**TITLE. Your family history and personal health might be more important for your memory than you thought!**

**GENERAL INTRODUCTION.** Alzheimer's disease (or "AD"), the leading cause of dementia, is a progressive brain disorder that causes problems with memory and thinking. More than five million patients in the United States are currently diagnosed with AD. The goal of our research is to help each person understand their risk for AD as early as possible. Also, to help them know what could be done today to potentially avoid the disease in the future.

**INTRODUCTION TO STUDY.** Two critical risk factors for AD are a family history of dementia and increasing age. Despite this knowledge, the effects of family history of AD on brain performance across the lifespan are poorly understood. There is currently no cure or even a long-lasting treatment for AD. So we decided to focus our efforts on identifying demographic, health, lifestyle, and medical factors that are linked to brain performance. We hoped to characterize the keys to a top-performing memory.

**METHODOLOGY.** To study brain function across a large group of people, we turned to the internet. We developed a short, free, easy-to-use, and fun internet-based memory quiz, bundled together with 22 demographic, health, lifestyle, and medical questions. We call it MindCrowd. The MindCrowd memory quiz is based on a version of a brain test developed over 100 years ago. It is essential to note that this quiz cannot diagnose AD and is not able to fully predict your risk for developing the disease in the future. To date, over 50,000 people from around the world, ranging in ages from 18-90, have participated in our study by completing the memory quiz and answering the questions. We also collected blood samples from a smaller group of participants. We purified DNA from these blood samples and examined each person's genetic information for a well-known risk factor for AD within a gene called APOE. We then combined three sources of information – the memory quiz, the answers to the 22 questions, and the genetic information – to identify the factors that influenced performance on the memory quiz. Our study is still open, and you can participate too by visiting [www.mindcrowd.org](http://www.mindcrowd.org).

**RESULTS.** Our study approach identified all of the previously known factors that were associated with the memory quiz score. These included things like age, biological sex, and educational attainment. This helped to show us that our new internet-based approach is a valid way to study the brain. We were also able to show that worse memory performance was found in participants under the age of 65 who had a family history of AD. Surprisingly, this was true even for participants in their early 20s. Lastly, we found that this effect was worsened by the presence of diabetes or the APOE genetic risk factor for AD. This finding is important as it suggests avoiding diseases like diabetes may be an excellent strategy to lower one's risk of AD. That is if dementia is known to run in your family.

**CONCLUSIONS.** The findings from this study show several things. First, that our internet-based approach to studying the brain works well. We confirmed associations identified by prior studies using a similar memory quiz. Second, we found that people with a family history of AD may have lower memory performance even when they are young adults. Importantly, this change in memory performance likely isn't noticeable to these individuals. However, it is detectable when you compare them to their peers in a study like ours. Third, we found that diabetes and genetics can make this effect of family history of AD worse. Having a family history of AD is a risk factor, but it doesn't mean you will get AD. It is important to know what things you can do to lower your risk. Indeed, reducing a person's risk of developing AD presents a significant opportunity.

**GENERAL CONCLUSIONS AND FUTURE PERSPECTIVES.** Our study suggests that several personalized factors converge to direct a person's memory performance. More work needs to be done to fully understand this. For example, more quiz/test types need to be done to get an entire picture of brain health. Also, we only looked at a single time point. It is also necessary to see how each person performs across time. If you have dementia in your family, it may increase your risk, but it doesn't mean you will get AD. In our current world, where there is no cure for AD, each of us may need to focus on things that we can change to reduce our risk for the disease.