Use of Medications for Management of Alzheimer's Disease in Ontario's Home Care Population

by

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Abstract

Background: Home care is an important care setting for those with Alzheimer's disease (AD). It provides support that allows individuals with AD to remain at home and may delay the transition to long-term care homes. Many clients with AD receive medications that are used for managing the symptoms of AD: cholinesterase inhibitors (ChEIs) and memantine. Ontario's provincial drug benefit plan (ODB) provides subsidies for some of these medications based on specific clinical criteria. These AD medications are costly and can have significant side effects, so it is important to understand how they are being used in practice.

Objectives: The objectives of this study were to report the proportion taking AD medications and which types were taken, show the change in receipt of AD medications over time, and show the covariates that were independently associated with receiving AD medications.

Methods: Analysis of secondary data was performed on the provincial home care dataset. All home care clients receiving long-term home care services were assessed using the RAI-Home Care (RAI-HC), which is a comprehensive and standardized assessment. One assessment from each individual over the age of 65 who was assessed between January 2004 and September 2008 was used, for a final sample size of 321,013.

Results: Overall, 65% of clients with a diagnosis of AD were receiving an AD medication. Logistic regression analysis among those diagnosed with AD showed that increased physical impairment and clinical complexity were associated with decreased odds of receiving AD medication. Contraindicating diagnoses such as congestive heart failure, lack of medical oversight and needing to make economic tradeoffs were also associated with decreased odds of receiving AD medication.

Conclusions: The multivariate model showed trends of rational prescribing, such as clients with contraindicating diagnoses or very high clinical complexity having decreased odds of receiving AD medications. At the same time, evidence of structural barriers to receiving the medications was shown. There is debate about the cost-effectiveness of these medications. The provincial government could consider expanding ODB guidelines to include all AD medications for those with all levels of cognitive impairment, but further analyses involving longitudinal outcomes available in this dataset should be performed to ensure it would be in the public interest.

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Dedication

This thesis is dedicated to my husband Greg for his patience and encouragement, and to my dear daughter Elise for waiting until I finished my revisions to arrive.

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1 Introduction and Overview

Alzheimer's disease (AD) is a progressive and degenerative disease of the brain that is the most prevalent form of dementia in older adults (Lindsay et al., 2004). It is generally slow in onset and progresses from forgetfulness to decreased ability to perform every-day tasks, inability to safely care for oneself and lack of awareness of people and surroundings. AD is sometimes accompanied by behavioural changes such as agitation, aggression and depression (McKhann et al., 1984). It is an important disease to study and understand because it has a large impact on health from levels of the individual and caregiver(s) to the health care system and society.

AD is a very difficult disease to live with because of the loss of memory and judgement in affected persons, but it is also very difficult for the caregiver. Informal caregivers can spend an average of 35 hours a week caring for someone with severe AD (Moore, Zhu & Clipp, 2001). A person with other chronic diseases may need more personal support, but they are able to appreciate and acknowledge the help they are receiving. It is also of great importance to the health care system because of the long duration of the disease and the cost of providing care to those affected by it. The cost to society as a whole with stress and lost time for caregivers is also significant, not to mention the costs associated with formal health and social services for this population.

The Canadian Study of Health and Aging found that 8% of those over 65 have dementia, but the proportions were not equal in subsets of that population. Dementia was found in 2.4% of those between 65 and 74, 11.1% of those between 75 and 84 and 34.5% of those over 85, and almost two-thirds of these cases were AD (Lindsay et al., 2004). This is particularly alarming in light of the aging population. By 2050, the number of people with AD is projected to quadruple, and even a major breakthrough in medications that would delay the onset of AD by six months would still result in a three-fold increase in those with AD by 2050 (Sloane et al., 2002).

As the health care system moves toward accommodating Canadians' desire to stay in their own homes for as long as possible, many more people with AD will receive home care services to delay the transition to residential care facilities. Therefore, home care is an important sector of Ontario's health care continuum. Home care provides health services in a person's home that they might otherwise need to be in a hospital or a nursing home to receive. Home care was referred to as the "next essential service" in Roy Romanow's report on the state of Canadian health care (Romanow, 2002). Home care continues to be a priority in Ontario as shown by the provincial government's $1.1 billion dollar "Aging at Home" strategy which provides funding for locally initiated small and large scale projects designed to help people stay in their own homes (Ministry of Health and Long-Term Care, 2007a).

Cholinesterase inhibitor (ChEI) medications and memantine are first choice pharmacotherapies for AD. According to the Canadian Consensus guidelines, there is evidence for modest effects of ChEIs when prescribed in mild to moderate AD and evidence for use of both ChEIs and memantine in moderate to severe AD (Herrmann, Gauthier & Lysy, 2007; Hogan et al., 2007). These medications are expensive. In 2002, ChEIs accounted for 25% of the mental health-related drug costs while representing less than 6% of mental health related drug prescriptions (Mamdani et al., 2005). Currently, the cost of ChEIs in Ontario is almost five dollars per day, which translates into about $1,600 per person per year (Ministry of Health and Long-Term Care, 2007b) so the cost-effectiveness of these medications given their modest effects is an important consideration.

AD is of particular interest in home care, because supervision and safety precautions can vary widely and there is a growing trend toward helping people stay at home longer. In Ontario, of the approximately 1.6 million people over 65 years of age, about 8% are receiving long-term home care services (Lindsay et al., 2004; Statistics Canada, 2007)

The literature review will give an overview of home care and AD, and provide background on the mechanisms, indications, evidence for use, regulatory framework and utilization of the ChEIs and memantine in Ontario. Additionally, prevalence and patterns of use of these medications will be explored and individual characteristics predicting use of these medications will also be examined.

2 Literature Review

2.1 Home Care

In Roy Romanow's 2002 report, home care is described as the next essential service for the Canadian healthcare system (Romanow, 2002). Home care provides services that allow clients to return home more quickly from hospital or stay at home longer before moving to a residential care setting. It has become an increasingly important part of the health care continuum across Canada. Currently about 900,000 Canadians are receiving some form of home care services and the majority of clients are 65 or older and require long-term supportive care (Canadian Home Care Association, 2008). All ten provinces and three territories provide home care to their residents and acknowledge that home care is an important part of primary care, chronic disease management and aging at home strategies. These strategies are intended to ease the current burden on the existing inpatient and residential care facilities and prepare for a future where demand for health care services will increase.

Home care services are meant to complement assistance and support from informal caregivers such as family members and friends and can include personal support such as bathing or dressing, or nursing services such as wound care or intravenous medications. Because home care is categorized under 'extended health services' in the Canada Health Act, it is not an insured health service. Each province and territory has their own Act, set of guidelines, or policies that direct the delivery of home care services according to the

needs of their population. This contributes to the variations in access and availability of services across the country.

In Ontario, home care services are accessed through the 14 Community Care Access Centres (CCACs), which determine a person's eligibility for funded services and provide case management for a variety of services contracted from provider agencies. They share the same geographic boundaries as the 14 recently created Local Health Integration Networks (LHINs) (See Appendix A for a map). The vast majority of clients who receive services receive them in a private home, but some may receive them while living in a long term care home, assisted living or supportive housing facility. One type of home care service recipient is a placement client, who is assessed in the hospital with the intent to place them in a Long Term Care Home (LTCH). Post-acute clients are those coming home from the hospital who need some short term nursing care such as dressing changes and IV medications. However, the majority are long-stay clients who are expected to be on service for 60 days or longer and tend to require services such as personal support, homemaking, and help with bathing.

2.2 Alzheimer's Disease

AD was first identified as a pathological condition in 1906 by Alois Alzheimer. He described the plaques and tangles in the brain that are now accepted as the hallmark of the disease (Alzheimer, 1906; Maurer, Volk & Gerbaldo, 1997). It is diagnosed by using clinical criteria to identify AD as well as by excluding other diseases that could cause the symptoms that the person is exhibiting. These diseases include Parkinson's disease, or

other forms of dementia such as vascular or Lewy body dementias (Bouchard, 2007; Patterson et al., 1999). Familial AD, which is a rare subtype of AD, can be diagnosed by investigating if there are gene mutations in genes such as presenilins 1 and 2, but other genetic markers, such as the E4 allele of apolipoprotein E are only associated with an increased risk of developing AD (Blennow, de Leon & Zetterberg, 2006).

There are two different sets of clinical criteria currently in use for diagnosing AD. The Diagnostic and Statistical Manual (4th ed.) (DSM-IV) describes dementia as "characterized by impaired memory and at least one of the following cognitive disturbances: aphasia, apraxia, agnosia, and disturbed executive function." To diagnose AD specifically, the dementia criteria should be present, as well as evidence of insidious onset and progressive decline (American Psychiatric Association, 1994). The National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association Work Group (NINCDS-ADRDA) have more complex diagnostic criteria for AD which consist of: dementia based on clinical examination and neuropsychological tests, with onset between ages 40 and 90, deficits in two or more areas of cognition, progressive worsening of memory and other cognitive functions and normal consciousness (McKhann et al., 1984).

A clinical diagnosis can be made using the criteria outlined above, but a pathological diagnosis can only be made by observing the plaques and tangles directly during an autopsy. Possible or probable AD are the diagnoses that are most often made in

practice. AD is often categorized into mild, moderate, or severe based on the stage of the disease. It is also possible for a diagnosis of probable AD to change to a diagnosis of another form of dementia if other symptoms emerge (Feldman et al., 2008). For these reasons, making a diagnosis of AD can be difficult.

2.2.1 Biological mechanisms

The classic hypothesis about the biological mechanism of AD is based on the acetylcholine (ACh) hypothesis. In normal brain signaling, ACh is a neurotransmitter that carries signals from one nerve cell to another. It is released from the end of one cell and travels across the space between nerve cells. When it binds with its receptors on the next neuron, the signal is passed along (Schliebs & Arendt, 2006). The ACh is normally broken down by acetylcholinesterase (AChE) so that too much does not accumulate in the space between the nerve cells (Hardy, 2006).

Bartus compiled evidence from many small studies in the late 1970s and early 1980s to show that significant changes in cholinergic markers were present in animal models of dementia (Bartus, Dean Iii, Beer & Lippa, 1982). These changes or dysfunctions were correlated with neuropathological markers and with the severity of cognitive impairments. AD was considered a cholinergic syndrome because of the selective degeneration of pre-synaptic cholinergic function (Perry, Perry, Blessed & Tomlinson, 1978; Whitehouse et al., 1982).

In AD, there is a relatively selective loss of cholinergic neurons in the basal forebrain nuclei, which is an area of the brain that when damaged in animal studies produced cognitive and learning deficits (Bartus, Dean, Beer & Lippa, 1982). ACh receptor binding is decreased in people with AD and is correlated with decreased cognitive function (Nordberg, 2005).

The observed cognitive deficits in those with decreased ACh receptor binding led to the hypothesis that increasing the availability of ACh in the brain could mitigate the cognitive decline associated with AD (Nordberg, 2006).
The cascade of pathophysiological events that is triggered does not happen to all neurons at the same time so the neurons that remain are good targets for treatment (Silvestrelli, 2006).

After the ACh hypothesis, the next hypotheses about the progression of AD involved amyloid plaques and tau tangles. These hypotheses will be further explained below, but it is not yet clear how the cholinergic dysfunction and the plaques and tangles work together to create AD (Nordberg, 2006; Silvestrelli et al., 2006).

2.2.2 Amyloid plaques

Amyloid plaques result from the accumulation of improperly processed proteins in the brain. The process starts with a large particle called amyloid precursor protein (APP). In healthy persons, the normal secretase-α enzyme cleaves the protein so that it is soluble. More rarely, secretase-β cleaves the APP instead and creates a protein called β-amyloid which is shorter and insoluble. Both are present in normal brains, but in AD there are very high amounts of β -amyloid. The clearing enzymes cannot keep up and are possibly defective. β-amyloid molecules clump together into small toxic aggregates and this is what forms the recognizable plaques
(Gouras, Almeida & Takahashi, 2005; Hardy & Higgins, 1992; Nordberg, 2006; Vardy, Catto & Hooper, 2005). It is not clear if these amyloid plaques are a cause or simply a byproduct of the disease (Hardy, 2006).

2.2.3 Tau Tangles

Another pathological hallmark of AD is the presence of tau tangles within neurons. These tangles are paired helical filaments that impede the normal transportation of nutrients within the neuron (Duara, Barker, Loewenstein & Bain, 2009). Normal tau helps to maintain the structure of the microtubules that transport nutrients within cells, but in those with AD it can become hyperphosphorylated, which changes its structure. This can lead to microtubule disassembly and destabilization of the neuronal cytoskeleton which can then lead to neuronal death (Z. Sun et al., 2008).

2.2.4 Loss of cholinergic neurons

Researchers are now finding interactions between the β-amyloid and tau tangle hypotheses. Experiments in mice show that in neurons where tau has been removed, the presence of β-amyloid alone does not cause degeneration, but where both are present, the neurons degenerate (Rapoport et al., 2002). Hypotheses about how they interact include the presence of β-amyloid leading to hyperphosphorylation of tau through oxidative stress or receptors on neuronal membranes. The neuronal membrane receptor hypothesis suggests that β-amyloid binds to certain subtypes of acetylcholine receptors and starts a cascade of changes which leads to the activation of glycogen synthase kinase-3 beta (GSK-3beta). This kinase has been shown to phosphorylate sites on tau and create tangles (Huang & Jiang, 2009).

2.3 Medications for use in those with AD

Even with continued research on the underlying biology of AD, there are still no treatments that delay the onset or underlying progression of the disease. The two types of medication that are currently available are cholinesterase inhibitors (ChEIs) and memantine (Birks, 2006).

2.3.1 Cholinesterase inhibitors (ChEIs)

Once the cholinergic hypothesis was accepted as a possible explanation for the development of AD, attempts were made to artificially increase cholinergic transmission. Early animal trials used direct injection of choline or lecithin and other methods. These were moderately successful, but were not well tolerated in humans (Bartus, Dean Iii et al., 1982). The first strategy to be approved for human use was a medication that helped keep the acetylcholine that the body already produced working longer in the brain.

Tacrine was the first medication approved for use in AD. It was approved in the US in 1997. This medication was not well accepted because of problems with liver toxicity and other side effects, though decreased mortality was found among those in nursing homes with AD who received tacrine when compared to those who did not receive the medication (Geldmacher, 2007; Ott & Lapane, 2002). In response to the adverse events, Health Canada did not approve tacrine for use in Canada. The next medication to be developed in this ChEI group was donepezil (Birks & Harvey, 2006a). It built on the strengths of tacrine and did not have the same problematic side effects (Geerts & Grossberg, 2006).

The three ChEI medications that are currently on the market in Canada are donepezil (brand name: Aricept, Eisai Inc and Pfizer Inc.), galantamine (brand name: Reminyl, Shire Pharmaceutical Inc.) and rivastigmine (brand name: Exelon, Novartis Pharmaceutical

Ltd). Donepezil was approved for use in Canada in 1997, while rivastigmine and galantamine were not available until 2000 and 2001, respectively.

The three ChEIs each have a slightly different pharmacological mechanism, but they all have the same general effects. As described previously, in normal cholinergic transmission, acetylcholine travels across the space between the nerve cells and ChE is the enzyme that breaks down acetylcholine so that the receptors are not overstimulated (Hardy, 2006). During the progression of AD, some nerve cells die so there is less acetylcholine available to make its way to the receptors. The less acetylcholine there is in the space between the neurons, the less likely it is that signals will pass from one neuron to the next. One way to increase the amount of acetylcholine in that space is to stop it from being broken down. The ChEIs work by stopping ChE from breaking down acetylcholine. The three medications were not found to have significantly different efficacies in a meta-analysis involving 13 randomized controlled trials (Birks, 2006).

2.3.2 Memantine

A more recent development is the N-Methyl-D-Aspartate (NMDA) receptor antagonist called memantine. It has a very different mechanism of action, but like the ChEIs it does not slow the progression of the disease (Parsons, Stoffler & Danysz, 2007). Memantine was approved for use in Canada in November 2004. It has been available in the United States and Europe since 2003 ("Alzheimer's drug approved with reservations," 2003;

Cosman, Boyle & Porsteinsson, 2007; Farlow, 2004). The brand name for memantine is Ebixa (Lundbeck Ltd.).

The exact mechanism of action of memantine is not as well characterized as that of the ChEIs. However, it is known that memantine is an inhibitor of glutamate N-Methyl-D-Aspartate (NMDA) receptors. These receptors are also in the brain and normally they are activated by glutamate and cause the nerve cell to fire. In a person with AD, there are elevated levels of glutamate. This can cause the neurons to fire too often, which can destroy them. Memantine blocks the receptors so the glutamate cannot access the receptor (Mobius, Stoffler & Graham, 2004).

2.4 Indications and Contraindications for use of AD medications

In Canada, Health Canada evaluates submissions from pharmaceutical companies for new medications and decides if the medication is approved for use in Canada. If it is to be approved, there are further decisions about what information goes on the label and what the drug can be used for. This is called the indication. Donepezil, galantamine and rivastigmine are indicated for use in mild-moderate AD and donepezil is also indicated for use in moderate-severe AD. Memantine is indicated for use in moderate-severe AD only.

The Canadian consensus guidelines suggest that ChEIs can be used in mild-moderate AD (Hogan, 2007), but in mid 2007 Health Canada agreed to expand the indication for donepezil to include severe AD (Health Canada, 2007b). There have also been some

reports of ChEIs and memantine being used for vascular and Lewy body types of dementia and in traumatic brain injury (Bourgeois, Bahadur & Minjares, 2002; Kaye et al., 2003; McKeith et al., 2000; Wilkinson et al., 2003).

The only true contraindication for the cholinesterase inhibitors is hypersensitivity or previous adverse events related to the drugs themselves. However, caution should be taken when prescribing to those with coronary artery disease and congestive heart failure because they may slow the heart rate (Gill et al., 2009); and those with unexplained syncope should also not receive them (Hogan et al., 2008). ChEIs may be expected to increase gastric acid secretion, so when prescribed to those at high risk of developing ulcers, careful monitoring should occur. Those with asthma or obstructive pulmonary disease should also be closely monitored as higher levels of acetylcholine can increase inflammation in the airway (Canadian Pharmacists Association, 2007). Rivastigmine has not been tested in those with severe liver or renal impairment, so it is contraindicated in those individuals (Canadian Pharmacists Association, 2005). Weight loss is associated with both AD (White, Pieper & Schmader, 1998) and with ChEIs so careful monitoring of weight should be done for those where it is a concern (Canadian Pharmacists Association, 2008). Memantine has fewer systemic effects, so gastrointestinal and respiratory effects are not of particular concern, but caution should still be used in those with cardiovascular conditions and seizures (Canadian Pharmacists Association, 2004).

Other medications can have an impact on how effective ChEIs can be. Anticholinergics, which are often used to help with urinary incontinence, have the opposite effect of ChEIs as they decrease the amount of acetylcholine available. These medications should never be used in those who are taking a ChEI (Han et al., 2001). Benzodiazepine medications are also sometimes used to deal with behavioural issues in those with AD, but they are also potentially inappropriate for use in those who are taking a ChEI because they can cause cognitive impairment (Gray, Lai & Larson, 1999).

2.4.1 Selected outcome measurements

It is important to understand the outcome measurements used in clinical trials to measure the efficacy of the medications. The Mini-Mental State Exam (MMSE) is the most commonly used scale, and is intended to measure cognitive functioning (Folstein, Folstein & McHugh, 1975). The MMSE evaluates cognitive functioning in five domains (attention and calculation, orientation, immediate recall, delayed recall, and language). It usually takes 10 minutes to perform, and results in scores ranging from 0 (severely impaired) to 30 (normal). It is sometimes used as the cutoff in determining whether AD is mild, moderate or severe. Mild-moderate disease is usually categorized as having MMSE scores anywhere between 10 or 11 and 24 or 26, while those with severe AD have MMSE scores less than 10 (Birks, 2006; Herrmann, Gauthier et al., 2007).

The cognitive portion of the Alzheimer's Disease Assessment Scale (ADAS-Cog) is a more sensitive measure of cognition and was developed for use in a population with AD. It consists of 11 items (spoken language, comprehension of spoken language, recall of test

instructions, word finding, following commands, naming objects, construction, ideational praxis, orientation, word recall, and word recognition). The score ranges from 0 to 70 and higher scores indicate greater impairment (Cummings, 1996; Logsdon, 1995; Rosen, Mohs & Davis, 1984).

2.5 Overview of evidence for use in AD

Authors from the Cochrane collaboration have produced four meta-analyses on ChEIs, one for each medication separately (Birks, Grimley Evans, Iakovidou & Tsolaki, 2000; Birks & Harvey, 2006a; Loy & Schneider, 2006), and one analyzing them concurrently (Birks, 2006). Overall, the evidence suggests that these medications do have a small but significant beneficial effect on cognitive function.

2.5.1 Donepezil

There have been several large-scale randomized controlled trials testing donepezil against a placebo in those with AD. Most of the studies that have been published show a small to moderate benefit in cognitive impairment from using the medication (Engedal et al., 2000; Feldman et al., 2001; Rogers et al., 1998). As these medications were approved and grew popular, concern grew in countries with single-payer drug plans (such as Canada and the UK) about the actual cost effectiveness of the medication to the system as a whole.

In the UK, the AD2000 study was publicly funded to examine donepezil in a more real-world situation. The authors concluded that based on outcome measures, such as delay

of nursing home placement or use of doctor's visits or hospital stays, donepezil was not cost effective (AD2000 Collaborative Group, 2004). However, there has been mixed reaction to this study. Birks (2006) decided not to include AD2000 in her Cochrane review because of a vastly different sample size than the investigators proposed (500 participants instead of 3,000) and a very complicated regimen and repeated washout periods that make interpretation of the results very difficult.

2.5.2 Galantamine, Rivastigmine

Overall, galantamine and rivastigmine were also shown to provide modest improvements in cognition and behavior in those with AD in both mild-moderate and severe AD, but many fewer trials have been performed using these medications as compared to those using donepezil (Lanctot et al., 2003; Takeda et al., 2006).

2.5.3 Evidence for Memantine

There have been several clinical trials for memantine, most showing a positive effect on cognitive decline (Cosman et al., 2007; Van Dyck, Tariot, Meyers & Malca Resnick, 2007). A Cochrane review of clinical trials for memantine has also been published (McShane, Areosa Sastre & Minakaran, 2006). McShane concludes that memantine has a small beneficial effect on cognition at six months in moderate to severe AD.

There is evidence for the efficacy of these medications in clinical trial settings. However, there is evidence that the representation of patients with dementia in clinical trials of

donepezil was not the same when compared to those who actually took the medication daily. Based on a cohort of all people receiving donepezil in Ontario, 50% to 80% of those that were actually taking it would have been excluded from all clinical trials because they were older than the upper age limit. Therefore, the small but significant effect demonstrated in clinical trials may not precisely reflect what might happen in the course of normal usage because of their older age, and presumably comorbid conditions that would also have led to their exclusion from the clinical trials (Evans, 1995; Gill et al., 2004).

2.6 Regulatory framework

2.6.1 Canada

In Canada, health care is the responsibility of the provinces but for some applications, it makes sense to use a more centralized approach. For approval of new drugs, the provinces have agreed to use the information contained in the Common Drug Review (CDR). Pharmaceutical companies submit information and evidence to the CDR committee at Health Canada that decides if the product is safe for use in Canada. The provinces can then use that information and decide if they will add the medication to their formulary, which is a list of medications that are included in a provincial drug plan (Kelly, Lazzaro & Peterson, 2007).

Each province makes the decision about whether or not to add the medication to their formulary independently, taking many factors into account, including cost-effectiveness

- whether the costs of providing the medications are outweighed by savings in other areas such as the costs of formal and informal care.

There is debate on cost effectiveness for AD medications. Studies done using modeling techniques generally showed cost-effectiveness for medication use, but there were few empirical studies, and their results were inconclusive. Therefore, further large-scale empirical studies need to be done in order to determine if these medications are cost-effective or not (Geldmacher, 2008; Wimo, 2004; Wimo & Norlund, 2007).

2.6.2 Ontario Drug Benefit Plan

In Ontario, the program that provides access to medications for those over 65 is called the Ontario Drug Benefit (ODB) plan. People receive subsidized medicines subject to their income. Some medications are provided through a program called Limited Access which means that certain clinical criteria need to be met in order for the medication to be provided. The ChEIs are such medications. In order for someone over 65 to receive subsidized donepezil, rivastigmine, or galantamine in Ontario, their physician needs to submit a form stating that their MMSE score is between 10 and 26. This form needs to be resubmitted after three months, and can subsequently be renewed for six month intervals. The medication continues to be subsidized until the person's MMSE score drops below 10. The cost to the ODB is about $5.00 per day. Donepezil, rivastigmine and galantamine were added to the ODB formulary list in 1999, 2001, and 2002, respectively.

2.6.3 Drug Benefit plans in other provinces

Across Canada, all those 65 years of age or older have access to subsidized drug programs, but access to specific drugs and the proportion covered can differ between provinces (Demers et al., 2008). Each province has its own formulary and rules for access.

Rules for access to ChEIs and memantine are generally the same across provinces, with a few notable exceptions. Memantine is available for purchase, but is not covered under any provincial drug plans. ChEIs are generally available as limited access medications through the provincial formularies. The criteria for access differs between provinces, but generally requires periodic cognitive tests showing mild-moderate disease and discontinues subsidized medication once a certain threshold is reached. Specific details for access in each province and territory are shown in Appendix B. The Canadian Rx Atlas does show large disparities in age standardized per capita spending on ChEIs between provinces. The spending in Saskatchewan is 52% lower than the national average, while the spending in Ontario is 30% higher than the national average. These differences are almost wholly due to differences in volume purchased and this could be attributed to the stricter criteria enforced in Saskatchewan as compared to the less restrictive criteria that exist in Ontario (Morgan, Raymond, Mooney & Martin, 2008).

2.7 Utilization rates of ChEIs and memantine

Medications can be used for many different reasons. Different forces can affect the use of medications within a population. Regulations can make a drug available or unavailable in a specific jurisdiction and, within a government-funded drug plan such as ODB, can restrict use based on characteristics of the disease. Those with low incomes can benefit from the medications within the regulatory framework of the ODB, but those with more resources are free to purchase the medications or receive them through private insurance plans when they are prescribed. Physician familiarity is another factor that can affect utilization, as they are the ones who decide which medication gets prescribed. Physicians are more likely to prescribe medications that they are familiar with (Hillmer et al., 2006; Sondergaard, Vach, Kragstrup & Andersen, 2009).

In Ontario there are studies that have looked at utilization of ChEIs, but none have been found about utilization of memantine. One study used ODB data linked to vital statistics and service utilization data to create a cohort of all Ontario residents 66 years of age or older who had a new prescription for a ChEI (Herrmann, Gill et al., 2007). The residents were followed until discontinuation, death or the end of the study period. Over half of those who died during the study period were still taking the medication when they died. Only 55% discontinued the medication before the end of follow-up (31 Mar 2005). This study also showed that 1.9% of the total Ontario population age 66 or older were

initiated on ChEI therapy in the initial cohort (Herrmann, Gill et al., 2007; Lanctot & Herrmann, 2007). Other observational studies considering persistence of ChEI therapy showed that 33% to 47% of the individuals studied remained on a ChEI with no significant gaps in therapy at one-year after initiation (Herrmann et al., 2009; Mauskopf, Paramore, Lee & Snyder, 2005; Singh et al., 2005; Suh et al., 2005). Increased persistence was associated with greater numbers of physician visits (Herrmann, Gill et al., 2007; Suh et al., 2005). Sex differences in persistence were not found to be significant (Kogut, El-Maouche & Abughosh, 2005; Mucha et al., 2008; Suh et al., 2005; Sun, Lai, Lu & Chen, 2008). Older age was associated with decreased persistence in one study (Y. Sun et al., 2008), increased persistence in another (Kogut et al., 2005), and had no association in others (Mucha et al., 2008; Suh et al., 2005). However, few studies examined characteristics associated with persistence beyond age and sex.

2.7.1 Characteristics of those who received ChEIs

Few studies have been found to date that investigate differences in demographic, clinical, behavioural, physical functioning, cognitive, and regional variables and how they influence receipt of an AD medication in a community-based population. Therefore it is difficult to hypothesize about which characteristics may predict receipt of these medications.

The vast majority of studies that have been published are randomized controlled trials, which artificially separate people into receipt or non-receipt groups. These trials are important for investigating the effects of medications, but they have strict inclusion and exclusion criteria which do not necessarily reflect the characteristics of those who use the medications in the community (Evans, 1995). In fact, investigation of a cohort of recipients of cholinesterase inhibitors in Ontario found that between 51% and 78% would have been excluded from most clinical trials based on their age or comorbidities, so it is important to show the characteristics of those who are receiving the medications as part of normal clinical practice (Gill et al., 2004).

Some observational studies have been performed, but they tend to use administrative prescription claims databases that contain minimal clinical information such as age, gender and diagnoses from previous hospital discharges. These studies cannot compare those that are using the medications to those who are not because only those who have been dispensed the medications appear in the prescription claims database (Gill et al., 2004; Herrmann, Gill et al., 2007; Mamdani et al., 2005).

There are a few studies that have reported on differences between groups that receive AD medications and those that do not. The Aged in Home Care (AdHOC) study which was carried out using the RAI-HC assessment in 11 European countries found that individuals who were cognitively impaired, unmarried and did not have a physician review their medications were more likely to discontinue their medications so some of

these same characteristics may protect against receipt of AD medications in the Ontario population (Cooper et al., 2005).

Using evidence from clinical trials, women were reported to be more likely to have adverse events, and since those who are older are less likely to have been included in the clinical trials, it is possible that physicians may be less likely to prescribe AD medications in those populations (Birks, 2006). Coronary artery disease, congestive heart failure, unexplained syncope, gastrointestinal disease, asthma or obstructive pulmonary disease, severe renal impairment, and weight loss may be expected to predict non-receipt of AD medications, because there are warnings against use of these medications in the presence of those conditions (Canadian Pharmacists Association, 2007).

Socioeconomic status could also have an impact on whether people receive AD medications. A study done in Quebec showed that medication utilization decreased when cost sharing measures were introduced to a public drug program for low-income residents (Blais, Couture, Rahme & LeLorier, 2003).

Regional differences could also have an impact on receipt of AD medications. As mentioned previously, Ontario's home care services are organized into 14 CCACs, which serve clients within geographic borders that are aligned to the borders of the 14 Local Health Integration Networks (LHINs). There are many differences between the LHINs

that could influence the receipt of services including size, both in land area and in population, proportion of the population that is over the age of 65, median income, urban/rural split, and the presence of teaching hospitals. The table showing characteristics of the 14 LHINs with data mostly drawn from Statistics Canada's Community Health Survey can be found in Appendix C. No studies were found that compared the rates of AD medication use across different LHINs. Other studies have found differences in rates of preventive care (influenza shot, mammogram, pap smear) and in minimally invasive biopsy for breast cancer diagnosis between LHINs (Holloway, Saskin & Paszat, 2008; Wang, Nie & Upshur, 2009). However, no differences between LHINs in gynecologic cancer outcomes were observed (Kwon et al., 2008).

2.8 Summary

Home care is an important care setting in Ontario that enables many elderly people to remain at home and delay the transition to long-term care homes. Many of those who receive home care services have a chronic disease, such as AD. There are two types of medications that are used for managing the symptoms of AD: ChEIs and memantine. According to the Canadian Consensus guidelines, all three ChEI medications are recommended treatments for mild to moderate AD. Donepezil and memantine are recommended for severe AD. Clinical trial evidence has focused on the effects of these medications in relatively young and healthy individuals, but population- based investigations using administrative prescription records show that they are being used in

a much older and more impaired population. These medications are fairly costly to taxpayers and their economic benefit to the health care system has not yet been established empirically. They can also have side effects for the persons receiving them, so it is important to understand how they are being used in practice. Those receiving home care services tend to be older and more impaired than the general population of seniors, so it is an appropriate population for these investigations.

3 Study Rationale

Answering the questions proposed below will make a contribution to knowledge about the use of AD medications in Ontario's home care population. An understanding can be gained of how widely ChEIs and memantine are used in those receiving HC services in Ontario, differences in characteristics between those who receive them and those who do not, and how utilization patterns have changed over time.

Studies that investigate the use of AD medications with administrative claims databases (specifically the Ontario Drug Benefit (ODB) database) provide information on how many people in Ontario use the medications and how many discontinue them (Herrmann et al., 2009; Herrmann, Gill et al., 2007). However, there is little information on the proportion of those in specific sub-populations (such as home care) who are reported to have AD, and who take AD medications. The claims databases also lack adequate clinical information to see if those who receive the medications are different in some way from those that have AD and do not receive them. The overall purpose of this study is to fill some of the gaps outlined above.

3.1 Research Questions

The following questions will be addressed in this research:

1. What proportion of those in home care with and without a diagnosis of AD are taking a ChEI or memantine?

2. Which types of AD medications are being taken among those with an AD diagnosis?
3. Are clients with AD that score 4 or higher on the CPS scale (comparable to 10 or lower on the MMSE) less likely to receive AD medications than those with other CPS scores?
4. How has the proportion of those taking AD medications changed from 2004-2008?
5. What covariates are associated with a greater likelihood of receiving an AD medication?

3.2 Relevance of research

It is important to consider past and current use of AD medications in the Ontario HC population to inform current decisions related to health policy and service delivery and to identify opportunities for future research on use of these medications.

If the results show that a specific subpopulation is underserved (e.g., women, different geographic regions) and there is no body of literature that suggests that the medications work any differently in that population, this research can highlight a health inequality for health care decision makers. In addition, home care case managers could target groups who may benefit from an AD medication but are not receiving one with health education strategies to encourage them to speak with primary care clinicians about their treatment options. It is also possible that these medications may be overused. In that case, information about the prevalence of use of AD medications in subpopulations

where the risks or costs of use may outweigh the benefits could be beneficial for decision-makers.

4 Methods section

4.1 Data source

4.1.1 The RAI-HC

The source of the data used for these analyses is an assessment instrument called the Resident Assessment Instrument for Home Care (RAI-HC) (see appendix D). This is a comprehensive, standardized assessment that was developed for use in the home care setting and consists of over 300 items. It covers many domains including cognitive and physical functioning, mood and behavior patterns, health conditions, and service utilization (Morris et al., 1997). The RAI-HC was developed by an international group of researchers called interRAI and is in use in many countries throughout the world (Bernabei, 2008). It has been found to be reliable and valid (Landi et al., 2000) and is intended to help caregivers create care plans by assisting them in collecting the same information about each client. It can also help planners at any level by allowing them to see the characteristics of the population they are serving and compare themselves accurately to other jurisdictions. interRAI has also developed other assessment instruments for use in different care settings that have similar core items and allow for comparisons across different care settings (Gray et al., 2009; Hirdes et al., 2008). interRAI assessments are always performed by trained assessors. These assessors are instructed to use the best available source to complete each item (a chart, the client, the family, etc.) and to use their best clinical judgement when completing an assessment.

4.1.2 Ontario RAI-HC datacut

In the Ontario home care context, there is a rich source of data based on the RAI-HC. Starting in 2003, the Ontario Ministry of Health and Long Term Care required that every person who was classified as a long-stay client (expected to receive services for 60 days or longer) received an initial assessment and semi-annual reassessments. One group that also receives RAI-HC assessments that are present in this datacut are those that are assessed while they are in an acute care hospital for the purposes of placement in a Long Term Care Home. Currently, this translates into about 150,000 assessments per year. The anonymized datacut used for the analyses described below was received in September 2008 and consists of over 900,000 records (Canadian Home Care Association, 2008).

4.1.3 Analytic Sample

To create the analytic sample, some exclusions were made from the dataset. Those under the age of 65 were excluded because they make up a small proportion of the long-stay home care population, but they tend to be very different than the rest of the population. Also, they are not eligible to receive medications through the Ontario Drug Benefit Program so their use of medications for AD could differ for that reason. Those who were in the hospital and receiving the assessment for the purpose of nursing home placement were excluded from the final model, but were analyzed separately in the other tables because they tend to have different characteristics than the community-based clients.

The RAI-HC was implemented in 2003, but CCACs did not get up to full capacity until 2004. There were no differences in the availability of ChEI medications through the ODB formulary in that time period. Therefore only those that were assessed between January 2004 and September 2008 were used in the analytic sample. For the cross-sectional analyses, only the first assessment on record for each unique individual was used, so as not to over-represent those that received service for longer periods of time. For the analyses that compare each year between 2004 and 2008, a different dataset was constructed. The same exclusion criteria were applied, but a cross-sectional dataset for each year was constructed independently so an individual contributed to the sample one time in each year that they were assessed.

4.2 Variables

4.2.1 Individual items

All the items that were used in these analyses (with the exception of the CCAC assessing the client and the location of the assessment, which are administrative variables contained in the datacut) are from the RAI-HC (see appendix D). The assessment is arranged with lettered sections, numbered items, and lettered sub-items. For example, behavioural symptoms is the third item in section E – Mood and Behaviour Patterns. The first sub-item is wandering, so the label for wandering would be e3a. In the lists of items below, the label will be given in parentheses to aid in the location of the exact item on the assessment.

The AD diagnosis variable used to categorize clients into AD or non AD groups is one of 28 diagnosis variables listed on the RAI-HC. Assessors use their best clinical judgement to code these diagnoses using the most accurate, reliable and valid information source available. Information sources can include the client's chart, or discharge information from other care settings. Assessors are trained not to indicate the presence of a diagnosis without an appropriate information source, so clients who have AD but have not yet been diagnosed would not be classified as having AD in this dataset.

Demographic variables that were used included sex (bb1), approximate age (calculated from the date of the assessment (a1) and the month and year of the birth date (bb2a)), marital status (bb4), living arrangement (cc6), and if the person has had to trade off medical expenses for food and/or shelter (p7).

Social variables included if the person's caregiver shows signs of distress (g2a or g2c) and if the client or caregiver thinks that the client would be better off in a different living environment (o2b).

Clinical variables included if the client has had a physician review their medications in the last six months (q3), diagnoses of the most common comorbid conditions from the assessment (section j) (hypertension, arthritis, diabetes, coronary artery disease, and cancer) as well as congestive heart failure (CHF), asthma/emphysema/chronic

obstructive pulmonary disease (COPD), renal failure, and bladder or bowel incontinence (i1a or i1b rated as 'occasionally incontinent' or more).
Behavioural symptoms (verbally abusive, physically abusive, socially inappropriate, resists care) (e3b-e) were also included.

The administrative variables used are the CCAC identifier (a map showing the CCAC boundaries is found in appendix A), and the location of the assessment. Most assessments are performed in the community with the intention of determining needs for initiating or continuing home-based services. However, some clients are assessed in the hospital as part of the admission process for long-term care homes.

The medication variables were compiled into binary variables for each of the three ChEIs as well as for memantine using the text entered medication names in items q51a through q525a. Medication data are collected by the case managers while they are completing the rest of the assessment. All medications, both prescription and over the counter, that were taken in the seven days before the assessment are included. Subsequently, two variables were created: one that is true if any one of the three ChEIs is present and one that is true if ChEIs or memantine is present. Lastly, one combination variable was constructed with four mutually exclusive groups: ChEI and Memantine, ChEI only, Memantine only, none). The dependent variable in the multivariate models was the variable that was coded as true if either ChEI or memantine use was recorded on the assessment.

4.2.2 Summary scales

A variety of embedded scales are available in the RAI-HC. These measures can be used cross-sectionally to summarize the person's clinical characteristics in various domain areas. The scales used in these analyses will be the Cognitive Performance Scale (CPS) which measures the person's cognitive skills, the Activities of Daily Living Hierarchy scale (ADLH) which measures early, medium, and late loss ADLs, the Changes in Health, End stage disease and Signs and Symptoms scale (CHESS) which is a measure of frailty and instability in health, the Depression Rating Scale (DRS) which can indicate possible depression, and the Pain scale which measures the frequency and severity of pain.

The CPS has seven levels (0-6, where 0 is cognitively intact). It uses items from the memory, cognitive skills for daily decision making, and communication sections as well as the eating ADL and has been validated against the MMSE. A score of 4 on the CPS correlates to an MMSE score of just under 10, the generally accepted cutoff for severe AD (Herrmann, Gauthier et al., 2007; Landi et al., 2000; Morris et al., 1994).

The ADLH is also a seven level scale (0-6, where 0 is independent in ADLs and 6 is the most dependent). It is a hierarchical algorithm based on the eating, locomotion in home, toilet use and hygiene ADL items from the RAI-HC (Landi et al., 2000; Morris, Fries & Morris, 1999).

The CHESS is a six level scale (0-5, where larger values indicate increasing frailty). It uses symptoms that may indicate frail or unstable health such as vomiting, dehydration, leaving food uneaten, weight loss, shortness of breath, and edema as well as decline in cognitive or ADL function and end-stage disease (Hirdes, Frijters & Teare, 2003).

The DRS is a 15 level scale (0-14, where larger values indicate more symptoms of possible depression), which has been validated against the Hamilton and Cornell depression scales. It uses items that indicate depression, anxiety or sad mood and a score of 3 or more is generally used to indicate possible depression (Burrows et al., 2000; Martin et al., 2008).

The Pain scale is a four level scale (0-3, where larger values indicate more frequent or intense pain), which was validated against the Visual Analogue Scale for pain. It is based on the items for frequency and intensity of pain (Fries et al., 2001).

4.3 Statistical Analyses

All statistical analyses were conducted using SAS version 9.1 software. Cross-sectional analyses were conducted using all home care clients from the analytic sample described above.

Univariate analyses were performed on selected variables to describe the characteristics of those with and without AD among those assessed in the community and in the

hospital setting. Univariate analyses were also performed to describe the types of AD medications being taken by four mutually exclusive groups: those with AD, those with no AD but with other dementia, those with no dementia but a CPS score of 1 or more, and those with no dementia and a CPS score of 0. These groups were constructed separately in the community and hospital settings.

Analyses were also performed to describe the distribution of CPS scores and the proportion receiving any AD medication among each score among those with AD in both community and hospital assessed clients. A chi-square test was used to determine if those with CPS scores of 4-6 were less likely to receive AD medications than those with CPS scores of 0-3.

In the year-over-year analyses, cross sectional datacuts were created as described in the analytic sample section above. Results for community and hospital assessed clients were reported separately. The proportion of clients in each of the mutually exclusive dementia groups that received AD medications was reported in each year that exists in the sample. Next, the sample was restricted only to those with AD and the proportion of clients receiving the different types of AD medications was reported in each year separately for those with CPS scores of 0-3 and 4-6.

The multivariate models were constructed in the group with AD and assessed in the community. The association of individual characteristics with receipt of any AD

medication as the outcome was investigated using binary logistic regression. Characteristics that had more than two categories were entered as class variables. All variables that were significant at the bivariate level (α=0.05) were entered into the multivariate model. Those that were not significant in the full model were removed one by one. The crude odds ratios were reported along with the adjusted odds ratios, maximum likelihood estimates and p-values in the final models. Three models were created. One included all those with AD and assessed in the community and the other two stratified that population by CPS score (0-3 and 4-6).

4.4 Ethics Approval

Ethics approval was obtained from the University of Waterloo Office of Research Ethics (certificate #15864).

5 Results

5.1 Sample characteristics

The original datacut received from OACCAC contained over 900,000 assessments. After restricting the sample to: a) assessments performed between January 2004 and September 2008; b) the first assessment available for each unique individual, and c) those who were 65 years of age or older at the time of the assessment, the final sample size was 321,013.

Tables 1 through 3 show the distributions of the demographic, social, clinical and psychological variables, as well as the scale scores for those with a diagnosis of AD compared to all other clients in both the community-assessed and hospital-assessed populations. The majority (90.2%, n=289,529) of the clients were assessed in the community, and similar proportions of clients had a diagnosis of AD recorded in both settings (7.9% in the community vs 8.5% in the hospital). Overall, those in the hospital had a mean age of 82.4 years (95% CI 82.3-82.5), as compared to 81.3 (95% CI 81.2-81.3) among those in the community.

5.1.1 Demographics

As shown in Table 1, there were higher proportions of women in both the community groups (64.1% and 65.8%) as compared to those in the hospital assessed groups (60.0% and 59.0%).

Table 1: Sample Characteristics (Demographic Variables)

		Community-Assessed (n=289,529)		Hospital-Assessed (n=31,484)	
		Alzheimer's disease	All Others	Alzheimer's disease	All Others
% (n)		7.9 (22,977)	92.1 (266,552)	8.5 (2,665)	91.5 (28,819)
Sex (Female)		64.1 (14,727)	65.8 (175,319)	60.0 (1,600)	59.0 (17,001)
Age Categories					
	65-74	14.1 (3,229)	21.8 (58,098)	11.2 (298)	17.7 (5,098)
	75-84	55.3 (12,706)	46.1 (122,839)	51.3 (1,367)	44.1 (12,703)
	85+	30.7 (7,042)	32.1 (85,615)	37.5 (1,000)	38.2 (11,018)
Marital Status					
	Married	49.6 (11,392)	38.7 (103,253)	41.7 (1,112)	29.9 (8,604)
	Widowed	6.9 (1,580)	10.9 (29,082)	11.3 (300)	16.4 (4,738)
	Other	43.5 (10,002)	50.4 (134,179)	47.0 (1,253)	53.7 (15,476)
Living Arrangement					
	Board & Care	10.3 (2,362)	6.1 (16,197)	9.3 (247)	7.9 (2,268)
	Facility	4.2 (956)	2.6 (6,846)	6.8 (182)	4.4 (1,262)
	Home alone	16.8 (3,849)	36.3 (96,806)	24.9 (663)	39.1 (11,262)
	Home others	67.7 (15,559)	54.1 (144,088)	53.4 (1,423)	42.9 (12,355)
	Missing	0.5 (104)	0.4 (1,112)	0.6 (15)	0.8 (226)
	Other	0.6 (147)	0.6 (1,503)	5.1 (135)	5.0 (1,446)
Economic Tradeoffs		0.6 (134)	1.3 (3,404)	item not collected	

Those with AD tended to have the smallest proportions in the youngest age group (65-74) (14.1% and 11.2% as compared to 21.8% and 17.7%, respectively) among both the community and hospital assessed groups. Of those with AD and assessed in the community, almost 50% were married and 42.5% were widowed, but in all of the other three groups, a higher proportion were widowed than were married. In both assessment settings, those with AD were less likely to reside in a private home alone than those without AD. The 'made economic tradeoffs' item was not collected in the hospital assessed groups. In the community groups, the proportion who reported making those tradeoffs was small, but was less than half as large in the AD group (0.6%) as in the rest of the community population (1.3%).

5.1.2 Summary scales

As would be expected, the distribution of CPS scale scores was more heavily weighted towards the higher, or more impaired, end among both AD groups but the difference was even more pronounced in the hospital assessed group (Table 2). Those in the hospital assessed group also had much more physical impairment than those in the community. One quarter of the hospital group had an ADL hierarchy score of 5 or 6 (severe or very severely impaired) while only 3.3% of those with AD in the community scored at that level. The non-AD hospital group had over three times more clients with the highest clinical complexity than did the community group.

Table 2: Sample Characteristics (Summary Scales)

	Community-Assessed (n=289,529)		Hospital-Assessed (n=31,484)	
	Alzheimer's disease	All Others	Alzheimer's disease	All Others
Cognitive Performance Scale (CPS)				
0-1	8.7 (2,000)	73.2 (195,049)	3.4 (90)	37.5 (10,795)
2-3	69.6 (16,000)	24.1 (64,311)	58.5 (1,558)	48.4 (13,938)
4-6	21.7 (4,975)	2.7 (7,151)	38.2 (1,017)	14.2 (4,084)
Activities of Daily Living Hierarchy (ADLH)				
0-1	69.1 (15,867)	81.3 (216,532)	22.6 (601)	21.4 (6,156)
2-4	27.6 (6,340)	16.9 (45,004)	52.4 (1,397)	55.6 (16,014)
5-6	3.3 (766)	1.8 (4,883)	25.0 (667)	23.1 (6,648)
Changes in Health End-stage Disease and Signs and Symptoms (CHESS)				
0-1	60.9 (13,989)	63.9 (170,314)	26.0 (692)	34.8 (10,020)
2-3	36.4 (8,353)	33.8 (89,938)	65.8 (1,754)	57.7 (16,623)
4-5	2.7 (628)	2.3 (6,211)	8.2 (219)	7.6 (2,175)
Depression Rating Scale (DRS)				
0	57.7 (13,242)	66.9 (178,052)	53.2 (1,418)	56.1 (16,165)
1-2	25.6 (5,879)	21.2 (56,376)	29.3 (780)	27.6 (7,945)
3-14	16.7 (3,832)	12.0 (31,878)	17.5 (467)	16.3 (4,701)
Pain Scale				
0	59.8 (13,728)	35.6 (94,701)	56.0 (1,493)	42.1 (12,121)
1	14.2 (3,252)	12.8 (34,086)	14.6 (390)	14.2 (4,092)
2	22.5 (5,177)	39.0 (103,824)	26.2 (697)	35.8 (10,323)
3	3.5 (812)	12.7 (33,812)	3.2 (85)	7.9 (2,278)

Just under 8% of those in hospital had CHESS scores of 4-5 while just over 2% of those in the community had that score. When measuring the DRS, the AD groups showed a higher prevalence of any depressive symptoms than the non-AD groups. The non-AD group in the community showed the lowest prevalence of possible depression (DRS of 3-14). Those in both AD groups reported a higher prevalence of no pain as compared to the non-AD groups.

5.1.3 Social and clinical variables

Table 3 shows that those who were diagnosed with AD had higher rates of caregiver distress than others in their care setting, but overall, those who were assessed in hospital showed higher rates of caregiver distress than those assessed in the community. Similarly, the clients themselves or the caregivers of those assessed in the hospital were much more likely to say that the person was “better off in another living environment” (93.1% of those with AD, 87.5% of all others) than if they were assessed in the community (34.2% vs 17.2%). Just under three percent had had no medication review in the last 6 months in the community. The item was not collected in hospital.

Incontinence (measured as at least occasionally incontinent in bladder or bowel) was present in 35.6% of those with AD in the community and in 64.9% of those with AD in the hospital. Those without AD had a prevalence of 23.9% and 53.1% respectively.

Table 3: Sample Characteristics (Social and Clinical Variables)

	Community-Assessed (n=289,529)		Hospital-Assessed (n=31,484)	
	Alzheimer's disease	All Others	Alzheimer's disease	All Others
Caregiver distress	16.9 (3,878)	8.3 (22,067)	35.5 (947)	21.4 (6,150)
Better off elsewhere	34.2 (7,857)	17.2 (45,848)	93.1 (2,482)	87.5 (25,216)
No medication review	3.0 (682)	2.8 (7,581)	item not collected	
Incontinence	35.6 (8,176)	23.9 (63,687)	64.9 (1,730)	53.1 (15,298)
Diagnoses				
Hypertension	44.1 (10,125)	54.1 (144,281)	50.4 (1,342)	58.1 (16,735)
Arthritis	36.7 (8,421)	50.5 (134,595)	26.4 (704)	32.3 (9,299)
Diabetes	16.1 (3,690)	23.5 (62,649)	19.6 (521)	25.3 (7,292)
CAD	16.9 (3,878)	25.1 (66,796)	21.7 (578)	28.3 (8,147)
Cancer	7.1 (1,619)	15.6 (41,472)	9.6 (256)	14.1 (4,076)
CHF	6.4 (1,464)	13.3 (35,322)	9.4 (251)	17.6 (5,061)
Behaviours				
Wandering	13.4 (3,085)	1.5 (3,858)	21.7 (577)	6.2 (1,799)
Verbally abusive	11.1 (2,548)	2.2 (5,760)	10.7 (286)	4.8 (1,375)
Physically abusive	3.5 (809)	0.4 (1,155)	7.3 (194)	2.4 (704)
Socially inappropriate	5.9 (1,359)	0.9 (2,472)	11.3 (301)	4.8 (1,393)
Resists care	17.6 (4,052)	3.3 (8,693)	24.7 (658)	11.6 (3,330)

Table 3 also shows the five most prevalent diagnoses in the study sample. Congestive heart failure was also reported because of its status as a contraindication for ChEI use. In general, the prevalence of the reported diseases is higher for persons with AD in the hospital compared to those with AD in the community. For persons without AD, prevalence of these diseases in hospital and community settings are similar. In addition, the diagnoses listed here are more prevalent in the non-AD population compared to AD clients.

All the behaviour items are more prevalent in the AD groups than the non-AD groups. In addition, the occurrence of these behaviours are usually highest in the hospital settings compared with the community. Resisting care was the most common behavior across all four groups (17.6% and 24.7% in the AD groups in community and hospital respectively, and 3.3% and 11.6% in the non-AD groups in community and hospital respectively).

5.2 Prevalence of AD medication use

In Table 4, the sample is further divided into mutually exclusive subgroups. All those with an AD diagnosis are in the first group, those with no AD and a diagnosis of other dementia are in the second group. The last two groups include those with neither diagnosis but consider CPS score for further differentiation into: those with any cognitive impairment (CPS score of 1 or more), and those with no cognitive impairment (CPS score of 0). As in the previous table, clients assessed in the community and those assessed in the hospital are reported separately. The biggest difference between the distributions of the subgroups in community and hospital assessed clients was in the others with no AD or dementia diagnosis and no cognitive impairment. Of those in the community, 51.1% were in that group, while only 19.7% of those in the hospital were in the no cognitive impairment group.

The next section of the table shows the proportion within each subgroup that reported receiving any of the three ChEI medications, and then shows the breakdown of which specific medications were received. In both assessment locations, those in the AD subgroup showed the highest prevalence of ChEI use, but use was more common among those with AD in the community (66.0%) as compared to those with AD in the hospital (45.0%). Donepezil was by far the most popular ChEI. It was used by 42.3% of the community AD subgroup, while rivastigmine and galantamine were used by 8.6% and 15.3% respectively.

Table 4: Prevalence of type of AD Medication use in different groups among Community and Hospital assessed individuals

	Community (n=289,529)				Hospital (n=31,484)			
	AD	Other Dementia (no AD)	Others with CPS1+	Others with CPS 0	AD	Other Dementia (no AD)	Others with CPS1+	Others with CPS 0
% (n)	7.9 (22,977)	11.3 (32,628)	29.7 (86,087)	51.1 (147,801)	8.5 (2,665)	26.7 (8,402)	45.1 (14,200)	19.7 (6,216)
Any Cholinesterase inhibitor	66.0 (15,174)	35.0 (11,404)	4.7 (4,052)	0.6 (849)	45.0 (1,199)	21.5 (1,803)	3.5 (492)	0.6 (35)
Donepezil	42.3 (9,729)	21.5 (7,026)	2.8 (2,434)	0.3 (472)	28.6 (762)	13.2 (1,106)	2.1 (300)	0.3 (18)
Rivastigmine	8.6 (1,966)	4.8 (1,572)	0.7 (619)	0.1 (160)	5.8 (154)	3.1 (258)	0.5 (71)	0.1 (4)
Galantamine	15.3 (3,522)	8.7 (2,839)	1.2 (1,009)	0.2 (218)	10.8 (287)	5.3 (446)	0.9 (123)	0.2 (13)
Number of ChEIs								
0	34.0 (7,803)	65.1 (21,224)	95.3 (82,035)	99.4 (146,952)	55.0 (1,466)	78.5 (6,599)	96.5 (13,708)	99.4 (6,181)
1	65.9 (15,132)	34.9 (11,371)	4.7 (4,042)	0.6 (848)	44.8 (1,195)	21.4 (1,796)	3.5 (490)	0.6 (35)
2	0.2 (41)	0.1 (33)	0.0 (10)	0.0 (1)	0.2 (4)	0.1 (7)	0.0 (2)	0.0 (0)
Memantine	5.6 (1,293)	1.6 (519)	0.2 (133)	0.0 (11)	3.3 (89)	1.0 (83)	0.1 (8)	0.0 (1)
Any ChEI or Memantine	67.2 (15,444)	35.4 (11,555)	4.8 (4,106)	0.6 (855)	46.2 (1,232)	21.9 (1,838)	3.5 (495)	0.6 (36)
Medication Status								
ChEI +Memantine	4.5 (1,023)	1.1 (368)	0.1 (79)	0.0 (5)	2.1 (56)	0.6 (1)	0.0 (5)	0.0 (0)
ChEI only	61.6 (14,151)	33.8 (11,036)	4.6 (3,973)	0.6 (844)	42.9 (1,143)	20.9 (21)	3.4 (487)	0.6 (35)
Memantine only	1.2 (270)	0.5 (151)	0.1 (54)	0.0 (6)	1.2 (33)	0.4 (0)	0.0 (3)	0.0 (1)
None	32.8 (7,533)	64.6 (21,073)	95.2 (81,981)	99.4 (146,946)	53.8 (1,433)	78.1 (78)	96.5 (13,705)	99.4 (6,180)

Home care clients who received a ChEI tended to use only one. The three do have similar mechanisms of action so it makes sense not to use more than one of these medications at once.

Memantine was used less often than ChEIs (5.6% in the AD in community group, 3.3% in the AD in hospital group), but it showed the same decreased rate of use across the subgroups as the ChEIs.

When receipt of any ChEI or memantine was calculated, 67.2% of those in the AD in community group had one of those medications, compared to 46.2% of those in the AD in hospital group. Those without a diagnosis received these medications less than 5% of the time in either setting even if they had signs of impaired cognition.

For the medication status variable, four mutually exclusive groups were created. ChEI use alone still had the highest prevalence within each subgroup. In the community AD group there is an interesting pattern where the majority of the clients who received memantine received it in combination with a ChEI (Overall 5.6% received memantine; 4.5% received it with a ChEI, 1.2% received memantine only). This same pattern of more use of memantine in combination with ChEIs does occur in the hospital AD group, but not to the same extent. Overall 3.3% received memantine; 2.1% received it with a ChEI, and 1.2% received memantine only.

5.3 AD medication use by CPS scores

Table 5 shows the CPS distribution among the community and hospital AD groups. Generally, the CPS scores are distributed more towards the higher end in the hospital group. Of those with AD in the community, 45.6% had a CPS score of 2, while 24.9% had the same score among those assessed in the hospital. At the most impaired, only 1.8% of the community group showed a CPS score of 6, while 8.3% of the hospital group had that score.

The next table (Table 6) uses the same community and hospital AD groups, but this time the numbers reported are the proportions receiving any AD medication within the CPS category. For example, within the community group, of those with a CPS score of 0, 51.7% received an AD medication.

Table 5: Cognitive Performance Scale (CPS) score distribution among Community and Hospital AD groups

CPS	AD in community (n=22,977), %(n)	AD in Hospital (2,665), %(n)
0	1.8 (422)	0.6 (17)
1	6.9 (1,578)	2.7 (73)
2	45.6 (10,480)	24.9 (664)
3	24.0 (5,520)	33.6 (894)
4	3.8 (879)	8.0 (214)
5	16.0 (3,682)	21.8 (582)
6	1.8 (414)	8.3 (221)

Table 6: Proportion receiving AD medications within each Cognitive Performance Scale (CPS) score among those with AD[1]

CPS	Received AD Medications (Community) (n=15,442), %(n)	Received AD Medications (Hospital) (n=1,232), %(n)
0	51.7 (218)	35.3 (6)
1	69.1 (1,090)	45.2 (33)
2	70.4 (7,376)	53.5 (355)
3	69.7 (3,846)	46.6 (417)
4	62.8 (552)	42.1 (90)
5	60.8 (2,239)	42.4 (247)
6	29.2 (121)	38.0 (84)

[1] The proportions in this table are related to the numbers in each CPS group from table 5. Of the 422 individuals in the community with CPS 0, 218 (51.7%) received an AD medication.

Overall, the proportions receiving AD medications were higher in the community. This was true for every individual CPS level, except for those with a CPS score of 6. A curvilinear pattern was observed in both settings, with lower proportions of those with CPS scores at the extreme ends of the scale receiving AD medications. A bigger drop-off in this curvilinear pattern was observed in the community group as compared to the hospital group. In the community group, 60.8% of those with a CPS score of 5 received AD medications and 29.2% of those with a CPS score of 6 received them. In the hospital group 42.4% of those with a CPS score of 5 received AD medications and 38.0% of those with a CPS score of 6 received them. In both settings the CPS scores with the highest proportion of AD medication use were 1 to 3, which corresponds to mild-moderate cognitive impairment.

Table 7 takes the data from Table 6 and collapses the CPS score categories into two groups in order to answer the question of if those with CPS scores of 4-6 are less likely to receive AD medications than those with CPS scores of 0-3. These splits are of interest because they correspond to the provincial drug formulary guidelines on when ChEIs are intended to be covered. In both community and hospital settings a lower proportion of those that were most cognitively impaired received the medications (58.5% and 41.4%, respectively) than those that were less impaired (69.6% and 49.2%, respectively). The differences were tested in each setting using a chi-squared test and the p-values for each setting were less than 0.0001.

Table 7: Proportion receiving AD medications among collapsed Cognitive Performance Scale (CPS) score groups, Chi-Square tested

	Community	Hospital
CPS 0-3	69.6 (12,532)	49.2 (811)
CPS 4-6	58.5 (2,912)	41.4 (421)
	p <0.0001	p <0.0001

5.4 AD medication use across time

In Table 8 and Table 9, the proportion who received a ChEI or memantine within the subgroups described in Table 4 were reported by year from 2004 to 2008. Memantine was extremely rare in 2004 as it was only approved for use in Canada in November of that year, but its use increased with each year in both the community and hospital groups. In 2005, 4.8% of the community AD group received memantine, but by 2008, 12.2% of that group received it. ChEI use increased only moderately across the years studied among the community AD group (63.4% to 69.1%), but the relative increase in use was more dramatic among those with other dementia (30.4% to 42.7%). In all years and settings, the use of ChEIs and memantine was negligible in the non-impaired populations.

Table 8: Prevalence of ChEI and Memantine use among mutually exclusive subgroups 2004-2008 In Community Assessed Individuals

Community	2004 (n=97,444)		2005 (n=111,644)		2006 (n=117,399)		2007 (119,430)		2008 (104,192)	
% (n)	ChEI	Memantine	ChEI	Memantine	ChEI	Memantine	ChEI	Memantine	ChEI	Memantine
AD	63.4 (4,871)	0.8 (59)	64.8 (5,478)	4.8 (408)	66.6 (6,053)	9.4 (853)	68.4 (6,391)	10.6 (992)	69.1 (5,499)	12.2 (972)
Other Dementia	30.4 (3,094)	0.1 (13)	33.6 (4,012)	1.2 (144)	36.8 (4,728)	2.6 (333)	39.1 (5,421)	3.0 (413)	42.7 (5,475)	3.6 (464)
Others with CPS1+	4.0 (1,175)	0.0 (3)	4.5 (1,502)	0.1 (31)	5.1 (1,856)	0.2 (67)	5.5 (2,068)	0.3 (100)	6.3 (2,097)	0.3 (100)
Others with CPS 0	0.5 (275)	0.0 (0)	0.6 (328)	0.0 (3)	0.7 (383)	0.0 (5)	0.7 (401)	0.0 (5)	0.8 (390)	0.0 (6)

Table 9: Prevalence of ChEI and Memantine use among mutually exclusive subgroups 2004-2008 in Hospital Assessed Individuals

Hospital	2004 (n=4,329)		2005 (n=8,047)		2006 (n=10,964)		2007 (12,191)		2008 (n=10,197)	
% (n)	ChEI	Memantine	ChEI	Memantine	ChEI	Memantine	ChEI	Memantine	ChEI	Memantine
AD	47.2 (214)	0.0 (0)	40.5 (324)	2.5 (20)	44.5 (461)	4.8 (50)	46.2 (539)	6.2 (72)	50.8 (460)	5.4 (49)
Other Dementia	18.9 (217)	0.0 (0)	19.1 (437)	0.7 (16)	22.5 (652)	1.7 (48)	23.2 (774)	1.3 (42)	27.1 (770)	1.8 (52)
Others with CPS1+	2.5 (48)	0.0 (0)	2.3 (84)	0.1 (2)	3.8 (188)	0.1 (3)	4.4 (231)	0.1 (7)	4.8 (208)	0.1 (6)
Others with CPS 0	0.3 (2)	0.0 (0)	0.9 (12)	0.0 (0)	0.6 (13)	0.0 (0)	0.9 (21)	0.0 (0)	1.1 (22)	0.1 (1)

In Table 10 and Table 11, only those with AD were included in the analysis. The proportions who received each type of medication were reported by year from 2004 to 2008, but separately for those with CPS scores of 0-3 (Table 10) and 4-6 (Table 11). The most striking differences across time in the community were seen in the proportion receiving ChEI with memantine. Among those in the community with CPS 0-3, in 2004 0.5% received the combination, but by 2008, 8.5% received it. Among those with CPS 4-6, 1.0% received a ChEI and memantine in 2004 while in 2008, 14.7% received the combination. The difference in prevalence between 2005 and 2008 is also larger in the CPS 4-6 group as compared to the CPS 0-3 group in the hospital-assessed clients (1.2% to 2.7% in the CPS 0-3 group and 1.9% to 4.9% in the CPS 4-6 group.

Table 10: Prevalence of type of AD medication use in each year 2004-2008, in Community and Hospital Assessed Individuals with AD, with Cognitive Performance Scale (CPS) scores between 0 And 3

	Community					Hospital				
% (n)	2004 (n=	2005	2006	2007	2008	2004	2005	2006	2007	2008
ChEI +Memantine	0.5 (27)	3.1 (191)	6.2 (422)	7.3 (524)	8.5 (523)	0.0 (0)	1.2 (6)	2.4 (15)	2.8 (20)	2.7 (14)
ChEI only	67.0 (3,666)	64.9 (3,971)	63.1 (4,331)	63.4 (4,552)	62.4 (3,833)	48.5 (130)	44.1 (216)	44.6 (279)	44.5 (313)	54.8 (283)
Memantine only	0.1 (3)	0.9 (54)	1.7 (119)	1.9 (133)	2.0 (125)	0.0 (0)	0.4 (2)	2.4 (15)	1.1 (8)	1.2 (6)
None	32.4 (1,774)	31.1 (1,899)	29.1 (1,995)	27.5 (1,973)	27.1 (1,665)	51.5 (138)	54.3 (266)	50.6 (317)	51.6 (363)	41.3 (213)
Donepezil	47.4 (2,595)	46.0 (2,810)	44.3 (3,045)	43.2 (3,099)	41.7 (2,564)	32.8 (88)	29.6 (145)	30.8 (193)	31.7 (223)	35.7 (184)
Rivastigmine	8.1 (443)	8.1 (495)	8.7 (596)	8.9 (642)	8.8 (539)	4.9 (13)	6.5 (32)	5.0 (31)	5.5 (39)	6.2 (32)
Galantamine	12.2 (665)	14.3 (877)	16.4 (1,124)	18.8 (1,351)	20.6 (1,268)	10.8 (29)	9.8 (48)	11.3 (71)	10.2 (72)	15.9 (82)

Table 11: Prevalence Of Type Of AD Medication Use In Each Year 2004-2008, In Community And Hospital Assessed Individuals With CPS Scores Between 4 And 6

	Community					Hospital				
	2004	2005	2006	2007	2008	2004	2005	2006	2007	2008
ChEI +Memantine	1.0 (22)	5.5 (128)	11.2 (248)	12.8 (277)	14.7 (266)	0.0 (0)	1.9 (6)	3.4 (14)	5.8 (27)	4.9 (19)
ChEI only	52.2 (1,156)	50.8 (1,188)	47.5 (1,052)	48.1 (1,038)	48.3 (877)	45.4 (84)	30.9 (96)	37.4 (153)	38.7 (179)	36.9 (144)
Memantine only	0.3 (7)	1.5 (35)	2.9 (64)	2.7 (58)	3.2 (58)	0.0 (0)	1.9 (6)	1.5 (6)	3.7 (17)	2.6 (10)
None	46.5 (1,031)	42.2 (986)	38.5 (852)	36.4 (785)	33.8 (614)	54.6 (101)	65.3 (203)	57.7 (236)	51.8 (240)	55.6 (217)
Donepezil	36.7 (813)	37.7 (880)	38.2 (847)	36.3 (784)	36.1 (656)	29.2 (54)	21.9 (68)	23.5 (96)	25.1 (116)	26.7 (104)
Rivastigmine	7.2 (160)	8.1 (190)	8.2 (182)	10.1 (218)	10.4 (189)	8.7 (16)	4.5 (14)	5.4 (22)	6.1 (28)	5.9 (23)
Galantamine	9.3 (207)	10.8 (252)	12.3 (272)	14.6 (316)	16.7 (303)	7.6 (14)	6.4 (20)	12.0 (49)	13.4 (62)	9.5 (37)

From 2004 to 2007, the majority of hospital assessed clients with CPS scores between 0 and 3 received neither ChEIs or memantine. However, in 2008 the majority in that group did receive either ChEI or memantine. Among those with CPS scores of 4-6 in the community, the majority did receive AD medications in each year studied and use has increased over time. In 2004, 53.5% received AD medications and by 2008, 66.2% received them. Donepezil was the most commonly received AD medication across all years, assessment settings, and CPS scores.

While the prevalence of donepezil and rivastigmine use remained fairly constant across the years reported, there was an observed increase in galantamine use in all four groups. The largest increase was seen in the community CPS 0-3 group where 12.2% of the group reported galantamine use in 2004 as compared to 20.6% in 2008.

5.5 Multivariate models predicting receipt of AD medications in the community sample

Candidate independent variables were entered into a logistic regression model (Table 12) that predicted the receipt of any AD medication among long-stay Ontario home care clients that were assessed in the community. The community sample alone was used because the economic tradeoffs item was found to be protective against receiving AD medication, but it was not collected in the hospital version of the assessment. Using only the community sample allowed that item to remain in the model.

The independent variables that were considered were found to be significant ($p<0.05$) in bivariate testing and included: gender, age group, marital status, living arrangement, presence of caregiver distress, CPS, ADL, CHESS, DRS 3+, Pain, congestive heart failure, incontinence, hypertension, coronary artery disease, emphysema/asthma/COPD, renal failure, economic tradeoffs, no medication oversight, and CCAC where the assessment was performed. The crude odds ratios were reported in Table 12. Interactions were tested but none were significant at the $p<0.05$ level so they were not included in the model.

The CPS was transformed because it has a curvilinear relationship with receipt of AD. A quadratic term (or squared term) for CPS was added to the model described above, in which the first order term for CPS was already included. Both the first order term and the quadratic term were significant.

In the final logistic regression model, as shown in Table 12, all of the independent variables entered were significant and independently predicted the receipt of AD medications except for living arrangement, incontinence, and presence of caregiver distress.

Women had decreased odds of receiving the medications as compared to men (odds ratio =0.89). Those in the 65-74 year old age range had the highest odds of receiving the medications, and the odds of receiving them decreased as the age group increased.

With all the scale scores except CPS, which will be discussed later, increasing impairment was associated with decreased odds of receiving AD medications. Increasing ADL Hierarchy scores, which indicate increasing impairment, were associated with decreased odds of receiving AD medications – most dramatically in those scoring 5 or 6 on the ADL Hierarchy scale. Those individuals had an odds ratio only 0.37 times as high as those who scored 0 or 1 on the scale. CHESS scores of 4 or 5 were associated with an odds ratio of 0.80 as compared to those with the lowest CHESS scores. A score of 3 or more on the DRS indicates a possible depression, and those who scored at that level had 0.90 times decreased odds of receiving AD medications. The pain scale was entered as the full 0-3 range, and so with each unit increase in the scale score, the odds of receiving AD medications was 0.93.

Table 12: Multivariate Model Predicting Use Of Any AD Medication Among Those Assessed In The Community

	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)	Parameter Estimate	p-value
Female	0.79 (0.75-0.84)	0.89 (0.84-0.96)	-0.11	0.001
Age (65-74 = reference)				
75-84	0.88 (0.80-0.96)	0.90 (0.82-0.98)	0.08	<.0001
85+	0.56 (0.51-0.61)	0.63 (0.57-0.69)	-0.27	<.0001
Married	1.43 (1.36-1.52)	1.28 (1.20-1.37)	0.25	<.0001
CPS[2]		--	0.41	<.0001
CPS squared		--	-0.07	<.0001
ADL (0-1 = reference)				
2-4	0.70 (0.66-0.74)	0.78 (0.73-0.84)	0.17	<.0001
5-6	0.22 (0.19-0.26)	0.37 (0.31-0.44)	-0.59	<.0001
CHESS (0-1 = reference)				
2-3	0.90 (0.85-0.95)	0.96 (0.90-1.02)	0.04	0.191
4-5	0.60 (0.51-0.71)	0.80 (0.68-0.95)	-0.13	0.022
DRS 3+	0.90 (0.83-0.96)	0.90 (0.83-0.97)	-0.10	0.008
Pain Scale	0.91 (0.88-0.94)	0.93 (0.90-0.96)	-0.07	<.0001
CAD	0.91 (0.84-0.98)	0.92 (0.85-1.00)	-0.08	0.039
CHF	0.57 (0.51-0.64)	0.67 (0.59-0.75)	-0.41	<.0001
Emphysema/Asthma/COPD	0.86 (0.78-0.95)	0.88 (0.79-0.97)	-0.13	0.014
Hypertension	1.06 (1.00-1.12)	1.07 (1.01-1.14)	0.07	0.016
Renal Failure	0.58 (0.48-0.70)	0.64 (0.53-0.78)	-0.44	<.0001
No Medication Oversight	0.53 (0.45-0.61)	0.54 (0.46-0.63)	-0.61	<.0001
Made Economic Tradeoffs	0.61 (0.44-0.85)	0.65 (0.46-0.92)	-0.43	0.014
CCAC (Toronto Central = reference)				
Waterloo Wellington	1.26 (1.09-1.47)	1.14 (0.98-1.33)	-0.01	0.834
South West	1.40 (1.22-1.61)	1.24 (1.07-1.43)	0.07	0.156
South East	1.22 (1.04-1.43)	1.09 (0.92-1.29)	-0.06	0.377
North West	1.46 (1.18-1.81)	1.27 (1.02-1.59)	0.10	0.289
North Simcoe Muskoka	1.44 (1.21-1.71)	1.24 (1.04-1.48)	0.07	0.299
North East	1.42 (1.20-1.67)	1.27 (1.07-1.51)	0.10	0.142
Mississauga Halton	1.26 (1.09-1.45)	1.25 (1.08-1.45)	0.08	0.127
Hamilton Niagara Haldimand Brant	1.18 (1.04-1.33)	1.03 (0.91-1.17)	-0.12	0.003
Erie St. Clair	1.29 (1.10-1.51)	1.16 (0.98-1.37)	0.00	0.939
Central West	1.17 (0.98-1.38)	1.07 (0.90-1.28)	-0.07	0.290
Champlain	1.32 (1.16-1.50)	1.18 (1.03-1.35)	0.02	0.591
Central	1.19 (1.05-1.35)	1.12 (0.98-1.28)	-0.03	0.477
Central East	1.29 (1.13-1.47)	1.13 (0.99-1.30)	-0.02	0.696
		c-statistic		0.627

[2] the odds ratio for CPS is not available because of its transformation in the equation

Of the five diagnoses included in the model (CHF, hypertension, CAD, emphysema/asthma/COPD and renal failure) all but hypertension were associated with decreased odds of receiving AD medications. Specifically, those with congestive heart failure (CHF) had an odds ratio of 0.67. The 'made economic tradeoffs' item was also protective of receiving AD medications (Odds Ratio=0.65).

There were also important regional differences in the use of these medications. Most of the individual p-values were not significant, but the wald chi-square value for the overall class variable was 24.9 with 13 degrees of freedom and a p-value of 0.02 so it is appropriate to keep the regional variable in the model. The Toronto Central CCAC was chosen as the reference group because the odds of receiving AD medications there were found to be the lowest among all the CCACs during bivariate testing. As compared to Toronto Central, the odds ratio for receiving an AD medication ranged from 1.03 in the Hamilton Niagara Haldimand Brant CCAC to 1.27 in the North East and North West CCACs.

Goodness of fit calculations indicated good predictive power of the final model. The c-statistic was 0.63, where 0.5 indicates chance prediction and 1 indicates perfect prediction.

Figure 1 illustrates the CPS quadratic relationship. It shows the curvilinear relationship between CPS and receipt of AD medications by reporting the odds ratio for receiving the AD medications separately for each level of CPS. A CPS score of 0 was set as the reference category, and the odds increased among those with scores of 1, 2, or 3, then started to decrease among those with scores of 4, 5, and 6.

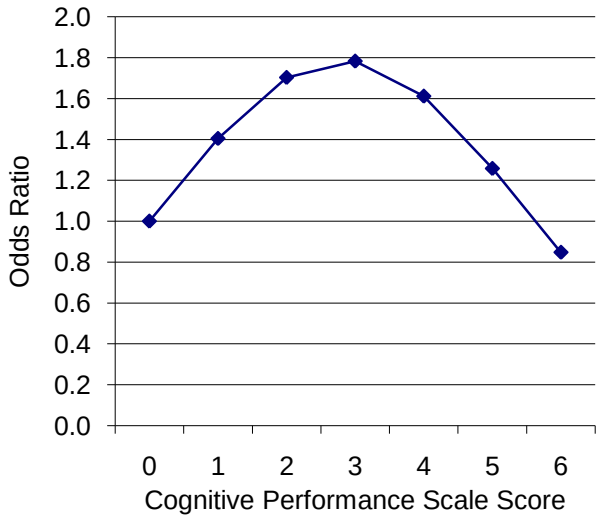

Figure 1 Quadratic relationship between the CPS and receipt of an AD medication: odds ratio by level of CPS

Separate models were constructed for those assessed in the community with CPS scores of 0-3 and for those with scores of 4-6 to see if there were differences in the predictors of AD medication receipt between those with mild-moderate AD and more severe disease.

The model for those with CPS scores of 0-3 (n=18,000) can be seen in Table 13. It was very similar to the full model in Table 12. The only variables that were not significant after controlling for all the other items were hypertension and made economic tradeoffs.

The 95% confidence limits of the adjusted odds ratios in this CPS 0-3 model all overlap with the 95% confidence limits of the full model in Table 12 so the adjusted odds ratios were not statistically different than the adjusted odds ratios found in the full model. The c-statistic for the CPS 0-3 model was 0.61, which is slightly lower than for the larger model.

Table 13: Logistic Regression among those assessed in the community with AD and a Cognitive Performance Scale score of 0-3 (n=18,000)

	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)	Parameter Estimate	p-value
Female	0.81 (0.76-0.87)	0.89 (0.82-0.96)	-0.12	0.002
Age (65-74 = reference)				
75-84	0.87 (0.79-0.96)	0.91 (0.82-1.01)	0.08	0.001
85+	0.58 (0.52-0.65)	0.65 (0.58-0.72)	-0.26	<.0001
Married	1.43 (1.34-1.52)	1.31 (1.22-1.41)	0.27	<.0001
ADL (0-1 = reference)				
2-4	0.78 (0.72-0.84)	0.82 (0.76-0.89)	0.15	0.017
5-6	0.35 (0.25-0.49)	0.43 (0.30-0.61)	-0.50	<.0001
CHESS (0-1 = reference)				
2-3	0.86 (0.80-0.91)	0.93 (0.87-1.00)	0.05	0.196
4-5	0.58 (0.47-0.70)	0.75 (0.61-0.92)	-0.17	0.013
DRS 3+	0.86 (0.79-0.94)	0.89 (0.82-0.97)	-0.12	0.011
Pain Scale	0.88 (0.85-0.91)	0.91 (0.88-0.94)	-0.10	<.0001
CAD	0.84 (0.77-0.91)	0.87 (0.80-0.95)	-0.14	0.001
CHF	0.54 (0.48-0.61)	0.64 (0.57-0.73)	-0.44	<.0001
Emphysema/Asthma/COPD	0.81 (0.73-0.91)	0.86 (0.77-0.97)	-0.15	0.010
Renal Failure	0.57 (0.46-0.71)	0.65 (0.52-0.81)	-0.43	<.0001
No Medication Oversight	0.53 (0.44-0.63)	0.52 (0.44-0.63)	-0.65	<.0001
CCAC (Toronto Central = reference)				
Waterloo Wellington	1.35 (1.14-1.61)	1.29 (1.08-1.54)	-0.01	0.888
South West	1.51 (1.28-1.77)	1.44 (1.22-1.69)	0.10	0.076
South East	1.30 (1.08-1.56)	1.25 (1.03-1.51)	-0.04	0.585
North West	1.58 (1.25-2.00)	1.55 (1.22-1.97)	0.17	0.083
North Simcoe Muskoka	1.51 (1.24-1.83)	1.42 (1.16-1.73)	0.09	0.260
North East	1.37 (1.14-1.66)	1.36 (1.12-1.65)	0.05	0.536
Mississauga Halton	1.47 (1.24-1.75)	1.44 (1.21-1.72)	0.11	0.098
Hamilton Niagara Haldimand Brant	1.26 (1.09-1.45)	1.17 (1.01-1.35)	-0.11	0.015
Erie St. Clair	1.38 (1.14-1.66)	1.30 (1.07-1.57)	0.00	0.972
Central West	1.29 (1.06-1.57)	1.23 (1.00-1.51)	-0.05	0.503
Champlain	1.43 (1.23-1.66)	1.32 (1.13-1.55)	0.02	0.701
Central	1.28 (1.10-1.49)	1.23 (1.05-1.43)	-0.06	0.244
Central East	1.38 (1.18-1.60)	1.30 (1.11-1.52)	0.00	0.984
			c-statistic	0.610

The model for those with CPS scores of 4-6 (n=4,977) is shown in table 14. Many fewer variables remained in the model than remained in the CPS 0-3 model. DRS, pain, CAD, and emphysema/asthma/COPD were all not significant at the bivariate level so they were not entered into the CPS 4-6 model. After controlling for all the other factors entered into the model only age, marital status, ADL, CHF, hypertension, renal failure and no medication oversight remained significant. The 95% confidence limits for the adjusted odds ratios for all the variables in this model overlapped with the 95% confidence limits for the adjusted odds ratios in the larger model in table 12.

The c-statistic for this model was 0.65, which is slightly higher than the c-statistic for the full model.

Table 14: Multivariable Model Predicting AD Medication use in those assessed in the Community, with AD and a Cognitive Performance Scale Score of 4-6 (n=4,977)

	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)	Parameter Estimate	p-value
Age (65-74 = reference)				
75-84	0.85 (0.72-1.01)	0.88 (0.74-1.05)	0.102	0.015
85+	0.47 (0.40-0.57)	0.57 (0.47-0.69)	-0.335	<.0001
Married	1.65 (1.47-1.85)	1.31 (1.14-1.50)	0.271	0.000
ADL (0-1 = reference)				
2-4	0.68 (0.60-0.78)	0.74 (0.65-0.84)	0.241	<.0001
5-6	0.23 (0.18-0.27)	0.26 (0.22-0.32)	-0.788	<.0001
CHF	0.67 (0.53-0.85)	0.74 (0.58-0.95)	-0.302	0.017
Hypertension	1.24 (1.10-1.39)	1.24 (1.10-1.40)	0.214	0.001
Renal Failure	0.56 (0.37-0.87)	0.58 (0.37-0.91)	-0.546	0.019
No Medication Oversight	0.58 (0.43-0.77)	0.59 (0.44-0.80)	-0.528	0.001
			c-statistic	0.65

6 Discussion

There have been many randomized controlled trials of AD medications, but few studies have investigated the utilization patterns in normal clinical practice. This study contributes to the literature by being the first to describe utilization of AD medications in Ontario home care clients. None so far have described utilization patterns in conjunction with individual clinical characteristics in this population. The objectives of the study were to: describe those diagnosed with AD in the home care population, report the proportion taking AD medications and which types were taken, show the change in receipt of AD medications over time, and to show the covariates that are independently associated with receiving AD medications.

6.1 Characteristics of the Sample

The sample of home care clients included was drawn using the first assessments for everyone 65 years or older who was a long-stay or hospital-assessed home care client in Ontario between January 2004 to September 2008. The prevalence of AD in this sample was close to 8%, which is higher than was found in the Canadian Study of Health and Aging (Lindsay et al., 2004). This is expected because those already receiving home care services are more likely to have illnesses than a random sample of all those over the age of 65. Both community and hospital assessed AD groups have a low proportion of clients in the youngest age category. This could be expected because of the nature of AD as an age-related disease that is much more common among the 75-84 and 85+ age groups (Lindsay et al., 2004).

Clients with AD were more likely to show signs of possible depression and behaviours such as wandering and resisting care. The hospital-assessed group had higher proportions of clients who were severely impaired in both cognition and activities of daily living. As well, those in the hospital scored higher on the CHESS scale and were more likely to have incontinence than those in the community. The hospital group also had much higher proportions indicating caregiver distress and clients or caregivers responding that the client would be better off in a setting different than their normal living environment.

With all these differences, it is clear that those assessed in the community and those assessed in the hospital are very different populations and it is appropriate to investigate them separately. Those who are very severely impaired and whose informal caregivers are not able to continue caring for the client safely at home are likely to be placed in a Long-Term Care Home and are less likely to appear in the community sample.

6.2 Prevalence and type of AD medication use

When investigating the prevalence of AD medication receipt, clients in the community and hospital assessed groups were further subdivided into four mutually exclusive subgroups. These subgroups were hypothesized to have different proportions receiving AD meds. Those with AD were indeed the most likely to receive any AD medication, and the proportion of those receiving any AD medications in the AD groups was almost twice

as high as the proportion receiving them in the respective community and hospital 'other dementia' groups. This shows that a diagnosis of AD is a driving factor for receiving AD medications, and is also evidence for the validity of the AD diagnosis on the assessment itself.

One may wonder why those with other dementia are receiving AD drugs. It is true that they are only indicated for use in AD, except for rivastigmine which received approval from Health Canada in late 2007 to add Parkinson's disease with mild-moderate dementia to the list of indications (Health Canada, 2007). However, there are reports of ChEIs being tested in randomized controlled trials for use in vascular and Lewy body dementias, and also in traumatic brain injury, with results showing improvement in various cognitive and functional scales (Kaye et al., 2003; McKeith et al., 2000; Wilkinson et al., 2003). Memantine has also been investigated for use in vascular dementia (Orgogozo et al., 2002). With these sorts of reports published in the literature, physicians may be prescribing ChEIs and memantine for these other types of dementias.

Donepezil is the ChEI that is used most often in all the groups that were studied. Some possible explanations are that it was the first medication approved in Canada. Consequently, it is most familiar to physicians and it is the drug with the largest body of evidence. On the other hand, it is indicated for mild-moderate and moderate-severe AD, while the other two ChEI medications are only indicated for mild-moderate AD. Therefore there is a broader range of clients to whom the medication is applicable.

The vast majority of those who receive any ChEIs receive only one because the mechanisms of action are very similar, so it is not advisable to take more than one at once (Birks, 2006). However, the assessor does record all medications that were taken in the seven days before the assessment date during the assessment process and it is possible that a switch from one type of ChEI to the other could have taken place within the 7-day window. Therefore, the presence of clients who are taking multiple AD medications may be explained, at least in part, by transitions in prescriptions.

Clients that were assessed in the hospital show an overall lower proportion of receipt of AD medications. This could be because ChEIs and memantine are used to stabilize and slow down the onset of symptoms of AD, and as such they may be described as preventive care. Those whose first RAI-HC assessments are in the hospital may be less likely to have sought preventive care with a family physician as well as not having sought HC services. Alternately, some medications may be discontinued while the person is in the hospital.

There was a higher proportion of high CPS scores among hospital assessed clients. Those who are severely cognitively impaired are likely not living in the community because their informal caregivers are not able to care for them safely and therefore these individuals do not appear in the community assessed sample. The curvilinear patterns seen in the proportion of those in the lowest to highest CPS levels among both the

community and hospital groups with AD show that clients with all CPS levels do receive AD medications. However, the groups with the least and most impaired cognition have the lowest proportions receiving them.

The Ontario Drug Benefit program allows access to ChEIs for individuals whose MMSE is 10-28. This range of MMSE scores corresponds to CPS scores of 0 (intact) to 3 (moderate) and is often used as an indication of mild-moderate AD. Clients with AD and a CPS score of 0-3 are significantly more likely to receive AD medications than those with higher CPS scores. This is an expected finding because all three ChEIs have been indicated for use in mild-moderate AD for the entire time period studied. It was not until 2007 that donepezil had its indication expanded to include moderate-severe AD. Memantine use is higher in those with moderate-severe AD, but it is still rare when compared to ChEI use. This is likely due to the relatively recent availability of memantine, as well as the fact that it is not available through the ODB.

In the community, almost 60% of clients with CPS scores of 4-6 are receiving AD medications. There is evidence for use of donepezil in moderate-severe AD, so such prescribing is supported by currently available literature (Feldman et al., 2001; Winblad et al., 2006). Based on ODB guidelines, those with moderate-severe AD would not receive ChEIs through the provincial formulary, so it is surprising that the prevalence of receipt is so high. Perhaps reluctance to discontinue the medications can result in clients continuing to receive AD medications after they progress to the moderate-severe stage

of AD. Also, in practice, MMSE scores from the physician are not always required in order for the prescription to be filled through ODB, making the guidelines difficult to enforce. These speculations cannot be verified in publically available sources, but could explain the large numbers of people with moderate-severe AD receiving the medications.

6.3 Changes over time in receipt of AD medications

The most striking changes over time in receipt of AD medications involve memantine. The time period of this study coincided with its introduction to the Canadian market in late 2004, so the uptake of this medication in its first four years is clearly evident. The rise in use is seen mostly among those with AD in the community with CPS scores of 4-6. This is expected because memantine is indicated for more severe AD. Use of ChEIs alone tended to decrease across the time period, while use of the combination of a ChEI and memantine increased. This is evidence of appropriate prescribing because the two types of medications have different mechanisms of action and have been shown to work well together (Tariot et al., 2004).

The largest differences in ChEI use between 2004 and 2008 were seen in the 'other dementia' groups in both community and hospital settings, which may reflect the growing body of evidence for use of ChEIs in other dementias.

Donepezil's indication was expanded in 2007 to include those with moderate-severe AD so we would expect to see an increase in use in 2008 among those with CPS 4-6. An

increase in donepezil use was not observed between 2004 and 2008 in community assessed clients with AD and a CPS score of 4-6, but use did stay fairly stable in that group while it dropped over the same time span in the CPS 0-3 group. That drop also coincided with an increase in galantamine use, so those in the CPS 0-3 group may be more likely to switch to galantamine, while those in the CPS 4-6 group may be more likely to remain on donepezil.

6.4 Covariates independently associated with AD medication use

The multivariate model shows which individual characteristics are independently associated with receipt of AD medications among those with AD who were assessed in the community. Women had decreased odds of receiving AD medications. This could be evidence of systematic undertreatment of women; however, it has been reported that women are more likely to have adverse events such as nausea and vomiting, possibly due to their generally lower body weight (Birks, 2006). Therefore, the decreased odds of receiving the medications could be due to them being previously tried and discontinued due to adverse events, or a reluctance to initiate for fear of those same events. If body mass index were included in the assessment, then low body weight could be controlled for.

Those in the 75-84 and 85+ age groups also had decreased odds of receiving AD medications and the odds were lowest among the oldest clients. Physicians may be reluctant to prescribe AD medications to this oldest age group because of lack of

perceived potential benefit to those who are older as compared to younger patients with AD. Frailty (as measured by the CHESS scale) and the major comorbid conditions have been controlled for in the model.

Clients who were married had odds of receiving AD medications that were 1.28 times higher than those who were not. This is likely a reflection of the importance of an informal caregiver who may be available to advocate for medication receipt on behalf of the client with AD.

The curvilinear relationship of CPS scores with receipt of AD medications is expected, because the medications are likely not yet prescribed at the low end of CPS and are not shown to be as effective at the highest CPS scores. These medications are supposed to be used for stabilization and maintenance of cognitive function, so it is surprising that only those with a CPS score of 6 had an odds ratio less than one when compared to the reference group of clients with CPS scores of 0.

Higher ADL Hierarchy scores were associated with lower odds of receiving AD medications. This could be a reflection of a reluctance to prescribe AD medications when the risks of side effects may outweigh the benefits of preserving the level of physical function that currently exists. ADL impairment could be considered to be a sign of reduced likelihood of improvement.

Higher CHESS scores, which indicate increased clinical complexity, are also associated with decreased odds of receiving AD medications and this could be due to competing priorities for physicians. If there are other more critical health problems aside from the comorbidities controlled for in the model that need to be dealt with, then prescription of AD medications may not be a priority.

Clients with a DRS score of 3 or more, which indicates possible depression, and those with higher pain scores have slightly decreased odds of receiving AD medications. As was evident for the CHESS score, this may also be influenced by competing clinical priorities.

Diagnoses of CAD, CHF, renal failure and emphysema, asthma, or COPD meant that clients had decreased odds of receiving AD medications. This is to be expected because in the prescribing guidelines physicians are instructed to be cautious in using the medications in individuals with these conditions. The effects are not all the same for these diagnostic groups. Clients with CHF and renal failure had odds ratios in the 0.60 range, while those with CAD and the airway diseases had odds ratios in the 0.90 range. This suggests that physicians were more cautious in light of more serious comorbidities.

Clients with no medication oversight – no one physician had reviewed all their medications in the last six months – had greatly decreased odds of receiving AD medications when compared to those who had had a medication review. This is likely

reflective of lack of contact with a physician and therefore lack of opportunity to be prescribed the medications.

Those who made economic tradeoffs, which is an item used as a proxy for low income, had odds of receiving AD medications that were 0.65 times lower than those who did not have to make those tradeoffs. A positive response to the economic tradeoffs item is very rare in this population – only 0.6% reported it – so it is surprising that it is significant in the multivariate model. This finding could be explained in several ways. It could be a social class effect where those with low income are less likely to be involved with physicians for preventive care. It could also be a resource issue where clients may wish to be in contact with a physician, but issues of access such as lack of transportation to the physician or to the pharmacy discourage medication use. It could be that the medication was prescribed and transportation was possible, but the required ODB co-payment of $2 per prescription was too onerous and other medications were prioritized. Finally, it could be that wealthier individuals receive the AD medications through private insurance or out-of-pocket payments even though they may not be eligible through ODB.

CCACs are the main unit of organization for Ontario's home care system. After all the individual clinical characteristics have been controlled for, those clients in the Toronto Central CCAC had the lowest odds of receiving AD medications. Toronto Central is a geographically small CCAC which is completely urban and has very high population

density. Clients residing in six of the 13 other CCACs had significantly greater odds of receiving AD medications when compared to those residing in Toronto Central. These CCACs were Champlain, South West and North Simcoe Muskoka (tie), Mississauga Halton, North East and North West (tie), in order of lowest to highest odds ratios. The most obvious pattern in these results is that the four most northern CCACs (North East, North West, North Simcoe Muskoka and Champlain) were among those that had higher odds ratios. It is unclear why the South West and Mississauga Halton CCACs showed higher odds ratios.

The models that were stratified based on CPS score showed many of the same variables as the full model. In fact, no new variables were significant in either model. The differences between the full and stratified models were that in the CPS 0-3 group, hypertension and economic tradeoffs were no longer significant. In the CPS 4-6 model, many fewer variables stayed in the model and only age, marital status, ADL, CHF, renal failure, hypertension and no medication oversight were significant.

A potential reason that the CPS 0-3 model is so similar to the full model is that 18,000 of the 22,977 clients in the AD group had CPS scores of 0-3 so they made up the majority of the cases in the full model. In the CPS 4-6 model, there were fewer clients (n=4,977) so that may have affected the significance of borderline items.

Non-patient determinants of medication use are likely also important predictors of whether a client receives AD medications or not. There is qualitative evidence that physician attitudes and expectations influence prescription of medications generally (Spinewine et al., 2005). A survey of Canadian family physicians found that reporting a lack of knowledge of AD medications, perceiving them to be ineffective, being a female physician, and lacking formulary coverage in the province were all associated with reduced prescribing rates of AD medications (Hillmer et al., 2006). Drug representative visits were associated with differing drug prescription patterns, but this was mostly related to the brand prescribed and not the category (Sondergaard et al., 2009).

Physician interpretation of patient expectations for prescription was shown to have an effect on prescription outcome (Lado et al., 2008). Since family members would likely be more involved with prescription of AD medication, it is possible that family factors such as attitudes towards physicians and actions such as advocacy for or against AD medications could affect receipt of the medications.

These physician and family factors are not measured in the RAI-HC dataset so it is likely that their absence from the models decreased the goodness of fit. However, it is debatable whether it is appropriate that these physician factors should have a large influence on prescription of a medication.

6.5 Limitations and Strengths

6.5.1 Limitations

There are limitations in this study that should be noted. The AD groups were created using the AD diagnosis checkbox on the RAI-HC assessment. Some may argue that it is not sensitive to the complicated nature of AD diagnosis, which is often mixed with other dementias. However, due to the professional nature of the assessors, the risk of a person being coded as having AD without a firm diagnosis from a physician is low. There is evidence that the diagnoses that are recorded on these assessments do correspond to hospital discharge information. Specifically, an MDS diagnosis of Alzheimer's disease compared with a recent hospital claim had a positive predictive value of 0.68 (Gambassi et al., 1998). In a more recent study conducted on Ontario Complex Continuing Care (CCC) patients, results suggested that when AD was listed as the primary diagnosis on the hospital discharge abstract immediately preceding the admission to the CCC bed, AD was listed on the RAI assessment with a sensitivity of 0.67 (0.64-0.70). When the discharge abstract form listed AD as any diagnosis and the presence of either AD or other dementia on the MDS was calculated, the sensitivity increased to 0.85 (Wodchis, Naglie & Teare, 2008).

The medication data that are used in this study are collected for the seven day period before the assessment date. It is not possible to determine a client's historical use of medications so those who were on the medications previously and have since

discontinued as well as those who have never received the medications are put together in the same group. This could have implications for the multivariate models, as covariates that predict discontinuation as well as those that predict never use could be important. The attitudes and expectations of clients, informal caregivers and physicians could also have an impact on whether or not a person receives an AD medication. That information is not available in this dataset.

The cross-sectional nature of the analytic sample used in this study means that the cases of AD that were identified are prevalent cases, not incident cases. The first assessment for all clients was used, but those who were not assessed using the RAI-HC were not represented in the sample. Because this study used prevalent cases it is not possible to establish a temporal order between the clinical characteristics of the clients and the receipt of AD medications.

Survivor bias, which can result from only following up on those who are still alive and able to be assessed, can underestimate incidence rates of AD in longitudinal studies (Tyas et al., 2006). It can also have implications for cross-sectional studies because individuals with rapidly progressing disease may die and are not available to be assessed (Zhou, Rahme, Abrahamowicz & Pilote, 2005). In this study, those with rapidly progressing dementia may die before receiving HC services and would therefore not be represented in the prevalence sample.

The Ontario HC dataset represents long-stay home care clients only. These are a large subset of the Ontario Home Care population, but they do not necessarily represent all home care clients. However, those with dementia that are receiving home care services do tend to be long-stay clients so the dataset likely does cover most of the population of interest. Those who are not receiving long-term home care services may be receiving community support services. These individuals could be assessed with the interRAI Community Health Assessment (CHA), which is an assessment designed for community settings with anticipated light care needs (Gray et al., 2009).

6.5.2 Strengths

One of the main strengths of this study is the dataset itself. The large sample size – over 300,000 records – and the breadth of clinical data available allows identification of specific rare subpopulations. Domains such as cognition, communication, and mood and behaviour patterns are assessed, as well as functional status, informal caregiving support, disease diagnoses, and many other clinically significant areas.

The client is always assessed by a trained professional who is usually a registered nurse. The data are used in many different ways in the Ontario home care sector. They are primarily used for care planning for the individual, but also for quality indicators and administrative planning so there is an incentive for both administrators and front-line workers to ensure that accurate data are collected.

Another strength of the dataset is the nature of the medication information. It is collected by the assessor at the person's home, so all medications are collected including over the counter and private insurance pay (not just those offered by ODB). Unlike the ODB administrative dataset, which reports the medications dispensed at the pharmacy level, the RAI-HC medication information reflects what was actually taken by the person over the seven days before the assessment.

The RAI-HC is a comprehensive assessment, and it is standardized so it is comparable across jurisdictions. All those who begin to receive HC services and who are expected to remain on-service for 60 days or longer receive an assessment, and continue to receive one every six months as long as they remain on-service. Thereforeit is census-level information for that group. Service utilization and discharge information is available for this dataset, though it is not used for these analyses.

6.6 Future research

In the future these analyses could be replicated across different jurisdictions and in different care settings. The Canadian Institute for Health Information has recently set up the Home Care Reporting System (HCRS), and several provinces are submitting their RAI-HC assessments. Once data are available, researchers can compare utilization and predictors of AD medication use across provinces as well as investigate implications of different policy decisions such as regulations for access to AD medications through provincial formularies.

It would also be interesting to look into the use of AD medications in other sectors that support people with AD such as long-term care homes, complex continuing care and inpatient mental health. Comparable studies could be carried out in both these sectors in Ontario because people in all three sectors are assessed using interRAI assessments so many of the items in each assessment are comparable to those in the HC assessment used in this study. A long-term care or complex continuing care study would need to use a cross-sectional sample from a research project that is currently being carried out, because completion of the medication section is not yet mandated in those settings. Data on those in geriatric psychiatry beds from the Ontario Mental Health Reporting System could be used to carry out a comparable study in the inpatient mental health setting.

Cross national comparisons can also be done among countries that use the same instruments and also collect medication information. The interRAI family of instruments have been used extensively for international comparisons, most notably in the 11 country Aged in Home Care (AdHOC) study based on the RAI-HC (Carpenter et al., 2004; Cooper et al., 2005; Fialova et al., 2005; Sørbye et al., 2009).

Other types of questions would also be of interest. Investigation into concurrent use of ChEIs and anticholinergics or benzodiazepines would be helpful to determine the extent of use of contraindicated medications. It would also be interesting to develop a

multivariate model to predict the use of AD medications among the 'other dementia' group and see if the predictors were the same as the ones found in the current study. Longitudinal analyses would be the next important step. Discharge information is now available up to September 2008, so trajectories of disease as measured by changes in scale scores over time could be studied as well as time to nursing home placement.

6.7 Policy Implications

The major policy implication involves the ODB and the availability of subsidized medications for those over the age of 65. This study showed that many home care clients are receiving AD medications when ODB guidelines would likely restrict their reimbursement. The available data do not allow a determination of which clients have received medications through the ODB and which obtained them through private means. However, it seems unlikely that all the clients with CPS scores of 4-6 are obtaining the medications through private means, as the prevalence of memantine use by 2008 was still low when compared to ChEI use, and memantine is not listed on the formulary.

Since those who do not have to make economic tradeoffs were found to be more likely to receive AD medications it is possible that people with no economic alternatives faced systematic barriers to receiving them. Those with CPS scores of 4-6 were less likely to receive the medications because of the stage of their disease, however some of these individuals continued to receive the medications perhaps because they, their caregivers

or their physicians were insistent. This could possibly have been facilitated by weak regulations based on MMSE scores.

Also, donepezil and memantine have been approved for use in moderate-severe AD and have been shown to be useful in RCTs, so consideration should be made to expanding the limited use guidelines, and possibly including memantine on the formulary. However, choices about which medications should be covered must always be made and economic analyses could be performed to see if it is in the public interest to cover these medications.

Use of these medications has been reported to delay time to nursing home placement, which would be an important cost consideration (Geldmacher et al., 2003). However, with delayed nursing home placement comes a need for more supports for informal caregivers. This would need to be considered in the economic analyses, but it would serve the needs of clients who wish to remain in their homes, and caregivers who desire to support them there for as long as possible.

6.8 Conclusions

The majority of home care clients who are diagnosed with AD do receive an AD medication and a much smaller proportion of those diagnosed with other dementias receive them as well. Donepezil is the ChEI that is used most often among all the groups. The use of ChEIs has not increased very much from 2004-2008, but the use of

memantine has grown substantially. Multivariate analysis showed trends of rational prescribing, such as clients with contraindicating diagnoses or very high clinical complexity being less likely to receive AD medications. At the same time, it also showed evidence of structural barriers to receipt of the medications, such as having to make economic tradeoffs and the CCAC where the person resides.

This multivariate model contributes to the body of knowledge about AD medication use in the Ontario home care population, specifically by linking clinical characteristics to receipt of AD medications. These analyses also show that the population using these medications is quite different than the population represented in most randomized controlled trials. In future, research using the RAI-HC dataset has the potential to measure real-world results of treatment in terms of changes in cognitive and physical impairment as well as transitions to long term care homes or death.

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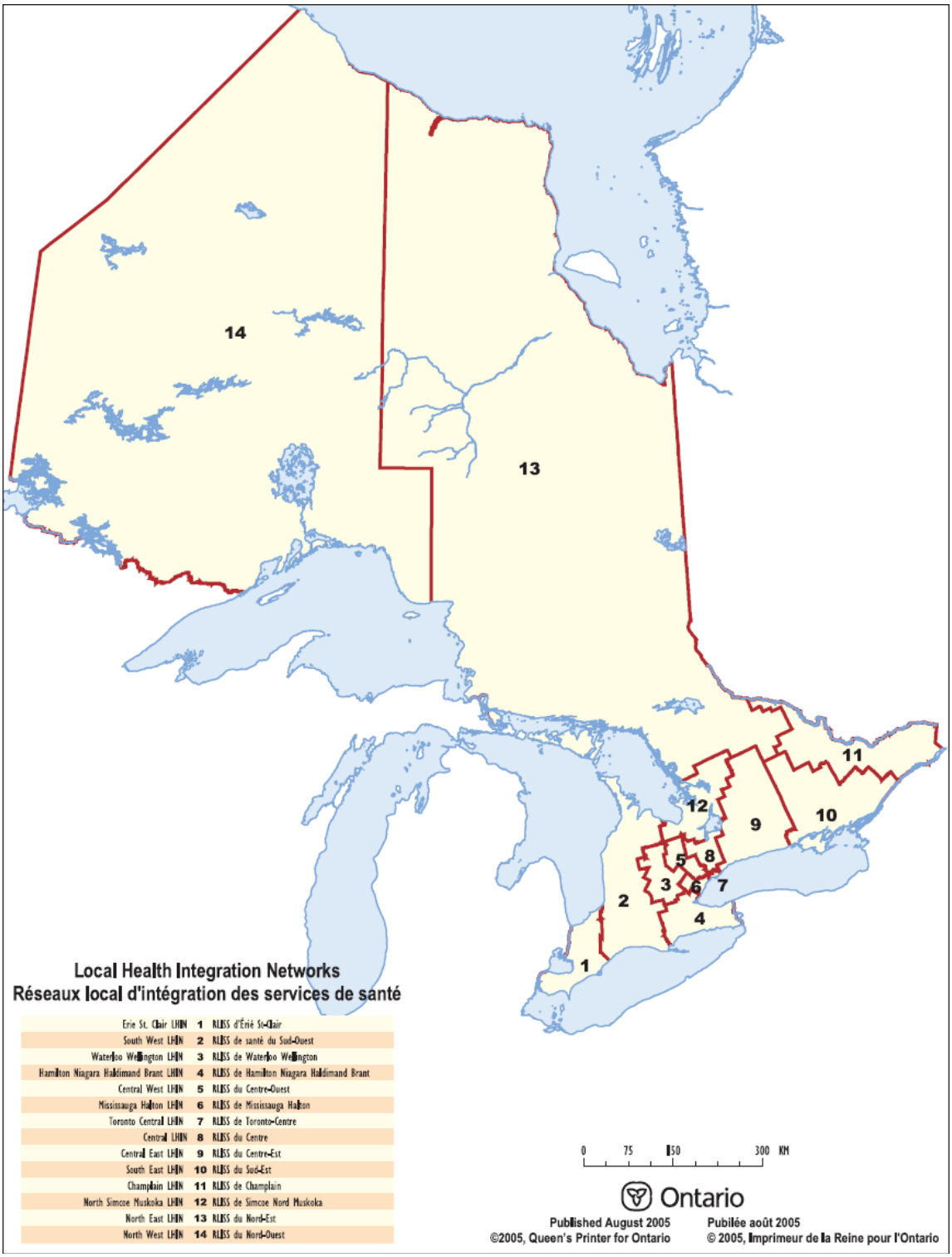
Appendices

Appendix A: LHIN/CCAC map



(Source: Ontario Ministry of Health and Long –Term Care)

Appendix B: Table of Provincial Formulary Access across Provinces

	Current status of ChEI	**Current status of Memantine**
British Columbia	Limited access to all ChEIs Requirements: • MMSE 10-26 • GDS 4-6 Initial authorization for 6 months Renewal requires form, algorithm to be completed	Available, but not through provincial formulary
Alberta	Limited access to all ChEIs Requirement: • MMSE 10-26 Initial authorization for 12 weeks Renewal requires MMSE drop less than 3 points in 12 weeks	Available, but not through provincial formulary
Saskatchewan	Limited access to all ChEIs Requirements: • Diagnosis of probable AD • MMSE 10-26 • FAQ score • Discontinuation of drugs with marked anticholinergic activity Initial authorization for 3 months Renewal requires improvement in MMSE (+2 points) or FAQ score (-1 point)	Available, but not through provincial formulary
Manitoba	Limited access to all ChEIs Requirements: • Confirmed AD diagnosis (DSMIV) with memory impairment and one of aphasia, apraxia, agnosia, disturbed executive function. • The deficits must have caused significant gradual and continued decline, are not due to other conditions, and do not occur only during delirium. • Normal test results for CBC, TSH, Electrolytes, VitB12 and glucose • MMSE score between 10-26 measured within 30 days of application Initial authorization for 3 months Renewal requires MMSE score of 10 or higher	Available, but not through provincial formulary

Ontario	Limited access to all ChEIs Requirements: • Diagnosis of AD • MMSE score 10-26 Initial authorization for 3 months Renewal requires MMSE of 10 or higher	Available, but not through provincial formulary
Quebec	Limited access to all ChEIs • MMSE 10-26 • Global evaluations of cognition, function, behaviour and social interactions Initial authorization for 6 months Renewal requires an MMSE of 10 or higher, maximum drop of 3 points on MMSE or significant improvement on evaluations of cognition, function, behaviour and social interactions	Available, but not through provincial formulary
New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador	Limited access to all ChEIs Requirements: • Diagnosis of probable AD or possible AD with vascular or Lewy bodies • MMSE 10-30 • FAST 4-5 • Target symptoms in each of three domains (out of cognition, function, behavior, social/leisure) Initial authorization for 6 months Renewal requires: • Stabilization or improvement in one target symptom (90 day continuation) • MMSE 10-30 and FAST 4-5 and stabilization or improvement in at least one target symptom (6 month renewal, if renewed at 6 months then annual renewal)	Available, but not through provincial formulary

(Source: Provincial Ministry of Health websites)

Appendix C: Table of LHIN/CCAC Characteristics

Local Health Integration Networks (LHIN) Characteristics: LHINs 1-7

	Ontario avg	1	2	3	4	5	6	7
LHIN Name	N/A	Erie St. Clair	South West	Waterloo Wellington	Hamilton Niagara Haldimand Brant	Central West	Mississauga Halton	Toronto Central
Major city	N/A	Windsor	London	Kitchener	Hamilton	Brampton	Mississauga	Toronto
Population	12,160,282	630,195	901,123	686,324	1,315,964	739,957	1,008,004	1,090,301
2001 -06 pop. change (%)	6.6	3.4	3.6	8.4	4.3	18.1	12.1	-0.3
% of Ontario population	N/A	5.2	7.4	5.6	10.8	6.1	8.3	9.0
Population density	13.4	86.1	43.1	144.6	203.3	285.7	956.7	5679.0
Total size (Km^2)	907,574	7,324	20,904	4,747	6,473	2,590	1,054	192
% Rural	14.9	20.1	28.5	12.1	11.9	6.8	2.1	0.0
% Age 65+	13.2	14.5	15.2	12.0	15.8	9.4	10.9	13.0
% Aboriginal	2.0	2.4	1.4	0.7	1.4	0.6	0.4	0.8
% Low income	14.7	12.2	11.1	9.8	13.8	14.6	13.3	24.2
Median income in 2005, all private households ($)	60,455	57,456	55,105	64,915	57,610	69,645	75,881	52,319
% Received influenza shots in the past year	36.6	40.1	39.2	35.6	33.5	35.3	31.9	32.7
% Contact with medical doctor in the past year	81.6	81.7	79.0	80.5	80.8	84.9	85.0	83.0
# of Community hospitals	60	5	7	5	5	2	3	2
# of Small hospitals	34	0	5	1	2	0	0	0
# of Teaching hospitals	16	0	2	0	2	0	0	5

Local Health Integration Networks (LHIN) Characteristics: LHINs 8-14

	Ontario avg	8	9	10	11	12	13	14
LHIN Name	N/A	Central	Central East	South East	Champlain	North Simcoe Muskoka	North East	North West
Major city	N/A	Markham	Oshawa	Kingston	Ottawa	Parry Sound	Timmins	Thunder Bay
Population	12,160,282	1,532,649	1,432,695	466,669	1,147,209	422,902	551,691	234,599
2001 to 2006 population change (%)	6.6	13.3	6.3	3.2	4.3	12.2	-0.3	0.6
% of Ontario population	N/A	12.5	11.0	3.8	9.4	3.5	4.5	1.9
Population density	13.4	561.3	93.8	26.1	65.1	50.5	1.4	0.6
Total size (Km^2)	907,574	2,730	15,274	17,887	17,631	8,372	395,577	406,820
% Rural	14.9	4.7	14.0	45.7	20.6	32.7	30.2	36.3
% Age 65+	13.2	12.6	13.7	17.2	13.2	15.2	16.5	14.1
% Aboriginal	2.0	0.4	1.2	2.7	2.0	3.3	9.4	19.6
% Low income	14.7	17.7	16.1	11.9	13.8	9.7	12.8	10.7
Median income in 2005, all private households ($)	60,455	75,881	61,114	52,454	64,555	59,148	49,592	54,111
% Received influenza shots in the past year	36.6	35.5	37.6	41.7	45.8	32.2	39.1	34.2
% Contact with medical doctor in the past year	81.6	83.4	80.8	78.9	82.0	78.2	79.1	74.2
# of Community hospitals	60	4	6	3	6	5	5	2
# of Small hospitals	34	1	1	1	6	0	9	8
# of Teaching hospitals	16	1	0	1	3	0	1	1

(Source: Statistics Canada Community Profiles, 2006; Statistics Canada Health Profiles, 2006)

Appendix D: RAI-HC Assessment Instrument

(Because of copyright considerations, the assessment instrument cannot be reproduced in the electronic version of this thesis. It can be obtained by contacting Dr. John P. Hirdes at the University of Waterloo)