

Alzheimer's disease currently affects more than 5 million Americans (NIA Alzheimer's Disease Progress Report). This number is expected to rise significantly over the coming years as baby boomers age. This progressive, neurodegenerative disease causes memory loss, cognitive decline, and dementia exacting a significant toll on families and caregivers over a long period of decline. Up until recently, Alzheimer's disease could only be confirmed in postmortem brain analysis. Three new tests for detecting the disease in individuals not yet manifesting symptoms have been developed. Each test capitalizes on different methodologies and incur different costs. In the following, you are asked to evaluate what is known regarding mechanisms of the disease, relate the new tests to these mechanisms, and consider the implications of the test availability as a routine screening tool.

Your answer should consist of the following parts:

- 1) The newly developed tests for Alzheimer's target blood lipid biomarkers (Mapstone et al., Nature Medicine 2014), misfolded amyloid beta oligomers in the CSF (Salvadores et al, Cell Reports 2014) and PET scans using the radioactive dye Amyvid (Doriaswamy et al., Molecular Psychiatry 2014). For each of the new tests, describe what the test is and how it works in detecting Alzheimer's disease. Relate these test markers to what is known (or not known) regarding mechanisms of the disease including cellular and molecular changes known to be associated with the disease, role of genetics, the specific brain regions and networks affected and the resultant behavioral and cognitive changes.
- 2) These tests identify individuals at risk for developing Alzheimer's prior to manifestation of symptoms. Currently, the US preventive services task force does NOT recommend widespread screening for dementia. What are the pros and cons for such screening? Does early detection affect the disease outcome? Alter it? What are the treatment options? What are the moral and ethical considerations of widespread availability of these tests? Be sure to support your opinion with empirical support. See Roberts and Uhlmann (2013) for a recent review of ethical and practice considerations regarding genetic testing including Alzheimer's disease.

Please limit your answer to the 10-15 page limit (excluding references). The weighting of each part is as follows: Part 1 -70%, Part 2- 30%. Be sure to support your statements with proper literature citations.