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Unintended Benefits: The Potential Economic Impact Of Addressing Risk Factors To Prevent Alzheimer's Disease

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ABSTRACT **Certain chronic conditions appear to be modifiable risk factors of Alzheimer's disease and related dementias. To understand the potential health and economic impacts of addressing those risk factors, we used data on a Medicare cohort to simulate four scenarios: a 10 percent reduction in the prevalence of diabetes, hypertension, cardiovascular diseases, respectively, and a 10 percent reduction in body mass index among beneficiaries who were overweight or obese. Our simulation demonstrated that reducing the prevalence of these conditions may yield "unintended benefits" by lowering the risk, delaying the onset, reducing the duration, and lowering the costs of dementia. More research is needed to clarify the exact relationship between various other chronic diseases and dementia. However, our findings highlight potential health gains and savings opportunities stemming from the better management of other conditions associated with dementia.**

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Therapeutic advances have led to substantial improvements in life expectancy among people living with chronic conditions such as diabetes, hypertension, and cardiovascular diseases.[1,2] But people with some conditions who live longer seem to be at greater risk than others of developing certain aging-related conditions, including Alzheimer's disease and related dementias (ADRD).[3–9] For example, patients with type 2 diabetes are roughly twice as likely as people without diabetes to develop dementia.[9]

The risk of Alzheimer's disease and related dementias also appears to increase with many conditions that damage the heart or blood vessels, such as congestive heart failure and stroke.[10–12] One study estimated that half of all Alzheimer's cases in the United States (2.9 million) may be attributable to a set of potentially modifiable risk factors such as diabetes, hypertension, obesity, and smoking and that reducing the prevalence rates of these risk factors by 10 percent could prevent as many as 184,000 cases of Alzheimer's disease.[13]

Numerous prevention strategies for Alzheimer's disease and related dementias have been proposed to address these risk factors.[14–21] For example, several epidemiological studies have reported that the use of statins is associated with a lower incidence of dementia in some populations.[18–20] Another recent analysis suggested that people who took certain medications commonly used for high blood pressure had a significantly lower risk for dementia, compared to people who did not take the medications.[21]

There is insufficient evidence to recommend the use of any of those therapeutic agents for the prevention of dementia. However, in advocating for the control of diabetes, high blood pressure, or body weight, it is useful to bear in mind these strategies' potential for reducing the effects of possible risk factors for dementia.[3,13]

Relatively little attention has been paid to potential unintended benefits stemming from the effective management of modifiable risk factors

related to dementia. How the reduction of these risk factors would affect disease burden and health care costs is a critical question, given the lack of effective interventions for Alzheimer's disease and related dementias; the potentially high cost of any new therapy; and the pressure from payers, employers, and governments to restrain spending growth. Anticipating the possible consequences of addressing modifiable risk factors could help government officials and policy makers assess potential future costs and health care needs and conduct public health planning for Alzheimer's disease and related dementias.

To explore potential benefits, we used a cohort-based simulation model to examine the relationship between the reduction of possible risk factors for dementia, the onset and duration of dementia, and its costs to Medicare and Medicaid. We investigated several hypothetical scenarios in which effective disease management would reduce the prevalence rates for the following four modifiable dementia-related conditions: overweight or obesity, diabetes, hypertension, and cardiovascular diseases.

Our study focused on the population with Alzheimer's disease and related dementias and thus differs from recent efforts that have examined the broader issue of delayed aging.[22] Our simulation also differs from other recent research that has quantified costs attributable to dementia[23] in that we explored potential savings opportunities that could result from the mitigation of dementia-related risk factors. Our results can serve as benchmarks for evaluating efforts to prevent dementia using different strategies, including hypothetical disease-modifying agents.

Study Data And Methods

DATA SOURCE AND SAMPLE We analyzed data from the 1997–2005 Medicare Current Beneficiary Survey (MCBS) Cost and Use Files. The data sets provide detailed information on sociodemographic characteristics and health status for a nationally representative sample of Medicare beneficiaries. Moreover, the survey data can be linked with Medicare claims.

Our study sample consisted of 8,586 Medicare beneficiaries ages sixty-five and older who had dementia and 105,225 beneficiaries in the same age group who did not. Beneficiaries were identified as having Alzheimer's disease or a related dementia based on one of the following three factors: self- or proxy report of dementia; an *International Classification of Diseases*, Ninth Revision, Clinical Modification (ICD-9-CM), diagnosis code of 290–99, 797, 292.82, 291.2, 294.1, 294.8, or 331.0–331.2; or self- or proxy report of use of any medications that target Alzheimer's disease and related dementias, such as donepezil (Aricept), rivastigmine (Exelon), galantamine (Reminyl or Razadyne), and memantine (Namenda).[24]

ESTIMATION OF RISK AND COSTS Using the 1997–2005 MCBS data, we estimated a multistage model to predict a person's risk of Alzheimer's disease and related dementias and Medicare and Medicaid costs conditional on dementia status (for more information about the model, see online Appendix 1).[25] Specifically, we first used logistic regression to estimate the probability of the person's having dementia in a particular year, adjusting for age; body mass index (BMI); comorbidities; acute medical events; and other sociodemographic characteristics, including sex, race, education, and income.

We then used a two-part model to predict the person's annual Medicare and Medicaid expenditures by dementia status, adjusting for the same set of covariates and time to death. The first part of the model was a logistic regression that predicted whether a person had any health care use that was reimbursed by Medicare or Medicaid. For beneficiaries who had any expenditures, we used an ordinary least squares model to predict the natural log of annual Medicare and Medicaid expenditures.

SIMULATION In light of the dynamic relationships between disease onset and health care costs over a person's lifespan, we constructed a cohort-based Dynamic Aging Process (DAP) simulation to characterize the aging process. Details of this model have been reported elsewhere.[26,27] Briefly, the model used a framework similar to that of the RAND Future Elderly Model[28] to track the development of chronic conditions, changes in body weight, changes in functional status, and annual health care costs from age sixty-five to death.

Based on the MCBS data, the model projected outcomes for a sixty-five-year-old virtual cohort born in the 1920s or 1930s. Our simulation followed the cohort from age sixty-five until death. The model projected five outcomes: Medicare and Medicaid costs, acute medical events, functional status transitions, BMI transitions, and mortality. All five model outcomes were simulated simultaneously using maximum likelihood estimation methods. Additional details about the model are provided in Appendix 2.[25]

Using the DAP model, we explored how a reduction of possible risk factors for Alzheimer's disease and related dementias might influence disease onset, course of illness, and Medicare and Medicaid costs. We did this by incorporating the parameters obtained from the dementia re-

gression model into the DAP model to simulate a beneficiary's potential development of dementia at a certain age. If the model predicted that the beneficiary would develop dementia, that condition was assumed to persist until death.

Next, using parameters from the two-part model, we simulated annual Medicare and Medicaid costs based on age, dementia status, time to death, education level, comorbidities, BMI, and other demographic characteristics. We used smearing factors to transform the predicted log expenditures to level expenditures, and the Monte Carlo process to estimate random error terms.

Most people who have Alzheimer's disease or a related dementia also have other coexisting conditions that may independently increase health care costs.[29] To isolate the costs attributable to dementia over a patient's lifespan, we conducted a counterfactual simulation, instead of simply comparing the costs for beneficiaries who had dementia with those for beneficiaries who did not.[23,30]

First, for beneficiaries with dementia, we used the DAP model to calculate lifetime Medicare and Medicaid costs from the onset of the disease until death. Second, we conducted a counterfactual simulation to estimate lifetime Medicare and Medicare costs for the same beneficiaries, assuming the same aging process and individual characteristics but without the development of dementia. We estimated Medicare and Medicaid costs attributable to dementia as the difference in costs between these two simulations.

For the purpose of this analysis, we explored the potential health and economic impacts of addressing four potentially modifiable risk factors: overweight or obesity (defined as BMI greater than or equal to 25); diabetes; hypertension; and cardiovascular diseases, including stroke and heart diseases. We conservatively assumed that the BMI of people who were overweight or obese and other risk factors could be reduced by 10 percent, and we simulated the consequences. We identified a plausible effect size for risk-factor reduction based on available evidence, such as Cochrane reviews and meta-analyses.[13,31–33] We considered these reductions to be plausible since they correspond to what has been observed in disease management programs in a real-world setting, such as the Diabetes Prevention Program.[34] All cost estimates were adjusted to 2012 dollars using the medical Consumer Price Index.

LIMITATIONS Several issues merit notice at the outset. First, we used a multiprong case definition for identifying patients with Alzheimer's disease or a related dementia. Prior research showed that an inclusive case definition, such as the one we used, is preferred to a single data source (such as a diagnosis of dementia in claims records) because the single source is more likely to underestimate the prevalence and costs of dementia and is liable to sample selection bias.[24,35]

Second, we did not directly assess the costs of interventions to modify risk factors.

Third, our estimates assumed a causal relationship between the risk factors and Alzheimer's disease and related dementias. However, dementia may be correlated with many unobserved factors, such as diet, exercise, and cognitive engagement. In addition, we simulated the impact of reducing the prevalence of each of these conditions independently.

Fourth, the underlying pathological processes that lead to Alzheimer's disease and related dementias may begin twenty to thirty years before any symptom appears.[36] The available data did not allow us to identify the optimal timing of implementing interventions to modify risk factors.

Finally, our analysis did not include the value of caregivers' time or lost productivity, which were not available in the MCBS data. Thus, our estimates of the economic impacts related to dementia are likely to be conservative.

Study Results

On average, beneficiaries who had Alzheimer's disease or a related dementia were older than those who did not (82.5 versus 71.3 years) (Appendix 3).[25] Compared to beneficiaries who did not have dementia, those who did had a lower BMI (24.5 versus 26.6), a greater risk of acute cardiovascular disease events (35.8 percent versus 27.1 percent), and higher mortality (15.9 percent versus 4.7 percent). All of these differences were significant ($p < 0.05$).

Our model predicted that later disease onset would reduce Medicare and Medicaid costs for Alzheimer's disease and related dementias (Exhibit 1). For example, an onset at age seventy would result in average Medicare dementia costs of roughly $35,000 over a lifetime, compared with average lifetime costs of less than $5,000 if the disease onset were at age eighty-five. Overall, costs for dementia paid by Medicare exceeded those paid by Medicaid across all ages. However, the cost difference was smaller among beneficiaries who developed dementia later in life.

At baseline, our model predicted that 14.5 percent of the sixty-five-year-old cohort would develop dementia at some point, the average onset age would be 80.72 years, and those who developed dementia would have the condition for an

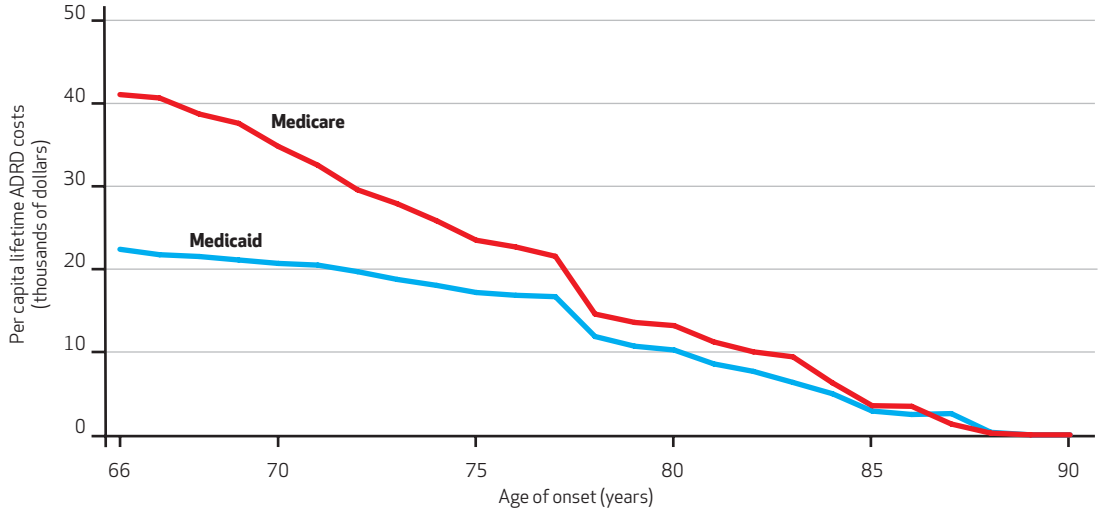
14.5%

Develop dementia

Our model predicted that 14.5 percent of the 65-year-old cohort would develop dementia, with the average age of onset being 80.72 years.

EXHIBIT 1

Estimated Per Capita Lifetime Medicare And Medicaid Costs Attributed To Alzheimer's Disease And Related Dementias (ADRD), By Age Of Onset



SOURCE Authors' calculations using the Dynamic Aging Process model. **NOTE** Costs are for a sixty-five-year-old cohort and were adjusted to 2012 dollars using the medical Consumer Price Index.

average of 5.03 years (Exhibit 2). Reducing the prevalence rate of cardiovascular diseases by 10 percent would decrease the risk of dementia by 0.6 percent, delay the onset of dementia by 0.1 year, and reduce the time spent living with it by 0.03 years (from 5.03 years to 5.00 years).

Estimated per capita lifetime costs attributable to Alzheimer's disease and related dementias are $12,366 for Medicare and $11,105 for Medicaid (Exhibit 2). Our estimated disease duration of 5.03 years implies annual per capita costs for dementia of roughly $2,400 for Medicare and $2,200 for Medicaid. Our cost estimates correspond closely to the annual Medicare cost estimate reported by Michael Hurd and coauthors of $2,752 (in 2010 dollars).[23] That dementia cost estimate reflects an adjustment for demographic characteristics and comorbidities and is based on data from the Aging, Demographics, and Memory Study subsample of the Health and Retirement Study.

Our model projected that reducing BMI by 10 percent among overweight or obese people would reduce Medicaid's lifetime dementia costs

EXHIBIT 2

Estimated Lifetime Risk Of Alzheimer's Disease And Related Dementias (ADRD), Course Of Illness, And Projected Per Capita Lifetime Medicare And Medicaid Costs Attributable To ADRD, By Scenario

		10 percent reduction in:							
		BMI among overweight or obese individuals		Diabetes		Hypertension		Cardiovascular diseases	
	Baseline	Estimate	Change	Estimate	Change	Estimate	Change	Estimate	Change
Probability of ADRD (%)	14.46	14.46	0.00	14.46	0.00	14.37	−0.09*	13.93	−0.53**
Duration of ADRD (years)	5.03	5.00	−0.03	5.02	−0.01	5.00	−0.03*	5.00	−0.03**
AGE (YEARS)									
At onset of ADRD	80.72	80.85	0.13	80.74	0.02	80.75	0.03*	80.81	0.09**
At death	85.75	85.85	0.10	85.76	0.01	85.75	0.00	85.81	0.06**
PER CAPITA LIFETIME COST OF DEMENTIA (2012 DOLLARS)[a]									
Medicare	12,366	11,779	−587**	11,715	−651**	11,375	−991**	10,953	−1,413**
Medicaid	11,105	7,866	−3,239**	10,981	−124**	10,058	−1,047**	9,897	−1,208**
Total	23,471	19,645	−3,826**	22,696	−775**	21,433	−2,038**	20,850	−2,620**

SOURCE Authors' calculations using the Dynamic Aging Process model. **NOTES** Overweight or obesity is body mass index (BMI) greater than or equal to 25. Change is from baseline. [a]Adjusted using the medical Consumer Price Index. *$p < 0.10$ **$p < 0.05$

by $3,239 per capita (Exhibit 2), primarily by delaying the onset of the disease. A 10 percent reduction in cardiovascular diseases would also yield substantial lifetime savings for both Medicare ($1,413 per capita) and Medicaid ($1,208 per capita).

To illustrate the impact on the US population, consider the following example. There are approximately seventy-six million baby boomers in the United States. A 10 percent decrease in cardiovascular diseases would eliminate twenty-eight million person-months living with dementia, reducing the total population time spent with the disease from 664 million to 635 million person-months (Exhibit 3). Reductions in BMI among overweight or obese individuals, in diabetes, or in hypertension would also reduce the duration of dementia and delay its onset, although by smaller amounts.

At the population level, we estimated that a 10 percent reduction in BMI among overweight or obese beneficiaries would save Medicare $6 billion and Medicaid $35 billion over the lifetime of the approximately seventy-six million baby boomers in the United States as a result of lower dementia costs (Exhibit 4). Similar reductions in cardiovascular diseases would save approximately $20 billion for Medicare and $17 billion for Medicaid; in diabetes, $7 billion for Medicare and $1 billion for Medicaid; and in hypertension, $12 billion each for Medicare and for Medicaid.

Discussion

Chronic conditions such as diabetes and cardiovascular diseases are major contributors to high health care costs in the United States. Some of these chronic conditions have been identified as potentially modifiable risk factors for Alzheimer's disease and related dementias, which substantially burden patients, caregivers, and the health care system. Using a cohort-based Dynamic Aging Process model, we simulated several scenarios to explore the potential impact of addressing modifiable risk factors for dementia on disease onset, course of illness, and lifetime Medicare and Medicaid costs. Our results suggest that reducing prevalence rates for certain chronic conditions, especially cardiovascular diseases, may yield unintended benefits related to Alzheimer's disease and related dementias, including lower risk, delayed onset, reduced duration, and a substantial reduction in costs.

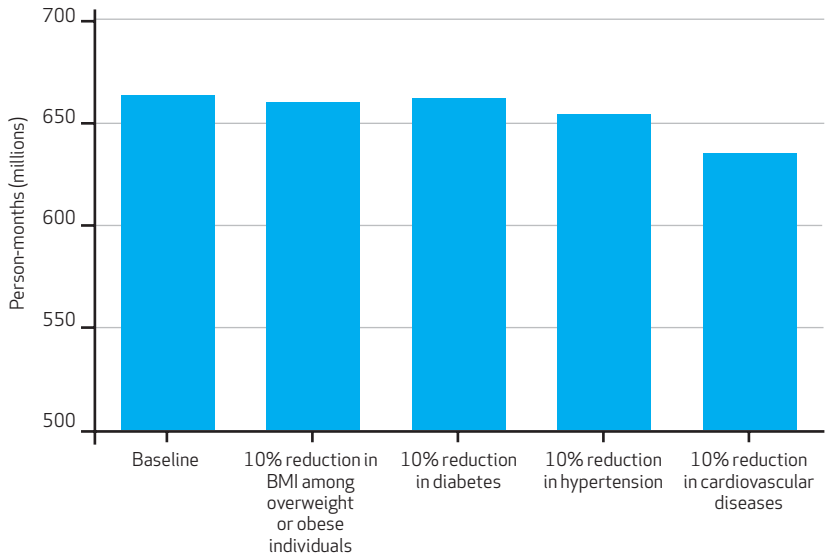
Our simulation indicates that the sixty-five-year-old cohort's lifetime risk of dementia is 14.5 percent, an estimate that is comparable to results reported by Brenda Plassman and coauthors in their analysis of the Aging, Demographics, and Memory Study subsample of the Health and Retirement Study.[30] The validity of our model is further supported by the close correspondence between our estimate of Medicare dementia costs and the results of Hurd and colleagues.[23,37]

As the costs of care for Alzheimer's disease and related dementias have risen, calls have increased for prevention and early intervention. The prevention of dementia remains an important goal because of the disease's high prevalence and associated economic burden. However, prevention trials are especially challenging in dementia because the disease's mechanism remains unclear, the selection of the target population for enrollment is difficult, and the trial would likely require a large sample and extended follow-up.[5,38,39] Our simulation provides an alternative approach for projecting the potential health and economic impacts of addressing risk factors associated with dementia.

In 2010 the National Institutes of Health published a state-of-the-science report that systematically reviewed the evidence on risk factors related to Alzheimer's disease and related dementias.[8] Despite many limitations in the available evidence, the report identified several potentially modifiable factors—including diabetes, depression, smoking, and physical inactivity—as being associated with an increased risk of dementia. Other studies have suggested that chronic conditions such as obesity, hypertension, and cardiovascular diseases and a poor diet—one

EXHIBIT 3

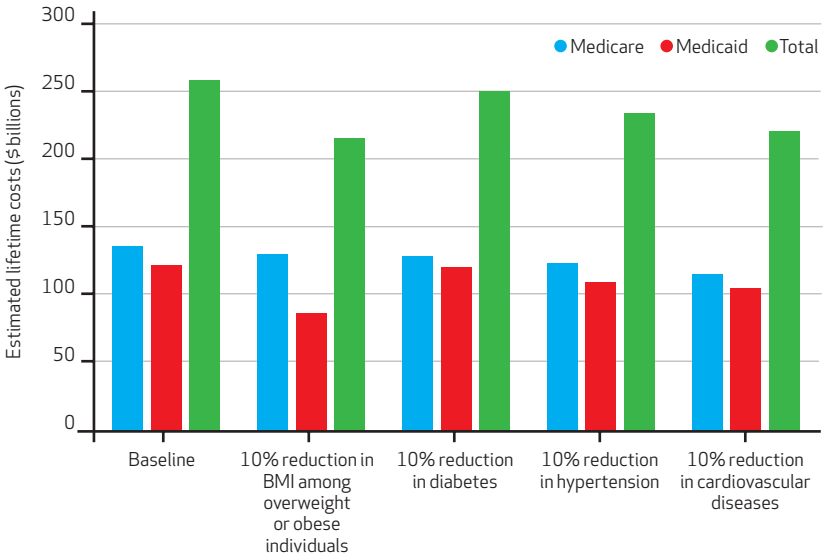
Estimated Time Spent Living With Alzheimer's Disease And Related Dementias Among The Seventy-Six Million US Baby Boomers, By Scenario



SOURCE Authors' calculations using the Dynamic Aging Process model.

EXHIBIT 4

Estimated Lifetime Medicare and Medicaid Costs Attributed To Alzheimer's Disease And Related Dementias (ADRD) For The Seventy-Six Million US Baby Boomers, By Scenario



SOURCE Authors' calculations using the Dynamic Aging Process model. **NOTE** Costs were adjusted to 2012 dollars using the medical Consumer Price Index.

high in saturated fat and low in vegetables—are also linked with a higher risk of dementia.[3–7,10–13,40] In other words, dementia appears to be a multifactorial disease associated with many observed and unobserved factors.

Our study focused on obesity or overweight, diabetes, hypertension, and cardiovascular diseases because they are biologically plausible risk factors and there is reasonably strong epidemiological evidence to support the associations. Addressing these risk factors could play an important role in reducing dementia. Because it is a progressive disease that begins long before any symptoms become apparent, our analysis did not assume that risk-factor modification interventions targeted only older adults. Our estimates did assume a causal relationship between the risk factors and dementia, however. The potential health and economic impacts related to dementia could be higher or lower, depending on the extent to which the risk factors could be modified.

To explore this uncertainty, we considered more-conservative scenarios in which risk-factor prevalence rates were 5 percent, instead of 10 percent, lower than the present levels (Appendix 2).[25] As an example, we found that reducing the prevalence rate of cardiovascular diseases by 5 percent would decrease the risk of dementia by 0.4 percent, delay its onset by 0.5 years, and save Medicare $700 per capita and Medicaid $600 per capita in dementia costs.

Many public- and private-sector interventions (such as counseling, education, lifestyle changes, and medication) that target the chronic conditions we analyzed are already under way.[41–44] For example, the Diabetes Prevention Program,[34] a major multicenter clinical research study, showed that diabetes may be prevented or delayed when people lose a modest amount of weight through diet and exercise. Program participants in the lifestyle intervention group reduced their risk of developing diabetes by 58 percent during the study.

Similarly, an analysis using the Archimedes model demonstrated that the aggressive application of eleven nationally recommended prevention interventions could prevent many cases of cardiovascular diseases.[42] This study estimated that if everyone received the interventions for which they were eligible, myocardial infarctions and strokes would be reduced by approximately 63 percent and 31 percent, respectively. Clinical trials of low-calorie diets (1,000–1,200 kilocalories per day) for weight loss[45] and the Trials of Hypertension Prevention[46] provide additional examples of effective disease prevention.

There is insufficient evidence to support recommending the use of any of the conventional therapies for chronic conditions to treat or prevent Alzheimer's disease and related dementias. However, we believe it is useful to explore the potential unintended benefits of these therapies. Opportunities for maintaining cognitive health are growing along with the understanding of risk factors related to dementia. For instance, some prospective randomized studies show that targeting vascular risk factors, such as systolic hypertension, is associated with lower prevalence of dementia,[47] and that certain therapies to lower blood pressure may protect against dementia in older adults.[16,17,21]

Maintaining cognitive health is a vital part of both healthy aging and quality of life. If the onset of dementia can be delayed and its duration shortened, healthy life expectancy—the number of years spent living in good health—can be extended. As a result, the lives of many older adults can be improved.

In addition to health benefits, our simulation also suggests that addressing potentially modifiable risk factors of dementia might substantially reduce health care costs. That finding is somewhat unexpected, because other efforts to prevent chronic disease have shown that greater longevity could increase health spending overall. This is because people who live longer are at an elevated risk of developing costly age-related conditions, including dementia. Yet our model predicted, for example, that a 10 percent reduction in cardiovascular diseases among baby

boomers would reduce lifetime Medicare costs for dementia by roughly $20 billion and corresponding Medicaid costs by $17 billion.

This result primarily reflects our finding that addressing risk factors for dementia would reduce morbidity but make only a minimal contribution to dementia-related longevity gains: For example, reducing cardiovascular diseases by 10 percent would extend life expectancy by roughly three weeks. Delaying the onset of dementia and reducing its duration would extend life expectancy without dementia. Therefore, our simulation demonstrated that by achieving a "compression of morbidity,"[48] reducing certain modifiable risk factors for dementia could lower lifetime health care costs.

Extending healthy life expectancy will be a critical part of any successful strategy for addressing an aging population.[49] One analysis estimated that delayed aging could increase life expectancy by roughly 2.2 years, most of which would be spent in good health.[22] The economic value of delayed aging was estimated at $7.1 trillion over fifty years.[22]

More research is needed to establish the relationship between other chronic diseases and dementia. However, our study suggests that by delaying the onset of dementia and reducing its duration, the mitigation of certain modifiable risk factors could increase dementia-free life expectancy and reduce dementia costs for Medicare and Medicaid.

Because many chronic diseases are correlated, multifaceted prevention efforts are probably needed to address multiple risk factors for dementia. In addition, the management of diabetes, hypertension, obesity, and cardiovascular diseases in many patients remains suboptimal. To build on the findings reported here, future research could assess how recognizing the unintended benefits of dementia prevention may encourage better adherence to treatment of the risk factors.

Conclusion

Evidence has suggested that some conventional therapies intended to address certain chronic conditions may have the added benefit of delaying the onset of Alzheimer's disease and related dementias or reducing the risk that dementia will develop at all. Clearly, more data are needed to support the control of risk factors such as obesity, diabetes, hypertension, and cardiovascular diseases as an effective way to prevent dementia. However, it is important to understand the potential consequences.

Our findings highlight potential health gains and saving opportunities stemming from the better management of other conditions associated with Alzheimer's disease and related dementias. Future research should assess the cost-effectiveness of dementia prevention by comparing interventions such as the use of disease-modifying agents, targeting of modifiable risk factors, and direct treatment of the condition. Such analyses could help payers, providers, and policy makers prioritize different strategies for managing dementia. ■

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25 To access the Appendix, click on the Appendix link in the box to the right of the article online.
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