Appendix H: Recommendations for future research

1. FULL LIST OF RECOMMENDATIONS FOR FUTURE RESEARCH

HP = high priority: 1, 2, 4, 5, 6

1.1 HP: Research recommendation 1

1.1.1 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?

1.2 HP: Research recommendation 2

1.2.1 In hospital patients with delirium, are atypical antipsychotics better than placebo or typical antipsychotics or benzodiazepines for treating delirium?

1.3 Research recommendation 3

1.3.1 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?

1.4 HP: Research recommendation 4

1.4.1 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?

1.5 HP: Research recommendation 5

1.5.1 How common is delirium and what are its adverse outcomes in people in long-term care?

1.6 HP: Research recommendation 6

1.6.1 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?

1.7 Research recommendation 7

1.7.1 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?

1.8 Research recommendation 8

1.8.1 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?

1.9 Research recommendation 9

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

1.10 Research recommendation 10

1.10.1 The development and validation of a new test for delirium

1.11 Research recommendation 11

1.11.1 Is the presence of immune system markers, particularly cytokines, a risk factor for the development of delirium?

1.12 Research recommendation 12

1.12.1 What is the resource use and cost of implementing a muticomponent prevention intervention in hospital or long term care settings as compared to usual care?

2 HIGH PRIORITY RECOMMENDATIONS FOR FUTURE RESEARCH

The criteria for selecting high-priority research recommendations were considered in accordance with process outlined in 'The guidelines manual' (NICE 2009).

2.1 HP: Research recommendation 1

2.1.1 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?

2.1.1.1 Summary– why the proposed research is important

The serious nature of delirium and its consequences makes all methods of prevention important to establish. Pharmacological agents may be a simple preventative treatment for delirium, but can also cause delirium, so the use of these agents should be treated with caution. The evidence is limited: three low quality studies were found, each of which was unrepresentative, either of the population or the drug used, but there was some indication of clinical effectiveness. A large randomised trial (with at least 100 patients in each arm) should be conducted in hospital patients at high risk of delirium to compare atypical antipsychotics, typical antipsychotics, benzodiazepines or acetylcholinesterase inhibitors with placebo for preventing delirium. It would be necessary to define the included population in terms of their

delirium risk (e.g. high risk patients could be those with two or more risk factors for delirium). The primary outcome should be the incidence of delirium, measured at least daily using a validated diagnostic tool. The severity and duration of delirium should also be recorded, together with adverse effects of the drugs, notably extrapyramidal symptoms and stroke.

Table H1: Criteria for Research Recommendation 1

Criterion	Explanation
Importance to patients or the population	Common condition, and commonly used drugs but unknown effectiveness for the prevention of this condition. Therefore new research would alter clinical practice either to increase their use in routine care, or stop use.
Relevance to NICE guidance	New knowledge/evidence that would improve strength of recommendations.
Relevance to the NHS	Potentially reduce lengths of stay but reducing the incidence of a condition that is known to extend lengths of stay
Current evidence base	Very weak
Equality	No equality issues
Feasibility	Standard trial methods
Other comments	Simple trial with potentially major implications for clinical practice and improving outcomes for the large group of people who are at risk of delirium.

2.2 HP: Research recommendation 2

2.2.1 In hospital patients with delirium, are atypical antipsychotics better than placebo or typical antipsychotics or benzodiazepines for treating delirium?

2.2.1.1 Summary– why the proposed research is important

Pharmacological interventions are currently used in clinical practice to manage symptoms of delirium, however the evidence for this is limited: one moderate quality study showed that typical and atypical antipsychotics were clinically and cost effective compared with placebo, but there is no evidence for benzodiazepines. Pharmacological agents that alter the course of delirium or control particular symptoms may be useful in treating delirium, but it needs to be determined if the drugs should be given routinely or for selected symptoms, and account needs to be taken of adverse drug events. A large randomised trial (with at least 100 patients in each arm) should be conducted in hospital patients with delirium to compare atypical antipsychotics, typical antipsychotics, or benzodiazepines with placebo for the treatment of delirium. The outcomes should be recovery from delirium (complete response) and the duration and severity of delirium, measured using a validated diagnostic tool. Adverse effects of the drugs, notably extrapyramidal symptoms and stroke, should also be recorded.

Table H2. Criteria for Research Recommendation 2

Criterion	Explanation
Importance to patients or the population	Common condition, and commonly used drugs but

	unknown effectiveness for the treatment of this condition. Therefore new research would alter clinical practice either to increase their use in routine care, or stop use.
Relevance to NICE guidance	New knowledge/evidence to strengthen the guidance.
Relevance to the NHS	Potentially reduce lengths of hospital stay but reducing the duration and severity of an episode of delirium.
Current evidence base	Very weak
Equality	No equity issues
Feasibility	Standard trial methods
Other comments	Simple trial with potentially major implications.

2.3 HP: Research recommendation 4

2.3.1 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?

2.3.1.1 Summary – why the proposed research is important

Although there is moderate quality evidence of clinical and cost effectiveness for multicomponent interventions for the prevention of delirium in patients in hospital, there is no evidence in a long term care setting. It is anticipated that such an intervention would be of benefit to this long term care population. A large randomised trial (adequately powered) or a large cluster randomised trial (adequately powered) should be conducted in people in long term care to compare a multicomponent intervention with usual care. The multicomponent intervention should include assessment by a trained and competent healthcare professional, who would recommend actions tailored to the person's needs. The intervention should include reorientation, drug review, hydration and sleep hygiene. The primary outcome should be the incidence of delirium, measured at least daily using a validated diagnostic tool. The severity and duration of delirium should also be recorded using a validated tool, together with consequences of delirium, including admission to hospital.

Table H3. Criteria for Research Recommendation 4

Criterion	Explanation
Importance to patients or the population	There are over 400,000 people resident in care homes in England. These people are at high risk of delirium through multiple long-term conditions and frailty. An episode of delirium is likely to be associated with a step deterioration in their dependency and care needs, and have a negative impact on their quality of life.
Relevance to NICE guidance	New knowledge /evidence to strengthen the guidance
Relevance to the NHS	Disproportionately high users of NHS care. Potential to avoid acute admissions.
Current evidence base	Very weak
Equality	Under-researched group
Feasibility	Large study needed
Other comments	

2.4 HP: Research recommendation 5

2.4.1 How common is delirium and what are its adverse outcomes in people in long-term care?

2.4.1.1 Summary– why the proposed research is important

Although there is evidence for adverse outcomes consequent to delirium in a hospital setting, there is very little evidence in a long term care setting. It is important to determine whether people in long term care, who already have a high risk of death, dementia and other adverse outcomes, also have increased risks of these outcomes when they have delirium. It is also unknown what is the risk of hospital admission as a consequence of delirium. A large cohort study should be conducted in people in long term care to determine (i) the prevalence of delirium in this setting, and (ii) if the presence of delirium is a prognostic factor for death, dementia, admission to hospital, falls and other adverse outcomes. The multivariate analysis conducted in this study should take into consideration the potential significant risk factors identified in the guideline. Such a study would also inform cost effectiveness analyses for the prevention and treatment of delirium.

Table H4. Criteria for Research Recommendation 5

Criterion	Explanation
Importance to patients or the population	There are over 400,000 people resident in care homes in England. These people are at high risk of delirium through multiple long-term conditions and frailty. Few data are available to facilitate NHS service responses to this group of people and to inform training of staff. design and training
Relevance to NICE guidance	New knowledge /evidence to strengthen guidance.
Relevance to the NHS	To design services more appropriate and responsive to the care needs of this large group of patients.
Current evidence base	Very weak
Equality	No equality issues
Feasibility	Study would need to be multi-centred to be sufficiently powered
Other comments	This study would also make a major contribution to the international literature on delirium as older people in care homes have been a hard to reach group internationally.

2.5 HP: Research recommendation 6

2.5.1 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?

2.5.1.1 Summary– why the proposed research is important

There is some evidence from multicomponent prevention studies to suggest that an education programme for health care professionals who care for people at risk of delirium, reduces the incidence of delirium in these people. However, the quality of this evidence is poor for the studies with a major educational component, and the better quality studies give an educational intervention only as part of their mullticomponent intervention, or not at all. Thus, there is a need to determine whether education on its own has an important preventative effect on the incidence of delirium. There is also a need to find out if an educational programme increases awareness of delirium, such that delirium is recorded accurately - which

is not the case in the UK at present. In order to avoid contamination effects and to prevent the problems of bed unavailability, it is proposed that a cluster randomised trial is performed, with whole hospitals being randomised to the interventions. A large cluster randomised trial should therefore be carried out to determine whether an interventional programme focussing solely on the education of staff about delirium reduces the incidence of delirium and/or improves the recording of delirium, compared with an education leaflet or usual care. The primary outcomes (incidence of delirium and recording of delirium in the patient's health care record) should be measured, before and after the intervention (time series design embedded in a cluster randomised trial).

Table H5. Criteria for Research Recommendation 6

Criterion	Explanation
Importance to patients or the population	We know that many cases of delirium are currently unrecognised in the NHS. Delayed diagnosis is associated with worse outcomes. Therefore an educational programme for improved awareness of delirium is likely to be associated with improved outcomes.
Relevance to NICE guidance	New knowledge/evidence to strengthen guidance.
Relevance to the NHS	Potential to improve patient outcomes and reduce lengths of stay
Current evidence base	Very weak
Equality	No equality issues
Feasibility	Standard trial methods
Other comments	Potentially cost effective approach to the prevention and management of delirium.