NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

Recommendation for Guidance Executive

Clinical guideline
CG103: Delirium: diagnosis, prevention and management

Publication date
July 2010

Surveillance report for GE
September 2014 (4 year surveillance review)

Surveillance recommendation
GE is asked to consider the following proposals and the attached paper for consultation:

- The clinical guideline CG103: Delirium should not be considered for an update at this time.
- The guideline should be transferred to the static list as the guidance meets the following criteria:
  - No evidence was identified that would impact on the current guidance and no major ongoing studies or research has been identified as due to be published in the near future (that is, within the next 3-5 years)

Key findings

	Potential impact on guidance	
	Yes	**No**
Evidence identified from Evidence Update	✓	
Evidence identified from literature search		✓
Feedback from Guideline Development Group		✓
Anti-discrimination and equalities considerations		✓

No update	CGUT update	Standard update	**Transfer to static list**	Change review cycle
✓			✓	

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Centre for Clinical Practice – Surveillance Programme

Surveillance review consultation document

4-year surveillance review of CG103: Delirium: diagnosis, prevention and management

Background information

Guideline issue date: July 2010
4-year review: 2014

Surveillance review recommendation

Surveillance review proposal put to consultees:

The clinical guideline CG103: Delirium should not be considered for an update at this time.

The guideline should be transferred to the static guidance list because it fulfils the following criteria:

- No evidence was identified that would impact on the current guidance and no major ongoing studies or research has been identified as due to be published in the near future (that is, within the next 3-5 years).

Main findings of the current 4 year surveillance review

An Evidence Update was produced for the guideline in 2012 and was used as a source of evidence for the review proposal. The Evidence Update considered new evidence from 17th August 2009 to 28th November 2011. New evidence that may impact on the guideline recommendations was identified in one area of the Evidence Update. This was in relation to the use of the PRE-DELIRIC tool to assess the risk of patients in intensive care for developing delirium. However, the evidence for the use of this tool is limited since only one study was

found during the Evidence Update and no other studies were identified through this 4 year surveillance review. Further evidence is likely to be required into the use of this tool before it can be recommended for inclusion in the guideline.

The literature search for this 4 year surveillance review was carried out between 28th November 2011 (the end of the search period for the Evidence Update) and 4th August 2014 to identify randomised clinical trials (RCTs) and systematic reviews. Relevant abstracts were assessed and clinical feedback was obtained from members of the guideline development group (GDG) through a questionnaire survey. The majority of questionnaire respondents were not aware of any evidence that would change the current guideline recommendations and felt that CG103: Delirium did not require an update at this time.

New evidence was identified for the current 4 year surveillance review relating to the following clinical areas within the Delirium guideline.

Clinical area: Epidemiology		
Q: What is the prevalence of delirium in different hospital settings and in long-term care?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) A systematic review[1] was identified which looked at the incidence and outcome of persistent delirium in older hospital patients. It included 18 prospective studies involving 1322 patients. The results showed that persistent delirium was common and was recorded for 44.7% of patients at discharge. Combined proportions of patients with persistent delirium were 32.8% at 1 month, 25.6 % at 3 months and 21% at 6 months. It was also found that those with persistent delirium had poorer outcomes (mortality, nursing home placement, function and cognition) compared to those who recovered. Another systematic review[2] assessed factors associated with persistent delirium in those with acute illness. It included 21 observational studies (n=1953). It was found that the rates of persistent delirium ranged from 0-78% and that persistent	None identified through GDG questionnaire.	The new evidence is supportive of the GDG's "Think delirium" prominent statement: Be aware that people in hospital and long-term care may be at risk of delirium. This can have serious consequences (such as increased risk of dementia and/or death) and, for people in hospital, may increase their length of stay in hospital and their risk of new admission to long-term care.

delirium was significantly associated with hypoactive delirium, increasing severity of delirium, cognitive impairment, multiple comorbidities and hypoxic illness.

A secondary analysis[3] used data from a prospective cohort study in patients with Alzheimer's disease to investigate the effect of delirium on cognitive function. There were 72 patients with dementia who developed delirium and 336 dementia patients who did not. Results showed that those who had delirium had significant acceleration in their cognitive decline compared to those without delirium.

4-year surveillance review (2014)

Stroke

A systematic review[4] was identified which examined incidence rates of delirium after stroke. Results showed that the incidence of delirium in acute stroke ranged from 2.3-66%.

Acute respiratory failure

A systematic review[5] investigated the prevalence of delirium in acute respiratory failure patients receiving non-invasive positive pressure ventilation. Three studies were included (n=239). Delirium prevalence was between 33% and 38% with a pooled prevalence of 37%. Furthermore, non-invasive ventilation failure was found to be associated with delirium.

Cardiac surgery

An RCT[6] was identified in which 92 patients undergoing coronary artery bypass grafting (CABG) were randomised to either high pressure or low pressure perfusion. Results showed that significantly more patients in the low pressure group developed postoperative delirium compared to the high pressure group. The authors concluded that maintaining perfusion at physiologic levels is associated with less postoperative delirium.

Subsyndromal delirium

A systematic review[7] investigated the prevalence and incidence of subsyndromal delirium (SSD) in older people. It included 12 studies. The combined prevalence of SSD was 23% whilst the combined incidence was 13%. The episodes tended to last up to 133 days and were often recurrent. However, there was significant unexplained heterogeneity in study results.

Clinical area: Diagnosis and accuracy of diagnostic tests		
Q: What is the diagnostic accuracy of practical diagnostic tests compared with the reference standard DSM IV, to identify delirium in people in hospital and long-term care settings?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No evidence identified. 4-year surveillance review (2014) **Generic assessment tools**	None identified through GDG questionnaire.	The new evidence suggests that the CAM is an appropriate assessment tool for delirium and that CAM-ICU is an effective tool for delirium detection in intensive care patients. The evidence is supportive of the current guideline recommendation which states: If indicators of delirium are identified,

A systematic review[4] investigated how delirium was identified after stroke. Nine studies were included on this topic. The study found that the methods most commonly used to identify delirium were generic assessment tools such as the Delirium rating scale, the Confusion Assessment Method (CAM) or both.

A systematic review[8] investigated the diagnostic accuracy of two delirium assessment tools (CAM and Confusion assessment method for the intensive care unit (CAM-ICU)) and compared them to the DSM IV. Twenty-two studies were included. The pooled sensitivity for the CAM was 82% and the pooled specificity was 99%. For the CAM-ICU the pooled sensitivity was 81% whilst the pooled specificity was 98%. Authors concluded that both of these tools had higher specificity than sensitivity and therefore their use should not replace clinical judgement.

Critically ill patients

A meta-analysis[9] was identified which examined the accuracy of delirium screening tools in critically ill patients. Sixteen studies were included (n=1523) which looked at five screening tools. Overall, the confusion assessment method for the intensive care unit (CAM-ICU) was the most specific tool for the assessment of delirium in critically ill patients. The pooled sensitivities and specificities for CAM-ICU were 75.7% and 95.8% respectively. However, the authors do point out that there was significant heterogeneity

carry out a clinical assessment based on the DSM-IV criteria or short Confusion Assessment Method (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.

present.

A meta-analysis[10] assessed the accuracy of the CAM-ICU and the Intensive care delirium screening checklist (ICDSC) for the diagnosis of delirium in critically ill patients. Nine studies (n=969) assessing CAM-ICU and four 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.

A systematic review[11] aimed to identify which types of delirium screening tools had been used in the emergency department. It included 22 studies with seven screening tools being identified. Minimal information was found to suggest when an ideal scheduling of a delirium assessment would be. Moreover, the study showed that there were several delirium screening tools that have been used in the emergency department but the validation of these tools in this setting has been minimal.

EEG-based monitoring

A systematic review[12] was conducted to examined EEG characteristics and delirium diagnosis for intensive care patients. Fourteen studies were included. The authors found that the relative power of the theta and alpha frequency band was most often able to distinguish delirium

from non-delirium.

Delirium superimposed on dementia

A systematic review[13] looked at delirium tools that explicitly included patients with dementia. Nine studies were included in which six delirium tools were evaluated. The confusion assessment method (CAM) was found to have a high specificity (96-100%) and moderate sensitivity (77%) in one study where 85% of patients had dementia. In two 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.

Cognitive impairment

A meta-analysis[14] was identified that examined the diagnostic test accuracy of assessment instruments to evaluate hip fracture surgery patients with cognitive impairment. Nine studies were included (n=690) and two assessment domains were recognised: pain and delirium. For delirium, 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.

Delirium at the end of life

A secondary analysis of an RCT[15] investigated the frequency and severity of delirium and the

clinical utility of the Nursing delirium screening scale (Nu-DESC) as scored by a care giver in patients admitted to home hospice. Seventy eight patients were included. 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.		

Clinical area: Risk factors for delirium

Q: What are the risk factors for delirium?

Evidence summary	GDG/clinical perspective	Impact
Evidence Update (2012) A systematic review[16] including randomised controlled trials, cohort studies and case-control studies investigated the relationship between medication and risk of delirium was identified. Fourteen studies were included (n=4652). The risk of delirium was found to increase with opioid, benzodiazepine and dihydropyridine usage. The evidence for antihistamines was inconclusive but a single RCT on haloperidol showed no increased risk with the use of this medication. The Evidence Update stated that specific groups of medications may be potential risk factors for development of delirium, however evidence is currently limited and further research was required. **Methods for assessing delirium risk** An observational multicentre study[17] used data	None identified through GDG questionnaire.	The new evidence is unlikely to impact on the guideline since it is mainly supportive of the risk factors already included in CG103. Furthermore, the evidence for a relationship between the identified factors and risk of delirium is limited, especially for pharmacological risk factors, and therefore further research is needed. With regards to electrolyte disturbance as a risk factor, the GDG were uncertain about the results when considering for inclusion in the original guideline. However, the new evidence identified during this surveillance review suggests that electrolyte imbalance may be a risk factor for delirium. Nonetheless, the new evidence is currently limited to only one study and so more research is likely to be needed on the association between this risk factor and delirium incidence before considering for inclusion in the guideline. There is also insufficient evidence for an association between cerebrospinal fluid biomarkers

collected within the first 24 hours of ICU admission to develop and validate a method for assessing the risk of delirium (PRE-DELIRIC (prediction of delirium in ICU patients)) (n=3056). This tool comprised of 10 risk factors: age, acute physiology and chronic health evaluation-II score, admission group, coma, infection, metabolic acidosis, use of sedatives, use of morphine, urea concentration, urgent admission. Results showed that PRE-DELIRIC was more successful than the clinical prediction of ICU nurses or physicians in identifying people at risk of delirium. Currently, a risk assessment tool is not recommended in CG103.

4-year surveillance review (2014)

Risk factors after cardiac surgery

A meta-analysis[18] was identified which investigated the risk factors of delirium after cardiac surgery. Twenty-five studies were included and 17 predisposing and 16 precipitating factors were identified. The most established predisposing risk factors were history of stroke, age, depression, cognitive impairment, atrial fibrillation and diabetes. The most established precipitating factors were duration of surgery, surgery type, prolonged intubation, red blood cell transfusion, elevation of inflammatory markers and plasma cortisol level, and postoperative complications. The authors also stated that sedation with dexmedetomidine may significantly predict the absence of postoperative delirium.

and delirium. More studies in this area are needed so that firm conclusions can be drawn. However, this evidence does relate to a research recommendation which asks: Is the presence of immune system markers, particularly cytokines, a risk factor for the development of delirium?

With regards to PRE-DELIRIC as an assessment method for risk of delirium, further research is needed before this can be recommended in the guideline. This is because no new evidence on this tool was found during this 4 year review and only one study was identified during the Evidence Update (2012).

A systematic review[19] was identified that investigated the risk factors for delirium in those who had undergone cardiac surgery. It identified 27 risk factors of which 12 were predisposing and 15 were precipitating factors. The most established predisposing risk factors were depression, atrial fibrillation, age, cognitive impairment, history of stroke, and peripheral vascular disease whilst the most established precipitating factor was a red blood cell transfusion. The use of an intra-aortic balloon pump, inotropic medication and a low cardiac output appeared to be the most relevant risk factors associated with postoperative delirium.

Delirium in acute stroke

A systematic review[4] looked at predictors in the development of delirium in acute stroke. Eleven studies reporting risk factors for delirium were included. Authors stated that increased age, aphasia, neglect or dysphagia, visual disturbance and elevated cortisol levels were associated with delirium development in at least one study.

Critically ill patients

A systematic review[20] was identified which aimed to identify the risk factors associated with acute delirium in critically ill adults. Twenty-four studies were included. Results showed that age was a common risk factor. For pharmacological factors, benzodiazepines were the most likely medication to be associated with delirium as compared to

other drugs used in intensive care. For biomarkers, there were a number that were implicated in causing delirium such as apolipoprotein 4 genotype, C-reactive protein, plasma tryptophan, cortisol and interleukin-6.

A meta-analysis[21] was conducted to look at potential risk factors for delirium in critically ill patients. Twenty-five observational studies were included. Overall, age, history of hypertension, clinical use of mechanical ventilation and higher APACHE II score were found to be associated with an increased risk of delirium.

Acute medical inpatients

A systematic review[22] was conducted which investigated risk factors most strongly related to the development of incident delirium during hospitalisation. Nine studies were included. Results showed that the most significant risk factors were dementia and cognitive impairment whilst a moderate association with delirium was found for functional impairment, severe illness and visual impairment. Patient's age was not found to be significantly related to delirium incidence.

A meta-analysis[23] investigated risk factors associated with incident delirium in older medical inpatients Eleven studies met the inclusion criteria (n=2338). The most common risk factors that were found to be significantly associated with incident delirium were: 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.

Pharmacological risk factors

A systematic review[24] examined the literature on medications related to delirium after cardiac surgery. Fifteen studies were included. Results found that two drugs (intraoperative fentanyl and ketamine) and two drug classes (preoperative antipsychotics and postoperative inotropes) were independently associated with delirium. Another seven drug classes (preoperative antihypertensives, anticholinergics, antidepressants, benzodiazepines, opioids, statins and postoperative opioids) and three single drugs (intraoperative diazepam, postoperative dexmedetomidine and postoperative rivastigmine) showed mixed findings. Risperidone was shown to prevent delirium when taken immediately upon waking.

Risk factors and timing of occurrence

A systematic review[25] was identified which investigated risk factors for postoperative delirium and categorised them according to timing of occurrence. Preoperative risk factors were categorised into four groups: demographics, comorbidities, surgery and anaesthesia-related. Intraoperative risk factors were categorised into two groups (surgery and anaesthesia – related) and post-operative risk factors included various

pathophysiological and environmental conditions.

Cerebrospinal fluid biomarkers

A systematic review[26] was identified which examined the association between cerebrospinal fluid biomarkers and delirium. Eight studies (n=235) were included. Delirium was found to be associated with elevated serotonin metabolites, interleukin-8, cortisol, lactate and protein and reduced somatostatin, beta-endorphin and neuron-specific enolase. It was also found that elevated acetylcholinesterase predicted poor outcomes after delirium. The authors concluded that no clear conclusions could be drawn.

Clinical area: Consequences of delirium		
Q: What are the consequences of delirium in terms of morbidity and mortality in a person in hospital or long-term care?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No evidence identified. 4-year surveillance review (2014) **Delusional memories** A systematic review[27] investigated the emotional consequences of delirium in intensive care patients. Fourteen studies were included of which five assessed delirium during intensive care admission and nine assessed delusional memories during or after admission. Results showed that there was no association between delirium and adverse emotional outcome.	None identified through GDG questionnaire.	The new evidence suggests that delirium results in higher morbidity, mortality, longer hospital stays and an increased likelihood of being discharged to long-term care. This is supportive of the prominent statement provided in the guideline which states: "THINK DELIRIUM" Be aware that people in hospital or long-term care may be at risk of delirium. This can have serious consequences (such as increased risk of dementia and/or death) and, for people in hospital, may increase their length of stay in hospital and their risk of new admission to long-term care.

Furthermore, results for delusional memories and adverse emotional outcome contradicted each other and so no conclusion could be drawn.

Acute stroke

A meta-analysis[28] assessed the outcomes of acute stroke patients with delirium. Ten studies fulfilled the inclusion criteria (n= 2004). Results showed that acute stroke patients with delirium had a higher inpatient mortality and morbidity at 12 months than non-delirious patients, tended to have longer hospital stays and were more likely to be discharged to nursing homes or other institutions.

Clinical outcomes

A meta-analysis[29] was identified that examined the association between clinical outcomes and delirium. Sixteen studies were identified. It was found that delirious patients had a higher mortality rate than non-delirious patients. Moreover, delirious patients were more likely to experience complications, to be discharged to skilled placement, have longer hospital stays and spend more time on mechanical ventilation compared to non-delirious patients.

A meta-analysis[30] was conducted to determine whether interventions effective at reducing delirium duration were associated with a reduction in short-term mortality. Seventeen trials with 2849 critically ill patients were included and the interventions included were pharmacological,

non-pharmacological and multimodal. Results showed that whilst average delirium duration was lower in the intervention groups short-term mortality was not reduced.		

Clinical area: Single component prevention: hydration and music		
Q: What are the most clinical and cost effective single-component, non-pharmacological interventions for the prevention of delirium in people in hospital?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012)	A GDG member stated that de-escalation training is not routinely received in acute hospitals and probably in care homes even though it's recommended in the guideline. Furthermore, the cost of de-escalation training may not have been included in the guideline analysis.	The new evidence for transfusion strategies and N-3 fatty acids for the prevention of delirium in hospital is currently inconclusive as no difference was found between groups for delirium outcomes. As such, this evidence is unlikely to impact on CG103.
No evidence identified.		
4-year surveillance review (2014)		
Earplugs		
An RCT[31] was identified which investigated the use of earplugs to prevent delirium in intensive care patients. One hundred and thirty six patients were randomised to either sleeping with earplugs during the night or to not sleeping with earplugs. It was found that using earplugs lowered the incidence of confusion and led to a later development of confusion.		The new evidence for earplugs, monitoring the depth of anaesthesia and fast track surgery shows some benefit of these interventions for delirium prevention. However, the current evidence is limited and so further research is required before inclusion in the guideline can be considered.
Monitoring the depth of anaesthesia		No new evidence was found on de-escalation training. However, practice variation in de-escalation training is an implementation issue and therefore should be addressed at a local level.
An RCT[32] investigated whether monitoring the depth of anaesthesia influenced the incidence of postoperative delirium. One thousand two hundred and seventy seven general anaesthesia patients were randomised to the anaesthetist using bispectral index (BIS) data to guide anaesthesia or the anaesthetist being blinded to the use of BIS. Results showed that delirium		No new cost-effectiveness evidence was found for any single-component non-pharmacological interventions.

incidence was lower in those with open guided BIS.

Transfusion strategies

An RCT[33] was carried out to see the effect of two different blood transfusion strategies on postoperative delirium. One hundred and eight six patients undergoing elective unilateral hip replacement surgery were randomised to a restrictive transfusion strategy or a liberal transfusion strategy. Results showed no difference between groups in the incidence of postoperative delirium.

Fast track surgery

An RCT[34] randomised 240 elderly patients with colorectal carcinoma to perioperative management with either traditional or fast-track surgery. It was found that the incidence of delirium was significantly lower in those receiving fast-track therapy compared to those in the traditional therapy group.

N-3 fatty acids

An RCT[35] investigated the effect of administering n-3 fatty acids on the incidence of sepsis-associated delirium. Fifty sepsis patients were randomised to 2ml/kg per day of a lipid emulsion containing highly refined fish oil for 7 days after intensive care admission or to standard treatment. The incidence of sepsis–associated delirium was found to be 75% in the intervention

group and 71% in the control group.		

Clinical area: Single component prevention: hydration and music

Q: What are the most clinical and cost effective single-component, non-pharmacological interventions for the prevention of delirium in people in long-term care?

Evidence summary	GDG/clinical perspective	Impact
<u>Evidence Update (2012)</u> No evidence identified. <u>4-year surveillance review (2014)</u> A Cochrane review[36] assessed the effectiveness of interventions for preventing delirium in older people in long-term care. Two trials met the inclusion criteria (n=3636). One small cluster RCT of a hydration-based intervention reported no reduction in the incidence of delirium in the intervention group compared to the control group. The large cluster RCT was of a computerised system to identify medications that may contribute to delirium risk and trigger a pharmacist led medication review. This reported a large reduction in delirium incidence but did not find any clear evidence for a decrease in hospital admissions, mortality, or falls risk.	None identified through GDG questionnaire.	The new evidence for hydration interventions is supportive of the evidence reported in the guideline as hydration interventions had no effect on delirium incidence. The guideline states that overall the evidence for this intervention is limited and the new evidence is supportive of this. More consistent evidence is needed before such interventions in this setting can be considered for inclusion within CG103. With regards to computerised interventions aimed at identifying medications that may contribute to delirium risk and trigger a pharmacist led medication review, the evidence is currently limited. More research into these interventions is needed before they can be considered for inclusion in the guideline.

Clinical area: Multicomponent prevention

Q: What are the most clinical and cost effective multicomponent interventions for the prevention of delirium in people in hospital?

Evidence Summary	GDG/clinical perspective	Impact
<u>Evidence Update (2012)</u> No evidence identified. <u>4-year surveillance review (2014)</u>	None identified through GDG questionnaire.	The new evidence for multidisciplinary geriatric interventions is unlikely to impact on the guideline recommendations. This is because the results from the studies are inconclusive. For example, one study shows these interventions

Nursing interventions

An RCT[37] was identified which aimed to investigate the effect of nursing interventions on delirium in patients admitted to an intensive care unit (ICU) (n=40) over five days. Patients were randomised to nursing interventions or routine care. The nursing interventions included: assuring, emotional support, clear information, effective communication with patients and families and family visits twice a day. Authors concluded that in using nursing interventions appropriately hypoactive delirium can be reduced.

Multidisciplinary geriatric intervention

An RCT[38] was identified that examined the impact of inpatient geriatric consultation teams on delirium and overall cognitive functioning in older adults with hip fracture. Patients (n=171) were randomised to a multidisciplinary geriatric intervention or to usual care. Results showed that significantly more controls were delirious at any point after surgery compared to patients in the intervention group. However, no significant difference was found between groups for duration or severity of delirium.

Another RCT[39] evaluated the effectiveness of a geriatric liaison intervention in frail elderly cancer patients. Patients were randomised to either a geriatric liaison intervention or standard treatment. The geriatric liaison intervention consisted of a preoperative geriatric

to significantly reduce delirium rates whilst two studies show multidisciplinary geriatric interventions to have no significant impact on delirium rates.

The new evidence on Non-pharmacological multicomponent interventions and general multicomponent interventions is generally supportive of guideline recommendation 1.3.2 which states: 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.

No new cost-effectiveness evidence was found for multicomponent interventions for those in hospital.

consultation, individual treatment plan targeted at delirium risk factors, daily visits by geriatric nurses during hospital stay and advice on any problems encountered. In the 261 patients analysed, there was no significant difference in the incidence of delirium between the intervention and the control group.

A third RCT[40] randomised 329 hip fracture patients to treatment in an acute geriatric ward or to a standard orthopaedic ward. Results showed no significant difference in delirium rates (49% intervention vs. 53% control) between groups.

Non-pharmacological multicomponent intervention

A systematic review[41] investigated the effectiveness and safety of in-facility multicomponent delirium prevention programs. It included 19 studies. The results showed that most multicomponent interventions were effective in preventing delirium in at-risk patients.

A meta-analysis[42] was identified which investigated non-pharmacological multi-component interventions for the prevention of delirium in hospitalised older adult patients who were not in intensive care. It included 10 studies. Overall, patients who received the interventions had a 31% lower risk of developing delirium than those receiving usual care. This was statistically significant.

Furthermore, the multi-component interventions were found to lessen the duration of delirium but this finding was not statistically significant. No difference was found between groups for the severity of delirium. An RCT[43] assessed the efficacy of a non-pharmacological multicomponent intervention on delirium prevention (n=287). Hospitalised patients were randomised to either the non-pharmacological intervention delivered by family members or standard management. Results showed that delirium occurred in 5.6 % of patients in the intervention group compared to 13.3% in the control group. An RCT[44] investigated a multidisciplinary postoperative intervention program and postoperative complications in people with dementia who had a femoral neck fracture. Sixty-four patients were randomised to the intervention or conventional routines. The intervention consisted of staff education, individualised care planning and rehabilitation, and active prevention, detection and treatment of postoperative complications (delirium). The staff also worked in teams to apply a comprehensive geriatric assessment. It was found that there were fewer postoperative complications (including delirium) in the intervention group. **Specialist medical and mental health unit**		

An RCT[45] randomised 600 patients admitted for acute medical care to a specialist medical and mental health unit or to standard care. Features of the specialist unit included joint staffing by medical and mental health professionals, enhanced staff training in delirium, dementia and person centred dementia care, provision of organised purposeful activity, environmental modification to meet the needs of those with cognitive impairment, delirium prevention and a proactive and inclusive approach to family carers. Results showed that specialist care improved the experience of patients and satisfaction of carers. However, the authors stated that there were no convincing benefits in health status or service use.

Exercise and cognitive programme

An RCT[46] was identified which examined the impact of an enhanced exercise and cognitive programme on incident delirium in elderly hospitalised patients. Consecutive medical inpatients (n=648) were randomly allocated to twice-daily progressive resistance exercise, mobilisation and orientation plus usual care or to usual care alone. Delirium occurred in 4.9% of patients in the intervention group compared to 5.9% in the control group. No difference was observed between groups. Furthermore, the intervention was found to have no effect on delirium duration, severity, discharge destination or length of stay.

General multicomponent interventions

A meta-analysis[47] investigated strategies for the prevention of postoperative delirium. Thirty eight studies were included that examined pharmacological, psychological and multicomponent interventions. The results showed that multicomponent interventions were effective in preventing delirium. A meta-analysis[48] was identified which examined the efficacy of peri-operative interventions in decreasing postoperative delirium. Twenty nine RCT's in non-cardiac patients were included. Overall, peri-operative geriatric consultation and lighter anaesthesia were found to be associated with a reduction in the incidence of delirium. Furthermore, there was possible protection with prophylactic haloperidol, bright light therapy and general rather than regional anaesthesia.		

Clinical area: Multicomponent prevention

Q: What are the most clinical and cost effective multicomponent interventions for the prevention of delirium in people in long-term care?

Evidence summary	GDG/clinical perspective	Impact
Evidence Update (2012) A cluster RCT[49] looked at the impact of a multidisciplinary integrated care intervention on the quality of care and quality of life of 340 elderly physically or cognitively impaired patients in residential care. Patients were randomised to the multidisciplinary integrated care intervention (this was based on identification and monitoring of disabilities caused by chronic disease and a	None identified through GDG questionnaire.	The evidence found is supportive of current guideline recommendations. CG103 advises: 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,

comprehensive geriatric assessment of functional health) or to usual care. Results indicated that, when compared to usual care, the intervention was associated with improved quality of care and led to a reduction in the occurrence of delirium. The Evidence Update concluded that this supports the advice provided in CG103 to ensure that care for people at risk of delirium is multicomponent and delivered by a multidisciplinary team. 4-year surveillance review (2014) No evidence identified.		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. The tailored multicomponent intervention package should be delivered by a multidisciplinary team trained and competent in delirium prevention.

Clinical area: Pharmacological prevention

Q: What are the most clinical and cost effective and safe pharmacological interventions for the prevention of delirium in people in hospital?

Evidence summary	GDG/clinical perspective	Impact
Evidence Update (2012) **Melatonin** A double-blind RCT[50] was identified that looked at the effect of melatonin on delirium incidence (n=145). Patients, who were admitted through the emergency department into a tertiary care hospital, were randomised to melatonin (0.5mg) or placebo. It was found that patients treated with melatonin had a lower risk of developing delirium compared to those receiving the placebo. The Evidence Update concluded that further research is required on the postulated	None identified	The new evidence found for acetylcholinesterase inhibitors is supportive of the evidence included in CG103. The new evidence suggests that this pharmacological intervention is not beneficial in reducing delirium incidence or severity. The RCT's included in the guideline also found no significant difference between acetylcholinesterase inhibitors and placebo in delirium incidence and severity. For melatonin, the new evidence suggests that it may be beneficial in preventing delirium. However, the evidence is currently limited and so further studies are required into the

mechanism of action and role of melatonin since no statistically significant effect of melatonin on sleep was found.

Antipsychotics

A single-blind RCT[51] investigated the effectiveness of prophylactic administration of olanzapine for the prevention of post-operative delirium in 495 elderly elective knee or hip replacement surgery patients. Patients were randomised to olanzapine 5mg or placebo both before and after surgery. Results showed that the incidence of delirium was lower in the intervention group compared to the placebo group and that the time-to-onset was longer for those receiving olanzapine. However, delirium that did occur was more severe and of a longer duration in the intervention group compared to the control.

The Evidence Update concluded that this evidence is consistent with CG103 in recommending new research to define the role of drugs in preventing delirium.

4-year surveillance review (2014)

Melatonin

A systematic review[52] was identified which examined the use of melatonin and melatonin agonist for the prevention and management of delirium in elderly patients. Three studies were

effectiveness of melatonin for the prevention of delirium before considering it for inclusion in the guideline.

The new evidence on atypical antipsychotics will have no impact on CG103 since the evidence identified is insufficient. More studies examining the effectiveness of atypical antipsychotics are needed before they can be considered for inclusion in the guideline. For typical antipsychotics, the new evidence is inconclusive since one study suggested haloperidol significantly reduced delirium incidence whilst the second study found no significant difference in delirium incidence in those receiving haloperidol and those not receiving the drug. The second study is supportive of the evidence included in the guideline which also found no significant effect of haloperidol on delirium incidence. However, the new evidence on haloperidol also suggests that those receiving this drug have significantly shorter hospital stays which is consistent with the evidence included in the guideline.

The evidence for typical and atypical antipsychotics does relate to a research recommendation which states: Are atypical antipsychotics more clinically and cost effective than placebo, typical antipsychotics, benzodiazepines or acetylcholinesterase inhibitors in preventing the development of delirium in hospital patients at high risk of delirium? However, more evidence comparing typical and atypical antipsychotics is needed

included. Two looked at melatonin and one examined a melatonin agonist. Data from the two studies evaluating melatonin showed melatonin to have some benefit in preventing delirium. However, no evidence for melatonin reducing the severity of delirium was found. The study looking at the melatonin agonist (ramelteon) found that it was beneficial in preventing delirium in medically ill patients when compared to placebo.

Acetylcholinesterase Inhibitors

A meta-analysis[47] investigated strategies for the prevention of postoperative delirium. Thirty eight studies were included that examined pharmacological, psychological and multicomponent interventions. Results showed that there was no difference in the incidence of delirium between acetylcholinesterase inhibitors and placebo.

A pilot RCT[53] investigated whether donepezil hydrochloride reduced the prevalence and severity of delirium in hip fracture repair patients (n= 16). Patients were randomised to either donepezil 5mg or placebo with daily treatment being given for 30 days or until side effects or the clinical situation needed termination. Results showed that those in the intervention group experienced significantly more side effects than those in the placebo group. Furthermore, there was no significant difference between arms in both delirium presence over time and delirium severity over time.

before the research recommendation is fulfilled.

No new evidence on the cost-effectiveness of pharmacological interventions for the prevention of delirium in hospital was identified.

Propofol or Desflurane

In an RCT[54] (n=180) patients undergoing CABG were randomised to propofol or desflurane and followed up for three months. No difference in delirium was found between the two groups at follow-up but desflurane was found to be associated with a reduction in early cognitive dysfunction.

Dexamethasone

An RCT[55] was identified which examined dexamethasone for the prevention of delirium after cardiac surgery (n=93). Patients were randomised to either 8mg dexamethasone before anaesthesia followed by 8mg every 8 hours for 3 days or to placebo. The authors found that delirium, extubation time and length of stay in intensive care significantly decreased in the intervention group without increasing serious complications. However, hyperglycaemia was found to increase in the intervention group. No significant differences were found between groups for renal, cardiac, cerebrovascular or respiratory complications.

Dexmedetomidine

A systematic review[56] investigated dexmedetomidine for ICU delirium. Eight clinical trials were identified. The evidence suggested that dexmedetomidine was a promising agent for the prevention and treatment of ICU delirium but

the authors concluded that larger, well-designed trials are needed.

A meta-analysis[47] investigated strategies for the prevention of postoperative delirium. Thirty eight studies were included that examined pharmacological, psychological and multicomponent interventions. Results for dexmedetomidine found that this sedation was associated with less delirium when compared to sedation produced by other drugs.

Another meta-analysis[57] also examined dexmedetomidine for delirium in intensive care patients. This included 14 trials (n=3029). Analysis showed that dexmedetomidine was associated with significant reductions in delirium incidence, agitation and confusion.

Antipsychotics

A meta-analysis[58] was identified which investigated antipsychotics for the prevention of postsurgical delirium. Five RCTs were include (n=1491). The pooled analysis showed that there was a reduction in delirium incidence with prophylactic antipsychotics. However, those receiving prophylactic antipsychotics showed no difference in total hospital days or the severity of delirium.

A systematic review[59] examined antipsychotic prophylaxis of delirium in elderly inpatients. Five studies (n=1491) looking at haloperidol, risperidone and olanzapine were included.

Overall, it was found that perioperative antipsychotics effectively reduced the risk of postoperative delirium compared to placebo.

A meta-analysis[47] investigated strategies for the prevention of postoperative delirium. Thirty eight studies were included that examined pharmacological, psychological and multicomponent interventions. Results for antipsychotics showed that both typical and atypical antipsychotics decreased delirium occurrence compared to placebo.

A meta-analysis[60] examined the efficacy and tolerability of antipsychotics for the prevention of delirium in surgical patients. It included six studies (n=1689) looking at haloperidol (three studies), olanzapine (1 study) and risperidone (2 studies). The authors found that antipsychotics, compared to placebo, were efficacious in reducing the occurrence of delirium. Furthermore, from sensitivity analysis, it was found that second-generation antipsychotics were superior to placebo compared to haloperidol which failed to show any superiority to placebo. No statistically significant differences were found between groups in delirium severity, rates of adverse events or discontinuation rate.

Haloperidol

An RCT[61] investigated haloperidol for the prevention of delirium in intensive care patients admitted after non-cardiac surgery (n=457).Patients were randomised to either

haloperidol or placebo. Results showed that haloperidol significantly reduced the incidence of postoperative delirium. Furthermore, the mean time to delirium onset and mean number of delirium free days were significantly longer in the haloperidol group compared with the placebo group whilst the median length of stay in intensive care was shorter. No difference in 28 day all-cause mortality was found between the two groups.

Another RCT[62] evaluated the safety and effectiveness of low-dose haloperidol on postoperative delirium in elderly patients undergoing elective surgery for digestive or orthopaedic disease. One hundred and nineteen patients were randomised to receive 2.5mg of haloperidol in the evening for three days after surgery or to no haloperidol. No side effects were found with haloperidol and no significant difference was found between groups for the incidence of postoperative delirium. Haloperidol was also found to have no significant effect on the severity or persistence of delirium.

Types of anaesthetic

A meta-analysis[47] investigated strategies for the prevention of postoperative delirium. Thirty eight studies were included that examined pharmacological, psychological and multicomponent interventions. The authors found no difference in the incidence of delirium between neuraxial and general anaesthesia or between epidural and intravenous analgesia.

Ondansetron

An RCT[63] was identified which examined the effect of postoperative ondansetron on postoperative delirium in patients undergoing surgery for femoral or hip fracture. One hundred and six patients were randomly assigned to 4ml of ondansetron 8mg postoperatively or placebo for five days. Results showed that ondansetron led to a lower incidence and duration of postoperative delirium.

Clinical area: Pharmacological prevention		
Q: What are the most clinical and cost effective and safe pharmacological interventions for the prevention of delirium in people in long-term care?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) **Medication review** A cluster RCT[64] assessed prospective pharmacy-led monitoring to facilitate early identification of potential adverse drug reactions. To do this they used the Geriatric Risk Assessment MedGuide (GRAM) which correlates the medications effects with physical, functional and cognitive decline. Twenty-five nursing homes participated. They found that newly admitted patients in the intervention group had a lower rate of possible delirium compared to those in the usual care group. The Evidence Update stated that this supports current CG103 advice to carry out a medication review for those at risk of delirium.	None identified through GDG questionnaire.	The evidence found is supportive of the current guideline recommendation which states: Carry out a medication review for people taking multiple drugs, taking into account both the type and number of medications (1.3.3.7). No new evidence was found on cost-effectiveness.

4-year surveillance review (2014) No evidence identified.		

Clinical area: Treatment of delirium: Multicomponent

Q: What are the most clinical and cost effective multicomponent interventions for treating people with delirium in hospital?

Evidence Summary	GDG/clinical perspective	Impact
Evidence Update (2012) **Bright light therapy** An RCT[65] investigating the effect of bright light therapy on post-operative arrhythmia and acute delirium in patients hospitalised for an oesophagectomy as corrective treatment for throat cancer was identified (n=22). Patients were randomised to either bright light therapy or control (normal light conditions). It was found that the frequency of post-operative delirium was lower in the bright light group compared to control. However, this difference was not statistically significant. The Evidence Update concluded that since the study population was small and because of the negative findings no firm conclusions can be drawn as to the effect of bright light therapy on the incidence of delirium. **Pain management** A systematic review[66] that included 83 studies was identified. This examined pain management in adults with acute hip fracture. The interventions assessed were: nerve blockade	None identified through GDG questionnaire.	Bright light therapy is not currently included in CG103. However, the new evidence on bright light therapy suggests that this intervention, when compared to control, is not beneficial for the treatment of delirium. As such, this intervention is unlikely to be considered for inclusion in CG103 and the evidence identified will not impact on this guideline. For family approaches to delirium treatment, the new evidence was inconclusive as the included study was unable to determine if the involvement of families in delirium treatment was effective. As such, this evidence is unlikely to impact on CG103. With regards to pain management, the Evidence Update in 2012 stated that the evidence supported the advice given in CG103 and may provide extra information on appropriate pain management. However, no new evidence on pain management was identified through this 4 year surveillance review and no new evidence was provided through clinical feedback. Finally, the evidence for delirium abatement programmes suggests that they have no impact on the duration of delirium. Therefore, this

(n=32), spinal anaesthesia (n=30), systematic analgesia (n=3), traction (n=11), multimodal pain management (n=2), neurostimulation (n=2), rehabilitation (n=1) and complementary and alternative medicine (n=2). Results showed that the effect of regional nerve blockades for acute pain and reducing delirium risk was not statistically significant. An RCT was also identified[67]. This assessed the prophylactic effect of fascia iliaca compartment block (FICB) on postoperative delirium in hip surgery patients (n= 219). Patients were randomised to either FICB or placebo. The frequency of delirium was found to be significantly lower in the FICB group compared to the placebo group. Subgroup analysis, however, showed that there was no difference between the FICB group and placebo group in incidence of delirium when only high risk patients were included. For patients at intermediate risk of delirium, FICB led to a significant reduction in the frequency of delirium when compared to placebo. Another RCT[68] investigated restricted sedation depth with propofol during spinal anaesthesia in elderly hip fracture surgery patients (n=114). Patients were randomly assigned to either light or deep sedation with propofol. Results showed that the incidence of post-operative delirium was significantly reduced in the light sedation group compared to the deep sedation group. Furthermore, the mean number of days of delirium during hospitalisation was significantly		evidence is unlikely to currently impact on the guideline.

lower in the light sedation group than in the deep sedation group. However, this study was conducted in the US and so would have used different post-operative treatment pathways that would be used in the UK.

The Evidence Update concluded that the above studies support the advice given in CG103.

Delivery of care

A cluster RCT[69] (n=457) was identified that assessed a nurse-led delirium abatement programme (DAP) in patients newly admitted to post-acute care units. DAP included assessment of delirium within 5 days of admission, identification and correction of common reversible causes of delirium, avoidance of complications associated with delirium and recovery of function. Facilities were randomised to either DAP or usual care. Nurses detected delirium in 41% of patients at DAP sites compared with 12% in usual care sites. However, implementation of DAP was found to have no impact on the duration of delirium at 2 weeks or 1 month.

4-year surveillance review (2014)

Bright light therapy

An RCT[70] was identified in which 36 patients with delirium were randomly assigned to risperidone or risperidone with light therapy. It was found that risperidone with light therapy led

to a significantly greater decrease in delirium rating scale scores and significant improvements in total sleep time and sleep efficiency. The scores on the memorial delirium assessment scale (MDAS) were not significantly different between groups.

Family approach

A systematic review[71] investigated family approaches to delirium management. It included 11 studies. The aspects of delirium care investigated by the included studies were diverse and included bedside interventions, screening strategies, family education and multi-component interventions. The authors concluded that this review was unable to determine if the involvement of families in delirium management improved patient outcomes.

Clinical area: Treatment of delirium: pharmacological		
Q: What are the most clinical and cost effective and safe pharmacological interventions for treating people with delirium in hospital?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) **Rivastigmine** A double-blind RCT[72] was identified which investigated the effect of rivastigmine on delirium duration in critically ill patients (n=109). Patients were randomised to rivastigmine or placebo. It was found that the median duration of delirium was longer with the intervention and that those	None identified through GDG questionnaire.	The new evidence suggests that benzodiazepines are beneficial for the treatment of delirium. However, the evidence is limited since only one small study was included in the Cochrane review identified. As such, more large studies examining this drug are needed before it can be considered for inclusion in the guideline.

treated with the intervention stayed in ICU for significantly longer than those receiving the placebo. It should also be noted that this study was finished early due to a higher incidence of mortality in the intervention group. Currently, rivastigmine is not a recommended treatment for delirium in CG103.

Benzodiazepines

A Cochrane review[73] of RCTs examined the efficacy and safety of benzodiazepines as a treatment for delirium. Only one study met the inclusion criteria. This compared lorazepam (benzodiazepine) to dexmedetomidine in mechanically ventilated patients in ICU (n=103). Results showed that those treated with dexmedetomidine had an increased number of days free from delirium and coma compared to those in the lorazepam group. Currently, CG103 does not include benzodiazepines as a recommended treatment for delirium.

Antipsychotics

A single-blind RCT[74] looked at the efficacy and safety of olanzapine and risperidone compared to haloperidol in delirium patients. Sixty-four patients were randomised to haloperidol (0.25-10mg), risperidone (0.25-4mg) or olanzapine (1.25-20mg). Results showed that all three treatments were equally effective for delirium treatment.

For rivastigmine, the new evidence is consistent with CG103 which currently does not recommend this for the treatment of delirium. This is because the new evidence showed rivastigmine to not reduce delirium duration and to be associated with an increase in mortality.

The new evidence also suggested that melatonin, morphine, dexmedetomidine and ramelteon were also beneficial for the treatment of delirium. However, currently there is not enough evidence to consider these treatments for inclusion in the guideline. Further studies are needed into the effectiveness of these treatments before considering inclusion.

With regards to pharmacological management and ondasetron the new evidence was insufficient and so no conclusion could be drawn at this time. As such, this evidence will not impact on CG103.

For typical antipsychotics the new evidence was generally supportive of recommendation 1.6.4 which states: 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) haloperidol or olanzapine. Start at the lowest clinically appropriate dose and titrate cautiously according to symptoms. Whilst quetiapine and risperidone also showed some benefit the evidence was limited and showed

The Evidence update concludes that the evidence identified is consistent with NICE CG103, which recommends haloperidol and olanzapine for the treatment of delirium. For risperidone, the included study provided some evidence of similar outcomes with this drug. However, the Evidence Update suggests that further studies that overcome the limitations of this evidence are required before the clinical value of risperidone in the treatment of delirium can be established.

4-year surveillance review (2014)

Melatonin

A systematic review[52] was identified which examined the use of melatonin and melatonin agonist for the prevention and management of delirium in elderly patients. Three studies were included. Two looked at melatonin and one examined a melatonin agonist. Data from the two studies looking at melatonin showed melatonin to have some benefit in managing delirium. However, no evidence for melatonin reducing the severity of delirium was found.

Pharmacological management

A systematic review[75] looked at the efficacy of the pharmacological management of delirium solely in adult intensive care patients. They found limited studies in intensive care patients and found that the results of pharmacological

quetiapine to be as effective as haloperidol. As such, further studies are needed into these antipsychotics before any recommendation on their use can be made.

The new evidence on atypical antipsychotics suggests that they are as efficacious as typical antipsychotics in treating delirium. However, further studies are needed to establish which atypical antipsychotics are most efficacious before the current recommendation (1.6.4) is changed. The new evidence does not currently, impact on this recommendation.

The new evidence is related to a research recommendation which states: In hospital patients with delirium, are atypical antipsychotics better than placebo or typical antipsychotics or benzodiazepines for treating delirium? However, further evidence is needed into atypical antipsychotics before this research recommendation can be fully addressed.

management studies in general medical patients are often extrapolated to intensive care patients. They concluded that there are few credible studies on this topic.

A Cochrane review[76] was identified which investigated the effectiveness of drug therapies for treating delirium in terminally ill adult patients. It included one trial (n=30) in AIDS patients receiving chlorpromazine, haloperidol and lorazepam. Authors concluded that there was insufficient evidence from which to draw conclusions with further research needed.

Another systematic review[77] investigated pharmacological treatment of ICU delirium. Four studies were included. The authors concluded that antipsychotic therapy may reduce the duration of delirium but more robust and methodologically rigorous studies are needed to demonstrate benefit. Overall, there is a lack of evidence supporting pharmacological treatments for ICU delirium.

Ondasetron

An RCT[78] examined the efficacy of ondasetron and haloperidol in 80 heart surgery patients who developed delirium. Patients were randomised to an IV of 8mg ondasetron or 5mg haloperidol. Results showed that there was no statistically significant difference between ondasetron and haloperidol in controlling the effects of delirium.

Antipsychotics

A systematic review [79] was identified which examined the efficacy of antipsychotics for the treatment of delirium in older hospitalised adults. Thirteen studies were included. The authors concluded that due to severe methodological problems with the included studies the use of antipsychotics for delirium treatment was not supported by this review.

Another systematic review[80] examined 28 studies investigating antipsychotics for the treatment of delirium. It found that around 75% of delirium patients treated with lose-dose antipsychotics experience a clinical response. Furthermore, from the studies included it was suggested that there was no significant differences in the efficacy of haloperidol compare to atypical agents but higher adverse events were reported. The included studies did not indicate any major differences between delirium subtypes in response rates.

Haloperidol

A systematic review[81] was identified which investigated haloperidol for the treatment of delirium in critically ill patients. Eleven studies were identified. The findings from the observational studies showed a benefit with haloperidol. The three included controlled trials had small sample sizes and methodological flaws and so no conclusions were drawn.

An RCT[82] investigated whether early haloperidol

treatment would decrease the amount of time that critical illness survivors were delirious or in a coma. In this double-blind, placebo-controlled study 142 adult intensive care patients were randomised to 25mg of haloperidol or 0.9% saline intravenously every eight hours. Results showed that those in the intervention group spent the same number of days alive, without delirium and without coma than those in the placebo group.

Quetiapine

A systematic review[83] investigated quetiapine for the treatment of delirium. It included two RCTs, five open-label studies and one retrospective cohort study. Overall the results suggested that quetiapine resolved delirium symptoms more quickly than placebo and was as efficacious as haloperidol and amisulpride.

An RCT[84] also looked at quetiapine versus haloperidol for the treatment of delirium. Within this, 52 medically ill patients with delirium were randomised to either 25-100mg a day of quetiapine or 0.5-2.0 mg a day of haloperidol. Overall, it was found that a low dose quetiapine was as effective as haloperidol and was safe for controlling delirium.

A post-hoc analysis was identified [85] which used data from an RCT to compare the duration and time to first resolution of delirium symptoms. Data between the quetiapine and placebo groups were compared for 29 critically ill patients. Results

showed that those in the quetiapine group had delirium symptoms resolved faster than those in the placebo group.

Risperidone

An RCT[86] investigated risperidone for the treatment of subsyndromal delirium in elderly patients who had undergone on-pump cardiac surgery (n=101). Patients were randomised to 0.5mg risperidone or placebo every 12 hours. Seven patients in the intervention group experienced delirium compared to 17 in the placebo group. Risperidone was found to be associated with a significantly lower incidence of delirium.

Atypical antipsychotics

A systematic review[87] was identified which assessed the efficacy and safety of atypical antipsychotics for the treatment of delirium. Six RCTs were included. Results showed that atypical antipsychotics were effective and safe for the treatment of delirium but there was no difference found between each agent. When compared with low-dose haloperidol the efficacy of atypical antipsychotics was similar.

Morphine

An RCT[88] investigated the effect of morphine compared to haloperidol in delirium patients after cardiac surgery (n=53). Patients were randomly assigned to 5mg haloperidol intramuscularly or

5mg of morphine sulphate intramuscularly. Results showed that patients receiving morphine responded more quickly compared to those receiving haloperidol. Statistically low Richmond agitation and sedation scale scores were found during morphine treatment and significantly more patients in the haloperidol group required additive sedatives.

Dexmedetomidine

A systematic review[56] investigated dexmedetomidine for ICU delirium. Eight clinical trials were identified. The evidence suggested that dexmedetomidine was a promising agent for the treatment of ICU delirium but the authors concluded that larger, well-designed trials are needed.

Ramelteon

A multicentre[89] RCT was identified which examined the effectiveness of ramelteon on delirium in elderly patients admitted for acute care. Sixty-seven patients were randomised to either 8 mg/d of ramelteon or placebo administered every night for seven days. Results showed that ramelteon was associated with a lower risk of delirium, even after risk factors were controlled for. Furthermore, the frequency of delirium was found to be lower in the intervention group compared to the placebo group.

Clinical area: Research Recommendation

Q: Does an education programme for staff reduce the incidence of delirium and improve the recording of delirium for patients in hospital, compared with an education leaflet or usual care?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No evidence identified. 4-year surveillance review (2014) A systematic review[90] investigated educational interventions for the prevention of delirium in hospitalised patients. Nineteen studies were included. Results showed that studies using predisposing, enabling and reinforcing strategies together were more effective in producing changes in staff behaviour and patient outcomes whilst studies using education and guidelines together had little effect. In addition, when strategies to enable and reinforce change were used in combination with education sessions patient outcomes were found to be more positive. A systematic review[91] aimed to determine the effects of education interventions on delirium recognition. The included strategies were more often effective in producing changes to staff behaviour and patient outcomes. Overall, education interventions to recognise delirium appeared to be most effective when formal teaching was interactive and was combined with other strategies such as engaging leadership and using clinical pathways and assessment tools. A cluster RCT[92] was identified which investigated the impact of a delirium specific educational	A GDG member stated that there were now qualitative studies on staff attitudes. However, no details for these studies were provided.	The new evidence is concerned with educational interventions for staff to prevent delirium and recognise delirium in hospitalised patients. The evidence for educational interventions is inconclusive and heterogeneous. Different modes of delivery and different components are compared within the included studies and the results suggest that different components to the educational interventions are effective. Further research is needed into which components and modes of delivery for educational interventions are effective before considering them for inclusion in the guideline. Currently, the new evidence in this area does not impact on CG103. No details on the qualitative studies highlighted by the GDG were provided therefore it is not possible to ascertain any impact on the guideline.

website on delirium knowledge and recognition in acute care nurses. Statistically significant differences were found between the intervention and non-intervention group with delirium knowledge scores being significantly higher in the intervention group. Overall, the study suggests that web-based delirium learning is effective for acute care nurses.

Clinical area: Research Recommendation

Q: Does an education programme for staff improve the recovery from delirium in patients in hospital compared with an education leaflet or usual care?

Evidence summary	GDG/clinical perspective	Impact
Evidence Update (2012) No evidence identified. 4-year surveillance review (2014) A systematic review[93] was identified which investigated interprofessional education interventions (IPE) on learning outcomes for delirium care. Ten studies were included. Authors concluded that IPE programs may influence team and patient outcomes in delirium care but the evidence is limited.	None identified through GDG questionnaire.	The new evidence is unlikely to impact on this guideline since the evidence to date is limited. More studies are needed which examine the effectiveness of educational programmes for staff.

For the following areas of the guideline no new evidence was identified:
- What are the symptoms that indicate a person may have delirium?
- What are the diagnostic criteria that must be fulfilled to identify that a person has delirium?
- What are the precipitating factors for delirium?
- What are the most clinical and cost effective single-component, non-pharmacological interventions for treating people with delirium in hospital?
- What are the most clinical and cost effective and safe pharmacological interventions for treating people with delirium in long-term care?

- What are the most clinical and cost effective single-component, non-pharmacological interventions for treating people with delirium in long-term care?
- What are the most clinical and cost effective multicomponent interventions for treating people with delirium in long-term care?
- What information should be given to people at risk of developing delirium, or people with delirium, and their families or carers?

Ongoing research

None identified.

Anti-discrimination and equalities considerations

None identified.

Conclusion

Through the 4 year surveillance review of CG103: Delirium no new evidence which may potentially change the direction of guideline recommendations was identified. The proposal is not to update the guideline at this time and to move this guidance onto the static list because it fulfils the following criteria:

- No evidence was identified that would impact on the current guidance and no major ongoing studies or research has been identified as due to be published in the near future (that is, within the next 3-5 years).

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