Delirium
An Evidence-Based Medicine (EBM) Monograph for Psychosomatic Medicine Practice

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Delirium – EBM Summary

INTRODUCTION

Objective and methods
This monograph summarizes current knowledge related to the diagnosis, epidemiology, etiology, and management of delirium. The monograph is based on the guideline 'delirium' of the National Institute of Clinical Excellence (NICE) [1], as well as on systematic reviews and pivotal trials. The quality of the evidence discussed in this monograph is graded as 'high', 'moderate', 'low' or 'very low', following the 'Grading of Recommendations Assessment, Development and Evaluation' (GRADE) system, which was developed by the Cochrane Center [1]. Readers are encouraged to consult the recommended readings for more detailed information (Appendix A).

Definition and symptoms: Delirium is an acute neuropsychiatric disorder characterized by a disturbed level of consciousness with reduced ability to focus, sustain, or shift attention, and accompanied by changes in cognition, such as memory deficits, disorientation, speech and language disturbances, delusions and perceptual abnormalities. These changes in cognition are not better accounted for by a pre-existing or evolving dementia. In addition, sleep-wake cycle disturbance, increased or decreased motor activity, and emotional disturbances are often present. The disturbance typically develops over a short period of time and tends to fluctuate during the course of the day [2].Clinically, a distinction between hyperactive and hypo-active delirium is often made on the basis of motor activity. Though this may be clinically useful, it has not found its way into the classification systems.

Diagnosis: The gold standard for the diagnosis of delirium are the criteria of the 4th edition of the Diagnostic and Statistical Manual (DSM IV; codes 291.0 to 293.0 and 780.09) or the 10th edition of the International Classification of Disease (ICD 10; code F05) [2, 3].

Prevalence and incidence: The occurrence of delirium depends on the setting.
- In the general population, the reported prevalence is low and ranges from <0.05 to 0.4%, with a higher prevalence in older people of 1.1% in those over 55 years [4, 5].
- For hospital inpatients, a median prevalence of 21.4%, a median incidence of 15.2%, and a median occurrence rate of 22% is reported on general medical wards. In the NICE guideline the term 'occurrence rate' is used when there is overlap between prevalence and incidence data, such as may occur when in incidence studies prevalent delirium upon entering the study is not excluded.
- The occurrence rate on general surgical wards is reported to be 44%; no data on prevalence and incidence rates in this setting are available [1].
- Occurrence rates are higher on Intensive Care Units, with a occurrence rates reported as high as 80%, depending on type of ICU [1].
- In long term care, low quality evidence shows a median occurrence rate of 15.9% [6].

Risk factors: Delirium is currently seen as the resultant of a complex interaction of *predisposing* and *precipitating* factors [7].
High quality evidence identifies the following risk factors for *incident* delirium:
- Older age
- Cognitive impairment

- Visual impairment [1]

Moderate quality evidence identifies the following risk factors for incident delirium:
- lllness severity
- Comorbidity
- Infection
- Fractures
- Vascular surgery
- Presence of a bladder catheter [1].

Moderate to low quality evidence identifies the following risk factors for *persistence* of delirium:
- Cognitive impairment
- Medical comorbidity
- Vision impairment)
- Use of physical restraints [1].

Low level evidence identifies the following risk factors for *increased severity* of delirium:
- Number of room changes
- Absence of clock or watch
- Cognitive impairment
- Not wearing glasses [1].

Low level of evidence shows no, or no clinically relevant, association for incidence or severity of with a variety of variables, such as sex, mobility, hearing impairment, incontinence, dehydration and polypharmacy [1]. Clinical experience however supports close attention for polypharmacy as a contributing cause of delirium.

Prognosis: Delirium has a number of negative prognostic implications.
High quality evidence
- Increased length of hospital stay, particularly for ICU patients [1, 9, 10]
- Increased and earlier post-discharge institutionalization [1]

Moderate to high quality evidence
- Increased mortality: the mortality of delirium patients during their hospital stay is 22 – 76%; the mortality in the first year after discharge is 35 – 40% [8].

Moderate quality evidence
- Delirium is a risk factor for cognitive decline and dementia after 3 years [1]

Low quality evidence.
- Delirium predisposes for worse functional abilities and activities of daily living [1] No study reported on the consequences of delirium for health related quality of life [1]

Costs:
Several studies have demonstrated significantly increased costs of health care for patients who develop delirium [9, 10]. One study estimated these costs to be at least 2.5 times greater per day for delirious patients compared to non-delirious patients [11].

SCREENING AND ASSESSMENT

Most health care providers recognize that delirium is a serious, underdiagnosed problem, but a minority routinely screen for delirium and few use a specific tool for assessment [12]. Failure to detect delirium has been associated with poorer outcomes, including increased mortality

[13], while explicit recognition of delirium has been associated with lower mortality and shorter inpatient stays [14].

Assessment consists of establishing the diagnosis, assessing severity and assessing clinical risks. Of the available diagnostic instruments, the Confusion Assessment Method (CAM) is preferred in a clinical setting, since it has the highest positive and lowest negative likelihood ratio (LR) (positive LR 9.6; 95% CI 5.8 – 16.0; negative LR 0.16; 95% CI 0.09 – 0.29) (moderate quality evidence) (http://www.healthcare.uiowa.edu/igec/tools/cognitive/CAM.pdf) [1, 15]. The MMSE score had the lowest discriminatory properties (moderate quality evidence) [15]. The MMSE should not be used alone to diagnose delirium.

In the ICU setting, moderate to high quality evidence shows that the CAM-ICU has the best data supporting its use, with positive LRs ranging from 13.42 to 36.36 [1]. Although there are a number of rating scales available for assessment of severity, no recommendation for a specific scale can be given. For most delirium rating scales, low to moderate evidence supports their use in the assessment of severity of delirium. [1, 16].

TREATMENT

Treatment of delirium consists foremost of treatment of the underlying medical condition. In addition, there is evidence that symptomatic treatment, including non-pharmacological and pharmacological treatment may be beneficial to the patient. (For a list or randomized pharmacological trials, see Appendix B).

Non-pharmacological treatment
There is moderate to very low quality evidence that suggests that enhanced treatment strategies for people with delirium are more effective than usual care. However, the various mono- and multi-component interventions vary substantially and most of the studies provide lower quality evidence, with much uncertainty around the results. For this reason, the NICE guideline development group abstained from recommending a specific strategy. There was consensus however that interventions targeting better orientation may be helpful in clinical practice [1].

Pharmacological symptomatic treatment

Antipsychotics
Moderate to low quality evidence shows that antipsychotic medications are effective in the treatment of symptoms of delirium. Compared to treatment with placebo, treatment with an antipsychotic medication is associated with a higher proportion of remission in patients, and a reduced severity of delirium. In one small study, haloperidol (0.25 – 10mg/d), risperidone (0.25-4mg/day), and olanzapine (1.25 – 20mg/day) were equally effective in treating delirium, with few adverse effects [17]. There is no consistent evidence on whether haloperidol results in more or more severe extrapyramidal side effects than olanzapine or risperidone [1]. Although some studies have evaluated the differential response to pharmacological treatment in patients with various motor subtypes of delirium, the low quality of available evidence does not allow any conclusion or recommendation in this respect.

Other medication

There is no evidence to support the use of benzodiazepines in the treatment of delirium not related to alcohol or benzodiazepine withdrawal [1]. There is no current evidence for the efficacy of cholinesterase inhibitors as treatment for delirium [1, 18-21]. In critically ill patients, treatment of delirium with the cholinesterase inhibitor rivastigmine is associated with increased mortality [21].

<u>Prevention</u>

Nonpharmacological prevention:
Mono-component interventions: there is no evidence of the effect of subcutaneous versus intravenous fluids on the incidence, duration or severity of delirium, both in a hospital setting and in a long term care setting (low quality evidence) [1].
Multi-component interventions: low quality evidence shows that multi-component interventions based on targeting modifiable risk factors (such as cognitive impairment, sleep deprivation, immobility, vision impairment, hearing impairment, dehydration), reduces the incidence of delirium (RR 0.66; 95% CI 0.46 to 0.95), reduces average delirium duration, and reduces the number of patients with urinary incontinence after 6 months follow up (RR 0.80; 95% CI 0.65 to 0.99). There was no difference in mortality, delirium severity, the median length of stay in hospital, post-discharge institutionalisation, the incidence of delirium after 6 months follow up, and the MMSE score after 6 months follow up [1].

Pharmacological prevention:

Antipsychotics
The NICE guideline summerizes that moderate to low quality evidence suggests that prophylactic treatment with typical antipsychotics does *not* reduce the incidence of delirium in hospital patients. One low quality RCT (level 2 evidence) with risperidone showed a significant reduction in delirium incidence (RR 0.35; 95% CI 0.16 to 0.77) which corresponds to a number needed to treat of 5 (95% CI 3 to 14) [22]. Another study with olanzapine (level 2 evidence) showed a decreased incidence but longer duration and severity of delirium in postoperative patients after joint surgery [23]. In contrast with this conclusion, a recent RCT of 457 patients after surgery randomized to haloperidol 0.5mg IV bolus and 0.1mg/hr continuous infusion for 12 hours versus placebo showed decreased incidence of delirium and shorter duration of ICU stay [24]. Prophylactic treatment with haloperidol may reduce the severity and duration of delirium, as well as the length of hospital stay [25].

Other medication:
Rivastigmine and donepezil do not reduce the duration of delirium, nor the length of stay in the ICU or in the general hospital (moderate quality evidence). Prophylactic treatment with risperidone did not reduce the length of hospital stay (level 2) [1, 26].

QUALITY INDICATORS

<u>Organization of detection and management:</u>
The available evidence does not allow for recommendation of a specific model of organization of delirium detection and management. However, the NICE guideline as well as available reviews and position papers stress the importance of a systematic and proactive approach to delirium identification and treatment. The approach to delirium should include systematic screening for patients with delirium risk factors, and then systematically following them for potential incident delirium and administer interventions known to help prevent

delirium. Once delirium is established, adequate pharmacological and non-pharmacological treatment should be provided. Follow-up contacts can be provided if indicated in order to taper medication or to follow the cognitive status of the patient.

Specific quality indicators
The following indicators provide insight into the quality of the organization of detection and management of delirium:
- The presence of an institutional protocol for delirium, based on a professional guideline
- The availability of professionals with expertise in delirium (psychiatrist/geriatrician) on a 24/7 basis
- Percentage of patients over 65-years that has been screened for delirium risk factors on admission or pre-operatively
- Percentage of patients at high-risk for delirium that is screened for incident delirium during the first few days of admission or post-operatively
- When delirium is present, treatment with antipsychotic medication is considered, unless medically contraindicated and benzodiazepines are avoided unless a clear reason for using them is provided (e.g., alcohol withdrawal).

(Based on: Inspectie voor de Gezondheidszorg (IGZ), Nederlandse Vereniging van Ziekenhuizen (NVZ), Nederlandse Federatie van Universitair Medische Centra (NFU), Orde van Medisch Specialisten (OMS): Quality indicator set for general hospitals: 2010. Utrecht, Health Care Inspectorate of the Netherlands, 2009.)

References

1   National Clinical Guideline Centre. Delirium: Diagnosis, prevention and management (clinical guideline 103). London, National Clinical Guideline Centre, 2010.
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4   Andrew MK, Freter SH, Rockwood K. Prevalence and outcomes of delirium in community and non-acute care settings in people without dementia: A report from the canadian study of health and aging. Biomed Central Medicine 2006 4
5   Folstein MF, Bassett SS, Romanoski AJ, Nestadt G. The epidemiology of delirium in the community: The Eastern Baltimore mental health survey. International Psychogeriatrics 1991;3:169-176.
6   Pitkala KH, Laurila JV, Strandberg TE, Tilvis RS. Prognostic significance of delirium in frail older people. Dementia Geriatric Cognitive Disorders 2005;19:158-163.
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8   McCusker J, Cole M, Abrahamowicz M, Primeau F, Belzile E. Delirium predicts 12-month mortality. Archives of Internal Medicine 2002;162:457-463.
9   Franco K, Litaker D, Locala J, Bronson D. The cost of delirium in the surgical patient. Psychosomatics 2001;42:68-73.

10   Mildrandt 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. Critical Care Medicine 2004;32:955-962.

11   Leslie DL, Marcantonio ER, Zhang Y, Leo-Summers L, Inouye SK. One-year health care costs associated with delirium in the elderly population. Archives of Internal Medicine 2008;168:27-32.

12   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. Critical Care Medicine 2004;32:106-112.

13   Kakuma R, du Fort GG, Aresnault L, Perrault A, Platt RW, Monette J, Moride Y, Wolfson C. Delirium in older emergency department patients discharged home: Effect on survival. Journal of the American Geriatric Society 2003;51:443-450.

14   Rockwood K, Cosway S, Stolee P, Kydd D, Carver D, Jarrett P, O'Brien B. Increasing the recognition of delirium in elderly patients. Journal of the American Geriatric Society 1994;42:252-256.

15   Wong CL, Holroyd-Leduc J, Simel DL, Straus SE: Does this patient have delirium? Value of bedside instruments. Journal of the American Medical Association 2010;304:779-786.

16   Schuurmans MJ, Deschamps PI, Markham SW, Shortridge-Bagget LM, Duursma SA: The measurement of delirium. Review of rating scales. Research and Theory of Nursing Practice 2003;17:207-224.

17   Grover S, Kumar V, Chakrabarti S. Comparative efficacy study of haloperidol, olanzapine and risperidone in delirium. Journal of Psychosomatic Research 2011;71:277-281.

18   Lonergan E, Britton AM, Luxenberg J. Antipsychotics for delirium. The Cochrane Database of Systematic Reviews 2007;Issue 2:Art. no CD005594.

19   Lonergan E, Luxenberg J, Areosa Sastre A. Benzodiazepines for delirium. The Cochrane Database of Systematic Reviews 2009;Issue4:Art. no. CD006379.

20   Overshott R, Karim S, Burns A. Cholinesterase inhibitors for delirium. The Cochrane Database of Systemaic Reviews 2008;Issue 1:Art. no CD005317.

21   van Eijk MM, Roes KC, Honing ML, Kuiper MA, Karakus A, van der Jagt M, Spronk PE, van Gool WA, van der Mast RC, Kesecioglu J, Slooter AJ. Effect of rivastigmine as an adjunct to usual care with haloperidol on duration of delirium and mortality in critically ill patients: A multicentre, double-blind, placebo-controlled randomised trial. Lancet 2010;376(9755):1829-1837.

22   Prakanrattana U, Prapaitrakool S. Efficacy of risperidone for prevention of postoperative delirium in cardiac surgery. Anaesthesiology and Intensive Care 2007;35:714-719.

23   Larsen KA, Kelly SE, Stern TA, Bode RH, Price LL, Hunter DJ, Gulczynski D, Bierbaum BE, Sweeney GA, Hoikala KA, Cotter JJ, Potter AW. Administration of olanzapine to prevent postoperative delirium in elderly joint-replacement patients: A randomized, controlled trial. Psychosomatics 2010;51:409-418.

24   Wang W, Li HL, Wang DX, Zhu X, Li SL, Yao GQ, Chen KS, Gu XE, Zhu SN. Haloperidol prophylaxis decreases delirium incidence in elderly patients after noncardiac surgery: A randomized controlled trial. Critical Care Medicine (accepted) 2011

25   Kalisvaart KJ, De Jonghe J, Bogaarts M, Vreeswijk R, Egberts ECG, Burger BJ, Eikelenboom P, Van Gool P. Haloperidol prophylaxis for elderly hip-surgery patients

at risk for delirium a randomized placebo-controlled study. Journal of the American Geriatric Society 2005;53:1658-1666.

26   Siddiqi N, Holt R, Britton AM, Holmes JD. Interventions for preventing delirium in hospitalised patients. The Cochrane Database of Systematic Reviews 2007;Issue 2:Art.no CD005563.

Appendix (Additional Materials)

A)   Recommended Readings
B)   Annotated List of Randomized Clinical Trials
C)   Assessment and Scales
D)   Areas for Future Research
E)   Multiple choice question(s)

APPENDIX A

Recommended Readings

Relevant practice guidelines:
- NICE clinical guideline 103 'Delirium: Diagnosis, prevention and management', NICE institute, London, UK: http://guidance.nice.org.uk/CG103

Relevant literature:
- Young J, Murthy L, Westby M, Akunne A, O'Mahony R, on behalf of the Guideline Development Group. Diagnosis, prevention, and management of delirium: summary of the NICE guidance. British Medical Journal 2010;341:247-249
- Wong CL, Holroyd-Leduc J, Simel DL, Straus SE. Does this patient have delirium? Value of bedside instruments. Journal of the American Medical Association 2010;304:779-786.

Relevant websites:
- American Delirium Society: http://americandeliriumsociety.org
- European Delirium Association: http://www.europeandeliriumassociation.com
- Hospital Elder Life Programme (HELP, Yale University School of Medicine, New Haven, USA): http://www.hospitalelderlifeprogram.org/public/public-main.php

APPENDIX B

Annotated List of Randomized Pharmacological Trials

A.   ACUTE TREATMENT

Antipsychotics

Breitbart W, Marotta R, Platt MM, Weisman H, Derevenco M, Grau C, et al. A double-blind trial of haloperidol, chlorpromazine, and lorazepam in the treatment of delirium in hospitalized AIDS patients. The American Journal of Psychiatry 1996;153(2):231-7.

> *30 hospitalized patients with AIDS were randomly assigned (double-blind) to receive low-dose chlorpromazine, low-dose haloperidol or lorazepam if they developed a delirium. The antipsychotics effectively treated the delirium while the benzodiazepine arm was terminated after it appeared to be ineffective while also causing side effects.*

Skrobik YK, Bergeron N, Dumont M, Gottfried SB. Olanzapine vs haloperidol: treating delirium in a critical care setting. Intensive Care Medicine 2004;30(3):444-9.

> *In this randomized trial (N=73), olanzapine and haloperidol reduced delirium symptoms to a similar degree; olanzapine had less EPS.*

Han CS, Kim YK. A double-blind trial of risperidone and haloperidol for the treatment of delirium. Psychosomatics 2004;45(4):297-301.

> *Small randomized trial (double-blind) of 28 patients that found no clear differences between a 7-day course of risperidone or haloperidol in patients with delirium.*

Lee KU, Won WY, Lee HK, Kweon YS, Lee CT, Pae CU, et al. Amisulpride versus quetiapine for the treatment of delirium: a randomized, open prospective study. International Clinical Psychopharmacology 2005;20(6):311-4.

> *Small randomized trial (N=40) comparing amisulpride with quetiapine for the treatment of delirium. Both interventions were comparable with regards to side effects and reduction of delirium symptoms.*

Devlin JW, Roberts RJ, Fong JJ, Skrobik Y, Riker RR, Hill NS, et al. Efficacy and safety of quetiapine in critically ill patients with delirium: a prospective, multicenter, randomized, double-blind, placebo-controlled pilot study Critical Care Medicine 2010;38(2):419-27.

> *36 patients with delirium received ancillary quetiapine in this small RTC (double-blind, placebo-controlled). All patients received as needed haloperidol. The added quetiapine led to more sedation but also reduced the duration of delirium and agitation.*

Girard TD, Pandharipande PP, Carson SS, Schmidt GA, Wright PE, Canonico AE, et al. Feasibility, efficacy, and safety of antipsychotics for intensive care unit delirium: the MIND randomized, placebo-controlled trial. Critical Care Medicine 2010;38(2):428-37.

In this double-blind, placebo-controlled RTC, 101 ventilated ICU patients received either haloperidol, ziprasidone or a placebo for 21 days. There were no differences in side effects or "days spent alive without delirium or coma."

Kim SW, Yoo JA, Lee SY, Kim SY, Bae KY, Yang SJ, et al. Risperidone versus olanzapine for the treatment of delirium. Human Psychopharmacology 2010;25(4):298-302.

Small randomized trial (N=32) that found no clear difference between risperidone and olanzapine in treating acute delirium.

Tahir TA, Eeles E, Karapareddy V, Muthuvelu P, Chapple S, Phillips B, et al. A randomized controlled trial of quetiapine versus placebo in the treatment of delirium. Journal of Psychosomatic Research 2010;69(5):485-90.

Small RTC (double-blind, placebo-controlled) of 42 patients that showed benefit from quetiapine for the treatment of delirium. With treatment, it resolved faster.

Acetylcholinesterase Inhibitors

Overshott R, Vernon M, Morris J, Burns A. Rivastigmine in the treatment of delirium in older people: a pilot study. International Psychogeriatrics 2010;22(5):812-8.

Very small RTC (double-blind, placebo-controlled) trial in 15 patients who were treated for delirium with either rivastigmine or placebo. The duration of delirium was comparable.

van Eijk MM, Roes KC, Honing ML, Kuiper MA, Karakus A, van der Jagt M, et al. Effect of rivastigmine as an adjunct to usual care with haloperidol on duration of delirium and mortality in critically ill patients: a multicentre, double-blind, placebo-controlled randomised trial. Lancet 2010;376(9755):1829-37.

Major multicenter RTC (double-blind, placebo-controlled) that examined if adding rivastigimine (12 mg TDD) to haloperidol in patients diagnosed with delirium would be helpful. The approach has face validity as cholinergic load is often increased in delirium. However, the intervention was not helpful. Worse, rivastigmine prolonged the delirium and increased mortality (22% in treatment group vs. 8% on placebo; p=0.07). The trial was prematurely terminated by the DSMB after 104 patients were enrolled because of the interim mortality findings.

B.   PROPHYLAXIS

Antipsychotics

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. Journal of the American Geriatrics Society. 2005;53(10):1658-66.

Large RTC (double-blind, placebo-controlled) of 430 patients over age 70 that examined if short-term, low-dose haloperidol (1.5 mg/day) treatment can prevent post-

operative delirium following hip surgery. The incidence of delirium was similar: 15.1% for the treatment group and 16.5% for the placebo group. However, those patients who developed delirium had a less severe delirium of shorter duration if they had received prophylactic haloperidol.

Prakanrattana U, Prapaitrakool S. Efficacy of risperidone for prevention of postoperative delirium in cardiac surgery. Anaesth Intensive Care 2007;35(5):714-9.

> *120 patients received a one-time sublingual dose of 1 mg risperidone or placebo immediately following regaining consciousness after elective cardiac surgery. The intervention reduced the risk of developing delirium (11.1% in the treatment group vs. 31.7% in the placebo group).*

Larsen KA, Kelly SE, Stern TA, Bode RH, Jr., Price LL, Hunter DJ, et al. Administration of olanzapine to prevent postoperative delirium in elderly joint-replacement patients: a randomized, controlled trial. Psychosomatics 2010;51(5):409-18.

Large RTC (double-blind, placebo-controlled) of 400 patients that examined if peri-operatively administered olanzapine (5 mg before and after surgery) would reduce delirium in elderly patients admitted electively for joint replacement surgery. While intervention reduced the incidence of delirium, the duration and severity of delirium was greater in the intervention group; nonetheless, dismissal to home rather than a rehabilitation facility was greater in the olanzapine-intervention group.

Acetylcholinesterase Inhibitors

Gamberini M, Bolliger D, Lurati Buse GA, Burkhart CS, Grapow M, Gagneux A, et al. Rivastigmine for the prevention of postoperative delirium in elderly patients undergoing elective cardiac surgery--a randomized controlled trial. Critical Care Medicine 2009;37(5):1762-8.

> *120 patients scheduled for elective cardiac received short-term, peri-operative rivastigmine (double-blind, placebo-controlled). The incidence of post-operative delirium was 30% in the placebo group and 32% in the treatment group.*

Melatonin

Al-Aama T, Brymer C, Gutmanis I, Woolmore-Goodwin SM, Esbaugh J, Dasgupta M. Melatonin decreases delirium in elderly patients: A randomized, placebo-controlled trial. International Journal of Geriatric Psychiatry 2011;26(7):687-94

> *165 medically admitted patients age 65 or above received low-dose melatonin (0.5) at night to see if delirium was prevented. The intervention effectively reduced the incident of delirium as determined by CAM (12% with melatonin vs. 31% with placebo).*
> *(This was a double-blind, placebo-controlled RTC.)*

APPENDIX C

Assessment and Scales

Many delirium scales are available. The choice of instrument depends on a number of factors, including time for completion, amount of training required, experience of the rater, the purpose of the scale (diagnosis, screening, severity measurement), and the clinical setting.

The scales listed below are the best in terms of psychometric properties and wide validation in multiple clinical settings/patient groups (see EBM main text for details regarding psychometric properties).

For non-psychiatric clinicians: Screening and diagnosis
- Confusion Assessment Method (CAM):
  http://www.medscape.com/viewarticle/481726
- For the ICU: CAM-ICU:
  http://www.mc.vanderbilt.edu/icudelirium/docs/CAM_ICU_worksheet.pdf

For psychiatric clinicians: Severity rating and diagnosis
- Delirium Rating Scale-98 (DRS-98)
  http://neuro.psychiatryonline.org/data/Journals/NP/3906/229.pdf
- Memorial Delirium Assessment Scale (MDAS)
  http://www.delirant.info/DreamHC/Download/MDAS.pdf

For nurses: Screening
- Neelon and Champagne Confusion Scale (NEECHAM)

References

Adamis D, Sharma N, Whelan PJ, Macdonald AJ. Delirium scales: A review of current evidence. Aging and Mental Health 2010;14(5):543-55

Dasgupta M, Dumbrell AC. Preoperative risk assessment for delirium after noncardiac surgery: a systematic review. Journal of the American Geriatric Society 2006;54(10):1578-89

Inouye SK, Zhang Y, Jones RN, Kiely DK, Yang F, Marcantonio ER. Risk factors for delirium at discharge: development and validation of a predictive model. Archives of Internal Medicine 2007;167(13):1406-13

Van Rompaey B, Elseviers MM, Schuurmans MJ, Shortridge-Baggett LM, Truijen S, Bossaert L. Risk factors for delirium in intensive care patients: a prospective cohort study. Critical Care 2009;13(3):R77

APPENDIX D

Areas of Future Research

- Determination of best pharmacological treatment
  - It remains unclear if and when second-generation antipsychotics are to be preferred over first-generation antipsychotics
  - RCT of amisulpride should be performed (see reference below)
  - Currently, there are no clear indications for the pharmacological prevention of delirium
- Identification of biomarkers that could aid in detection and diagnosis of delirium (including subclinical delirium)
- Comparing efficacy of pharmacologic treatment in certain delirium subtypes (hyperactive versus hypoactive delirium).
- Identification of elements of underlying pathophysiology of delirium and its symptoms
- Further development of prevention and detection strategies and their impact on incidence, mortality, morbidity, and cost
- Identification of elements of psychiatric consultation that have the most impact on clinical and financial outcomes of delirium prevention and treatment
- Development of a new practice guideline that incorporate recent research findings

Reference:
Pintor, L, Fuente, E, Bailles, E, Matrai. S. Study on the efficacy and tolerability of amisulpride in medical/surgical inpatients with delirium admitted to a general hospital. European Psychiatry 2009;24:450-455
> *Open label prospective study of 40 hospital inpatients with delirium treated with amisulpride 200-300mg/day for 1 week. Patients treated with amisulpride showed significant improvement in DRS, PANSS and MMSE.*

APPENDIX E

Multiple choice questions

Which of the following is a specific quality indicator for delirium care in a hospital?

    A. Percentage of patients over 65-years that has been screened for risk factors for delirium upon admission or pre-operatively
    B. The percentage of patients who receive a routine psychiatric consultations in the ICU
    C. The percentage of orthopaedic patients who receive peri-operative delirium prophylaxis for hip surgery (e.g., an antipsychotic)
    D. The percentage of patients with delirium who require restraint

(Correct answer: A.)

What is the best treatment for managing delirium?

    A. Haloperidol
    B. Valproate
    C. Lorazepam
    D. Donepezil
    E. Citalopram

(Correct answer: A)

Which of the following factors have highest evidence of being associated with delirium?

    A. Gender
    B. Premorbid cognitive impairment
    C. Hypertension
    D. Incontinence
    E. Social support

(Correct answer: B)

Best assessment for delirium is which of the following?

    A. MMSE
    B. History from family
    C. CAM
    D. CT head
    E. Review of medications

(Correct answer: C)

Best evidence exists for delirium negatively impacting which of the following?

    A. Development of dementia
    B. Mortality of caregivers

C. Impairment of ADL's longterm
D. Length of hospitalization
E. Marital status

(Correct answer: D)