

PRELIMINARY STATISTICAL OVERVIEW

ALZHEIMER'S DRUG THERAPY INITIATIVE RESEARCH PROGRAM

The Alzheimer's Drug Therapy Initiative (ADTI) is a four-phase initiative that started in July 2006. Phase I was a policy forum of key stakeholders. Phase 2 was the developmental phase involving clinical experts, stakeholders and policymakers. We are currently in Phase 3, providing evidence-based coverage of cholinesterase inhibitors (ChEIs) through PharmaCare and gathering demographic information for the research program. Phase 4 is the reporting phase in which an informed listing decision will be made prior to the projected end date of April 2012.

Basic eligibility for ADTI coverage:

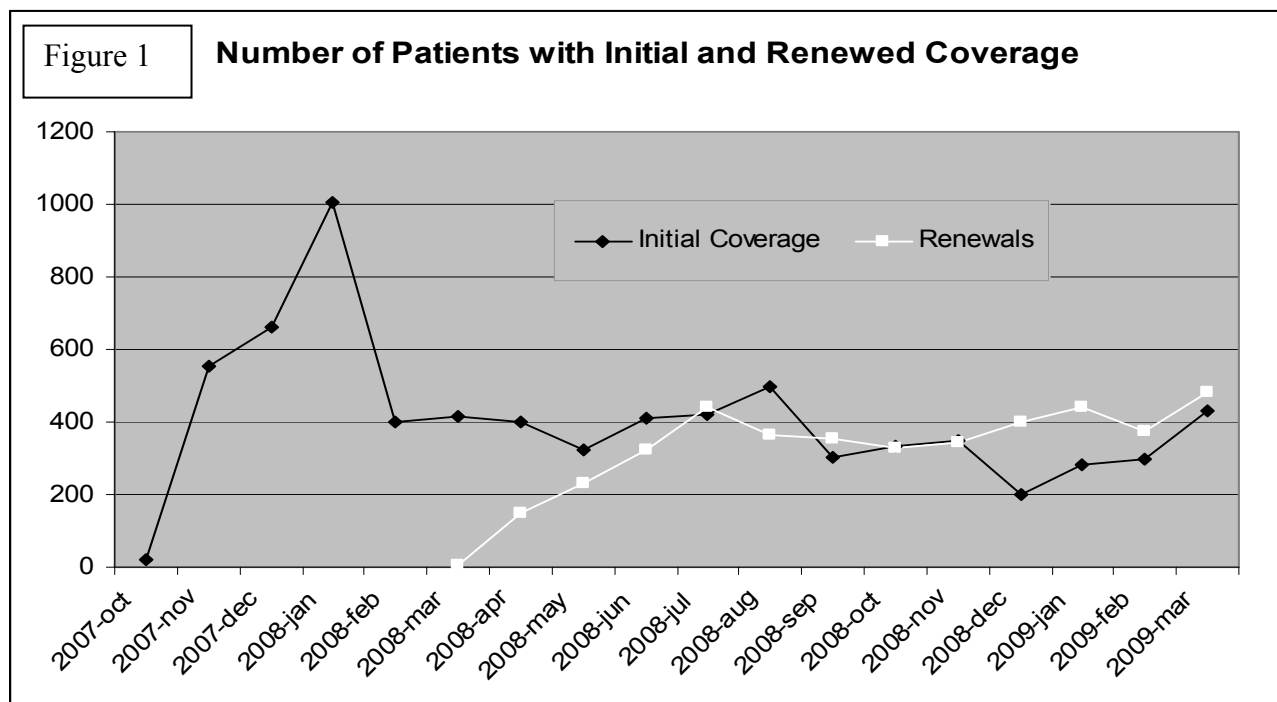
- mild to moderate AD defined by a SMMSE score 10 to 26 and a GDS rating 4 to 6, AND
- at 6 month renewal intervals, a SMMSE score of ≥ 10 and GDS 4 to 6.

Eligibility for Research Project

- patient and caregiver consent
- patient classified as indeterminate responder (no significant side effects, no increase in SMMSE score, little or no decrease in SMMSE score and/or no significant clinical improvement)

Following is a selection of BC provincial statistics gathered to date on Alzheimer's disease and participation in the ADTI.

As of March 31, 2009, 7,800 individuals were registered for initial coverage through the ADTI. Physicians are required to apply for renewal of coverage before the end of the 6-month coverage period. Over the past 6 months, an average of 315 patients per month received initial coverage, with an average of 395 patients per month renewing coverage at 6 or 12 months.



There are approximately 636,000 seniors (individuals 65+) in the Province of British Columbia and it is estimated that 4.3 percent, or 27 000 patients, have AD. Of these individuals, an estimated 60 percent are classified in the mild to moderate stages of AD and are therefore eligible for coverage under the ADTI. Figure 2 depicts the percentage of seniors with mild to moderate AD currently taking a ChEI with and without ADTI coverage by Health Authority.

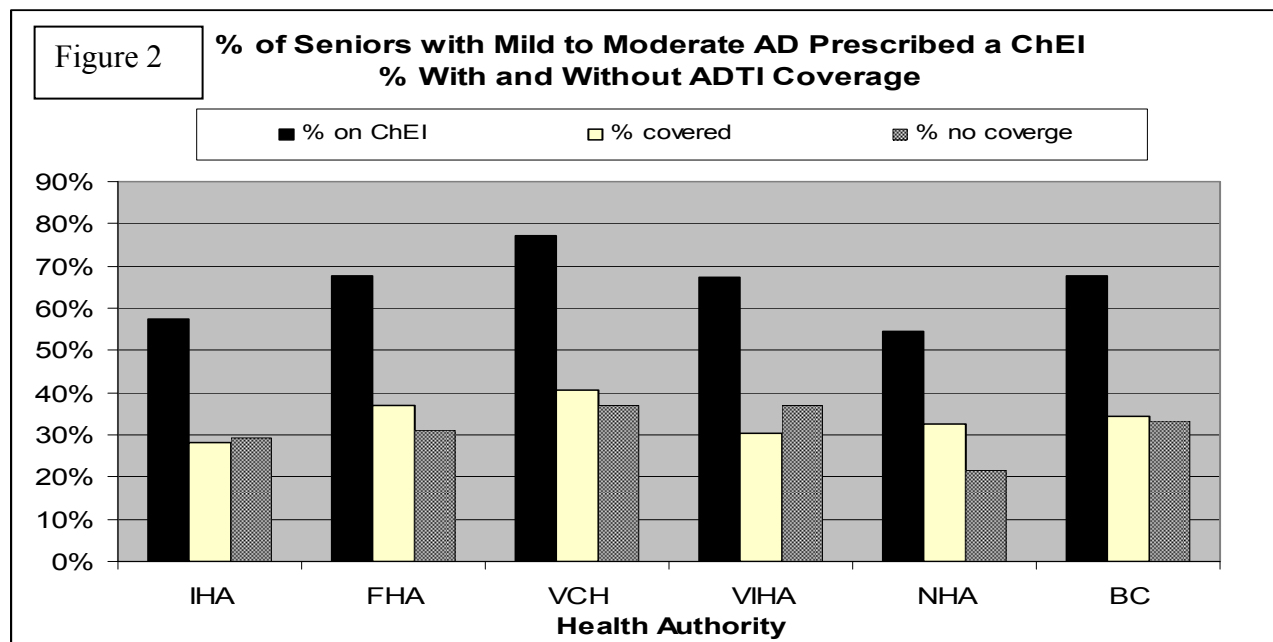
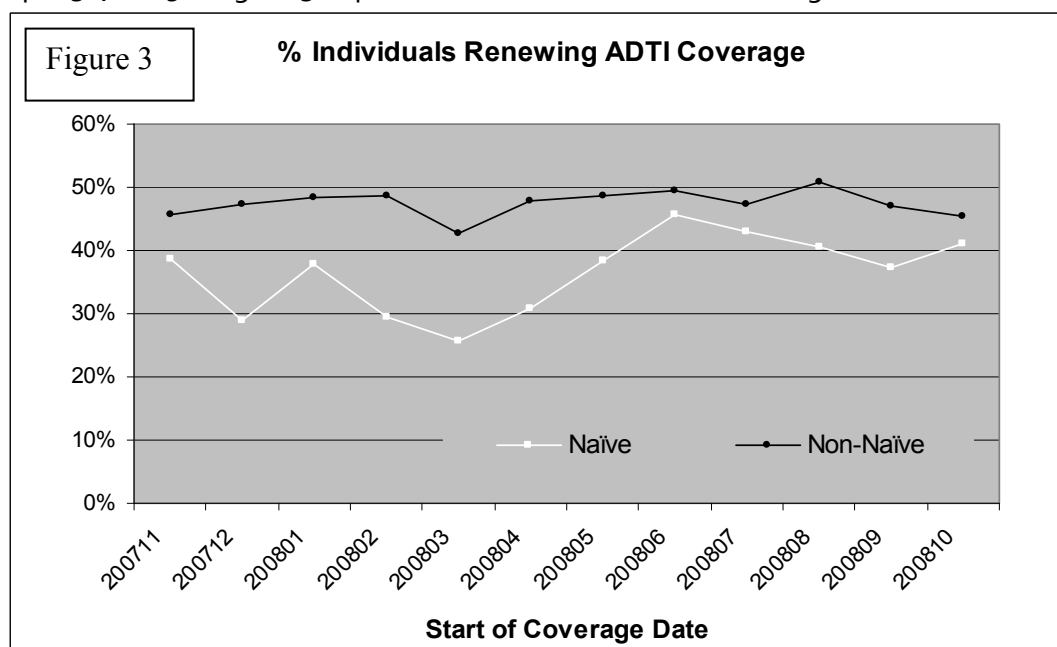


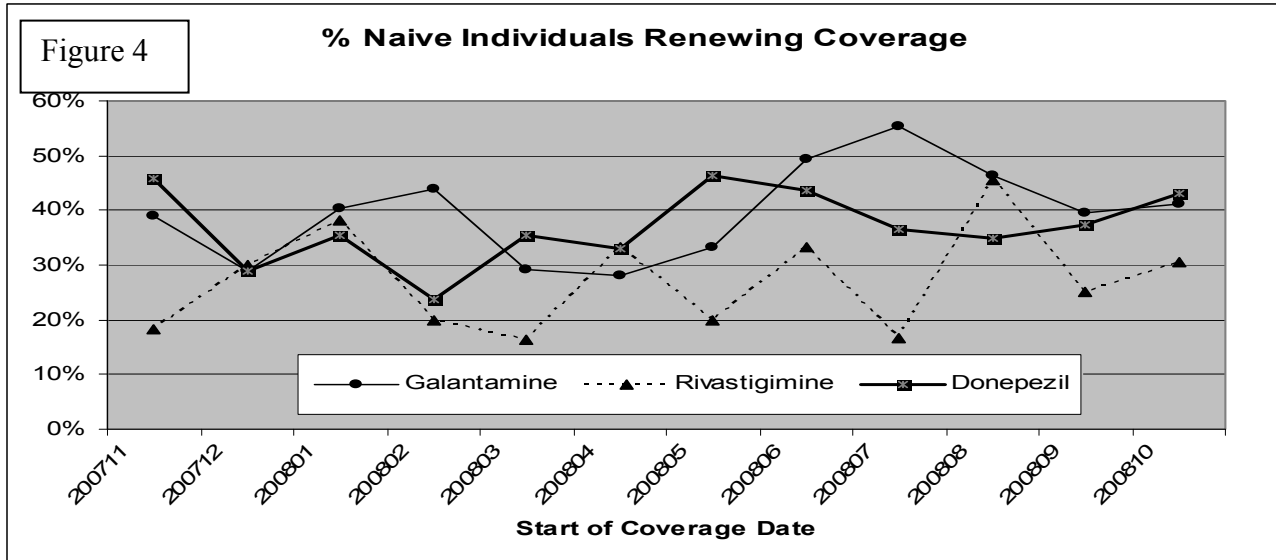
Figure 3 and figure 4 show the percentage of individuals registered for ADTI coverage between October 2007 and November 2008 whose coverage had been renewed and were still registered as of April 30, 2009. Figure 3 depicts the difference in ADTI coverage renewal rates between ChEI-naïve



and non-ChEI-naïve individuals. As defined by the Ministry, ChEI-naïve individuals are those who, when they receive their initial ADTI coverage for a specific ChEI, have not filled a prescription for that ChEI in the past 6 months. As expected, the average

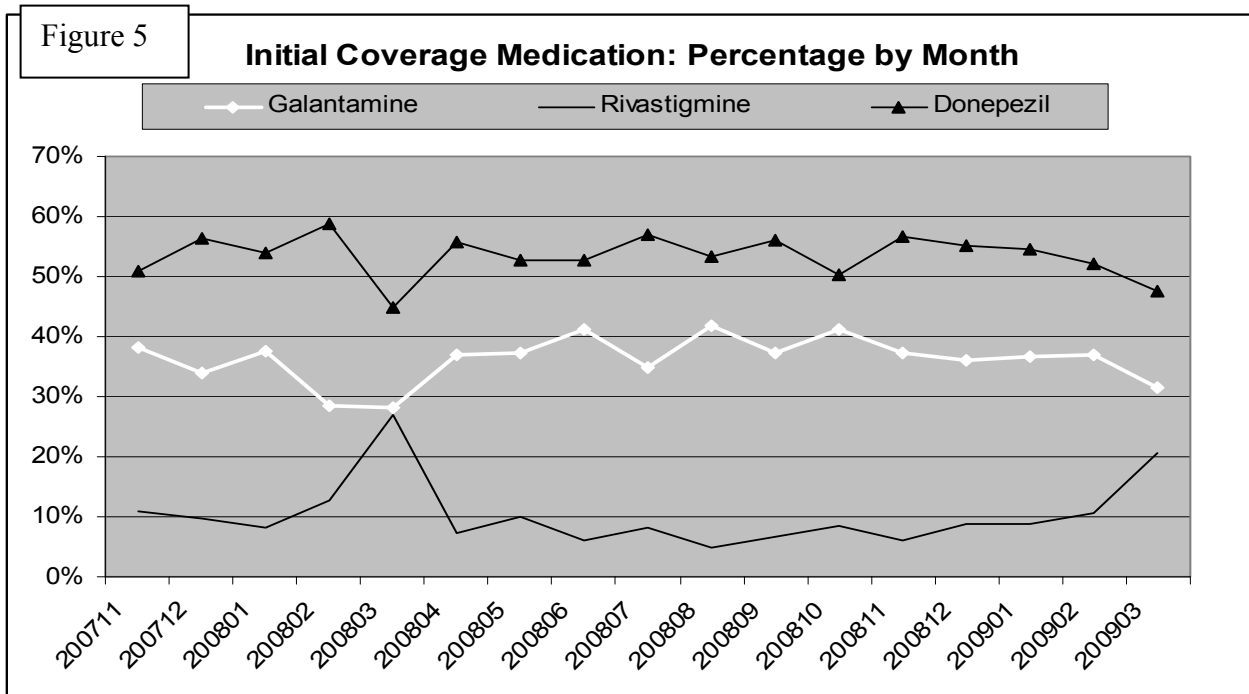
coverage renewal rate is lower for naïve individuals; 36 percent for ChEI-naïve individuals to 47 percent for non-ChEI-naïve individuals.

For ChEI-naïve individuals registered between October 2007 and November 2008, over 58 percent no longer had ADTI coverage as of April 30, 2009. As depicted in Figure 4, the average renewal rate for this period is 40 percent for galantamine, 37 percent for donepezil and 27 percent for rivastigmine.



To address the high dropout rate, a process has been implemented to remind patients and physicians that coverage is expiring and a reassessment appointment is needed.

Figure 5 shows that initial coverage of medication by percent has remained relatively consistent over the past 18 months; 56 percent for donepezil, 37 percent for galantamine, and 10 percent for

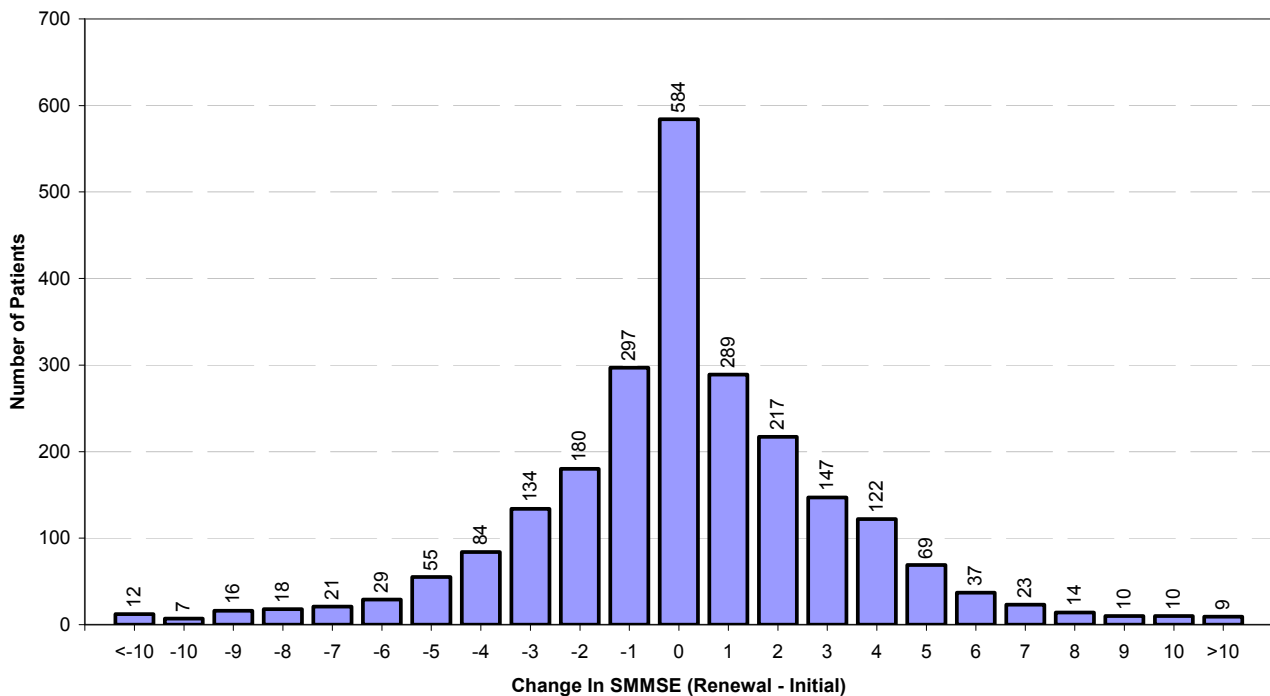


rivastigmine. There were two notable increases in rivastigmine: the jump in March 2008 was an unrelated practice anomaly which is unlikely to reoccur while the March 2009 increase corresponds to the addition of the rivastigmine transdermal patch to the ADTI.

The initial average SMMSE score for ChEI-naïve individuals was 20.3. There were differences in the average score depending on education level; for education levels of 0 to 8 years, 9 to 12 years and 13+ years the average SMMSE scores were 18.7, 20.5 and 21.3, respectively. The corresponding GDS scores were 4.61, and 4.56, respectively for education levels of 0 to 8 years and 9 to 12 years, and 4.59 for 13+ years.

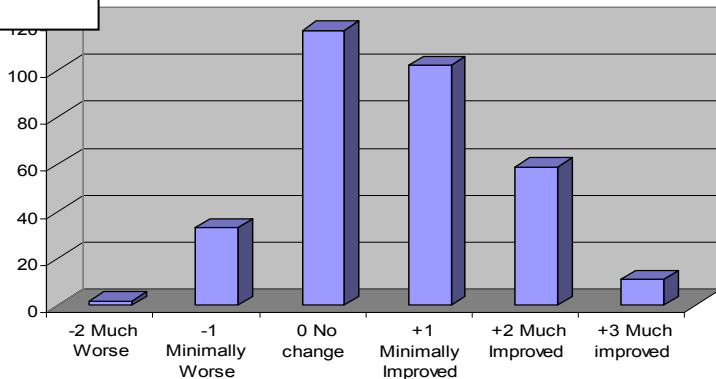
Figure 6 shows the change in SMMSE scores for ChEI-naïve individuals from their initial Special Authority assessment to first renewal when the Special Authority form was submitted by the same physician.

Figure 6 *Changes in SMMSE Scores from Initial Application to First Renewal When Conducted by Same Physician June 11, 2009*



While insufficient analysis has been undertaken to draw extensive conclusions, approximately 52 percent of individuals had a change in their SMMSE score of between +/- 1, while approximately 35 percent had a decrease in their score and 40 percent had an increase in their score.

Figure 7 *OPAR Scores for Naive Individuals*



The ADTI's Study Design Working Group—the group established to design and conduct the ADTI research projects—developed the Overall Patient Assessment Rating (OPAR) to assess the

change in patient's abilities (cognition, function and behaviour) between assessments. This assessment rating was established to assist physicians determine whether or not to continue treatment with the medication and to establish eligibility to participate in the research studies. Figure 7 shows the OPAR for 325 ChEI-naïve individuals 6 months after initial ADTI coverage. Approximately 53 percent are 'Positive Responders,' 46 percent are 'Indeterminate Responders,' and 1 percent were 'Non-responders'. However, as 60 percent of ChEI-naïve individuals did not renew their coverage, the percentage of non-responders is considered to be under-represented by these statistics.

When developing the ADTI Special Authority form, ADTI researchers included demographic data that, while not necessary to evaluate the efficacy of the ChEI-treatment for a particular patient, could be helpful in understanding whether individual patient characteristics affect tolerability or can be used to predict a better or worse response to cholinesterase inhibitor therapy.

Figure 8 provides the reported ethnicity of ADTI participants. The majority is noted as having European ethnicity. The second largest group is 'unknown' – or missing data. It is expected that ethnicity statistics will improve as the Research Program progresses.

