Running head: ANTIPSYCHOTIC MEDICATIONS AND DEMENTIA

The effects of antipsychotic medications on older adults with dementia in Canadian complex and long-term care facilities

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Goldfish for the win!

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Abstract

Dementia is a neurodegenerative disease that involves progressive cognitive and functional decline. Symptoms vary and commonly include behaviour and psychological disturbances that can result in patients being prescribed antipsychotic medications. The use of these medications in managing the behavioural and psychological symptoms of dementia is controversial and have been the subject of numerous safety warnings. Research has consistently shown that high numbers of patients with dementia are still being prescribed antipsychotic medications despite these warnings and that there is a significantly higher rate of death for these individuals, compared to those who were not taking this type of medication.

Through descriptive statistics and generalized linear mixed modelling this study aimed to show the nature of antipsychotic medication use in Canadian complex and long-term care facilities, as well the effects these medication have on various areas of functioning, health, and death rates in those with dementia. Approximately 40% of those diagnosed with dementia in Canadian care facilities are prescribed antipsychotic medications. Contrary to earlier studies, there was actually a slightly lower death rate for those individuals' prescribed antipsychotic medications daily but a significantly higher death rate for those who were taking this form of medication inconsistently (1 to 6 days a week). These results suggest that there may be fundamental differences between the individuals receiving antipsychotic medications as a PRN and those who received them everyday, or that medical professionals and caregivers should ensure that patients with dementia consistently take antipsychotic medication, if required, rather than prescribing it on an as needed basis. Future research into the differences in death rate based on the frequency of antipsychotic medication use would be highly beneficial to confirm these findings, which contradict past research, to provide further insight into the safety of these medications for older adults with and without dementia.

The effects of antipsychotic medications on older adults with dementia in Canadian complex and long-term care facilities

Dementia

Dementia is a neurodegenerative disease caused by a variety of illnesses that involves progressive cognitive and functional decline. Symptoms of dementia vary between people but they typically include memory impairment with diminished capacity in other areas such as reasoning, communication skills, the ability to complete activities of daily living (ADL), and in the development of behavioural and psychological symptoms (BPSD). Dementia is an irreversible progressive syndrome with symptoms starting gradually and becoming more numerous and intense over time.

Causes

Dementia is caused by structural and chemical changes in the brain resulting in the death of brain tissue. There are many illnesses that can cause dementia by damaging different parts of the brain while inducing relatively similar symptoms. Alzheimer's disease is the most well known and common cause of dementia and accounts for 63% of all dementias in Canada (Alzheimer Society of Canada, 2010). Alzheimer's disease is due to a deficiency in acetylcholine neurotransmitters (Neef & Walling, 2006), which causes the parieto-temporal regions, including the hippocampus and surrounding cortical structures of the brain, to atrophy (Braaten, Parsons, McCue, Sellers & Burns, 2006). The second most common form of dementia, vascular dementia, is caused by issues related to heart disease, including strokes, high blood pressure, endocarditis, and brain aneurisms. Vascular dementia is relatively unique in that the root cause of the dementia is highly variable and dependent on where the lesion or clot occurs in

the brain (Cummings & Benson, 1992). However it is generally primarily cortical, subcortical, or a combination of both (Braaten et al., 2006).

Fronto-temporal dementia is caused by a degeneration of the frontal and anterior temporal lobes (Braaten et al, 2006), while dementia due to multiple sclerosis is related to atrophy in deep grey matter and the mesial temporal lobe (Benedict, Ramasamy, Munschauer, Weinstock-Guttman & Zivadinov, 2009). Parkinson's disease can also cause dementia due to the death of dopamine generating cells in the pars compacta region of the substantia nigra (Obeso et al., 2008). The death of these cells has been shown to cause a loss of gray matter in the temporal, occipital, and subcortical regions of the brain (Burton, McKeith, Burn, Williams & O'Brien, 2004). In addition, Lewy bodies, eosinophilic cytoplasmic inclusions that contain deposits of a protein called alpha-synuclein, develop in the brain in Parkinson's disease resulting in further damage and dementia symptoms. Contrasting dementia due to Parkinson's, dementia with Lewy bodies is caused by the development of Lewy bodies in the subcortical and cortical areas of the brain, as well as amyloid plaques (McKeith et al., 2004), without the further pathology related to Parkinson's disease.

Several additional forms of dementia are the result of disease or injury to white matter in the brain. Typically the diseases or injuries that affect white matter in the brain are diffuse or multifocal and cause dementia rather than specific cognitive deficits or behavioural issues (Rao, 1996). Some of the causes of dementias related to cerebral white matter are: multiple sclerosis, due to demyelination and white matter lesions; acquired immune deficiency syndrome (AIDS), caused by issues such as generalized atrophy, areas of myelin pallor, and patches of demyelination; traumatic brain injury, due to axonal shearing, or broad axonal injury, that causes

ventricular enlargement and atrophy of white matter; and alcoholic dementia, caused by heavy long-term drinking which damages white matter through toxicity (Rao, 1996).

Demographics

In 2008, it was estimated that approximately 480,600 people in Canada suffered from some form of dementia, with an annual incidence rate of 103,700 (Alzheimer Society of Canada, 2010). The risk of developing dementia increases with age, with less than 1% of Canadians under 65 suffering from dementia compared to 2.5% of people between 65 and 74 years of age, and increasing to 35% for those over 85 years of age (Canadian Study of Health and Aging Working Group, 1994). As the oldest of the large 9.9 million Canadian baby-boomer (those born between 1947-1966) generation are starting to turn 65 years of age this year, this cohort is beginning to enter the age range of greatest risk for developing dementia (Forbes & Neufeld, 2008). It is estimated that within the next 25 years the number of new cases of dementia in Canadians 65 years of age and older is expected to increase by 2.5 times, leading to the diagnosis of 257,800 new dementia patients annually. This will bring the estimated total number of Canadians suffering with dementia to a staggering 1,125,200, the equivalent of about 2.8% of the Canadian population (Alzheimer Society of Canada, 2010).

With the significant increase in the numbers of people being diagnosed with dementia in Canada over the next 25 years, dementia related care requirements are expected to soar as well. The need for long-term care beds is expected to increase from 280,000 in 2008, to 690,000 in 2038 (Alzheimer Society of Canada, 2010). Unfortunately, many of the people needing long-term care beds will not have access to them due to projected shortfalls of availability. These individuals will be forced to reside in the community under the care of their family or hired caregivers. The number of hours spent caring for people with dementia in the community by

informal caregivers (e.g. family, friends) is expected to more than triple in the same time period to 756 million hours per year. Economically, the cost of caring for people with dementia is expected to increase from $15 billion in 2008, to an incredible $153 billion in 2038, taking inflation into account.

Symptoms

Pre-clinical dementia. Pre-clinical dementia is generally defined as the period of five years prior to formal diagnosis with dementia (Ramakers et al., 2007). It is during this period of time that physical, cognitive, and behavioural symptoms begin to become noticeable but are not significant enough to be diagnosable as dementia. During this time an individual may be diagnosed with mild cognitive impairment, meaning that he or she is showing signs of cognitive decline along a continuum between a normal elderly person and one with clear dementia (Fratiglioni, Grut, Forsell, Viitanen & Winblad, 1992). Increased visits to family physicians are common (Wilkinson, Stave, Keohane & Vincenzino, 2004), with a significant increase of medical visits within the two years prior to diagnosis (Ramakers et al., 2007).

In a review of pre-diagnosis medical records of 74 patients with dementia and 125 non-demented controls it was found that the earliest predictor of dementia is gait disturbances (Ramakers et al., 2007). This symptom was predictive of dementia five years before diagnosis. Cognitive complaints, especially regarding memory issues, became predictive of dementia two years before formal diagnosis. Other research studies have shown that there is a strong relationship between gait and cognition, as well as gait-related motor disturbances and dementia (Scherder et al., 2007; Scherder, Eggermont, Visscher, Scheltens, Swaab, 2011; Waite, Grayson, Piguet, Creasey, Bennet & Broe, 2005). BPSD only appeared approximately one year prior to diagnosis (Ramakers et al., 2007). The researchers of this study hypothesize that the BPSD

symptoms develop later in the neurodegenerative process or only became severe enough to start reporting to the family physician in the year prior to diagnosis.

Cognitive symptoms. Cognitive symptoms of dementia are highly variable between individuals, including individuals who are suffering from the same form of dementia, and as a result there are two principles that form the concept of dementia (Knopman, Boeve & Petersen, 2003). The first principle is that the person suspected of suffering from dementia has experienced a decline from some form of previously higher level of functioning. This decline has to be above and beyond what would be considered normal aging such as an increase in forgetfulness greater than what would be typical for others of the same age. The second principle is that the symptoms of the suspected dementia significantly interfere with ADL such as work or social activities.

There are five main cognitive areas that may be impaired to a varied degree in those people suffering from dementia. They include: memory, language, apraxia, agnosia, and executive functioning (American Psychiatric Association [DSM-IV-TR], 2000). Memory impairment is a requirement for the diagnosis of all dementias and is usually one of the first apparent symptoms. Dementia may cause a decline in the ability to learn, retain, and retrieve newly learned information (Knopman, Boeve & Petersen, 2003), or may negatively impact the person's remote memory which includes the ability to recall personal information as well as information learned historically (American Psychological Association, 2000). The degree and nature of memory impairment in a person with dementia may help differentiate between which form of dementia he or she are suffering from. For example, in Alzheimer's disease, the most obvious symptom is typically pervasive forgetfulness which may include paying bills, repeating questions because the person has forgotten that the question has been asked and answered,

geographic disorientation, and lapses in judgement (Knopman, Boeve & Petersen, 2003). In contrast, memory is relatively preserved in frontotemporal dementia to the point where these patients may score in the normal range in tests of delayed recall.

Impairment in language function causes decline in the ability to comprehend and express verbal information (Knopman, Boeve & Petersen, 2003). Patients may develop aphasia (difficulty producing the names of people and objects), echolalia (echoing what they hear), and/or palilalia (continuous repetition of sounds or words) (American Psychological Association, 2000). In addition, the individual suffering from dementia may have impairment in comprehension of spoken and written language.

Apraxia (reduction in ability to complete physical tasks despite intact motor abilities, sensory function, and understanding of the desired task) is another cognitive area that may be compromised due to dementia (American Psychological Association, 2000). Individuals with apraxia may have difficulty completing activities such as picking up a mug, brushing their teeth, or getting dressed. Agnosia is defined as the inability to recognize or identify objects even though sensory function is intact (American Psychological Association, 2000). For people with agnosia, the ability to recognize everyday objects, is impaired which may progress into the inability to recognize love ones or themselves.

Problems with executive functioning are present when a person has impairment in the ability to perform higher-order functioning such as abstract reasoning, problem-solving, mental manipulation of more than one idea at a time, and maintaining mental focus (Knop, Boeve & Petersen, 2003). The Diagnostic Statistical Manual of Mental Disorders (DSM)(2000) describes executive functioning as, "... the ability to think abstractly and to plan, initiate, sequence, monitor, and stop complex behavior" (p. 149).

Cognitive symptoms of dementia develop at a varied pace based on the individual as well as the cause of the dementia. Cognitive symptoms may be present at least two years prior to diagnosis (Ramakers et al., 2007) although patients may not express cognitive complaints until much later (Ganguli et al., 2006). This may be due to patients feeling ashamed and therefore not reporting their cognitive symptoms or patients assuming that their cognitive impairment is normal for their age. Alternatively, patients may be unaware of their cognitive symptoms (Ramakers et al., 2007). Rate of decline may occur slowly, as in some cases of Alzheimer's disease, or progress rapidly, as seen in non-vasculitic autoimmune inflammatory meningoencephalopathies such as Hashimoto encephalopathy (Knopman, Boeve & Petersen, 2003). Women, and those with more education, have been shown to have more rapid decline in cognitive functioning and older age has been shown to be predictive of greater cognitive and functional impairment (Tschanz et al., 2011).

Behavioural and psychological symptoms. Alois Alzheimer described behavioural and psychological disturbances prominently in his original case study of the disease, subsequently named after him, in the early twentieth century (Alzheimer, 1906). Alzheimer described the subject of his case study as suffering from paranoia, delusions of sexual abuse, hallucinations, and screaming. While BPSD was a focus of this case study, research on the cognitive factors related to dementia dominated the field for many years. In the early 1980s research on BPSD began to increase substantially (International Psychogeriatric Association, 2002).

In 1996 the International Psychogeriatric Association (IPA) convened a Consensus Conference on the behavioural disturbances of dementia. The Consensus group consisted of approximately 60 experts in the dementia field from 16 different countries (Kozman, Wattis & Curran, 2006). They created a definition of BPSD to increase consistency within future research

that stated, "the term behavioral disturbances should be replaced by the term behavioral and psychological symptoms of dementia (BPSD), defined as: Symptoms of disturbed perception, thought content, mood or behavior that frequently occur in patients with dementia". The consensus group also acknowledged that it may be helpful to group specific symptoms into clusters, such as behavioural symptoms and psychological symptoms, to aid in research, which is how BPSD will be described below.

Behavioural symptoms. Behavioural symptoms of dementia include all physical and verbal symptoms displayed by a person suffering from the disease.

Agitation and aggression. Agitation is a state of psychological and physical restlessness, and can manifest as behaviours such as pacing, general irritation, and repetitive actions such as nail biting or skin picking. Aggression includes acts of verbal and physical abuse towards others, including acts such as threats of assault, physical violence, emotional abuse, verbal sexual harassment, and sexual assault (Boström, Squires, Mitchell, Sales & Estabrooks, 2011). Aggression commonly results from agitation and therefore the two are routinely combined in research (International Psychogeriatric Association, 2002; Lövheim, Sandman, Karlsson, & Gustafson, 2009; Lyketsos, Steinberg, Tschanz, Norton, Steffens, & Breitner, 2000).

Agitation and aggression are two of the most significant behavioural symptoms in dementia, occurring in between 20% to 50% of patients (International Psychogeriatric Association, 2002; Jost & Grossberg, 1996; Lyketsos et al., 2000). Among restless behaviours, it has been shown that women are more likely to roll up table cloths, while men will more commonly stack or overturn chairs and other furniture (Lövheim et al., 2009). In regards to restless wandering, women are more likely to hide things than men, while men more frequently stand at an outside door wanting to go out. Aggressive behaviours, such as hitting others,

making violent threats, resisting being dressed or undressed, and becoming easily annoyed, are more common among men. Agitation and aggressive behaviour typically peak in the middle stages of dementia, and reduction in these behaviours later in the disease is hypothesized to be due to reduced language and communication ability, as well as restricted motor functions (Lövheim et al., 2008).

Verbally disruptive and attention seeking. Verbally disruptive and attention seeking behaviours can add significant stress and pressure on caregivers and loved ones. These types of behaviours can include symptoms such as constantly seeking the attention and/or help of staff, repeated complaining, continuously shrieking or shouting (Lövheim et al., 2009), moaning, and wailing (Runci, Redman & O'Connor, 2006). Attention seeking behaviour occurs in 40% to 52% of dementia patients living in long-term care facilities (Lövheim et al., 2008). The different behaviours are consistent between men and women, however, women are more likely to exhibit help seeking behaviours and make complaints (Lövheim et al., 2009). This gender difference may occur due to higher rates of depression diagnosis in women with dementia which leads them to seek support and complain.

Verbally disruptive behaviour is observed in 12-50% of patients with dementia in long-term care facilities (Bourbonnais & Ducharme, 2010). It has been found that people who scream due to dementia have higher levels of depression, are more prone to falling, are more often restrained, have lower cognitive functioning, less autonomy, and have a poorer social network than patients who do not scream (Cohen-Mansfield, Werner & Marx, 1990; Cohen-Mansfield, Marx & Werner, 1992). Verbally disruptive behaviour in dementia patients is said to be due to the person residing in a state of confusion because they continue to live in a highly cognitive world but no longer have the capacity to interpret it (Boubannais & Ducharme, 2010). This can

make the external world very confusing and frightening, which can lead some people with dementia to express themselves with verbally disruptive behaviour, purposefully or not. It has been found that screams (and other disruptive behaviour) can express seven different factors such as dissatisfaction or satisfaction, pain, emotions, physical needs, desire to modify environment, and enigmatic (Burbannais & Ducharme, 2010). No significant gender differences have been found for this behaviour between men and women.

Inappropriate and regressive. Inappropriate and regressive behaviour includes behaviours such as being unruly in bed; urinating in inappropriate places such as wastebaskets, wash basins, and on the floor; smearing feces on clothing, walls, and furniture; laying in other peoples beds; taking other people's possessions; and undressing in public rooms (Lövheim et al., 2009). These behaviours may occur for several reasons including confusion, poor memory, disinhibition, or lack of judgement. Inappropriate and regressive behaviour occurs in 7% to 21% of dementia patients in long-term care facilities (Lövheim et al., 2008). Research shows that these symptoms are more common in men than in women, with the exception of undressing in public rooms and smearing feces where there is equal prevalence (Lövheim et al., 2009).

Sexual. Sexual disinhibition can be difficult for caregivers, families, and medical practitioners to manage, causing distress and embarrassment. Sexually inappropriate behaviours have been divided into two types: intimacy seeking and disinhibited (de Medeiros, Rosenberg, Baker & Onyike, 2008). Intimacy seeking consists of normal behaviours that are misplaced in social context (e.g. kissing, hugging). Disinhibited behaviour consists of rude and intrusive behaviours that would be considered inappropriate in most contexts (e.g. fondling, exhibitionism). Dealing with inappropriate sexual behaviour can be a difficult issue in care facilities. There is a need to respect the patient's sexuality and understand that he or she is still a

sexual being, while trying to balance the emotional and physical safety of other patients, family members, and staff. Unfortunately, the line between respect and safety is often very blurry.

Occurrence of inappropriate sexual behaviours varies dramatically depending on the setting, ranging from estimates of 1.8% to 25%, with it being more common in higher-level care (Tucker, 2010). It has been shown that Alzheimer's disease is associated with intimacy seeking behaviours while non-Alzheimer's dementia is associated with disinhibited behaviours (de Medeiros et al., 2008). The majority of the people who exhibit these behaviours are men who frequently have other conditions contributing to their dementia such as subdural hemorrhage or long-standing alcoholism (Tucker, 2010). It has also been found that there is an over-representation of men who engage in sexually inappropriate behaviours that have early onset dementia between 40 and 60 years of age.

Psychological symptoms. Psychological symptoms of dementia include all mental and emotional symptoms displayed by a person suffering from the disease.

Personality changes. As many as 90% of people diagnosed with dementia experience changes in their personality (International Psychogeriatric Association, 2002). Approximately half of the people who develop dementia, or have the neurological markers of Alzheimer's disease at autopsy, experience personality change prior to diagnosis (Balsis, Carpenter & Storandt, 2005). In comparison, less than one quarter of seniors who do not develop dementia experience personality change prior to death. In a study by Balsis et al., (2005), it was found that people became increasingly self-centred and inflexible before their diagnosis of dementia. Some people also became increasingly withdrawn and apathetic, while others became more impulsive and emotionally labile.

Throughout the course of dementia, common personality changes based on the five-factor model of personality (Costa & McCrae, 2002) include increased neuroticism while extroversion, openness, and conscientiousness decreased (Siegler, Dawson & Welsh, 1994). Other studies have looked at personality change in dementia based on the Blessed Dementia Scale (Blessed, Tomlinson & Roth, 1968). This scale identifies changes in the person's personality, drives, and interests. It has been found that people with dementia are frequently rigid and self-centred, lack concern for others, and display rigidity of affect (Bozzola, Gorelick & Freels, 1992). Balsis et al., (2005) summarized his study by saying that people with dementia change in negative ways relative to their former selves and become more erratic, passive, aloof, withdrawn, rash, and immature.

Apathy. Apathy in dementia is characterized by a lack of initiative (Lövheim et al., 2009) and motivation that is not due to diminished level of consciousness, cognitive impairment, or emotional distress (Marin, 1991). Depending on the individual, apathy can cause patients to no longer talk spontaneously, cooperate with others, and to not enjoy previously enjoyed activities (Lövheim et al., 2009). Prevalence estimates of apathy in community dwelling individuals with dementia are between 17% and 37% (Onyike et al., 2007). Estimates drastically increase for individuals living in long-term care facilities with prevalence rates estimated up to 80% (Lövheim et al., 2008). Gender is not correlated with apathy (Lövheim et al., 2009), and while it does not affect cognitive decline, apathy is significantly correlated with functional decline (Clarke, Ko, Lyketsos, Rebok & Eaton, 2010). It has been shown that apathy is the only BPSD that becomes continually worse throughout the progression of dementia, until the patient dies (Lövheim et al., 2008),

Depression. Depression is a serious psychological symptom of dementia. It can cause sadness, loss of interest, weakness and fatigue, sleep difficulties, agitation, and feelings of worthlessness or guilt. Depression can also cause an alteration in eating habits and non-purposeful fluctuations in weight. When severe, it can make the individual want to die and/or consider suicide (Park et al., 2007). While depression can be very difficult for the individual with dementia to deal with, caregivers also experience a negative impact from these symptoms which can lead to early institutionalization for the dementia patient (Teri & Wagner, 1992).

There is much debate regarding the nature of depression in dementia. Some say that depression is a risk factor for dementia (Mondrego & Ferrandez, 2004; Andersen, Lolk, Kragh-Sorensen, Petersen & Green, 2005), while others have shown that depression and its symptoms are actually part of a prodromal phase of dementia and therefore not a risk factor (Vinkers, Gussekloo, Stek, Westendorp & Van Der Mast, 2004; Ganguli, Du, Dodge, Ratcliff & Chang, 2006). Depression is more common in people with dementia than those without dementia (Lövheim et al., 2008; Bergdahl, Allard & Gustafson, 2011). Up to 80% of individuals with dementia are said to suffer from depression during the course of their illness (International Psychogeriatric Association, 2002), with more significant depressive symptoms in the early and middle stages of the disease, and reducing in the later stages when there is more severe cognitive impairment (Lövheim et al., 2008). Some studies have shown that there is a difference in prevalence rates of depression between vascular dementia and Alzheimer's disease, with vascular dementia having significantly higher rates (Park et al., 2007). Other studies have found that there are no differences in rates of depression between forms of dementia (Thompson, Brodaty, Trollor & Sachdev, 2010). Depression in dementia has been shown to be significantly

more common in women, which is consistent with life-time prevalence rates of depressive disorders (Lövheim et al., 2009).

Anxiety. Anxiety involves apprehensive expectation and worry (Smith et al., 2008), and may include symptoms of restlessness, being easily fatigued, difficulty concentrating, irritability, muscle tension, and sleep disturbances (American Psychological Association, 2000), as well as suspiciousness (Ferretti, McCurry, Logsdon, Gibbons & Teri, 2001) . Anxiety in dementia can be explained through the Progressively Lowered Stress Threshold model (PLST) (Hall & Buckwalter, 1987). PLST posits that dementia related anxiety is increased due to confusing or overwhelming aspects of the physical and social environment, overstimulation, physical illness, and demands that exceed the individual's ability to function. This model suggests that anxiety signals the onset of more intense and challenging behaviours that increase the risk of behavioural incidents. These incidents may promote the unnecessary use of medications to manage the behaviour and increase the potential that the individual is moved to a higher level of care (Smith et al., 2008).

Prevalence rates for anxiety in individuals with dementia are conservatively estimated to be 35% (Seignourel, Kunik, Snow, Wilson & Stanley, 2008). Anxiety symptoms appear to be stable throughout the course of dementia, until the later stages when impairment is profound. In regards to differences in anxiety between dementia types, anxiety appears to be greater in vascular dementia than in Alzheimer's disease (Seignourel et al., 2008), as well as frontotemporal dementia (Porter et al., 2003) and dementia associated with Parkinson's disease (Aarsland Cummings & Larsen, 2001). Dementia related anxiety has been shown to cause poor quality of life which includes more functional limitations, poor physical health, and reduced activities, after controlling for depression, problem behaviours, and dependency (Hoe, Hancock,

Livingston & Orrell, 2006). Unmet needs, including lack of daytime activities, psychological distress, lack of company, and memory and communication problems, have been associated with higher levels of anxiety in individuals with dementia living in long-term care facilities (Hancock, Woods, Challis & Orrell, 2006). It does not appear that there is a gender difference in anxiety levels in individuals with dementia (Mendez et al., 2006), which contrasts with the finding that anxiety symptoms and disorders are more common in women amoung those not suffering from dementia (Stanley & Beck, 2000).

Delusions. A delusion is defined as a false belief, based on incorrect beliefs and assumptions about an external reality, which is firmly held despite what most people believe and despite undeniable evidence and obvious proof to the contrary (American Psychological Association, 2000). Common delusions associated with dementia include delusions of theft, abandonment, danger, 'one's house is not one's home' (where an individual believes that their house is not theirs), misidentification, infidelity, and non-paranoid delusions (Fischer, Bozanovic-Sosic & Norris, 2004). Delusions regarding theft and 'one's house is not one's home' are the most commonly experience delusions, followed by delusions related to suspiciousness and abandonment (Shaji, Bose & Kuriakose, 2009).

Delusional symptoms are commonly associated with the individual being disoriented regarding time, physical location, and other people (Cohen-Mansfield, Golander, Ben-Israel & Garfinkel, 2011). For example, in a 'one's house is not one's home' delusion, the individual may not recognize the nursing home they are in or may not remember actually moving into a nursing home. Loneliness and insecurity can influence delusions of abandonment, which may cause individuals with dementia to believe that their families have left them or that they have no one that loves them. Boredom is a risk factor for increased delusional symptoms. It has been

found that delusions are more common when there are no activities occurring or when an individual is looking for stimulation. Other common triggers for delusions can be environmental phenomena including not being able to find an object, watching the news, staff shift change, talking about the past, and people going in and out of care facilities with bags.

Delusions occur in an estimated 20% to 73% of individuals with dementia (International Psychogeriatric Association, 2002). Those with Alzheimer's disease have delusions more often than people with vascular dementias (Lyketsos et al., 2000). Individuals with poor vision, or who are blind, have significantly more delusions regarding theft, abandonment, and danger, than those with minor or no vision problems (Cohen-Mansfield et al., 2011). Delusions are not a significant predictor of mortality, but are associated with greater cognitive and functional decline and institutionalization rates (Scarmeas et al., 2005).

Hallucinations. Hallucinations are perceived sensory experiences that an individual believes are real, when these experiences are not, or have not, actually occurred (American Psychological Association, 2000). Hallucinations can occur in any sensory modality, but visual hallucinations are the most common in dementia. Hallucinations are believed to be caused by the activation of specific cortical areas, due to damage in the brain associated with the dementia, related to the specific hallucination (Howard et al., 1997). For example, hallucinations of faces are accompanied by the activation of cortical areas involved in face perception on magnetic resonance imaging. While auditory hallucinations are more common than visual hallucinations in other psychotic disorders (American Psychological Association, 2000), auditory hallucinations rarely occur without a concurrent visual hallucination in patients with dementia (Inzelberg, Kipervasser & Korczyn, 1998).

It has been reported that 15% to 49% of people with dementia suffer from hallucinations (International Psychogeriatric Association, 2002). Hallucinations can be either simple or complex (Mosimann et al., 2006). Simple hallucinations include flashes, dots, or grids, while complex hallucinations are well formed typically of people, animals, or objects. Simple hallucinations in isolation are rare; rather it is more common for people with dementia to experience complex visual hallucinations (Mosimann et al., 2006). Hallucinations are more common in dementia due to Parkinson's disease, as well as dementia with Lewy bodies, than other forms of dementia (Lövheim et al., 2008). This is due to the nature of damage caused by Lewy bodies in the brain in these two forms of dementia. As with most other BPSD, hallucination symptoms tend to be most severe during moderate dementia and decrease at later stages of dementia when the individual has severe cognitive impairment (Lövheim et al., 2008). Prevalence of auditory and visual hallucinations are equal for both males and females (Lövheim et al., 2009).

Impact of Behavioural and Psychological Symptoms

Families and other caregivers. Quite often, family members may know the formal diagnosis of their loved ones' dementia, before the individual knows themselves. A doctor might discuss the diagnosis of dementia with a direct family member in order to ascertain the best way to go about informing the patient. Bamford et al., (2004) revealed that one third to two thirds of medical practitioners have difficulty revealing the diagnosis of dementia to their patients. Their study also showed that family members are reluctant to disclose the diagnosis of dementia to their loved one, due to fear of causing emotional stress, the stigma associated with dementia, and questions regarding the ability of the individual to understand and remember the diagnosis. If the individual with dementia does not possess positive coping skills or the ability to deal with

their diagnosis for whatever reason, BPSD may increase directly affecting those around them (Aminzadeh et al., 2007).

Family members typically become the primary caregivers, providing up to 90% of in-home care for people with dementia (Keating, Fast, Frederick, Cranswick & Perrier, 1999). Because BPSD are a major cause of distress for caregivers, and dementia is recognized as one of the hardest illnesses to care for, caregivers of people with dementia are at extremely high-risk to suffer from burn-out (Canadian Institute for Health Information; CIHI, 2010). BPSD plays a major role in the risk of burn-out, which occurs when caregivers are physically, mentally, and emotionally depleted from caring for another person (Pinquart & Sorensen, 2004). Burn-out, and simply the stress of caring for an individual with dementia, may cause caregivers to suffer symptoms such as decreased personal health, injury, depression, anxiety, fatigue, financial problems, and employment losses (Lilly, Robinson, Holtzman & Bottorff, 2012).

Caring for an individual with dementia is very demanding work, even when burn-out is not present. Research has shown that caregivers often feel taken for granted by healthcare providers and the health care system, other family members, as well as the individual with dementia himself/herself (Lilly et al., 2012). Caregivers in Canada feel that they do not receive enough support from professionals to help care for their loved ones, and that the availability for respite and relief services is lacking (Lilly et al., 2012). When caregivers are tired and feeling overwhelmed, they may become reactionary to the individual with dementia (Pulsford & Duxbury, 2006). This can increase the risk for elder abuse and neglect.

While it is a difficult decision to make, when the family caregivers become burnt out from caring for a loved one with significant symptoms due to dementia, they are typically forced to place the individual in long-term care (CIHI, 2010). BPSD are commonly cited by caregivers

as one of the primary reasons for the institutionalization of their relative (International Psychogeriatric Association, 2002). This is often the time when BPSD are very disruptive and may cause safety concerns for the individual with dementia and/or their caregivers (Logsdon, McCurry & Teri, 2007).

Individuals with dementia. By the time of dementia diagnosis, cognitive decline and BPSD tend to be easily observed by others (Ramakers et al., 2007). In some cases, the individual with dementia is also aware that they are going through cognitive and behavioural changes (Aminzadeh, Byszewski, Molnar & Eisner, 2007). When individuals are formally diagnosed, they not only have to deal with the impending losses associated with a disabling and terminal illness, but they will also have to deal with the stigma that comes with the label 'dementia' (Harman & Clare, 2006). Powerful emotional reactions are associated with the diagnosis of dementia, including fear of stigma and devaluation, mourning associated with actual and anticipated losses, and a sense of increased vulnerability of self (Aminzadeh et al., 2007). This is especially the case with Alzheimer's disease, presumably due to the negative stereotypes associated with the disease, as well as the well-known devastation it causes. Limited research has shown that emotional and behavioural reactions to the diagnosis of dementia, and the threat of destruction of self, may have a more significant impact on the disease outcomes than the actual cognitive changes (Bryden, 2002).

Quality of life (QOL) assessments have been used to measure the subjective perception of quality of life in those with dementia, their family, and caregivers (International Psychogeriatric Association, 2002). These assessments measure the individual's health status, including health associated disabilities; environment, including restrictions, stigma, opportunity for choice; subjective perceptions of mood, physical discomfort, and frustration; other's

observations of activity, affect, and social involvement; and caregiver's report of mood and behaviour. A recent study that looked at QOL ratings in dementia patients also looked at what family and paid caregivers would rate the QOL for the individual with dementia (Crespo, Bernaldo de Quirós, Gómez & Hornillios, 2012). It was found that the individuals with dementia believe they have a better quality of life than did their family or caregivers, which was seen in factors such as mood, yourself overall, life overall, energy, relationship with family, and relationship with friends. Paid caregivers gave the second highest QOL rating, with family giving the poorest. This may be due to the fact that the family has been able to witness the full decline of the individual with dementia, and the patient themself has either mentally accommodated their circumstances, or has lost insight into their full situation.

The individual with dementia will need increased care and support in order to complete ADL and function day to day. When BPSD are present, most can be deemed disruptive and cause psychological distress to those around them (Pinquart & Sorensen, 2004), which may cause negative reactions that effect the individual. BPSD can also impact the person with dementia by causing earlier long-term care referral and poorer prognosis (Lyketsos et al., 2000). When residing in a long-term care facility, BPSD may also cause the individual to be put on more medication than those patients without BPSD, as well as be physically restrained (Feng et al., 2009). There are many questions surrounding the efficacy of medications used for BPSD, and potential health ramifications.

Management of Behavioural and Psychological Symptoms

Psychosocial Interventions. Due to the impact that BPSD has on individuals with dementia, their families, and caregivers, as well as the often disruptive nature of the symptoms, management of BPSD is seen as very difficult and highly important. Psychosocial interventions

aimed at the treatment of BPSD in long-term care facilities are being developed as an alternative to pharmacological management (Vernooij-Dassen, Vasse, Zuidema, Cohen-Mansfield, & Moyle, 2010), but at this point most have been poorly researched. These strategies try to improve the quality of life of those with dementia by focusing on the patients' abilities and strengths, while compensating for existing deficits. Psychosocial interventions consist of a wide range of approaches, and can focus on training staff who work with individuals with dementia, or interventions which can be directed at those with dementia.

Some of the most promising and researched psychosocial interventions focus on training staff who work with people with dementia. It has been found that staff training in long-term care facilities can significantly reduce resident behavioural issues, improve communication between staff and residents, and improve quality of life indicators for those with dementia. Staff who are trained in verbal and non-verbal communication techniques, and are able to recognize potential resident needs through behaviour and attitudes, are able to improve staff-resident interactions and life satisfaction and reduce behavioural issues and depression (Kuske, Hanns, Luck, Angermeyer, Behrens, & Riedel-Heller, 2007; Levy-Storms, 2008; Vasse, Vernooij-Dassen, Spijker, Olde-Rikkert, & Koopmans, 2010).

In 2004, a new approach to managing problematic behaviour related to dementia was developed in South Central Ontario and has been implemented in many Ontario and Canadian long-term care homes since (Pettit, 2012). The intervention is called the Gentle Persuasive Approach (GPA), which reframes how aggressive behaviours in those with dementia are viewed by staff in long-term care settings (Speziale, Black, Coatsworth-Puspoky, Ross & O'Regan, 2009). Instead of focusing on aggressive and disruptive behaviours in relation to neuropathology caused by dementia, staff are trained to look at these behaviours occurring as a result of unmet

needs, and a way for the individual with dementia to communicate, protect themselves, and re-exert control over their lives. GPA teaches that these behaviours may be the only way the cognitively impaired individual can deal with a life that has become, or is increasingly becoming, unfamiliar and frightening.

In a study by Speziale et al. (2009), pre and post effectiveness of GPA on aggressive and disruptive behaviour was analyzed for the three months immediately proceeding staff training in this intervention. Staff was comprised of various professions working with dementia patients in a tertiary treatment facility for older adults in Ontario. It was found that over 95% of staff that went through GPA training thought the course was very good or excellent, and that they would recommend it to coworkers. Approximately 70% of staff reported that GPA was most useful with patients who were verbally and physically aggressive. Physical aggression by patients was reduced by 50%, with 42 patients being involved in 370 reported aggressive incidents prior to GPA training, and 39 patients involved in only 194 incidents after GPA training. In addition, staff reported a better understanding of the presenting features of dementia, and that a respectful and tolerant approach worked best with the dementia patients.

There are a few psychosocial interventions, directed at individuals with dementia, which have shown potential for reducing BPSD, although research in this area is scant and little is known about their true efficacy. Cognitive stimulation therapy (CST), which focuses on issues such as mental alertness, orientation, reminiscence, and language and executive functioning stimulation, has been shown to help reduce depression with a limited effect on reducing behavioural symptoms, in several short term studies (Livingston et al., 2005). One study, with 201 individuals with dementia recruited from long-term care homes and day treatment centres, randomly divided participants into a CST group or treatment as usual. It was found that after

eight weeks, there was significant improvement in quality of life in the CST group, with lower levels of depression and dependency, and increased cognitive functioning, but no effect on behavioural symptoms (Woods, Thorgrimsen, Spector, Royan & Orrell, 2006).

Behavioural management techniques that focus on an individual patient's needs have also been shown to reduce behavioural symptoms and depression (Livingston et al., 2005). Some strategies that have been utilized in these studies have been problem solving techniques, progressive muscle relaxations, reminiscence, and positive reinforcement. A recent placebo-controlled study, involving 167 elderly long-term care residents with dementia in 12 facilities in Maryland, USA, looked at whether individualized behavioural intervention programs would reduce agitated and aggressive behaviours (Cohen-Mansfield, Libin & Marx, 2007). Six of the facilities were used as the intervention facilities, while the other 6 conducted treatment as usual. Interventions were designed to match the needs of individual residents in areas such as cognitive, physical and sensory abilities, as well as their lifelong habits and roles, and occurred for 10 days during the 4 hours of greatest agitation for each resident. At the end of the study, it was found that there were significant reductions in overall agitation and aggression for the intervention group. It was also found that this group had a significant increase in pleasure and interest.

Increasing physical activity for those with dementia also appears to be a promising intervention. Several studies have shown that increased physical activity can improve fitness ability, physical function, positive behaviour and cognitive functioning (Heyn, Abreu, & Ottenbacher, 2004; Kemoun et al., 2010; Lindenmuth & Moose, 1990). A recent randomized control trial looked at the effect of exercise in people with dementia living in long-term care facilities (Kemoun et al., 2010). It involved three 1-hour physical activity sessions per week (including one session a week of walking, stamina exercises, and dance) and demonstrated that

the participants in the intervention group improved their cognitive performance scores and walking abilities. In contrast, the participants in the control group had a reduction in their baseline cognitive performance scores, and a reduction in both their walking speed and stride length. In a large meta-analysis reviewing 30 randomized control trials with older adults with cognitive impairment living either at home or in long-term care facilities, improvements were found for both cognitive performance (ES = 0.57, 95% CI = 0.43-1.17), and positive behaviour (e.g. reduction in aggression, agitation)(ES = 0.54, 95% CI = 0.36-0.72) for the exercise groups (Heyn, Abreu & Ottenbacher, 2004).

Psychopharmacological Interventions. Psychopharmacological treatments of BPSD are frequently used in individuals with dementia, with medications such as cholinesterase inhibitors, mood stabilizers, antidepressants and benzodiazepines, but most commonly with antipsychotics (Trifirò, Spina & Gambassi, 2009). Antipsychotics have been shown to be the most consistent medications used for treatment of BPSD over the other psychotropic medications (Madhusoodanan, Shah, Brenner & Gupta, 2007).

Antipsychotic medications were first developed in the 1950s for treatment of schizophrenia (Banerjee, 2009). Over the next 40 years, many new antipsychotic medications were developed and prescribed to those with psychotic illnesses. Older antipsychotic medications, including haloperidol and thioridazine, are referred to as conventional or typical antipsychotics. These medications bind to the D_2 dopaminergic receptors and have been shown to cause extrapyramidal symptoms including tardive dyskinesia and parkinsonism (Salzman et al., 2008). Most of the newer antipsychotic medications were developed in the early 1990s and are termed atypical antipsychotics (Ministry of Health, 2011). These medications, which include drugs such as clozapine, risperidone, olanzapine, loxapine, and quetiapine, have significantly

more complex and heterogeneous receptor binding profiles than conventional antipsychotics, and have substantially lower rates of extrapyramidal side effects (Trifirò et al., 2009).

In Canada, antipsychotic medications are approved for the treatment of psychiatric illnesses where there is psychosis, such as schizophrenia and bipolar disorder. No antipsychotic medications, except risperidone, are approved for the treatment of BPSD in people with dementia. Risperidone has been approved for the, "short-term symptomatic management of inappropriate behaviour due to aggression and/or psychosis in patients with severe dementia" (Health Canada, 2005, p.1). With the exception of risperidone, the prescription of antipsychotic medications to manage BPSD is considered off-label, as the safety and effectiveness of these drugs for this purpose has not been proven (Kales et al., 2011).

In an older study, dispensing trends of antipsychotic medications in Ontario long-term care homes were analyzed (Bronskill, Anderson, Sykora, Wodchis, Gill, Shulman & Rochon, 2004). Participants included 19,780 residents who were 66 years old and older, had not taken an antipsychotic medication in the previous year, had no evidence of major psychosis, and had been newly admitted to a long-term care facility in Ontario. It was found that antipsychotic medications were prescribed to 17% of the residents within 100 days, and 24% of residents within the first year since admission. Risk of being prescribed an antipsychotic medication was less likely in women (OR = 0.7, 95% CI = 0.6-0.8), and more likely in residents with dementia (OR = 3.5, 95% CI = 3.2-3.8). In addition, it was found that long-term care residents were prescribed an initial does that exceeded recommended thresholds, and that only 14% of those newly prescribed an antipsychotic medication had prior contact with a geriatrician or a psychiatrist.

Between April 2010 and June 2011, 50.3% of seniors in British Columbia on PharmaCare Plan B (public drug plan) who resided in long-term care facilities were prescribed an antipsychotic medication (Ministry of Health, 2011). The most commonly prescribed antipsychotics for these individuals were atypical, including quetiapine, risperidone, loxapine, and olanzapine, followed by the conventional antipsychotics haloperidol and methotrimeprazine. The rest of Canada had an antipsychotic prescription rate of approximately 37.7% for seniors living in long-term care facilities in 2007 (Canadian Institute for Health Information, 2009). Trends show that antipsychotic prescription rates for those seniors in long-term care facilities have increased in BC over the years from 37% in 2001/02, 47% in 2006/07, to 50.3% in 2011 (Ministry of Health 2011), and the same trend can be assumed for the rest of Canada.

Efficacy. There is much debate throughout the medical field regarding the efficacy of antipsychotic medications for the management of BPSD. A few studies have found benefits of conventional and atypical antipsychotic medications for these symptoms. In a meta-analysis looking at the effects of haloperidol in agitated dementia patients, found that there was significant improvement in symptoms of aggression, modest improvement in psychotic symptoms, but no improvements in agitation (Lonergan, Luxenberg, Colford & Birks, 2002). There is very little clinical trial evidence for other conventional antipsychotics with BPSD. In another meta-analysis looking at the effects of atypical antipsychotics on aggression, agitation and psychosis in dementia patients, it was found that risperidone provided overall benefits for behavioural symptoms including aggression, modest benefits for psychosis, and no evidence for non-aggressive agitation (Ballard & Howard, 2006). A further meta-analysis looked at the effects of risperidone and olanzapine on BPSD in Alzheimer's disease, and reported a modest effect in reducing aggression and psychosis (Ballard & Waite, 2006).

The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) was a 42 site, double-blind, placebo-controlled drug trial, with 421 outpatient participants with Alzheimer's disease and psychosis, aggression, or agitation (Schneider et al., 2008). This study compared the efficacy of risperidone, olanzapine, and quetiapine with the placebo for a duration of three to nine months. Benefits of these medications were limited, with 32% of patients receiving olanzapine, 26% of patients receiving quetiapine, 29% of patients receiving risperidone, and 21% of patients receiving placebo, exhibiting improved behaviour. Furthermore, this study showed that the placebo group had significantly lower health costs than the participants on the antipsychotic medications. The authors of this study noted that the adverse events of these atypical antipsychotics offset any advantages in the efficacy of these medications.

A large scale randomized, double-blind, placebo-controlled study, involving 235 long term care facility residents with dementia and psychosis, looked at the effectiveness of risperidone in the treatment of clinically significant psychosis in Alzheimer's disease (Mintzer et al., 2006). It was found that this medication had no benefit over placebo in reducing psychosis rating on the BEHAVE-AD, and that the patients receiving risperidone had more adverse events (74% versus 64%), greater and more frequent somnolence (16.2% versus 4.6%), and higher rate of mortality (3.8% versus 2.5%), than those taking placebo. Beyond the conflicted research findings as to whether there are benefits with using antipsychotic medications for BPSD, it has been found that antipsychotic medications do not appear to improve functioning, care needs, or quality of life for people with dementia (Sultzer et al., 2008).

Warnings. In 2002, warnings began to be issued regarding adverse side effects (discussed further in next section) of antipsychotic medications when taken by patients with dementia. Clinical trials were starting to show that people with dementia were at a significantly

higher risk for life-threatening adverse events when taking antipsychotic medications (Banjeree, 2009). In October 2002, the manufacturer of risperidone made an unprecedented announcement to Canadian healthcare professionals. They shared that in drug-sponsored clinical trials for risperidone, it had been found that people with dementia had a higher rate of cerebrovascular adverse events (CVAE) compared to those taking placebo (Banjeree, 2009).

In 2003, the United States Food and Drug Administration (FDA) published its own warnings regarding the safety of risperidone for dementia patients, requiring changes to the prescribing information (Black & Almeida, 2004). Then, in 2004, the European Medicines Agency alerted the public that olanzapine increased the risk of CVAEs and mortality in people with dementia. Also in 2004, the United Kingdom Committee of Safety of Medicines recommended that physicians avoid prescribing risperidone and olanzapine to elderly people with dementia with BPSD due to an increased risk of strokes (Committee on Safety of Medicines, 2005).

In April 2005, the United States FDA issued an alert to health professionals regarding increased mortality risk in patients with dementia related psychosis (Federal Drug Administration, 2005). This alert was based on the findings of seventeen independent randomized clinical trials using the antipsychotic drugs olanzapine, aripiprazole, risperidone, and quetiapine. 5106 elderly patients with BPSD took part in the studies as well as additional control participants. The drug trials showed that the risk of death was 1.6 to 1.7 times higher for those participants taking the antipsychotic medications than the control participants on a placebo over an approximate 10 week period. Causes of the deaths were identified as primarily cardiovascular (e.g. heart failure) and infectious (e.g. pneumonia). The FDA found similar results of increased

risk for death with conventional antipsychotics, but refrained from issuing an alert because data was only based on one randomized control trial with haloperidol (Trifirò et al., 2009).

Health Canada also issued a warning in June 2005 regarding the safety of using atypical antipsychotic medications for the treatment of behavioural and psychological symptoms in elderly patients with dementia (Health Canada, 2005). This warning was based on the results of thirteen placebo-controlled studies using the atypical antipsychotics risperidone, quetiapine, and olanzapine for the treatment of behavioural and psychological symptoms in elderly patients (n = 3965) with dementia. It was found that the risk of death was 1.6 times greater in the participants receiving the antipsychotics. Cause of death was typically due to cardiovascular events and infections, or consistent with what was found in the American studies. Due to these findings, Health Canada requested the manufacturers of atypical antipsychotic medications include a warning on their Product Monograph describing the risks of these medications and noting that they are not approved for treatment of behavioural and psychological symptoms in elderly patients with dementia, with the exception of risperidone. In 2008, the FDA followed suit and required their antipsychotic medication manufacturers to provide warnings of the increased risk of death in elderly patients with BPSD with off-label use (Trifirò et al., 2009).

These warnings fueled the debate over whether antipsychotic medications should be used to treat behavioural and psychological symptoms in elderly patients with dementia. Mowat, Fowlie and MacEwan (2004) sent a letter to the editor of the British Medical Journal stating that they believe atypical antipsychotics are highly effective and that "the blanket injunction issued by the Committee on Safety of Medicines is oversimplified and may prove detrimental to patient care" (p. 1262). A large number of other studies have been conducted since the warnings were

issued, confirming an increased risk of death for elderly dementia patients taking antipsychotic medications, as well as finding numerous other health concerns related to antipsychotics.

Side Effects.

All-cause mortality. All-cause mortality refers to the overall death rate for a population regardless of specific cause (e.g. heart attacks, strokes). At this point, there is significant evidence that antipsychotic medications increase the risk of mortality. Large scale meta-analyses have consistently shown increased risk of death when people with dementia are treated with atypical antipsychotic medications. A meta-analysis of seventeen independent randomized controlled trials with 5106 elderly demented patients with BPSD, including the atypical antipsychotic medications olanzapine, aripiprazole, risperidone, and quetiapine, found that overall mortality was 4.5% for patients treated with these antipsychotic medications compared to 2.6% for patients on placebo (Federal Drug Administration, 2005). In another meta-analysis of thirteen controlled studies with 3965 participants with BPSD, it was found that the risk of death was 1.6 times higher for those taking the atypical antipsychotics olanzapine, risperidone, and quetiapine, than those taking placebo (Health Canada, 2005).

These meta-analyses were said to provide conclusive evidence that atypical antipsychotic medications increased risk for all-cause mortality in older adults with dementia, so the focus of drug trials was redirected towards the risks associated with conventional antipsychotics (Trifirò et al., 2009). In a study with 27,259 match pairs of dementia patients, it was found that there is a significant increase in the risk for death for those taking antipsychotic medications at 30 days, when compared to those not taking an antipsychotic, which persisted to the end of the study at 180 days (Gill et al., 2007). The risk of death in this study was greater for those prescribed conventional antipsychotic medications than those who were taking atypical antipsychotics.

A large scale study, conducted in the United States, looked at the risk of death in elderly people taking either a conventional or atypical antipsychotic medication and found that conventional antipsychotic medications were at least as likely to increase risk of death than atypical medications (Wang et al., 2005). In the conclusion of this study, it was warned that conventional medications should not replace the use of atypical medications that were involved in recent FDA warnings. A study looking at elderly patients in British Columbia who were taking either a conventional or atypical antipsychotic medication, it was found that within the first 180 days of starting the medication, 14.1% of those in the conventional medication group died, while only 9.6% of those taking an atypical antipsychotic passed away (Schneeweiss, Setoguchi, Brookhart, Dormuth & Wang, 2007). In an Italian study, it was found that elderly people with dementia who took an atypical antipsychotic medication were at a two-fold risk for death, whereas those taking a conventional antipsychotic were at a four-fold risk for death, compared to controls (Musicco et al., 2011).

In a study looking at the long-term survival rates for those with Alzheimer's disease taking either an atypical or a conventional antipsychotic medication, or a placebo, showed similar results (Ballard et al., 2009). Participants were randomly assigned to take either thioridazine, chlorpromazine, haloperidol, trifluoperazine, risperidone, or placebo. It was found that survival rate for the antipsychotic group was 46% compared to 71% in the placebo group at 24 months, 30% versus 59% at 36 months, and 26% versus 53% at 42 months.

A study was recently conducted, looking at the risk of short-term mortality in 508 Ontario long-term care facilities based on dispensing rates of antipsychotic medications (Bronskill et al., 2009). The study included 60,105 individuals 66 years of age and older who were newly admitted to a long-term care facility between the years of 2000 and 2004. Facilities

were assigned to one of five groups (quintiles), with Q1 having the lowest antipsychotic dispensing rate and Q5 having the highest. It was found that the average dispensing rate of antipsychotic medications ranged from 11.6% of residents in Q1, and increased to an average of 30.0% in Q5. When looking at individuals who did not have a recent hospitalization, it was found that all-cause mortality rates at 30 days was 2.5% for Q1 and 3.3% for Q5. At 120 days, this rate increased to 9.3% for Q1 and 11.7% for Q5. This study showed that despite similar admission characteristics, those long-term care residents who were simply admitted to a facility that dispensed greater quantities of antipsychotic medications (e.g. Q5 versus Q1), faced an increased risk of death.

Cardiovascular events. In 2005, Health Canada issued a warning about the increased risk of death and adverse events from the use of atypical antipsychotic medications in the elderly patients with dementia (Health Canada, 2005). This warning stemmed from the review of thirteen placebo-controlled studies using risperidone, quetiapine, and olanzapine in elderly patients with BPSD, that showed a mean 1.6 fold increase in death rate this population taking these medications. The majority of deaths in these studies were due to heart related events including heart failure and sudden-death. The United States also issued a warning in 2005 based on seventeen studies focusing on older adults with dementia (Federal Drug Administration, 2005). These studies found that cardiovascular events, including sudden cardiac death and myocardial infarction, were the most common reason for death in older adults with dementia taking either an atypical or conventional antipsychotic.

In a recent study looking at community-dwelling older adults who take antipsychotic medications, it was found that the unadjusted risk of death associated with taking antipsychotic medications was approximately three times that of people who did not use these medications,

and double that of non-users after adjusting for demographics, diagnostic differences, an antidepressant use (Gisev, Hartikainen, Chen, Korhonen & Bell, 2012). In this study, the highest adjusted risk of death was found in those people using antipsychotic medications who had a baseline diagnosis of respiratory disease. Another study that looked at the risk for serious cardiac events in older adults taking antipsychotic medications found that after controlling for duration of therapy and other exposures probable to induce cardiovascular risk, participants taking conventional antipsychotics were 20% more likely to have a serious cardiac event (Mehta, Chen, Johnson & Aparasu, 2011).

Cardiac arrhythmias have been associated with antipsychotic medications in older adults. Conventional antipsychotics have been shown to contribute to serious cardiac events by increasing the risk of prolongation of cardiac repolarization and the QTc interval, causing orthostasis, and tachyarrhythias (Drici & Priori, 2007). Atypical antipsychotics may trigger sinus tachycardia, atrial and ventricle extrasystoles, as well as rate-corrected QTc inverval prolongation, T wave inversion, ST segment depression, and atrioventricular blocks (Haddad & Anderson, 2002).

In studies related to venous thrombosis (a blood clot in a vein), pulmonary embolisms (a blockage in the main artery of the lung or one of its branches), and venous thromboembolism (VTE) (a venous thrombosis that causes a pulmonary embolism), an association has been made between occurrences of these conditions and older people taking antipsychotic medications. One study looked at the risk of hospitalization for VTE among elderly patients living in long-term care facilities who were taking either an atypical or conventional antipsychotic (Liperoti, Pendone, Lapane, Mor, Bernabei & Gambassi, 2005). After adjusting for potential confounding factors, it was found that users of atypical antipsychotics including risperidone, olanzapine,

clozapine and quetiapine had an increased risk of hospitalization for VTE, while those taking a conventional antipsychotic had no increased risk compared to controls. A case-control study showed that the risk of VTE was 3.5 times greater for those using antipsychotic medications than those who are not, which occurred at the rate of 4:1 for atypical and conventional antipsychotics respectively, in people 68 years of age (Lacut et al., 2007).

Cerebrovascular adverse events. Cerebrovascular adverse events (CVAE), such as strokes and transient ischaemic attacks (TIA), are caused by disruption of blood supply to the brain, typically caused by a cerebral infarction or hemorrhage. It has been found that dementia patients taking risperidone or olanzapine had a risk three times greater for strokes and TIAs than those taking placebo (De Deyn, Katz, Brodaty, Lyons, Greenspan & Burns, 2005; Wooltorton, 2004). A post hoc analysis of pooled results from eleven randomized controlled trials of risperidone and olanzapine in elderly dementia patients found statistically significant differences in the occurrence of CVAEs, with 2.2% of drug treated patients experiencing these events compared to 0.8% of placebo treated patients (Herrmann & Lanctot, 2005).

In a meta-analysis including 15 controlled trials using atypical antipsychotics (aripiprazole, olanzapine, quetiapine, and risperidone) with placebos, it was found that there is an increased odds ratio by meta-analysis for CVAEs in those on antipsychotics of 1.9% versus 0.9% pooled (Schneider, Dagerman & Insel, 2006). When risperidone was specifically looked at in this meta-analysis, the risk was even greater at 3.1% versus 1.0% pooled. In case control studies, it has been found that patients with dementia taking antipsychotic medications had a 1.3 to 2 times greater risk of a CVAE, than those not taking these medications (Sacchetti, Turrina & Valsecchi, 2010). Sacchetti et al. (2010), determined that the highest risk of stroke is within the first weeks of treatment with antipsychotic medications, and risk factors for strokes in this

population include older age, cognitive impairment, and pre-existing vascular illness. In a comprehensive literature review, it was found that risk for CVAEs in dementia patients being treated with antipsychotic medications for BPSD was similar for conventional and atypical antipsychotics, and increased due to factors such as male gender, higher severity of dementia, greater functional impairment, and comorbid conditions such as atrial fibrillation (Mittal, Kurup, Williamson, Muralee & Tampi, 2011).

Cognitive decline. Cognitive decline has been shown to be accelerated in older people with dementia taking antipsychotic medications. People with dementia taking olanzapine or risperidone have been documented in one study to have significantly greater rates of cognitive decline than patients receiving placebo, when they took the medication for at least two weeks prior to assessment (Vigen et al., 2011). Another study, looking at the effects of quetiapine on cognitive impairment in older adults with Alzheimer's disease, found there was significant decline compared to placebo (Ballard et al., 2005). Participant's cognitive impairment level was measured with the Severe Impairment Battery, that has a maximum score of 152. At the six-week follow-up, the quetiapine group scored an average of 14.6 points less (worse) than the placebo group and 15.4 points less at 26 weeks.

In a two year prospective longitudinal study, it was reported that cognitive decline was doubled for older people with dementia taking a conventional antipsychotic medication, compared to those who did not (McShane, Keene, Gedling, Fairburn, Jacoby & Hope, 1997). It was also found in this study that the rate of cognitive decline was more rapid when the antipsychotic medication was initiated, rather than towards the end of study, and that cortical Lewy body pathology did not explain the association between antipsychotic use and faster cognitive decline at autopsy. Atypical antipsychotics were also confirmed to significantly

increase the rate of cognitive decline in a meta-analysis (Schneider et al., 2006). This analysis looked at Mini-Mental State Exam scores over 12 weeks in placebo-controlled trials, and showed that atypical antipsychotic medications caused more rapid cognitive decline in dementia patients.

Extrapyramidal. Extrapyramidal symptoms (EPS) are movement disorders such as Parkinsonism, akathisia, dystonia, and tardive dyskinesia, caused by the effects of antipsychotic medications on dopamine receptors. It has been well documented that conventional antipsychotics are highly associated with developing EPS, and less so with atypical antipsychotics (Czarnecki, Kumar & Josephs, 2008). The inequality in EPS prevalence between conventional and atypical antipsychotics is believed to be due to the differences in their pharmacological mechanisms on dopamine receptors (Weiden, 2007).

Acute EPS develops within hours to weeks of the initiation of antipsychotic medications and can include Parkinsonism, akathisia, and acute dystonia (Czarnecki et al., 2008). Parkinsonism refers to motor issues that mirror those of Parkinson's disease, commonly caused by antipsychotic medications. Motor issues may include a decrease in facial expressions, difficulty starting and controlling movement, loss or weakness of movement (paralysis), tremor, and stiffness of the body or limbs (American Psychological Association, 2000). Akathisia is a syndrome of persistent restlessness which may be perceived as extreme anxiety. People with akathisia have compulsive movements, such as fidgeting, marching in one spot, pacing, or swinging legs when sitting in a chair, in order to help relieve their restlessness (Chang & Friedman, 2009). Acute dystonia involves sustained abnormal body postures or muscle spasms (American Psychological Association, 2000). Abnormal positioning commonly includes the head and neck but can also target the body and limbs. Spasms can affect the jaw muscles, as

well as effect ability to swallow, speak or breath. At times, acute dystonia can affect the eyes causing an oculogyric crisis, causing the eyes to deviate up, down, or sideways.

Conventional and atypical antipsychotics have been compared to see what group of medications cause the most risk for EPS. The conventional antipsychotic haloperidol has been consistently shown to induce the highest risk for EPS (Geddes, Freemantle, Harrison & Bebbington, 2000; Bagnall et al., 2003; Crespo-Facorro, Perez-Inglesias, Ramirez-Bonilla, Martinez-Garcia, Llorca, Vazquez-Barquero, 2006). Risperidone is believed to cause the greatest risk of Parkinsonism than all other atypical antipsychotics (Yang, Kao Yang, Chong, Yang, Chang & Lai, 2007). One study found that risperidone caused Parkinsonism in 42% of participants, with haloperidol only causing parkinsonism in 29% (Knable, Heinz, Raedler & Weinberger, 1997). Another study found no differences in the incidence of developing parkinsonism, acute dystonia, or akathisia when treated with risperidone or haloperidol (Rosebush & Mazurek, 1999). When looking at the risk for EPS between atypical antipsychotics, it has been found that risperidone was associated with the highest risk, and clozapine and quetiapine had the lowest risk (Weiden, 2007).

Tardive dyskinesia has a late onset and may appear months or years after initial treatment with antipsychotic medications. Tardive dyskinesia involves involuntary movements of the tongue, jaw, body or limbs due specifically to the use of antipsychotic medications (American Psychological Association, 2000). The involuntary movements may include choreiform (rapid, jerky, non-repetitive), athetoid (slow, sinuous, continual), or rhythmic (stereotypies). Conventional antipsychotics are known to cause the highest risk of tardive dyskinesia, with an incidence of 5% per year in a study non-specific to older people with dementia, compared to atypical antipsychotics that have an incidence of 1% per year (Tarsy & Baldessarini, 2006).

Elderly people are seen as the highest risk group for tardive dyskinesia (Trifirò et al., 2009), and the incidence of EPS has been shown to be higher in elderly dementia patients at a conservative rate of 2.6% per year (Jeste, Okamoto, Napolitano, Kane & Martinex, 2000).

Pneumonia. In studies regarding the development of pneumonia in elderly people taking antipsychotics the results are fairly consistent. While some of these studies do not focus specifically on dementia, they regularly show that there is an increased risk for pneumonia for older adults taking antipsychotic medications. A study containing 22,944 elderly participants who had received a prescription for antipsychotic drugs (Knol, van Marum, Jansen, Souverein, Schobben & Egberts, 2008). It was found that after controlling for confounding factors, the current use of antipsychotics in older adults was associated with a 60% greater risk of pneumonia than controls using no antipsychotics. In this study, risk for developing pneumonia was equal for both conventional and atypical antipsychotics.

A study that looked at the risk for developing pneumonia after the initiation of atypical antipsychotics in older adults found that there was a 70% increased risk compared to controls (Pratt, Roughead, Ramsay, Salter & Ryan, 2011). In another study, using 258 older adults hospitalized with pneumonia who were taking antipsychotic medications, it was found that 25% died within 30 days, which was significantly greater than controls (Trifirò et al., 2010). It was also found that there was a dose dependent increase in the risk for pneumonia when taking antipsychotic medications in this population, but only atypical antipsychotics were associated with an increased risk for fatal pneumonia. Risk for the development of pneumonia for both conventional and atypical antipsychotics in older adults has been found to be the highest in the first week of taking the medication, and then returning to base-line levels after 90 days of treatment (Knol et al., 2008).

Falls and fractures. Some research has found that the risk of falls and fractures is increased for dementia patients taking antipsychotic medications. A study by Kolanowski, Fick, Waller and Ahern (2006), showed that the risk of falls and hip fractures was increased for those people taking either a conventional or atypical antipsychotic. These results mirror what was found in a study looking at risk of hospitalization for a femur fracture (Liperoti et al., 2007). Risk for femur fracture was increased for those on atypical antipsychotics (OR = 1.37, 95% CI = 1.11 to 1.69) and conventional antipsychotics (OR - 1.35, 95% CI = 1.06 to 1.71) compared to non-users. Haloperidol posed the highest risk for femur fracture (OR = 1.53, 95% CI = 1.18 to 2.26) followed by risperidone (OR = 1.42, 95% CI = 1.12 to 1.80) and olanzapine (OR = 1.34, 95% CI = 0.87 to 2.07). In an observational study in Australia with residents in long-term care, it was found that the participants taking either atypical or conventional antipsychotics had a 35% to 70% increased risk for falls (Hien et al., 2005). Conversely, other studies looking at the rate of falls in people with dementia did not show increased risk for those taking risperidone when compared with placebo (Katz, Mintzer, Brodaty, De Deyn & Greenspan 2005).

Summary

Dementia is a neurodegenerative disease that currently effects 480,600 people in Canada, with estimates that this number will grow to 1,125,200 within the next 25 years (Alzheimer Society of Canada, 2010). Beyond the cognitive symptoms, dementia can cause severe behavioural and psychological symptoms, including disruptive behaviours such as aggression and agitation. These symptoms have a significant negative effect on the individual suffering from dementia, as well as their family, caregivers, and others around them (CIHI, 2010). When BPSD is severe, most families have no choice other than to admit their loved one to a long-term care facility (Lyketsos et al., 2000).

Strategies to manage BPSD include psychosocial interventions as well as psychopharmacology. The psychosocial interventions that have the most support within the literature involve staff training within the long-term care facilities. This type of training teaches the staff ways to improve the quality of life of those with dementia, by understanding the potential causes of disruptive behaviour, how to focus on the individual's strengths, and how to compensate for their existing functional deficits (Vernooij-Dassen et al., 2010). The GPA, is a well-regarded intervention that is being taught and implemented in long-term care facilities throughout Ontario and other parts of Canada (Pettit, 2012). This approach also trains staff to understand that the aggressive and agitated behaviours displayed by those with dementia typically result from unmet needs, and may be the only way the individual with dementia is able to communicate issues, protect themselves, and take control over their increasingly unfamiliar and frightening world (Speziale et al., 2009).

Other psychosocial interventions are created directly for those suffering from dementia. Cognitive stimulation therapy tries to stimulate brain function and alertness, and has been shown to help reduce depression and potentially mildly reduce behavioural symptoms (Livingston et al., 2005). Behavioural management techniques focusing on individual patient's needs, such as problem solving techniques, progressive muscle relaxation, reminiscence, and positive reinforcement have shown positive effects on reducing aggression and agitation, while increasing pleasure and interest (Cohen-Mansfield, Libin & Marx, 2007). Increased physical activity has also been shown to have a promising effect on reducing behavioural issues including aggression, as well as increasing physical fitness, physical function, cognitive functioning, and mood (Kemoun et al., 2010). While some positive results have been shown in these psychosocial interventions, the research in this area is sparse and not well developed.

Psychopharmacological interventions are frequently used to help manage BPSD. The most common form of medication prescribed for these symptoms, especially for aggression and agitation and antipsychotics (Trifirò et al., 2009). These medications were first developed in the 1950s, conventional antipsychotics, to treat psychotic illnesses, such as schizophrenia. In the early 1990s, the receptor binding profiles of conventional antipsychotics were made more complex and heterogeneous, creating a new class of antipsychotics, termed atypical antipsychotics (Trifirò et al., 2009). No conventional or atypical antipsychotics, with the exception of the atypical antipsychotic risperidone, have been approved to treat BPSD in Canada. Risperidone is only approved to be prescribed short-term to manage aggression and/or psychosis in those with severe dementia (Health Canada, 2005). While antipsychotic medications are not approved to manage BPSD, up to 50% of seniors residing in long-term care facilities in Canada, most would be diagnosed with dementia, are taking at least one of these medications (Ministry of Health, 2011).

While antipsychotic medications are commonly prescribed to people with dementia, there is controversy as to whether they are effective in treating BPSD. The research in this area is rife with conflicting results showing that these medications are and are not beneficial. When taken together, it appears that there may be some limited effectiveness of both conventional and atypical antipsychotics in reducing BPSD, including aggression and agitation.

Warnings over the safety of antipsychotic medications in older people with dementia started to emerge in 2002, when the manufacturer of risperidone announced to Canadian healthcare professionals that there is a significantly increased risk of CVAE in people with dementia taking this medication. At least seven subsequent warnings regarding the safety of all antipsychotic medications, conventional and atypical, were issued in the United States, Europe

and Canada over the next six years, stating that there is an increase in cardiovascular events, CVAEs and death in dementia patients taking these medications.

Over the past 10 years, a plethora of research has warned about significant side effects with the use of this medication in dementia patients. It has been shown that people with dementia taking an atypical antipsychotic are at a twofold risk of death, and those taking a conventional antipsychotic are at a fourfold risk of death, than people with dementia not taking these medications (Musicco et al., 2011). In a large meta-analysis of 17 studies focusing on older adults with dementia, it was found that cardiovascular events, such as sudden cardiac death and myocardial infarction, were the most common reason for death in this population taking either an atypical or conventional antipsychotic medication (Federal Drug Administration, 2005). The risk for CVAEs, including strokes and TIAs, are significantly increased for people with dementia taking these medications, with one study showing that people with dementia taking either risperidone or olanzapine having a risk three times greater for strokes and TIAs than controls (De Deyn et al., 2005).

Cognitive decline has been shown to be accelerated in people with dementia taking these medications (Vigen et al., 2011), and the development of EPS well documented, especially with conventional medications (Czarnecki et al., 2008). The risk of developing pneumonia is also increased for elderly people taking antipsychotic medications, regardless of dementia diagnosis. One study found that those individuals taking an atypical or conventional antipsychotic medication were at a 60% greater risk for developing pneumonia (Knol et al., 2008). Lastly, some studies have shown that the risk for falls and fractures in people with dementia taking an antipsychotic medication are significantly increased compared to controls (Hien et al., 2005; Kolanowski et al., 2006; Liperoti et al., 2007).

While it is evident that there is promise for psychosocial interventions in the treatment of BPSD, especially for aggressive and agitated behaviours, antipsychotic medications appear to be the intervention most commonly used. Even with significant government warnings regarding the use of antipsychotic medications in older adults with dementia, and research showing undeniable evidence of severe, and sometimes deadly, side effects, these medications are being widely prescribed in Canada to individuals in this population, especially in long-term care homes. At this point, it is important to gain a clear picture of the current prescribing trends of antipsychotic medications in older adults with dementia in Canada. It will also be beneficial to determine the side effects these medications are having on individuals with dementia in our long-term care homes, and whether there are any visible benefits with their use.

Current Study

Antipsychotic medications continue to be prescribed to older adults with BPSD, even after significant safety warnings were issued from Health Canada in 2004, with very limited evidence for any meaningful benefit within this population. As previously shown, side effects from these medications in older adults with dementia are numerous and potentially severe, including increased risk of death.

The current study provides the most comprehensive look at the current use, and effects, of antipsychotic medications in older adults in continuing care facilities in Canada. Although earlier studies (except those with interventional designs) were mainly cross-sectional, the present research will focus on longitudinal trends. The main dataset in the study is the Resident Assessment Instrument - Minimum Data Set 2.0 (MDS). A brief history of its use in continuing care follows. In 1996, complex continuing care facilities (CCC) in Ontario started to collect data using MDS 2.0. The MDS tool gathers information that includes behaviours (e.g.,

aggressive behaviour), physical competence (e.g., activities of daily living), cognitive status (e.g., overall performance, delirium), and indicators of overall health status (e.g., frailty) and specific diagnoses. In 2005, long-term care (LTC) facilities in Ontario also started to collect MDS 2.0 data, at which time the Ontario Ministry of Health and Long-Term Care mandated its use in all LTC facilities use by June 2010. This process was gradual, with 20 facilities collecting data in 2005, and 217 facilities (39%) by the spring of 2009. The remaining 411 facilities in Ontario were collecting data by the summer of 2010. The data used in this study was the full year census level data for 2010/2011 and 2011/2012 when all facilities in Ontario were using the MDS 2.0.

The MDS 2.0 data are available from the Canadian Institute for Health Information (CIHI), which also provided linkages with two other datasets. First, all Canadian hospitals (except those in Quebec) submit their separations records directly to CIHI for inclusion in the Discharge Abstract Database (DAD). The database contains demographic, administrative and clinical data for hospital discharges (inpatient acute, chronic, rehabilitation) and day surgeries. Second, the National Ambulatory Care Reporting System (NACRS) contains data for hospital-based and community-based emergency and ambulatory care (for example, day surgery and outpatient clinics). The main purposes of these additional datasets are to provide information on mortality in other than the primary CCC or LTC residence.

Issues within study

There were problematic issues related to medications that were known prior to running this study. The first was regarding the type of antipsychotic administered to participants during the study period. This information was not recorded on the RAI. Consequently, the analyses did not take into account the differences regarding the class of antipsychotic medication participants

were taking (e.g. atypical versus typical), nor did they look at the differences between specific medications (e.g. risperidone versus quetiapine versus olanzapine). Second, the database contains no information on dosage, meaning that dosage effects could not be analyzed. Therefore, the use of antipsychotic medications was only analyzed with respect to indexes based on frequency of use per week within the specified period of time. In addition, the frequency of administration, was not recorded within the database.

Lastly, antipsychotic medications are also prescribed to older adults for reasons other than to help manage the behavioural symptoms of dementia. Older adults with schizophrenia (Jeste & Maglione, 2013), bipolar disorder (Dolder & Mckinsey, 2011), and cancer (Fisch & Kim, 2004) are regularly prescribed antipsychotic medications to help control symptoms related to the respective illnesses, which may confound the results in the current study if not taken into account. Rather than excluding participants with a diagnosis of any of these illnesses, as done in a previous study (Huybrechts, Gerhard, Crystal, Olfson, Avorn, Levin, Lucas & Schneeweiss, 2012), participants with these illnesses were controlled for within the multilevel modeling analyses in this study.

Purpose of Research

The purpose of this research study was threefold. First, this study aimed to explore the nature of demographics within CCC and LTC facilities, regarding issues such as health and behaviour. Second, detailed information on the use of antipsychotic medications in these facilities was sought, with specific reference to those participants using this class of medication who also a diagnosis of dementia or were exhibiting aggressive behaviour. It was hypothesized that based on preceding evidence, approximately 40% to 50% of residents in CCC or LTC

facilities would be receiving antipsychotic medications at any given time (CIHI, 2009; Ministry of Health, 2011).

It was also hypothesized that those participants receiving antipsychotic medications would be more likely to have a diagnosis of dementia and have a higher level of aggressive behaviours than those who are not. With that being said, it is estimated that those with severe cognitive impairment would be prescribed antipsychotic medications less frequently than those with moderate or no cognitive impairment due to the reduction of mental and physical abilities, including aggressive behaviour, commonly witnessed in these patients.

Lastly, this study aimed to identify the effects of antipsychotic medication use on mortality in those residing in CCC and LTC facilities. It is hypothesized that those participants receiving antipsychotic medications will have a higher rate of mortality than those who are not taking them, consistent with past research (Federal Drug Administration, 2005; Health Canada, 2005; Musicco et al., 2011). Banarjee (2009) adjusted a refinement of this hypothesis, which was tested in the present research, that there is a higher risk of mortality associated with longer durations of antipsychotic medication use.

Method

Participants

MDS 2.0 assessment data for all CCC and LTC facilities in Ontario were obtained from CIHI for the financial years 2010-2011 and 2011-2012. The data was census level for both CCC and LTC, with data collected quarterly, containing 102,658 participants in total. The composite data set also included linkages to mortality and other relevant entries in the DAD and NACRS datasets. These datasets were merged into one to include all participants age 65 and older that

had census level data for the time period analyzed. The primary analyses were on residents entering a facility during the time period encompassed by the study.

MDS 2.0 Indexes

The MDS is a system of standardized instruments that assess complex populations across various health and social service sectors, including CCC and LTC facilities (Hirdes, Mitchell, Maxwell & White, 2011). These instruments are widely used around the world including North America, Europe, Asia, the Middle East, South America, New Zealand, and Australia. The MDS has been continuously evaluated and refined through research to ensure and maintain high levels of reliability (Hirdes et al., 2008; Poss et al, 2008; Sgadari et al., 1997) and validity (Carpenter, 2006; Fries, Simon, Morris, Flodstrom & Bookstein, 2001; Morris, Jones, Fries & Hirdes, 2004) across care settings.

The current study included MDS 2.0 outcome measures and morbidity related variables, in addition to mortality data. Status and outcome scales are embedded within the MDS and can be used to evaluate a resident's current clinical status, and change in clinical status where longitudinal data is collected on a particular resident. Illness related variables, such as dementia, cognitive decline, aggression, and depression, were used to evaluate the effects that antipsychotics had on these symptoms. The variable related to the change in MDS scale scores indicated the difference in each score from the first assessment to last assessment, for the five MDS scales. Variables were selected for relevance as well as for known reliability and validity against gold standard measures. Additionally, some variables that are caused by antipsychotic medications, like falls, were not included in the analyses because they are already accounted for within the variables related to antipsychotic medications.

Outcome Measures

Activities of Daily Living (ADL) Scale. The ADL Scales (Short Form, Long Form, and Self-Performance Hierarchy) looked at the resident's ability to perform normal day to day activities, for example dressing, personal hygiene, toilet use, locomotion, transfer, bed mobility, and eating. The ADL scales assessed these activities according to the level of impairment faced by the resident, with ADLs that are lost early in disability, such as dressing, are given lower scores than those ADLs that are lost later in disability, such as eating. All the ADL scales have been shown to have good reliability and validity with positive predictive values between .6 and .7 and the long form achieving an alpha inter-consistency level exceeding .85 (Mor, Intrator, Unruh & Cai, 2011). The present study will use the hierarchy measure.

Aggressive Behaviour Scale (ABS). The ABS is a summary scale of four MDS items, including verbal abusive (e.g. screaming at others), physical abusive (e.g. hitting others), socially inappropriate or disruptive behaviour (e.g. throwing food), and resisting care (e.g. pushing caregiver during ADL assistance) (Perlman, & Hirdes, 2008). Aggressive behaviour is coded over seven days on ABS items, as not exhibited (0), behaviour occurred 1 to 3 days in the past 7 days (1), behaviour occurred 4 to 6 days in the past 7 days but less than daily (2), or behaviour occurred daily (3). Scores range from 0 to 12, with more frequent measured behaviours resulting in a higher score. Reliability for the ABS is good, with alphas of 0.79 and 0.93, and strong concurrent validity (correlation coefficient = 0.72, $P<.001$) when compared to the aggression subscale of the well validated Cohen-Mansfield Agitation Inventory (CMAI)(Perlman & Hirdes, 2008). Similar results were found in a more recent study comparing the ABS and CMAI ($p = 0.54$, $P = .004$), however, in this study, the ABS did not correlate with the Neuropsychiatric

Inventory-Nursing Home Edition (NPI) Agitation/aggression subscale (p = 0.10, P = .628) (Smart, Herrmann, & Lanctôt, 2011).

Changes in Health, End-Stage Disease and Symptoms and Signs Scale (CHESS). The CHESS scale predicts mortality and clinical instability, and identifies individuals at risk of serious health decline. The CHESS scale is a six point scale with 0 = not at all unstable to 5 = highly unstable, with higher scores being predictive of worse outcomes such as mortality, hospitalization, pain, caregiver stress, and poor self-rated health (Hirdes, Frijters & Teare, 2003). Symptoms measured on this scale included shortness of breath, edema, weight loss, leaving food uneaten, vomiting, dehydration, end-stage disease, decline in cognition, and decline in ADLs. The CHESS scale is a strong predictor of mortality (P <.001) independent of age, gender, ADL impairment, and cognition, in addition to being strongly associated with physician involvement, complex medical procedures, and pain (P <.001 for each) (Hirdes, Frijters & Teare, 2003). These results have been confirmed by a large scale study looking at the predictability of mortality in nursing home residents using the CHESS scale (Lee, Chau, Hui, Chan, & Woo, 2009). It was found that shorter survival was independently associated with more frail CHESS scale scores (HR = 1.150 per 1-unit increment, 95% CI 1.042-1.268, P = 0.005) in individuals after admission to a nursing home care facility.

Cognitive Performance Scale (CPS). The CPS is used to determine the cognitive status of residents in CCC and LTC facilities. It is based on five items: comatose, short-term memory, cognitive skills for daily decision making, expressive communication, and eating self performance. Scores range from 0 to 6, with 0 being intact cognitive functioning and 6 being very severe impairment. The CPS has been validated against the Mini Mental State Exam

(MMSE) and the Test for Severe Impairment (TSI), Eta2 = 0.75 for the MMSE and 0.80 for MMSE and TSI combined (Morris et al., 1994).

The diagnostic accuracy of the CPS has been shown to be similar to the MMSE in another study (Paquay, De Lepeleire, Schoenmakers, Ylieff, Fontaine, & Buntinx, 2007). The diagnostic values of a CPS score of two or more for the detection of cognitive impairment in this study were: sensitivity = 0.81, specificity = 0.80, PPV = 0.92, and NPV = 0.57. The diagnostic values of a MMSE score of less than or equal 23 in the same study were: sensitivity = 0.97, specificity = 0.59, PPV = 0.88, and NPV = 0.85. For CPS, the area under the receiver operating characteristic (ROC) curve was 0.87 (95% CI, 0.81–0.91), and not significantly different (p = 0.63) from the MMSE score, 0.88 (0.83–0.93. A recent study looking at the validity between the CPS and MMSE found similar results (p = -0.57, P = .003, sensitivity = 0.69, specificity = 0.70, PPV = 0.79, NPV = 0.58)(Smart, Herrmann, & Lanctôt, 2011). Inter-rater reliability is also good with the Spearman-Brown inter-rater reliability coefficients for the CPS items averaging .85 (Morris et al., 1994).

Depression Rating Scale (DRS). The DRS is used to measure symptoms of depression including: negative statements; persistent anger; expression of unrealistic fears; repetitive health complaints; repetitive anxious complaints; sad, pained, worried expression; and tearfulness. The scale is based on frequency of symptoms within the last seven days, with scores of 0 if symptoms are not present, 1 if present at least once in the last 30 days or up to 5 days a week, and 2 if present 6 or 7 days a week.

The DRS has been correlated with the Cornell Scale for Depression ($r = 0.69$, $P < 0.05$, sensitivity = 78%, specificity = 77%) and the Hamilton Depression Rating Scale ($r = 0.70$, $P < 0.05$, sensitivity = 94%, specificity = 72%)(Burrows, Morris, Simon, Hirdes & Phillips, 2000). In

addition, the DRS has been correlated to the NPI Depression subscale showing a significant correlation (p = 0.41, P = .040), and NPI total score (p = 0.42, P = .038), with a sensitivity = 0.44, a specificity = 0.71, a PPV = 0.80, and a NPV = 0.33 (Smart, Herrmann, & Lanctôt, 2011). When compared to the DSM-IV Geriatric Psychiatry Assessment, the DRS has shown sensitivity of 91% and specificity of 69% (Burrows et al., 2000). While the DRS has been significantly correlated to these scales, it has been found that the DRS may have difficulty detecting mild depressive symptoms in those with severe dementia (Smart, Herrmann, & Lanctôt, 2011). This has been suggested due to the difficulty this population can have with verbally communicating symptoms and the fact that 3 of 7 items on the DRS scale are related to speech.

Mortality Indicators

Mortality data was provided within the RAI, DAD and NACRS datasets.

Antipsychotic Medication Use

The MDS 2.0 records the frequency of usage per week during the preceding measurement period. Previous findings suggest that the vast majority of residents administered antipsychotics receive daily use (Stones, Stewart & Kirkpatrick, 2003).

Analyses

Descriptive statistics obtained for all the preceding measures include graphical and tabular trends. This included information related to the measures such as gender or age, type of facility resided in, and antipsychotic medication use. The main analyses made use of binomial logistic mixed modeling from the SPSS 2.0 generalized linear mixed model battery. The reasons for this form of analysis include (a) non-independence of observations from residents within the same facilities, (b) non-normal distributions for the dependent variables, and (c) capability to take account of missing data. Due to the dependence of observations within facilities, as shown

later on, and because of non-normal distributions, conventional types of tests such as t-tests, chi squares, and analyses of variance inappropriate.

The generalized linear mixed models were hierarchical, with mortality being the target variable. Initial models included demographics, such as age, gender, and type of facility (CCC, LTC), as covariates and time of measurement as a categorical variable (with the intake assessment as reference category). Subsequent models sequentially included MDS 2.0 outcome measures, diagnostic variables, change in MDS 2.0 outcomes over time, and antipsychotic medication use. All the models included facilities as a random intercepts (given that residents are grouped by facility) and measurement periods as random slopes. The random covariance matrices will be unstructured. All continuous variables were centred on grand means. Antipsychotic medication use was measured in two ways, based on change in use over time and percent of daily occurrences. The antipsychotic medication variable measuring change in use over time contained nine levels, based on the participant either using the medication every day, inconcsistently throughout the week (medically termed pro re nata)(PRN), or none at all. Antipsychotic medication use on initial assessment was then matched with use on the last assessment, for example everyday to everyday, everyday to PRN, everyday to none, and so on for PRN use and non use. The antipsychotic medication use variable related to percent of daily occurrences measured overall use based on the percent of participants who used these medications everyday, as a PRN, or none at all.

Results

Descriptives

This section describes the trends for variables in this study through distributions. It does not include inferential statistics because of the possibility of correlated error within facilities.

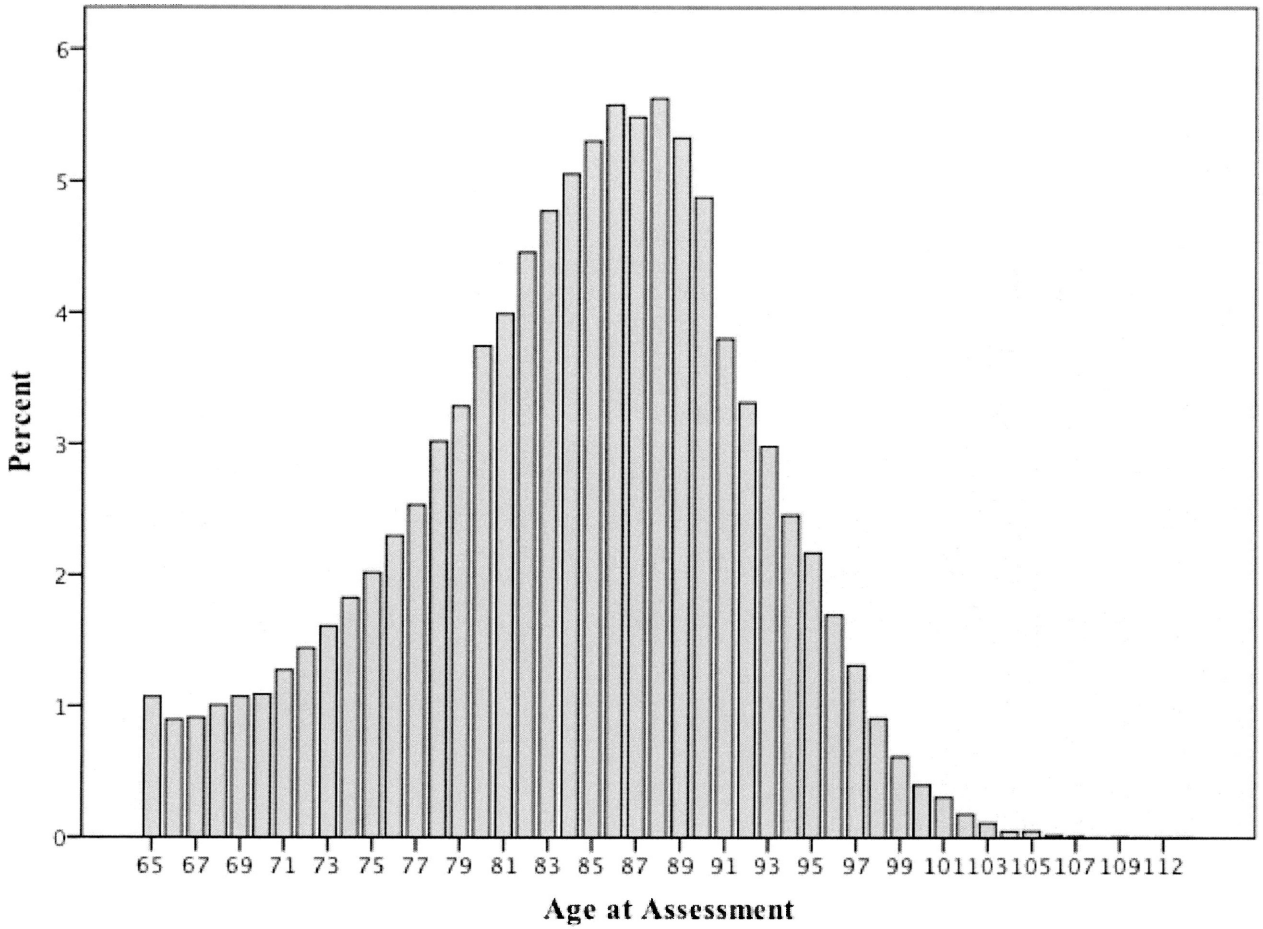
Participants. There were 102,658 participants included in this study over the two years of data collection.

Gender. There were three gender categories included in this study, based on the information contained on the MDS assessments: male, female, and other. Females made up 69.1% (N = 70,961) of participants, while 30.8% (N = 31,628) were males, and 0.1% (N = 69) were classified as 'other'. It is believed that the classification of 'other' may have been used when a gender was not specified, or if the person identified as transgendered or was clinically a hermaphrodite. Omitting the 'other' gender variable would have been inappropriate due to its consistent usage within the data. In addition, the number of individuals classified as 'other' (N = 69) was large enough to have adequate findings.

Age. Due to the nature of the study, participants included in the analyses were 65 years of age and older. The average age of participants was 84.2 years (SD = 7.72), ranging from 65 to 114 years (median = 85.0, mode = 88.0)(Figure 1). Due to the wide distribution of age and potential differences related to older versus younger participants, such as normal variations in health, physical abilities and behaviour, three age categories were created to facilitate descriptive depiction: 65-79 (N = 26057, 25.4%), 80-89 (N = 50654, 49.3%), and 90-114 (N = 25947, 25.3%) years. Categories were created to have a normal curve, with roughly 25 percent of participants falling into the first group, 50 percent into the second, and 25 percent in the third.

Figure 1.

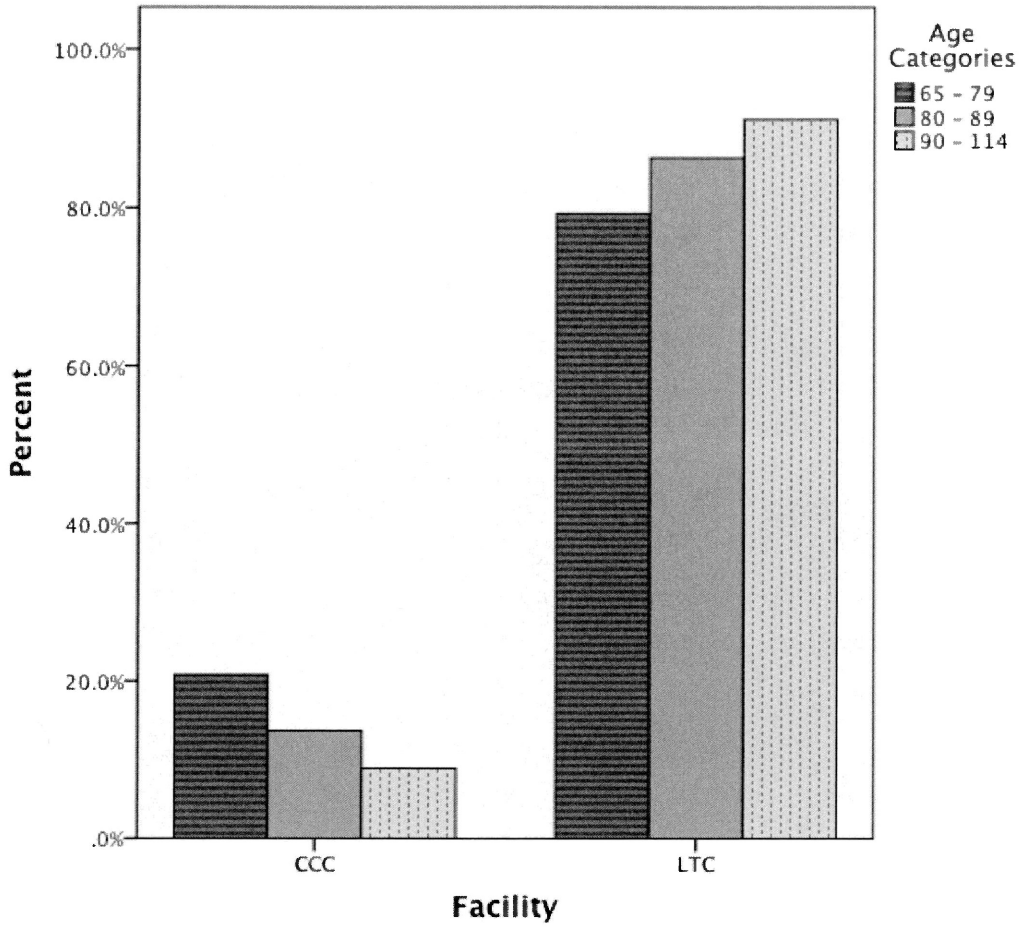
Age distribution at first assessment



Facilities. A higher proportion of participants resided in the 668 LTC facilities (85.7%) than in the 92 CCC facilities (14.3%) during the course of this study. Within these facilities, 12.1% (N = 8570) of female participants resided in CCCs, as did 19.2% (N = 6069) of males, and 11.6% (N = 8) of participants classified as 'other'. Younger participants were more likely to reside in CCC facilities, while older adults were more likely to reside in LTC facilities (Figure 2).

Figure 2

Age distribution in CCC and LTC facilities



Observations. The MDS 2.0 assessment is given to all LTC and CCC residents within 14 days of initial admission to the care facility. Subsequently, the MDS 2.0 is re-administered on a quarterly basis, or within 14 days of transferring to a new facility. Of the 102,658 participants in this study, the MDS 2.0 was administered an average of 5.83 times per participant, with a range of 1-18 times (SD = 2.878)(Table 1).

Table 1

Frequency of Observations

Observations	Frequency	
1	14177	(13.8%)
2	7574	(7.4%)
3	6246	(6.1%)
4	5542	(5.4%)
5	7063	(6.9%)
6	7301	(7.1%)
7	7219	(7.0%)
8	32059	(31.2%)
9	13526	(13.2%)
10	1692	(1.6%)
11	186	(.2%)
12	51	(.0%)
13	9	(.0%)
14	4	(.0%)
15	2	(.0%)
16	3	(.0%)
17	3	(.0%)
18	1	(.0%)
Total	102658	(100.0%)

MDS 2.0 Summary Scales

Activities of Daily Living Scale (ADL). Only 7.3% of participants in this study did not need any support with their activities of daily living (range = 0-6)(Table 2). Over half of the participants (53.1%) required a moderate or higher level of support. The distribution of scores on this scale was negatively skewed, with a greater number of participants requiring a higher level of support with their activities of daily living (Figure 3).

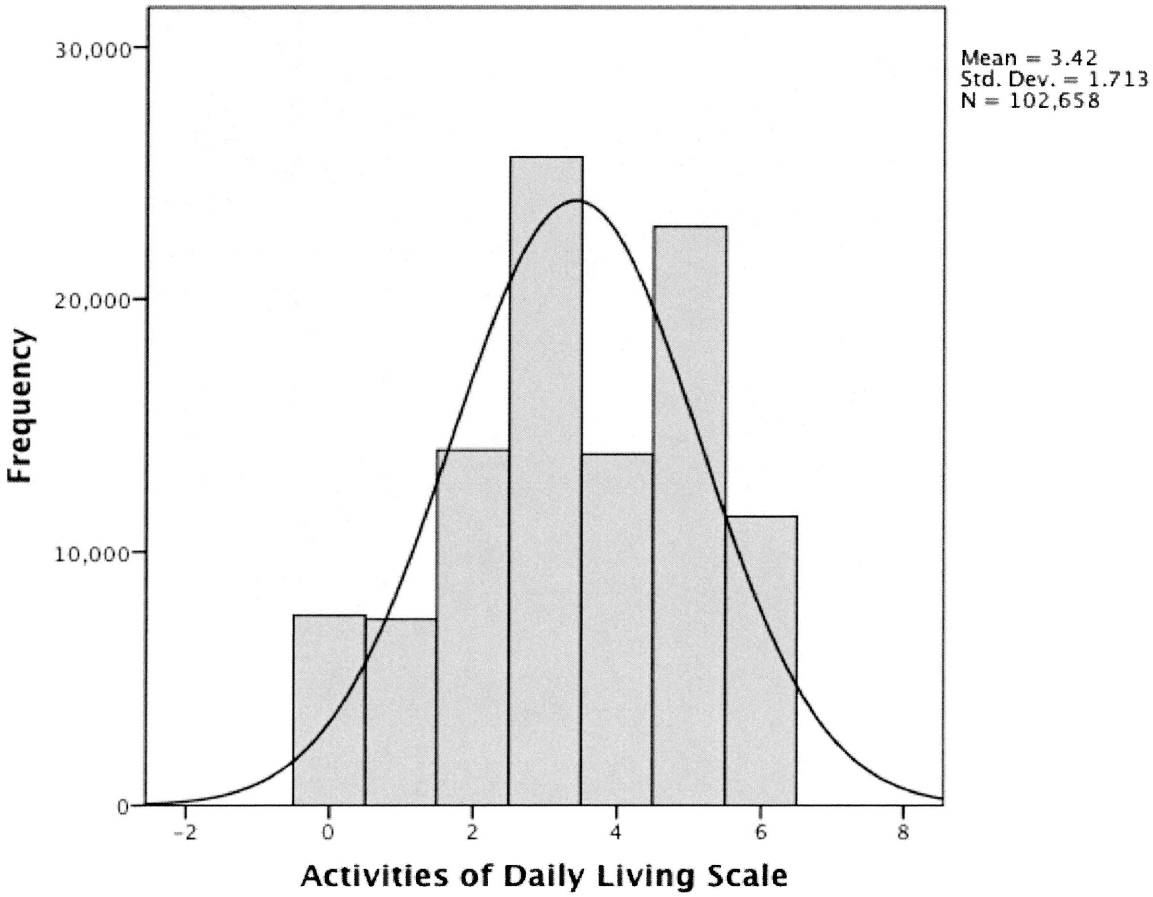
Table 2

Activities of Daily Living scores

Scale Score	Frequency	
0	7495	(7.3%)
1	7340	(7.1%)
2	14027	(13.7%)
3	25648	(25.0%)
4	13861	(13.5%)
5	22879	(22.3%)
6	11408	(11.1%)
Total	102658	(100.0%)

Figure 3

Distribution of Activities of Daily Living scores



Aggressive Behaviour Scale (ABS). For 59.8% of individuals in this study, no ABS items were endorsed. A total of 90.1% of participants received an ABS score of 4 or less, which is within the mild to moderate categories of aggressive behaviour (range = 0-12)(Table 3). Only 9.9% of people received a score of 5 or more, indicating severe aggression (Figure 4). When looking at the differences in participants with and without dementia, those who were diagnosed with dementia (Table 4) were much more likely to display aggressive behaviour than those who were not (Table 5). Only 41.8% of individuals diagnosed with dementia displayed no aggressive behaviour, compared to 70.4% of those without this diagnosis. Furthermore, only 83.6% of people with dementia received a score on the ABS of 4 or less, compared to 95.7% of those without dementia.

Table 3

Aggressive Behaviour Scale scores

Scale Score	Frequency	
0	61290	(59.7%)
1	10565	(10.3%)
2	7944	(7.7%)
3	8834	(8.6%)
4	3773	(3.7%)
5	2468	(2.4%)
6	2760	(2.7%)
7	1285	(1.3%)
8	1097	(1.1%)
9	1042	(1.0%)
10	437	(.4%)
11	290	(.3%)
12	749	(.7%)
Total	102534	(99.9%)

Figure 4

Distribution of Aggressive Behaviour Scale scores

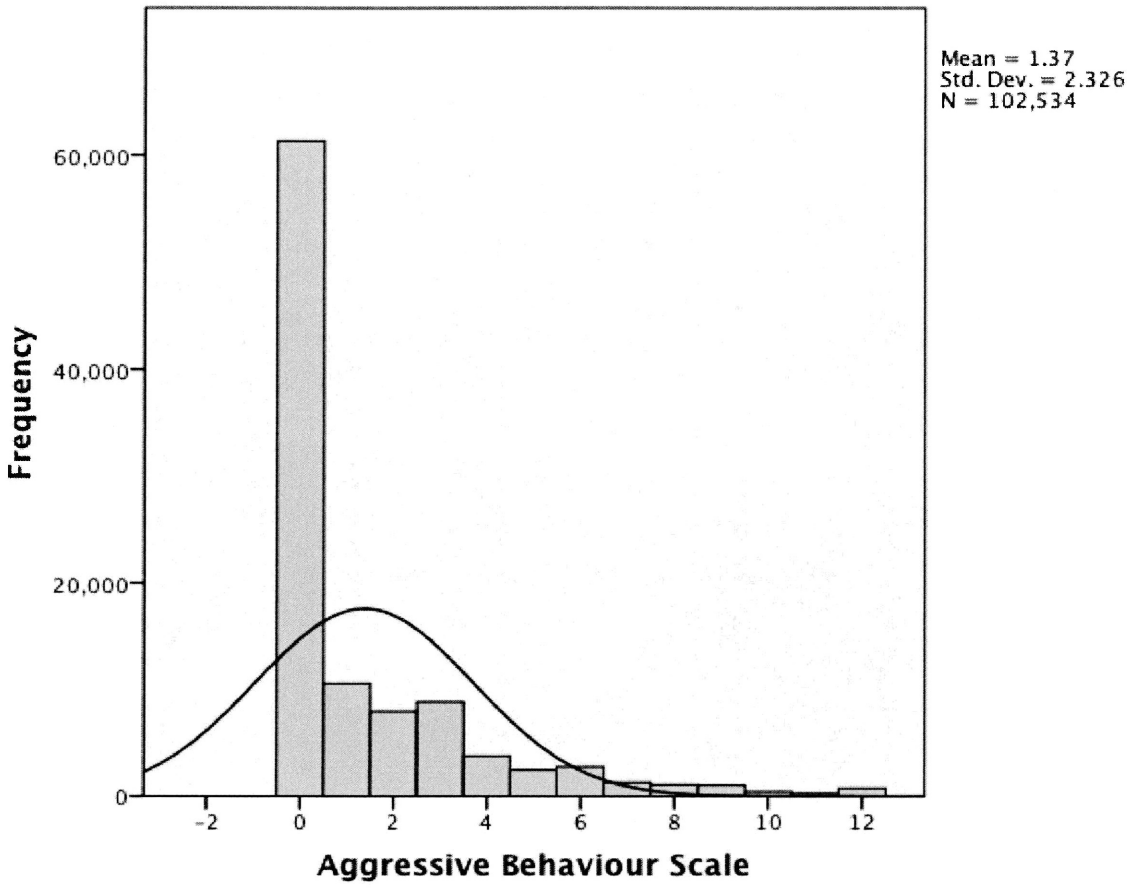


Table 4

Aggressive Behaviour Scale scores with dementia

Score	Frequency	
0	25105	(41.7)
1	7260	(12.1)
2	6599	(11.0)
3	7747	(12.9)
4	3513	(5.8)
5	2347	(3.9)
6	2680	(4.5)
7	1274	(2.1)
8	1041	(1.7)
9	1123	(1.9)
10	460	(.8)
11	279	(.5)
12	668	(1.1)
Total	60096	(99.9)
Missing	60	(.1)
Total	60156	(100.0)

Table 5

Aggressive Behaviour scale scores without dementia

Score	Frequency	
0	29865	70.3
1	4323	10.2
2	2873	6.8
3	2506	5.9
4	1014	2.4
5	553	1.3
6	537	1.3
7	247	.6
8	171	.4
9	163	.4
10	54	.1
11	33	.1
12	77	.2
Total	42416	99.8
Missing	64	.2
Total	42480	100.0

Changes in Health, End-Stage Disease and Symptoms and Signs (CHESS) Scale.

The majority of participants in this study, 44.7%, obtained a score of zero on the CHESS scale, indicating 'no health instability'(range = 0-5)(Table 6). A total of 90.4% of people received a score of 2 or less, indicating 'low health instability', while the remaining 9.6% received a score of 3 to 5, indicating a range from 'moderate' to 'very high' health instability (Figure 5).

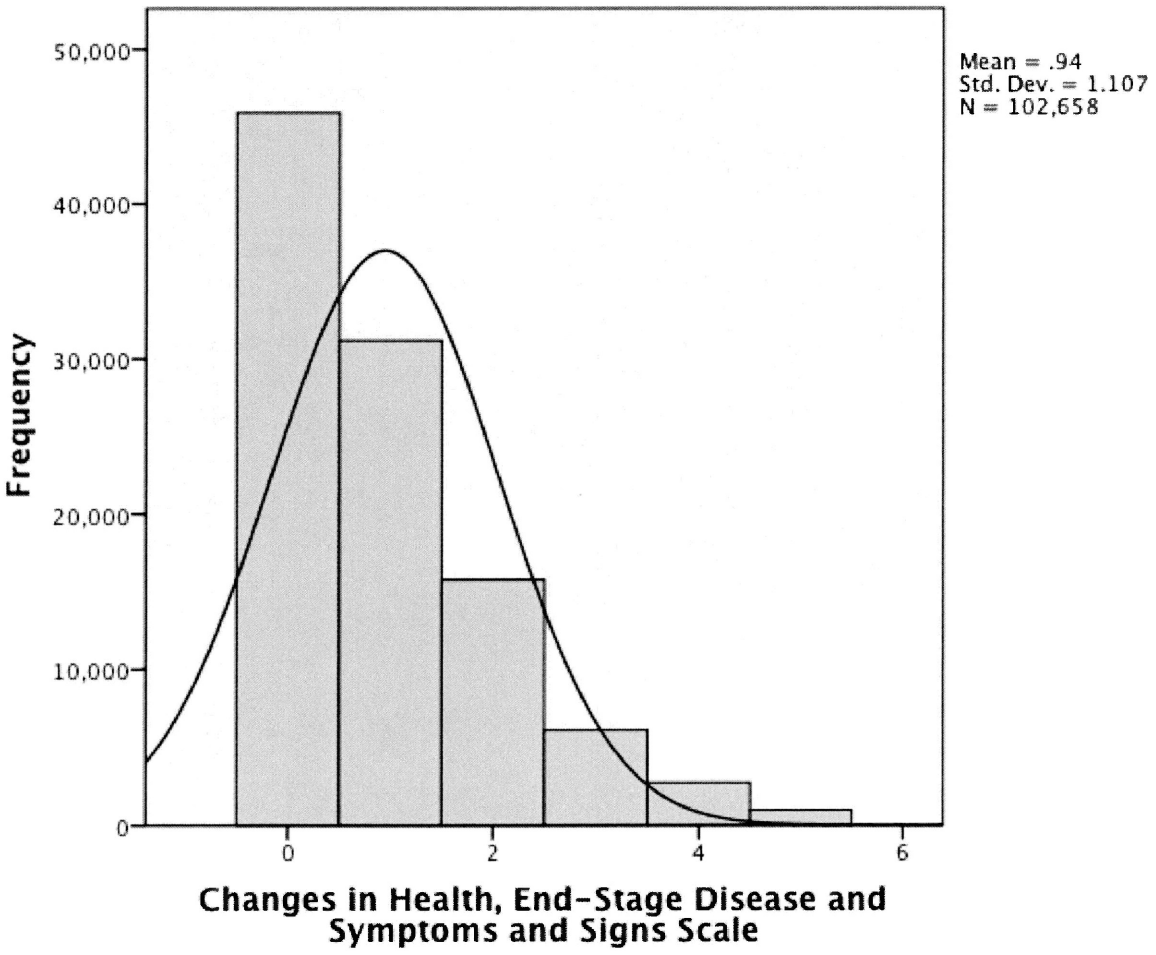
Table 6

Changes in Health, End-Stage Disease and Symptoms and Signs Scale Scores

Scale Scores	Frequency	
0	45899	(44.7)
1	31190	(30.4)
2	15764	(15.4)
3	6104	(5.9)
4	2728	(2.7)
5	973	(.9)
Total	102658	(100.0)

Figure 5

Distribution of CHESS scale scores



Cognitive Performance Scale (CPS). Only 16.7% of participants in this study had a score of zero on the CPS, indicating 'intact' cognitive abilities (Table 7). Just under half of people, 46.0%, received scores within the 'mild' cognitive impairment range or less (scores 0 – 2) (Figure 6). In contrast, 54% of participants were classified in the 'moderate' to 'very severe' range of cognitive impairment (scores 3 – 6).

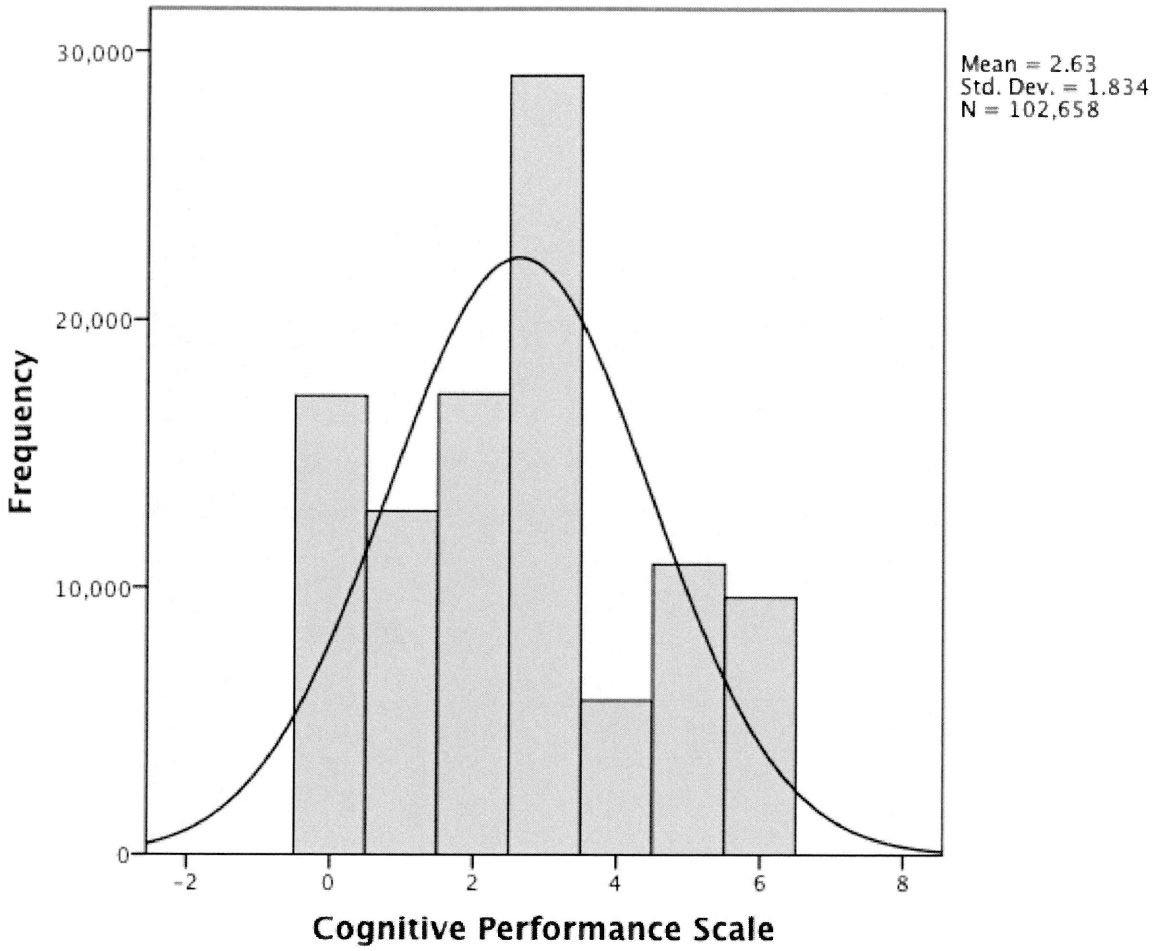
Table 7

Cognitive Performance Scale scores

Scale Scores	Frequency	
0	17169	(16.7)
1	12861	(12.5)
2	17238	(16.8)
3	29097	(28.3)
4	5775	(5.6)
5	10880	(10.6)
6	9638	(9.4)
Total	102658	(100.0)

Figure 6

Distribution of Cognitive Performance Scale scores



Depression Rating Scale (DRS). Of the participants included in this study, 66.7% obtained a score of 0 – 2, indicating no significant level of depression (range = 0-14)(Table 8). The subsequent 33.3% of participants had a score of 3 – 14 which indicates minor to major depressive disorders (Figure 7). There was no substantial difference between depression rates in those with (Table 9) or without a diagnosis of dementia (Table 10). A graph is included to visually show the difference depression rates for those with and without (Figure 8).

Table 8

Depression Rating Scale scores

Scale Scores	Frequency	
0	33523	(32.7)
1	16544	(16.1)
2	18280	(17.8)
3	10018	(9.8)
4	8731	(8.5)
5	4872	(4.7)
6	4060	(4.0)
7	2315	(2.3)
8	1778	(1.7)
9	943	(.9)
10	735	(.7)
11	321	(.3)
12	263	(.3)
13	85	(.1)
14	66	(.1)
Total	102534	(99.9)
Missing	124	(.1)
Total	102658	(100.0)

Table 9

Depression Rating Scale scores with dementia

Scale Scores	Frequency	
0	17029	(28.3)
1	9997	(16.6)
2	11796	(19.6)
3	6229	(10.4)
4	5457	(9.1)
5	3034	(5.0)
6	2467	(4.1)
7	1462	(2.4)
8	1120	(1.9)
9	612	(1.0)
10	433	(.7)
11	212	(.4)
12	163	(.3)
13	50	(.1)
14	35	(.1)
Total	60096	(99.9)
Missing	60	(.1)
Total	60156	(100.0)

Table 10

Depression Rating Scale scores without dementia

Scale Scores	Frequency	
0	16485	38.8
1	6545	15.4
2	6480	15.3
3	3787	8.9
4	3271	7.7
5	1837	4.3
6	1593	3.8
7	853	2.0
8	658	1.5
9	331	.8
10	302	.7
11	109	.3
12	100	.2
13	35	.1
14	30	.1
Total	42416	99.8
Missing	64	.2
Total	42480	100.0

Figure 7

Distribution of Depression Rating Scale scores

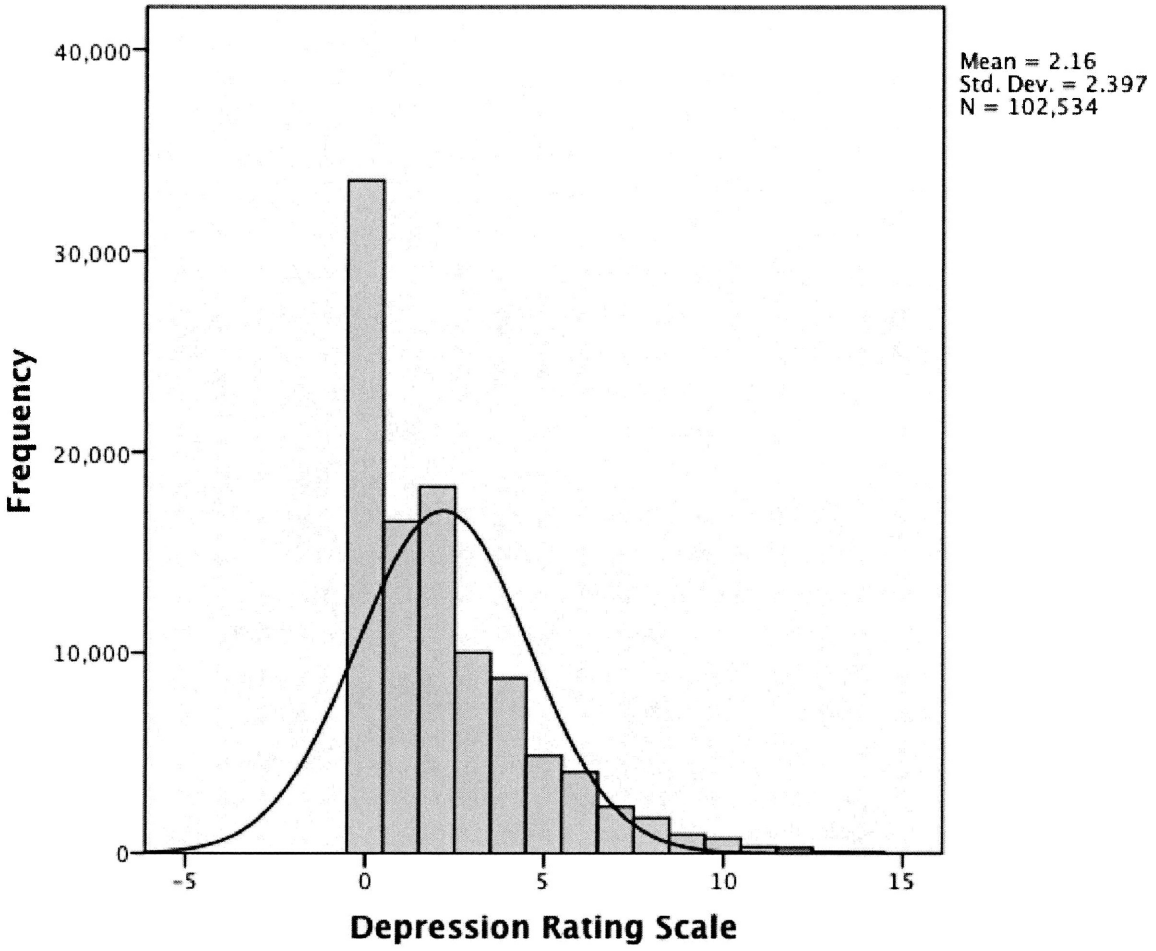
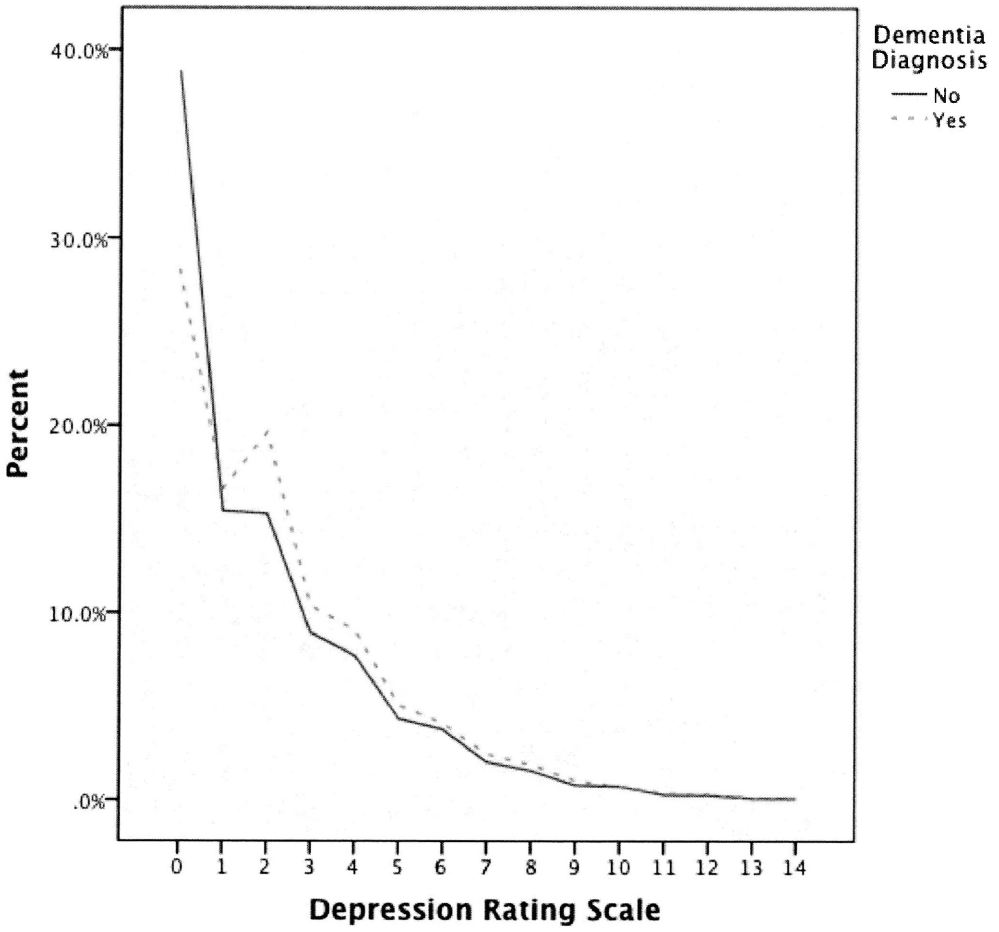


Figure 8

Depression Rating Scale scores and dementia



Antipsychotic Medication Use

Participants. Of the 102,658 participants included in this study, 31,803 (31%) people were on an antipsychotic medication at least once per week, with the majority of those (29.2%) receiving these medications 7 days per week (Table 11).

Table 11

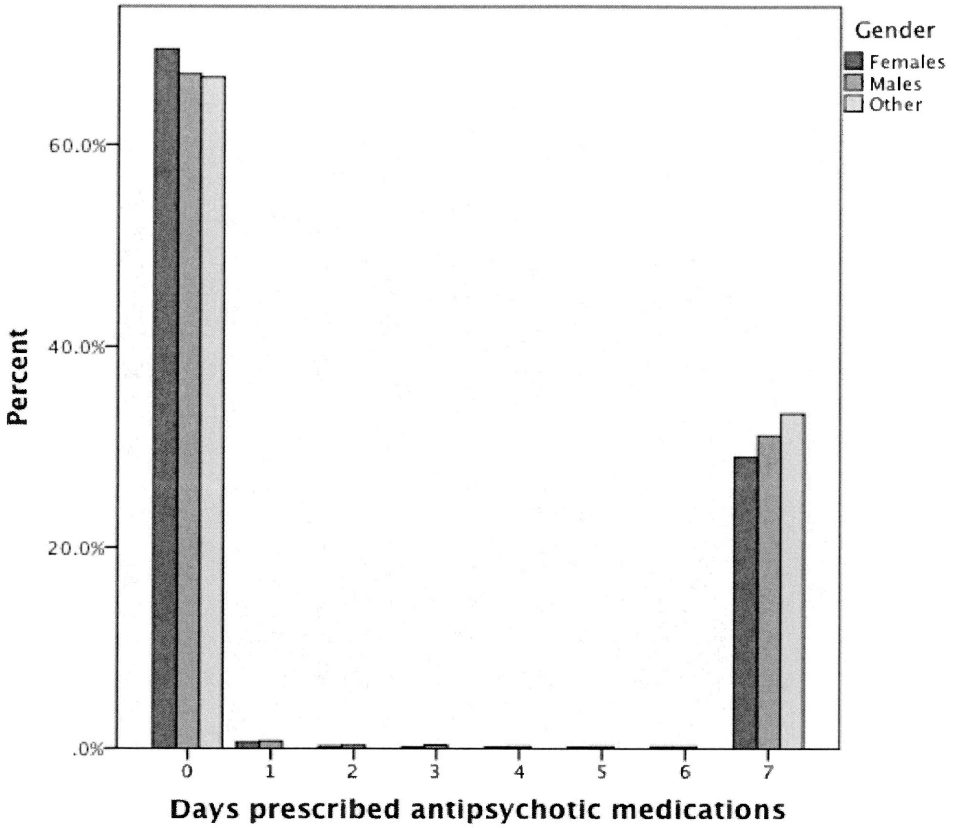
Weekly administration rate of antipsychotic medications

Observations	Frequency	
0	70855	(69.0)
1	530	(.5)
2	293	(.3)
3	259	(.3)
4	221	(.2)
5	220	(.2)
6	271	(.3)
7	30009	(29.2)
Total	102658	(100.0)

Gender. Males were prescribed antipsychotic medications more than females, with 31.1% of males receiving these medications seven days a week, while the same can be said for 29.0% of females (Figure 9). Consistent with this finding, 69.4% of females did not take antipsychotic medications compared to 67.0% of males. Those participants whose gender was classified as 'other' had the highest rate of antipsychotic medication use, with 33.0% of these participants taking them seven days a week.

Figure 9

Gender differences in antipsychotic medication use



Age. Younger people were more likely to be prescribed antipsychotic medications, than those in the older age categories (65-79 = 34.5%; 80-89 = 29.8%; 90-114 = 22.9%) (Table 12). This observation is also most prevalent when looking at those participants who were prescribed an antipsychotic medication for either 0 or 7 days out of the week. Gender differences in the rate of antipsychotic medication use are also shown to diminish with age (Figure 10).

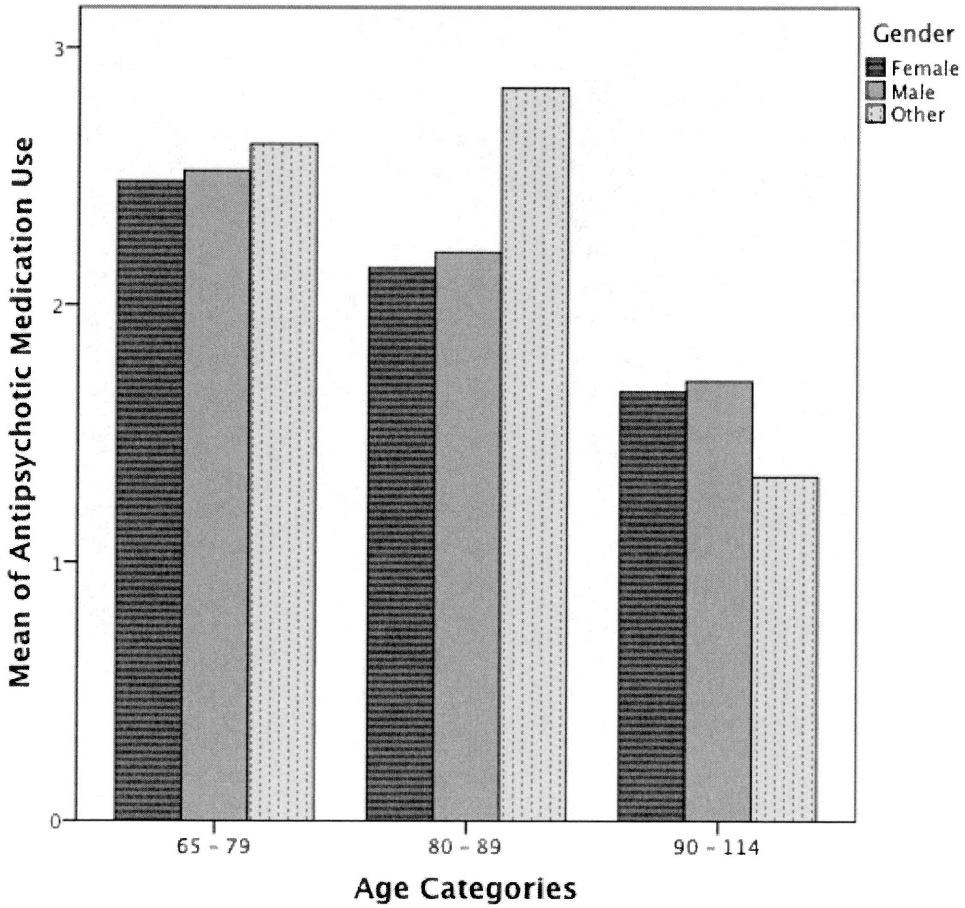
Table 12

Within age group percentages for antipsychotic medication use

Days taking Antipsychotics	Age Categories 65-79		80-89		90-114		Total	
0	16627	(63.8%)	34704	(68.5%)	19524	(75.2%)	70855	(69.0%)
1	157	(0.6%)	234	(0.5%)	139	(0.5%)	530	(0.5%)
2	59	(0.2%)	150	(0.3%)	84	(0.3%)	293	(0.3%)
3	79	(0.3%)	116	(0.2%)	64	(0.2%)	259	(0.3%)
4	47	(0.2%)	114	(0.2%)	60	(0.2%)	221	(0.2%)
5	43	(0.2%)	120	(0.2%)	57	(0.2%)	220	(0.2%)
6	57	(0.2%)	135	(0.3%)	79	(0.3%)	271	(0.3%)
7	8988	(34.5%)	15081	(29.8%)	5940	(22.9%)	30009	(29.2%)
Total	26057	(100%)	50654	(100%)	25947	(100%)	102658	(100%)

Figure 10

Age and gender relationship with antipsychotic medication use



Facility. Participants residing in LTC facilities (31.0%) were more likely to be prescribed antipsychotic medications seven days a week than those living in CCC (18.7%) facilities (Table 13). This was true for both males and females; however, there was a reduction in antipsychotic medication use for those with a gender classified as 'other' (Figure 11).

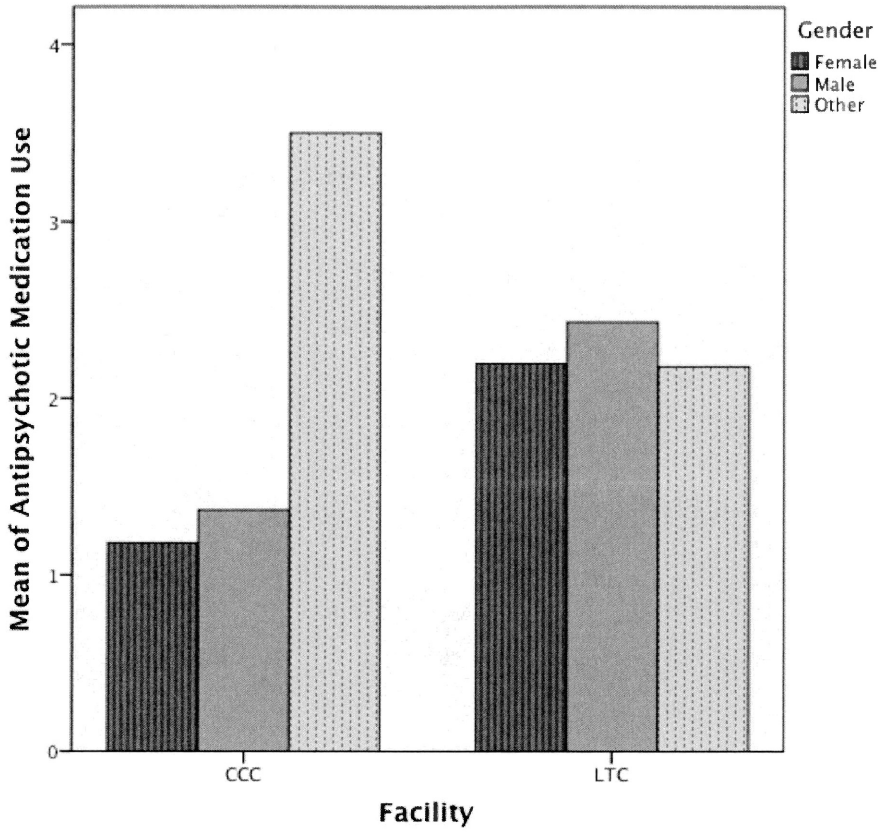
Table 13

Within facility percentages for antipsychotic medication use

Days taking Antipsychotics	Facility Type CCC		LTC		Total	
0	11512	(78.6%)	59343	(67.4%)	70855	(69.0%)
1	135	(0.9%)	395	(0.4%)	530	(0.5%)
2	75	(0.5%)	218	(0.2%)	293	(0.3%)
3	73	(0.5%)	186	(0.2%)	259	(0.3%)
4	41	(0.3%)	180	(0.2%)	221	(0.2%)
5	37	(0.3%)	183	(0.2%)	220	(0.2%)
6	36	(0.2%)	235	(0.3%)	271	(0.3%)
7	2738	(18.7%)	27271	(31.0%)	30009	(29.2%)
Total	14647	(100%)	88011	(100%)	102658	(100%)

Figure 11

Facility and gender relationship with antipsychotic medication use



Dementia. Participants with dementia were far more likely to be prescribed antipsychotic medications than the general participant population. A total of 37.7% of participants with dementia were taking antipsychotic medications seven days a week (Table 14), compared to only 17.2% of those participants without a diagnosis of dementia (Table 15). Of participants who were taking antipsychotic medications, those with a diagnosis of dementia were over twice as likely to be taking these medications inconsistently throughout the week (Table 16).

Table 14

Antipsychotic medication use for participants with dementia

Days taking Antipsychotics	Frequency	
0	36236	(60.2%)
1	323	(0.5%)
2	198	(0.3%)
3	181	(0.3%)
4	151	(0.3%)
5	169	(0.3%)
6	212	(0.4%)
7	22686	(37.7%)
Total	60156	(100%)

Table 15

Antipsychotic medication use for participants without dementia

Days taking Antipsychotics	Frequency	
0	34606	(81.5%)
1	207	(0.5%)
2	95	(0.2%)
3	78	(0.2%)
4	70	(0.2%)
5	51	(0.1%)
6	59	(0.1%)
7	7314	(17.2%)
Total	42480	(100%)

Table 16

Dementia and antipsychotic medication use

Days taking Antipsychotics	Dementia Diagnosis No		Yes		Total	
0 Days	34606	(48.8%)	36236	(51.2%)	70842	(100%)
1 – 6 Days	560	(31.2%)	1234	(68.8%)	1794	(100%)
7 Days	7314	(0.2%)	22686	(75.6%)	30000	(100%)

When looking at cognitive impairment using the CPS scores, regardless of a diagnosis of dementia, it was found that 74.1% of individuals with moderate to severe cognitive impairment were taking antipsychotic medications at least once a week, compared to only 14.5% with mild impairment, with 69.6% taking them 7 days a week (Table 17). Results also show that of all the people taking antipsychotic medications in this study 7 days a week, 89.1% were classified as having moderate to severe cognitive impairment.

Table 17

Cognitive impairment and antipsychotic medication use

Days taking Antipsychotics	Cognitive Impairment Mild		Moderate		Severe	
0 Days	20355	(85.5%)	34241	(66.3%)	16259	(59.7%)
1 – 6 Days	167	(0.7%)	872	(1.7%)	755	(2.8%)
7 Days	3278	(13.8%)	16494	(32.0%)	30000	(37.6%)
Total	23800	(100%)	51607	(100%)	27251	(100%)

Aggressive behaviour. Aggressive behaviour was analyzed using ABS scores, distributing them between mild, moderate, and severe categories. It was shown that 60.1% of participants with severe aggression took antipsychotic medications 7 days a week, as did 50% of those with moderate aggression, and 25% of those with mild aggression (Table 18). Only 35.7%

of participants with severe aggression did not take any form of antipsychotic medication.

Table 18

Level of aggression and antipsychotic medication use

Days taking Antipsychotics	Level of Aggression					
	Mild		Moderate		Severe	
0 Days	63464	(73.5%)	6271	(46.9%)	1019	(35.7%)
1 – 6 Days	1241	(1.4%)	425	(3.2%)	120	(4.2%)
7 Days	21591	(25.0%)	6684	(50.0%)	1719	(29.3%)
Total	86296	(100%)	13380	(100%)	2858	(100%)

Mortality

Of the 102,658 participants in this study, 32.2% (N = 33,071) died during the data collection period. Those classified with a gender of 'other' had the highest rate of death during the study at 39.1%, followed by males, 35.3%, and then females, 30.8% (Table 19).

Table 19

Rate of overall death based on gender

Survival	Gender					
	Female		Male		Other	
Alive	49088	(69.2%)	20457	(64.7%)	42	(67.8%)
Deceased	21873	(30.8%)	11171	(35.3%)	27	(32.2%)
Total	70961	(100%)	31628	(100%)	69	(100%)

Substantially more people died in CCC facilities (43.8%) during this study, than in LTC facilities (30.8%)(Table 20). There was a small difference in rate of death during this study between those with (33.6%) and without (30.3%) a diagnosis of dementia (Table 21).

Table 20

Rate of overall death based on facility

Survival	Facility			
	CCC		LTC	
Alive	6097	(56.2%)	63490	(69.2%)
Deceased	4748	(43.8%)	28323	(30.8%)
Total	10845	(100%)	91813	(100%)

Table 21

Rate of overall death for participants with and without dementia

Survival	Dementia Diagnosis				Total	
	No		Yes			
Alive	29608	(69.7%)	39973	(66.4%)	69581	(67.8%)
Deceased	12872	(30.3%)	20183	(33.6%)	33055	(32.2%)

When looking at participant deaths in relation to antipsychotic medication use, there was a large difference in death rate based on the frequency of dispensation of these medications within a one week period (Table 22). Participants who took these medications inconsistently throughout the week (1 – 6 times per week) had a higher rate of death (61.2%) than those participants who were not on this type of medication at all (32.2), while participants who were taking antipsychotic medications seven days a week were the least likely to die (30.4%)(Figure 12). This pattern was the same for those with (Table 23) and without (Table 24) dementia.

Table 22

Rate of overall death based on frequency of antipsychotic use

Days taking Antipsychotics	Died			
	No		Yes	
0	48011	(67.8%)	22844	(32.2%)
1	247	(46.6%)	283	(53.4%)
2	118	(40.3%)	175	(59.7%)
3	89	(34.4%)	170	(65.6%)
4	67	(30.3%)	154	(69.7%)
5	71	(32.3%)	149	(67.7%)
6	104	(38.4%)	167	(61.6%)
7	20880	(69.6%)	9129	(30.4%)
Total	69587	(67.8%)	33071	(32.2%)

Figure 12

Rate of death based on antipsychotic dispensation categories

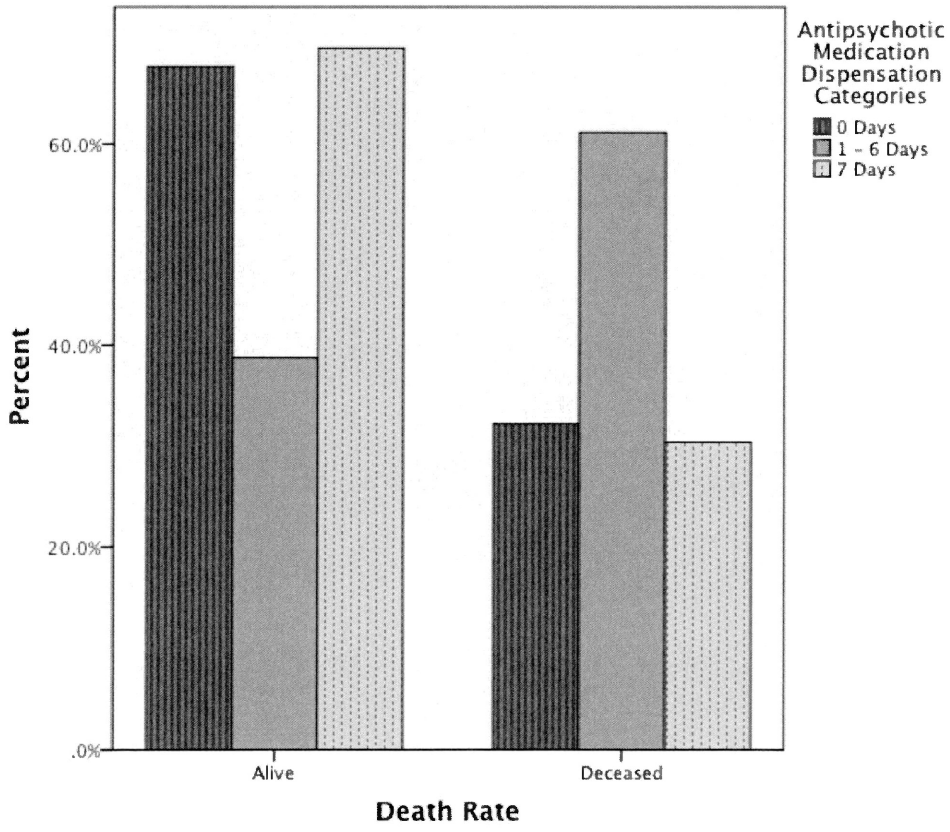


Table 23

Rate of death for those using antipsychotic medications with dementia

Days taking Antipsychotics	Died: No		Yes		Total	
0 Days	23793	(65.7%)	12443	(34.3%)	36236	(100.0%)
1 – 6 Days	503	(40.8%)	731	(59.2%)	1234	(100.0%)
7 Days	15677	(69.1%)	7009	(30.9%)	22686	(100.0%)

Table 24

Rate of death for those using antipsychotic medications without dementia

Days taking Antipsychotics	Died: No		Yes		Total	
0 Days	24214	(70.0%)	10392	(30.0%)	34606	(100.0%)
1 – 6 Days	193	(34.5%)	367	(65.5%)	560	(100.0%)
7 Days	5201	(71.1%)	2113	(28.9%)	7314	(100.0%)

Generalized Linear Mixed Modeling. Generalized linear mixed modeling was used to explore the relationship between the use of antipsychotic medications and overall death within different contexts. Initially, a series of six models were developed to serve as the foundation to explore these relationships, which were then manipulated depending on the context that was being explored. Eight contexts were explored using these models providing a thorough examination of the relationship between antipsychotic medications and death within this data set. To aid in clarity, only the final complete model will be reported for these eight contexts.

GLMM set one – All participants. The preliminary series of six models were developed to build on one another. All models used the facilities participants resided in as a random variable, due to the similarities found when people live in the same residence (e.g. same staff, nutritional/recreational options, medication protocols). Sector (LTC or CCC) was used as a

fixed variable. The death related variable, died, was entered as the target dependent variable. The distribution for the dependent variable in this series of models was interval censored survival, which uses a binomial distribution with a complementary log-log link. This type of distribution has been shown to be useful in survival analyses, such as the ones in the current study, when some participants do not die during the study period (Douglas & Homan, 1998). All continuous variables used within the models in this study were centred on their grand means, in order to give results consistent meaning.

The first set one model, the null model, was run using the information above, with no added fixed effects. The purpose of this model was to provide a base measure for all subsequent models. All participants were included in this model. It was found that the overall correct classification for this model was 68.1%. The random variable of facility had a significant effect on the death rate (Wald $Z = 14.610$, $p < .001$)(Table 25).

Table 25

GLMM set one – null model intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.097	.007	14.610	.000	.085	.111

The next model, Model 2, was built using the null model as a foundation while also including demographic information on participants. Overall correct classification went up to 68.9% (Wald Z = 14.401, $p < .001$)(Table 26). Demographic variables included participants' age at assessment, gender, and whether they resided in a LTC or CCC facility. This model showed that older individuals had a greater chance of dying, as did those living in CCC (Table 27).

Males had a higher death rate than females as did participants who had a gender classified as 'other'.

Table 26

GLMM set one – model 2 intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.092	.006	14.401	.000	.081	.106

Table 27

GLMM set one – model 2

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence Lower	Upper
Intercept	-.840	.0364	-23.059	.000	-.911	-.768
Age	.045	.0008	56.773	.000	.044	.047
Gender - Other	.326	.1987	1.643	.100	-.063	.716
Gender - Male	.279	.0122	22.837	.000	.255	.303
Gender - Female	0	.	.	.	.	.
CCC	-.250	.0387	-6.457	.000	-.326	-.174
LTC	0	.	.	.	.	.

Model 3 was then built to include the variables in model 2, with the addition of the MDS Summary Scales as fixed effects. These five scales, ABS, ADL, CPS, CHESS, and DRS, increased the overall correct classification to 72.4% (Wald Z = 14.244, $p < .001$)(Table 28). Results from this model showed that participants who had higher scores on these scales (had more/worse symptoms), except for the ABS, had a higher rate of death than those who did not (Table 29). Unlike the other MDS scales, ABS score was found not to be related to rate of death. In addition, when the MDS Summary Scales are added to the model, the difference in death rate between those living in LTC and CCC loses significance ($p > .05$) (Table 29).

Table 28

GLMM set one – model 3 intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.095	.007	14.244	.000	.082	.109

Table 29

GLMM set one – model 3

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence Lower	Upper
Intercept	-1.222	.0380	-32.182	.000	-1.296	-1.148
Age	.041	.0008	51.348	.000	.040	.043
Gender – Other	.334	.2057	1.622	.105	-.070	.737
Gender – Male	.351	.0126	27.883	.000	.327	.376
Gender – Female	0	.	.	.	.	.
CCC	.075	.0402	1.875	.061	-.003	.154
LTC	0	.	.	.	.	.
ADL Scale	.206	.0044	46.702	.000	.197	.215
ABS Scale	.000	.0027	.130	.896	-.005	.006
CHESS Scale	.269	.0054	49.771	.000	.258	.280
CPS Scale	.066	.0038	17.193	.000	.058	.073
DRS Scale	.021	.0027	7.507	.000	.015	.026

The next model, model 4, was built by adding diagnostic variables as additional fixed effects. These variables related to manic depression, schizophrenia, cancer, and dementia increased the overall correct classification to 72.7% (Wald Z = 14.154, $p < .001$)(Table 30). Surprisingly, this model indicated that those participants who had a diagnosis of manic depression, schizophrenia, or dementia had lower rates of death than those participants without

such a diagnosis[1] (Table 31). Those with a diagnosis of cancer had a higher rate of death than those participants without this diagnosis. When the diagnostic variables were added to the model, the difference in death rate for participants residing in LTC or CCC returned, with those living in CCC facilities having an increased risk for death ($p < .01$).

Table 30

GLMM set one – model 4 intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.094	.007	14.154	.000	.081	.107

[1] It is possible that the lower death rate for dementia may be due to shared variance with the CPS. Analysis that omitted the CPS as a fixed effect showed a significantly higher death rate for residents with dementia ($p < .05$).

Table 31

GLMM set one – model 4

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence Lower	Upper
Intercept	-1.266	.0385	-32.871	.000	-1.342	-1.191
Age	.041	.0008	50.503	.000	.039	.043
Gender – Other	.358	.2078	1.724	.085	-.049	.766
Gender – Male	.314	.0127	24.763	.000	.289	.339
Gender – Female	0	.	.	.	.	.
CCC	.139	.0402	3.464	.001	.060	.218
LTC	0	.	.	.	.	.
ADL Scale	.201	.0044	45.239	.000	.193	.210
ABS Scale	.004	.0027	1.489	.136	-.001	.009
CHESS Scale	.253	.0055	46.388	.000	.242	.264
CPS Scale	.084	.0043	19.765	.000	.076	.092
DRS Scale	.021	.0027	7.539	.000	.015	.026
Manic Depression Yes	-.146	.0517	-2.830	.005	-.248	-.045
Manic Depression No	0	.	.	.	.	.
Cancer – Yes	.481	.0165	29.201	.000	.449	.514
Cancer – No	0	.	.	.	.	.
Schizophrenia – Yes	-.160	.0485	-3.305	.001	-.256	-.065
Schizophrenia – No	0	.	.	.	.	.
Dementia – Yes	-.096	.0139	-6.917	.000	-.123	-.069
Dementia – No	0	.	.	.	.	.

The change in MDS Summary Scale scores over time was added next to the series of set one models, in model 5. This increased the overall correct classification of the model to 77.7% (Wald Z = 14.367, $p < .001$)(Table 32). A change in scores over MDS assessments appears to reduce death rate for those participants with changes in their CPS and ABS scores, while increasing the risk for death for those with changes in their CHESS score (Table 33). No significant relationship was found for rate of death due to change in ADL or DRS scores. After

adding the change in MDS Summary Scale scores to the model, the risk of death for those individuals diagnosed with schizophrenia lost significance ($p > .05$), and became equivalent to those who were not diagnosed with this disorder.

Table 32

GLMM set one – model 5 intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.107	.007	14.367	.000	.093	.123

Table 33

GLMM set one – model 5

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence Lower	95% Confidence Upper
Intercept	-1.389	.0412	-33.695	.000	-1.470	-1.309
Age	.037	.0008	43.576	.000	.035	.038
Gender – Other	.428	.2185	1.961	.050	.000	.857
Gender – Male	.325	.0133	24.370	.000	.299	.351
Gender – Female	0[b]	.	.	.	.	.
CCC	.145	.0430	3.376	.001	.061	.229
LTC	0[b]	.	.	.	.	.
ADL Scale	.316	.0059	54.060	.000	.305	.328
ABS Scale	-.002	.0032	-.671	.502	-.008	.004
CHESS Scale	.538	.0067	80.274	.000	.525	.551
CPS Scale	.080	.0049	16.269	.000	.070	.090
DRS Scale	.013	.0034	3.832	.000	.006	.020
Manic Depression Yes	-.146	.0530	-2.748	.006	-.250	-.042
Manic Depression No	0	.	.	.	.	.
Cancer – Yes	.378	.0177	21.290	.000	.343	.412
Cancer – No	0	.	.	.	.	.
Schizophrenia – Yes	-.057	.0496	-1.143	.253	-.154	.041
Schizophrenia – No	0	.	.	.	.	.
Dementia – Yes	-.082	.0147	-5.585	.000	-.111	-.053
Dementia – No	0	.	.	.	.	.
ADL Change	.209	.0067	31.240	.000	.196	.222
ABS Change	-.010	.0032	-3.068	.002	-.016	-.004
CHESS Change	.466	.0052	89.649	.000	.455	.476
CPS Change	-.002	.0059	-.386	.700	-.014	.009
DRS Change	-.003	.0032	-.831	.406	-.009	.004

The Final Model was created to include the change in antipsychotic medication use over assessments. This increased the overall correct classification to 77.8% (Wald Z = 14.366, $p <$ .001)(Table 34). A change in the frequency of receiving antipsychotic medications was a risk factor for death in participants who were receiving no antipsychotic medications and then started

as a PRN, those who stayed on antipsychotics as a PRN, and those who were taking antipsychotics everyday and reduced their use to an as needed basis (PRN)(Table 35). A decrease for risk of death occurred for individuals who went from using antipsychotics from everyday to none, and vise versa, as well as those who moved away from PRN use to either taking this medication everyday or not at all.

Table 34

GLMM set one – final model intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.107	.007	14.366	.000	.093	.123

Table 35

GLMM set one – final model

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence	
					Lower	Upper
Intercept	-1.362	.0414	-32.866	.000	-1.443	-1.281
Age	.036	.0008	42.928	.000	.035	.038
Gender – Other	.452	.2187	2.068	.039	.024	.881
Gender – Male	.326	.0134	24.358	.000	.299	.352
Gender – Female	0	.	.	.	.	.
CCC	.146	.0431	3.394	.001	.062	.231
LTC	0	.	.	.	.	.
ADL Scale	.314	.0059	53.511	.000	.302	.325
ABS Scale	.000	.0033	-.114	.909	-.007	.006
CHESS Scale	.533	.0067	79.099	.000	.519	.546
CPS Scale	.082	.0049	16.613	.000	.072	.092
DRS Scale	.015	.0034	4.376	.000	.008	.022
Manic Depression Yes	-.146	.0533	-2.744	.006	-.251	-.042
Manic Depression No	0	.	.	.	.	.
Cancer – Yes	.375	.0178	21.117	.000	.340	.410
Cancer – No	0	.	.	.	.	.
Schizophrenia – Yes	-.069	.0501	-1.374	.169	-.167	.029
Schizophrenia – No	0	.	.	.	.	.
Dementia – Yes	-.070	.0148	-4.729	.000	-.099	-.041
Dementia – No	0	.	.	.	.	.
ADL Change	.211	.0067	31.444	.000	.197	.224
ABS Change	-.008	.0032	-2.562	.010	-.014	-.002
CHESS Change	.462	.0052	88.302	.000	.451	.472
CPS Change	.002	.0059	.383	.702	-.009	.014
DRS Change	-.002	.0032	-.545	.586	-.008	.005
Everyday to Everyday	-.005	.0160	-.337	.736	-.037	.026
Everyday to PRN	.227	.0606	3.750	.000	.109	.346
Everyday to None	-.205	.0244	-8.408	.000	-.253	-.158
PRN to Everyday	-.328	.0827	-3.960	.000	-.490	-.165
PRN to PRN	.228	.0758	3.009	.003	.080	.377
PRN to None	-.323	.0855	-3.781	.000	-.491	-.156
None to Everyday	-.302	.0273	-11.036	.000	-.355	-.248
None to PRN	.157	.0672	2.340	.019	.026	.289
None to None	0	.	.	.	.	.

GLMM set two – More than one assessment. GLMM set two was run using the same pattern as the preliminary models, however, only included participants who had more than one assessment within the database. Therefore, individuals that were included in this analysis had two or more completed MDS assessment entries. Examining the models with only participants with more than one entry provides longitudinal information as it removes individuals who only had one record, due to situations such as death or moving to a private residence to die.

Using only participants with more than one observation increased the overall correct classification of the final model from 77.8% in the preliminary model set to 79.5% (Wald Z = 13.941, $p < .001$)(Table 36). When examining the differences between the preliminary model and current model, it was found that those individuals who had their gender classified as 'other' no longer had a significantly higher death rate than females (Table 37). In turn, it also showed that those participants who had a change in CPS score had a higher death rate than those who did not ($p < .05$), while those with a change in ABS score were no longer significantly different than those who did not ($p > .05$). The final difference between these two models was that those participants were maintained their use of antipsychotics as a PRN throughout their assessments, were no longer at an increased risk of death than those who were not taking these medications ($p > .05$).

Table 36

GLMM set two – final model

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.124	.009	13.941	.000	.107	.142

Table 37

GLMM set two – final model

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence Lower	95% Confidence Upper
Intercept	-1.520	.0482	-31.563	.000	-1.615	-1.426
Age	.041	.0010	41.243	.000	.039	.042
Gender – Other	.393	.2491	1.579	.114	-.095	.882
Gender – Male	.318	.0155	20.456	.000	.287	.348
Gender – Female	0	.	.	.	.	.
CCC	.108	.0496	2.171	.030	.010	.205
LTC	0	.	.	.	.	.
ADL Scale	.344	.0072	47.977	.000	.330	.358
ABS Scale	-.001	.0037	-.298	.766	-.008	.006
CHESS Scale	.559	.0085	65.451	.000	.543	.576
CPS Scale	.100	.0059	16.889	.000	.089	.112
DRS Scale	.014	.0040	3.596	.000	.006	.022
Manic Depression Yes	-.134	.0593	-2.266	.023	-.251	-.018
Manic Depression No	0	.	.	.	.	.
Cancer – Yes	.279	.0218	12.804	.000	.236	.322
Cancer – No	0	.	.	.	.	.
Schizophrenia – Yes	-.061	.0558	-1.089	.276	-.170	.049
Schizophrenia – No	0	.	.	.	.	.
Dementia – Yes	-.067	.0169	-3.958	.000	-.100	-.034
Dementia – No	0	.	.	.	.	.
ADL Change	.265	.0076	35.021	.000	.250	.280
ABS Change	-.006	.0034	-1.844	.065	-.013	.000
CHESS Change	.497	.0057	86.797	.000	.486	.508
CPS Change	.029	.0064	4.487	.000	.016	.041
DRS Change	.001	.0035	.395	.693	-.005	.008
Everyday to Everyday	-.017	.0185	-.928	.353	-.053	.019
Everyday to PRN	.306	.0627	4.886	.000	.183	.429
Everyday to None	-.091	.0253	-3.585	.000	-.140	-.041
PRN to Everyday	-.188	.0839	-2.236	.025	-.352	-.023
PRN to PRN	.239	.1742	1.372	.170	-.102	.580
PRN to None	-.208	.0872	-2.383	.017	-.379	-.037
None to Everyday	-.167	.0281	-5.943	.000	-.222	-.112
None to PRN	.218	.0690	3.162	.002	.083	.353
None to None	0	.	.	.	.	.

GLMM set three – New admissions. GLMM set three was run using only individuals who were new to the data set during the study period, using the same pattern as the preliminary models. Therefore, only individuals who were new admissions to either CCC or LTC facilities during the study period, and not those who were already residing in these facilities when the study began, were included in these analyses. This allows us to look at census level new admissions across all CCC and LTC facilities in Ontario, reducing potential confounds such as reporting differences between facilities.

When this model was run using only individuals who were new admissions to CCC and LTC facilities during the study period, it was found that the overall correct classification of the final model increased from 77.8% in the preliminary model set to 80.5% (Wald Z = 9.057, $p <$ .001)(Table 38). When looking at the differences between the preliminary model and current model, it was found that in relation to risk of death, significance was lost for those participants who had a gender marked as 'other', had a higher DRS score, were diagnosed with a manic depressive disorder, had a change in their ABS score over time, and those who went from taking antipsychotic medications everyday to using them as a PRN ($p > .05$)(Table 39). In contrast, there was a significant decrease risk of death for those participants who had a change in their DRS score over time ($p < .05$).

Table 38

GLMM set three – final model intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.110	.012	9.057	.000	.089	.137

Table 39

GLMM set three – final model

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence Lower	95% Confidence Upper
Intercept	-1.365	.0483	-28.280	.000	-1.459	-1.270
Age	.025	.0016	15.946	.000	.022	.028
Gender – Other	-.523	.5740	-.910	.363	-1.648	.602
Gender – Male	.289	.0236	12.257	.000	.243	.335
Gender – Female	0	.	.	.	.	.
CCC	.110	.0492	2.244	.025	.014	.207
LTC	0	.	.	.	.	.
ADL Scale	.287	.0099	28.993	.000	.268	.307
ABS Scale	.008	.0073	1.086	.277	-.006	.022
CHESS Scale	.524	.0118	44.448	.000	.501	.547
CPS Scale	.046	.0091	5.021	.000	.028	.064
DRS Scale	.006	.0067	.856	.392	-.007	.019
Manic Depression Yes	-.185	.1300	-1.425	.154	-.440	.070
Manic Depression No	0	.	.	.	.	.
Cancer – Yes	.552	.0279	19.756	.000	.497	.607
Cancer – No	0	.	.	.	.	.
Schizophrenia – Yes	-.071	.1305	-.545	.586	-.327	.185
Schizophrenia – No	0	.	.	.	.	.
Dementia – Yes	-.132	.0285	-4.618	.000	-.187	-.076
Dementia – No	0	.	.	.	.	.
ADL Change	.242	.0116	20.828	.000	.219	.265
ABS Change	-.013	.0068	-1.953	.051	-.027	-.001
CHESS Change	.449	.0101	44.291	.000	.429	.469
CPS Change	.011	.0109	1.020	.308	-.010	.032
DRS Change	-.015	.0061	-2.394	.017	-.026	-.003
Everyday to Everyday	.018	.0330	.545	.586	-.047	.083
Everyday to PRN	.096	.1408	.681	.496	-.180	.372
Everyday to None	-.191	.0557	-3.435	.001	-.300	-.082
PRN to Everyday	-.436	.1276	-3.412	.001	-.686	-.185
PRN to PRN	.270	.0934	2.895	.004	.087	.454
PRN to None	-.332	.1225	-2.710	.007	-.572	-.092
None to Everyday	-.301	.0497	-6.046	.000	-.398	-.203
None to PRN	.410	.1170	3.508	.000	.181	.640
None to None	0	.	.	.	.	.

GLMM set four – New admissions and more than one assessment. GLMM set four was run using only individuals who were new to the data set during the study period and had more than one assessment, using the same pattern as the preliminary models. Therefore, only individuals who were new admissions to either CCC or LTC facilities during the study period, not those who were already residing in these facilities when the study began, and also had two or more assessments completed, were included in these analyses. This allowed us to look at census level new admissions across all CCC and LTC facilities in Ontario, who were in the study long enough to provide some longitudinal information.

When this model was run using only individuals who were new admissions to CCC and LTC facilities and had more than one assessment during the study period, it was found that the overall correct classification of the final model increased from 77.8% in the preliminary model set to 83.6% (Wald Z = 7.470, $p < .001$)(Table 40). Many variables in this model lost significance when looking at increased death rate, when compared to the preliminary model ($p > .05$), including the increased risk for those having a gender marked as 'other', the difference between CCC and LTC facilities, having a higher DRS score, being diagnosed as having a manic depressive disorder, and having a change in ABS scores over assessments (Table 41). In addition, all variables related to taking antipsychotic medications were found to be not significant in this model, with the exception of changing from not taking an antipsychotic to taking one as a PRN showed to increase the risk of death ($p < .001$). The last difference for this final model, when compared to the preliminary final model, was an increased risk of death for those individuals with a higher CPS score ($p < .05$).

Table 40

GLMM set four – final model intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.121	.016	7.470	.000	.093	.157

Table 41

GLMM set four - final model

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence Lower	95% Confidence Upper
Intercept	-1.614	.0594	-27.196	.000	-1.731	-1.498
Age	.031	.0022	14.190	.000	.027	.035
Gender – Other	-12.644	336.5532	-.038	.970	-672.311	647.024
Gender – Male	.279	.0322	8.642	.000	.215	.342
Gender – Female	0	.	.	.	.	.
CCC	-.001	.0585	-.013	.989	-.115	.114
LTC	0	.	.	.	.	.
ADL Scale	.328	.0149	21.953	.000	.298	.357
ABS Scale	.005	.0097	.473	.636	-.014	.024
CHESS Scale	.630	.0184	34.284	.000	.594	.666
CPS Scale	.041	.0135	3.005	.003	.014	.067
DRS Scale	.007	.0092	.768	.443	-.011	.025
Manic Depression Yes	-.166	.1709	-.969	.332	-.501	.169
Manic Depression No	0	.	.	.	.	.
Cancer – Yes	.420	.0410	10.227	.000	.339	.500
Cancer – No	0	.	.	.	.	.
Schizophrenia – Yes	-.092	.1652	-.557	.578	-.416	.232
Schizophrenia – No	0	.	.	.	.	.
Dementia – Yes	-.121	.0375	-3.217	.001	-.194	-.047
Dementia – No	0	.	.	.	.	.
ADL Change	.313	.0146	21.418	.000	.284	.341
ABS Change	-.011	.0076	-1.391	.164	-.026	.004
CHESS Change	.523	.0120	43.665	.000	.499	.546
CPS Change	.029	.0123	2.310	.021	.004	.053
DRS Change	.000	.0069	.069	.945	-.013	.014
Everyday to Everyday	.053	.0454	1.176	.240	-.036	.142
Everyday to PRN	.235	.1468	1.602	.109	-.052	.523
Everyday to None	.047	.0593	.790	.429	-.069	.163
PRN to Everyday	-.173	.1326	-1.305	.192	-.433	.087
PRN to PRN	-.103	.2959	-.348	.728	-.683	.477
PRN to None	-.135	.1271	-1.060	.289	-.384	.114
None to Everyday	-.049	.0528	-.922	.357	-.152	.055
None to PRN	.522	.1239	4.209	.000	.279	.765
None to None	0	.	.	.	.	.

GLMM set five – Dementia. GLMM set five was run using only individuals who were diagnosed with dementia. Therefore, individuals who had a diagnosis of manic depression, cancer, or schizophrenia were eliminated from this analysis. As people with these disorders are also commonly prescribed antipsychotic medications, removing them from this analysis allowed us to look specifically at the effects of antipsychotic medications on those participants with dementia.

When this model was run using only participants with dementia, it was found that the overall correct classification of the final model decreased from 77.8% in the preliminary model set to 76.4% (Wald Z = 12.047, $p < .001$)(Table 42). This result showed that the fit of this model was not as good when using only individuals who had a diagnosis of dementia. Three variables lost significance in this model, when compared to the preliminary model. When looking at the current model, the variables related to participants who had a gender classified as 'other', had a change in their ABS score, and those who were not on antipsychotics and then started taking them on a PRN basis, were no longer at an increased risk of death, as was the case in the preliminary model (Table 43).

Table 42

GLMM set five – final model intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.108	.009	12.047	.000	.092	.127

Table 43

GLMM set five – final model

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence Lower	95% Confidence Upper
Intercept	-1.624	.0557	-29.155	.000	-1.733	-1.515
Age	.041	.0013	32.173	.000	.038	.043
Gender – Other	.552	.2988	1.848	.065	-.033	1.138
Gender – Male	.358	.0194	18.446	.000	.320	.397
Gender – Female	0	.	.	.	.	.
CCC	.307	.0565	5.435	.000	.196	.418
LTC	0	.	.	.	.	.
ADL Scale	.342	.0093	36.988	.000	.324	.361
ABS Scale	-.003	.0041	-.715	.475	-.011	.005
CHESS Scale	.514	.0099	51.655	.000	.494	.533
CPS Scale	.090	.0079	11.379	.000	.075	.106
DRS Scale	.023	.0048	4.776	.000	.014	.033
Manic Depressive	0	.	.	.	.	.
Cancer	0	.	.	.	.	.
Schizophrenia	0	.	.	.	.	.
Dementia	0	.	.	.	.	.
ADL Change	.205	.0102	20.041	.000	.185	.225
ABS Change	-.007	.0040	-1.847	.065	-.015	.000
CHESS Change	.465	.0072	64.204	.000	.450	.479
CPS Change	-.005	.0092	-.569	.569	-.023	.013
DRS Change	.001	.0046	.300	.764	-.008	.010
Everyday to Everyday	.000	.0205	-.014	.989	-.041	.040
Everyday to PRN	.261	.0729	3.578	.000	.118	.404
Everyday to None	-.231	.0298	-7.742	.000	-.289	-.172
PRN to Everyday	-.389	.1026	-3.787	.000	-.590	-.188
PRN to PRN	.405	.1181	3.432	.001	.174	.637
PRN to None	-.246	.1083	-2.269	.023	-.458	-.033
None to Everyday	-.278	.0367	-7.581	.000	-.350	-.206
None to PRN	.117	.0914	1.286	.199	-.062	.297
None to None	0	.	.	.	.	.

GLMM set six – Dementia and new admissions. GLMM set six was run using the same pattern as the preliminary models, however, only included participants who had a diagnosis of dementia, and had more than one assessment within the database. Therefore, individuals that were included in this analysis had dementia with two or more completed MDS assessment entries. Examining the models with only participants with dementia and more than one assessment entry provided longitudinal information as it removed individuals who only had one record, as well as helped to remove potential confounds related to participants taking antipsychotic medications for reasons other than managing symptoms related to dementia.

Using only participants with dementia and more than one assessment increased the overall correct classification of the final model from 77.8% in the preliminary model set to 78.1% (Wald Z = 13.941, $p < .001$)(Table 44). When comparing the variables in the preliminary final model to this one, three variables lost significance. It was found that when looking specifically at participants with dementia who had more than one assessment completed, a change in the ABS score was no longer significant, nor was staying on an antipsychotic medication as a PRN across assessments, or reducing the use of an antipsychotic medication from a PRN to not using one at all (Table 45).

Table 44

GLMM set six – final model intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.125	.011	11.838	.000	.106	.147

Table 45

GLMM set six – final model

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence Lower	95% Confidence Upper
Intercept	-1.790	.0656	-27.305	.000	-1.919	-1.662
Age	.042	.0014	30.060	.000	.039	.045
Gender – Other	.631	.3172	1.988	.047	.009	1.252
Gender – Male	.336	.0215	15.632	.000	.294	.378
Gender – Female	0	.	.	.	.	.
CCC	.292	.0661	4.421	.000	.163	.422
LTC	0	.	.	.	.	.
ADL Scale	.367	.0106	34.757	.000	.346	.387
ABS Scale	-.007	.0046	-1.571	.116	-.016	.002
CHESS Scale	.538	.0117	46.009	.000	.515	.561
CPS Scale	.104	.0090	11.622	.000	.087	.122
DRS Scale	.023	.0054	4.293	.000	.013	.034
Manic Depressive	0	.	.	.	.	.
Cancer	0	.	.	.	.	.
Schizophrenia	0	.	.	.	.	.
Dementia	0	.	.	.	.	.
ADL Change	.256	.0111	22.920	.000	.234	.277
ABS Change	-.008	.0042	-1.818	.069	-.016	.001
CHESS Change	.494	.0077	64.039	.000	.479	.510
CPS Change	.017	.0097	1.699	.089	-.003	.036
DRS Change	.001	.0050	.285	.776	-.008	.011
Everyday to Everyday	.002	.0229	.078	.938	-.043	.047
Everyday to PRN	.348	.0750	4.641	.000	.201	.495
Everyday to None	-.118	.0307	-3.834	.000	-.178	-.058
PRN to Everyday	-.249	.1037	-2.405	.016	-.452	-.046
PRN to PRN	.295	.2405	1.226	.220	-.177	.766
PRN to None	-.126	.1102	-1.143	.253	-.342	.090
None to Everyday	-.144	.0375	-3.843	.000	-.218	-.071
None to PRN	.194	.0933	2.081	.037	.011	.377
None to None	0	.	.	.	.	.

GLMM set seven – Dementia with more than one assessment. GLMM set seven was run using the same pattern as the preliminary models, however, only included participants who had a diagnosis of dementia, and were classified as a new admission within the database. Therefore, individuals that were included in this analysis had dementia and entered a CCC or LTC facility after the study had begun. Examining the models with only participants diagnosed with dementia who were new admissions provides a consistent and complete picture of residents with dementia in CCC and LTC facilities, as it helped reduce reporting differences seen prior to the MDS assessments becoming mandatory in all facilities in Ontario.

Using only participants with dementia who were new admissions to CCC and LTC facilities increased the overall correct classification of the final model from 77.8% in the preliminary model set to 80.0% (Wald Z = 6.009, $p < .001$)(Table 46). Several variables lost significance for risk of death in this model when compared to the final preliminary model, including those participants with a gender classified as 'other', a high DRS score, and a change in ABS score (Table 47). In addition, participants who switched from taking antipsychotic medication everyday to PRN use, and those who went from taking them as a PRN to not at all, and vise versa, were not significantly different than those who not prescribed these medications.

Table 46

GLMM set seven – final model intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.113	.019	6.009	.000	.082	.157

Table 47

GLMM set seven – final model

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence Lower	95% Confidence Upper
Intercept	-1.566	.0698	-22.435	.000	-1.703	-1.429
Age	.037	.0029	12.787	.000	.031	.043
Gender – Other	-12.358	429.5776	-.029	.977	-854.396	829.680
Gender – Male	.363	.0397	9.144	.000	.285	.440
Gender – Female	0	.	.	.	.	.
CCC	.174	.0696	2.499	.012	.037	.310
LTC	0	.	.	.	.	.
ADL Scale	.322	.0181	17.842	.000	.287	.358
ABS Scale	.018	.0096	1.862	.063	-.001	.037
CHESS Scale	.500	.0210	23.791	.000	.459	.541
CPS Scale	.063	.0171	3.701	.000	.030	.097
DRS Scale	.000	.0106	.047	.963	-.020	.021
Manic Depressive	0	.	.	.	.	.
Cancer	0	.	.	.	.	.
Schizophrenia	0	.	.	.	.	.
Dementia	0	.	.	.	.	.
ADL Change	.237	.0193	12.257	.000	.199	.275
ABS Change	-.006	.0087	-.643	.520	-.023	.012
CHESS Change	.458	.0156	29.296	.000	.427	.489
CPS Change	-.002	.0182	-.121	.904	-.038	.033
DRS Change	-.016	.0093	-1.760	.078	-.035	.002
Everyday to Everyday	-.019	.0472	-.404	.686	-.112	.073
Everyday to PRN	.158	.1592	.994	.320	-.154	.470
Everyday to None	-.288	.0737	-3.913	.000	-.433	-.144
PRN to Everyday	-.535	.1652	-3.236	.001	-.858	-.211
PRN to PRN	.644	.1623	3.968	.000	.326	.962
PRN to None	-.314	.1618	-1.943	.052	-.631	.003
None to Everyday	-.290	.0691	-4.201	.000	-.426	-.155
None to PRN	.299	.1665	1.797	.072	-.027	.626
None to None	0	.	.	.	.	.

GLMM set eight – Dementia and new admissions and more than one assessment.

GLMM set eight was run using the same pattern as the preliminary models, however, only included participants who had a diagnosis of dementia, were classified as a new admission within the database, and had more than one assessment. Therefore, individuals that were included in this analysis had dementia, entered a CCC or LTC facility after the study had begun, and had two or more assessments completed. Analyzing the models this way allowed for a very clean and specific view of census level CCC and LTC facility admissions across Ontario for those diagnosed with dementia over time.

When this model was run using only individuals diagnosed with dementia, who were new admissions to CCC and LTC facilities, and had more than one assessment during the study period, it was found that the overall correct classification of the final model increased from 77.8% in the preliminary model set to 83.6% (Wald Z = 5.317, $p < .001$)(Table 48). Many variables lost significance in this model, when compared to the final preliminary model. Having a gender classified as 'other', residing in a CCC rather than a LTC, having a high DRS score, or having a change in ABS score, no longer changed the risk of death for participants (Table 49). In addition, all variables related to antipsychotic medication use lost significance when looking at risk of death, except for those participants who went from not using this type of medication to using it as a PRN. These participants still had a significantly increased risk for death compared to those who were not using these medications at all. It must be noted that findings in this table (49) may be inflated due to the unusual sex distribution.

Table 48

GLMM set eight – final model intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.128	.024	5.317	.000	.088	.184

Table 49

GLMM set eight – final model

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence Lower	95% Confidence Upper
Intercept	-1.759	.0849	-20.730	.000	-1.926	-1.593
Age	.038	.0035	10.848	.000	.031	.045
Gender – Other	-15.196	2159.816	-.007	.994	-4248.836	4218.445
Gender – Male	.329	.0479	6.879	.000	.235	.423
Gender – Female	0	.	.	.	.	.
CCC	.032	.0835	.382	.703	-.132	.195
LTC	0	.	.	.	.	.
ADL Scale	.334	.0230	14.498	.000	.289	.379
ABS Scale	.006	.0120	.467	.640	-.018	.029
CHESS Scale	.556	.0278	20.048	.000	.502	.611
CPS Scale	.067	.0218	3.075	.002	.024	.110
DRS Scale	.017	.0129	1.323	.186	-.008	.042
Manic Depressive	0	.	.	.	.	.
Cancer	0	.	.	.	.	.
Schizophrenia	0	.	.	.	.	.
Dementia	0	.	.	.	.	.
ADL Change	.297	.0226	13.182	.000	.253	.342
ABS Change	-.006	.0097	-.640	.522	-.025	.013
CHESS Change	.513	.0177	29.009	.000	.478	.547
CPS Change	.019	.0201	.936	.349	-.021	.058
DRS Change	-.001	.0102	-.052	.959	-.021	.020
Everyday to Everyday	.031	.0588	.520	.603	-.085	.146
Everyday to PRN	.312	.1657	1.882	.060	-.013	.637
Everyday to None	-.051	.0778	-.652	.514	-.203	.102
PRN to Everyday	-.264	.1691	-1.560	.119	-.595	.068
PRN to PRN	.290	.4163	.698	.485	-.526	1.106
PRN to None	-.084	.1664	-.503	.615	-.410	.243
None to Everyday	-.027	.0729	-.364	.716	-.169	.116
None to PRN	.450	.1733	2.598	.009	.110	.790
None to None	0	.	.	.	.	.

GLMM set nine – Antipsychotic medication categories. GLMM set nine was run using all participants, however, instead of looking at the change in antipsychotic medication use, the frequency of antipsychotic medication use was analyzed. For this purpose, frequency of antipsychotic medication use was broken down into three categories: 1. daily use (7 days per week), 2. used as a PRN (1 to 6 days per week), or 3. no use (0 days per week). The measure was the proportion of assessments per person that fell into each category. This analysis provided a picture of whether there was a difference in death based on whether these medications were used, not used, or used as a PRN.

When this model was run using the variables related to the categories of antipsychotic medication use, it was found that the overall correct classification of the final model decreased from 77.8% in the preliminary model set to 77.7% (Wald Z = 14.363, $p < .001$)(Table 50). This result showed that the fit of this model was not as good as when the change of antipsychotic medication was analyzed. With that being said, no variables lost significance in this model, and it was shown that those participants who were taking antipsychotic medications as a PRN or daily had a lower risk of death then those participants who were not taking them at all (Table 51). This result may be due to confounds related to the prescribing of antipsychotic medications to help manage symptoms of other illnesses.

Table 50

GLMM set nine – final model intercept

Random Effect Covariance	Estimate	Std. Error	Z	Sig.	95% Confidence Lower	Upper
Intercept	.107	.007	14.363	.000	.093	.122

Table 51

GLMM set nine – final model

Model Term	Coefficient	Std. Error	t	Sig.	95% Confidence Lower	95% Confidence Upper
Intercept	-1.393	.0413	-33.754	.000	-1.474	-1.312
Age	.037	.0008	43.199	.000	.035	.038
Gender – Other	.431	.2184	1.971	.049	.002	.859
Gender – Male	.325	.0134	24.362	.000	.299	.351
Gender – Female	0	.	.	.	.	.
CCC	.148	.0430	3.439	.001	.064	.232
LTC	0	.	.	.	.	.
ADL Scale	.316	.0059	53.894	.000	.304	.327
ABS Scale	-.002	.0033	-.539	.590	-.008	.005
CHESS Scale	.536	.0067	79.667	.000	.522	.549
CPS Scale	.080	.0049	16.298	.000	.071	.090
DRS Scale	.013	.0034	3.921	.000	.007	.020
Manic Depression Yes	-.139	.0532	-2.601	.009	-.243	-.034
Manic Depression No	0	.	.	.	.	.
Cancer – Yes	.377	.0177	21.257	.000	.342	.412
Cancer – No	0	.	.	.	.	.
Schizophrenia – Yes	-.049	.0501	-.985	.324	-.148	.049
Schizophrenia – No	0	.	.	.	.	.
Dementia – Yes	-.079	.0148	-5.365	.000	-.108	-.050
Dementia – No	0	.	.	.	.	.
ADL Change	.209	.0067	31.246	.000	.196	.222
ABS Change	-.010	.0032	-3.029	.002	-.016	-.003
CHESS Change	.464	.0052	89.242	.000	.454	.474
CPS Change	-.002	.0059	-.322	.747	-.013	.010
DRS Change	-.003	.0032	-.811	.417	-.009	.004
Percent Daily	-.002	.0006	-3.637	.000	-.004	-.001
Percent PRN	-.002	.0006	-3.242	.001	-.003	-.001
Percent None	0	.	.	.	.	.

Discussion

The current study provides the most comprehensive look at the current use of antipsychotic medications in older adults residing in CCC and LTC facilities in Canada, with specific attention given to those individuals diagnosed with dementia. This study is the first to provide census level data for this type of information across Ontario for all continuing care facilities using the MDS 2.0, NACRS, and DAD databases. Having this level of data allows for a complete view of the effects antipsychotic medications have in this population, which has never been seen before. This study was completed with the goals of providing information regarding, 1) the nature of older adults living in CCC and LTC facilities; 2) the use of antipsychotic medications in these facilities, with specific reference to those individuals diagnosed with dementia or who were exhibiting aggressive behaviour; and 3) whether taking antipsychotic medications increased the risk of mortality in older adults.

Resident information for CCC and LTC facilities

There were more than 100,000 individuals, age 65 and older, living in residential care facilities in Ontario during the study period. Females made up approximately two thirds of this population (69.1%), while males made up the rest (30.8%), with the exception of 69 individuals (0.1%) who were classified as 'other'. It is surmised that for those individuals who had a gender was classified as 'other', it was either due to a data collection error by the residential facility, the participant may have identified as transgendered, or was clinically a hermaphrodite. The average age of participants included in the study was 84.2 years, ranging from 65 to 114 years old.

The majority of individuals in this study resided in LTC (85.7%) facilities compared to CCCs (14.3%). Males (19.2%) were more likely to live in CCCs then females (12.1%), and those living in CCCs were typically younger than people living in LTC facilities. It is believed

that individuals in CCCs were younger due to the nature of care within these facilities compared to LTCs. CCCs are hospital-based facilities that would typically provide care for individuals suffering from issues related to acute illnesses and events (e.g. heart attack), surgery, or rehabilitation (e.g. strokes), while patients with chronic and progressive illnesses are more likely to reside in LTC facilities (e.g. Parkinson's disease, cognitive decline). While living in these facilities, the average person was assessed using the MDS 2.0 approximately 8 times (31.2%), with a range of 1 to 18 assessments.

The MDS 2.0 summary scales provided valuable information regarding the functional abilities of individuals living in CCC and LTC facilities. Very few individuals residing in these facilities did not require any support with their activities of daily living (7.3%). Over half (53.1%) of the participants in the study required a moderate or higher level of support in order to successfully make it through their day.

Approximately 60% of people in this study did not exhibit any aggressive behaviours in CCC and LTC facilities, while 90% displayed aggression at moderate or lower levels. Only 10% of individuals in these facilities displayed severe aggression. This picture is quite different when looking at the differences in aggressive behaviour for those individuals with and without a diagnosis of dementia. Almost 60% of participants in the study who were diagnosed with dementia showed at least a minimal level of aggression compared to 30% of those without this diagnosis.

When looking at severe aggression in those with dementia, the rate drops dramatically to only 12.5% of individuals exhibiting these behaviours, and 3% for those without dementia. While the total of aggressive behaviour is far above the findings in previous studies relating to dementia patients, with 20% to 50% exhibiting this behaviour in community samples (Jost &

Grossberg, 1996; Lyketsos et al., 2000), it is quite a bit lower when only looking at severe aggression. It may be that the difference in this high number of aggressive behaviour is due to the admitting practices and protocols of residential facilities in Canada, where all attempts are typically made to keep individuals out of residential care until absolutely necessary. Due to this, a trend may be seen that most individuals admitted to a CCC or LTC facility would be displaying more significant symptoms than those with dementia still living in the community, even though they are not necessarily considered 'severe'.

While participants in this study may have been showing a higher level of aggressive symptoms than those still residing in the community, the CHESS scale showed that the majority of participants (90.4%) had very low physical health instability. Only 9.6% of people in these facilities had moderate to very high health instability. Cognitively, results showed through the CPS that 54% of participants had moderate to very severe cognitive impairment, only approximately 17% had intact cognitive abilities. The results in this current study indicate that while physical health may be generally good in older adults residing in CCC and LTC facilities, cognitive decline and impairment are more common than not.

Approximately one third of participants in this study also had symptoms of depression ranging from minor to major, according to the DRS. There was not a substantial difference in symptoms of depression level for those with (35.4%) or without dementia (30.4%), when looking at scores 3 and above, indicating minor to major depressive issues. While this finding contrasts the International Psychogeriatric Association's (2002) finding that up to 80% of individuals with dementia suffer from symptoms of depression within the course of their illness, it may be consistent with their assertion that symptoms of depression are more prevalent in the early and

middle stages of dementia and cognitive impairment, as people in CCC and LTC facilities may be further along in their illnesses and impairment.

Use of antipsychotic medications in CCC and LTC facilities

Past research has indicated that approximately 40% to 50% of residents residing in CCC and LTC facilities were being prescribed antipsychotic medications (CIHI, 2009; Ministry of Health, 2011). This is despite the fact that research has shown the efficacy of antipsychotic medications in older adults with and without dementia was questionable (Ballard & Howard, 2006; Mintzer et al., 2006; Schneider et al., 2008), and there were multiple health warnings from government agencies regarding an increased risk of mortality in people with dementia (Committee on Safety of Medicines, 2005; Federal Drug Administration, 2005; Health Canada, 2005), as well as a plethora of other significant side effects (Ballard et al., 2005; Herrmann & Lanctot, 2005; Lacut et al., 2007; Trifirò et al., 2010).

The current study indicates that 31% of people in CCC and LTC facilities in Ontario were taking antipsychotic medications at least once per week, with the majority of individuals (29.2%) taking them seven days a week, during the study period. While this is less then what was indicated in past research, when looking only at individuals with a diagnosis of dementia, it was found that 39.8% of residents took antipsychotic medications at least once per week, with a total of 37.7% taking them seven days a week. This compares to only 17.2% of individuals without a diagnosis of dementia taking these medications seven days a week. This finding is consistent with the hypothesis that individuals with dementia would be more likely to receive antipsychotic medications than those without this diagnosis.

Males (31.1%) and females (29.0%) were prescribed antipsychotic medications at roughly the same rate. A total of 33.0% of individuals with a gender classified as 'other'

received this medication. Younger individuals were much more likely to be prescribed these medications seven days a week, when looking at the three age categories (65-79 = 34.5%; 80-89 = 29.8%; 90-114 = 22.9%). This may be due to greater physical impairment and decreased strength, leading to less physical aggression, progressively in the older age groups. Individuals residing in LTC facilities were much more likely to be prescribed antipsychotic medications (31%) seven days a week and those living in CCC facilities (18.7%), regardless of gender. Again, this may be attributable to the reasons behind why individuals are admitted to either a CCC or LTC facility, such as the nature of illness.

When looking at cognitive impairment using the CPS in the use of antipsychotic medications, it was found that 74.1% of individuals with moderate to severe cognitive impairment were prescribed these medications, with 69.6% taking them 7 days a week. This compares to only 14.5% of participants with mild cognitive impairment being prescribed these medications. When looking at only individuals prescribed antipsychotic medications, it was found that a staggering 89.1% were classified as having moderate to severe cognitive impairment. Results are not consistent with the hypothesis that those with more severe cognitive impairment were prescribed antipsychotic medications less often than those with milder impairment.

While the finding related to cognitive impairment and antipsychotic medication use was not consistent with the study hypothesis, the finding was consistent to the one related to aggressive behaviour. It was shown that 60.1% of participants with severe aggression took antipsychotic medication seven days a week, while only 50% of those with moderate aggression, and 25% of those with mild aggression did so. This is despite the fact there are many studies

questioning the limited effectiveness and safety of using antipsychotic medications to treat agitation and aggression (Ballard & Howard, 2006; Schneider et al., 2008; Sultzer et al., 2008).

Use of antipsychotic medications and mortality risk

Of the 102,658 individuals included in this study, 32.2% died during the data collection period. Those with the gender classified as 'other' (39.1%) had the highest death rate, followed by males (35.3%), and then females (30.8%). Difference in death rate for males and females may well be due to the fact females live longer on average. Results also showed that individuals living in CCC facilities (43.8) had a higher death rate than those in LTC facilities (30.8%). As stated earlier, CCC facilities typically admit patients with more acute health problems, such as heart attacks and strokes, while LTC facilities typically admit patients with chronic conditions such as dementia, which would explain the higher death rate in CCC facilities.

Only one antipsychotic medication, risperidone, has been approved for the treatment of behavioural and psychological symptoms of dementia in Canada for, "*short-term symptomatic management* [emphasis added] of inappropriate behaviour due to aggression and/or psychosis in patients with severe dementia" (Health Canada, 2005, p.1). Many quality research studies have shown that the use of antipsychotic medication in older adults with dementia increased overall mortality rate in this population (Gill et al., 2007; Health Canada, 2005; Trifirò et al., 2009; Musicco et al., 2011), which led to multiple warnings within Canada from drug manufacturers (Banjeree, 2009) and Health Canada itself (2005).

Increased risk of death been found for both conventional and atypical antipsychotic medications (Wang et al., 2005; Schneeweiss et al., 2007), with research showing that elderly people with dementia taking an atypical antipsychotic were at a twofold risk for death, while those taking a conventional antipsychotic were at a fourfold risk of death, compared to controls

(Musicco et al., 2011). Despite this, the current study shows that almost 40% of residents in CCC and LTC facilities with dementia are prescribed this type of medication.

Results from this study paint a different picture than previous research in regards to increased risk in overall death for older adults. Of the 102,658 participants included in this study, there was no substantial difference in death rate for those who were not taking this type of medication (32.2%) and those who were taking this type of medication seven days a week (30.4%). This trend for death rates related to antipsychotic medication use was similar for both those with dementia, 34.3% and 30.9% respectively, and those without dementia, 30.0% and 28.9% respectively.

An interesting finding occurred when further analysis was done to explore the rate of death associated with antipsychotic medications for those individuals who were taking this type of medication as a PRN, between 1 to 6 days a week. Those individuals who took antipsychotic medications infrequently throughout the week, one to six times, had a much higher rate of death (61.2%) than those who did not take it at all (32.2%) or took it seven days a week (30.4%). When looking at individuals with and without dementia the results were the same. Rate of death for individuals with dementia increased to 59.2% when these medications were taken as a PRN throughout the week, versus 30.9% when taken 7 days a week, and 34.3% when not taken at all. For those without dementia, death rate was 65.5% when these medications were taken 1 to 6 times throughout the week, compared to 20.9% when taken seven days a week, and 30.0% when not taken it all.

These results suggest that regardless of dementia diagnosis, the risk of increased death rate correlates with frequency of antipsychotic medication use when taken inconsistently throughout the week, rather than consistently at seven days a week. Furthermore, results actually

suggest that there may be a slight protective factor when older adults take these medications everyday, or that these two groups (PRN versus 7 days a week) are fundamentally different based on other factors. Overall, individuals who were not prescribed antipsychotic medications had a death rate 1.8% higher than those who were taking these medications seven days a week. These medications appear to have the most protective effect for those individuals diagnosed with dementia, with results showing that people with dementia who were not taking antipsychotic medications died at a rate of 3.4% greater than those who were taking them seven days a week. In relation to individuals without a diagnosis of dementia, these participants died 1.1% more frequently without antipsychotic medication, than while taking this medication seven days a week. These findings are not consistent with the study hypothesis that those individuals receiving antipsychotic medications will have a higher rate of mortality than those who were not.

No other studies could be found related to the rate of death associated with the frequency of antipsychotic medication use in older adults with or without dementia, to help provide an explanation for these findings. It is surmised that the increase rate of death in those individuals who took antipsychotic medications 1 to 6 days a week may be related to a few different factors. First, antipsychotic medications are quite potent and it may be that when older adults take them infrequently throughout the week, their bodies are constantly trying to regulate and accommodate the medication and related side effects, adding stress to already potentially frail and compromised systems (Van Der Hooft et al., 2005). Second, the reasons behind individuals being prescribed these medications as a PRN inconsistently throughout the week may be the reason behind the increased death rate, rather than the medication itself.

It is unclear why this study found a lower rate of death for individuals taking antipsychotic medications seven days a week compared to those not taking them all. It may

actually be that similar findings in previous studies were overlooked as the methodology only looked at whether participants were, or were not, taking antipsychotic medications. If there is a protective factor for those individuals taking antipsychotic medications seven days a week, rather than not at all, it is proposed that the lower rate of death in those taking antipsychotic medications seven days a week its due to the benefit they have on managing BPSD and other symptoms.

GLMM findings

Rate of death was explored further in this study using multilevel linear modelling. This provided information regarding the relationships between different variables and the rate of death of participants in this study, within a variety of contexts. Understanding the factors related to increased death rate could prove valuable to medical professionals working in CCC and LTC facilities, as well as physicians working with older adults with and without dementia.

A summary table was created to provide an opportunity to view the differences of the final models with ease (Table 52). Using the legend below, final models can be compared in regards to what final models led to significance for each variable included.

Final Models:

Name	*Description of Model*
1	All participants model
2	More than one assessment
3	New admissions
4	New admissions and more than one assessment
5	Dementia
6	Dementia with more than one assessment
7	Dementia and new admissions
8	Dementia and new admissions and more than one assessment
9	Antipsychotic medication categories

H = Significantly higher mortality due to higher scores on the continuous variable or due to differences between the target and reference categories
L = Significantly lower mortality due to lower scores on the continuous variable or due to differences between the target and reference categories
. = Not included in analysis

Table 52

Summary of significance for final models

Model Term	1	2	3	4	5	6	7	8	9
Percent/Intercept	77.8 L	79.5 L	80.5 L	83.6 L	76.4 L	78.1 L	80.0 L	83.6 L	77.7 L
Age	H	H	H	H	H	H	H	H	H
Gender – Other	H					H			H
Gender – Male	H	H	H	H	H	H	H	H	H
Gender – Female	.	.	.	.	.	.	.	.	.
CCC	H	H	H		H	H	H		H
LTC	.	.	.	.	.	.	.	.	.
ADL Scale	H	H	H	H	H	H	H	H	H
ABS Scale									
CHESS Scale	H	H	H	H	H	H	H	H	H
CPS Scale	H	H	H	H	H	H	H	H	H
DRS Scale	H	H			H	H			H
Manic Depression Yes	L	L			.	.	.	.	L
Manic Depression No	.	.	.	.	.	.	.	.	.
Cancer – Yes	H	H	H	H	.	.	.	.	
Cancer – No	.	.	.	.	.	.	.	.	.
Schizophrenia – Yes					.	.	.	.	
Schizophrenia – No	.	.	.	.	.	.	.	.	.
Dementia – Yes	L	L	L	L	.	.	.	.	
Dementia – No	.	.	.	.	.	.	.	.	.
ADL Change	H	H	H	H	H	H	H	H	H
ABS Change	L								L
CHESS Change	H	H	H	H	H	H	H	H	H
CPS Change		H		H					
DRS Change			L						
Everyday to Everyday									.
Everyday to PRN	H	H			H	H			.
Everyday to None	L	L	L		L	L	L		.
PRN to Everyday	L	L	L		L	L	L		.
PRN to PRN	H		H		H		H		.
PRN to None	L	L	L		L				.
None to Everyday	L	L	L		L	L	L		.
None to PRN	H	H	H	H		H		L	.
None to None	.	.	.	.	.	.	.	.	.
Percent Daily	.	.	.	.	.	.	.	.	L
Percent PRN	.	.	.	.	.	.	.	.	L
Percent None	.	.	.	.	.	.	.	.	.

Demographic Variables. The first set of models, set one, used all participants in this study and was used as a base to compare subsequent models, which were run using different contexts (e.g. new admissions, only dementia patients). After running the null model in this set of models, demographic characteristics were entered. It was found that when no other variables were included in the model, males had a higher rate of death than females, and those living in CCC facilities had a lower rate of death compared to those living in LTC facilities.

MDS 2.0 Scales. Higher scores on all of these scales, except the ABS, increased the risk of death. As soon as these scales were included in model three, those residing in CCC facilities no longer had a significantly different rate of death than those residing in LTC facilities. This may be due to the fact that higher scores on these scales, indicating more significant levels of impairment, can be related to seriousness of illness. Those who are more seriously ill have a greater chance of residing in a CCC due to the nature of care they provide.

Diagnostic Variables. Diagnostic variables were added next to control for confounding illnesses within the MDS 2.0 related to manic depression, schizophrenia, and cancer, in model 4. Previous research has shown that older adults with schizophrenia (Jeste & Maglione, 2013), bipolar disorder (Dolder & Mckinsey, 2011), and cancer (Fisch & Kim, 2004), are often prescribed antipsychotic medications to help control symptoms. The current study showed that those individuals who were diagnosed with bipolar disorder, schizophrenia, or dementia, had a lower death rate than did those who were not diagnosed with these illnesses. However, those individuals diagnosed with cancer had a higher death rate than those who did not. These findings were consistent for these variables in model five and the final model, when the variable related to antipsychotic medications was included, with the exception of schizophrenia, which lost its significance in model 5 and 6. The lower death rate for individuals with schizophrenia,

bipolar disorder, and dementia, maybe due to the potentially protective nature of antipsychotic medications, as discussed earlier. In contrast, these individuals' psychiatric condition may have expedited their admission into a care facility, even though they were not as medically ill, as their clinical presentation may have been more difficult to continue managing in the home or in community settings. The higher rate of death for those with cancer may be attributable to the organic nature of this illness.

MDS 2.0 Change Scales. Model five was developed to include variables related whether participants had a change in the MDS 2.0 scales over assessments. It was found that a change in the ADL and CHESS scales increased the rate of death of participants, while change in ABS score decreased the rate of death. Having a change in CPS or DRS scales was not related to death rate. These findings were consistent with what was seen in the final model. The finding that changes in the ADL and CHESS scales is related to death is consistent with previous research (Mor et al., 2011; Smart, Herrmann, & Lanctôt, 2011). Changes in these scores most likely indicate that individuals are at a stage with their health that they are losing their basic abilities and are becoming very frail. Having a change in ABS score decreasing death rate would be consistent with the fact that these people are still physically healthy enough to display the sort of behaviour.

Antipsychotic Medication Use. Variables related to antipsychotic medication use were added to the series to create the final model. These variables looked at consistent frequency of antipsychotic medication use over time, as well as changes in the use of antipsychotics overtime, in relation to rate of death. This model confirmed the results that were discussed earlier in relation to death rate and antipsychotic medication use. Death rate was not related to the everyday use antipsychotic medications, however switching from taking these medications every

day to inconsistently increased death rate, while switching from everyday use to none at all decreased death rate, when compared to those individuals who were not taking antipsychotic medications at all.

In addition, when individuals switched from using antipsychotic medications as a PRN to taking them every day, or stop taking them all together, death rate decreased. Those who continued to use antipsychotic medications as a PRN were at an increased risk of death compared to those who were not taking at all. Lastly, it was found that individuals who were not taking antipsychotics and started to take them as a PRN had an increased risk of death, but those who went from not taking them to taking them every day had a decreased risk of death. As discussed earlier, it is hypothesized that these results may be due to the potential that inconsistent use of antipsychotic medications has a negative impact on the bodies of older adults, and may also be due to the reasons behind why these medications were being prescribed as a PRN.

Context Models. This set of models was run again using eight different contexts, with the final models being reported from each context and compared with the first final model, which used all participants in this study. These contexts included all participants (set 1), individuals with more than one assessment (set 2), new admissions (set 3), and new admissions and more than one assessment (set 4). Additionally, matching models were then run for those who were only diagnosed with dementia (set 5), dementia and one assessment (set 6), dementia and new admissions (set 7), and dementia and new admissions who had more than one assessment (set 8). The last model (set 9) was run with all participants but used the antipsychotic medication categories, rather than changes to antipsychotic medications.

The contexts using new admissions with more than one assessment, as well as those with dementia that were new admissions with more than one assessment, had best fit with this model,

both explaining 83.6% of the variance, compared to only 77.8% of variance when using all participants. These models may have been able to explain the most variance because they were the contexts contained the most complete information. For example, these contexts included participants that were new residents of CCC and LTC facilities once census level data was being collected throughout Ontario, and were also in the study long enough to have more than one assessment completed. It is interesting that in these contexts, and only these contexts, all of the variables related to antipsychotic medication use lost significance, except for those who went from not using these medications to using them as a PRN throughout the week, which increased the rate of death. No logical explanation of this could be developed.

The context that included only participants with dementia, with no other stipulations, was found have the worst fit in these models explaining only 76.4% of the variance. This was marginally less than set one (77.8%) which used all the participants. It may be that because the diagnostic variables were taken out of the model, some of the sources of variance were naturally lost. These findings did follow the pattern found with the other matched contexts between those with and without dementia.

Study Implications and Future Research

Results from this study may have a dramatic effect on how people view the use of antipsychotic medications with older adults, with and without dementia, and how physicians prescribe them. This is the first study to look at whether there is a difference in death rate based on frequency of medication use for older adults taking antipsychotics. Results consistently showed, over different forms of analysis, that contrary to previous research, antipsychotic medication does not necessarily increase death rate. Rather, it only increases death rate in those individuals taking these medications inconsistently throughout the week, for both individuals

with and without dementia. Furthermore, it appears that regular use (7 days a week) of antipsychotic medications may actually reduce death rate when compared to individuals who are not taking this medication at all. This finding was the strongest for participants with dementia.

Based on the results from this study, it is strongly advised that further research is conducted focusing on the differences in death rate for older adults who are 1) not taking antipsychotics, 2) are taking antipsychotics as a PRN, and 3) taking antipsychotics 7 days a week, for those with and without dementia. The purpose of this would be to confirm and expand this body of knowledge. If other studies find that antipsychotic medications do increase death rates when taken inconsistently, medical professionals will have to be informed and adjust their prescription and dispensing practices accordingly, in order to prevent further deaths related to a very easy fix.

If it is found that results from this study are not an anomaly, and taking antipsychotic medications seven days a week actually reduces the risk of death compared to those not taking it at all, further research would need to explore the factors surrounding why this protective effect is occurring. This may encourage the prescription of antipsychotic medications for specific groups of older adults, reducing death rate in this population significantly. Of course, this would need to be done while monitoring quality of life as living longer can be better in most circumstances, but living longer in a stupor or in pain may not be.

It may also be that taking antipsychotic medications consistently actually reduces the risk of other health conditions or events, such as strokes or heart attacks, hence the findings of lower death rates in these participants, when those using this form of medication as a PRN are factored out. Replicating past studies that looked at the risk of side effects in those using this medication, as a PRN and seven days a week, would be highly beneficial. This will help show whether using

this medication as a PRN also induces more side effects, than when it is used consistently, as was the case with death rate.

In summary, the major findings from this study contradicted what has been found in previous research in relation to antipsychotic medications increasing death rate for older adults with dementia. The current study looked at the frequency antipsychotic medications were taken throughout the week, in the categories of 1) none at all, 2) inconsistently throughout the week – 1 to 6 days, and 3) consistently at seven days a week. This appears to be the first study to have done this, and results suggest through different forms of analyses that those taking antipsychotic medications as a PRN have an increased death rate, however those taking them 7 days a week have a lower death rate, when compared to those who are not taking these medications at all, both for those with and without dementia.

Further research should be conducted to confirm and expand these findings. This may lead to a change in prescription and dispensing rates of antipsychotic medications. It may be that recommendations are made for physicians to stop prescribing these medications on an as needed basis (PRN), and actually encourage the prescribing of antipsychotics for older adults with dementia, and sometimes for those without. This may increase quality of life if it is found that taking these medications inconsistently is increasing other side effects, and expand life by using these medications regularly as a protective agent.

Research Limitations

Despite the contribution to the area of antipsychotic use in older adults with dementia, there are limitations to the current study. The most significant limitation is regarding factors related to the antipsychotic medications. Information regarding the specific type of antipsychotic medication participants were taking was unavailable, nor was it available for the class of

antipsychotic, conventional or atypical. This information may have helped further explain the unique findings of this study or enabled more detailed results regarding death rates in older adults taking these medications.

The dosage of antipsychotic medication that people were taking was also not included in the dataset. This could provide information related to death rate that could also help further explain these unexpected results. For example, it may be that those individuals who were taking antipsychotic medications as a PRN were on a stronger single dose than those individuals who were taking it consistently throughout the week, leading to a higher risk of side effects and death. It may also be found in subsequent studies that the individuals who were taking antipsychotic medications as a PRN may have been closer to death to begin with, hence their inflated death rate, as disruptive behaviours naturally decline with more profound stages of illness so daily antipsychotics use may not have been necessary. In addition, other medications that participants were on were not included in the analysis, as it was out of the scope of this study. Future research may find that there is a correlation between higher death rate when people are taking an antipsychotic medication and another specific type of medication.

Lastly, as the participants in this study were residents of CCC and LTC facilities, the results and potential prescription recommendations may not be fully attributable to community based older adults. There may be some unique factors related to older adults in residential care, such as severity of illness, comorbid illnesses, or age, that may attribute to these results, that would not be consistent for older adults living in the community. It would be beneficial for future research to see if the results from this study can be replicated with a large community based sample.

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