Published in final edited form as:
Health Aff (Millwood). 2010 ; 29(1): 102–108. doi:10.1377/hlthaff.2009.0525.

Genetic Testing For Alzheimer's And Long-Term Care Insurance

Donald H. Taylor Jr [assistant professor],
public policy at Duke University in Durham, North Carolina

Robert M. Cook-Deegan [director],
Institute for Genome Sciences and Policy Center for Genome Ethics, Law, and Policy at Duke University

Susan Hiraki [genetic counselor and project coordinator],
REVEAL II study at Boston University

J. Scott Roberts [assistant professor],
Department of Health Behavior and Health Education at the University of Michigan in Ann Arbor

Dan G. Blazer [J.P. Gibbons Professor], and
Psychiatry and Behavioral Sciences and vice chair for Education and Academic Affairs at Duke University

Robert C. Green [codirector]
Boston University's Alzheimer's Disease Center, as well as a professor of neurology, genetics, and epidemiology, in Boston, Massachusetts

Donald H. Taylor: don.taylor@duke.edu

Abstract

A genetic marker known as apolipoprotein E provides a clear signal of a person's risk of developing Alzheimer's disease and thus that person's future need for long-term care. People who find that they have the variant of the trait that increases Alzheimer's disease risk are more likely to purchase long-term care insurance after receiving this information. If the information is widely introduced into the insurance market, coverage rates could be affected in different ways, depending on who possesses that information. Policymakers will eventually need to confront the issue of the use of this and other markers in the pricing of long-term care insurance.

Advances in genetic testing and the increased knowledge that results have presented both opportunities and challenges. From consumers' point of view, testing for a specific genetic marker that indicates the likelihood of needing long-term care as a result of Alzheimer's disease could affect their interest in purchasing long-term care insurance. The insurance industry would, not surprisingly, take a different view, seeing potential adverse selection and its impact on insurance premiums and the availability of coverage.[1]

One genetic test now enables people to gain information about their future risk of Alzheimer's disease, a condition that frequently results in the need for long-term care. This is a test for a variant of apolipoprotein E, or APOE. People inherit one of three genetic traits from each of their parents: APOE2 (e2), APOE3 (e3), or APOE4 (e4). Having two e3 traits is most common and represents average risk of developing Alzheimer's disease. Having at least one e4 trait increases a person's risk of developing Alzheimer's, and having at least one e2 trait reduces it. A person who has two e4 traits (one from each parent) has a greatly increased risk of developing Alzheimer's disease.

Anticipating the future impact of genetic testing, Congress passed the Genetic Information Nondiscrimination Act (GINA) of 2008. This act makes it illegal for health insurers and

employers to discriminate based on the results of genetic testing. However, it does not address long-term care, disability, or life insurance. Thus, determining whether the information provided by APOE genotyping might affect long-term care insurance markets provides an example of consumer and insurance industry behavior in markets that are not subject to the nondiscrimination law.

This paper examines the role of genetic testing as it applies to the market for long-term care insurance, focusing on propensity for Alzheimer's disease and effects on consumers' and insurance companies' behavior. We examine the long-term care insurance market and explore the reasons why so few consumers purchase this coverage. We conclude by considering the likely effect of the availability of APOE testing on consumers and insurers in the long-term care insurance market, assuming four different scenarios.

Long-Term Care

Long-term care is provided in both community and institutional settings and is financed by private and public sources.[2] Medicaid pays for a great deal of nursing home care, while Medicare covers only a limited amount. Private long-term care policies cover both community-based and nursing home care. Fewer than 10 percent of Americans age fifty and older have such coverage.[3]

Long-term care is a common risk that brings potentially catastrophic costs: seven of ten people who reach age sixty-five use some long-term care. Mean out-of-pocket long-term care spending for those reaching age sixty-five is $21,100, and more than $100,000 (in 2005 dollars) for the one of five people who use such care for five years or more.[4] A recent estimate is that $1.5 million in liquid wealth would be needed to self-finance the maximum period that a person might expect to use long-term care from age sixty-five until death.5 Thus, virtually the entire U.S. population is at some risk of using more care than their assets can finance.

Why Do So Few People Buy Private Long-Term Care Insurance?

There are six primary reasons that people do not purchase long-term care insurance. First, there are no clear risk signals for future long-term care need when people are relatively young and premiums are low. Even if one could predict a health event such as a stroke at age seventy-five, some will die suddenly, some will recover fully, while others will experience severe disability and use extended long-term care.

Second, most people do not understand the cost of long-term care, especially the nonfinancial burden imposed on caregivers.[6,7] Third, three of ten people who reach age sixty-five experience sudden death and never use long-term care, while some using long-term care for only a few months would not receive the benefits of insurance because of benefit triggers and deductibles.[4] Fourth, Medicaid may crowd out, or cause people not to buy, long-term care insurance.[8]

Fifth, a sizable portion of the population has neither sufficient wealth to protect nor income to pay long-term care insurance premiums.[9] Sixth, the structure of policies themselves (benefits denominated in dollars per day, inflation risk of purchasing insurance for an event that is probabilistically far away, increases in premiums for everyone when insurance companies face insolvency, denial of applications)[10,11] reduces purchase rates.

There are several motivations for increasing private long-term care insurance coverage. Doing so could reduce Medicaid long-term care costs; Medicaid now pays for approximately half of U.S. nursing home care.[2] Tax credits and partnership programs[12] are examples of public policies whose goal is to shift long-term care spending from Medicaid to private insurance. Expanding insurance also could ensure that elderly people receive needed care. And expanded

rates of insurance coverage could reduce premiums for low- or average-risk people who nevertheless wanted to purchase a policy, simply because an expanded risk pool should lead to reduced premiums.

Study Data And Methods

We turn now from a general discussion of long-term care insurance to examine genetic testing for Alzheimer's risk and its role in the long-term care insurance market.

The APOE genetic marker has been consistently shown to be associated with risk of Alzheimer's disease.[13] Because 75 percent of people developing this disease eventually move to a nursing home, this makes APOE a plausible genetic marker to use to identify those at risk of future long-term care use.[14] We tested whether APOE genotype independently predicts actual nursing home placements in a community-based sample, the Piedmont Health Survey of the Elderly. Further, we analyzed whether participants in the second REVEAL clinical trial reported being more likely to purchase long-term care insurance upon finding out they had an variant of APOE that increased the risk of Alzheimer's disease. In this way, we provide evidence of how well APOE predicts actual long-term care use, as well as how a selected sample of consumers respond to receipt of information about their APOE genotype.

The Piedmont Health Survey of the Elderly is a population-based survey of a community cohort of people age sixty-five and older; it is designed to investigate physical, psychological, and social functioning.[15] Participants lived in five contiguous counties (one urban, four rural) in the North Central Piedmont region of North Carolina. A baseline interview in 1986–87 was followed by three additional in-person interviews and four telephone interviews; the last in-person interview was in 1996–97. Six years after baseline, blood was drawn from consenting subjects, and APOE genotype was assessed using standard procedures.[16] The number of subjects with useable genotyping for this study was 2,089.

We used individual APOE genotype as a predictor of moving to a nursing home from study inception (1986–87 in home interview) until 31 December 2006. People with at least one e2 trait and no e4 trait ($n = 308$) were hypothesized to be at low risk for moving to a nursing home; those with at least one e4 trait ($n = 578$) were hypothesized to be at high risk; and those with two e3 traits ($n = 1$; 113) were hypothesized to have average risk. The group with two e3 traits served as the comparison group in all analyses. People who had one e2 trait and one e4 trait ($n = 90$) were excluded from analyses following the normal convention in the literature.[17] We also controlled for self-reported age, sex, marital status, and race, and we estimated a logistic regression model that identified the effect of APOE on the likelihood of moving to a nursing home.

The REVEAL study[18,19] is a series of multisite randomized clinical trials designed to assess the impact of APOE genotype disclosure on first-degree relatives (that is, adult children, siblings) of people with Alzheimer's disease. In each of the study protocols, genetic counselors provide education, APOE genotyping, and disease risk information to interested participants, who are then followed up to a year after risk disclosure to determine its psychological and behavioral impact. In the initial trial ($n = 162$), we found that people who were told they had at least one e4 trait were more likely than those who did not have an e4 trait to report changes in long-term care insurance after receiving this information.[1]

We report here on results from the second trial ($n = 276$, mean age = 58 years), where all participants received APOE genotype information, via the original Extended Protocol (two in-person sessions, mean duration = 76 minutes total) or a more clinically feasible Condensed Protocol (one in-person session, mean duration = 33 minutes total). Participants were asked

about their long-term care insurance holdings at baseline; in follow-up, they were asked to describe any changes made in this insurance domain.

New Empirical Evidence/Results

DOES APOE STATUS AFFECT FUTURE USE OF LONG-TERM CARE?

From study data, we find that having at least one e4 trait increased the likelihood of moving to a nursing home, controlling for other factors, among elderly people living in a community setting (Exhibit 1). People with at least one e4 trait were around 50 percent (odds ratio = 1.48; 95 percent confidence interval [CI] = 1.09–2.01) more likely than those who had two e3 traits to enter a nursing home during a ten-year follow-up period. In past work with the study database, having at least one e4 trait did not predict quality-of-life declines among people remaining in the community.[20] Other research has shown that people with at least one e4 trait are around 4.6 times more likely to develop Alzheimer's disease (95 percent CI = 1.3–16.1; Exhibit 1) than people with two e3 traits.[17] Thus, APOE is both a direct predictor of nursing home admission and an indirect predictor of long-term care use via its link with Alzheimer's.

HOW DO CONSUMERS RESPOND WHEN THEY LEARN THEIR APOE GENOTYPE?

Adverse selection occurs when people with a higher probability of making a claim against insurance know their risk while the insurer does not, making the consumer more likely to purchase coverage. If this takes place on a systematic basis, then the premiums charged across the risk pool are not adequate to cover the payout for long-term care services. Adverse selection assumes that the buyer has inside information and that the buyer acts upon this information.

From REVEAL II data, we find that consumers who discover that they have at least one e4 trait are 2.3 times more likely than those with two e3 traits to increase their long-term care insurance holdings, or report planning to do so (Exhibit 1). In terms of absolute likelihood of making a change, people with at least one e4 trait had a probability of 0.237 of making such a change, compared to 0.087 for those with two e3 traits. These new results extend past findings suggesting the presence of adverse selection into long-term care insurance based on one's knowledge of one's APOE genotype.[1]

Thus, the APOE genotype provides information that could be useful for assigning premiums for long-term care policies, because it predicts nursing home use, it increases risk for Alzheimer's disease, and the disclosure of the risk-increasing variant of the APOE genotype motivates consumers to make changes in their insurance holdings (adverse selection).

How The Long-Term Care Insurance Market Would Respond To APOE Genotype Information

GINA prohibits the use of genetic information for underwriting or setting health insurance premiums, and it bans employment discrimination based on genetic information unless it is job-related. It has already begun to take effect for health insurance, and all provisions were to be in effect by the end of November 2009. GINA does not, however, address long-term care insurance. Some state laws prohibit the use of genetic information in long-term care insurance, and states have the primary role in regulating insurance unless that role is superseded by federal legislation.[21] Although there is no widespread prohibition, private insurers do not use APOE genotyping or other genomic or biological markers to determine long-term care insurance eligibility or to set premiums.

Exhibit 2 outlines potential responses in the private long-term care insurance market to different scenarios regarding the availability of APOE genotype information for insurance applicants.

These scenarios illustrate the range of potential responses to the use of genetic testing in a market that is not regulated by the 2008 nondiscrimination law. They assume varying degrees of knowledge about results on the part of consumers and insurers.

STATUS QUO: NEITHER INSURERS NOR INDIVIDUALS KNOW APOE GENOTYPE

In this scenario, insurers do not use APOE or other genetic testing to underwrite policies or set premiums, and most people do not know their APOE genotype. Under the assumption that people seeking coverage have inside information, whether from APOE or otherwise, insurers increase all premiums out of caution. This further serves to drive out lower risks from the insurance pool, keeping coverage rates low and premiums high. Within the insured pool, people with low APOE-based risk subsidize those with higher risk. Under this scenario, it is unlikely that APOE genotyping will have any effect on long-term care insurance rates.

INCOMPLETE INFORMATION: ONLY CONSUMERS KNOW THEIR GENOTYPE

The second scenario, like scenario 1 (status quo), represents current reality. The technology for widespread availability of APOE genotyping exists, although it is not easily obtained by consumers. This could change in the near future, and widespread consumer knowledge of APOE genotype could lead to better understanding of long-term care risk.[22]

The company Navigenics, for example, includes an indirect marker of APOE in its direct- to-consumer “personal genomics” service. APOE status can also be inferred from other personal genomics services such as offered by 23andMe, deCODEme, SeqWright, and others. When Alzheimer’s disease risk is not reported directly, it can be inferred by use of freely available Internet resources such as SNPedia. And the company Smart Genomics offered direct-to-consumer APOE genotyping from March to October 2008.[23]

We have demonstrated adverse selection among research participants who sought and received their APOE status, so increasing consumers’ awareness of their APOE status could increase adverse selection in long-term care insurance markets. However, people in the REVEAL II sample might be more likely than a general sample of people to act on genetic information since participants had a loved one with Alzheimer’s disease, making Alzheimer’s risk information highly salient.

Adverse selection is typically viewed as hurting only the insurer, but it could also hurt low- or average-risk consumers who desire long-term care insurance, in one of two ways. First, if insurers increase all premiums because of fears of adverse selection, higher premiums than warranted will be charged to those of low or average risk. Second, if adverse selection results in higher-than-anticipated claims, then an insurance company may have to raise premiums for all people in a risk pool or face insolvency. This scenario and the status quo scenario would harm consumers of low or average risk.

INCOMPLETE INFORMATION: ONLY THE INSURER KNOWS INDIVIDUALS’ GENOTYPES

Under this scenario, which doesn’t currently exist, an insurance company might run a variety of tests for the purpose of underwriting and setting a premium for a given individual. But the insurer might not disclose the effect of the APOE genotype on the premium. A person who did not know or understand how genotype influenced his or her risk of needing long-term care might view the premium offered as too high and decline insurance, even if the company offered a fair premium.

Such one-sided use of information was a major policy argument for the passage of GINA. Using APOE to underwrite for long-term care insurance is not illegal except when banned by a few states, although it might prove highly damaging to the public image of any firm engaging

in APOE genotyping without sharing information with long-term care insurance applicants. The concern here is “adverse underwriting” in which the insurance company has “inside information” that is not available to the consumer—a situation that would be viewed by most as genetic discrimination based on APOE genotype. This discrimination would be exacerbated by failure to disclose the basis for charging higher premiums and failing to report increased risk of Alzheimer’s disease and nursing home use to insurance applicants.

Extending the GINA provisions to ban the use of genetic information for long-term care insurance underwriting would have one of several effects. It might have no effect, because insurers do not now use APOE to underwrite; it is unclear whether or not they desire to do so. However, if APOE genotyping becomes more readily available to the public, banning its use in long-term care insurance might further restrict the market to only those who are at high risk or who perceive their risk to be high. This could artificially raise premiums for people who are of average or low risk with respect to APOE, because premiums cannot be adjusted to APOE-based risk.

This could be corrected by forced risk pooling, but this would require a long-term care insurance mandate so that those at all levels of risk would be forced to buy insurance. This, of course, would also have the effect of forcing those at low risk to subsidize those at high risk. Another policy solution would be to explicitly organize such a subsidy through government action that provides premium support to those at higher risk, thus spreading the subsidy costs across a larger group of people (all taxpayers).

FULL INFORMATION: INSURERS AND INDIVIDUALS KNOW APOE STATUS

If both parties to an insurance transaction know the APOE status, and if the risk pool is big enough, then an actuarially fair premium—one that takes account of APOE and other factors known to delineate risk—would be possible. From a pure risk-adjustment standpoint, using a genetic marker is no different from charging smokers higher premiums for life insurance. The use of genotyping differs from smoking, because people are not responsible for their genotype, whereas smoking is often viewed as a choice. This feature of discriminatory pricing strikes many as unfair: it pits the notion of actuarial fairness against moral intuitions of fairness.[24]

The varying perspectives represented in the four scenarios would have to be fully discussed and policy decisions made regarding which was most important if a policy goal of increasing private long-term care insurance coverage is to be realized.

Key Policy Goal: Fair Premiums For Long-Term Care Insurance

APOE provides a clear signal of individual risk for long-term care and could be used in the setting of premiums. Developing a stable insurance market that assigns fair premiums is good for everyone. But “fair” has two highly distinct meanings to insurers and to individuals. To an actuary, it means priced according to risk; but to a consumer, it means priced according to factors that seem morally fair, and one’s genes are not a matter of choice or control. Actuarial fairness can be achieved by ensuring that long-term care insurance buyers and sellers have complete information with respect to APOE, and it could lead to an increase in the purchase of long-term care insurance via market mechanisms. However, extending the intuitions of fairness that underlie GINA to long-term care insurance will not likely lead to increases in coverage.

If APOE genotyping remains fairly uncommon and “under the radar” of long-term care insurance underwriting, it might not perturb current practice. If APOE testing becomes more common, however, then policymakers will confront a choice between actuarial fairness and fairness as embodied in GINA, if it were expanded to long-term care insurance. If the proportion

of the population insured rose from less than 10 percent toward one-third, then it seems plausible that a more robust and sustainable private insurance market could exist, aided by use of APOE testing to assign actuarially fair premiums. This would require public acceptance of actuarial fairness as being the correct policy goal. If, however, the policy goal is more in line with fairness as embodied in GINA, not risk stratification according to genetic risk, then a major policy intervention would be needed to increase long-term care insurance rates, such as a mandate to purchase long-term care insurance or a subsidy larger than that provided by current tax credits.

A reform option that was under consideration in December 2009 during the national health reform discussion, the Community Living Assistance Services and Support (CLASS) Act, would create a public long-term care insurance plan that would provide limited community-based long-term care benefits (on the order of $75 per day, on average, in 2009 dollars). People would be automatically enrolled when they began working, and there would be no underwriting, but they could opt out. One would expect such a plan to have adverse selection risks, but the degree to which this was true would depend upon employees' opt-out behavior. The Congressional Budget Office (CBO) says that it will take a premium on the order of $123–$146 per month to make the CLASS Act self-financing. People would have to pay in for five years before they could claim benefits, which would differ based on disability levels, and private insurance companies could offer wraparound policies that would cover long-term care costs above those paid for by the CLASS provisions.

Whatever reform option ultimately prevails will force policymakers, insurers, and individuals to confront the thorny equation of genetic risk markers, adverse selection, and industry reaction.

NOTES

1. Zick CD, Mathews CJ, Roberts JS, Cook-Deegan R, Pokorski RJ, Green RC. Genetic testing for Alzheimer's disease and its impact on insurance purchasing behavior. Health Aff (Millwood) 2005;24 (2):483–490. [PubMed: 15757934]
2. Kaiser Family Foundation. Medicaid/CHIP: long-term care [Internet]. Menlo Park (CA): KFF; [[cited 2009 Nov 19]]. Available from: http://www.kff.org/medicaid/longtermcare.cfm
3. Brown JR, Finkelstein A. The private market for long-term care insurance in the United States: a review of the evidence. J Risk Uncertaint 2009;76:5–29.
4. Kemper P, Komisar HL, Alecxih L. Long-term care over an uncertain future: what can current retirees expect? Inquiry 2005;42(4):335–350. [PubMed: 16568927]
5. Finkelstein A, McGarry K, Sufi A. Dynamic inefficiencies in insurance markets: evidence from long-term care insurance. Am Econ Rev 2005;95:224–228.
6. Langa KM, Chernew ME, Kabeto MU, Herzog AR. National estimates of the quantity and cost of informal caregiving for the elderly with dementia. J Gen Intern Med 2001;16(11):770–778. [PubMed: 11722692]
7. Taylor DH Jr, Schenkman M, Zhou J, Sloan FA. The relative effect of Alzheimer's disease and related dementias, disability, and comorbidities on cost of care for elderly persons. J Gerontol B Psychol Sci Soc Sci 2001;56(5):S285–S293. [PubMed: 11522810]
8. Brown JR, Finkelstein A. The interaction of public and private insurance: Medicaid and the long-term care insurance market. Amer Econ Rev 2008;98(3):1083–1102.
9. Merlis, M. Private long-term care insurance: who should buy it and what should they buy?. Menlo Park (CA): Kaiser Family Foundation; 2003. p. iii-viii.
10. Murtaugh CM, Kemper P, Spillman BC. Risky business: long-term care insurance underwriting. Inquiry 1995;32(3):271–284. [PubMed: 7591041]
11. Temkin-Greener H, Mukamel DB, Meiners MR. Long-term care insurance underwriting: understanding eventual claims experience. Inquiry 2000/01;37(4):348–358. [PubMed: 11252445]

12. Wiener, JM.; Illston, LH.; Hanley, RJ. Sharing the burden: strategies for public and private long-term care insurance. Washington (DC): Brookings Institution; 1994.

13. Farrer LA, Cupples LA, Haines JL, Hyman B, Kukull WA, Mayeux R, et al. Effects of age, sex, and ethnicity on the association between apolipoprotein e genotype and alzheimer disease: a meta analysis. JAMA 1997;278(16):1349–1356. [PubMed: 9343467]

14. Welch HG, Walsh JS, Larson EB. The cost of institutional care in Alzheimer's disease: nursing home and hospital use in a prospective cohort. J Am Geriatr Soc 1992;40(3):221–224. [PubMed: 1538039]

15. Blazer D, Burchett B, Service C, George LK. The association of age and depression among the elderly: an epidemiologic exploration. J Gerontol A Biol Sci Med Sci 1991;46(6):M210–M215.

16. Blazer D, Burchett B, Fillenbaum G. APOE e4 and low cholesterol as risks for depression in a biracial elderly community sample. Am J Geriatr Psychiatry 2002;10(5):515–520. [PubMed: 12213685]

17. Slooter AJ, Cruts M, Kalmijn S, Hofman A, Breteler MM, Van Broekhoven C, et al. Risk estimates of dementia by apolipoprotein E genotypes from a population-based incidence study: the Rotterdam study. Arch Neurol 1998;55(7):964–968. [PubMed: 9678314]

18. BU Alzheimer's Disease Study. REVEAL [Internet]. Boston (MA): Boston University; [[cited 2009 Nov 19]]. Available from: http://www.bu.edu/alzresearch/research/genetics/reveal/index.html

19. Roberts JS, LaRusse SA, Katzen H, Whitehouse PJ, Barber M, Post SG, et al. Reasons for seeking genetic susceptibility testing among first-degree relatives of people with Alzheimer's disease. Alzheimer's Dis Assoc Disord 2003;17(2):86–93.

20. Blazer DG, Fillenbaum GC, Gold DT, Burchett BM, Hays JC. APOE e4 as a predictor of subjective quality of life in a biracial older person community sample. J Aging Health 2003;15(4):645–660. [PubMed: 14594022]

21. National Conference of State Legislatures. Genetics and life, disability, and long-term care insurance [Internet]; NCSL; Denver (CO). [[cited 2009 Nov 19]]. Available from: http://www.ncsl.org/IssuesResearch/Health/GeneticNondiscriminationLawsinLifeDisability/tabid/14283/Default.aspx

22. Genetics and Public Policy Center. Direct-to-consumer genetic testing companies [Internet]. Washington (DC): Genetics and Public Policy Center; [[last updated 2009 May 27; cited 2009 Nov 19]]. Available from: http://www.dnapolicy.org/resources/DTCcompanieslist.pdf This document lists thirty-nine companies providing direct-to-consumer genetic testing as of 27 May 2009.

23. Skeehan, K.; Heaney, C.; Cook-Deegan, R. Impact of gene patents and licensing practices on licensing practices on access to genetic testing for Alzheimer's disease. Durham (NC): Duke University Center for Genome Ethics, Law, and Policy; 2009 Feb.

24. Pokorski R. A test for the insurance industry. Nature 1998;391(6670):835–836. [PubMed: 9495331]

EXHIBIT 1

Associations Between APOE Genotype And Outcomes Of Interest

	Piedmont Health Survey of the Elderly		Rotterdam Study	REVEAL II	
	Odds ratio of nursing home admission [95% CI][a]	Probability[b] of nursing home admission	Odds ratio of developing Alzeimer's disease [95% CI][c]	Odds ratio of changing long-term care insurance [95% CI]	Probability[d] of changing long-term care insurance
At least one e2 trait and no e4 trait	0.80 [0.52–1.22]	0.082	0.5 [0.0–5.4]	1.55 [0.43–5.60]	0.149
Two e3 traits	1.00	0.101	1.00	1.00	0.087
At least one e4 trait	1.48 [1.09–2.01]	0.127	4.6 [1.3–16.1]	2.31 [1.11–4.81]	0.237
N	1,999	1,999	134	253	253
Percent of sample with two e3 traits	68.0	68.0	56.4	50.8	50.8

SOURCES See below.

[a] Based on authors' calculations. Odds ratios and 95 percent confidence intervals (CIs) from logistic regression. Model adjusted for sex, age, race, and marital status.

[b] Based on authors' calculations. Full sample probability of nursing home admissions: 0.104.

[c] Slooter AJ et al. Risk estimates of dementia by apolipoprotein E genotypes from a population-based incidence study: the Rotterdam Study. Arch Neurol. 1998;55:964–8.

[d] Based on authors' calculations. Full sample probability of changing or planning to change long-term care insurance: 0.137.

EXHIBIT 2

Potential Responses In Long-Term Care Insurance Markets To APOE Genotyping

Knows individual APOE genotype			
Individual	**Insurer**	**Likely to lead to increase in coverage?**	**Expected response in current market**
No	No	Unlikely (status quo)	Typical situation today; most individuals don't know status, and insurers don't require APOE; therefore, premium not adjusted with respect to risk; insurers may increase all premiums because of uncertainty and assumed adverse selection; if the proportion of population covered by insurance increases, the risk associated with APOE is spread, and lack of knowledge of APOE status is lessened
Yes	Yes	Possibly	Fair premium based on APOE risk most likely to be assigned, with both parties operating based on full information; could be operationalized via an individual mandate for insurance, or advocating genotyping for individuals to make them aware of their risk, and allowing insurers to genotype under either scenario
No	Yes	Possibly, with individual mandate or compulsory purchase	Fair premium based on APOE risk likely to be assigned, but potential purchasers may not understand why they have received a higher premium, so uptake of insurance by high-risk group may be lower if they expect an average premium with respect to APOE; could result in an insured risk pool that is primarily low risk, with higher-risk individuals being less likely to be covered
Yes	No	Unlikely	Adverse selection, whereby consumers with highest risk will seek insurance, making the risk pool more likely to be unsustainable; if insurers are banned from using APOE to underwrite, then they will likely increase all premiums assuming adverse selection, further driving out better risks

SOURCE Content based on authors' assessments.