Reducing Potential Overuse of Dementia Drugs Could Lead to Considerable Savings

Dementia medications typically provide modest, short-term benefits and have no proven effectiveness beyond one year of use. Nevertheless, our findings indicate that some adults with dementia remained on these drugs for as long as a decade, increasing the potential for adverse health outcomes and costing patients and insurers nearly $20,000. As much as 90 percent of this spending occurred after drug treatment was no longer supported by clinical evidence.

INTRODUCTION

Dementia is defined as a loss of cognitive functioning—the ability to think, remember, problem solve, or reason—that interferes with daily life and activities. While earlier stages of the disease may be relatively mild, dementia eventually progresses to the point that those with the disease are completely dependent on others for basic activities of daily living.1

As many as half of all people ages 85 and older may have some form of dementia.1 As the US population continues to age, the prevalence of dementia is expected to rise, with a corresponding increase in related spending. In 2018, annual costs associated with dementia will total more than $270 billion in the United States and could rise as high as $1.1 trillion by 2050.2

While clinical trial evidence indicates that some dementia medications, specifically cholinesterase inhibitors (ChEI) and memantine, may briefly address dementia symptoms like memory loss and confusion, these drugs do not affect the underlying cause of the disease.3 Further, because ChEI and memantine typically provide modest benefits for only a limited time, the decision to start or continue treatment must be balanced against the potential adverse effects of the drugs. For example, ChEI use has been linked to fainting, abnormally slow heart rate, and hip fracture.5 Another consideration is cost: the price of some dementia drugs can exceed $700 per month.6

Despite the limited effectiveness of dementia drugs, most clinicians receive little guidance on when and how to de-prescribe them—that is, taper or discontinue the drugs to improve patient outcomes. Further, it is common for physicians to continue prescribing these drugs to patients for considerably longer than the duration supported by clinical evidence.8,9 The associated costs can be substantial for both patients and health care payers.
BACKGROUND
Current dementia drugs have shown limited efficacy. Two types of drugs have been approved by the US Food and Drug Administration for the treatment of dementia symptoms: (a) ChEI, including donepezil (Aricept), galantamine (Razadyne), and rivastigmine (Exelon); and (b) memantine (Namenda, Namenda XR).* Clinical evidence indicates that ChEI and memantine may delay cognitive impairment for approximately 3 to 12 months among certain adults with dementia, while other patients will not benefit at all.10 Some researchers suggest that a combination therapy of ChEI and memantine is the optimal treatment for dementia,7,11,12 but others report that adding memantine to donepezil treatment is not superior to treatment with donepezil alone.13 Notably, the evidence supporting dementia drugs’ effects on cognitive impairment is typically based on cognitive test results** and not on real-world behavior: ChEI and memantine, in combination or separately, have not been shown to appreciably delay institutionalization, improve quality of life, or lessen caregiver burden.4 Nevertheless, there is some research that indicates that a small subset of patients may see a meaningful benefit from using dementia drugs, although such results remain subject to debate.14,15 Considering these drugs’ limited efficacy, potential adverse effects, and cost, we took a closer look at their use. Specifically, we examined the duration and costs of treatment with these dementia medications, including costs incurred after clinical evidence no longer supported their use.

METHODOLOGY
We conducted a retrospective analysis of de-identified claims obtained from the OptumLabs® Data Warehouse, a comprehensive, longitudinal, real-world data asset containing medical, pharmacy, and eligibility information for enrollees in plans offered by a large U.S. insurance company.16 Our sample consisted of 70,987 Medicare Advantage (MA) enrollees ages 65 years or older with a new dementia diagnosis between 2006 and 2015.

A new case of dementia was defined as a documented dementia diagnosis on an insurance claim between January 1, 2006, and December 31, 2015, or a documented prescription for one or more of the following dementia drugs: donepezil, rivastigmine, galantamine, or memantine. We defined the diagnosis date as the date of first dementia diagnosis or the date of the first prescription for a dementia drug.

Study subjects were required to have a 12-month “clean period” during which there was no documentation of a dementia diagnosis or a prescription for a dementia drug. Study subjects were also required to have at least 12 months of continuous enrollment following the diagnosis date, with some having over 10 years of follow-up through December 31, 2016. Study subjects with diagnoses of alcohol or drug abuse were excluded. We also excluded subjects who had a prescription for memantine with no dementia diagnosis and one of the following diagnoses: obsessive compulsive disorder, attention-deficit hyperactivity disorder, migraine headaches, or posttraumatic stress disorder, as memantine is indicated for the treatment of these conditions.

Statistical Analysis
Patients with a dementia diagnosis were classified into one of four drug groups: (a) none, (b) ChEI only, (c) memantine only, and (d) a combination of ChEI and memantine. Chi-square tests were used to compare proportions across these drug groups. Analysis of variance (ANOVA) models (generalized linear models for unbalanced designs) were used to compare means of continuous variables across groups.

We calculated allowable costs (combined amounts paid by patients and insurers) from each insurance claim on the date of dementia drug prescription fill. To reduce the effect of extreme outliers, a 99 percent Winsorisation method was used for the drug costs:

* A NMDA (N-methyl-D-aspartate) receptor antagonist.
** Such as the Standardized Mini-Mental State Examination or Bristol Activities of Daily Living Scale.
all values above the 99th percentile were set to the 99th percentile and all values below the 1st percentile were set to the 1st percentile.

**Study Limitations**
Our sample consists of enrollees in MA plans offered by one insurance company; therefore, our results are not generalizable to the MA population as a whole or to Medicare fee-for-service beneficiaries. The insurance claims did not contain information on the severity of dementia. Also, we were not able to determine the reasons for loss to follow-up, such as death or switching insurance products. Many patients likely continued to take the drugs after switching insurance plans, so the duration and costs of treatments reported here are likely underestimates. Finally, the costs presented are allowable costs (patient paid plus provider paid) and are not broken down to show out-of-pocket burden.

**RESULTS**

**Even Split between Dementia Patients Treated and Not Treated with Dementia Drugs**
Half of our study sample (50.7 percent) was prescribed a dementia drug within one year of their dementia diagnosis, while the other half (49.3 percent) was not prescribed ChEI or memantine (figure 1).

**Majority of Older Adults with Dementia Were Treated with Drugs for Longer Than Clinically Indicated**
Most older adults with dementia in our sample (70 percent) were prescribed dementia drugs for 13 months or longer. Eleven percent were treated with dementia drugs for 1 month or less, while the remaining 19 percent were treated for between 2 and 12 months (figure 2).

**Cholinesterase Inhibitor Was the Most Common Treatment**
Of the 36,000 MA enrollees in our sample who initiated drug treatment for dementia, the majority (58 percent) were prescribed ChEI, 33 percent were prescribed ChEI and memantine, and 8 percent were prescribed memantine only. Notably, 16 percent of patients in our sample were prescribed ChEI or memantine without an accompanying diagnosis of dementia on the insurance claim.

**Older Adults with Dementia Incurred Substantial Drug Costs**
Total dementia drug costs were highest for those taking ChEI and memantine together: an average of $151 per month (up to $1,050) and more than $4,800 (up to $19,316) over the 10-year study period (table). Costs for memantine alone averaged $200 per month and $3,163 between 2006 and 2015. Costs for ChEI alone were substantially lower, averaging $59 per month and $997 total over the 10-year study period.

As much as $18,000 of total dementia drug spending occurred after the first year of use—that is, beyond the duration of treatment supported by clinical evidence.
FIGURE 2
Duration of Dementia Drug Treatment among MA Enrollees 65+, N = 36,000

![Bar chart showing percentage of dementia drug treatment duration among MA enrollees 65+.

TABLE
Costs and Duration of Dementia Drug Treatment among MA Enrollees 65+, 2006–15, N = 36,000

<table>
<thead>
<tr>
<th></th>
<th>ChEI ( N = 21,034 )</th>
<th>Mem ( N = 2,971 )</th>
<th>ChEI + Mem ( N = 11,995 )</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up Duration (days)</td>
<td>1,029 (SD = 601)</td>
<td>1,005 (SD = 599)</td>
<td>1,243 (SD = 685)</td>
<td>&lt; 0.01</td>
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<tr>
<td>Duration of Dementia Drug</td>
<td>583 (SD = 549)</td>
<td>532 (SD = 512)</td>
<td>1,031 (SD = 650)</td>
<td>&lt; 0.01</td>
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<tr>
<td>Treatment (days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monthly Dementia Drug</td>
<td>$59 (SD = 89) Min = 1</td>
<td>$200 (SD = 127) Min</td>
<td>$151 (SD = 108) Min = 1</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Cost</td>
<td>Max = 1,200</td>
<td>Max = 1,489</td>
<td>Max = 1,050</td>
<td></td>
</tr>
<tr>
<td>Total Dementia Drug Cost</td>
<td>$997 (SD = 2,004) Min</td>
<td>$3,163 (SD = 3,301)</td>
<td>$4,806 (SD = 4,343) Min = 14</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>Max = 19,228</td>
<td>Max = 19,078</td>
<td>Max = 19,316</td>
<td></td>
</tr>
<tr>
<td>Percentage on Dementia</td>
<td>60.2%</td>
<td>56.8%</td>
<td>90.3%</td>
<td>&lt; 0.01</td>
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<tr>
<td>Drugs More than One Year</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Total Dementia Drug Cost</td>
<td>$754 (SD = 2,004) Min</td>
<td>$2,261 (SD = 2,179)</td>
<td>$3,598 (SD = 4,343) Min = 14</td>
<td>&lt; 0.01</td>
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<tr>
<td>after One Year</td>
<td>Max = 18,033</td>
<td>Max = 17,328</td>
<td>Max = 17,549</td>
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</tr>
</tbody>
</table>

ChEI=Cholinesterase inhibitor; Mem=Memantine; SD=Standard Deviation
DISCUSSION

Of the MA enrollees ages 65 and older with dementia in our sample who were prescribed dementia drugs, the majority (70 percent) took the drugs for longer than the duration of treatment supported by clinical evidence. ChEI was the most commonly used drug treatment, followed by a combination of ChEI and memantine. Some patients took dementia drugs for the entire 10-year study period at a cost of nearly $20,000. It is unclear why patients were prescribed dementia drugs for such long periods, although this may be related to perceived benefit or lack of other treatment options. The latter could warrant additional attention, as there is strong evidence that some non-pharmacological treatment options can have positive effects for dementia patients and their caregivers.

Nearly half of patients with a dementia diagnosis did not initiate dementia drugs within one year of diagnosis. It is unclear whether the overriding factor is patients (or their caregivers) not filling a prescription or never receiving a prescription at all.

CONCLUSION

Despite a lack of clinical evidence supporting the practice, many clinicians continue to prescribe dementia drugs long term at a substantial cost to patients and the overall health care system. While it is not uncommon for drugs to be prescribed in ways that do not fit with clinical trial evidence, clinicians, patients, and caregivers using dementia drugs should ensure that the cost and side effects associated with such products are appropriately balanced with cognitive benefits.

Notably, these findings are not unique to dementia drugs. Older adults typically use multiple prescription drugs, often on a long-term basis, and see multiple health care providers without meaningful oversight of their overall prescription drug regimens. Health care providers must regularly assess patients and their prescription drug regimens to ensure regimens remain appropriate given changing health status and needs. Accessible and up-to-date information on a drug’s effectiveness and side effects is essential to help increase the practice of de-prescribing medications that may no longer be of benefit, or even cause harm.

REFERENCES


