

Appendix B: Stakeholder consultation comments table

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

Consultation dates: 31 August 2018 to 13 September 2018

Do you agree with the proposal to not update the guideline?			
Stakeholder	Overall response	Comments	NICE response
Department of Health and Social Care		I wish to confirm that the Department of Health and Social Care has no substantive comments to make, regarding this consultation.	Thank you for your response.
Intensive Care Society	No	No comments provided.	Thank you for your response.
British Association of Psychopharmacology	No	Delirium is a severe neuropsychiatric syndrome, which affects up to 1 in 5 people in hospital. It is distressing for	Thank you for your comment. In response to the individual points raised: <ul style="list-style-type: none"> Our literature search for this surveillance review included newly published studies from 5th August 2014 to 1st May

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	<p>sufferer, carer and staff. Despite this impact, it remains undetected and poorly managed.</p> <p>There have been significant additions to the literature since the last guidelines, and many of the recommendations have been potentially superseded. This is particularly true in the area of screening, where the 4AT tool is now used most often by units to screen, and has a growing evidence base behind it.</p> <p>A nationwide audit of standards against current NICE guidelines has been carried out, due to report at the end of the year – this will add important information.</p> <p>I believe the decision not to update the guideline will lead to a delay in this new research becoming best practice, and therefore a missed opportunity to improve the care of a great many older people in hospital</p> <p>Section 2, 2.1/2.2 Research recommendations – the current recommendation is for a head to head study of typical antipsychotics, atypical antipsychotics, benzodiazepines, acetylcholinesterase inhibitors and placebo for both the treatment or prevention of delirium. In our opinion approach is limited without a clear drug target. Basic research to identify the underlying biological mechanisms of delirium is required 1) to identify pharmacological and other therapeutic targets for prevention and treatment of delirium. 2) a method to be able to stratify at risk or delirium patient to appropriate treatments. It may then be possible to conduct appropriate clinical trials. There is unlikely to be one cause or treatment for all delirium.</p>	<p>2018. This covers the period from the end of the previous surveillance review for this topic in 2014 to the start of this review in 2018. A very small number of studies were identified during this literature search regarding the 4AT tool, and unfortunately these were not the correct study types to be included in our surveillance review. We are aware of an NIHR study on the development and validation of the 4AT tool. We are awaiting publication of this study so we can consider if there is an impact on the current recommendations when results are available.</p> <ul style="list-style-type: none"> • Thank you for highlighting the forthcoming audit. We will log this activity and consider it at the next surveillance review. • New research was considered as part of the 5-year surveillance review for this guideline. Where new research provides a clear signal for changes to the guideline we endeavour to make relevant changes. However, in most areas the new evidence did not provide a clear signal to update the guideline at this surveillance review time point. • Thank you for your feedback on the research recommendations. Unfortunately it is outside the scope of the surveillance process to amend research recommendations or add new ones. However, we will log your feedback and pass the information over to developers if this guideline is updated in the future. • We feel that the research recommendations are sufficient for new research at this time. However we have mechanisms in place to review the evidence base earlier than the scheduled review process if new evidence is brought to our attention.
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	<p>Haloperidol (a typical antipsychotic) has been shown not to be beneficial in the prevention of delirium in older at risk patients.</p> <p>Ref: Schrijver, E.J., de Vries, O.J., van de Ven, P.M., Bet, P.M., Kamper, A.M., Diepeveen, S.H., van Marum, R.J., van Strien, A.M., Anten, S., Lagaay, A.M. and Boelaarts, L., 2017. Haloperidol versus placebo for delirium prevention in acutely hospitalised older at risk patients: a multi-centre double-blind randomised controlled clinical trial. <i>Age and ageing</i>, 47(1), pp.48-55.</p> <p>There is still not clear evidence for the use of antipsychotics, for example see recent systematic review:</p> <p>Ref: Burry, L., Mehta, S., Perreault, M.M., Luxenberg, J.S., Siddiqi, N., Hutton, B., Fergusson, D.A., Bell, C. and Rose, L., 2018. Antipsychotics for treatment of delirium in hospitalised non-ICU patients. <i>Cochrane Database of Systematic Reviews</i>, (6).</p> <p>1.6.4 haloperidol and olanzapine are recommended for distressed patients (for tranquilisers effect), Quetiapine and risperidone are also commonly used.</p> <p>New drug targets need investigation e.g. Serotonin 2A antagonist Pimervanserin indicated for parkinsons hallucinations may offer a new pharmacological approach to treat some delirium and should be investigated.</p>	<ul style="list-style-type: none"> • Thank you for highlighting the RCT by Schrijver et al. This was included in our surveillance review as reference number 124. The section on Antipsychotics-haloperidol for prevention in appendix A includes several RCTs, including this one, which stated there was no significant improvement in delirium incidence, duration or severity with prophylactic haloperidol. The evidence regarding haloperidol for prevention continues to be mixed and as such is insufficient to consider changing recommendation 1.3 at this time. • Thank you for highlighting the Cochrane review by Burry et al. This was published in June 2018 and as such not captured by our search period which ended on the 1st May 2018. <p>We have incorporated a summary of this review into appendix A as it was also highlighted in our search for relevant Cochrane protocols. The evidence found for antipsychotic treatment at this review was mixed and as such no impact is anticipated at this time. This issue will be considered again at the next review.</p> <ul style="list-style-type: none"> • Regarding recommendation 1.6.4, we will be removing the olanzapine recommendation now that haloperidol has UK licensing for this indication. Evidence for quetiapine was considered at the 2014 review which found it to be effective. In addition, the evidence identified at the 2018 review found no difference between quetiapine and haloperidol. Although some new evidence has been identified during the current review, there remains insufficient evidence to suggest changing the current guideline recommendations. <p>Evidence from the 2014 review found that risperidone was as effective as haloperidol, and this was also raised by a topic</p>
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			<p>expert. However no evidence was found to support this at the 2018 review and the evidence remains insufficient to recommend changing the guideline at this time.</p> <ul style="list-style-type: none"> • Thank you for highlighting the new drug Pimavanserin, however we did not find any evidence relating to this drug in for the prevention or treatment of delirium. We will log this for consideration at the next surveillance review.
RCN	Yes	We have reviewed the current guidelines and agree that these are still relevant.	Thank you for your response.
British Geriatrics Society	No	<p>Delirium affects at least 15% of hospital patients and recent studies show that although there has been some progress, less than half of delirium remains undetected.</p> <p>There has been progress in some areas, notably (1) detection tools, with the 4AT now having 7 published validation studies involving >1800 patients (NB a research recommendation from the 2010 guidelines was to develop new research tools – NIHR funded a 4AT vs CAM study which has now reported, finding 4AT superior to CAM – this has very important implications for practice because the current NICE guidelines recommend CAM); (2) Cochrane Library finding no clear evidence for antipsychotic use in delirium; (3) No clear evidence of benefit of other drug treatments; (4) An expanded evidence base re delirium risk reduction.</p>	<p>Thank you for your comment. In response to the individual points raised:</p> <ul style="list-style-type: none"> • (1) Thank you for highlighting the 4AT validation studies. As there is an NIHR study considering the development and validation of 4AT awaiting publication we will monitor this study and review the results once published and consider the impact on the guideline recommendations. • (2) Thank you for highlighting the Cochrane Library findings. This review by Burry et al. was published in June 2018 and as such not captured by our search period which ended on the 1st May 2018. We have added a summary of this Cochrane review to appendix A as this was, also highlighted in our search for relevant Cochrane protocols. As the evidence in this area is mixed no impact is anticipated at this time. • (3) We have reviewed the evidence treating delirium, where this would be relevant to recommendation 1.6. As the evidence found for new drug treatments was mixed, we are

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			<p>not proposing to change the guideline at this time. We will consider drug treatment again at the next review,</p> <ul style="list-style-type: none"> • (4) We found new evidence which supported the current recommendations on risk factors, but limited new evidence to suggest additional risk factors. Evidence in this area will be considered again at the next review.
Association of British Neurologists	Yes	No comments provided.	Thank you for your response.
Royal College of Anaesthetists	No. There are a number of strong arguments as to why it should be updated at this iteration.	<p>- Risk factor assessment – agree with the topic expert that a patient having major surgery and in particular emergency surgery, should be considered high risk for delirium (not just patients with hip fractures). Already established that patients having surgery have a delirium rate of between 10-50% (compared to medical patients where the rate is 20-30%). In emergency surgery – the risk is higher compared with elective (reference – Ansaloni L et al). The risk factors and incidence of post-operative delirium in elderly patients after elective and emergency surgery. Br J Surg 2010;97:273-280.</p> <p>1.3.3.5 – Fast track surgery – although no new evidence is provided except for the one study in the 2014 surveillance report, fast track surgery is well established in the majority of hospitals and represents a multicomponent package which</p> <p>1.3.2 Advocates: multicomponent intervention package – fast track contains many of these interventions and should be emphasised for patients at high risk of delirium undergoing surgery.</p>	<p>Thank you for your comments. In response to the individual points raised:</p> <ul style="list-style-type: none"> • We found mixed evidence relating to major surgery as a risk factor for delirium, with studies mainly seeking to identify which personal factors prior to surgery were associated with post-operative delirium. The 'think delirium' statement mentions that people in hospital may be at risk of delirium. This would include those undergoing surgery. We will log this issue for consideration at the next review. • Thank you for providing information regarding fast track surgery (recommendations 1.3.3.5 and 1.3.2). Evidence from 1 study at the 2014 review found that patients who had fast track surgery has a lower rate of delirium, however no additional evidence was found at the 2018 review. We will log this for consideration at the next review and aim to identify new evidence on this topic. • CG103 cross-refers to NICE guideline NG97- dementia: assessment, management and support for people living with dementia and their carers. There are 3 recommendations in

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	<p>1.3.3.6 – Patients with dementia – need to suggest a tool for pain assessment rather than blanket statement of looking for non-verbal signs (example of a suitable tool would be the Abbey Pain Assessment tool).</p> <p>1.3.3 – Although Comprehensive Geriatric Assessment shows good evidence in reducing delirium, it is not explicitly mentioned – it should be as it will encourage users of the guidelines to seek appropriate support from the geriatricians</p> <p>1.6. – Use of dexmedetomidine in surgical patients – as surgery is a risk factor (between 10 to 50% risk of delirium), it represents a significant hospital workload and the statement that it relates to a narrow subgroup of the population is inconsistent. The guidelines should emphasise areas where delirium has the highest incidence especially as surgery is a large part of any hospital workload and will have the largest impact.</p> <p>There is much in terms of an infrastructural approach to clinical practice that could be improved. The USA is more advanced nationally in delirium prevention, recognition and treatment as a priority.</p> <p>The Hospital Elder Life programme website is very helpful and this is not referenced in the document for pragmatic approaches in clinical practice. https://www.hospitalelderlifeprogram.org.</p>	<p>NG97 relating to pain assessments, including 1.8.3 Consider using a structured observational pain assessment tool.</p> <ul style="list-style-type: none"> • The comprehensive geriatric assessment (CGA) is not specifically mentioned in the recommendation, however the current recommendations reflect the activities that are covered by the CGA. As limited evidence was found regarding the CGA at this surveillance review, there is insufficient evidence to suggest a change to the recommendations at this time. • Although new evidence was found regarding the potential benefit of dexmedetomidine for treating delirium, the results were mixed in the 2 studies identified. The majority of evidence regarding dexmedetomidine is in recommendation 1.3 – prevention of delirium. We agree that surgery represents a high workload in hospitals. However we have found that the evidence for dexmedetomidine for the prevention of post-operative delirium was largely from RCTs comparing dexmedetomidine to a placebo rather than alternative sedatives. The 1 systematic review we identified compared dexmedetomidine with propofol, midazolam and lorazepam and found no evidence for dexmedetomidine reducing delirium risk. This issue will be logged and considered again at the next review. • Thank you for providing a link to the hospital elder life programme. NICE uses cross-references to external sources or guidelines sparingly, and rarely where the products are not NICE accredited. In addition, cross-references to external sources are difficult to manage when changes occur. For those reasons, we don't plan to add a cross-reference to the hospital elder life programme.
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<p>Recommendation 1.5.1 covers diagnosis and states: ‘carry out a clinical assessment based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria or short Confusion Assessment Method (short CAM) to confirm the diagnosis’. We propose to change the recommendation by replacing the reference to DSM-IV with the updated DSM-V criteria. Do you agree with the proposal to refer to the new version, DSM-V, in the context of this recommendation?</p>			
Stakeholder	Overall response	Comments	NICE response
Department of Health and Social Care	Not answered		
Intensive Care Society	Yes	No comments provided.	Thank you for your response.
British Association of Psychopharmacology	Yes	No comments provided.	Thank you for your response.
RCN	Yes	This seems appropriate.	Thank you for your response.
British Geriatrics Society	Yes	However the section on diagnosis requires significant enhancement, as per suggestions below.	Thank you for your response.
Association of British Neurologists	Yes	No comments provided.	Thank you for your response.
Royal College of Anaesthetists	Yes	The document has failed to mention the 4-AT which is a simple to use widespread diagnostic and surveillance tool. It is used in many NHS hospitals https://www.the4at.com/	Thank you for your comment. No evidence was identified at this surveillance review for the 4AT. We are aware of an NIHR study on the development and validation of the 4AT tool . We are awaiting publication of this study so we can

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		Recommend for it to be included here.	consider if there is an impact on the current recommendations when results are available.
Do you have any comments on areas excluded from the scope of the guideline?			
Stakeholder	Overall response	Comments	NICE response
Department of Health and Social Care	Not answered		
Intensive Care Society	Yes	Critical care delirium required separate management and considerations. Of course there are specific ITU guidelines regarding this, but a mention in the NICE guideline would be beneficial.	Thank you for highlighting the area of critical care. Two recommendations currently mention critical care, however as no new evidence regarding specific advice for this area was identified at this review, we are not able to add further information at this time.
British Association of Psychopharmacology	Yes	<p>Recent work has shown the high proportion of undiagnosed dementia in people with delirium – and this should be addressed. Informant tools, such as the Informant Questionnaire of Cognitive Decline in the Elderly (IQCODE) have been validated to detect dementia in people with dementia, so should ideally be recommended.</p> <p>The guidelines should include clear recommendations for treating distress in delirium, as a symptoms – and in what settings this would be appropriate (ie haloperidol). This should be separate from the treatment of delirium by diligent investigation for, and treatment of, underlying cause(s).</p>	<p>Thank you for your comment. In response to the individual points raised:</p> <ul style="list-style-type: none"> • Several recommendations in CG103 reference dementia, including recommendation 1.6.6 'if delirium does not resolve: re-evaluate for underlying causes, follow up and assess for possible dementia'. There are also several footnotes which provide cross-referrals to NICE guideline NG97- Dementia: assessment, management and support for people living with dementia and their carers, including CG103 recommendation 1.6.6. NICE guideline NG97 recommendation 1.2.5 refers to IQCODE to support diagnosis of dementia.

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		Delirium occurs in specific settings, such as palliative care, paediatric intensive care, liver disease. The guidelines should attempt to be clear about which guidelines may be specific to those settings.	<ul style="list-style-type: none"> The guideline recommendation 1.2 covers indicators of delirium. Recommendation 1.5 is focused on treatment options. Palliative care, those aged under 18 and those suffering from delirium as a result of withdrawal from intoxicating substances are excluded from the scope of this guideline. We will add the following editorial amendment to the 'think delirium' section: For recommendations on delirium in palliative care please see NICE guideline NG31- care of dying adults in the last days of life
RCN	No	No comments provided.	Thank you for your response.
British Geriatrics Society	See comments	<ol style="list-style-type: none"> Update on risk factors, eg Parkinsons disease, multiple medications, sensory impairment. Diagnosis: there are multiple other tools now available and we would expect a literature review with recommendations. The tool that is chosen depends on the time available and the clinical setting. For example in the context of assessing for new confusion for the NEWS2 in intentional rounding a CAM would not be appropriate due to time constraints. Diagnostic tools MUST include an appraisal of the 4AT as it is increasingly widely used (see above). However there are multiple other tools now available eg SqID, RADAR etc. Importantly, the field now understands better the distinction between screening/assessment tools like the 4AT, and tools for ongoing surveillance of incident delirium in high risk groups, like the RADAR. Because of the enormous resource implications, it is crucial that this is made clearer to deter inappropriate use of screening tools in 1- 	<p>Thank you for your comment. In response to the individual points raised:</p> <ul style="list-style-type: none"> (1) The new evidence found regarding risk factors at this review was limited and inconsistent and is insufficient to support any changes to the recommendations. (2) Thank you for highlighting the screening tools now available, however no new evidence was found for these tools during our surveillance review. We are tracking a study that is awaiting publication that may provide more information on screening tools and will assess the impact on the guideline once results are available. (3) No evidence was found at any surveillance review for the indication of CT scans for investigation. (4) The guideline currently recommends the cautious use of haloperidol for distressed patients in which all other methods have failed, for short term use only. The evidence

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		<p>3 times daily use of screening tools for delirium surveillance.</p> <ol style="list-style-type: none"> 3. There is no advice on investigations, in particular when CT head may be indicated. 4. Pharmacological treatment for distress, must include consideration of important negatives. The Cochrane Library finds no clear evidence for antipsychotic use in delirium, neither is there clear evidence of benefit of other drug treatments. The recommendation for haloperidol must mention the risk of known side effects, for this reason it is rarely used outside of the ICU setting. 5. The section on research recommendations is in need of updating as some of these areas have been completed eg 2.5 on education 6. Sections on what and who should receive education on delirium 7. There should be additional sections on delirium in special circumstances eg palliative care 8. There should be firmer guidance on avoiding ward moves out of ours and no multiple bed moves 9. There should be a section about prevalence of undiagnosed dementia and requirement for follow up, and at the very least there should be a link to the new dementia guidance. <p>Note also that the Scottish Intercollegiate Guidelines Network is producing a delirium guideline which is due for publication in February 2019 (the draft and consultation phases are now complete) – this work will help to inform the NICE revision, and appropriate alignment of NICE and SIGN is desirable.</p>	<p>found regarding side effects has been mixed and inconclusive and as such is insufficient to recommend a change at this time.</p> <ul style="list-style-type: none"> • (5) Thank you for your feedback on the research recommendations. We did not find evidence to suggest this research recommendation has been fully satisfied, as such there are no plans to remove it at this time. • (6) Recommendation 1.7.1 states to offer information to people who are at risk of delirium and their family and or carers. As no evidence was found for this section, this recommendation will not be updated at this time. • (7) Palliative care is outside the scope of CG103 and is covered by NICE guideline NG31 - Care of dying adults in the last days of life. That guideline makes recommendations on managing delirium in end of life care. • (8) Recommendation 1.3.1. Contains a strong statement regarding relocation of patients: 'Avoid moving people within and between wards or rooms unless absolutely necessary.' • (9) Dementia is covered by NICE guideline NG97- Dementia: assessment, management and support for people living with dementia and their carers, cross-referrals are made from the footnotes of appropriate sections of the current guideline to NG97. We will log the issue of prevalence for consideration at the next review of NICE guideline NG97. • Thank you for highlighting the upcoming SIGN guidance on delirium. We have checked the draft document and note the recommendations are generally consistent with the current NICE guideline. Where the guidelines differ are areas that
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			we have not found sufficient evidence at this review to suggest updating the recommendations.
Association of British Neurologists	No	No comments provided.	Thank you for your response.
Royal College of Anaesthetists	Yes	<p>The statement 'anaesthesia is not covered by the guideline' – It should be included in the guideline as it is artificial to separate out anaesthesia and surgery when it comes to factors contributing to delirium – it is part of the perioperative care of the surgical patient. BIS guided anaesthesia has been shown to reduce delirium (Cochrane review) and this is an effective strategy to reduce delirium. In one study – the NNT to reduce the delirium rate is 12 compared to the NNT of 42 for the efficacy of low dose aspirin and STEMI. (Reference- Chan M et al 2013 J Neurosurg Anesthesiol 25; 33-42.)</p> <p>A previous episode of delirium is a significant risk factor for outcome – this should be added as suggested by the topic experts.</p> <p>The guidelines underplay the severity and significance of an episode of delirium to long-term outcome. The document fails to enumerate the benefit of prevention (33% can be prevented).</p> <p>It also fails to state how important screening and prevention is in terms of socio-economic burden. The document hardly references Prof Sharon Inouye (https://jamanetwork.com/journals/jamapsychiatry/article-abstract/2598160) and her extensive work around delirium prevention. This has become a leading area in monitoring</p>	<p>Thank you for your comment. In response to the individual points raised:</p> <ul style="list-style-type: none"> • Thank you for highlighting the importance of anaesthesia. We have revised the response in recommendation A in line with your comment. We will also add a cross-referral from this guideline to our diagnostics guideline DG6 - Depth of anaesthesia monitors – Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M which recommends the use of BIS guided anaesthesia. • Thank you for highlighting the study by Chan et al. As this study is outside the search dates for the current review we will not include it at this time, however we have included the above cross-referral to diagnostics guideline DG6 to highlight the use of BIS guided anaesthesia. • The evidence found at this review for risk factors for delirium supported the risk factors listed in recommendation 1.1.1. Evidence for other risk factors was mixed and as such will not have an impact at this review. • The NICE quick guide on recognising and preventing delirium highlights that delirium is preventable in 30% of cases. • Thank you for highlighting the article on Delirium, Dementia and Decline, however our study type inclusion criteria for

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		and is regarded as seriously as HAI in the USA with delirium being reported at board level in many hospitals (e.g. Johns Hopkins). The guidance does not reference the benefits of 'sitters'.	this guideline is limited to systematic reviews and randomised controlled trials and as such this does not meet the criteria for inclusion. <ul style="list-style-type: none"> No evidence was found at this review relating to the use of sitters.
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Do you have any comments on equalities issues?

Stakeholder	Overall response	Comments	NICE response
Department of Health and Social Care	Not answered		
Intensive Care Society	No	No comments provided.	Thank you for your response.
British Association of Psychopharmacology	Yes	The Scottish Intercollegiate Guidelines Network is producing a delirium guideline (due for publication in February 2019) - I would imagine this would be an important piece of work to inform the NICE revision, and appropriate alignment of NICE and SIGN is desirable.	Thank you for your comment. From the draft guidance available the SIGN document is largely consistent with the current NICE guideline. The difference in recommendations are areas we have not found substantial evidence for at this review.
RCN	No	No comments provided.	Thank you for your response.
British Geriatrics Society	No	No comments provided.	Thank you for your response.
Association of British Neurologists	No	No comments provided.	Thank you for your response.

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Royal College of Anaesthetists	No	No comments provided.	Thank you for your response.
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