

Undiagnosed long-term cognitive impairment in acutely hospitalised older medical patients with delirium

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- 1 Undiagnosed long-term cognitive impairment in acutely hospitalised older
- 2 medical patients with delirium: a prospective cohort study

3

4 **Abstract**

5 Background

6 Delirium and dementia are common in the general hospital, being present in nearly 50% of
7 older unselected admissions to hospital. Cognitive impairment is a risk factor for delirium,
8 but the prevalence of previously undiagnosed cognitive impairment (dementia or mild
9 cognitive impairment) in patients with delirium is unknown.

10 Methods

11 We performed a prospective cohort study of people over 70 years admitted to hospital with
12 delirium to establish the prevalence of previously unrecognised prior cognitive impairment.
13 Delirium was diagnosed at baseline using the Diagnostic and Statistical Manual of Mental
14 Disorders (DSM-IV-TR). Mild cognitive impairment and dementia were diagnosed 3 months
15 following recruitment in survivors using the International Working Group on Mild Cognitive
16 Impairment criteria and DSM-IV criteria, respectively.

17 Results

18 Delirium was identified in 17.9% of older patients and 82 participants with delirium were
19 assessed at 3 months: 5 (6%) had persistent delirium, 14 (17%) had mild cognitive
20 impairment and 47 (57%) had dementia. In 17 participants with prior dementia and 14 with
21 prior mild cognitive impairment the diagnosis had been unrecognised, amounting to 31/82
22 (38%) of all patients with delirium having some form of previously undiagnosed cognitive
23 impairment.

24 Conclusion

25 Given that over 1/3 of older patients with delirium were found to have a previously
26 undiagnosed cognitive impairment, the development and evaluation of services to follow-up
27 and manage patients with delirium is warranted.

28

29 Key words: Delirium, dementia, mild cognitive impairment, MCI, general hospital,
30 prevalence, aged

31 Key Phrases:

32 17% of patients with delirium had mild cognitive impairment

33 57% of patients with delirium had DSM-IV dementia

34 One third of patient with dementia had previously undiagnosed dementia

35 1/3 of older patients with delirium were found to have a previously undiagnosed cognitive
36 impairment

38 **Background**

39 Delirium is a neuropsychiatric syndrome characterised by an acute change in cognition,
40 attentional deficits and altered arousal [1]. It accounts for 20% of emergency hospital
41 admissions in older people [2]. Delirium is associated with multiple adverse consequences
42 including increased mortality and new institutionalisation [3].

43 Dementia is a chronic neurodegenerative syndrome with multiple causes, usually
44 characterised by progressive cognitive change including amnesic and executive deficits and
45 functional decline [4]. It is common in the general hospital setting, affecting up to 40% of
46 acute hospital admissions [5]. The true contribution of dementia on the demand for unplanned
47 hospital care of older people may be underestimated because up to half of all cases of
48 dementia found in hospital in research had been previously undiagnosed [5]. Older people
49 with dementia admitted to general hospitals also have increased adverse events [6] and higher
50 mortality [7]. In fact delirium and/or dementia was present in 49% of older unselected
51 admissions in a recent cohort study [8].

52 People with dementia are six times more likely to be admitted to hospital with delirium [9].

53 Given the high proportion of undiagnosed dementia in acutely hospitalised patients in
54 general, we hypothesised that patients with delirium are likely to have an especially high
55 prevalence of undiagnosed dementia.

56 Mild cognitive impairment (MCI) is a syndrome of reported memory loss and measurable
57 cognitive deficit, but with the deficit not severe enough to affect activities of daily living.

58 MCI affects approximately 5% of older people, and is associated with a 5-10% yearly risk of

59 development into dementia [10]. MCI is a risk factor for delirium [11]. Little is known about
60 the prevalence of MCI in general hospital or in hospitalised people with delirium.

61 The prevalence of dementia in older hospital patients with delirium ranges from 51% to 68%
62 from eight individual cohort studies [8, 12-20]. Only two studies however used recognised
63 reference criteria for the diagnosis of both delirium and dementia [19, 20]. Two studies
64 reported the prevalence of unrecognised cognitive impairment. No studies reported the
65 prevalence of mild cognitive impairment. These studies are summarised in supplemental
66 table 1 in the supplementary data on the journal website
67 <http://www.ageing.oxfordjournals.org/>. No previous studies to our knowledge report the true
68 prevalence of undiagnosed dementia in hospital inpatients patients with delirium by reference
69 criteria. The objective of this prospective study was to identify accurately the proportion of
70 people admitted as unplanned admissions to hospital with delirium with both previously
71 diagnosed and undiagnosed dementia and mild cognitive impairment. By determining these
72 proportions, we aimed to determine the extent to which prevalent delirium is a marker of
73 previously undiagnosed dementia and mild cognitive impairment.

74 **Method**

75 A prospective cohort study was carried out. Unselected patients aged 70 years and over with
76 an unplanned medical admission to a UK teaching hospital between March 2013 and
77 November 2014 were screened by a single trained assessor (a specialist in geriatric medicine)
78 for delirium. The screening used the Confusion Assessment Method (CAM) [21],
79 Abbreviated Mental Test Score (AMTS) [22], the Digit Span test, and a detailed review of
80 the medical notes. Participants were eligible for the study if they met the Diagnostic and
81 Statistical Manual of Mental Disorders fourth edition (DSM-IV-TR) criteria for delirium
82 [23]. The screening took place on 143 days evenly spread over the period. Potential

83 participants who were unable to communicate because of severe sensory impairment or
84 inability to communicate in English were excluded, as were those deemed to be at risk of
85 imminent death.

86 Patients with delirium were then invited to participate. Informed consent was sought from the
87 potential participant if they had the mental capacity to give it. For those who lacked the
88 mental capacity to give informed consent, the next of kin was consulted in accordance with
89 the provisions of the Mental Capacity Act with respect to participation in research, and they
90 were asked also to agree to act as informants.

91 Baseline data were collected including demographic data, the Charlson Co-morbidity Index
92 and the Clinical Frailty Index [24, 25]. Review of the medical record accompanied an
93 informant interview that enquired about a previous diagnosis of dementia or MCI, and a
94 history of prior cognitive function, but no new diagnoses of dementia were made at baseline
95 due to the difficulties of distinguishing dementia from delirium in the presence of the latter.

96 At 3 months, a follow-up assessment was undertaken in survivors, at the patient's own home
97 or hospital if they were still an in-patient, by the same assessor who had seen them at
98 baseline. The presence of persistent delirium was first established using DSM-IV-TR criteria
99 for delirium. If no delirium was present a standardised history and examination, including the
100 Addenbrooke's Cognitive Examination III (ACEIII) [26], was performed to establish the
101 presence or absence of dementia or mild cognitive impairment before the onset of the
102 delirium. Dementia and subtype was diagnosed using the DSM-IV-TR criteria [27]: (1) the
103 development of multiple cognitive deficits, including memory impairment, and (2) the
104 impairment is sufficiently severe to cause impairment in occupational or social function. MCI
105 was diagnosed using the current consensus definition [28]: (1) the person is neither normal

106 nor demented, (2) there is evidence of cognitive decline, and (3) that activities of daily living
107 are preserved and complex instrumental functions are either intact or minimally impaired.

108 The final diagnosis was made synthesising all available information in relation to the 6 month
109 period before delirium hospitalisation, to make the diagnosis of either dementia or MCI at the
110 index admission. The symptoms of cognitive and functional decline had to have been present
111 for at least 6 months prior to the admission with delirium, as indicated by DSM-IV. It is not
112 possible to diagnose DSM-IV dementia in the presence of delirium so follow-up at three
113 months was chosen as the best balance to allow recovery from delirium and ensuring an
114 accurate and near-contemporaneous diagnosis of dementia at the index admission.

115 Data were analysed using IBM SPSS version 20 for Windows. Descriptive statistics were
116 used to describe the proportions of cognitive diagnoses given to the cohort with 95%
117 confidence interval calculated. Differences between common clinical variables were
118 analysed, using the independent t-test, Kruskal-Wallis test or chi-squared test depending on
119 the normality of the variables and whether the variables were continuous or categorical.
120 Odds ratios to predict the risk of having previously undiagnosed dementia were calculated
121 using univariate binary logistic regression.

122 The study was reported using the Strengthening the Reporting of Observational Studies in
123 Epidemiology (STROBE) statement [29].

124

125

126 **Ethics, consent and permissions**

127 Ethical and regulatory approvals were obtained (Bradford Ethics Committee, part of the
128 Yorkshire and Humber National research and Ethics Service, ref: 12/YH/0534). The
129 consent process is described in the methods.

130

131 **Results**

132 Of 1668 available older people admitted to hospital, 1327 were screened for delirium
133 between March 2013 and November 2014. Of these, 228/1327 (17.2%) were diagnosed with
134 DSM-IV-TR delirium. 125 of 228 (54.8%) were recruited. The main reason for non-
135 recruitment was lack of an available next of kin to act as consultee (57/103).

136 Of the 125 recruited, 45 (36%) had a previously recognised diagnosis of dementia. The
137 diagnosis had been made by a GP in 4/45 (9%) cases, a geriatrician in 7/45 (16%) cases and
138 an old age psychiatrist in 34/45 (76%) cases. 32/45 (71%) had been assessed in a memory
139 clinic and 17/45 (38%) were on cognitive enhancing drugs.

140 Of the 125 recruited, 82 (66%) were followed up at 3 months: 25 (20%) had died, 10 (8%)
141 declined the follow-up visit and 8 (6%) were not contactable. There was no difference in age,
142 gender or admission dementia status between those followed up and those not. The mean age
143 of the followed up sample was 84.4 years and 65.9% were female. 21/82 (24%) were from a
144 care home. Figure 1 shows participant flow.

145 At 3 months 5/82 (6%) had persistent delirium, 14/82 (17%) were diagnosed with prior MCI,
146 47/82 (57%) were diagnosed with dementia and 16/82 (20%) had no evidence of prior
147 cognitive impairment. Of the 47 with dementia, 31/47 (66%) had Alzheimer's disease, 12/47
148 (26%) had vascular dementia, 3/47 (6%) had mixed dementia and 1/47 (2%) had dementia
149 with Lewy bodies: 17 (21%) had probable dementia that was present at index admission but

150 not diagnosed. MCI had not been previously diagnosed in any of those in whom it was
151 diagnosed at the 3-month follow up. Of these newly diagnosed cases, 12 were diagnosed with
152 Alzheimer's disease and 5 with vascular dementia. In total, 31/82 patients who had been
153 admitted to hospital with delirium had previously undiagnosed cognitive impairment, that is
154 either dementia or MCI. Figure 2 illustrates these proportions with 95% confidence intervals.

155 The group with prior cognitive impairment had a higher burden of co-morbidity (median co-
156 morbidity index 2.0 vs 0.0, $p=0.002$) and frailty (median clinical frailty scale 5.5 vs 4.0,
157 $p<0.0005$) than the group with no prior cognitive impairment. See table 1.

158 Fifty of the 82 had no recognised diagnosis of dementia when admitted to hospital with 17/50
159 (34%) of those diagnosed with dementia at follow-up. When trying to predict unrecognised
160 dementia at admission from the group admitted with no recognised diagnosis of dementia,
161 age and frailty were significantly associated with having unrecognised dementia. Univariate
162 logistic regression demonstrates every increased year of age was associated with a 12%
163 increased risk of having unrecognised dementia (OR 1.12, 95% CI 1.01-1.25) and every
164 increased point in the Rockwood clinical frailty scale was associated with a two and a half
165 fold increased risk of having unrecognised dementia (OR 2.58, 95% CI 1.34-4.97). Please
166 see supplementary table 2 in the supplementary data on the journal website
167 <http://www.ageing.oxfordjournals.org/> .

168

169

170 **Discussion**

171 The main findings in this study are that nearly 4 in 5 older emergency medical patients with
172 delirium also have dementia or MCI, and that half of those with dementia or MCI did not

173 have a prior diagnosis. Our findings are consistent with previous studies of dementia
174 prevalence in older patients with delirium, which report a range of 51-68% [8, 17]. Delirium
175 was diagnosed on admission in 17% of older people in our cohort, which also is in keeping
176 with previously reported prevalence rates (15-25%) [2, 30].

177 This study adds to prior reports finding that unrecognised cognitive impairment is common
178 among patients with delirium. However, no previous studies have reported the proportion of
179 cases of delirium who had undiagnosed dementia at presentation diagnosed according to the
180 reference standard, and none have previously reported the prevalence of prior mild cognitive
181 impairment patients presenting with delirium. Two studies report the prevalence of
182 unrecognised cognitive impairment. In a study measuring drug metabolism in older patients
183 with delirium, 'probable dementia' was recorded using a validated informant questionnaire
184 (Informant Questionnaire of Cognitive Decline in the Elderly, IQCODE) and informant
185 interview [15]. The assessment was carried out at the time of admission and 63/105 patients
186 with delirium had probable dementia. Of those 37/105 (35%) had no prior diagnosis. A
187 further study reported the proportion of undiagnosed cognitive impairment in delirium,
188 reporting that in only 5 of 28 participants with delirium and cognitive impairment, a
189 diagnosis of dementia was recorded in medical notes [18]. Here the IQCODE administered
190 over the telephone was used to classify previous cognitive impairment.

191 The ascertainment at three months of pre-delirium dementia and MCI used standardised
192 diagnostic processes which included the assessment of cognition at that point, and hence
193 post-delirium cognitive impairment could potentially have led to an over-estimation of the
194 number of cases of prior dementia or prior MCI in borderline cases. We judge this risk to be
195 small, as the amount of post delirium cognitive impairment is small, and the diagnoses of
196 prior MCI and prior dementia rarely relied solely upon the cognitive assessment made at
197 three months.

198 Although the study did not recruit all patients admitted to hospital with delirium, the main
199 reason for non-recruitment was a lack of a consultee. There was no difference between the
200 age or sex of those who were and were not recruited, so this is unlikely to have caused a
201 significant bias in our results. Recognising the difficulty of separating delirium from
202 dementia, we applied formal reference standard criteria for the diagnosis of delirium and
203 dementia, using a trained assessor and using assessment at three months rather than solely on
204 admission: for these reasons we believe these findings to be robust. Persistent symptoms of
205 delirium were present at three months in 5 (6%) participants, though this may have
206 represented a new episode at assessment.

207 The significance of the finding of a high proportion of people with delirium having prior
208 undiagnosed cognitive impairment is that, not only is delirium an important diagnosis to
209 make in older patients admitted to hospital [31], it also presents a strong opportunity to
210 identify dementia and MCI [32]. A timely diagnosis of dementia during hospital admission
211 may ameliorate adverse events associated with a hospital stay [6], allow suitable resource
212 allocation, such as signposting to a cohort ward [33] or a trigger for comprehensive geriatric
213 assessment [34]. In the longer term, diagnosing patients with dementia allows identification
214 of those who would benefit from pharmacological therapy [35]. Patients could then be
215 counselled, advised and offered post diagnostic support, or offered the opportunity to
216 participate in research. This would not be possible without these diagnoses being recognised.
217 In the UK there is a government drive to improve dementia diagnosis rates through the
218 National Dementia Strategy[36] and the Prime Minister's dementia challenge[37], and
219 similar activities are also occurring worldwide. Routine follow up of patients who have
220 presented with delirium could therefore be of value - to identify those with persisting
221 delirium as well as to identify previously unrecognised dementia and mild cognitive
222 impairment.

223 A frailty measure, the Clinical Frailty Scale, would appear to have discriminating ability in
224 identifying those with delirium who also have dementia (Tables 1 and supplementary table
225 2). This suggests that there is also value in the assessment of frailty in this cohort.

226 Further work is now required to develop follow-up procedures to identify unrecognised
227 dementia, and to evaluate their cost effectiveness. Although screening tools for dementia in
228 the acute hospital setting exist [38] future work should concentrate on developing optimised
229 tools to identify dementia and MCI accurately in people with delirium, as well as evaluating
230 the potential benefits timely diagnosis in hospital offers.

231 **Conclusions**

232 Dementia in acutely hospitalised older patients is common and is associated with poor acute
233 and long-term health outcomes, yet it is currently under diagnosed. Our findings confirm that
234 older people in hospital with delirium are a high-risk group for undiagnosed cognitive
235 impairment (dementia and MCI). Delirium is therefore a target condition to screen or case-
236 find for dementia in general hospitals. However, improved identification in hospitals and
237 validated methods of evaluation and follow-up of older people with delirium in hospitals are
238 needed. Practitioners should consider adopting informant interviews and other methods in
239 detecting possible dementia in older acute hospital patients with delirium.

240

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245 in the study

246 **Declaration of interests**

247 The authors have no declaration of interests to declare

248 **Author contributions**

249 TAJ conceived and designed the study with significant contributions from AMJM, JRG, JML
250 and BS. TAJ carried out all assessments, data analysis and wrote the first manuscript draft.

251 All authors contributed to data interpretation and further revisions of the manuscript. The
252 final paper has been approved by all authors.

Table 1: Demographic and illness data of patients organised by diagnosis at 3 month follow up. MCI=mild cognitive impairment, ACEIII = Addenbrooke's Cognitive Assessment III, carried out at 3 month follow-up, Difference = Difference between cognitive impairment and no cognitive impairment, using independent samples Kruskal-Wallis test as data not normally distributed, NS=not significant, *=statistically significant.

	Cognitive impairment at 3 months						Difference
	Persistent delirium N=5	MCI N=14	Dementia – previously recognised N=30	Dementia – not previously recognised N=17	Combined cognitive impairment N=66	No cognitive impairment N=16	
Age Years, mean, SD	84.4±3.7	82.7±5.0	84.6±6.5	87.2±7.0	84.4±6.5	82.3±7.6	NS
Gender % female	20.0	64.3	76.0	64.7	66.7%	62.5	NS
Co-morbidity (Charlson co-morbidity index) Median, IQR	3(3)	1.5(3)	2(2)	2(2)	2(2)	0.0 (2)	.002 *
Frailty (Rockwood clinical frailty scale) Median (IQR)	6(4)	5(1)	6(1)	6(2)	5.5(1)	4(2)	<0.0005*
Cognitive assessment (ACEIII) Mean, SD	NA	66.4 (8.7)	20.1(23.7)	29.4(26.5)	33.2(28.7)	86.8(7.2)	<0.0005*

Figure 1: Flowchart of participant flow through the study. ♀=female.

Figure 2: Flow chart of diagnosis of prior cognitive impairment made at 3-month follow-up.

95% confidence intervals for all proportions shown in brackets.

References

PLEASE NOTE: The very long list of references supporting this report has meant that only the most important are listed here and are represented by bold type throughout the text. The full list of references is available on the journal website

<http://www.ageing.oxfordjournals.org/> as appendix 1

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