Psychosis symptoms in nursing home residents with and without dementia – cross-sectional analyses from the COSMOS study

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Abstract:

Objective: To investigate the characteristics of nursing home residents with psychosis and the association with potential underlying factors, such as pain, sleep disturbances, and antipsychotic medication.

Method: 545 residents with and without dementia from 67 Norwegian nursing home units were included in the cross sectional analyses. Psychosis was the main outcome measure in our study; other outcome measures include quality of life (QoL), ADL function, cognitive function, pain, and antipsychotic medication.

Results: 112 residents had one or more symptoms of psychosis, and compared to residents without psychosis, they had lower QoL (p <0.001), ADL function (p = 0.003) and cognitive functioning (p = 0.001). Adjusted logistic regression analyses showed that psychosis was associated with the prevalence of pain (OR: 3.19, 95% CI: 1.94-5.24), sleep disturbances (OR: 4.51, 95% CI: 2.91-6.99), and total number of medication (OR: 1.10, 95% CI: 1.03-1.17). Residents with psychosis but without antipsychotic medication, had better quality of life (p = 0.005) compared with residents receiving any antipsychotics.

Conclusion: Psychosis in NH residents is associated with pain, sleep disturbances and number of medications. Residents with psychosis have poor quality of life, though better quality of life was observed among those who did not use antipsychotic medication.

Keywords: Psychosis, Neuropsychiatric symptoms, Nursing Home, Psychotropic drugs, Dementia, Quality of Life, Pain

Key Points:

- Symptoms of psychosis are common in a nursing home population
- Nursing Home residents with symptoms of psychosis had lower Quality of Life, ADL and cognitive function
- Pain, sleep disturbances and number of drugs prescribed were associated to psychosis, and should be evaluated when making treatment decisions for symptoms of psychosis.

Background:

In an increasingly older population, more people are in need of institutional care, and in Norway, almost 50% of all deaths occurs in a nursing home (NH).¹ These individuals are characterized by complex care needs, multiple acute and chronic conditions, and over 80% have dementia.² Neuropsychiatric symptoms (NPS) such as agitation, psychosis and depression are often related to dementia, and over 90% experience at least one such symptom during the course of the disease.^{3,4} Symptoms of psychosis such as delusion and hallucinations are frequent, and the prevalence of delusion and hallucinations in a NH population vary between 14-33%, and 5-27% respectively.^{2,5-7} Along with neuropsychiatric symptoms, pain is frequent in NHs and between 30-60% of residents experience pain on a daily basis.⁸⁻¹⁰

Psychosis symptoms can be distressing for residents, families, and carers alike, increases the risk of admission to a health care institution, and is associated with poor Quality of Life (QoL).¹¹⁻¹⁴ In older residents, symptoms of psychosis have a multifactorial aetiology, and are often a result of delirium or dementia.¹⁵ In 2016 Helvik et al. found that psychosis in NH residents was associated with poor activities of daily living (ADL) functioning, and dementia severity.³ In 2012 Tosato et al. found an association between delusion and pain in a European NH population.¹⁶ The association between psychosis and pain was further studied by Habiger et al., who found that symptoms of psychosis such as delusion were ameliorated in residents receiving pain treatment.¹⁷

Recent guidelines on the treatment of neuropsychiatric symptoms in people with dementia, recommend the use of non-pharmacological interventions as a first-line approach.^{18,19} For psychosis symptoms that are not in an acute phase, these guidelines highlight the importance of identifying and treating possible underlying causes when deciding on treatment options for NPS.^{18,19} However, the treatment of psychosis is complex, and the medication of choice for psychosis symptoms is often antipsychotics such as haloperidol and risperidone, which are also known for harmful side effects such as accelerated cognitive decline and cerebrovascular events, in this vulnerable population.²⁰⁻²² Psychotropic drugs in NHs are frequently prescribed, and in 2016, Gulla et al. found that 73% of Norwegian NH residents used at least one psychotropic drug, but only 14% of the residents used antipsychotic medication.²³ Janus et al. found that the antipsychotic prescription rate in Western European NHs ranges from 12% to as high as 59% in some countries.²⁴

The aim of this study is to explore the characteristics of NH residents with psychosis and to investigate whether residents with psychosis using antipsychotic medication differ from those not using antipsychotic medication. We aim to investigate possible underlying factors associated with symptoms of psychosis and hypothesize that these symptoms are associated with poor QoL, cognitive function, and ADL function. We also hypothesize that there are few clinical differences between residents with psychosis with and without antipsychotic drug prescription.

Method:

This study is based on baseline data from the COSMOS study. COSMOS is an acronym and stands for COmmunication, Systematic assessment and treatment of pain, Medication review, Occupational therapy and Safety. The study protocol was published by Husebo et al. in 2015, and is fully described elsewhere.²⁵

The study was conducted from 2014 to 2015 and included 545 residents from 67 NH units, in both western and eastern Norway. The COSMOS study is a cluster randomized controlled trial (RCT), investigating the effect of the implementation of a complex intervention with focus on the four key COSMOS subjects lasting for 4 months and followed up at month 9. Inclusion criteria were NH residents ≥65 years old, with and without dementia. Residents

with a life expectancy ≤ 6 months or residents with schizophrenia were excluded from the study. The data in this article is based on the baseline data collection.

Outcome measures:

The primary measure for assessment of psychosis was the Neuropsychiatric Inventory Nursing Home version (NPI-NH), which was developed by Cummings et al. ²⁶, translated into Norwegian and thoroughly tested for reliability and validity by Selbaek et al..²⁷ The NPI-NH assesses 12 different NPS such as delusion, hallucinations, depression and sleep disturbances, and assesses the frequency (F) and severity (S) of each symptom. Frequency is measured on a scale from 0–4, where 0 represents not present and 4 represents symptom present on a daily basis. Severity is measured on a scale from 1-3, where 1 represents mild severity with little stress for the resident, and 3 represents a severe symptom with much stress on the resident. The frequency and severity score are then multiplied together to generate a total score for each symptom (FxS) ranging from 0-12. A resident was defined as having an NPS, when he had an FxS score ≥ 4 , as this is deemed a clinically significant score.²⁸ The different symptoms can be clustered together in various ways, and symptom clusters contain the NPS that are closely related in the clinical setting, such as depression and anxiety in a mood cluster, agitation and irritability in an agitation cluster, and delusion and hallucination in a psychosis cluster.²⁹⁻³¹ The psychosis cluster in our study includes both hallucinations and delusion, and residents were classified as having psychosis if they had an FxS score \geq 4 on either one or both of these symptoms. Sleep disturbances and appetite disturbances were assessed using their respective items on the NPI-NH.

For investigation of associations with psychosis, we included assessment tools for cognitive function, depression, QoL, behavioral disturbances, activities of daily living (ADL) function and pain. Cognitive performance was assessed using the Mini Mental State Exam (MMSE) generating a score from 0 to 30, where a low score indicates poor cognitive function.³² The category Activities of daily living was assessed using the Lawton and Brody's ADL assessment tool, generating a score from 0 to 30, where higher scores indicate lower functional independence.³³ Depression was assessed using the Cornell Scale for Depression in Dementia (CSDD) generating a score of 0–38, where a high score indicates a severe degree of depression.³⁴ QoL was assessed using the 18-item version of Quality of life in dementia (QUALIDEM) generating a score from 0 to 54 where a low score indicates poor QoL while a

high score indicates a high QoL.³⁵ QoL was also assessed using Quality of life in late stages of Dementia (QUALID), generating a score from 11 to 55 where a high score indicates poor QoL.³⁶ Behavioral disturbances were evaluated by the Cohen-Mansfield Agitation Inventory (CMAI) generating a score from 29 to 203, where a high score indicates a high level of behavioral disturbance.³⁷ Pain was evaluated by the Mobilisation – Observation – Behavioral - Intensity - 2 Pain Scale (MOBID-2) which assesses pain related to the musculoskeletal system, internal organs, head and skin, and generates a score from 0–10, where 0 indicates no pain, and 10 indicates the highest pain possible.^{38,39} Information about diagnoses and medication were obtained from the residents' medical records. Psychotropic drugs were defined as the group noted N05 in the Anatomical Therapeutic Chemical (ATC) register. Psychotropic drugs were also divided into the subgroups antipsychotics (N05A), anxiolytics (N05B) and hypnotics and sedatives (N05C) in line with ATC register. The MMSE were performed by one of four full-time researchers in the COSMOS team consisting of one physician, one nurse and two medical students. All other assessments were performed by a caregiver who knew the resident well, after receiving training from the COSMOS team on using the different assessment tools.

Statistics

To test differences in characteristics between residents with and without clinically significant psychosis symptoms, independent sample t-test were used for normally distributed variables; a chi-squared test was used for categorical variables and Mann Whitney U-test for non-normally distributed variables. To test associations between symptoms of psychosis and other factors (ADL function, pain, depression, medication, QoL, nighttime disturbances and appetite disturbances as measured with the NPI-NH), logistic regression with robust standard error estimation adjusting for clustered design was used. Odds Ratios were calculated for each factor and adjusted for age, gender, dementia diagnosis and cognitive functioning. Statistical analyses were performed using IBMs Statistical Package for Social Sciences (SPSS) version 23 and StataCorps Stata version 15.0.

Ethics:

Verbal and written informed consent was obtained from residents who were cognitively able to understand the information regarding the COSMOS study. In residents lacking the ability

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to consent, a verbal and written presumed consent was obtained, after explaining the study procedure, from the residents' next of kin or legal guardian, with the resident present if possible. The trial was approved by the Regional Committee for Medical and Health Research Ethics, West Norway (REK 2013/1765), and registered at clinicaltrials.gov (NCT02238652).

Results:

Five hundred and forty-five residents from 67 NH units were included in the study; 33 residents had incomplete data for the NPI-NH assessment of psychosis symptoms, resulting in 512 participants in the final analyses. The mean age was 87 years, and 73% were women (Table 1). One-hundred and twelve residents (21.9%) had one or more symptoms of psychosis, 94 (18.4%) had delusion, and 45 (8.8%) had hallucinations. Compared to residents without psychosis, those with psychosis more often had dementia (p = 0.004, df: 510), poorer QoL on both the QUALIDEM (p <0.001, df: 502) and QUALID (p <0.001, df: 502) assessment tool, more behavioral disturbances (p < 0.001, df: 493) and lower ADL function (p = 0.003, df: 505). (Table 1) Residents with psychosis also had higher depression scores assessed by CSDD (p <0.001, df: 415), more sleep disturbances (X² = 47.7, p <0.001), poorer cognitive function on the MMSE (p = 0.001, df: 472) and more pain (p = 0.002, df: 438) (Table 1). More psychotropic drugs were prescribed to residents with psychosis (p = 0.015, df = 503), without differences between antipsychotics, anxiolytics and hypnotics and sedatives (Table 1 & Figure 1). Residents with psychosis using no antipsychotic medication, had better QoL on the QUALIDEM (p = 0.005, df = 108) and lower total scores on the NPI-NH (p = 0.035, df = 108) compared to those treated with antipsychotic medication. Residents with psychosis using antipsychotic medication did not differ from residents using no antipsychotic medication in ADL function, pain and cognitive function. (Figure 2)

In the logistic regression analyses with adjustment for clustered design, age, sex, dementia diagnose and cognitive function, psychosis was found to be associated with poor QoL (adjusted Odds Ratio: 0.89, 95% CI: 0.86-0.92, p <0.001), depression (aOR: 1.21, 95% CI: 1.15-1.27, p <0.001), number of prescribed drugs (aOR: 1.10, 95% CI: 1.03-1.17, p = 0.005), nighttime disturbances (aOR: 4.51, 95% CI: 2.91-6.99, p <0.001), appetite disturbances (aOR: 3.46, 95% CI: 1.65-7.27, p = 0.001) and pain (aOR: 3.19, 95% CI: 1.94-5.24, p <0.001). The same associations were found for the individual symptoms of delusion and hallucinations,

with the exception of an association between hallucinations and ADL function (aOR: 1.19, 95% CI: 1.07-1.33, p = 0.773) (Table 2). Psychosis symptoms were found to be associated with all other NPS measured with the NPI (Table 2). The same associations were found for the individual symptom delusion, while hallucinations were found to not be associated with apathy (aOR: 2.02, 95% CI: 0.91 - 4.48, p = 0.082), disinhibition (aOR: 1.37, 95% CI: 0.56 - 3.31, p = 0.490), and euphoria (aOR: 1.40, 95% CI: 0.30 - 6.57, p = 0.668) respectively. (Table 2)

Discussion:

The study showed that NH residents with psychosis had poorer QoL compared to residents without psychosis, and that residents with psychosis not using any antipsychotic medication had better QoL compared to residents not using antipsychotics. Psychosis was found to be associated with pain, number of drugs prescribed, sleep disturbances, appetite disturbances and depression. The findings are important for the clinician because they highlight the detrimental impact that symptoms of psychosis have on NH residents, the importance of treating the symptoms and possible underlying causes, and the complexity of such treatment.

Our study is one of the largest studies focusing on psychosis in NH residents, and adds important knowledge about psychosis in NH residents. The findings regarding psychosis and QoL are in line with previous studies where psychosis was found to have a negative impact on QoL. Mjorud et al. investigated variables associated with QoL in Norwegian NH residents with dementia, and found an association between poor QoL and psychosis,¹⁴ while Wetzels et al. studied determinants of QoL in Dutch NH residents with dementia and found that psychosis was associated to lower QoL.¹³ As in our study, the NPI-NH was used to measure psychosis, making the studies comparable. The association between psychosis and sleep disturbances is an important finding. Previous studies on psychosis and sleep disturbances have found an association between psychosis and insomnias. ^{40,41} These studies, however, were only performed on patients aged 16–74 years, and there is a lack of studies on the association between psychosis and sleep disturbances in patients aged 75 years and older. Sleep disturbances in our study are also a more broad term as it includes all types of sleep

disturbances, not only insomnia. It is also important to note that a recent study by Blytt et al. found a large discrepancy between the NPI-NH item sleep disturbances and objectively measured sleep disturbances with actigraphy.⁴² Since our results are cross-sectional, we cannot claim causality, so there is a need for further studies, and the use of a more reliable measure of sleep disturbances may be warranted in the future.

A previous study by Helvik et al. on the severity of NPS in 2898 Norwegian NH residents, found an association between psychosis severity and ADL function.³ Though residents with psychosis had lower ADL function than residents without psychosis in our study, no significant association was found between psychosis and ADL function when adjusting for confounding factors such as age, and cognitive function. A reason for this difference could be that the two symptoms of psychosis impact ADL function in different ways. This is supported by our results, as hallucinations were found to be associated with poor ADL function when adjusting for confounding factors, while no such association was found for delusion. It is also worth noting that Helvik et al. investigated the association between psychosis severity and ADL function, and not between ADL function and the presence of psychosis as in our study.

The finding that NH residents with psychosis using any antipsychotic medication had poorer QoL when compared to residents with psychosis using no antipsychotics highlights a challenge in treating psychosis in NH residents. Antipsychotic medication may be necessary in the acute setting where the resident can cause harm to himself and others, but the use of antipsychotics in treatment of psychosis in a chronic phase is a more complex matter. Guidelines state that non-pharmacological options such as environmental and psychosocial measures should be first-line treatment for psychosis in a chronic phase before antipsychotics are used, but few concrete suggestions are made.¹⁹ Knowledge about the effect of non-pharmacological measures on psychosis is scant, and few studies have been performed.⁴³ In a study conducted by Chen et al. in 2014, it was found that delusions and hallucinations in 104 older Taiwanese men with dementia were reduced in response to an organized program of non-pharmacological measures.⁴⁴ The number of patients was low, however, and the study only included men.⁴⁴ Arguments can be made that residents using antipsychotic medication have a more severe degree of psychosis than residents not using antipsychotics do. However, this does not seem to be the case in our study as there were no significant difference in the total NPI-NH score of psychosis for residents with psychosis using any antipsychotic medication and those who did not use any antipsychotic medication (Figure 2). When interpreting the results regarding antipsychotic medication, it is important to have some limitations mind. Residents with psychosis experienced more behavioral disturbances such as aggression, than residents without psychosis. The use of antipsychotic medication such as Risperidone, and in some cases Haloperidol in delirious residents, are recommended in treating aggression, and there is a possibility that some of the use of antipsychotic medication in the psychosis group are due to aggression and not psychosis. The number of antipsychotic medication used in order to treat psychosis may therefore be lower than the total number of antipsychotics prescribed in residents with psychosis symptoms. One also has to take into consideration the somewhat low number of residents and the design of the study, but the findings are an important stepping-stone for future studies. The efficacy of non-pharmacologically treatment approaches to psychosis is a key point that needs further investigations.

We also found that the total number of drugs was associated with symptoms of psychosis. Polypharmacy is a well-known challenge in NH residents and increases the risk of hospital admission, circulatory and endocrine co-morbidity and neurological motor dysfunction.⁴⁵ The number of drugs also increases the possibility of anti-cholinergic side effects, such as confusion and delirium.⁴⁶ Delirium is often hard to distinguish from psychosis and has many of the same symptoms such as delusion and hallucinations.¹⁵ Our findings support the hypothesis that psychosis is associated with polypharmacy, and they highlight the importance of a thorough medication review by physicians so as to avoid unnecessary drug prescription and development of possible debilitating side effects.

The association between pain and psychosis is supported to a certain degree by previous studies. Tosato etal. found an association between pain and delusion in NH residents with cognitive impairment; however, they did not find an association between pain and hallucinations.¹⁶ An explanation for this is perhaps the use of different assessment tools for psychosis symptoms, as the NPI-NH is more suited to detect and differentiate between psychosis symptoms than the minimum dataset residents assessment instrument. Our own findings suggest that symptoms of psychosis, especially delusions, were ameliorated in response to pain treatment in residents with behavioral disturbances and dementia.¹⁷ In

contrast to the present study, we did not find a cross-sectional association between pain and symptoms of psychosis. A reason for this may be the more selected group of residents in the 2016 study, as it consisted of NH residents with dementia and behavioral disturbances. Our findings have clinical importance in that they indicate the need for a thorough pain assessment before making treatment decisions for residents with psychosis. If psychosis is caused, or triggered, by an underlying treatable factor such as pain, then treatment of this factor can ameliorate the symptoms of psychosis without the need for antipsychotic medication. Pain as a cause for NPS can be treated using a stepwise protocol for treating pain or a multidisciplinary approach, which has shown an effect in previous studies.⁴⁷⁻⁴⁹ Our findings are cross-sectional, however, and there is a need to look at the association of pain and psychosis over time to gain more solid knowledge.

Strengths and Limitations:

One of the strengths of this study is the broad inclusion criteria where all NH residents \geq 65 years of age, a life expectancy >6 months and without schizophrenia were included. The greatest limitation lies perhaps in the cross-sectional design of the study, which cannot differentiate properly between psychosis in an acute and chronic setting, and makes conclusions on causality difficult. More longitudinal studies are needed to draw conclusions on causality. Another limitation regarding the design of the study, is that it is based on secondary analysis from an already existing database, where power calculations were made on the basis of other assessment tools and designs than our study. Therefore there is a possibility that our study group may be underpowered. As it is not clear-cut which symptoms are possible confounders, the regression analyses was not adjusted for the impact of other NPS. This is a limitation, which is important to keep in mind when interpreting the results. There is also a lack of information regarding the cause of psychosis in residents without dementia which is a limitation. The assessment of many of the outcome measures were made by proxy-raters who knew the resident well. While studies have shown this to be an accurate assessment, especially for symptoms of psychosis, it cannot replace self-report for other symptoms such as pain.

Conclusion:

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Symptoms of psychosis in NH residents lead to poorer QoL, more sleep disturbance, and are associated with pain and number of prescribed drugs. The use of antipsychotic medication in treatment of psychosis symptoms is associated with poorer QoL. The findings highlight that a thorough and broad evaluation of possible underlying causes should be made before making treatment decisions on chronic psychosis in NH residents.

References

- 1. Ramm J. Eldres bruk av helse og omsorgstjenester. *Statistisk Sentralbyrå.* 2013:107.
- 2. Selbaek G, Kirkevold O, Engedal K. The prevalence of psychiatric symptoms and behavioural disturbances and the use of psychotropic drugs in Norwegian nursing homes. *International journal of geriatric psychiatry*. 2007;22(9):843-849.
- 3. Helvik AS, Engedal K, Wu B, et al. Severity of Neuropsychiatric Symptoms in Nursing Home Residents. *Dementia and geriatric cognitive disorders extra*. 2016;6(1):28-42.
- 4. Selbaek G, Engedal K, Benth JS, Bergh S. The course of neuropsychiatric symptoms in nursinghome patients with dementia over a 53-month follow-up period. *International psychogeriatrics / IPA*. 2014;26(1):81-91.
- 5. Bergh S, Holmen J, Saltvedt I, Tambs K, Selbaek G. Dementia and neuropsychiatric symptoms in nursing-home patients in Nord-Trondelag County. *Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke.* 2012;132(17):1956-1959.
- 6. Bjork S, Lovheim H, Lindkvist M, Wimo A, Edvardsson D. Thriving in relation to cognitive impairment and neuropsychiatric symptoms in Swedish nursing home residents. *International journal of geriatric psychiatry*. 2017.
- Roen I, Selbaek G, Kirkevold O, Engedal K, Testad I, Bergh S. Resourse Use and Disease Couse in dementia - Nursing Home (REDIC-NH), a longitudinal cohort study; design and patient characteristics at admission to Norwegian nursing homes. *BMC health services research*. 2017;17(1):365.
- 8. Achterberg WP, Gambassi G, Finne-Soveri H, et al. Pain in European long-term care facilities: cross-national study in Finland, Italy and The Netherlands. *Pain.* 2010;148(1):70-74.
- 9. Sandvik RK, Selbaek G, Seifert R, et al. Impact of a stepwise protocol for treating pain on pain intensity in nursing home patients with dementia: A cluster randomized trial. *European journal of pain (London, England).* 2014.
- 10. Husebo BS, Strand LI, Moe-Nilssen R, Borgehusebo S, Aarsland D, Ljunggren AE. Who suffers most? Dementia and pain in nursing home patients: a cross-sectional study. *Journal of the American Medical Directors Association*. 2008;9(6):427-433.
- 11. Okura T, Plassman BL, Steffens DC, Llewellyn DJ, Potter GG, Langa KM. Neuropsychiatric symptoms and the risk of institutionalization and death: the aging, demographics, and memory study. *Journal of the American Geriatrics Society*. 2011;59(3):473-481.
- 12. Wergeland JN, Selbaek G, Bergh S, Soederhamn U, Kirkevold O. Predictors for Nursing Home Admission and Death among Community-Dwelling People 70 Years and Older Who Receive Domiciliary Care. *Dementia and geriatric cognitive disorders extra*. 2015;5(3):320-329.
- Wetzels RB, Zuidema SU, de Jonghe JF, Verhey FR, Koopmans RT. Determinants of quality of life in nursing home residents with dementia. *Dementia and geriatric cognitive disorders*. 2010;29(3):189-197.
- 14. Mjorud M, Kirkevold M, Rosvik J, Selbaek G, Engedal K. Variables associated to quality of life among nursing home patients with dementia. *Aging & mental health.* 2014;18(8):1013-1021.
- 15. Engedal K. *Alderspsykiatri i praksis.* 2 ed. Aldring og Helse: Aldring og Helse; 2008.
- 16. Tosato M, Lukas A, van der Roest HG, et al. Association of pain with behavioral and psychiatric symptoms among nursing home residents with cognitive impairment: results from the SHELTER study. *Pain.* 2012;153(2):305-310.
- 17. Habiger TF, Flo E, Achterberg WP, Husebo BS. The Interactive Relationship between Pain, Psychosis, and Agitation in People with Dementia: Results from a Cluster-Randomised Clinical Trial. *Behavioural Neurology.* 2016;2016:8.
- 18. Kales HC, Gitlin LN, Lyketsos CG. Management of neuropsychiatric symptoms of dementia in clinical settings: recommendations from a multidisciplinary expert panel. *Journal of the American Geriatrics Society.* 2014;62(4):762-769.

- 19. Helsedirektoratet. *Nasjonal faglig retningslinje om demens.* Helsedirektoratet 11/30/2017 2017.
- 20. Ballard C, Hanney ML, Theodoulou M, et al. The dementia antipsychotic withdrawal trial (DART-AD): long-term follow-up of a randomised placebo-controlled trial. *The Lancet Neurology.* 2009;8(2):151-157.
- 21. Huybrechts KF, Gerhard T, Crystal S, et al. Differential risk of death in older residents in nursing homes prescribed specific antipsychotic drugs: population based cohort study. *BMJ* (*Clinical research ed*). 2012;344:e977.
- 22. Forlenza OV, Loureiro JC, Pais MV, Stella F. Recent advances in the management of neuropsychiatric symptoms in dementia. *Current opinion in psychiatry*. 2017;30(2):151-158.
- 23. Gulla C, Selbaek G, Flo E, Kjome R, Kirkevold O, Husebo BS. Multi-psychotropic drug prescription and the association to neuropsychiatric symptoms in three Norwegian nursing home cohorts between 2004 and 2011. *BMC geriatrics.* 2016;16:115.
- 24. Janus SI, van Manen JG, MJ IJ, Zuidema SU. Psychotropic drug prescriptions in Western European nursing homes. *International psychogeriatrics / IPA*. 2016;28(11):1775-1790.
- 25. Husebo BS, Flo E, Aarsland D, et al. COSMOS-improving the quality of life in nursing home patients: protocol for an effectiveness-implementation cluster randomized clinical hybrid trial. *Implement Sci.* 2015;10(1):131.
- 26. Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology.* 1994;44(12):2308-2314.
- 27. Selbaek G, Kirkevold O, Sommer OH, Engedal K. The reliability and validity of the Norwegian version of the Neuropsychiatric Inventory, nursing home version (NPI-NH). *International psychogeriatrics / IPA*. 2008;20(2):375-382.
- 28. Margallo-Lana M, Swann A, O'Brien J, et al. Prevalence and pharmacological management of behavioural and psychological symptoms amongst dementia sufferers living in care environments. *International journal of geriatric psychiatry*. 2001;16(1):39-44.
- 29. Cheng ST, Kwok T, Lam LC. Neuropsychiatric symptom clusters of Alzheimer's disease in Hong Kong Chinese: prevalence and confirmatory factor analysis of the Neuropsychiatric Inventory. *International psychogeriatrics / IPA.* 2012;24(9):1465-1473.
- 30. Selbaek G, Engedal K. Stability of the factor structure of the Neuropsychiatric Inventory in a 31-month follow-up study of a large sample of nursing-home patients with dementia. *International psychogeriatrics / IPA.* 2012;24(1):62-73.
- 31. Hollingworth P, Hamshere ML, Moskvina V, et al. Four components describe behavioral symptoms in 1,120 individuals with late-onset alzheimer's disease. *Journal of the American Geriatrics Society*. 2006;54(9):1348-1354.
- 32. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of psychiatric research*. 1975;12(3):189-198.
- 33. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *The Gerontologist.* 1969;9(3):179-186.
- 34. Alexopoulos GS, Abrams RC, Young RC, Shamoian CA. Cornell Scale for Depression in Dementia. *Biological psychiatry*. 1988;23(3):271-284.
- 35. Ettema TP, Droes RM, de Lange J, Mellenbergh GJ, Ribbe MW. QUALIDEM: development and evaluation of a dementia specific quality of life instrument--validation. *International journal of geriatric psychiatry*. 2007;22(5):424-430.
- 36. Weiner MF, Martin-Cook K, Svetlik DA, Saine K, Foster B, Fontaine CS. The quality of life in late-stage dementia (QUALID) scale. *Journal of the American Medical Directors Association*. 2000;1(3):114-116.
- 37. Cohen-Mansfield J, Marx MS, Rosenthal AS. A description of agitation in a nursing home. *Journal of gerontology*. 1989;44(3):M77-84.

- 38. Husebo BS, Strand LI, Moe-Nilssen R, Husebo SB, Snow AL, Ljunggren AE. Mobilization-Observation-Behavior-Intensity-Dementia Pain Scale (MOBID): development and validation of a nurse-administered pain assessment tool for use in dementia. *Journal of pain and symptom management.* 2007;34(1):67-80.
- 39. Husebo BS, Ostelo R, Strand LI. The MOBID-2 pain scale: reliability and responsiveness to pain in patients with dementia. *European journal of pain (London, England)*. 2014;18(10):1419-1430.
- 40. Sheaves B, Bebbington PE, Goodwin GM, et al. Insomnia and hallucinations in the general population: Findings from the 2000 and 2007 British Psychiatric Morbidity Surveys. *Psychiatry research.* 2016;241:141-146.
- 41. Freeman D, Stahl D, McManus S, et al. Insomnia, worry, anxiety and depression as predictors of the occurrence and persistence of paranoid thinking. *Social psychiatry and psychiatric epidemiology*. 2012;47(8):1195-1203.
- 42. Blytt KM, Bjorvatn B, Husebo B, Flo E. Clinically significant discrepancies between sleep problems assessed by standard clinical tools and actigraphy. *BMC geriatrics.* 2017;17(1):253.
- 43. de Oliveira AM, Radanovic M, de Mello PC, et al. Nonpharmacological Interventions to Reduce Behavioral and Psychological Symptoms of Dementia: A Systematic Review. *BioMed research international.* 2015;2015:218980.
- 44. Chen RC, Liu CL, Lin MH, et al. Non-pharmacological treatment reducing not only behavioral symptoms, but also psychotic symptoms of older adults with dementia: a prospective cohort study in Taiwan. *Geriatrics & gerontology international.* 2014;14(2):440-446.
- 45. Jokanovic N, Tan EC, Dooley MJ, Kirkpatrick CM, Bell JS. Prevalence and factors associated with polypharmacy in long-term care facilities: a systematic review. *Journal of the American Medical Directors Association*. 2015;16(6):535.e531-512.
- 46. Duran CE, Azermai M, Vander Stichele RH. Systematic review of anticholinergic risk scales in older adults. *Eur J Clin Pharmacol.* 2013;69(7):1485-1496.
- 47. Husebo BS, Ballard C, Sandvik R, Nilsen OB, Aarsland D. Efficacy of treating pain to reduce behavioural disturbances in residents of nursing homes with dementia: cluster randomised clinical trial. *BMJ (Clinical research ed).* 2011;343:d4065.
- 48. Pieper MJ, van der Steen JT, Francke AL, Scherder EJ, Twisk JW, Achterberg WP. Effects on pain of a stepwise multidisciplinary intervention (STA OP!) that targets pain and behavior in advanced dementia: A cluster randomized controlled trial. *Palliative medicine*. 2017:269216316689237.
- 49. Pieper MJ, van Dalen-Kok AH, Francke AL, et al. Interventions targeting pain or behaviour in dementia: A systematic review. *Ageing research reviews*. 2013;12(4):1042-1055.

Table 1: Characteristics of residents with and without psychosis

	Psychosis	Without psychosis	p-value	Total population
	(n = 112)	(n = 400)		(n = 512)
Women (%)	87 (77,7)	292 (73,0)	0.318ª	379 (74.0)
Age (SD)	86,6 (7.5)	86,7 (7.4)	0.629 ^b	86.9 (7.4)
Dementia diagnosis (%)	86 (76.8)	248 (62.0)	0.004 ^a	334 (65.2)
MMSE score (SD)	9,0 (6.7)	11,8 (7.8)	0.001 ^c	11.2 (7.7)
ADL score (SD)	18,5 (5.6)	16,8 (5.1)	0.003 ^c	17.1 (5.3)
Cornell score (SD)	12,5 (7.2)	5,7 (5.0)	<0.001 ^c	7.1 (6.2)
CMAI score (SD)	55,2 (18.7)	38,6 (11.8)	<0.001 ^c	42.3 (15.3)
QUALID score (SD)	26,9 (8.3)	20,0 (6.5)	<0.001 ^c	21.5 (7.5)
QALIDEM score (SD)	32.7 (8.8)	41.2 (8.1)	<0.001 ^b	39.2 (8.9)
MOBID-2 score (SD)	3,2 (2.6)	2,3 (2.6)	0.002 ^c	2.5 (2.6)
NPI-NH total score (SD)	40,1 (23.3)	11,6 (14.0)	<0.001 ^b	17.8 (20.2)
NPI-NH total carer strain (SD)	15.4 (9.3)	4.8 (6.0)	<0.001 ^c	7.0 (8.1)
Agitation/Aggression (%)	57 (50.9)	61 (15.3)	<0.001ª	118 (23.0)
Depression (%)	53 (47.3)	66 (16.5)	<0.001 ^a	119 (23.2)
Anxiety (%)	50 (44.6)	67 (16.8)	<0.001 ^a	117 (22.9)
Euphoria (%)	8 (7.1)	12 (3.0)	0.044ª	20 (3.9)
Apathy (%)	26 (23.2)	47 (11.8)	0.002ª	73 (14.3)
Disinhibition (%)	33 (29.5)	48 (12.0)	<0.001 ^a	81 (15.8)
Irritability (%)	74 (66.0)	87 (21.8)	<0.001 ^a	161 (31.4)
Aber. motor behaviour (%)	28 (25.0)	30 (7.5)	<0.001 ^a	58 (11.3)
Appetite disturbances (%)	20 (17.9)	25 (6.3)	<0.001 ^a	45 (8.8)
Sleep Disturbances (%)	46 (41.0)	61 (15.3)	<0.001 ^a	107 (20.9)
Drugs as prescribed (SD)	8,4 (3.7)	7,9 (3.8)	0.226 ^c	8.0 (3.8)
Psychotropics (%) ⁺	66 (58.9)	185 (46.3)	0.015ª	251 (49.0)
Antipsychotics (%)	20 (17.9)	57 (14.4)	0.333ª	77 (15.0)
Anxiolytics (%)	28 (25.0)	79 (19.8)	0.216ª	107 (20.9)
Hypnotic and Sedatives (%)	41 (36.6)	115 (28.8)	0.101 ^a	156 (30.5)
Analgesics (%)	74 (66.0)	227 (56.8)	0.064ª	301 (58.8)
Antidepressants (%)	46 (41.1)	163 (40.8)	0.951 ^a	209 (40.8)
Antidementia drugs (%)	24 (20.8)	55 (13.8)	0.047 ^a	79 (15.4)
Anti-Parkinson drugs (%)	6 (5.4)	21 (5.3)	0.964ª	27 (5.3)
Drugs as needed (SD)	4.0 (2.0)	3.2 (2.2)	<0.001 ^c	3.4 (2.2)
Psychotropics (%) [†]	90 (80.4)	230 (57.5)	<0.001ª	320 (62.5)
Antipsychotics (%)	8 (7.1)	21 (5.3)	0.444ª	29 (5.7)
Anxiolytics (%)	73 (65.2)	172 (43.0)	<0.001ª	245 (47.9)
Hypnotic and Sedatives (%)	42 (37.5)	99 (24.8)	0.008ª	141 (27.5)
Analgesics (%)	93 (83.0)	289 (72.3)	0.020ª	382 (74.6)
Notes: MMSE indicates Mini M				. ,

Agitation Inventory; QUALID, Quality of Life in late-stage Dementia; QUALIDEM, Quality of Life in Dementia; MOBID-2, Mobilization-Observation-Behavior-Intensity-Dementia-2 pain scale; NPI-NH. Neuropsychiatric Inventory Nursing Home version

^aChi Squared test

^bIndependent t-test samples

^cMann-Whitney U-test

⁺Use of any Antipsychotic, Anxiolytic and Hypnotic and Sedative

Table 2: Symptoms	of Psychosis and	associated features
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Psychosis	OR (95% CI)	p-value ^a
Pain (MOBID2 ≥3)	3.19 (1.94 – 5.24)	<0.001
ADL function	1.03 (0.98 – 1.09)	0.213
Quality of life (QUALIDEM)	0.89 (0.86 – 0.92)	<0.001
Depression (CSDD)	1.21 (1.15 – 1.27)	<0.001
Number of prescribed drugs	1.10 (1.03 – 1.17)	0.005
Sleep disturbances	4.51 (2.91 – 6.99)	<0.001
Appetite disturbance	3.46 (1.65 – 7.27)	0.001
Agitation/Aggression	5.37 (3.21 – 8.97)	<0.001
Depression (NPI-NH)	4.49 (2.73 – 7.37)	<0.001
Anxiety	4.60 (2.67 – 7.93)	<0.001
Apathy	2.27 (1.38 – 3.73)	0.001
Disinhibition	2.65 (1.45 – 4.83(0.001
Aberrant Motor Behaviour	3.51 (1.72 – 7.17)	0.001
Euphoria	3.30 (1.39 – 7.85)	0.007
Irtitability	6.27 (3.95 – 9.96)	<0.001
Delusion		
Pain (MOBID2 ≥3)	2.89 (1.75 – 4.76)	<0.001
ADL function	1.01 (0.95 – 1.07)	0.773
Quality of life (QALIDEM)	0.89 (0.86 – 0.92)	<0.001
Depression (CSDD)	1.22 (1.17 – 1.28)	<0.001
Number of prescribed drugs	1.11 (1.04 – 1.20)	0.003
Sleep disturbances	4.06 (2.57 – 6.42)	<0.001
Appetite disturbance	3.13 (1.49 – 6.55)	0.003
Agitation/Aggression	5.47 (3.06 – 9.81)	<0.001
Depression (NPI-NH)	4.29 (2.56 – 7.20)	<0.001
Anxiety	4.28 (2.47 – 7.42)	<0.001
Apathy	2.17 (1.27 – 3.69)	0.004
Disinhibition	3.03 (1.70 – 5.39)	<0.001
Aberrant Motor Behaviour	3.02 (1.51 – 6.05)	0.002
Euphoria	4.03 (1.69 – 9.65)	0.002
Irtitability	6.41 (3.87 – 10.61)	<0.001
Hallucinations	· · · · · ·	
Pain (MOBID2 ≥3)	2.78 (1.23 – 6.28)	0.014
ADL function	1.19 (1.07 – 1.33)	0.001
Quality of life (QALIDEM)	0.88 (0.84 – 0.93)	<0.001
Depression (CSDD)	1.15 (1.09 – 1.22)	<0.001
Number of prescribed drugs	1.09 (1.01 – 1.18)	0.029
Sleep disturbances	5.02 (2.55 – 9.90)	<0.001
Appetite disturbance	4.33 (1.87 – 10.02)	0.001
Agitation/Aggression	3.67 (1.90 – 7.11)	<0.001
Depression	2.91 (1.36 – 6.22)	0.006
Anxiety	4.17 (2.05 - 8.48)	<0.001
Apathy	2.02 (0.91 - 4.48)	0.082
Disinhibition	1.37 (0.56 – 3.31)	0.490
Aberrant Motor Behaviour	3.32 (1.61 – 6.84)	0.001
Euphoria	1.40 (0.30 – 6.57)	0.668
Irtitability	2.56 (1.29 – 5.08)	0.007

of Daily Living; QUALIDEM, Quality of Life in Dementia; CSDD, Cornell Scale of Depression in Dementia ^aLogistic regression, with associations adjusted for age, sex, dementia diagnose and cognitive function

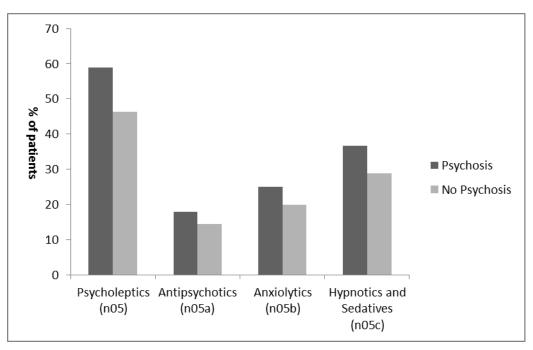


Figure 1: Psychotropic drug prescription in residents with and without psychosis

