



Pilot study of a preventive multicomponent nurse intervention to reduce the incidence and severity of delirium in hospitalized older adults: MID-Nurse-P

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ABSTRACT

Background: Although multicomponent interventions are the gold standard for delirium management, few nurse-led interventions in Acute Geriatric Units (AGU) are described.

Objectives: To analyze if a preventive multicomponent non-pharmacologic nurse-led intervention randomized clinical trial (MID-Nurse Study) is feasible (pilot study), and can reduce the incidence, duration, and severity of delirium in hospitalized older adults in an AGU.

Design: Parallel-group double-blind randomized clinical trial (pilot Study).

Setting: AGU Complejo Hospitalario Universitario, Albacete (Spain).

Participants: 50 patients ≥ 65 years hospitalized in the AGU. Intervention group (IG) 21, control group (CG) 29.

Intervention: After risk factor analysis, all participants in the IG received a daily multicomponent non-pharmacologic intervention (orientation, sensorial deficit, sleep, mobilization, hydration, nutrition, drug chart review, elimination, oxygenation, pain) by the intervention nurses. The CG received usual care.

Measurements: Daily delirium presence with the Confusion Assessment Method (CAM), and severity with the Delirium Rating Scale-Revised-98 (DRS). Outcome measures were delirium incidence, prevalence, severity, and number of days with delirium, mortality, length of stay, use of physical restraint measures, and use of drugs for delirium control.

Results: Mean age 86.5 (48% women). 21 participants presented delirium during hospitalization (14CG and 7 IG). Process, resources, management, and scientific objectives were considered positive, making the study feasible. Delirium prevalence (33.3% vs 48.3%) and incidence (14.3% vs 41.4%; $p = 0.039$) were reduced in the IG compared to CG. Total delirium severity was lower in the IG compared to the CG (35.0 vs 65.0; $p = 0.040$). Mortality was not different between groups (CG 17.2% vs IG 19.0%).

Conclusion: The MID-Nurse Study is feasible, and a multicomponent nurse-led intervention on patients with delirium in an AGU can reduce delirium prevalence, incidence, and severity.

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1. Introduction

Delirium is an acute impairment of attention and other cognitive functions like memory, orientation, thinking, language, or perception that appears during a short period of time with daily

fluctuations [1]. It is one of the most common complications in hospitalized older adults, it is potentially reversible, and can be prevented. However, it is associated with an increased risk of morbidity and mortality, loss of independence, length of stay, and institutionalization in this population [2]. Prevalence ranges from 29% to 64% in hospitalized older adults although it is commonly an infra-diagnosed syndrome [3], and contributes to more than \$164 billion in health care costs in the United States annually [4]. It has been described that up to 30–40% of the cases could be prevented [5]. Older adults with delirium should be considered as a

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vulnerable population, due to the high rates of dementia, mortality, and institutionalization [2].

The etiology is multifactorial, with an interaction between internal individual predisposing factors of vulnerability (susceptibility) and external precipitating factors (triggers) [3,5,6]. Therefore, multifactorial interventions have been described as the cornerstone of delirium prevention and treatment [7]. However, multicomponent non-pharmacologic targeted interventions have been effective only in the prevention of incident delirium in multiple systematic reviews, overviews, and meta-analysis [5,7,8,9], but not in the treatment of this condition [9].

Different standardized approaches for improving quality of care in hospitalized older adults with delirium have been described. The Hospital Elder Life Program (HELP) [10] is a preventive program including mobility, orientation, nutrition, hydration, sleep care, and sensory impairment evaluation. More recently, Vidán et al., analyzed the effectivity of a preventive intervention in hospitalized older adults, with a 6.8% reduction in the delirium incidence [11].

Nurses are the major providers of bedside care, and must possess the knowledge to recognize delirium, identify risk factors, and provide safe and effective interventions to prevent it [12]. Therefore, nurses specialized in geriatrics should be an important support for the clinical management of these patients. However, a lack of nurse knowledge regarding delirium has been identified [13,14], and only few studies following cardiac surgery [15], in emergency departments or in intensive care units [16,17] have analyzed specific nurse-led interventions. Furthermore, there are no randomized clinical trials that have analyzed a pure nurse-led intervention in hospitalized older adults, in order to prevent and treat delirium, and for this reason we designed the MID-Nurse study. However, we first decided to conduct a feasibility study (pilot study), MID-Nurse-P, in order to analyze process, resources, management and scientific challenges for realizing the clinical trial [18].

2. Methods

2.1. Study design

Parallel-group, simple blind (evaluation and analysis), randomized clinical trial (pilot study). The design was based on recommendations for conducting pilot studies [18]. The study is registered at [ClinicalTrials.gov](https://clinicaltrials.gov) ID: NCT02558777.

2.2. Main objective of the MID-Nurse (randomized clinical trial)

To analyze if a preventive multicomponent non-pharmacologic nurse-led intervention reduces the incidence, duration, and severity of delirium in hospitalized older adults in an Acute Geriatric Unit (AGU).

2.3. Specific objectives and evaluating criteria of the MID-Nurse-P (pilot study)

- **Process:** to determine the recruitment rate (criteria: at least 70% of the eligible patients can be recruited), the complete follow-up rate (criteria: at least 85% of the included participants complete the follow-up), and the adherence to intervention (criteria: at least 80% of the included participants receive every scheduled intervention).
- **Resources:** to assess capacity of the team and process time to conduct the trial. Criteria: less than 10% of the participants can't complete the intervention program due to study team problems, and daily time employed per participant is not longer than 30 min.
- **Management:** to analyze potential study personnel and data managing problems.

- **Scientific:** to estimate the intervention effect and the variance.

2.4. Setting

AGU of the *Complejo Hospitalario Universitario of Albacete*, Albacete, Spain, a tertiary University Hospital.

2.5. Study population

Patients with an age equal or older than 65 years, hospitalized at the AGU of the *Complejo Hospitalario Universitario of Albacete* from October 2013 until February 2014, with a valid signed informed consent by the patient or legal representative. Exclusion criteria were agonic situation, non-Spanish speaking, severe cognitive decline (Reisberg's Global Deterioration Scale = 7) [19], and patients sharing the same room with a previously included participant to avoid contamination bias (every room at the AGU has two beds).

2.6. Sample size

Based on previous studies [11], MID-Nurse sample size was calculated to detect a 6.8% reduction in the incidence of delirium, from 18.5% in the control group to 11.7% in the intervention group, with a 95% confidence and 80% potency. Using the Epidat 3.0 program, 437 participants per group should be necessary. However, to determine the sample size for the MID-Nurse-P, we followed the recommendations of Cocks and Torgerson [20] suggesting that to estimate the main study's standard deviation a sample size of at least 50 should be needed, and that with a 20% control group proportion and a 10% difference to be detected, a pilot sample size (80% level) of 46 participants should be necessary (upper one-sided 80% confidence limit 0.0993). For these reasons, we chose a sample size of 50 participants for the MID-Nurse-P Study that later on could be pooled in the MID-Nurse study, if no significant variations in the methodology were assumed.

2.7. Randomization

Randomization was computer based, using computer-generated random numbers, with a proportion of 1:1 between control group and intervention group. The block size used for the computer generation of randomization codes was 874 participants, the complete sample size for the MID-Nurse Study. For this reason there was a discrepancy in the numbers between the two groups. After randomization before participant allocation, opaque envelopes were used to store the data with sequential study numbers.

2.8. Blinding

Blinding of investigator and participants was not possible to perform due to the nature of the intervention. However, several measures were used to avoid contamination between both groups. Only one patient per room was allowed (all rooms have two beds for two patients), because interventions on a patient could be observed by the other inpatient or caregivers, leading to contamination. Intervention and evaluation were always conducted by different study personnel, to avoid measurement biases. For these reasons, we created the roles of "intervention nurse" and "evaluation nurse". One of the strengths of this study is the blinding of the outcome assessor. Last, all statistical analyses were realized by study personnel that did not take part in the evaluation or intervention process.

2.9. Study variables

In the first 24 h from admission, all the following data were collected by the evaluation nurses, once the informed consent was signed, and randomization performed by one investigator, who did not take part in the rest of the data collection, analysis, and clinical intervention.

Socio-demographic data including age and sex. We also registered the Charlson comorbidity index [21], the mean clinical diagnosis for admission, and the usually consumed drugs before admission.

Disabilities in basic activities of daily living previous to hospitalization were assessed with the Barthel index [22], and previous ambulation with the Holden's FAC instrument [23]. Cognitive impairment was determined with the Pfeiffer's Short Portable Mental Status Questionnaire [24], and with the Reisberg's Global Deterioration Scale [19]. Pain was assessed with the visual analogical scale [25], and pressure ulcers risk with the Braden scale [26].

Vital signs were determined on admission, including blood pressure, heart rate, temperature, hydration level, and oxygen saturation. Medical or nurse procedures were recorded, including bladder catheterization, nasogastric tube placement, venous or arterial access, blood sample acquisition, and other invasive procedures.

Blood sample was collected, and haemoglobin, leukocyte and neutrophil count, reactive C protein, sedimentation rate, glucose, urea, sodium, potassium, albumin, total proteins, cholesterol, thyroid stimulating hormone, transferrin, ferritin, total iron, folic acid, and B12 vitamin, were recorded.

2.10. Delirium assessment and main outcome variables

After patient enrollment, nurses performed a daily delirium evaluation with the Confusion Assessment Method scale (CAM) [27] in the afternoon. CAM is an easy and short time administered instrument, with a specificity of 90–95%, and a sensitivity of 95–100%, and is the gold standard for delirium assessment.

Delirium was analyzed with several constructs: (1) delirium incidence: new cases of delirium across the follow-up. (2) Delirium prevalence: presence of delirium at any moment throughout the follow-up, including admission (first day). (3) Delirium prevalence excluding the first day: presence of delirium at any moment throughout the follow-up, excluding admission (first day) to avoid bias for this reason. (4) Number of days with delirium per participant including and excluding first day.

In the case that the CAM was positive for delirium, patients also were evaluated with the Delirium Rating Scale-Revised-98 (DRS-R-98) [28] to determine delirium severity. This scale is composed of 13 items scoring from 0 (lower severity) to 3 (higher severity), with a final range between 0–39. Total delirium severity was calculated by adding the severity of delirium during all days of hospitalization (sum of DRS-R-98 during the complete follow-up), and mean severity per day was calculated dividing the global severity per number of days with delirium.

Subsequently, main outcome variables were (1) Delirium incidence (dichotomic variable, yes/no). (2) Delirium prevalence including and excluding first day (dichotomic variables, yes/no). (3) Number of days with delirium per participant including and excluding first day (continuous variable). (4) Total delirium severity per participant (continuous variable) including and excluding first day. (5) Mean delirium severity per day including and excluding first day (continuous variable).

2.11. Other outcome variables

Other outcome variables were in-hospital mortality, length of hospital stay (days), necessity of physical restraint measures (yes/no), and the necessity of drugs for delirium control (neuroleptics or benzodiazepines). Name, dose, and number of doses required were recorded.

2.12. Intervention

Participants in the intervention group received the initial intervention in the first 24 h from admission, and thereafter daily until hospital discharge. Participants in the control group received usual medical and nurse care during all the hospitalization process. Fig. 1 presents the study flow diagram.

The intervention was carried out exclusively by the “intervention nurses”, and was composed of two main parts, being the first one a risk factor analysis, and the second one the intervention on the risk factors detected. Table 1 describes the intervention on each specific risk factor. Furthermore, the intervention nurses identified the principal caregiver in the first 24 h from admission, and provided an informative booklet about strategies and recommendations to prevent delirium incidence, including ambient strategies, orientation abilities, and identification of alert signs (Fig. 2).

2.13. Statistical methods

A descriptive analysis of the study variables was conducted (means, standard deviation, number of cases and proportions). Normal distribution of all the continuous variables was analyzed. Prevalence, incidence, and severity of delirium were described. Thereafter, *t*-test, Mann–Whitney-U test, and ANOVA were used to compare continuous variables between control and intervention groups, and chi square and Fisher exact test to compare proportions between both groups. The efficacy of the intervention was analyzed with the relative risk ratio (RR) and 95% confidence interval (95% CI). All analyses were calculated under an intention to treat approach.

Data were anonymized, codified and included in a data base for further analysis. The analysis was realized with the statistical package SPSS15.

2.14. Ethical aspects

This study complies with the Declaration of Helsinki and with the Organic Personal Data Protection Spanish Law 15/1999. The study was approved by the Institutional Review Board of the Albacete Health Area and the Clinical Research Committee of the *Complejo Hospitalario Universitario of Albacete*. All participants or legal tutors gave their written signed consent before being included in the study. When the study team found a new clinical condition, this was put in consideration of the staff geriatrician.

3. Results

Fig. 3 presents the participant flow (CONSORT 2010) [29]. 132 patients were assessed for eligibility, and 65 met inclusion criteria (49.2%). Regarding the specific objectives of the MID-Nurse-P study, 50 patients (77%) of the 65 eligible patients meeting inclusion criteria, were randomized, 21 to the intervention group and 29 to usual care or control group. All randomized participants completed the follow-up without reallocations. Moreover, adherence to scheduled intervention was also 100%. All participants completed the intervention in less than 30 min and in less than 20 min if risk factor

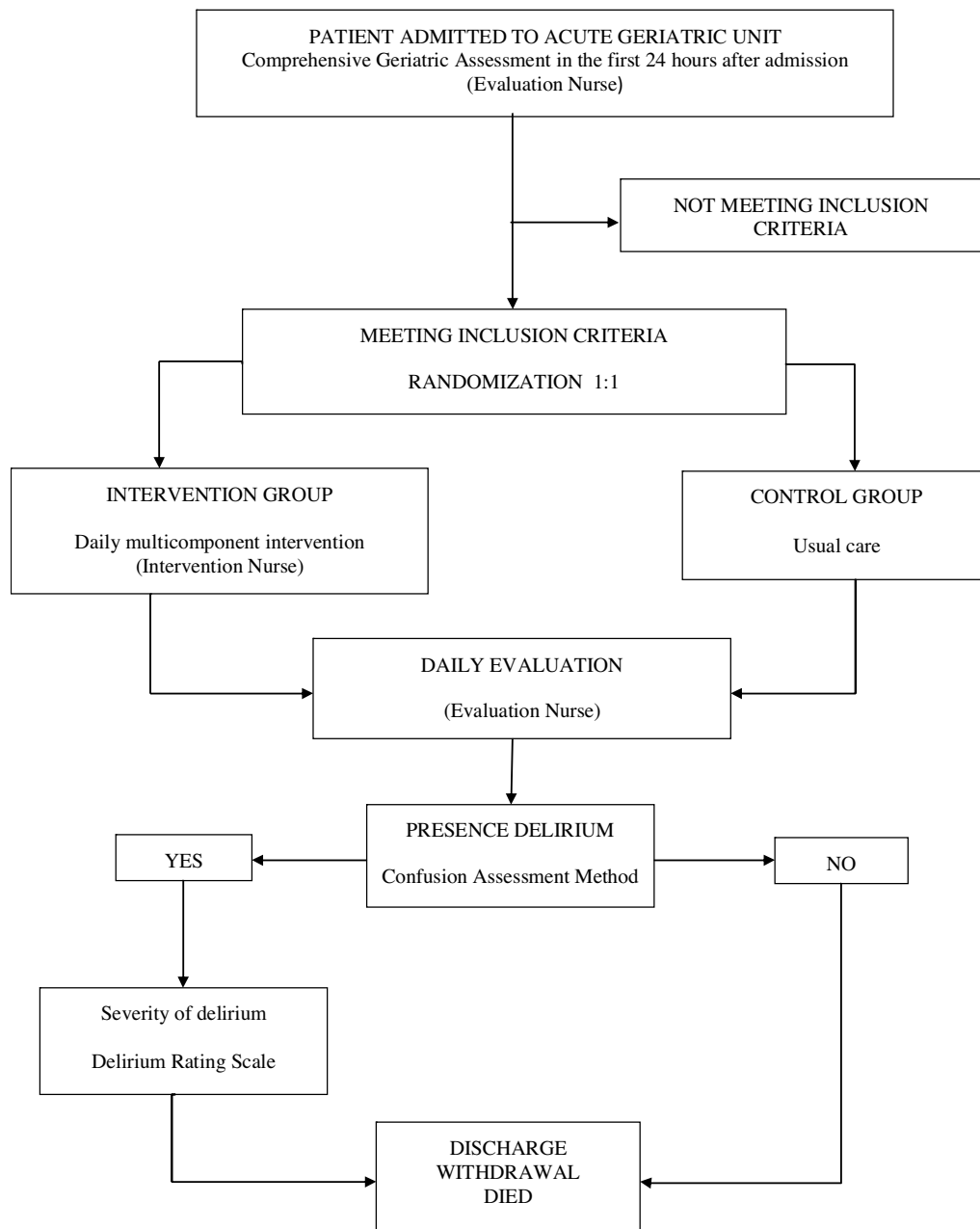


Fig. 1. Flow diagram.

analysis was not necessary. There were neither team problems with the intervention nor data managing difficulties.

Table 2 presents the basal characteristics of the sample. 21 participants presented delirium at any moment during hospitalization, 14 in the control group and 7 in the intervention group. Nine patients presented delirium on admission (first day), and three of them presented delirium only in the first day of admission. Thirty five participants presented incident delirium at any moment during hospitalization. Fig. 4 presents the number of participants with delirium (panel A), and mean delirium severity (panel B), per day of hospitalization in both groups.

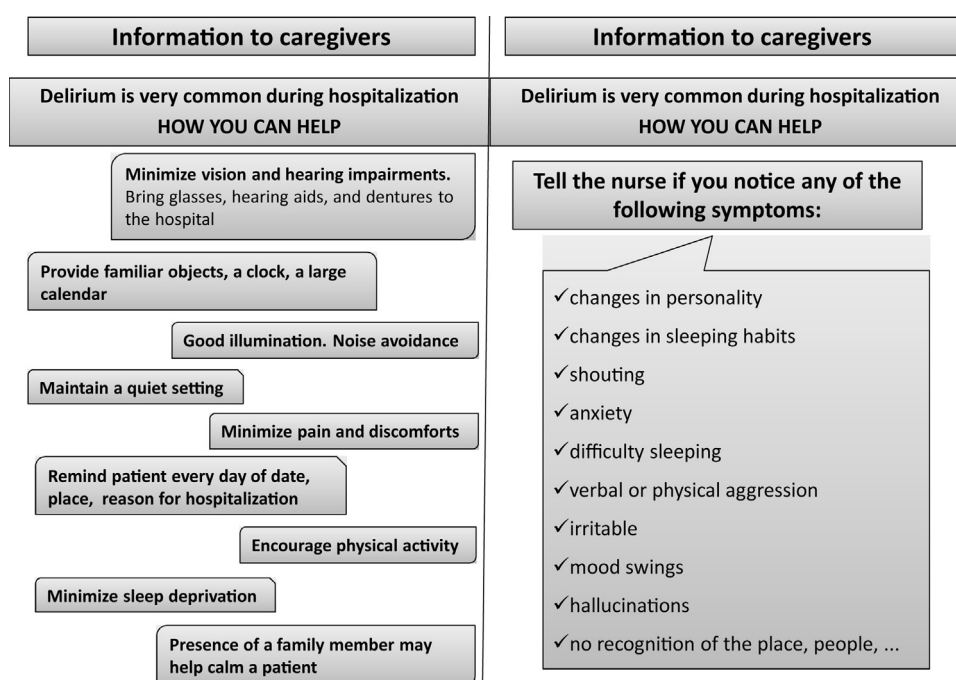
Table 3 presents the main delirium-related outcomes during hospitalization. Intervention decreased delirium prevalence during hospitalization (33.3% vs 48.3%; RR 0.54; 95% CI 0.17–1.72), delirium prevalence excluding the first hospitalization day (23.8% vs 48.3%; RR 0.34; 95% CI 0.10–1.16), and incident delirium during hospitalization (14.3% vs 41.4%; RR 0.24; 95% CI 0.06–0.99; $p = 0.039$).

Mean number of hospitalization days with delirium in the complete sample was 2.9 (SD 2.0; range 1–8), 3.4 days in the control group (range 1–13), and 1.7 days in the intervention group (range 1–6 days). Excluding the first day of hospitalization, mean number of days with delirium in the complete sample was 2.8 (SD 2.0; range 1–8), 3.4 in the control group (range 1–13 days) and 2.0 in the intervention group (range 1–6 days).

Mean delirium severity during hospitalization in the complete sample was 55.0 (SD 40.6; range 12.5–133.0), and mean severity per day with delirium was 19.4 (SD 7.8; range 10.3–43.0). Same data excluding the first day of hospitalization were 55.6 (SD 42.0; range 13.0–133.0), and 19.1 (SD 7.6; range 8.8–43.0) respectively. Delirium severity was lower in the intervention group than in the control group (35.0 vs 65.0; mean difference 30.0, 95% CI 1.5–58.5; $p = 0.040$), but mean severity per day with delirium was higher in the intervention group (21.1 vs 18.6). Excluding the first day of admission, delirium severity was lower in the intervention than in

Table 1
Multicomponent intervention.

Risk factor	Daily evaluation	Intervention
Orientation	Pfeiffer	Information booklet to caregiversexplaining preventive measures Temporospatial orientation intervention(Remind patients every day of date, place, and reason for hospitalization)
Sensorial deficit	Need of glasses or hear aids	Reminding of the use of own glasses or hearing aids Non-verbal language Good illumination Noise avoidance
Sleep	Presence of insomnia Sleep preservation	Alert if insomnia detection Non-pharmacologic intervention Drug chart review and treatment Avoid treatments during sleep time if possible
Mobilization	Evaluation of mobilization	Early mobilization protocol (Get patients out of bed each day during admission) Removal of urinary catheter if possible Avoidance of physical restraints Mobilization after toileting Information to caregivers explaining mobilization strategies
Hydration	Evaluation of mucosal hydration Daily voiding registry	Alert if dehydration Scheduled oral intake or i.v. fluids Alert if diuresis < 1000 cc/day
Nutrition	Evaluation of intake	Daily intake registry Scheduled oral intake Alert if absolute diet Nutritional supplements administration
Drugs	List of potential drugs	Alert if drug risk detection Psychotropic drugs avoidance Control of drug deprivation
Oxygenation	Oxygen saturation	Oxygen adjust
Elimination	Intestinal (constipation or diarrhea) and urinary elimination pattern assessment	Alert if constipation, diarrhea, or urinary incontinence/obstruction Avoidance of indwelling catheters
Pain	Pain assessment with visual analogic scale	Alert if pain detection, drug chart review and administration

**Fig. 2.** Information to caregivers sheet.

the control group (35.2 vs 59.9; NS), but also mean severity per day with delirium was higher in the intervention group (20.1 vs 18.8; NS).

Mortality was higher in patients with delirium on admission compared to those without delirium (33.3% vs 14.6%). Patients with delirium at any moment during hospitalization or with incident delirium presented higher mortality than those without delirium

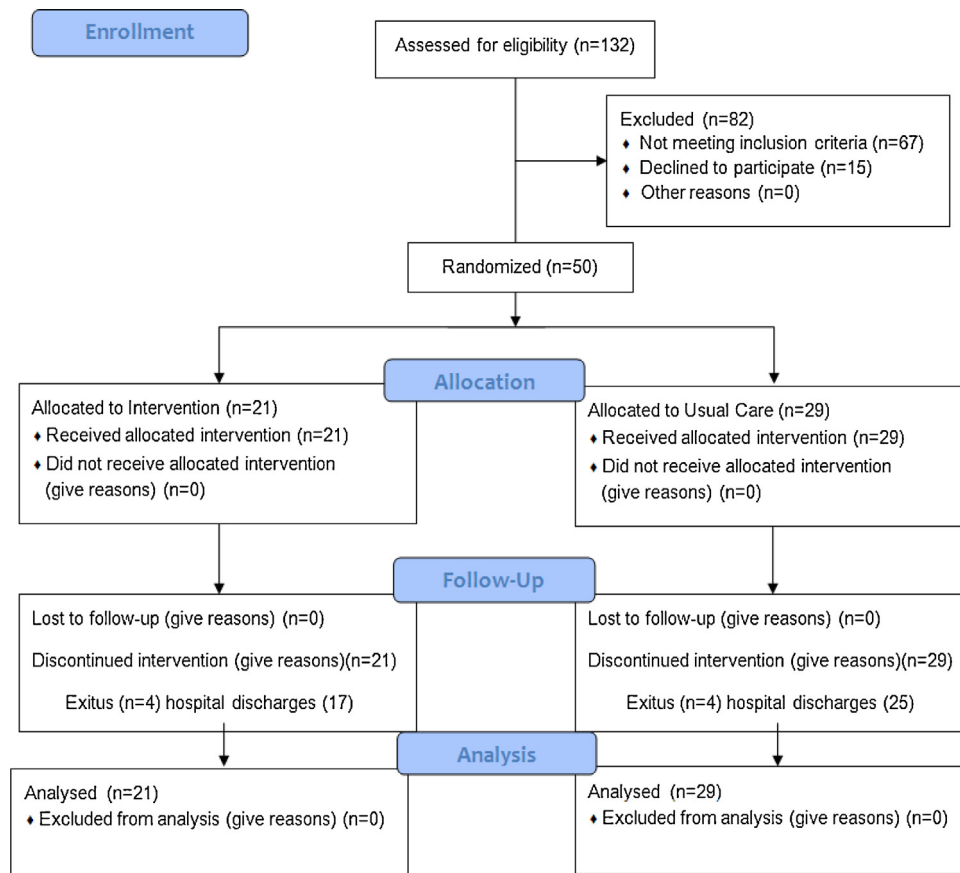


Fig 3. Participant flow (CONSORT 2010).

Table 2
Basal characteristics.

	Complete sample (n = 50)	Control group (n = 29)	Intervention group (n = 21)
Age	86.5 (5.5)	87.0 (4.9)	85.8 (6.2)
Gender			
Male	26 (52.0)	16 (55.2)	10 (47.6)
Female	24 (48.0)	13 (44.8)	11 (52.4)
FAC	2.4 (1.9)	2.6 (1.9)	2.2 (2.1)
Barthel index	53.0 (33.6)	53.5 (33.5)	52.4 (34.6)
Braden scale	15.3 (3.7)	15.4 (3.7)	15.3 (3.7)
Pfeiffer	4.5 (2.9)	5.0 (2.8)	3.8 (3.0)
Charlson index	2.2 (1.5)	2.2 (1.3)	2.1 (1.7)
VAS pain	4.2 (5.0)	4.6 (5.2)	3.7 (4.8)
Drugs			
Neuroleptics (previous)	7 (14)	6 (20.7)	1 (4.8)
BZD (previous)	12 (24)	6 (20.7)	6 (28.6)
SBP (mmHg)	137.9 (24.7)	135.8 (23.5)	140.9 (26.4)
DBP (mmHg)	73.4 (14.0)	68.4 (11.7)**	80.4 (14.1)**
Heart rate (bpm)	79.1 (14.7)	74.6 (14.3)*	85.1 (13.2)*
Temperature (°C)	36.5 (0.9)	36.5 (1.1)	36.7 (0.5)
Oxygen saturation (%)	94.7 (2.8)	94.2 (3.0)	95.2 (2.4)
Interventions on admission			
Urethral catheter	33 (66)	18 (64.3)	15 (71.4)
Venous access	50 (100)	29 (100)	21 (100)
Oxygen	34 (68.0)	19 (67.9)	15 (71.4)
Physical barriers			
Bed rails	43 (86.0)	23 (82.1)*	20 (100)*
Wristbands	3 (6.0)	2 (7.1)	1 (5.0)
Urinary incontinence	40 (80.0)	8 (27.6)	2 (9.5)
Constipation	7 (14.0)	4 (14.3)	3 (14.3)
Dehydration	15 (30.0)	6 (23.1)	9 (42.9)
Absolute intake	20 (40.0)	14 (48.3)	6 (28.6)

All data are means (SD) or number of participants (%). FAC: functional ambulation classification holden. VAS: visual analogic scale. SBP: systolic blood pressure. DBP: diastolic blood pressure. BZD: benzodiazepines.

* $p < 0.05$.

** $p < 0.01$.

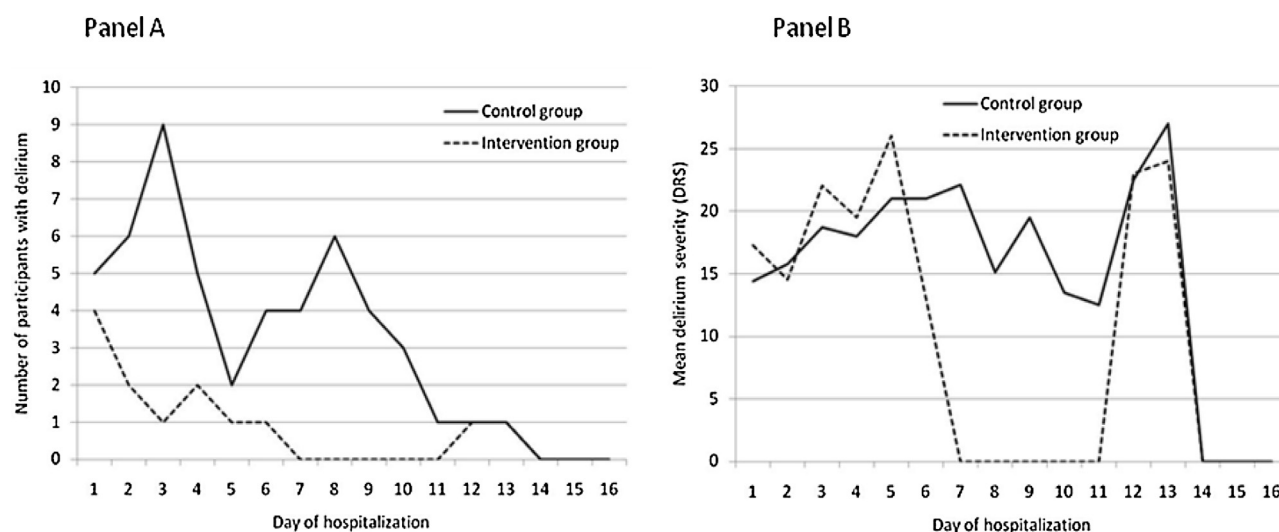


Fig. 4. Prevalence and severity of delirium during hospitalization.

Panel A: number of participants with delirium per day of hospitalization; panel B: mean delirium severity per day of hospitalization.

Table 3

Delirium-related outcomes during hospitalization.

Delirium-related outcome	Control group	Intervention group	p-value
Delirium incidence, n (%)	12 (41.4)	3 (14.3)	0.039
Delirium prevalence, n (%)	14 (48.3)	7 (33.3)	0.291
Delirium prevalence excluding first day, n (%)	14 (23.8)	5 (48.3)	0.079
Delirium severity, mean (SD)	65.0 (45.9)	35.0 (15.0)	0.040
Delirium severity excluding first day, mean (SD)	59.9 (46.4)	35.2 (19.3)	0.122
Number of days with delirium, mean (SD)	3.4 (2.2)	1.7 (0.8)	0.063
Number of days with delirium excluding first day, mean (SD)	3.4 (2.2)	2.0 (0.7)	0.176
Mean delirium severity per day, mean (SD)	18.6 (8.2)	21.1 (7.2)	0.477
Mean delirium severity per day, excluding first day, mean (SD)	18.8 (8.6)	20.1 (3.5)	0.773

(38.1% vs 3.4%; $p = 0.002$) and (40.0% vs 8.6%; $p = 0.008$) respectively. However, we could not find differences in mortality between control group and intervention group (17.2% vs 19.0%).

Mean hospitalization length was 7.4 days (SD 4.1; range 1–18). In the complete sample, length of hospitalization was higher in participants with delirium compared to those without delirium (7.7 [SD 4.1] vs 7.1 [SD 4.2]; NS), and also in participants with delirium at any moment during hospitalization (10.2 [SD 3.3] vs 7.6 [SD 5.7]; NS), in participants with delirium excluding the first day of hospitalization (10.2 [SD 3.3] vs 7.8 [SD 4.1]; NS), and in patients with incident delirium (10.2 [SD 3.2] vs 6.2 [SD 3.9]; mean difference 4.0; 95% CI 1.7–6.3; $p = 0.001$), always compared to those without delirium.

Patients in the intervention group needed less restraint measures than those in the control group (9.5% vs 17.2%; NS) and used less frequently neuroleptic drugs (33.3% vs 48.3%; NS) during hospitalization, without reaching statistical significance. The use of benzodiazepines during hospitalization was similar between groups respectively (42.9% vs 41.4%; NS).

4. Discussion

The main conclusion of our study is that the MID-Nurse Study, a scheduled non-pharmacologic nurse-led intervention in an AGU is feasible, and that the intervention may decrease delirium incidence, prevalence, and severity. Although the results are positive, confirmation from the complete MID-Nurse study are needed before establishing that the intervention is effective.

Our study has several innovations with respect to previous studies identified in recent meta-analysis [5,8]. The first one is the

design and development of a pilot (feasibility) study, in which we have analyzed the process, resources, management, and scientific objectives of the complete randomized clinical trial, the MID-Nurse Study, based on recommendations given by a tutorial in pilot studies [18]. This approach has been described to increase the efficiency of the main study [30].

Second, nurses, without active participation of geriatricians, exclusively delivered intervention. Geriatricians only received nurses' alerts, but decisions on treatment changes were not protocolized. In previous studies, intervention was delivered by nurses, residents and geriatricians in different proportions [11,31,32]. Our approach has only been used by two studies, the REVIVE Study [33], although nurses were volunteers only employed for individual nursing of delirious patients, and the study from Chen et al. [34] with trained nurses using HELP methodology.

Third, our study included patients with delirium on admission (first day). We had three reasons for this approach. (1) Although our intervention was aimed to be mainly preventive, we also wanted to know if it could have a treatment component. (2) Patients with delirium on admission are at risk of presenting recurrent episodes of delirium, and these new episodes could be prevented. (3) Our intervention was also aimed at reducing delirium severity, not only incidence.

Forth, our intervention was based on the HELP program [35], which includes as risk factors cognitive impairment, vision/hearing impairment, immobilization, psychoactive medication use, dehydration, and sleep deprivation. However, in order to include all possible risk factors, we decided to add three more risk factors with their corresponding interventions, elimination, oxygenation, and pain, included in the NICE guidelines 2010 [36]. Another difference with the HELP program was that geriatric nurses exclusively

conducted it, while the HELP program included Elder Life Specialist, volunteers, Elder Life Nurse Specialist, Geriatrician, and had administrative support.

Fifth, regarding methodology, only five studies on delirium prevention were randomized clinical trials [32,37–40], and among them, only one was single blind [38]. Furthermore, three of them included patients on surgical wards with hip fracture [32,37,38], in another one the intervention was delivered by family members [40], and in the last one the intervention only included exercise, mobilization and orientation [39]. Other studies in medical acute wards were controlled clinical trials [11,31]. Thus, our study is the first preventive multicomponent non-pharmacologic randomized trial to be performed in a medical ward [9]. Our study also adds a double blinding to improve validity, and to reduce contamination bias.

Previous studies have focused mainly on targeted patients like those with dementia [41], those with abdominal surgery [34], those at orthopedic wards [11,37,38], and those at medical/surgical wards [42], although some of them have been conducted in medical acute wards as ours [11,31,43].

Another innovation of our study is the intervention applied. The most widely disseminated approach is the HELP [31], a multicomponent intervention strategy with proven effectiveness and cost-effectiveness in the prevention of delirium and functional decline [44,45]. Previous studies have included cognition/orientation therapies [11,31,33,34,39–41,43,46], hydration review [11,31,43,46], feeding/nutrition [11,31,33,34], avoidance of vision and hearing deprivation [11,31,40,43,46], early mobilization/rehabilitation [11,31,33,37,38,43], constipation prevention [43], pain assessment [43], exercise [39], staff education [11,31,37,38], family/caregiver education [40], and sleep-wake cycle preservation [11,31]. In our study we included all aforementioned interventions, plus drug chart review, urinary elimination, and oxygenation, in order to cover all possible delirium risk factors described in the literature. Subsequently, our study could be meta-analyzed with those from Inouye et al. [31], and Vidán et al. [11] because we included seven common components, namely staff education, orientation protocol, avoidance of sensory deprivation, sleep protocol, early mobilization, hydration and nutrition [9].

Main limitations of our study are those derived from a pilot study. We can't assume that results are valid until the complete MID-Nurse Study is finished. Furthermore, the sample size is based on the outcome delirium incidence; therefore caution is needed in the interpretation of the secondary outcomes' results.

Nurses are the cornerstone of Geriatric care in AGU, and protocolization of main geriatric syndromes following gold standards of care should be a priority. Our pilot study has shown that a scheduled non-pharmacologic nurse-led intervention on old medical inpatients to prevent delirium is feasible, and could reduce delirium incidence, prevalence and severity, leading to shorter length of stay and higher quality of life for these patients.

Conflicts of interest

None declared.

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Author contributions

Almudena Avendaño-Céspedes conceived and designed the study and drafted and revised the manuscript. Nuria García-Cantos, María del Mar González-Teruel, Mónica Martínez-García, and Elena Villarreal-Bocanegra were responsible for data collection. José Luis Oliver-Carbonell designed the study and was responsible for data analysis. Pedro Abizanda conceived and designed the studies was responsible for acquisition/ analysis/ interpretation of data and drafted and revised the manuscript. All authors approved the final manuscript.

Sponsor's role

The sponsor had any role in the study.

Ethics

This study was approved by the local Ethics Committee (reference number and date of approval if supplied). Informed consent was obtained from all participants or legal representatives.

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References

- [1] S.K. Inouye, Delirium in older persons, *N. Engl. J. Med.* 354 (2006) 1157–1165.
- [2] J. Witlox, L.S. Eurelings, J.F. de Jonghe, et al., Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis, *JAMA* 304 (2010) 443–451.
- [3] S.K. Inouye, R.G. Westendorp, J.S. Saczynski, Delirium in elderly people, *Lancet* 383 (2014) 911–922.
- [4] D.L. Leslie, E.R. Marcantonio, Y. Zhang, et al., One-year health care costs associated with delirium in the elderly population, *Arch. Intern. Med.* 168 (2008) 27–32.
- [5] T.T. Hsieh, J. Yue, E. Oh, et al., Effectiveness of multicomponent nonpharmacological delirium Interventions: a meta-analysis, *JAMA Intern Med* 175 (2015) 512–520.
- [6] S.K. Inouye, P.A. Charpentier, Precipitating factors for delirium in hospitalized elderly persons: Predictive model and interrelationship with baseline vulnerability, *JAMA* 275 (1996) 852–857.
- [7] N. Siddiqi, R. Stockdale, A.M. Britton, et al., Interventions for preventing delirium in hospitalised patients, *Cochrane Database Syst. Rev.* (2) (2007), CD005563.
- [8] F. Martinez, C. Tobar, N. Hill, Preventing delirium: should nonpharmacological, multicomponent interventions be used? A systematic review and meta-analysis of the literature, *Age Ageing* 44 (2015) 196–204.
- [9] I. Abraha, F. Trotta, J.M. Rimland, et al., Efficacy of non-pharmacological interventions to prevent and treat delirium in older patients: a systematic overview the SENATOR project ONTOP series, *PLoS One* 10 (2015) e0123090.
- [10] M.J. Strijbos, B. Steunenbergh, R.C. van der Mast, et al., Design and methods of the Hospital Elder Life Program (HELP), a multicomponent targeted intervention to prevent delirium in hospitalized older patients: efficacy and cost-effectiveness in Dutch health care, *BMC Geriatr.* (2013) 13–78.
- [11] M.T. Vidán, E. Sánchez, M. Alonso, E.T. al, An intervention integrated into daily clinical practice reduces the incidence of delirium during hospitalization in elderly patients, *J. Am. Geriatr. Soc.* 57 (2009) 2029–2036.
- [12] B. Middle, M. Miklancie, Strategies to Improve Nurse Knowledge of Delirium: A Call to the Adult-Gerontology Clinical Nurse Specialist, *Clin. Nurse Spec.* 29 (2015) 218–229.
- [13] J. McCrow, K.A. Sullivan, E.R. Beattie, Delirium knowledge and recognition: a randomized controlled trial of a web-based educational intervention for acute care nurses, *Nurse Educ. Today* 34 (2014) 912–917.
- [14] A.P. Wand, W. Thoo, H. Sciuriaga, et al., A multifaceted educational intervention to prevent delirium in older inpatients: a before and after study, *Int. J. Nurs. Stud.* 51 (2014) 974–982.
- [15] T. Mailhot, S. Cossette, A. Bourbonnais, et al., Evaluation of a nurse mentoring intervention to family caregivers in the management of delirium after cardiac surgery (MENTOR.D): a study protocol for a randomized controlled pilot trial, *Trials* 15 (2014) 306.
- [16] M. Reimers, C. Miller, Clinical nurse specialist as change agent: delirium prevention and assessment project, *Clin. Nurse Spec.* 28 (2014) 224–230.

- [17] M. Hare, G. Arendts, D. Wynaden, et al., Nurse screening for delirium in older patients attending the emergency department, *Psychosomatics* 55 (2014) 235–242.
- [18] L. Thabane, J. Ma, R. Chu, et al., A tutorial on pilot studies: the what, why and how, *BMC Med. Res. Methodol.* 10 (1) (2010).
- [19] B. Reisberg, S.H. Ferris, M.J. De León, et al., The Global Deterioration Scale (GDS): an instrument for the assessment of primary degenerative dementia, *Am. J. Psychiatry* 139 (1982) 1136–1139.
- [20] K. Cocks, D.J. Torgerson, Sample size calculations for pilot randomized trials: a confidence interval approach, *J. Clin. Epidemiol.* 66 (2013) 197–201.
- [21] M. Charlson, P. Pompei, K.L. Ales, et al., A new method of classifying prognostic comorbidity in longitudinal studies: development and validation, *J. Chronic Dis.* 40 (1987) 373–383.
- [22] F.I. Mahoney, D.W. Barthel, Functional evaluation: the Barthel Index. A simple index of independence useful in scoring improvement in the rehabilitation of the chronically ill, *Md. State Med. J.* 14 (1965) 61–65.
- [23] M.K. Holden, M.K.K.M. Gill, M.R. Magliozzi, et al., Clinical gait assessment in the neurologically impaired: reliability and meaningfulness, *Phys. Ther.* 64 (1984) 35–40.
- [24] E. Pfeiffer, A short portable mental status questionnaire for the assessment of organic brain deficits in the elderly, *J. Am. Geriatr. Soc.* 23 (1975) 433–441.
- [25] J. Scott, E.C. Huskisson, Graphic representation of pain, *Pain* 2 (1976) 175–184.
- [26] N. Bergstrom, B. Braden, A. Laguzza, The Braden Scale for predicting pressure sore risk, *Nurs. Res.* 36 (1987) 205–210.
- [27] S.K. Inouye, C.H. van Dyck, C.A. Alessi, et al., Clarifying confusion: the confusion assessment method: A new method for detection of delirium, *Ann. Intern. Med.* 113 (1990) 941–948.
- [28] S.E. De Rooij, B.C. van Munster, J.C. Korevaar, et al., Delirium subtype identification and the validation of the delirium rating scale–revised–98 (Dutch version) in hospitalized elderly patients, *Int. J. Geriatr. Psychiatry* 21 (2006) 876–882.
- [29] D. Moher, K.F. Schulz, D.G. Altman, The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials, *Ann. Intern. Med.* 134 (2001) 657–662.
- [30] J. Wittes, E. Brittain, The role of internal pilot studies in increasing the efficiency of clinical trials, *Stat. Med.* 9 (1990) 65–71.
- [31] S.K. Inouye, S.T. Bogardus Jr., P.A. Charpentier, et al., A multicomponent intervention to prevent delirium in hospitalized older patients, *N. Engl. J. Med.* 340 (1999) 669–676.
- [32] E.R. Marcantonio, J.M. Flacker, R.J. Wright, et al., Reducing delirium after hip fracture: a randomized trial, *J. Am. Geriatr. Soc.* 49 (2001) 516–522.
- [33] G.A. Caplan, E.L. Harper, Recruitment of Volunteers to Improve Vitality in the Elderly: the REVIVE study, *Intern. Med. J.* 3 (2007) 95–100.
- [34] C.C. Chen, M.T. Lin, Y.W. Tien, et al., Modified hospital elder life program: effects on abdominal surgery patients, *J. Am. Coll. Surg.* 213 (2011) 245–252.
- [35] HELP website. Available at: <http://hospitalelderlifeprogram.org>.
- [36] National Institute for Health and Care Excellence (NICE). Delirium: diagnosis, prevention and management. Available at: www.nice.org.uk/guidance/CG103.
- [37] M. Lundström, B. Olofsson, M. Stenvall, et al., Postoperative delirium in old patients with femoral neck fracture: a randomized intervention study, *Aging Clin. Exp. Res.* 19 (2007) 178–186.
- [38] M. Stenvall, B. Olofsson, M. Lundström, et al., A multidisciplinary, multifactorial intervention program reduces postoperative falls and injuries after femoral neck fracture, *Osteoporos. Int.* 18 (2007) 167–175.
- [39] K.J. Jeffs, D.J. Berlowitz, S. Grant, et al., An enhanced exercise and cognitive programme does not appear to reduce incident delirium in hospitalised patients: a randomised controlled trial, *BMJ Open* 3 (2013), pii: e002569.
- [40] F.T. Martinez, C. Tobar, C.I. Beddings, et al., Preventing delirium in an acute hospital using a non-pharmacological intervention, *Age Ageing* 41 (2012) 629–634.
- [41] E. Androm. Comps, S. Estivin, et al., Prevention of delirium in demented hospitalized patients, *Eur. J. Intern. Med.* 23 (2012) 124–125.
- [42] A. Kratz, Use of the acute confusion protocol: a research utilization project, *J. Nurs. Care Qual.* 23 (2008) 331–337.
- [43] R. Holt, J. Young, D. Heseltine, Effectiveness of a multi-component intervention to reduce delirium incidence in elderly care wards, *Age Ageing* 42 (2013) 721–727.
- [44] J.A. Rizzo, S.T. Bogardus Jr., L. Leo-Summers, et al., Multicomponent targeted intervention to prevent delirium in hospitalized older patients: what is the economic value, *Med. Care* 39 (2001) 740–752.
- [45] D.L. Leslie, Y. Zhang, S.T. Bogardus, et al., Consequences of preventing delirium in hospitalized older adults on nursing home costs, *J. Am. Geriatr. Soc.* 53 (2005) 405–409.
- [46] M. Bo, B. Martini, C. Ruatta, et al., Geriatric ward hospitalization reduced incidence delirium among older medical inpatients, *Am. J. Geriatr. Psychiatry* 17 (2009) 760–768.