

INTRODUCTION

Delirium: The term ‘delirium’ was first used in the 1st century, meaning to be out of furrow or a track. By the nineteenth century, it had been understood to be a syndrome of symptoms with multifactorial organic aetiology. Delirium is a common condition that occurs in approximately 10-15% of hospitalised patients. In the elderly, this proportion increases to 30-50%. Despite its high prevalence, it is not always diagnosed in medical settings. Managing delirium can be challenging, as patients can be restless, agitated, and confused. Good medical practice promotes the use of behavioural and environmental techniques for managing acutely confused patients, but some clinical situations might require pharmacological management.

Guidelines about choice of medication, dose, and frequency are needed for better management and care. They can provide this comprehensive information and are important tools in providing evidence-based recommendations for various clinical situations. In a group where guidelines were used, recognition of delirium was significantly better (93% versus the control group 43%; P < 0.01), average length of hospital stay was shorter by 1.7 days (p = 0.03), fewer consultations were requested in the intervention group (p < 0.01), and a net cost saving of £57,138 over a 6-week period was achieved.

Evidence-based delirium guidelines: There has been a move towards developing national guidelines. In the UK, the National Institute of Clinical Excellence (NICE) guidelines are the most recent and comprehensive guide to clinically managing delirium. These guidelines for delirium broadly focus on behavioural management, multi-disciplinary consultation, psychological support, effective communication and environmental adaptations.

A common factor amongst all the guidelines for management of delirium is the limited evidence for pharmacological treatments, a point which is highlighted by NICE. The Australian guidelines recommend the use of low-dose haloperidol, olanzapine or risperidone. The Canadian guidelines, specifically aimed at management of delirium in the elderly, recommend a very low dose (0.25-0.5mg) of haloperidol in the first instance, and atypical antipsychotics as an alternative. The NICE guideline recommends considering haloperidol or olanzapine if non-pharmacological approaches have not been evaluated for their use and acceptability. They are multi-page, difficult to read, and embedded in lengthy documents.

AIMS

The aim of this quality improvement (QI) project was to evaluate the use and acceptability of evidence-based one page Delirium Management Guidelines in a tertiary care general hospital, University Hospital of Wales, Cardiff, UK. The first version of these guidelines was developed as an ethics requirement for a randomised control trial (RCT) for treatment of delirium. It ensured that both the treatment groups were given uniform non-drug management.

Clinical scenario 1

Mild delirium:
An 84 year old independently retired teacher had interrupted sleep and was restless. He reported seeing things and hearing voices. He was diagnosed with UTI and had a history of benign prostatic enlargement. Antibiotics were prescribed leading to resolution of mild symptoms of delirium.

METHODOLOGY

A multi-professional guidelines development group (GDG), including consultation and liaison psychiatrists, psychologists, old age psychiatrist, old age physicians and statistical analyst, formulated the first draft of the guidelines. Updated versions were published. Besides information from this survey, up-to-date information from research literature was incorporated for clinical use in the most recent version of
these guidelines. Tahir et al (2010) was approved by the ethics committee. Improved versions were part of a QI project and did not require ethics approval.

**DESIGNING DELIRIUM MANAGEMENT GUIDELINES**

A detailed literature search was undertaken using Ovid, Medline, Embase, Cochrane and PubMed. The literature was searched for three areas; previous delirium management guidelines, drug treatment for delirium, and non-drug interventions for management of delirium. The terms 'delirium' or 'acute confusion' or 'organic brain syndrome' were used in combination with other terms including, 'management' or 'guidelines.' To find literature for drug treatment of delirium, these terms were used in combination with 'treatment', 'drug therapy', 'non-drug interventions', 'management', 'antipsychotics', 'risperidone', 'quetiapine', 'olanzapine', 'haloperidol', ' amisulpride', ' benzodiazepines', ' lorazepam', 'psychotropic medication', 'anticholinesterases' and ' benzodiazepines.' For non-drug treatments, additional terms were used; 'multi-factorial', 'multi-disciplinary', 'systemic'. A more recent literature search was undertaken in March 2020 for obtaining comprehensive information prior to appraisal of literature and review of previously published guidelines.

After the initial literature search, three papers on designing delirium management guidelines were identified. They did not evaluate their use. A low level of evidence was identified for drug treatment of delirium. Information for antipsychotics, including haloperidol, olanzapine, risperidone, quetiapine and ziprasidone was based on case reports and case series. Only a few RCTs (randomised control trials) were identified. Recent reviews also confirm a small number of randomised trials for treatment of delirium. For non-drug treatment of delirium, the search strategy identified 76 references. After a review of the abstracts, a further 9 papers were identified for detailed review.

The literature search identified evidence recommendations for abbreviated one-page guidelines. In drafting these guidelines, clarity of language, local organisational impact, practical and applicable use in day-to-day clinical practice, as well as guidance for management of varied presentations in delirium, were considered.

It was considered that this was possible without any bias, as only one member of the GDG (TT) was involved in the drafting of the first version. The primary aim of this pilot was to ensure that the recommendations are presented in a user-friendly language and in an easy to follow format.

**EVALUATION OF DELIRIUM MANAGEMENT GUIDELINES**

For this QI project, an electronic Google Forms questionnaire was designed to conduct a survey for the acceptability of these guidelines. Ten questions were selected to evaluate various aspects of the guidelines using a five-point Likert Scale, ranging from 'totally agree' to 'totally disagree.' An additional three open-ended questions enquired for any information which the respondents would have liked to add or remove from the guidelines. The survey link was emailed to members of staff within Cardiff & Vale University Health Board.

The quantitative analysis included a brief description of the sample that responded to the questionnaire and the details of the responses in percentages. The qualitative analysis included the analysis of themes as suggestions by the respondents in reply to the three open-ended questions.

To complete the QI audit cycle, the guidelines were edited in response to the survey and recirculated amongst a group of colleagues interested in delirium management for further comments.

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**Clinical scenario 2**

**Moderate delirium:**

A 78 year old lady was recently diagnosed with mixed vascular and Alzheimer's dementia with history of diabetes and colon cancer. Family thought that she was calling more during the night and thought that she was depressed for 2-3 days. On cognitive functions assessment she was disoriented in time and place. On physical examination she had decreased breath sounds in left lower lobe. Chest infection was treated with antibiotics. She was prescribed low dose quetiapine to help her sleep. On follow up she had improved in attention and cognition.

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**RESULTS**

Fifty-nine questionnaires were completed. Most respondents were junior doctors (35.6%) and consultants (35.6%). Medicine (39.0%) and Psychiatry (32.2%) were the two main clinical areas from which completed questionnaires were received. The guidelines were found to be simple to read (79.6% totally agree/agree) and understandable (96.6% totally agree/agree). The majority of responses suggested the guidelines can help in confirming the diagnosis (77.9% totally agree/agree) and in the management of delirium (88.1% totally agree/agree). Most respondents (79.6% totally agree/agree) also reported that they would consider using them again.

Suggestions and responses to the open-ended questions guided improvements to the piloted version of these guidelines. As expected, some responses to the open-ended questions were positive, while some were critical. Positive comments included: 'They are very straightforward and easy to read,' 'Excellent work - Had made management of delirium simple,' and 'Overall a very useful guideline that I will definitely employ in the future.'

Critical comments included suggestions for improvement of either the presentation or content of the guidelines. Regarding presentation, one consultant commented: 'you need, I would argue, a much simpler initial flowchart (basically the headings of each box, with no more than one or two lines after) that grabs the attention, help the flow of thinking and gets people
to read the rest. As it is, the initial view is of a detailed, possibly complex flowchart, which will put people off actually reading it and it will end up in the back of the ring binder of guidelines, unread and unnoticed. Which would be a pity, given that it is a great guideline.‘ A medical doctor remarked: ‘I found it difficult to navigate around. There is too much information on one page. The text is small, and it isn’t clear how to navigate section to section.’ Other comments included requests for ‘reduce(d) amount of text’ and ‘larger print and calm colours’.

Regarding content, a major theme was that the guidelines needed to be clearer on the order of suggested interventions. Specifically, many respondents felt that environmental management options should be prioritised over pharmacological options, and that this needed to be better reflected in the guidelines: ‘I’d consider a stepwise approach when it comes to management, trying environmental and psychological approaches first, prior to medications’; ‘The presented order suggests that management with medication is the first line. It may be an idea to re-order to emphasise the importance of non-medication management first?’; ‘More practical tips on the psychological management of distress in delirium or links to other information on potential interventions to use instead of or as well as medication… I am concerned that people will skip the environmental and psychological steps and go straight for medication.’

Finally, some feedback was given on the pharmacological management section regarding the dosages of recommended medications and required monitoring. For example, a pharmacist said: ‘Change elderly dose to ‘quarter to half that of adult dose’ - in practice would not routinely give 150mg quetiapine prn in a day,’ and ‘ECG is required before haloperidol adult dose’ - in practice would not routinely give 150mg quetiapine and Lorazepam were given. After 2 weeks he was more settled but continued to exhibit fluctuations of cognition and was misidentifying relatives. He was restless and agitated of TIA with intermittent right sided weakness. He was paranoid and was misidentifying relatives. He was restless and agitated

A number of changes to the Guidelines were made in light of these comments. This new updated version (Figure) has been implemented in routine clinical practice and for educating doctors and nurses. To complete the feedback cycle, this version was distributed to a selected group of senior clinicians who were asked whether they thought the changes had addressed the comments described above. The feedback at this stage was positive. Comments included: ‘Much less overwhelming and much more focused on non-pharmacological approaches’; ‘I think this is much more straightforward to follow and am happy with the edited version.’; ‘I much prefer the revised guidelines. Simplified, it’s easier on the eye to read and follow, it makes perfect sense and the steps flow well. The drug and dose medication section is particularly helpful.’

### Clinical scenario 3

**Chronic delirium:**
An 75 year old man was admitted to hospital with a diagnosis of TIA with intermittent right sided weakness. He was paranoid and was misidentifying relatives. He was restless and agitated and wanted to leave the hospital against medical advice. Both quetiapine and Lorazepam were given. After 2 weeks he was more settled but continued to exhibit fluctuations of cognition at night time.

### Table 1: Details of respondents – number of respondents (%)

<table>
<thead>
<tr>
<th>Professional</th>
<th>SALT</th>
<th>Pharmacist</th>
<th>Nurse</th>
<th>Junior / trainee Doctor</th>
<th>Consultant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicine</td>
<td>33</td>
<td>13 (20.3%)</td>
<td>21 (35.6%)</td>
<td>23 (38.0%)</td>
<td>0 (0.0%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>Anaesthetics / Intensive Care</td>
<td>34</td>
<td>2 (3.4%)</td>
<td>21 (35.6%)</td>
<td>25 (42.4%)</td>
<td>3 (5.1%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>Trauma &amp; Orthopaedics</td>
<td>37</td>
<td>5 (8.5%)</td>
<td>21 (35.6%)</td>
<td>19 (32.2%)</td>
<td>1 (1.7%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>Accident &amp; Emergency</td>
<td>38</td>
<td>1 (1.7%)</td>
<td>21 (35.6%)</td>
<td>1 (1.7%)</td>
<td>25 (42.4%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>Obstetrics &amp; Gynaecology</td>
<td>39</td>
<td>1 (1.7%)</td>
<td>21 (35.6%)</td>
<td>1 (1.7%)</td>
<td>25 (42.4%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>Psychiatry</td>
<td>4 (6.8%)</td>
<td>6 (10.2%)</td>
<td>13 (22.0%)</td>
<td>23 (39.0%)</td>
<td>0 (0.0%)</td>
<td>59 (100%)</td>
</tr>
</tbody>
</table>

Note: SALT=Speech and Language Therapy

### Table 2: Responses to questions 1-10 from 59 respondents – number of responses (%)

<table>
<thead>
<tr>
<th>Question</th>
<th>Totally agree</th>
<th>Agree</th>
<th>Don't know</th>
<th>Disagree</th>
<th>Totally disagree</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The guidelines are simple to read</td>
<td>33 (55.9%)</td>
<td>13 (22.0%)</td>
<td>2 (3.4%)</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>2. The language used is simple</td>
<td>33 (55.9%)</td>
<td>13 (22.0%)</td>
<td>2 (3.4%)</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>3. The language is understandable</td>
<td>33 (55.9%)</td>
<td>13 (22.0%)</td>
<td>2 (3.4%)</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>4. The guidelines are simple to follow</td>
<td>33 (55.9%)</td>
<td>13 (22.0%)</td>
<td>2 (3.4%)</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>5. The guidelines help confirm the diagnosis of delirium</td>
<td>33 (55.9%)</td>
<td>13 (22.0%)</td>
<td>2 (3.4%)</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>6. The guidelines help identify risks associated with delirium, e.g. non-compliance, aggression, etc.</td>
<td>33 (55.9%)</td>
<td>13 (22.0%)</td>
<td>2 (3.4%)</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>7. The guidelines help in the management of delirium</td>
<td>33 (55.9%)</td>
<td>13 (22.0%)</td>
<td>2 (3.4%)</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>8. The guidelines help me use environmental factors in the management of delirium</td>
<td>33 (55.9%)</td>
<td>13 (22.0%)</td>
<td>2 (3.4%)</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>9. It is easy to use the guidelines</td>
<td>33 (55.9%)</td>
<td>13 (22.0%)</td>
<td>2 (3.4%)</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
<td>59 (100%)</td>
</tr>
<tr>
<td>10. I would use these guidelines in the future</td>
<td>33 (55.9%)</td>
<td>13 (22.0%)</td>
<td>2 (3.4%)</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
<td>59 (100%)</td>
</tr>
</tbody>
</table>
**Figure: Delirium Management Guidelines**

### Step 1: Confirm Diagnosis

#### History
- Acute onset
- Fluctuating course
- Symptoms: DSM-5 and ICD-11 criteria
  - Impaired attention, orientation, focus, memory, language, disturbed sleep
  - Perceptual disturbance: hallucinations / illusions
  - Activity levels: hyperactive / hypoactive / mixed

#### Screening Tests
- Use a standard and culturally appropriate test e.g. 4AT CAM, Clock Drawing Test or SQID.

### Step 2: Risk Assessment

#### Investigations of underlying cause:
- FBC, U&E, LFT, CRP, urinalysis, CXR, brain imaging.
- Other causes to consider:
  - Substance intoxication
  - COVID-19 infection
  - Constipation & pain

#### Agitation & restlessness
- Self-neglect

#### Non-compliance factors
- Patient-related
- Staff-related

#### Consider Legal Framework
- Mental Capacity Act (MCA)
- Deprivation of Liberty Safeguards (DoLS)

### Step 3: Management

#### General / Environmental
- Assess regularly
- Address causes of delirium e.g. infections, constipation, dehydration, low sodium, pain, medication side effects/interactions.
- 1:1 nursing in separate cubicle
- Staff continuity
- Adequate lighting and room temperature
- Hydration & nutrition
- Regular day-night cycle

#### Psychological / Behavioural
- Break down complicated tasks
- Acknowledge distress, validate feelings
- Ensure use of sensory aids (hearing/visual)
- Use environmental cues (clock, calendar, newspaper, television) to aid orientation
- Inform, educate and counsel the family
- Do not confront false beliefs (delusions) or perceptual disturbances (hallucinations / illusions)
- Offer reassurance and foster independence
- Improve mobility

#### Medication
- **General principles**
  - Start low, go slow; avoid polypharmacy; monitor for side effects.
  - Benzodiazepines – avoid long-acting agents, use low doses (half of adult doses) in elderly.
  - Antipsychotics – use low doses, get baseline ECG to monitor QTc (esp. Haloperidol), monitor for akathisia which can mimic agitation.
  - Consider monotherapy with one of the following antipsychotics.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose (mg)</th>
<th>Frequency</th>
<th>Max dose/24h (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam</td>
<td>0.25 – 1</td>
<td>OD</td>
<td>4</td>
</tr>
<tr>
<td>*Quetiapine</td>
<td>12.5 – 50</td>
<td>BD – QDS</td>
<td>300</td>
</tr>
<tr>
<td>*Olanzapine</td>
<td>1.25 – 5</td>
<td>BD – QDS</td>
<td>10</td>
</tr>
<tr>
<td>*Risperidone</td>
<td>0.25 – 1</td>
<td>BD – QDS</td>
<td>3</td>
</tr>
<tr>
<td>*Haloperidol</td>
<td>0.5 – 1</td>
<td>BD – QDS</td>
<td>4</td>
</tr>
</tbody>
</table>

* In doubt contact liaison psychiatry

Rule out drug interactions between psychotropic medications and other medications for underlying disorders e.g.


DISCUSSION

Summary of results: Evidence for the use of multimodal management of delirium was incorporated in the current version of guidelines (Figure). Our survey demonstrated that most respondents found the guidelines to be simple to read and understand. The majority of respondents suggested they can help in confirming the diagnosis and management of delirium, and also that they would consider using them again. In response to some suggestions, alterations have been made to these guidelines. They have been implemented by using in the clinical setting as part of RCT and for educating doctors and nurses.

Strengths of this QI project: A rigorous methodology was used to design these guidelines. A comprehensive review has presented information on delirium guidelines. This included an appraisal of an up-to-date literature review of guidelines for the pharmacological and non-pharmacological management of delirium. Evidence-based recommendations were made to the GDG, which was involved in making alterations to the first draft. The inclusion of a pilot phase and a carefully designed questionnaire to evaluate various aspects of the guidelines to improve the final version were also methodological strengths. The up-to-date version of the guidelines was published. Not only were these guidelines reported as easy to use and read, they also highlighted the multifactorial non-drug and environmental factors for the management of delirium. Although previous peer review is a key strength, it was important to evaluate the user friendliness of these guidelines. None of the previous delirium guidelines have been evaluated in this manner.

Limitations of this QI project: Despite the methodological strengths, there were several practical limitations that might have restricted the scope and results of this project. The membership of the GDG was limited to local professionals who had expressed an interest in the subject. Ideally, a wider focus group on delirium management, semi-structured interviews, or a combination of both could have been used to gather information. It would probably have been helpful to pilot the guidelines with a small number of patients being managed for delirium. This would have allowed further refinement prior to their use. To improve the response rate, strategies like posting reminders on the walls of staff rooms and sending written notices could have been used.

Lessons learnt and implications: These guidelines reflect an up-to-date evidence base. Early identification and initiation of management should assist early recovery. Educational and organisational changes are required to implement the guidelines, as guidelines alone do not appear to improve the management of delirium. Any effort to implement and develop the existing guidelines should help bring clinical practice and research closer.

Delirium should not only be part of a curriculum for those working in hospitals but also those taking care of patients in the community, palliative care and residential care. Multi-page guidelines usually contain a detailed description of how the guidelines were drawn. Therefore, in comparison with the multi-page guideline document, these one-page evidence-based guidelines can be an effective teaching tool. Education to implement these guidelines could raise consideration of prioritising recommendations to meet identified gaps within individual clinical settings. For example, rather than reliance on medication alone, education can highlight the importance of environmental and psychological management, nursing support, use of strategies for reorientation and a need for regular review. Education can also alter the perception and demands of staff in general hospitals to transfer patients with behavioural symptoms to psychiatric units. Education strategies can range from bedside teaching to formal classroom teaching. These guidelines take into account variants of delirium: Importantly, hypoactive delirium might not be managed as intensively as hyperactive or mixed type delirium. Therefore, the use of guidelines in hypoactive delirium needs to be encouraged and evaluated.

The information in guidelines can also be used to develop shared care pathways between psychiatric and medical units to treat patients suffering from delirium. As the non-drug strategies described in lengthy documents can be difficult to use in a busy general ward with competing demands, the use of brief and simple delirium management guidelines can be easily justified.

Although the NICE guideline is comprehensive and a major development to guide the clinical management of a complex neuropsychiatric syndrome, this extensive document also highlights the limited evidence base for the pharmacological treatment of delirium. It has, however, given a comprehensive review of the non-pharmacological management. The evidence presented for pharmacological intervention and used by NICE is based on only three studies. Some of the detailed documents for delirium management guidelines include algorithms which have not been evaluated for their use in hospital settings. Therefore, after designing any guideline, it is equally important to evaluate their use and impact.

The previously published version of these guidelines included management of Covid-19-related delirium with specific reference to drug interactions for medications used for management for Covid-19. These were further modified by the Faculty of Old Age Psychiatry of the Royal College of Psychiatrists. It is important to regularly update any guidelines through a regular literature review. However, as the quality and level of evidence in the treatment of delirium improves, these guidelines will have to be redrafted and further evaluated, for example, through a similar audit cycle.
There are two methods which can be considered to evaluate the latest version of these one-page guidelines. A case-control method, similar to Webster et al. (1999) and the Appraisal of Guidelines Research & Evaluation (AGREE) Instrument could be used which is an international collaboration project involving researchers and policymakers seeking to improve the quality and effectiveness of clinical guidelines. It helps in establishing a shared and structured framework for their development, reporting and assessment.

While the case-control study can assess the use of guidelines in two patient groups, the AGREE instrument can assess the design of guidelines, evidence on which guidelines are designed, their quality of reporting, and the acceptability of these guidelines. This would be a development on the previous evidence on designing of guidelines and their use leading to acceptability.

Although the national guidelines recommend several strategies, they fail to acknowledge the importance of local services and strategies for implementing guidelines.

**CONCLUSION**

These one-page evidence-based guidelines have been evaluated for use in a general hospital and found to be helpful. These guidelines need to be implemented through education and use in clinical settings. They have the potential to improve patient care through early recognition and management. Use of these guidelines will not only help with patient management, it will also influence the required changes in the ward environment where they are treated.

**KEY MESSAGES**

1. Undertake a thorough assessment of physical status and mental state with an evaluation of investigations for comorbid physical disorders.
2. Evaluate risk factors for delirium
3. Use guidelines for non-pharmacological and judicious use of antipsychotic medications.

**Competing interests**

Tayyeb A. Tahir: Tahir et al. was an investigator-initiated study: in terms of the Clinical Trials Directive, AstraZeneca, UK had legally sponsored and provided funding for recruitment of a research assistant and trial medication.

Dr Christopher C Ng, Dr Ankit Saxena and Dr Radhika Oruganti: none declared.

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