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

Jackson, Thomas; MacLullich, Alasdair MJ; Gladman, J; Lord, Janet; Sheehan, Bart

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

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 following recruitment in survivors using the International Working Group on Mild Cognitive 15 Impairment criteria and DSM-IV criteria, respectively. 16

17 Results

Delirium was identified in 17.9% of older patients and 82 participants with delirium were assessed at 3 months: 5 (6%) had persistent delirium, 14 (17%) had mild cognitive impairment and 47 (57%) had dementia. In 17 participants with prior dementia and 14 with 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

3

- 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

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

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

Dementia is a chronic neurodegenerative syndrome with multiple causes, usually 43 characterised by progressive cognitive change including amnesic and executive deficits and 44 45 functional decline [4]. It is common in the general hospital setting, affecting up to 40% of acute hospital admissions [5]. The true contribution of dementia on the demand for unplanned 46 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 mortality [7]. In fact delirium and/or dementia was present in 49% of older unselected 50 admissions in a recent cohort study [8]. 51

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.

Mild cognitive impairment (MCI) is a syndrome of reported memory loss and measurable
cognitive deficit, but with the deficit not severe enough to affect activities of daily living.
MCI affects approximately 5% of older people, and is associated with a 5-10% yearly risk of

37

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

A prospective cohort study was carried out. Unselected patients aged 70 years and over with 75 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 Statistical Manual of Mental Disorders fourth edition (DSM-IV-TR) criteria for delirium 81 [23]. The screening took place on 143 days evenly spread over the period. Potential 82

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

86 Patients with delirium were then invited to participate. Informed consent was sought from the potential participant if they had the mental capacity to give it. For those who lacked the 87 mental capacity to give informed consent, the next of kin was consulted in accordance with 88 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 and the Clinical Frailty Index [24, 25]. Review of the medical record accompanied an 92 93 informant interview that enquired about a previous diagnosis of dementia or MCI, and a history of prior cognitive function, but no new diagnoses of dementia were made at baseline 94 due to the difficulties of distinguishing dementia from delirium in the presence of the latter. 95 At 3 months, a follow-up assessment was undertaken in survivors, at the patient's own home 96 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

for delirium. If no delirium was present a standardised history and examination, including the 99

Addenbrooke's Cognitive Examination III (ACEIII) [26], was performed to establish the 100

presence or absence of dementia or mild cognitive impairment before the onset of the 101

103

delirium. Dementia and subtype was diagnosed using the DSM-IV-TR criteria [27]: (1) the 102

development of multiple cognitive deficits, including memory impairment, and (2) the impairment is sufficiently severe to cause impairment in occupational or social function. MCI 104

105 was diagnosed using the current consensus definition [28]: (1) the person is neither normal nor demented, (2) there is evidence of cognitive decline, and (3) that activities of daily living
are preserved and complex instrumental functions are either intact or minimally impaired.

The final diagnosis was made synthesising all available information in relation to the 6 month 108period before delirium hospitalisation, to make the diagnosis of either dementia or MCI at the 109 index admission. The symptoms of cognitive and functional decline had to have been present 110 for at least 6 months prior to the admission with delirium, as indicated by DSM-IV. It is not 111 possible to diagnose DSM-IV dementia in the presence of delirium so follow-up at three 112 113 months was chosen as the best balance to allow recovery from delirium and ensuring an accurate and near-contemporaneous diagnosis of dementia at the index admission. 114 115 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% confidence interval calculated. Differences between common clinical variables were 117 analysed, using the independent t-test, Kruskall-Wallis test or chi-squared test depending on 118 119 the normality of the variables and whether the variables were continuous or categorical. Odds ratios to predict the risk of having previously undiagnosed dementia were calculated 120 using univariate binary logistic regression. 121

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

124

125

126 Ethics, consent and permissions

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

130

131 **Results**

- 132 Of 1668 available older people admitted to hospital, 1327 were screened for delirium
- 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-

- 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
- 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 $2 \cdot 0$ vs $0 \cdot 0$, p=0.002) and frailty (median clinical frailty scale $5 \cdot 5$ vs $4 \cdot 0$,
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/ .

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170 Discussion

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

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

This study adds to prior reports finding that unrecognised cognitive impairment is common 177 178 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 impairment patients presenting with delirium. Two studies report the prevalence of 181 182 unrecognised cognitive impairment. In a study measuring drug metabolism in older patients with delirium, 'probable dementia' was recorded using a validated informant questionnaire 183 (Informant Questionnaire of Cognitive Decline in the Elderly, IQCODE) and informant 184 185 interview [15]. The assessment was carried out at the time of admission and 63/105 patients with delirium had probable dementia. Of those 37/105 (35%) had no prior diagnosis. A 186 187 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 diagnosis of dementia was recorded in medical notes [18]. Here the IQCODE administered 189 over the telephone was used to classify previous cognitive impairment. 190

The ascertainment at three months of pre-delirium dementia and MCI used standardised diagnostic processes which included the assessment of cognition at that point, and hence post-delirium cognitive impairment could potentially have led to an over-estimation of the number of cases of prior dementia or prior MCI in borderline cases. We judge this risk to be small, as the amount of post delirium cognitive impairment is small, and the diagnoses of prior MCI and prior dementia rarely relied solely upon the cognitive assessment made at 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 age or sex of those who were and were not recruited, so this is unlikely to have caused a 200 201 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 undiagnosed cognitive impairment is that, not only is delirium an important diagnosis to 208 make in older patients admitted to hospital [31], it also presents a strong opportunity to 209 210 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 of those who would benefit from pharmacological therapy [35]. Patients could then be 214 215 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 National Dementia Strategy[36] and the Prime Minister's dementia challenge[37], and 218 219 similar activities are also occurring worldwide. Routine follow up of patients who have presented with delirium could therefore be of value - to identify those with persisting 220 221 delirium as well as to identify previously unrecognised dementia and mild cognitive 222 impairment.

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

Further work is now required to develop follow-up procedures to identify unrecognised dementia, and to evaluate their cost effectiveness. Although screening tools for dementia in the acute hospital setting exist **[38]** future work should concentrate on developing optimised tools to identify dementia and MCI accurately in people with delirium, as well as evaluating 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 and long-term health outcomes, yet it is currently under diagnosed. Our findings confirm that 233 234 older people in hospital with delirium are a high-risk group for undiagnosed cognitive impairment (dementia and MCI). Delirium is therefore a target condition to screen or case-235 find for dementia in general hospitals. However, improved identification in hospitals and 236 validated methods of evaluation and follow-up of older people with delirium in hospitals are 237 needed. Practitioners should consider adopting informant interviews and other methods in 238 239 detecting possible dementia in older acute hospital patients with delirium.

240

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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
- 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 Kruskall-Wallis test as data not normally distributed, NS=not significant, *=statistically significant.

	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	Difference
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*

Cognitive impairment at 3 months

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

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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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