# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

# Centre for Clinical Practice – Surveillance Programme

## *Recommendation for Guidance Executive (post-consultation)*

## Clinical guideline
CG103: Delirium: diagnosis, prevention and management

## Publication date
July 2010

## Surveillance report for GE (post-consultation)
December 2014

## Surveillance recommendation
GE is asked to consider the following proposal which was consulted on for two weeks:

- The clinical guideline CG103: Delirium should not be considered for an update at this time.
- The guideline should remain on the active surveillance list in light of the results emerging from ongoing trials examining magnesium for delirium prevention and from existing trials investigating haloperidol.

## 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 |
| ✓ | | | | |

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Centre for Clinical Practice – Surveillance Programme

### Surveillance review of CG103: Delirium: diagnosis, prevention and management

### *Recommendation for Guidance Executive (post consultation)*

## *Background information*

Guideline issue date: July 2010
4 year review: 2014

NCC: National Clinical Guidelines Centre

## *Four year surveillance review*

1. An Evidence Update was produced for the guideline in 2012 and was used as a source of evidence for the 4 year surveillance review. 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.

2. 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.

3. No new evidence was identified through the literature search which would invalidate the guideline recommendations.

## *Ongoing research*

4. During consultation the United Kingdom Clinical Pharmacy Association highlighted an ongoing study investigating magnesium for the prevention of delirium. In this RCT 62 intensive care unit patients were randomised to either magnesium or saline in addition to the usual sedation protocol. This study will provide important data on delirium incidence and duration as well as data assessing the impact of magnesium on sedation consumption.

## *Anti-discrimination and equalities considerations*

5. None identified.

## *Implications for other NICE programmes*

6. A Quality Standard on Delirium was published in July 2014. The current surveillance review recommendation to not update the guideline does not impact on the Quality Standard. However, the following should be noted:

- Stakeholders indicated through consultation for the Quality Standard that recommendation 1.6.4 could be impacted because haloperidol or olanzapine may present a significant increased risk of mortality or increased confusion. No new evidence was identified during this surveillance review concerning this issue and no comments on this issue were received during consultation for the surveillance decision. As such, it was decided not to update the delirium guideline at this time but to review this issue at the next surveillance review point.
- There was a general consensus among the Quality Standard Advisory Committee that the content is generally tailored to health rather than social care. For example, the scope is limited to hospital and long-term care settings, however it does not apply to some community care settings, notably the home. The 4-year surveillance review of CG103 considered evidence outside of the guideline scope however, no evidence on community care settings was identified. Furthermore, this issue was not raised by GDG members during initial intelligence gathering.

## *Summary of stakeholder feedback*

7. Stakeholders were consulted on the following proposal over a two week consultation period:

| |
|---|
| The Delirium guideline should not be considered for an update at this time.<br><br>The guideline should be transferred to the static guidance list because it fulfils the following criteria:<br><br>• 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). |

8. In total, 12 stakeholders commented on the surveillance review proposal recommendation during the two week consultation period. The table of stakeholder comments can be viewed in Appendix 1. Nine stakeholders provided comments on the surveillance review proposal and the remaining three stakeholders stated that they had no substantive comments to make.

9. Of the nine stakeholders that provided comment, four agreed that CG103 did not need to be updated whilst five stakeholders disagreed.

10. Three stakeholders agreed with the decision to place CG103 on the static list whilst five stakeholders disagreed. One stakeholder did not comment on the static list proposal.

11. The following is a summary of the general comments made by the stakeholders that disagreed with the surveillance review proposal:

12. Pharmacological Interventions.

*Dexmedetomidine.*

One stakeholder stated that there was accumulating evidence for an association between lower delirium incidence and dexmedetomidine use in the ICU and highlighted a relevant systematic review. This study was not identified during the surveillance review because it was published after the literature search cut-off date. From assessment of the abstract, the review indicated that the use of dexmedetomidine is associated with lower delirium incidence. This is consistent with the evidence identified during this surveillance review. However, the evidence included in the surveillance review is currently limited since the systematic reviews included either did not state the population and did not state how many studies on dexmedetomidine were included or concluded that more larger well-designed trials are needed in order

to define the role of this drug in delirium prevention. As such, further methodologically rigorous studies are needed that examine dexmedetomidine before it can be considered for inclusion in the guideline.

*Pharmacological interventions including antipsychotics.*

One stakeholder also stated that the new evidence identified through the surveillance review on pharmacological interventions for the prevention and treatment of delirium, specifically antipsychotics, tended to be earmarked as being weak, as was the study by Hu et al which was included in the original guideline. They stated that it was not clear why historically weak evidence is a better guide than new weak evidence. However, as only the abstracts of studies are evaluated in a surveillance review, the included studies are not assessed for methodological rigour. However, from an assessment of abstracts, the studies that were included tended to be small and inconclusive. As such, methodologically rigorous studies conducted in larger populations are needed before recommendations on the pharmacological interventions for the prevention and treatment of delirium and for antipsychotics can be changed.

*Haloperidol and Mortality.*

One stakeholder stated that there is evidence for an association between haloperidol and mortality and highlighted a recent study. This study was not identified during the surveillance review because it was published after the literature search cut-off date. However, an assessment of the abstract identified this study as a retrospective cohort study. The primary study design for the prevention and treatment sections of CG103 were RCTs and quasi-randomised trials. Non-randomised studies were to be included only if no other evidence was available. As RCTs for haloperidol and the prevention and treatment of delirium were included in the guideline and contributed to the evidence base, the cohort study highlighted would not currently impact on CG103. In addition, a number of studies were identified investigating haloperidol for the prevention and treatment of delirium during this surveillance review. The evidence for prevention tended to be inconclusive with one study finding haloperidol to be beneficial and another study finding no beneficial effect. However in the study finding benefit, no difference in 28 day all-cause mortality was found between haloperidol and placebo. For treatment of delirium, the evidence identified in this surveillance review suggested that haloperidol was beneficial. Furthermore, in one RCT results showed that those receiving haloperidol spent the same number of days alive, without delirium and coma compared to the placebo group. However, sample sizes tended to be small in these studies. As such, larger trials into the use of haloperidol for the prevention and treatment of delirium and its association with mortality are needed before firm conclusions can be drawn.

*Magnesium and the prevention of delirium*

One stakeholder stated that they expected to see some discussion about magnesium for the prevention of delirium and highlighted a preliminary report of an ongoing study. This study was an ongoing RCT in which 62 intensive care unit patients were randomised to either magnesium or saline in addition to the usual sedation protocol. However, no new evidence investigating magnesium for the prevention of delirium was identified during this surveillance review and no evidence on this topic was identified during the development of the guideline. Moreover, as this preliminary report was published in 2009, any published trial results may have been identified and considered during the development of the Evidence Update of this guideline in 2012. Magnesium for the prevention of delirium and the impact of magnesium on sedation consumption will be considered again at the next surveillance review of the guideline.

13. Multicomponent prevention of delirium.

Two stakeholders highlighted a study investigating multicomponent, multidisciplinary interventions for the prevention of delirium and stated that this study should be considered for inclusion within the guideline. From an assessment of the abstract, this study was identified as a before and after study. The guideline states that for prevention of delirium the primary trial designs were RCTs and quasi-randomised trials. Non-randomised studies were only included if no other evidence was available. Furthermore, before and after studies were to be considered with caution. As the guideline includes RCT evidence in the section on prevention and since the highlighted study was a small before and after study the evidence provided by the stakeholders is unlikely to be included in this guideline or drive an update at this time.

## *Conclusion*

14. Through the 4 year surveillance review of CG103: Delirium and subsequent consultation with stakeholders no new evidence was identified which may potentially change the direction of current guideline recommendations. The proposal is not to update the guideline at this time. However, stakeholders highlighted uncertainty around the association between haloperidol and mortality, the use of dexmedetomidine and the use of magnesium but from the evidence identified through the surveillance review there was uncertainty about the consistency of effects, methodological limitations or not enough evidence to currently consider an update. Nonetheless, after consideration of the comments provided by stakeholders it was determined that the guidance should not be recommended for the static guidance list. Further research outcomes related to the use of haloperidol for the prevention and treatment of delirium in Intensive Care Units and on the use of dexmedetomidine may become available and ongoing studies, such as the study examining magnesium, may

impact on the guidance in the future. Therefore the guideline should remain on the active surveillance list and continue on a 2 yearly surveillance cycle.

Mark Baker – Centre Director
Sarah Willett – Associate Director
Louise Hartley – Technical Analyst

Centre for Clinical Practice
January 2015

# Appendix 1 Surveillance review consultation

Surveillance review consultation comments table
30 October 2014 - 13 November 2014

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| Orion Pharma (UK) Ltd | Disagree | No | | We believe that there is accumulating evidence that suggests that there are lower incidences of delirium associated with dexmedetomidine use in the ICU, for example Crit Care Med. 2014 Sep 23. [Epub ahead of print], A Systematic Review of Risk Factors for Delirium in the ICU. Zaal IJ et al.<br>As such the guideline should be updated to reflect this. | Thank you for your comment and for highlighting a reference for this consultation. This study was not identified through the surveillance review because it was published after the literature search cut-off date.<br><br>In terms of the Zaal et al. study, the results reported in the abstract indicate that the use of dexmedetomidine is associated with lower delirium prevalence. This is consistent with the evidence found during this surveillance review. However, the evidence included in this review is currently limited and therefore would not justify an update at this time. This is because of the three systematic reviews included, one did not state the population and did not state how many studies on dexmedetomidine were included and another concluded that more larger well-designed trials are needed in order to define the role of this drug in |

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| | | | | | delirium prevention.<br><br>This guideline is remaining on the active surveillance list in light of the results emerging from ongoing trials examining magnesium for delirium prevention and from existing trials investigating haloperidol highlighted by stakeholders. This area will be considered further at the next surveillance review point. |
| NICE Social Care | Probably, although there are aspects of managing delirium in care homes that might not be too well covered. | Again, probably | Even though the guidance covers the diagnosis, prevention and management of delirium in hospital in-patients and residents in long-term care, the surveillance report is written in a very clinical way and appears to consider little general guidance on care, accessible to care staff and managers. | If it were reviewed, there could be more accessible and relevant information for care home staff. | We conducted a broad search for RCTs and systematic reviews investigating the diagnosis, prevention, and management of delirium. No studies examining general care issues for care home staff and managers were identified. Furthermore, this issue was not highlighted by GDG members during initial intelligence gathering. However, this aspect will be considered at the next surveillance review of the guideline. |
| British Geriatrics Society | Agree | Agree | We are disappointed to see that there is no recommendation of what medication to | | Thank you for your comments.<br><br>The scope of CG103 covers all adults in a hospital setting or in long-term residential |

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| | | | use for delirium in Parkinsons disease. On a practical level it is not particularly helpful to simply state medications to avoid. | | care and so studies involving patients with Parkinsons disease and delirium would have been included in the guideline and therefore the surveillance review.<br><br>However, in conducting a broad search for RCTs and systematic reviews investigating the diagnosis, prevention and management of delirium we did not identify any evidence during this surveillance review that examined which medications to use for delirium in Parkinson's disease. As such, further evidence is needed before the guideline can make specific recommendations about medications.<br><br>Currently, CG103 states: Use antipsychotic drugs with caution or not at all for people with conditions such as Parkinsons disease or dementia with Lewy bodies (1.6.5) and cross refers to CG35: Parkinsons disease. However, the Parkinsons disease guideline is currently being updated and so your comments will be passed to the relevant group undertaking this update. |
| College of Emergency Medicine | Agree | Agree | None | It is the right decision. Totally agree with translation of updated evidence | Thank you for your comment |

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| | | | | | |
| Lancashire Teaching Hospitals NHS Foundation Trust | Disagree | Disagree | | **Following a research study undertaken in our Critical Care Unit, the stakeholders propose that the significant findings of this trial should be considered for inclusion within the evidence for multi component prevention of delirium. The full reference for the trial is as follows;**<br>***Patel J, Baldwin J, Bunting P, Laha S, The effect of a multicomponent multidisciplinary bundle of interventions on sleep and delirium in medical and surgical intensive care patients. Anaesthesia. 2014 Jun; 69(6):540-9.***<br>The outcomes of this trial demonstrated that improving patient sleep reduced the incidence of delirium by >50%. It also decreased the length of time patients spent in a delirious state and delayed the onset of delirium. The bundle of non-pharmacological interventions to promote sleep and reduce delirium, involved simple adjustments to practice and | Thank you for your comment.<br><br>This study was not identified in the literature search for this surveillance review. An assessment of the abstract indicates that this study is a before and after study. The guideline states that for prevention the primary trial designs were RCTs and quasi-randomised trials. Non-randomised studies were only included if no other evidence was available. Furthermore, before and after studies were to be considered with caution. As the guideline includes RCT evidence in the prevention section and since the highlighted study was a small before and after study the highlighted evidence is unlikely to be included in this guideline or drive an update at this time.<br><br>This guideline is remaining on the active surveillance list in light of the results emerging from ongoing trials examining magnesium for delirium prevention and from existing trials investigating haloperidol highlighted by stakeholders. |

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| | | | | environment and had minimal resource implications. A further staged programme of study is planned for the next 12 months. This will initially explore the sustained implementation of the bundle in order to measure the impact of the intervention under real life conditions without additional input from an investigator. This will lead to the development of a tool kit to facilitate the roll out and adoption of the intervention across other regional critical care units. The final stage will involve the adaptation of the tool kit for use throughout the wider hospital setting. The ultimate aim is to demonstrate how simple improvements in practice can dramatically reduce the incidence of delirium in hospital patients and for this reason we feel the guideline should be reviewed to incorporate the recommendations from evidence outlined above. | |
| The Royal College of Psychiatrists | Disagree | No | Depression is not mentioned in the guidance. It is noted that dementia may | <u>Comments on proposal not to update the guideline</u><br><br>There is more evidence that | Thank you for your comments.<br><br>This study was not identified through the surveillance review because it was |

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| | | | be confused with delirium. However, with a hypo-active delirium, the differential diagnosis includes depression. In clinical practice, I see far too many people put on anti-depressants inappropriately when they have a hypo-active delirium. For these common diagnoses, the 3Ds approach to diagnosis is required: dementia-delirium-depression. | haloperidol is associated with mortality. (see Comparative mortality risks of antipsychotic medications in community-dwelling older adults*,† T. Gerhard, K. Huybrechts, M. Olfson, S. Schneeweiss, W. V. Bobo, P. M. Doraiswamy, D. P. Devanand, J. A. Lucas, C. Huang, E. S. Malka, R. Levin and S. Crystal BJ Psych Oct 2014) Precisely how this relates to delirium is unclear, but it makes me uneasy about the current recommendation by NICE to use it. | published after the literature search cut-off date. However, assessment of the abstract shows this study to be a retrospective cohort study. The primary study design for the prevention and treatment sections of CG103 were RCTs and quasi-randomised trials. Non-randomised studies were to be included only if no other evidence was available. As RCTs for haloperidol and the prevention and treatment of delirium were identified in the guideline, the cohort study highlighted is unlikely to impact on CG103.<br><br>Through the surveillance review a number of studies which examined haloperidol were identified. Two were for the prevention of delirium and two for the treatment of delirium. From the prevention studies, the evidence for the effectiveness of haloperidol was inconclusive since one study found haloperidol to be beneficial in reducing the incidence of delirium whilst the other study found no difference between haloperidol and no haloperidol in the incidence of post-operative delirium. One study did find, however, that there was no difference between haloperidol and placebo in 28 day all-cause mortality. For the studies investigating the treatment of delirium, the systematic review of |

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| | | | | | observational studies found that haloperidol was beneficial whilst the RCT showed that those in the haloperidol group spent the same number of days alive, without delirium and coma as those in the placebo group.<br><br>This guideline is remaining on the active surveillance list in light of the results emerging from ongoing trials examining magnesium for delirium prevention and from existing trials investigating haloperidol highlighted by stakeholders. |
| The Royal College of Nursing | | | | This is to inform you that the Royal college of Nursing have no comments to submit to inform on the Delirium: Diagnosis, prevention and management surveillance review proposal. | Thank you. |
| Department of Health | | | | I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation. | Thank you. |
| CC3N | Disagree | Disagree | | Following a research study undertaken in a Critical Care Unit at Lancashire Teaching Hospitals NHS Trust, we propose that the significant findings of the trial | Thank you for your comment.<br><br>This study was not identified in the literature search for this surveillance review. An assessment of the abstract indicates that |

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| | | | | should be considered for inclusion within updated guidance. The full reference for the trial is as follows; ***Patel J, Baldwin J, Bunting P, Laha S, The effect of a multicomponent multidisciplinary bundle of interventions on sleep and delirium in medical and surgical intensive care patients. Anaesthesia. 2014 Jun; 69(6):540-9.***<br>The outcomes of this trial demonstrated that improving patient sleep reduced the incidence of delirium by >50%. It also decreased the length of time patients spent in a delirious state and delayed the onset of delirium. The bundle of non-pharmacological interventions to promote sleep and reduce delirium, involved simple adjustments to practice and environment and had minimal resource implications. A further staged programme of study is planned for the next 12 months. This will initially explore the sustained implementation of the bundle in order to measure the | this study is a before and after study.<br>The guideline states that for prevention the primary trial designs were RCTs and quasi-randomised trials. Non-randomised studies were only included if no other evidence was available. Furthermore, before and after studies were to be considered with caution. As the guideline includes RCT evidence in the prevention section and since the highlighted study was a small before and after study the highlighted evidence is unlikely to be included in this guideline or drive an update at this time.<br><br>This guideline is remaining on the active surveillance list in light of the results emerging from ongoing trials examining magnesium for delirium prevention and from existing trials investigating haloperidol highlighted by stakeholders. |

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| | | | | impact of the intervention under real life conditions without additional input from an investigator. This will lead to the development of a tool kit to facilitate the roll out and adoption of the intervention across other regional critical care units. The final stage will involve the adaptation of the tool kit for use throughout the wider hospital setting. The ultimate aim is to demonstrate how simple improvements in practice can dramatically reduce the incidence of delirium in hospital patients and for this reason we feel the guideline should be reviewed to incorporate the recommendations from evidence outlined above. | |
| United Kingdom Clinical Pharmacy Association | Disagree | | | The team from NICE have done a good job of collating and summarising new publications that have emerged since the previous guideline.<br><br>1. We note that new data that may affect the sections on pharmacological interventions (both prophylactic and for established delirium) tend to be earmarked as | Thank you for your comments.<br><br>1. For recommendation 1.6.4 the GDG weighed up the evidence from the included studies and the cost effectiveness analysis. In doing this, they decided that the benefits of pharmacological interventions outweighed the risks and so decided that they should recommend drug treatment after other treatment interventions had been tried. Due to the uncertainty surrounding |

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| | | | | being of weak evidence<br><br>E.g.<br>*"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 quetiapine to be as effective as haloperidol. As such, further studies are needed into these antipsychotics before any* | the evidence and the adverse events associated with these drugs for long term use, the GDG did not want to recommend the routine use of these drugs for everyone with delirium. It was therefore decided to make a cautious recommendation that healthcare professionals consider giving pharmacological treatment as short term treatment. Short-term treatment was defined as 1 week or less, based on the evidence from the Hu (2006) study and usual practice.<br><br>During a surveillance review only the abstracts of identified relevant studies are assessed. As such, we are unable to assess the methodological rigour of our included studies and so cannot ascertain if they are weak. However, the majority of included studies investigating pharmacological interventions were small and many of the studies reported that there were methodological problems. This meant that no conclusions could be drawn. More large, longer term RCTs that are methodically rigorous are needed before the recommendations are likely to be changed.<br><br>2. The original Devlin study was published |

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| | | | | *recommendation on their use can be made."*<br><br>The study the original NICE guidance was based on (Hu et al) is similarly weak (not blinded, no placebo). It is not at all clear why historically weak evidence is a better guide to national policy than new weak evidence, particularly when the new weak evidence tends to arise from (on the face of it) less biased trial methodology.<br><br>2. Also noted that some Devlin evidence is included (ref 85), but the original study by Devlin that looked at Quetiapine vs Placebo (not haloperidol) is excluded Crit Care Med. 2010 Feb;38(2):419-2.<br><br>*3. "The new evidence suggests that benzodiazepines are beneficial for the treatment of delirium"*<br><br>The evidence cited actually supports the reverse, this may be because of the wording | before the search period for this surveillance review (28/11/11 to 4/8/14) and so would not have been included.<br><br>3. Thank you for highlighting this. The wording has been changed to say that benzodiazepines are not beneficial for the treatment of delirium.<br><br>4. During the surveillance review no evidence was found relating to Magnesium and delirium. The RCT provided was published in 2009 and so is outside of the search period for this surveillance review. However, the study should have been identified by guideline developers when the CG103 was being produced.<br>However, NICE recognises the potential impact the findings from this study may have on the guidance recommendations in the future. Therefore we propose not to update the guidance at this time but will retain the guideline on the active surveillance list and consider any published results at the next review of the guidance in 2 years. |

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| | | | | *"Results showed that those treated with dexmedetomidine had an increased number of days **free** from delirium and coma compared…"*<br><br>4. Expected to see some discussion about Magnesium http://ccforum.com/content/13/S1/P412<br><br>Thank you for the opportunity to comment, this submission was rushed in the last hour before deadline so I apologise for brevity and any typo's, spelling errors, etc. | |
| NHS England | | | | I wish to confirm that NHS England has no substantive comments to make regarding this consultation. | Thank you. |
| The Royal College of Anaesthetists | Yes, at this moment in time a full review is not necessary | No, as this could mean that the guidance is not reviewed for five years. | n/a | We have consulted with experts in delirium occurring in the postoperative period and in the critical care setting and we have been advised that there is ongoing research in this field. We are concerned that moving the current | Thank you for your comment.<br><br>At present, we do not update clinical guidelines if there is no new significant evidence that would impact on their recommendations. Guidelines where there is new impacting evidence are given priority |

| Stakeholder | Do you agree that the guidance should not be updated? | Do you agree that the guidance should be put on the static list | Comments on equality issues or areas excluded from the original scope | Comments<br>If you disagree please explain why | Response |
|---|---|---|---|---|---|
| | | | | guidance to the static list will delay any new evidence being considered for too long a period of time and we would advise that a full review should take place within three to four years at the latest. | for updating. This is because of time and resource restraints. We are of course aware that this will mean that the evidence base in the guideline will not be up to date although the recommendations remain valid. The guideline will be reviewed again in two years time.<br><br>This guideline is remaining on the active surveillance list in light of the results emerging from ongoing trials examining magnesium for delirium prevention and from existing trials investigating haloperidol highlighted by stakeholders. |

# Appendix 2 Decision matrix

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| 103-01: What is the prevalence of delirium in different hospital settings and in long-term care? | | | |
| 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.<br><br>Another systematic review[2] assessed factors associated with persistent delirium in those with acute illness. It included 21 observational studies | **Stroke**<br><br>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%.<br><br>**Acute respiratory failure**<br><br>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. | 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. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| (n=1953). It was found that the rates of persistent delirium ranged from 0-78% and that persistent delirium was significantly associated with hypoactive delirium, increasing severity of delirium, cognitive impairment, multiple comorbidities and hypoxic illness.<br><br>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. | **Cardiac surgery**<br><br>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.<br><br>**Subsyndromal delirium**<br><br>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 | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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. | | |
| 103-02: What are the symptoms that indicate a person may have delirium? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| 103-03: 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? | | | |
| None identified. | **Generic assessment tools**<br><br>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.<br><br>A systematic review[8] investigated the diagnostic accuracy of two delirium assessment tools (CAM | 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, 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 |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**Critically ill patients**<br><br>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 CAM-ICU was the most specific tool for the assessment of delirium in critically ill patients. The pooled | | distinguishing between the diagnoses of delirium, dementia or delirium superimposed on dementia, treat for delirium first. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | sensitivities and specificities for CAM-ICU were 75.7% and 95.8% respectively. However, the authors do point out that there was significant heterogeneity present.<br><br>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.<br><br>A systematic review[11] aimed to identify which types of delirium | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**EEG-based monitoring**<br><br>A systematic review[12] was conducted to examine 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. | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | **Delirium superimposed on dementia**<br><br>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.<br><br>**Cognitive impairment** | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**Delirium at the end of life**<br><br>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. | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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. | | |
| 103-04: What are the diagnostic criteria that must be fulfilled to identify that a person has delirium? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| 103-05: What are the risk factors for delirium? | | | |
| A systematic review[16] including randomised controlled trials, cohort studies and case-control studies investigated the relationship between medication and risk of delirium. 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. | **Risk factors after cardiac surgery**<br><br>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 | 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.<br><br>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 |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| The Evidence Update stated that specific groups of medications may be potential risk factors for the development of delirium. However evidence is currently limited and further research is required.<br><br>**Methods for assessing delirium risk**<br><br>An observational multicentre study[17] used data 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 and 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. | 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.<br><br>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- | | 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.<br><br>There is also insufficient evidence for an association between cerebrospinal fluid biomarkers 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?<br><br>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, no evidence was provided by GDG members |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| Currently, a risk assessment tool is not recommended in CG103. | aortic balloon pump, inotropic medication and a low cardiac output appeared to be the most relevant risk factors associated with postoperative delirium.<br><br>**Delirium in acute stroke**<br><br>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.<br><br>**Critically ill patients**<br><br>A systematic review[20] was identified which aimed to identify the risk factors associated with acute delirium in critically ill adults. | | or stakeholders and only one study was identified during the Evidence Update (2012). In particular, further studies comparing this tool to recognised prediction methods are needed before PRE-DELIRIC can be considered for inclusion in the guideline. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>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. | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | **Acute medical inpatients**<br><br>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.<br><br>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: | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**Pharmacological risk factors**<br><br>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, | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**Risk factors and timing of occurrence**<br><br>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 | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | various pathophysiological and environmental conditions.<br><br>**Cerebrospinal fluid biomarkers**<br><br>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. | | |
| 103-06: What are the precipitating factors for delirium? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| 103-07: What are the consequences of delirium in terms of morbidity and mortality in a person in hospital or long-term care? | | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| None identified. | **Delusional memories**<br><br>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. Furthermore, results for delusional memories and adverse emotional outcome contradicted each other and so no conclusion could be drawn.<br><br>**Acute stroke**<br><br>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 | 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:<br><br>“THINK DELIRIUM”<br><br>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. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**Clinical outcomes**<br><br>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. | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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. | | |
| 103-08: What are the most clinical and cost effective single-component, non-pharmacological interventions for the prevention of delirium in people in hospital? | | | |
| None identified. | **Earplugs**<br><br>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 | 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. Currently the guideline recommends:<br><br>Address dehydration and/or constipation by: |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | confusion and led to a later development of confusion.<br><br>**Monitoring the depth of anaesthesia**<br><br>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 incidence was lower in those with open guided BIS.<br><br>**Transfusion strategies**<br><br>An RCT[33] was carried out to see the effect of two different blood transfusion strategies on postoperative delirium. One | | • ensuring adequate fluid intake to prevent dehydration by encouraging the person to drink – consider offering subcutaneous or intravenous fluids if necessary<br>• taking advice if necessary when managing fluid balance in people with comorbidities (for example, heart failure or chronic kidney disease).<br><br>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.<br><br>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.<br><br>No new cost-effectiveness evidence was |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**Fast track surgery**<br><br>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.<br><br>**N-3 fatty acids**<br><br>An RCT[35] investigated the effect of | | found for any single-component non-pharmacological interventions. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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. | | |
| 103-09: What are the most clinical and cost effective single-component, non-pharmacological interventions for the prevention of delirium in people in long-term care? | | | |
| None identified. | 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 | 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. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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. | | 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. This is because only one study was identified which assessed this intervention. Furthermore, the study identified was conducted in the U.S.A and so the practicality of the intervention may not be generalisable to a UK setting. More research into these interventions is needed before they can be considered for inclusion in the guideline. |
| 103-10: What are the most clinical and cost effective multicomponent interventions for the prevention of delirium in people in hospital? | | | |
| None identified. | **Nursing interventions**<br><br>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 | 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 to significantly reduce delirium rates whilst two studies show multidisciplinary geriatric interventions to have no significant impact on delirium rates. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**Multidisciplinary geriatric intervention**<br><br>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 | | 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:<br>• Within 24 hours of admission, assess people at risk for clinical factors contributing to delirium.<br>• 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.<br><br>No new cost-effectiveness evidence was found for multicomponent interventions for those in hospital. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | between groups for duration or severity of delirium.<br><br>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 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.<br><br>A third RCT[40] randomised 329 hip fracture patients to treatment in an acute geriatric ward or to a standard orthopaedic ward. Results | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | showed no significant difference in delirium rates (49% intervention vs. 53% control) between groups.<br><br>**Non-pharmacological multicomponent intervention**<br><br>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.<br><br>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 | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>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.<br><br>An RCT[44] investigated a multidisciplinary postoperative | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**Specialist medical and mental health unit**<br><br>An RCT[45] randomised 600 patients admitted for acute medical care to a specialist medical and mental health unit or to standard care. | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**Exercise and cognitive programme**<br><br>An RCT[46] was identified which examined the impact of an enhanced exercise and cognitive programme on incident delirium in | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**General multicomponent interventions**<br><br>A meta-analysis[47] investigated strategies for the prevention of postoperative delirium. Thirty eight studies were included that examined pharmacological, psychological and multicomponent | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | interventions. The results showed that multicomponent interventions were effective in preventing delirium.<br><br>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. | | |
| 103-11: What are the most clinical and cost effective multicomponent interventions for the prevention of delirium in people in long-term care? | | | |
| 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 | None identified | None identified through GDG questionnaire. | The evidence found is supportive of current guideline recommendations. CG103 advises:<br><br>Give a tailored multicomponent |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| 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 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.<br><br>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. | | | intervention package:<br><br>• Within 24 hours of admission, assess people at risk for clinical factors contributing to delirium<br>• 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.<br>• The tailored multicomponent intervention package should be delivered by a multidisciplinary team trained and competent in delirium prevention. |
| 103-12: What are the most clinical and cost effective and safe pharmacological interventions for the prevention of delirium in people in hospital? | | | |
| **Melatonin**<br><br>A double-blind RCT[50] was identified that looked at the effect of melatonin | **Melatonin**<br><br>A systematic review[52] was identified which examined the use | None identified through GDG questionnaire. | The new evidence found for acetylcholinesterase inhibitors is supportive of the evidence included in CG103. The new evidence suggests that |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| 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.<br><br>The Evidence Update concluded that further research is required on the postulated mechanism of action and role of melatonin since no statistically significant effect of melatonin on sleep was found.<br><br>**Antipsychotics**<br><br>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 | 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 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.<br><br>**Acetylcholinesterase Inhibitors**<br><br>A meta-analysis[47] investigated strategies for the prevention of postoperative delirium. Thirty eight studies were included that examined pharmacological, | | 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.<br><br>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 effectiveness of melatonin for the prevention of delirium before considering it for inclusion in the guideline.<br><br>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 |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| 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.<br><br>The Evidence Update concluded that this evidence is consistent with CG103 in recommending new research to define the role of drugs in preventing delirium. | psychological and multicomponent interventions. Results showed that there was no difference in the incidence of delirium between acetylcholinesterase inhibitors and placebo.<br><br>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. | | 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.<br><br>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 |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | **Propofol or Desflurane**<br><br>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.<br><br>**Dexamethasone**<br><br>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 | | needed before the research recommendation is fulfilled.<br><br>No new evidence on the cost-effectiveness of pharmacological interventions for the prevention of delirium in hospital was identified. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**Dexmedetomidine**<br><br>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.<br><br>A meta-analysis[47] investigated strategies for the prevention of postoperative delirium. Thirty eight studies were included that | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>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.<br><br>**Antipsychotics**<br><br>A meta-analysis[58] was identified which investigated antipsychotics for the prevention of postsurgical delirium. Five RCTs were included (n=1491). The pooled analysis showed that there was a reduction | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | in delirium incidence with prophylactic antipsychotics. However, those receiving prophylactic antipsychotics showed no difference in total hospital days or the severity of delirium.<br><br>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.<br><br>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 | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | typical and atypical antipsychotics decreased delirium occurrence compared to placebo.<br><br>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. | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | *Haloperidol*<br><br>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.<br><br>Another RCT[62] evaluated the safety and effectiveness of low-dose haloperidol on postoperative | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**Types of anaesthetic**<br><br>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 | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | delirium between neuraxial and general anaesthesia or between epidural and intravenous analgesia.<br><br>**Ondansetron**<br><br>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. | | |
| 103-13: What are the most clinical and cost effective and safe pharmacological interventions for the prevention of delirium in people in long-term care? | | | |
| **Medication review**<br><br>A cluster RCT[64] assessed prospective | None identified. | None identified through GDG questionnaire. | The evidence found is supportive of the current guideline recommendation which states: Carry out a medication review for |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| 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. | | | people taking multiple drugs, taking into account both the type and number of medications (1.3.3.7).<br><br>No new evidence was found on cost-effectiveness. |
| 103-14: What are the most clinical and cost effective single-component, non-pharmacological interventions for treating people with delirium in hospital? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| 103-15: What are the most clinical and cost effective single-component, non-pharmacological interventions for treating people with delirium in long-term care? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| 103-16: What are the most clinical and cost effective multicomponent interventions for treating people with delirium in hospital? | | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| **Bright light therapy**<br><br>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.<br><br>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.<br><br>**Pain management** | **Bright light therapy**<br><br>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.<br><br>**Family approach**<br><br>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 | 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.<br><br>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.<br><br>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 |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| 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 (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.<br><br>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 | multi-component interventions. The authors concluded that this review was unable to determine if the involvement of families in delirium management improved patient outcomes. | | evidence was provided through clinical feedback.<br><br>Finally, the evidence for delirium abatement programmes suggests that they have no impact on the duration of delirium. Therefore, this evidence is unlikely to currently impact on the guideline. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| 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.<br><br>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 lower in the light sedation group than in the deep sedation group. However, | | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| this study was conducted in the US and so would have used different post-operative treatment pathways than would be used in the UK.<br><br>The Evidence Update concluded that the above studies support the advice given in CG103.<br><br>**Delivery of care**<br><br>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 | | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| DAP was found to have no impact on the duration of delirium at 2 weeks or 1 month.<br><br>The Evidence Update concluded that this study supports current guidance. It states that although CG103 recommends multicomponent interventions delivered by a multidisciplinary team to prevent delirium, similar advice is not given for treatment of established delirium. | | | |
| 103-17: What are the most clinical and cost effective multicomponent interventions for treating people with delirium in long-term care? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| 103-18: What are the most clinical and cost effective and safe pharmacological interventions for treating people with delirium in hospital? | | | |
| **Rivastigmine**<br><br>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 | **Melatonin**<br><br>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 | None identified through GDG questionnaire. | The new evidence suggests that benzodiazepines are not beneficial for the treatment of delirium. This is consistent with CG103 which currently does not recommend benzodiazepines for delirium treatment.<br><br>For rivastigmine, the new evidence is consistent with CG103 which currently |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| the intervention and that those 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.<br><br>**Benzodiazepines**<br><br>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 | 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.<br><br>**Pharmacological management**<br><br>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 management studies in general medical patients are often extrapolated to intensive care patients. They concluded that there are few credible studies on this topic.<br><br>A Cochrane review[76] was identified which investigated the | | 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.<br><br>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.<br><br>With regards to pharmacological management and ondasetron the new evidence was insufficient. For ondasetron only one study was identified and this showed no benefit of this drug. For pharmacological management, few studies were identified and the included systematic reviews concluded that the studies assessing pharmacological management were not methodologically |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| recommended treatment for delirium.<br><br>**Antipsychotics**<br><br>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.<br><br>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 | 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.<br><br>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.<br><br>**Ondasetron**<br><br>An RCT[78] examined the efficacy of | | rigorous meaning that no conclusion could be drawn. As such, this evidence is unlikely to impact on CG103.<br><br>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 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.<br><br>The new evidence on atypical antipsychotics suggests that they are as |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| clinical value of risperidone in the treatment of delirium can be established. | 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.<br><br>**Antipsychotics**<br><br>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. | | 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.<br><br>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, the current evidence was from small studies and so further large, RCTs are needed into atypical antipsychotics before this research recommendation can be fully addressed. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>*Haloperidol*<br><br>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 | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | studies showed a benefit with haloperidol. The three included controlled trials had small sample sizes and methodological flaws and so no conclusions were drawn.<br><br>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.<br><br>*Quetiapine*<br><br>A systematic review[83] investigated quetiapine for the treatment of | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>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.<br><br>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 | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>*Risperidone*<br><br>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.<br><br>*Atypical antipsychotics*<br><br>A systematic review[87] was | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>**Morphine**<br><br>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. | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | Statistically low Richmond agitation and sedation scale scores were found during morphine treatment and significantly more patients in the haloperidol group required additive sedatives.<br><br>**Dexmedetomidine**<br><br>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.<br><br>**Ramelteon**<br><br>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 | | |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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. | | |
| 103-19: What are the most clinical and cost effective and safe pharmacological interventions for treating people with delirium in long-term care? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| 103-120: What information should be given to people at risk of developing delirium, or people with delirium, and their families or carers? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| Research recommendation: 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? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| Research recommendation: In hospital patients with delirium, are atypical antipsychotics better than placebo or typical antipsychotics or benzodiazepines for treating delirium? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| Research recommendation: Is music therapy that is tailored to the individual's preferences, more clinically and cost effective than non-tailored music or usual care in preventing the development of delirium in hospital patients at risk of delirium? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| Research recommendation: For patients in long-term care, is a multicomponent non-pharmacological intervention more clinically and cost effective than usual care in preventing the development of delirium? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| Research recommendation: How common is delirium and what are its adverse outcomes in people in long-term care? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| Research recommendation: 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? | | | |
| None identified. | 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 | 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 |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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.<br><br>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.<br><br>A cluster RCT[92] was identified which investigated the impact of a delirium specific educational | | 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.<br><br>No details on the qualitative studies highlighted by the GDG were provided therefore it is not possible to ascertain any impact on the guideline. |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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. | | |
| Research recommendation: Does giving information about delirium to people in a UK hospital or long-term care, who are at risk of delirium, increase their ability to cope if delirium subsequently occurs, and does the information decrease the duration of delirium? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| Research recommendation: In people with dementia, does an education programme in delirium for carers improve the recognition of acute confusion and reduce the severity and duration of delirium, compared to an education leaflet or usual care? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| Research recommendation: Does an education programme for staff improve the recovery from delirium in patients in hospital compared with an education leaflet or usual care? | | | |
| None identified. | A systematic review[93] was identified which investigated interprofessional education interventions (IPE) on learning | 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 |

| Conclusions of Evidence Update (2012) | Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion? | Clinical feedback from the GDG | Conclusion of this 4-year surveillance review (2014) |
|---|---|---|---|
| | 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. | | programmes for staff. |
| Research recommendation: The development and validation of a new test for delirium | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| Research recommendation: Is the presence of immune system markers, particularly cytokines, a risk factor for the development of delirium? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |
| Research recommendation: What is the resource use and cost of implementing a multicomponent prevention intervention in hospital or long term care settings as compared to usual care? | | | |
| None identified. | None identified. | None identified through GDG questionnaire. | No relevant evidence identified. |

# References


1. Cole MG CABEeal. (2009) Persistent delirium in older hospital patients: a systematic review of frequency and prognosis. Age and Ageing 38:19-26.

2. Dasgupta M HL. (2010) Factors associated with prolonged delirium: a systematic review. International Psychogeriatrics 22:373-394.

3. Fong TG JRSPeal. (2009) Delirium accelerates cognitive decline in Alzheimer disease. Neurology 72:1570-1575.

4. Carin-Levy G, Mead GE, Nicol K et al. (2012) Delirium in acute stroke: screening tools, incidence rates and predictors: a systematic review. Journal of Neurology 259:1590-1599.

5. Charlesworth M, Elliott MW, and Holmes JD. (2012) Noninvasive positive pressure ventilation for acute respiratory failure in delirious patients: understudied, underreported, or underappreciated? A systematic review and meta-analysis. Lung 190:597-603.

6. Siepe M, Pfeiffer T, Gieringer A et al. (2011) Increased systemic perfusion pressure during cardiopulmonary bypass is associated with less early postoperative cognitive dysfunction and delirium. European Journal of Cardio-Thoracic Surgery 40:200-207.

7. Cole MG, Ciampi A, Belzile E et al. (2013) Subsyndromal delirium in older people: a systematic review of frequency, risk factors, course and outcomes. International Journal of Geriatric Psychiatry 28:771-780.

8. Shi QW. (2013) Confusion assessment method: A systematic review and meta-analysis of diagnostic accuracy. Neuropsychiatric Disease and Treatment 9:-1370.

9. Neto AS, Nassar AP, Jr., Cardoso SO et al. (2012) Delirium screening in critically ill patients: a systematic review and meta-analysis. Critical Care Medicine 40:1946-1951.

10. Gusmao-Flores DFS. (2012) The confusion assessment method for the intensive care unit (CAM-ICU) and intensive care delirium screening checklist (ICDSC) for the diagnosis of delirium: a systematic review and meta-analysis of clinical studies. Critical Care 16.

11. LaMantia MA, Messina FC, Hobgood CD et al. (2014) Screening for delirium in the emergency department: a systematic review. Annals of Emergency Medicine 63:551-560.

12. van der Kooi AW, Leijten FS, van der Wekken RJ et al. (2012) What are the opportunities for EEG-based monitoring of delirium in the ICU?. Journal of Neuropsychiatry & Clinical Neurosciences 24:472-477.

13. Morandi A, McCurley J, Vasilevskis EE et al. (2012) Tools to detect delirium superimposed on dementia: a systematic review. [Erratum appears in J Am Geriatr Soc. 2013 Jan;61(1):174 Note: Ely, Wesley E [corrected to Ely, E Wesley]]. Journal of the American Geriatrics Society 60:2005-2013.

14. Smith T, Hameed Y, Cross J et al. (2013) Assessment of people with cognitive impairment and hip fracture: a systematic review and meta-analysis. Archives of Gerontology & Geriatrics 57:117-126.

15. de la Cruz M, Noguera A, San Miguel-Arregui MT et al. (20-2-2014) Delirium, agitation, and symptom distress within the final seven days of life among cancer patients receiving hospice care. Palliative & Supportive Care 1-6.

16. Clegg A YJB. (2011) Which medications to avoid in people at risk of delirium: a systematic review. Age and Ageing 40:23-29.

17. van den Boogaard M PPSAeal. (2012) Development and validation of PRE-DELIRIC (PREdiction of DELIRium in ICu patients) delirium prediction model for intensive care patients: observational multicentre study. BMJ 344:e420.

18. Lin Y, Chen J, and Wang Z. (2012) Meta-analysis of factors which influence delirium following cardiac surgery. Journal of Cardiac Surgery 27:481-492.

19. Koster S, Hensens AG, Schuurmans MJ et al. (2011) Risk factors of delirium after cardiac surgery: a systematic review. European Journal of Cardiovascular Nursing 10:197-204.

20. Mattar IC. (2012) Factors causing acute delirium in critically ill adult patients: A systematic review. JBI Database of Systematic Reviews and Implementation Reports 10:187-231.

21. Huai J and Ye X. (17-5-2014) A meta-analysis of critically ill patients reveals several potential risk factors for delirium. General Hospital Psychiatry .

22. Cull E.Kent. (2013) Risk factors for incident delirium in acute medical in-patients: A systematic review. JBI Database of Systematic Reviews and Implementation Reports 11:62-111.

23. Ahmed S.Leurent. (2014) Risk factors for incident delirium among older people in acute hospital medical units: A systematic review and meta-analysis. Age and Ageing 43:326-333.

24. Tse LS. (2012) Pharmacological risk factors for delirium after cardiac surgery: A review. Current Topics in Medicinal Chemistry 12:181-196.

25. Bilotta F, Lauretta MP, Borozdina A et al. (2013) Postoperative delirium: risk factors, diagnosis and perioperative care. Minerva Anestesiologica 79:1066-1076.

26. Hall RJ, Shenkin SD, and Maclullich AM. (2011) A systematic literature review of cerebrospinal fluid biomarkers in delirium. Dementia & Geriatric Cognitive Disorders 32:79-93.

27. Nouwen MJ, Klijn FA, van den Broek BT et al. (2012) Emotional consequences of intensive care unit delirium and delusional memories after intensive care unit admission: a systematic review. Journal of Critical Care 27:199-211.

28. Shi Q, Presutti R, Selchen D et al. (2012) Delirium in acute stroke: a systematic review and meta-analysis. Stroke 43:645-649.

29. Zhang Z, Pan L, and Ni H. (2013) Impact of delirium on clinical outcome in critically ill patients: a meta-analysis. General Hospital Psychiatry 35:105-111.

30. Al-Qadheeb NS, Balk EM, Fraser GL et al. (2014) Randomized ICU trials do not demonstrate an association between interventions that reduce delirium duration and short-term mortality: a systematic review and meta-analysis. Critical Care Medicine 42:1442-1454.

31. Van Rompaey BE. (2012) The effect of earplugs during the night on the onset of delirium and sleep perception: A randomized controlled trial in intensive care patients. Critical Care 16.

32. Radtke FM, Franck M, Lendner J et al. (2013) Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction. British Journal of Anaesthesia 110 Suppl 1:i98-105.

33. Fan Y-XL. (2014) Comparison of restrictive and liberal transfusion strategy on postoperative delirium in aged patients following total hip replacement: A preliminary study. Archives of Gerontology and Geriatrics 59:181-185.

34. Jia YJ. (2014) Fast-track surgery decreases the incidence of postoperative delirium and other complications in elderly patients with colorectal carcinoma. Langenbeck's Archives of Surgery 399:77-84.

35. Burkhart CSD. (2014) Effect of n-3 fatty acids on markers of brain injury and incidence of sepsis-associated delirium in septic patients. Acta Anaesthesiologica Scandinavica 58:689-700.

36. Clegg A, Siddiqi N, Heaven A et al. (2014) Interventions for preventing delirium in older people in institutional long-term care. Cochrane Database of Systematic Reviews 1:CD009537.

37. Khalifezadeh A, Safazadeh S, Mehrabi T et al. (2011) Reviewing the effect of nursing interventions on delirious patients admitted to intensive care unit of neurosurgery ward in Al-Zahra Hospital, Isfahan University of Medical Sciences. Iranian Journal of Nursing and Midwifery Research 16:106-112.

38. Deschodt M, Braes T, Flamaing J et al. (2012) Preventing delirium in older adults with recent hip fracture through multidisciplinary geriatric consultation. Journal of the American Geriatrics Society 60:733-739.

39. Hempenius LS. (2013) Outcomes of a Geriatric Liaison Intervention to Prevent the Development of Postoperative Delirium in Frail Elderly Cancer Patients: Report on a Multicentre, Randomized, Controlled Trial. PLoS ONE [Electronic Resource] 8.

40. Watne LOT. (2014) The effect of a pre- and postoperative orthogeriatric service on cognitive function in patients with hip fracture: Randomized controlled trial (Oslo Orthogeriatric Trial). BMC Medicine 12.

41. Reston JT and Schoelles KM. (5-3-2013) In-facility delirium prevention programs as a patient safety strategy: a systematic review. Annals of Internal Medicine 158:375-380.

42. Thomas E.Smith. (2014) The effectiveness of non-pharmacological multi-component interventions for the prevention of delirium in non-intensive care unit older adult hospitalized patients: A systematic review. JBI Database of Systematic Reviews and Implementation Reports 12:180-232.

43. Martinez FT, Tobar C, Beddings CI et al. (2012) Preventing delirium in an acute hospital using a non-pharmacological intervention. Age & Ageing 41:629-634.

44. Stenvall M, Berggren M, Lundstrom M et al. (2012) A multidisciplinary intervention program improved the outcome after hip fracture for people with dementia--subgroup analyses of a randomized controlled trial. Archives of Gerontology & Geriatrics 54:e284-e289.

45. Goldberg SE, Bradshaw LE, Kearney FC et al. (2013) Care in specialist medical and mental health unit compared with standard care for older people with cognitive impairment admitted to general hospital: randomised controlled trial (NIHR TEAM trial). BMJ 347:f4132.

46. Jeffs KJB. (2013) An enhanced exercise and cognitive programme does not appear to reduce incident delirium in hospitalised patients: A randomised controlled trial. BMJ Open 3.

47. Zhang HL. (2013) Strategies for prevention of postoperative delirium: A systematic review and meta-analysis of randomized trials. Critical Care 17.

48. Moyce Z, Rodseth RN, and Biccard BM. (2014) The efficacy of peri-operative interventions to decrease postoperative delirium in non-cardiac surgery: a systematic review and meta-analysis. Anaesthesia 69:259-269.

49. Boorsma M FDKDeal. (2011) Effects of multidisciplinary integrated care on quality of care in residential care facilities for elderly people: a cluster randomized trial. Canadian Medical Association Journal 183:E724-E732.

50. Al-Aama T BCGIeal. (2011) Melatonin decreases delirium in elderly patients: a randomized, placebo-controlled trial. International Journal of Geriatric Psychiatry 26:687-694.

51. Larsen KA KSSTeal. (2010) Administration of olanzapine to prevent postoperative delirium in elderly joint-replacement patients: a randomized, controlled trial. Psychosomatics 51:409-418.

52. Chakraborti D, Tampi DJ, and Tampi RR. (18-6-2014) Melatonin and Melatonin Agonist for Delirium in the Elderly Patients. Am.J.Alzheimers.Dis.Other Demen .

53. Marcantonio ER, Palihnich K, Appleton P et al. (2011) Pilot randomized trial of donepezil hydrochloride for delirium after hip fracture. Journal of the American Geriatrics Society 59 Suppl 2:S282-S288.

54. Royse CF, Andrews DT, Newman SN et al. (2011) The influence of propofol or desflurane on postoperative cognitive dysfunction in patients undergoing coronary artery bypass surgery. Anaesthesia 66:455-464.

55. Mardani DB. (2012) The effect of dexamethasone prophylaxis on postoperative delirium after cardiac surgery: A randomized trial. Journal of Research in Medical Sciences 17:S113-S119.

56. Mo Y and Zimmermann AE. (2013) Role of dexmedetomidine for the prevention and treatment of delirium in intensive care unit patients. Annals of Pharmacotherapy 47:869-876.

57. Pasin L, Landoni G, Nardelli P et al. (14-7-2014) Dexmedetomidine Reduces the Risk of Delirium, Agitation and Confusion in Critically Ill Patients: A Meta-analysis of Randomized Controlled Trials. Journal of Cardiothoracic & Vascular Anesthesia .

58. Gilmore ML and Wolfe DJ. (2013) Antipsychotic prophylaxis in surgical patients modestly decreases delirium incidence--but not duration--in high-incidence samples: a meta-analysis. General Hospital Psychiatry 35:370-375.

59. Teslyar P, Stock VM, Wilk CM et al. (2013) Prophylaxis with antipsychotic medication reduces the risk of post-operative delirium in elderly patients: a meta-analysis. Psychosomatics 54:124-131.

60. Hirota T and Kishi T. (2013) Prophylactic antipsychotic use for postoperative delirium: a systematic review and meta-analysis. Journal of Clinical Psychiatry 74:e1136-e1144.

61. Wang W, Li HL, Wang DX et al. (2012) Haloperidol prophylaxis decreases delirium incidence in elderly patients after noncardiac surgery: a randomized controlled trial*. Critical Care Medicine 40:731-739.

62. Fukata S, Kawabata Y, Fujisiro K et al. (16-2-2014) Haloperidol prophylaxis does not prevent postoperative delirium in elderly patients: a randomized, open-label prospective trial. Surg.Today .

63. Papadopoulos GP. (2014) The effect of ondansetron on postoperative delirium and cognitive function in aged orthopedic patients. Minerva Anestesiologica 80:444-451.

64. Lapane KL HCDLeal. (2011) Effect of a pharmacist-led multicomponent intervention focusing on the medication monitoring phase to prevent potential adverse drug events in nursing homes. Journal of the American Geriatrics Society 59:1238-1245.

65. Ono H TTKYeal. (2011) The usefulness of bright light therapy for patients after oesophagectomy. Intensive and Critical Care Nursing 27:158-166.

66. Abou-Setta AM BLRSeal. (2011) Comparative effectiveness of pain management interventions for hip fracture: a systematic review. Annals of Internal Medicine 155:234-245.

67. Mouzopoulos G VGLNeal. (2014) Fascia iliaca block prophylaxis for hip fracture patients at risk for delirium: a randomized placebo-controlled study. Journal of Orthopaedics and Traumatology 10:127-133.

68. Sieber FE ZKGAeal. (2010) Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair. Mayo Clinic Proceedings 18-26.

69. Marcantonio ER BMKDeal. (2010) Randomized trial of a delirium abatement program for postacute skilled nursing facilities. Journal of the American Geriatrics Society 58:1019-1026.

70. Yang J, Choi W, Ko YH et al. (2012) Bright light therapy as an adjunctive treatment with risperidone in patients with delirium: a randomized, open, parallel group study. General Hospital Psychiatry 34:546-551.

71. Halloway S. (2014) A family approach to delirium: a review of the literature. Aging & Mental Health 18:129-139.

72. van Eijk MMJ RKHMeal. (2010) Effect of rivastigmine as an adjunct to usual care with haloperidol on duration of delirium and mortality in critically ill patients: a multicentre, double-blind, placebo-controlled randomised trial. Lancet 376:1829-1837.

73. Lonergan E LJASA. (2009) Benzodiazepines for delirium. Cochrane Database of Systematic Reviews .

74. Grover S KVCS. (2011) Comparative efficacy study of haloperidol, olanzapine and risperidone in delirium. Journal of Psychosomatic Research 71:277-281.

75. Bledowski J and Trutia A. (2012) A review of pharmacologic management and prevention strategies for delirium in the intensive care unit. Psychosomatics 53:203-211.

76. Candy B, Jackson KC, Jones L et al. (2012) Drug therapy for delirium in terminally ill adult patients. [Update of Cochrane Database Syst Rev. 2004;(2):CD004770; PMID: 15106261]. Cochrane Database of Systematic Reviews 11:CD004770.

77. Bathula M and Gonzales JP. (2013) The pharmacologic treatment of intensive care unit delirium: a systematic review. Annals of Pharmacotherapy 47:1168-1174.

78. Tagarakis GI, Voucharas C, Tsolaki F et al. (2012) Ondasetron versus haloperidol for the treatment of postcardiotomy delirium: a prospective, randomized, double-blinded study. Journal Of Cardiothoracic Surgery 7:25.

79. Flaherty JH, Gonzales JP, and Dong B. (2011) Antipsychotics in the treatment of delirium in older hospitalized adults: a systematic review. Journal of the American Geriatrics Society 59 Suppl 2:S269-S276.

80. Meagher DJ, McLoughlin L, Leonard M et al. (2013) What do we really know about the treatment of delirium with antipsychotics? Ten key issues for delirium pharmacotherapy. American Journal of Geriatric Psychiatry 21:1223-1238.

81. Wang EH, Mabasa VH, Loh GW et al. (2012) Haloperidol dosing strategies in the treatment of delirium in the critically ill. Neurocritical Care 16:170-183.

82. Page VJ, Ely EW, Gates S et al. (2013) Effect of intravenous haloperidol on the duration of delirium and coma in critically ill patients (Hope-ICU): a randomised, double-blind, placebo-controlled trial.[Erratum appears in Lancet Respir Med. 2013 Oct;1(8):592]. The Lancet Respiratory Medicine 1:515-523.

83. Hawkins SB, Bucklin M, and Muzyk AJ. (2013) Quetiapine for the treatment of delirium. Journal of Hospital Medicine (Online) 8:215-220.

84. Maneeton B, Maneeton N, Srisurapanont M et al. (2013) Quetiapine versus haloperidol in the treatment of delirium: a double-blind, randomized, controlled trial. Drug design, development & therapy 7:657-667.

85. Devlin JW, Skrobik Y, Riker RR et al. (2011) Impact of quetiapine on resolution of individual delirium symptoms in critically ill patients with delirium: a post-hoc analysis of a double-blind, randomized, placebo-controlled study. Critical Care (London, England) 15:R215.

86. Hakim SM, Othman AI, and Naoum DO. (2012) Early treatment with risperidone for subsyndromal delirium after on-pump cardiac surgery in the elderly: a randomized trial. Anesthesiology 116:987-997.

87. Wang HR, Woo YS, and Bahk WM. (2013) Atypical antipsychotics in the treatment of delirium. Psychiatry & Clinical Neurosciences 67:323-331.

88. Atalan N, Efe SM, Akgun S et al. (2013) Morphine is a reasonable alternative to haloperidol in the treatment of postoperative hyperactive-type delirium after cardiac surgery. Journal of Cardiothoracic & Vascular Anesthesia 27:933-938.

89. Hatta K, Kishi Y, Wada K et al. (2014) Preventive effects of ramelteon on delirium: a randomized placebo-controlled trial. JAMA Psychiatry 71:397-403.

90. Wand AP. (2011) Evaluating the effectiveness of educational interventions to prevent delirium. Australasian Journal on Ageing 30:175-185.

91. Yanamadala M, Wieland D, and Heflin MT. (2013) Educational interventions to improve recognition of delirium: a systematic review. Journal of the American Geriatrics Society 61:1983-1993.

92. McCrow J, Sullivan KA, and Beattie ER. (2014) Delirium knowledge and recognition: a randomized controlled trial of a web-based educational intervention for acute care nurses. Nurse Educ.Today 34:912-917.

93. Sockalingam S, Tan A, Hawa R et al. (2014) Interprofessional education for delirium care: a systematic review. Journal of Interprofessional Care 28:345-351.