

The “CHROME criteria”: Tool to optimize and audit prescription quality of psychotropic medications in institutionalized people with dementia

Ruben Muñiz,¹ Alia I. Pérez-Wehbe,² Francisco Couto,³ María Pérez,³ Noemí Ramírez,³ Alejandro López,³ Javier Rodríguez,³ Teresa Usieto,³ Lietzan Lavin,³ Ana Rigueira,⁴ Luis Agüera-Ortiz,⁵ Jorge López-Alvarez,⁵ Manuel Martín-Carrasco,⁶ and Javier Olazarán^{1,7}

¹Maria Wolff Foundation, Madrid, Spain

²Universidad de la Laguna, Sta Cruz de Tenerife, Spain

³Centro Sociosanitario El Pino, Instituto de Atención Social y Sociosanitaria (IAS), Las Palmas de Gran Canaria, Spain

⁴Servicio de Farmacia, Hospital Universitario San Agustín, Avilés, Spain

⁵Servicio de Psiquiatría, Hospital Universitario 12 de Octubre, Madrid, Spain

⁶Clinica Padre Menni, Hermanas Hospitalarias, Pamplona, Spain

⁷Servicio de Neurología, Hospital General Universitario Gregorio Marañón, Madrid, Spain

ABSTRACT

Objective: Describe and validate the CHROME (CHemical Restraints avOidance MEthodology) criteria.

Design: Observational prospective longitudinal study.

Setting: Single nursing home in Las Palmas de Gran Canaria, Spain.

Participants: 288 residents; mean age: 81.6 (SD 10.6). 77.4% had dementia.

Intervention: Multicomponent training and consultancy program to eliminate physical and chemical restraints and promote overall quality care. Clinicians were trained in stringent diagnostic criteria of neuropsychiatric syndromes and adequate psychotropic prescription.

Measurements: Psychotropic prescription (primary study target), neuropsychiatric syndromes, physical restraints, falls, and emergency room visits were semi-annually collected from December 2015 to December 2017. Results are presented for all residents and for those who had dementia and participated in the five study waves (completer analysis, $n=107$).

Results: For the study completers, atypical neuroleptic prescription dropped from 42.7% to 18.7%, long half-life benzodiazepines dropped from 25.2% to 6.5%, and hypnotic medications from 47.7% to 12.1% ($p<0.0005$). Any kind of fall evolved from 67.3 to 32.7 (number of falls by 100 residents per year). Physicians' diagnostic confidence increased, while the frequency of diagnoses of neuropsychiatric syndromes decreased ($p<0.0005$).

Conclusions: Implementing the CHROME criteria reduced the prescription of the most dangerous medications in institutionalized people with dementia. Two independent audits found no physical or chemical restraint and confirmed prescription quality of psychotropic drugs. Adequate diagnosis and independent audits appear to be the keys to help and motivate professionals to optimize and reduce the use of psychotropic medication. The CHROME criteria unify, in a single compendium, neuropsychiatric diagnostic criteria, prescription guidelines, independent audit methodology, and minimum legal standards. These criteria can be easily adapted to other countries.

Key words: Chemical restraint, Nursing home, Pharmacological restraint, Pharmacological treatment, Neuropsychiatric symptoms, Dementia, Psychotropic medication, Non-pharmacological therapies

Correspondence should be addressed to: Javier Olazarán, MD, PhD, Fundación Maria Wolff, Río Sil 15 bis, 28660 Boadilla del Monte, Madrid, Spain. Phone: +34 916322507; Fax: +34 914336033. Email: javier@mariawolff.es. Received 04 Feb 2019; revision requested 22 Mar 2019; revised version received 07 Jun 2019; accepted 19 Jun 2019.

Introduction

Despite their modest efficacy and the significant risks derived from their use, psychotropic medications are widely utilized among elderly adults with cognitive

impairment, often in a nonspecific way (Majic *et al.*, 2010). Neuroleptics and long half-life benzodiazepines are the most deleterious drugs associated with faster cognitive decline, higher rate of cerebrovascular events and falls, and unexpected high mortality (Ballard *et al.*, 2009; Olazarán *et al.*, 2013; Schneider *et al.*, 2005). The term chemical restraint has been created to designate the inappropriate prescription of drugs that have the ability to limit personal freedom.

Namely, the Centers for Medicare & Medicaid Services (CMS) and the federal law of the United States defined chemical restraint as “any drug used for discipline or convenience and not required to treat medical symptoms.” The CMS defines “convenience” (Interpretive Guidelines §483.13(a)) as *any action taken by the facility to control a resident’s behavior with a lesser amount of effort by the facility and not in the resident’s best interest.* “Medical symptom” is defined as *an indication or characteristic of a physical or psychological condition.*

Although these definitions and interpretations help identify extreme cases of malpractice, less obvious cases of pharmacological restraining or suboptimal prescription quality might pass undetected as concepts like “resident’s best interest” or “physical or psychological condition” are vague and prone to biased interpretation. This is possibly one of the reasons why there is little research on chemical restraints as such, and most studies approach the subject via prevalence of psychotropic medication prescription with focus on antipsychotics, anxiolytics, and hypnotics (Hughes and Lapane, 2005; Phillips *et al.*, 2000; Richter *et al.*, 2012).

To reduce the use of chemical restraint and promote quality prescription of psychotropic drugs in institutionalized settings, a panel of experts created the CHROME (CHEMical Restraints avOidance METHodology) criteria (Olazarán-Rodríguez *et al.*, 2016). The panel members were experts from psychiatry, neurology, geriatrics, psychology, pharmacology, as well as the legal and managerial fields. The organizational and procedural aspects of the CHROME criteria were designed for institutionalized people with dementia. However, the diagnostic and treatment recommendations allow application in other situations where disruptive disorders may potentially put the person at risk of being subjected to chemical restraint.

The CHROME criteria define chemical restraint as: a) any drug prescribed out of organizational convenience and/or b) any drug that is not prescribed to treat any of the six neuropsychiatric syndromes (as defined in Appendix Table 1) that cause significant patient suffering. In contrast to the definition of the CMS, this more precise definition

allows an external physician to more accurately identify possible or definite chemical restraint as well as making quality prescription audits feasible. Furthermore, these criteria provide listings of admissible drugs and dosages for each syndrome; norms for the acquisition, use, and disposal of psychotropic drugs; legal requirements like the kind of informed consent by type of situation; and most importantly, a method to externally verify (audit) the prescription quality of psychotropic drugs of any given nursing home. In the case of a favorable audit result, the home is awarded an accreditation of “Chemical restraint-free home according to the CHROME criteria,” backed by the Confederación Española de Asociaciones de Familiares de Enfermos de Alzheimer (CEAFA) i.e. the Spanish National Alzheimer’s Association. An updated version of the CHROME criteria is freely available as an online appendix to this article.

The objective of this validation study was to describe the evolution of psychotropic drug prescription as well as other potentially related variables during the training and consultancy process. The several components involved culminated with the accreditation of a nursing home as a “chemical restraint-free center,” issued by CEAFA, which independently made the audit applying Maria Wolff Foundation’s CHROME criteria. On November 2017, the Association’s chairperson issued the accreditation confirming that the facility fully complied with all the requirements set by the CHROME criteria. Neither definitive nor possible chemical restraints were found, and quality prescription criteria were met on randomly selected cases as well as those cases picked by the auditor after visual inspection of the home (Appendix Table 1). The figures of the study’s last wave were recorded two weeks after the audit. In addition to drug-related figures, the study reports the evolution of fall rates, physical restraints, and diagnoses of neuropsychiatric syndromes.

Methods

Design

This was an observational, longitudinal, prospective study in which data of residents of a single nursing home were semi-annually extracted at six dates (study waves) from December 2015 to December 2017.

Ethics

Approval for the study was obtained from an institutional ethics committee (University of La Laguna, Tenerife, Spain).

Setting

The nursing home that was object of the present study is integrated in a larger sociosanitary complex located in the city of Las Palmas on the island of Gran Canaria (Spain). Five wards with 215 beds for people with dementia or highly dependent elderly people were included in the study. The other four wards offer day care for the elderly with or without dementia and 72 mental health beds. A total of 448 people are cared for. The “Centro Sociosanitario El Pino” has been managed since 2010 by the ICOT Health Group through a contract with the local authority “Instituto de Atención Social y Sociosanitaria” of the “Cabildo de Gran Canaria.” Led by the Maria Wolff Foundation, El Pino initiated in 2014 a comprehensive training program for all its professionals aimed at preventing and treating behavioral and psychological symptoms of dementia (BPSD), eliminating physical and chemical restraints, and promoting dementia-friendly care and person-centered care to all its residents. Since the program was conceived and developed for the care of institutionalized people with dementia, the psychiatric and day care residents were not included in the study.

It is noteworthy that El Pino holds unusually good staffing ratios for Spanish standards. For example, nurse aid staffing is more than adequate (e.g. two nurse aids in the night shift per ward of 40 residents, in addition to other medical staff like registered nurses or 24-hour medical doctor). In addition, four full-time psychologists and five medical doctors under one medical coordinator provide psychological and medical care for the 215 residents. Activities manager, occupational therapists, and physiotherapists are also available with an adequate staff to resident ratio. Senior and middle management positions are held in part by psychologists, which contributes to the organization’s commitment with nonpharmacologic treatment and psychoactive drug treatment containment.

Study variables

The primary outcome variable was the frequency of prescription of psychotropic medications, which were divided into the following categories: typical neuroleptics, atypical neuroleptics, antidepressants, hypnotics (short/intermediate half-life benzodiazepines, benzodiazepine derivatives, clomethiazole), long half-life benzodiazepines, dementia-specific medications (cholinesterase inhibitors [CEI], memantine), and antiepileptics. The prescription of psychotropics was coded as yes or not, either continuous or PRN prescription, in the previous week to the study wave. In the case of continuous prescriptions, the daily dose was also registered.

In addition, the following study variables were collected:

- Age and sex, in the first date of study inclusion.
- Total number of prescribed medications for any condition, as registered in the electronic medical history, at the date of the study wave.
- Dementia, when the resident was first included in the study, according to American Psychiatric Association criteria (2013) or <24 score in the Spanish version of the Mini-Mental State Examination (Lobo *et al.*, 1999).
- Presence of neuropsychiatric syndromes, according to CHROME criteria (Appendix Table 1), at the date of the study waves, as diagnosed by the consensus of psychologist and physician. The category of possible syndrome was utilized when there was suspicion of neuropsychiatric syndrome without sufficient diagnostic confidence or information.
- Performance in basic activities of daily living, according to the Barthel Index (Cid-Ruzafa and Damián-Moreno, 1997), closest to the study waves.
- Risk of falling, according to the Downton Index (Aranda-Gallardo *et al.*, 2015), closest to the study waves.
- Falls accumulated in the six months before the date of the study wave. Three types of falls were recorded: non-injurious falls, falls with hip fracture, and falls with any other complication.
- Any kind of physical restraint for at least a week, at the date of the study wave. Bed rails were excluded from the definition of physical restraint in accordance with previous reports (Ljunggren *et al.*, 1997).
- Referrals to the emergency room department in the six months previous to the date of the study waves.
- Death, when occurred between two consecutive study waves.

Since the specific CHROME training was initiated on April 2016 (i.e. between the dates of the first and second study waves), the diagnoses of neuropsychiatric syndromes were not collected at the first study wave. Falls and emergency room referrals began to be systematically recorded on December 1, 2015, and, for that reason, data regarding those variables were also lacked for the first wave. All the other study variables were prospectively collected as part of the center’s usual assessment protocol. Figures of falls, emergency room referrals, and death were expressed as number of events per 100 fully occupied beds per year (RPY).

Intervention

A total of four training sessions adding up to 16 hours per employee were delivered to about 200 staff members over a period of three years. The employees who were trained ranged from senior management and physicians to nurse aids or maintenance personnel. These programs had the transformative

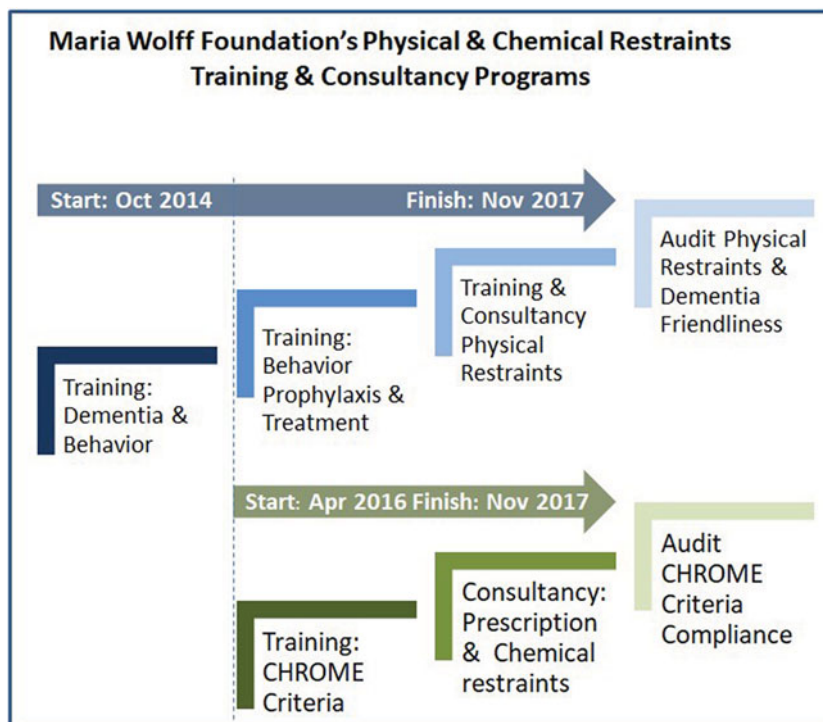


Figure 1. Maria Wolff Foundation's physical and chemical restraints training and consultancy programs.

aims to a) build a dementia friendly culture, b) prevent and treat BPSD non-pharmacologically or in combination with drugs, and c) implement a comprehensive physical restraint reduction program. Implementation of the three programs was systematically followed up with formal videoconferences covering consultancy and discussion of clinical cases. The essential components of the Maria Wolff Foundation physical restraint-free care program for nursing homes have been described in detail elsewhere (Muñiz *et al.*, 2016). These components are basically training, consultation, and consultancy provided at various levels of the organization with special focus on genesis, prophylaxis and management of BPSD, environmental modifications, and person-centered care philosophy. The steps and contents of the intervention implemented in El Pino are summarized in Figure 1.

Once the physical restraint reduction program was fully under way, the CHROME criteria were implemented simultaneously: medical doctors, psychologists, nurses, managers, and the pharmacist received eight hours of training in CHROME criteria. To identify possible or definitive chemical restraints or inappropriate prescription, all the patients had to be diagnosed at each study wave. To ensure diagnostic accuracy, psychologists and medical doctors made their diagnoses separately and tried to reach diagnostic consensus case by case. These diagnoses were the basis by which physicians then applied the

prescription guidelines delivered by the CHROME criteria. The center's pharmacist helped to avoid undesired interactions and kept the study database up to date regarding drugs. The study director of the CHROME criteria (JO) provided *ad libitum* videoconference, e-mail, and telephone support.

Data extraction and statistical analysis

Pharmacological and medical data were extracted from the center's software/database (Aegerus, Sabadell, Spain) to MS Excel 2010 (Microsoft, Redmond, WA) by the center investigators. Diagnostic data were produced by the medical doctors and psychologists and manually recorded in the mentioned spreadsheet. Data were reviewed for potential artifacts and errors by the principal investigator (RM), the study director (JO), and one of the center's psychologists (FC) and then exported from MS Excel into SPSS v.15.0 (SPSS Inc., Chicago, IL) for analysis.

Measures of frequency, central tendency, and dispersion were utilized to describe the residents' characteristics and to analyze the evolution of the study variables across the five study waves. The evolution of residents who had dementia and remained in the nursing home throughout the complete study period was specifically analyzed (completer analysis) as these were the cases that can benefit most from the study intervention and therefore validate the CHROME criteria. Nonparametric statistics

Table 1. Study variables in the total sample of residents across the five study waves

	12/01/2015 (<i>n</i> = 205)	06/01/2016 (<i>n</i> = 217)	12/01/2016 (<i>n</i> = 214)	06/01/2017 (<i>n</i> = 219)	12/01/2017 (<i>n</i> = 214)
Age	82.7 (10.1)	82.5 (10.6)	81.9 (10.5)	81.6 (10.6)	81.3 (10.7)
Sex (% female)	66.3	64.8	62.6	62.4	61.6
Basic ADL (BI)	22.2 (26.6)	25.0 (28.3)	23.8 (28.0)	25.1 (27.4)	24.3 (27.5)
Physical restraint (%)	35.1 (28.6-41.7)	10.6 (6.5-14.7)	7.5 (4.0-11.0)	6.4 (3.2-9.6)	0
Risk of falling (DI)	4.5 (1.5)	4.5 (1.5)	4.4 (1.5)	4.4 (1.5)	4.5 (1.5)
Fall of any type (RPY)	NC	100.7	136.6	90.0	135.4
Noninjurious falls	NC	88.7	118.6	68.2	105.1
Falls with hip fracture	NC	0.00	1.99	0.95	0.00
Falls other complications	NC	12.0	15.9	20.8	30.3
Emergency room referral (RPY)	NC	35.9	78.7	49.2	44.5
Death (RPY)	29.4	20.9	18.9	17.0	16.1
Medications (n)1	8.2 (3.2)	7.1 (3.3)	6.9 (3.1)	7.1 (3.2)	6.4 (3.4)
Typical neuroleptics (%)	7.5 (3.8-11.1)	5.6 (2.5-8.7)	5.7 (2.5-8.8)	5.1 (2.2-8.1)	3.8 (1.2-6.5)
Atypical neuroleptics (%)	43.8 (36.9-50.6)	36.0 (29.6-42.4)	37.4 (30.9-43.9)	38.2 (31.8-44.7)	27.8 (21.7-33.7)
Antidepressants (%)	45.0 (38.1-51.9)	38.2 (32.1-45.2)	40.2 (34.1-47.2)	43.3 (37.2-50.4)	41.6 (35.4-48.7)
Hypnotics (%)	35.6 (29.1-42.2)	34.7 (28.4-41.0)	34.1 (27.8-40.5)	30.1 (24.2-36.1)	16.4 (11.5-21.3)
Long half-life BZD (%)	24.4 (18.5-30.3)	13.2 (8.8-17.7)	14.5 (9.8-19.2)	13.5 (9.1-18.0)	9.6 (5.7-13.5)
CEI/memantine (%)	38.0 (31.3-44.7)	35.4 (28.9-41.8)	36.0 (29.6-42.4)	36.9 (30.4-43.3)	35.5 (29.1-41.9)
Antiepileptics (%)	18.4 (13.1-23.8)	17.3 (12.2-22.4)	17.9 (12.8-23.1)	19.8 (14.5-25.1)	19.2 (13.9-24.4)

Figures represent mean (SD), frequency (95% confidence interval), or number of events per 100 beds per year (RPY); ¹PRN prescriptions are included. ADL: activities of daily living; BI: Barthel Index; BZD: benzodiazepines; CEI: cholinesterase inhibitors; DI: Downton Index; n: number; NC: not collected.

were applied for the analysis of psychotropic medication prescription and other study variables in those subjects, taking as reference the first measurement. Given that frequency of psychotropic prescription was the primary study outcome and since there were seven groups of psychotropic medications, the level of statistical significance was set at $p < 0.007$.

Results

A total of 288 residents were studied across the five study waves. Mean age at study inclusion was 81.6 years (SD 10.6, range 38-104), 183 (63.5%) of the participants were female and 223 (77.4%) of them had dementia. The demographic and clinical variables of the residents across the five study waves are presented in Table 1. As expected, the participants were polymedicated, had a high risk of falls, and had high functional dependence. There was a prevalence of physical restraint of 35.1% in the first wave, which was progressively reduced and culminated with complete absence of physical restraints at the end of the study. Those results were accompanied by an increase of noninjurious falls (from 88.7 to 105.1 RPY), falls with complication different from hip fracture (from 12.0 to 30.3 RPY), and emergency room referrals (from 35.9 to 44.5 RPY). However, falls with hip fracture did not increase significantly,

and demise was progressively decreased across the study waves (Table 1).

The mean number of psychotropic prescriptions per resident was 1.6 (SD 1.3, range 0-5) at the beginning of the study and 1.0 (SD 1.1, range 0-5) at the end. At the beginning of the study, prescription was particularly frequent for antidepressants (45.0%), atypical neuroleptics (43.8%), and hypnotics (35.6%). At the end of the study, frequency of prescription was significantly reduced for atypical neuroleptics, long half-life benzodiazepines, and hypnotic medications (Table 1). "As needed" (PRN) prescriptions were frequently observed for neuroleptics, long half-life benzodiazepines, or hypnotics at the beginning of the study (30.7% [CI 95% 22.4-37.0]) but were reduced at the end (4.7% [CI 95% 1.8-7.5]). Significant dose changes could not be detected across the study waves, although the number of patients that remained on the different medications was low. For instance, the mean dose (SD) of quetiapine - the most frequently prescribed neuroleptic- was 140.6 (115.7) mg/d in the first wave ($n = 28$) and 132.1 (77.5) mg/d in the last wave ($n = 14$); the corresponding figures for lormetazepam, which was the most frequently prescribed hypnotic, were 1.4 (0.9) mg/d ($n = 12$) and 0.9 (0.2) mg/d ($n = 7$) (all p values > 0.05 , results of medication dose are not shown).

Table 2. Results in the residents which had dementia and completed the five study waves ($n = 107$)

	12/01/2015	06/01/2016	12/01/2016	06/01/2017	12/01/2017	p^2
Basic ADL (BI)	19.2 (23.8)	20.8 (24.2)	17.8 (23.1)	17.3 (21.9)	16.8 (21.7)	0.021
Physical restraint (%)	43.0 (33.6-52.4)	15.9 (9.0-22.8)	12.1 (6.0-18.3)	11.2 (5.2-17.2)	0	0.000
Risk of falling (DI)	4.6 (1.4)	4.6 (1.5)	4.3 (1.6)	4.0 (1.7)	3.6 (1.7)	0.000
Fall, any type (RPY)	NC	67.3	72.0	35.5	32.7	NA
Non-injurious fall	NC	59.8	68.2	27.1	23.4	NA
Falls with hip fracture	NC	0	0.9	0	0	NA
Falls with other complication	NC	7.5	2.8	8.4	9.3	NA
Emergency room referral (RPY)	20.6	12.1	34.6	9.3	7.5	NA
Medications (n) ¹	8.3 (3.5)	6.7 (3.0)	6.6 (3.2)	6.5 (2.9)	5.6 (2.8)	0.000
Typical neuroleptics	5.8 (1.3-10.3)	2.9 (0.0-6.1)	2.8 (0.0-6.0)	1.9 (0.0-4.5)	1.9 (0.0-4.5)	0.102
Atypical neuroleptics	42.7 (33.2-52.3)	33.3 (24.3-42.4)	34.6 (25.6-43.6)	34.6 (25.6-43.6)	18.7 (11.3-26.1)	0.000
Antidepressants	45.6 (36.0-55.3)	40.0 (30.6-49.4)	43.0 (33.6-52.4)	42.1 (32.7-51.4)	40.2 (30.9-49.5)	0.257
Hypnotics	47.7 (38.2-57.1)	40.2 (30.9-49.5)	38.3 (29.1-47.5)	38.3 (29.1-47.5)	12.1 (6.0-18.3)	0.000
Long half-life BZD (%)	25.2 (17.0-33.5)	11.2 (5.2-17.2)	15.0 (8.2-21.7)	14.0 (7.4-20.6)	6.5 (1.9-11.2)	0.000
CEI/memantine	53.4 (43.8-63.0)	48.6 (39.0-58.1)	47.7 (38.2-57.1)	45.8 (36.4-55.2)	46.7 (37.3-56.2)	0.059
Antiepileptics	15.5 (8.5-22.5)	14.3 (7.6-21.0)	15.0 (8.2-21.7)	15.0 (8.2-21.7)	14.0 (7.4-20.6)	0.739

Figures represent mean (SD), frequency (95% confidence interval), or number of events per 100 beds per year (RPY).

¹PRN prescriptions are included; ²for the comparison between the last and the first measurement (Wilcoxon test). ADL: activities of daily living; BI: Barthel Index; BZD: benzodiazepines; CEI: cholinesterase inhibitors; DI: Downton Index; n: number; NA: not applicable; NC: not collected; RPY: per 100 beds and year.

There were 107 residents with dementia, who remained in the nursing home during the complete study period. The mean (SD) age of those residents was 84.2 (8.5) years, and 76.6% of them were female. The evolution of the study variables of these completer subjects is presented in Table 2. In this group, a significant reduction of psychotropic medication was confirmed for atypical neuroleptics, which fell from 42.7% to 18.7% of prescription frequency; for hypnotics, which fell from 47.7% to 12.1%, and for long half-life benzodiazepines, which fell from 25.2% to 6.5%. Considering only neuroleptic, long half-life benzodiazepines, and hypnotic medications, the total number of prescriptions per patient fell from 1.1 (SD 1.1, range 0-5) to 0.4 (SD 0.7, range 0-3), $p < 0.05$ (Figure 2). The observed reduction of psychotropic prescription and elimination of physical restraints were accompanied by a decrease of falls (from 67.3 RPY to 32.7 RPY) and a decrease of emergency room referrals (from 20.6 to 7.5).

An increase in the confidence in the diagnosis of neuropsychiatric syndromes was observed, along with trends of decrease in frequency for the diagnoses of psychotic syndrome (from 13.1% to 4.7%), impulsive syndrome (from 14.0% to 7.5%), maniform syndrome (from 4.7% to 0.0%), and sleep alteration (from 15.9% to 8.4%). Only the frequency of anxiety syndrome remained elevated (31.8%) at the end of the study period (Table 3 and Figure 2).

Discussion

The external audit and the results herein reported show a complete elimination of physical and chemical restraints, along with an overall reduction of psychotropic medication, particularly for residents with dementia. In these patients, falls and emergency room referrals were also reduced. Overall, these results validate the CHROME criteria as a feasible, efficient, and safe tool to optimize the quality prescription of psychotropic medications in institutionalized people with dementia.

We believe that the definition of relatively stringent diagnostic criteria for people with dementia who present clinically significant neuropsychiatric syndromes (Appendix Table 2) turned out to be the primary key success factor to change prescription behavior, attain quality prescription, and secondarily reduce the frequency of the most dangerous medications. The observed trends of decrease in frequency of diagnoses for most neuropsychiatric syndromes suggests a previous overdiagnosis and supports the usefulness of the definitions provided. Figure 2 reflects how reduced frequency of diagnoses (all except anxiety syndrome) was associated with the reduction of neuroleptic, benzodiazepine, and hypnotic prescriptions.

The second key success factor had an organizational nature: attaining the *Quality Seal of CHROME Criteria Compliance*, which was awarded by an

Table 3. Evolution of neuropsychiatric diagnoses ($n=107$)

	12/01/2015	06/01/2016	12/01/2016	06/01/2017	12/01/2017
Depressive syndrome					
Possible	NC	6.5	5.6	5.6	0.9
Certain	NC	8.4	6.5	8.4	12.1
Total	NC	15.0 (8.2-21.7)	12.1 (6.0-18.3)	14.0 (7.4-20.6)	13.1 (6.7-19.5)
Anxiety syndrome					
Possible	NC	5.6	5.6	6.5	0.9
Certain	NC	21.5	20.6	19.6	30.8
Total	NC	27.1 (18.7-35.5)	26.2 (17.8-34.5)	26.2 (17.8-34.5)	31.8 (23.0-40.6)
Psychotic syndrome					
Possible	NC	2.8	1.9	0.9	0.0
Certain	NC	10.3	11.2	10.3	4.7
Total	NC	13.1 (6.7-19.5)	13.1 (6.7-19.5)	11.2 (5.2-17.2)	4.7 (0.7-8.7)
Impulsive syndrome					
Possible	NC	4.7	5.6	2.8	0.0
Certain	NC	9.3	6.5	7.5	7.5
Total	NC	14.0 (7.4-20.6)	12.1 (6.0-18.3)	10.3 (4.5-16.0)	7.5 (2.5-12.5)
Maniform syndrome					
Possible	NC	0.9	0.9	0.9	0.0
Certain	NC	3.7	3.7	3.7	0.0
Total	NC	4.7 (0.7-8.7)	2.8 (0.7-8.7)	4.7 (0.7-8.7)	0.0 (0-0)
Sleep alteration					
Possible	NC	4.7	2.8	5.6	0.0
Certain	NC	11.2	10.3	8.4	8.4
Total	NC	15.9 (9.0-22.8)	13.1 (6.7-19.5)	14.0 (7.4-20.6)	8.4 (3.2-13.7)

Figures represent frequency (95% confidence interval). NC: not collected.

external audit, motivated management, psychologists, physicians, and other staff to make the effort in treating behavioral or psychological symptoms with environmental and nonpharmacological strategies more thoughtfully. The temptation of using drugs as shortcuts was avoided through the stringency of the CHROME criteria.

In contrast to the rest of the syndromes, the prevalence of anxiety remained high at the end of the study. There are three explanatory factors for that result: 1) Sleep disorder or even impulsive and psychotic syndromes might have been reclassified to anxiety as the primary syndrome; 2) At the beginning of the study, physicians and psychologists did not clearly differentiate symptoms from syndromes. Put in a blunt example, sadness (reactive) due to nursing home placement does not necessarily meet depressive syndrome criteria; 3) Anxiety disorders are highly prevalent in older adults living in long-term care facilities (Seitz *et al.*, 2010). In an observational study conducted in people with dementia, significant anxiety was found in 33.7% of the residents remaining so after one year (31.2%) (Goyal *et al.*, 2018).

The present study has several limitations. Though large, we described results of only one nursing home. Prevention of delirium and other potential physical benefits of the psychotropic

medication reduction were not specifically recorded. The frequency and severity of behavioral and psychological symptoms at the beginning and end of the study were not quantitatively measured, as were not quality of life of residents and professional caregivers. The authors, nevertheless, believe that the changes in drug prescription did in no way worsen patient well-being (agitation, etc.). The four study psychologists (FC, MP, NR, AL) were vigilant in regard to the improvement-worsening of all residents and did not report any salient negative effects besides some residents being more demanding. Moreover, cases considered difficult were treated in clinical sessions with the study director (JO), and the principal investigator (RM) and solved acceptably.

The CHROME criteria require some investigative efforts on the physician's side, which might be perceived as more time consuming, especially in the beginning. Future research must clarify if optimized prescription settles in as a constant cultural component of the care home, since turnover of both residents and clinicians might thin a home's achievements over time.

Most articles published to improve prescription of psychotropics in people with dementia have focused on frequency (Janus *et al.*, 2016; Richter *et al.*, 2012), prescription factors (Brimelow *et al.*,

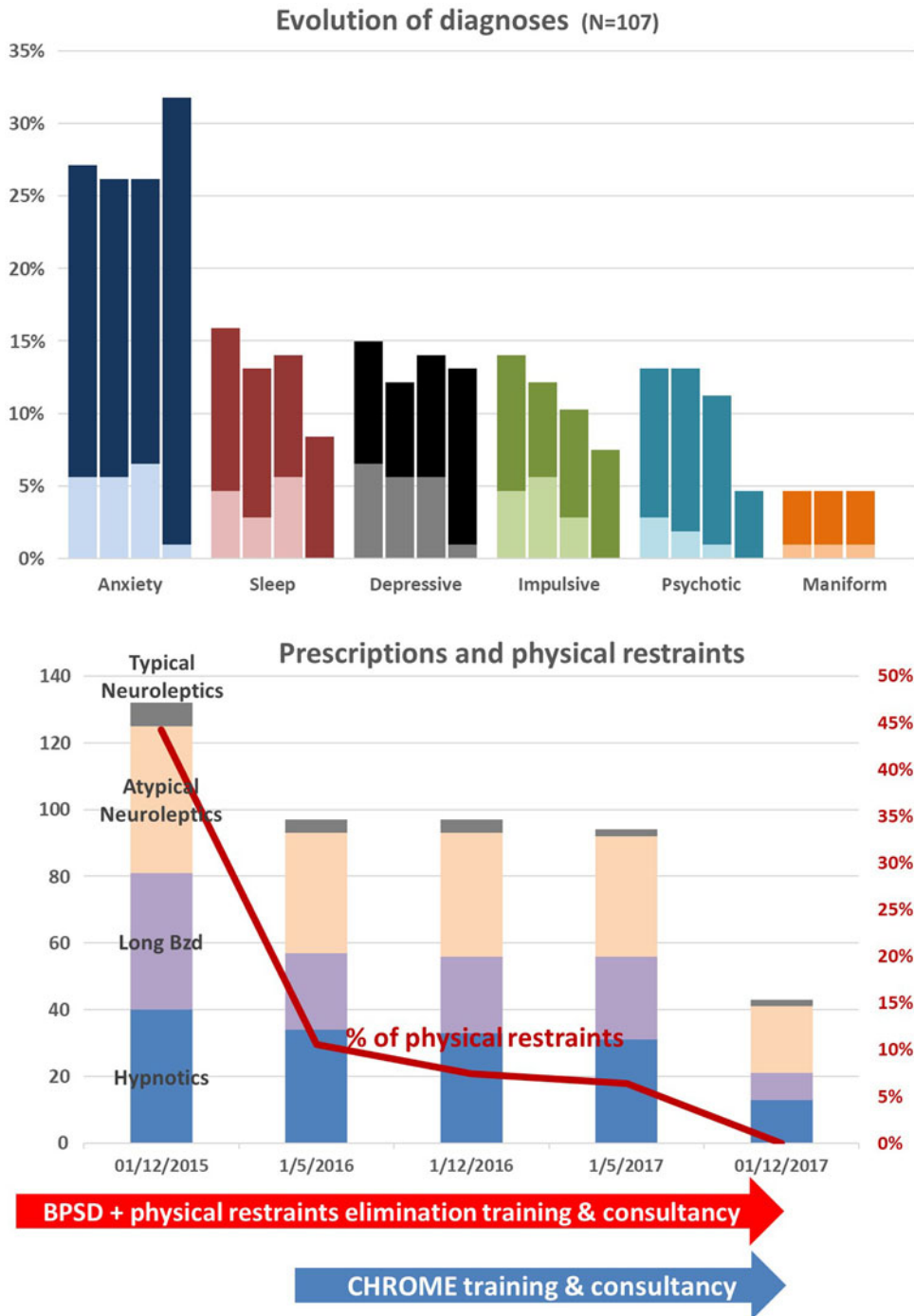


Figure 2. Evolution of certain (solid) and possible (light) neuropsychiatric diagnoses while physicians learned to use the CHROME criteria (up), total number of prescriptions for the most dangerous medications and frequency of physical restraints (down), across the study waves. BZD: benzodiazepines.

in press; Nørgaard *et al.*, 2017), and BPSD. The “frequency and BPSD” approach has recently been described in an intervention using patient-centered medication reviews for BPSD (Massot Mesquida *et al.*, 2019). In contrast to this more common approach, the CHROME criteria propose to focus on adequacy of prescription based on predefined

neuropsychiatric syndromes, which appear as a result of a cerebral biological imbalance. From there, adequacy and frequency issues are implicitly solved in a relatively simpler and safer way (Appendix Tables 2 and 3).

The CHROME criteria can easily be applied by any physician, be it for community dwelling or

institutionalized people with dementia. Clear definition of chemical restraint and ease for third-party verification add objectivity and organizational possibilities. The criteria can easily be adapted to other countries adjusting to local drugs, legal requirements concerning drug purchase, storage and disposal, as well as kinds of informed consent.

Conflict of interest

RM and JO received honoraria from ICOT for their consultancy and training services outside of this study.

Description of the authors' roles

R. Muñiz conceived the CHROME criteria, contributed to the study design, supervised the data collection, conducted statistical analyses, wrote part of the article, and coordinated all other coauthors' contributions. A.I. Pérez-Wehbe organized the study inception and reviewed the paper. F. Couto participated in neuropsychiatric diagnoses, supervised data extraction, and reviewed the paper. M. Pérez oriented physicians in treatment options, collected data, and reviewed the paper. N. Ramírez participated in neuropsychiatric diagnoses, collected data, and reviewed the paper. A. López supervised the entire study process, organized the external audits, and reviewed the paper. J. Rodríguez coordinated the physician's participation and reviewed the paper. T. Usieto and L. Lavin implemented prescriptions according to the CHROME criteria and gave valuable feedback to the research team. A. Rigueira provided CHROME criteria's pharmaceutical drug management and reviewed the manuscript. L. Agüera-Ortiz and J. López-Alvarez contributed to the definition of neuropsychiatric syndromes and to the treatment guidelines and reviewed the paper. M. Martín-Carrasco assisted in writing the manuscript. J. Olazarán contributed to the definition of neuropsychiatric syndromes, participated in the study design, trained the study physicians, and wrote the paper.

Acknowledgments

The principal investigator and the study director thank Juan Luis Beltrán and Pilar García for their invaluable support regarding legal and bio-ethic issues related to both physical and pharmacological restraints that are woven into this article. Jesús M^a López-Arrieta for his contributions from the geriatric perspective.

Supplementary material

To view supplementary material for this article, please visit <https://doi.org/10.1017/S104161021900111X>.

References

- American Psychiatric Association.** (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*, 5th Ed. Arlington, VA: American Psychiatric Association.
- Aranda-Gallardo, M. et al.** (2015). [Consequences of errors in the translation of questionnaires: Spanish version of Downton index]. *Revista de Calidad Asistencial*, 30, 195–202. doi: [10.1016/j.cali.2015.04.003](https://doi.org/10.1016/j.cali.2015.04.003). [Article in Spanish]
- Ballard, C. et al.** (2009). The dementia antipsychotic withdrawal trial (DART-AD): long-term follow-up of a randomised placebo-controlled trial. *Lancet Neurology*, 8, 151–157. doi: [10.1016/S1474-4422\(08\)70295-3](https://doi.org/10.1016/S1474-4422(08)70295-3).
- Brimelow, R. E., Wollin, J. A., Byrne, G. J. and Dissanayaka, N. N.** (in press). Prescribing of psychotropic drugs and indicators for use in residential aged care and residents with dementia. *International Psychogeriatrics*, 31, 837–847. doi: [10.1017/S1041610218001229](https://doi.org/10.1017/S1041610218001229).
- Cid-Ruzafa, J. and Damián-Moreno, J.** (1997). [Disability evaluation: Barthel's index]. *Revista Española de Salud Pública*, 71, 127–137. [Article in Spanish]
- Goyal, A. R., Bergh, S., Engedal, K., Kirkevold, M. and Kirkevold, Ø.** (2018). The course of anxiety in persons with dementia in Norwegian nursing homes: a 12-month follow-up study. *Journal of Affective Disorders*, 235, 117–123. doi: [10.1016/j.jad.2018.04.015](https://doi.org/10.1016/j.jad.2018.04.015).
- Hughes, C. M. and Lapane, K. L.** (2005). Administrative initiatives for reducing inappropriate prescribing of psychotropic drugs in nursing homes: how successful have they been? *Drugs & Aging*, 22, 339–351.
- Janus, S. I., van Manen, J. G., IJzerman, M. J. and Zuidema, S. U.** (2016). Psychotropic drug prescriptions in Western European nursing homes. *International Psychogeriatrics*, 28, 1775–1790.
- Ljunggren, G., Phillips, C. and Sgadari, A.** (1997). Comparisons of restraint use in nursing homes in eight countries. *Age & Ageing*, 26(Suppl 2), 43–47.
- Lobo, A. et al.** (1999). [Revalidation and standardization of the cognition mini-exam (first Spanish version of the Mini-Mental Status Examination) in the general geriatric population]. *Medicina Clínica (Barcelona)*, 112, 767–774. [Article in Spanish]
- Majic, T. et al.** (2010). The pharmacotherapy of neuropsychiatric symptoms of dementia: a cross-sectional study in 18 homes for the elderly in Berlin. *Deutsches Ärzteblatt International*, 107, 320–327. doi: [10.3238/arztebl.2010.0320](https://doi.org/10.3238/arztebl.2010.0320).
- Massot Mesquida, M., Tristany Casas, M., Franzi Sisó, A., García Muñoz, I., Hernández Vian, Ó. and Torán Monserrat, P.** (2019). Consensus and evidence-based medication review to optimize and potentially reduce psychotropic drug prescription in institutionalized dementia patients. *BMC Geriatrics*, 19, 7. doi: [10.1186/s12877-018-1015-9](https://doi.org/10.1186/s12877-018-1015-9).
- Muñiz, R. et al.** (2016). Reducing physical restraints in nursing homes: A report from Maria Wolff and Sanitas.

- Journal of the American Medical Directors Association*, 17, 633–639. doi: [10.1016/j.jamda.2016.03.011](https://doi.org/10.1016/j.jamda.2016.03.011).
- Nørgaard, A., Jensen-Dahm, C., Gasse, C., Hansen, E. S. and Waldemar, G.** (2017). Psychotropic polypharmacy in patients with dementia: prevalence and predictors. *Journal of Alzheimer's Disease*, 56, 707–716. doi: [10.3233/JAD-160828](https://doi.org/10.3233/JAD-160828).
- Olazarán, J., Valle, D., Serra, J. A., Cano, P. and Muñiz, R.** (2013). Psychotropic medications and falls in nursing homes: a cross-sectional study. *Journal of the American Medical Directors Association*, 14, 213–217. doi: [10.1016/j.jamda.2012.10.020](https://doi.org/10.1016/j.jamda.2012.10.020).
- Olazarán-Rodríguez, J. et al.** (2016). [The CHROME criteria for the accreditation of centers free of chemical restraints and for a quality prescription of psychotropic medications]. *Psicogeriatría*, 6, 91–98. [Article in Spanish]
- Phillips, C. D., Spry, K. M., Sloane, P. D. and Hawes, C.** (2000). Use of physical restraints and psychotropic medications in Alzheimer special care units in nursing homes. *American Journal of Public Health*, 90, 92–96.
- Richter, T., Mann, E., Meyer, G., Haastert, B. and Köpke, S.** (2012). Prevalence of psychotropic medication use among German and Austrian nursing home residents: a comparison of three cohorts. *Journal of the American Medical Directors Association*, 13, 187.e7–187.e13. doi: [10.1016/j.jamda.2011.03.007](https://doi.org/10.1016/j.jamda.2011.03.007).
- Schneider, L. S., Dagerman, K. S. and Insel, P.** (2005). Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. *Journal of the American Medical Association*, 294, 1934–1943.
- Seitz, D., Purandare, N. and Conn, D.** (2010). Prevalence of psychiatric disorders among older adults in long-term care homes: a systematic review. *International Psychogeriatrics*, 22, 1025–1039. doi: [10.1017/S1041610210000608](https://doi.org/10.1017/S1041610210000608).

SUPPLEMENTARY MATERIAL

Appendix 1. The CHROME criteria for a quality prescription of psychotropic medications in institutionalized people with dementia

1. Definition of chemical restraint

Chemical restraint is defined as a psychoactive drug that is prescribed:

- a) not complying with any of the six neuropsychiatric syndromes defined by the CHROME criteria or
- b) for organizational convenience.

Some examples of chemical restraints are: prescriptions to suppress or reduce “demanding behaviors, like seeking constant “attention or care”, “screaming”, “singing”, “behaviors that can give a bad impression to visitors”, induce patients to extend their stay in bed, treat unspecific “agitation”, wandering, etc.

2. Neuropsychiatric syndromes: key to quality prescription of psychotropics

Neuropsychiatric syndromes define clinical pictures of persistent and significant discomfort or risk that arises from a pathological substrate (anatomical-chemical) and are not mere consequences of the environment.

Another condition for symptoms to be included under the umbrella of neuropsychiatric syndromes, in dementia, is that cognitive impairment cannot fully explain these.

The CHROME criteria’s proposal is to prescribe based on strict compliance with six dementia-relevant neuropsychiatric syndromes. This syndromic prescription approach should improve prescription quality based on behavioral and psychological symptoms of dementia (BPSD). Prescriptions on a BPSD basis have to date, produced no prescription agreements. This may be because many underlying pathologies can cause these symptoms. Instead, the neuropsychiatric approach proposes to target (as far as possible) the underlying pathology of symptoms. Environmental, and non-pharmacological approaches remain first choices.

Table 1 summarizes the definitions of relevant neuropsychiatric syndromes, developed by the CHROME expert panel.

3. Check-list before prescribing pharmacological treatment

The following issues should be considered once the manifestation or target symptom has been identified and before starting pharmacological treatment:

- Is it an adaptive phenomenon that will tend to fade once the environmental cause disappears?
- Has an organic cause, other than dementia, been ruled out (e.g. pain, infection ...)?
- May non-pharmacological measures and/or adjustment of the current medication be enough?
- Have dementia medications (i.e., cholinesterase inhibitors and memantine) been optimized?
- Is it a pathological phenomenon susceptible to specific pharmacological treatment effective beyond sedation (i.e., neuropsychiatric syndrome)?

- Do the short, medium, and long-term benefits of pharmacological treatment exceed the inherent risks of the medication to be used?

The suitable medications for the different neuropsychiatric syndromes, according to the existing literature and CHROME expert opinion (evidence level C) are presented in Table 2.

4. Accreditation of chemical restraint free facilities

As CHROME criteria are designed to allow external diagnostic audit (by a physician), nursing homes or similar facilities can be evaluated for compliance.

The accreditation process consists of four phases:

1. Training
2. Implementation and consultancy
3. External auditing/verification
4. Final report and accreditation (if requirements are met)

Training, implementation and consultancy phases include exchange of information between the home's medical and other staff and the CHROME criteria consultants. In addition, the CHROME experts implement a consultancy program to facilitate the organization of all the involved departments.

The on-site audit checks for:

1. Quality prescription of psychoactive drugs in accordance to the CHROME criteria, and therefore:
2. If chemical restraints are present or not
3. Compliance with minimum legal standards of psychotropic prescriptions
4. Compliance with pharmacy standards (drug acquisition, storage, administration and disposal)

The methodology and steps of the auditing/verification phase are the following:

- The physician to conduct the audit is external (e.g.: hired by the National Alzheimer's Society), very experienced in BPSD treatment, as well as previously trained by the CHROME criteria panel experts
- Identification of all the residents of the facility with dementia
- Random selection of 20% of residents with dementia for verification, as well as:
- Selection of all residents receiving more than three psychotropic drugs
- The auditing physician, accompanied by the center physician, evaluates the information available in the medical records of the selected residents and explores those residents where they usually live
- In addition, the auditing doctor may spontaneously select any resident which, by reason of his or her appearance, might be at risk of chemical restraint (residents looking bloated, claiming attention, being restless, etc.)
- The auditor assesses aspects which will be individually verified and introduced systematically on the assessment sheets: diagnosis of dementia, prescription of drugs for BPSD, informed consent, initial adjustment of the prescription, response to the drug, control of possible adverse effects, current dose, and adequacy of maintaining prescription and dose

The verification phase ends with the completion of a report by the auditing physician, which is written outside the premises. The report includes suggestions for improvement and whether the “accreditation of chemical restraint free center” can or cannot be granted.

The audit(or) distinguishes between “definitive” and “possible” chemical restraints, which are defined in Table 3. The accreditation of “chemical restraint free facility” is only granted if there is less than one definitive chemical restraint and less than three possible chemical restraints for every 100 people with dementia in the center.

Appendix Table 1. Definitions of “Definitive” and “Possible” chemical restraints

<p>DEFINITIVE CHEMICAL RESTRAINT The criteria a, b and c must be fulfilled:</p> <ul style="list-style-type: none"> a) Any kind of neuropsychiatric syndrome clearly absent b) The drug was clearly prescribed for organizational convenience c) Absence of any ongoing withdrawal plan
<p>POSSIBLE CHEMICAL RESTRAINT At least one of the following criteria is met:</p> <ul style="list-style-type: none"> a) There is insufficient information regarding the existence of neuropsychiatric syndrome b) There is no clear response to the drug or the balance between response and tolerance is not admissible c) There was acceptable response and tolerance, but withdrawal should have been attempted
<p>The accreditation of “chemical restraint free facility” will only be issued if there is less than one definitive chemical restraint and less than three possible chemical restraints for every 100 people with dementia in the center.</p>

Appendix Table 2. Working definitions of the relevant neuropsychiatric syndromes

SYNDROME*	DEFINITION and CAVEATS
Depressive syndrome	<p>DEFINITION Mood disturbance that manifests itself as sadness, anhedonia, feeling of being a burden or lack of hope, which occurs persistently (most of the time for at least two weeks) and is a change regarding a previous state.</p>
	<p>CAVEATS In patients with advanced dementia or impaired verbal communication, symptoms can be inferred from attitudes (negative, withdrawn, lack of interest) or from body language (appearance of sadness, crying, etc.).</p> <p>The clinical presentation of anergia, lack of interest and reduced enjoyment in the absence of sadness, feelings of uselessness, guilt, hopelessness or suicidal ideation might instead suggest an apathetic syndrome.</p>

Anxiety syndrome	DEFINITION Excessive or unjustified fear or feeling of loss of control, expressed as fear or apprehension about the present or future, somatic complaints (headache, gastric discomfort, urge to urinate, dry mouth, etc.), repetitive thoughts or obsessive behaviors, which occur persistently (most of the time for at least two weeks) and produce significant distress or loss of functioning.
	CAVEATS Patients with advanced dementia or impaired verbal communication, symptoms can be inferred from attitudes (distress, shadowing the caregiver, etc.), body language (quick or deep breathing, getting too easily alarmed, sweating, etc.). De novo manifestation of symptoms of anxiety in patients with dementia must not only imply a reevaluation of previous medical processes and drug treatments, but also an organic assessment in search of a possible medical trigger. Therefore, an anxiety syndrome of neuropsychiatric nature is a diagnosis of exclusion.
Psychotic syndrome	DEFINITION False beliefs or stories (ideas of theft, abandonment, prejudice, infidelity, etc.) or false perceptions (visual, auditory or other), which occur persistently (most days for at least seven days) and cause significant suffering or risks, or a loss of functioning.
	CAVEATS Given the potential risks and suffering of a psychotic syndrome, pharmacologic treatment can be justified even if a systemic illness (or another condition different from dementia) is contributing to the symptoms. In these cases, de-prescription must be attempted as soon as the associated process is controlled. The psychotic syndrome tends to grow smaller and disappear as dementia progresses. In patients with advanced dementia, or in those with important verbal communication deficits, the presence of a psychotic syndrome can rarely be proven. False recognitions, if coexistent with anosognosic manifestations are not going to improve with antipsychotics, thus excluding their indication.
Impulsive syndrome	DEFINITION Lack of foresight, or social tact in verbal language, body language or other behaviors (e.g., eating) that occurs persistently (most days for the last two weeks) and causes significant suffering or risk, a loss of functioning, dignity, or social rejection.
	CAVEATS Due to the lack of specific pharmacologic treatments (more even than for the previously described syndromes), modification of institutional or family environment must be considered as the primary variable to be modified. Use of medication must be limited to those situations where impulsiveness puts patient, mates or caregivers at risk, or an important loss of dignity. Due to its different origin and treatment, a differential diagnosis regarding the maniform syndrome has to be performed.
Maniform syndrome	DEFINITION Elevated mood and perception of one's own capabilities, feeling abnormally energetic, hyperactive, decreased need for rest, impulsiveness, irritability

	and anger, which occurs persistently (most of the time for at least a week), associated with significant risk or a loss of functioning.
	<p>CAVEATS</p> <p>Should be considered in case of patients with a history of bipolar disorder. Even in these patients, there is high likelihood that symptoms have a secondary cause. For this reason, a new organic assessment needs to be made. The neuropsychiatric origin of the maniform syndrome is therefore a diagnosis of exclusion.</p> <p>The maniform syndrome requires drug treatment, which has to be initiated as soon as antidepressive medication (in case of being present) starts to be decreased or withdrawn.</p>
Sleep alteration	<p>DEFINITION</p> <p>Loss of the physiological sleep-wake cycle (hypersomnia, insomnia, cycle inversion, fragmented sleep, etc.) that occurs persistently (more than half of the days) in the last two weeks</p>
	<p>CAVEATS</p> <p>Primary sleep alteration in elderly with dementia is frequent. It is however mandatory to always check for another syndrome to better explain the disturbance; for example: anxiety, depressive or psychotic syndromes. The organizational need to keep patients in bed longer than desired by them or needed for their physiological rhythms can never justify drug treatments.</p>
<p>* In order to diagnose any of the syndromes, the disturbances should never be entirely explainable due to a medical condition (infection, pain, anemia, thyroid disorders, etc.), drugs (including excessive psychotropics), caregiver attitude, stressing environment, lack of stimuli, lack of basic needs (social, respect, etc.), critical event (death of a loved one, change of environment, etc.) or as a reaction to cognitive impairment. Manifestations of other syndromes can always coexist within the frame of a primary syndrome (e.g. sleep alteration or delusional ideation in case of a patient with primarily a depressive syndrome) “Syndromes” should never be confused with “traits” or “symptoms”. Being extremely sad due to the recent passing away of a loved one, or due to being placed in a nursing home are both normal human reactions that as such have no neuropsychiatric origin. Therefore, in principle there is no need for drug treatment. Instead, these conditions usually need compassionate attention in a wider sense.</p>	

Appendix Table 3. Medications indicated for the different neuropsychiatric syndromes

	First choice	Second choice
Depressive syndrome	SSRI, SNRI, other antidepressants (mirtazapine, vortioxetine, bupropion)	
Anxiety syndrome	SSRI, SNRI, other antidepressants (mirtazapine, trazodone)	Short/middle half-life benzodiazepines; gabapentin, pregabalin; atypical antipsychotics (quetiapine, olanzapine)
Psychotic syndrome	Atypical antipsychotics	

Impulsive syndrome	Serotonergic medications (sertraline, citalopram, escitalopram, trazodone)	Antiepileptic drugs (valproate, gabapentin, pregabalin, carbamazepine, oxcarbamazepine, zonisamide), atypical antipsychotics
Maniform syndrome	Antiepileptic drugs (valproate, carbamazepine, oxcarbamazepine, topiramate), atypical antipsychotics (e.g., quetiapine)	Lithium
Sleep alteration	Short half-life benzodiazepines (lorazepam, lormetazepam), benzodiazepine analogs (zolpidem, zopiclone), other medications (clomethiazole, trazodone, mirtazapine, gabapentin, pregabalin, melatonin), natural products (valeriana, passiflora)	Atypical antipsychotics (quetiapine, olanzapine)

SNRI: Serotonin and norepinephrine reuptake inhibitors; SSRI: selective serotonin reuptake inhibitors