

Appendix A: Summary of evidence from surveillance

2018 surveillance of [Delirium: prevention, diagnosis and management](#) (2010) NICE guideline CG103

Summary of evidence from surveillance

Studies identified in searches are summarised from the information presented in their abstracts.

Feedback from topic experts who advised us on the approach to this surveillance review, was considered alongside the evidence to reach a final decision on the need to update each section of the guideline.

Risk factor assessment

Recommendations in this section of the guideline

- 1.1.1 When people first present to hospital or long-term care, assess them for the following risk factors. If any of these risk factors is present, the person is at risk of delirium.
- Age 65 years or older.
 - Cognitive impairment (past or present) and/or dementia⁴. If cognitive impairment is suspected, confirm it using a standardised and validated cognitive impairment measure.
 - Current hip fracture.
 - Severe illness (a clinical condition that is deteriorating or is at risk of deterioration)⁵.
- 1.1.2 Observe people at every opportunity for any changes in the risk factors for delirium.

⁴ For guidance on diagnosing dementia, see [diagnosis](#) in the NICE guideline on dementia.

⁵ For further information on recognising and responding to acute illness in adults in hospital, see the NICE guideline on [acutely ill adults in hospital](#).

Surveillance decision

These recommendations should not be updated.

Risk factor assessment

Risk factors for the general population

Age

Previous surveillance summary

The 2014 review identified 2 systematic review's(1,2) and meta-analysis(3) which found that age over 65 years was associated with the development of delirium.

2018 surveillance summary

A systematic review and meta-analysis(4) of 24 studies of 5364 elderly patients with hip fracture, assessed the risk factors for delirium following hip surgery. They found that advanced age was more likely to lead to sustained delirium.

Cognitive impairment

Previous surveillance summary

No new evidence was identified at the 2012 review. The 2014 review identified a meta-analysis(5) which found the NEECHAM confusion scale had high internal consistency and the delirium rating scale-revisited-98 (DRS-R-98) had high inter-rater reliability, sensitivity and specificity for assessing fracture surgery patients with cognitive impairment.

2018 surveillance summary

None found.

Pharmacological risk factors

Previous surveillance summary

In the 2012 surveillance review and a second surveillance review in 2014, 2 systematic reviews(6,7) showed that some drugs were associated with an increased risk of delirium but there was insufficient

evidence to justify updating of the recommendation.

2018 surveillance summary

A systematic review(8) of 29 studies evaluated preoperative medicine use as a risk factor for postoperative delirium in patients aged 18 years or older undergoing major surgery. Medicines were an independent predictor of delirium in 4 studies, with preoperative beta-blockers and benzodiazepines being significant predictors of delirium following vascular and orthopaedic surgery respectively in single studies. The remaining studies included multiple medications or interventions making direct association difficult to determine. Preoperative nifedipine use was significantly associated with postoperative delirium following cardiac surgery.

Cerebrospinal fluid biomarkers

Previous surveillance summary

No new evidence was identified at the 2012 review.

The 2014 review identified a systematic review(9) in which delirium was associated with 8 CSF markers, however the significance of the results was not stated. Elevated acetylcholinesterase levels predicted poor outcomes after delirium.

2018 surveillance summary

An RCT(10) (n=217) investigated whether levels of acetylcholinesterase (AChE) or butyrylcholinesterase (BChE) were associated with postoperative delirium. The study found 27.6% of patients developed delirium even though AChE and BChE levels were within the normal range in these patients.

A secondary analysis of 2 RCTs(11) investigated whether S100 biomarker predicts postoperative delirium (n=92

patients undergoing off-pump coronary heart bypass surgery). Presence of the S100 biomarker was tested at baseline, end of surgery and postoperative day 1; presence of delirium was assessed daily until postoperative day 5 using either the confusion assessment method (CAM) or CAM-ICU. The authors state that S100-values on postoperative day 1 significantly predicted the occurrence of postoperative delirium during the later hospital stay.

Genetic risk factors

[Previous surveillance summary](#)

No new evidence was identified at the 2012 or 2014 reviews.

[2018 surveillance summary](#)

A systematic review and meta-analysis(12) of 10 studies examined the relationship between apolipoprotein E (APOE) and delirium. Meta-analysis of data from 8 papers (n=1762) found a small but non-significant effect on the presence of delirium in patients with the APOE allele.

Risk factors for specified sub-populations

Risk factors after cardiac surgery

[Previous surveillance summary](#)

No new evidence was found at the 2012 review.

The 2014 review found a systematic review(13) and meta-analysis(14) that investigated risk factors for delirium following cardiac surgery. A number of risk factors were identified including history of stroke, age, cognitive impairment, atrial fibrillation and red blood cell transfusion. The authors also stated that sedation with dexmedetomidine may significantly predict the absence of postoperative delirium.

[2018 surveillance summary](#)

None found.

Acute stroke

[Previous surveillance summary](#)

No new evidence was found at the 2012 review.

One systematic review(1) from the 2014 review found that increased age, aphasia, neglect or dysphagia, visual disturbance and elevated cortisol levels were associated with delirium development in patients with acute stroke.

[2018 surveillance summary](#)

None found.

Critically ill patients

[Previous surveillance summary](#)

No new evidence was found at the 2012 review.

In the 2014 review, a systematic review(2) found that age was a common risk factor for delirium. Benzodiazepines were the medication most likely to be associated with delirium and 5 biomarkers were implicated in causing delirium.

Another systematic review(15) which found 7 screening tools used to identify delirium in the emergency department however tools were not validated. A meta-analysis(3) found age, history of hypertension, clinical use of mechanical ventilation and higher APACHE II score were associated with an increased risk of delirium.

[2018 surveillance summary](#)

None found.

Acute medical inpatients

[Previous surveillance summary](#)

No new evidence was identified at the 2012 review.

The 2014 review identified 1 systematic review(16) which found dementia, cognitive impairment, functional impairment, severe illness and visual impairment were related to delirium incidence. Age was not significantly related to delirium incidence. A meta-analysis(17) found dementia, age, co-morbid illness, severity of medical illness, infection, “high risk” medication use, diminished activities of daily living, immobility, sensory impairment, urinary catheterisation, length of hospital stay, urea and electrolyte imbalance and malnutrition were risk factors for incident delirium in medical inpatients.

2018 surveillance summary

None found.

Blood transfusion

Previous surveillance summary

No new evidence was identified at the 2012 or 2014 reviews.

2018 surveillance summary

A systematic review(18) of 23 RCTs and cohort studies investigated the treatment of anaemia with blood transfusion and its association with delirium. The authors stated that in 4 studies, delirium may have occurred following transfusion, with 1 of these studies stating that transfusion was a significant risk factor. However no association was found in the remaining 3 studies. The authors state that it was not possible to determine when delirium occurred in the remaining 17 studies. Overall, there was no clear evidence of blood transfusion as a risk factor for delirium.

An RCT(19) investigated whether delirium was precipitated by anaemia and blood transfusions in 415 patients aged 65-102 years admitted for hip fracture surgery.

Anaemia was associated with increased incidence of delirium. But in patients with a low haemoglobin level, blood transfusion was a protective factor for delirium.

Surgery related risk factors

Previous surveillance summary

No new evidence was identified at the 2012 review.

From the 2014 surveillance review, a systematic review(20) found that identifying when risk factors occurred (pre, intra or post operatively) and implementing effective prevention or treatment strategies, could prevent postoperative delirium.

2018 surveillance summary

A systematic review(21) of 10 prospective observational studies examined preoperative clinical risk factors for postoperative delirium following hip fracture surgery. After adjustment for other risk factors in multivariate models, only cognitive impairment was a significant predictor of postoperative delirium.

A systematic review and meta-analysis(4) of 24 studies of 5364 elderly patients with hip fracture, assessed the risk factors for delirium following hip surgery. The following factors were more likely to lead to sustained delirium: advanced age, living in an institution, heart failure, hip arthroplasty, multiple co-morbidities and morphine use. Females were less likely than males to develop delirium.

A secondary analysis of an RCT(22) evaluated the effect of intraoperative blood pressure on postoperative delirium in elderly hip fracture patients (n=23). No significant association was observed between intraoperative blood pressure and postoperative delirium.

A systematic review and meta-analysis(23) examined risk factors for delirium in 16 studies (n=3817 patients) that had used validated delirium assessment tools in vascular surgery patients. The following risk factors were identified: American Society of Anaesthesiologists (ASA) score >2, renal failure, previous stroke, neurologic comorbidity and male sex. Patients with delirium had lower preoperative haemoglobin levels and were older than patients who did not develop delirium.

A systematic review and meta-analysis(24) of 15 studies investigated delirium in patients undergoing vascular surgical. Older age, hypertension, pre-existing cognitive impairment or depression, and open aortic surgery were significantly associated with delirium.

A systematic review and meta-analysis(25) of 41 studies (n=9384 patients) examined postoperative risk factors for delirium in older adults having elective surgery. Significant risk factors identified were history of delirium, frailty, cognitive impairment, impairment in instrumental activities of daily living and potentially modifiable factors such as smoking and use of psychotropic medication.

A systematic review and meta-analysis(26) of 6 studies investigated delirium risk factors following spinal surgery. The following risk factors were associated with development of delirium: age >65 years, female sex, number of medications, low preoperative haematocrit, albumin, durations of surgery, intraoperative blood loss, low postoperative haematocrit, haemoglobin, sodium and postoperative fever.

A systematic review and meta-analysis(27) assessed risk factors for delirium in patients undergoing surgery for head and

neck cancer (n=1940). The following risk factors were found to be statistically significant: old age, age >70, male sex, duration of surgery, history of hypertension, blood transfusions, tracheotomy, ASA grade 3 or above, flap reconstruction and neck dissection.

Methods for assessing delirium risk

Previous surveillance summary

In the 2012 surveillance review 1 study(28) found that the PRE-DELIRIC tool (prediction of delirium in ICU patients) was more successful than the clinical prediction of ICU nurses or physicians for identifying people at risk of delirium. The 2014 review identified a systematic review(1) that found generic assessment tools such as the delirium rating scale and/or CAM were the most commonly used to identify delirium in patients who had experienced a stroke. A second systematic review(29) compared CAM and CAM-ICU to DSM-IV and found that both tools had higher specificity than sensitivity and therefore should not replace clinical judgement. Two meta-analyses(30,31) found that CAM-ICU was the most specific and one of the most suitable tools (along with the Intensive care delirium screening checklist (ICDSC)) for the assessment of delirium in critically ill patients.

2018 surveillance summary

A systematic review(32) of 22 studies aimed to review the use of the Months Backwards Test (MBT). The MBT can be used to predict risk of delirium in surgical patients as well as many other cognitive impairment diagnoses. The authors state that the MBT can be used across a variety of conditions including delirium, but with little consistency. However no results for

delirium have been specified in the abstract.

A systematic review and meta-analysis(33) of 13 studies investigated the accuracy of the Mini-Mental State Examination (MMSE) in adult patients (n=2017) in medical settings. Overall the sensitivity was 84.1 % with specificity of 73% which increased to 81.1% and 82.2%, respectively in some subgroups. The authors state the MMSE may be a useful screening tool (with 93% accuracy), as patients with high scores were unlikely to have delirium.

A systematic review(34) of 27 studies reviewed screening tools for delirium in older patients (n=4766) in the hospital and nursing home setting, including attention, arousal and rapid bedside screening. The observation scale of level of arousal (OSLA) and Richmond agitation sedation scale (RASS) arousal tests had high sensitivity and specificity (>80%) and were suitable for daily use by nursing staff. Other tests varied from 17-100% for sensitivity and 38-99% for specificity. The authors did not comment on the suitability for these tests.

A secondary analysis of a randomised trial(35) (n=996) investigated whether postoperative impairment of cerebral function could predict postoperative delirium. Three tools were assessed: post anaesthetic recovery score (PARS), RASS and the nursing delirium screening scale (Nu-DESC) within 10 minutes after admission to the recovery room. Abnormal RASS and Nu-DESC scores were significantly associated with postoperative delirium within 7 days, with abnormal PARS scores being significantly associated with a longer stay in the recovery room.

Intelligence gathering

Topic experts highlighted the following:

- One topic expert stated that the age cut off of over 65 in the recommendation is artificial and should instead be based on the physical age of the patient.
- One topic expert suggested expanding the risk factors to include a previous episode of delirium, medication and surgery.
- One topic expert raised that any fracture should be considered a risk factor for delirium, rather than just hip fractures.

Impact statement

Risk factors for the general population

Age

The 2014 review found evidence from 2 studies that increased age (over 65 years) was a common risk factor for critically ill or stroke patients. New evidence from the 2018 review found that age over 65 years in surgical patients was significantly associated with an increased incidence of delirium. This is supportive of recommendation 1.1.1 which lists age 65 years or older as a risk factor for delirium.

One topic expert in the 2018 review acknowledged that age was an artificial risk factor, and physical age was a better indicator of risk, however, no new evidence was found to support this.

Cognitive impairment

Evidence from the 2014 review found that NEECHAM and DRS-R-98 were acceptable for assessing delirium in hip fracture patients with cognitive impairment. There is insufficient evidence here to suggest adding these assessment tools to the current recommendations. This is supportive of recommendation 1.1.1 regarding assessment of those with cognitive impairment.

Pharmacological risk factors

The 2012 evidence update found specific groups of medications may be potential risk factors for development of delirium. However, evidence from the 2014 review on the effects of these drugs provided mixed results. One topic expert in 2018 highlighted medication as a risk factor for delirium. Medication is not currently listed as a risk factor in recommendation 1.1. A systematic review from the 2018 review found that nifedipine use prior to cardiac surgery was significantly associated with postoperative delirium. However, the evidence was limited in scope and does not support including medications as a risk factor at this time.

Cerebrospinal fluid biomarkers

The 2014 review found an association between delirium and 8 CSF biomarkers. New evidence from 2 studies identified in the 2018 review also found biomarkers may predict delirium, however, there was limited evidence and an impact on the recommendations is unlikely.

Genetic risk factors

The 2018 review found evidence for APOE as a potential indicator for delirium, however the effect seen was non-significant and is unlikely to impact on the current recommendations.

Risk factors for specified sub-populations

Risk factors after cardiac surgery

The 2014 summary found evidence from 2 studies that identified potential risk factors from cardiac surgery such as length of surgery and red cell transfusion, although no changes to recommendations were proposed at that time. As no further evidence was found during the current review, there is insufficient evidence to suggest updating the recommendations.

Delirium in acute stroke

One study from the 2014 review found a number of risk factors were associated with delirium in acute stroke patients. This included increased age, aphasia, visual disturbances and elevated cortisol levels. Recommendation 1.1 does not describe risk factors specifically for patients with acute stroke, and as no further evidence was identified for the general population at the 2018 review these findings are unlikely to have an impact on the recommendations.

Critically ill patients

The 2014 review found 2 studies relating to critically ill patients which found that increased age was a common risk factor for delirium. Further evidence from the 2014 review found several delirium screening tools were in use in emergency departments with minimal validation in 1 study.

No evidence was found for the current review and as such no impact on the recommendations is anticipated.

Acute medical inpatients

Two studies from the 2014 review found that dementia was a risk factor for delirium in hospital inpatients. But there was conflicting evidence for age as a risk factor. Age is currently listed as a risk factor in recommendation 1.1.1, as the evidence from 2014 is inconclusive and no further evidence was found in the current review there is not enough evidence to suggest changing the current recommendation. One of these studies also highlighted cognitive impairment as a risk factor for delirium which is consistent with recommendation 1.1.1 as no further evidence was found at the 2018 review it is unlikely to have an impact on the recommendations at this time.

Blood transfusion

New evidence from 1 study found mixed results for blood transfusion as a risk factor for delirium. Another found anaemia to be associated with delirium. This is not an area covered by recommendation 1.1.1 and as the evidence is mixed and limited it is unlikely to have an impact.

Surgery related risk factors

Evidence from the 2014 review categorised potential risk factors for delirium, however no clear conclusions could be drawn. The new evidence in 2018 found that older age (>65) was significantly associated with postoperative delirium in surgical patients which supports age as a risk factor in recommendation 1.1.

ASA score >3 was a significant risk factor for delirium in one study of vascular surgical patients from the 2018 review, and ASA>2 was associated with delirium in a second study of head and neck cancer surgical patients (significance not stated). Surgery is not listed as a risk factor in recommendation 1.1 and the 2 identified studies are unlikely to have an impact on the recommendations at this time.

Gender was highlighted in 4 studies of pre- and postoperative patients, however the results were mixed with 1 study finding male sex to be a significant risk factor, 1 finding female sex to be significant and 2 others found male sex to be associated with delirium as an outcome but did not report statistical significance. Gender is not currently listed as a risk factor in recommendation 1.1 and as the evidence is mixed it is unlikely to have an impact at this time.

Six studies reported on risk factors associated with surgery and delirium, and duration of surgery was significantly associated with delirium in 2 studies on

postoperative risk factors. Two of the studies reported on hip fracture surgical patients, no evidence was found for other types of fracture as a risk factor as raised by one topic expert. It was also raised by one topic expert that surgery may be a risk factor for delirium, however the evidence found relates only to which risk factors increase the risk of postoperative delirium in patients undergoing surgery. As the evidence regarding this area is mixed it is unlikely to have an impact on the recommendations at this time.

Methods for assessing delirium risk

The 2012 evidence identified a screening tool for delirium, however as no further evidence was identified in the subsequent reviews, it is unlikely to impact on the recommendations at this time.

Evidence from 1 study in the 2014 review found that CAM and CAM-ICU were found to have higher specificity than sensitivity and as such they should be used alongside clinical judgement. Two studies found CAM-ICU had a higher degree of specificity than sensitivity in critically ill patients, although sensitivity was also high. The MBT and MMSE may be a useful screening tool as those with high scores were unlikely to have delirium. The OSLA and RASS arousal tests had high sensitivity and specificity and were suitable for daily use. Abnormal RASS and Nu-DESC scores were significantly associated with postoperative delirium, however this was in a high dementia prevalence sample.

Screening tools are not currently listed in this recommendation and as there is limited evidence on individual tools it would be unlikely to have an impact on the recommendations at this time.

Overall conclusions

Overall, there was a range of new evidence across different patient groups and risk factors. However, the evidence is limited and inconsistent and is insufficient to support any changes to the recommendations.

There was evidence to support the risk factors age and current hip fracture that are reported in the guideline recommendation 1.1.1.

New evidence is unlikely to change guideline recommendations.

Indicators of delirium: at presentation

1.2.1 At presentation, assess people at risk for recent (within hours or days) changes or fluctuations in behaviour. These may be reported by the person at risk, or a carer or relative. Be particularly vigilant for behaviour indicating hypoactive delirium (marked*). These behaviour changes may affect:

- Cognitive function: for example, worsened concentration*, slow responses*, confusion.
- Perception: for example, visual or auditory hallucinations.
- Physical function: for example, reduced mobility*, reduced movement*, restlessness, agitation, changes in appetite*, sleep disturbance.
- Social behaviour: for example, lack of cooperation with reasonable requests, withdrawal*, or alterations in communication, mood and/or attitude.

If any of these behaviour changes are present, a healthcare professional who is trained and competent in diagnosing delirium should carry out a clinical assessment to confirm the diagnosis.

Surveillance decision

No new evidence has been identified at any surveillance review.

This recommendation should not be updated.

Interventions to prevent delirium

Recommendations in this section of the guideline

- 1.3.1 Ensure that people at risk of delirium are cared for by a team of healthcare professionals who are familiar to the person at risk. Avoid moving people within and between wards or rooms unless absolutely necessary.
- 1.3.2 Give a tailored multicomponent intervention package:

- Within 24 hours of admission, assess people at risk for clinical factors contributing to delirium.
 - Based on the results of this assessment, provide a multicomponent intervention tailored to the person's individual needs and care setting as described in recommendations 1.3.3.1–1.3.3.10.
- 1.3.3 The tailored multicomponent intervention package should be delivered by a multidisciplinary team trained and competent in delirium prevention.
- 1.3.3.1 Address cognitive impairment and/or disorientation by:
- providing appropriate lighting and clear signage; a clock (consider providing a 24-hour clock in critical care) and a calendar should also be easily visible to the person at risk
 - talking to the person to reorientate them by explaining where they are, who they are, and what your role is
 - introducing cognitively stimulating activities (for example, reminiscence)
 - facilitating regular visits from family and friends.
- 1.3.3.2 Address dehydration and/or constipation by:
- ensuring adequate fluid intake to prevent dehydration by encouraging the person to drink – consider offering subcutaneous or intravenous fluids if necessary
- taking advice if necessary when managing fluid balance in people with co-morbidities (for example, heart failure or chronic kidney disease).
- 1.3.3.3 Assess for hypoxia and optimise oxygen saturation if necessary, as clinically appropriate.
- 1.3.3.4 Address infection by:
- looking for and treating infection
 - avoiding unnecessary catheterisation
 - implementing infection control procedures in line with [healthcare-associated infections](#).
- 1.3.3.5 Address immobility or limited mobility through the following actions:
- Encourage people to:
 - mobilise soon after surgery
 - walk (provide appropriate walking aids if needed – these should be accessible at all times).
 - Encourage all people, including those unable to walk, to carry out active range-of-motion exercises.
- 1.3.3.6 Address pain by:
- assessing for pain
 - looking for non-verbal signs of pain, particularly in those with communication difficulties (for example, people with learning difficulties or dementia, or people on a ventilator or who have a tracheostomy)

- starting and reviewing appropriate pain management in any person in whom pain is identified or suspected.
- 1.3.3.7 Carry out a medication review for people taking multiple drugs, taking into account both the type and number of medications.
- 1.3.3.8 Address poor nutrition by:
- following the advice given on nutrition in [Nutrition support in adults](#) (NICE clinical guideline 32)
 - if people have dentures, ensuring they fit properly.
- 1.3.3.9 Address sensory impairment by:
- resolving any reversible cause of the impairment, such as impacted ear wax
 - ensuring hearing and visual aids are available to and used by people who need them, and that they are in good working order.
- 1.3.3.10 Promote good sleep patterns and sleep hygiene⁶ by:
- avoiding nursing or medical procedures during sleeping hours, if possible
 - scheduling medication rounds to avoid disturbing sleep
 - reducing noise to a minimum during sleep periods.

⁶ For more information on good sleep hygiene, see the NICE guideline on [Parkinson's disease](#).

Surveillance decision

This recommendation should not be updated.

Editorial amendments

- The overview page currently has a cross referral to the guideline [alcohol-related physical health problems](#). We will add the following cross referral to this paragraph: For guidance on bispectral-index guided anaesthesia please see Diagnostics guidance DG6 - [Depth of anaesthesia monitors – Bispectral Index \(BIS\), E-Entropy and Narcotrend-Compact M](#).
- Recommendation 1.3.3.7: we will include the following cross-referral as a relevant guideline has been published: “For information on medicines optimisation see [NICE guideline NG5](#)”.
- Recommendation 1.3.3.10: The information about sleep hygiene is no longer included in NICE guideline NG71, so we plan to remove the footnote.

Recommendation 1.3

Non-pharmacological prevention: single component interventions

Earplugs

Previous surveillance summary

No evidence was identified at the 2012 review.

The 2014 review identified an RCT(36) which found using earplugs lowered the incidence and delayed the development of confusion.

2018 surveillance summary

A systematic review and meta-analysis(37) of 9 intervention studies (n=1,455) assessed the efficacy of earplugs for reducing the incidence of delirium in the ICU. The authors state that the use of earplugs significantly reduced the incidence of delirium for ICU patients (based on 2 studies). This study is also reported in an [NIHR signal](#).

A systematic review and meta-analysis(38) of 30 RCTs and quasi-RCTs (n=1569) aimed to assess the efficacy, safety, clinical effectiveness and cost effectiveness of non-pharmacological sleep improvement interventions in adult ICU patients on a number of outcomes including delirium. Meta-analysis of 3 trials which used earplugs, eye masks or both, found a significantly lower incidence of delirium during ICU stay (based on 2 studies, n=177). Total sleep time was also significantly improved.

Transfusion strategies

Previous surveillance summary

No evidence was identified at the 2012 review.

An RCT(39) identified in the 2014 review found no difference in postoperative delirium incidence between liberal or restrictive blood transfusion strategies.

2018 surveillance summary

A *post-hoc* analysis of an RCT(40) (n=179 frail anaemic patients admitted for hip fracture surgery from nursing homes) investigated a liberal blood transfusion strategy and the risk of POD, compared with a restrictive transfusion strategy. The effect of POD on 90 day mortality was also investigated. Delirium was assessed using the MMSE and CAM on days 1 and 10. The liberal blood transfusion significantly reduced POD at day 10 compared with the restrictive transfusion strategy. POD at day 10 was a significant risk factor for 90 day mortality.

Fast-track surgery

Previous surveillance summary

No evidence was identified at the 2012 review.

An RCT(41) from the 2014 review found patients who received fast-track surgery had a significantly lower incidence of delirium.

2018 surveillance summary

None identified.

N-3 fatty acids

Previous surveillance summary

No evidence was identified at the 2012 review.

An RCT(42) from the 2014 review found that administration of n-3 fatty acids did not affect the incidence of sepsis-associated delirium.

2018 surveillance summary

None identified.

Hydration-based intervention

Previous surveillance summary

No evidence was identified at the 2012 review.

A Cochrane review(43) identified in the 2014 review found that hydration-based interventions did not reduce delirium incidence in older people in long-term care. The review also found that a computerised medication identification system resulted in a large reduction in delirium incidence for older people in long-term care.

2018 surveillance summary

None identified.

Geriatric care/protocols

Previous surveillance summary

No evidence was identified at the 2012 or 2014 reviews.

2018 surveillance summary

A systematic review and meta-analysis(44) of 16 RCTs and observational studies assessed the effect of flexible versus restricted ICU visiting policies on patient, relative and staff outcomes. Patients experienced significantly reduced frequency of delirium and less severe anxiety symptoms with the flexible visiting policy.

A systematic overview(45) of 24 systematic reviews assessed the efficacy of non-pharmacological interventions for prevention and treatment of delirium in older people. Staff education, reorientation protocols and Geriatric Risk Assessment software were found to be effective single component interventions in preventing delirium.

An RCT(46) (n=123) compared application of a delirium preventative protocol delivered to patients for the first 7 days of ICU hospitalisation (n=60) with usual care

(n=63). No significant effect on delirium incidence, in hospital mortality, 30 day in hospital mortality, ICU re-admission or length of ICU stay was seen in the intervention group; however, a significant decrease in 7 day in hospital mortality was seen in the intervention group compared with the control group.

Education

Previous surveillance summary

No evidence was identified at the 2012 or 2014 reviews.

2018 surveillance summary

An RCT(47) (n=129 patients undergoing pulmonary thromboendarterectomy) investigated effect of preoperative education on delirium, anxiety and patient knowledge postoperatively. The intervention group (n=63) received preoperative 45 minute multifaceted education and the control group (n=66) received standard education. The State Trait Anxiety Inventory and Knowledge test was completed by participant's pre and post education. There was no significant difference between the control and intervention groups for delirium or length ICU stay.

Oxygen related interventions

Previous surveillance summary

No evidence was identified at the 2012 or 2014 reviews.

2018 surveillance summary

A systematic review and meta-analysis(48) of 15 RCTs (n=1,018 intervention and n=1,039 control group patients) evaluated the use of cerebral oximetry to guide intraoperative management on postoperative delirium. There was no significant reduction in postoperative delirium incidence.

A prospective RCT(49) (n=40 patients with moderate acute respiratory distress syndrome) investigated whether synchronised intermittent mandatory ventilation with pressure support (SIMV+PS) would improve clinical outcomes for patients including delirium compared with the usual method of assist/control (A/C) ventilation. SIMV+PS did not reduce delirium incidence.

An RCT(50) (n=114) investigated whether the use of perioperative continuous positive airway pressure (CPAP) could improve acute postoperative delirium compared with usual care, in patients at risk of obstructive sleep apnoea. The incidence of delirium was 21% in the intervention group and 16% in the usual care group (no significant difference). The residual preoperative apnoea-hypopnea index showed a significant reduction in delirium severity in CPAP participants.

An RCT(51) (n=249) investigated regional cerebral oxygen desaturation and its impact on POD in patients >60y undergoing cardiac surgery. An oxygen restoration algorithm was commenced if cerebral oximetry dropped below 75% of baseline for 1 minute or more during surgery in the intervention group, compared with no action in the control group. Delirium was assessed using CAM-ICU twice daily for 7 days postoperatively. There was no significant difference in delirium incidence between the control and intervention groups.

Light therapy

Previous surveillance summary

No evidence was identified at the 2012 or 2014 reviews.

2018 surveillance summary

An RCT(52) (n=734) investigated whether the use of dynamic light application

compared with usual lighting between 9am and 4pm would reduce the incidence of delirium in medical and surgical patients admitted to the ICU. The intervention (n=361) consisted of ceiling mounted blue-white light up to 1700 lux compared with control (n=373) lighting at 300 lux. The study was terminated early following a futility analysis, which found delirium had occurred in 38% of the intervention and 33% of the control groups.

Glucose control

Previous surveillance summary

No evidence was identified at the 2012 or 2014 reviews.

2018 surveillance summary

An RCT(53) (n=198) investigated the effect on postoperative delirium of tight glucose control during cardiac surgery. Patients received either tight intraoperative glucose control with a hyperinsulinemic-normoglycemic clamp or standard therapy. Postoperative delirium was diagnosed if CAM was positive at any assessment. Tight glucose control was significantly associated with an increase in postoperative delirium, however severity of delirium did not differ significantly between the groups.

Non-pharmacological prevention: multicomponent interventions

Nursing interventions

Previous surveillance summary

A cluster RCT(54) from the 2012 review found that a nurse-led delirium abatement programme detected delirium in 41% of patients at DAP sites compared with 12% in usual care sites. An RCT(55) from the 2014 review found that hypoactive delirium can be reduced with nursing interventions.

2018 surveillance summary

A systematic review and meta-analysis(56) of 7 randomised trials (n=1691) investigated whether delirium in hospitalised patients could be prevented by nursing staff using multicomponent interventions. Incident delirium and accidental falls were significantly reduced by the intervention, but the reduction in delirium duration, was not statistically significant.

Comprehensive geriatric assessment

Previous surveillance summary

No evidence was identified at the 2012 or 2014 reviews.

2018 surveillance summary

A systematic review(57) of 4 trials (2 ward based models on geriatric wards, 2 team based models on orthopaedic wards, n=973 participants) assessed the efficacy of delirium prevention following hip fracture using the comprehensive geriatric assessment (CGA). Overall a significant reduction in delirium was seen, which was maintained in the team based trials following post-hoc subgroup analysis.

A meta-analysis(58) of 7 RCTs (n=1840 elderly patients with hip fractures) compared the CGA (intervention) with routine orthopaedic treatment.

Perioperative delirium incidence was significantly reduced and there was higher cognitive status associated with the CGA. Duration of delirium was not significantly different between the control and intervention groups.

An RCT(59) (n=176 patients >65 years scheduled for surgery) compared a preoperative CGA and optimisation with standard preoperative assessment to investigate the effect on length of hospital stay, new co-morbidities and postoperative complications. A

significantly lower incidence of delirium and reduction in hospital stay was seen in the intervention group

Hospital based geriatric interventions

Previous surveillance summary

A cluster RCT(60) from the 2012 review found that a multidisciplinary integrated care intervention led to a reduction in the occurrence of delirium.

The 2014 review identified a systematic review(61), a meta-analysis(62) and an RCT(63) which found that multicomponent non-pharmacological interventions were effective at preventing or reducing the risk of delirium in patients. Three RCTs(64–66) found that geriatric interventions, consultant teams or wards had no significant difference on delirium severity, duration or incidence. One RCT(67) in dementia patients found multicomponent interventions lead to fewer postoperative complications including delirium.

2018 surveillance summary

A randomised trial(68) in 260 frail elderly cancer patients undergoing a surgical solid tumour procedure investigated long-term outcomes following the implementation of a geriatric liaison intervention to prevent postoperative delirium. The intervention group (n=127) received preoperative consultation, individual treatment plans for targeted risk factors for delirium and daily geriatric nurse visits. At 3 months post discharge, no difference was seen between the intervention and control groups for any outcome.

Specialist medical and mental health unit

Previous surveillance summary

No evidence was identified at the 2012 review.

An RCT(69) from the 2014 review found that specialist care for people with

delirium and dementia improved the experience of patients and satisfaction of carers. However the effects on prevention were unclear.

2018 surveillance summary

None identified.

Exercise and cognitive programme

Previous surveillance summary

No evidence was identified at the 2012 review. The 2014 review identified an RCT(70) that found no difference in incidence of delirium when elderly hospitalised patients undertook an enhanced exercise and cognitive programme.

2018 surveillance summary

None identified.

General multicomponent interventions

Previous surveillance summary

No evidence was identified at the 2012 review. A meta-analysis(71) from the 2014 review found that multicomponent interventions were effective in preventing postoperative delirium. A second meta-analysis(72) found perioperative geriatric consultation with multicomponent interventions and lighter anaesthesia were associated with a reduction in delirium incidence.

2018 surveillance summary

A systematic overview(45) of 24 systematic reviews assessed the efficacy of non-pharmacological interventions for prevention and treatment of delirium in older people. The incidence of delirium on medical and surgical wards was reduced significantly by multicomponent interventions (based on 2 RCTs). Non-pharmacological interventions were unable to prevent delirium in this population in 1 RCT but the authors of the review noted

that that delirium was not the primary outcome in this study.

A systematic review(73) assessed multicomponent interventions compared with usual care and found a reduction in delirium incidence, however no effect was seen in a subgroup of patients with pre-existing dementia.

A systematic review(74) of 9 studies investigated the effectiveness of multicomponent interventions on delirium in patients with hip fractures. When data was pooled from 3 RCTs, the incidence of delirium was reduced significantly by the multicomponent intervention (components not stated) Results from the other 6 studies showed effect on duration or severity of delirium.

A meta-analysis(75) of 14 interventional studies aimed to evaluate non-pharmacological multicomponent interventions for reduction of delirium and associated poor outcomes. Significant reductions in delirium incidence were seen in 11 studies, with the rate of falls reduced significantly in 4 studies. The length of stay in an institution was also found to decrease with the intervention however this was not significant. The individual components of the interventions assessed was not reported in the abstract.

Anaesthesia

Previous surveillance summary

A systematic review(76) from the 2012 review found regional nerve blockades did not significantly reduce delirium risk. However one RCT(77) found the frequency of delirium was significantly lower in hip surgery patients who underwent fascia iliaca compartment block. A meta-analysis(71) from the 2014 review found no difference in the incidence of delirium between neuraxial

and general anaesthesia or between epidural and intravenous analgesia. An RCT(78) found no difference between desflurane or propofol for delirium incidence in cardiac surgery patients.

2018 surveillance summary

An RCT(79) (n=96) compared propofol and desflurane maintenance anaesthesia for delirium incidence as assessed by CAM in obese patients following primary total knee replacement surgery. No significant difference in delirium incidence was seen between groups.

An RCT(80) (n=256) assessed xenon based compared with sevoflurane based general anaesthesia for the incidence of POD in elderly (>75 years) hip fracture patients. No significant difference was seen between group for delirium within 4 days postoperatively or any time after surgery.

Depth of anaesthesia

Previous surveillance summary

One RCT(81) from the 2012 review found that postoperative delirium was significantly reduced by light sedation compared with heavy sedation. No evidence was identified 2014 review.

2018 surveillance summary

A systematic review and meta-analysis(82) of 9 studies (n = 4,521 patients) sought to quantify the impact of deep sedation within 48 hours of mechanical ventilation on a number of outcomes including delirium. Delirium frequency was significantly lower in the light sedation group (28%) compared with the heavy sedation group (49%).

Monitoring the depth of anaesthesia

Previous surveillance summary

No evidence was identified at the 2012 review.

An RCT(83) from the 2014 review found that delirium incidence was lower in surgical patients whose anaesthesia was guided using bispectral index (BIS).

2018 surveillance summary

A systematic review(73) assessed a number of prevention interventions for non-ICU hospitalised patients. A reduction in delirium incidence was seen with BIS guided anaesthesia, when compared with BIS-blinded anaesthesia or clinical judgement alone. This study is described in more detail in the [melatonin](#) section.

Pharmacological prevention

Melatonin

Previous surveillance summary

An RCT(84) from the 2012 review found that melatonin reduced the risk of developing delirium compared with placebo. The 2014 review found a systematic review(85) which found melatonin may reduce incidence but not severity of delirium. A melatonin agonist (ramelteon) also prevented delirium in medically ill patients.

2018 surveillance summary

A systematic review(73) of 39 trials investigated interventions for preventing delirium in non-ICU patients. Delirium prevention interventions were compared with usual care in 15 trials, and another intervention in 10 trials. No clear evidence was found for reducing the incidence of delirium with melatonin or melatonin agonists compared with placebo.

A meta-analysis(86) of 4 RCTs (n=669 elderly patients) assessed whether melatonin reduced delirium incidence. Overall melatonin was associated with a decreased incidence of delirium compared with the control group. In a subgroup analysis, a significant reduction in delirium

incidence was found with melatonin in medical wards but no difference was seen for surgical wards.

An RCT(87) (n=378 elderly patients admitted for hip surgery) investigated the effect of melatonin 3 mg administered each evening for 5 days within 8 days of admission. The incidence of delirium was 29.6% compared with 25.5% in a placebo group but the difference was not significant.

An RCT(88) (n=56 patients) investigated the impact of melatonin on delirium duration in patients with organophosphate compound poisoning admitted to the ICU. Melatonin tablets or placebo tablets were given each night during the ICU stay, with CAM-ICU used to assess delirium 3 times a day. The melatonin intervention group had a significantly decreased prevalence and duration of delirium compared with placebo.

An RCT(89) (n=88 ICU patients who could take medication orally or via nasogastric tube) assessed the use of ramelteon, a melatonin receptor agonist on delirium incidence and duration, and length of ICU stay. The intervention group (n=45) received 8 mg/d ramelteon daily until discharge. The control group (n=43) received 1g/d lactose powder. There was a statistically significant decrease in the rate of onset and duration of delirium with ramelteon compared with control. Note that ramelteon is not licensed in the UK.

Acetylcholinesterase inhibitors

Previous surveillance summary

No evidence was identified at the 2012 review.

A meta-analysis(71) from the 2014 review showed no difference in the incidence of postoperative delirium between acetylcholinesterase inhibitors and

placebo. A pilot RCT(90) found no difference in delirium prevalence or severity with donepezil hydrochloride compared with a placebo.

2018 surveillance summary

A systematic review(73) assessed a number of prevention interventions for non-ICU hospitalised patients. Acetylcholinesterase inhibitors were not effective at reducing delirium incidence compared with placebo. Fuller details of this study are available in the [melatonin](#) section.

Dexmedetomidine

Previous surveillance summary

No evidence was identified at the 2012 review.

A systematic review(91) was found in the 2014 review where the authors reported dexmedetomidine as a promising agent (details not stated) for the prevention and treatment of delirium in the ICU. A meta-analysis(92) found significant reductions in delirium incidence with dexmedetomidine compared to non-invasive ventilation, midazolam, and in general ICU patients.

2018 surveillance summary

A systematic review(93) of 7 RCTs (n=1624) investigated dexmedetomidine compared with alternative sedatives (propofol, midazolam, lorazepam) for long-term sedation (>24 hours) in critically ill, mechanically ventilated patients. The authors noted that the risk of delirium was highly heterogeneous but, because of the low number of studies, were unable to determine its source. There was no evidence for dexmedetomidine reducing the risk of delirium. No effect on mortality was identified, however bradycardia was a common side effect.

Five meta-analyses(94–98), assessed the effect of dexmedetomidine as a sedative

(16 RCTs), compared with lorazepam, midazolam and propofol (16 RCTs), midazolam alone (2 meta-analyses 14 RCTs, 6 studies), propofol alone (8 RCTs) on delirium incidence, and for prevention of delirium, agitation and confusion (14 studies). In all 5 meta-analyses, dexmedetomidine significantly reduced the incidence of delirium compared with other medications. There was a significant increase in bradycardia in 3 analyses, and reduction in confusion and agitation in 1 analysis with dexmedetomidine. One analysis found a significant association between dexmedetomidine and hypotension, however a second found no significant association between dexmedetomidine and hypotension. Six RCTs(99–104) assessed the use of dexmedetomidine on cardiac surgery patients for the POD. Dexmedetomidine was compared with saline control (3 studies), midazolam (1), propofol (1) or placebo (1). CAM or CAM-ICU was used for daily delirium assessment in 3 studies, the delirium rating scale was used daily in a 4th study. The remaining 2 studies stated daily delirium assessment but did not report the method used. Overall, a non-significant decrease in postoperative delirium risk was seen in 2 studies, significant decrease in delirium incidence was seen in 3 studies and 1 study stated that both control and intervention groups had similar incidence and duration of delirium but did not report significance. Two RCTs(105,106) assessed the use of dexmedetomidine for the prevention of POD compared with propofol or saline controls in hip (n=296) and hip and knee (n=200) surgery patients. Both studies used CAM to assess delirium. Patients in the study of hip and knee surgery also had amnestic mild cognitive impairment prior to surgery. The hip surgery study reported

a decrease in POD but did not state if this was significant, the hip and knee surgery study reported significant decreases in POD compared with the saline control group.

Three RCTs(107–109) investigated the use of dexmedetomidine intra and postoperatively compared with saline (n=390, n= 80) or placebo (n=700) for the prevention of POD. Delirium was assessed daily in 2 studies and twice daily in a third, using either CAM or CAM-ICU. The 2 studies with saline controls reported non-significant decreases in the risk of POD with dexmedetomidine, while the placebo controlled study found a significant decrease in POD with dexmedetomidine. An RCT(110) (n= 100 critically ill adults) investigated the use of nocturnal dexmedetomidine compared with placebo to increase sleep and prevent delirium. Twelve hourly delirium assessments were performed using the ICDSC. In the dexmedetomidine group, a significant number of patients did not suffer delirium compared with the placebo group. There was no significant difference in hypotension and bradycardia seen between the 2 groups.

Antipsychotics - general

Previous surveillance summary

An RCT(111) from the 2012 review found the incidence of delirium was lower for patients receiving prophylactic olanzapine compared with a placebo. However, delirium that did occur was more severe and of a longer duration in the intervention group compared with the control.

The 2014 review identified 1 systematic review(112) and 3 meta-analyses(63,113,114) which found that postoperative delirium was reduced by prophylactic antipsychotic use, including

typical and atypical antipsychotics. Another RCT(115) found that prophylactic risperidone was associated with a significantly lower incidence of delirium.

2018 surveillance summary

A systematic review and meta-analysis(116) investigated antipsychotics for prevention of postoperative delirium. The number of studies was not stated, however 1710 subjects were included in the analysis. Antipsychotics significantly reduced the incidence of postoperative delirium, however the individual antipsychotics used were not reported in the abstract.

A systematic review and meta-analysis(117) of 19 studies of adult medical and surgical inpatients assessed the effectiveness of (unstated) antipsychotics on delirium incidence. Antipsychotics had no significant effect on postoperative delirium incidence in 7 studies compared with placebo or no treatment. No change in delirium severity or duration was found when comparing data from all 19 studies.

A systematic review(118) of 13 RCTs assessed the effect of pharmacological agents on delirium following cardiac surgery. Ten studies considered delirium prevention, with a large study on dexamethasone accounting for 77% of the 5848 total sample size. Other agents assessed were rivastigmine, risperidone, ketamine, dexmedetomidine, propofol and clonidine. The authors state that moderate quality evidence supports the use of pharmacologic agents for the prevention of delirium.

A systematic review(73) of 39 studies assessed interventions for non-ICU hospitalised patients. Three trials assessed antipsychotic medication as a group; there was no effect on delirium incidence. One study found olanzapine was associated

with a significantly lower delirium incidence compared with placebo. See the [melatonin](#) section for a fuller details of this study.

Antipsychotics - Haloperidol

Previous surveillance summary

No evidence was identified at the 2012 review. A meta-analysis(72) from the 2014 review found a possible protective effect on postoperative delirium with prophylactic haloperidol. One RCT(119) found haloperidol was significantly more effective than a placebo at reducing postoperative delirium however another RCT(120) found when haloperidol was given after surgery there was no effect on postoperative delirium.

2018 surveillance summary

A systematic review(121) of 12 RCTs evaluated haloperidol for the prevention and treatment of delirium in hospitalised patients. Four placebo controlled studies addressed delirium prevention and 3 of these found significant reduction delirium incidence, severity and duration in ICU. Data could not be pooled because of heterogeneity between the studies.

A systematic review and meta-analysis(122) of 10 RCTs and prospective cohort studies investigated haloperidol for delirium prophylaxis and treatment compared with either placebo (8 studies n=1,734) or with second generation antipsychotics (2 studies n=127). A high dose of prophylactic haloperidol (>5 mg/d) may reduce incidence of delirium in surgical patients, however significance was not stated. There was no significant difference between haloperidol and placebo groups for any secondary outcome including delirium duration and mortality.

A systematic review(73) assessed a number of preventative interventions for non-ICU hospitalised patients. Two studies evaluated haloperidol but no evidence for effectiveness was found. For a full summary see the [melatonin](#) section.

Three RCTs(123–125) (n= 68, 242 and 1789 respectively) investigated the prophylactic use of 1 mg or 2 mg oral or intravenous (IV) haloperidol 2, 3, or 4 times a day compared with placebo. There was no significant improvement in delirium incidence, duration or severity in the intervention group for any study. Haloperidol significantly reduced agitation in 1 study and no treatment limited side effects were found in another study.

Ondansetron

[Previous surveillance summary](#)

No evidence was identified at the 2012 review. The 2014 review identified one RCT(126) which found postoperative ondansetron led to a lower incidence of postoperative delirium.

[2018 surveillance summary](#)

None identified.

Ketamine

[Previous surveillance summary](#)

No evidence was identified at the 2012 or 2014 reviews.

[2018 surveillance summary](#)

An RCT(127) (n=1360) investigated low (0.5 mg/kg) or high (1.0 mg/kg) dose ketamine and placebo following anaesthesia for the prevention of postoperative delirium in patients >60y undergoing surgery. Delirium was assessed using the CAM twice daily for 3 days post-surgery, with no significant differences seen between the low or high dose intervention group and the placebo group.

Other pharmacological preventions

[Previous surveillance summary](#)

No evidence was identified at the 2012 review. The 2014 review identified an RCT(128) which found that dexamethasone pre and post cardiac surgery can lead to significant decreases in incidence of delirium.

[2018 surveillance summary](#)

An RCT(129) investigated the use of peri-procedural medication for the prevention of post-procedure delirium in 93 elderly patients undergoing elective cardiac surgery. The investigation group received oral diphenhydramine and diazepam (25 mg/5 mg) with the control group receiving no medication. Patients were assessed using the CAM before the procedure, 4 hours after and at discharge. Neither the intervention nor control group reported any cases of delirium.

An RCT(130) (n=72) investigated the use of suvorexant for delirium prevention in patients aged 65-89 years on acute wards or in ICU. Participants received suvorexant 15 mg per day for 3 days at night or a placebo. Delirium incidence was significantly less in the intervention group compared with the placebo group, with no significant differences in adverse events. Note that suvorexant is not licensed in the UK.

An RCT(131) (n=697 non-cardiac surgery patients) investigated whether pre and postoperative gabapentin could reduce delirium incidence. Gabapentin 900 mg or a placebo was administered preoperatively and for 3 days post-surgery and patients were assessed with CAM. There was no significant difference in incidence of delirium between the 2 groups.

An RCT(132) (n=116) investigated the use of postoperative tryptophan on incidence of postoperative hyperactive and overall

delirium in elderly patients undergoing major surgery requiring ICU admission. Patients received 1 g oral L-tryptophan or a placebo 3 times daily after surgery and for 3 days postoperatively, with delirium assessed by CAM-ICU and RASS. There was no significant differences between groups for incidence of either hyperactive or overall delirium.

An RCT(133) (n=498) investigated whether methylprednisolone has an effect on POD in patient undergoing cardiac surgery. Patients received either 250 mg methylprednisolone or a placebo at induction and before cardiopulmonary bypass. Delirium was assessed daily for 3 days postoperatively using CAM. There was no significant difference in incidence of delirium or its subdomains between groups.

Medication review

Previous surveillance summary

A cluster RCT(134) from the 2012 review found a lower rate of possible delirium when pharmacy-led monitoring using the Geriatric Risk Assessment MedGuide was implemented.

No evidence was identified at the 2014 review.

2018 surveillance summary

None found.

Intelligence gathering

One topic expert suggests that the medication review mentioned in recommendation 1.3.3.7 should be prioritised above other interventions, however recommendation 1.3.3 does not detail in which order these prevention methods should be used. One topic expert suggested that use of a 'communication passport' may aid identification of behaviour changes in a patient and ensure

they are treated by healthcare professionals who are trained to recognise delirium. Another topic expert felt that promoting awareness and increasing education around delirium for all patient facing staff would be of benefit, as early identification and management would prevent cases.

The following studies were highlighted by topic experts:

- An RCT(125) (n=1789) investigated the effect of prophylactic haloperidol use at 1 mg or 2 mg intravenously compared with a placebo in critically ill patients at high risk of delirium. The primary outcome was patient survival at 28 days, with additional outcomes including incidence of delirium and 28 days delirium free. No significant differences were seen between the intervention group and placebo group for any outcome.
- A trial(135) compared a quality improvement initiative to usual care in patients at high risk of complications. Primary outcomes included length of stay, 7- and 30-day readmissions, and level of care at discharge, secondary outcomes included delirium and postoperative complications. The study found that length of stay was shorter with less frequent readmissions for the intervention group, however rates of delirium were significantly higher in this group.
- An RCT(107) investigated the use of a dexmedetomidine infusion during surgery and for 2 hours after to prevent delirium. No difference was seen between the intervention and control groups for the primary outcome of postoperative delirium or postoperative cognitive decline.

Impact statement

The committee for the full guideline used hospital care evidence and extrapolated findings for long-term care settings outside of hospital. For the 2018 evidence summary we have considered evidence from hospital, long-term care and community settings, however, no studies have been identified for community based care.

Non-pharmacological prevention: single component interventions

Ear plugs

The 2014 surveillance found earplugs lowered the incidence of confusion in ICU patients. This is supported by new evidence from 2 studies that also found that earplugs reduced the incidence of delirium in ICU patients. The use of earplugs is consistent with recommendation 1.3.3.10 which promotes good sleeping patterns and reducing noise to a minimum during sleep periods. Earplugs are not specifically mentioned and may represent a cheap and simple measure to reduce the impact of uncontrolled noise. However, as the evidence was limited to ICU patients, evidence of benefit in other populations would be required before adding to the current recommendations on sleep hygiene.

Transfusion strategies

The 2014 surveillance review found no difference between the incidence of delirium with either restrictive or liberal blood transfusion strategies, whereas new evidence from the 2018 review from 1 study found a liberal transfusion strategy reduced postoperative delirium at day 10. Transfusion strategies are not currently covered by the recommendations, as the evidence is conflicting it would not be

sufficient to update the recommendations at this time.

Fast-track surgery

The 2014 surveillance review found in 1 study that delirium incidence was lower in elderly patients who received fast-track surgery. No new evidence has been identified on this topic and as such no impact on the current guidelines is anticipated.

N-3 fatty acids

The 2014 surveillance review found inconclusive evidence for N-3 fatty acids in the prevention of delirium outcomes and no new evidence has been identified. Therefore fatty acids should not be considered further at this time.

Hydration-based interventions

The 2014 surveillance found 1 review of 1 small trial relating to hydration interventions, which found no effect. Recommendation 1.3.3.2 already gives information on dehydration and the evidence found is not sufficient to change the current recommendation.

Geriatric care/protocols

The 2014 surveillance review found no evidence that a geriatric intervention had an impact on delirium.

The 2018 evidence found a preventative protocol had no significant effect on delirium incidence in 1 study. Increased flexibility of visiting hours was found to reduce delirium in one study, however significance was not stated. One study found no significant difference in any outcome including delirium when a geriatric liaison intervention was introduced. One topic expert highlighted a study on quality improvement initiatives however they did not result in a reduction in delirium incidence. Another study highlighted by a topic expert found that

perioperative optimisation of senior health initiative (an interdisciplinary perioperative care intervention) had higher levels of delirium. Geriatric protocols are not currently mentioned in recommendation 1.3 and there is insufficient evidence here to suggest adding it to the recommendations at this time.

Comprehensive geriatric assessment

New evidence from 2 hip fracture studies regarding the CGA found it significantly reduced peri-and postoperative delirium. A third study of elderly surgical patients found CGA led to a significantly lower incidence of delirium. The recommendations do not currently mention the CGA. However, the recommendations reflect activities that would be covered by the CGA; this includes, assessment of medical condition, functional ability and other patient circumstances to help prevent delirium. Therefore, evidence is complementary to existing recommendations.

Education

New evidence found that preoperative patient education had no effect on delirium incidence. There are no current recommendations regarding education. One topic expert highlighted that a communication passport may aid identification of behaviour changes. Another topic expert felt that increasing education for all patient facing staff would have a beneficial impact on delirium. Education is not currently covered by recommendation 1.3 and the evidence here is insufficient to suggest adding to the recommendations at this time.

Oxygen related interventions

New evidence found no differences in delirium for SIMV+PS compared with normal ventilation in patients with moderate acute respiratory distress

syndrome. No significant difference was seen between CPAP and usual care in one study of acute postoperative patients. Cerebral oximetry guided intraoperative management had no effect on delirium incidence in 1 study. No significant difference was seen in delirium incidence when an oxygen restoration algorithm was applied compared with usual care in patients >60y undergoing cardiac surgery. Recommendation 1.3.3 suggests optimising oxygen saturation, after assessing for hypoxia however this new evidence in a specific subpopulation cannot be extrapolated to the broader population covered by this recommendation and as such no change to this recommendation is anticipated.

Light therapy

One study that investigated dynamic light therapy was found, which was terminated early due to lack of effectiveness, with no significant difference between the intervention and usual lighting. Lighting in this context is not currently included in the recommendations and as this study was inconclusive there is no impact on the current guideline recommendations.

Glucose control

New evidence from the 2018 review on tight glucose control during cardiac surgery indicated that it was significantly associated with an increased incidence of postoperative delirium. Glucose control is not currently covered by recommendation 1.3, and as only 1 small study has been identified it is not sufficient to suggest updating the recommendations at this time.

Non-pharmacological prevention: multicomponent interventions

Nursing interventions

Evidence from the 2014 surveillance found that a selection of nursing interventions could reduce hypoactive delirium in ICU patients. New evidence also found that nursing interventions significantly reduced incident delirium in hospitalised patients in 2 studies. The current recommendations cover nursing interventions, multiple healthcare associated interventions, including orientation support and cognitive activities. They also recommend staff facilitate regular visits. This evidence is supportive of recommendation 1.3.3.1 and as such no impact is anticipated.

Geriatric interventions

The 2012 evidence update found that a multidisciplinary approach reduced delirium incidence in elderly patients. The 2014 review found 3 studies in which multicomponent interventions significantly reduced or prevented delirium in the elderly, 1 study that had a lower percentage of delirium cases and 1 study that had an overall reduction in complications including delirium. However 2 studies also found that geriatric liaison interventions or geriatric ward care had no significant effect on delirium incidence. New evidence found from 1 study found no effect on delirium. Therefore, the evidence does not indicate that recommendations should be revised at this time.

Exercise and cognitive programme

The 2014 review found no difference in delirium outcomes between the exercise intervention and usual care. Recommendation 1.3.3.5 recommends motion exercises, to address mobility or immobility. There is insufficient evidence

to consider changing the current recommendations given at this time.

General multicomponent interventions

The 2014 review found evidence from 2 studies on general multicomponent interventions that was supportive of the current guideline recommendations. This is supported by new evidence from 3 studies which found multicomponent non-pharmacological interventions significantly reduced delirium incidence in older adults and those at high risk of delirium. This is consistent with recommendation 1.3.2 which suggests a multicomponent approach.

Anaesthesia

Two studies from the 2014 review found that different types of anaesthesia had no impact on delirium incidence. New evidence from 2 studies within the current review found no significant difference in delirium incidence when comparing propofol and desflurane anaesthesia or xenon and sevoflurane anaesthesia respectively. One study found that nerve block did not significantly reduce delirium and a second study found that fascia iliaca compartment block was associated with a significantly lower incidence of delirium. Two studies found significantly less delirium when light rather than deep sedation was used.

Monitoring depth of anaesthesia

The 2014 surveillance found that guiding anaesthesia using BIS was associated with a lower incidence of delirium. This is supported by new evidence from a Cochrane review which found that BIS guided anaesthesia had a lower incidence of delirium compared with BIS-blinded or clinically guided anaesthesia.

Comments received during stakeholder consultation support the evidence found

for BIS guided anaesthesia. As a result we will add a cross-referral to diagnostics guidance DG6 - [Depth of anaesthesia monitors – Bispectral Index \(BIS\), E-Entropy and Narcotrend-Compact M](#) as detailed in editorial amendments.

Pharmacological prevention

Melatonin

Evidence from 2012 and 2014 found that melatonin was associated with a lower incidence of delirium. New evidence identified during the current review found a significant decrease in delirium incidence, prevalence and duration with melatonin (2 studies) or a melatonin reception agonist (1 study). However, 1 Cochrane review and 1 RCT found no clear evidence for the effect of melatonin on delirium. As the evidence found is inconclusive further evidence would be required in this area before an effect on the current recommendations can be determined.

Acetylcholinesterase inhibitors

Three studies from the 2014 review found that there was no significant difference between acetylcholinesterase inhibitors and placebo for the prevention of delirium. No new evidence was identified by the current review. This is not an area mentioned in the guideline and is likely to have no impact.

Dexamethasone

The 2014 review found that dexamethasone was associated with a decreased incidence of delirium. The guideline does not currently recommend dexamethasone and as no further evidence has been found it is unlikely to have an impact.

Dexmedetomidine

The 2014 review found that dexmedetomidine was associated with a reduced incidence of delirium in 3 studies. New evidence from 21 studies was found in the current review regarding dexmedetomidine for the prevention or resolution of delirium, most investigated postoperative delirium. In most studies, dexmedetomidine was used intra- or post-operatively for sedation including in mechanically ventilated ICU patients, 2 studies investigated the role of perioperative dexmedetomidine and 1 investigated nocturnal use in the ICU. A significant reduction in delirium incidence was seen in 13 studies, with non-statistically significant reductions in delirium incidence seen in a further 5 studies, with 3 studies finding no difference in delirium incidence. Bradycardia was listed as a common significant side effect in 3 studies with hypotension also listed as concern. One topic expert highlighted a study which found no difference between a dexmedetomidine infusion and a control. The recommendations do not currently mention dexmedetomidine for delirium prevention, or name a preferred method of sedation. New medications for prevention were also raised by a topic expert who highlighted a study on dexmedetomidine. The majority of the evidence found compares dexmedetomidine to a placebo, rather than other sedatives. The 1 systematic review which compares dexmedetomidine to propofol, midazolam and lorazepam found that dexmedetomidine had no significant effect on delirium incidence. As the evidence here is mixed it is not sufficient to impact the guideline recommendations at this time.

Antipsychotics

Evidence from the 2012 update found less delirium occurrence with olanzapine use, however the delirium that occurred lasted longer and was more severe.

The 2014 surveillance review found evidence on typical and atypical antipsychotics for delirium prevention was inconclusive in 1 study and evidence of reduced incidence of delirium with prophylactic risperidone use in a second study.

New evidence from the current review was found from 5 studies relating to the general use of antipsychotics for delirium prevention. One found a significant decrease in POD incidence, a second showed a decrease in incidence but significance was not stated. The remaining 3 studies did not find that antipsychotics generally prevented delirium, however 1 study found that olanzapine was effective. Antipsychotics are not currently recommended for the prevention of delirium in recommendation 1.3, and as the available evidence is inconclusive it would be unlikely to have an impact on the guideline.

Haloperidol

The 2014 review found 3 studies on haloperidol. One found no effect on incidence, duration or severity of delirium, 1 found a possible protective effect against delirium and 1 found significant reductions in postoperative delirium.

New evidence identified during the current review from 1 study suggests haloperidol may prevent delirium in surgical patients, however significance was not stated. A second study found haloperidol to significantly reduce incidence of delirium in ICU patients. Further findings from 1 SR and 4 RCTs found no significant effects of haloperidol

on delirium incidence, duration or severity. No safety concerns were reported in any study. Antipsychotics are not currently recommended for the prevention of delirium in recommendation 1.3, and as the available evidence is inconclusive it would be unlikely to have an impact on the guideline.

Ondansetron

One study from the 2014 surveillance found ondansetron led to a lower incidence and duration of postoperative delirium. However, as no further evidence was identified this is unlikely to impact the current recommendations.

Ketamine

New evidence from one study found no significant effect on delirium when adding ketamine following anaesthesia for the prevention of postoperative delirium. This is unlikely to impact on the guideline.

Other pharmacological preventions

Five studies provided new evidence of other pharmacological preventions. Diphenhydramine/diazepam, gabapentin, tryptophan, methylprednisolone had no significant effect on delirium incidence, with suvorexant (not licensed in the UK) significantly decreasing delirium incidence. Dexamethasone was also found to significantly reduce delirium incidence in 1 study from the 2014 review. This mixed evidence is inconclusive and would not currently influence the guideline recommendations.

Medication review

The 2012 update found that pharmacy-led medication review might lower the incidence of delirium for patients. This is supportive of recommendation 1.3.3.7 which suggests a medication review is performed. In addition, a topic expert highlighted that the medication review

should be prioritised above other prevention methods.

Overall conclusion

There is new evidence regarding potential prevention measures for delirium across a number of intervention areas such as ear plugs for hospitalised patients and dexmedetomidine sedation for surgical patients. However, the evidence for

dexmedetomidine related to a narrow subgroup of the population and as such further research is required in both of these areas before the impact on recommendations can be considered.

New evidence is unlikely to change guideline recommendations.

Indicators of delirium: daily observations

Recommendations in this section of the guideline

- 1.4.1 Observe, at least daily, all people in hospital or long-term care for recent (within hours or days) changes or fluctuations in usual behaviour (see recommendation 1.2.1). These may be reported by the person at risk, or a carer or relative. If any of these behaviour changes is present, a healthcare professional who is trained and competent in the diagnosis of delirium should carry out a clinical assessment to confirm the diagnosis.

Surveillance decision

No new information was identified at any surveillance review.

This recommendation should not be updated.

Diagnosis (specialist clinical assessment)

Recommendations in this section of the guideline

- 1.5.1 If indicators of delirium are identified, carry out a clinical assessment based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria or short CAM to confirm the diagnosis. In critical care or in the recovery room after surgery, CAM-ICU should be used. A healthcare professional who is trained and competent in the diagnosis of delirium should carry out the assessment. If there is difficulty distinguishing between the diagnoses of delirium, dementia or delirium superimposed on dementia, treat for delirium first.
- 1.5.2 Ensure that the diagnosis of delirium is documented both in the person's hospital record and in their primary care health record.

Surveillance decision

This recommendation should not be updated.

Editorial amendments

- Recommendation 1.5.1 currently states to confirm delirium diagnosis using DSM-IV. This will be replaced with DSM-V: "If indicators of delirium are identified, carry out a clinical assessment based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria or short Confusion Assessment Method (short CAM) to confirm the diagnosis."

Recommendation 1.5

Generic assessment tools

Previous surveillance summary

No evidence was identified at the 2012 or 2014 reviews.

A systematic review(29) of 22 studies investigated the diagnostic accuracy of 2 delirium assessment tools (CAM & CAM-ICU) and compared them to the DSM-IV. The pooled sensitivity for the CAM was 82% and the pooled specificity was 99%. For the CAM-ICU the pooled sensitivity was 81% while the pooled specificity was 98%. The authors concluded that although these tools have a role in diagnosis, they should be used in addition to clinical judgement. 2018 surveillance summary

A cross-sectional study(136) (n=200 patients in a skilled nursing facility) investigated the diagnostic accuracy of DSM and international classification of disease (ICD) criteria. Over half of the patients had pre-existing dementia. The delirium rating scale-revised-98 (DRS-R98), DSM-III-R, DSM-IV, DSM-5 and ICD-10 criteria were assessed. A cluster analysis of delirium features categorised 49 patients as having delirium. Diagnosis accuracy was highest for DSM-III-R at 87.5% and lowest for DSM-5 at 84.5%. The best balance of sensitivity (81.6%) and specificity was seen in DSM-III-R, with the highest inter-rater reliability seen in DSM-5.

A meta-analysis(31) assessed the accuracy of the CAM-ICU and the ICDSC for the diagnosis of delirium in critically ill patients. Nine studies (n=969) assessing CAM-ICU and 4 studies (n=361) evaluating ICDSC were included. The pooled sensitivity of the CAM-ICU was 80% and the pooled specificity was 95.9%. For the ICDSC the pooled sensitivity was 74% and the pooled specificity was 81.9%. The authors conclude that both tools can be used as a screening tool for delirium in critically ill patients and also state that due to its high specificity CAM-ICU is an excellent tool for delirium diagnosis.

EEG-based monitoring

Previous surveillance summary

No new evidence was identified at the 2012 review. A systematic review(137) was identified at the 2014 review which found that the theta and alpha frequency band during EEG was most often able to distinguish delirium from non-delirium.

2018 surveillance summary

None found.

Delirium superimposed on dementia

Previous surveillance summary

No new evidence was identified at the 2012 review. The 2014 review identified a systematic review(138) which found the CAM to have a high specificity (96-100%)

and moderate sensitivity (77%) in one study where 85% of patients had dementia. In 2 studies conducted in intensive care, CAM was reported to have 100% sensitivity and specificity in those with dementia. In another study, electroencephalography was found to have 67% sensitivity and 91% specificity in a population with dementia.

2018 surveillance summary

None found.

Delirium at the end of life

Previous surveillance summary

No new evidence was identified at the 2012 review. The 2014 review identified an RCT(139) which found delirium was diagnosed in 44% of patients using the Memorial delirium assessment scale (MDAS) and the Nu-DESC was found to have a sensitivity of 35% and specificity of 80% when used by care givers, however end of life care is outside the scope of CG103 and is now covered by NICE guideline NG31 – care of dying adults in the last days of life, which was published in December 2015.

2018 surveillance summary

None found.

Intelligence gathering

One topic expert mentioned that the DSM-IV criteria referenced in recommendation 1.5.1 is out of date. It has been updated to DSM-V.

Impact statement

Generic assessment tools

One topic expert highlighted that reference to the DSM-IV requires updating in the guideline, and to be replaced by

DSM-V. DSM and ICD criteria were found to have a high degree of accuracy in 1 study with DSM-V having the highest degree of inter-rater reliability.

Recommendation 1.5.1 currently recommends using CAM, CAM-ICU or DSM-IV for assessment of delirium. There is insufficient evidence to recommend assessment based on the DSM-V or adding additional diagnosis methods to the recommendation at this time. We will ask stakeholders for their view on replacing the DSM-IV with DSM-V in this recommendation.

EEG-based monitoring

Evidence from the 2014 review found theta and alpha frequency bands were able to distinguish between delirium and non-delirium in 1 study. This is not an area covered by the recommendation and there is insufficient evidence here to change that recommendation.

Delirium superimposed on dementia

The 2014 review found evidence from 1 study that stated CAM had high sensitivity and specificity for detecting delirium in dementia patients. This is supportive of recommendation 1.5.1 which recommends the use of CAM.

Delirium at the end of life

The 2014 review found evidence from 1 study that Nu-DESC had low sensitivity and high specificity. There is insufficient evidence here to suggest adding this assessment tool to the current recommendations. People receiving end of life care are outside the scope of this guideline, however at the time of the 2014 review there was not an alternative guideline for this information. End of life care is now covered by a new guideline, NG31.

New evidence is unlikely to change guideline recommendations.

Treating delirium

Recommendations in this section of the guideline

Initial management

- 1.6.1 In people diagnosed with delirium, identify and manage the possible underlying cause or combination of causes.
- 1.6.2 Ensure effective communication and reorientation (for example explaining where the person is, who they are, and what your role is) and provide reassurance for people diagnosed with delirium. Consider involving family, friends and carers to help with this. Provide a suitable care environment (see recommendation 1.3.1).

Distressed people

- 1.6.3 If a person with delirium is distressed or considered a risk to themselves or others, first use verbal and non-verbal techniques to de-escalate the situation. For more information on de-escalation techniques, see [Violence](#) (NICE clinical guideline 25). Distress may be less evident in people with hypoactive delirium, who can still become distressed by, for example, psychotic symptoms.
- 1.6.4 If a person with delirium is distressed or considered a risk to themselves or others and verbal and non-verbal de-escalation techniques are ineffective or inappropriate, consider giving short term (usually for 1 week or less) haloperidol⁷ or olanzapine⁷. Start at the lowest clinically appropriate dose and titrate cautiously according to symptoms.
- 1.6.5 Use antipsychotic drugs with caution or not at all for people with conditions such as Parkinson's disease or dementia with Lewy bodies⁸.

If delirium does not resolve

- 1.6.6 For people in whom delirium does not resolve:
 - Re-evaluate for underlying causes.
 - Follow up and assess for possible dementia⁹.

⁷ Haloperidol and olanzapine do not have UK marketing authorisation for this indication.

⁸ For more information on the use of antipsychotics for these conditions, see the NICE guidelines on [Parkinson's disease](#) and [dementia](#).

⁹ For guidance on dementia, see the NICE guideline on [dementia](#).

Surveillance decision

This recommendation should not be updated.

Editorial amendments

- Recommendation 1.6.4: footnote 7 states that haloperidol and olanzapine do not have UK marketing authorisation for delirium treatment, however haloperidol does now have marketing authorisation. Olanzapine will be removed from recommendation 1.6.4 to follow the process set out in [Developing NICE guidelines: the manual](#) as the clinical need can now be met by a licensed product. Footnote 7 will be removed because it no longer applies to haloperidol.

Recommendation 1.6

Non-pharmacological interventions.

Bright light therapy

Previous surveillance summary

The 2012 review identified an RCT(140) which found the frequency of postoperative delirium was lower (not significantly) when bright light therapy was used compared with a control. An RCT(141) from the 2014 review found that risperidone used with light therapy led to a significantly greater decrease in delirium rating scale scores.

2018 surveillance summary

None found.

Family approach

Previous surveillance summary

No new evidence was identified at the 2012 review. The 2014 review identified a systematic review(142) which was unable to determine if the involvement of families in delirium management improved patient outcomes.

2018 surveillance summary

An RCT(143) (n=111) investigated the use of a stimulated family presence on the agitation level of patients with hyperactive or mixed delirium. A control group

received usual care with 2 control arms receiving either a family video message or a nature video for 1 minute. The family video was associated with significantly better agitation scores on the agitated behaviour scale during the intervention, with no group being significantly different at either of the post group assessments.

Pharmacological interventions

Benzodiazepines

Previous surveillance summary

The 2012 review identified a Cochrane review(144) of RCTs which showed that those treated with dexmedetomidine had an increased number of days free from delirium and coma compared with those treated with lorazepam group. An RCT(145) found the median duration of delirium was longer with rivastigmine compared with a control.

No evidence was identified at the 2014 review.

2018 surveillance summary

None found.

Melatonin

Previous surveillance summary

No new evidence was identified at the 2012 review. The 2014 review identified a systematic review(85) which found melatonin to have some benefit for

managing delirium, however no evidence for melatonin reducing the severity of delirium was found.

2018 surveillance summary

None found.

Pharmacological management

Previous surveillance summary

No new evidence was identified at the 2012 review. The 2014 review identified a systematic review(146) which investigated the pharmacological management of delirium in adult intensive care patients but found that limited studies were available and no results were reported.

2018 surveillance summary

None found.

Ondansetron

Previous surveillance summary

No new evidence was identified at the 2012 review. The 2014 review identified an RCT(147) which found no statistically significant difference between ondansetron and haloperidol in controlling the effects of delirium.

2018 surveillance summary

None found.

Antipsychotics

Previous surveillance summary

No new evidence was identified at the 2012 review. The 2014 review identified a systematic review(148) which concluded that antipsychotic therapy may reduce the duration of delirium in ICU patients. Another systematic review(149) found that due to severe methodological problems with the included studies the use of antipsychotics for delirium treatment was not supported by this review.

One systematic review(150) found that 75% of patients with delirium treated with

low-dose antipsychotics experience a clinical response. It also found there was no significant differences in the efficacy of haloperidol compared with atypical agents but higher adverse events were reported. A Cochrane review(151) was found which investigated drug therapies for terminally ill patients however there was insufficient evidence and no results were stated.

2018 surveillance summary

None found.

Haloperidol

Previous surveillance summary

No new evidence was identified at the 2012 review. The 2014 review identified a systematic review(152) which found that haloperidol was of benefit in the treatment of delirium and an RCT(153) which found no difference in the time a patient remained alive or in a coma following critical illness when early haloperidol was given.

2018 surveillance summary

A systematic review(121) of 12 RCTs evaluated haloperidol (administration method not stated) for the prevention and treatment of delirium in hospitalised patients. Eight studies compared haloperidol with other typical and atypical antipsychotics, lorazepam, mianserin, ondansetron or morphine and indicated that haloperidol reduced the severity of delirium

An RCT(154) (n=100) compared the efficacy of haloperidol and olanzapine for delirium treatment. Patients received either 1-4 mg/day haloperidol or 2.5-10 mg/day olanzapine orally or via nasogastric tube and were assessed for severity of delirium using the MDAS. Delirium severity improved in both groups, and there was no significant difference in

treatment duration or MDAS score between the groups.

Quetiapine

[Previous surveillance summary](#)

No evidence was identified at the 2012 review. The 2014 review identified a systematic review(155) which found that quetiapine resolved delirium symptoms more quickly than placebo and was as effective as haloperidol and amisulpride. One RCT(156) found that quetiapine was as effective as haloperidol and safe for controlling delirium. A post-hoc analysis(157) found delirium symptoms resolved more quickly with quetiapine compared with a placebo.

[2018 surveillance summary](#)

An RCT(158) (n=63 patients with delirium) compared the effectiveness of haloperidol and quetiapine (administration route not stated) for delirium treatment at baseline and for the 6 consecutive days after. Delirium was assessed using DRS-R-98 and MMSE. There was no difference on any assessment for either treatment group.

Risperidone

[Previous surveillance summary](#)

The 2012 review identified an RCT(159) which found that olanzapine, risperidone and haloperidol were equally effective at improving delirium.

[2018 surveillance summary](#)

None found.

Atypical antipsychotics

[Previous surveillance summary](#)

No new evidence was identified at the 2012 review. The 2014 review identified a systematic review(160) which found that atypical antipsychotics were effective and

safe for the treatment of delirium but there was no difference in effectiveness between each agent. There was no difference in effectiveness between low-dose haloperidol and atypical antipsychotics.

[2018 surveillance summary](#)

None found.

Morphine

[Previous surveillance summary](#)

No new evidence was identified at the 2012 review. The 2014 review identified an RCT(161) which found that receiving morphine responded more quickly compared with those receiving haloperidol.

[2018 surveillance summary](#)

None found.

Dexmedetomidine

[Previous surveillance summary](#)

No new evidence was identified at the 2012 review. The 2014 review identified a systematic review(91) which suggested that dexmedetomidine was a promising agent for the treatment of ICU delirium.

[2018 surveillance summary](#)

An RCT(162) (n=74 patients with severe agitation and delirium) assessed the use of dexmedetomidine or placebo given by nursing staff until the required physician directed sedation goal had been achieved. A significant acceleration of delirium resolution was seen in the dexmedetomidine group.

An RCT(163) compared use of dexmedetomidine (1 microgram/kg) or ondansetron (4 mg) to haloperidol (5 mg) (administration route not stated) for delirium treatment in 96 adult patients with trauma. Medication was administered twice daily for 3 days. Outcomes included

number of patients with delirium and patients needing rescue haloperidol. There was no significant difference in the number of patients with delirium between the 3 groups, and between the dexmedetomidine and haloperidol groups for number of patients needing rescue haloperidol. Significantly more patients in the ondansetron group required rescue haloperidol than the haloperidol group.

Ramelteon

Previous surveillance summary

No new evidence was identified at the 2012 review. The 2014 review identified an RCT(164) which found ramelteon was associated with a lower risk of delirium and a lower frequency of delirium compared with a placebo.

2018 surveillance summary

None found.

Simvastatin

Previous surveillance summary

No new evidence was identified at the 2012 or 2014 reviews.

2018 surveillance summary

An RCT(165) (n=142 adult ICU patients) investigated whether early treatment with simvastatin decreased delirium or coma in survivors of critical illness. Patients received either simvastatin 80 mg or a placebo daily for up to 28 days, with delirium assessed using CAM-ICU. There was no significant difference between the 2 groups for the number of days alive without delirium or coma.

Intelligence gathering

One expert suggested that CG103 should cover antipsychotic use for delirium in palliative care, however this is out of scope. One topic expert mentioned that

the recommended pharmacological treatments are not licensed for treatment of delirium; this is already stated in the footnotes of the recommendation. However, since publication haloperidol is now licensed for this indication. Another topic expert also had concerns about recommending olanzapine or haloperidol because of concerns about the anticholinergic load; the expert suggested that risperidone may be preferable to these agents. Experts also raised that antipsychotics should be used with caution in people with hypoactive delirium. One topic expert highlighted that new trials have been published on delirium treatment and suggest current guidance on antipsychotics may need revising. One topic expert suggested including the use of newer antipsychotics for short term treatments. They also highlighted a number of studies, 3 of which met our inclusion criteria and were summarised above in recommendation 1.3.

Impact statement

Non-pharmacological treatment interventions

Bright light therapy

Previous reviews found limited evidence for bright light therapy for the treatment of delirium. Bright light therapy is not currently part of this recommendation and more evidence would be required in this area before it could be changed.

Family approach

The 2014 review found evidence from 1 study regarding family based interventions, however the review was unable to determine whether delirium was improved. New evidence from 1 study identified during the current review found that a stimulated family presence was associated with a non-significant reduction in

agitation. Family involvement is already mentioned in recommendation 1.6.2 and there is no evidence here to suggest that should be changed.

Pharmacological interventions

The 2012 evidence update found that dexmedetomidine was associated with increased delirium free days compared with lorazepam in 1 study. Rivastigmine was associated with increased delirium duration in 1 study. Rivastigmine is not currently included for treatment in this recommendation and as such no impact is anticipated as no further evidence was found in the more recent reviews.

Melatonin

Evidence from the 2014 review found that melatonin may have benefit in delirium prevention and management but the authors state no evidence for melatonin on delirium duration was found. Melatonin is not currently mentioned in recommendation 1.6, and as no new evidence has been found it is unlikely to have an impact on the recommendations at this time.

Pharmacological management

Evidence from the 2014 review found 1 study regarding pharmacological management however it was inconclusive. This is unlikely to have an impact on the current recommendations as no further evidence was found at the 2018 review and the recommendation does not currently suggest pharmacological management.

Ondansetron

Ondansetron was compared with haloperidol in one study from the 2014 review, which found no significant difference between groups. There is currently insufficient evidence to consider

adding ondansetron to recommendation 1.6.4.

Antipsychotics

Four studies from the 2014 review found inconclusive results for the pharmacological treatment of delirium.

A Cochrane review found no difference for delirium severity, resolution or overall mortality with antipsychotics compared to nonantipsychotics, however the authors state that the evidence found was low or very low quality, with no evidence found for delirium duration. Topic experts highlighted that antipsychotics should be used with caution for hypoactive delirium, and suggested new evidence may be available for the general use of antipsychotics. The guideline currently recommends short term and low-dose treatment with 2 named antipsychotics, this evidence on general antipsychotics is unlikely to have an impact.

Haloperidol

Two studies from the 2014 review had mixed evidence regarding the use of haloperidol. One study found a beneficial effect however there were methodological issues, and the other found no difference between haloperidol and a placebo for delirium incidence.

New evidence in the current review from 1 study found that delirium incidence was reduced with haloperidol. One study found no significant difference in delirium incidence with either haloperidol or olanzapine. One topic expert raised that haloperidol was not licensed for this indication, however it is now licensed. This requires 2 footnotes to be amended as detailed in the editorial corrections.

A study highlighted by a topic expert found that no significant differences were found between haloperidol and a placebo.

Within the guideline it is recommended that either haloperidol or olanzapine are considered for short term use, in recommendation 1.6.4. Given the mixed nature of evidence over the surveillance time points, the evidence is generally supportive of the recommendation.

Quetiapine

Two studies from the 2014 surveillance found that quetiapine was as effective as haloperidol in reducing delirium and it was well tolerated. One study found that treatment with quetiapine led to faster resolution of delirium compared with a placebo. New evidence from the current review also found no difference between quetiapine and haloperidol for delirium treatment. Recommendation 1.6.4 currently recommends haloperidol or olanzapine and more evidence would be required to change this recommendation. Although some new evidence has been identified during the current review, there remains insufficient evidence to suggest changing the current guideline recommendations.

Risperidone

Evidence from the 2012 update from 1 study found that risperidone was as effective as haloperidol and olanzapine in the treatment of delirium. Risperidone was also found to be associated with a significantly lower incidence of delirium in 1 study from the 2014 review. One topic expert suggested risperidone could be used for delirium treatment. But the evidence remains insufficient to recommend changing the guideline.

Atypical antipsychotics

The 2014 review found that atypical antipsychotics effective for the treatment of delirium and were well tolerated, with no difference seen in efficacy when compared with haloperidol. No new

evidence was found at the current review and further evidence would be required to clarify which individual atypical drugs are effective. As the guideline currently recommends the use of haloperidol this is unlikely to have an impact.

One topic expert suggested that the current recommendations for haloperidol and olanzapine could be changed by new research, with another topic expert also suggesting newer antipsychotics could be more appropriate than haloperidol. However we did not find any evidence to support this.

Morphine

The 2014 review found that patients with delirium responded more quickly to morphine than haloperidol and had less sedation. No further evidence has been identified during the current review and there remains insufficient evidence to change guideline recommendations.

Dexmedetomidine

The 2014 review found that dexmedetomidine was a promising agent for delirium treatment. This is supported by new evidence from 1 study which found a lower incidence of delirium with dexmedetomidine, however a second study found no difference between dexmedetomidine and haloperidol. This does not impact on the current recommendations as the evidence is mixed.

Ramelteon

The 2014 review found that ramelteon was associated with a lower risk of delirium, however as no new evidence was found this is unlikely to impact the guideline recommendations.

Simvastatin

New evidence found no significant difference between treatment with

simvastatin or a placebo for delirium. This would not affect the recommendations as there is insufficient evidence here.

New evidence is unlikely to change guideline recommendations.

Information and support

Recommendations in this section of the guideline

- 1.7.1 Offer information to people who are at risk of delirium or who have delirium, and their family and/or carers, which:
- informs them that delirium is common and usually temporary
 - describes people's experience of delirium
 - encourages people at risk and their families and/or carers to tell their healthcare team about any sudden changes or fluctuations in behaviour
 - encourages the person who has had delirium to share their experience of delirium with the healthcare professional during recovery
 - advises the person of any support groups.
- 1.7.2 Ensure that information provided meets the cultural, cognitive and language needs of the person.

Surveillance decision

No new evidence was found at any surveillance review
This recommendation should not be updated.

Areas not currently covered in the guideline

In surveillance, evidence was identified for areas not covered by the guideline. This new evidence has been considered for possible addition as a new section of the guideline.

New section considered in surveillance

No new areas were found during surveillance.

Research recommendations

4.1 Pharmacological prevention

In people in hospital who are at high risk of delirium, which medication (atypical antipsychotics, typical antipsychotics, benzodiazepines or acetylcholinesterase inhibitors), compared with placebo or each other, is more clinically and cost effective in preventing the development of delirium?

Summary of findings

New evidence was found in relation to [dexmedetomidine](#) (21 studies), [melatonin](#) (2 studies), [general antipsychotics](#) (3 studies), [other pharmacological interventions](#) (suvorexant, beta-blockers and benzodiazepines, gabapentin, parecoxib, ramelteon and tryptophan), [haloperidol](#) (4 studies), and [propofol anaesthesia](#). The evidence for the pharmacological prevention methods was mixed and will be considered again at the next surveillance review.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

4.2 Pharmacological treatment

In people in hospital who have delirium, which is the most effective medication (atypical antipsychotics, typical antipsychotics or benzodiazepines) compared with placebo or each other for treating delirium?

Summary of findings

New evidence was found regarding [pharmacological treatments](#) for delirium: dexmedetomidine, haloperidol and olanzapine, general antipsychotic use, and other pharmacological agents (quetiapine, simvastatin and acetylcholinesterase inhibitors).

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

4.3 Multicomponent intervention

For people in long-term care, is a multicomponent non-pharmacological intervention more clinically and cost effective than usual care in preventing the development of delirium?

Summary of findings

Evidence was found relating to [multicomponent non-pharmacological interventions](#) for delirium prevention in 2 studies.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

4.4 Delirium in long-term care

How common is delirium and what are its adverse outcomes in people in long-term care?

Summary of findings

No new evidence was found for this recommendation.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

4.5 Education programme

Does a staff education programme (compared with an educational leaflet or usual care) reduce the incidence of delirium and improve the recognition and recording of delirium in people in hospital?

Summary of findings

Evidence was found regarding [pre-operative education](#).

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

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