Presentation Notes

Background

* An Aging Population: This is an infographic I found on the US Census website and I am sure this comes as no surprise to those of you in this room that the projected number of individuals over 65 are expected to increase, here, we can see that in the United States alone the number of individuals over 65 is expected to almost double by 2060.
* As the population ages, the need to manage and provide healthcare for this distinct population grows
* To this end, how can we use already published observational data to provide insight into what genetic factors contribute to healthy aging?

Methods

* It has traditionally been difficult to evaluate observational studies for causal associations in risk factors in human longevity due to confounding , etc.
  + Solution: Mendelian Randomization approach. A statistical approach to find causal associations among observational data
  + Uses genetic variants /SNP/instrumental variable as a proxy for an exposure
  + Mendel’s Law of Inheritance: genes are inherited from parent to child are random.
    - We can utilize this randomness (e.g. an assumption of no confounding associated with SNPs in population) to approximate a RCT using observational data.
      * Genes are the ‘’random” assignments for an exposure or exposure levels
    - Temporality: a requirement for determining causality
      * Genetic factors are determined at birth, therefore our exposure precedes our outcome
  + Risk factors: limit by genetic associations of risk factors
* Specifically for this project, we used Two Sample MR, which obtains significant SNP-Exposure from other studies and compares SNP-outcome relationships in another study. In this way we can make causal association among the Exposure-Outcome relationship.

Assumptions

Assumption #1

SNPs are truly associated with an Exposure as seen from independent studies.

Limitations

Developmental compensation – unlike RCTs genetic variants reflect a life-long exposure, (not one of short duration), and associations might be due to developmental compensations that arise due this exposure, not the exposure itself