3-year scoping report

Topic: SIGN 157: Risk reduction and management of delirium

Literature published since most recent searches for SIGN 157 in 2018 (publication dates from 2019–2022)

Date of search: May 2022

Searched by: Donald Nicolson

Key concepts: Delirium, risk reduction, management

Summary of findings

The purpose of this 3–year scoping is to identify significant new evidence relating to SIGN 157 and whether any sections of the guideline require updating. A rapid search of the literature was conducted with sources and references detailed below.

Comments from the Co-Chairs

Co-Chair	Comments
Professor Alasdair MacLullich, Professor of Geriatric Medicine	With respect to our broad recommendations there are probably not any major changes in the evidence. I haven't fully kept up to date with the intensive care unit (ICU) literature however, but I am not aware of any major practice-changing trials.
Dr Ajay Macharouthu, Consultant in Liaison Psychiatry for the Elderly	The initial SIGN157 guideline recommendations are broad and there is no new convincing evidence from the scoping document to amend the existing guideline.

Relevant evidence and implications for SIGN recommendations

Reference	Details	How does this potentially change current recommendations?
Medicines and Healthcare products Regulatory Agency December 2021 Haloperidol (Haldol): reminder of risks when used in elderly patients for the acute treatment of delirium - GOV.UK (www.gov.uk)	Elderly patients are at an increased risk of adverse neurological and cardiac effects when being treated with haloperidol for delirium. The lowest possible dose of haloperidol should be used for the shortest possible time, and cardiac and extrapyramidal adverse effects should be closely monitored.	SIGN 157 does not recommend haloperidol, but further caution on its use could be added.

Recommendations for research

Reference	Details	What area for further research does this address?
Zayed et al, 2019 Haloperidol for the management of delirium in adult ICU patients: a systematic review and meta-analysis of randomised controlled trials. Journal of critical care, 50, pp.280-286. Haloperidol for the management of delirium in adult intensive care unit patients: A systematic review and meta-analysis of randomized controlled trials - ScienceDirect **Systematic review**	Systematic review and meta-analysis of six randomised controlled trials (RCTs) comparing haloperidol versus placebo for treatment and/or prophylaxis of delirium in the ICU. Haloperidol use was not associated with decreased short-term all-cause mortality, ICU length of stay or mechanical ventilation days when compared to placebo in management of ICU related delirium. There was **no** significant difference between haloperidol and placebo in coma and/or delirium-free days in patients with ICU-related delirium. Haloperidol use was not associated with increased risk of serious adverse events, corrected QT interval prolongation or extrapyramidal symptoms in comparison to placebo. Among critically ill patients, haloperidol administration compared with placebo does not significantly affect short-term mortality, incidence of delirium, ICU length of stay, or delirium or coma-free days.	RCTs on the efficacy and safety of haloperidol in the reduction of the severity and duration of delirium in non-ICU settings. Could be considered for sections 5.2 and 7.1

Fiest et al 2020 A study protocol for a randomised controlled trial of family-partnered delirium prevention, detection, and management in critically ill adults: the ACTIVATE study. BMC health services research, 20(1), pp.1-11. https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-020-05281-8 **RCT protocol**	Protocol of an ongoing RCT to determine the effect of family-administered delirium prevention, detection and management in critically ill patients on family member symptoms of depression and anxiety, compared to usual care. To determine the effect of family-administered delirium prevention, detection and management in critically ill patients on family member symptoms of psychological distress, compared to usual care. To determine the effect of family-administered delirium prevention, detection, and management on the prevalence (ever/never delirium as indicated by an ICU Delirium Screening Checklist [ICDSC] score ≥ 4), duration (total days of an ICDSC score ≥ 4), and severity of delirium (as indicated by the ICDSC score, which ranges from 0 to 8) in critically ill patients, compared to usual care. To determine the effect of family-administered delirium prevention, detection, and management on the diagnosis of the patient with delirium (ICDSC score ≥ 4), compared to usual care. To determine the effect of family-administered delirium prevention, detection and management on family member knowledge of delirium in critically ill patients, compared to usual care. To determine the effect of family-administered delirium prevention, detection, and management on the burden of delirium (eg feelings of helplessness) experienced by family members of critically ill patients, compared to usual care.	Research into detection and management of people with delirium in primary care, community and long-term care settings. Publication date to be advised.
MacLullich et al 2019 The 4 As test for detecting delirium in acute medical patients: a diagnostic accuracy study. Health Technology Assessment, 23(40). The 4 'A's test for detecting delirium in acute medical patients : a diagnostic	The 4 As test (Arousal, Attention, Abbreviated Mental Test–4, Acute change) (4AT) is a screening tool for delirium. This study evaluated its usability, diagnostic accuracy and cost, measured with two surveys and two qualitative studies. The study found evidence that delirium awareness is increasing, but also that there is a need for education on delirium in general and on the 4AT in particular. Most users	Validation of tools for routine monitoring of patients with delirium with clarification of the frequency of using these tools and their impact on outcomes and cost effectiveness. Could be considered for section 3.1

accuracy study (whiterose.ac.uk) **Diagnostic accuracy study** **BMJ 2021** Best Practice Assessment of Delirium Assessment of delirium - Differential diagnosis of symptoms	BMJ Best Practice **Practice guidance**	reported that the 4AT was useful, and it was in widespread use both in the UK and beyond. The 4AT (n=392) had an area under the receiver operating characteristic curve of 0.90. A positive 4AT score (> 3) had a specificity of 95% (95% confidence interval (CI) 92% to 97%) and a sensitivity of 76% (95% CI 61% to 87%) for reference standard delirium. The Confusion Assessment Method (CAM) (n=382) had a specificity of 100% (95% CI 98% to 100%) and a sensitivity of 40% (95% CI 26% to 57%) in the subset of participants in whom it was possible to assess using this. Patients with positive 4AT scores had longer lengths of stay (median 5 days, interquartile range 2.0–14.0 days) than did those with negative 4AT scores (median 2 days, interquartile range 1.0–6.0 days), and they had a higher 12-week mortality rate (16.1% and 9.2%, respectively). The estimated 12-week costs of an initial inpatient stay for patients with delirium were more than double the costs of an inpatient stay for patients without delirium (eg in Scotland, £7,559, 95% CI £7,362 to £7,755, vs. £4,215, 95% CI £4,175 to £4,254). The estimated cost of false-positive cases was £4,653, of false-negative cases was £8,956, and of a missed diagnosis was £2,067. Limitations: Patients were aged ≥70 years and were assessed soon after they were admitted, limiting generalisability. The treatment of patients in accordance with reference standard diagnosis limited the ability to assess comparative cost effectiveness. Conclusions: These findings support the use of the 4AT as a rapid delirium assessment instrument. The 4AT has acceptable diagnostic accuracy for acute older patients aged >70 years.	
Wiegand et al 2022 Electroencephalography in delirium assessment: a scoping review. BMC neurology, 22(1), pp.1-23. Electroencephalography in delirium assessment: a scoping review	BMC	Electroencephalogram (EEG) seems to offer manifold possibilities in diagnosing delirium. All 33 studies showed a certain degree of qualitative or quantitative EEG alterations in delirium. Thus, normal routine (rEEG) and continuous EEG (cEEG) make presence of delirium very unlikely.	Studies of the practicalities and diagnostic yield of performing EEG in adults presenting with delirium. This may change the recommendation in section 3.4.2 which currently recommends EEG only when there is a suspicion of epileptic activity as a cause of a patient's delirium.

Neurology | Full Text (biomedcentral.com) **Scoping review**		
Li et al 2022 Benzodiazepines for treatment of patients with delirium excluding those who are cared for in an ICU. Cochrane Database of SRs, (2). https://research.birmingham.ac.uk/en/publications/effect-of-regional-vs-general-anesthesia-on-incidence-of-postoper **RCT**	In patients aged 65 years and older undergoing hip fracture surgery, regional anaesthesia without sedation did not significantly reduce the incidence of postoperative delirium compared with general anaesthesia.	RCTs on the efficacy of depth of anaesthesia monitoring in reducing postoperative delirium in patients with dementia undergoing surgery and patients undergoing emergency surgery or trauma orthopaedic surgery. Could be considered for section 4.2.1.
Kim et al 2022 Effects of non-pharmacological interventions for preventing delirium in general ward inpatients: A SR & MA of RCTs. PloS one, 17(5), p.e0268024. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0268024 **Systematic review**	Non-pharmacological multicomponent intervention was effective in reducing the incidence of delirium in both the internal and surgical wards. It was confirmed by quantitative evidence that non-pharmacological interventions, especially multicomponent interventions, were effective in preventing delirium in general ward inpatients.	Trials of multicomponent interventions for the treatment of patients with delirium in general hospital settings. The findings are in agreement with the current recommendations in section 4 non-pharmacological risk reduction.
Chen et al 2022 Comparative effectiveness of non-pharmacological interventions for preventing delirium in critically ill adults: A SR and network MA. International Journal of Nursing Studies, p.104239. Comparative effectiveness of non-pharmacological	Multicomponent strategy was the most effective non-pharmacological intervention in reducing the incidence of ICU delirium. Early mobilisation and family participation involvement in non-pharmacological interventions seemed to be more effective in reducing the incidence of delirium in ICU.	

interventions for preventing delirium in critically ill adults: A systematic review and network meta-analysis - ScienceDirect **Systematic review**		
Rood et al 2021 The impact of nursing delirium preventive interventions in the ICU: a multicenter cluster-randomised controlled clinical trial. American Journal of Respiratory and Critical Care Medicine, 204(6), pp.682-691. The Impact of Nursing Delirium Preventive Interventions in the ICU: A Multicenter Cluster-randomised Controlled Clinical Trial | American Journal of Respiratory and Critical Care Medicine (atsjournals.org) **RCT**	A stepped-wedge cluster-randomised controlled trial conducted in ICUs of ten centres to determine the effects of a multicomponent nursing intervention programme on delirium. There was a limited increase in the use of nursing interventions, and no change in the number of delirium-free and coma-free days alive in 28 days could be determined.	Large multicentre trials detailing a package of non-pharmacological interventions in the ICU with evidence of implementation. Could be considered for sections 4.3 and 6
Lee et al 2022 Can we improve delirium prevention and treatment in the emergency department? A SR. Journal of the American Geriatrics Society. https://agsjournals.onlinelibrary.wiley.com/doi/pdf/10.1111/jgs.17740 **Systematic review**	Few interventions initiated in the emergency department (ED) were found to consistently reduce the incidence or duration of delirium.	RCTs on the efficacy and safety of antipsychotics in reducing the risk of delirium in patients in ICU or other hospital settings.
Khan et al 2018 Preventing postoperative delirium after major non-cardiac thoracic surgery—a randomised clinical trial.	Objective: To assess the efficacy of haloperidol in reducing postoperative delirium in individuals undergoing thoracic surgery. No significant differences were observed between those receiving haloperidol and those receiving placebo in incident delirium (n=15 (22.1%) vs n=19 (28.4%); p =0.43),	RCTs on the efficacy and safety of haloperidol in the reduction of the severity and duration of delirium in non-ICU settings. Could be considered in section 7.1

Journal of the American Geriatrics Society, 66(12), pp.2289-2297. [Preventing Postoperative Delirium After Major Non-cardiac Thoracic Surgery—A Randomized Clinical Trial (wiley.com)](...) **RCT**	time to delirium (p =0.43), delirium duration (median 1 day, interquartile range (IQR) 1–2 days vs median 1 day, IQR 1–2 days; p=0.71), delirium severity, ICU length of stay (median 2.2 days, IQR 1–3.3 days vs median 2.3 days, IQR 1–4 days; p=0.29), or hospital length of stay (median 10 days, IQR 8–11.5 days vs median 10 days, IQR 8-12 days; p=0.41). In the oesophagectomy subgroup (n=84), the haloperidol group was less likely to experience incident delirium (n=10 (23.8%) vs n=17 (40.5%); p=0.16). There were no differences in time to delirium (p=0.14), delirium duration (median 1 day, IQR 1–2 days vs median 1 day, IQR 1–2 days; p=0.71), delirium severity, or hospital length of stay (median 11 days, IQR 10–12 days vs median days 11, IQR 10–15 days; p=0.26). ICU length of stay was significantly shorter in the haloperidol group (median 2.8 days, IQR 1.1–3.8 days vs median 3.1 days, IQR 2.1–5.1 days; p=0.03). Safety events were comparable between the groups. Low-dose postoperative haloperidol did not reduce delirium in individuals undergoing thoracic surgery but may be efficacious in those undergoing oesophagectomy.	
Li et al, 2020. Benzodiazepines for treatment of patients with delirium excluding those who are cared for in an ICU. Cochrane Database of SRs, (2). https://www.cochranelibrary.com/ cdsr/doi/10.1002/14651858.CD012670.pub2/full **Systematic review**	There is not enough evidence to determine whether benzodiazepines are effective when used to treat patients with delirium who are cared for in non-ICU settings.	RCTs on the efficacy and safety of antipsychotics, benzodiazepines or dexmedetomidine in the reduction of the severity and duration of delirium in patients in ICU. Could be considered for section 7.4

Potentially important new evidence

Reference	Details	Why might this be important to include in the guideline?
Woodhouse et al 2019 Woodhouse, R., Burton, J.K., Rana, N., Pang, Y.L., Lister, J.E. and Siddiqi, N., 2019. Interventions for preventing delirium in older people in institutional long-term care. Cochrane Database of SRs, (4). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6478111/pdf/CD009537.pdf	The introduction of a computerised system to identify medications that may contribute to delirium risk and trigger a medication review was probably associated with a reduction in delirium incidence (12-month HR 0.42, CI 0.34 to 0.51; 1 study, 7,311 participant-months; moderate certainty evidence downgraded for risk of bias) but probably had little or no effect on mortality (HR 0.88, CI 0.66 to 1.17; 1 study, 9,412 participant-months; moderate certainty evidence downgraded for imprecision), hospital admissions (HR 0.89, CI 0.72 to 1.10; 1 study, 7,599 participant-months; moderate certainty evidence downgraded for imprecision) or falls (HR 1.03, CI 0.92 to 1.15; 1 study, 2,275 participant-months; low certainty evidence downgraded for imprecision and risk of bias).	This could be included under section 5.1 Medicines optimisation.

Consultation feedback

Former members of the SIGN 157 guideline development group were invited to comment on the report and the proposed areas for update.

Reviewer	Comments
Dr Sweyn Garrioch, Consultant Anaesthetist	I don't see anything that makes me think the sections I was most involved with need updated. Some comments below on the most relevant papers to my sections: https://research.birmingham.ac.uk/en/publications/effect-of-regional-vs-general-anesthesia-on-incidence-of-postoper I don't feel this adds anything new. Very low rates of reported delirium when the incidence in this group is normally 20% or more. Factors not reported such as pain control method, opiate consumption, Median pain score of zero in each group which is difficult to believe in patients with hip fractures. **Woodhouse et al 2019** Could be added to 5.1 but difficult to recommend something with significant resource implications on the basis of one trial. I do not work in primary care so a GP may be better placed to comment.
Dr Roy Soiza, Consultant Physician	I do not think there is a need for an update as most of the new evidence supports our recommendations or finds little new persuasive evidence to support changing any of the current recommendations.

Ms Alyson Warren, Lead Pharmacist	I have looked at the document attached and the guideline, but only focused on the sections which I was involved in at the time, mainly to do with medication. Based on what I have read in these references, I do not think that the guideline would need updated at this time. Whilst some of the references are very interesting, and some more current (others including trials and studies already referenced in SIGN 157) the ones which I looked at did not change any of the recommendations or content significantly. In fact many of them added strength or bulk to the body of evidence already reported. If a review was required now (based on the references which I have not looked at), or in the future it may be worth adding some of them in, to ensure that more current studies are referenced.
Dr Maria Wybrew, General Practitioner	I would support the addition of computerised assessment of potential drug induced delirium and think that would be a valuable addition to the current guideline It seems well accepted in Highland and I think has improved patient care.

Concluding remarks (Dr Lola Adewale, Programme Manager)

Comments from the guideline development group suggest that there is no new evidence that will significantly change the recommendations in the existing guideline.

The literature search identified a study that could possibly be included in section 5.1 Medicines Optimisation (Woodhouse et al, 2019). This study suggests that the introduction of a computerised system to identify medications that might contribute to delirium risk and trigger a medication review was probably associated with a reduced incidence of delirium. However, concern was raised about recommending an intervention with significant resource implications on the basis of one randomised controlled trial.

The recommendation is: **there is no significant new evidence that will affect existing recommendations and the guideline should not be reviewed at this time.**

Decision

The recommendation was ratified by Healthcare Improvement Scotland Evidence Senior Management Team on 7 July 2022.

This guideline was **revalidated** in 2022 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: www.sign.ac.uk

Annex 1

Evidence sources

Resource	Results
Dynamed	Nil
BMJ Best Practice	**BMJ 2021** Best Practice Assessment of Delirium Assessment of delirium - Differential diagnosis of symptoms | BMJ Best Practice
Guidelines and guidance	
Previous HIS projects/advice/guidance relating to this topic	Nil
NICE	NICE [CG 103] update in progress, and expected publication date is February 2023 https://www.nice.org.uk/guidance/indevelopment/GID-NG10332 The update is to incorporate evidence on the 4AT tool.
HTW	Nil
HTA database	MacLullich, A.M., Shenkin, S.D., Goodacre, S., Godfrey, M., Hanley, J., Stíobhairt, A., Lavender, E., Boyd, J., Stephen, J., Weir, C. and MacRaild, A., 2019. The 4 'A's test for detecting delirium in acute medical patients: a diagnostic accuracy study. *Health Technology Assessment*, 23(40).The 4 'A's test for detecting delirium in acute medical patients : a diagnostic accuracy study (whiterose.ac.uk)
Additional searching (if required)	
Cochrane library	Burton JK, Craig L, Yong SQ, Siddiqi N, Teale EA, Woodhouse R, Barugh AJ, Shepherd AM, Brunton A, Freeman SC, Sutton AJ, Quinn TJ. Non-pharmacological interventions for preventing delirium in hospitalised non-ICU patients. Cochrane Database of SRs 2021, Issue 11. Chen, T.J., Traynor, V., Wang, A.Y., Shih, C.Y., Tu, M.C., Chuang, C.H., Chiu, H.Y. and Chang, H.C.R., 2022. Comparative effectiveness of non-pharmacological interventions for preventing delirium in critically ill adults: A SR and network MA. *International Journal of Nursing Studies*, p.104239. Finucane AM, Jones L, Leurent B, Sampson EL, Stone P, Tookman A, Candy B. Drug therapy for delirium in terminally ill adults. Cochrane Database of SRs 2020, Issue 1, Kim, Y.H., Kim, N.Y. and Ryu, S., 2022. Effects of non-pharmacological interventions for preventing delirium in general ward inpatients: A systematic review & MA of RCTs. *PloS one*, 17(5), p.e0268024.

	Li, Y., Ma, J., Jin, Y., Li, N., Zheng, R., Mu, W., Wang, J., Si, J.H., Chen, J. and Shang, H.C., 2020. Benzodiazepines for treatment of patients with delirium excluding those who are cared for in an ICU. *Cochrane Database of SRs*, (2).
	Woodhouse, R., Burton, J.K., Rana, N., Pang, Y.L., Lister, J.E. and Siddiqi, N., 2019. Interventions for preventing delirium in older people in institutional long-term care. *Cochrane Database of Systematic Reviews*, (4).
Grey Literature Search	Medicines and Healthcare products Regulatory Agency December 2021 [Haloperidol (Haldol): reminder of risks when used in elderly patients for the acute treatment of delirium - GOV.UK (www.gov.uk)](http://www.gov.uk)
	Fiest, K.M., Krewulak, K.D., Sept, B.G., Spence, K.L., Davidson, J.E., Ely, E.W., Soo, A. and Stelfox, H.T., 2020. A study protocol for a randomised controlled trial of family-partnered delirium prevention, detection, and management in critically ill adults: the ACTIVATE study. BMC health services research, 20(1), pp.1-11.
	Khan, B.A., Perkins, A.J., Campbell, N.L., Gao, S., Khan, S.H., Wang, S., Fuchita, M., Weber, D.J., Zarzaur, B.L., Boustani, M.A. and Kesler, K., 2018. Preventing postoperative delirium after major non-cardiac thoracic surgery—a randomised clinical trial. *Journal of the American Geriatrics Society*, *66*(12), pp.2289-2297.
	Lee, S., Chen, H., Hibino, S., Miller, D., Healy, H., Lee, J.S., Arendts, G., Han, J.H., Kennedy, M. and Carpenter, C.R., 2022. Can we improve delirium prevention and treatment in the ED? A systematic review. *Journal of the American Geriatrics Society*.
	Rood, P.J., Zegers, M., Ramnarain, D., Koopmans, M., Klarenbeek, T., Ewalds, E., van der Steen, M.S., Oldenbeuving, A.W., Kuiper, M.A., Teerenstra, S. and Adang, E., 2021. The impact of nursing delirium preventive interventions in the ICU: a multicenter cluster-randomised controlled clinical trial. *American Journal of Respiratory and Critical Care Medicine*, *204*(6), pp.682-691.
	Wiegand, T.L., Rémi, J. and Dimitriadis, K., 2022. Electroencephalography in delirium assessment: a scoping review. BMC neurology, 22(1), pp.1-23.
	Zayed, Y., Barbarawi, M., Kheiri, B., Banifadel, M., Haykal, T., Chahine, A., Rashdan, L., Aburahma, A., Bachuwa, G. and Seedahmed, E., 2019. Haloperidol for the management of delirium in adult ICU patients: a SR and MA of RCTs. Journal of critical care, 50, pp.280-286.