Monitoring drug Efficacy through Multi-Omics Research initiative in Alzheimer's Disease (MEMORI-AD): A protocol for a multisite exploratory prospective cohort study on the drug response-related clinical, genetic, microbial and metabolomic signatures in Filipino patients with Alzheimer's disease

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INTRODUCTION

Dementia is one of the leading causes of disability among older people aged 60 years and above, with majority eventually being diagnosed with Alzheimer's disease (AD). Pharmacological agents approved for dementia include acetylcholinesterase enzyme (AChE) inhibitors like rivastigmine, donepezil and galantamine and the N-methyl-D-aspartate (NMDA) receptor antagonist memantine, prescribed as monotherapy or in combination with each other, depending on the severity of disease. There is currently no available study demonstrating the clinical response to these drugs for AD in the Filipino population. Hence, this protocol aims to characterize the clinical, genetic, microbial and metabolic factors associated with drug responses to donepezil, rivastigmine and/or memantine for AD in a cohort of Filipinos with late-onset AD.

METHODS

This protocol involves a multisite descriptive study that will use two study designs: (1) a descriptive, cross-sectional study to characterize the clinical profile of Filipino dementia patients with AD and (2) an exploratory prospective cohort study to investigate drug response-related genetic, gut microbiome and metabolome signatures of a subset of the recruited AD patients. At least 153 patients with mild or moderate AD aged 65 years old and above will be recruited regardless of their treatment status. A subset of these patients (n=60) who meet inclusion and exclusion criteria will be included further in the exploratory cohort study. These patients will be grouped according to their baseline medications and will be observed for treatment response in 6 months. The cognitive, functional and behavioral domains of patients and levels of functioning will be measured using different assessment tools. Drug responses of Filipino patients will then be investigated employing multi-omics technology to characterize genetic variations via whole exome sequencing, gut microbiome profile via shotgun metagenomic sequencing and metabolome profile via liquid chromatography with mass spectrometry.

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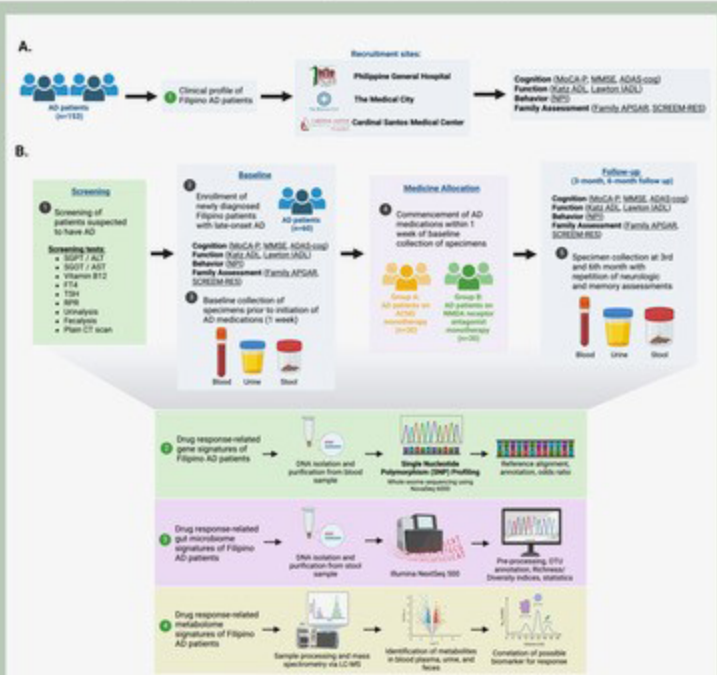

MEMORI-AD workflow. This study will recruit at least 153 patients with dementia aged 65 years old and above. Patients who meet inclusion and exclusion criteria will be enrolled, and their sociodemographic and clinical profiles will be recorded. A subset of recruited AD patients will be followed up for further observation as part of the exploratory prospective cohort to investigate gene, gut microbiome and gut metabolome signatures for treatment response. Patients will be observed from baseline, at 3 month and at 6 month follow-up.