

## ABSTRACT

Alzheimer's disease (AD) is the sixth-leading cause of death in the United States [1]. AD is characterized by a progressive increase in neuropathology resulting in the loss of brain matter and consequent symptoms of cognitive impairment and functional limitation [2]. Early in the disease, AD traditionally presents as mild cognitive impairment (MCI) that increase in severity as the disease progresses. During disease-progression, symptoms emerge from at least two processes. Critically, as Amyloid plaques mature the amyloid binds directly to the arterial walls thereby causing increased neuroinflammation and glial activation [5-7]. Secondly, amyloid plaques and subsequent glial activation can elicit tauopathy and hasten its spread through the brain. Thus, cerebrovascular health is a critical point of intervention in AD [3, 4]. Recently, in a ground-breaking discovery the SPRINT Research Group reported that controlling hypertension in a large clinical trial (N=9,361) reduced risk of onward progression from mild cognitive impairment (MCI) to dementia due to AD [8].

**At Stony Brook, our team has already built the first cloud-based Diabetes Prevention Program (CB-DPP).** The DPP was recently approved by the Center for Disease Control (CDC) to help prevent or delay the onset of diabetes in individuals that have prediabetes [9]. The CB-DPP program includes a web app focused on user education and a mobile app that serves as an electronic diary and virtual coach. The CB-DPP has been shown to successfully support lifestyle change by e-coaching individuals to help them improve eating habits, increased physical activity, successful weight loss, and reduce blood sugar for overweight users with prediabetes [9]. This program was highly successful: while in-person diabetes prevention programs have typically seen success rates of ~5% when measuring ability to meet CDC blood sugar control standards after one year, our coaching-focused DPP exhibited 60% success [9].

Controlling risk of AD requires similar lifestyle improvements as controlling diabetes: it requires sustained interventions in lifestyle behaviors. **Noting the promise that the SPRINT trial results could imply, our team embarked on adapting our CB-DPP app to create the "engAgeD" app.** In the engAgeD app, the virtual coach starts every day with a multiple-choice question that assures users retain educational information provided by the web app. This question period ensure that users start each day mindful of their lifestyle choices, and the virtual coach reminds users to follow-up on these choices throughout the day. User summaries are provided along with artificial intelligence derived performance-based advice each day and each week. While refocusing the CB-DPP on hypertension control was a manageable shift, we felt it could be a good time to also expand our focus to a range of lifestyle issues associated with AD. To this end, we expanded the engAgeD app to help users improve eating habits and control weight [10], increase physical activity [11], control blood sugar [12] while also supporting blood pressure control [13], increased social engagement [14] and cognitive engagement [15]. User diary data are stored for review by human coaches and the user's physician that help keep the user on track using instant notifications to meet their goals.

**The engAgeD app is now ready for human testing to determine safety, usability, and user friendliness.** To assess the acceptability and power to determine impact of the engAgeD app among older individuals with MCI, we follow implementation-science guidance and propose to recruit 30 adults aged  $\geq 55$  years with MCI and hypertension who are healthy enough to exercise and have a mobile phone, PC and will complete a magnetic resonance imaging (MRI) protocol. Treated participants will be trained to use engAgeD and a trained coach will oversee progress. Participants randomized to control conditions will be provided standard of care including information about lifestyle risk factors for AD and resources from the Alzheimer's Association. At baseline and 12-month visits, participants will complete a cognitive and physical screening interview alongside a magnetic resonance imaging (MRI) protocol using an arterial spin labeling (ASL), T1-MPRAGE, and DTI sequences to quantitate cerebral perfusion and neurodegeneration.