

ADHERENCE OF ANTIPSYCHOTROPIC DRUGS IN GERIATRIC PATIENTS AND ITS IMPACT ON THEIR QUALITY OF LIFE: A REVIEW

¹Lincy George, ²Alba Annex, ³Treesa Mariya, ⁴Sona Jose, ⁵Angel Nixen

¹Associate. Prof., Dept. of Pharmacy Practice, St. James' College Of Pharmaceutical Sciences (NAAC Accredited), Chalakudy, KUHS University, Kerala, India

²⁻⁵PharmD Student, St. James' College Of Pharmaceutical Sciences (NAAC Accredited), Chalakudy, KUHS University, Kerala, India

ABSTRACT: The most accurate definition of psychosis or psychiatric disorder is a condition with a recognizable set of symptoms, such as delusions, hallucinations, slurred speech, and agitated and disorganized behavior. Misinterpretation of reality is a characteristic of psychosis. Psychotic symptoms in elderly adults are generally categorized into organic and functional reasons. Organic conditions include delirium due to underlying sickness or due to psychosis driven drug usage. Schizophrenia, affective or mood disorders, and delusional disorders are examples of functional illnesses that manifest with psychotic symptoms. Some patients might need some pharmacological treatments to treat behavioral issues brought on by psychotic symptoms. Older patients with psychosis are frequently given psychotropic drugs such as antipsychotics, antidepressants, and benzodiazepines. The risk of negative medication responses rises with advancing age and polypharmacy. Almost half of elderly patients with psychotic illnesses who are taken antipsychotic medication struggle greatly with treatment non-adherence. In the worst-case situation, poor adherence could lead to suicide. Clinical implications of poor adherence include deteriorating symptoms, relapse, psychosocial decline, higher costs, and increased costs. The quality of life for older individuals suffers from non-adherence to medication. This article reviews typical psychotropic medications, their compliance, and the effects of antipsychotic medications on older patients. It also discusses several types of psychotic diseases that affect geriatric patients.

KEYWORDS: Psychosis, Antipsychotropics, Geriatrics, Adherence, Quality of life

INTRODUCTION

The best way to define psychosis or psychotic illness is as a syndrome with a recognisable set of symptoms, such as delusions, hallucinations, incoherent speech, agitated and disorganised behaviour, and loss of insight^[1]. The primary characteristic of psychosis is the misinterpretation of reality, which manifests as disordered speech and behaviour patterns, impaired perception and interpretation of the environment, and incorrect beliefs. In professional settings, the term "psychosis" is frequently used to refer to a severe form of mental disease in which hallucinations and delusions predominate^[2]. The ageing of the brain, issues with physical health, cerebral pathologies, socioeconomic variables including decreased economic independence and a breakdown of the family support system, and increased susceptibility to psychiatric morbidities among the older population all contribute to this^[3]. Older adults may have psychotic symptoms in a wide range of diseases that have historically been classified as having organic and functional origins. Among organic disorders, delirium brought on by a medical sickness or psychosis brought on by drug abuse or withdrawal both exhibit acutely seeming psychotic symptoms. Neurodegenerative diseases like Alzheimer's disease, vascular dementia, dementia with Lewy bodies, and Parkinson's disease are characterised by the slow emergence of psychotic symptoms. Affective or mood disorders, delusional disorders, and schizophrenia (chronic and late onset) are some functional illnesses that manifest with psychotic symptoms^[1]. Gross brain atrophy, ventricular enlargement, selective regional neuronal loss, remodeling of dendritic, axons, and synapses are only a few examples of age-related alterations in the central nervous system that are frequently observed in the ageing process. The ageing of the frontal and temporal cortices, age-related neurochemical changes, social isolation, sensory deficiencies, cognitive loss, and polypharmacy all raise the risk of psychosis in the elderly^[1].

DIFFERENTIAL DIAGNOSIS OF PSYCHOSIS IN ELDERLY

The presence of ailments and medications may make it difficult to recognise psychotic symptoms. Aggression and agitation are triggers for seeking mental health treatment since they are linked to psychosis in the elderly. The underlying causes of the psychotic symptoms must be taken into account by the doctor. Before beginning any pharmacological treatment, the differential diagnosis must take into account the range of illnesses that can present with psychotic symptoms^[5].

1.1 Schizophrenia

Older people with schizophrenia can be divided into two groups depending on the time of onset of illness: those who have suffered from the illness from a young age and have now grown old and those who have developed the illness in the later part of their lives (late-onset schizophrenia). The second group has been further divided into late-onset (onset after 40 years of age) and very late onset (onset after 60 years of age) on the basis of research evidence. The late onset have a similar genetic risk and positive symptoms as the early onset but show fewer negative symptoms and a better response to antipsychotics. The very late-onset group are less likely to have a genetic link, more likely to have sensory impairment and are more sensitive to extrapyramidal side-effects of antipsychotics^[1].

1.2 Delirium

Delirium, an acute, reversible state of disorientation marked by modifications in cognition and consciousness, commonly goes undetected or receives an incorrect diagnosis in the elderly. Disorientation, difficulty focusing or maintaining attention, poor memory, perceptual disturbances (delusions and hallucinations), psychomotor changes of hypoactivity or hyperactivity, labile mood, anxiety, impaired speech, sleep/wake impairment, and disruptive behaviour are some of the symptoms these patients exhibit^[5].

1.3 Delusional Disorder

Patients with persistent delusions without obvious hallucinations in the absence of dementia, schizophrenia, or mood disorders are classified as having delusional disorder (DSM-IV code 297.10). These individuals typically have well-defined, nonbizarre delusions, which may include notions of physical ailments, persecution, thievery, adultery, and mistaken identity. Delusional illnesses typically manifest in males between the ages of 40 and 49 and in females between the ages of 60 and 69^[5].

1.4 Mood Disorder with Psychosis

In older patients, depression is the most common psychiatric disorder. Retirement, relocation, loss of social support, bereavement, financial problems, and chronic medical illnesses all increase the elderly's risk of depression. In elderly patients, psychotic symptoms are frequently associated with depression. Mania can also occur in the elderly. Elderly manic patients are rarely euphoric, instead exhibiting irritability, paranoia, and mild confusion^[5].

1.5 Dementia with Psychosis

During the course of their illness, dementia patients who are elderly are at a significant risk of developing psychotic symptoms and behavioural disturbances. Patients with dementia typically express visual and auditory hallucinations as well as basic paranoid delusions. Dementia with Lewy bodies is yet another dementia syndrome receiving more attention (DLB). Patients with Parkinson's disease and Alzheimer's disease have been found to contain Lewy bodies, which are inclusion bodies that are immunoreactive to ubiquitin^[5].

1.6 Substance Abuse and Psychosis

Among senior people, substance addiction due to boredom, loneliness, or excessive use of prescription medications (such as barbiturates) is a typical issue. As a result, both short-term and long-term substance use can contribute to the emergence of psychosis in this population. Alcohol withdrawal symptoms that are severe can cause delirium, complete with vivid hallucinations and delusions^[5].

1.7 Psychotic Disorder due to Medical or Neurologic Condition

The development of psychotic symptoms in older persons may be predisposed by medical conditions. Elderly psychosis has been linked to a number of common conditions, including thyroid disease, diabetes, vitamin B12 and folate insufficiency, sodium-potassium imbalance, sleep deprivation, and dehydration. Hallucinations and/or delusions are common signs of delirium and can be present. When an underlying metabolic disorder is the cause of the psychosis, vivid visual hallucinations and disorientation are very frequent symptoms. It's also important to rule out any structural brain abnormalities or mild seizure diseases. The majority of older people who have neurologic diseases exhibit behavioural problems. Multiple sclerosis, Huntington's disease, Parkinson's disease, and amyotrophic lateral sclerosis are all conditions that might result in the emergence of psychotic symptoms ^[5].

MAJOR GROUPS OF DRUGS USED IN ELDERLY

- 2.1. Antipsychotic medications
- 2.2. Antidepressant medications
- 2.3. Mood stabilizers
- 2.4. Benzodiazapines and other anxiolytics
- 2.5. Anti-dementia drugs

2.1 Antipsychotic Medications

2.1.1 Typical Antipsychotics

Specific target symptoms must be identified before the start of antipsychotic medications and regular monitoring over the course of the illness needs to be done as exposing elderly patients to unwarranted medications may lead to various untoward effects like anticholinergic side effects (poor attention, impaired memory and behavioral problems), extrapyramidal side effects (tremor, rigidity, akathisia, dyskinesia), cardiovascular side effects (orthostatic hypotension and arrhythmias), Sedation, Hypersalivation. Gastrointestinal effects like nausea, constipation and diarrhea, Liver effects like Cholestatic jaundice and Raised transaminase enzyme activities, Endocrine effects like weight gain and diabetes mellitus and Epilepsy ^[3].

2.1.2 Atypical Antipsychotics

2.1.2.1 Clozapine

Although clozapine continues to have positive neurological side-effects, its usage in the older population is constrained due to its significant side-effects, such as drowsiness, disorientation, and agranulocytosis, which necessitate regular blood count monitoring. When prescribing clozapine, it is advisable to initiate treatment with a dose of 6.25 mg/day, followed by weekly titration of 6.25 mg/day until a therapeutic effect is achieved ^[3].

2.1.2.2 Risperidone

In elderly psychotic patients, risperidone is beneficial in lowering violent behaviour, paranoia, and delusions, but it is also known to cause EPS symptoms at low dosages (1-2 mg per day) in older patients, especially those who already have dementia. Risperidone's daily maximum dose for older patients is 2-3 mg ^[3].

2.1.2.3 Olanzapine

In comparison to Risperidone, Olanzapine appears to be more effective at maintaining control over negative symptoms in older patients with schizophrenia and similar psychotic diseases. The ideal dosing range is 2.5 to 15 mg per day ^[3].

2.1.2.4 Quetiapine

According to reports, quetiapine is more effective at inhibiting 5-HT₂ receptors than D₂ and mesolimbic pathways than nigrostriatal ones, which explains why it has a low propensity to generate EPS and is effective at treating positive symptoms. It is recommended that Quetiapine should be started with the lowest possible dose (25 mg) and slowly titrated up to 100– 300 mg/day ^[3].

2.2 Antidepressant Medications

The elderly is known to have more stressors in their lives like ageing of brain, problems with physical health, cerebral pathologies, socio-economic factors such as decrease in economic independence and breakdown of the family support system. These problems have been found to be associated with the development of depression in the elderly. Medications used to treat depression in the elderly are Selective serotonin reuptake inhibitors (SSRIs) (e.g., fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, and escitalopram), Non-Selective Serotonin Reuptake Inhibitors (bupropion, venlafaxine, and mirtazapine) and Tri-cyclic antidepressants (TCA) (e.g., amitriptyline, imipramine, doxepin, trimipramine, desipramine, nortriptyline and protriptyline).

2.3 Mood Stabilizers

2.3.1 Lithium

As the elderly have a lower renal function as compared to the younger population, they suffer from side-effects of lithium therapy like diarrhea, tremor, polyuria and polydipsia more commonly^[3].

2.3.2 Valproate

Valproate is considered an acceptable alternative to lithium in manic elderly patients, particularly in those who develop deterioration of cognitive performance during lithium treatment. Dosages of Valproate in the elderly should be adjusted to attain plasma levels of around 50 and 120 µg/mL. Prescribing 400-1000mg of Valproate per day in divided doses usually produces the desired concentration in blood^[3].

2.3.3 Carbamazepine

Treatment for the symptoms of both mania and depression with carbamazepine is successful. Antimanic effects start to manifest after four to seven days when carbamazepine dosages (usually starting at 200 mg orally twice a day) are adjusted to produce blood levels between 4 and 12 ng/mL^[3].

2.4 Benzodiazepines and Other Anxiolytics

The preferred medication for treating acute or subacute anxiety is still benzodiazepines. Shorter-acting benzodiazepines, such as lorazepam or oxazepam, which undergo single-step conjugation in the liver and have no active metabolites, are typically preferred for anxiety disorders requiring treatment for more than 4-6 weeks. When used for such a long time, longer acting benzodiazepines have a tendency to build up in the body and have undesirable side effects. Buspirone is nonbenzodiazepine that has been shown to be an effective anxiolytic agent in elderly patients. Zolpidem is amongst the most widely used hypnotic in the elderly and zaleplon is much shorter acting and as effective as zolpidem^[3].

2.5 Anti Dementia Drugs

Anti-cholinesterase drugs Tacrine, donepezil, rivastigmine, and galantamine are a few cholinesterase inhibitors that can be used to treat mild to moderate cognitive impairment brought on by Alzheimer's disease. All of these substances boost central cholinergic neurotransmission by preventing acetylcholinesterase from degrading acetylcholine^[3].

2.5.1 Memantine

Memantine is the first non-cholinesterase inhibitor that has been shown in randomized controlled clinical trials, to be effective in reversing or slowing cognitive and functional decline in Alzheimer's disease.

ADHERENCE OF ANTIPSYCHOTROPICS IN ELDERLY

People over 50 are more likely to have various chronic conditions, necessitating the use of numerous drugs to enhance quality of life, prevent comorbidities, and prevent mortality^[6]. Mental illness is prevalent among the elderly population. In a population of 65 years or older, depression is more prevalent than dementia^[7]. The term 'extent to which patient's treatment-related behaviour conform to healthcare professionals' advice is used to describe adherence. One of the greatest obstacles to patients with psychiatric diseases receiving successful therapy is nonadherence to psychotropic drugs. Noncompliance could increase the healthcare cost, morbidity, and mortality^[8].

3.1 Factors Affecting Medication Adherence in Elderly

In clinical practice, medication compliance is multifaceted. Negative health outcomes for individuals with mental health conditions, such as suicide, early mortality, rehospitalization, delays in remission, and violence, are mostly predicted by nonadherence to psychotropic drugs^[8]. Elderly nonadherence is influenced by a number of factors, including:

3.1.1 Socioeconomic Related

The risk of poor treatment management and unfavorable outcomes is increased for older persons who self-administer medication therapy for extended periods of time without proper supervision and assistance. Lack of social support from friends or carers, expensive medicine costs, death of a spouse or other close family member, loneliness, feeling like a burden to others, feeling neglected, busy job schedules, spiritual and cultural attitudes regarding diseases are all contributing factors^[9]. Retirement has an impact on personality since the entire environment will change after retirement and it will be quite challenging to adjust^[10].

3.1.2 Health Care System

Approximately 50% of elderly people don't follow the treatment plan. Most healthcare providers do not give their patients their whole attention, which might result in poor adherence. Medication adherence is positively impacted by a good doctor-patient relationship. Adequate information about the drug and its benefit how to administrate, instructions for use and adverse effects. The length of the treatment is crucial for a successful medical outcome^[9].

3.1.3 Condition Related

Many chronic disorders that affect older people frequently call for long-term medication therapy. Furthermore, major cardiac procedures and diminishing of sensory organs causes older adults to depend on others. One of the primary causes of drug nonadherence is psychological changes associated with ageing, which include: poor sleep, lack of sleep, dislike of small things, rigidity of personality, emotional instability, and diminished learning capacity, withdrawal from society, constant grumbling and even a propensity towards suicide, diminished enjoyment of ordinarily pleasurable activities.^[10]

3.1.4 Treatment Related

The patient always finds it difficult to follow a complicated treatment plan. Increasing daily doses, lengthy treatment for chronic illness, the simultaneous administration of medications, and the absence of an instant improvement or therapeutic benefit all have a negative impact on adherence^[9].

3.1.5 Patient Related

The causes of nonadherence in elderly people include cognitive impairment, hearing and vision loss, and swallowing difficulties. Inadequate comprehension of the benefits of therapy, the necessity of taking medications, anxiety about potential side effects, a lack of social support, and substance addiction all contribute to nonadherence^[9].

3.2 Strategies to Improve Medication Adherence in Geriatrics

People are living longer today. Medical nonadherence is more likely in older patients with mental health concerns. Several strategies created by researchers can be used to increase adherence to psychiatric medication.

3.2.1 Psychosocial Interventions

These interventions are aimed at specific individuals, groups, families, or communities. Psychoeducation, motivational interviewing, and cognitive behavioural therapy are essential elements. The objectives of the psychosocial therapies are to enhance general functioning and quality of life^[11].

3.2.1.1 Psychoeducation

It tries to educate patients and their families about their condition, the best course of treatment, and any potential side effects. It also provides counselling to individuals, patient groups, and families^[12]. Essential components of psychoeducation are ;

- Informing patients about their condition and teaching them problem-solving skills.
- Self-assertiveness and communication training

3.2.1.2 Cognitive behavioural therapy (CBT)

CBT is a type of psychological therapy that uses explicit, goal-oriented procedures to challenge patients' maladaptive behaviours and thought processes. Patients who follow to treatment can achieve great outcomes and maintain their health throughout life. It teaches patients how to recognise and change negative habitual thoughts regarding drugs. It places a strong emphasis on changing behaviour, thinking, and reducing distress through emotional control. Regular sessions, constant feedback, learning how to calm one's mind and body, gradually exposing one to their worst fears, and encouraging positive behavioural changes are some of the activities included^[11].

3.2.1.3 Assertive Community Treatment

AST is a multidisciplinary team-led paradigm for assisting senior citizens with severe mental health issues. Individuals get mental health care, family education, occupational training, integrated dual disorder treatment, wellness skills, and rehabilitation in AST. The AST team also attends to the clients' complete needs, which may include housing, employment, and outpatient psychotherapy. Additional psychosocial therapies include cognitive adaption training, motivational interviewing, and adherence coping education. By assisting clients in exploring and resolving ambivalence, motivational interviewing is a client-centered counselling method that promotes behaviourchange^[12].

3.2.2 Pharmacological Interventions

Using long-acting injections, switching, and dose tweaking are pharmacological approaches to promote adherence. In order to prevent side effects, patients must first and foremost be informed about their symptoms, drugs, and decision-making processes. By forming a solid therapeutic alliance with the doctor, the patient can get insights into what causes nonadherence and have a personalised treatment plan made for them^[12].

3.2.3 Technological Interventions

- Electronic drug monitoring measures pill intake or pill count using smart or electronic pill containers.
- Electronic reminders - It will remind patients to take daily medications via apps on a phone or device.
- Digital medicine system - A adherence monitoring tool, can track the actual intake of medicine via inbuilt sensor^[12].

Other Interventions Include

By adopting tools like alarm clocks, journals, and mind games to improve memory and might delay cognitive decline. Life-affirming perspectives are encouraged. Physical assistance is provided for dressing, washing, and walking. Sometimes you need to have joint discussions with your spouse. More effective is cognitive behavioural therapy They must mingle with people of similar ages. Family counselling is offered to enhance communication and mental wellness within the family. Reading and writing can help with memory. The health of seniors depends on their remaining active and exercising regularly. Taking up new interests can aid in maintaining an active lifestyle after retirement^[10]

IMPACT OF ANTIPSYCHOTROPICS ON QUALITY OF LIFE

The WHO defines quality of life as an individual's view of their position in life in relation to their objectives, aspirations, standards, and concerns within the framework of the culture and value systems in which they live^[13].

Quality of life is also defined as health brought on by a confluence of physical, functional, emotional, and social components^[14]. The most important component of quality of life (QOL), which is a complex of various aspects affecting human performance and achievement, is pain, which is followed by mobility, mood, and social situation. The emotional level is the key level of QOL that psychotropic medications mighteffect^[15].

Antipsychotic usage in people with dementia has been linked to an elevated risk of cardiovascular events and mortality in several pooled studies and meta-analyses^[16,17,18,19]. This was observed in senior citizens living in

nursing homes, and it may be related to advanced dementia, which would increase the baseline mortality risk [20-26]. To treat the signs of increased mortality and stroke risk, the American Geriatric Society's 2015 Beers criteria for safe pharmaceutical use in older individuals advise against using antipsychotics [27].

Erica Ito et al randomized controlled trial indicates that psychiatric medications may be dangerous to elderly patients' quality of life [28]. More exposure to psychotropic drugs was associated with lower quality of life in the cross-sectional study by Stephanie L. Harrison et al. on older persons with high levels of dementia and cognitive impairment living in Australian residential care facilities. Both benzodiazepines and antipsychotics have been independently linked to a lower quality of life. There was a decline in the use of psychotropic drugs in residential care institutions that had adopted a small group home-like approach [29].

Cardiovascular problems and negative mental stage alterations are only a few of the side effects that psychotropic medicines can cause [30]. Some drugs, such as benzodiazepines and antipsychotics, have been advised against using in elderly and dementia patients [31]. Yet, personnel in residential care may have a huge difficulty as people with dementia are very likely to develop BPSD at some point [32].

Elderly patients who are prescribed psychotropic medications need to have their prescriptions frequently reviewed to determine if the potential risks, which could include a reduced quality of life, outweigh the benefits of the medication and if any non-pharmacological alternatives might be used instead. With moderate quality evidence and without the side effects associated with psychotropic medicines, functional analysis-based therapies have been found to significantly reduce global BPSD [33].

CONCLUSION

Because of comorbid diseases and age-related physical changes in the geriatric population, psychiatric disorders may manifest differently and have a more difficult course. Many patient, systemic, and environmental factors are linked to older patients' non-adherence to psychiatric medication. Increased adherence to psychiatric drugs would lower the risk of readmission and lower healthcare expenses, alleviating this population's financial burden. The quality of life of the older population is seriously threatened by antipsychotropic medications. Antipsychotropic drugs were linked to a higher risk of death, according to the majority of investigations. We draw the conclusion from this work that additional research is necessary to improve older patients' compliance with antipsychotic medications, which will ultimately improve their quality of life.

REFERENCES

- [1] Salman Karim MSc, FRCP, *Diagnosis and management of psychosis in older people. Prescriber* ;19 (2) 2008: 38-43
- [2] Salman Karim & Eleanor J. Byrne , *Treatment of psychosis in elderly people. Advances in Psychiatric Treatment*;11, 2005: 286-296
- [3] Samidhya Varma, Himanshu Sareen, J.K. Trivedi , *The Geriatric Population and Psychiatric Medication. Mens Sana Monographs*;8(1), 2010: 30-50
- [4] Shiv Gautam, et al. *Clinical Practice Guideline for Management of Psychoses in Elderly. Indian Journal of Psychiatry*;60(3), 2018: S363S370
- [5] Steven D. Targum, M.D. *Treating Psychotic Symptoms in Elderly Patients. Primary Care Companion to The Journal of Psychiatry*; 3(4), 2001: 156-163
- [6] Murray MD, Morrow DG et al. *A conceptual framework to study medication adherence in older adults. Am J Geriatr Pharmacother*;2(1), 2004: 36-43.
- [7] Gureje O, Kola L, et al. *Epidemiology of major depressive disorder in elderly Nigerians in the Ibadan Study of Ageing: A community-based survey. Lancet. 2007; 370:957–964.*
- [8] Tsikada, Omah S., "Evidence-Based Strategies for Improving Medication Adherence Among Psychiatric Patients: A Systematic Review". *Walden Dissertations and Doctoral Studies*.(2020); 8811.
- [9] Dwajani S., Prabhu Mr, Ranjana G., Sahajananda H, *Importance of medication adherence and factors affecting it. IP Int J Compr Adv Pharmacol*;3(2), 2018:69-77.
- [10] Sahoo Srinibash, et al. *Psychological problems of the aged and its management. Int. J. Res. Ayurveda Pharm.*;4(5),2013 :656-660
- [11] Dolder CR, Lacro JP, Leckband S, et al. *Interventions to improve antipsychotic medication adherence: review of recent literature. J Clin Psychopharmacol*;23, 2003:389–399
- [12] Kane JM, Kishimoto T, et al. *Non-adherence to medication in patients with psychotic disorders: epidemiology, contributing factors and management strategies. World Psychiatry*;12(3), 2013:216-26
- [13] Nejati V, Shirinbayan P, Akbari A, Foroughan M, Taheri P, Sheikhatvan M. *Quality of life in elderly people in Kashan, Iran. Middle East J Age Ageing*; 5 (2), 2008:21–25.
- [14] Ware JE Jr, Sherbourne CD. *The MOS-36 item short-form health survey (SF-36) Med Care*; 30 (6), 1992:473–83.
- [15] Olli Pekka Ryyanen ; *Psychotropic medication and quality of life in the elderly. Nordic Journal Of Psychiatry*;47, 2009:67-72
- [16] Schneider LS, Tariot PN, Dagerman KS, et al. ; *CATIE-AD Study Group. Effectiveness of atypical antipsychotic drugs in patients with Alzheimer's disease. N Engl J Med*;355, 2006:1525–1538.
- [17] Rossom RC, Rector TS, Lederle FA, Dysken MW. *Are all commonly prescribed antipsychotics associated with greater mortality in elderly male veterans with dementia? J Am Geriatr Soc*;58, 2010:1027–1034.
- [18] Maust DT, Kim HM, Seyfried LS, et al. *Antipsychotics, other psychotropics, and the risk of death in patients with dementia: number needed to harm. JAMA Psychiatry*;72, 2015:438–445.

- [19] Wooltorton E. Olanzapine (Zyprexa): increased incidence of cerebrovascular events in dementia trials. *CMAJ*;170, 2004:1395
- [20] Wooltorton E. Risperidone (Risperdal): increased rate of cerebrovascular events in dementia trials. *CMAJ*;167, 2002:1269–1270.
- [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*;344, 2012:977.
- [22] Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. *JAMA*;294, 2005:1934–1943.
- [23] Kales HC, Kim HM, Zivin K, et al. Risk of mortality among individual antipsychotics in patients with dementia. *Am J Psychiatry*;169, 2012:71–79.
- [24] Goff DC, Cather C, Evins AE, et al. Medical morbidity and mortality in schizophrenia: guidelines for psychiatrists. *J Clin Psychiatry*;66, 2005:183–94; quiz 147, 273.
- [25] Nerius M, Johnell K, Garcia-Ptacek S, Eriksdotter M, Haenisch B, Doblhammer G. The impact of antipsychotic drugs on long-term care, nursing home admission, and death in dementia patients. *J Gerontol A Biol Sci Med Sci*;73, 2018:1396–1402.
- [26] Wei YJ, Simoni-Wastila L, Lucas JA, Brandt N. Fall and fracture risk in nursing home residents with moderate-to-severe behavioral symptoms of Alzheimer's disease and related dementias initiating antidepressants or antipsychotics. *J Gerontol A Biol Sci Med Sci*;72, 2017:695–702.
- [27] American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American geriatrics society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*;63(11), 2015:2227–46.
- [28] Erika Ito , Line Iden Berge et al The Negative Impact of Psychotropic Drug Use on Quality of Life in Nursing Home Patients at Different Stages of Dementia: Cross-Sectional Analyses from the COSMOS Trial. *J Am Med Dir Assoc*;21(11), 2020:1623-1628
- [29] Harrison SL, Bradley C, Milte R, Liu E et al Psychotropic medications in older people in residential care facilities and associations with quality of life: a cross-sectional study. *BMC Geriatr*: 26;18(1), 2018:60.
- [30] Australian Medicines Handbook. In. Adelaide: Australian Medicines Handbook Pty Ltd; 2016.
- [31] American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*.;63(11), 2015:2227–46.
- [32] Koder D, Hunt GE, Davison T. Staff's views on managing symptoms of dementia in nursing home residents. *Nurs Older People*;26(10), 2014:31–6.
- [33] Dyer SM, Harrison SL, Laver K, Whitehead C, Crotty M. An overview of systematic reviews of pharmacological and non-pharmacological interventions for the treatment of behavioral and psychological symptoms of dementia. *Int Psychogeriatr*. 2017:1–15.