Journal of the American Medical Directors Association

Understanding factors associated with psychomotor subtypes of delirium in older inpatients with dementia

--Manuscript Draft--

Manuscript Number:	JAMDA-D-19-00303R3
Article Type:	Original Study
Keywords:	motor subtypes of delirium; dementia; elderly
Corresponding Author:	Alessandro Morandi, MD, MPH Fondazione Teresa Camplani Cremona, Cremona ITALY
First Author:	Alessandro Morandi, MD, MPH
Order of Authors:	Alessandro Morandi, MD, MPH
	Antonella Zambon
	Simona Di Santo
	Andrea Mazzone
	Antonio Cherubini
	Enrico Mossello
	Mario Bo
	Alessandra Marengoni
	Giuseppe Bellelli
Abstract:	Objectives: Few studies have analyzed factors associated with delirium subtypes. In this study we investigate factors associated with subtypes of delirium only in patients with dementia to provide insights on the possible prevention and treatments. Design: This is a cross-sectional study nested in the "Delirium Day" study, a nationwide Italian point-prevalence study. Setting and participants: Older patients admitted to 205 acute and 92 rehabilitation hospital wards. Measures: Delirium was evaluated with the 4-AT and the motor subtypes with the Delirium Motor Subtype Scale. Dementia was defined by the presence of a documented diagnosis in the medical records and/or prescription of Acetylcholinesterase inhibitors or memantine prior to admission. Results: Out of 1057 patients with dementia, 35% had delirium with 25.6% hyperactive, 33.1% hypoactive, 34.5% mixed, and 6.7% non-motor subtype. There were higher odds of having venous catheters in the hypoactive (OR 1.82, 95% CI: 1.18-2.81) and mixed type of delirium (OR 2.23, CI: 1.43-3.46), while higher odds of urinary catheters in the hypoactive (OR 2.91, CI: 1.92-4.39), hyperactive (OR 1.99, CI: 1.23-3.21) and mixed types of delirium (OR 2.05, CI: 1.36-3.07). We found higher odds of antipsychotics both in the hyperactive (OR 2.87, CI: 1.81-4.54) and mixed subtype (OR 1.84, CI: 1.24-2.75), while higher odds of antibiotics was present only in the mixed subtype (OR 1.91, CI 1.26-2.87). Conclusions and implications: In patients with dementia the mixed delirium subtype is the most prevalent followed by the hypoactive, hyperactive, and non-motor subtype. Motor subtypes of delirium may be triggered by clinical factors, including the use of venous and urinary catheters, and the use of antipsychotics. Future studies are necessary to provide further insights on the possible pathophysiology of delirium in patients with dementia and to address the optimization of the management of potential risk factors.

October 8th 2019

Dear Editor,

We are pleased to resubmit our manuscript, "**Understanding factors associated with psychomotor subtypes of delirium in older inpatients with dementia**" for consideration for publication in the *Journal of the American Medical Directors Association*. We have responded to each query from the Reviewers and included these in a point-by-point response in the Response Letter to the Reviewers. We have shown the changes in the manuscript bold and underline.

February 15th, 2020

Dear Editor,

We thank the Editor and the Reviewer for the excellent critiques of our manuscript titled, "***Understanding factors associated with psychomotor subtypes of delirium in older inpatients with dementia***" submitted to *JAMDA*. We have responded to each query from the Reviewers and included these in a point-by-point response below. For each critique, we reproduce each Reviewers' question followed by our response in a normal font and the actual changes in the manuscript shown in bold and underline.

Reviewer and editor comments:

1) Table 1. The previous comment was “Please include column headings as “N (%) or Median (IQR)” and omit them from the rows. Please remove the aberrant asterisk after feeding tubes and the quotation mark in the functional status footnote. Please use the types of footnote symbols as shown in the guidelines for authors.”
I do not see that these changes were made. More so, I point out that you have two separate footnotes – “Data are expressed as Median + Interquartile ranges (IQR) unless otherwise specified” and “Variables are expressed as n (%) or median (IQR).” Also, there is nothing that is "otherwise specified."
And, as you correct the footnotes as above, please notice that it seems (1) you are currently using a single asterisk for two separate pieces of information; and (2) the double asterisks next to feeding tubes seems incorrect.

RESPONSE: we have corrected Table 1 as suggested.

2) Title page: Correct the superscript attributions (v follows h); also, a location of v is not provided.

RESPONSE: we have modified the attributions.

Understanding factors associated with psychomotor subtypes of delirium in older inpatients with dementia

Alessandro Morandi MD, MPH,[a] Antonella Zambon, PhD,[b] Simona G Di Santo, MS[c], Andrea Mazzone, MD,[d] Antonio Cherubini, MD, PhD [e], Enrico Mossello, MD, PhD,[f,] Mario Bo, MD, PhD, [g,] Alessandra Marengoni, MD, PhD [h], Giuseppe Bellelli, MD,[,c,iv] on behalf of the Italian Study Group on Delirium (ISGoD)

[a] Department of Rehabilitation and Aged Care "Fondazione Camplani" Hospital, Cremona, Italy, [b] School of Medicine and Surgery, University of Milano-Bicocca; [c]Department of Clinical and Behavioral Neurology, Neuropsychiatry Laboratory, IRCCS Foundation S Lucia, Roma, Italy; [d] Redaelli Geriatric Institute, Milan, Italy; [e] Geriatria, Accettazione geriatrica, Centro di ricerca per l'invecchiamento, IRCCS-INRCA, Ancona, Italy; [f] Research Unit of Medicine of Ageing, Department of Experimental and Clinical Medicine, University of Florence and Azienda Ospedaliero-Universitaria Careggi, Firenze, Italy; [g] Section of Geriatrics, Città della Salute e della Scienza – Molinette, Torino, Italy, [h] Department of Clinical and Experimental Sciences, University of Brescia, Italy; Geriatric Unit, S. Gerardo Hospital, Monza, Italy; [iv]

Abstract: 293

Text: 2791

References: 42

Tables: 1

Figures: 1

Running title: subtypes of delirium in patients with dementia**.**

Key words: motor subtypes of delirium; dementia; elderly;

Brief Summary: Mixed delirium is the most prevalent subtype in people with dementia. Motor subtypes of delirium may be triggered by clinical factors, including the use of venous and urinary catheters, and the use of antipsychotics.

Corresponding author:

Alessandro Morandi, MD, MPH

Rehabilitation Hospital Ancelle di Cremona (Italy)

Geriatric Research Group (Italy)

Center for Quality of Ageing (Nashville, TN, USA)

ICU delirium group (Nashville, TN, USA)

Tel: +39 03725357753

E-mail: morandi.alessandro@gmail.com

alessandro.morandi@unibs.it

Understanding factors associated with psychomotor subtypes of delirium in older inpatients with dementia

Alessandro Morandi MD, MPH,[a] Antonella Zambon, PhD,[b] Simona G Di Santo, MS[c], Andrea Mazzone, MD,[d] Antonio Cherubini, MD, PhD [e], Enrico Mossello, MD, PhD,[f,] Mario Bo, MD, PhD, [g,] Alessandra Marengoni, MD, PhD [h], Giuseppe Bellelli, MD,[,c,i] on behalf of the Italian Study Group on Delirium (ISGoD)

[a] Department of Rehabilitation and Aged Care "Fondazione Camplani" Hospital, Cremona, Italy, [b] School of Medicine and Surgery, University of Milano-Bicocca; [c]Department of Clinical and Behavioral Neurology, Neuropsychiatry Laboratory, IRCCS Foundation S Lucia, Roma, Italy; [d] Redaelli Geriatric Institute, Milan, Italy; [e] Geriatria, Accettazione geriatrica, Centro di ricerca per l'invecchiamento, IRCCS-INRCA, Ancona, Italy; [f] Research Unit of Medicine of Ageing, Department of Experimental and Clinical Medicine, University of Florence and Azienda Ospedaliero-Universitaria Careggi, Firenze, Italy; [g] Section of Geriatrics, Città della Salute e della Scienza – Molinette, Torino, Italy, [h] Department of Clinical and Experimental Sciences, University of Brescia, Italy; Geriatric Unit, S. Gerardo Hospital, Monza, Italy; [i]

Abstract: 293

Text: 2791

References: 42

Tables: 1

Figures: 1

Running title: subtypes of delirium in patients with dementia**.**

Key words: motor subtypes of delirium; dementia; elderly;

Brief Summary: Mixed delirium is the most prevalent subtype in people with dementia. Motor subtypes of delirium may be triggered by clinical factors, including the use of venous and urinary catheters, and the use of antipsychotics.

Corresponding author:

Alessandro Morandi, MD, MPH

Rehabilitation Hospital Ancelle di Cremona (Italy)

Geriatric Research Group (Italy)

Center for Quality of Ageing (Nashville, TN, USA)

ICU delirium group (Nashville, TN, USA)

Tel: +39 03725357753

E-mail: morandi.alessandro@gmail.com

alessandro.morandi@unibs.it

ABSTRACT

Objectives: Few studies have analyzed factors associated with delirium subtypes. In this study we investigate factors associated with subtypes of delirium only in patients with dementia to provide insights on the possible prevention and treatments.

Design: This is a cross-sectional study nested in the "Delirium Day" study, a nationwide Italian point-prevalence study.

Setting and participants: Older patients admitted to 205 acute and 92 rehabilitation hospital wards.

Measures: Delirium was evaluated with the 4-AT and the motor subtypes with the Delirium Motor Subtype Scale. Dementia was defined by the presence of a documented diagnosis in the medical records and/or prescription of Acetylcholinesterase inhibitors or memantine prior to admission.

Results: Out of 1057 patients with dementia, 35% had delirium with 25.6% hyperactive, 33.1% hypoactive, 34.5% mixed, and 6.7% non-motor subtype. There were higher odds of having venous catheters in the hypoactive (OR 1.82, 95% CI: 1.18-2.81) and mixed type of delirium (OR 2.23, CI: 1.43-3.46), while higher odds of urinary catheters in the hypoactive (OR 2.91, CI: 1.92-4.39), hyperactive (OR 1.99, CI: 1.23-3.21) and mixed types of delirium (OR 2.05, CI: 1.36-3.07). We found higher odds of antipsychotics both in the hyperactive (OR 2.87, CI: 1.81-4.54) and mixed subtype (OR 1.84, CI: 1.24-2.75), while higher odds of antibiotics was present only in the mixed subtype (OR 1.91, CI 1.26-2.87).

Conclusions and implications: In patients with dementia the mixed delirium subtype is the most prevalent followed by the hypoactive, hyperactive, and non-motor subtype. Motor subtypes of delirium may be triggered by clinical factors, including the use of venous and urinary catheters, and the use of antipsychotics. Future studies are necessary to provide further insights on the possible pathophysiology of delirium in patients with dementia and to address the optimization of the management of potential risk factors.

INTRODUCTION

Several studies have shown a strong association between delirium and dementia[1], being that delirium is a risk factor for both dementia onset and worsening of a pre-existing dementia.[2] The coexistence of delirium and dementia is referred to as delirium superimposed on dementia (DSD) and its prevalence in community populations and hospitalized patients ranges from 22% to 89%.[3] This prevalence is probably underestimated given the challenge of diagnosing delirium, especially in late dementia.[4-6] The occurrence of DSD is associated with significant adverse outcomes including functional and cognitive decline, increased mortality and institutionalization. [3, 7, 8]

An important and neglected issue in DSD is the psychomotor manifestation. When delirium is diagnosed, it can be classified in four psychomotor subtypes: hyperactive, hypoactive, mixed and non hyperactive-hypoactive subtype.[9] These different manifestations often increase the complexity of delirium diagnosis especially in the context of dementia. Few studies have investigated the prevalence of different delirium subtypes and their association with worse outcomes but not specifically in patients with dementia.[10] The hypoactive form seems to be associated with worse outcomes in terms of mortality compared to the hyperactive and mixed subtypes. [11, 12 13] Further complexity in the interpretation of delirium subtypes is related to the identification of specific risk factors, which could provide key information for delirium prevention.[14] Risk factor profiles might be different in people with dementia, who may have aberrant motor behavior irrespectively of delirium. Finally, medical treatment can vary in different delirium subtypes; to date, the hyperactive and mixed delirium have been associated with a higher use of antipsychotics.[15, 16] To the best of our knowledge, few studies were carried out to investigate delirium motor subtypes in patients with dementia, their prevalence and associated factors. A previous multicenter study showed that dementia was associated with hyperactive, hypoactive and mixed type of delirium in 275 elderly patients of whom 59% had dementia.[17] In another study evaluating a large cohort of acutely ill elderly patients admitted to geriatric wards, dementia prevalence was slightly higher in the hypoactive delirium subtype, and specifically severe dementia.[18]

Given the high worldwide prevalence of dementia and its projected increase by 2050, it is imperative to increase awareness of these two clinical conditions in daily clinical practice. [19-20, 21]

In 2015 and 2016, a point-prevalence study named "Delirium day" was conducted in Italy to evaluate the prevalence of delirium among patients admitted to acute hospital and rehabilitation wards.[8, 22] As part of the study protocol the presence of dementia and delirium subtypes classification were recorded. In the current study we aim to investigate the prevalence of delirium subtypes and the associated factors in patients with dementia admitted to acute hospital wards and rehabilitation units in Italy.

METHODS

This is a cross-sectional study nested in the "Delirium Day" study. The aims of the "Delirium Day" were previously described.[22] The "Delirium Day" study is a nationwide point-prevalence study conducted in Italy evaluating the prevalence of delirium on an index day; two editions (2015 and 2016) have been carried out up to now. A total of 205 acute and 92 rehabilitation hospital wards were involved in the study. The Ethics Committee of the IRCCS Fondazione Santa Lucia, Roma (CE/PROG.500) approved the 2015 study protocol while the Ethical Committee of the Monza Brianza Province approved the 2016 study protocol (Prot n 18904, 1/06/2016). Informed consent was obtained from all participants. When participants were not capable to provide informed consent because of delirium or dementia and a legal representative was not available, we obtained the informed consent from their next of kin.

Study protocol

Delirium assessment

Delirium was assessed using the 4AT that was administered by the attending physician at each hospital ward as part of the study protocol on the index day.[23] The 4AT is relatively novel tool for the assessment of delirium validated against the Diagnostic and Statistical Manual for Mental Disorders-IV (DSM-IV) criteria in acute and rehabilitation hospital wards, with a sensitivity of 89.7% and specificity of 84.1% for delirium detection. [23] In the subgroup of patients with dementia the sensitivity was 94% and the specificity 64.9%.[23] The area under the receiver operating characteristic curves (ROC) for delirium diagnosis was 0.93 in the entire studied population, 0.92 in patients without dementia, and 0.89 in patients with dementia.[23] The 4AT has shown good accuracy in other settings including palliative care and emergency departments.[24, 25] A recent large multicenter study of older acute medical inpatients showed the 4AT had a sensitivity of 76% and a specificity of 94%, with a ROC curve of 0.90.[26] Important characteristics of the 4AT are its brevity (generally < 2 minutes) and the fact that does not require a specific training for its use making this tool appealing for large multicentre studies. A 4AT score of 0 indicates the absence of dementia or

delirium, a score between 1 and 3 suggests a possible cognitive impairment but not delirium, while a score ≥ 4 is strongly suggestive of delirium.

Delirium motor subtype evaluation

When the 4AT score was 4 or above, then the attending physician evaluated the motor subtypes of delirium with the Delirium Motor Subtype Scale (DMSS). The DMSS is a 11-item scale items, [27, 28] that can be rated by any healthcare professional. Each item assesses specific patient's behaviours occurring in the previous 24 h or more (4 hyperactive and 7 hypoactive features). Each item is scored as positive or negative when at least 2 symptoms are present from either the hyperactive or hypoactive list to meet subtype criteria. Patients meeting both hyperactive and hypoactive criteria classified in the mixed subtype while those meeting neither criterion were classified as non-motor subtype.

Dementia evaluation

Dementia was defined by the presence of a documented diagnosis in the medical records and/or prescription of Acetylcholinesterase inhibitors (AChE-I) or memantine prior to admission. The documentation used to ascertain the presence of a previous dementia was gathered from the hospital medical records and from the documentation delivered by the caregivers. The information regarding the drugs prescription was collected from the medical history based on the patients/caregivers interview, medical records and availability of the actual drugs boxes.

Clinical assessment

Demographics and the date of hospital admission were recorded. The presence of comorbidity was assessed using the Charlson Index,[29] excluding dementia from the total score. Functional status before admission was evaluated using the Katz Activities of Daily Living (ADL) scale with a score ranging from 0 (patient dependent) to 6 (patient completely independent).[30] A Katz score of 4 or above is indicative of moderate impairment. [30] The presence of specific drugs (i.e., anti-hypertensives, antiplatelets, antiarrhythmics, statins/lipid lowering drugs, antidiabetics, antiulcers, antibiotics, benzodiazepines, antipsychotics, antidepressants, antiepileptics and AChE-I/memantine)

received by each patient on the index day was recorded. We also collected, on the index day, information on the use of feeding tubes [i.e., nasogastric tube (NT) or percutaneous endoscopic gastrostomy (PEG)], peripheral venous catheters, urinary catheters and physical restraints (i.e., vests, wrists, inguinal restraints and bedrails).

Statistical analysis

Continuous variable were reported as median and interquartile range and categorical variables as count and relative frequency. Comparisons between psychomotor subtypes of delirium were made with Kruskal-Wallis tests for non-continuous variables and chi-square or Fisher exact test for categorical data. A generalized logit model was used to model relationships between the polytomous response variable without an ordered structure (psychomotor subtype of delirium) and the set of regressor variables (clinical and socio-demographic variables listed in Table 1). In brief, the generalized logit model consists of a combination of several binary logits estimated simultaneously considering the same reference category for the response variable. The exponential of the estimated coefficient for each response category is reported as odds ratio and corresponding 95% confidence intervals are reported. To select a parsimonious model we applied a stepwise approach to select variables. We considered a $p = 0.15$ as the critical value for entering and remaining in the model.

Finally, in the model selected by the stepwise approach, we performed all head-to-head comparisons for testing linear hypotheses of the parameters. Specifically, we tested the hypothesis that the logOR for the i-th level of the response variable respect to the reference category was equal to those of the j-th level (with j>i). This test is a Wald test, which is based on the asymptotic normality of the parameter estimators, and follows an asymptotic χ^2 distribution.

For all hypothesis tests, statistical significance was set at a P value of less than 0.05. All analyses were performed by the Statistical Analysis System Software (version 9.4; SAS Institute, Cary, North Carolina, USA).

RESULTS

Of 4514 patients enrolled in 2015 and 2016 (1856 in 2015 and 2658 in 2016), dementia was recognized as already present before the index hospitalization in 1057 (23%) (441 in 2015 and 616 in 2016). A total of 1057 patients with dementia were included in the study, 969 admitted to acute hospital and 88 to rehabilitation wards. Delirium overall prevalence was 35% (N= 371) with the following categorization of motor subtypes: 25.6% (N=95) hyperactive, 33.1% (N=123) hypoactive, 34.5% (N=128) mixed, and 6.7% (N=25) non-motor subtype of delirium. In the acute settings the prevalence of delirium was 36% (N=357), with 25% (N=90) hyperactive, 34% (N=121) hypoactive, 34% (N=121) mixed, and 7% (N=25) non-motor subtype. In the rehabilitation settings the prevalence of delirium was 16% (N=14), with 40% (N=5) hyperactive, 10% (N=2) hypoactive, 50% (N=7) mixed, and 0% non-motor subtype.

Table 1 shows the characteristics of patients with and without delirium according to delirium subtypes. Patients with hyperactive delirium had a higher impairment in the ADLs at baseline (19%). Overall, the median number of drugs was greater in patients with mixed delirium. Among the specific drugs we found a higher prevalence of antiplatelets drugs in the mixed delirium (66.4%), statins/lipid-lowering drugs in the hyperactive delirium (12.6%), antibiotics in the mixed delirium (56.3%), and antipsychotics in the hyperactive delirium (64.2%). Finally, venous catheters were more prevalent in the mixed delirium (73.4%), urinary catheters in the hypoactive delirium (57.7%) and physical restraints in the hyperactive delirium (24.2%).

In the multivariable model (Figure 2) there was no difference in the comparison between the non-motor subtype of delirium vs. absence of delirium. There were higher odds of having venous catheters in the hypoactive (OR 1.82, 95% CI: 1.18-2.81) and mixed type of delirium (OR 2.23, CI: 1.43-3.46), while higher odds of urinary catheters were present for the hypoactive (OR 2.91, CI: 1.92-4.39), hyperactive (OR 1.99, CI: 1.23-3.21) and mixed types of delirium (OR 2.05, CI: 1.36-3.07). We found higher odds of antipsychotics both in the hyperactive (OR 2.87, CI: 1.81-4.54) and mixed subtype (OR 1.84, CI: 1.24-2.75), with higher odds of antibiotics only in the mixed

subtype (OR 1.91, CI 1.26-2.87). Finally in the head-to-head comparisons of the different variables included in the model of Figure 2 and the four delirium subtypes we found that there was no difference in the association between venous and urinary catheters. Physical restraints were significantly different when comparing the non-motor subtype and the hyperactive subtype **(χ2; p=.05**) and the hypoactive and the hyperactive subtypes **(χ2; p=.02**). There was a significant difference in the ADLs at baseline between the mixed and the hyperactive delirium subtype **(χ2; p=.01**). The association between antibiotics and delirium was different when comparing the hypoactive and the hyperactive delirium subtype **(χ2; p=.03**) and the mixed and hyperactive subtypes **(χ2; p=.01**). Antibiotics were significantly different in the hypoactive and mixed delirium subtypes **(χ2; p=.01**), and in the hypoactive and hyperactive subtypes **(χ2; p<.01).** Antiplatelets drugs were different in the hypoactive and mixed delirium subtypes **(χ2; p=.03**).

DISCUSSION

Findings from this large multicenter study showed that delirium is highly prevalent in older hospitalized patients with dementia. The most frequent delirium subtype was the mixed followed by the hypoactive, hyperactive, and non-motor subtype. Urinary catheters were significantly associated with all delirium subtypes, while the presence of venous catheter was associated only with the hypoactive and the mixed delirium subtype. Antipsychotics prescriptions were associated with both mixed and hyperactive delirium, while antibiotics only with the mixed subtype.

To the best of our knowledge, this is the first multicenter study that specifically investigated factors potentially associated with different delirium subtypes in patients with dementia, though the cross sectional nature of the study limits our ability to draw any causal-effect association.

In previous investigations the hypoactive delirium subtype has been shown to be the most common. However, there might be some differences in delirium subtype distribution if we consider the incidence and not the prevalence. For instance, it has been shown that in orthogeriatric patients the most frequent incident delirium subtypes are the hyperactive and the mixed.[31] In the same study, dementia was more prevalent in the mixed delirium subtype followed by the hyperactive and the hypoactive delirium.[31] In a large single center prospective cohort of 1409 elderly patients admitted to an acute geriatric ward, hypoactive delirium was the most prevalent followed by mixed and hyperactive delirium.[18] In the same study, about half of the patients had dementia but the authors did not report the prevalence of delirium according to the presence and severity of dementia. It should, however, be noticed that dementia prevalence was slightly higher in the hypoactive delirium subtype. In a previous study from our research group, dementia was equally associated with the three delirium subtypes (hypoactive, hyperactive, mixed).[17] One single center study of 37 older patients admitted for hip fracture found the hyperactive delirium being the most prevalent (47%), followed by the hypoactive (26%) and mixed subtype (26%).[32] In the same study, dementia was more prevalent in the hyperactive subtype (44%) followed by the hypoactive (33%) and mixed subtype (22%). Finally, in a recent investigation on 352 older patients with multimorbidity admitted

to a subacute care unit, hyperactive delirium was the most frequent (40%), followed by the mixed (31%) and hypoactive (31%) subtypes.[33] Dementia was more prevalent in the hypoactive delirium (87%) followed by the hyperactive (70%) and mixed (68%) subtypes.

Few studies tried to investigate the factors associated with different delirium subtypes but none has specifically analyzed patients with DSD. Studies on delirium subtypes have been hindered by the tendency to consider dementia and delirium as caused by a single etiology rather than multiple interacting etiologies.[10] Avelino-Silva and colleagues found that older age, and malnutrition were associated with the mixed delirium subtype, greater ADL impairment and malnutrition with both mixed and hypoactive delirium, while signs of possible infections (i.e. leucocytes count and elevated C Reactive Protein) were similar in the three subtypes delirium groups.[18] Other studies focused on delirium subtypes but not on the presence of dementia. In a small study of 49 older patients with delirium, three possible etiological categories were described: an anticholinergic group, a group with drug-related causes, and another group including metabolic and infectious illnesses. Drug-related causes showed the highest severity score for delirium, and the anticholinergic causes the lowest. The authors concluded that the study supports the possibility that the etiological cause may influence the different symptom patterns.[34]

An emerging literature supported the phenomenon of exaggerated Central Nervous System (CNS) effects of systemic inflammation in elderly people with dementia.[35] The explanation for this phenomenon appears to lie in the 'priming' of microglial cells. Microglial cells are primed in older patients with dementia leading to a greater pro-inflammatory response subsequent to an infection.[35] It has been described a greater prevalence of hypoactive delirium subtype in aged mice with dementia after a challenge with infectious trigger.[35] The use of antibiotics is an indirect sign of the presence of an infection. Our findings of the association of a possible infection with a mixed delirium subtype are in line with a previous investigation. [36] However, one might expect that in patients with infections and, especially severe infections, the hypoactive subtype might be more prevalent, as previously described in a cohort of palliative care patients.[15] Other studies have

228 reported that patients with sepsis are more likely to have hypoactive behaviors, including weakness,
229 and inability to concentrate.[37] However, further studies are necessary to investigate this etiological
230 mechanism in the subgroup of patients with dementia.

231 Bo and colleagues in a large cohort of 1867 patients with an overall 60% prevalence of
232 dementia patients found that urinary catheter was associated with an acute change and a fluctuating
233 course, a possible expression of a mixed delirium subtype.[38] In our study, we found that urinary
234 catheter was associated with all three delirium subtypes. It should be noticed that the prevalence of
235 urinary catheter in patients with delirium compared to patients without delirium was almost double.
236 These findings combined with previous publications support the indication of the Hospital Elder
237 Life Program (HELP) protocol to avoid unnecessary catheterization and to remove it as soon as
238 possible.[39]

239 On the other hand, the association between venous catheters with hypoactive and mixed
240 delirium is not clear. In our study, venous catheters were more prevalent in the hypoactive and
241 mixed delirium subtypes. A previous study of 73 patients with hypoactive or mixed postoperative
242 delirium showed that 23.3% had at least 1 delirium-related adverse event including inadvertent tube
243 or line removals.[40] The higher association we found in our investigation might be related to the need
244 to administrate drugs, which might lead to a hypoactive or mixed delirium subtypes. Other
245 explanations might be that patients with hypoactive delirium are sicker and require fluid
246 administration also related to the low ability to drink and eat. Previous studies showed that patients
247 with hypoactive delirium were sicker on admission with longer hospital stays and suffered from a
248 more persistent delirium.[41]

249 Finally, previous investigations have shown atypical antipsychotics to be more prevalent in
250 older patients with hyperactive and mixed delirium regardless of the presence of dementia.[20] We
251 also found that antipsychotics were more prevalent in the mixed and hyperactive delirium.
252 Antipsychotics were prescribed to 60% of patients with hyperactive delirium, 50% with mixed
253 delirium and 30% with hypoactive delirium. Though we cannot rule out causality, it is likely that

these patients receive more antipsychotics because of agitation and aggressive behaviors. However, it might be that these patients were already receiving antipsychotics because of behavioral disorders associated with the pre-existing dementia. These are relevant information given the lack of benefits of antipsychotics for the prevention and treatment of delirium as well as their deleterious effect in patients with dementia. [41-43] A recent seminal trial in critical care patients did not show any effect of antipsychotics on both hyperactive and hypoactive delirium not supporting their use in the treatment of delirium.[42, 44] Longitudinal studies are warranted to further elucidate the association between delirium subtypes and antipsychotics prescription.

Our study has strengths along with limitations. This is the first real-world multicenter study evaluating delirium subtypes in a large cohort of older patients with dementia. We used validated tools (i.e., 4AT and the DMSS) both to assess for the presence of delirium and to categorize the subtypes of delirium. A possible limitation of the use of the DMSS is that an Italian validation of this tool is not currently available. However, the DMSS does not require to ask specific questions to the patients but it is scored according to the evaluation of the patient's behaviours by the health care providers thus reducing the bias of using a tool not specifically validated in an Italian population.

The main limitation of the study relies in the cross sectional design; thus, we cannot establish causality between factors associated with different delirium subtypes. We were also limited in the investigation of the non-motor delirium subtype given the low number of patients in this subgroup. Future prospective studies are needed to further investigate risk factors and to establish interventions to reduce the impact of these factors on the development of delirium in this frail population. Additionally, future larger studies are needed to explore delirium subtypes across different types of dementia: Alzheimer Disease, vascular disease, Lewy Body dementia, and Parkinson Disease. It will be also informative to further study psychomotor activities during hospitalization in patients with dementia, with or without delirium. Finally, the ascertainment of dementia in our investigation might have underestimated the true prevalence of this condition.

However, we found a 23% prevalence of dementia in the population included in our study, which is in line with a previous large investigation on dementia in elderly patients admitted to acute hospital showed a prevalence of dementia ranging from 23% to 48% in patients with 70-79 years to 80-89 years respectively.[42]

CONCLUSION AND IMPLICATIONS

Delirium is highly prevalent in patients with dementia; the mixed subtype is the most prevalent manifestation followed by the hypoactive, hyperactive, and non-motor subtype. Urinary catheters were significantly associated with all delirium subtypes, while the presence of venous catheter only with the hypoactive and mixed delirium subtypes. Antipsychotics were associated with both mixed and hyperactive delirium, while antibiotics only with the mixed subtype. Though we cannot assess causality due to the cross-sectional nature of the study, these findings suggest that clinicians should carefully review the need of urinary catheters in older hospitalized patients since we found an association with all delirium subtypes. Additionally, further attention should be given to antipsychotic prescription in patients with dementia either if they are prescribed for behavioral disturbances or hyperactive delirium. In fact, it has been widely shown that there is no current evidence of their use to treat delirium besides for the presence of distressing psychotic features, as indicated in the most recent guidelines.[43] Future longitudinal studies are necessary to provide further insights on the possible pathophysiology of delirium in patients with dementia and to address the optimization of potential risk factors such as medications (i.e. antipsychotics) and the use of urinary catheters

Acknowledgments: we acknowledge for their collaboration in data collection all the participants of the Delirium Day 2015-2016. The full list of the investigators of investigators and members of the Italian Study Group on Delirium (ISGoD) is included in the Appendix.

Conflict of interests: The authors do not report any financial or personal conflict of interest.

Funding: This research did not receive any funding from agencies in the public, commercial, or not-for-profit sectors.

References

1. Davis DH, Muniz-Terrera G, Keage HA, Stephan BC, Fleming J, Ince PG, Matthews FE, Cunningham C, Ely EW, MacLullich AM and Brayne C. Association of Delirium With Cognitive Decline in Late Life: A Neuropathologic Study of 3 Population-Based Cohort Studies. *JAMA psychiatry*. 2017;74:244-251.
2. Davis DH, Skelly DT, Murray C, Hennessy E, Bowen J, Norton S, Brayne C, Rahkonen T, Sulkava R, Sanderson DJ, Rawlins JN, Bannerman DM, MacLullich AM and Cunningham C. Worsening cognitive impairment and neurodegenerative pathology progressively increase risk for delirium. *The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry*. 2015;23:403-15.
3. Fick DM, Agostini JV and Inouye SK. Delirium superimposed on dementia: a systematic review. *Journal of the American Geriatrics Society*. 2002;50:1723-32.
4. Morandi A, Han JH, Meagher D, Vasilevskis E, Cerejeira J, Hasemann W, MacLullich AM, Annoni G, Trabucchi M and Bellelli G. Detecting Delirium Superimposed on Dementia: Evaluation of the Diagnostic Performance of the Richmond Agitation and Sedation Scale. *Journal of the American Medical Directors Association*. 2016;17:828-33.
5. Morandi A, Davis D, Bellelli G, Arora RC, Caplan GA, Kamholz B, Kolanowski A, Fick DM, Kreisel S, MacLullich A, Meagher D, Neufeld K, Pandharipande PP, Richardson S, Slooter AJ, Taylor JP, Thomas C, Tieges Z, Teodorczuk A, Voyer P and Rudolph JL. The Diagnosis of Delirium Superimposed on Dementia: An Emerging Challenge. *Journal of the American Medical Directors Association*. 2017;18:12-18.
6. Bellelli G, Speciale S, Morghen S, Torpilliesi T, Turco R and Trabucchi M. Are fluctuations in motor performance a diagnostic sign of delirium? *Journal of the American Medical Directors Association*. 2011;12:578-83.
7. Morandi A, Davis D, Fick DM, Turco R, Boustani M, Lucchi E, Guerini F, Morghen S, Torpilliesi T, Gentile S, Maclullich AM, Trabucchi M and Bellelli G. Delirium superimposed on dementia strongly predicts worse outcomes in older rehabilitation inpatients. *Journal of the American Medical Directors Association*. 2014;15:349-54.
8. Morandi A, Di Santo SG, Zambon A, Mazzone A, Cherubini A, Mossello E, Bo M, Marengoni A, Bianchetti A, Cappa S, Fimognari F, Antonelli Incalzi R, Gareri P, Perticone F, Campanini M, Penco I, Montorsi M, Di Bari M, Trabucchi M and Bellelli G. Delirium, dementia and in-hospital mortality: the results from the Italian Delirium Day 2016, a national multicenter study. *The journals of gerontology Series A, Biological sciences and medical sciences*. 2018.
9. ZJ. L. *Delirium: acute confusional states.*: New York: Oxford University Press; 1990.
10. Meagher D. Motor subtypes of delirium: past, present and future. *International review of psychiatry*. 2009;21:59-73.
11. Yang FM, Marcantonio ER, Inouye SK, Kiely DK, Rudolph JL, Fearing MA and Jones RN. Phenomenological subtypes of delirium in older persons: patterns, prevalence, and prognosis. *Psychosomatics*. 2009;50:248-54.
12. Bellelli G, Speciale S, Barisione E and Trabucchi M. Delirium subtypes and 1-year mortality among elderly patients discharged from a post-acute rehabilitation facility. *The journals of gerontology Series A, Biological sciences and medical sciences*. 2007;62:1182-3.
13. Kiely DK, Jones RN, Bergmann MA and Marcantonio ER. Association between psychomotor activity delirium subtypes and mortality among newly admitted post-acute facility patients. *The journals of gerontology Series A, Biological sciences and medical sciences*. 2007;62:174-9.
14. Slor CJ, Adamis D, Jansen RW, Meagher DJ, Witlox J, Houdijk AP and de Jonghe JF. Delirium motor subtypes in elderly hip fracture patients: risk factors, outcomes and longitudinal stability. *Journal of psychosomatic research*. 2013;74:444-9.

15. Meagher DJ, Leonard M, Donnelly S, Conroy M, Adamis D and Trzepacz PT. A longitudinal study of motor subtypes in delirium: Relationship with other phenomenology, etiology, medication exposure and prognosis. *Journal of psychosomatic research*. 2011;71:395-403.
16. Meagher DJ, Leonard M, Donnelly S, Conroy M, Adamis D and Trzepacz PT. A longitudinal study of motor subtypes in delirium: frequency and stability during episodes. *Journal of psychosomatic research*. 2012;72:236-41.
17. Morandi A, Di Santo SG, Cherubini A, Mossello E, Meagher D, Mazzone A, Bianchetti A, Ferrara N, Ferrari A, Musicco M, Trabucchi M and Bellelli G. Clinical Features Associated with Delirium Motor Subtypes in Older Inpatients: Results of a Multicenter Study. *The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry*. 2017;25:1064-1071.
18. Avelino-Silva TJ, Campora F, Curiati JAE and Jacob-Filho W. Prognostic effects of delirium motor subtypes in hospitalized older adults: A prospective cohort study. *PloS one*. 2018;13:e0191092.
19. Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W and Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimer's & dementia : the journal of the Alzheimer's Association*. 2013;9:63-75 e2.
20. Bellelli G, Morandi A, Trabucchi M, Caironi G, Coen D, Fraticelli C, Paolillo C, Prevaldi C, Riccardi A, Cervellin G, Carabellese C, Putignano S, Maggi S, Cherubini A, Gnerre P, Fontanella A, Latronico N, Tommasino C, Corcione A, Ricevuti G, Ferrara N, De Filippi F, Ferrari A, Guarino M, Ruggieri MP, Modesti PA, Locatelli C, Hrelia P, Toscano MO, Bondi E, Tarasconi A, Ansaloni L and Perticone F. Italian intersociety consensus on prevention, diagnosis, and treatment of delirium in hospitalized older persons. *European Geriatric Medicine*. 2017;8:293-298.
21. Pozzi C, Lucchi E, Lanzoni A, Gentile S, Trabucchi M, Bellelli G and Morandi A. Preliminary Evidence of a Positive Effect of Occupational Therapy in Patients With Delirium Superimposed on Dementia. *Journal of the American Medical Directors Association*. 2017;18:1091-1092.
22. Bellelli G, Morandi A, Di Santo SG, Mazzone A, Cherubini A, Mossello E, Bo M, Bianchetti A, Rozzini R, Zanetti E, Musicco M, Ferrari A, Ferrara N and Trabucchi M. "Delirium Day": a nationwide point prevalence study of delirium in older hospitalized patients using an easy standardized diagnostic tool. *BMC medicine*. 2016;14:106.
23. Bellelli G, Morandi A, Davis DH, Mazzola P, Turco R, Gentile S, Ryan T, Cash H, Guerini F, Torpilliesi T, Del Santo F, Trabucchi M, Annoni G and MacLullich AM. Validation of the 4AT, a new instrument for rapid delirium screening: a study in 234 hospitalised older people. *Age and ageing*. 2014;43:496-502.
24. Baird L and Spiller JA. A quality improvement approach to cognitive assessment on hospice admission: could we use the 4AT or Short CAM? *BMJ open quality*. 2017;6:e000153.
25. O'Sullivan D, Brady N, Manning E, O'Shea E, O'Grady S, N OR and Timmons S. Validation of the 6-Item Cognitive Impairment Test and the 4AT test for combined delirium and dementia screening in older Emergency Department attendees. *Age and ageing*. 2018;47:61-68.
26. Shenkin SD, Fox C, Godfrey M, Siddiqi N, Goodacre S, Young J, Anand A, Gray A, Hanley J, MacRaild A, Steven J, Black PL, Tieges Z, Boyd J, Stephen J, Weir CJ and MacLullich AMJ. Delirium detection in older acute medical inpatients: a multicentre prospective comparative diagnostic test accuracy study of the 4AT and the confusion assessment method. *BMC medicine*. 2019;17:138.
27. Meagher D, Moran M, Raju B, Leonard M, Donnelly S, Saunders J and Trzepacz P. A new data-based motor subtype schema for delirium. *The Journal of neuropsychiatry and clinical neurosciences*. 2008;20:185-93.
28. Godfrey A, Leonard M, Donnelly S, Conroy M, Olaighin G and Meagher D. Validating a new clinical subtyping scheme for delirium with electronic motion analysis. *Psychiatry research*. 2010;178:186-90.

29. Charlson ME, Pompei P, Ales KL and MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373-83.
30. Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. *J Am Geriatr Soc*. 1983;31:721-7.
31. Bellelli G, Carnevali L, Corsi M, Morandi A, Zambon A, Mazzola P, Galeazzi M, Bonfanti A, Massariello F, Szabo H, Oliveri G, Haas J, d'Oro LC and Annoni G. The impact of psychomotor subtypes and duration of delirium on 6-month mortality in hip-fractured elderly patients. *International journal of geriatric psychiatry*. 2018.
32. Santana Santos F, Wahlund LO, Varli F, Tadeu Velasco I and Eriksdotter Jonhagen M. Incidence, clinical features and subtypes of delirium in elderly patients treated for hip fractures. *Dementia and geriatric cognitive disorders*. 2005;20:231-7.
33. Gual N, Inzitari M, Carrizo G, Calle A, Udina C, Yuste A and Morandi A. Delirium Subtypes and Associated Characteristics in Older Patients With Exacerbation of Chronic Conditions. *The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry*. 2018;26:1204-1212.
34. Meagher DJ, O'Hanlon D, O'Mahony E, Casey PR and Trzepacz PT. Relationship between etiology and phenomenologic profile in delirium. *Journal of geriatric psychiatry and neurology*. 1998;11:146-9; discussion 157-8.
35. Cunningham C. Systemic inflammation and delirium: important co-factors in the progression of dementia. *Biochemical Society transactions*. 2011;39:945-53.
36. van Munster BC, Korevaar JC, Zwinderman AH, Levi M, Wiersinga WJ and De Rooij SE. Time-course of cytokines during delirium in elderly patients with hip fractures. *Journal of the American Geriatrics Society*. 2008;56:1704-9.
37. Dantzer R. Cytokine-induced sickness behaviour: a neuroimmune response to activation of innate immunity. *European journal of pharmacology*. 2004;500:399-411.
38. Bo M, Porrino P, Di Santo SG, Mazzone A, Cherubini A, Mossello E, Bianchetti A, Musicco M, Ferrari A, Ferrara N, Filippini C, Trabucchi M, Morandi A and Bellelli G. The association of indwelling urinary catheter with delirium in hospitalized patients and nursing home residents: an explorative analysis from the "Delirium Day 2015". *Aging clinical and experimental research*. 2018.
39. Yue J, Tabloski P, Dowal SL, Puelle MR, Nandan R and Inouye SK. NICE to HELP: operationalizing National Institute for Health and Clinical Excellence guidelines to improve clinical practice. *Journal of the American Geriatrics Society*. 2014;62:754-61.
40. Robinson TN, Raeburn CD, Tran ZV, Brenner LA and Moss M. Motor subtypes of postoperative delirium in older adults. *Archives of surgery*. 2011;146:295-300.
41. Liptzin B and Levkoff SE. An empirical study of delirium subtypes. *The British journal of psychiatry : the journal of mental science*. 1992;161:843-5.
42. Sampson EL, Blanchard MR, Jones L, Tookman A and King M. Dementia in the acute hospital: prospective cohort study of prevalence and mortality. *The British journal of psychiatry : the journal of mental science*. 2009;195:61-6.
43. Network SIG. Risk Reduction and management of delirium. https://www.sign.ac.uk/sign-157-delirium.html.

Tables and Figures legend

Table 1: Patients characteristics according to delirium subtypes

Figure 1: Study flowchart of 1057 patients older patients admitted to acute and rehabilitation hospital wards.

Figure 2: Multivariate analysis of factors associated with different psychomotor subtypes of delirium.

Table

Table 1. Baseline characteristics of the population with dementia according to delirium psychomotor subtypes.

	No delirium (N=686)	Delirium (N=371)				
		Delirium psychomotor subtypes				
Variables		**Non-motor (N=25, 6.7%)**	**Hypoactive (N=123, 33.1%)**	**Mixed (N=128, 34.5%)**	**Hyperactive (N=95, 25.6%)**	**p-value***
Age, years	85 (80 – 89)	87 (82 – 90)	86 (81 – 90)	86 (82 – 90)	86 (81 - 89)	0.1415
Female gender	345 (50.3)	12 (48.0)	64 (52.0)	58 (45.3)	51 (53.7)	0.7544
ADL score >4/6‡#	157 (22.9)	2 (8.0)	13 (10.6)	8 (6.3)	18 (19.0)	<0.001
Charlson Index (excluding dementia),	2 (1 - 3)	2 (1 – 3)	2 (1 – 3)	1.5 (1 – 4)	2 (1 – 3)	0.7330
Number of drugs	4 (3 - 5)	3 (2 – 4)	3 (2 – 5)	4 (3 – 6)	3 (2 – 4)	0.0043
Diuretics	324 (47.2)	14 (56.0)	62 (50.4)	71 (55.5)	37 (39.0)	0.1324
Antihypertensive drugs	409 (59.6)	14 (56.0)	70 (56.9)	85 (66.4)	55 (57.9)	0.5491
Antiplatelet drugs	337 (49.1)	10 (40.0)	45 (36.6)	63 (49.2)	33 (34.7)	0.0122
Antiarrhythmic drugs	65 (9.5)	4 (16.0)	6 (4.9)	13 (10.2)	7 (7.4)	0.3128
Statins/lipid-lowering drugs	124 (18.1)	1 (4.0)	14 (11.4)	13 (10.2)	12 (12.6)	0.0269
Antidiabetics	121 (17.6)	3 (12.0)	21 (17.1)	20 (15.6)	18 (19.0)	0.9127
Antiulcer drugs	467 (68.1)	17 (68.0)	86 (69.9)	87 (68.0)	57 (60.0)	0.5774
Antibiotics	229 (33.4)	10 (40.0)	65 (52. 9)	72 (56.3)	29 (30.5)	<0.0001
Benzodiazepines	166 (24.2)	5 (20.0)	31 (25.2)	24 (18.8)	29 (30.5)	0.3474

Antipsychotics	239 (34.8)	12 (48.0)	36 (29.3)	64 (50.0)	61 (64.2)	<0.001
Antidepressants	244 (35.6)	6 (24.0)	38 (30.9)	38 (29.7)	25 (26.3)	0.2206
Antiepileptics	65 (9.5)	0 (0.0)	9 (7.3)	12 (9.4)	10 (10.5)	0.5022
AChE-I/memantine	58 (8.5)	1 (4. 0)	8 (6.5)	10 (7.8)	4 (4.2)	0.5714
Feeding tubes (NT/PEG)**	10 (1.5)	0 (0.00)	5 (4.1)	4 (3.1)	5 (5.3)	0.0551
Venous catheter	338 (49.3)	15 (60.0)	86 (69.9)	94 (73.4)	55 (57.9)	<0.001
Urinary catheter	188 (27.4)	13 (52.0)	71 (57.7)	67 (52.3)	40 (42.1)	<0.001
Physical restraints	49 (7.1)	1 (4.0)	10 (8.1)	16 (12.5)	23 (24.2)	<0.001

Data are expressed as n (%) -or Median (+ Interquartile ranges (IQR). unless otherwise specified.
Abbreviations: AChE-I= Acetylcholinesterase inhibitor; NT = Nasogastric tube; PEG = Percutaneous Endoscopic Gastrostomy
**Comparisons between psychomotor subtype of delirium were made with Kruskal-Wallis tests for non-continuous variables and chi-square or Fisher exact test for categorical data.
†# Functional status before admission was evaluated using the Katz Activities of Daily Living (ADL) scale with a score ranging from 0 (patient dependent) to 6 (patient independent). A Katz score of 4 or above is indicative of moderate impairment."

Formatted: Superscript
Formatted: Left
Formatted: Font: Times, 10 pt, Italian (Italy)

Table

Table 1. Baseline characteristics of the population with dementia according to delirium psychomotor subtypes.

	No delirium (N=686)	Delirium (N=371)				
		Delirium psychomotor subtypes				
Variables		**Non-motor (N=25, 6.7%)**	**Hypoactive (N=123, 33.1%)**	**Mixed (N=128, 34.5%)**	**Hyperactive (N=95, 25.6%)**	**p-value***
Age, years	85 (80 – 89)	87 (82 – 90)	86 (81 – 90)	86 (82 – 90)	86 (81 - 89)	0.1415
Female gender	345 (50.3)	12 (48.0)	64 (52.0)	58 (45.3)	51 (53.7)	0.7544
ADL score >4/6†	157 (22.9)	2 (8.0)	13 (10.6)	8 (6.3)	18 (19.0)	<0.001
Charlson Index (excluding dementia),	2 (1 - 3)	2 (1 – 3)	2 (1 – 3)	1.5 (1 – 4)	2 (1 – 3)	0.7330
Number of drugs	4 (3 - 5)	3 (2 – 4)	3 (2 – 5)	4 (3 – 6)	3 (2 – 4)	0.0043
Diuretics	324 (47.2)	14 (56.0)	62 (50.4)	71 (55.5)	37 (39.0)	0.1324
Antihypertensive drugs	409 (59.6)	14 (56.0)	70 (56.9)	85 (66.4)	55 (57.9)	0.5491
Antiplatelet drugs	337 (49.1)	10 (40.0)	45 (36.6)	63 (49.2)	33 (34.7)	0.0122
Antiarrhythmic drugs	65 (9.5)	4 (16.0)	6 (4.9)	13 (10.2)	7 (7.4)	0.3128
Statins/lipid-lowering drugs	124 (18.1)	1 (4.0)	14 (11.4)	13 (10.2)	12 (12.6)	0.0269
Antidiabetics	121 (17.6)	3 (12.0)	21 (17.1)	20 (15.6)	18 (19.0)	0.9127
Antiulcer drugs	467 (68.1)	17 (68.0)	86 (69.9)	87 (68.0)	57 (60.0)	0.5774
Antibiotics	229 (33.4)	10 (40.0)	65 (52. 9)	72 (56.3)	29 (30.5)	<0.0001
Benzodiazepines	166 (24.2)	5 (20.0)	31 (25.2)	24 (18.8)	29 (30.5)	0.3474

Antipsychotics	239 (34.8)	12 (48.0)	36 (29.3)	64 (50.0)	61 (64.2)	<0.001
Antidepressants	244 (35.6)	6 (24.0)	38 (30.9)	38 (29.7)	25 (26.3)	0.2206
Antiepileptics	65 (9.5)	0 (0.0)	9 (7.3)	12 (9.4)	10 (10.5)	0.5022
AChE-I/memantine	58 (8.5)	1 (4. 0)	8 (6.5)	10 (7.8)	4 (4.2)	0.5714
Feeding tubes (NT/PEG)	10 (1.5)	0 (0.00)	5 (4.1)	4 (3.1)	5 (5.3)	0.0551
Venous catheter	338 (49.3)	15 (60.0)	86 (69.9)	94 (73.4)	55 (57.9)	<0.001
Urinary catheter	188 (27.4)	13 (52.0)	71 (57.7)	67 (52.3)	40 (42.1)	<0.001
Physical restraints	49 (7.1)	1 (4.0)	10 (8.1)	16 (12.5)	23 (24.2)	<0.001

Data are expressed as n (%) or Median (Interquartile range).
Abbreviations: AChE-I= Acetylcholinesterase inhibitor; NT = Nasogastric tube; PEG = Percutaneous Endoscopic Gastrostomy
*Comparisons between psychomotor subtype of delirium were made with Kruskal-Wallis tests for non-continuous variables and chi-square or Fisher exact test for categorical data.
†Functional status before admission was evaluated using the Katz Activities of Daily Living (ADL) scale with a score ranging from 0 (patient dependent) to 6 (patient independent). A Katz score of 4 or above is indicative of moderate impairment."

Figure 2

Click here to access/download;Figure;Figure_2_R1.tif

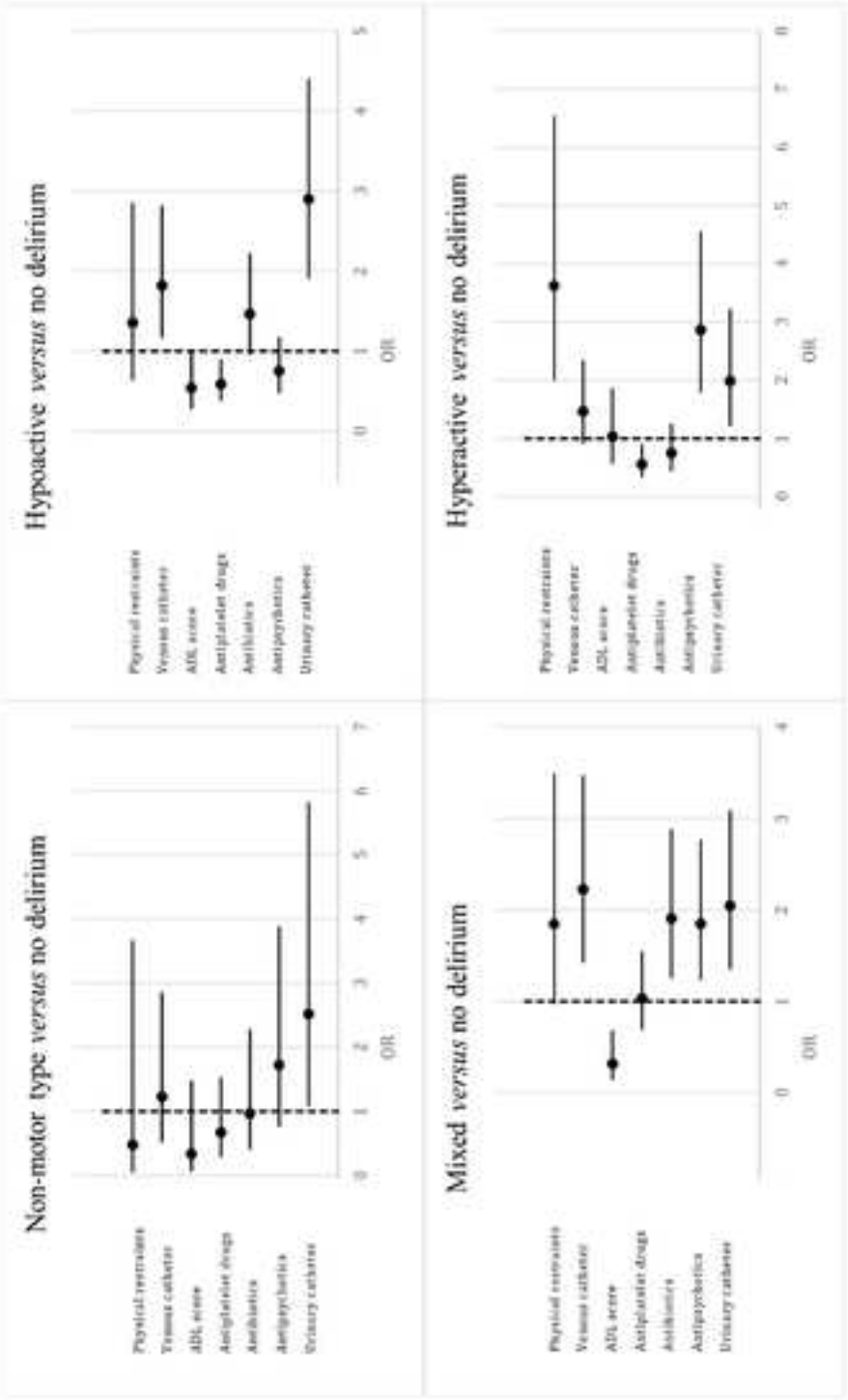
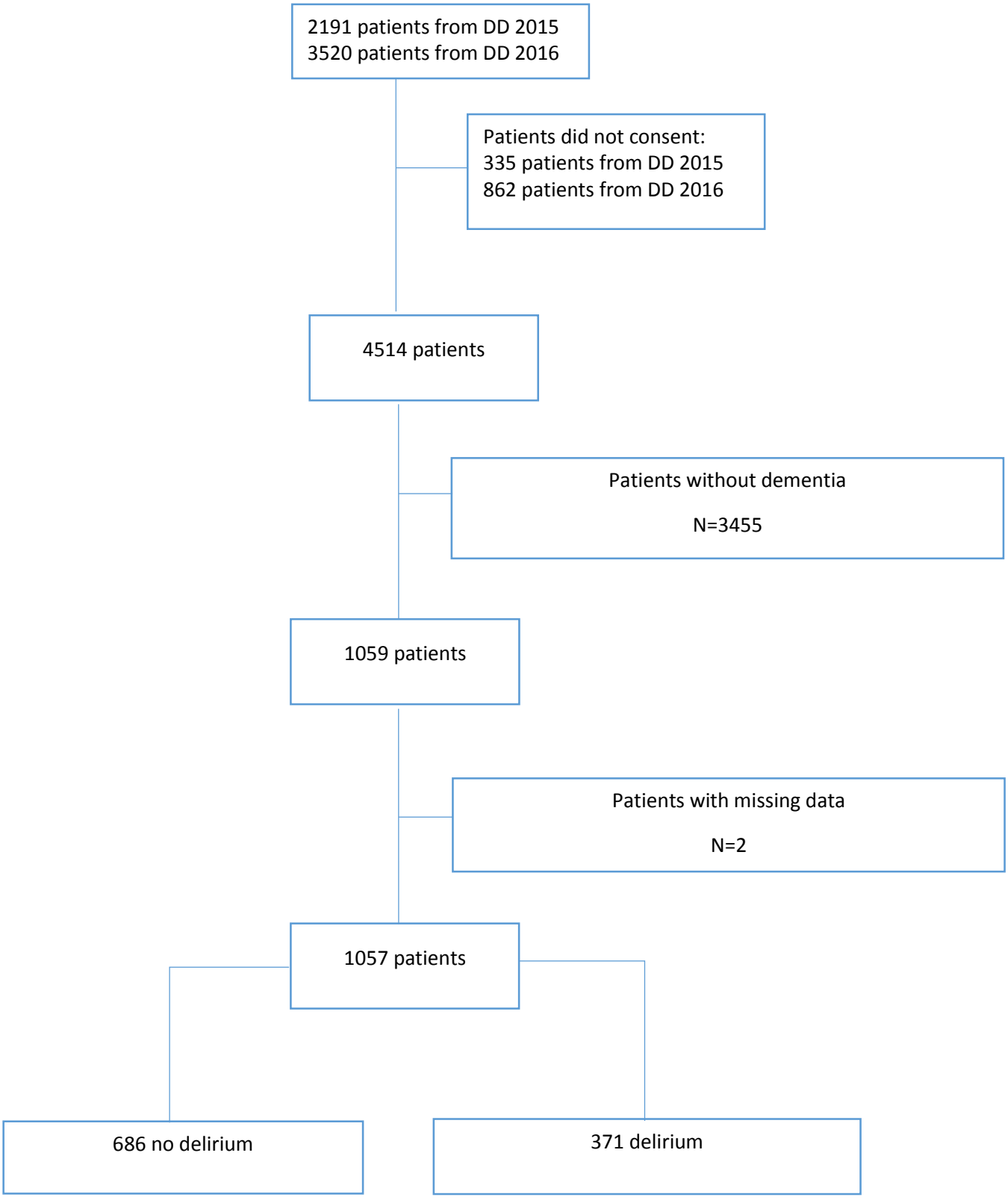


Figure 1

Figure 1. Study flowchart of 1057 patients older patients admitted to acute and rehabilitation hospital wards.



Click here to access/download
Supplementary Material
Appendix .docx