

Potential Harms Posed by Advances in Predicting Alzheimer's Disease

¹ Falcia Elenberg, ² Edmund Howe

¹ Falcia Elenberg, 8311 Aqueduct Rd, Potomac, MD 20854, Phone: 301-461-6642

² Professor of Psychiatry & Medicine Director, Medical School Programs in Ethics, Senior Scientist

Uniformed Services University of the Health Sciences, Disclaimer: The opinions or assertions contained herein are the private views of the authors and are not necessarily those of the AFRRRI, USUHS, or the Department of Defense.

4301 Jones Bridge Rd, Bethesda, MD 20814

Corresponding author: **Falcia Elenberg**

Abstract: In recent years, predictive tests for Alzheimer's disease have increased in accuracy and availability to the public. These tests carry with them complex implications in that the development of Alzheimer's disease has such profound negative impacts on those effected and there is no known cure. This paper seeks to explore the possible benefits and detriments of receiving such tests and concludes by discussing the ethical considerations that follow as well as propose potential policy recommendations.

INTRODUCTION

For some time, it has been possible to predict that an individual is at exceptionally high risk for acquiring Alzheimer's disease in his or her later years. This has predominantly been possible in research settings. Note that it is understood that this source of dementia begins decades earlier in life than the onset of symptoms, and the focus of research has been to provide interventions at relatively earlier stages in life to prevent these causes from later bringing this disorder about.

The ability to predict a person's susceptibility to Alzheimer's disease is rapidly becoming more accurate and cost effective. Most recently, a team of researchers from Washington University in St. Louis reported that they have created the most sensitive blood test yet, that capitalizes on the presence of amyloid, a protein that is a significant risk factor. They found that in combining this information with other risk factors examined, their test is 94 percent effective in predicting the presence of plaques [1]. Additionally, consumer genetic websites such as 23andme offer people to see their estimated likelihood of developing Alzheimer's disease based on genetic predispositions. Customers can access their results from their personal electronic devices, given that they provide consent to seeing such results and read a disclaimer about how to interpret them. It is unknown under what context they will receive their results, how they will be affected, and what resources will be made available to these individuals after hearing such potentially life altering news.

These new early warning systems could be revolutionary, and they have cost and scalability advantages over current methods, suggesting that there will be an increase in clinical access to Alzheimer's predictive tests. While there are some clear benefits that could arise as a result of this, there are also potential harms posed by these advances that will require thoughtful consideration from healthcare professionals and society as a whole.

POTENTIAL BENEFITS OF PREDICTIVE SCREENING

One of the many possible benefits from early detection includes the ability of people to modify their behavior, which research suggests can have an impact, albeit relatively small, on mitigating Alzheimer symptoms [2]. There also exists early treatment options, though again their effects on the progression of the disease are minimal, which patients can engage in upon hearing their results [3]. Another possible benefit is that people who have been identified as likely to develop Alzheimer's disease can participate in clinical trials. Furthermore, if young individuals know with almost certainty that they will develop the disease, they may be better able to plan their lives accordingly in terms of finances and setting up long term care. Lastly, certain risk indicators have been known to have predictive value for other diseases. For example, the genetic variant predictive of Alzheimer's disease, APOE4, is known to have some association with cardiovascular risk [4]. Perhaps other risk factors used in new tests can be predictive of more than just Alzheimer's disease and allow patients a greater wealth of information about their predispositions. Similarly, early detection may allow researchers to find these associations through studying those patients who opt to receive testing at earlier ages.

POTENTIAL HARMS OF PREDICTIVE SCREENING

Despite these many possible benefits that can arise from tests predicting Alzheimer's disease, there are also numerous complex concerns that have the possibility of outweighing these benefits. One of the

biggest concerns associated with testing for life ending diseases with no known cure is that they will cause people immense emotional distress. Many studies, however, indicate that for most people this is not the case. One such study followed the long term psychological morbidity of people who had received test results regarding whether or not they had Huntington's Disease, another incurable life ending condition, and found that patients who received positive test results (i.e. they were going to develop the disease) on average did not become more stressed long term, and those who received negative test results did not, on average, experience long term lower levels of stress either [5,6]. Even in the immediate aftermath, those who found out they would develop the disease typically fell under the normal range of distress [6,7]. Nevertheless, people with histories of mental health struggles and those who lack a social support system or psychological resources may have a severely compromised ability to cope, and physicians should thus be cautious of the circumstances of the patient when discussing whether testing be done.

Further, while the patient themselves may not be largely affected emotionally long term by the news of their results, their families may be. Another study regarding Huntington's disease found that partners of those who tested positive for the disease had greater difficulties coping than the carriers. Partners typically reported higher levels of stress and lower quality of life than did their spouse who got tested [6]. Therefore, physicians must be cognizant of not only possible negative emotional impacts to the patients, but to their family members as well. Is the Alzheimer's test worth it if it negatively impacts the patient's support system? If one decides that it is still worth administering the test, it would be very important for physician's to be aware of the fact that the family members may not be offered the same type of support (i.e. post-test counseling) as the patient, and perhaps protocol can be put in place to remedy this.

The wide-ranging implications of an early detected positive test result on many facets of the patient's life lead to very complex ethical considerations. The diagnosis of diseases leading to dementia can have legal effects on a person, including their right to hold a driver's license or own a gun, and can also affect the way society views their potential and utility. Therefore, an early and more precise positive result can lead to stigmatization, and even worse, possible discrimination, especially when considering employment, insurance, or the right to drive or carry a weapon as discussed above. If a patient requests the test be done, one would think that their autonomy should be respected and the test carried out, but the very results of the test could then impede on their autonomy in the future.

Another complex ethical issue arises when considering one of the earlier cited benefits of receiving

test results: future planning. How does one plan for a future of cognitive decline? Can we reliably predict what will be best for ourselves in the future, and can we confidently assume that who are today will be fundamentally similar to who we are in the future? With a disease such as Alzheimer's, people experience radical behavioral and personality shifts, and thus our notions of psychological continuity will likely face challenges [8,9]. There are already questions regarding to what extent one should respect the autonomy of a patient who is cognitively impaired, and at exactly which level of cognitive impairment it would be acceptable to begin to depart from patient autonomy. Mixing in considering what the younger version of the patient wanted as compared to what the patient currently wants only further complicates the discussion. Additionally, given that these tests can be administered decades before the onset of the disease, what happens when a patient requests a treatment plan that would later no longer be in their best interest, for reasons such as that option being outdated and replaced with better treatment options or that their chosen course of action is no longer considered humane? While many of these questions existed long before the introduction of these new Alzheimer's tests, their importance has only become heightened and their considerations more complex.

POLICY AND HEALTHCARE REGULATION

An important step in protecting patients and their families who undergo Alzheimer's tests can include strengthening the requirements for giving informed consent before the tests are administered. Patients could be informed of the possible benefits of receiving the tests as well as possible consequences and be encouraged to discuss with their loved ones whether this is an option they truly wish to pursue. These requirements, if applied to hospitals, should also extend to consumer websites, and perhaps there be even stricter. For example, consumer websites could be required to include information about coping recourses since these patients can access this information under any circumstance within any context. This practice is in keeping with the recently adopted new rules for gaining consent in research which requires presenting would be participants with the information they most need to know to decide whether to enter research initially [10]. The concern has been raised that many people with a fatal illness may enter even Phase 1 studies without really having a choice because they so wish to pursue any plausible means of surviving longer. People at risk of Alzheimer's may similarly seek to know whether they are at high risk without assessing how they might respond to this dark cloud thoughtfully.

Significant time and resources should be used in training healthcare providers to best help guide patients through these complex issues with compassion, and best support balancing their wellbeing

with autonomy. In regard to consumer websites, regulatory bodies should take steps in making sure that companies are providing their customers not only with information about resources but also ensure that those resources are actually accessible to those people.

CONCLUSION

If effective treatments for Alzheimer's disease are discovered, it will certainly alter the conversation about these ethical concerns dramatically, but until then, as these tests reach greater numbers of individuals, these are very important issues for society to consider. As more tests are being developed to predict a greater number of diseases with greater accuracy, one must address the notion that simply because we can offer patients information about themselves, that does not necessarily mean we should. It is important to take a step back and think about how to approach these tests in the most responsible manner possible that serves to promote the well-being of patients. Just as past studies on Huntington's disease can inform conversations happening presently, so too can the emotional and societal impact of these new test results inform future conversations regarding incurable diseases.

REFERENCES

- [1] Schindler S, Bollinger JG, Ovod V, Mawuenyega KG, Li Y, Gordon BA, Holtzman DM, Morris JC, Benzinger T, Xiong C, Fagan AM, Bateman RJ. High-precision plasma β -amyloid 42/40 predicts current and future brain amyloidosis. *Neurology*. 2019. DOI:10.1212/WNL.00000000000008081. (Accessed August 30, 2019).
- [2] Rege SD, Geetha T, Broderick TL, Babu JR. Can Diet and Physical Activity Limit Alzheimer's Disease Risk? *Current Alzheimer Research*. 2017; 14(1): 76-93.
- [3] Cummings JL, Tong G, Ballard C. Treatment Combinations for Alzheimer's Disease: Current and Future Pharmacotherapy Options. *Journal of Alzheimer's Disease*. 2019; 67(3): 779-794.
- [4] Clark D, Skrobot OA, Adebisi I, Susce MT, de Leon J, Blakemore AF, Arranz MJ. Apolipoprotein-E gene variants associated with cardiovascular risk factors in antipsychotic recipients. *European Psychiatry*. 2009; 24(7): 456-463.
- [5] Tibben A, Timman R, Bannink EC, Duivenvoorden HJ. Three-year follow-up after presymptomatic testing for Huntington's disease in tested individuals and partners. *Health Psychol*. 1997;16:48-63.
- [6] Marteau TM, Croyle RT. Psychological Responses to Genetic Testing. *BMJ*. 1998; 316(7132): 693-696.
- [7] Wiggins S, Whyte P, Huggins M, Adam S, Theilmann J, Bloch M, et al. The psychological consequences of predictive testing for Huntington's disease. *New England Journal of Medicine*. 1992;1401-5.
- [8] Mattsson N, Brax D, Zetterberg H. To know or not to know: ethical issues related to early diagnosis of Alzheimer's disease. *International Journal of Alzheimer's Disease*. 2010. <http://www.hindawi.com/journals/ijad/2010/841941/>. (Accessed August 30, 2019).
- [9] Growdon ME. Ethical Issues in the Early Diagnosis of Alzheimer Disease. *Virtual Mentor*. 2011; 13(12):868-872.
- [10] Attachment C -New "Key Information" Informed Consent Requirements. *U.S. Department of Health and Human Services*. 2018. <https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-november-13-2018/index.html>. (Accessed August 30, 2019).