**Introduction**

*Momentum in Science* is the story of many scientists working independently and collaboratively to uncover the causes of Alzheimer’s and to ultimately treat and prevent it. We hope this Discussion Guide will enrich your viewing of the film by providing questions to help you probe more deeply into the content, a glossary to explain some of the technical language, and resources and facts to help you learn more about the disease including steps you can take to fight Alzheimer’s.

**Alzheimer’s Basics**

1. *Can you describe what Alzheimer’s disease is?*
   
   Alzheimer’s disease (AD) is an irreversible, progressive brain disease that slowly destroys memory and other thinking skills and, eventually, even the ability to carry out the simplest tasks. Ultimately, the person with AD dies, often years earlier than he/she would have otherwise. In most people with AD, symptoms first appear after age 60.

2. *What do scientists and researchers say are the “hallmarks” of the disease?*
   
   The brains of people with AD have an abundance of two abnormal structures: amyloid plaques and neurofibrillary tangles. A third characteristic of AD is the loss of connections between nerve cells (neurons) in the brain.

3. *As you watched people taking the various tests for AD, did you find yourself taking those tests, too? What was that like? Will you go home repeating apple, table, and penny?*

4. *What are some of the established potential risk factors for developing the disease? Which ones are controllable? What factors can’t be controlled?*
   
   We can’t control the fact that we age, nor can we control our genetic make-up which we inherit from our parents. Increasing age is the best established risk factor for AD.
   
   Other factors may be potentially under our control. Researchers are studying many factors that are important to overall health and well-being and are looking closely at the role of physical activity, diet, control of chronic diseases, social engagement, and intellectual stimulation in brain health. They are hoping to discover whether these factors could also play a role in the prevention of Alzheimer’s disease.

5. *Scientists use cerebrospinal fluid (CSF) as one way to learn more about Alzheimer’s disease. What do scientists hope studying CSF will tell them?*
   
   CSF is the fluid found in and around the brain and spinal cord. Its function is to transport substances to and away from the brain itself and to cushion the brain hydraulically. Measuring cerebrospinal fluid and its contents helps scientists understand chemistry of the brain. CSF is collected by a procedure called lumbar puncture. Biological markers found in CSF can be used to measure changes in people who have MCI or AD or who are cognitively normal. The measurements may one day identify people early in the disease process and also help physicians assess the response to treatment much more rapidly and less expensively than is possible today.

6. *Plaques and tangles may begin to accumulate in the brain long before anyone notices any problems or symptoms. What do you think that means for diagnosis and treatment of the disease?*
Genetics

7. The scientists in the film describe two different forms of AD: late-onset and early-onset. What are the big differences between these two forms of the disease?

Early-onset Alzheimer’s disease is a rare form of AD that usually affects people between ages 30 and 60. It is called familial AD (FAD) if it runs in the family.

Late-onset Alzheimer’s disease is the most common form of AD. It occurs in people aged 60 and older. Scientists studying the genetics of late-onset AD have found that the mutations seen in early-onset AD are not involved in this form of the disease.

8. Does having a family member with AD increase your risk of developing the disease?

Having a parent or sibling with Alzheimer’s disease is a known risk factor for Alzheimer’s. However, having a family member with late-onset Alzheimer’s disease does not mean that a person is certain to get the disease. Scientists are using new technologies to learn about factors, both genetic and environmental, that may make some people more susceptible to developing Alzheimer’s than others. Enormous efforts are being devoted to understanding the role of genetics in late-onset Alzheimer’s. Not only is more research needed into the role genes play in developing late onset Alzheimer’s, but we also need more information about how environmental factors may play a role in the disease and how they interact with genetics in any one individual.

9. How would you describe what a susceptibility gene is and why it might be important?

Susceptibility genes are also called risk factor genes. Scientists believe that small changes or variants in a cell’s DNA may increase the chance that a person will develop a disease. These changes do not cause the disease, but may increase a person’s susceptibility to disease. One form of the gene, ApoE, is considered a susceptibility gene because it is associated with a higher risk of developing late-onset Alzheimer’s. Scientists think that other risk-factor genes exist as well. Finding AD risk-factor genes is essential for understanding the very early biological steps that lead to the vast majority of AD cases and for developing drugs and other prevention and treatment strategies. Finding these genes also will help scientists develop better ways to identify people at risk of AD and determine how the genes may interact with other genes, or with lifestyle or environmental factors, to affect an individual’s AD risk.

10. The DeMoe family is one of the 200–300 families in the world who have early-onset familial Alzheimer’s disease. Why are they so important to AD research?

In the early days of AD genetics research, scientists realized that some cases, particularly of the rare early-onset AD, ran in families. This led them to examine DNA samples from these families to see whether they had some genetic trait in common. Chromosomes 21 first, then 14, and 1 became the focus of attention. The scientists found that some families have a mutation in selected genes on these chromosomes. Early-onset AD is very rare and mutations in these three genes do not play a role in the more common late-onset AD. However, these findings were crucial because they showed that genetics was indeed a factor in AD, and they helped to identify some key cell pathways involved at the onset of the AD disease process. They showed that mutations in amyloid precursor protein can cause AD, highlighting the presumed key role of beta-amyloid in the disease.

11. What do you think it would be like to be the only sibling without the gene that causes early onset Alzheimer’s disease?
12. What other diseases related to aging may play a role in the development of Alzheimer’s disease?

Several common chronic diseases that affect older people, including heart disease, stroke, and type 2 diabetes, also affect the body’s vascular system and have been tied to declines in cognitive function or increased AD risk.

13. Why is glucose so important to the body and the brain?

Glucose comes from foods we eat that contain carbohydrates. The blood stream carries glucose to the organs of the body, including the brain. Insulin, which is made in the pancreas, helps glucose enter the organs, where it provides fuel. Glucose is the only fuel normally used by brain cells. Because neurons cannot store glucose, they depend on the bloodstream to deliver a constant supply of this important fuel.

14. What do you think about the idea that inflammation is always a “two-edged sword”? When is it a good thing? When is it bad for you?

Inflammation is a way that the body responds to cellular injury by attempting to eliminate foreign matter and damaged tissue to protect the body. Inflammation in the brain is a common feature of AD. In response to injury and the deposition of plaques, factors are released that attract scavenger cells, the microglia, which attempt to remove plaque. However, some aspects of an uncontrolled immune response can lead to tissue damage, inadvertently destroying neurons and their connections (the synapses) in the parts of the brain most intimately connected with memory and cognition.

15. What did you learn about how clogged arteries, heart disease, strokes, diabetes, high cholesterol, and high blood pressure might be related to Alzheimer’s or might make the disease worse? Do you think these other conditions could be important in the development or eventually in the prevention of Alzheimer’s disease?

Scientists have been finding clues that damage to the vascular system (the body’s vast system of large and small blood vessels) may contribute to the development of AD or affect its severity. Several common chronic diseases that affect older people, including heart disease, stroke, and type 2 diabetes, also affect the body’s vascular system and have been tied to declines in cognitive function or increased AD risk. In addition, heart disease, high blood pressure, and diabetes to a large extent can be modified by drugs, but also by diet, exercise, and other lifestyle changes. Therefore, scientists are keenly interested in learning whether reducing the risks of or controlling these conditions through drug and/or lifestyle changes also may reduce the risks of cognitive decline or AD.

16. Scientists are investigating many different ideas about how Alzheimer’s disease begins. What are a few of the areas that are actively under study?

We do not yet fully understand what causes AD, but we believe it develops because of a complex series of events that take place in the brain over a long period of time. Many studies are exploring the factors involved in the cause and development of AD, including genetics, beta-amyloid, tau, protein misfolding, vascular disease, lifestyle factors, and the aging process itself.
**Brain Imaging**

17. Until recently the only way to see plaques and tangles was to examine brain tissue from someone who had died from the disease. Now, we see how imaging – such as MRI and PET scans – has changed the way researchers can study Alzheimer’s disease. Why is being able to see inside a living brain so important for Alzheimer’s research?

These imaging techniques provide “windows” on the living brain that may help scientists measure the earliest changes in brain function or structure in order to identify people who are at the very first stages of the disease – well before they develop clinically apparent signs and symptoms. The ability to monitor these brain changes may also be important in analyzing the effectiveness of interventions to treat or prevent AD.

18. Pittsburgh Compound B (known as PiB) is an exciting new development in Alzheimer’s disease research. What is PiB allowing researchers to see and do?

Pittsburgh Compound B (PiB) is the radioactive tracer compound that is used during a Positron emission tomography (PET) scan of the brain to show beta-amyloid deposits. This imaging technique allows researchers to observe and measure activity in different parts of the brain by monitoring blood flow and concentrations of substances such as oxygen and glucose, as well as other specific constituents of brain tissues. Initial studies showed that people with AD take up more PiB in their brains than do cognitively healthy older people. Since then, scientists have found high levels of PiB in some cognitively healthy people, suggesting that the damage from beta-amyloid may already be underway. The next step will be to follow these cognitively healthy people who have high PiB levels to see whether they do, in fact, develop AD over time.

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**Participating in Research**

19. What was it like to watch the DeMoe family talking about their experience with AD? Families like the DeMoes are rare in many ways. How do they feel about participating in research? How do the researchers treat the family?

20. Have you ever participated in clinical research or a clinical trial? Did families like the DeMoes and others inspire you to consider participating?

21. Why are researchers interested in studying people without memory problems as well as people who have them?

People with AD, those with MCI, those with a family history of AD, and healthy people with no memory problems and no family history of AD may be able to take part in clinical trials. Study volunteers help scientists learn about the brain in healthy aging as well as what happens in AD. Results of AD clinical trials are used to improve prevention and treatment approaches. Participating in clinical trials is an effective way to help in the fight against AD.
22. The study involving older religious sisters, brothers, and priests takes a somewhat different approach from the previous studies presented in this film. Why do you think this kind of study, which involves repeated observations of people over long periods of time, is useful in studying the development of Alzheimer’s disease?

23. In the film, a number of scientists talk about needing people to participate in research studies and clinical trials. What do you think will happen (or not happen) if people aren’t willing to join studies? Why are randomized clinical trials so important?

Rapid advances in our knowledge about AD have led to the development of many promising new drugs and treatment strategies. However, before these new strategies can be used in clinical practice, they must be shown to work in people. This means that clinical trials – and volunteer participants – are an essential part of AD research. Advances in prevention and treatment are only possible thanks to volunteers who participate in clinical trials. Clinical trials are the primary way that researchers find out if a promising treatment is safe and effective. They can also tell researchers who might benefit most from a given treatment.

24. If someone experiences forgetfulness, it can be difficult to tell the difference between what’s called age-related memory decline and Alzheimer’s disease. How are researchers trying to tell the difference?

In the early stages, it is difficult to differentiate between the onset of AD and other types of age-related cognitive decline. We have improved our ability to diagnose AD correctly, and doctors experienced in this area can diagnose the disease with up to 90 percent accuracy, primarily through a series of neuropsychological tests and other assessments over time. A definitive diagnosis of AD, however, is still only possible after death, during an autopsy, and we are still far from the ultimate goal: a reliable, valid, inexpensive, and early diagnostic marker that can be used in any doctor’s office.

Scientists are now exploring ways to help physicians diagnose AD earlier and more accurately. For example, some studies are focusing on changes in mental functioning. These changes can be measured through memory and recall tests, such as you saw in the film. Tests that measure a person’s abilities in areas such as abstract thinking, planning, and language can help pinpoint changes in these areas of cognitive function. Researchers are working to improve current testing methods, so that they might be used to point to AD even earlier or predict which individuals are at higher risk of developing AD in the future.

Other studies are examining the relationship between early damage to brain tissue and imaging changes in the brain. Still others are looking for changes in biomarkers in the blood or cerebrospinal fluid that may indicate the progression of AD.

25. When the researchers compared brains of the two nuns from Dubuque, they seemed surprised by the results. What theories did they have about why both sisters had plaques and tangles, but only one of them appeared to have symptoms of Alzheimer’s?

A growing body of research suggests that, even in the presence of AD plaques, the more formal education a person has, the better his or her memory and learning abilities.
Studies have also shown that keeping the brain active is associated with reduced AD risk. In the Religious Orders Study, for example, investigators periodically asked more than 700 participants – older nuns, priests, and religious brothers – to describe the amount of time they spent in seven information-processing activities. These activities included listening to the radio, reading newspapers, playing puzzle games, and going to museums. After following the participants for 4 years, investigators found that the risk of developing AD was 47 percent lower, on average, for those who did the activities most often than for those who did them less frequently. Other studies have shown similar results. However, it is possible that the correlations found in this kind of epidemiological study might not translate into effective therapies for AD, especially if a person has one or more of the risk factor genes for late onset AD.

26. How did the researchers describe “cognitive reserve?”

Cognitive reserve is the brain's ability to operate effectively even when some damage to cells or brain cell communications has occurred.

27. Almost everyone has heard about doing crossword puzzles to keep your brain active. What do you think about the idea that a big social network might be good for your brain too? What are other ways to keep your brain active?

Studies of animals and of older people living both in nursing homes and in the community have suggested a link between social engagement and cognitive performance. Older adults who have a full social network and participate in many social activities tend to have less cognitive decline and a decreased risk of dementia than those who are not socially engaged. The reasons for this apparent link between social engagement or intellectual stimulation and AD risk aren’t entirely clear, and scientists are working to understand this better.

28. Many people want to know if there are ways to prevent AD. How did the scientists answer that question? Why do you think scientists are so careful when they answer that question?

Our knowledge about AD is growing rapidly as scientists expand their understanding of the many factors involved in this devastating disease. Although no treatments or drugs have yet been proven to prevent or delay AD, people can take some actions that are beneficial for healthy aging and that also might reduce the effect of possible risk factors for AD. For example, you can:

- Exercise regularly.
- Eat a healthy diet that is rich in fruits and vegetables.
- Engage in social and intellectually stimulating activities.
- Control type 2 diabetes.
- Lower high blood pressure levels.
- Lower high blood cholesterol levels.
- Maintain a healthy weight.

These actions lower the risk of other diseases and help maintain and improve overall health and well-being. However, it is important to remember that they will not necessarily prevent or delay AD in any one person. Even if these actions were eventually proven effective, they might not offset a person’s individual genetic and other risk factors enough to prevent the development of AD.

29. In the film, it appears that mice that get regular exercise learn faster than “couch-potato” mice. Researchers who are pursuing this idea are excited about the possible benefits, but do we know yet if exercise will prevent or delay AD?

Clinical trials in people are underway now to expand our knowledge about the relationship of exercise to healthy brain aging, reduced risk of cognitive decline, and development of AD. Previous epidemiologic studies, animal studies, and human clinical trials assessing the influence of exercise on cognitive function found intriguing evidence:

- Animal studies have shown that exercise increases the number of capillaries that supply blood to the brain and improves learning and memory in older animals.
- Epidemiologic studies show that higher levels of physical activity or exercise in older people are associated with reduced risk of cognitive decline and reduced risk of dementia. Even moderate exercise, such as brisk walking, is associated with reduced risk.
- Clinical trials show some evidence of short-term positive effects of exercise on cognitive function, especially executive function (cognitive abilities involved in planning, organizing,
and decision making). One trial showed that older adults who participated in a 6-month program of brisk walking showed increased activity of neurons in key parts of the brain.

**GENERAL**

30. What would you say is the main message of this film? Are there one or two new ideas that you take away from the film? How would you describe this film to your family and friends?

31. Before watching this film, how concerned were you about AD? After watching the film, has your thinking about AD changed? In what ways? Will you do anything differently as a result?

32. Even though scientists have not found a specific way to prevent or cure Alzheimer’s disease, they are very optimistic about the prospects of treating and preventing AD in the not too distant future. What does that mean to you? Do you have any difficulty reconciling the optimism of the scientists with the day-to-day struggles that families with AD face? Is there reason for hope?

33. How is Alzheimer’s disease research paid for in the United States? Do taxpayers play a role? What about other groups, such as non-profit organizations, foundations, and businesses?

Funding for AD research comes, by and large, from the public through tax dollars and from private contributions to organizations and foundations. The National Institute on Aging, the lead U.S. Government agency for AD research, and other parts of the National Institutes of Health are supported by tax dollars. The Alzheimer’s Association®, the nation’s leading voluntary health organization in Alzheimer’s care, support and research, has committed more than $250 million to over 1,700 best-of-field research proposals since 1982. The Geoffrey Beene Gives Back® Alzheimer’s Initiative, Fidelity® Charitable Gift Fund, and numerous other organizations, foundations, and businesses also donate to or directly fund AD research.

34. The film shows many different research studies being conducted in the United States. If you wanted to participate in research, how can you learn about studies that are accepting participants?

NIA, which is part of the National Institutes of Health (NIH), leads the federal government’s research efforts on AD. NIA-supported Alzheimer’s Disease Centers located throughout the United States conduct many clinical trials and carry out a wide range of research, including studies of the causes, diagnosis, and management of AD. NIA also sponsors the Alzheimer’s Disease Cooperative Study (ADCS), a consortium of leading AD researchers throughout the U.S. and Canada who conduct clinical trials on promising AD treatments.

To find out more about AD clinical trials, talk to your health care provider or contact NIA’s ADEAR Center at 1-800-438-4380. Or, visit the ADEAR Center clinical trials database at [www.nia.nih.gov/Alzheimers/ResearchInformation/ClinicalTrials](http://www.nia.nih.gov/Alzheimers/ResearchInformation/ClinicalTrials). You also can sign up for email alerts that let you know when new clinical trials are added to the database. More information about clinical trials is available at [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov).
35. How can people support efforts to prevent or cure Alzheimer’s?

There are many ways to join the fight against Alzheimer’s disease, including participating in research, writing letters to Congress, supporting people with the disease, and donating time or money. To learn how you can become an Alzheimer’s Champion, visit the Alzheimer’s Association at www.actionalz.org.

36. A number of scientists mentioned that they became interested in Alzheimer’s disease because the disease had affected their family. How often do you think this kind of personal experience helps people to choose a career path? Would you encourage someone in your family to pursue a career in science?
RECAP FORM

Thank you for hosting a screening and discussion panel on HBO's The Alzheimer's Project. Please fill in the form below and return it in the accompanying self addressed envelope, via fax or email per the instructions at the end of this document. We value your feedback and use it to advance public awareness of Alzheimer's disease, so please be candid.

1. Name:_____________________________________________________________________________________________

2. City:_______________________________________________________________________________________________

3. Date of screening:___________________________________________________________________________________

4. Number of guests attended:__________________________________________________________________________

5. Where was screening held? (e.g., community center, school, religious facility):______________________________

6. Was the screening hosted by an organization? If so, please provide the name of your organization:___________________________

7. Please provide a brief description of the event. Please include details about how you structured the screening and discussion.

Description of event:
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8. How did this screening benefit your organization?
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9. Comments – Please include any memorable comments from guests (attach additional pages as necessary):
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10. Did you use the customizable press release?__________________________________________________________

11. Did any local media cover the event? If so, please specify: _____________________________________________
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Your name:_______________________________________Title: _______________________________________________
Phone/Email:_________________________________________________________________________________________

If possible, please return this form by May 12, 2009. If your screening occurs at a later date, your feedback is still valuable to us.

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