GRAM Model Documentation

Individual Attributes

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| ALIVE | Alive status | 0 = Dead  1 = Alive |
| SEX | Sex | 1 = Male  2 = Female |
| EDU | Highest level of education | 1 = College degree or more  2 = High school or GED  3 = Less than high school |
| RACEETH | Ethnicity | 0 = Not Hispanic or Black  1 = Hispanic or Black |
| OBES | Obesity status | 0 = Not obese  1 = Obese |
| APOE4 | APOE4 allele carrier status | 0 = Not a carrier  1 = Hetero  2 = Homo |
| SYN | Cognitive syndrome status | 0 = Cognitively intact  1 = Mild cognitive impairment  2 = Dementia |
| SEV | Dementia severity | 1 = Mild dementia  2 = Moderate dementia  3 = Severe dementia |
| AB | Amyloid beta status (determined by ???) | 0 = No amyloid beta accumulation  1 = Amyloid beta accumulation |
| TX | Treatment status | 0 = Treatment on/provided  1 = Treatment off/stopped |
| AGE | Age | Numeric between  50 . . . 100 |
| COG | Cognitive assessment based on the CDR-SB | Numeric between  0 . . . 18  At increments of 0.5 |
| FUN | Functional assessment based on the FAQ |  |
| QALY | Quality-adjusted life years | Numeric |
| COST | Costs incurred | Numeric (USD) |

Update time: Each cycle represents one year. At the beginning of each cycle, the TIME attribute is increased by 1.

Update alive: Mortality rates are applied based on age and cognitive status. Individual probabilities for death are calculated by adjusting life table probabilities (CITE) for the increased mortality rate for MCI and dementia (including differing severity). Adjusted death rates are calculated, then compared to the random number generated for each individual at each cycle to determine outcome.

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| **Severity** | **Risk ratio for death (CITE)** |
| Healthy | 1 (ref) |
| MCI | 1.82 |
| Mild dementia | 2.92 |
| Moderate dementia | 3.85 |
| Severe dementia | 9.52 |

Update age: For those who remain alive, age is updated by 1 year. Other are assigned NA.

Update sex, race/ethnicity, obesity, education: For those who remain alive, these fixed attributes are kept the same. Others are assigned NA.

Update syndrome: Two separate models are used to update cognitive status. A logistic regression (Getsios et al?) is used to generate transition probabilities from cognitively intact to mild cognitive impairment. The predictors are age, education, race/ethnicity, and obesity. Transition probabilities from MCI to dementia (any) are obtained from a Weibull distribution (Green et al?). No backwards transitions are possible. People who are no longer alive are not assigned a syndrome status.

Update cognitive status score: Cognition is measured and monitored with the Clinical Demenita Rating – sum of boxes score. This scale incorporates both cognitive and functional status and ranges between 0-18 in increments of 0.5. *Healthy individuals* are assigned a score of 0. *Individuals who newly transition in MCI* (in the current cycle) get assigned a random CDR-SB score between 0.5 and 4.0. These values are drawn from a right-skewed beta distribution to allow more people to have lower CDR-SB scores at diagnosis. Individuals who remain in MCI (but did not newly transition) incur an increase of 1.67 point (on average, allowing for random variability across individuals). Individuals who newly transition into dementia are first assigned a severity (mild/moderate/severe) based on pre-defined landing probabilities for dementia severity. They are then assigned a CDR-SB score between 4.5-9.0, 9.5-15.5, 16.0-18.0 from a uniform distribution, for mild/moderate/severe dementia respectively (CITE O’BRYANT). Individuals who maintain their dementia syndrome attribute from the prior cycle incur an increase in CDR-SB score by 2 points on average, allowing for random variability across individuals. People who are no longer alive do not have a CDR-SB score.

Update dementia severity: Dementia severity is reassessed for those with dementia, using the same CDR-SB cutoff scores described above. People who are no longer alive or do not have dementia (i.e., are cognitively intact or have mild cognitive impairment) are not assigned a severity.

Update functional status: A post-hoc FAQ score is calculated for those who are alive. This is based on the correspondence of CDR-SB and FAQ scales. An explicit FAQ progression is not depicted.

Update treatment status: ???