and delirium severity and by targeting high-risk populations. Most work has been done in homogeneous patient groups which can make it difficult to generalize to other populations. But the evidence already found can improve patient outcomes. The medical consultant has a key role in providing this care and managing the preoperative conditions and postoperative complications that may affect optimal functional recovery. However, much more evidence will need to be found for patient groups, more heterogeneous populations, in order to provide good care to all patients. Also, the knowledge, skills and attitude of healthcare staff with regard to delirium risk assessment, prevention of delirium patients deserves improvement.

References

1. Meagher DJ, Maclullich AM, Laurila JV. Defining delirium for the international classification of diseases, 11th revision. J Psychosom Res. 2008;65(3):207–14.
2. Meagher DJ, Morandi A, Inouye SK, Ely W, Adamis D, Maclullich AJ, Rudolph JL, Neufeld K, Leonard M, Bellelli G, et al. Concordance between DSM-IV and DSM-5 criteria for delirium diagnosis in a pooled database of 768 prospectively evaluated patients using the delirium rating scale-revised-98. BMC Med. 2014; 12:164.
3. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet. 2014;383(9920):911–22.
4. Cole MG, You Y, McCusker J, Ciampi A, Belzile E. The 6- and 12-month outcomes of older medical inpatients who recover from delirium. Int J Geriatr Psychiatry. 2008;23(3):301–7.
5. Meagher DJ, Leonard M, Donnelly S, Conroy M, Adamis D, Trzepacz PT. A longitudinal study of motor subtypes in delirium: frequency and stability during episodes. J Psychosom Res. 2012;72(3):236–41.
6. Rudiger A, Begdeda H, Babic D, Kruger B, Seifert B, Schubert M, Spahn DR, Bettex D. Intra-operative events during cardiac surgery are risk factors for the development of delirium in the ICU. Crit Care. 2016; 20:264.
7. Mehta S, Cook D, Devlin JW, Skrobik Y, Meade M, Fergusson D, Herridge M, Steinberg M, Granton J, Ferguson N, et al. Prevalence, risk factors, and outcomes of delirium in mechanically ventilated adults. Crit Care Med. 2015;43(3):557–66.
8. Morandi A, Jackson JC, Ely EW. Delirium in the intensive care unit. Int Rev Psychiatry. 2009;21(1):43–58.
9. Pandharipande P, Cotton BA, Shintani A, Thompson J, Pun BT, Morris JA Jr, Dittus R, Ely EW. Prevalence and risk factors for development of delirium in surgical and trauma intensive care unit patients. J Trauma. 2008;65(1):34–41.
10. Morandi A, Jackson JC. Delirium in the intensive care unit: a review. Neurol Clin. 2011;29(4):749–63.
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 Jul 28;304(4):443-51.
12. Leslie DL, Zhang Y, Holford TR, et al. Premature death associated with delirium at 1-year follow- up. Arch Intern Med. 2005; 165:1657–1662. [PubMed: 16043686]
13. Zywiel MG, Hurley RT, Perruccio AV, Hancock-Howard RL, Coyte PC, Rampersaud YR. Health economic implications of perioperative delirium in older patients after surgery for a fragility hip fracture. J Bone Joint Surg Am. 2015;97(10):829–36.
14. Milbrandt EB, Deppen S, Harrison PL, Shintani AK, Speroff T, Stiles RA, Truman B, Bernard GR, Dittus RS, Ely EW. Costs associated with delirium in mechanically ventilated patients. Crit Care Med. 2004;32(4):955–62.
15. 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(1):27–32.
16. Weinrebe W, Johannsdottir E, Karaman M, Füsgen I. What does delirium cost? An economic evaluation of hyperactive delirium. Z Gerontol Geriat 2016 · 49:52–58
17. Schubert M, Schürch R, Boettger S, Garcia Nuñez D, Schwarz U, Bettex D, Jenewein J, Bogdanovic J, Staehli ML, Spirig R, Rudiger A. A hospital-wide evaluation of delirium prevalence and outcomes in acute care patients - a cohort study. BMC Health Serv Res. 2018 Jul 13;18(1):550.

18. Rizzo JA, Bogardus ST Jr. Leo-Summers L, et al. Multicomponent targeted intervention to prevent delirium in hospitalized older patients: What is the economic value? Med Care. 2001; 39:740–752. [PubMed: 11458138]
19. Leslie DL, Zhang Y, Bogardus ST, et al. Consequences of preventing delirium in hospitalized older adults on nursing home costs. J Am Geriatr Soc. 2005; 53:405–409. [PubMed: 15743281]
20. Rubin FH, Neal K, Fenlon K, et al. Sustainability and scalability of the Hospital Elder Life Program (HELP) at a community hospital. J Am Geriatr Soc. 2011 in press.
21. 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
22. Morandi A, Davis D, Taylor JK, Bellelli G, Olofsson B, Kreisel S, Teodorczuk A, Kamholz B, Hasemann W, Young J, Agar M, de Rooij SE, Meagher D, Trabucchi M, MacLullich AM. Consensus and variations in opinions on delirium care: a survey of European delirium specialists. Int Psychogeriatr. 2013 Dec; 25(12): 2067–2075.
23. Sinvani L, Kozikowski A, Pekmezaris R, Akerman M, Wolf-Klein G. Delirium: A Survey of Healthcare Professionals' Knowledge, Beliefs, and Practices. J Am Geriatr Soc. 2016 Dec;64(12)
24. Trogrlić Z, Ista E, Ponssen HH, Schoonderbeek JF, Schreiner F, Verbrugge SJ, Dijkstra A, Bakker J, van der Jagt M. Attitudes, knowledge and practices concerning delirium: a survey among intensive care unit professionals. Nurs Crit Care. 2017 May;22(3):133-140
25. Verloo H, Goulet C, Morin M, Von Gunten A. Association between frailty and delirium in older adult patients discharged from hospital Clinical Interventions in Aging 2016:11 55–63
26. Lindesay J., Rockwood K, Macdonald A. Delirium in Old Age. 2002: Oxford University Press
27. Lindroth H, Bratzke L, Purvis S, Brown R, Coburn M, Mrkobrada M, Chan MTV, Davis DHJ, Pandharipande P, Carlsson CM, Sanders RD. Systematic review of prediction models for delirium in the older adult inpatient. BMJ Open. 2018 Apr 28;8(4):e019223.
28. Marcantonio ER, Goldman L, Mangione CM, Ludwig LE, Muraca B, Haslauer CM, Donaldson MC, Whittemore AD, Sugarbaker DJ, Poss R. A clinical prediction rule for delirium after elective noncardiac surgery. JAMA. 1994 Jan 12;271(2):134-9.
29. Koster S, Oosterveld FG, Hensens AG, Wijma A, van der Palen J. Delirium after cardiac surgery and predictive validity of a risk checklist. Ann Thorac Surg. 2008 Dec;86(6):1883-7
30. Vochteloo AJ, Moerman S, van der Burg BL, de Boo M, de Vries MR, Niesten DD, Tuinebreijer WE, Nelissen RG, Pilot P. Delirium risk screening and haloperidol prophylaxis program in hip fracture patients is a helpful tool in identifying high-risk patients, but does not reduce the incidence of delirium. BMC Geriatr. 2011 Aug 11; 11:39.
31. van den Boogaard M, Pickkers P, Slooter AJ, Kuiper MA, Spronk PE, van der Voort PH, van der Hoeven JG, Donders R, van Achterberg T, Schoonhoven L. Development and validation of PRE-DELIRIC (PREdiction of DELIRium in ICu patients) deliriumprediction model for intensive care patients: observational multicentre study. BMJ. 2012 Feb 9;344
32. Kennedy M, Enander RA, Tadiri SP, Wolfe RE, Shapiro NI, Marcantonio ER. Delirium risk prediction, healthcare use and mortality of elderly adults in the emergency department. J Am Geriatr Soc. 2014 Mar;62(3):462-9.

33. Ettema R, Heim N, Hamaker M, Emmelot-Vonk M, van der Mast R, Schuurmans M. Validity of a screening method for delirium risk in older patients admitted to a general hospital in the Netherlands. Gen Hosp Psychiatry. 2018 Nov - Dec; 55:44-50.
34. Vreeswijk R, Kalisvaart I, Maier AB, Kalisvaart KJ. Development and Validation of the Delirium Risk Assessment Score (DRAS). International Journal of geriatric Psychiatry 2019 submitted
35. Kennelly SP, Morley D, Coughlan T, Collins R, Rochford M, O'Neill D. Knowledge, skills and attitudes of doctors towards assessing cognition in older patients in the emergency department. Postgrad Med J. 2013 Mar;89(1049):137-41.
36. Morandi, D. Davis, J. K. Taylor, G. Bellelli, B. Olofsson, S. Kreisel, A. Teodorczuk, B. Kamholz, W. Hasemann, J. Young, M. Agar, S. E. de Rooij, D. Meagher, M. Trabucchi, A. M. MacLullich. Consensus and variations in opinions on delirium care: a survey of European delirium specialists. Int Psychogeriatr. 2013 Dec; 25(12): 2067–2075.
37. Sinvani L, Kozikowski A, Pekmezaris R, Akerman M, Wolf-Klein G. Delirium: A Survey of Healthcare Professionals' Knowledge, Beliefs, and Practices. J Am Geriatr Soc. 2016 Dec;64(12)
38. Ontario Psychogeriatric Association (OPGA) (2005) https://connectability.ca/Garage/wp-content/uploads/2012/11/ThreeDcomparison-TPADD-CONFERENCE.pdf
39. O'Malley G, Leonard M, Meagher D, O'Keeffe ST. The delirium experience: a review. J Psychosom Res. 2008 Sep;65(3):223-8.
40. Fuller V. Delirium recall - an integrative review. J Clin Nurs. 2016 Jun;25(11-12):1515-27.
41. Lou MF, Dai YT. Nurses' experience of caring for delirious patients. J Nurs Res 2002; 10: pp. 279-290
42. Kristiansen S, Konradsen H, Beck M. Nurses' experiences of caring for older patients afflicted by delirium in a neurological department. 2018 J. Clin. Nursing
43. Davis D, MacLullich A. Understanding barriers to delirium care: a multicenter survey of knowledge and attitudes amongst UK junior doctors. Age Ageing. 2009 Sep;38(5):559-63.
44. WHO 2019 https://www.who.int/classifications/icd/en/?
45. Laurila, JV, Pitkala KH, Strandberg TE, Tilvis RS. (2004). Impact of different diagnostic criteria on prognosis of delirium: a prospective study. Dementia and Geriatric Cognitive Disorders, 18, 240-44.
46. 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 Ageing. 2015 Mar;44(2):196-204.
47. Zhang H, Lu Y, Liu M, Zou Z, Wang L, Xu FY, Shi XY. Strategies for prevention of postoperative delirium: a systematic review and meta-analysis of randomized trials. Crit Care. 2013 Mar 18;17(2): R47.
48. de Jonghe J.F.M., Kalisvaart K.J., Dijkstra M., van Dis H., Vreeswijk R., Kat M.G., Eikelenboom P., van der Ploeg T., van Gool W.A.. Early Symptoms in the Prodromal Phase of Delirium: A Prospective Cohort Study in Elderly Patients Undergoing Hip Surgery. Am J Geriatr Psychiatry 2007 Feb;15(2):112-21. doi: 10.1097/01.JGP.0000241002.86410.c2.

Chapter 2

Primary Prevention of Delirium in the elderly

Kalisvaart KJ
Vreeswijk R

Rev Esp Geriatr Gerontol. 2008;43 Suppl 3:19-24. Review

ABSTRACT

The incidence of delirium in the elderly in general hospitals is up to 20 to 65%. Delirium is associated with high mortality, increased morbidity, increased need for nursing surveillance, longer hospital stays and a high rate of institutionalization following discharge. Delirium is not recognized by clinicians in one- to two-thirds of all cases and is commonly overlooked or misattributed to dementia, depression, or senescence; confusional states in the hospitalized elderly are considered the rule, rather than the exception and cognitive function is rarely assessed. For prevention of delirium it is necessary to look for patients "at-risk" for delirium and to use instruments for screenings and severity. Also should the medical and nursing staff be made aware of prodromal symptoms for delirium, indicating a delirium is developing. Prevention requires multidisciplinary action with pharmacological and non pharmacological interventions (multifactor intervention). A pro-active consultation team (doctors and nurses) resulting in good basic medical- and nursing care have the best results concerning the prevention of delirium, reducing delirium incidence with more than 25%.

INTRODUCTION

Hospitals do not acknowledge the fact that delirium within the elderly is a major problem. Most times they do not have a policy regarding the problem and there is a lack in expertise about delirium in the elderly. Knowledge about the subject and the use of instruments is low not only among doctors but also among nurses. And most times they need the expertise of a geriatrician, psychiatrist or a specialized nurse.

The incidence of delirium in the elderly in general hospitals is up to 20 to 65%. Delirium is associated with high mortality, increased morbidity, increased need for nursing surveillance, longer hospital stays and a high rate of institutionalization following discharge. The burden for patients, families and nursing staff as well as economic costs are enormous. Furthermore, delirium in the elderly is characterized by a more prolonged persistence of cognitive symptoms 6 to 12 months after hospitalization. Thus, additional costs are incurred as a result of rehabilitation services, nursing home placement, and home care. The proportion of older people in hospital is growing and will account, for almost half of all inpatient days in the near future. As a result, the incidence of delirium will also rise steeply the coming years.

Despite the high prevalence of delirium, the severity of the clinical implications and the high economical burden, it has attracted little attention from clinical researchers and almost no attention at all from health care management, insurance companies and governmental agencies.

Previous studies suggest that a 25% reduction of delirium can be achieved with simple preventive measures, such as decreased use of psychoactive medications, treatment of dehydration and early mobilization, with substantial cost savings [1]. Delirium serves as an indicator of how hospital care is failing older patients, due to iatrogenesis, overmedication, failure to carry out proper geriatric assessments, reduction in skilled nursing staff, rapid pace of care and poor attitudes towards care of elderly patients. Examining delirium provides an opportunity to improve the quality of hospital care for older persons in more general terms.[2]

In comparison to the fields of research on depression and dementia, the research activity focusing specifically on delirium is relatively small. There are many white spots and there is very little knowledge on basic aspects of delirium. Especially in clinical practice it is clear that, despite of clinical guidelines, most of the ‘golden standards’ for the assessment, prevention and treatment of delirium are based on clinical experience rather firmly established clinical evidence.[3]

Delirium is not recognized by clinicians in one- to two-thirds of all cases. The reasons for this failure to recognize this serious clinical condition are complex and manifold, including failure to appreciate that delirium is a potential medical emergency and that it is often the first, and sometimes the only, sign of serious underlying illness, such as pneumonia, sepsis, or myocardial infarction, in older patients. Delirium is commonly overlooked or misattributed to dementia, depression, or senescence; confessional states in the hospitalized elderly are considered the rule, rather than the exception and cognitive function is rarely assessed.[4]

Moreover, characteristics of the delirium itself, such as its fluctuating nature, lucid intervals, and predominance of the hypoactive form in the elderly, make its recognition more difficult.

Varying definitions of delirium do not make things easier. Two influential diagnostic classification systems exist. The Diagnostic and Statistical Manual for Mental Disorders (DSM) criteria of the American Psychiatric Association, with revised versions over the last decade (DSMIII, DSM-III-R, DSM-IV and DSM-IV-TR) and The International Classification of Diseases (ICD) versions 9 and 10. Although differences between the systems appear to be small, some studies have pointed out that these differences can lead to diverging results on the recognition and diagnosis of delirium.5 The use of assessment scales for the recognition and diagnosis of delirium based on these classification systems must be evaluated with this in

mind, especially when used for research purposes. Much early work on delirium has been done with no clear concept of valid delirium scales at all, making interpretation of existing data very hard indeed. Some of the work on assessment scales was either not available in a Dutch translation or not validated for use in different populations, while the use of rating scales can be helpful in detecting delirium and in measuring symptom severity.

Delirium screenings and severity scales

In a systematic review 13 scales were examined. Out of seven similar rating scales the Confusional Assessment Method (CAM), NEECHAM en Delirium Observation Scale (DOS) appear to be most suitable as a screening instrument for the diagnosis of delirium, depending on the type of raters (physician or nurse). The revised Delirium Rating Scale (DRS-R-98) that is rated by either physicians or trained research nurses seems to be particularly useful for measuring delirium severity or monitoring change.[10]

The fluctuating course of delirium symptoms over the day or even hours makes 24-hour observation and assessment of duration and severity important. Treatment decisions are based on these observations made by nurses during their shifts over the day. In the systematic review there was no severity scale found which can be used especially by nurses. In the review the Delirium O Meter (DOM) was not mentioned because at that time it was not developed. The DOM is a new rating scale for delirium-severity. It is a nurses' rating scale for monitoring delirium severity. The scale is based on the symptoms of delirium. Both the 'hypo-active' and 'hyper-active' symptoms were included in the scale, to allow for making distinction between these subtypes of delirium. In practice the DOM performs well in measuring the severity of delirium by nurses[13]

Risk-assessment and prediction of delirium

Much research work has been done to identify risk factors for delirium. Since etiology of delirium is multifactorial, involving the inverse relationship between patient's vulnerability. predisposing factors on admission and the severity of noxious insults and aggravating factors and precipitating factors during hospitalisation, it has been tried to combine the most important factors into a predictive model. Only one model had been validated in another population than the development cohort: the Inouye et al. model [11], developed in a medical population and did not include post-surgery patients.

Risk factors

Several risk factors have been identified. In several studies more than 60 predisposing and precipitating risk factors have been found. Table 1 and table 2

Prodromal symptoms of delirium

In clinical practice and also in a few studies' attention is drawn towards symptoms patients have before the diagnosis of delirium is made. These early symptoms can consist of a variety of symptoms, psychological and motor, but not the pathognomonic symptom of clouding of consciousness (yet). The nursing staff often reports especially wild and livid dreams, restlessness, orientation disturbance and tiredness. Even days before formal criteria of postoperative delirium were met, patients who developed a frank delirium later on were already experiencing problems with the sleep-wake cycle, perception, thinking, psychomotor changes, orienting, concentrating and memory (DRS-R-98). Most patients with postoperative delirium already have early symptoms in the prodromal phase of delirium. These prodromal symptoms are potentially useful for screening purposes and for optimizing prevention strategies targeted at reducing the incidence of postoperative delirium[12].

Primary prevention of delirium

Some work is done on influencing the risk factors to prevent delirium or to prevent the worsening of delirium once it has occurred. In a review involving a systematic search of MEDLINE, the Cochrane- and CINAHL Databases and subsequent examining of reference lists about primary prevention of delirium based on not pharmacological interventions, only six studies found.[8]

Not all the researchers used the same criteria for the diagnosis of delirium and the studies were done in different populations and often not very well controlled. Despite the methodological weaknesses of most of the studies, several different kinds of interventions to prevent delirium are effective in practice. Systemic interventions regarding medical, nursing, environmental and educational items were effective in preventing delirium in those studies. They showed a reduction of 3% to 18% in delirium. In a large study about prevention of delirium in elderly hip surgery patients done in the Netherlands there was use of a Best Supportive Care protocol for the prevention of delirium. This protocol was developed out of the scientific research which was already done. The protocol consisted about advises on aspects of orientation, sleep, pain, food and fluid intake, information to family and aspects of education of care towards nursing staff. During this study there was a reduction of delirium of more than 25%.

A multifactor intervention is the best way for the prevention of delirium, and a pro-active consultation team (doctors and nurses) seems to have the best results concerning the prevention of delirium.

Gold Standard

Since long there was a feeling among physicians in the Netherlands that, when the risk of developing delirium mounts up to almost a 100% in specific groups of patients, e.g., those with severe dementia and a hip-fracture, it might be advisable to start with the "golden standard" treatment on admission to the hospital instead of waiting for a frank delirium. Although solid evidence of controlled studies is lacking, haloperidol is used as the treatment of first choice.

In a review found in Cochrane about interventions for preventing delirium in hospitalised patients by Siddiqi et al. 2007 there were only two studies mentioned with a quality assessment of A.[7] These studies were done by Marcantonio 2001 and Kalisvaart 2005. Only Kalisvaart was a medical trial about haloperidol prophylaxes for the prevention of delirium.[9] In this study a total of 430 hip-surgery patients aged 70 and older at risk for postoperative delirium were randomized, double blind, in a placebo-controlled trial. Haloperidol 1.5 mg/day or placebo was started preoperatively and continued up to 3 days postoperatively. Pro-active geriatric consultation was provided for all randomized patients.

The primary outcome of the study was the incidence of postoperative delirium (DSM-IV and Confusion Assessment Method criteria). Secondary outcomes were the severity of delirium (Delirium Rating Scale revised version-98), the duration of delirium and the length of hospital stay. The overall incidence of postoperative delirium was 15.7%.

The percentage of patients with postoperative delirium in the haloperidol and placebo treatment condition was 15.1% vs 16.5%. The severity of delirium as reflected by the mean of the highest DRS-R-98 score for each episode with delirium was 14.4 in patients receiving prophylaxis vs 18.4 in patients with placebo. Also, the delirium duration was much shorter with haloperidol prevention: 5.4 vs 11.8 days and the mean number of days in the hospital for both groups was17.1 vs 22.6. No haloperidol-related side effects were noted. The conclusion of this study was|: Low-dose haloperidol prophylactic treatment demonstrated no efficacy in reducing the incidence of postoperative delirium. It did have a positive effect on the severity

and duration of delirium. Moreover, haloperidol reduced the number of days patients stayed in the hospital, while the therapy was well tolerated.

Clinical implications

As cited above, Inouye has described the high incidence of delirium as a prototypical symptom of the weaknesses in our current hospital care, combining iatrogenic incidents, overmedication, failure to carry out proper geriatric assessment, reduction in skilled nursing staff, rapid pace of care and poor attitudes towards care of elderly patients. Although this picture is sombering it also offers a perspective on opportunities to improve the quality of hospital care for older people. By simply providing a good standard of basic care we can prevent some deliria and reduce overall delirium incidence in our hospitals. When educating students or nurses on the subject of prevention of delirium the standard reaction is always: "this seems such basic normal care". With the increasing number of old and above all frail patients in hospital, the first thing to do is provide good normal care.

The use of a model for predicting delirium in patients by forming 'at-risk' groups on the basis of higher vulnerability gives us the opportunity to provide extra, high-cost care to those who really need it.

The assessment of the early symptoms in the prodromal phase of delirium may result in earlier diagnosis, because physicians as well as nursing staff will become more focused on detecting delirium. Furthermore, it is potentially useful for screening purposes and for optimizing prevention strategies targeted at reducing the incidence of postoperative delirium.

The construction and implementation of a 'best-supportive care' program makes it possible to provide the best possible care for patients either at risk for or with incident delirium. The program requires the use of cognitive and delirium assessment scales, even when administering these instruments imposes costs and changes routine in the hospital. The scales are easy to use, reliable, validated and translated into several languages.

The construction of the Delirium-O-Meter provides a good tool for nurses to follow the patient with delirium and detect change, both in severity and form of the delirium over the day. It takes very little time to administer. In one glance it provides a different picture of patients who are 'confused' and it completes insight in how patients have been over the last days' In daily practice it seems to result in more adequate use of psychoactive drugs and of restraining devices.

The implementation of the 'best-supportive care' program resulted in a decrease in incidence of delirium. The reduction in complications, related medical costs, and the duration of hospital admission resulting from a reduction of delirium severity, can be expected to be significant too. Haloperidol prophylaxis has an effect on severity and duration, which is in itself very important. For daily practice it is recommended to use low dose of haloperidol for the prevention of delirium in patients at high risk for delirium.

This concentration of preventive strategies should become part of normal practice for all elderly

FUTURE RESEARCH

More research is needed on all fronts of delirium. Continuing research into the conceptualisation of delirium is needed, because it is by no means clear that the current diagnostic constructs in ICD-10 and DSM-IV fully capture the unique, defining aspects of this disorder, especially in relation to dementia. More work on aetiology and pathogenesis will lead to better understanding of how all these totally different predisposing and precipitating factors can lead to such a complicated syndrome of delirium. Sophisticated models are probably needed to help to decide which possible causal factors are there to be influenced first

to get a ‘cure’ for delirium that can replace all the symptomatic treatments of today. There is still much work to be done on improving the understanding of the psychometric properties of delirium rating scales. One important issue that is still insufficiently appreciated is that concepts such as validity and reliability are not inherent attributes of scales, but functions of the context in which they are used. If researchers are using an instrument in a population that is substantially different from that in which the instrument was developed, they need to show that it is suitable to be used in their specific studied patient sample.
The validation of measures of change is difficult and complex. More work has to be done on this issue. In general, research into the specific symptoms (such as attention) of delirium will require the development of more sophisticated measures than are currently available, and this development will in turn need to be grounded in more detailed study of delirium phenomenology, including its fundamental neuropsychological characteristics. Better measures of specific symptoms (as we did with our work on early symptoms) will contribute to our reliability to identify patients in the earliest stages of delirium. Prevention and risk-assessment need refining and testing in other more specific populations. Research should have longer follow-up periods and shorter intervals between assessments to characterize better the course of delirium, e.g. in the course of depression and dementia. And to get a better understanding of the long-term outcomes. Still there is very little knowledge about the relation between delirium and dementia. The evidence base for effective management strategies is still very limited; indeed, it is non-existent for some important groups, such as delirium in the elderly with cognitive impairment.[6] Treatment programs (medical, pharmacological, social and psychological) must be studied in all populations by means of randomised, controlled trials. The concept of ‘education’- changing the knowledge, skills, and attitudes of staff- needs to be extended to the whole system that deals with delirious older people.

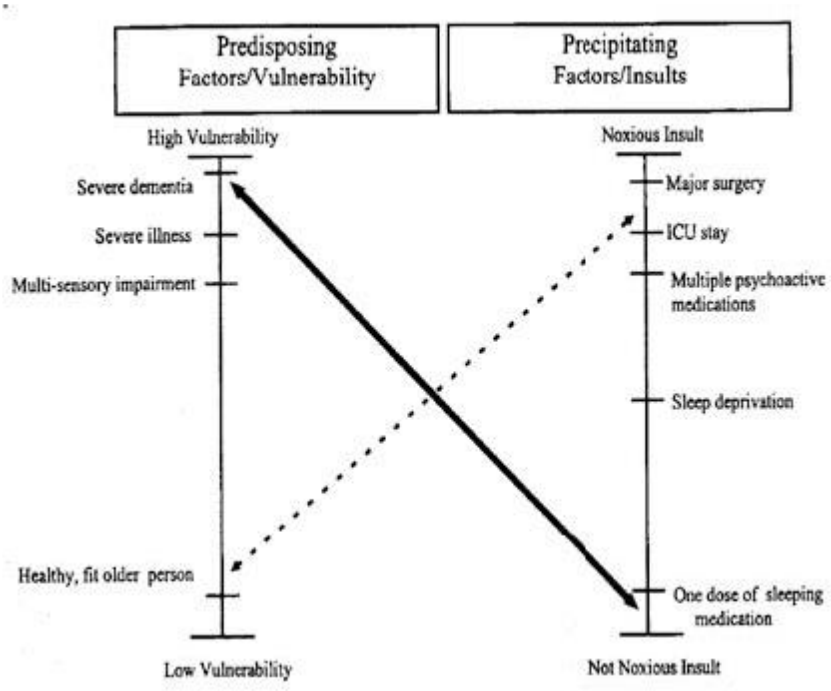
CLOSING REMARKS

Delirium is a very common problem in the elderly. But only a few are researching this subject. This does not seem right in respect to this syndrome being one of the ‘geriatric giants’. Delirium research deserves a more prominent place on the academic agenda. However, to get more knowledge on diseases it is of the utmost importance that every physician is willing to play a part in research. Even by ‘only’ constantly monitoring and evaluating our work we provide material for answering some of the existing questions. This study shows that, with affordable means, patient research is perfectly possible in a large, non-academic, hospital. Affiliations with medical schools are very helpful and provides a good basis for working.

References

1. Brook RH, McGlynn EA, Cleary PD. Quality of health care. Part 2: measuring quality of care. N Engl J Med 1996;335:966-70.
2. Inouye SK, Schlesinger MJ, Lydon TJ. Delirium: a symptom of how hospital care is failing older persons and a window to improve quality of hospital care. Am.J.Med. 1999;106:565-73.
3. Lindesay J, Rockwood K, Macdonald A. The future, In: Lindesay J, Rockwood K, Macdonald A, editors. Delirium in old age. New York: Oxford University Press; 2002. p. 213-22.
4. Inouye SK. The dilemma of delirium: clinical and research controversies regarding diagnosis and evaluation of delirium in hospitalized elderly medical patients. Am.J Med 1994;97:278-88.
5. Laurila JV, Pitkala KH, Strandberg TE, Tilvis RS. The impact of different diagnostic criteria on prevalence rates for delirium. Dement.Geriatr.Cogn Disord. 2003; 16:156-62.
6. Britton A, Russell R. Multidisciplinary team interventions for delirium in patients with chronic cognitive impairment. Cochrane.Database.Syst.Rev. 2001; CD000395.
7. Siddiqi N, Srockdale R, Britton AM, Holmes J. Interventions for prevention in delirium in hospitalised patients (review). Cochrane.Database.Syst.Rev. 2007
8. Kalisvaart KJ, Vreeswijk R, de Jonghe JFM, Milissen K. A review of multifactorial intervention studies for the primary prevention of delirium in the elderly. TGG. 2005: 5
9. Kalisvaart KJ, de Jonghe JFM, Bogaards MJ, Vreeswijk R, et al. Haloperidol prophylaxis for elderly hip surgery patients at risk for delirium. A randomized placebo-controlled study. JAGS 2005;53: 1658-1666
10. Timmers JFM, Kalisvaart KJ, Schuurmans M, de Jonghe JFM. A review of assessment scales for delirium. TGG. 2004; 35: 5-14
11. Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. JAMA 1996; 275:852-57
12. De Jonghe JF, Kalisvaart KJ, Dijkstra M, Van Dis H, Vreeswijk R, Kat MG, et al. Early symptons in the prodromal phase of delirium: a prospective cohort study in elderly patients undergoing hip surgery. Am J Geriatr Psychiatry. 2007; 15:112-21.
13. De Jonghe JF, Kalisvaart KJ, Timmers JF, Kat MG, Jackson JC. Delirium- O-Meter: a nurses'rating scale for monitoring delirium severity in geriatric patients. Int J Geratr Psychiatry. 2005; 20:1158-66.

Fig 1. Multifactorial model of delirium.



Inouye, 1996.

Table 1. Predisposing causes for delirium

- Demographic and social factors
  - Older age
  - Male gender
  - Institutional setting
  - Social isolation*
- Process of care
  - Iatrogenesis
  - Inadequate skills in recognition of delirium
  - Negative attitudes toward the care of the elderly
  - Rapid pace and technological focus of acute care
  - Reductions in skilled nursing staff
- Special sensory inpairement
  - Visual impairment
  - Hearing impairment
- Cognitive and psychatric comorbidy
  - Dementia
    - Degree of stage of dementia
    - Late onset Alzheimer's dementia
    - Vascular dementia
  - Cognitive impairment
  - Depression
- Functional impairments and disability
  - Functional dependence
  - Immobility
  - Fracture on admission
- Malnutrition
  - Dehydration
  - Alcoholisme
- Medical comorbidity
  - Hugh burden of Illness
  - Previous stroke
  - Parkinson's disease
  - Azotemia

Table 2. Precipitating causes for delirium

- Medications
  - Substance withdrawal
    - Alcohol
    - Sedative hypnotics
  - Substance intoxication
    - Sedative hypnotics
    - Narcotics
    - Anticholinergics
    - Antipsychotics
    - Antiparkinsnians
    - Antideprssants
- Severe acute illness infections
  - Urinary tract infections
  - Pneumonia
- Metabolic abnormalities
  - Hyperglycemia/hypoglycemia
  - Hypercalcemia/hypocalcemia
  - Thyrotoxicosis/Myxedema
- Adrenal Insufficiency
  - Hepatic Failure
  - Renal Failure
  - Hypernatremia/Hyponatremia
  - Hyperkalemia/Hypokalemia
- Hypoperfusion States and Pulmonary compromise
  - Hypoxemia
  - Shock
  - Anemia
  - Congestive Heart Failure
  - Chronic Obstructive Pulmonary disease
- Urinary and fecal retention
- Environmental-Psychological contributors
  - Sensory deprivation
  - Sensory overload
  - Psychological stress
  - Sleep deprivation
  - Pain
  - Physical restraine use
  - Bladder catheter use
  - Any iatrogenic event
  - Intensive care unit treatment
- Surgery, anaesthesia and other procedures
  - Orthopedic surgery
  - Cardiac surgery
    - Duration of cardiopulmonary bypass
  - Non cardiac surgery
  - High number of procedures in hospital
- Neurologic Illness
  - Subdural hematoma
  - Stroke
  - Malignancy
  - Cerbral Infection
  - Seizures

Chapter 3

Risk factors and prediction of postoperative delirium in elderly hip surgery patients. *Implementation and Validation of the Inouye Risk Factor Model.*

Kalisvaart KJ
Vreeswijk R
De Jonghe JFM
Van der Ploeg T
Van Gool WA
Eikelenboom P

J Am Geriatr Soc. 2006 May;54(5):817-22.

ABSTRACT

Objectives: To evaluate risk factors for postoperative delirium in a cohort of elderly hip-surgery patients and to validate a medical risk stratification model.

Design: Prospective cohort study.

Setting: Medical school-affiliated general hospital in Alkmaar, the Netherlands.

Participants: Six hundred three hip-surgery patients aged 70 and older screened for risk factors for postoperative delirium.

Measurements: Predefined risk factors for delirium were assessed on admission. One point was assigned for each of four risk factors present, resulting in three groups: low, intermediate, and high risk. Baseline screening and assessment included the Mini-Mental State Examination, the standardized Snellen test for visual impairment, chart review to determine Acute Physiological and Chronic Health Evaluation II score, and blood urea nitrogen to creatinine ratio. The primary outcome was postoperative delirium, as defined using Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, and Confusion Assessment Method criteria. All patients were screened daily for delirium.

Results: Incidence of delirium was 3.8% in the low-risk group (P<.001), 11.1% in the intermediate-risk group (P=.27, relative risk (RR)=3.0), and 37.1% in the high-risk group (P<.001, RR=9.8). Cognitive impairment at admission had the highest predictive value for postoperative delirium (coefficient of determination=0.15). Contrary to previous findings, age was an independent predictive factor for delirium. Moreover, postoperative delirium was four times as frequent in acute patients as in elective hip-replacement patients.

Conclusion: The medical risk factor model is valid for elderly hip-surgery patients. Cognitive impairment, age, and type of admission are important risk factors for delirium in this surgical population.

INTRODUCTION

Delirium is a serious postoperative complication in elderly patients. [1-3] It is associated with high morbidity and mortality, longer hospital stays and a high rate of institutionalization following discharge.[2,4-7] Incidence rates for delirium of 5 to 45% in orthopedic patients emphasize the need for primary and secondary prevention. [2,3,8,9] Effective prevention requires identification of risk factors for delirium.

Risk factors for delirium reflect the patient's predisposition or vulnerability for delirium or they may be present as precipitating events i.e., occurring during admission. [10,11] Predisposing and precipitating factors that have been identified are cognitive impairment, sensory impairment, severity of illness and dehydration, malnutrition, metabolic disturbances, intoxications, use of bladder catheter, use of physical restraints. [11-13] The etiology of delirium is still largely unknown and risk factors are likely to interact in a complex way. [13] In a pivotal study Inouye et al (1993) developed a predictive model of risk factors for delirium. [10] Patient characteristics present on admission were assessed and related to the incidence of delirium during hospital stay. Four risk factors for delirium were identified: *visual impairment, severe illness, cognitive impairment* and *dehydration*. Patients were classified as low, intermediate or high risk, based on the number of risk factors present. Nine percent of the people in the low-risk sample had delirium compared to 23% and 83% in the intermediate and high-risk samples. Subsequent validation of the model in an independent patient sample showed similar albeit somewhat less impressive results. [10]

The Inouye model has some clear advantages over other: results have been replicated in a similar patient sample: model variables are readily identifiable upon clinical examination and they can be quantified and monitored by trained nurses. Also, the risk on delirium can be influenced when changes occur in patient status over the course of hospitalization. However, some other issues need further clarification. Results have not been replicated in other patient samples; thus, the external validity of the model remains uncertain. Secondly, in contrast to others, Inouye et al. did not find an effect for age on the risk for delirium. [10,14-16] This counter-intuitive finding requires further exploration.

The focus of this study was to evaluate baseline vulnerability characteristics that could be helpful in identifying patients at risk for developing postoperative delirium. Our aims were to estimate the incidence of delirium in a general hospital cohort of elderly hip surgery patients; to validate the four-factor predictive model by Inouye et al.; and to investigate whether age, type of admission, depression and functional status are associated with the risk of delirium.

METHOD

Ethical Considerations

The study was done in accordance with the Declaration of Helsinki and the guidelines on Good Clinical Practice. Approval of the regional research ethics committee was obtained. All patients or their relatives gave fully informed, written consent.

Study Design and Objectives

We evaluated baseline risk factors for delirium and conducted a validation study of the Inouye delirium risk criteria, as part of a randomized, double blind, placebo-controlled clinical trial, comparing elderly hip-surgery patients at intermediate or high risk for delirium treated with either haloperidol or placebo before surgery. Details of the intervention study are described

elsewhere [26]. The intervention study showed that the duration and severity of delirium were different for haloperidol and placebo treated patients but not the incidence. Therefore, data of both the intervention groups and the low-risk group were pooled for this study. Baseline patient characteristics of incident and non-incident cases with postoperative delirium were compared. Postoperative delirium was defined as delirium occurring within a period of five postoperative days.

Risk classification was based on the presence of one or more predictive risk factors as described by Inouye et al.: *Visual impairment,* defined as binocular near vision worse than 20/70 after correction, *Severe illness,* measured by the Apache II (Acute Physiology Age and Chronicle Health Examination, scale of 0 to 70), with a cut-off score of > 16 indicating increased severity[17], *Cognitive impairment* (Mini Mental Status Examination (MMSE) score of <24 on a scale of 0 to 30)) [18] and *Dehydration* (ratio of blood urea nitrogen to creatinine of ≥18).

Analogous to Inouye et al., 'low', 'intermediate', and 'high risk' for postoperative delirium at baseline were defined as no risk factors present, one or two risk factors present or three or four risk factors present, respectively. [10] Furthermore, potentially significant risk factors, not used in the stratification model, i.e. age, base-line functional status, mood-status and type of admission were evaluated.

Participants

The study was conducted in a series of patients consecutively admitted for hip surgery to a 915-bed teaching hospital in Alkmaar, The Netherlands. During the study period, from August 2000 to August 2002, 603 hip-surgery patients aged 70 or over, fulfilled criteria for low-, intermediate-, or high risk for delirium at baseline. Patients were ineligible if they had delirium at admission; were not up to being interviewed (profound dementia, language barrier, intubation, respiratory isolation, aphasia, coma or terminal illness), or had a delay of surgery of more than 72 hours after admission.

Eligibility was checked against the patient's clinical notes and their own recall. Patients were enrolled in the study after the trial had been explained to them and they had provided written informed consent. According to procedures approved by the medical ethics committee, a proxy, usually a close relative gave informed consent for patients with cognitive impairment.

Measurements and Procedures

Members of the research team not involved in the clinical care of the patients carried out all assessments. The research team was composed of research nurses and experienced geriatricians, who were trained extensively and followed standard procedures. All data were collected on standardized patient record forms and were thoroughly checked on errors and validity.

Assessment

The baseline screening and assessments were completed before surgery and within 12 hours after admission, included the MMSE, the standardized Snellen test for visual impairment[19], chart review to determine the APACHE II score, blood urea nitrogen to creatinine ratio, the GDS-15 for assessment of mood disorders [20] and the Barthel index for the assessment of base line activities of daily living (ADL). [21]

Outcomes

The primary outcomes were post-operative delirium and predefined risk factors. Diagnosis of the syndrome was defined by DSM-IV and Confusion Assessment Method criteria (CAM). [22;23] Daily patient assessments with the MMSE, DRS-R-98 for delirium severity, range 0 (no severity) to 45 (high severity) and the Digit span test (assessment of attention, range 0 (no attention) to 42 (good attention) were used to make the DSM-IV and CAM diagnoses possible and to assess delirium severity. [24;25] CAM and DRS-R-98 assessments were continued once delirium was diagnosed.

Statistical analysis

Statistical calculations were performed using SPSS for Windows, version 11.5 (SPSS, Inc. Chicago, IL). Proportions of patients were compared using chi^2 analysis. Two-tailed p- values of less than 0.05 were considered to indicate statistical significance. Parametric values were tested with Student t-test. The results are expressed as relative risks with 95% confidence intervals (95%CI) for the delirium group compared to the non-delirium group and the acute versus the elective patient groups, with a relative risk of less than 1.0 in the CI indicating a beneficial effect. Performance of the risk stratification models was measured using receiver-operating characteristic (ROC) analysis. The values for area under the ROC curve range from 0 to 1, with 1 corresponding to perfect prediction, 0.5 to random performance (equivalent to chance alone), and 0 to completely incorrect prediction. Multivariate, logistic regression models were used to calculate the predictive values of independent predictive parameters for delirium, using Nagelkerke R^2 to evaluate the performance of the models.

RESULTS

A description of the 603 study participants; demographics, medical status and type of admission is provided in Table 1. A total of 123/603 patients had no risk points (low risk), 409/603 had one or two risk points (intermediate risk), and 62/603 had 3 or 4 risk points (high risk). Overall, seventy- four patients 74/603 (12.3%) (CI, 9.6-14.9) developed delirium within 5 days following admission, which is comparable to Inouye et al.'s validation cohort: 16.7% (CI, 11.0-22.1). Individuals in the delirium group had significantly more cognitive disturbances, as measured with the MMSE, poorer visual acuity scores and lower Apache-II scores. (table 1) There was no difference for the BUN/creatinine ratio in the two groups. The estimated risk for delirium of the four Inouye risk factors and the comparison with the results in the original validation cohort of Inouye et al. is provided in Table 2. Of the patients with a delirium 48/74 (64.9%) vs 103/529 (19.5%), *P*=< .001; without delirium had a MMSE score lower than 24. For the Apache-II score higher than 16: 27/74 (36.5%) versus 57/529 (10.8), *P*< .001; For vision impairment (score >20/70): 15/74 (20.3%) versus 60/529 (11.3%), *P*= .029. The combination of the four risk factors in the stratification model (low-, intermediate-, and high risk) and the estimated risk for delirium as an indicator of the performance of the predictive model is provided in Table 3. The incidence of delirium in the low (0 points) risk group was taken as a reference; 5/132 (3.8%), for the intermediate (1-2 points) risk group the risk was: 46/409 (11.1%, RR=3.0), and in the high (3-4 points) risk group: 23/62 (37.1%, RR= 9.8.). Documenting a substantially higher risk for developing delirium in the higher risk patient groups compared with the low-risk patients for this population. The area under the ROC curve was: 0.73 (CI, 0.65 to 0.78) versus 0.66 (CI, 0.55 to 0.77) for the Inouye validation cohort. Varying the cut-off value of the MMSE (<=24) and the Apache-II (>=16, being the 2 independent predictors of delirium in this cohort, did not improve the predictive value of the model. (Area under the ROC curve; 0.73 (CI, 0.67 to 0.78). A separate, multivariate, stepwise logistic regression analysis of 3 of the 4, in univariate analysis,

significant Inouye et al. factors shows that cognitive impairment and illness severity predicted delirium (Nagelkerke $R^2 = .17$). (table 4a) At baseline, patients in the delirium group were older, had higher GDS-15 scores and were more likely to have been acutely admitted. (table1). Multivariate, stepwise, logistic regression analysis of all the significant base-line variables, including the 3 Inouye criteria significant in univariate analysis, shows that cognitive status, type of admission and age achieved statistical, predicting significance at baseline (Nagelkerke $R^2 = .21$) (table 4b).

DISCUSSION

This study adds new evidence in support of the predictability of postoperative delirium by independent significant risk factors. The Inouye et al. risk stratification model proved to be useful for this purpose.[10] Implementation of the model in this study showed that the presence at baseline of one or more predefined risk factors at baseline predicted postoperative delirium in elderly hip- surgery patients, as good as in the original development and validation cohorts. Moreover, other findings on baseline vulnerability and precipitating factors may add to the model's predictive power.

The prevalence of postoperative delirium was 12.3%. This rate is comparable to those in the Inouye study cohorts of medical patients and to the range of 5-45% in hip-surgery patients reported by others.[3;10] Inouye et al. found that the incidence of delirium in the development and validation cohorts of elderly general medical patients was 9% and 3% for the low-risk groups, 23% and 16% for the intermediate risk groups and 83% and 32% for the high-risk groups. In the present study the incidence of delirium in the low, intermediate and high-risk patients was: 3.8%, 11.1% and 37.1%, respectively. The median onset of delirium in the Inouye et al. study was 4 and 6 days. In this study the observation period was 5 postoperative days. The significant baseline differences found between patients with or without subsequent delirium suggests high vulnerability in the group at risk. This coincides well with the theory that the predisposing factors are present the higher the baseline vulnerability and so the higher the risk on delirium.[11] As in the Inouye et al. study we found that the risk of postoperative delirium was high when patients were cognitively impaired, severely ill or had vision impairment. Contrary to previous findings, dehydration, as measured by the BUN/ creatinine ratio, did not predict postoperative delirium in this surgical cohort. Explanations for the apparent difference concern the use of different samples and measure validity. Dehydration is probably more of a problem in a medical population than in a combined acute-elective surgical population. Alternatively, in an interim analysis -results not reported here- the BUN/creatinine ratio only marginally correlated with another measure of dehydration, as measuring with an impedance meter. This finding may challenge validity of the BUN/creatinine ratio and, together with the sample differences; it may explain why dehydration did not predict delirium in this study. The other 3 risk factors of the Inouye model performed well in this surgical cohort as patients at a higher risk of developing delirium were efficiently identified at baseline. In multivariate, logistic regression analysis only the MMSE and the Apache-II scores were found to be independent predictors of delirium.

The predictive value of the Inouye model in this surgical cohort was as good as in the original study. These findings underline generalizability of the model. Varying the cut-off value of the MMSE (<=24) and the Apache-II (>=16), being the 2 independent predictors of delirium in this cohort did not enhance the predictive value of the model. Strengths of the risk stratification model are its simplicity and feasibility in clinical practice: either a physician or a

trained nurse easily and quickly assesses all of the risk factors. Moreover, the assessment is minimally intrusive to the patient.

Strengths of this study include the prospective, controlled design, the sample size, the use of a predefined risk stratification model, and the use of a standardized, validated diagnostic instrument for delirium, the Confusion Assessments Method, as well as the use of daily assessments for delirium throughout the study. Screening (CAM) for delirium started on admission, in order to exclude delirious patients. Results may well be generalized to other orthopedic patient populations.

In addition to the predefined risk factors for delirium other baseline characteristics, indicating a risk for delirium in hip-surgery patients were identified. Age and acute admission were independent predictors of delirium. Age was a predictor of delirium in other studies.[14-16] Contrary to these findings, age was not a predictor of delirium in the Inouye et al. study, nor was acute admission. One explanation of the apparent differences is that falls (and hip-fractures) are associated with age. In this study acute hospital admittance because of fractures was associated with a fourfold increase in the risk of delirium (29.6% vs 7.3%). It goes without saying that falls were not a relevant baseline patient characteristic in the Inouye's et al. medical patient samples. Unlike elective admission (e.g. hip replacement), acute admission (e.g. fractures) indicates increased vulnerability in general, with higher risk of falling, more co-morbidity, more pain and more stress factors that may associated with postoperative delirium. Baseline scores on the GDS-15 self-rating scale of depression were also higher in the patients with postoperative delirium than in those without. However, the mean scores for the GDS-15 (1.5+1.7 vs 1.0+1.5) are well within normal range and no cases of depression were observed. In multivariate, logistic regression analysis not only the MMSE, but also age and acute admission were found to be independent risk factors for delirium in this hip-surgery sample. ROC analysis shows that the area under the curve was 0.77 (CI, 0.71-0.82) for the extended model and 0.73 (CI, 0.65 to 0.78) for the four-factor model. As with overlapping confidence intervals, no conclusions on which model is superior can be drawn. Age and type of admission may be added to the predictive model, but the results need further confirmation in an independent patient cohort.

Study limitations to be addressed are that this is a single site study; risk factors were studied in the context of a delirium prevention clinical trial; and the selection of risk factors from all possible risk factors. This study included all eligible patients from several orthopedic and surgical wards in one general teaching hospital. The large number of patients included underlines that results are robust. Nevertheless, generalizability of the conclusions would have benefited had this been a multi-center trial. Patients were participants in a delirium prevention study. An intervention targeted at preventing postoperative delirium may influence the incidence rate of delirium or it may act as a confounder of baseline risk factors. The overall incidence of delirium was lower than we had expected based on previous reports. [2;3;8] Perhaps non-specific effects, e.g. being a participant in a clinical trial, contributed to the low incidence. Furthermore, proactive geriatric consultation was provided to all patients and that too may have contributed to the relatively low incidence of delirium. However, the incidence of postoperative delirium was not statistically different in the haloperidol and placebo cohorts. Therefore, we assume that treatment condition was not a strong confounding variable in this study. Perhaps not all major risk factors for postoperative delirium were evaluated, thereby challenging content validity of the study. Many risk factors for delirium have been identified. [11-13;16] Not all of them were evaluated in this study. The focus of this study was on the risk factors identified by Inouye et al., and to elaborate and replicate some of the previous findings

in a new sample of hip-surgery patients. Important variables were selected from the wide range of possible risk factors. These include age, sex, type of admission, functional ability and symptomatology of mood disorders. Nevertheless, it is possible that other important risk factor for postoperative delirium in hip-surgery patients were not evaluated in the study.

The results from the Inouye et al. study have now been replicated in a different patient sample. A predictive model that helps to differentiate between surgery patients who are at risk for postoperative delirium is of great clinical importance. Patients at higher risk can be targeted for multifunctional, intensive, delirium prevention programs that are expensive and require substantial manpower, whereas patients with low risk can be integrated in a more simplified prevention program.

References

1. Dyer CB, Ashton CM, Teasdale TA. Postoperative delirium. A review of 80 primary data-collection studies. Arch.Intern. Med. 1995; 155:461-65.
2. Galanakis P, Bickel H, Gradinger R, Von Gumppenberg S, Forstl H. Acute confusional state in the elderly following hip surgery: incidence, risk factors and complications. Int.J.Geriatr.Psychiatry 2001;16:349-55.
3. Lindesay J, Rockwood K, Rolfson DB. The epidemiology of delirium, In: Lindesay J, Rockwood K, Macdonald AJ, editors. Delirium in old age, 1 ed. New York: Oxford University Press; 2002. p. 27-50.
4. Marcantonio ER, Flacker JM, Michaels M, Resnick NM. Delirium is independently associated with poor functional recovery after hip fracture. J.Am.Geriatr.Soc. 2000;48:618-24.
5. Marcantonio ER, Simon SE, Bergmann MA, Jones RN, Murphy KM, Morris JN. Delirium symptoms in post-acute care: prevalent, persistent, and associated with poor functional recovery. J.Am.Geriatr.Soc. 2003;51:4-9.
6. McCusker J, Cole MG, Dendukuri N, Belzile E. Does delirium increase hospital stay? J Am.Geriatr.Soc. 2003;51:1539-46.
7. O'Keeffe S, Lavan J. The prognostic significance of delirium in older hospital patients. J Am.Geriatr.Soc. 1997;45:174-78.
8. Berggren D, Gustafson Y, Erikson B. Postoperative confusion after anaesthesia in elderly patients with femoral neck fractures. Anesthesia and Analgesia 1987; 66:497-504.
9. Williams-Russo P, Urquhart BL, Sharrock NE, Charlson ME. Post-operative delirium: predictors and prognosis in elderly orthopedic patients. J.Am.Geriatr.Soc. 1992;40:759-67.
10. Inouye SK, Viscoli CM, Horwitz RI, Hurst LD, Tinetti ME. A predictive model for delirium in hospitalized elderly medical patients based on admission characteristics. Ann.Intern.Med. 1993;119:474-81.
11. Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. JAMA 1996; 275:852-57.
12. Rolfson DB. The causes of delirium, In: Lindesay J, Rockwood K, Rolfson DB, editors. Delirium in Old age, 1 ed. Oxford: Oxford University Press; 2002. p. 101-22.
13. Inouye SK. Predisposing and precipitating factors for delirium in hospitalized older patients. Dement.Geriatr.Cogn Disord. 1999; 10:393-400.
14. Gustafson Y, Berggren D, Brannstrom B, Bucht G, Norberg A, Hansson LI *et al.* Acute confusional states in elderly patients treated for femoral neck fracture. J.Am.Geriatr.Soc. 1988;36:525-30.
15. Rockwood K. Acute confusion in elderly medical patients. J Am.Geriatr.Soc. 1989;37:150-54.
16. Schor JD, Levkoff SE, Lipsitz LA, Reilly CH, Cleary PD, Rowe JW *et al.* Risk factors for delirium in hospitalized elderly. JAMA 1992;267:827-31.
17. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985; 13:818-29.
18. Folstein MF, Folstein SE, McHugh PR. «Mini-mental state». A practical method for grading the cognitive state of patients for the clinician. J Psychiatr.Res. 1975; 12:189-98.
19. Hetherington R. The Snellen chart as a test of visual acuity. Psychol.Forsch. 1954; 24:349-57.

20. Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M *et al.* Development and validation of a geriatric depression screening scale: a preliminary report. J.Psychiatr.Res. 1982;17:37-49.
21. Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. Md State Med.J. 1965;14:61-65.
22. American Psychiatric Association (APA). Diagnostic and statistical manual of mental disorders, fourth edition revised (DSM-IV). Washington DC: American Psychiatric Association; 1994.
23. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann.Intern.Med. 1990;113:941-48.
24. Cummings JL. Clinical neuropsychiatry. Orlando, FL.: Grune & Stratton; 1985.
25. Trzepacz PT, Mittal D, Torres R, Kanary K, Norton J, Jimerson N. Validation of the Delirium Rating Scale-revised- 98: comparison with the delirium rating scale and the cognitive test for delirium. J Neuropsychiatry Clin Neurosci. 2001; 13:229-42.
26. Kalisvaart KJ, Jonghe JF, Bogaards MJ, Vreeswijk R, Burger BJ, Eikelenboom P et al. Haloperidol Prophylaxis for Elderly Hip-Surgery Patients at Risk for Delirium. A Randomized Placebo-Controlled Study. J Am Geriatr Soc 2005; 53:1658-1666

Table 1. Baseline Characteristics of the Patients on Admission

Characteristic	Delirium (N=74)	no-delirium (N=529)	*P*- value
Age, mean ±SD	81.8 + 6.7	77.4 + 5.7	<.001
Female, n (%)	53 (71.6)	412 (77.9	.230
MMSE, mean ±SD*	21.7 + 4.6	25.7 +3.9	<.001
Visual acuity mean ±SD†	0.34 + 0.14	0.43 + 0.16	<.001
Apache-II, mean ±SD‡	14.8 + 3.8	12.8 + 2.8	<.001
BUN/creatinine ratio, mean ±SD§	19.5 + 6.6	20.5 + 6.1	.262
GDS-15 mean ±SD □□	1.5 + 1.7	1.1 + 1.6	.013
Barthel Index, mean ±SD**	18.3 + 3.1	18.8 + 3.1	.196
Acute Admission (fracture), n (%)	40 (54.1)	95 (18.0)	<.001

* Range 0 (severe cognitive impairment) to 30 (no cognitive impairment).
† Range 20/20 (no visual impairment) to 20/800 (severe visual impairment).
‡ Range 0 (no acute health problems) to 70 (severe acute health problems).
§ Ratio over 18 indicating dehydration.
□□ Range 0 (depression not likely) to 15 (depression very likely).
** Range 0 (severe disability) to 20 (no disability).
SD = standard deviation.
Because of rounding, percentages may not total 100

Table 2. Estimated Risk for Delirium: Inouye Criteria Factors on Admission in Comparison with the Original Validation Cohort.

Characteristic	Delirium (N=74)	No-delirium (N=529)	*P*-value	RR (95% CI)	Inouye validation cohort Relative Risk
MMSE, n risk point (%)*	48 (64.9)	103 (19.5)	< .001	5,53 (3.56-8.58)	4.0**
Apache, n risk point (%)*	27 (36.5)	57 (10.8)	< .001	3.55 (2.35-5.37)	4.3**
Vision, n risk point (%)*	15 (20.3)	60 (11.3)	.029	1.79 (1.07-2.99)	3.0**
BUN/creat ratio, n risk point (%)*	52 (70.3)	353 (66.7)	.544	1.16 (0.72-1.85)	2.9**

The cut-off point as used by Inouye et al. 1993 determined each patient's risk: * MMSE score < 24
Vision score > 20/70 Apache score > than 16 Bun/creatine ratio > 18
** For these factors, in the Inouye development cohort, the 95% CI excludes 1.0 (*P* < .05) Because of rounding, percentages may not total 100.

Table 3. Performance of the Predictive Model in an Elderly Hip-Surgery Cohort Compared to the Inouye Validation Cohort

		Studygroup		Inouye validation cohort	
Risk Group*	points	n/N (%)	Relative Risk	n/N (%)	Relative Risk
Low	0	5/132 (3.8) **	1.0	1/30(3) ***	1.0
Intermediate	1-2	46/ 409 (11.2) **	3.0	16/103(16) ***	4.7
High	3-4	23/ 62 (37.1) **	9.8	12/38(32) ***	9.5

Each patient's risk group was determined by adding 1 point for each risk factor present:
* MMSE score < 24
Vision score > 20/70
Apache score > than 16
Bun/reatine ratio > 18
** Chi-square, *P*< .000, using low risk group as reference group.
***Chi-square trend, *P*< .002
Because of rounding, percentages may not total 100.

Table 4a. Stepwise Logistic Regression Analysis of Three of the Four Inouye's Risk Factors in Patients with Postoperative Delirium (n=74) and without (n=529)

Outcome	Predictor	ß	Wald Statistic	Standard error	*P*-value	Exp(B)	NagelkerkeR²
Postoperative delirium	APACHE	-0.12	8.721	.041	. 003	.887	
	MMSE	.153	28.990	.028	<.001	1.166	.172

Table 4b. Stepwise Logistic Regression Analysis of Three of the Four Inouye's Risk Factors and Age, Type of admission and GDS-15 in Patients with Postoperative Delirium (n=74) and without (n=529)

Outcome	Predictor	ß	Wald Statistic	Standard error	*P*-value	Exp(B)	NagelkerkeR²
Postoperative delirium	MMSE	.147	17.81	.035	<.001	1.159	
	Age	-.059	5.70	.025	.017	.946	
	Admission type	.686	4.20	.335	.040	1.986	.206

Chapter 4

Risk assessment of delirium; development and validation of the Delirium Risk Assessment Score (DRAS)

Vreeswijk R
Kalisvaart I
Maier AB
Kalisvaart KJ

Eur Geriatr Med. 2020 Apr;11(2):307-314.

ABSTRACT
Purpose: Development and validation of a delirium risk assessment score. Predisposing risk factors for delirium were used, which are easily assessed at hospital admission without additional clinical or laboratory testing.

Methods: A systematic literature search identified ten risk factors: acute admission, alcohol use > 4 units/day, cognitive impairment, ADL impairment, age > 75 years, earlier delirium, hearing/vision problems, number of medication ≥ 5, number of morbidities > 2 and male. The DRAS was developed in a mixed patient population (N = 842) by the use of univariate and multivariate analyses and -2 log-likelihood calculation to weigh the risk factors. Based on the sensitivity and specificity, a cutoff score was calculated. The validation was performed in 3 cohorts (N = 408, N = 186, N = 365). In cohort 3, the DRAS was compared (AUC, sensitivity and specificity) to 3 instruments (Inouye, Kalisvaart, VMS rules).

Results: The delirium incidence was 31.8%, 20.3%, 15.6% and 15.1%. All risk factors were independently predictive for delirium, except male. The multivariate analyses excluded morbidities. The final DRAS consists of 8 items; acute admission, cognitive impairment, alcohol use (3 points), ADLimpairment/mobilityproblems (2 points), higher age, earlier delirium, hearing/vision problems, and medication (1 point). The total score is 15 points and at a cut-of score of 5 or higher the patient is at risk of developing a delirium. The cutoff was at 5 or more points, AUC: 0.76 (95% CI 0.72-0.79), sensitivity 0.77, specificity 0.60. Validation cohorts AUC was 0.75 (95% CI 0.96-0.81), 0.76 (95% CI 0.70-0.83) and 0.78 (95% CI 0.70-0.87), sensitivity 0.71, 0.67 and 0.89 and specificity 0.70, 0.72 and 0.60. The comparison revealed the highest AUC for the DRAS.

Conclusion: Based on an admission interview, the delirium risk can be easily evaluated using the DRAS shortlist score of predisposing risk factors for delirium in older inpatients.

INTRODUCTION

Delirium is a serious complication in older inpatients. [1-3] It is multifactorial determined and based on a combination of predisposing and precipitating risk factors. Incidence rates for delirium vary among various hospital patient populations ranging from 5 to 87%. [3] Patients with delirium often have high morbidity and mortality, prolonged hospital length of stay and high rates of institutionalization and dementia following discharge. [2-7]
Current guidelines and trials suggest that about one third of all delirium episodes could have been prevented by assessing systematic programs, and that delirium prevention would be a cost-effective strategy. [8,9] Recent studies also showed that there is a lack of knowledge, competence, awareness regarding delirium, prevention of delirium and use of screening tools for detection and severity of delirium amongst clinicians. [10-12] There is also a relation between frail elderly and delirium due to the fact that frail elderly people have also more predisposing risk factors for delirium than dose who are not frail. [13,14] Therefore, it seems prudent to screen hospitalized patients for their risk for delirium to create awareness that a patient is at risk and because clinicians can develop plans to mitigate the risk. Understanding delirium risk factors may even help clinicians, patients, and caregivers in targeting non-pharmacological and pharmacological interventions aimed at lessening its burden.
Identification of modifiable predisposing and precipitating risk factors for delirium is a prerequisite for an individual approach for the prevention of delirium. The predisposing delirium risk factors are already identifiable on admission and the amount of predisposing risk factors present denotes the elderly patient's vulnerability for delirium during admission. [6]
Several screening instruments have been suggested to detect patients at risk of delirium. Lindroth found 23 prediction screening instruments. The instruments in this review showed that they were often based on complex methods such as scale administration (MMSE, Barthel, KATZ, GDS) and interpretation of laboratory measurements which need time and knowledge to perform, and they were developed for specific patient populations and are not validated. [9,15-20, 35-37]

The aim of this study was to evaluate whether patient characteristics of older patients admitted to a hospital, which can be assessed quickly and easily on admission based on an admission interview and without additional clinical or laboratory testing, may serve to stratify older inpatients with respect of their delirium risk.

METHOD

Participants and Setting

In this study four different patient cohorts were used, a development cohort and three validation cohorts. The development cohort, consisting of a population of 842 elderly patients (mixed surgical/non-surgical) who were admitted to a teaching hospital in the Spaarne Gasthuis in Haarlem from 2009 till 2011, was used to develop the prediction screening instrument Delirium Risk Assessment Score (DRAS). The DRAS was validated using three cohorts. Validation cohort one is a cohort of 408 orthopaedic patients admitted to the same hospital in 2010 till 2012. Validation cohort two is a cohort of 186 surgical patients admitted in 2016 to a hospital in the Spaarne Gasthuis in Haarlem. Validation cohort three is a cohort of 365 of 603 orthopaedic patients from the Haloperidol study population that took place in 2000 to 2002 in a hospital at the Medisch Centrum Alkmaar in Alkmaar, the Netherlands. [22]
The validation was done retrospective because data was already available. The haloperidol study included in total 603 patients but due to missing data at admission 238 out of 603 patients had to be excluded from analysis of the third validation cohort.

In and exclusion criteria were in all populations the same. Included were all people with the age 65 or over, no delirium on admission (CAM and confirmation by a geriatrician) and admission ≥ 72 hours. Consent was obtained by patient or relative (if the patient was not able to give consent).

Risk factors and assessment on admission

The potential predisposing risk factors for delirium were selected after a systematic review of literature published from 1990 to 2008 and using reviews published from 2008 to 2011. [21-28] Risk factors which are independent associated with delirium found in literature were: Older age, male gender, sensory impairment (Visual and hearing impairment), cognitive comorbidity (dementia, cognitive impairment, depression), acute admission, functional impairments and disability (immobility, functional dependence, fracture on admission), malnutrition (alcoholism, dehydration), polypharmacy and medical comorbidity (high burden of illness). The predisposing risk factors that were selected were based on their characteristics to be easy to assess without additional clinical or laboratory test results. This resulted in the following potential predisposing risk factors for delirium: acute vs planned admission, alcohol use ≥ four units per day vs < four units, cognitive impairment yes vs no, hearing/ vision problems yes vs no , help needed for activities of daily living (ADL) yes vs no, age ≥75 vs <75 years, previous delirium yes vs no, number of medication ≥5 vs <5, number of morbidities >two vs ≤ two, and male yes vs no. Cognition was scored as diagnosis of dementia, or if patient or their relative mentioned any cognition problems. The patient ability to perform activities of daily living (ADL) was scored if patients and/or relatives mentioned any help for ADL at home and or needed devices as support for their mobility. Patients and/or their relatives were asked if they have experienced delirium, confusion or disorientation in a previous admission. Hearing and vision problems were scored if patient were not able to solve hearing and/or vision problems by using glasses or a hearing aid.
In the validation cohort 3 data were used out of an existing database, the risk factors for the DRAS were established as follows; for cognition, a Mini Mental State Examination (MMSE) score of ≤ 24 points was used [30], for vision problems the Snellen vision test (> 20/70) [32]. Other risk factors were measured in the same way as in the development cohort.

Test characteristics of the DRAS were compared with the Inouye risk score and the Kalisvaart risk screening instrument and the VMS screening instrument. [9,20,29] The variables used in these tools are already available in the data. The Inouye model is a well-known risk model cited in more than 800 articles and often used in research. The Dutch hospitals uses the Dutch Safety Monitoring (Veiligheids Management Systeem (VMS)) in daily practice to screen for patients at risk.

For the Inouye risk screening instrument the following 4 risk factors were scored: Cognitive impairment (MMSE) [30] score of ≤24 points on a scale of 0 to 30 points, visual impairment, defined as binocular near vision, Snellen vision test worse than 20/70 after correction vision [31], index of dehydration (ratio of blood urea nitrogen to creatinine of ≥18) and severity of illness, measured by the Apache II (Acute Physiology Age and Chronicle Health Examination,) score of ≥16 on a scale of 0 to 70 [32], and for the Kalisvaart risk screening instrument the factors; age, cognition (MMSE ≤ 24 points) and acute admission. The VMS screening instrument for delirium, uses 3 questions; ‘Do you experience cognitive problems?’, ‘Have you needed ADL support within 24 hours before admission?’, Did you had a delirium during another admission?. The VMS was not developed and validated in a scientific study but already used in the Dutch hospitals. That is why it is used to compare the DRAS with the VMS in this study.

Delirium Assessment

In the development cohort and the validation cohorts a brief delirium assessment (<15 minutes) was preformed daily from day one till three days after admission or operation by trained interviewers which could be a research nurse, or a doctor not involved in the patient's treatment to screen for delirium symptoms by use of Confusion Assessment Method (CAM) [33] assessed delirium. If the patient scored positive on the CAM, a geriatrician confirmed the diagnosis based on DSM-IV and DSM-V. The daily assessment was augmented with medical and nursing record review for evidence of intervening delirium features (e.g. acute onset, inattention, disorganized thinking, altered level of consciousness, disorientation, memory impairment, perceptual disturbances, psychomotor agitation or retardation, and altered sleep-wake cycle) and medical treatment for delirium.

Statistics

Statistical calculations were performed using SPSS for Windows, version 18.0 (SPSS, Chicago Inc. Chicago, IL). Each potential risk factor for delirium was tested with the primary outcome measurements using Chi-square tests for nominal variables, the Mann-Whitney U test for ordinal variables and the unpaired 2-tailed t-test for continuous variables. A logistic univariate regression analyses were preformed to establish if the predisposing risk factor was related to the development of delirium. All used risk factors with a value of $P < 0.2$ were included in the multivariate stepwise logistic regression analysis. To facilitate use of the DRAS score, we developed weights for all risk factors based on the Odds Ratios (OR) of the estimate risk factor.

The performance of the risk model (DRAS) was measured using receiver-operating characteristic (ROC) analysis. For the best performance of the DRAS a cut-off point was calculated using the best score on sensitivity and specificity. Furthermore, for the comparison part of this study the sensitivity and specificity were calculated of the other screening instruments used.

The studies were done in accordance with the Declaration of Helsinki and the guidelines on Good Clinical Practice. Local approval of the METC was obtained. The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

RESULTS

The delirium incidence was 268/842 (31.8%) in the development cohort, 83/408 (20.3%) in validation cohort one, 28/186 (15.1%) in cohort two and 57/365 (15.6%) in validation cohort three. Demographic characteristics of the participants in the cohorts are described in Table 1. Nine out of ten risk factors for delirium described in the literature were related to the development of delirium in the development cohort. Male gender was not significantly associated with delirium ($P = 0.051$). In the multivariate stepwise logistic regression analysis, comorbidity was the only risk factor which lost significance predicting delirium (Table 2). Of the 10 used variables 8 remain in the final model. The OR of the delirium risk factors was calculated to attribute weight to them. After weighing the risk factors, the final DRAS consisted of three points for acute admission, alcohol use, and cognition impairment, two points to ADL impairment and one point to the other risk factors. The final DRAS had a ROC curve: AUC 0.76 (95% CI 0.72 – 0.79). The cut-off point of the DRAS using the best score for sensitivity and specificity showed that at ≥ 5 points on the DRAS the prediction for delirium was the best. In the development cohort 211 patients had five DRAS points or more accounting for 79 % of the delirium incidence. Furthermore, the higher the score the more patients developed delirium, at a score of 11 it was 82.4% and with a score of 12 till 14 it was

100%. The AUC of the validation cohorts ranges from 0.75 – 0.87, the sensitivity 0.67 – 0.89 and specificity from 0.60 – 0.72 (Table 3). The final DRAS with the descriptions of the description of the different risk factors is presented in table 4.

The comparison of the DRAS with other screening instruments for delirium (Kalisvaart, Dutch VMS and Inouye) revealed a somewhat higher AUC for the DRAS but overlapping confidence intervals; DRAS 0.75 (95% CI: 0.69 – 0.82), Kalisvaart AUC 0.74 (95% CI: 0.67-0.81), VMS AUC 0.69 (95% CI: 0.62-0.77), Inouye AUC 0.66 (95% CI: 0.59-0.74). (Fig 1) The sensitivity for the DRAS was 0.67, Kalisvaart 0.78, VMS 0.75 and Inouye 0.97. The specificity for the DRAS was 0.72, Kalisvaart 0.66, VMS 0.58 and Inouye 0.14. (Table 3)

DISCUSSION

The Delirium Risk Assessment Score (DRAS), based solely on information that is most times readily available, or easy to obtain and easy to interpret by nurses and doctors has been shown to be highly accurate in the assessment of risk for delirium. Despite evidence of a high risk for developing delirium in all kinds of patient populations, reliable studies on risk factors and prediction of delirium by nurses and doctors are rare. In a review article of Lindroth et al. (2017) 23 delirium prediction models for different patient populations were identified of which 14 were externally validated. Of these 14 models the overall predictive ability was moderate to high with an AUC ROC range from 0.52 to 0.94. Besides these 14 studies two other studies can be found which are externally validated. [39,40] Most of the found models used scales (MMSE, Clock drawing, Geriatric Depression Scale (GDS) APACHE II) and/or laboratory tests, which are labor and time intensive and require training to be used in daily practice.[38] Furthermore, the results of cognition testing e.g. MMSE or other patient reported tests done on admission are known to have low reliability when the patient is in stress of the admission, is severe ill, unable to respond or is being tested at busy emergency departments. [34] Another point made by Woodford was that small cognitive screening test for unselected populations may result in more false positives than true positive cases. And the best method of classifying cognitive impairment is a comprehensive clinical evaluation.[41]
Methodological shortcomings of the prediction model studies have been reported. The assessment of the outcome variable delirium was largely non-systematic, only once daily and not in weekends or every 48 hours. In the studies that assessed delirium more than once per day, the assessment was performed by routine clinical staff, decreasing consistency. [38] This is a major limitation for an acute condition that fluctuates, may occur suddenly and is dependent on precise, objective assessment. Most studies used the Confusion Assessment Method (CAM) but only a few confirmed the diagnoses by a geriatrician or psychiatrist.
To improve delirium prediction models, future models should consider using standard risk factors (predisposing and/or precipitating) used in daily care and should preferably be applicable for more populations. In the Netherlands patients receive an admission interview administered by doctors and nurses when they are admitted to a hospital. In this admission interview most predisposing risk factors for delirium are established.
The DRAS, is a simple delirium risk screenings instrument. It showed good validity to predict delirium in the development cohort and three validation cohorts. It's AUC lays within the range of AUC's of the other delirium prediction screenings instruments found. But the strength of the DRAS is its simplicity and feasibility in clinical practice: each nurse and doctor can easily and quickly assess and interpret all of the DRAS risk items based solely on brief admission interview or just asking six simple questions to the patient or his/her relative. The DRAS performs as accurately or somewhat better compared to the other screening instruments like the Kalisvaart screening tool [10], the Inouye screening tool [9] and the VMS

screening tool [15]. The DRAS does not require elaborate testing (of which the outcome may not be reliable) [34,41], laboratory results and/or training of nurses and doctors. Due to this there is no delay in starting preventive interventions for delirium.
The strength in this study lays also in the fact that the DRAS was developed in a heterogenous patient population makes it possible to use the DRAS in different patient populations. The large number of patients included underlines that our results are robust. Furthermore, the assessment of delirium in all our studies was done by a trained person on a daily basis using the Confusion Assessment Method and the diagnose was confirmed by a geriatrician.

Study limitations to be addressed are that the development and validation was not externally validated. There was a validation done in cohort 3 which came from another hospital, but this cohort was data already available from another study. Also, preventive interventions for delirium done by the geriatric liaison service in our hospital may have possibly influenced the incidence rate of delirium. This study included all eligible patients from several wards, a heterogenous patient population, in a general teaching hospital., so the fact that the validation was limited to an orthopaedic and surgical population may raise questions but nevertheless, the results on DRAS risk assessment in the third validation cohort were the same or better compared to the other screening instruments.

CONCLUSION

Based on the admission interview the delirium risk can be very easily evaluated by using the DRAS shortlist score of predisposing risk factors for delirium in older inpatients.

References

1. Dyer CB, Ashton CM, Teasdale TA. Postoperative delirium. Arch Intern Med. 1995; 155:461–465.
2. Galanakis P, Bickel H, Gradinger R, Von Gumppenberg S, Förstl H. Acute confusional state in the elderly following hip surgery: incidence, risk factors and complications. Int J Geriatr Psychiatry. 2001 Apr;16(4):349- 55.
3. Lindesay, J., Rockwood, K. and Rolfson, D. The epidemiology of delirium. In Delirium in Old Age. Eds. Lindesay, J., Oxford University Press; 2002 pp 27-50.
4. McCusker J, Cole M, Abrahamowicz M, Primeau F, Belzile E. Delirium predicts 12-month mortality. Arch Intern Med 2002; 162: 457–63.
5. Witlox J, Eurelings LS, de Jonghe JF, Kalisvaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of post discharge mortality, institutionalization, and dementia: a meta-analysis. JAMA. 2010 Jul 28;304 (4):443-51.
6. Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. JAMA. 1996 Mar 20;275(11):852-7.
7. Inouye SK. Predisposing and precipitating factors for delirium in hospitalized older patients. Dement Geriatr Cogn Disord. 1999 Sep-Oct;10(5):393-400.
8. Cole MG, McCusker J, Bellavance F, Primeau FJ, Bailey RF, Bonnycastle MJ, et al. Systematic detection and multidisciplinary care of delirium in older medical inpatients: a randomized clinical trial. CMAJ 2002; 167:753-9
9. Inouye SK, Viscoli CM, Horwitz RI, Hurst LD, Tinetti ME. A predictive model for delirium in hospitalized elderly medical patients based on admission characteristics. Ann Intern Med. 1993; 119;474-481
10. Morandi A, Davis D, Taylor JK, Bellelli G, Olofsson B, Kreisel S, Teodorczuk A, Kamholz B, Hasemann W, Young J, Agar M, de Rooij SE, Meagher D, Trabucchi M, MacLullich AM. Consensus and variations in opinions on delirium care: a survey of European delirium specialists. Int Psychogeriatr. 2013 Dec; 25(12): 2067–2075.
11. Yaghmour S.M., Gholizadeh L. Review of Nurses' knowledge of delirium, dementia and depression (3Ds): systematic literature review. Journal of nursing 2016, 6, 193-203
12. Kristiansen S., Konradsen H., Beck M., Nurses'experiences of caring for older patients afflicted by delirium in a neurological department. 2018 J. Clin. Nursing
13. Verloo H, Goulet C, Morin D, Von Gunten A. Association between frailty and delirium in older adult patients discharged from hospital Clinical Interventions in Aging 2016:11 55–63
14. Quinlan N, Marcantonio ER, Inouye SK, Gill TM, Kamholz B, Rudolph JL. Vulnerability: The Crossroads of Frailty and Delirium. J Am Geriatr Soc. 2011 November; 59(Suppl 2): S262–S268.
15. Kalisvaart KJ, Vreeswijk R, de Jonghe JF, van der Ploeg T, van Gool WA, Eikelenboom P. Risk factors and prediction of postoperative delirium in elderly hip-surgery patients: implementation and validation of a medical risk factor model. J Am Geriatr Soc. 2006 May;54(5):817-22.
16. Marcantonio ER, Goldman L, Mangione CM, Ludwig LE, Muraca B, Haslauer CM, et al. A clinical prediction rule for delirium after elective noncardiac surgery. JAMA. 1994 Jan 12;271(2):134-9.
17. Rudolph JL, Jones RN, Levkoff SE, Rockett C, Inouye SK, Sellke FW, et al. Derivation and validation of a preoperative prediction rule for delirium after cardiac surgery. Circulation 2009, 119:229-36.
18. Vochteloo AJ, Moerman S, van der Burg BL, de Boo M, de Vries MR, Niesten DD, et al. Delirium risk screening and haloperidol prophylaxis program in hip fracture patients is a

helpful tool in identifying high-risk patients, but does not reduce the incidence of delirium. BMC Geriatr. 2011 Aug 11; 11:39.
19. Koster S, Oosterveld FG, Hensens AG, Wijma A, van der Palen J. Delirium after cardiac surgery and predictive validity of a risk checklist. Ann Thorac Surg. 2008 Dec;86 (6):1883-7.
20. Praktijkgids Kwetsbare ouderen (online). Available at www.vmszorg.nl
21. Raats JW, Steunenberg SL, de Lange DC, van der Laan L, Risk factors of post-operative delirium after elective vascular surgery in the elderly: A systematic review. Int.J.Surg 2016 Nov;35:1-6.
22. Scholz AF, Oldroyd C, McCarthy K, Quinn TJ, Hewitt J, Systematic review and meta-analysis of risk factors for postoperative delirium among older patients undergoing gastrointestinal surgery. Br.J.Surg. 2016 Jan;103(2).
23. Van Meenen LC, van Meenen DM, de Rooij SE, ter Riet G. Risk prediction models for postoperative delirium: a systematic review and meta-analysis. J. Am. Geriatric Soc. 2014 Dec;62(12):2383-90
24. Ahmed S, Leurent B, Sampson FL. Risk factors for incident delirium among older people in acute hospital medical units: a systematic review and meta-analysis. Age and Aging. 2014 May;43(3):326-33
25. Vasilevskis EE, Han JH, Hughes CG, Ely EW. Epidemiology and risk factors
26. For delirium across hospital settings. Best Pract. Res Clin Anaesthesiol. 2012 Sep;26(3):277-87.
27. Oh ES, Li M, Fafowora TM, Inouye SK, Chen CH, Rosman LM, Lyketsos CG, Sieber FE, Puhan MA. Preoperative risk factors for postoperative delirium following hip fracture repair: a systematic review. Int J Geriatr Psychiatry. 2015 Sep;30(9):900-10.
28. Lindesay J., Rockwood K, Macdonald A. The causes of delirium, in Delirium in Old Age. 2002: Oxford University Press
29. Laurila JV, Laakkonen ML, Tilvis RS, Pitkala KH. Predisposing and precipitating factors for delirium in a frail geriatric population. J Psychosom Res. 2008 Sep;65(3):249-54. Review.
30. Kalisvaart KJ, de Jonghe JF, Bogaards MJ, Vreeswijk R, Egberts TC, Burger BJ, et al. Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: a randomized placebo- controlled study. J Am Geriatr Soc. 2005 Oct;53(10):1658-66.
31. Folstein MF, Folstein SE, McHugh PR. «Mini-mental state». A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12: 189-198
32. Hetherington R. The Snellen chart as a test of visual acuity. Psychol Forsch 1954;24: 349-357
33. Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. Crit Care Med 1985;13: 818-829
34. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann Intern Med. 1990 Dec 15;113(12):941-8.
35. Kat M.G., Vreeswijk R., de Jonghe J.F.M., van der Ploeg T., van Gool W.A. Eikelenboom P., Kalisvaart K.J. Long-Term Cognitive Outcome of Delirium in Elderly Hip Surgery Patients Dement Geriatr Cogn Disord. 2008;26(1):1-8.
36. Fortes-Filho SQ, Apolinario D, Melo JA, Suzuki I, Sitta Mdo C, Garcez Leme LE. Predicting delirium after hip fracture with a 2-min cognitive screen: prospective cohort study. Age Ageing. 2016 Sep;45(5):713-7.
37. Freter S, Dunbar M, Koller K, MacKnight C, Rockwood K. Risk of Pre-and Post-Operative Delirium and the Delirium Elderly At Risk (DEAR) Tool in Hip Fracture Patients. Can Geriatr J. 2015 Dec 23;18(4):212-6.

38. Douglas VC, Hessler CS, Dhaliwal G, Betjemann JP, Fukuda KA, Alameddine LR, et al. The AWOL tool: derivation and validation of a delirium prediction rule. J Hosp Med. 2013 Sep;8(9):493-9.
39. Lindroth H, Bratzke L, Purvus S, Brown R, Coburn M, Mrkobrada M, et al. Systematic review of prediction models for delirium in the older adult inpatient. BMJ Open 2018;8 March.
40. van den Boogaard M, Pickkers P, Slooter AJ, Kuiper MA, Spronk PE, van der Voort PH, van der Hoeven JG, Donders R, van Achterberg T, Schoonhoven L. Development and validation of PRE-DELIRIC (PREdiction of DELIRium in ICU patients) delirium prediction model for intensive care patients: observational multicentre study. BMJ. 2012 Feb 9;344
41. Fan H, Ji M, Huang J, Yue P, Yang X, Wang C, Ying W. Development and validation of a dynamic delirium prediction rule in patients admitted to the Intensive Care Units (DYNAMIC-ICU): A prospective cohort study. Int J Nurs Stud. 2019 May; 93:64-73.
42. Woodford HJ, George J. Cognitive assessment in the elderly: a review of clinical methods. QJM. 2007; 100:469–484.

Table 1. Patient characteristics of the development and three validation cohorts stratified by delirium.

	Development cohort N = 842		Validation cohort 1 N= 408		Validation cohort 2 N = 186		Validation cohort 3 N = 365	
	No delirium N = 574	Delirium N = 268	No delirium N = 325	Delirium N = 83	No delirium N = 158	Delirium N = 28	No delirium N = 308	Delirium N=57
Age		81.8, (6.45)	78.5, (5.82)	82.7, (5.87)	79.7, (7.3)	80.6, (6.45)	78.3, (5.72)	82.1, (6.11)
- mean (SD)	79.3 (6.19)							
- 75 years or older	428, (64.8)	233, (35.2)	236, (75.9)	75, (24.1)	102, (64.6)	23, (18.4)	218, (81.3)	50, (18.7)
Gender (male)	175, (30.5)	100, (37.3)	59, (18.2)	25, (30.1)	62, (83.8)	12, (16.2)	54, (17.5)	17, (29.8)
Acute admission	231, (54.1)	196, (45.9)	79, (59.4)	54, (40.6)	91, (78.4)	25, (21.6)	68, (68.7)	31, (31.3)
Alcohol, 4 or more units/daily	24, (54.5)	20, (45.5)	16, (76.2)	5, (23.8)	5, (83.3)	1, (16.7)	16, (80.0)	4, (20.0)
Cognitive impairment	141, (50.0)	141, (50.0)	90, (66.7)	45, (33.3)	17, (58.6)	12, (41.4)	84, (68.3)	39, (31.7)
ADL problems	172, (53.8)	148, (46.2)	86, (73.5)	31, (26.5)	42, (72.4)	16, (27.6)	80, (78.4)	22, (21.6)
History of delirium	34, (56.7)	26, (43.3)	11, (68.8)	5, (31.2)	10, (66.7)	5, (33.3)	10, (71.4)	4, (28.6)
Vision/hearing problems	147, (56.8)	112, (43.2)	52, (67.5)	25, (32.5)	63, (80.8)	15, (19.2)	43, (75.4)	14, (24.6)
Medication 5 or more	229, (60.4)	150, (39.6)	102, (74.5)	35, (25.5)	71, (77.2)	21, (22.8)	90, (82.6)	19, (17.4)
Comorbidity, 2 or more illnesses	132, (55.5)	106, (44.5)	48, (60.8)	31, (39.2)	46, (75.4)	15, (24.6)	47, (65.3)	25, (34.7)

Results prescribed as N, (%) unless otherwise stated

Table 2. Development of the Delirium Risk Assessment Score (DRAS) to predict delirium in the development cohort (N=842), Univariate and Multivariate analyses.

	Univariate			Multivariate			Final DRAS
Risk factors	**OR**	**95% CI**	**P**	**OR**	**95% CI**	**P**	**Points**
Acute admission	4.04	2.94 – 5.55	<0.001	2.99	2.12 - 4.22	<0.001	3
Alcohol, 4 or more units/day	1.85	1.00 – 3.41	0.046	2.70	1.34 – 5.45	0.01	3
Cognitive impairment	3.41	2.51 – 4.63	<0.001	2.40	1.72 – 3.36	<0.001	3
ADL problems	2.88	2.14 – 3.89	<0.001	1.91	1.36 – 2.68	<0.001	2
Age, 75 years or older	2.27	1.52 – 3.39	<0.001	1.46	0.93 – 2.28	0.14	1
Vision/hearing problems	2.09	1.54 – 2.83	<0.001	1.34	0.95 – 1.90	0.10	1
Medication, 5 or more prescriptions	1.92	1.43 – 2.57	<0.001	1.35	0.97 – 1.88	0.10	1
History of delirium	1.71	1.01 – 2.92	0.045	1.54	0.84 – 2.83	0.16	1
Comorbidity, 2 or more ilnesses	2.19	1.60 – 1.49	<0.001	excluded		0.83	Excluded
Gender (male)	1.36	1.00 – 1.84	0.051	Excluded			Excluded

Table 3. Validity of the Delirium Risk Assessment Score (DRAS) in the development cohort, three validation cohorts and the comparison of with two other delirium risk screening instruments in cohort 3.

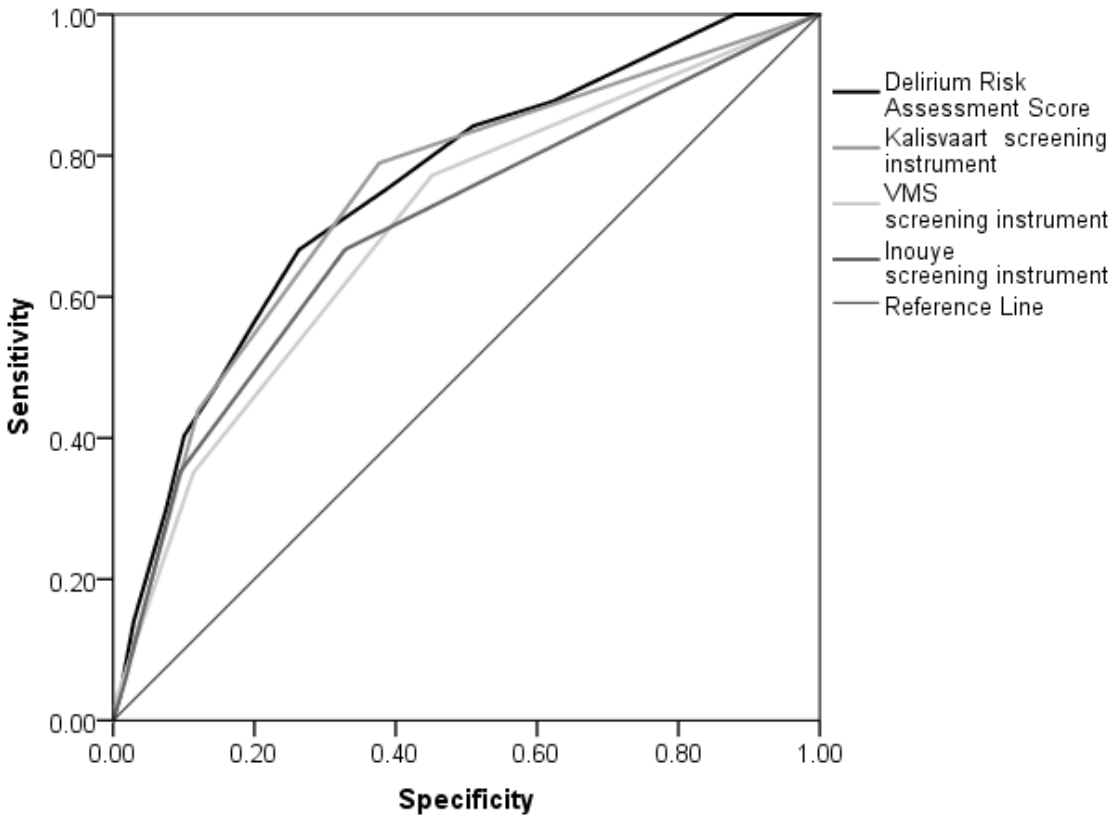
			Asymptomatic				
	N	AUC	95% CI		P	Sensitivity	Specificity
Validity of the DRAS in the development cohort							
Development cohort	842	0.75	0.72	0.79	<0.001	0.79	0.58
Validity of the DRAS in three validation cohorts							
Validation – cohort 1	408	0.75	0.69	0.81	<0.001	0.71	0.72
Validation – cohort 2	186	0.78	0.70	0.87	<0.001	0.60	0.89
Validation – cohort 3	365	0.75			<0.001	0.67	0.74
Validity of three other delirium risk screening tools in cohort 3							
Kalisvaart screening tool	365	0.74	0.67	0.81	<0.001	0.78	0.66
VMS-screening tool	365	0.69	0.62	0.77	<0.001	0.75	0.58
Inouye screening tool	365	0.66	0.59	0.74	<0.001	0.97	0.14

VMS: Dutch Safety Management System

Table 4. Delirium Risk Assessment Score (DRA

	Risk factor	Risk factor description	Points
1	Acute Admission	Acute admission to hospital	3
2	Cognitive impairment	Every mentioned cognitive problem by patient or family	3
3	Alcohol abuse	4 or more units of alcohol used daily	3
4	ADL/mobility problems	Help needed with ADL and/or mobility	2
5	Vision/hearing problems	Vision and/or hearing problems which cannot be solved by using glasses or hearing aid	1
6	Medication ≥5	5 or more medications at admission	1
7	Age ≥ 75	Age 75 years or over	1
8	Earlier delirium	Have you experienced an earlier delirium or were you confused at an earlier admission	1
		Patient at risk at cut-of score 5, maximum score is 15	

Fig 1. ROC curve in the comparison study of the DRAS with, Kalisvaart screening instrument, Dutch VMS screening instrument and Inouye screening instrument (N=365)



Chapter 5

Risk of delirium is increased in hospitalised older adults with COVID-19.

Vreeswijk R
Maier AB
Kalisvaart KJ

Submitted

ABSTRACT

Background: Delirium is a severe complication in hospitalised older adults, with an incidence up to 70% in older inpatients with COVID-19. Identification of patients at risk for delirium is essential for preventative interventions. The Delirium Risk Assessment Score (DRAS) is a rapid and easy to administer delirium prediction screening instrument based on predisposing risk factors for delirium. This study aims to describe the delirium risk and incidence of delirium in older COVID-19 patients.
Method: A retrospective cohort study
Setting: COVID-19 ward of a university-affiliated top clinical hospital in the Netherlands
Patients: COVID-19 diagnosed patients of 70 years and older
Results: Ninety-seven patients (78,8 years (6.06 SD), 51 male) were included in the study. The mean Clinical Frailty Score (CFS) was 3.57 (SD 1.61)) and 31 patients died during admission. Patients with delirium (28/79) had a higher CFS score, were cognitive impairment (11/14), had a higher Body Mass Index (>25 kg/m2) 16/36), more comorbidity >2 (21/51), lived in a long-term care facility (5/5) or received care at home (4/8). Thirteen patients have been admitted to the ICU, of which ten patients had delirium. The DRAS mean score was 6.16 (SD 2.20). The DRAS had an AUC 0.80 (95% CI 0.69 - 0.90). The higher the DRAS-score, the more patients developed delirium. Twelve patients with a DRAS of > 9 and were all diagnosed with delirium.
Conclusion: Delirium is highly prevalent in older COVID-19 positive inpatients, and the DRAS a delirium risk score of predisposing risk factors for delirium predicts delirium in older COVID-19 patients.

INTRODUCTION

Delirium is an acute fluctuating syndrome with features of inattention, altered consciousness and cognitive disturbances. [1] It is common among hospitalised older patients, affecting up to 50% of post-operative older persons and 80% of older intensive care unit (ICU) patients. [2,3] And the frailer a patient is, the higher the risk for delirium. [4,5] Patients with delirium often have high morbidity and mortality, prolonged hospital length of stay and high rates of institutionalization and dementia the following discharge. [6] Delirium is a preventable condition in 30 - 40% of cases. [7]
The incidence of delirium amongst Coronavirus disease 2019 (COVID-19) patients varies from 15 - 70% on non-ICU-COVID-19 wards [8–13] and 13 - 84% on ICUs. [14]
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes COVID-19. Angiotensin-converting enzyme 2 (ACE2) is the functional receptor for SARS-CoV-2, present in multiple human organs, including the nervous system and skeletal muscles. Besides the lungs, it can also damage other organs like the heart, liver, kidneys and brain. Patients admitted to a hospital with COVID-19 are more likely to be frail and prone to develop delirium due to direct central nervous system (CNS) invasion, induction of CNS inflammatory mediators, a secondary effect of other organ system failure, the effect of sedative strategies, prolonged mechanical ventilation time, immobilization, and environmental factors including social isolation and quarantine without family. [8,12] Delirium, the most frequent clinical expression of acute brain dysfunction, is especially important in the context of COVID-19. Therefore, delirium prevention programs are also highly needed in COVID-19 care pathways. Mortality in the first wave (first months of 2020) in COVID-19 patients aged $\geq$ 65 years was up to 46%. [13,14] The mortality of hospitalized patients with COVID-19 above the age of 80 years is up to 54% in international studies. [15] Coupled with delirium, which independently increases the risk for prolonged mechanical ventilation, longer ICU and hospital stay, institutionalization, functional dependence, long-term cognitive impairment, and higher mortality up to two years after discharge, COVID-19 poses a considerable risk for older patients. [16 – 18] Delirium prevention starts with an assessment of delirium risk. Several delirium risk assessment instruments have been developed, e.g. Risk model for Delirium (RD), PREdiction of DELIRium on the IC (PREDELIRIC), AWOL-score, DYNAMIC-ICU. [19] These delirium risk assessment instruments often rely on convenient complex methods such as scale administration (Mini Mental State Examination, Barthel, Katz Activities of daily living scale, Geriatric Depression Scale), which is not always possible in COVID-19 patients, e.g. due to isolation or psychological state because of their illness.
The Delirium Risk Assessment Score (DRAS) is a valid delirium prediction tool in orthopaedic and surgical populations that do not rely on scale assessment or laboratory measurements based on readily available inpatient data. [20] The aim of this study is to establish the delirium incidence and the risk for delirium using the DRAS in older COVID-19 positive inpatients.

METHOD

A retrospective, single-center observational study was performed among COVID-19 positive patients aged 70 years and older admitted to dedicated COVID-19 wards and COVID-19 ICU of the Spaarne Gasthuis, a university-affiliated teaching hospital in the Netherlands in March and April 2020. The exclusion was age < 70 years and delirium on admission based on the Confusion Assessment Method (CAM). [23]
The following patient characteristics are collected from the electronic patient records: gender, comorbidity (number of chronic illnesses present on admission), amount of medication,

cognitive impairment, hearing/vision impairment, alcohol use, delirium in history, living circumstances, Body Mass Index (BMI). The level of frailty was established using the Clinical Frailty Score ranging from not frail (scores 1-4), mildly frail (score 5), moderately frail (score 6), to severely frail (score 7-9). [21]
Electronic patient charts were screened by the researcher (RV) for delirium symptoms based on clinical notations of nurses and doctors, and/or the presence of a Delirium Observation Screening Score (DOSS) [22] and/or Confusion Assessment Method (CAM) [23] and/or diagnosis of delirium. The diagnosis of delirium was based on the data found and made by the research team. Because due to lack of knowledge, use of screening tools and workload a diagnose of delirium could be missed by the treating doctor. The final diagnosis of delirium was confirmed by a geriatrician (KK) based on the DSM-V. [24]

The Delirium Risk Assessment Score (DRAS)
The risk for delirium was calculated using the DRAS. The DRAS [20], a valid and easily applicable delirium risk assessment tool was applied and includes the following predisposing risk factors for delirium; acute admission (3 points), cognitive impairment (3 points), ADL/mobility problems (2 points), age ≥ 75 years (1 point), earlier delirium (1 point), hearing/vision problems (1 point), number of medications ≥ 5 (1 point), number of alcohol use > 4 units/day (1 point). The total score is 15 points, and at a cut-off score of 5 or higher, the patient is at risk of developing delirium (Table 1). The DRAS has an AUC: 0.76-0.78, a sensitivity of 0.71-0.89, and a specificity of 0.60-0.72.

Statistics
Statistical calculations were performed using SPSS for Windows, version 24 (SPSS, Chicago Inc. Chicago, IL). Continuous variables are reported as mean and standard deviation (SD) or median based on the distribution of the variable. Categorical variables are reported as number and proportion (percentage). The performance of the DRAS was measured using receiver operating characteristic (ROC) analysis for calculation of the area under the curve (AUC), the sensitivity and the specificity.

RESULTS

Ninety-seven COVID-19 positive patients were eligible for inclusion in this study. One patient was excluded because of missing data. Baseline characteristics are shown in table 2. Mean age was 78.7 years (SD 6.06, range70 - 96), 51 patients were male. The CFS mean score was 3.57 (SD 1.61). The mean score BMI was 26.1 (SD 4.57). In 51/79 patients had more than two illness present, the median score was 3 (range 0 - 8). The number of medications the median score 6 (range 0 - 20). The majority of patients, 66/79, lived independently, eight had received community care, and five came from a long-term care facility. The 32/79 patients died, of which five patients had been admitted to the ICU during admission. Of these 32 patients, 29 died while they were in the hospital. Thirteen patients were also admitted to the ICU during their admission.

Delirium was diagnosed in 28/79 patients, of which 10/13 patients were in the ICU. Not all patients had a delirium diagnosis made directly by the treating physician, only 13/28 had a diagnosis of delirium by the treating physician, but the researcher did not label two as delirious. The described symptoms were more related to cognitive impairment. Delirium was more present in patients with cognitive problems (11/14). Patients who received care (4/8) or are living in a long-term care facility (5/5) were more diagnosed with delirium than a patient who lived independently (19/66). Delirium was more diagnosed in patients with a CFS of 7 or

8 (4/5). Of the patients which died, 16/32 had delirium. Of the patients with a BMI of > 25 kg/m2 (36/70), 16 patients had delirium. The mean difference of days spent in the hospital was 2.6 days shorter in patients without delirium (7.78 days, SD 5.39) than in patients with delirium (10.35 days, SD 5.39). Sixteen of the 32 patients who died had delirium during admission.
The DRAS at a cut-off score of 5 points had an AUC of 0.80 (95% CI .69 – 0.90), a sensitivity of 82% and a specificity of 61%. The higher the score, the more patients developed delirium; 12 patients had a DRAS of $\geq$ 9 points and were all diagnosed with delirium (Fig. 1.).

DISCUSSION

Considering the high incidence of delirium in COVID-19 older patients and the potential serious consequences, attention is needed in order to reduce disability and mortality in this vulnerable category of patients. Identifying patient at risk for delirium based on predisposing risk factors for delirium can help reducing delirium and complications related with delirium in these patients. Several delirium risk models have been developed.[19] The DRAS as one of these models can identify patients at risk for delirium. To our knowledge there are no other studies on delirium risk assessment using a delirium risk model for older COVID-19 patients, although these patients are often frail and suffer from comorbidities.
In this study, the DRAS was used to predict delirium risk in COVID-19 patients, a tool based on readily available (admission data), easy to obtain, and easy to interpret by nurses and physicians. This may be an advantage due to the high workload of clinicians and nurses during the pandemic. According to the DRAS criteria of a score of 5 or higher a patient is at risk for developing delirium, the majority of patients in this population are a risk for developing delirium. The DRAS showed to be very effective and accurate to establish the risk for delirium in COVID-19 patients. The specificity of the DRAS was not as high as expected but is acceptable also because false-positive patients will receive preventive interventions for delirium, which can be considered as 'regular good care'. Establishing the delirium risk with the DRAS make it possible to focus a multi-component prevention regimen on the patients at need with a higher likelihood of benefit.

This study also has some limitations, mainly due to our retrospective study design. The data were obtained from the electronic patient records. Missing data may have introduced bias, e.g. delirium symptoms.
Delirium risk assessment and detection can also be influenced by the fact that COVID-19 treatment was more of a priority than delirium detection and prevention. But also, as a result of a lack of knowledge about delirium and delirium prevention, as shown in a European study. It showed that amongst 200 respondents from different countries delirium awareness (34%), knowledge (33%), and lack of education (13%) were the most commonly reported barriers. [25]

Another limitation is that it is a single-site study in a hospital where delirium prevention is considered part of routine care for patients at risk for delirium. This could affect the incidence of delirium. Although, to the circumstances and unfamiliarity with the treatment of COVID-19 patients, prevention of delirium may not have been a priority at the time. The at-risk patient is more exposed to accelerating (precipitating) delirium risk factors such as intense social isolation due to the ban on family members and caregivers, minimal staff exposure and staff are often rushed and stressed, and wear protective gear that masks faces and muffles voices, makes communication and human connection difficult. This is even more problematic for people with hearing or vision impairments. [26,27]

These conditions make it difficult to perform non-pharmacological preventive interventions for delirium. [24] The priority of care for COVID-19 positive patients are more on organizational aspects and care for personal safety than on the prevention of delirium. The ability to recognize, manage delirium and perform (excellent) delirium prevention for those patients at risk for delirium will directly affect clinical outcomes in this population.

CONCLUSION

Delirium incidence in COVID-19 patients is high and very high when admitted to ICU. The DRAS predicts delirium with high sensitivity. As the tool is easily implementable, it is recommended to use the DRAS in clinical practice to identify patients with COVID-19 at risk for delirium and initiate interventions to prevent delirium.

References

1. European Delirium Association, American Delirium Society. The DSM-5 criteria, level of arousal and delirium diagnosis: inclusiveness is safer. BMC Med. 2014; 12:141
2. Inouye SK. Delirium in older persons. N Engl J Med. 2006;354(11):1157-1165.
3. Kotfis K, Marra A, Ely EW.ICU delirium - a diagnostic and therapeutic challenge in the intensive care unit. Anaesthesiol Intensive Ther. 2018;50(2):160-167.
4. Sillner AY, McConeghy RO, Madrigal C, Culley DJ, Arora RC, Rudolph JL. The Association of a Frailty Index and Incident Delirium in Older Hospitalized Patients: An Observational Cohort Study. Clin Interv Aging. 2020; 15: 2053–2061.
5. Quinlan N, Marcantonio ER, Inouye SK, Gill TM, Kamholz B, Rudolph JL. Vulnerability: The Crossroads of Frailty and Delirium. J Am Geriatr Soc. 2011 November; 59(Suppl 2): S262–S268.
6. Witlox J, Eurelings LS, de Jonghe JF, Kalisvaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of post discharge mortality, institutionalisation, and dementia: a meta-analysis. JAMA. 2010 Jul 28: 304 (4):443-51.
7. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet. 2014 Mar 8;383(9920):911-22.
8. Kotfis K, Williams Roberson S, Wilson JE, Dabrowski W, Pun BT, Ely W. COVID-19: ICU delirium management during SARS-CoV-2 pandemic. Crit Care. 2020; 24: 176.
9. Poloni TE, Carlos AF, Marco Cairati, Cutaia C, Medici V, Marelli E, Ferrari D, Galli A, Bognetti P, Davin A, Cirrincione A, Ceretti A, Cereda C, Ceroni M, Tronconi L, Vitali S, Guaita A. Prevalence and prognostic value of Delirium as the initial presentation of COVID-19 in the elderly with dementia: An Italian retrospective study. EClinicalMedicine. 2020 Jul 30
10. Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalised patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol 2020; 77: 1–9.
11. O'Hanlon S, Inouye S. Delirium: a missing piece in the COVID-19 pandemic puzzle. Editorial in Age and Aging 2020; 49:497-498
12. Hawkins M, Sockalingam S, Bonato S, Rajaratnam T, Ravindran M, Gosse P, Sheehan KA. A rapid review of the pathology, presentation, and management of delirium in adults with COVID-19. J Psychosom Res. 2021 Feb; 141:110350.
13. De Smet R, Mellaerts B, Vandewinckele H, Lybeert P, Frans E, Ombelet S, Lemahieu W, Symons R, Ho E, Frans J, Smismans A, Laurent MR. Frailty and Mortality in Hospitalized Older Adults With COVID-19: Retrospective Observational Study. J Am Med Dir Assoc. 2020 Jul; 21(7): 928–932.e1.
14. Blomaard LC, van der Linden CMJ, van der Bol JM, Jansen SWM, Polinder-Bos HA, Willems HC, Festen J, Barten DG, Borgers AJ, Bos JC, van den Bos F, de Brouwer EJM, van Deudekom FJA, van Dijk SC, Emmelot-Vonk MH, Geels RES, van de Glind EMM, de Groot B, Hempenius L, Kamper AM, Kampschreur LM, de Koning MMM, Labots G, Looman R, Lucke JA, Maas HAAM, Mattace-Raso FUS, El Moussaoui R, van Munster BC, van Nieuwkoop C, Oosterwijk LBLE, Regtuijt MEM, Robben SHM, Ruiter R, Salarbaks AM, Schouten HJ, Smit OM, Smits RAL, Spies PE, Vreeswijk R, de Vries OJ, Wijngaarden MA, Wyers CE, Mooijaart SP.**Frailty** is associated with in-hospital mortality in older hospitalised COVID-19 patients in the Netherlands: the COVID-OLD study. Age Ageing. 2021 May 5;50(3):631-640.
15. Wirth R, Becker C, Djukic M, Drebenstedt C, Heppner HJ, Jacobs AH, Meisel M, Michels G, Nau R, Pantel J, Bauer JM. [COVID-19 in old age-The geriatric perspective]. Z Gerontol Geriatr. 2021 Mar;54(2):152-160.
16. Duggan MC, Van J, Ely EW. Delirium Assessment in Critically Ill Older Adults Considerations During the COVID-19 Pandemic. Crit Care Clin (2021) 37; 175-190

17. Rebora P, Rozzini R, Bianchetti A, Blangiardo P, Marchegiani A, Piazzoli A, Mazzeo F, Cesaroni G, Chizzoli A, Guerini F, Bonfanti P, Morandi A, Faraci B, Gentile S, Bna C, Savelli G, Citerio G, Valsecchi MG, Mazzola P, Bellelli G; CoViD-19 Lombardia Team.Delirium in Patients with SARS-CoV-2 Infection: A Multicenter Study. J Am Geriatr Soc. 2021 Feb;69(2):293-299.
18. Morandi A, Rebora P, Isaia G, Grossi E, Faraci B, Gentile S, Bo M, Valsecchi MG, Deiana V, Ghezzi N, Miksza J, Blangiardo P, Bellelli G. Delirium symptoms duration and mortality in SARS-COV2 elderly: results of a multicenter retrospective cohort study. Aging Clin Exp Res. 2021 Aug;33(8):2327-2333. doi: 10.1007/s40520-021-01899-8. Epub 2021 Jun 26.
19. Lindroth H, Bratzke L, Purvis S, Brown R, Coburn M, Mrkobrada M, Chan MTV, Davis DHJ, Pandharipande P, Carlsson CM, Sanders RD. Systematic review of prediction models for delirium in the older adult inpatient. BMJ Open. 2018 Apr 28;8(4):e019223.
20. Vreeswijk R, Kalisvaart I, Maier AB, Kalisvaart KJ. Development and validation of the delirium risk assessment score (DRAS). Eur Geriatr Med. 2020 Apr;11(2):307-314.
21. Sablerolles RSG, Lafeber M., van Kempen JAL, van de Loo BPA, Boersma, Rietdijk WJR, Polinder-Bos HA, Mooijaart SP, van der Kuy H, Versmissen J, Faes MC. Association between Clinical Frailty Scale score and hospital mortality in adult patients with COVID-19 (COMET): an international, multicentre, retrospective, observational cohort study The Lancet, health Longevity 2021
22. Schuurman, M.J., Shortridge-Baggett, L.M., & Duursma, S.A. (2003). The delirium observation screening scale: a screening instrument for delirium. Research and theory for nursing practice: an international journal, 17, 31- 50.
23. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann Intern Med. 1990 Dec 15;113(12):941-8. doi: 10.7326/0003-4819-113-12-941.
24. DSM-V. American Psychiatric Association. May 2013. ISBN9780890425541
25. Morandi A, Davis D, Taylor J.K., Bellelli G, Olofsson B, Kreisel S, A. Teodorczuk A, Kamholz B, Hasemann W, Young J, Agar M, de Rooij S.E, Meagher D, Trabucchi M, MacLullich A.M, Consensus and variations in opinions on delirium care: a survey of European delirium specialists. Int Psychogeriatr. 2013 Dec; 25(12): 2067–2075.
26. Inouye SK, The Importance of Delirium and Delirium Prevention in Older Adults During Lockdowns JAMA. 2021;325(17):1779-1780.
27. Suman A, Baptiste L, Sampson EL. Risk factors for incident delirium among older people in acute hospital medical units: a systematic review and meta-analysis Age and Ageing 2014; 43: 326–333

Table 1. Delirium Risk Assessment Score (DRAS)

	Risk factor	Risk factor description	Points
1	Acute Admission	Acute admission to hospital	3
2	Cognitive impairment	Every mentioned cognitive problem by patient or family	3
3	Alcohol abuse	4 or more units of alcohol used daily	3
4	ADL/mobility problems	Help needed with ADL and/or mobility	2
5	Vision/hearing problems	Vision and/or hearing problems which cannot be solved by using glasses or hearing aid	1
6	Medication ≥5	5 or more medications at admission	1
7	Age ≥ 75	Age 75 years or over	1
8	Earlier delirium	Have you experienced an earlier delirium or were you confused at an earlier admission	1
		Patient at risk at cut-of score ≥5, maximum score is 15	

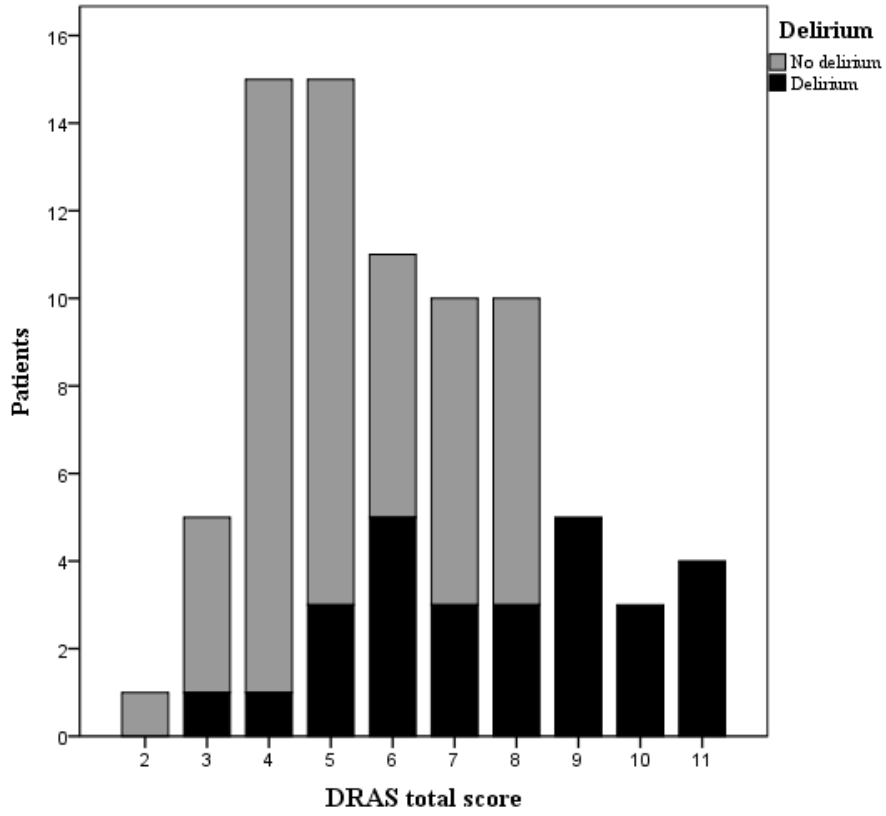
Table 2. Demographics, CFS score and DRAS score of COVID-19 patients, survivals and non-survivals

	All (N = 79)		Survivals (N = 47)		Non-survivals (N = 32)	
	Delirium N = 28	No-delirium N = 51	Delirium N = 12	No-delirium N = 35	Delirium N = 16	No-delirium N = 16
Age						
- Mean (SD)	80.4 (6.4)	77.8 (5.7)	79.1 (6.2)	77.5 (5.9)	81.4 (6.5)	78.6 (5.4)
- 75 years or older	23 (28.8)	34 (42.5)	10 (21.3)	23 (48.9)	13 (40.6)	11 (34.4)
Gender, male	20 (25.3)	31 (39.2)	7 (14.9)	19 (40.4)	13 (40.6)	12 (37.5)
Acute admission*	27 (35.0)	50 (62.5)	12 (25.5)	34 (72.3)	15 (46.9)	16 (50.0)
Cognitive impairment*	11 (13.9)	3 (3.8)	3 (6.4)	2 (4.3)	8 (25.0)	1 (3.1)
ADL/mobility problems*	19 (24.1)	12 (15.2)	6 (12.8)	6 (12.8)	13 (40.6)	6 (18.8)
History of delirium*	7 (8.9)	0 (0.0)	3 (6.4)	0 (0.0)	4 (12.5)	0 (0.0)
Vision/Hearing Problems*	11 (13.9)	19 (24.1)	5 (10.6)	10 (21.3)	6 (18.8)	9 (28.1)
Medication 5 or more*	22 (27.8)	35 (44.3)	9 (19.1)	23 (48.9)	13 (40.6)	12 (37.5)
Alcohol use 4 or more units/daily*	1 (1.3)	1 (1.3)	1 (2.1)	0 (0.0)	0 (0.0)	1 (3.1)
Comorbidity > 2*	21 (26.6)	30 (38.0)	9 (19.1)	20 (42.6)	12 (37.5)	10 (31.3)
BMI (N=70)						
- BMI 18.5 - 24.9 (normal weight)	8 (11.4)	26 (37.1)	3 (7.3)	18 (43.9)	8 (27.6)	5 (17.2)
- BMI 25 - 30 (overweight)	10 (14.3)	12 (17.1)	4 (9.8)	7 (17.1)	5 (17.2)	6 (20.7)
- BMI > 30 (obese)	6 (8.6)	8 (11.4)	3 (7.3)	6 (14.6)	2 (6.9)	3 (10.3)
ICU admission	10 (12.7)	3 (3.8)	7 (14.9)	1 (2.1)	3 (9.4)	2 (6.3)

Living place						
- Independent	47 (59.5)	19 (24.1)	10 (21.3)	33 (70.8)	9 (28.1)	14 (43.8)
- Independent with care	4 (5.1)	4 (5.1)	2 (4.3)	2 (4.3)	2 (6.3)	2 (6.3)
- Long-term Care	5 (6.3)	0 (0.0)	--	--	5 (15.6)	0 (0.0)
Clinical Frailty Score (CFS)						
- Not Frail	14 (17.7)	45(57.0)	8 (17.0)	33 (70.2)	6 (18.8)	12 (37.5)
- Mildly Frail	4 (5.1)	2 (2.5)	1 (2.1)	1 (2.1)	3 (9.4)	1 (3.1)
- Moderately Frail	6 (7.6)	3 (3.8)	3 (6.4)	1 (2.1)	3 (9.4)	2 (6.3)
- Severely Frail	4 (5.1)	1 (1.3)	--	--	4 (12.8)	1 (3.1)
Delirium Risk Assessment Score (DRAS)	2 (2.5)	19 (24.1)	2 (4.3)	16 (34.0)	0 (0.0)	3 (9.4)
- Score 0 - 4	26 (32.9)	32 (40.5)	10 (21.3)	19 (40.4)	16 (50.0)	13 (40.6)
- Score 5 - 15						

Results prescribed as N, (%) unless otherwise stated, *variable is present in the patient.

Fig 1. DRAS score and delirium incidence per score



Chapter 6

Assessment scales for delirium.

Vreeswijk R
Timmers JF
de Jonghe JFM
Kalisvaart KJ

Aging Health volume 5 number 3 June 2009 409-425 (17)

ABSTRACT

Delirium is a severe psychiatric syndrome that is highly prevalent in elderly general hospital patients. However, the diagnosis of delirium is often missed. The use of rating scales can be helpful in detecting and measuring delirium symptom severity. This article reviews recent developments regarding psychometric qualities, measurement goals, content and rating procedures of some of the available rating scales in clinical practice. Literature from the Medline files up to 2008 were collected, using the following search entries: delirium, (acute) confusion, assessment/rating scale and screening. Articles were selected if their title or summary were related to the development or applicability of delirium rating scales. The reference lists of relevant articles were searched for additional references. The rating scales were split up according to their purposes, screening or severity rating and were discussed for the following aspects: content (theoretical background, rating domains and items), interview (duration, format and assessors" expertise) and psychometric qualities (reliability and validity). There were eight screening scales (Confusion Assessment Method [CAM], CAM for the Intensive Care Unit [CAM-ICU], Intensive Care Delirium Screening Checklist [ICDSC], Delirium Symptom Interview [DSI], NEECHAM Confusion Scale [NEECHAM], Cognitive Test for Delirium [CTD], Delirium Observation Screening [DOS] and Nursing Delirium Screening Scale [Nu-DESC]) and seven severity rating scales (Delirium Rating Scales [DRS], Memorial Delirium Assessment Scales [MDAS], Confusional State Evaluation [CSE], Delirium Severity Scales [DSS], Delirium Index [DI], Delirium-O-Meter [DOM] and Delirium Detection Scale [DDS]) selected for further research. The CAM, NEECHAM and DOS and the CAM-ICU for the ICU appear to be the most suitable as screening instruments, depending on the type of rater (trained) physician or nurse. The (revised) Delirium Rating Scale (DRS-R-98) and the DOM appear to be particularly useful for measuring delirium severity or monitoring change.

INTRODUCTION

Delirium, a severe psychiatric syndrome, is highly prevalent among elderly, general hospital patients, and is associated with elevated morbidity, mortality, longer-stay duration, impeded rehabilitation and higher costs. [1–8] Therefore, early recognition and treatment of delirium and its underlying causes are of major importance. [3] The patient's rehabilitation and wellbeing in any setting is, among other things, dependent on whether delirium is detected and properly treated or not. Owing to the high prevalence of delirium in hospitals guidelines suggest routine screening for delirium. Therefore, valid and reliable screening and severity scales are necessary; these scales are also good reminders of what should be looked for in order to detect the symptoms of delirium.

Delirium is often unrecognized by physicians, nurses and other healthcare workers. One survey carried out in a first aid ward showed that delirium is a frequently missed diagnosis in elderly patients. [9] Provided with a simple checklist for 'mental status', the accuracy with which the diagnosis was made rose a modest 11.8%. Another survey undertaken amongst 912 healthcare workers demonstrated that 78% did not recognize delirium symptoms, 40% screened on a routine basis and only 16% used a screening scale [7]. In a study performed by Devlin et al., it was shown that when using a valid rating scale, the detection of delirium increased [10]. Rating scales can be useful in diagnosing, interpreting and monitoring symptoms of delirium, such as the sudden onset of fluctuating symptoms, disturbances of consciousness, concentration, cognition and perception. [10] Others have found that a standard screening protocol, consisting of an orientation–memory– concentration test and a delirium algorithm, leads to more accurate recognition of delirium in elderly patients.[11] Furthermore, nursing staff was generally pleased using the protocol, as it boosted their awareness and knowledge of changes in mental status. This is a major, additional advantage, as delirious patients are often agitated, afraid or indeed apathetic, and there- fore in need of specific and intensive nursing staff care. [12]

For both research and clinical purposes, there is a need for reliable and valid delirium rating scales. Scales can be used for measuring presence absence or severity of delirium symptoms, for measuring change in intervention trials, or as a means to measure change in day-to-day patient management. Symptom coverage and detailed phenomenological study is an additional important function of delirium assessment scales that can facilitate studies that improve our under- standing of delirium as a syndrome.

Many diagnostic scales contain items that are diagnostic in nature such as 'sudden onset of symptoms', which does not change during repeated assessments, and items measuring symptom severity. Totaling the item scores may therefore not be a measure of severity of the disorder but may rather reflect the degree of confidence in the diagnosis. [14]

The validity and reliability of scales depends on several factors, such as functions of the scale design, the items structure and definition of, and training and experience of raters. As there are many different ways to calculate the accuracy of these measures, it is often hard to compare different scales in this respect. Sometimes, validity and reliability may partly be in contrast to each other. [13]

Several scales for screening and severity of delirium have been developed. However, which one should be used is determined by a number of factors. Besides reliability and validity, purpose (screening, diagnostics and severity rating), interviewer (physician, nurse and researcher) and location (general hospital or nursing home) are important aspects. The selection is also determined by aspects such as the patient's expected cooperation and the amount of time available for training and completion. A number of rating scales have been discussed (some more fully than others) in reviews published earlier. [13–18] This review aims to provide a survey of up-to-date rating scales suitable for clinical practice. Scales (screening

and severity) will be evaluated on content, objective, completion and psychometric qualities.

METHOD

A comprehensive literature search was conducted for all original research articles in Dutch and English literature on validity of delirium rating scales using the following search criteria: delirium, (acute) confusion, assessment/rating scale and screening up to August 2008 using Medline and CINAHL. The total hits for Medline were n = 369 and for CINAHL n = 145. Articles were selected if title or summary were related to the development or applicability of delirium rating scales. The reference lists of relevant articles were searched for additional references. Articles were excluded if they did not meet the inclusion criteria, that is, if they were review articles, foreign-language article, case reports, letter to the editor, abstracts or book chapters. A total of 21 articles were included in the final review. Articles excluded were:

- The Confusion Rating [19] with only one publication.
- The Saskatoon Delirium Checklist [20] because no psychometric data was available.
- The Global Accessibility Rating Scales (GARS) [21] and the Visual Analog Scale for Confusion (VAS-C) [22], which are visual analog scales and only rate one particular symptom.
- The Clinical assessment of Confusion (CAC- A) [23] and the Delirium assessment Scale (DAS) [24], because they have no actual list of items.

The remaining scales were split up into screening scales (n = articles): Confusion Assessment Scale (n = 10); Delirium Observation Scale (n = 1); Delirium Symptom Interview (n = 1); Nursing Delirium Screening scale (n = 1); NEECHAM (n = 4); Cognitive Test for Delirium (n = 1); Confusion Assessment Method for the ICU (n = 3) and the Intensive Care Delirium Screening Checklist (n = 1), and severity scales Delirium Rating Scales (n = 6); Memorial Delirium Assessment Scale (n = 3); Confusional State Evaluation (n = 1); Delirium Severity Scale (n = 1); Delirium Index (n = 1); Delirium-O-Meter (n = 1) and the Delirium Detection Scale (n = 1). In total, 21 original research articles were relevant for this review. At least two of the authors evaluated the scales independently and blindly and discrepancies in information were resolved in a consensus meeting with all authors. The scales were scored on the criteria mentioned below and if the scales met the criteria mention they were rated '+', if the score was lower than the criteria but reason- able the scale was rated '-/+' and if no information was found in the validation study article the scale was scored 'blank'.

The validation studies were defined as articles that examined scale performance characteristics including sensitivity, specificity and reliability. The scales were evaluated on content (theoretical background, rating domains and items), interview (duration, format and assessors' expertise) and psychometric qualities (reliability and validity). The scale reliability assessment is based on internal consistency data ($a > 0.70$) and inter-rater agreement ($k > 0.40$ or intraclass correlation (ICC) > 0.70). No test– retest reliability was performed owing to the fluctuating nature of delirium symptoms. Scale validity was evaluated on content and criterion validity ($r < 0.80$ with 'golden standard' and $0.30 < r > 0.70$ with other ratings). The scales also evaluated for the quality of the validation, which means size, and composition of the study population, use of control groups and objective diagnostic standards and independent raters.

RESULTS

Fifteen scales were evaluated, eight screening scales and seven severity scales.

Screening scales

Confusion assessment method

The Confusion Assessment Method (CAM) [54] is based on consensus judgments by experts and it largely corresponds to the operational delirium criteria of the Diagnostic and Statistical manual of Mental Disorders, third edition-revised (DSM-III-R). [26] The following nine items: acute onset and fluctuating course, impaired concentration, disorganized thinking, altered level of consciousness, disorientation, memory impairment, distorted perception, psychomotor agitation/retardation and altered sleep/awake rhythm, are scored using a simple system. In addition, clinical data can be gathered asking open questions. After a structured patient interview, for instance with the Mini-Mental State Evaluation (MMSE) [27] as a guideline, physicians can diagnose delirium by applying the CAM-algorithm. This diagnostic algorithm is geared to four CAM items. Completing the entire CAM takes approximately 20 min and the CAM-algorithm takes approximately 5 min.

Several studies addressed psychometric quality of the CAM among geriatric patients admitted to a variety of general hospital wards. In a double-blind study using the CAM among a group of 56 elderly patients (dementia and depression included), 26 of whom suffer from delirium (DSMIII- R), 94–100% were correctly assessed to be delirious and 90–95% were correctly considered non delirious. In a study in which the CAM was completed by phone, it also proved a practical and sensitive (92.8%) scale for detecting postsurgical delirium in the elderly [28]. Recent research using fewer exclusion criteria and therefore possibly with more 'vulnerable' geriatric patients taking part (n = 81), showed lower sensitivity and specificity (0.81–0.86 and 0.63–0.84, respectively), compared with different diagnostic criteria (DSM-III, DSM-III-R, DSM-IV and ICD-10). [29] These authors favor the CAM as a screening scale and not as a diagnostic tool. The CAM's reliability is very high (k = 0.81–1.00). [25] The same study showed a moderate to high degree of concurrence between the CAM and external criteria (MMSE, a memory test, the GARS and memory span (r = 0.64, r = 0.59, r = 0.82 and r = 0.66, respectively). The CAM was initially developed for physicians. The use of the CAM by nurses/research assistants has been studied several times. [30–35] Sensitivity and specificity varied considerably, depending on experience, training and the type of information available, that is to say observation only or also detailed, cognitive testing (0.68/0.97; 0.46/0.92; 0.89/1.00; 0.13/1.00; 0.19/96). Until there is more clarity on this matter, the CAM should only be used by experienced physicians.

In the palliative care setting, the CAM is widely used but not well validated. Ryan et al. undertook a study to determine the sensitivity and specificity of the CAM when used by non-consultant hospital doctors (NCHDs) working in a specialist palliative care unit. [36]

In a pilot phase with a 1-h training session, the sensitivity of the CAM was only 0.5 (0.22–0.78) and specificity was 1.0 (0.81–1.0). An 'enhanced' training program with two 1-h sessions that involved case-based learning focused on the areas where the NCHDs were experiencing difficulty saw the performance of the CAM improve significantly. Sensitivity was 0.88 (0.62–0.98) and specificity was 1.0 (0.88–1.0). Again, the results suggest that the CAM is a valid screening tool for delirium in the palliative care setting, but its performance is dependent on the skill of the operator. [36]

In most studies, physicians performed the CAM, but nurses and study personnel have also been reported as raters, Rockwood et al. and Rolfson et al. found that the CAM performed poorly as a screening instrument for delirium when administered by non-physicians. They

concluded that there is a need for training in the use of the CAM, especially by non-physicians. [31,32]
In a study by Inouye in 2001 comparing (untrained) nurses' ratings with research ratings using the CAM, nurses identified only 19% of observations and 31% of patients. Sensitivities of nurses' ratings for delirium and its key features were generally low (15–31%); however, specificities were high (91–99%). The conclusion was: recognition of delirium can be enhanced with education of nurses in delirium features, cognitive assessment and factors associated with poor recognition. [34]

Confusion assessment method-ICU

The confusion assessment method-ICU (CAM- ICU) [37,38] was developed to detect delirium in mechanically ventilated or retrained ICU patients and is based on the CAM. It uses non-verbal tasks such as picture recognition, vigilance task, simple yes/no logic questions and simple commands to rate the features of the CAM algorithm. The CAM-ICU has four key delirium criteria: first, acute mental status change (change from baseline or fluctuation course); second, inattention; third, disorganized thinking, and fourth, altered level of consciousness. Delirium is considered to be present if criteria 1 and 2 and either criteria 3 or 4 are present. Completion of the CAM-ICU takes only 2–5 min and can be completed during daily care and can be done by nurses and physicians.
The CAM-ICU was validated in several studies. In these studies, psychometric research was done according to standard guidelines. The first study was carried out in 38 medical ICU patients, CAM-ICU assessments of two nurses and two intensivists were compared with each other and with a diagnosis based on the DSM-IV criteria made by an expert. The sensitivity and specificity were high, and the CAM-ICU produced reliable results in 87% of the patients with delirium. Demographic features such as dementia at baseline did not affect the overall results. The inter-rater reliability varies from k=0.79tok=0.96. In a secondstudy by Ely et al. in 2001 amongst 111 consecutive patients, 471 daily paired evaluations made by two study nurses were compared with a reference standard for diagnosing delirium the CAM-ICU and they had a sensitivity of 100% and 93% respectively, and a specificity of 98% and 100%. The inter- rater reliability was k = 0.96 and measured across subgroups k values varied from 0.92 for those over 65 years of age, 0.99 for the group with a suspected dementia and 0.92 for the group with a median value of 23 on the APACHE II. There was no difference found in sensitivity and specificity when these groups were compared.

Intensive care delirium screening checklist

The intensive care delirium screening checklist (ICDSC) is an eight-item list based on DSM-IV criteria and other delirium features. [39] It is a scale especially developed for use in an ICU where patients have difficulties with communication owing to, for example, intubation. The scale includes assessment of consciousness, orientation, hallucinations or delusions, attentiveness, psychomotor activity (agitation or retardation), inappropriate speech or mood, sleep/wake rhythm disturbances and symptom fluctuation. Each domain (when present) is given one point during the evaluation; the maximum total score is eight and with a score of greater than three delirium is present. Data gathering can be per- formed at the bedside by a nurse or a physician and during routine patient care. The validation was performed in a mixed medical/surgical ICU amongst 93 medical-ventilated patients. Independent assessment was carried out daily in groups by patient nurse–research and nurse- intensivist–psychiatrist (psychiatrist = 'gold standard'). The ICDSC versus the diagnosis made by the psychiatrist had a sensitivity of 99% and a specificity of 64%. The item reliability had a homogeneity coefficient of 0.71–0.79. When the consciousness item was left out, the a was higher 0.78–0.85. The inter-observer reliability between nurse–nurse and nurse–physician was high.

Delirium symptom interview

The Delirium Symptom Interview (DSI) is an interview protocol screening for delirium, based on the seven DSM-III symptoms. [40] These symptoms are: disorientation, consciousness and perception disorders, interrupted sleep/awake cycle, incoherent speech, altered psychomotor activity and fluctuating behavior. Scoring of the DSI is done through direct observation and asking direct questions. The 32 items of the DSI can be rated by a (layman) research assistant. The interview takes approximately 15 min, but with seriously deranged patients it takes longer. Interrater agreement is high (r = 0.90). [40] Internal item consistency for the different symptoms varied from insufficient to good (a = 0.45–0.80). The DSI largely concurred with specialist opinions of neurologists and geriatricians (r = 0.93). The DSI was found sensitive (90%) and specific (80%) in a group of 50 elderly, acutely admit- ted patients, 30 of whom were suffering from delirium. No evaluation has taken place to see if the DSI is suitable to distinguish delirium from dementia.

NEECHAM confusion scale

The NEECHAM confusion scale (NEECHAM) is a nursing screening tool allowing a relatively quick and inconspicuous 'bedside' evaluation of patients' behavioral functioning. [41] The scale consists of nine items, based on review of the literature and a consensus of expert opinions. The items are subdivided into three domains: information processing (attention, performing tasks and orientation: 0–14), behavior (appearance, locomotion and speech: 0–10) and physiological control (vital functions, oxygen saturation and urinary continence: 0–6). Based on the total score, a distinction can be made between normal functioning (27–30), 'possibly delirious' (25– 26), 'slightly confused' (20–24) and 'confused' (0–19). Completion takes 8–10 min and can largely be done during the daily routine. With a margin score of 24 out of 25 on the NEECHAM, 95% of 21 delirium patients were correctly classified and 78% of 137 patients with no delirium were correctly classified as 'not delirious'. A validation study by Neelon et al. in 1996 among 426 elderly patients in a general hospital (including pre-existing cognitive problems), showed a high internal consistency (a = 0.90) and a high inter-assessor reliability (k = 0.91). [41] Concurrence between the NEECHAM and external criteria (MMSE and DSM-III-R) ranged from moderate to good (r = 0.87; r = 0.70/-0.54, respectively). The NEECHAM is fairly well distinguished from measures for ADL and IADL (r = 0.47–0.70). Csokasy (1999) too studied the psychometric qualities of the NEECHAM among nineteen elderly patients admitted to an intensive care unit. [42] They found an internal consistency of a = 0.81, which was high, and the concurrence with external criteria was reason- able to good (physiological scale, DSM-III-R; r = 0.93; r = 0.68, respectively). There is also one validation study found that was carried out in an in-house setting (n = 74). [43] A specialized nurse did the assessment and here the scale turned out reliable (a=0.80; r=0.87) and valid; there was reasonable concurrence with external criteria (MMSE-R: -0.62; DSM-IV-R: -0.70) and low correspondence with a mood scale (GDS r = -0.30). The sensitivity of the scale was 89.7% and the specificity was 69.6%.

Cognitive test for delirium

The cognitive test for delirium (CTD) is a screening scale developed for delirium screening in an ICU. [44] The scale is based on DSM-III-R and cognitive symptoms are often described with delirium. This screening tool was developed to assess orientation, concentration span, memory, understanding/conceptual reasoning and vigilance/ alertness. The scores for each of these five domains range from zero to six and amount to a total score with a maximum of 30. All visual stimuli are big representations and there are parallel items for memory, understanding/conceptual reasoning and vigilance. Patients respond nonverbally to all test

items. Completion takes 10–15 min.
Hart et al. validated the scale among 103 adults with different psychiatric diagnoses (DSM-III-R), admitted to an ICU. [44] The CTD score, among others, was useful in distinguishing between delirium and other psychiatric diagnoses (dementia, depression and schizophrenia). At a cut-off score of less than or equal to 18 on the CTD, all 22 delirium patients were rightly identified as delirious and the scale had a sensitivity of 100% and a specificity of 95.1%. The delirium and dementia groups showed strong concurrence between the CTD-scores and the MMSE (0.81–0.82). This relation was less pronounced in the other two groups (0.48 and 0.51). Furthermore, the internal consistency proved high (a = 0.87). In the validation study, a psychologist carried out the CTD.
Although elderly patients were included (>65 years of age), the scale was not validated for this group specifically. Psychologists did the CTD. In addition, the CTD short version, consisting of attention span and memory items appears suitable to scan for delirium.[41] The short version turned out reliable (a =0.79) and useful to distinguish between delirium and dementia, depression and schizophrenia. With a marginal value of less than 11, sensitivity was 94.7% and specificity 98.8%. [46]
The CTD was tested by Kennedy et al. in a population of 65 patients with a traumatic brain injury. [45] In this study, the receiver operating characteristic analysis showed an optimal cut-off value of less than 22, the sensitivity was 72% and the specificity was 71% compared with the DSM-IV diagnosis. The cut-off of 22 is slightly higher and of a lower sensitivity and specificity than that which Hart et al. found. These results suggest that the Cognitive Test for Delirium provides an acceptable level of differentiation between delirious and nondelirious patients with traumatic brain injury. [45]

Delirium observation screening
The Delirium Observation Screening (DOS) Scale is a 25-item scale especially designed for early recognition of delirium by nursing staff. [16] It is a screening instrument based on DSM-IV criteria for delirium, review of the literature and clinical experience. This 25-item scale deals with eight symptoms: consciousness disorders (three items), attention and concentration (three items), thinking (five items), memory/orientation (three items), psychomotor activity (four items), sleep/ awake pattern (three items), mood (two items) and perception (two items). Incidence for each item is scored on a five-point scale, resulting in a total score. Completing the scale takes less than 5 min and is based on observations during daily care. The psychometric qualities were studied in two elderly patient populations: geriatric patients (n = 82) and a population of patients with a fractured hip (n = 92), and a group of patients from a psychiatric consultation service (n = 57). The DOS has a content validity and internal consistency of a = 0.96/0.97/0.92 in these populations. In these populations the inter-rater reliability showed poor to good scores (for each single item; k = 0.0–1.0). Between the DOS and external criteria (MMSE and CAM) the concurrence varied from reasonable to high (r = -0.66/-0.79; r = 0.63), with a different cognitive assessment scale it was variable (r = 0.33/0.74), with a pre-existing psychiatric diagnosis it was moderate (r = 0.42/0.43), and it was low to moderate with an ADL-scale (r = 0.26/-0.55). Based on the DOS total scores, the delirious group could be distinguished from the non-delirious group. There is also a short version of 13 items available.

Nursing Delirium Screening Scale
The Nursing Delirium Screening Scale (Nu-DESC) is a five-item observation scale that can be completed quickly and is based on the Confusion Rating Scale. [47] The five items are: disorientation, inappropriate behavior, inappropriate communication, illusions/hallucinations and psychomotor retardation. Symptoms are rated from 0–2 based on the presence and

intensity of each symptom. It takes only a few minutes to complete the Nu-DESC. The scale was tested by Gaudreau et al. in a hemato–oncological /internal medicine patient population admitted to a general hospital. The validity of the Nu-DESC was established by determining the scale against the CAM, expert opinions and DSM-III-R criteria. To estimate concur- rent validity, the scale test performance relative to the CAM was compared with those of the CRS, DSM-IV and the MDAS. The convergent validity was established by determining the agreement of the scale with the results of the DSM-IV and the MDAS. The sample size was 52 patients, of which seven had a CAM assessment twice, so 59 CAM assessments were completed. Of 59 CAM assessments, 21 were found to be delirium positive. A psychiatrist re-evaluated 72.9% of all 59 CAMs. The inter-rater reliability (research nurse–psychiatrist) for the CAM was 0.89. To compare the discriminating ability of each method, area under receiver operating characteristic curve test was performed as an index of global test performance. The AUC of the Nu-DESC was 0.902, the CRS 0.823, the DSM-IV 0.952 and the MDAS 0.970. When comparing the AUCs, there was a significant difference between the Nu-DESC and CRS, but not between the others. The Nu-DESC had a sensitivity of 85.7% and a specificity of 86.8%.

Severity scales

Delirium Rating Scale

The Delirium Ratting Scale (DRS) rates the severity of a delirium. [48] The scale's content is based on DSM-III criteria for delirium and consists of ten items; temporal onset of the symptoms, perceptual disturbances, hallucination type, delusions, psychomotor behavior, cognitive status during formal testing, physical disorders, sleep–wake cycle disturbance, liability of mood and variability of symptoms. Items of inattention and disorganized thinking which are usually regarded as essential features of delirium are not included, 'because of vague and varying definition of these terms'. [48] Each item produces a qualitatively described score (0–2/3/4), resulting in a total score (max. 32). The recommended cut-off score for the DRS is 12 points. [53] Over a period of at least 24 h, psychiatrists/ physicians conduct the assessment, consisting of an interview, concise cognitive testing and/ or information from medical files or third par- ties. How long it takes to complete the DRS is not mentioned. Good quality research into the psychometric aspects of the scale has been done. In an adult patient population, the authors found higher, not overlapping DRS scores for delirious patients (DSM-III-R) compared with demented, schizophrenic and 'normal' controls.[48] Inter-rater agreement was high (k = 0.97). In the delirium group, a correlation was found between the severity of the delirium and the results for some cognitive tests (r = -0.43; r = 0.66). In a study with a psychogeriatric setting, the DRS-score did not differentiate between delirium and dementia with super- posed delirium [49]. Rosen et al. found significantly higher DRS-scores for elderly, delirious patients (DSM-III-R) in comparison to scores for geronto–psychiatric patients with a dementia or other syndrome. [50] At a cut-off score greater or equal to ten, 94% of all 'deliria' and 82% of the nondelirious patients were correctly classified. Rockwood et al. also evaluated the psychometric qualities of the DRS among a psychogeriatric study population [51]. They found a high internal consistency (a = 0.90) and interassessor reliability (ICC = 0.91). 'Face validity' was considered good, despite a lacking item for attention deficit. Concurrence with a cognitive test (MMSE) was high (r = -0.78), with an ADL scale reasonable (r = -0.63) and with a dementia scale low (r = 0.22). At a cut- off score of greater of equal to ten, sensitivity was 82% and specificity 94%. [50,51]

None of these studies compared the DRS with other severity scales, they were actually more focused on the distinguishing or diagnostic potential of the DRS. Factor analysis showed that the different DRS items measure one single construct, the delirium syndrome. [52] A couple of

studies proved the DRS to be almost equally reliable when scored by trained research assistants instead of psychiatrists (ICC = 0.59–0.75; ICC = 0.69–0.99). [49,50,52] In a survey article, Trzepacz states that the DRS is the most frequently used delirium scale and there are at least seven translated versions into other languages. [53] The author also refers to research using the DRS for psychomotor subtyping of delirium (hypoactive-, hyperactive and combined type) and for measuring temporal changes and changes in treatment effects. [54] Meagher et al. found that the average DRS score in adult patients with hyperactive delirium was significantly higher compared with the hypoactive or combined type, meaning that the DRS detects the first mentioned best. [55] For recur- rent assessments, there are seven-and eight-item versions, from which the items temporal onset, variability and somatic cause have been removed. [56] Unfortunately, the psychometric qualities of these shortened and therefore 'new' scales have not been studied.

In 2001, Trzepacz developed the revised version of the DRS, the Delirium Rating Scale-revised-98 (DRS-R-98), a 16-item scale, with three diagnostic tests (onset, varying symptom severity and physical disorders) and 13 severity-rating items. [57] Compared with the DRS, there is one extra item for attention/concentration and one for malfunctions in the thinking process. The cognition-item has been replaced with the following five items: language, orientation, 3D insight and short- and long-term memory. The item for psychomotor behavior has been changed into an item for motor agitation and motor retardation. The original items for perception disorders and hallucinations have been merged into one item (perception disorders). A study of the psychometric qualities of the DRS-R-98 was done with an adult research population, according to international guide- lines. The DRS-R-98 total- and severity-scores allowed delirious patients to be distinguished from patients with dementia, schizophrenia, depression or any other psychiatric disorder ($p < 0.001$). At a cut-off score greater than 17.75 for the DRS-R-98 total score, sensitivity was 92% and specificity 95% and at a cut-off score of greater than 15.25 for the DRS-R-98 severity score, sensitivity was 92% and specificity 93%. The total score proved best suited to distinguish between delirium and dementia. Internal consistency turned out high ($a = 0.90$ total score, $a = 0.87$ severity score). Inter-rater agreement was good (ICC = 0.98–0.99). The DRS-R-98 total score largely concurred with the DRS-R- 98 severity score ($r = 0.99$), the DRS ($r = 0.83$), the CTD ($r = -0.62$) and a disorder severity rating scale ($r = 0.62$). In addition, the DRS-R-98 severity score corresponded well with these scales ($r = 0.80$; $r = -0.63$; $r = 0.61$). The DRS-R-98 proved especially suitable for detecting changes over time.

Memorial delirium assessment scale

The memorial delirium assessment scale (MDAS) is a delirium severity assessment scale. [58] The ten items reflect, among other things, the DSM-IV delirium criteria: failing alertness and consciousness, impaired cognitive functioning (memory, attention, orientation and thinking disorders) and psychomotor activity. The items come with four different severity and intensity categories. The scale is considered highly suitable for multiple ratings within 24 h. Completing the scale takes approximately 10 min and is based on observed behavior and concise, cognitive testing. Including third party information is an option. The MDAS is done by a physician.

The MDAS was tested by Breitbart, Lawlor and Marcantonio. Breitbart used a group of 84 adult patients with cancer and AIDS (with/ without pre-existing cognitive problems). The scale varied significantly ($p < 0.0002$) between delirious, psychiatric and demented patients. The MDAS showed a high internal consistency and inter-rater reliability ($k = 0.92$, $a = 0.91$). [53] There was a high concurrence between the MDAS and external criteria such as the DRS ($r = 0.88$), the MMSE ($r = -0.91$) and a 'clinician's global rating of delirium severity' ($r = 0.89$). [58 - 60]

Lawlor et al. also found high inter-rater agreement (k = 0.89) and high internal consistency (a = 0.78) in a group of adult patients with advanced cancer. [59] They found at a cut-off score of seven a sensitivity of 98% and a specificity of 96% (maximum 30), this was the highest sensitivity and specificity found. Correlation with an external criterion (MMSE) was moderate (r = 0.55). Marcantonio researched the MDAS in a group of elderly, general hospital patients. [60] In contrast with Lawlor, Marcantonio found the highest sensitivity (87%) and specificity (86%) at a cut-off score of five for the average MDAS- score and not seven, and the scale proved suitable for distinguishing between delirious and nondelirious patients. Thus, there is a possibility for using the MDAS as a screening scale for delirium, but more research is needed. However, in this study assessors were not 'blind' to the diagnosis and the proportion of demented patients in this sample was not evaluated. The MDAS was used to distinguish between 'hypoactive delirium' and 'hyperactive'. The former occurred more frequently in the study population and was related to lower severity scores. Although it is claimed that this scale is suitable to be completed several times within 24 h, this has not been evaluated.

Confusional state evaluation

The confusional state evaluation (CSE) is a severity scale and its 22 items were selected on the basis of literature study and clinical experience. [61] Twelve of these items are considered core characteristics – disorientation in person, time, place and situation, memory-, concentration- and thinking disorders, distractedness, per- severance, limited contact, paranoid delusions and hallucinations – all together yielding a confusion score. In addition, there are seven items related to associated characteristics, such as agitation and emotional instability. The remaining three items are regarding duration and intensity.

There are five qualifying statements to each item (0–5), each of which can be scored half a point as well. Assessment is primarily based on interviews conducted by physicians, nurses or psychologists (observations included) and additional, third-party information. Completion time is not specified (max. 30 min.).

Robertsson et al. validated the scale in a study among 71 elderly, delirious (DSM-III-R) patients in a general hospital or nursing home – with or without dementia. The scale showed good inter- rater agreement (k = 0.58). Internal consistency was reasonable (a = 0.69). Concurrence was high between the CSE and the clinical diagnosis r = 0.79, the MMSE r = 0.87 and the attention- motivation scale r = 0.59–0.78. Changes measured with the CSE over 3 weeks time matched those found with a global clinical scale.

Delirium Severity Scale

The Delirium Severity Scale (DSS) [62] aims to rate delirium severity on the basis of cognitive testing, 'digit span' and 'similarities', based on subtests of the Wechsler Memory Scale-Revised (WRS-R) and the Wechsler Adult Intelligence Scale-Revised (WAIS-R). [63,64] The total score is the sum of its parts (max. 59). Research assistants can complete the DSS in approximately 10 min. The authors claim that the DSS is probably not suitable for rating delirium severity in elderly patients with underlying dementia, as attention and verbal reasoning have often already been affected.

Bettin et al. performed a qualitatively good study among 37 elderly patients with/without delirium (CAM diagnosis) admitted to a general hospital and showed excellent inter-rater agreement (k = 0.99). Various reading moments showed reasonable concurrence between the DSS scores and quantified clinical assessments (DSM-III-R) (r = -0.44; r = -.52). The DSS proved sensitive to change; scores improved considerably over time ($p<0.001$). Furthermore, this study population showed minimal bottom or upper limit effects with the DSS.

Delirium Index

The Delirium Index (DI) contains seven items – attention, disorganized thinking, level of consciousness, disorientation, memory, distorted perception and motor activity – based on the CAM (DSM-III-R) and the MMSE. [65,66] The severity of each item is scored qualitatively (0–3), resulting in a total score. Completing the scale takes 5–10 min and is based on recent observations and concise cognitive testing (completed MMSE) by a physician or research assistant.

McCusker conducted two studies in a general hospital among acutely admitted, elderly patients, with or without delirium/underlying dementia syndrome. The inter-rater reliability was high (k = 0.78–0.88). [65,66] The concurrence was high (r = 0.84) between the DI and an external criterion (the revised DRS). It should be noted that the same assessor completed both scales. There was a reasonable concurrence with the MMSE (r = -0.70) and an ADL- scale (r = -0.60). Validity appeared to diverge when compared with an IADL- scale (r = -0.42) and another cognitive scale (r = 0.26). The DI also proved suitable for monitoring changes over time.

Delirium-O-Meter (DOM)

The Delirium-O-Meter (DOM) is a severity scale, and its 12 items were based on key aspects of other delirium rating scales (DOS, NEECHAM, CAM and DRS). [69] The 12 items are: sustained attention, shifting attention, orientation, consciousness, apathy, hyperkinesias/ psychomotor retardation, incoherence, fluctuations in functioning, restlessness, delusions (thinking), hallucinations (perceiving) and anxiety/fear. Each item is scored on a four- point scale (0 = absent, 1 mild, 2 = moderate, 3 severe) with severity levels described in detail for all items. The content of the scale was designed to reflect both hyperactive and hypoactive symptoms as well as the criteria from the DSM-IV. The total score ranges from 0 till 36. Assessment is primarily based on observations and small interviews conducted by nurses. Completion time is 3–5 min. The scale is especially developed for nurses because there was no delirium severity scale found to be suitable for use by nurses.

De Jonghe et al. conducted a study among 92 consecutively admitted elderly patients to a general hospital. [69] Of the patients, 95 were admit- ted to a specialized geriatric ward and 33 were referred for geriatric consultation and admitted to other wards. Of these, 56 were diagnosed with delirium, 24 with dementia or other cognitive disturbances and 12 had other psychiatric disorders or no mental disorders at all. Measures that were done were the DOM, DOS, DRS-98, GIP and MMSE.

The reliability of the DOM was high, the Cronbach's a was calculated and ranged from 0.87 to 0.92, The ICC range was 0.84 to 0.91 for total scores and 0.40 to 0.97 for item scores. The DOM is highly correlated to other measures of delirium severity DOS, DRS-98, GIP apathy, GIP cognitive, GIP affect, MMSE (Spearmans rho: 0.89, 0.92, 0.86, 0.56, 0.87 and 0.83). Inter- rater agreement on item level varied from low to high. Specificity was modest in the combined nondelirious sample that included dementia patients (66.7%) and high in the nondelirious sample including psychiatric/normal control patients (83.3%). The specificity was higher for the sample without cognitive disturbances.

Delirium Detection Score

The delirium detection score (DDS) is a delirium severity scale especially developed for the ICU. [68] The scale is modified from the Clinical Institute Withdrawal Assessment for Alcohol Scale (CIWA-Ar) to the ICU and is composed of eight criteria: agitation, anxiety, hallucinations, orientation, seizures, tremor, paroxysmal sweating and altered sleep–wake rhythm. For each criterion zero, one, four or seven points can be allocated depending on the symptoms. A total of 56 points are possible. The authors first validated the scale against the

CIWA-Ar (which was not considered as a gold-standard for delirium) later on the measurements were repeated against the DSM criteria. The validation was performed in 1073 consecutive patients in a surgical ICU using the DDS together with the Ramsay sedation scale (RSS), the scoring was done by intensivists and nurses. In total, 3588 paired assessments were done. Otter et al. used the ROC to show differentiation between no-delirium and mild, moderate and severe symptoms of delirium. If the DDS was greater than seven the sensitivity was 69% and the specificity was 75%. The AUC was 0.808 (CI: 0719–0.898; $p < 0.001$). For the reliability of the DDS a Cronbach's a was calculated (0.667). And after items with a Cronbach's a of less than four were detected (myoclonus/ convulsions, paroxysmal sweating and tremor) and deleted the Cronbach's a was 0.699. The paired comparisons (nurse–nurse and medical doctor–nurse) showed an interclass correlation between 0.64 and 0.76. The item correlation revealed a k from 0.339 (altered sleep waking rhythm and tremor) to 0.667 (agitation). The sensitivity was low using a cut-off score of seven; the authors found the specificity perfect and they also found the ROC analysis not different as for another score and, therefore. it seems that the cut-off is unclear for the different settings.

DISCUSSION

This study reviews fifteen delirium rating scales and shows remarkable differences in content, objective, completion and psychometric qualities. Many scales mentioned in this study are not used in daily practice or outside the centers where they have been developed. Furthermore, it is noted that most scales are only used in research regarding delirium. The only exceptions are the CAM, CAM-ICU, DRS-R-98 and the MDAS. Most scales that have been developed are not implemented into daily practice. The content of a scale is closely related to its theoretical background, in most cases the DSM delirium criteria. However, this classification system itself has been developed further over the years and some rating scales are based on DSM-III and others on DSM-III-R or DSM-IV. The DSM-IV criteria are clearly 'broader' than those in previous DSM versions. DSM/IV criteria focus primarily on consciousness disorder, leaving out criteria such as psychomotor agitation and disoriented thinking. [65,66] These changes have consequences for diagnostics and subsequently scale construction (e.g., item selection) and validation research (e.g., concurrence with 'the golden standard').

A number of scales are based on a review of the literature or factor analysis. The source of the DSS is unknown. Consciousness or attention disturbances are considered core delirium symptoms. Apart from the original DRS, all scales have items for measuring these symptoms. Also, they all contain items registering, to some extent, cognitive changes such as, memory, language, thinking, and perception disorders. Considering these cognitive aspects, it is important if a (screening) tool distinguishes between delirium and other psychiatric disorders such as dementia or depression. Research has shown that the CAM, NEECHAM, CTD, DOS, DOM, DRS(-R-98) and the MDAS can do so.

Most scales do not include all delirium phenomena. Symptoms included are the ones that are more or less easy to observe. A core symptom of delirium such as clouding of consciousness is notoriously hard to operationalize and scoring the symptom may be subject to low inter-rater agreement. Psychometric quality of rating scales would benefit when (core) symptoms of delirium are clearly defined and are accessible via behavioral observations.

Some scales do not allow for sensitive weighting of symptom severity. Given the nonspecific nature of delirium symptoms, this is a major flaw. There is a considerable difference between mild insomnia versus sleep–wake cycle reversal, yet few scales distinguish between these degrees of sleep disruption. Although the present–absent format is usually preferred for screening purposes, delirium severity scales should incorporate items that differentiate between mild, moderate and severe symptoms.

Most researchers and clinicians would agree that delirium can be divided into three subtypes: hyperactive, hypoactive and combined type. [5] Although psychomotor behavior is included in most scales, the primary aim of these scales appears not to be to distinguish between the different subtypes. Possible exceptions are the DOM, DRS(R-98), Nu-DESC and the MDAS. Notably, most rating scales are based on the DSM criteria. However, DSM hardly provides any criteria for hypoactive delirium and therefore, most rating scales are not suited for differentiating between delirium types. For a better understanding of delirium subtypes, rating scales should be used that incorporate all relevant aspects of delirium. It should be noted that the (French) Clinical Subtype Assessment Scale of Camus et al., not discussed in this survey, was especially developed for this purpose and we recommend translation and validation research. [70]

Most scales are sensitive to the fluctuating course of delirium. Only the CAM, CAM-ICU, DRS-R-98 and the CSE have an item for 'acute onset' of the symptoms. The DRS-R-98 does give codes for underlying somatic causes. Eight scales aim to contribute to detecting delirium. Ideally, these screening tools need to cover a wide range of delirium symptoms. Furthermore, it is important that screening tools have been validated for delirium detection. The CAM, CAM- ICU, DSI, NEECHAM, CTD, but also the DOM, DRS-R-98 and the MDAS proved both sensitive and specific. Scales quickly completed (CAM-algorithm and DOS) and scales primarily based on behavioral observations, instead of actual testing and NEECHAM and DOS) are pre-eminently suitable to be used with delirious patients. Only the NEECHAM requires additional (physiological) readings.

Another seven scales aim at rating the severity of delirium already diagnosed. In this respect, not so much the sensitivity towards the diagnosis, but the registration of the frequency and severity of and the temporal changes in symptoms are important. The DRS-R-98, MDAS, CSE, DSS, DOM, DDS and the DI proved suitable for rating severity and/or frequency. It should be noted that, unlike the original version, the revised DRS distinguishes between diagnostic and severity items. Apart from the DSS, the severity scales appeared suitable to be used with delirious patients suffering from an underlying dementia syndrome. All severity scales have a multiple point scoring system, using qualifying statements. The CSE allows half points to be scored, so that small differences in the symptoms presented can be registered. The DOM, DRS-R-98, CSE, DSS and the DI were found to be sensitive in measuring temporal changes. None of the severity scales purely focuses on behavioral observations, all entail interviews with and/or (concise) testing of delirious patients. Apart from the extra time or actions needed to complete a scale, its user-friendliness is also determined by its clarity and the assessor's assumed expertise. Incidentally, for correct completion of all scales, training is considered necessary.

Next, availability is important. Nearly all scales are in English. Scales of which there is a translation into a different language, for example, the CAM and DRS-R-98, have often not been studied on reliability and validity in the specific language situation, there is an exception for the CAM-ICU for which the translation in several languages was validated. [71,72]

On the whole, research into the psychometric qualities of these scales has been limited. Instead of studying existing scales further, new scales keep being developed, which might say something regarding these scales' practical use. The reliability and validity of six scales only – the CAM, CAM-ICU, NEECHAM, DOS, DRS-R-98 and MDAS – have been researched in more than one study. Moreover, validation research quality regularly left much to be desired on aspects such as, study population size and included control groups, diagnostic standards and independent assessors.

A large majority of these studies was carried out in general hospitals among elderly patient populations. Wards varied from first aid, intensive care, surgery and geriatrics to psychiatry, thus restricting generalization of the research findings. Validation research so far shows that

the CAM, CAM-ICU, NEECHAM, DOS, DOM, DRS-R-98 and the MDAS are reliable and valid. How suitable the scales are in different settings and patient populations as well as the psychometric qualities of the DSI, CTD, DRS-R-98, CSE, DSS, Nu-DESC, DOM, DDS and the DI need further research.

CONCLUSION

Fifteen delirium rating scales were studied and assessed on purpose, content, administration and psychometric aspects. Of the eight screening tools discussed, the CAM comes out best when assessments are done by physicians or specialists. And for the ICU the CAM-ICU. The DRS-R-98, though primarily designed for severity rating, appears to be a reasonable alternative. However, the CAM has the advantage that it detects delirium quickly and accurately. The NEECHAM and DOS are the most suit- able delirium screening tools for nurses. Both scales have the advantage of being observation based, although the NEECHAM requires some physiological parameter readings.

The DRS-R-98 and the DOM came out best of the seven severity rating scales. One advantage of the DRS-R-98 and the DOM over the MDAS is that the delirium course is registered and that the scales can be used by physicians and research assistants, and the DOM by nurses as well. There are no severity scales that are based on observation only. The DOM was specifically designed for nurses; it is a concise test, making it easy to use during daily nursing routine and enabling multiple comparisons between multiple shifts. Moreover, it is a sensitive measure of change. The CSE is a possible candidate, but it is comprehensive and insufficiently studied. The DSS cannot be used with patients with pre- existing cognitive problems. Although assessment scales do not render good clinical diagnostics and monitoring of delirium obsolete, they do contribute to improved detection and in standardizing observations and monitoring of behavioral changes involved.

FUTURE PERSPECTIVE

More research is needed on all fronts of delirium. Continuing research into the conceptualization of delirium is needed, because it is by no means clear that the current diagnostic constructs in ICD-10 and DSM-IV fully capture the unique, defining aspects of this disorder, especially in relation to dementia. More work on etiology and pathogenesis will lead to better understanding of how all these totally different predisposing and precipitating factors can lead to such a complicated syndrome of delirium. Sophisticated models are probably needed to help decide which possible causal factors are there to be influenced first to find a ‘cure’ for delirium that can replace all the symptomatic treatments of today. There is still much work to be done on improving the understanding of the psychometric properties of delirium rating scales. One important issue that is still insufficiently appreciated is that concepts such as validity and reliability are not inherent attributes of scales, but functions of the context in which they are used. If researchers are using an instrument in a population that is substantially different from that in which the instrument was developed, they need to show that it is suitable to be used in their specific studied patient sample.

The validation of measures of change is difficult and complex. More work has to be done on this issue. In general, research into the specific symptoms (such as attention) of delirium will require the development of more sophisticated measures than are currently available, and this development will in turn need to be grounded in more detailed study of delirium phenomenology, including its fundamental neuropsychological characteristics. Better measures of specific symptoms will contribute to our reliability to identify patients in the earliest stages of delirium. Prevention and risk-assessment need refining and testing in other more specific populations. Research should have longer follow-up periods and shorter

intervals between assessments to better characterize the course of delirium, for example, in the course of depression and dementia. And to get a better understanding of the long-term outcomes. Still, there is very little knowledge regarding the relation between delirium and dementia. The evidence base for effective management strategies remains very limited; indeed, it is nonexistent for some important groups, such as delirium in the elderly with cognitive impairment. Treatment programs (medical, pharmacological, social and psychological) must be studied in all populations by means of randomized, controlled trials. The concept of 'education' – changing the knowledge, skills, and attitudes of staff – needs to be extended to the whole system that deals with delirious older people.

CLOSING REMARKS

Delirium is a very common problem in the elderly. But only a few are researching this subject. This does not seem right in respect to this syndrome being one of the 'geriatric giants'. Delirium research deserves a more prominent place on the academic agenda. However, to get more knowledge on diseases it is of the utmost importance that every physician is willing to play a part in research. Even by 'only' constantly monitoring and evaluating our work we provide material for answering some of the existing questions.

References.

1. Cole MG, Primeau FJ, Elie LM. Delirium: prevention, treatment, and outcome studies. J. Geriatr. Psychiatry Neurol. 11(3), 126–137 (1998).
2. Fann JR. The epidemiology of delirium: a review of studies and methodological issues. Semin. Clin. Neuropsychiatry 5(2), 64–74 (2000).
3. Francis J, Martin D, Kapoor WN. A prospective study of delirium in hospitalized elderly. JAMA 263(8), 1097–1101 (1990).
4. Levkoff SE, Evans DA, Liptzin B et al. Delirium. The occurrence and persistence of symptoms among elderly hospitalized patients. Arch. Intern. Med. 152(2), 334–340 (1992).
5. Lipowski ZJ. Delirium in the elderly patient. N. Engl. J. Med. 320(9), 578–582 (1989).
6. O'Keeffe S, Lavan J. The prognostic signicance of delirium in older hospital patients. J. Am. Geriatr. Soc. 45(2), 174–178 (1997).
7. Kakuma R, du Fort GG, Arsenault L et al. Delirium in older emergency department patients discharged home: effect on survival. J. Am. Geriatr. Soc. 51(4), 443–450 (2003).
8. McAvay GJ, Van Ness PH, Bogard ST Jr et al. Older adults discharged from the hospital with delirium: 1- outcomes. J. Am. Geriatr. Soc. 54(8), 1245–1250 (2006).
9. Ely EW, Stephens RK, Jackson JC et al. Current opinions regarding the importance, diagnosis, and management of delirium in the intensive care unit: a survey of 912 healthcare professionals. Crit. Care Med. 32(1), 106–112 (2004).
10. Devlin JW, Fong JJ, Howard EP et al. Assessment of delirium in the intensive care unit: nursing practices and perceptions. Am. J. Crit. Care 17(6), 555–565 (2008).
11. Lacko L, Bryan Y, Dellasega C, Salerno F: Changing clinical practice through research: the case of delirium. Clin. Nurs. Res. 8(3), 235–250 (1999).
12. Levkoff SE, Safran C, Cleary PD, Gallop J, Phillips RS. Identification of factors associated with the diagnosis of delirium in elderly hospitalized patients. J. Am. Geriatr. Soc. 36(12), 1099–1104 (1988).
13. Musselman DL, Hawthorne CN, Stoudemire A. Screening for delirium: a means to improve outcome in hospitalised elderly patients. Rev. Clin. Gerontol. 7, 235–256 (1997).
14. Robertsson B. The instrumentation of delirium. In: Delirium in Old Age. Lindesay J, Rockwood K, McDonald A (Eds.). Oxford University Press Inc, NY, USA, 9–25 (2002).
15. Rapp CG, Wakeeld B, Kundrat M et al. Acute confusion assessment instruments: clinical versus research ability. Appl. Nurs. Res. 13(1), 37–45 (2000).
16. Schuurmans MJ. Early recognition of delirium. Univesritair Medisch Centrum Utrecht, The Netherlands (2001).
17. Smith MJ, Breitbart WS, Platt MM. A critique of instruments and methods to detect, diagnose, and rate delirium. J. Pain Symptom Manage. 10(1), 35–77 (1995).
18. Trzepacz PT. A review of delirium assessment instruments. Gen. Hosp. Psychiatry 16(6), 397–405 (1994).
19. Williams MA, Ward SE, Campbell EB. Confusion: testing versus observation. J. Gerontol. Nurs. 14(1), 25–30 (1988).
20. Miller PS, Richardson JS, Jyu CA et al. Association of low serum anticholinergic levels and cognitive impairment in elderly presurgical patients. Am. J. Psychiatry 145(3), 342–345 (1988).
21. Anthony JC, LeResche LA, Von Korff MR, Niaz U, Folstein MF. Screening for delirium on a general medical ward: the tachistoscope and a global accessibility rating. Gen. Hosp. Psychiatry 7(1), 36–42 (1985).
22. Nagley S. Predicting and preventing confusion in your patients. J. Gerontol. Nurs. 12(3), 27–31 (1986).
23. Vermeersch PE. The clinical assessment of confusion-A. Appl. Nurs. Res. 3(3), 128–133

(1990).
24. Rockwood K. The occurrence and duration of symptoms in elderly patients with delirium. J. Gerontol. 48(4), M162–M166 (1993).
25. Inouye SK, van Dyck CH, Alessi CA et al. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann. Intern. Med. 113(12), 941–948 (1990).
26. American Psychiatric Association (APA). In: Diagnostic and Statistical Manual of Mental Disorders, Third Edition Revised (DSM-III-R). American Psychiatric Publishing, Washington DC, USA (1987).
27. Folstein MF, Folstein SE, McHugh PR. Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. J. Psychiatr. Res. 12(3), 189–198 (1975).
28. Fisher BW, Flowerdew G. A simple model for predicting postoperative delirium in older patients undergoing elective orthopedic surgery. J. Am. Geriatr. Soc. 43(2), 175–178 (1995).
29. Laurila JV. Confusion assessment method in the diagnostics of delirium among aged hospital patients: would it serve better in screening than as a diagnositc instrument? Int. J. Geriatr. Psychiatry 17, 1112–1119 (2002).
30. Pompei P, Foreman M, Cassel CK, Alessi C, Cox D. Detecting delirium among hospitalized older patients. Arch. Intern. Med. 155(3), 301–307 (1995).
31. Rockwood K, Cosway S, Stolee P et al. Increasing the recognition of delirium in elderly patients. J. Am. Geriatr. Soc. 42(3), 252–256 (1994).
32. Rolfson DB, McElhaney JE, Jhangri GS, Rockwood K. Validity of the confusion assessment method in detecting postoperative delirium in the elderly. Int. Psychogeriatr. 11(4), 431–438 (1999).
33. Zou Y, Cole MG, Primeau FJ et al. Detection and diagnosis of delirium in the elderly: psychiatrist diagnosis, confusion assessment method, or consens diagnosis? Int. Psychogeriatr. 10(3), 303–308 (1998).
34. Inouye SK. Nurses' recognition of delirium and its symptoms. Arch. Intern. Med. 161, 2467–2473 (2001).
35. Monette J, Galbaud du Fort G, Fung SH et al. Evaluation of the confusion assessment method (CAM) as a screening tool for delirium in the emergency room. Gen. Hosp. Psychiatry 23, 20–25 (2001).
36. Ryan K, Leonard M, Guerin S et al. Validation of the confusion assessment method in the palliative care setting. Palliat. Med. 23(1), 40–45 (2009).
37. Ely EW, Margolin R, Francis J et al. Evaluation of delirium in critically ill patients: validation of the confusion assessment method for the intensive care unit. Crit. Care Med. 29, 1370–1379 (2001).
38. Ely EW, Inouye SK, Bernard GR et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). JAMA 286(21), 2703–2710 (2001).
39. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. Intensive care delirium screening checklist: evaluation of a new screening tool. Intensive Care Med. 27, 859–864 (2001).
40. Albert MS, Levkoff SE, Reilly C et al. The delirium symptom interview: an interview for the detection of delirium symptoms in hospitalized patients. J. Geriatr. Psychiatry Neurol. 5(1), 14–21 (1992).
41. Neelon VJ, Champagne MT, Carlson JR, Funk SG. The NEECHAM Confusion Scale: construction, validation, and clinical testing. Nurs. Res. 45(6), 324–330 (1996).
42. Csokasy J. Assessment of acute confusion: usee of the NEECHAM Confusion Scale. Appl. Nurs. Res. 12(1), 51–55 (1999).
43. Cacchione PZ. Four acute confusion assessment instruments. J. Gerontol. Nurs. 12–19

(2002).
44. Hart RP, Levenson JL, Sessler CN, Best AM, Schwartz SM, Rutherford LE. Validation of a cognitive test for delirium in medical ICU patients. Psychosomatics 37(6), 533–546 (1996).
45. Kennedy R, Nakase-Thompson R, Nicj TG, Sherer M. Use of the cognitive test for delirium in patients with traumatic brain injury. Psychosomatics 44, 283–289 (2003).
46. Hart RP, Best AM, Sessler CN, Levenson JL: Abbreviated cognitive test for delirium. J. Psychosom. Res. 43(4), 417–423 (1997).
47. Gaudreau JD, Gagnon P, Harel F, Tremblay A, Roy MA. Fast, systematic, and continuo delirium assessment in hospitalized patients: the nursing delirium screening scale. J. Pain Symptom Manage. 29(4), 368–375 (2005).
48. Trzepacz PT, Baker RW, Greenho J. A symptom rating scale for delirium. Psychiatry Res. 23(1), 89–97 (1988).
49. Trzepacz PT, Mulsant BH, Amanda DM et al. Is delirium different when it occurs in dementia? A studying the delirium rating scale. J. Neuropsychiatry Clin. Neurosci. 10(2), 199–204 (1998).
50. Rosen J, Sweet RA, Mulsant BH et al. The delirium rating scale in a psychogeriatric inpatient setting. J. Neuropsychiatry Clin. Neurosci. 6(1), 30–35 (1994).
51. Rockwood K, Goodman J, Flynn M, Stolee P. Cross-validation of the Delirium Rating Scale in older patients. J. Am. Geriatr. Soc. 44(7), 839–842 (1996).
52. Trzepacz PT, Dew MA. Further analyses of the delirium rating scale. Gen. Hosp. Psychiatry 17(2), 75–79 (1995).
53. Trzepacz PT. The Delirium Rating Scale. Its use in consultation–liaison research. Psychosomatics 40(3), 193–204 (1999).
54. Liptzin B, Levkoff SE. An empirical study of delirium subtypes. Br. J. Psychiatry 161, 843–845 (1992).
55. Meagher DJ, O'Hanlon D, O'Mahony E, Casey PR. The use of environmental strategies and psychotropic medication in the management of delirium. Br. J. Psychiatry 168(4), 512–515 (1996).
56. Uchiyama M, Tanaka K, Isse K, Toru M. Efficacy of mianserin on symptoms of delirium in the aged: an open trial study. Prog. Neuropsychopharmacol. Biol. Psychiatry 20(4), 651–656 (1996).
57. Trzepacz PT, Mittal D, Torres R et al. Validation of the delirium rating scale- revised-98: comparison with the delirium rating scale and the cognitive test for delirium. J. Neuropsychiatry Clin. Neurosci. 13(2), 229–242 (2001).
58. Breitbart W, Rosenfeld B, Roth A et al. The Memorial Delirium Assessment Scale. J. Pain Symptom Manage. 13(3), 128–137 (1997).
59. Lawlor PG, Nekolaichuk C, Gagnon B et al. Clinical utility, factor analysis, and further validation of the memorial delirium assessment scale in patients with advanced cancer: assessing delirium in advanced cancer. Cancer 88(12), 2859–2867 (2000).
60. Marcantonio E, Ta T, Duthie E, Resnick NM. Delirium severity and psychomotor types: their relationship with outcomes after hip fracture repair. J. Am. Geriatr. Soc. 50(5), 850–857 (2002).
61. Robertsson B, Karlsson I, Styrud E, Gottfries CG. Confusional State Evaluation (CSE): an instrument for measuring severity of delirium in the elderly. Br. J. Psychiatry 170, 565–570 (1997).
62. Bettin KM, Maletta GJ, Dysken MW et al. Measuring delirium severity in older general hospital inpatients without dementia. The delirium severity scale. Am. J. Geriatr. Psychiatry (1998) 6(4), 296–307.
63. Wechsler D. In: Wechsler Adult Intelligence Scale-Revised Manual. Psychological

Corporation, NY, USA(1981).
64. Wechsler D. In: WMS-R: Wechsler Memory Scale-Revised Manual. Psychological Corporation, NY, USA (1987).
65. McCusker J, Cole M, Bellavance F, Primeau F. Reliability and validity of a new measure of severity of delirium. Int. Psychogeriatr. 10(4), 421–433 (1998).
66. McCusker J, Cole M, Dendukuri N, Belzile E. The Delirium Index, a measure of the severity of delirium: new findings on reliability, validity, and responsiveness. J. Am. Geriatr. Soc. 52(10), 1744–1749, (2004).
67. Hertogh CM, Eikelenboom P. Delirium in the elderly and DSM IV: is there clarity about confusion? Tijdschr. Gerontol. Geriatr. 26(2), 51–56 (1995).
68. Otter H, Martin J, Bäsell K et al. Validity and reliability of the DDS for severity of delirium in the ICU. Neurocrit. Care 2, 150–158 (2005).
69. De Jonghe JFM, Kalisvaart KJ, Timmers JFM, Kat MG, Jackson JC. Delirium-O-Meter: a nurses' rating scale for monitoring delirium severity. Int. J. Ger. Psych. 20(12), 1158–1166.
70. Camus V, Burtin B, Simeone I et al. Factor analysis supports the evidence of existing hyperactive and hypoactive subtypes of delirium. Int. J. Geriatr. Psychiatry 15(4), 313–316 (2000).
71. Larsson C, Axell AG, Ersson A. Confusion assessment method for the intensive care unit (CAM-ICU): translation, retranslation and validation into Swedish intensive care settings. Acta Anaesthesiol. Scand. (7), 888–892 (2007).
72. Chuang WL, Lin CH, Hsu WC et al. Evaluation of the reliability and validity of the Chinese version of the confusion assessment method for the intensive care unit. Hu Li Za Zhi 54(4), 45–52 (2007).
73. McNicoll L, Pisani MA, Ely EW, Gifford D, Inouye SK. Detection of delirium in the intensive care unit: comparison of the confusion assessment method for the intensive care unit with confusion assessment method ratings. J. Am. Geriatric. Soc. 53, 495–500 (2005).

Table 1. Background, purpose, content and completion of delirium scales.

Study	Based on	Screening	Discriminating power	Distinction hypo/ hyperactive delirium	Consciousness/ attention	Other (cognitive) disorders‡	Acute onset/ fluctuations
CAM	DSM-III-R	+	+	-	+	+	+
CAM-ICU	CAM	+	+	-	+	+	+
NEECHAM	RESEARCH	+	+	-	+	+	-
CTD	DSM-III-R	+	+	-	+	+	-
ICDSC	DSM-IV	+	-	+	+	+	+
DSI	DSM-III	+	-	-	+	+	+
DOS	DSM-IV	+	+	-	+	+	-
Nu-DESC	CRS	+	-	+	-	+	
DRS	DSM-III-R	-	+	+	-	+	+
DRS-R-98	DRS, RESEARCH	-	+	+	+	+	+
MDAS	DSM-IV	-	+	+	+	+	-
CSE	RESEARCH	-	-	-	+	+	+
DSS	?	-	-	-	+	+	-
DI	DSM-III-R	-	-	-	+	+	-
DOM	DSM-IV/ DRS-98	-	+	+	+	+	+
DDS	CIWA-AR	-	-	-	+	+	-

**Distinguishes delirium from other psychiatric disorders and dementia.*
‡Impeded thinking, speech, orientation, memory, perception, psychomotor, sleep/awake rhythm and effect.
+: Yes/present, ~: Possible, insufficiently researched; ?: Unknown; –: No/absent; i: Interview; N: Nurse; o: (Behavioral) observation; P: Physician/psychiatrist/ geriatrician/neurologist; Ps: Psychologist; R: Research assistant; t: Cognitive test.

Table 1. Background, purpose, content and completion of delirium scales (cont.).

Study	Somatic cause	Severity rating	Sensitive to temporal changes	Information gathering	Assessor in daily practice	Completion time (min)	Tested in the ICU
CAM	-	-	-	i,t	P	5-20	-
CAM-ICU	-	-	-	i,o	P,N	5	+
NEECHAM	-	-	-	o	N	10	+
CTD	-	-	-	t	Ps	>15	+
ICDSC	-	-	-	i,o	N,P	?	+
DSI	-	-	-	i,o	R	15	-
DOS	-	-	-	o	N	5	-
Nu-DESC	-	-	-	o	N	<5	-
DRS	+	+	+	i,o,t	P,R	?	-
DRS-R-98	+	+	+	i,o,t	P	?	-
MDAS	-	+	+	i,t	P	10	-
CSE	-	+	+	i,o	P,N,PS	<30	-
DSS	-	+	+	t	R	10	-
DI	-	+	+	i,t	P,R	10	-
DOM	-	+	+	i,o,t	N,R	5-10	-
DDS	-	+	+	i,o	P,N	?	+

**Distinguishes delirium from other psychiatric disorders and dementia.*
ǂImpeded thinking, speech, orientation, memory, perception, psychomotor, sleep/awake rhythm and effect.
+: Yes/present, ~: Possible, insufficiently researched; ?: Unknown; –: No/absent; i: Interview; N: Nurse; o: (Behavioral) observation; P: Physician/psychiatrist/ geriatrician/neurologist; Ps: Psychologist; R: Research assistant; t: Cognitive test.

Table 2. Psychometric aspects of delirium screening scales.

Study	Design	Internal consistency	Interrater reliability*	CV based on a classification system	CV based on other delirium scales	CV based cognitive ratings	CV based on attention tests	CV based on other behavioral ratings	Diverging validity	Assess-ment	Setting	Study population	Ref.
CAM	Pr	-	+	+	=/-	+/-	-	-	-	+	H+	E	30
	Pr	-	-	+	-	-	-	-	-	+/-	H	E	32
	Pr	-	-	?	-	-	-	-	-	+/-	H	E	28
	Pr	-	-	+	-	-	-	-	-	+/-	H	E	31
	Pr	-	+	+	-	-	-	-	-	+/-	H	E	34
	Pr	-	-	+	-	-	-	-	-	+/-	H	E	33
	Pr	-	-	-	+	-	-	-	-	+/-	H	E	35
	De	-	+	+	-	-	-	-	-	+/-	H	E	36
	Pr	-	+	-	-	-	-	-	-	+	H+	E	29
	Pr	-	-	+	-	-	-	-	-	+	PC	A	37
DOS	Pr	+	+	+	+	+/-	-	+/-	+	+	H+	E	16
DSI	De	+/-	+	+	-	-	-	-	-	+/-	H	E	42
Nu-DESC	Pr	-	-	+	+	-	-	-	-		H	A	49
NEECHAM	Pr	+	+	+/-	-	-	-	+/-	+	+	H	E	43
	Pr	+	-	+/-	-	-	-	+	-	+/-	H	E	44
	Pr	+	-	-	-	+/-	-	-	-	+/-	H	E	74
	De	+	-	-	-	-	-	-	+	+/-	N	E	45
Intensive care unit screening scales													
CTD	Pr	+	+	+		+	-	-	-	+	H	E	46
CAM-ICU	Pr	+	+	+		+/-	+	+	-	+	H	A	38
	Pr	+	+	-	+/-	+		+/-	-	+	H	A	38
	Pr	+	+	-	-	-	-	-	-	+/-	H	A	75
ICDSC	Pr	+	+	+	-	-	-	-	-	+	H	A	41

Converging validity..

+: Good; +/-: Reasonable; –: Mediocre/poor; ?: Unknown; A: Adults; CV: Converging value; De: Descriptive; E: Elderly (age >55 years); H: General hospital ward; H+: Psycho geriatric/geronto psychiatric wards in general hospitals; N: Nursing home; Ob: Observational; PC: Palliative Care; Pr: Prospective; Re: Retrospective.

Table 3. Psychometric aspects of delirium severity scales.

Study	Design	Internal consistency	Interrater reliability*	CV based on a classification system	CV based on other scales	CV based cognitive ratings	CV based on attention tests	CV based on other behavioral ratings	Diverging validity	Assess-ment	Setting	Study population	Ref.
DRS	Pr	+	+	+	-	+/-	-	-	-	+	H	A	50
	Pr	-	+	+	-	-	-	-	-	+	H+	E	53
	De	+	-	-	-	-	-	-	-	+	H	E	55
	Pr	-	+	+	-	+	-	+/-	+	+	H+	E	54
	Pr	-	+	+	-	-	-	-	-	+	H+	E	52
DRS 98	Pr	+	+	+	+/-		-	+/-	-	+	H+	A	57
MDAS	Pr	+	+	+	+	+	+	-	-	+	H	A	59
	Pr	+	+	+	-	+/-	-	-	-	+/-	H	A	60
	Pr	-	-	+	-	-	-	-	-	+/-	H	E	61
CSE	De	+/-	+	+	+	-	-	+/-	-	+/-	H+	E	62
DI	Pr	-	+	-	+	+/-	-	+/-	+	+/-	H	E	66
DSS	Pr	-	+	+/-	-	-	-	-	-	+	H	E	63
DOM	Pr	+	+	+	-	+/-	-	-	+	+	H	E	68
Intensive care unit severity scales													
DDS	Pr	+	+	+			+	+		+	H	A	69

**Converging validity..*

+: Good; +/-: Reasonable; –: Mediocre/poor; A: Adults; CV: Converging value; De: Descriptive; E: Elderly (age >55 years); H: General hospital ward; H+: Psychogeriatric/geronto-psychiatric wards in general hospital; Ob: Observational; Pr: Prospective; Re: Retrospective.

Chapter 7

Validation of the dutch version of the Confusion Assessment Method (CAM-ICU) for delirium screening in the Intensive Care Unit.

Vreeswijk R
Toornvliet A
Honing MIH
Bakker K
De Man T
Daas, G
Spronk PE
De Jonghe JFM
Kalisvaart KJ

Published: Neth J Crit Care April 2009;13(2): 73-78

ABSTRACT

Background Delirium is frequently encountered in hospital settings especially in the Intensive Care Unit (ICU), with an inci- dence of 42% to 87%. The aetiology of delirium is still unknown but research has shown that prevention and treatment is possible. Early detection is a necessary first step for successful treatment and prevention in the ICU. The Confusion Assessment Method for the ICU (CAM-ICU) is a rapid and easily administered screening instrument to detect delirium in the ICU setting and is based on the Diagnostic and Statistic Manual of Mental Disorders IV criteria (DSM-IV)

The aim of this study was to validate the Dutch version of the CAM-ICU.

Methods The CAM-ICU was translated in accordance with standard translation guidelines. The validation study of the Dutch CAM-ICU version was performed in a large Dutch community hospital with a mixed ICU. The patients were tested by a geriatrician or a psychiatrist for clinical symptoms of delirium according to the DSM IV criteria (= reference standard), and the results were compared with indepen- dently scored CAM-ICU outcomes.

Results Thirty consecutive adult patients with Richmond Agitation and Sedation Scale (RASS) ≥ -3 were assessed for delirium using the CAM-ICU and the DSM-IV criteria, resulting in 60 paired tests. Twenty-nine patients were included in the analysis. Based on the DSM-IV criteria 11 of 29 patients had delirium and 9 of 29 scored positive on the CAM-ICU. Only three patients were diagnosed differently by the geriatrician or psychiatrist and the CAM-ICU, two had a psychiatric disorder and one had been sedated and was therefore excluded. Agreement was calculated using crosstabs analysis, overall agreement was 93.1%. In our validation cohort the incidence of delirium was 37.9%.

Conclusion The translation of the Dutch CAM-ICU showed good correlation with the original English version and can therefore be used in a Dutch ICU. The results of the validation study showed very good agree- ment between the clinical diagnoses made by the experts and the detection of delirium using the Dutch CAM-ICU. The Dutch CAM-ICU reliably detects ICU delirium. It therefore provides the means for early detection, treatment and secondary prevention of ICU delirium.

INTRODUCTION

Delirium is a common psychiatric syndrome in Intensive Care Units (ICU). Incidence estimates for delirium vary from 5% for non-ICU patients to 87% for ICU patients. [1-3] ICU delirium is associated with increased morbidity and negatively affects 6-months survival and weaning from mechanical ventilation and contributes to the increased length of stay. [4-7] Delirium is often under-diagnosed by ICU professionals. [8,9] Establishing a diagnosis of delirium can be difficult because of the fluctuating course of delirium symptoms. Delirium receives little attention in the ICUs, because it is, 1. Rarely a primary reason for admission, 2. Often believed to be iatrogenic due to medications, 3. Frequently rationalized as "ICU psychosis", and 4. Believed to have no adverse consequences in terms of patient outcome. [5] Despite international and national guidelines [29,30], no more than 7% of ICUs in the Netherlands have routinely evaluated the presence of delirium with a validated instrument. Less than one-third of Dutch ICUs use a protocol to treat ICU delirium.[10] ICU patients and particularly mechanically ventilated patients are at risk of delirium. The outcome of delirium is negative: more ventilation days, longer hospitalization and higher morbidity and mortality, therefore detecting and treating this syndrome is very important. [4-7]
The CAM-ICU was developed as a screening instrument for the detection of delirium in nonverbal ICU patients. As a screening instrument for delirium the CAM-ICU is the best-validated and studied instrument. [9, 12-15] Versions of the CAM- ICU are available in various languages, thus making international comparison of results possible. (www.icudelirium.org, also Dutch version). Implementation of a screening instrument such as the CAM-ICU leads to improved detection of delirium. [6, 17-18]
The aim of this study was to assess validity of the Dutch translation of the CAM-ICU by comparing delirium as assessed by the Dutch CAM-ICU with a reference standard, i.e. the DSM-IV diagnosis of delirium.

METHOD

Patients

This study was undertaken in a 14-bed ICU at a large teaching hospital in the Netherlands between October 2007 and January 2008. Consecutively admitted, mechanically ventilated patients who had a RASS score of ≥ -3 were included in the study. Patients with a known addiction to alcohol or narcotics were excluded (because of withdrawal delirium); patients with no possible means of communication (e.g. prior neurological disease); and patients for whom medical interventions changed during assessments (for example after sedation with benzodiazepines), were also excluded.
The research nurse checked daily whether newly admitted patients met the inclusion criteria and during the index ICU period assessed the CAM-ICU independently from the psychiatrist or geriatrician. All assessments were planned between 10.00 and 11.00. None of the raters had access to any of the other's evaluations or ratings. A psychiatrist or geriatrician made the diagnosis of delirium using DSM-IV criteria, the research nurse used the CAM-ICU algorithm. Both physician and nurse raters had access to medical charts and were allowed to interview the nurses involved in daily care of the patient.

Translation process

In general, when directions relating to an instrument are translated, the text should be understandable and meaningful, and the translation must be as close to the original text as possible. As a consequence, results of measurements done with the translated instrument should be the same as if the original instrument were used.

After consent was obtained from the author, the CAM-ICU, Attention Screening Examination (ASE) and Richmond Agitation and Sedation Scale (RASS) were translated into Dutch by members of our research group (RV, JJ, KK) a senior geriatrician, a neuropsychologist and a Master of Science in Nursing.

The Richmond Agitation-Sedation Scale (RASS) [19]
The RASS measures sedation and agitation and is necessary to establish if the patient can be tested. It is a brief 10-point rating scale (-5 unarousable to +4 combative). The CAM-ICU can only be assessed in patients with RASS > -4. (Appendix 3)

The Confusion Assessment Method for the ICU. [2-3, 20] The CAM-ICU is a screening instrument specifically adapted from the CAM for use in ICU patients. CAM-ICU items are non-verbal tasks such as picture recognition, vigilance A task, simple yes/no logic questions and simple commands. A positive CAM-ICU screen is based on an algorithm including four key criteria for delirium. The validity and reliability of the English version of the CAM-ICU was established in two large studies (N= 750) with Kappa as high as 0.96 and sensitivity 100% and specificity > 93%.

Diagnostic and Statistical Manual of Mental Disorders IV (DSM- IV). [21,22] The DSM-IV is a categorical classification system. The categories are prototypes, and a patient with a close approximation to the prototype is said to have that disorder. (Appendix 4)

The translation
The translation was done according the principles of good translation. The process of translation involved preparation, forward translation, translation review, harmonization, cognitive debriefing and validation of the translated CAM-ICU. [23]
Consensus on the translation was reached on the instrument's contents and structure. Experienced nurses working in a large Dutch hospital commented on the Dutch translation in respect of ambiguous wording, concepts or other elements that they were unable to understand. The Dutch version was judged to be similar to the original English version of the CAM-ICU as checked by a professional translator. The author of the original CAM-ICU accepted the translation of the Dutch CAM-ICU and published it on the website (www.icudelirium.org). Appendix 1, 2, 3.

Statistics
Means or proportions were used to describe demographic and clinical characteristics of the study sample. Absolute agreement between the two tests (DSM-IV and CAM-ICU) was examined using a two-by-two table. SPSS software version 14 (SPSS Inc., Chicago, Il) was used for analyses. For the validation of the Dutch version, we followed the method Ely et al used. In a pilot study they found a test sensitivity of 95% averaging across raters, and a test specificity of 88%. They stated that instrument sensitivity was the critical feature and that the lower limit of 95% confidence interval had to be 85% or higher, while an acceptable specificity would be 75% or higher. [3] After consulting a statistician, we discussed the lower limit of the sensitivity and specificity and reached a consensus that the lower limit for sensitivity should be 80%, and for specificity 70%. The sample size was calculated to ensure the appropriate number of patients necessary to achieve the expected lower limit of the 95% confidence interval for the CAM-ICU sensitivity and specificity in alert or lethargic patients. Because there are no data on prevalence of delirium in Dutch ICUs, we assumed an incidence of delirium of 50%, which would require 30 patients. Because the CAM-ICU has been well validated in several studies we did not have to do an extended study with a large population.

In a two-by-two table we only needed five patients per cell and for comparison we needed a minimum of 20 patients. The performance test characteristics for the CAM-ICU were estimated from simple two-by-two tables, a cross tab analysis to compare the outcome (delirium yes/no) of the CAM-ICU and DSM-IV.

RESULTS

A total of 30 patients were included. One patient was excluded because sedatives had been given between clinical and CAM- ICU assessments. The average age of the patients was 61.2 years, (27-87), male/female ratio was 15/14, the average stay on the ICU was 16.93 days and average stay in hospital was 46.86 days. Reasons for being admitted to ICU were pulmonary disease 20.7%, malignancy 27.6 %, cardiovascular 20.7%, internal medical conditions 20.7%, trauma 6.9% and other 3.4%. (Table 1)
Eleven of 29 patients had delirium (DSM-IV, 37.9%), and 9 of 29 patients screened positive on the CAM-ICU (31%). Absolute agreement between clinical diagnosis and CAM-ICU was 93.1%. CAM-ICU sensitivity was 81.8% and specificity 100%. (Table 2) Evaluation of discordant cases showed that two CAM-ICU positive patients were diagnosed with a primary psychiatric disorder (schizophrenia).

DISCUSSION

Screening instruments can be useful for detecting delirium. Besides the CAM-ICU, instruments available for the ICU include the Cognitive Test for Delirium (CTD) by Hart (1996) with a sensitivity of 100% and a specificity of 95.1%, and the Intensive Care Delirium Screening Checklist (ICDSC) by Bergeron (2001) with a sensitivity of 99% and a specificity of 64%. The CTD and ICDSC scales are not well-validated instruments and more research needs to be done. [11] With the rise in clinician and nursing workload and the ever-increasing numbers of protocols being implemented into ICU practice, ICU staff may feel that there is little time available to routinely evaluate their patients. [28] The CAM-ICU is easy to administer and takes two minutes to complete, the CTD takes > 15 minutes to complete and the time it takes to complete the ICDSC is not known.
This study evaluated CAM-ICU (Dutch version) validity compared with a diagnosis of delirium (based on the DSM-IV) in ICU patients. Absolute agreement between research nurse-based CAM-ICU assessments and clinical diagnosis of delirium based on the DSM-IV was 93.1%. A sensitivity of 81.8% and a specificity of 100% demonstrate that the CAM-ICU Dutch version is a valid measure of delirium in ICU patients. Our sensitivity of 81.8% was under the lower limit of 85% stated by Ely et al. [3] We discussed this in our group and found the sensitivity acceptable. If patients with a history of psychosis were excluded (as in the study of Ely [3]), sensitivity would be even higher - up to 100% - which is far above the lower limit, and also the absolute agreement would be 100%. Our results confirm those of others using the CAM- ICU. Studies using the English, Swedish and Chinese versions of CAM-ICU showed sensitivity values ranging from 73% to 100% and specificity values ranging from 89% to 100%. [2-3, 24-25] Because the results were the same, we do not think it is necessary to perform another validation study for the CAM-ICU.
A high level of agreement between CAM-ICU ratings and diagnosis of delirium is clinically important. Eleven of 29 patients had delirium (DSM-IV); all but two screened positive on the CAM-ICU, and none of the patients without delirium did. So, nurse-based assessments of delirium can be an efficient way of detecting delirium in the ICU. These are positive findings and need to be further implemented in daily practice in ICUs in the Netherlands.
In most studies different assessments are planned on the same day. Because of the fluctuating

nature of delirium symptoms, with nighttime restlessness, often no symptoms during the day and worsening of symptoms starting at sundown, different raters may see different behaviors and classify patients accordingly. In other studies, the time interval between CAM-ICU assessments and clinical judgments varied from 10 minutes to 4 hours or was based on a chart review. [2-3, 6, 13, 20] It could in part explain some of the lower CAM-ICU sensitivity values found, although Ely et al. found no differences in the diagnosis, where they were up to four hours apart. [2] To our knowledge this is the first study carefully doing CAM-ICU ratings and making the clinical diagnosis of delirium at the same time, so as to avoid measuring unwanted inter-assessment score variances due to symptom fluctuations. In our study we planned assessments not more than one hour apart from each other, but never together and with blinding of the results. Strict adherence to the assessment protocol was achieved throughout the study. In fact, this may be the reason why nurse-based CAM-ICU ratings predicted delirium diagnosis so well.

The first problem was making the clinical diagnosis. In a previous study delirium recognition was very poor. [8] The clinical diagnosis made by an ICU physician could therefore not be automatically used as a reference standard against the CAM-ICU. In this study the CAM-ICU ratings were compared with a clinical diagnosis made by a psychiatrist or geriatrician who were well trained in all aspects of delirium. In other studies, the validation procedure was done differently. In one study agreement between the two measures was based on a chart-based method and research nurse CAM-ICU ratings comparison. [20] And in some studies, it is not clear if CAM-ICU ratings had been related to clinical judgment by experts. [6, 24-25]

A potential limitation is that our research nurse selected the patients to be included and also made the CAM-ICU assessments. This may have biased the results thus challenging validity. However, subjects both with and without delirium were selected. Patient selection was in part based on RASS sedation evaluation and not based on the presence or absence of delirium as measured with the CAM-ICU. Therefore, we believe that the validity of our results is not challenged. Another limitation is that assessment, although done at the time of clinical diagnosis, took place in the morning for practical reasons and often the first signs of delirium start to appear at sun downing. [26] The small number of patients was also a limitation of this study, although this does not influence its validity it can affect the precision of its estimates. During this study all the CAM-ICU measurements were performed by one trained research nurse. This was not a limitation because all CAM-ICU assessments were done in the same way, so a possible bias due to different raters was anticipated. Further study on if CAM-ICU administered by nurses in daily practice has the same results on sensitivity and specificity is indicated. However, before implementation of the CAM-ICU into daily practice, nurses should be educated on delirium. Pun et al. established that it only takes minimal training to record excellent compliance by bedside nurses in using delirium instruments. Education should be considered the core component of the implementation, as it has been shown to improve delirium assessment reliability. [27]

The validation of a delirium instrument for the ICU opens new frontiers for investigation. [3] Aspects such as the impact of delirium on relation to outcome, determination of risk factors for delirium in the ICU, prevention, but also incidence of delirium in Dutch ICUs need to be further studied.

References

1. Lindesay J, Rockwood K, MacDonald A. Delirium in old age. 2002 Oxford Press New York
2. Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, Speroff T, Gautam S, Bernard GR, Inouye SK. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Crit Care Med. 2001 Jul; 29(7):1370-9.
3. Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, Truman B, Speroff T, Gautam S, Margolin R, Hart RP, Dittus R. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). JAMA. 2001 Dec 5;286(21): 2703-10
4. Ely EW, Gautam S, Margolin R, Francis J, May L, Speroff T, Truman B, Dittus R, Bernard R, Inouye SK. The impact of delirium in the intensive care unit on hospital length of stay. Intensive Care Med. 2001 Dec;27(12):1892-900.
5. Ely EW, Shintani A, Truman B, Speroff T, Gordon SM, Harrell FE Jr, Inouye SK, Bernard GR, Dittus RS. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. JAMA. 2004 Apr 14;291(14):1753-62
6. Lin SM, Liu CY, Wang CH, Lin HC, Huang CD, Huang PY, Fang YF, Shieh MH, Kuo HP. The impact of delirium on the survival of mechanically ventilated patients. Crit Care Med. 2004 Nov;32(11):2254-9.
7. Thomason JW, Shintani A, Peterson JF, Pun BT, Jackson JC, Ely EW. Intensive care unit delirium is an independent predictor of longer hospital stay: a prospective analysis of 261 non-ventilated patients. Crit Care. 2005 Aug; 9(4): R375-81.
8. Ely EW, Stephens RK, Jackson JC, Thomason JW, Truman B, Gordon S, Dittus RS, Bernard GR. Current opinions regarding the importance, diagnosis, and management of delirium in the intensive care unit: a survey of 912 healthcare professionals. Crit Care Med. 2004 Jan; 32(1):106-12.
9. Ely EW, Siegel MD, Inouye SK. Delirium in the intensive care unit: an under-recognized syndrome of organ dysfunction. Semin Respir Crit Care Med. 2001;22(2):115-26.
10. Van Eijk MM, Kesecioglu J, Slooter AJ. Intensive care delirium monitoring and standardised treatment: a complete survey of Dutch Intensive Care Units. Intensive Crit Care Nurs. 2008 Aug;24(4):218-21. Epub 2008 Jun 3.
11. R. Vreeswijk, J.F. Timmers, J.F.M. de Jonghe, K.J. Kalisvaart. Assessment scales for delirium: a review. Health and Aging (2008/2009) Submitted for publication
12. Bergeron N, Skrobik Y, Dubois MJ. Delirium in critically ill patients. Crit Care 2002, 6:181-182
13. Truman B, Ely EW. Monitoring delirium in critically ill patients. Using the confusion assessment method for the intensive care unit. Crit Care Nurse. 2003 Apr;23(2):25-36;
14. McNicoll L, Pisani MA, Ely EW, Gifford D, Inouye SK. Detection of delirium in the intensive care unit: comparison of confusion assessment method for the intensive care unit with confusion assessment method ratings. J Am Geriatr Soc. 2005 Mar;53(3):495-500.
15. Micek ST, Anand NJ, Laible BR, Shannon WD, Kollef MH. Delirium as detected by the CAM-ICU predicts restraint use among mechanically ventilated medical patients. Crit Care Med. 2005 Jun;33(6):1260-5.
16. Laurila JV, Pitkala KH, Strandberg TE, Tilvis RS. Confusion assessment method in the diagnostics of delirium among aged hospital patients: would it serve better in screening than as a diagnostic instrument? Int J Geriatr Psychiatry. 2002 Dec;17(12):1112-9.

17. Flaatten H. Prognostic scoring systems in the ICU. Acta Anaesthesiol Scand 2006 50:1175-6
18. McNicoll L, Pisani MA, Zhang Y, Ely EW, Siegel MD, Inouye SK. Delirium in the intensive care unit: occurrence and clinical course in older patients. J Am Geriatr Soc. 2003 May;51(5):591-8.
19. W, Truman B, Shintani A., et al. Monitoring sedations over time in ICU patients; reliability and validity of the Richmond Agitation-Sedation Scale (RASS) JAMA June 11, 2003 Vol.289, No.22, 2983-2991
20. Pisani MA, Araujo KL, Van Ness PH, Zhang Y, Ely EW, Inouye SK. A research algorithm to improve detection of delirium in the intensive care unit. Crit Care. 2006;10(4): R121.
21. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th ed (DSM-IV). Washington DC, APA, 1994.
22. American Psychiatric Association: Practice Guideline for the treatment of Patients with Delirium. Washington DC, APA, 1999.
23. Wild D, Grove A, Martin M et al. Principles of good practice for the translation and cultural adaptation process for patient reported outcomes (PRO) measures: report of the ISPOR taskforce for translation and cultural adaptation. Value Health 2005; 8: 94–104.
24. Larsson C, Axell AG, Ersson A. Confusion assessment method for the intensive care unit (CAM-ICU): translation, retranslation and validation into Swedish intensive care settings. Acta Anaesthesiol Scand. 2007 Aug; 51(7): 888-92.
25. Chuang WL, Lin CH, Hsu WC, Ting YJ, Lin KC, Ma SC. Evaluation of the reliability and validity of the Chinese version of the confusion assessment method for the intensive care unit. Hu Li Za Zhi. 2007 Aug; 54(4):45-52. Chinese.
26. Jos F. M. de Jonghe, Kees J. Kalisvaart, Marty Dijkstra, Huib van Dis, Ralph Vreeswijk, et al.. Early Symptoms in the Prodromal Phase of Delirium: A Prospective Cohort Study in Elderly Patients Undergoing Hip Surgery. Am J Geriatr Psychiatry, Feb 2007; 15: 112 - 121.
27. Pun BT, Gordon SM, Peterson JF et al. Large scale implementation of sedation and delirium monitoring in the intensive care unit: a report from two medical centres. Crit Care Med. 2005;6: 1199-205.
28. Bolton DL Delirium the costs of inattention. Crit Care Med. 2004; 32: 1080-1081.
29. http://www.psychiatryonline.com/pracGuide/pracGuideTopic_2.aspx
30. http://www.cbo.nl/product/richtlijnen/folder20021023121843/delirium_rl_2005. pdf

Table 1. Patient Characteristics

Variabele	Value
Characteristics	
Age (years: mean ± SD)	61.2 ± 15.48
Male/female seks (n)	15/14
Days on ICU (days mean ± SD)	16.93 ± 22.53
Days in hospital (days mean ± SD	46.86 ± 44.28
Admitting diagnosis (n [%])	
Respiratory problems	6 (20.7)
Malignancy	8 (27.6)
Heart/vascular system problems	6 (20.7)
Other internal problems	6 (20.7)
Trauma	2 (6.9)
Other	1 (3.4)

Table 2. Performance of clinical diagnosis compared with CAM-ICU

			DSM-IV diagnosis Delirium		**Total**
			No Delirium	**Delirium**	
Delirium CAM-ICU	**No Delirium**	Count	18	2	20
		% within the clinical diagnose delirium	100.0%	18.2%	69.0%
	Delirium	Count	0	9	9
		% within the clinical diagnose delirium	0.0%	81.8%	31.0%
Total		Count			
		% within the clinical diagnose delirium	100.0%	100.0%	100.0%

Appendix 1. CAM-ICU

CAM-ICU onderdelen en beschrijvingen.

1. Acuut begin en fluctuerende beloop.	**Afwezig**	**Aanwezig**

1A: Zijn er aanwijzingen voor een acute verandering in het psychisch/cognitief functioneren vergeleken met hoe het was in het begin?

Of

1B: Was er sprake van fluctuaties in het gedrag gedurende de afgelopen 24 uur, dus d.w.z. was het aanwezig en verdween het, nam het toe of af in ernst zoals bleek uit scores op een meetschaal voor sedatie (bijv.RASS), GCS, of een vorige delirium beoordeling?

2. Verminderde aandacht. Aanwezig als in elk geval 2A of 2B kleiner dan 8 is Probeer de ASE letters eerst, als de patiënt in staat is deze uit te voeren noteer de uitslag en ga naar onderdeel 3. Als de patiënt niet in staat is tot de uitvoer van de test of de score is onduidelijk doe dan de plaatsjes. Als beide testen gedaan worden noteer dan de score van de plaatjes als score voor dit onderdeel.	**Afwezig**	**Aanwezig**

2A. ASE letters: noteer score (noteer NG als er niet getest is) **Score (uit 10): _____**

Aanwijzing: Zeg tegen de patiënt, "Ik ga een reeks van 10 letters opnoemen. Wanneer U de letter A hoort knijpt U in mijn hand". Lees de volgende reeks letters voor zonder nadrukkelijk te articuleren (houdt met het volume rekening met de geluiden op de ICU) en met een snelheid van 1 letter per seconde.

S A V E A H A A R T

Score: Een respons is fout als de patiënt niet knijpt bij een letter "A" of knijpt bij een andere letter dan "A" .

2B: ASE Pictures: noteer score (noteer NG als er niet getest is) **Score (uit 10): _____**

Voor aanwijzingen zie plaatjes

3. Ongeorganiseerd denken Aanwezig als de gecombineerde score lager dan 4 is.	**Afwezig**	**Aanwezig**

3A: Ja / Nee vragen

(Wissel set A en set B af op opeen volgende dagen)

Set A	**Set B**
1. Blijft een steen drijven in water?	1. Blijft een blad drijven in water?
2. Zijn er vissen in de zee?	2. Zijn er olifanten in de zee?
3. Weegt 1 pond meer dan 2 ponden?	3. Wegen 2 ponden meer dan 1 pond?
4. Kun je met een hamer een spijker inslaan?	4. Kun je met een hamer hout snijden?

Score:_____ (patiënt krijgt 1 punt voor ieder correct antwoord van de 4 vragen)

3B: Opdrachten:

Zeg tegen de patiënt: "Kunt U zoveel vingers opsteken" (onderzoeker houdt 2 vingers omhoog), "Doe hetzelfde met de andere hand" (onderzoeker laat nu niet de twee vingers zien).

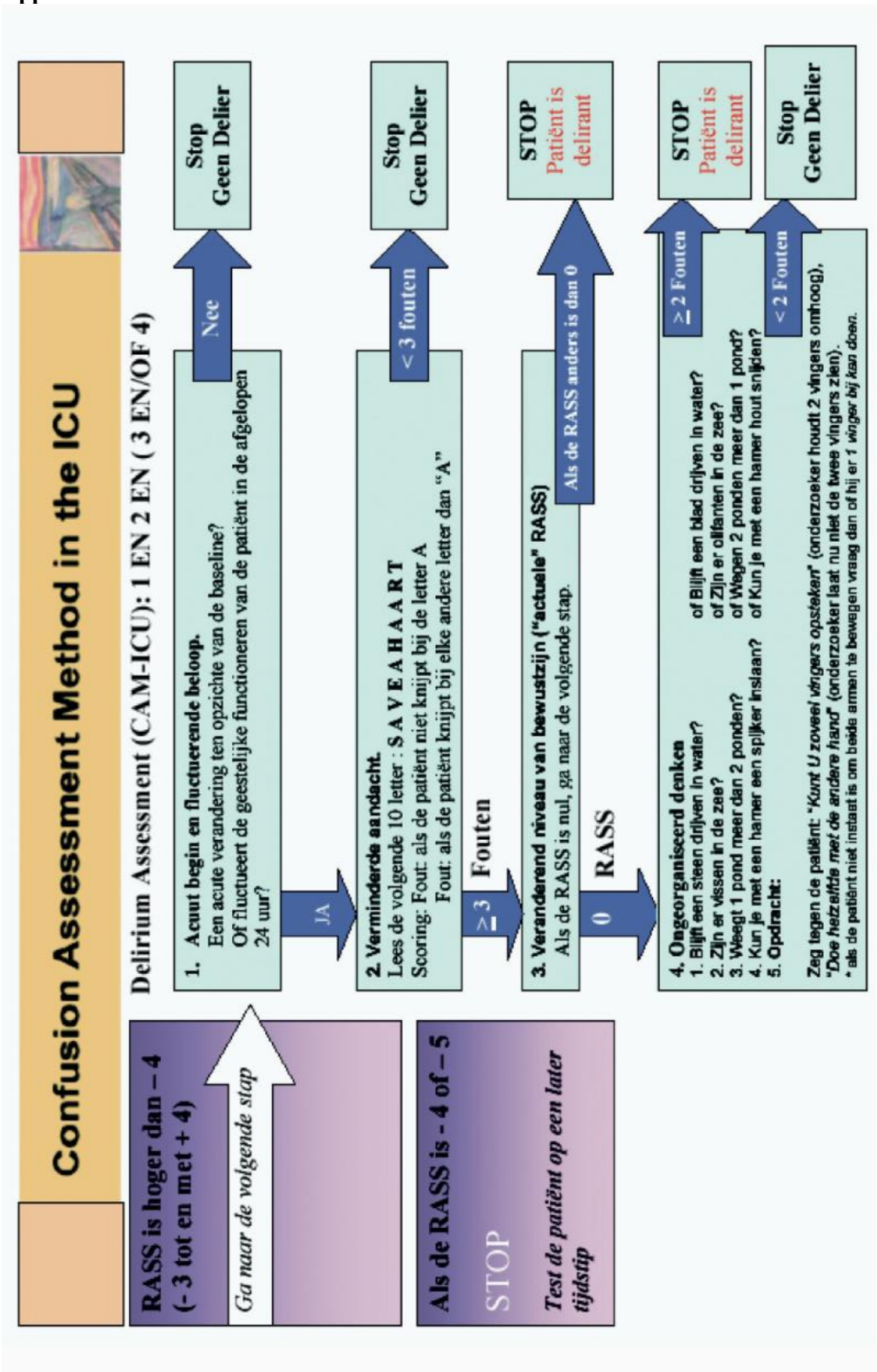
** als de patiënt niet instaat is om beide armen te bewegen vraag dan of hij er 1 vinger bij kan doen.*

Score:_____ (patiënt krijgt 1 punt voor het correct uitvoeren van de totale opdracht)

Combineer Score (3A + 3B): _____ (totaal van 5)

4. Veranderend niveau van bewustzijn **Aanwezig als de RASS score anders is dan "0" (nul)**	**Afwezig**	**Aanwezig**
In totaal CAM-ICU (onderdelen 1 en 2 en op zijn minst onderdeel 3 of 4)	**Ja**	**Nee**

Appendix 2 Flowchart CAM-ICU



Appendix 3. RASS

Verbinding tussen sedatie en deliermonitoring.
Een tweetraps benadering van onderzoek naar bewustzijn.

Stap 1: Vaststelling van de mate van sedatie.

De Richmond Agitatie en Sedatie schaal: de RASS*

Score	Begrip	Beschrijving	
+4	strijdlustig	openlijk strijdlustig, gewelddadig, direct gevaar voor personeel	
+3	erg geagiteerd	trekt aan of verwijderd katheter(s) of tube(s); agressief	
+2	geagiteerd	regelmatig niet doelgerichte bewegingen, afwerende reacties	
+1	onrustig	angstig maar bewegelijkheid is niet agressief krachtig.	
0	alert en kalm		
-1	slaperig	niet volledig alert maar is in staat wakker te blijven (ogen open/oogcontact) bij stemgeluid (≥ 10 seconde)	verbale stimulatie
-2	lichte sedatie	kort wakker met oogcontact bij stemgeluid (< 10 seconde)	verbale stimulatie
-3	matige sedatie	beweging of ogen open bij stemgeluid (geen oogcontact)	verbale stimulatie
-4	diepe sedatie	geen reactie op stemgeluid, maar wel beweging en ogen open bij lichamelijke prikkeling	lichamelijke stimulatie
-5	niet wekbaar	geen reactie op stemgeluid of lichamelijke prikkeling	lichamelijke stimulatie

Als RASS score –4 0f –5 is dan **stoppen** en patiënt op een later tijdstip **hertesten**.
Als RASS boven de –4 (-3 tot +4) ligt dan **stap 2 toepassen**.

Appendix 4. DSM-IV criteria

THE DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS (DSM-IV) CRITERIA FOR DELIRIUM

a. Disturbance of consciousness:That is, reduced clarity of awareness of the environment, with reduced ability to focus, sustain,or shift attention.

b. A change in cognition: such as memory deficit, disorientation, language disturbance or the development of a perceptual disturbance that is not better accounted for by a pre-existing established or evolving dementia.

c. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.

Chapter 8

A review of multifactorial intervention studies for the primary prevention of delirium in the elderly.

Kalisvaart KJ
Vreeswijk R
de Jonghe JFM
Milisen K

Tijdschr Gerontol Geriatr. 2005 Dec;36(6):224-31. Review. Dutch.

ABSTRACT

Delirium is a severe psychiatric syndrome that is highly prevalent in elderly patients in a general hospital. Primary prevention is important to prevent delirium. This article reviews recent developments with regard to multifactorial intervention trials for primary prevention of delirium. The review process involved a systematic search in MEDLINE, The Cochrane Database and CINAHL Database and subsequent examination of reference lists. Six studies were selected. Four studies showed that systemic interventions regarding medical-, nurse-led, environmental-, and educational items, were effective in preventing delirium. In one study a reduction was found in duration and severity of duration only. One study showed no effect on delirium at all. Despite the methodological weaknesses of the studies, conclusions are that different kinds of non-pharmacological interventions can be effective in preventing delirium.

INTRODUCTION

Delirium is a severe psychiatric syndrome that is highly prevalent among elderly, general hospital patients and it is associated with elevated morbidity, increased mortality, longer stays, impeded rehabilitation and higher costs. [1-3] Prevention, early recognition and treatment of delirium and its underlying causes are therefore of major importance. Because of the high prevalence rates of up to 65% it seems that primary prevention (before delirium), with both somatic-, and psychosocial interventions, is of major importance. [4-6] However, the use of primary preventive strategies is not common in daily practice, yet.

Pharmacological interventions are important for preventing and treating delirium. They are useful for treating underlying medical conditions and for preventing worsening of the condition (secondary prevention). A special form of pharmacological interventions is used to prevent delirium. This so-called primary prevention concerns the prophylactic use of antipsychotics, cholinesterase inhibitors or other medications used likewise. The term 'multifactorial' does not preclude certain pharmacological interventions, like antibiotics and pain killers, because they are aimed at treating underlying somatic conditions. There have been several studies into primary delirium prevention. Several factors can determine the choice of a particular preventive intervention: effectiveness, location (e.g. emergency or nursing wards, operating theatres.) and agents (e.g. physicians, nurses or relatives), time (e.g. immediately on admission, just before an operation) and purpose (e.g. training, medical evaluation or family education) are all important. It is also important to know how much effort it takes for nurses, physicians and relatives to apply these interventions or to be trained to do so. Some studies have been briefly to extensively discussed in earlier review articles and the CBO guidelines. [7-9]

The 1996 review article by Cole et al. provides a very thorough, extensive survey of all studies carried out up to then. Absolute risk reduction (ARR) for the surgery studies varied from 8% to 16% and for the medical population from –3% to 3%. [8] The Weber et al. survey (2004) also comprises four recent studies in the field of delirium prevention. The studies included yielded a delirium prevalence of 5%-32% and the control population showed 15%-50%. [9] Cole and Weber concluded that, despite methodological shortcomings in several studies, there is a wide range of interventions that may be effective in preventing delirium and that preventive interventions are more successful with surgery patients than with general medicine patients. [8;9]

The objectives this article is to extensively review studies of multifactorial interventions for the primary prevention of delirium in elderly, general hospital patients, and to evaluate the quality of the scientific evidence brought forward by these studies.

METHOD

We gathered Dutch and English literature from the MEDLINE, CINAHL and Cochrane-files from 1966 up to October 2004, using the following search items: delirium, (hospital) confusion, (primary) prevention and intervention. Papers were selected if the title or summary had bearing on the development or applicability of interventions for the primary, multifactorial prevention of delirium. General pharmacological interventions aimed at treatable underlying disorders (e.g. pain) were accepted. The papers' reference lists were checked for possible other studies dealing with delirium, (hospital) confusion, (primary) prevention and intervention but no new articles were found. Other selection criteria were:

research population of elderly patients (>65) admitted to a general hospital, original data, and DSM-based criteria for the diagnosis of delirium (Diagnostic and Statistical Manual of Mental disorders).[10-12] Using the Evidence based review methodology, the selected studies were evaluated according to a hierarchy in study designs [13] and the five criteria defined by the Evidence Based Medicine Working Group. [14]

- Level 1. randomized, controlled study
- Level 2. non-randomized, controlled study
- Level 3. observation study with control population
- Level 4. observation study without control population

The following criteria were used to assess study validity and reliability:
1. Random patient selection?
2. Were all patients participating rightly included in this study and its conclusion?
2a. Was there a complete follow-up?
2b. Were patients analyzed within their study groups?
3. Were patients, health care workers and researchers 'blind' in reference to the treatment? 4. Were groups equal at the start of the study?
5. Apart from the experimental interventions, were groups treated the same?

RESULTS

Forty-four papers were the result of the MEDLINE search. The Cochrane systematic review database provided eight other new articles. Searching the CINAHL (Nursing and Allied Health Database) produced no new articles.

From the 52 potential articles, nineteen were selected. The other articles were not selected because they were not related to the subject. The nineteen remaining articles were checked for relevance for this review. This resulted in the exclusion of another thirteen articles, for the following reasons: six articles were based on studies published earlier (same study population), [8;15-19] one follow-up study [20], one article on a secondary prevention study [21], one with a younger adults study population [22], two studies because the diagnosis of delirium was not operationalized according to DSM-criteria [23;24] and the two review articles of Cole and Weber. [8;9] These two reviews are not part of our review because we only wanted to discuss original work.

The remaining six articles are one randomized, controlled study [25] and five non-randomized, controlled studies of hip-surgery and general medical patients. [26-30]

Methodological quality of intervention studies for primary prevention

The results of the reliability and validity assessment are presented in table 2.
The Marcantio et al. study is the only one that has with a randomized, controlled design, scoring 5/5 of the Evidence Based Medicine Working Group criteria. [25] Of the non-randomized studies the Inouye et al. study was the only one that scored 5/5 of the Evidence Based Medicine Working Group criteria.[27] The studies of Gustafson et al. and Lundstrom et al. fulfil only a few of the criteria: Historical control groups are used. [26;28] The studies of Milisen et al. and Wanich et al. were not blinded and there was no equality between research and control populations. [29;30]

Type-, and effectiveness of the interventions

Gustafson et al. (1991) [26] studied the effect of a geriatric-anesthesiological intervention program for the prevention and treatment of delirium in elderly with a hip-fracture. The intervention consisted of pre- and post-operative, geriatric assessments, administering oxygen, short waiting for the operation, prevention and treatment of peri-operative dropping of blood pressure and treatment of post-operative complications. Post-operative delirium incidence (based on DSM-III-R criteria[11]) was lower for the intervention group (46.7% versus 61.3%, *P* < .005). Delirium duration (percentage longer than seven days; 9.1% versus 28.1%, *P*<.001) and severity (percentage of patients that makes good nursing care difficult; 6.8% versus 29.7%, *P*<.001) were also less than in the control group. Measured in days, hospital stays were shorter (11.6 versus 17.4, *P*<.001).

Wanich et al (1992) [30] studied the effect of nursing interventions, performed by two nursing specialists on a daily basis, in general medical patients. The focus was both on delirium onset (DSM-III criteria[10]) and functional decline. The interventions consisted of nursing staff training, patients' orientation and communication, mobilization, setting adjustments, instructing care providers and/or relatives, medication adjustments and release planning. The study shows no difference in delirium incidence between intervention and control group, respectively 19.0% versus 22%; *P*= .61, nor was there a significant difference in clinical outcome (complications; 19.0% versus 16.0%, *P* = .62 and mortality; 8.0% versus 5.0%, *P* = .36) between the two groups. Although the intervention group was admitted 1.2 days shorter, there was no significant difference with the control group (*P*= .53).

Inouye et al. (1999) [27] focussed on the effectiveness of a multi-component, intervention strategy to prevent delirium in general medical patients. Interventions consisted of structured, standardized protocols for six proven delirium risk factors. These factors are cognitive disorder, sleep, immobility, visus and hearing problems and dehydration. The study shows a difference in delirium incidence (Confusion assessment Method, based on DSM-III-R criteria[11;31]) between the intervention and control groups, 9.9% versus 15% respectively (OR 0.60; 95%CI=0.39-0.92). The two groups also differed significantly in the total number of delirium days (on average 105 days for the intervention group and 161 days for the control group, *P*=.02) and the total number of delirium episodes (intervention: 62 versus control: 90 episodes, *P*=.03). Delirium severity (3.85 versus 3.52, *P* =.025) and recurrence rate (31.0% versus 26.6%, *P*=.62) did not vary between the groups.

Lundstrom et al. (1999) [28] studied the effects of a nursing and medical intervention programme to prevent and treat delirium in patients with fractured hips. The intervention programme consisted of training staff, coordinating orthopaedics and geriatrics, individual care planning and rehabilitation, improved ward settings, active nutrition involvement, improved care continuity in preventing and treating delirium complications. Delirium incidence (based on DSM-III-R criteria[11]) was significantly lower than in earlier studies. The study distinguishes between pre- and post-operative delirium. Pre-operative delirium: control study I: 33.3%, control study II: 29.1% (*P*=.098), intervention study 20.4% (*P*=.253). Post-operative delirium control study I:61.3%, control study II: 47.6% (*P*<.001), intervention study 30.6% (*P*=.047).

Marcantonio et al. (2001) [25] studied whether pre-operative, geriatric consultations and daily visits by geriatrics furthered the prevention of delirium in non-delirious patients in patients with a hip- fracture. Visits took place during admission and specific recommendations were

given using a structured protocol. Examples of these recommendations are: how to apply oxygen adequately, electrolyte- and fluid levels, pain management, pharmacological clearance, miction and defecation measures, good nutrition, early mobilization and rehabilitation, prevention, detection and treatment of post-operative complications and applied setting changes. (multi-component strategy). The intervention group ran a relatively lower risk for having delirium (based on the CAM, DSI (Delirium Symptom Interview- DSM-III criteria[32]) 32% versus 50%; RR 0.64; 95% CI= 0.37-0.98). No significant difference in hospital stay duration was found between the two groups (median ± IQR= 5 ± 2 days), possibly because of a (limited stay) duration determined by protocol. The severity of delirium, as assessed with MDAS (Memorial Delirium Assessment Scale based on DSM-IV criteria[12;33]) was less in the intervention group (12% versus 29%, *P*=.02).

Milisen et al. (2001) [29] focused on the effects of a nurse-guided, interdisciplinary intervention program on delirium incidence and course (duration and severity) in elderly patients with fractured hips. Furthermore, cognitive functioning, recovered functioning (rehabilitation), mortality and duration of stay were evaluated. The intervention consisted of training nursing staff, systematic cognitive screening, consultation of a nurse specialized in the elderly or a psycho-geriatrician and a pain protocol. No significant difference in delirium incidence, as measured with the CAM [31] was found between the intervention (20.0%) and the control group (23.3%); *P*=.82. However, there was a difference in delirium duration (intervention median =1 day, control median =4 days; *P*=.03) and severity as rated with an adjusted CAM-version (score of seven delirium symptoms; 1.9 versus 5.0, *P*=.0049). The hospital admission duration was not different for the groups (median 13.5 days versus 14 days, *P*=.60).

The type of interventions and effectiveness of the studies are presented in table 2.

DISCUSSION

This paper reviews studies that evaluated the effectiveness of multifactorial interventions for the primary prevention of delirium in elderly, general hospital patients. A total of six studies (1 RCT and 5 non-randomized studies) were found. [25-30] One may conclude that precious little thorough research into this field has been carried out. Effective interventions focus on active, geriatric consultation and a combination of several medical, nursing and setting factors.

Of the studies excluded most did not meet the research criteria set forth by Evidence Based Medicine Working Group criteria. The included studies showed methodological shortcomings also: e.g., no randomization of participating patients, there were baseline differences between control and intervention groups and study blinding was not always maintained. Two of the studies lack sufficient scientific value because of this. [26;28]

Furthermore, it is not clear whether patients were checked for delirium on admission. In a study on primary prevention this should be made clear. Two of the six studies provide information on this subject. [27;28] In one of these studies patients with delirium were included.

The diversity in study populations (in- and exclusion criteria, vulnerability of the study population on admission, different study designs, patient selection, intervention types and population sizes, etc) and when, how and by whom delirium was diagnosed might explain the wide range of prevalence rates for delirium between the studies. No two studies used

diagnostic criteria based on the same version of the DSM and not one used the DSM-IV criteria. [12] Differences between diagnostic classification systems leads to varying delirium detection percentages in one and the same population. The DSM-IV criteria are most sensitive for making the diagnosis. [12;34]

Both Marcantonio et al. and Inouye et al. showed that specific consultation and multi-component recommendations lead to a significantly reduced delirium incidence in hip fracture patients and general medical patients. [25;27] Two of the six studies showed no effectiveness of the interventions on delirium. [29;30] Milisen et al. did show a positive effect on delirium severity and duration. [29] Gustafson et al. and Lundstrom et al. did find a reduction of delirium incidence, but these results should be interpreted with caution. [26;28] The studies mentioned above indicate that a combination of interventions (multi-component) can be useful to prevent delirium.

The success of an intervention also depends on its applicability and adherence of both patient and staff. Inouye et al. showed that adherence is an independent predictor for the rate of delirium. [18] Marcantonio indicates that the sheer number of interventions is an indicator for adherence by nursing staff. Interventions should be applied when really necessary and therefore their numbers should be limited. [25] For the selected and discussed studies no details are mentioned, except for Marcantonio et al. and Inouye et al. on the control of adherence check.

The question arises what this review adds to other reviews and existing guidelines. One earlier review contains mostly older studies. [8] Another contains more recent studies in the English language. [9] The valuable CBO guideline “Delirium” offers a global review of the prevention studies from 1996 until now. [7] The NHG-guidelines (Dutch General Practitioners guidelines) has no chapter on prevention. [35] As far as we know this review offers the only broad discussion of all the relevant research on the primary multifactorial prevention of delirium.

CONCLUSION

Six intervention studies on primary, multifactorial delirium prevention were evaluated for content and methodology. Best of these six is the one by Marcantonio, as this is a randomized, controlled study (RCT) and the only one meeting all Evidence Based Medicine criteria.

Recommendations for peri-operative geriatric consultation in combination with structured protocols for general interventions focusing on determined problems and the improvement of a patient’s situation as a whole (multi-component strategy) proved useful in a population of elderly, hip surgery patients.[25]

The Inouye et al. study also meets sufficient Evidence Based Medicine demands and it is recommended to apply the interventions used. [27]

Therefore, for daily practice it is recommended to have a geriatric consultation team for peri-operative monitoring and checkup and for giving recommendations on administering oxygen adequately, electrolyte- and fluid levels, pain management, pharmacological clearance, miction and defecation measures, good nutrition, early mobilization and rehabilitation, prevention, detection and treatment of post-operative complications and applied setting

changes. (multi-component strategy). [25]
For general medical patients recommendations are therefore: apply interventions focussed on cognition, sleep, immobility, vision, hearing and dehydration. [27] It is also recommended to have the cognitive status of patients assessed by nursing staff on a regular basis (using a standardized assessment scale). [29]

Further research into multifactorial interventions aiming to prevent delirium is necessary. Methodology, research populations and size (power analysis should be used) should be taken into account. The 'outcome' measure delirium should be assessed blindly. A clear definition for delirium and operationalized diagnostic methods are necessary.

Furthermore, possible distortions of the results that might occur when control and intervention groups are studied on one and the same ward or when both groups do not get the same care, should be taken into the equation. For daily practice it is important that the interventions (multi-component strategy) are actually applied. Considering the results found, co-operation between different disciplines (medical and nursing) seems indispensable.

References

1. Galanakis P, Bickel H, Gradinger R, Von Gumppenberg S, Forstl H. Acute confusional state in the elderly following hip surgery: incidence, risk factors and complications. Int.J. Geriatr.Psychiatry 2001;16:349-55.
2. Lindesay J, Rockwood K, Rolfson DB. The epidemiology of delirium., In: Lindesay J, Rockwood K, Macdonald AJ, editors. Delirium in old age., 1 ed. New York: Oxford University Press; 2002. p. 27-50.
3. Rockwood K. The occurrence and duration of symptoms in elderly patients with delirium. J Gerontol 1993;48:M162- M166.
4. Meagher DJ. Delirium: optimising management. BMJ 2001; 322:144-49.
5. O'Keeffe ST, Lavan JN. Predicting delirium in elderly patients: development and validation of a risk-stratification model. Age Ageing 1996; 25:317-21.
6. Rowe JW. Geriatrics, prevention, and the remodeling of Medicare. N.Engl.J.Med. 1999;340:720-21.
7. CBO. Multidisciplinaire richtlijn delirium. 2004. Report
8. Cole MG, Primeau F, McCusker J. Effectiveness of interventions to prevent delirium in hospitalized patients: a systematic review. CMAJ. 1996; 155:1263-68.
9. Weber JB, Coverdale JH, Kunik ME. Delirium: current trends in prevention and treatment. Intern.Med.J. 2004;34:115-21.
10. American Psychiatric Association (APA). Diagnostic and statistical manual of mental disorders, third edition (DSM-III). Washington DC: American Psychiatric Association; 1980.
11. American Psychiatric Association (APA). Diagnostic and statistical manual of mental disorders, third edition revised (DSM- III-R). Washington DC: American Psychiatric Association; 1987.
12. American Psychiatric Association (APA). Diagnostic and statistical manual of mental disorders, fourth edition revised (DSM-IV). Washington DC: American Psychiatric Association; 1994.
13. Markowitz, A. M. Making Health Care Safer. 2004. Internet Communication
14. Guyatt GH, Haynes RB, Jaeschke RZ, Cook DJ, Green L, Naylor CD *et al.* Users' Guides to the Medical Literature: XXV. Evidence-based medicine: principles for applying the Users' Guides to patient care. Evidence-Based Medicine Working Group. JAMA 2000; 284:1290-96.
15. Cole MG. Delirium: effectiveness of systematic interventions. Dement.Geriatr. Cogn Disord. 1999; 10:406-11.
16. Inouye SK, Bogardus ST, Jr., Baker DI, Leo-Summers L, Cooney LM, Jr. The Hospital Elder Life Program: a model of care to prevent cognitive and functional decline in older hospitalized patients. Hospital Elder Life Program. J.Am.Geriatr.Soc. 2000;48:1697-706.
17. Inouye SK. Prevention of delirium in hospitalized older patients: risk factors and targeted intervention strategies. Ann.Med. 2000;32:257-63.
18. Inouye SK, Bogardus ST, Jr., Williams CS, Leo-Summers L, Agostini JV. The role of adherence on the effectiveness of nonpharmacologic interventions: evidence from the delirium prevention trial. Arch.Intern.Med. 2003;163:958-64.
19. Rizzo JA, Bogardus ST, Jr., Leo-Summers L, Williams CS, Acampora D, Inouye SK. Multicomponent targeted intervention to prevent delirium in hospitalized older patients: what is the economic value? Med.Care 2001;39:740-52.
20. Bogardus ST, Jr., Desai MM, Williams CS, Leo-Summers L, Acampora D, Inouye SK. The effects of a targeted multicomponent delirium intervention on postdischarge outcomes for hospitalized older adults. Am.J.Med. 2003;114:383- 90.

21. Cole MG, McCusker J, Bellavance F, Primeau FJ, Bailey RF, Bonnycastle MJ *et al.* Systematic detection and multidisciplinary care of delirium in older medical inpatients: a randomized trial. CMAJ. 2002; 167:753-59.
22. Owens JF, Hutelmyer CM. The effect of preoperative intervention on delirium in cardiac surgical patients. Nurs.Res. 1982; 31:60-62.
23. Nagley SJ. Predicting and preventing confusion in your patients. J. Gerontol.Nurs. 1986; 12:27-31.
24. Williams MA, Campbell EB, Raynor WJ, Mlynarczyk SM, Ward SE. Reducing acute confusional states in elderly patients with hip fractures. Res Nurs Health 1985; 8:329-37.
25. Marcantonio ER, Flacker JM, Wright RJ, Resnick NM. Reducing delirium after hip fracture: a randomized trial. J.Am.Geriatr.Soc. 2001;49:516-22.
26. Gustafson Y, Brannstrom B, Berggren D, Ragnarsson JI, Sigaard J, Bucht G *et al.* A geriatric-anesthesiologic program to reduce acute confusional states in elderly patients treated for femoral neck fractures. J.Am.Geriatr.Soc. 1991;39:655-62.
27. Inouye SK, Bogardus ST, Jr., Charpentier PA, Leo-Summers L, Acampora D, Holford TR *et al.* A multicomponent intervention to prevent delirium in hospitalized older patients. N.Engl.J.Med. 1999;340:669-76.
28. Lundstrom M, Edlund A, Lundstrom G, Gustafson Y. Reorganization of nursing and medical care to reduce the incidence of postoperative delirium and improve rehabilitation outcome in elderly patients treated for femoral neck fractures. Scand. J.Caring.Sci. 1999;13:193-200.
29. Milisen K, Foreman MD, Abraham IL, De Geest S, Godderis J, Vandermeulen E et al. A nurse-led interdisciplinary intervention program for delirium in elderly hip-fracture patients. J.Am.Geriatr.Soc. 2001;49:523-32.
30. Wanich CK, Sullivan-Marx EM, Gottlieb GL, Johnson JC. Functional status outcomes of a nursing intervention in hospitalised elderly. Image 1992; 24:201-07.
31. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann.Intern.Med. 1990;113:941-48.
32. Albert MS, Levkoff SE, Reilly C, Liptzin B, Pilgrim D, Cleary PD *et al.* The delirium symptom interview: an interview for the detection of delirium symptoms in hospitalized patients. J Geriatr.Psychiatry Neurol. 1992;5:14-21.
33. Breitbart W, Rosenfeld B, Roth A, Smith MJ, Cohen K, Passik S. The Memorial Delirium Assessment Scale. J Pain Symptom.Manage. 1997; 13:128-37.
34. Laurila JV, Pitkala KH, Strandberg TE, Tilvis RS. Impact of different diagnostic criteria on prognosis of delirium: a prospective study. Dement.Geriatr.Cogn Disord. 2004; 18:240-44.
35. Ritmeijer CA, Vesseur-Baak JA. [Summary of the Dutch College of General Practitioners' practice guideline 'Delirium in elderly people']. Ned.Tijdschr.Geneeskd. 2003; 147:1527-28.

Tabel 1. Summary of the Study Properties

		Patient population								
Study /year/ref	**Rating outcome**	**Intervention**		**Control**		**Intervention type, *by whom***	**Patient population**	**Absolute Risk reduction**		**NNT**	
Gustafson 1991 25	DSM-III-R	N=103 Delier 47,6%		N=111 Delier 61,3%		Pre- and postoperative assessment, oxygen therapy, quick operation, prevention and treatment of peri-operative dropping blood pressure and treatment of post-operative complications. *MD.*	Hip-surgery	13,7%		7	
Wanich 1992 30	DSM-III	N = 135 Delier 19%		N = 100 Delier 22%		Training nursing staff, orientation and communication, Mobilisation, setting adjustments, contacting and training care providers and/or relatives, adjusted medication, release planning. *Nurse.*	Medical	3%		33	
Lundstrom 1999 # 27	DSM-III-R	**I*** N=111 Delier 33,3% (61,3%)	**II *** N= 103 Delier 29,1% (47,6%)	**I*** N=111 Delier 33,3% (61,3%)	**II *** N= 103 Delier 29,1% (47,6%)	Training staff, co-operation between orthopaedics and geriatrics, individual care plans, improved ward settings, active nutrition involvement, improved care continuity in relation to treatment and prevention. *MD./Nurse*..	Hip-surgery	**I[&]** 12,9% (30,7%)	**II[&]** 8,7% (17%)	**I[&]** 9 (3)	**II[&]** 12 (6)
Inouye 1999 26	CAM	N=426 Delier 9,9%		N=426 Delier 15%		Training staff, co-operation between orthopaedics and geriatrics, individual care plans, improved ward settings, active nutrition involvement, improved care continuity in relation to treatment and prevention. *Multidisciplinary team*	Medical	5,1%		20	
Marcantonio 2001 28	CAM, DSI MDAS	N=62 Delier 32%		N=64 Delier 50%		Pre-operative geriatric consultation consisting of visits during admission, specific recommendations, structured examining protocols. *MD.*	Surgery	18%		6	
Milisen 2001 29	CAM	N=60 Delier 20%		N=60 Delier 23,3%		Pre-operative geriatric consultation consisting of visits during admission, specific recommendations, structured examining protocols. MD./Nurse.	Surgery	3,3%		30	

[#.] Lundstrom made a difference between pre- en postoperative ( ) delirium patients
*. Historical control population (control study **I** en control study **II**).
[$.] Absolute risk reduction (ARR) of the intervention study in relation to control study **I** and **II.**
[&.] Numbers Needed to Treat (NNT) of intervention study in relation to control study **I** and control study **II**.

Tabel 2. Methodological quality of intervention studies for primary prevention.

Study	Ref.	Study design	Similarity of populations at baseline	Similarity of treatment	Blindness	Complete follow-up	Intention to treat
Gustafson 1991	25	NRCT	-	-	-	+	?
Wanich 1992	30	NRCT	-	+	-	+	+
Lundstrom 1999	27	NRCT	-	-	-	+	-
Inouye 1999	26	NRCT	+	+	+	+	+
Marcantonio 2001	28	RCT	+	+	+	+	+
Milisen 2001	29	NRCT	-	+	-	+	+

RCT = randomised controlled study
NRCT = non- randomised controlled study

Chapter 9
Recipe for primary prevention of delirium in horpitalized older patients.

Vreeswijk R
Maier AB
Kalisvaart KJ

Aging Clinical and Experimental Research. 2022 Sep 22. Online ahead of print

ABSTRACT

Delirium is an acute fluctuating syndrome characterized by a change in consciousness, perception, orientation, cognition, sleep-wake rhythm, psychomotor skills, and the mood and feelings of a patient. Delirium and delirium prevention remain a challenge for healthcare professionals, especially nurses who form the basis of patient care. It also causes distress for patients, their caregivers and healthcare professionals. However, delirium is preventable in 30-40% of cases. The aim of this article is to summarize the delirium risk models, delirium screening tools, and (non-pharmacological) delirium prevention strategies. A literature search of review articles supplemented by original articles published in PubMed, Cinahl, and Cochrane between 1 January 2000 and 31 December 2020 was carried out. Among the older patients, delirium is a common condition with major consequences in terms of mortality and morbidity, but prevention is possible. Despite the fact that delirium risk models, delirium screening scales and non-pharmacological prevention are available for the development of a hospital delirium prevention programme, such a programme is still not commonly used on a daily basis.

INTRODUCTION

Delirium is described in the DSM-5 as an acute fluctuating syndrome characterised by a change in consciousness, perception, orientation, cognition, sleep–wake rhythm, psychomotor skills, and the mood and feelings of a patient. [1] The delirium prevalence varies among hospital patient populations ranging from 5% for elective orthopaedic surgery to 87% for intensive care unit (ICU) patients. [2, 3] The causes of delirium vary, but there is almost always a somatic cause, putting frail and cognitively impaired patient and patients with multimorbidity at the highest risk of delirium. [4–6] Patients with delirium often have a risk of morbidity, mortality, prolonged hospital length of stay, high rates of institutionalization, and cognitive decline. [7, 8] Delirium is also associated with long-term cognitive decline. [9] Delirium increases the cost of the index hospitalization as well as the need for post-acute care and the demands on unpaid, often older caregivers. [10, 11] Delirium and delirium prevention continue to be a challenge for healthcare professionals, especially for nurses who form the basis of patient care. It also causes distress for patients, their caregivers, and healthcare professionals. [12–14] In 30–40% of cases, delirium is a preventable condition.[15] Prevention starts by patients at risk of delirium being identified using a delirium risk model, followed by management of these patients using delirium screening tools and non-pharmacological preventive interventions. Delirium prevention increases patient well-being, as well as decreasing staff workload and reducing costs. Nevertheless, several studies reveal a shortfall in nurses´ knowledge of delirium prevention, which has a negative impact on the number of appropriate outcomes. In addition, despite the fact that the knowledge from research on delirium detection, control and prevention is available, its application in daily practice can still be improved. [16–19]

A successful implementation in daily practice starts with knowledge and the attitude of nurses and doctors. The aim of this article is to summarize the delirium prediction models, screening tools, and the non-pharmacological prevention of delirium.

DATA SOURCES AND SEARCH STRATEGY

Search strategy

A literature search of review articles supplemented by original articles published in PubMed, Cinahl, and Cochrane between 1 January 2000 and 31 December 2020 was carried out. The published review articles were supplemented by the original articles that were not included in the reviews (Fig. 1). In addition, the reference list for additional studies in these articles was reviewed.

The Mesh terms and all field keywords per phase were:
Screening for Delirium risk and prediction:
Delirium, postoperative, hospital, prediction, model, risk*, older patient.
Assessment for delirium and preventive interventions:
Delirium, postoperative, hospital, prevention, non-pharmacology, screening, older patient.

Criteria for inclusion of articles

Articles for delirium risk were included if the authors had investigated risk assessment of delirium based on predisposing risk factors for delirium as the main purpose of the study and including older patients admitted to hospital. Only articles written in English were included. Reviews supplemented by original articles that were not in the reviews were also included.

All study designs were included and there was no limitation by time frame of delirium development. Studies were excluded if they study a patient population (emergency departments, palliative care or hospice) of which the results are not generalizable to a medical or surgical inpatient hospital setting. These specific patient populations have specific characteristics requiring specific care regarding delirium prevention. Furthermore, studies in populations related to alcohol withdrawal or delirium tremens were excluded. Titles and abstracts of the search results were reviewed for eligibility, followed by the full text of the paper by the author (RV) and any duplicates were removed. Where there was doubt, papers were assessed by another author (KK). Selected studies were then subject to a full text review, based on the inclusion and exclusion criteria, ultimately resulting in a final list of included articles. The inclusion criteria were delirium, hospital, prevention (non-pharmacological), and screening. Exclusion criteria: non-hospital, delirium treatment.

Data items

Data were collected on the year of publication, study design, population, evaluation of delirium (screening and severity), delirium risk models, and (non-pharmacological) interventions for delirium prevention.

RESULTS OF THE DELIRIUM RISK MODELS

Since the aetiology of delirium is multifactorial, predisposing factors on admission and precipitating factors during hospitalization vary and prediction models for delirium are numerous (Table 1). However, only a few models have been independently validated and implemented into clinical practice. [20] The literature search resulted in five review articles on delirium prediction models [21–25] and four original articles. [26–29]

In total, 28 delirium prediction models were found of which 15 were validated in another patient population (Table 2). 23 articles were prospective cohort studies, 4 were retrospective cohort studies, and 1 was an observational study. Nine studies included internal medicine patients (internal (6), neurology (1), acute geriatric (1), cardiology (1)), 11 studies were surgical patient populations (elective non-cardiac (3), elective orthopaedic (2), hip fracture (3), elective cardiac (1), oncology (2)), 6 studies were a mixed population and 2 were ICU patient populations. The area under the curve (AUC) of the different delirium risk models varied in the development cohort from 0.72 to 0.91 with a range of 0.61– 0.94, and in the validation cohorts the AUC varied from 0.53 to 0.94 with a range of 0.42–0.97. Not all the delirium risk models had an AUC calculated. [30–32] The omission of an AUC makes it more difficult to compare the model with other models and more difficult to gain insight into the predictive value of the model. The models used varying combinations of risk factors for delirium with inconsistency in the definitions and measurements of these risk factors. The risk factors used were pre-existing cognitive disorders (20 models), sensory disorders (10 models), higher age (11 models), activities of daily life (ADL) problems (9 models), degree of illness (number of chronic diseases present) (9 models), abnormal laboratory values (7 models), infections present (6 models), alcohol/drug abuse (7 models) and prior delirium (6 models). Furthermore, the type of admission (acute), depression, malnutrition, and amount of medication before and during hospital admission were also risk factors. Some models also showed catheter use, acute surgery, fracture at admission, history of stroke, iatrogenic event, and ICU admission variables in the final model. Cognitive impairment in models were based on an MMSE screening, telephone interview for cognitive status (TICS), or clock-drawing score (Table 2). There are several limitations. Firstly, the research design, application, and

reporting of statistical methods seem inadequate. The assessment of delirium varied both in method and personnel; the Confusion Assessment Method (CAM) was used most, but the screening moment, when mentioned, varied from three times a day to once every 48 h. Screening for delirium was done by nurses, doctors, or research personnel. The way of screening (time, method, and personnel) could have had consequences for delirium incidence, because there is a chance that delirium would have been missed due to symptoms varying during the day. Also, the incidence of delirium varied among retrospective and prospective studies. The retrospective design of studies may have consequences for the adequate diagnosing of delirium because of being less accurate. Only eight studies mentioned that the diagnosis of delirium was confirmed by a geriatrician, psychiatrist, psychologist, or independent screening of patient charts. Moreover, the models were developed for specific patient populations and therefore impeded the generalizability to other populations. Even if patient populations in different studies were the same (e.g. hip fracture), the inclusion and exclusion criteria were different per study which makes generalizability difficult.

DELIRIUM SCREENING AND SEVERITY SCALES

Delirium is commonly overlooked or misattributed to dementia, depression, or senescence; confessional states in the hospitalized elderly are considered the rule rather than the exception, and cognitive function is rarely assessed. [33] Moreover, characteristics of the delirium itself, such as its fluctuating nature, lucid intervals and predominance of the hypoactive form in the older patients, make its recognition more difficult. [33] But two influential diagnostic classifica- tion systems exist. The Diagnostic and Statistical Manual for Mental Disorders (DSM) criteria of the American Psychi- atric Association, with revised versions over the last decade (DSM-III, DSM-III-R, DSM-IV, DSM-IV-TR, and DSM-V) [34] and the International Classification of Diseases (ICD) version 11. [35] Although differences between the systems appear to be small, some studies have pointed out that these differences can lead to diverging results in the recognition and diagnosis of delirium. [36]
For prevention of delirium, it is necessary to look for patients "at risk" of delirium and to use instruments for screening and severity. Also, the medical and nursing staff should be made aware of prodromal symptoms for delirium, which indicate a delirium is developing. Most patients with postoperative delirium already have early symptoms in the prodromal phase of delirium. These findings are potentially useful for screening purposes and optimizing prevention strategies targeted at reducing the incidence of postopera- tive delirium. [37] Early symptoms can be detected by the use of assessment scales for the recognition and diagnosis of delirium.

Several delirium screening and severity scales for hospital inpatients are described in different review articles. [38–44] (Table 3) The scales can be divided into screening scales for the detection of delirium and severity scales for measur- ing the severity of delirium. In total, 21 delirium screening scales were found and 9 severity scales which can be used in hospitals. The first screening scale was published in 1992 and the first severity scale in 1994. (Table 3)

The delirium screening scales are: Delirium Symptom Interview (DSI), Saskatoon Delirium Checklist (SDC), Visual Analog Scale for Acute Confusion (VAS-AC), Confusion Assessment Method (CAM), Clinical Assessment of Confusion–A and B (CAC-A and B), Confusion Rating Scale (CRS), Delirium Symptom Interview (DSI), Cognitive Test for Delirium (CTD), Neelon–Champagne Confusion Scale (NEECHAM), Delirium Index (DI), Intensive Care Delirium Screening Checklist (ICDSC), Delirium Observa- tion Screening Scale (DOS), Nursing Delirium Screening Scale (Nu-DESC), Single Question for Delirium,

4-A's Test (4-AT), Confusion Assessment Method-ICU (CAM-ICU), Delirium Triage Screen (DTS), Informant Assessment of geriatric delirium (IAGeD), 3D-Confusion Assessment Method (3D-CAM), Stanford Proxy Test for Delirium (S-PTD), Ultra-Brief Confusion Assessment Method (UB-CAM).

The delirium severity scales are: Delirium Assess- ment Scale (DAS), Memorial Delirium Assessment Scale (MDAS), Confusion State Evaluation (CSE), Delirium Index (DI), Delirium Severity Scale (DSS), Delirium Rating Scale-Revised-98 (DRS-R-98), Delirium-O-Meter (DOM), Delirium Detection Score (DDS), Confusion Assessment Method-severity scale (CAM-S).

Three delirium screening scales can be used as a diagnos- tic scale: Confusion Assessment Method (CAM), Delirium Rating Scale-Revised-98 (DRS-R-98), and Memorial Delir- ium Assessment Scale (MDAS). [45]

Many of the scales mentioned have not been implemented into daily practice or outside the centres where they were developed. Furthermore, it is noted that most scales are only used in research regarding delirium in specific patient popu- lations. The exceptions are the CAM, CAM-ICU, DOSS, NEECHAM, DRSR-98, MDAS, and the 4AT. The content of a scale is closely related to its theoretical background, in most cases the DSM delirium criteria. However, this classification system itself has been developed further over the years and also the rating scales are based on DSM-III, DSM-IV, or DSM-V. Consciousness or attention distur- bances are considered core delirium symptoms. All scales have one or more items for measuring these symptoms. Also, they all contain items registering, to some extent, and cogni- tive changes, such as memory, language, thinking, and per- ception disorders. Considering these cognitive aspects, it is important that a (screening) scale distinguishes between delirium and other psychiatric disorders such as dementia or depression.

The delirium screening scales are developed for doctors, nurses, psychologists or psychiatrists. Nine of the screening scales and four of the severity scales use cognitive screen- ing scales such as MMSE, clock drawing, and months of the year backwards. The time taken varies from less than 1 min to up to 30 min. Some scales, however, need time for a patient to be observed during shifts (e.g. CRS, DOSS) or for all the information to be gathered (e.g. chart review, physical tests) (e.g. NEECHAM). No training is needed for three screening scales (IAGed, 4-AT, Single Question for Delirium) and one severity scale (DOM). Only two scales (IAGed, Single Question for Delirium) get the information from a source other than the patient.

NON-PHARMACOLOGICAL STRATEGIES FOR THE PREVENTION OF DELIRIUM

The majority of studies that investigated non-pharmacological prevention of delirium were designed as explanatory studies with the aim of demonstrating the efficacy of the intervention. No intervention or group of interventions reliably prevents delirium, but there are a number of non-pharmacological interventions aimed at predisposing and precipitating risk factors of delirium that appear to reduce the incidence. [46–48]
A research article by Abraha (2015) describes 16 prevention studies which studied single or multi-component interventions, organization of care, or the effect of education. In this article, only four randomized clinical trials, four clinical controlled trials, and eight before and after studies were found on the prevention of delirium. The overall conclusion was that in older

patients, multi-component non-pharmacological interventions as well as some single-component interventions were effective in preventing delirium. [49] Other reviews came to the same conclusion. Martinez's review (2015) found seven studies of differing quality. The overall conclusion was that a multi-component intervention strategy reduced delirium incidence (relative risk 0.73, 95% confidence interval 0.63–0.85, $P < 0.001$) and there was no difference in the effectiveness with regard to the department or degree of dementia. An additional advantage of a multi-component strategy was that the number of fall incidents also decreased during hospitalization. [48] The Zhang review (2013) demonstrated that a multi-component intervention strategy from the two randomized clinical trials found could prevent delirium. One of the RCTs belonged to Marcantonio, and he demonstrated that the reduction could be as high as 40% due to proactive geriatric consultation in hip fracture patients. [50] A systematic review and meta-analysis that identified 14 high-quality trials showed that a bundle of non-pharmacological and multi-component interventions decreased the incidence of delirium by 44%.[51] Wang's review about the use of comprehensive geriatric assessment (CGA) for the prevention of perioperative delirium in hip fractures, in which six RCTs and one quasi- RCT were investigated, concluded that CGA may provide a reduction in delirium incidence. As Wang indicates, the outcome should be used with some restraint. [52] The review and meta-analysis by Ludolph (2020) also found eight studies and the conclusion, in line with the current guidelines, was that multi-component interventions are effective in preventing delirium. [53]

Although all the review articles mentioned that the quality of the studies are diverse, the overall conclusions were the same, namely that non-pharmacological interventions for the prevention of delirium are effective.

Non-pharmacological treatment involves providing an unambiguous, supportive environment to improve the orientation and maintain the competence of the patients. The components of non-pharmacological prevention can be divided into providing support and orientation, providing an unambiguous environment, measures at maintaining competence, and providing other supportive measures. Several non-pharmacological interventions consist of an orientation plan, therapeutic activities, sleep enhancement, (early) mobilization, a vision and/or hearing protocol, encouraging fluid intake, feeding assistance, family involvement, or an individual care plan. Possible interventions for the prevention of delirium are shown in Table 4.

IMPLICATIONS FOR DAILY PRACTICE

Twenty years ago, Inouye described the high incidence of delirium in hospitals as a prototypical symptom of the weaknesses in our hospital care, a combination of iatrogenic incidents, overmedication, failure to perform proper geriatric assessment, reduction of skilled nursing staff, rapid pace of care, and poor attitude when it comes to caring for elderly patients. [54, 55] More than 20 years after Inouye's conclusion, there are more and more improvements in the care for the prevention of delirium in hospitals, but still not enough. More guidelines are developed, and the construction and implementation of a delirium prevention programme makes it possible to provide the best possible care for patients either at risk of or with incident delirium. A delirium prevention programme requires prediction of risk of delirium, the use of cognitive and delirium assessment scales, and non-pharmacological preventive interventions.

To assess whether a patient is at risk of delirium, this review showed that there are already delirium prediction models based on different risk factors for delirium and developed for different patient populations. It is because of this diversity that it is not possible to give a statement about which is the best prediction model to use in daily practice. It is difficult because of the difference in quality of the research, the variables used for the model, and the groups for which the model was developed. Despite the fact that more and more prediction models based on (evidence based) risk factors for delirium have been developed for different patient groups, the use of prediction models in daily practice is not yet common. A small survey on knowledge and attitude towards delirium amongst European delirium specialists gave no information about the use of delirium prediction models in daily practice [56] Also, no study was found about the use of delirium prediction models in daily practice. Even so, the use of a prediction model for delirium in patients by forming 'at-risk' groups on the basis of higher vulnerability for delirium gives healthcare workers the opportunity to provide extra, high-cost preventive care to those who really need it.

By identifying the early symptoms in the prodromal phase of delirium using a delirium screening instrument, an early diagnosis can be made, and both doctors and nurses can focus more on detecting and preventing delirium. Most of the screening scales developed are easy to use, reliable, and validated, and some of them have already been translated into several languages. Furthermore, it is potentially useful for optimizing prevention strategies targeted at reducing the incidence of postoperative delirium. The most validated and used screening scales in daily practice are the CAM, DOSS, and CAM-ICU. However, the use of a screening scale in daily practice is not common despite that several screening scales are available. A study done amongst healthcare workers in different European countries showed that only 26% of these healthcare workers always use a scale to assess delirium. Most of the time, the CAM (52%) or the DOS (30%) is used. [56] Sinvani´s study found that only 50.3% of the participants indicated that a formal scale like the CAM should be used. Also, clinicians who had undergone delirium training were more confident about using delirium scales (59.3% vs 32.3%).[57] Amongst UK doctors, there was some improvement in the use of a validated delirium assessment scale, as in 2006 only 9% used such a scale, but this increased to 35% in 2016. [58, 59] Screening routinely varied from 26.8% to 59%. There is also a variation in daily use of the scale for screening. Routine screening was done once a day (23.6–54%), or once per shift (11.1–12%), depending on the situation. [56, 60, 61]

Non-pharmacological strategies are often applied for the prevention and management of delirium. By providing a good standard of basic care, it is possible to prevent most types of delirium and reduce overall delirium incidence in hospitals. When educating students or nurses on the subject of the prevention of delirium, the standard reaction is always: "this seems such basic normal care". With the increasing numbers of old and above all frail patients in hospital, the first thing to do is provide good normal care. A delirium prevention programme must be a combination of multi-factor intervention (which is the best way for the prevention of delirium), and a proactive consultation team (doctors and nurses) seems to have the best results concerning the prevention of delirium. However, there is a difference in how non-pharmacological preventive interventions are applied. Overall, despite strong evidence supporting their value, the implementation of delirium preventive measures is still not a common practice and varies in different places. The main barriers to implementation include time constraints on the staff and cultural gaps among physicians and nurses. [62, 63] In addition, a lack of knowledge and attitude create a barrier. A survey amongst European delirium specialists showed that in hyperactive delirium, 60.6% combined pharmacological and non-pharmacological strategies, 30% used only non-pharmacological interventions and 9.4% used

only pharmacological management. In hypoactive delirium patients, a non-pharmacological intervention approach was more common (67.5%), followed by a combination of non-pharmacological and pharmacological (29.4%) and pure pharmacological treatment (3%). [56] A survey in Italy showed similar or lower figures. Only 11.1% of the nurses performed preventive non-pharmacological interventions. [64]

Although the overall picture on delirium prevention is somewhat negative, it also offers a perspective on opportunities to improve the quality of hospital care for older people. The scales and preventive interventions are already available for the development of a hospital delirium prevention programme. As Inouye already showed in the Hospital Elderly Life Program (HELP), the implementation of a delirium risk assessment and prevention programme results in a decrease in incidence of delirium. [55] The expected significant benefits of delirium prevention are the reduction in complications, related medical costs, and the reduction in duration of hospital admission resulting from a reduction of delirium incidence and its severity. [54, 55] An improvement in nurses´ and doctors´ knowledge about the different aspects of delirium prevention leads to better preventive care for delirium. [57, 58, 64, 65]

In summary, delirium is a common and dangerous condition in older adults, but as Inouye said in 2000 prevention is possible. This article on the development of delirium risk models, screening scales, and non-drug prevention demonstrates that all necessary tools are in place for the development of a hospital delirium prevention programme. There is no reason whatsoever for any hospital not to implement all available knowledge into practice and to allow patients to benefit from it. Despite the fact that it is difficult to identify a single “best” device or “best” (multicomponent) non-pharmacological intervention. Also, because there is a lack of calibration and classification measures between the included risk model studies, as well as the lack of consistency between risk models developed in different clinical settings.

References

1. European Delirium Association, American Delirium Society. The DSM-5 criteria, level of arousal and delirium diagnosis: inclusiveness is safer. BMC Med. 2014; 12:141. https://doi:10.1186/s12916-014-0141-2.
2. Inouye SK. Delirium in older persons. N Engl J Med. 2006;354(11):1157-1165. https://doi:10.1056/NEJMra052321.
3. Kotfis K, Marra A, Ely EW. ICU delirium - a diagnostic and therapeutic challenge in the intensive care unit. Anaesthesiol Intensive Ther. 2018;50(2):160-167. https://doi:10.5603/AIT.a2018.0011
4. Sillner AY, McConeghy RO, Madrigal C, Culley DJ, Arora RC, Rudolph JL. The Association of a Frailty Index and Incident Delirium in Older Hospitalized Patients: An Observational Cohort Study. Clin Interv Aging. 2020; 15: 2053–2061. https://doi:10.2147/CIA.S249284
5. Quinlan N, Marcantonio ER, Inouye SK, Gill TM, Kamholz B., Rudolph JL. Vulnerability: The Crossroads of Frailty and Delirium. J Am Geriatr Soc. 2011 November; 59(Suppl 2): S262– S268. https://doi:10.1111/j.1532-5415.2011.03674.x
6. Lindesay J., Rockwood K., Rolfson D. The epidemiology of delirium. In Delirium in Old Age. Eds. Lindesay, J., Oxford University Press; 2002
7. Witlox J, Eurelings LS, de Jonghe JF, Kalisvaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of post discharge mortality, institutionalization, and dementia: a meta-analysis. JAMA. 2010 Jul 28: 304 (4):443-51. https://doi:10.1001/jama.2010.1013
8. Pereira JV, Zin Aung Thein M, Nitchingham A, Caplan GA. Delirium in older adults is associated with development of new dementia: a systematic review and meta-analysis. International Journal of Geriatric Psychiatry 36(1) February 2021. Jul;36(7):993-1003. https://doi:10.1002/gps.5508
9. Goldberg TE, Chen C, Wang Y, Jung E, Swanson A, Ing C, Garcia PS, Whittington RA, Moitra V. Association of Delirium with Long-term Cognitive Decline A Meta-analysis JAMA Neurol. 2020;77(11):1373-1381. https://doi:10.1001/ jamaneurol.2020.2273
10. Weinrebe W., Johannsdottir E., Karaman M., Füsgen I.. What does delirium cost? An economic evaluation of hyperactive delirium. Z Gerontol Geriat 2016 · 49:52–58. https://doi:10.1007/s00391-015-0871-6.
11. Leslie DL, Marcantonio ER, Zhang Y, et al. One-year health care costs associated with delirium in the elderly population. Arch Intern Med. 2008; 168:27–32. https://doi:10.1001/archinternmed.2007.4
12. Mc Donnell S, Timmins F. A quantitative exploration of the subjective burden experienced by nurses when caring for patients with delirium. J. Clin. Nurs. 2012. 21 2488–2498. https://doi:10.1111/j.1365-2702.2012. 04130.x
13. Morandi A, Lucchi E, Turco R, Morghen S, Guerini F, Santi R, et al. Delirium superimposed on dementia: a quantitative and qualitative evaluation of informal caregivers and health care staff experience. J. Psychosom. Res. 2015. 79 272–280. https://doi:10.1016/ j.jpsychores.2015.06.012
14. Schmitt EM, Gallagher J, Albuquerque A, Tabloski P, Lee HJ, Gleason L, et al.. Perspectives on the delirium experience and its burden: common themes among older patients, their family caregivers, and nurses. Gerontologist 201959 327–337. https://doi:10.1093/geront/gnx153
15. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet. 2014 Mar 8;383(9920):911-22. https://doi:10.1016/S0140-6736(13)60688-1.
16. Godfrey M, Smith J. Green, J, Cheater, F, Inouye, SK, Young, JB. Developing and implementing an integrated delirium prevention system of care: A theory driven,

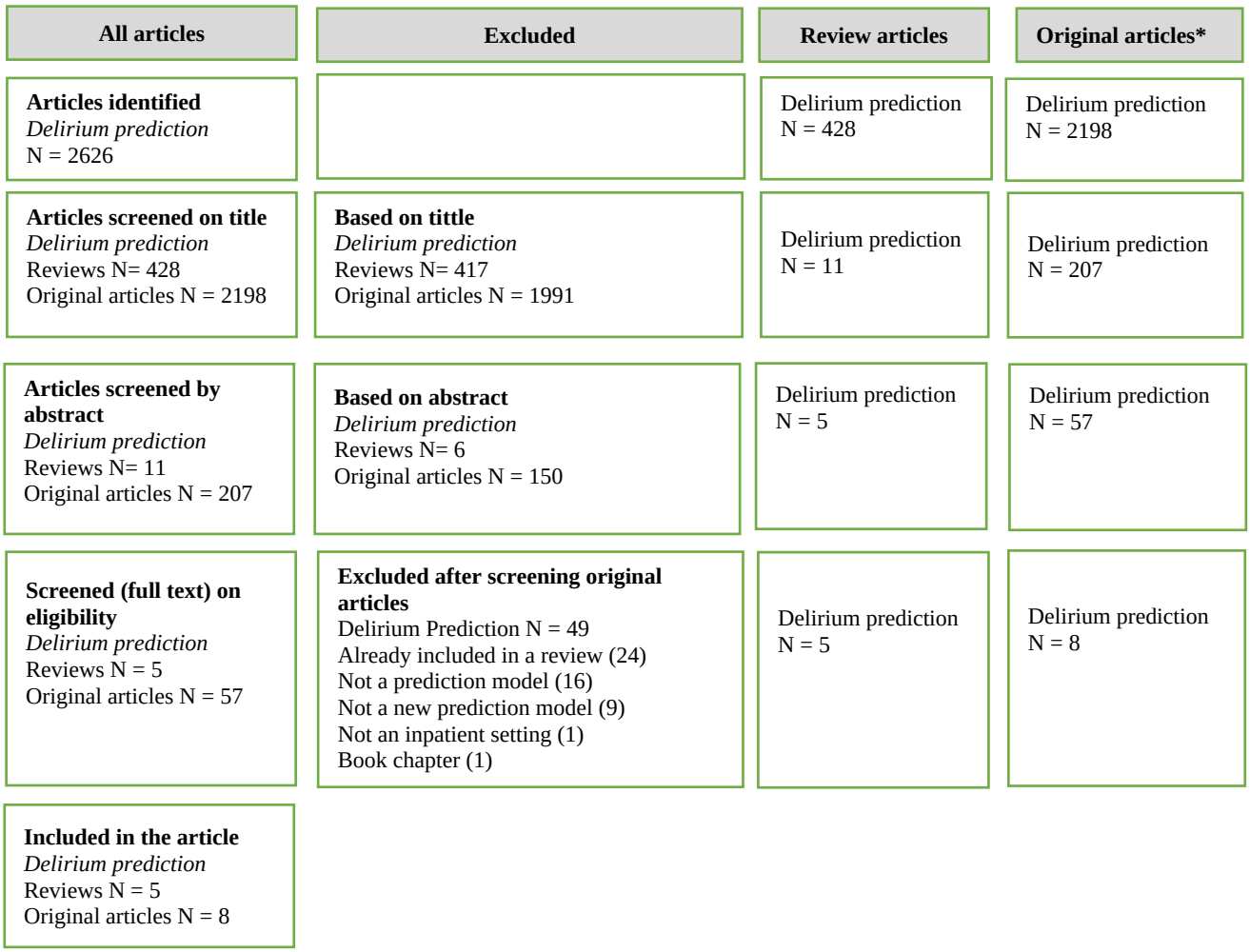
participatory research study. BMC Health Serv. Res. 2013, 13, 1–15. https://doi:10.1186/1472-6963-13-341
17. Kristiansen S, Konradsen H, Beck M. Nurses' experiences of caring for older patients afflicted by delirium in a neurological department. J. Clin. Nurs. 2018, 28, 920–930. https://doi:10.1111/jocn.14709
18. Martins S, Pinho E, Correia R, Moreira E, Lopes L, Paiva JA, Azevedo L, Fernandes L. What effect does delirium have on family and nurses of older adult patients? Aging Ment. Health 2017, 22, 903–911. https://doi:10.1080/13607863.2017.1393794
19. Christensen M. Nurses' knowledge of delirium: A survey of theoretical knowing. Kai Tiaki Nurs. Res. 2016, 7, 11–18.
20. Siddiqi N, Harrison JK, Clegg A, Teale EA, Young J, Taylor J, Simpkins SA. Interventions for preventing delirium in hospitalised non-ICU patients Cochrane Database Syst Rev. 2016 Mar 11;3:CD005563. https://doi:10.1002/14651858 .
21. Newman MW, O'Dwyer LC, Rosenthal L. Predicting delirium: a review of risk stratification models. Gen Hosp Psychiatry. Sep-Oct 2015;37(5):408-13. https://doi:10.1016/j.Genhosppsych.2015.05.003.
22. Kalimisetty S, Askar W, Fay B, Khan A. Models for Predicting Incident Delirium in Hospitalized Older Adults: A Systematic Review. J Patient Cent Res Rev. 2017 Apr 25;4(2):69-77. https://doi: 10.17294/2330-0698.1414
23. Lee S, Harland K, Mohr NM, Matthews G, Hess EP, Bellolio MF, Han JH, Weckmann M, Carnahan R. Evaluation of emergency department derived delirium prediction models using a hospital-wide cohort. J Psychosom Res. 2019 Dec; 127:109850. https://doi:10.1016/j.jpsychores.2019.109850
24. Lindroth H, Bratzke L, Purvis S, Brown R, Coburn M, Mrkobrada M, Chan MTV, Davis DHJ, Pandharipande P, Carlsson CM, Sanders RD. Systematic review of prediction models for delirium in the older adult inpatient. BMJ Open. 2018 Apr 28;8(4): e019223. https://doi:10.1136/bmjopen-2017-019223
25. Dylan F, Byrn G, Mudge AM. Delirium risk in non-surgical patients: systematic review of predictive tools. Arch Gerontol Geriatr. Jul-Aug 2019; 83:292-302. https://doi:10.1016/j.archger.2019.05.013.
26. Vochteloo AJ, Moerman S, van der Burg BL, de Boo M, de Vries MR, Niesten DD, Tuinebreijer WE, Nelissen RG, Pilot P. Delirium risk screening and haloperidol prophylaxis program in hip fracture patients is a helpful tool in identifying high-risk patients, but does not reduce the incidence of delirium. BMC Geriatr. 2011 Aug 11; 11:39. https://doi:10.1186/14712318-11-39
27. Ettema R, Heim N, Hamaker M, Emmelot-Vonk M, van der Mast R, Schuurmans M. Validity of a screening method for delirium risk in older patients admitted to a general hospital in the Netherlands. Gen Hosp Psychiatry. 2018 Nov - Dec; 55:44-50. https://doi:10.1016/j.genhosppsych.2018.09.004
28. Fan H, Ji M, Huang J, Yue P, Yang X, Wang C, Ying W. Development and validation of a dynamic delirium prediction rule in patients admitted to the Intensive Care Units (DYNAMIC-ICU): A prospective cohort study. Int J Nurs Stud. 2019 May; 93:64-73. https://doi:10.1016/j.ijnurstu.2018.10.008
29. Vreeswijk R, Kalisvaart I, Maier AB, Kalisvaart KJ. Development and Validation of the Delirium Risk Assessment Score (DRAS). Eur Geriatr Med. 2020 Apr;11(2):307-314. https://doi:10.1007/s41999-019-00287-w.
30. Pompei P, Foreman M, Rudberg MA, et al. Delirium in hospitalized older persons: outcomes and predictors. J Am Geriatr Soc 1994; 42:809–15. https://doi:10.1111/j.15325415.1994.tb06551.x

31. Liang CK, Chu CL, Chou MY, et al. Developing a prediction model for post-operative delirium and long-term outcomes among older patients receiving elective orthopedic surgery: a prospective cohort study in Taiwan. Rejuvenation Res 2015; 18:347–55. https://doi:10.1089/rej.2014.1645
32. Maekawa Y, Sugimoto K, Yamasaki M, et al. Comprehensive geriatric assessment is a useful predictive tool for postoperative delirium after gastrointestinal surgery in old-old adults. Geriatr Gerontol Int 2016;16. https://doi:10.1111/ggi.12587
33. Kalisvaart KJ, Vreeswijk R, Prevention of delirium in the elderly. Rev Esp Geriatr Gerontol. 2008;43 Suppl. 3:19-24.
34. DSM-V. American Psychiatric Association. May 2013. ISBN9780890425541
35. ICD. www.who.int/standards/classifications/classification-of-diseases
36. Laurila JV, Pitkala KH, Strandberg TE, Tilvis RS. The impact of different diagnostic criteria on prevalence rates for delirium. Dement.Geriatr.Cogn Disord. 2003; 16:156-62. https://doi:10.1159/000071004
37. de Jonghe JF, Kalisvaart KJ, Dijkstra M, van Dis H, Vreeswijk R, Kat MG, Eikelenboom P, van der Ploeg T, van Gool WA. Early symptoms in the prodromal phase of delirium: a prospective cohort study in elderly patients undergoing hip surgery. Am J Geriatr Psychiatry. 2007 Feb;15(2):112-21. https://doi:10.1097/01.JGP.0000241002.86410.c2.
38. Vreeswijk R., Timmers JF., Jonghe de JFM., Kalisvaart KJ. 2009 Assessment scales of delirium. Aging Health 2009;5 (3): 409-425
39. Adamis D, Sharmab N, Whelanc PJP., Macdonaldd AJD.. Delirium scales: A review of current evidence. Aging & Mental Health. Vol. 14, No. 5, July 2010, 543–555. https://doi:10.1080/13607860903421011
40. Grover S, Kate N. Assessment scales for delirium: A review. World J Psychiatr 2012 August 22; 2(4): 58-70. https://doi:10.5498/wjp.v2.i4.58
41. Carvalho JPL, Pinto de Almeida AR, Gusmao-Flores D. Delirium rating scales in critically ill patients: a systematic literature review. Rev Bras Ter Intensiva. 2013;25(2):148-154. https://doi:10.5935/0103-507X.20130026
42. van Velthuijsen EL, Zwakhalen SMG, Warnier RMJ, Mulder WJ, Verhey FRJ, Kempen G. Psychometric properties and feasibility of instruments for the detection of delirium in older hospitalized patients: a systematic review. Int J Geriatr Psychiatry. 2016;31(9):974-989. https://doi:10.1002/gps.4441
43. Jones RN, Cizginer S, Pavlech L, Albuquerque A, Daiello LA, Dharmarajan K, Gleason LJ, Helfand B, Massimo L, Oh E, Okereke OI, Tabloski P, Rabin LA, Yue J, Marcantonio ER, Fong TG, Hshieh TT, Metzger ED, Erickson K, Schmitt EM, Inouye S.K. Better Assessment of Illness (BASIL) Study Group. Assessment of Instruments for Measurement of Delirium Severity: A Systematic Review. JAMA Intern Med. 2019 Feb 1;179(2):231-239. https://doi:10.1001/jamainternmed.2018.6975
44. Helfand BKI, D'Aquila ML, Tabloski P, Erickson K, Yue J, Fong TG, Hshieh TT, Metzger ED, Schmitt EM, Boudreaux ED, Inouye SK, Jones RN. Detecting Delirium: A Systematic Review of Identification Instruments for Non-ICU Settings. J Am Geriatr Soc 00:1-9, 2020. https://doi:10.1111/jgs.16879
45. Samuel MJ. Postoperative Delirium in Older Adults: Best Practice Statement from the American Geriatrics Society. J Am Coll Surg. 2015. Vol.220 No.2. https://doi:10.1016/j.jamcollsurg.2014.10.019
46. Kalisvaart CJ, Vreeswijk R, de Jonghe JF, Milisen K. A systematic review of multifactorial interventions for primary prevention of delirium in the elderly. Tijdschr Gerontol Geriatr. 2005 Dec;36(6):224-31.
47. Clegg A, Siddiqi N, Heaven A, et al. Interventions for preventing delirium in older people in institutional long-term care. Cochrane Database Syst Rev 2014; 1:CD009537.

48. 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 Ageing. 2015 Mar;44(2):196-204. https://doi:10.1093/ageing/afu173
49. IAbraha J, Trotta F, Rimland JM, Cruz-Jentoft A, LozanoMontoya I, Soiza RL, Pierini V, Fulgheri PD, Lattanzio F, O'Mahony D, Cherubini A. Efficacy of Non-Pharmacological Interventions to Prevent and Treat Delirium in Older Patients: A Systematic Overview. The SENATOR project ONTOP Series PLoS One. 2015 Jun 10;10(6):e0123090. https://doi:10.1371/journal.pone.0123090.
50. Zhang H, Lu Y, Liu M, Zou Z, Wang L, Xu FY, Shi XY. Strategies for prevention of postoperative delirium: a systematic review and meta-analysis of randomized trials. Crit Care. 2013 Mar 18;17(2): R47. https://doi:10.1186/cc12566.
51. Hshieh TT, Yue J, Oh E, Puelle M, Dowal S, Travison T, et al.. Effectiveness of multicomponent nonpharmacological delirium interventions: a meta-analysis. JAMA Intern. Med. 2015. 175 512–520. https://doi:10.1001/jamainternmed.2014.7779
52. Wang Y, Tang J, Zhou F, Yang L, Wu J. Comprehensive geriatric care reduces acute perioperative delirium in elderly patients with hip fractures: A meta-analysis. Medicine (Baltimore). 2017 Jun;96(26):e7361. https://doi:10.1097/MD.0000000000007361
53. Ludolph P, Stoffers-Winterling J, Kunzler AM, Rösch R, Geschke K, Vahl CF, Lieb K, Non-Pharmacologic Multicomponent Interventions Preventing Delirium in Hospitalized People. JAGS. 2020 68:1864-1871. https://doi:10.1111/jgs.16565
54. Inouye SK, Schlesinger MJ, Lydon TJ. Delirium: a symptom of how hospital care is failing older persons and a window to improve quality of hospital care. Am J Med 1999 May;106(5):565-73. https://doi:10.1016/s0002-9343(99)00070-4.
55. Inouye SK, Bogardus ST, Baker DI, Leo-Summers L, Cooney LM. The Hospital Elder Life Program: a model of care to prevent cognitive and functional decline in older hospitalized patients. Hospital Elder Life Program. J. Am. Geriatr. Soc. 2000. 48 1697–1706. https://doi:10.1111/j.1532-5415.2000.tb03885.x
56. Morandi A, Davis, Taylor JK, Bellelli G, Olofsson B, Kreisel S, Teodorczuk A, Kamholz B, Hasemann W, Young J, Agar M, de Rooij SE, Meagher D, Trabucchi M, MacLullich AM. Consensus and variations in opinions on delirium care: a survey of European delirium specialists. Int Psychogeriatr. 2013 Dec; 25(12): 2067–2075. https://doi:10.1017/S1041610213001415
57. Sinvani L, Kozikowski A, Pekmezaris R, Akerman M, Wolf-Klein G. Delirium: A Survey of Healthcare Professionals' Knowledge, Beliefs, and Practices. J Am Geriatr Soc. 2016 Dec;64(12). https://doi:10.1111/jgs.14544
58. Davis D, MacLullich A. Understanding barriers to delirium care: a multicentre survey of knowledge and attitudes amongst UK junior doctors. Age Ageing. 2009 Sep;38(5):559-63. https://doi:10.1093/ageing/afp099
59. Jenkin RP, Al-Attar A, Richardson S, Myint PK, MacLullich AM, Davis DH. Increasing delirium skills at the front door: results from a repeated survey on delirium knowledge and attitudes. Age Ageing. 2016 Jul;45(4):517-22. https://doi:10.1093/ageing/afw066.
60. Xing J, Sun Y, Jie Y, Yuan Z, Liu W. Perceptions, attitudes, and current practices regards delirium in China: A survey of 917 critical care nurses and physicians in China. Medicine (Baltimore). 2017 Sep;96(39):e8028. https://doi:10.1097/MD.0000000000008028.
61. Patel RP, Gambrell M, Speroff T, Scott TA, Pun BT, Okahashi J, Strength C, Pandharipande P, Girard TD, Burgess H, Dittus RS, Bernard GR, Ely EW. Delirium and sedation in the intensive care unit: survey of behaviours and attitudes of 1384 healthcare professionals. Crit Care Med. 2009 Mar;37(3):825-32. https://doi:10.1097/CCM.0b013e31819b8608.

62. Greysen SR. Delirium and the “know-do” gap in acute care for elders. JAMA Intern. Med. 2015.175 521–522. https://doi:10.1001/jamainternmed.2014.7786
63. Bellelli G, Morandi A, Zanetti E, Bozzini M, Lucchi E, Terrasi M, Trabucchi M, AIP delirium study group. Recognition and management of delirium among doctors, nurses, physiotherapists, and psychologists: an Italian survey. Int Psychogeriatr. 2014 Dec;26(12):2093-102. https://doi:10.1017/S1041610214001653.
64. Griffiths A, Knight A, Harwood R, Gladman JR. Preparation to care for confused older patients in general hospitals: a study of UK-health professionals. Age Ageing. 2014 Jul;43(4):521-7. https://doi:10.1093/ageing/aft171
65. Yaghmour SM., Gholizadeh L, Review of Nurses’ knowledge of delirium, dementia and depression (3Ds): systematic literature review. Journal of nursing 2016, 6, 193-203. https://doi:10.4236/ojn.2016.63020

Fig. 1. Flowchart Review articles supplemented with original articles Delirium Prediction Models.



*Final inclusion were original articles not included in the found and used reviews

Table 1: Predisposing and precipitating risk factors for delirium [6]

Predisposing Risk Factors for delirium	**Precipitating Risk Factors for delirium**
Demographic and social factors: - Older age - Male gender - Institutional setting - Social isolation *Process of care:* - Iatrogenesis - Inadequate skills in recognition of delirium - Negative attitudes toward the care of the elderly - Rapid pace and technological focus of acute care - Reductions in skilled nursing staff *Special sensory impairment:* - Visual impairment - Hearing impairment *Cognitive and psychiatric comorbidity:* - Dementia - Degree of stage of dementia - Late onset Alzheimer's dementia - Vascular dementia - Cognitive impairment - Depression *Functional impairments and disability:* - Functional dependence Immobility Fracture on admission *Malnutrition:* - Dehydration - Alcoholism *Medical comorbidity:* - Hugh burden of Illness - Previous stroke - Parkinson's disease - Azotaemia	*Medications:* Substance withdrawal - Alcohol - Sedative hypnotics Substance intoxication - Sedative hypnotics - Narcotics - Anticholinergics - Antipsychotics - Antiparkinsonians - Antidepressants *Severe acute illness infections:* - Urinary tract infections - Pneumonia *Metabolic abnormalities:* - Hyperglycaemia/hypoglycaemia - Hypercalcemia/hypocalcaemia - Thyrotoxicosis/Myxoedema *Adrenal Insufficiency:* - Hepatic Failure - Renal Failure - Hypernatremia/Hyponatremia - Hyperkalaemia/Hypokalaemia *Hypoperfusion States and Pulmonary compromise:* - Hypoxemia - Shock - Anaemia - Congestive Heart Failure - Chronic Obstructive Pulmonary disease *Urinary and faecal retention* *Environmental-Psychological contributors:* - Sensory deprivation - Sensory overload - Psychological stress - Sleep deprivation - Pain - Physical restrain use - Bladder catheter use - Any iatrogenic event - Intensive care unit treatment *Surgery, anaesthesia and other procedures:* - Orthopaedic surgery - Cardiac surgery Duration of cardiopulmonary bypass - Non cardiac surgery - High number of procedures in hospital *Neurologic Illness:* - Subdural hematoma - Stroke - Malignancy - Cerebral Infection - Seizures

Table 2: Delirium prediction models

	Author **Name instrument** **Year** **Journal**	**Study design** **patient population N**	**Delirium screening** **Delirium incidence N (%)**	**Instrument variables**	**AUC**
1	**Inouye Model** Inouye *et al* 1993 Ann Int. Med.	Prospective Cohort Internal patients Age > 70 years Development cohort: 107 Validation cohort: 174	CAM, daily Development cohort: 27 (25) Validation cohort: 29 (17)	Predisposing factors - MMSE ≤ 24 >16 1 point - Vision impairment20/70 1 point - High urea/creatinine ratio 1 point - APACHE II >16 1 point	No AUC calculation
	Rudolph *et al* Inouye model 2011	Prospective Cohort Internal patients Validation cohort: 100	DSM-IV, daily interview Development cohort: 23 (23)		Validation cohort: AUC 0.53 (95% CI: 0.42 – 0.74)
2	**Risk stratification model** Pompei *et al* 1994 JAGS	Prospective Cohort Internal and surgical patients Age >65 years Development cohort: 432 Validation cohort: 323	CAM, 2 x a week, confirmation according DSM-III Development cohort: 64 (14.8) Validation cohort: 86 (26.3)	- Cognitive impairment - Comorbidity - Depression - Alcohol use	No AUC calculation
3	**Marcantonio model** Marcantonio *et al* 1994 JAMA	Prospective cohort Elective non cardiologic surgery Age >50 years Development cohort: 1341	CAM and patient file Development Cohort:117 (9)	- Alcohol abuse - TICS - Deviating lab (serum sodium, potassium, glucose) - Aortic aneurysm surgery - Non cardiac/thoracic surgery	Development cohort: AUC 0.81
4	**Two variables model** Fisher and Flowerdew 1995 JAGS	Prospective Cohort Elective orthopaedic Age >60 years Development cohort: 80	CAM, 2× daily Development cohort: 14 (17,5)	- Clock-drawing score ≤ 6 - Male gender	No AUC calculation
5	**Risk stratification model** O'Keeffe and Lavan 1996 Age Ageing	Prospective Cohort Acute geriatric unit patients Development cohort: 100 Validation cohort: 84 Age not mentioned	DAS, every 48 hour (DSM III) Development cohort: 28 (28) Validation cohort: 25 (30)	- Dementia - Severe illness - Raised serum urea	Development cohort: AUC 0.79 (95% CI: 0.69 – 0.90) Validation cohort: AUC 0.75 (95% CI: 0.63 – 0.86)
6	**DEAR** Freter *et al* 2005 Age aging 2015 Can Geriatric Journ.	Prospective Cohort Hip fracture Development cohort: 132 Age ≥65 years Validation cohort: 283 Age ≥65 years	CAM, daily Development cohort:24 (24) CAM, day 1, 3 and 5 Validation cohort: 119 (42)	- Age ≥80 years - Cognitive impairment (MMSE <24) - Substance use (alcohol > 3/week or benzodiazepine >3/week - Sensory impairment - Functional dependence (Need for ADL)	Development cohort: 0.77 (95% CI: 0.64 – 0.87) Validation cohort No AUC calculation

	Author **Name instrument** **Year** **Journal**	**Study design** **patient population N**	**Delirium screening** **Delirium incidence N (%)**	**Instrument variables**	**AUC**
7	**Kalisvaart model** Kalisvaart *et al* 2006	Prospective Cohort Hip fracture patients Age >65 years Validation cohort: 603	CAM, DRS-98, daily max 5 days after surgery confirmation by geriatrician. Validation cohort: 74 (12)	- Age - Acute admission - MMSE $\leq$ 24	Validation cohort: AUC 0.73 ((95% CI: 0.65 – 0.78)
8	**Delirium Risk Checklist** Koster et al 2008 Ann Thorac Surg Revised Delirium Risk Checklist Koster et al 2012 Eur. J. Cardiovasc. nursing	Observational cohort Elective cardiology Development cohort: 112 Age $\geq$45 years Elective cardiac surgery Validation (original version) and Development (revised version) cohort: 300 Age $\geq$45 years	DOSS and psychiatrist Development cohort: 24 (21) DOSS Development and validation cohort: 52 (17.3)	Delirium Risk Checklist original version - Lab values; electrolyte sodium and potassium - EURO score Revised delirium Risk Checklist - Higher EURO-score - Age $\geq$ 70 years - Cognitive impairment (MMSE ,23) - Number of comorbidities - History of delirium - Alcohol use - Type of surgery	Development cohort: AUC 0.75 (95% CI: 0.66 – 0.85) Validation cohort original version: 0.75 (95% CI: 0.66 – 0.85) Development cohort revised version: 0.89 (95% CI: 0.83 – 0.94)
9	**Risk stratification model** Rudolph *et al* 2009 Circulation	Prospective Cohort Cardiologic surgery Age >60 years Development cohort: 122 Validation cohort: 109	CAM, MDAS, DSI, daily Development cohort: 63 (52) Validation cohort: 48 (44)	- Stroke of transient ischemic attack in medical history 1 point - MMSE $\leq$ 23 2 points - MMSE 24 – 27 1 point - GDS $\geq$ 4 1 point - Albumin divergent 1 point	Development cohort: AUC 0.74 Validation cohort: AUC 0.75
10	**Risk Model for Delirium (RD)** Vochteloo 2011 BMC Geriatr. Moerman *et al* 2012	Prospective cohort Hip fracture Age >65 years Development cohort 445 Prospective Cohort Hip fracture Age >65 years Validation cohort: 378	DSM-IV Development cohort: 120 (27) Nursing observation 3× daily Confirmed by chart review Validation cohort: 102 (27)	- Earlier delirium 5 points - Dementia 5 points - Clock drawing; Minor fault 1 point Major fault 2 points - Hearing problem 1 point - Vision problem 1 point - ADL-problem: IADL impairment 0,5 point ADL impairment 0,5 point - Use heroin, methadone, morphine 1 point - Alcohol > 4 units 1 point	Development cohort: AUC 0.72 (95% CI 0.67 – 0.77) Validation cohort: AUC 0.73 (95% CI: 0.68 – 0.77)
11	**Risk stratification model** Isfandiaty *et al* 2012 Acta Med Indonesia	Retrospective Cohort Internal patients Age > 60 years Age >60 years Development cohort: 457	Not known, daily Development cohort: 87 (19)	- Infection (without sepsis) - Cognitive impairment - Decrease functional status	Development cohort: AUC 0.82 (95% CI: 0.78 – 0.88)

	Author Name instrument Year Journal	Study design patient population N	Delirium screening Delirium incidence N (%)	Instrument variables	AUC
12	**Clinical Prediction model** Martinez *et al* 2012 BMJ Open	Prospective Cohort Internal patients Age >18 years Development cohort: 397 Validation cohort: 302	CAM Development cohort: 53 (13) Validation cohort: 76 (25)	- Age >85 1 point - ADL >5 1 point - Medication at admission Medication 1 point Antipsychotic 2 points	Validation cohort 1: AUC 0.85 (95% CI: 0.80 – 0.88) Validation cohort 2: AUC 0.78 (95% CI: 0.68 – 0.88)
13	**PREDELIRIC** Boogaard et al 2012 BMJ.	Prospective cohort ICU Age >18 years Development cohort 1613 Validation cohort: 549	CAM-ICU, EPD patient, DSM-IV Development cohort: 411 (25.5) Validation cohort: 171 (31.1)	- APACHE - Reason admission - Coma - Infection - Metabolic acidosis - Sedatives/morphine use - Urea concentration - Acute admission - Age	Development cohort: AUC 0.87 (95% CI: 0.85 – 0.89) Validation cohort: AUC 0.89 (95% CI: 0.86 – 0.92) External validation: AUC 0.84 (95% CI: 0.82 – 0.87)
14	**AWOL** Douglas *et al* 2013 J Hosp. Med.	Prospective Cohort Internal patients Age >50 years Development cohort: 209 Validation cohort: 165	Short CAM, daily Development cohort: 25 (12) Validation cohort: 14 (8.5)	- Age ≥ 80 - World cannot spell backwards - Disorientation in location - Higher Nurse rated illness severity	Development cohort AUC 0.81(95% CI: 0.73 – 0.90) Validation cohort AUC 0.69 (95% CI: 0.54 – 0.83)
15	**Predictive Risk Score** Carrasco *et al* 2014 Age Aging	Prospective Cohort Internal patients Age > 65 years Development cohort: 374 Validation cohort: 104	CAM, every 48 hour Development cohort: 25 (0.06) Validation cohort: 12 (12)	- Barthel score - Dehydration (urea/creatinine level)	Development cohort: AUC 0.86 (95% CI: 0.82 – 0.91) Validation cohort: AUC 0.78 (95% CI: 0.66 – 0.90)
16	**Kennedy model** Kennedy et al. 2014 J. Am. Geriatr. Soc.	Prospective observational Cohort SHE Age >65 years Development Cohort: 700	CAM Development cohort: 63 (9)	- Age - CVA or ischemic attack in medical history - Dementia - Suspected infection - Acute intracranial bleeding	Development cohort AUC 0.77 (95% CI: 0.71 – 0.83)
17	**Dutch Safety Management (VMS)** Ettema *et al* 2018 Gen. Hosp. Psychiatry	Retrospective cohort Mixed population Age >70 years Validation cohort: 3786	DOSS, review patient file on antipsychotics, notes from either geriatrician or psychiatrist Validation cohort: (16,8)	Dutch National Safety Program: 3 questions; - Did you need assistance in ADL 24 hours before admission? 1 point - Do you have memory problems? 1 point - Have you experienced confusion during an earlier admission? 1 point Addition of more variables: - Age - Functional barriers (KATZ) - Number of medications prescribed - Vision problem	Validation cohort 3 question instrument AUC 0.81 (95% CI: 0.79 – 0.83) Validation cohort extended AUC 0.86 (95% CI: 0.84 -0.87)

	Author **Name instrument** **Year** **Journal**	**Study design** **patient population N**	**Delirium screening** **Delirium incidence N (%)**	**Instrument variables**	**AUC**
18	**CGA** Korc-Grodzicki *et al* 2015 Ann Surg.	Prospective Cohort Oncological surgery Age >75 years Development cohort: 416	CAM, daily Development cohort: 79 (19)	- Charlson Comorbidity Index score ≥ 3 - IADL =D - Fall = yes - Abnormal mini Cog	Development cohort: AUC 0.64
19	**CGA** Liang *et al* 2015 Rejuvenation	Prospective Cohort Elective orthopaedic surgery Age >60 years Development cohort: 461	CAM, daily, confirmed by psychologist (DSM-IV) Development cohort: 37 (8)	Comprehensive Geriatric Assessment: - Polypharmacy - Hearing impairment - ADL (Barthel ≤75) - Cognition (MMSE <24) - GDS-15 ≥ 5 Demographic factors: - Age ≥75 - Male - CCI ≥2 - Type of surgery (knee, hip spine)	No AUC calculation
20	**CGA** Maekawa *et al* 2016 Geriatric Gerontology Int.	Prospective Cohort Oncologic; gastrointestinal surgery Age >75 years Development cohort: 517	CAM Development cohort: 124 (24)	Comprehensive Geriatric Assessment	No AUC calculation
21	**DElirium MOdel (DEMO)** De Wit *et al* 2016 Int. J. Clin. Pharm. Gonzalvo et al. 2017 BMJ Open	Retrospective cohort Mixed population Age >60 years Development cohort: 1291 Observational Mixed population Age >60 years Validation cohort: 383	Chart review Development cohort: 225 (17) Chart review Delirium screening on 1, 3 and 5 day Validation cohort: 98 (25.6)	Automated delirium prediction model CDSS - Age - Polypharmacy - Anxiolytics - Anti-dementia - Antidepressant - Anti-Parkinson's agents - Antidiabetic - Psychopharmaca - Analgetics - Sleep medication	Development cohort: AUC 0.77 (95% CI: 0.74 – 0.81) Validation cohort:
22	**Mini-COG** Dworkin *et al* 2016 JAGS	Prospective Cohort Elective non-cardiac surgery Age >65 years Development cohort: 76	CAM of FAM-CAM, 1× after operation Development cohort 10 (13)	Mini-COG	Development cohort: AUC 0.77 (95% CI: 0.61 – 0.93)
23	**DELPHI** Kim *et al* 2016 Medicine	Prospective Cohort Major surgery Development cohort: 561 Validation cohort: 533	Nu-Desc: every shift by nurses' confirmation by CAM Development cohort: 112 (20) Validation cohort: 99 (18)	- Age; 60– 69 0 points 70 – 79 1 point ≥80 1 point - Low physical activity:	Development cohort AUC 0.91 (95% CI: 0.88 n- 0.94) Validation cohort AUC 0.94 (95% CI: 0.91 – 0.97)

	Author **Name instrument** **Year** **Journal**	**Study design** **patient population N**	**Delirium screening** **Delirium incidence N (%)**	**Instrument variables**	**AUC**
				Self-reliant 0 points Help needed 2 points - Lots of alcohol; No 0 points Yes 2 points - Hearing problem No 0 points Yes 1 point - Earlier delirium No 0 points Yes 2 points - Acute surgical No 0 points Yes 1 point - Open surgical procedure No 0 points Yes 2 points - ICU admission No 0 points Yes 3 points - CRP (mg/dL) <10 0 points ≥10 1 point	
24	**E-NICE risk** **Risk stratification model** Rudolph *et al* 2016	Retrospective cohort Development cohort: 27 625 Prospective Cohort Validation cohort: 246 Internal and surgical population	Development cohort: audit patient File Val: DSM-IV Daily interview Development cohort: 2342 (8) Validation cohort: 64 (26)	- Cognition 4 points - Age: ≥ 65 year. 2 points ≥ 80 year 3 points - Infection 2 points - Fracture 4 points - Vision problem 1 point - Severe Illnesses 2 points	Development cohort: AUC 0.81 (95% CI: 0.80 – 0.82) Validation cohort: AUC 0.69 (95% CI: 0.61 – 0.77)
25	Pendlebury *et al* 2017 Age Ageing	Prospective Cohort Internal patients Age ≥65 years Validation cohort: 308	CAM, every 48-hour confirmation by a DSM-IV-interview Validation cohort: 95 (31)	- Age ≥ 80 years 2 points - Cognitive problem 2 points - Severe illness 1 point - Infection. 1 point - Vision problem 1 point	Validation cohort: AUC 0.78 (95% CI: 0.71 – 0.84)
26	**DYNAMIC-ICU** Fan et al 2019 Int. J. Nurs. Stud.	Prospective cohort ICU patients: 560 Development Cohort: 336 Validation Cohort: 224	Development cohort: 68 (20.2) Validation cohort: 46 (20.5)	Predisposing factors: - History of chronic illnesses - Hearing impairment Illness related factors: - Infection - High APACHE II score on admission	Development cohort: AUC 0.91 (95%CI: 0.87 – 0.94) Validation cohort: AUC 0.90 (95% CI: 0.86 – 0.94)

	Author **Name instrument** **Year** **Journal**	**Study design** **patient population N**	**Delirium screening** **Delirium incidence N (%)**	**Instrument variables**	**AUC**
				- Iatrogenic and environmental factors - Use of sedatives and analgesics, - Indwelling catheter - Sleep disturbance	
27	**PANDA** Nakamizo et al. 2020 J. Neurological Sciences	Prospective cohort 387 Development cohort: Acute stroke patients	Intensive Care Delirium Screening Checklist Development cohort; 42 (12.1)	- Prior delirium - Alcohol (> 40g ethanol/day) - Stroke severity (HIHSS $\geq$ 5) - Dementia (diagnosed prior to admission) - Auditory/visual impairment	Development cohort: AUC 0.84 (95% CI: 0.78 – 0.89)
28	**Delirium Risk Assessment Score (DRAS)** Vreeswijk et al 2020 EUGM	Prospective cohort Development cohort: 842 Mixed population Validation cohort 1: 408 Orthopaedic population Validation cohort 2: 186 Surgical population Validation cohort 3: 365 Orthopaedic/surgical Age $\geq$70 years	CAM and geriatrician daily Development cohort:268 (31.8) Validation cohort 1: 83 (20.3) Validation cohort 2: 28 (15.1) Validation cohort 3: 57 (15.6)	- Acute admission 3 points - Cognitive impairment 3 points - Alcohol abuses > 4 units 3 points - ADL-impairment 2 points - Vision/hearing impairment 1 point - Earlier delirium 1 point - Medication 5 of more 1 point - Age $\geq$75 1 point	Development cohort: AUC 0.75 (95% CI: 0.79 – 0.58) Validation cohort 1: AUC 0.75 (95% CI: 0.71 – 0.72) Validation cohort 2: AUC 0.78 (95% CI: 0.60 – 0.89) Validation cohort 3: AUC 0.75 (95% CI: 0.67 – 0.74)

MMSE: Mini Mental State examination
CAM: Confusion Assessment Method
ADL: Activities of Daily Living
GDS: Geriatric depression scale
TICS: Telephone Interview for Cognitive Status
EPD: Electronic patient chart

Table 3: Delirium screening and severity scales.

								DSM-criteria					
Scale	**Year**	**Type of Scale**	**Examiner**	**Time**	**DSM**	**Cognitive test**	**Training**	**Acute onset**	**Fluctuating course**	**Inattention**	**Disorientation**	**Cognitive impairment**	**Ward**
Delirium Symptom Interview (DSI)	1992	Screening	Clinician	10-15 min	DSM-III	no	yes	no	yes	yes	yes	no	non-icu
Saskatoon Delirium Checklist (SDC)	1988	Screening	Clinician	5 min	DSM-III	no	yes	yes	yes	yes	yes	yes	non-icu
Visual Analog Scale for Acute Confusion (VAS-AC)	1986	Screening	Nurses	5 min	?	no	yes	no	no	yes	yes	no	non-icu
Confusion Assessment Method (CAM)	1990	Screening	Clinician	5-10 min	DSM-IV	yes	yes	yes	yes	yes	yes	no	non-icu
Clinical Assessment of Confusion–A and B (CAC-A & B)	1990	Screening	Nurses	10 min	DSM-III	yes	yes	no	no	no	yes	yes	non-icu
Confusion Rating Scale (CRS)	1991	Screening	Nurses	1-2 min	?	no	yes	no	yes	yes	yes	no	non-icu
Delirium Symptom Interview (DSI)	1992	Screening	Clinician	1-2 min	DSM-III	no	yes	no	yes	yes	yes	no	non-icu
Cognitive Test for Delirium (CTD)	1996	Screening	Clinician	10-15 min	DSM-III	yes	yes	no	no	yes	yes	yes	ICU
Neelon and Champagne Confusion Scale (NEECHAM)	1996	Screening	Clinician	3 min	DSM-IV	no	yes	no	yes	yes	yes	no	non-icu
Delirium Index (DI)	1998	Screening	Clinician	10 min	DSM-III	yes	yes	no	no	yes	yes	yes	non-icu
Intensive Care Delirium Screening Checklist (ICDSC)	2001	Screening	Nurses	10-15 min	DSM-IV	no	yes	no	yes	yes	yes	no	ICU
Delirium Observation Screening Scale (DOS)	2003	Screening	Nurses	5 min	DSM-IV	no	yes	no	no	yes	yes	no	non-icu
Nursing Delirium Screening Scale (Nu-DESC)	2005	Screening	Nurses	1-2 min	DSM-IV	no	yes	no	no	yes	yes	no	non-icu
Single Question for delirium	2010	Screening	Nurses	< 5 min	DSM-IV	no	no	no	no	no	yes	no	non-icu
4-A's Test (4-AT) Rapid Clinical test for delirium	2011	Screening	Clinician	< 2 min	DSM-IV	yes	no	yes	no	yes	yes	yes	non-icu
Confusion Assessment Method-ICU (CAM-ICU)	2011	Screening	Clinician	2-3 min	DSM-IV	yes	yes	yes	yes	yes	yes	no	ICU
Delirium Triage Screen (DTS)	2013	Screening	Clinician	< 1 min	DSM-IV	no	yes	no	no	yes	no	no	non-icu
Informant Assessment of geriatric delirium (IAGeD)	2013	Screening	?	5 min	DSM-IV	no	no	yes	no	yes	yes	no	non-icu
3D-Confusion Assessment Method (3D-CAM)	2014	Screening	Clinician	1 min	DSM-IV	yes	yes	yes	yes	yes	yes	no	non-icu
Stanford Proxy Test for Delirium (S-PTD)	2018	Screening	Clinician	< 1 min	DSM-V	no	yes	yes	yes	yes	yes	no	non-icu
Ultra-Brief Confusion Assessment Method (UB-CAM)	2020	Screening	Clinician	< 1 min	DSM-V	yes	yes	yes	yes	yes	yes	no	non-icu
Delirium Assessment Scale (DAS)	1994	Severity	Clinician	?	DSM-III	yes	yes	yes	yes	yes	yes	yes	non-icu
Memorial Delirium Assessment Scale (MDAS)	1997	Severity	Psychiatrist	< 30 min	DSM-IV	yes	yes	no	no	yes	yes	yes	non-icu
Confusion State Evaluation (CSE)	1997	Severity	Clinician	< 30 min	DSM-III	no	yes	yes	yes	yes	yes	no	non-icu
Delirium Index (DI)	1998	Severity	Clinician	10 min	DSM-IV	yes	yes	no	yes	yes	yes	no	non-icu

Delirium Severity Scale (DSS)	1998	Severity	Clinician	10 min	?	yes	yes	no	no	yes	no	no	non-icu
Delirium Rating Scale-Revised-98 (DRS-R-98)	2001	Severity	Clinician	20-30 min	DSM-IV	no	yes	yes	yes	yes	yes	yes	non-icu
Delirium-O-Meter (DOM)	2005	Severity	Nurses	3-5 min	DSM-IV	no	no	no	no	yes	yes	yes	non-icu
Delirium Detection Score (DDS)	2005	Severity	Nurses	?	DSM-IV	no	yes	no	no	no	yes	no	ICU
Confusion Assessment Method-severity scale (CAM-S)	2014	Severity	Clinician	< 5 min	?	yes	yes	yes	yes	yes	yes	no	non-icu

---

Time: time to perform,

DSM: on which DSM version the scale is based,

Cognitive test needed (yes or no)

Observation time necessary (yes or no)

Patient: screening done with or without patient

Training necessary (yes or no)
DSM criteria incorporated in scale (yes or no)

Table 4: Non-pharmacological interventions for prevention of delirium (for nurses).

	Risk factor	**Intervention**	
1	Orientation	Well known objects from home (e.g. pictures)	A
		Bed at window side/corner side /appropriate lighting	D
		Clock, calendar	A
		Passing by, short conversation, introduce yourself Orientation/test, give information	D D
		If room is to lively for this patient - 1 or 2-person room - same nurse constantly	A A
2	Cognitive problems MMSE < 25	Appropriate lighting, nightlight on	A
		Regular visits from family and friends	D
		Detailed orientation conversation (who, what, why, where)	D
		Nurse tells who she is, why she comes and what she is doing	A
3	Mobility	Encourage early mobility (e.g. walk, exercises, physiotherapy)	D
		Remove CAD/infuse/drain a.s.a.p	D
		Day schedule for mobilisation (rather often and shorter out of bed)	D
		Avoid restrains	A
4	Senses -Hearing - Sight	Screening for visual and hearing impairment	A
		Address sensory impairment by resolving any reversible cause of impairment (e.g. impacted ear wax)	A
		Are hearing aids available and working and used by the patient	A
		Are visual aids available and used by the patient	A
		Approach the patient from his/her best side	D
5	Intake - Fluid - Nutrition	Stimulate fluid intake by encouraging the patient to drink	D
		If patient is dehydrated, consider infusion and fluid balance	A
		Address poor nutrition (using SNAQ, MNA,)	A
		Stimulate food intake	D
		Bad intake - consult a Nutritionist	A
6	Pain	Address pain by using instruments (e.g. VAS)	D

		Looking for non-verbal signs of pain	D
		Initiate and reviewing appropriate pain management	A
		If pain medication, then attention for side effects	D
7	Sleep	Promote good sleep patterns and sleep hygiene by; - avoid nursing procedures during sleep hours - avoid medical procedures during sleep hours - reduce noise to a minimum during sleep hours - scheduling medications rounds to avoid sleep disturbance	 A A A A
		Stimulate activity during the daytime	D
		If possible, out of bed and mobilize the patient	D
		Use patient's rituals before going to sleep	D
		Use sleep medication (only if necessary)	A
8	Micturition & defecation	Echo for bladder retention	A
		Attention for constipation, ask for defecation	D
9	Patient	Educate patient at risk	A
		Inform patient about delirium prevention	A
10	Family	Inform family about delirium prevention and involve them if necessary in delirium prevention interventions.	A
11	Other	Educate each other /staff	A
		Use Delirium risk assessment model and delirium screening tool	D
12	Patient	Educate patient at risk	A
		Inform patient about delirium prevention	A

D = Daily checked/to do, A = Point of attention

Samenvattingen, discussie en conclusie

Delier is een serieuze complicatie welke veel voorkomt bij oudere patiënten die opgenomen worden in een algemeen ziekenhuis. Nog steeds is het aantal nieuwe gevallen van delier hoog, al wisselt het wel per specialisme. De incidentie percentages lopen op tot 65% en bij ICU-patiënten zelfs op tot 80%. Een delier periode kan voor de patiënt en zijn familie als zeer onaangenaam worden ervaren en kan lijden tot angst, onzekerheid en posttraumatisch stresssyndroom. Het doormaken van een delier kan lijden tot complicaties (vallen, functieverlies gedurende de opname) en een verhoogde kans op mortaliteit, cognitieve achteruitgang en institutionalisatie. Ook voor de verpleegkundige zorg is de belasting zeer groot, delirante patiënten verhogen de werkdruk, maar geven de verpleegkundigen ook gevoelens van te kort schieten als het gaat om zorg aan delirante patiënten en andere patiënten op hun afdeling. Daarnaast zijn de kosten die extra gemaakt moeten worden met betrekking tot de zorg bij delirante patiënten van belang. De extra ziekenhuiskosten worden gemiddeld geschat op 1200 Euro per delirante patiënt. Gemiddeld liggen delirante patiënten langer in het ziekenhuis, gebruiken meer materiaal, etc.. Ook na een ziekenhuisopname kunnen er extra kosten gemaakt moeten worden op het gebied van zorg (revalidatie, verzorgingshuis/verpleeghuis) en/of thuiszorg.
In de afgelopen 20 jaren is er veel gepubliceerd op het gebied van delier in al zijn facetten. Onderzoeken op het gebied van risicofactoren, preventieve interventies (farmacologisch en non-farmacologisch), screeningsinstrumenten, kennis en attitude van gezondheidzorg personeel en ervaringen van patiënten. Ook zijn er diverse delierrichtlijnen opgesteld. Maar desondanks de veelheid aan onderzoeken en de toename aan kennis, is in de praktijk nog weinig echt toegepast en geborgd als het gaat om het voorkomen van delier bij patiënten opgenomen in een algemeen ziekenhuis.
Onderzoek in de afgelopen 10 jaar toont nog steeds aan dat er een gebrek aan kennis is om delier te onderkennen, preventieve interventies toe te passen en screeningsinstrumenten te gebruiken. Zeker als onderzoek heeft aangetoond dat door simpele preventieve interventies een delier kan worden voorkomen. Sharon Inouye geeft percentages van 30 tot 40%. Zij geeft zelfs aan dat het percentage patiënten met een delier gedurende een ziekenhuisopname een indicatie kan zijn voor de kwaliteit van zorg van het ziekenhuis.

In het kader van deze introductie is de doelstelling van dit proefschrift:

- Vroegtijdig risicofactoren te onderkennen om het risico op een delier bij oudere patiënten die opgenomen worden in een algemeen ziekenhuis vast te stellen en daaruit een delier risico assessment instrument te ontwikkelen en te valideren. Het instrument moet eenvoudig in gebruik zijn. *(Prediction of delirium)*
- Welke meetschalen zijn er voorhanden om delier te herkennen, te diagnosticeren (screeningschalen)) en om de behandeling te evalueren (ernstschalen). *(Assessment of delirium)*
- Welke preventieve (non-)farmacologische interventies zijn er voorhanden om een delier te voorkomen.
  (Primary prevention of delirium)

DELIER RISICO VASTSTELLING

Delier preventie start met de juiste kennis en attitude van artsen en verpleegkundigen. Maar diverse studies hebben aangetoond dat onder andere verpleegkundigen de richtlijnen en ziekenhuisprotocollen met betrekking tot delier niet kennen. In de meeste gevallen worden protocollen niet gevolgd en het gebruik van screeningsinstrumenten in de dagelijks praktijk is niet gebruikelijk. [1,2] Verpleegkundigen gaven aan dat ze meer vertrouwen op de adviezen van een collega dan op richtlijnen. [3] Er zijn 4 barrières te onderscheiden waarom delierdetectie in de dagelijkse praktijk moeilijk verloopt, namelijk: bewustwording dat een patiënt een delier heeft, kennis en competentie, gebrek aan scholing en tijd. Kijken we naar

delier management dan geeft men de volgende redenen: gebrek aan kennis, organisatorische problemen, gebrek aan training en slechte attitude. [4]
Dit kan tot gevolg hebben dat bij oudere patiënten het risico op het krijgen van een delier onderschat wordt, het toepassen van preventieve interventies niet of te laat gebeurt en de symptomen van een delier verkeerd geïnterpreteerd worden of toegeschreven worden aan een dementie of depressie.
Er zijn reeds veel onderzoeken verricht naar (predisponerende en precipiterende) risicofactoren voor delier en van daaruit zijn delier risicomodellen ontwikkeld. Sharon Inouye en haar collega's waren een van de eerste die een voorspellend model ontwikkelde welke getest werd bij een interne geneeskunde patiëntenpopulatie.
Dit risico-stratificatie model is gebruikt in een studie naar haloperidol profylaxe voor de preventie van een delier bij heupfractuur patiënten. [5] Dit gaf de mogelijk om het risico stratificatie model te valideren in deze chirurgische populatie van 603 patiënten van 70 jaar en ouder. (**Hoofdstuk 3**) Het vaststellen van het risico op delier vond plaats bij opname en op basis van het model van Sharon Inouye en bestond uit 4 onderdelen die elk 1 punt kregen. De onderdelen waren: 1. Cognitie problemen op basis van de Mini Mental State Examination (MMSE), visus problemen op basis van de Snellen visustest, Apache II score en dehydratie op basis van de bloed ureum/creatine ratio. De mate van risico werd gedaan aan de hand van de gescoorde punten en resulteerde in 3 groepen: laag (0 punten), matig (1 of 2 punten) en hoog risico (3 of 4 punten). De uitkomstmaat was een postoperatief delier waarbij de diagnose vastgesteld werd op basis van de DSM-IV en de Confusion Assessment Method (CAM) welke dagelijks werd afgenomen.
Het resultaat was dat in de laag risicogroep 3.8%, in de matig risicogroep 11% en in de hoog risicogroep 37.1% delieren werden gediagnostiseerd. Daarbij hadden patiënten die acuut werden opgenomen een 4 keer zo grote kans om delirant te worden dan de electief opgenomen patiënten. Ook patiënten met een risicopunt op de MMSE wat aangaf dat er sprake zou kunnen zijn van cognitieve problemen hadden hoge samenhang met een later optredend delier. Als onafhankelijke voorspellende factor kwam nog de variabele leeftijd naar voren, een hogere leeftijd gaf meer risico.
De conclusie van dit onderzoek was dan ook dat het Sharon Inouye risicostratificatie model in een populatie oudere heupfractuur patiënten valide is. Dat mogelijke cognitieve stoornissen (op basis van MMSE), acute opname en hoge leeftijd de belangrijkste risicofactoren zijn in deze populatie. Verder geeft dit de mogelijkheid voor het ontwikkelen van een nieuw model, bestaande uit onafhankelijke risicofactoren gevonden in deze studie namelijk de MMSE, leeftijd en acute opname. Dit "nieuwe" model heeft in deze populatie minstens dezelfde voorspellende waarde als het Sharon Inouye risicostratificatie model voor de niet chirurgische patiëntenpopulatie.

Door de eerdergenoemde barrières als tijd, kennis en attitude die bij o.a. verpleegkundigen geconstateerd zijn kan het dagelijks gebruik van een risico stratificatie model weerstand opwekken doordat het arbeidsintensief is door gebruik van testen (MMSE), extra training behoeft of laboratorium waarden gebruikt die geïnterpreteerd moeten worden. Tevens moet vermeld worden dat een cognitieve screening als bijv de MMSE bij opname niet geheel betrouwbaar is. (Kat) Het gebruik van delier risicostratificatie modellen in de dagelijkse praktijk is mogelijk daarom nog minimaal. In geen van de gevonden onderzoeken naar kennis en attitude bij artsen en verpleegkundigen is onderzocht of er gebruik wordt gemaakt van delier risicostratificatie modellen. In Nederland is er de regel dat bij opname (binnen 24 uur) de patiënt gescreend wordt aan de hand van 3 vragen op het aanwezig zijn van een risico op delier (Veiligheid Management Systeem (VMS)). Deze methode is niet op wetenschappelijke basis ontwikkelend en nauwelijks gevalideerd. Naast de in Nederland gehanteerde VMS zijn er nog 30 andere risico stratificatie modellen ontwikkeld voor verschillende patiëntenpopulatie en voor de screening gebruik maken van testen, en/of bloedwaarden. Er

moet dus een eenvoudigere methode zijn om risico op een delier vast te stellen die voor verpleegkundigen makkelijk te gebruiken is en minder belastend is voor de patiënt.
De Delirium Risk Assessment Score (DRAS) is ontwikkeld als instrument om op eenvoudige en snelle manier vast te stellen of een patiënt een verhoogd risico heeft om een delier tijdens ziekenhuisopname te ontwikkelen. (**Hoofdstuk 4**) Er zijn daarvoor geen extra testen, bloedwaarden of training van verpleegkundigen nodig, veelal de informatie al aanwezig is of omdat de informatie tijdens het opnamegesprek gevraagd kan worden. De belasting voor de patiënt is minimaal. De DRAS is ontwikkeld in een gemengde patiëntenpopulatie (N = 842) en bestaat uit de variabelen: acute opname, cognitieve problemen, alcoholgebruik meer dan 4 eenheden per dag, zelfzorg en/of mobiliteitsproblemen, leeftijd 75 jaar of ouder, medicijn gebruik 5 of meer dagelijks, visus en/of gehoorproblemen en een eerder delier gehad. De maximale score is 15 punten en bij 5 of meer is er een risico op een delier. De validatie werd uitgevoerd in 3 cohorten (N = 408, N = 186, N = 365). En in cohort 3, de DRAS werd vergeleken) met 3 risicomodellen (Inouye, Kalisvaart, VMS-regels). De incidentie van delirium was 31,8%, 20,3%, 15,6% en 15,1%. Bij 5 of meer punten was AUC: 0,76 (95% BI 0,72-0,79), gevoeligheid 0,77, specificiteit 0,60. In de validatiecohorten was de AUC respectievelijk 0,75 (95% BI 0,96-0,81), 0,76 (95% BI 0,70-0,83) en 0,78 (95% BI 0,70-0,87), sensitiviteit 0,71, 0,67 en 0,89 en specificiteit 0,70, 0,72 en 0,60. De vergelijking met de andere 3 risicomodellen bracht de hoogste AUC voor de DRAS aan het licht.
Conclusie: Op basis van een opnamegesprek kan het deliriumrisico eenvoudig worden beoordeeld aan de hand van de DRAS bij oudere opgenomen patiënten. Het vergt van de verpleegkundige geen extra trainingen of testen en de tijd die nodig is om te scoren is $\pm$ 2 minuten. Daarbij is de DRAS niet ontwikkeld voor een specifieke patiëntenpopulatie zoals veel andere risicomodellen.
Ook in een meer specifieke populatie als oudere COVID-19 patiënten is een delier een ernstige complicatie die veel voorkomt. **(Hoofdstuk 5)** Van de 79 patiënten hadden er 28 een delier en van de patiënten die op de ICU lagen was het aantal hoger namelijk 10/13. Ook in deze populatie patiënten bleek de DRAS een model te zijn wat goed te gebruiken zou zijn om een delier te voorspellen, mede door zijn eenvoud en korte tijd van afname. De DRAS heeft in deze populatie een AUC 0.80 (95% CI 0.69-0.90). Daarbij werden alle patiënten met een score van 9 of hoger delirant.
De conclusie van dit onderzoek was dat delier veel voorkomt bij oudere COVID-19-patiënten en de DRAS voorspelt delier bij oudere COVID-19-patiënten.

ASSESSMENT VAN DELIER

Als bij een patiënt eenmaal een risico op het krijgen van een delier is vastgesteld zou een vervolg stap zijn om de patiënt te screenen op vroege symptomen van een zich ontwikkelend delier. Al voordat de diagnose delier gesteld kan worden zijn er al signalen/symptomen aanwezig. [7] De vroege symptomen die men kan signaleren zijn zowel van motorische (bijv. onrust, plukkerig) als psychologische aard (bijv. gedesoriënteerdheid, incoherentie). Vroegtijdige onderkenning van een delier kan aan de hand van ontwikkelde meetschalen voor een delier.
Er is een uitgebreid literatuuronderzoek uitgevoerd naar alle originele onderzoeksartikelen in de Nederlandse en Engelse literatuur over de validiteit van deliriummeetschalen. **(Hoofdstuk 6)** Het totaalaantal hits voor Medline was n = 369 en voor CINAHL n = 145. Artikelen werden geselecteerd als de titel of abstract verband hield met de ontwikkeling of toepasbaarheid van deliriumbeoordelingsschalen. In de referentielijsten van relevante artikelen is gezocht naar aanvullende referenties. In totaal werden 21 artikelen opgenomen in de eindbeoordeling. De gevonden meetschalen zijn opgesplitst in 8 screeningschalen: Confusion Assessment Scale (CAM); Delirium Observation Scale (DOS); Delirium Symptom Interview (DSI); Nursing Delirium Screening Scale (Nu-DESC); NEECHAM; Cognitive test

for Delirium (CTD); Confusion Assessment Method for IC (CAM-ICU) en de Intensive Care Delirium Screening Checklist (ICDS) en 7 ernstschalen: Delirium Rating Scales (DRS); Memorial Delirium Assessment Scale (MDAS); Confusional State Examination (CSE); Delirium Severity Scale (DSS); Delirium-index (DI); Delirium-O-Meter (DOM) en de Delirium Detection Scale (DDS). De betrouwbaarheidscoëfficiënten van de schalen varieerde van 0.59 tot 1.00 en de correlatie met externe criteria varieerde van 0.44 tot 0.93. Van de screenings schalen waren de CAM, de NEECHAM en de DOS het meest geschikt als screenings instrument voor de diagnose delier. Als ernst schaal voor delier lijkt de DRS-R-98 goed bruikbaar maar alleen als hij door getrainde artsen of verpleegkundigen wordt afgenomen.

Voor de Nederlandse situatie bleek er nog geen screeningsschaal voor de ICU voorhanden te zijn. Daarom is gekeken welke meetschaal er reeds ontwikkeld was om screening op delier te kunnen doen bij ICU-patiënten. Voor de ICU was alleen de CAM-ICU ontwikkeld in Amerika door Wes Ely. Om de CAM-ICU geschikt te maken voor de Nederlandse situatie moest hij vertaald en gevalideerd worden. **(Hoofdstuk 7)** De CAM-ICU werd eerst vertaald volgens de standaard richtlijnen voor vertalen. Daarna werd het validatieonderzoek van de Nederlandse CAM-ICU-versie uitgevoerd op de ICU van een groot Nederlands ziekenhuis. De patiënten werden door een geriater of een psychiater getest op klinische symptomen van delirium volgens de DSM IV-criteria (=referentiestandaard) en de resultaten werden vergeleken met onafhankelijk gescoorde CAM-ICU-uitkomsten van de onderzoeker. Dertig patiënten met Richmond Agitation and Sedation Scale (RASS) ≥ –3 werden beoordeeld op delirium met behulp van de CAM-ICU en de DSM-IV-criteria, wat resulteerde in 60 gepaarde tests. Negenentwintig patiënten werden opgenomen in de analyse. Op basis van de DSM-IV-criteria hadden 11 van de 29 patiënten een delier en 9 van de 29 scoorden positief op de CAM-ICU. Slechts drie patiënten werden anders gediagnosticeerd door de geriater of psychiater en de CAM-ICU, twee hadden een psychiatrische stoornis en één was gesedeerd en werd daarom uitgesloten. De algehele overeenkomst was 93,1%. In dit validatiecohort was de incidentie van delier 37,9%.
Conclusie De vertaling van de Nederlandse CAM-ICU vertoonde een goede correlatie met de originele Engelse versie en kan daarom worden gebruikt op een Nederlandse IC. De resultaten van het validatieonderzoek lieten een zeer goede overeenkomst zien tussen de klinische diagnoses die door de experts werden gesteld en de detectie van delirium met behulp van de Nederlandse CAM-ICU. De Nederlandse CAM-ICU detecteert betrouwbaar IC-delirium. Het biedt daarmee de middelen voor vroege opsporing, behandeling en secundaire preventie van IC-delier.

PRIMAIRE PREVENTIE VAN DELIER

Voor de preventie van een delier is het niet alleen noodzakelijk om aan delierrisico en vroegtijdige onderkenning van een delier te doen maar ook om preventieve interventies toe te passen om zo een delier proberen te voorkomen. Zo zijn er diverse non-farmacologische interventies variërend van oriëntatie tot training van medewerkers. In een literatuuronderzoek werd een systematische zoekactie gedaan in Medline, de Cochrane en CHINAL-database naar relevante onderzoeksartikelen. **(Hoofdstuk 8)** Referenties werden gecontroleerd op mogelijke andere artikelen. In totaal werden er 52 potentiele artikelen gevonden waarvan er 19 werden geselecteerd en daarvan bleven er uiteindelijk 6 over. Ondanks dat veel van de gevonden onderzoeken methodologische tekortkomingen hadden, bleken de toegepaste interventies wel effect te hebben op de preventie van een delier. De toegepaste interventies waren gericht op medische aspecten, verpleegkundige aspecten, omgevingsfactoren en educatie. In een aantal onderzoeken is er een combinatie te vinden en kan men spreken van een multi-factoren interventie preventie aanpak.

Ondanks de methodologische tekortkomingen van de onderzoeken, is de conclusie dat verschillende soorten medische, verpleegkundige, omgevings- en educatieve interventies (multifactorieel) om een delier te voorkomen in de praktijk effectief zijn.

In het laatste **hoofdstuk 9** is getracht een verbinding te leggen tussen de diverse onderdelen als delier risico, delier screening en preventieve interventies voor delier. Het hoofdstuk geeft een overzicht welke delier risicomodellen er in de afgelopen 20 jaar ontwikkeld zijn, welke meetschalen er nog verder ontwikkeld zijn om delier vroegtijdig vast ts stellen en delier ernst te meten en welke non-farmacologische interventies men kan toepassen. Er is daarnaast ook gekeken hoe de resultaten van de onderzoeken, dus de ontwikkelde modellen, schalen en interventies door de praktijk worden toegepast. Helaas is opvallende van dit hoofdstuk dat in de dagelijkse praktijk het gebruik van risicomodellen voor delier, screeningsschalen en preventieve interventies nog steeds niet goed geborgd is. Met betrekking tot risicomodellen gebruik is er geen onderzoek te vinden. Verder blijkt dat maar 26% tot 50% van gezondheidzorg medewerkers een screeningsschaal gebruik voor delier en dan nog niet eens op een routinematige basis. Ook als het gaat om preventieve interventies zijn de percentages niet hoger, het percentage varieert per onderzoek van 30% tot 67%.
De oorzaak hiervan is te vinden in een aantal barrières die uit onderzoek naar voren kwamen namelijk, de tijdsdruk, kennis en attitude die wijdverbreid zijn onder artsen en verpleegkundigen.

Dit hoofdstuk over de ontwikkeling van delierrisicomodellen, screeningsschalen en niet-medicamenteuze preventie laat zien dat alle benodigde instrumenten aanwezig zijn voor de ontwikkeling van een ziekenhuisdelierpreventieprogramma. Waardoor bij patiënten met een risico voor delier getracht kan worden een delier te voorkomen, aangezien screeningschalen voor delierdetectie beschikbaar zijn en niet-farmacologische preventieve interventies effectief zijn gebleken voor de preventie van delier. Maar een goede implementatie in de dagelijkse praktijk begint bij kennis en houding van verpleegkundigen en artsen.

WAT IS HET BELANG VAN DEZE ONDERZOEKEN?

Twintig jaar geleden beschreef Sharon Inouye de hoge incidentie van delier in ziekenhuizen als een prototypisch symptoom van de zwakke punten in onze ziekenhuiszorg, een combinatie van iatrogene incidenten, overmedicatie, het niet uitvoeren van een goede geriatrische beoordeling, afname van geschoold personeel, hoge zorgtempo en een slechte attitude met betrekking tot de zorg voor oudere patiënten. [8] Meer dan twintig jaar na de conclusie van Sharon Inouye zijn er steeds meer verbeteringen in de zorg voor de preventie van delier in ziekenhuizen, maar nog steeds niet genoeg. Er worden meer richtlijnen ontwikkeld en de opzet en implementatie van een deliriumpreventieprogramma maakt het mogelijk om de best mogelijke zorg te bieden aan patiënten met een risico op of met een delier. Een ziekenhuisdelierpreventieprogramma vereist predictie van het risico op delier, het gebruik van cognitieve en delierbeoordelingsschalen en niet-farmacologische preventieve interventies. De gevolgen van een delier zijn ingrijpend, zo is er een verhoogde kans op mortaliteit, cognitieve achteruitgang, opname in een instelling en functieverlies gedurende de ziekenhuisopname. Delier moet daarom ook gezien worden als een complicatie tijdens een ziekenhuisopname. De huidige praktijk laat zien dat er nog steeds onvoldoende besef is dat delier een ingrijpende gebeurtenis is voor zowel patiënt, zijn/haar familie als verpleegkundig personeel. Onderzoek toonde aan dat er gebrek aan kennis is en de attitude van o.a. de verpleegkundige richting (kwetsbare) oudere patiënten laat nog te wensen over. In de Nederlandse ziekenhuiszorg is de tendens om minder administratieve druk in de zorg te hebben, dit kan leiden tot minder alert zijn op patiënten met risico op delier om dat de daarbij behorende delierrisicomodellen, screeningsschalen en preventieve interventies niet worden toegepast. Maar het toepassen van

een eenvoudig te scoren risicomodel als bijv. de DRAS om patiënten met een verhoogd delier te onderkennen biedt de mogelijkheid om gericht preventieve interventies toe te passen bij diegene die het, het meest nodig hebben. Ieder delier dat voorkomen wordt zorg niet alleen voor een betere uitkomst voor de patiënt maar zorg ook voor minder werkdruk voor een verpleegkundige. Een delirante patiënt vergt namelijk veel extra zorg in ondersteuning, begeleiding en preventie van complicaties (bijv. verslikken, vallen, verwonding). Daarnaast zijn er nog de hogere kosten die een patiënt met een delier met zich meebrengt gedurende de ziekenhuisopname maar ook daarna.
Kijkend naar de non-farmacologische preventieve interventies valt op dat het geen hoog complexe zorg is. De preventieve interventies die onderzocht zijn eigenlijk normale basale zorghandelingen geleerd tijdens de opleiding tot verpleegkundige en die door iedere verpleegkundige uitgevoerd kan worden. Er moet alleen een bewustwording bij verpleegkundigen komen dat deze basale verpleegkundige zorg ook bijdraagt tot de preventie van een delier en dat deze interventies geen extra tijd kosten maar ook uitgevoerd kunnen worden gedurende de dagelijkse zorg.
Een goed ziekenhuisdelierpreventieprogramma vereist naast een delierrisico vaststelling en preventieve interventies ook het gebruik van een meetschaal om een delier vroegtijdig te onderkennen om zo erger te voorkomen. De meetschalen die ontwikkeld zijn, zijn veelal makkelijk in gebruik, betrouwbaar en gevalideerd en vergen minimale training. Het gebruik van een meetschaal kan bijdragen aan een goede uitvoer van een delier preventieplan voor de individuele patiënt.

WAT IS ER NODIG VOOR EEN GOEDE PREVENTIE VAN DELIER?

Zoals al aangegeven veel is al voorhanden om goede delierpreventie te kunnen toepassen in een algemeen ziekenhuis. Diverse risicomodellen voor delier en delier screeningschalen voor specifieke patiëntenpopulatie zijn ontwikkeld en preventieve interventies zijn beschreven. Waarom lukt het dan niet om delier in algemene ziekenhuizen te voorkomen?
Allereerst kan men nog zoveel ontwikkelen als er in de praktijk geen gebruik van wordt gemaakt of onderzoek bereikt de werkvloer niet heeft het geen enkele zin. Onderzoek heeft al aangetoond dat de kennis en attitude van gezondheidspersoneel te wensen overlaat en als er enige vorm van training (tijdens opleiding of werk) wordt gegeven dat men zich meer vertrouwd voelt in het gebruik van schalen en preventieve interventies.
Daarnaast is de verscheidenheid van risicomodellen en screeningschalen nog erg groot. Ze zijn voor specifieke populaties ontwikkeld of (nog) niet goed gevalideerd in andere populaties. Welke te kiezen blijft dus veelal voor een gebruiker op de werkvloer moeilijk. Preventie en risicovaststelling behoeft meer verfijning en onderzoek in andere populaties. Validering in andere populaties kan bijdragen in het meer algemeen gebruik van risicomodellen.

AFSLUITEND

Delier komt veelvuldig voor bij oudere opgenomen patiënten en het wisselt per populatie. Delier moet gezien worden als een complicatie van de zorg die er verleend wordt en preventie is zeker mogelijk. In de afgelopen 20 jaar is er veel onderzoek verricht naar de diverse aspecten van delier waaronder preventie, maar er is nog weinig toepassing daarvan in de dagelijkse praktijk. Dat het weinig nog wordt toegepast in de dagelijkse praktijk is vreemd zeker omdat delier een grote impact kan hebben voor de patiënt en zijn naaste, maar ook voor verpleegkundigen en de maatschappij.

Referenties

1. Selim AA, Ely EW. Delirium the under-recognized syndrome: survey of healthcare professionals' awareness and practice in the intensive care units. J Clin Nurs. 2017 Mar;26(5-6):813-824.
2. Trogrlić Z, Ista E, Ponssen HH, Schoonderbeek JF, Schreiner F, Verbrugge SJ, Dijkstra A, Bakker J, van der Jagt M. Attitudes, knowledge and practices concerning delirium: a survey among intensive care unit professionals. Nurs Crit Care. 2017 May;22(3):133-140
3. Emme C. "It should not be that difficult to manage a condition that is so frequent": A qualitative study on hospital nurses' experience of delirium guidelines. J Clin Nurs. 2020 Aug;29(15-16):2849-2862. doi: 10.1111/jocn.15300. Epub 2020 May 11.
4. Morandi D. Davis JK. Taylor G. Bellelli B. Olofsson, Kreisel S, Teodorczuk A, Kamholz B, Hasemann W, Young J, M. Agar, de Rooij SE, Meagher D, Trabucchi M, MacLullich AM. Consensus and variations in opinions on delirium care: a survey of European delirium specialists. Int Psychogeriatr. 2013 Dec; 25(12): 2067–2075.
5. Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. JAMA. 1996 Mar 20;275(11):852-7.
6. Kalisvaart KJ, de Jonghe JFM., Bogaards MJ, Vreeswijk R, Egberts TC, Burger BJ, Eikelenboom P, van Gool WA. Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: a randomized placebo-controlled study. J Am Geriatr Soc. 2005 Oct;53(10):1658-66. doi: 10.1111/j.1532-5415.2005.53503. x.
7. de Jonghe JFM, Kalisvaart KJ, Dijkstra, van Dis H, Vreeswijk ., Kat MG, Eikelenboom P, van der Ploeg T, van Gool WA.. Early symptoms in the prodromal phase of delirium: a prospective cohort study in elderly patients undergoing hip surgery. Am J Geriatr Psychiatry. 2007 Feb;15(2):112-21. doi: 10.1097/01.JGP.0000241002. 86410.c2.
8. Inouye SK, Schlesinger MJ, Lydon TJ. Delirium: a symptom of how hospital care is failing older persons and a window to improve quality of hospital care. Am J Med. 1999 May;106(5):565-73. doi: 10.1016/s0002-9343(99)00070-4.

Summaries, discussion and conclusion

Delirium is a serious complication that is common in elderly patients admitted to a general hospital. The number of new cases of delirium is still high, although it varies per specialism. The incidence percentages are up to 65% and in ICU patients even up to 80%. A period of delirium can be experienced as very unpleasant for the patient and his family and can lead to anxiety, insecurity and post-traumatic stress syndrome. Going through delirium can lead to complications (fall, loss of function during hospitalization) and an increased risk of mortality, cognitive decline and institutionalization. The burden on nursing care is also very great, delirious patients increase the workload, but the nurses also feel that they are falling short when it comes to caring for delirious patients and other patients in their ward. In addition, the extra costs that have to be incurred with regard to the care of delirious patients are important. The extra hospital costs are estimated on average at 1200 Euros per delirious patient. On average, delirious patients spend longer in hospital, use more equipment, etc. Even after hospitalization, additional costs may have to be incurred in the field of care (rehabilitation, care home/nursing home) and/or home care.
In the past 20 years, much has been published in the field of delirium in all its facets. Research into risk factors, preventive interventions (pharmacological and non-pharmacological), screening instruments, knowledge and attitude of health care personnel and experiences of patients. Various delirium guidelines have also been drawn up.
But despite the multitude of studies and the increase in knowledge, little has been really applied and guaranteed in practice when it comes to preventing delirium in patients admitted to a general hospital.
Research over the past 10 years still shows that there is a lack of knowledge to identify delirium, apply preventive interventions and use screening tools. Especially if research has shown that delirium can be prevented by simple preventive interventions. Sharon Inouye gives percentages from 30 to 40%. She even indicates that the percentage of patients with delirium during hospitalization can be an indication of the quality of hospital care.

In the context of this introduction, the aim of this thesis is:
- Early identification of risk factors to determine the risk of delirium in elderly patients admitted to a general hospital and to develop and validate a delirium risk assessment tool. The instrument must be easy to use. (Prediction of delirium)
- Which measurement scales are available to recognize, diagnose delirium (screening scales) and to evaluate the treatment (severity scales). (Assessment of delirium)
- Which preventive (non-) pharmacological interventions are available to prevent delirium. (Primary prevention of delirium)

DELIRIUM RISK ASSESSMENT

Delirium prevention starts with the right knowledge and attitude of doctors and nurses. But several studies have shown that nurses, among others, do not know the guidelines and hospital protocols regarding delirium. In most cases protocols are not followed and the use of screening instruments in daily practice is not common. [1,2] Nurses indicated that they rely more on the advice of a colleague than on guidelines. [3] Four barriers can be distinguished why delirium detection is difficult in daily practice, namely: awareness that a patient has delirium, knowledge and competence, lack of training and time. If we look at delirium management, the following reasons are given: lack of knowledge, organizational problems, lack of training and bad attitude. [4]
As a result, the risk of developing delirium in older patients is underestimated, preventive interventions are applied too late or not at all, and the symptoms of delirium are misinterpreted or attributed to dementia or depression.

Many studies have already been conducted into (predisposing and precipitating) risk factors for delirium, and delirium risk models have been developed from this. Sharon Inouye and her colleagues were among the first to develop a predictive model that was tested in an internal medicine patient population.
This risk-stratification model was used in a study on haloperidol prophylaxis for the prevention of delirium in hip fracture patients. [5] This allowed the validation of the risk stratification model in this surgical population of 603 patients aged 70 years and older. (Chapter 3) The assessment of the risk of delirium took place on admission and was based on the model of Sharon Inouye and consisted of 4 parts, each of which received 1 point. The components were: 1. Cognition problems based on the Mini Mental State Examination (MMSE), vision problems based on the Snellen vision test, Apache II score and dehydration based on the blood urea/creatine ratio. The degree of risk was based on the points scored and resulted in 3 groups: low (0 points), moderate (1 or 2 points) and high risk (3 or 4 points). The outcome measure was postoperative delirium with the diagnosis based on the DSM-IV and the Confusion Assessment Method (CAM), which was administered daily.
The result was that in the low-risk group 3.8%, in the moderate-risk group 11% and in the high-risk group 37.1% were diagnosed with delirium. In addition, acutely admitted patients were 4 times more likely to become delirious than the electively admitted patients. Also, patients with a risk point on the MMSE that indicated that there could be cognitive problems had a high correlation with a later onset delirium. The variable age also emerged as an independent predictive factor, while a higher age gave more risk.
The conclusion of this study was therefore that the Sharon Inouye risk stratification model is valid in a population of older hip fracture patients. That possible cognitive impairment (based on MMSE), acute admission and advanced age are the most important risk factors in this population. Furthermore, this provides the opportunity to develop a new model, consisting of independent risk factors found in this study, namely the MMSE, age and acute admission. This “new” model has at least the same predictive value in this population as the Sharon Inouye risk stratification model for the non-surgical patient population.

Due to the aforementioned barriers such as time, knowledge and attitude that have been observed among nurses, the daily use of a risk stratification model can generate resistance because it is labor-intensive due to the use of tests (MMSE), requires extra training or uses laboratory values that have to be interpreted. . It should also be noted that a cognitive screening such as the MMSE upon admission is not entirely reliable. (Kat) The use of delirium risk stratification models in daily practice may therefore still be minimal. None of the studies that were found into knowledge and attitude among doctors and nurses have examined whether delirium risk stratification models are used. In the Netherlands there is a rule that on admission (within 24 hours) the patient is screened on the basis of 3 questions for the presence of a risk of delirium (Safety Management System (VMS)). This method has not been developed on a scientific basis and has hardly been validated. In addition to the VMS used in the Netherlands, 30 other risk stratification models have been developed for different patient populations and using tests and/or blood values for screening. There must therefore be a simpler method of assessing risk of delirium that is easy for nurses to use and less burdensome for the patient.
The Delirium Risk Assessment Score (DRAS) has been developed as an instrument to quickly and easily determine whether a patient has an increased risk of developing delirium during hospitalization. (Chapter 4) No additional tests, blood values or training of nurses are required, often the information is already available or because the information can be requested during the admission interview. The burden on the patient is minimal. The DRAS was developed in a mixed patient population (N = 842) and consists of the variables: acute admission, cognitive problems, alcohol consumption more than 4 units per day, self-care and/or mobility problems, age 75 years or older, drug use 5 or more daily, vision and/or

hearing problems and had a previous delirium. The maximum score is 15 points and with 5 or more there is a risk of delirium. The validation was performed in 3 cohorts (N = 408, N = 186, N = 365). And in the cohort 3, the DRAS was compared) with 3 risk models (Inouye, Kalisvaart, VMS rules). The incidence of delirium was 31.8%, 20.3%, 15.6% and 15.1%. At 5 or more points, AUC was: 0.76 (95% CI 0.72-0.79), sensitivity 0.77, specificity 0.60. In the validation cohorts, AUC was 0.75 (95% CI 0.96-0.81), 0.76 (95% CI 0.70-0.83) and 0.78 (95% CI 0.70-0.83), respectively. 0.87), sensitivity 0.71, 0.67 and 0.89 and specificity 0.70, 0.72 and 0.60. The comparison with the other 3 risk models revealed the highest AUC for the DRAS.
Conclusion: Based on an admission interview, the risk of delirium can be easily assessed using the DRAS in older admitted patients. It requires no extra training or testing from the nurse and the time needed to score is + 2 minutes. In addition, the DRAS has not been developed for a specific patient population like many other risk models.
Delirium is also a serious complication that occurs frequently in a more specific population such as older COVID-19 patients. (Chapter 5) Of the 79 patients, 28 had delirium and the number of patients in the ICU was higher, namely 10/13. Also, in this population of patients, the DRAS proved to be a good model to use to predict delirium, partly due to its simplicity and short administration time. The DRAS in this population has an AUC of 0.80 (95% CI 0.69-0.90). In addition, all patients with a score of 9 or higher became delirious.
The conclusion of this study was that delirium is common in elderly COVID-19 patients and the DRAS predicts delirium in elderly COVID-19 patients.

ASSESSMENT OF DELIRIUM

Once a patient has been identified at risk of developing delirium, the next step would be to screen the patient for early symptoms of developing delirium. Signs/symptoms are already present before the diagnosis of delirium can be made. [7] The early symptoms that can be identified are both motor (e.g., restless, picky) and psychological (e.g., disorientation, incoherence). Early identification of a delirium is possible on the basis of developed measuring scales for a delirium.
An extensive literature search was performed on all original research articles in the Dutch and English literature on the validity of delirium measurement scales. (Chapter 6) The total number of hits for Medline was n = 369 and for CINAHL n = 145. Articles were selected if the title or abstract was related to the development or applicability of delirium rating scales. Additional references were searched in the reference lists of relevant articles. A total of 21 articles were included in the final assessment. The measurement scales found are divided into 8 screening scales: Confusion Assessment Scale (CAM); Delirium Observation Scale (DOS); Delirium Symptom Interview (DSI); Nursing Delirium Screening Scale (Nu-DESC); NEECHAM; Cognitive test for Delirium (CTD); Confusion Assessment Method for IC (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDS) and 7 severity scales: Delirium Rating Scales (DRS); Memorial Delirium Assessment Scale (MDAS); Confusional State Examination (CSE); Delirium Severity Scale (DSS); Delirium Index (DI); Delirium-O-Meter (DOM) and the Delirium Detection Scale (DDS). The reliability coefficients of the scales ranged from 0.59 to 1.00 and the correlation with external criteria ranged from 0.44 to 0.93. Of the screening scales, the CAM, NEECHAM and DOS were the most suitable screening instruments for the diagnosis of delirium. The DRS-R-98 seems useful as a severity scale for delirium, but only if administered by trained doctors or nurses.

For the Dutch situation, there appeared to be no screening scale for the ICU. Therefore, it was examined which measurement scale had already been developed to enable screening for delirium in ICU patients. Before the ICU, only the CAM-ICU was developed in America by Wes Ely. To make the CAM-ICU suitable for the Dutch situation, it had to be translated and

validated. (Chapter 7) The CAM-ICU was first translated according to standard translation guidelines. After that, the validation study of the Dutch CAM-ICU version was performed in the ICU of a large Dutch hospital. Patients were tested by a geriatrician or psychiatrist for clinical signs of delirium according to the DSM IV criteria (= reference standard) and the results were compared with the investigator's independently scored CAM-ICU outcomes. Thirty patients with Richmond Agitation and Sedation Scale (RASS) ≥ –3 were assessed for delirium using the CAM-ICU and DSM-IV criteria, resulting in 60 paired tests. Twenty-nine patients were included in the analysis. Based on the DSM-IV criteria 11 of 29 patients had delirium and 9 of 29 scored positive on the CAM-ICU. Only three patients were diagnosed differently by the geriatrician or psychiatrist and the CAM-ICU, two had a psychiatric disorder and one was sedated and therefore excluded. The overall agreement was 93.1%. In this validation cohort, the incidence of delirium was 37.9%.
Conclusion The translation of the Dutch CAM-ICU showed a good correlation with the original English version and can therefore be used on a Dutch IC. The results of the validation study showed a very good agreement between the clinical diagnoses made by the experts and the detection of delirium using the Dutch CAM-ICU. The Dutch CAM-ICU reliably detects IC delirium. It thus provides the means for early detection, treatment and secondary prevention of IC delirium.

PRIMARY PREVENTION OF DELIRIUM

For the prevention of delirium, it is not only necessary to deal with delirium risk and early recognition of a delirium, but also to apply preventive interventions in order to try to prevent a delirium. There are various non-pharmacological interventions, ranging from orientation to employee training. In a literature search, a systematic search was performed in Medline, the Cochrane and CHINAL database for relevant research articles. (Chapter 8) References were checked for possible other articles. In total, 52 potential articles were found, of which 19 were selected and of which 6 ultimately remained. Despite the fact that many of the studies found had methodological shortcomings, the applied interventions did appear to have an effect on the prevention of delirium. The applied interventions focused on medical aspects, nursing aspects, environmental factors and education. In a number of studies, a combination can be found, and one can speak of a multi-factor intervention prevention approach.
Despite the methodological shortcomings of the studies, it is concluded that different types of medical, nursing, environmental and educational interventions (multifactorial) to prevent delirium are effective in practice.

In the last chapter 9 an attempt was made to establish a connection between the various components such as delirium risk, delirium screening and preventive interventions for delirium. The chapter provides an overview of which delirium risk models have been developed in the past 20 years, which measurement scales have been further developed to diagnose delirium early and measure delirium severity and which non-pharmacological interventions can be applied. In addition, it was also examined how the results of the studies, i.e. the models, scales and interventions developed, are applied in practice. Unfortunately, what is striking about this chapter is that the use of risk models for delirium, screening scales and preventive interventions is still not well secured in daily practice. There is no research to be found with regard to risk models use. Furthermore, it appears that only 26% to 50% of healthcare professionals use a screening scale for delirium and even on a routine basis. Even when it comes to preventive interventions, the percentages are not higher, the percentage varies per study from 30% to 67%.
The reason for this can be found in a number of barriers that have emerged from research, namely the time pressure, knowledge and attitude that are widespread among doctors and nurses.

This chapter on the development of delirium risk models, screening scales and non-drug prevention shows that all necessary tools are in place for the development of a hospital delirium prevention program. Therefore, in patients at risk for delirium, efforts can be made to prevent delirium, as screening scales for delirium detection are available and non-pharmacological preventive interventions have been shown to be effective for the prevention of delirium. But a good implementation in daily practice starts with the knowledge and attitude of nurses and doctors.

WHAT IS THE IMPORTANCE OF THESE STUDIES?

Twenty years ago, Sharon Inouye described the high incidence of delirium in hospitals as a prototypical symptom of the weaknesses in our hospital care, a combination of iatrogenic incidents, overmedication, failure to perform proper geriatric assessment, reduction in skilled staff, high rate of care and poor attitude towards the care of elderly patients. [8] More than twenty years after Sharon Inouye's conclusion, there have been more and more improvements in care for the prevention of delirium in hospitals, but still not enough. More guidelines are being developed and the design and implementation of a delirium prevention program makes it possible to provide the best possible care to patients at risk for or with delirium. A hospital delirium prevention program requires prediction of the risk of delirium, the use of cognitive and delirium rating scales and non-pharmacological preventive interventions.
The consequences of delirium are serious, for example there is an increased risk of mortality, cognitive decline, admission to an institution and loss of function during hospitalization. Delirium should therefore also be seen as a complication of hospitalization.

Current practice shows that there is still insufficient awareness that delirium is a major event for the patient, his/her family and nursing staff. Research has shown that there is a lack of knowledge and the attitude of, among others, the nurse towards (vulnerable) older patients still leaves much to be desired. In Dutch hospital care there is a tendency to have less administrative burden in care, which can lead to less alertness to patients at risk of delirium because the associated delirium risk models, screening scales and preventive interventions are not applied. But applying an easy-to-score risk model such as the DRAS to identify patients with increased delirium offers the possibility to apply preventive interventions in a targeted manner to those who need it most. Any delirium that is prevented not only ensures a better outcome for the patient, but also reduces the workload for a nurse. A delirious patient requires a lot of extra care in support, guidance and prevention of complications (e.g. choking, falling, injury). In addition, there are the higher costs that a patient with delirium entails during hospitalization and afterwards.

Looking at the non-pharmacological preventive interventions, it is striking that it is not a highly complex care. The preventive interventions studied are actually normal basic care practices learned during nurse training and can be performed by any nurse. The only thing that needs to be done is to make nurses aware that this basic nursing care also contributes to the prevention of delirium and that these interventions do not cost extra time but can also be carried out during daily care.

In addition to a delirium risk assessment and preventive interventions, a good hospital delirium prevention program also requires the use of a measurement scale to recognize delirium early in order to prevent it from getting worse. The measuring scales that have been developed are often easy to use, reliable and validated and require minimal training. The use of a measurement scale can contribute to the proper implementation of a delirium prevention plan for the individual patient.

WHAT ELSE IS NEEDED FOR EFFECTIVE PREVENTION OF DELIRIUM?

As already indicated, much is already available to be able to apply good delirium prevention in a general hospital. Various risk models for delirium and delirium screening scales for specific patient populations have been developed and preventive interventions have been described. Why is it not possible to prevent delirium in general hospitals?
First of all, so much can still be developed if it is not used in practice or if research does not reach the workplace, it makes no sense. Research has already shown that the knowledge and attitude of health personnel leaves something to be desired and that if any form of training (during education or work) is provided, people feel more comfortable in the use of scales and preventive interventions.
In addition, the diversity of risk models and screening scales is still very large. They have been developed for specific populations or have not (yet) been well validated in other populations. Which one to choose often remains difficult for a user on the work floor. Prevention and risk assessment needs more refinement and research in broader scope of patient populations. Validation in other populations may contribute to the more widespread use of risk models, followed by using screening tools and preventive interventions.

CLOSING REMARKS

Delirium is common in older hospitalized patients and varies by population. Delirium must be seen as a complication of the care provided and prevention is certainly possible. In the past 20 years a lot of research has been done on the various aspects of delirium, including prevention, but there is still little application in daily practice. It is strange that it is still little used in daily practice, because delirium can have a major impact on patients and their loved ones, but also on nurses and society.

References

1. Selim AA, Ely EW. Delirium the under-recognized syndrome: survey of healthcare professionals' awareness and practice in the intensive care units. J Clin Nurs. 2017 Mar;26(5-6):813-824.
2. Trogrlić Z, Ista E, Ponssen HH, Schoonderbeek JF, Schreiner F, Verbrugge SJ, Dijkstra A, Bakker J, van der Jagt M. Attitudes, knowledge and practices concerning delirium: a survey among intensive care unit professionals. Nurs Crit Care. 2017 May;22(3):133-140
3. Emme C.. "It should not be that difficult to manage a condition that is so frequent": A qualitative study on hospital nurses' experience of delirium guidelines. J Clin Nurs. 2020 Aug;29(15-16):2849-2862. doi: 10.1111/jocn.15300. Epub 2020 May 11.
4. Morandi D. Davis JK. Taylor G. Bellelli B. Olofsson, Kreisel S, Teodorczuk A, Kamholz B, Hasemann W, Young J, M. Agar, de Rooij SE, Meagher D, Trabucchi M, MacLullich AM. Consensus and variations in opinions on delirium care: a survey of European delirium specialists. Int Psychogeriatr. 2013 Dec; 25(12): 2067–2075.
5. Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. JAMA. 1996 Mar 20;275(11):852-7.
6. Kalisvaart KJ, de Jonghe JFM., Bogaards MJ, Vreeswijk R, Egberts TC, Burger BJ, Eikelenboom P, van Gool WA. Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: a randomized placebo-controlled study. J Am Geriatr Soc. 2005 Oct;53(10):1658-66. doi: 10.1111/j.1532-5415.2005.53503. x.
7. de Jonghe JFM, Kalisvaart KJ, Dijkstra, van Dis H, Vreeswijk ., Kat MG, Eikelenboom P, van der Ploeg T, van Gool WA.. Early symptoms in the prodromal phase of delirium: a prospective cohort study in elderly patients undergoing hip surgery. Am J Geriatr Psychiatry. 2007 Feb;15(2):112-21. doi: 10.1097/01.JGP.0000241002. 86410.c2.
8. Inouye SK, Schlesinger MJ, Lydon TJ. Delirium: a symptom of how hospital care is failing older persons and a window to improve quality of hospital care. Am J Med. 1999 May;106(5):565-73. doi: 10.1016/s0002-9343(99)00070-4.

Publications
Presentations
Awards

Publications

2022
Vreeswijk R, Maier AB, Kalisvaart KJ.
Recipe for primary prevention of delirium in hospitalized older patients.
Aging Clin Exp Res. 2022 Sep 22. doi: 10.1007/s40520-022-02249-y. Online ahead of print.

2021
Tillemans MPH, Butterhoff-Terlingen MH, Stuffken R, Vreeswijk R, Egberts TCG, Kalisvaart KJ.
The effect of the anticholinergic burden on duration and severity of delirium in older hip-surgery patients with and without haloperidol prophylaxis: A post hoc analysis.
Brain Behav. 2021 Dec;11(12): e2404

Blomaard LC, van der Linden CMJ, van der Bol JM, Jansen SWM, Polinder-Bos HA, Willems HC, Festen J, Barten DG, Borgers AJ, Bos JC, van den Bos F, de Brouwer EJM, van Deudekom FJA, van Dijk SC, Emmelot-Vonk MH, Geels RES, van de Glind EMM, de Groot B, Hempenius L, Kamper AM, Kampschreur LM, de Koning MMM, Labots G, Looman R, Lucke JA, Maas HAAM, Mattace-Raso FUS, El Moussaoui R, van Munster BC, van Nieuwkoop K, Oosterwijk LB, Regtuijt ME, Robben SHM, Ruiter R, Salarbaks AM, Schouten HJ, Smit OM, Smits RAL, Spies PE, Vreeswijk R, de Vries OJ, Wijngaarden MA, Wyers CE, Mooijaart SP.
Frailty is associated with in-hospital mortality in older hospitalised COVID-19 patients in the Netherlands: the COVID-OLD study.
Age and Ageing 2021 Jan 30; afab018.

2020
Jutten RJ, Harrison JE, Brunner AJ, Vreeswijk R, van Deelen RAJ, de Jong FJ, Opmeer EM, Ritchie CW, Aleman A, Scheltens P, Sikkes SAM.
The Cognitive-Functional Composite is sensitive to clinical progression in early dementia: Longitudinal findings from the Catch-Cog study cohort.
Alzheimers Dement (N Y). 2020 Apr 17;6(1): e12020.

Vreeswijk R, Kalisvaart I, Maier AB, Kalisvaart KJ.
Development and Validation of the Delirium Risk Assessment Score (DRAS).
Eur Geriatr Med. 2020 Apr;11(2):307-314.

Visser LNC, van Maurik IS, Bouwman FH, Staekenborg S, Vreeswijk R, Hempenius L, de Beer MH, Roks G, Boelaarts L, Kleijer M, van der Flier WM, Smets EMA.
Clinicians' communication with patients receiving a MCI diagnosis: The ABIDE project.
PLoS One. 2020 Jan 21;15(1): e0227282.

2019
Jutten RJ, Harrison JE, Lee Meeuw Kjoe PR, Ingala S, Vreeswijk R, van Deelen RAJ, de Jong FJ, Opmeer EM, Aleman A, Ritchie CW, Scheltens P, Sikkes SAM.
Assessing cognition and daily function in early dementia using the cognitive-functional composite: findings from the Catch-Cog study cohort.
Alzheimers Res Ther. 2019 May 15;11(1):45.

2018
Legdeur N, Badissi M, Carter SF, de Crom S, van de Kreeke A, Vreeswijk R, Trappenburg MC, Oudega ML, Koek HL, van Campen JP, Keijsers CJPW, Amadi C, Hinz R, Gordon MF,

Novak G, Podhorna J, Serné E, Verbraak F, Yaqub M, Hillebrand A, Griffa A, Pendleton N, Kramer SE, Teunissen CE, Lammertsma A, Barkhof F, van Berckel BNM, Scheltens P, Muller M, Maier AB, Herholz K, Visser PJ.
Resilience to cognitive impairment in the oldest-old: design of the EMIF-AD 90+ study.
BMC Geriatr. 2018 Nov 26;18(1):289.

2016
Wassenaar A, Van den Boogaard M, Beishuizen A, Van den Bergh WM, Hoogendoorn M, Königs M, Kuiper MA, Müller MC, Oldenbeuving A, Schuurmans MJ, Simons K, Slooter AJC, Van der Steen M, Vreeswijk R, Van der Woude M, Schoonhoven L, Pickkers P.
Determination of the feasibility of a multicomponent intervention program to prevent delirium in the intensive care unit: a modified RAND Delphi study.
Australian Critical Care · December 2016

2011
Slor CJ, de Jonghe JF, Vreeswijk R, Groot E, Ploeg TV, van Gool WA, Eikelenboom P, Snoeck M, Schmand B, Kalisvaart KJ.
Anesthesia and postoperative delirium in older adults undergoing hip surgery.
J Am Geriatr Soc. 2011 Jul;59(7):1313-9.

2009
Kat MG, de Jonghe JF, Vreeswijk R, van der Ploeg T, van Gool WA, Eikelenboom P, Kalisvaart KJ. Mortality associated with delirium after hip-surgery: a 2-year follow-up study.
Age Ageing. 2011 Mar 17.
Cadogan FL, Riekerk B, Vreeswijk R, Rommes JH, Toornvliet AC, Honing ML, Spronk PE.
Current awareness of delirium in the intensive care unit: a postal survey in the Netherlands.
Neth J Med. 2009 Jul-Aug;67(7):296-300.

Vreeswijk R, Timmers JF, de Jonghe JFM, Kalisvaart KJ.
Assessment scales for delirium. Aging Health,
June 2009, Vol. 5, No. 3, Pages 409-425.

Vreeswijk R, Toornvliet A, Honing MLH, Bakker K, de Man T, Daas G, Spronk PE, de Jonghe JFM, Kalisvaart KJ.
Validation of the Dutch version of the Confusion Assessment Method (CAM-ICU) for delirium screening in the Intensive Care Unit.
Neth.Journal of Critical Care. vol 13 - no 2 - april 2009

2008
Kat MG, Vreeswijk R, de Jonghe JFM, van der Ploeg T, van Gool WA, Eikelenboom P, Kalisvaart KJ. Long-term cognitive outcome of delirium in elderly hip surgery patients. A prospective matched controlled study over two and a half years.
Dement Geriatr Cogn Disord. 2008;26(1):1-8. Epub 2008 Jul 9.

Lemstra AW, Kalisvaart KJ, Vreeswijk R, van Gool WA, Eikelenboom P.
Pre-operative inflammatory markers and the risk of postoperative delirium in elderly patients.
Int J Geriatr Psychiatry. 2008 Sep;23(9):943-8.

Kalisvaart K, Vreeswijk R.
Prevention of delirium in the elderly.
Rev Esp Geriatr Gerontol. 2008;43 Suppl 3:19-24. Review.

2007
De Jonghe JF, Kalisvaart KJ, Dijkstra M, van Dis H, Vreeswijk R, Kat MG, Eikelenboom P, van der Ploeg T, van Gool WA.
Early symptoms in the prodromal phase of delirium: a prospective cohort study in elderly patients undergoing hip surgery.
Am J Geriatr Psychiatry. 2007 Feb;15(2):112-21.
2006
Kalisvaart KJ, Vreeswijk R, de Jonghe JF, van der Ploeg T, van Gool WA, Eikelenboom P.
Risk factors and prediction of postoperative delirium in elderly hip-surgery patients: implementation and validation of a medical risk factor model.
J Am Geriatr Soc. 2006 May;54(5):817-22.

2005
Kalisvaart CJ, Vreeswijk R, de Jonghe JF, Milisen K.
A systematic review of multifactorial interventions for primary prevention of delirium in the elderly.
Tijdschr Gerontol Geriatr. 2005 Dec;36(6):224-31. Review. Dutch.

Kalisvaart KJ, de Jonghe JF, Bogaards MJ, Vreeswijk R, Egberts TC, Burger BJ, Eikelenboom P, van Gool WA.
Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: a randomized placebo-controlled study.
J Am Geriatr Soc. 2005 Oct;53(10):1658-66.

Expected publications:

Vreeswijk R, Maier AB, Kalisvaart KJ
Risk of delirium increases in older adults hospitalised with COVID-19.
Submitted

Eecen C, Vreeswijk R, Souverein D, Euser SM, Kalisvaart KJ.
The role of Dutch guidelines in the diagnostic outcomes and treatment decisions of hospitalized older patients with a suspected urinary tract infection: a retrospective cohort study.
Submitted

Kalisvaart KJ, Vreeswijk R, Kievit S, Heetveld M.
The use of routine pre-operative chest x-rays in elderly patients undergoing acute hip surgery.
Submitted

Poster publications:

Vreeswijk R, Kalisvaart KJ, van Schagen M, van Stralen K.
Value based health care for the frail elderly patient with a hip fracture.
International journal of integrated care 18(s2):231 · October 2018

Vreeswijk R, Kalisvaart I, Kalisvaart KJ.
Development and validation of the Delirium Risk Assessment Score (DRAS).
Journal of Geriatric Oncology 5(2): S48-S49 · October 2014

Kalisvaart KJ, Vreeswijk R.
Souvenaid in a real-life prospective clinical setting.
European Geriatric Medicine Volume 5, Supplement 1, September 2014, Page S98
Vreeswijk R, Kalisvaart KJ.
The evaluation of the effects of souvenaid on the quality of live in patient with the diagnosis M. Alzheimer; real-life prospective clinical cohort study.
European Psychiatry. 2014, 29, supplement 1

Kalisvaart KJ, Vreeswijk R.
The effect of Souvenaid on the quality of life of patients with the diagnosis of Alzheimers disease in a real-life prospective clinical setting.
Alzheimer's and Dementia, 2014 July 10, 4:454-455

Baden M, Vreeswijk R, Keijzers M, Kalisvaart KJ.
The incidence, severity and duration of delirium at the coronary care unit.
European Geriatric Medicine 3(1): S10 · September 2012

Donders E, Vreeswijk R, Tillemans M, Kalisvaart KJ.
Effect of haloperidol dosing frequencies on the duration and severity of delirium in elderly hip fracture patients. A prospective randomized trial.
European geriatric medicine 3(1): S118-S119 · September 2012

Presentations

May 2018	Poster presentation Value Based Health Care, ICIC, Utrecht
September 2017	Poster AND Pitch presentation DRAS, EUGMS Nice
July 2014	Poster presentation Souvenaid study AAIC Copenhagen
September 2014	Poster presentation Souvenaid study EUGMS Rotterdam
March2014	Poster presentation Souvenaid study EPA Munchen
October 2014	Poster presentation DRAS, SIOG, Lissabon
September 2013	Presentation primaire prevention of delirium. EUGMS Venetie
Januari 2013	Poster presentation Linneauswetenschapssymposium Haarlem
September 2012	Poster presentation and presentation EUGMS Brussel
Februari 2012:	Presentation Geriatric congress Den Bosch
Januari 2012:	Presentation Linneaus wetenschapssymposium Haarlem
September 2011:	Posterpresentation EUGMS Malaga Spanje
September 2010:	Presentation Internationaal Intensivisten Symposium HAI Berlijn
April 2010:	Presentation Verenso regiosymposium Delier
September 2009:	Presentation Internationaal Intensivisten Symposium HAI Berlijn
March 2009:	Presentation AAGP-symposium Honolulu, Hawaii
October 2008:	Presentation 3de symposium European Delirium Association Helsinki
September 2008:	Presentation Internationaal Intensivisten Symposium HAI Berlijn
May 2008:	Presentation Venticare congres Utrecht
March 2008:	Poster presentation Internationaal ICU-congres Brussel
Februari 2008:	Presentation "Meet the expert congres" AMC Amsterdam
Januari 2007:	Presentation VENTICARE Utrecht.
March 2006:	Presentation AAGP-symposium San Juan, Puerto Rico.
Januari 2006:	Presentation symposium delirium prevention MCA Alkmaar.
September 2005:	Poster presentation IPA-symposium Stockholm, Zweden.
March 2005:	Two presentations de Geriatriedagen Noordwijkerhout.
November 2003:	Presentation symposium delirium prevention Brugge, België.
Augustus 2003:	Poster presentation, delirium prevention, IPA symposium Chicago, USA.

Awards

2021 Third Place Scientific symposium Spaarne Gasthuis 2021
The role of Dutch guidelines in the diagnostic outcomes and treatment decisions of hospitalized older patients with a suspected urinary tract infection: a retrospective cohort study.

2018 Samenwerkende Topklinische opleidingsziekenhuizen (STZ) Topresearcher 2018
Awarded best poster/research of 109 enteries.
Development and validation of the Delirium Risk Assessment Score (DRAS).

2012. Best Poster Scientific symposium Kennemer Gasthuis/Spaarne Gasthuis 2012.
The incidence, severity and duration of delirium at the coronary care unit.

Dankwoord

Als je na de basisschool een vervolgopleiding gaat doen denk je er nog niet aan om uiteindelijk te eindigen als een gepromoveerde aan een universiteit, zeker niet als de start een mavo-opleiding is. Maar zoals in het begin van het proefschrift is aangegeven: “Great things are not done by impulse, but by a series of small things brought together.” Dit geldt niet alleen voor mijn gehele opleiding, maar ook voor mijn proefschrift.
Maar om door te leren heb je mensen nodig die je stimuleren en je “potentie” zien. En om onderzoek te doen (naast je werk) heb je mensen nodig die je stimuleren.
Wetenschappelijk onderzoek doe je niet alleen daarvoor heb je mensen nodig of het nu collega’s, patienten of familie zijn zonder hen wordt het moeilijker.

Een aantal mensen wil ik hierbij dan ook persoonlijk bedanken.

Prof.dr. Andrea Maier mijn promotor. Dank dat je mij de mogelijkheid hebt geven om bij jou een promotietraject in te gaan. Door de afstand en tijdsverschil met Melbourne maar ook door mijn fulltimebaan, was het voor mij niet altijd makkelijk om een moment van overleg te hebben of deel te nemen aan de bijeenkomsten die georganiseerd werden vanuit jouw studentengroep. Maar in de contacten die wij hadden heb ik veel geleerd. Dank daarvoor.

Kees Kalisvaart, geriater en co-promotor. Wie had gedacht dat ik toen ik in 1997 op de geriatrie afdeling in het MCA als verpleegkundige kwam werken zou eindigen als dr..
Jij bood mij de kansen en wist mij te stimuleren en te motiveren tot waar ik nu ben. Ik weet nog goed de eerste keer dat ik uitnodiging kreeg voor een presentatie moest doen in Brugge, Belgie over delierpreventie, jij zei dat ik dat kon en zoveel zouden er toch niet in de zaal zitten. Uiteindelijk zaten er 180 mensen in de zaal.
Een van je uitspraken is dat ieder een “Ralph” nodig heeft, maar dat geld ook voor jou, eenieder heeft een “Kees” nodig als je kijkt wat er in al die jaren bereikt is op wetenschappelijk gebied maar ook op het gebied van de ontwikkeling van de geriatrie in het MCA en in het Spaarne Gasthuis. Dank voor je samenwerking, steun en vriendschap.

Imke Kalisvaart. Dank je voor het doornemen van alle patiëntendossiers die ik nodig had voor het ontwikkelen van de delier risico assessment score (DRAS) in een periode dat nog niet alles digitaal was vastgelegd in een electronisch patienten dossier. Het is een heel werk geweest.

Tjeerd van der Ploeg. Beste Tjeerd, ik heb de samenwerking en ondersteuning met betrekking van de methodologische en statistische onderbouwing bij een groot deel van mijn onderzoek als prettig ervaren, ik heb veel van je geleerd tijdens de gesprekken over het onderzoek. Je opmerking dat je als je de basis van de statistiek goed beheerst je al een heel eind kan komen. Het is niet altijd nodig om gecompliceerde statische berekeningen te doen om tot een antwoord te komen.

Karlijn van Stralen. Beste Karlijn, zoals Tjeerd mij in het begin van mijn onderzoek heeft geholpen heb jij gedaan in het laatste deel van het traject. Was het niet telefonisch dan wel live. Uitleg welke statistische berekening te gebruiken of hoe formuleer je de tekst voor een artikel goed. Je was altijd bereid “even” mee te denken.

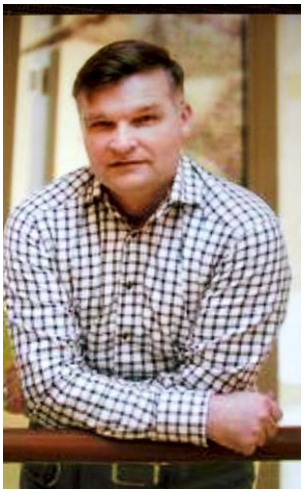
Prof. Dr. Piet Eikelenboom. Beste Piet, ik vind de gesprekken als je weer even langsliep op de geriatrie erg stimulerend met betrekking tot delieronderzoek. Ook je adviezen met betrekking tot een paar artikelen heb ik erg gewaardeerd, het gaf mij de mogelijkheid om zaken in een ander licht te zien waardoor ik weer door kon.

José Bouwman als bibliothecaresse heb je mij geholpen met het verkrijgen van de artikelen die ik nodig had voor mijn onderzoeken. Niets was je te veel en je snelheid van reageren was verbazingwekkend in vele gevallen kreeg ik met kerende post de gevraagde artikelen.

De Spaarne Gasthuis Academy wil ik bedanken voor de PI subsidie die Kees Kalisvaart en ik hebben gekregen om onderzoek te kunnen doen. Het gaf mij de mogelijkheid om iets tijd vrij te maken om naast mijn dagelijkse werkzaamheden ook onderzoek te doen.

Peter mijn vader. Jij gaf mij de mogelijkheid om door te leren omdat jezelf niet de kansen hebt gehad. Het halen van een diploma was belangrijk, uiteindelijk heb ik er 6 behaald. Het is zoals je weet een lang traject geworden met veel ups en downs, maar uiteindelijk is het resultaat dat telt. Je hebt daarvoor momenten van chagrijn, frustratie en nog meer van mijn kant moeten ondergaan (helaas). Maar dank je dat je het geaccepteerd hebt. Je blijft belangrijk in mijn leven.

Curriculum Vitae



Ralph Vreeswijk was born in Amsterdam in 1964.
He took the long road in his education from MAVO, HAVO, VWO where he graduated from the OSG West-Friesland in 1986. At the University of Maastricht, he studied Health Science at the University of Maastricht from 1986 till 1992 but did not graduate. During his work in a nursing home and he parttime studied Nursing at the HBO-v in Alkmaar where he finished in two years instead of four.
In 1997 he started working as a nurse at the newly opened Department of Geriatric Medicine at the Medical Center of Alkmaar.
Dr. Kalisvaart asked Ralph in 2000 to become a research nurse of dr. Kalisvaart his PhD study. In the same year Ralph started the study to become a specialized geriatric nurse which he finished in 2001 and he also started the study Nursing Science at the University of Utrecht where he graduated in 2005.
In 2009 he started working at the Geriatric Department of the Spaarne Gasthuis in Haarlem where he is currently working. He has diverse responsibilities: Advisor elderly care, specialized nurse, official secretary of the department of geriatrician, and science.
His research interests are in the fields of delirium and geriatric traumatology. But also supervises medical students during their scientific internship.
As congress committee member of the geriatric department, he organized scientific conferences in 2007, 2010, 2017 and 2022 and was also involved in organizing the founding conference of the European Delirium Association in 2006.
Further more he has been a boardmember of the Vereniging Verpleegkundigen Geriatrie Nederland, and Samenwerkende Topklinische opleidingsziekenhuizen (STZ) verpleegkundig onderzoek.
Furthermore, there is involvement in regional and national committees with the main topic of "vulnerable" elderly patients/people.