Manual 30

ARIC Analysis Manual

Version 3.0

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List of Abbreviations

##	A reference to the current version of a dataset from a specific visit, such as DERIVE##
2D	Two Dimensional
3D	Three Dimensional
A/V	Arterio-Venous
ABI	Ankle Brachial Index
ACA	Anterior Cerebral Artery
ACHIEVE	Aging and Cognitive Health Evaluation in Elders
AD8	Eight-item Interview to Differentiate Aging and Dementia
ADP	Adenosine Diphosphate
AF	Atrial Fibrillation
AFU	Annual Follow-Up
ALT	Alanine Aminotransferase
AIC	Akaike information criterion
AMD	Age-related Macular Degeneration
ANS	Animal Naming Score
ANSI	American National Standards Institute
ANT	Anthropometry
ARIC	Atherosclerosis Risk in Communities
ARIC NCS	Atherosclerosis Risk in Communities Neurocognitive Study
ASE	American Society of Echocardiography
AST	Aspartate Aminotransferase
ATP	Adenosine Triphosphate
ATS	American Thoracic Society
BIC	Bayesian information criterion
BBMRI	Black Blood Magnetic Resonance Imaging
BNT	Boston Naming Test
BRVO	Branch Vein Occlusion
CAC	Coronary Artery Calcium
CBC	Complete Blood Count
CC	Coordinating Center
CDART	Carolina Data Acquisition and Reporting Tool
CDR	Clinical Dementia Rating
CERAD	Consortium to Establish a Registry for Alzheimer's Disease
CFA	Confirmatory Factor Analysis
CHE	Cholesterol Esterase
CHO	Cholesterol Oxidase
CMIA	Chemiluminescent Microparticle Immunoassay
CNV	Choroidal Neovascularization
CRAE	Central Retinal Arteriole Equivalent
CRP	High Density C-Reactive Protein
CRVE	Central Retinal Venule Equivalent
CRVO	Central Vein Occlusion

CSME	Clinically Significant Macular Edema
cTnI	Cardiac Troponin I
CV	Coefficient of Variation
CVD	Cerebrovascular Disease
dB HL	Decibel Hearing Level
Dcf	Path length from the carotid to the femoral artery
Dfa	Path length from the femur to the ankle
Dhb	Path length from the suprasternal notch to brachial artery
Dhf	Path length from the suprasternal notch to femur
DSB	Digit Span Backwards
DSBmT	N, N-Bis (4-Sulfobutyl)-M-Toluidine Disodium Salt
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th
DSS	Digit Symbol Substitution
DT	Deceleration Time
DTI	Diffusion Tensor Imaging
DWR	Delayed Word Recall
ECG	Electrocardiograph
ECLIA	Electrochemiluminescence
EDTA	Ethylenediaminetetraacetic Acid
EGTA	Ethyleneglycol-bis(β-aminoethylether)-N,N,N′,N′-tetraacetic acid
EPICARE	Epidemiological Cardiology Research Center
EMF	Electromotive Gorce
ERM	Epiretinal Membrane
ERS	European Respiratory Society
ETDRS	Early Treatment Diabetic Retinopathy Study
FA	Fractional Anisotropy
FAQ	Functional Activities Questionnaire
FDA	Food and Drug Administration
FEV1	Forced Expiratory Volume in One Second
FLAIR	Fluid-Attenuated Inversion Recovery
FPD	Fibrous Proliferation on the Disc
FPE	Fibrous Proliferation Elsewhere
FVC	Forced Vital Capacity
G-6-P	Glucose-6-Phosphate
G6P-DH	Glucose-6-phosphate dehydrogenase
GEE	Generalized Estimating Equations
GGT	Gamma-Glutamyltransferase
GK	Glycerol Kinase
GM	Gray Matter
GPO	Glycerol Phosphate Oxidase
H2O2	Hydrogen Peroxide
HbA1c	Glycated Haemoglobin
HDL	High Density Lipoprotein
HDL-C	High Density Lipoprotein Cholesterol
HE	Hard Exudate
HK	Hexokinase

HMA	Hemorrhages and Microaneurysms
HPLC	High-Performance Liquid Chromatography
HS cTnT	High Sensitive Cardiac Troponin T
Hz	Hertz
ICAD	Intracranial Atherosclerotic Disease
ICD	International Classification of Diseases
ICT	Informed Consent Tracking
IDMS	Isotope Dilution Mass Spectroscopy
IFCC	International Federation of Clinical Chemistry
ILR	Incidental Learning
IPW	Inverse Probability Weighting
IPCW	Inverse Probability-of-Censoring Weighting
IRMA	Intraretinal Microvascular Abnormalities
ISE	Ion-Selective Electrode
KAOD	Ketoamine Oxidase
LA	Left Atrial
LAVi	Left Atrial Volume Index
LDH	Lactate Dehydrogenase
LDL	Low Density Lipoprotein
LDL-C	Low Density Lipoprotein Cholesterol
LICA	Left Internal Carotid Artery
LMCA	Left Middle Cerebral Artery
LMT	Logical Memory Test
LOWESS	Locally Weighted Scatterplot Smoothing
LPCA	Left-Posterior Communicating Artery
LTC	Long-Term Care
LV	Left Ventricular
LVEF	Left Ventricular Ejection Fraction
LVH	Left Ventricular Hypertrophy
LVMi	Left Ventricular Mass Index
MADB	N,N-Bis(4-Sulfobutyl)-3,5-Dimethylaniline, Disodium Salt
MAR	Missing At Random
MCAR	Missing Completely At Random
MCI	Mild Cognitive Impairment
mCi	Millicurie
MD	Mean Diffusivity
MDH	Malate Dehydrogenase
ME	Macular Edema
MICE	Multiple Imputation by Chained Equations
MMSE	Mini-Mental States Exam
MNAR	Missing Not At Random
MNI	Montreal Neurologic Institute
MPRAGE	Magnetization Prepared Rapid Acquisition Gradient-Echo
MRI	Magnetic Resonance Imaging
NAD+	Nicotinamide Adenine Dinucleotide
NADH	Nicotinamide Adenine Dinucleotide, Reduced

NADP	Nicotinamide Adenine Dinucleotide Phosphate
NADPH	Dihydronicotinamide Adenine Dinucleotide Phosphate
NBT	Nitrotetrazolium-Blue
NGSP	National Glycohemoglobin Standardization Program
NHANES	National Health and Nutrition Examination Survey
NIA-AA	National Institute on Aging–Alzheimer's Association
NIST	National Institute of Standards and Technology
non-HDL-C	Non-High-Density Lipoprotein Cholesterol
NT-proBNP	Nterminal Pro-Brain Natriuretic Peptide
NURBS	Non-Uniform Rational B-Splines
NVD	New Vessels on the Disc
NVE	New Vessels Elsewhere
OTMTA	Oral Trail Making Test A
OTMTB	Oral Trail Making Test B
PACS	Picture Archiving and Communication System
PASL	Pulsed Arterial Spin Labeling
PEP	Phosphoenol Pyruvate
PET	Positron Emission Tomography
PK	Pyruvate Kinase
POD	Peroxidase
PRH	Preretinal Hemorrhage
PRP	Platelet-Rich Plasma
PTA	Pure-Tone Average
PWV	Pulse Wave Velocity
ROI	Region of Interest
QC	Quality Control
QXQ	Question by Question
QuickSIN	Speech-in-Noise Measurement
RICA	Right Internal Carotid Artery
RMCA	Right Middle Cerebral Artery
ROI	Region of Interest
RPCA	Right-Posterior Communicating Artery
RVF	Repeat Visit Form
RWT	Relative Wall Thickness
SAS	Statistical Analysis System
SBM	Source-based Morphometry
SBP	Sitting Blood Pressure
SE	Soft Exudates or Cottonwool Spots
SIS	Six-Item Screener
SPM	Statistical Parametric Map
SUVR	Standard Uptake Value Ratio
Tba	Time delay between right brachial and tibial arteries
Tcf	Time delay between carotid and femoral arteries
Tfa	Time delay between femoral and tibial arteries
TG	Triglycerides
TICS	Telephone Interview for Cognitive Status

TMTA	Trail Making Test A
TMTB	Trail Making Test B
TPO	Thyroid Peroxidase
TSH	Thryoid Stimulating Hormone
VB	Venous Beading
VBM	Voxel-based Morphometry
VH	Vitreous Hemorrhage
VLDL	Very Low-Density Lipoprotein
WFT	Word Fluency Test
WG	Working Groups
WGEE	Weighted Generalized Estimating Equations
WMH	White Matter Hyperintensity

1. INTRODUCTION

1.1. Purpose

The purpose of this working document is to provide guidance to analysts working on ARIC manuscripts. The collaborative document includes information about data available to ARIC investigators, documentation sources, and suggestions for specific types of analyses. These suggestions provide a means to ensure methodological consistency across publications.

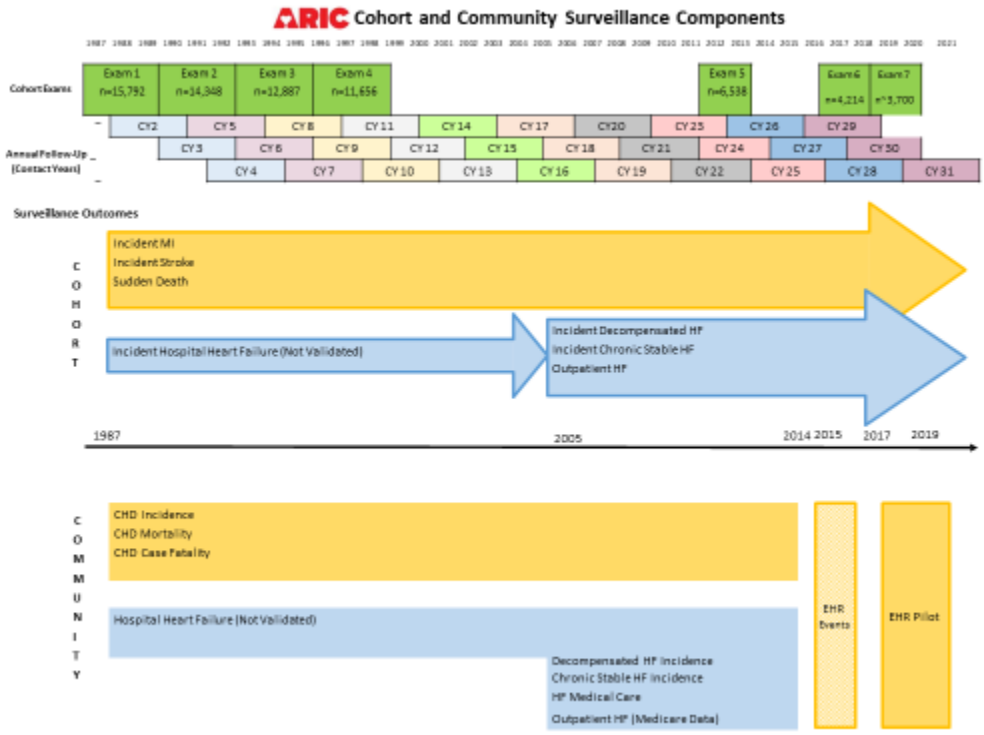
1.2. Available data

1.2.1. Overview

The diagram below depicts ARIC data collection from 1987 to present (Figure 1.2.1.1). In addition to the data collected at each visit, participants are contacted via telephone semi-annually and are given a short battery of data collection forms (AFU). The cohort is also tracked for cardiac-related events and hospitalizations (ARIC cohort surveillance). The AFU and surveillance data were necessary for investigators to track the cohort in the long gap between Visit 4 and Visit 5.

Comprehensive descriptions of datasets collected during the visits, neurocognitive study, AFU, and surveillance are found on the ARIC web site under the Cohort tab on the main menu (https://sites.cscc.unc.edu/aric/).

Figure 1.2.1.1. ARIC data collection from 1987 to present



1.2.2. Datasets

All supporting dataset documentation, codebooks, and derived data dictionaries for closed visits, AFU, and surveillance data have been posted to the study website. There are three types of datasets:

1. Case report form datasets: Data entered into the data management system Carolina Data Acquisition and Reporting Tool (CDART) by the sites or reading centers are retrieved into a corresponding Statistical Analysis System (SAS) dataset. Two accompanying datasets distributed with the form data include the notelog and field status datasets. These datasets include additional information beyond the response, such as comments or the reasons for non-response. The comments are added by the data collector as needed for each question. The data collector's notes are particularly helpful when trying to determine the reasons for suspicious values contained in the

dataset. Some of the visit case report forms were collected during repeat visits for quality control (QC) purposes. The repeat visit data may be linked to the participant using the repeat visit form (RVF) dataset.

2. Transfer datasets: Data transferred to the ARIC coordinating center (CC) from either the sites, such as the Ankle Brachial Index (ABI) and Pulse Wave Velocity (PWV) data, or a reading center/central laboratory, such as Magnetic Resonance Imaging (MRI) data, and converted into a corresponding SAS dataset. Some of the lab datasets have corresponding repeat visit data. The repeat visit data may be linked to the participant using the RVF dataset.
3. Derived datasets: Variables that have undergone transformations, such as calibrated analytes, or new variables created from data found in either the case report form datasets or transfer datasets.

Case Report Form Datasets

Each ARIC case report form yields a corresponding dataset. All 'paper' versions of the case report forms are found on the ARIC website under the 'Cohort' tab, organized by the relevant visit or phone call the form was collected. Supplemental documents for each case report form that contain the field-specific instructions, or Question by Question (QXQ), may be found on the same web page as the forms.

Each form is assigned a 3 or 4-character code as its ‘name.’ For example, the Informed Consent Tracking form is the ‘ICT’. This 3 or 4-character code is used for variable names within each dataset. For example, item #1 on the ICT form is called ICT1 in the ICT dataset. Each ARIC case report form dataset has a codebook that contains descriptive information, labels, and distributions of each variable in the form datasets.

Transfer Data Sets

The transfer datasets are data from labs and reading centers. There are no corresponding ‘paper’ forms nor QxQs. Codebooks and some dictionaries are created for transfer datasets to provide additional documentation about the variables.

Derived Data Sets

The CC, ARIC working groups (WG), and analysts collaborate to create derived datasets. The WG's and analysts have supplied specifications for analysis variables and have reviewed and validated the CC's calculations of the newly created variables. The naming convention for all visit-derived datasets includes the visit number embedded in the dataset name and a version number. For instance, Version 1 of the derived dataset for Visit 5 is [DERIVE51] and Version 2 of the derived dataset for Visit 6 is [DERIVE62]. Throughout the manual, these datasets are referenced with a '##', e.g. [DERIVE##], to indicate the most current version of a dataset from the desired visit. Only those participants who were defined as completing the visit will have a record in [DERIVE##]. A participant is defined as completing the visit when either a weight from the anthropometry or 'ANT' form or blood pressure measurement from the sitting blood pressure or 'SBP' form are present.

Another important derived dataset is [STATUS##], which has been created for analysts. [STATUS##] contains a myriad of indicators for all members of the ARIC cohort (N=15,792) that are determined at the conclusion of the data collection for a specific visit. These indicators are useful for analyses accounting for attrition. This dataset contains the leveled dementia variables.

Several longitudinal datasets are created for ARIC analysts. The analyte dataset, V1_V5_ANALYTES.sas7bdat, contains analyte data from Visits 1-5 and some ancillary studies. Another longitudinal, derived dataset, V2_V#_CNFA.sas7bdat, contains the neurocognitive battery z-scores and factor scores calculated from the neurocognitive testing collected from Visit 2 onward.

The documentation for all the derived datasets is included on the study website under the Cohort tab. These documents are updated regularly as derived datasets undergo version changes as variables are added and/or reviewed.

2. GENERAL METHODS SECTIONS

2.1. Study design

2.1.1. Overview

The ARIC Study is a prospective cohort study investigating the etiology of atherosclerotic disease in a middle-aged, predominantly biracial population. A detailed study design description has been published[1]. The cohort was selected by probability sampling in four U.S. communities, Forsyth County, NC; Jackson, MS; northwestern suburbs of Minneapolis, MN; and Washington County, MD. In Jackson only African Americans were recruited whereas in the other sites the racial composition of the cohort reflected that of the community. In 1987-1989, 15,792 men and women aged 45-64 attended the baseline clinic examination (Visit 1). There were three subsequent visits at approximately three-year intervals (Visit 2 in 1990-1992; Visit 3 in 1993-1995; Visit 4 in 1996-1998) followed by Visit 5 in 2011-2013 and Visit 6 in 2016-2017. Participants have been contacted annually (semi-annually beginning in 2012) since baseline, to obtain information about hospitalizations and for additional data collection.

The ARIC Study protocol was approved by the institutional review board of each participating site and informed consent was obtained from participants at each visit.

References

(1) The ARIC investigators. The Atherosclerosis Risk in Communities (ARIC) study: design and objectives. *American Journal of Epidemiology*. 1989;129(4):687-702.

2.1.2. Neurocognitive Study

The ARIC Neurocognitive Study (ARIC NCS) was integrated operationally with the ARIC examination at Visit 5. Its overall objectives are to determine the prevalence of cognitive impairments and the associations of mid-life vascular risk factors and markers with later-life cognitive impairments and cognitive change. Genetic markers and cerebral imaging features are also studied. Participants are invited for exams in clinic or in their homes or long-term care (LTC) facilities. Those who cannot be examined in person are assessed by telephone. Additional information about participant's cognitive and functional status is sought from informants when

necessary. Some participants are invited for further evaluation including magnetic resonance imaging (MRI). An expert committee reviews data and classifies dementia, mild cognitive impairment (MCI), and their subtypes.

ARIC Cohort Visit 5 participants were selected to Stages 2/3 under a stratified random sampling plan designed to oversample for participants with evidence of cognitive impairment ("atypical"). Details of the selection process and the definition of atypical are provided in Manual 17. In brief, 100% of atypical participants, i.e. low Mini-Mental States Exam (MMSE) score or a low Z-score within a cognitive domain and definite cognitive decline, as well as 100% of ARIC Brain MRI participants were invited to Stage 2. A random sample of the remaining participants was also invited. Sampling fractions varied by site and age group (<80, ≥80 years) and were selected to achieve a sample size of 2000 participants. The final sampling fractions are provided below:

Table 2.1.2.1. Sampling fractions

Site	Age Group	
	< 80	**≥80**
Forsyth	0.18	0.36
Jackson	0.65	1.0
Minneapolis	0.23	0.46
Washington	0.39	0.78

Since participants in the resulting sample are not equally representative of individuals participating in ARIC at Visit 5, the CC has calculated weights that take into account the probability of selection ([V5_V11_MRI_DERV] SAMWT1). The sampling weights are the product of a base weight ([V5_V11_MRI_DERV] BASEWT1) and an adjustment for refusal ([V5_V11_MRI_DERV] REFADJ1). The base weight is the inverse of the proportion of participants completing clinic visits who were selected to Stage 2. The weights were normalized to the number of participants completing clinic visits. The adjustment for refusal is the inverse of the site-specific probability of completing an exam, though analysts may choose to re-calculate to account for informative failure to complete the visit.

2.2. Laboratory Analyte Measurements – Advanced Research and Diagnostic Laboratory (University of Minnesota) – Visits 5 through 7

2.2.1. Thryoid Stimulating Hormone, TSH (mIU/L) – Visit 5

Thryoid Stimulating Hormone (TSH) was measured in serum using a sandwich immunoassay method on the Roche Elecsys 2010 Analyzer (Roche Diagnostics, Indianapolis, IN) using a sandwich immunoassay method (Roche Diagnostics). In the first incubation, the patient sample is mixed with a biotinylated monoclonal TSH-specific antibody and a monoclonal TSH-specific antibody labeled with a ruthenium complex to form a sandwich complex. During the second incubation, streptavidin-coated microparticles are added, and the complex becomes bound to the solid phase via interaction of biotin and streptavidin. The microparticles are then captured magnetically and unbound material is removed. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. The amount of light produced is directly proportional to the amount of TSH in the sample. The inter-assay coefficients of variation (CVs) of the method are 7.6% at a concentration of 0.195 mIU/L and 4.5% at a concentration of 1.98 mIU/L.

2.2.2. Thyroxine (free), fT4 (ng/dL) – Visit 5

Thyroxine (free) was measured in serum on a Roche Elecsys 2010 Analyzer (Roche Diagnostics, Indianapolis, IN) using a competition immunoassay method (Roche Diagnostics). In the first incubation, the patient sample is mixed with T4-specific antibody labeled with a ruthenium complex. Biotinylated T4 and streptavidin-coated microparticles are added during the second incubation. The still-free binding sites of the labeled antibody become occupied, with formation of an antibody-hapten complex. The entire complex becomes bound to the solid phase via interaction of biotin and streptavidin. The microparticles are then captured magnetically and unbound material is removed. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. The amount of light produced is inversely proportional to the amount of T4 in the sample. The inter-assay CVs for the method are 4.2% at a concentration of 1.22 ng/dL and 4.5% at a concentration of 2.84 ng/dL.

2.2.3. Triiodothyronine, T3 (ng/dL) – Visit 5

Triiodothyronine (T3) was measured in serum on a Roche Elecsys 2010 Analyzer (Roche Diagnostics, Indianapolis, IN) using a competition immunoassay method (Roche Diagnostics). Bound T3 is released from the binding proteins in the sample by 8-anilino-1-naphthalene sulfonic acid. In the first incubation, T3 in the patient sample reacts with T3-specific antibody labeled with a ruthenium complex. Biotinylated T3 and streptavidin-coated microparticles are added during the second incubation. The still-free binding sites of the labeled antibody become occupied, with formation of an antibody-hapten complex. The entire complex becomes bound to the solid phase via interaction of biotin and streptavidin. The microparticles are then captured magnetically and unbound material is removed. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. The amount of light produced is inversely proportional to the amount of T3 in the sample. The inter-assay CVs for the method are 7.2% at a concentration of 121 ng/dL and 5.4% at a concentration of 354 ng/dL.

2.2.4. Thyroid peroxidase antibody, anti-TPO (IU/mL) – Visit 5

Thyroid peroxidase antibody (anti-TPO) is measured in serum or plasma on a Roche Elecsys 2010 Analyzer (Roche Diagnostics, Indianapolis, IN) using a competition immunoassay method (Roche Diagnostics). In the first incubation, the patient sample is mixed with anti-TPO-antibodies labeled with a ruthenium complex. Biotinylated TPO and streptavidin-coated microparticles are added during the second incubation. The anti-TPO antibodies in the sample compete with the ruthenium-labeled anti-TPO antibodies for the biotinylated TPO antigen. The entire complex becomes bound to the solid phase via interaction of biotin and streptavidin. The microparticles are then captured magnetically and unbound substance is removed. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. The amount of light produced is inversely proportional to the amount of anti-TPO in the sample. The CV for the method is 10.2% at concentrations below the assay cut-off (34 IU/mL) and 6.0% for concentrations above the assay cut-off.

2.2.5. HbA1c (%) – Visits 5 through 7

HbA1c was measured in EDTA whole blood on the Tosoh HPLC Glycohemoglobin Analyzer (Tosoh Medics, Inc., San Francisco, CA) using an automated high performance liquid chromatography method. Calibration of this method is evaluated utilizing standard values derived by the National Glycohemoglobin Standardization Program (NGSP). The laboratory CV was 1.9% at Visit 5. At Visit 6 and Visit 7 the laboratory inter-assay CVs were 1.16% at a mean HbA1c value of 5.34% and 0.55% at a mean HbA1c value of 10.11%.

2.2.6. Creatinine, Serum (mg/dL) – Visits 5 through 7

Creatinine was measured in serum on a Roche Modular P Chemistry Analyzer (Roche Diagnostics, Indianapolis, IN) using a creatinase enzymatic method (Roche Diagnostics). In this enzymatic method creatinine is converted to creatine under the activity of creatininase. Creatine is then acted upon by creatinase to form sarcosine and urea. Sarcosine oxidase converts sarcosine to glycine and hydrogen peroxide, and the hydrogen peroxide reacts with a chromophore in the presence of peroxidase to produce a colored product that is measured at 546 nm (secondary wavelength = 700 nm). This is an endpoint reaction that agrees well with recognized high-performance liquid chromatography (HPLC) methods, and has the advantage over Jaffe picric acid-based methods that are susceptible to interferences from non-creatinine chromogens. The CV for the method was 2.3% at Visit 5. At Visit 6 and Visit 7 the laboratory inter-assay CVs were 2.9% at a mean concentration of 0.835 mg/dL and 2.8% at a mean concentration of 3.93 mg/dL.

2.2.7. Cystatin C (mg/dL) – Visits 5 through 7

Cystatin C was measured in serum using Gentian Cystatin C reagent (Gentian AS, Moss, Norway) on the Roche Modular P Chemistry analyzer at Visit 5 and the Roche Cobas 6000 chemistry analyzer at Visit 6 and Visit 7 (Roche Diagnostics, Indianapolis, IN). Serum sample from human is mixed with Gentian Cystatin C immunoparticles. Cystatin C from the sample and anti-Cystatin C from the immunoparticles aggregates. The complex particles created absorb light, and by turbidimetry the absorption is related to Cystatin C concentration via interpolation on an established standard calibration curve. The laboratory inter-assay CVs are 4.3% at a value of 0.75 mg/L and 3.2% at a value of 3.83 mg/L.

2.2.8. Uric Acid, Serum (mg/dL) – Visit 5

Uric acid was measured in serum using an enzymatic colorimetric assay kit and read on the Roche Modular P Chemistry analyzer (Roche Diagnostics, Indianapolis, IN). In this method uric acid is oxidized by uricase to produce allantoin, CO2, and peroxide. Then the peroxide produced from this reaction is acted upon by peroxidase in the presence of 4-aminophenazone and TOOS (N-ethyl-N-(2-hydroxy-3-sulfopropyl)-3-methylaniline) to produce a red quinoneimine dye end product. It is a two-point, end-point reaction, with measurement occurring at 546 nm (secondary wavelength 700 nm). The laboratory inter-assay CV is 1.9% at a mean concentration of 4.6 mg/dL and 1.6% at a mean concentration of 8.9 mg/dL.

2.2.9. Urine Albumin –UMALI (mg/L) – Visits 5 through 7

At Visit 5, urine albumin was measured using an immunoturbidimetric method on the ProSpec nephelometric analyzer (Dade Behring GMBH, Marburg, Germany). A solution of rabbit-derived anti-human albumin is incubated with the urine specimen. An immunocomplex forms between the antibody and the albumin in the specimen, resulting in an increase in light scatter. The higher the concentration of albumin, the more intense the degree of light scatter. The albumin concentration of the test specimen is determined by comparing its light scatter to that observed using known standards in a calibration curve. The laboratory inter-assay CV is 6.9% at a mean concentration of 19 mg/L and 2.2% at a mean concentration of 127 mg/L.

At Visit 6 and Visit 7, urine albumin was measured using an immunoturbidimetric method on the Roche Cobas 6000 chemistry analyzer (Roche Diagnostics, Indianapolis, IN). Anti-albumin antibodies react with the antigen in the sample to form antigen/antibody complexes which, following agglutination, are measured turbidimetrically. This method has been standardized against the reference preparation of the Institute for Reference Materials and Measurements BCR470/CRM470 Reference Preparation for Proteins in Human Serum. The laboratory inter-assay CVs are 4.0% at a mean concentration of 19.7 mg/L and 2.1% at a mean concentration of 117.7 mg/L.

2.2.10. Urine Creatinine (mg/dL) – Visits 5 through 7

At Visit 5, creatinine was measured in urine on a Roche Modular P Chemistry Analyzer at Visit 5 and a Roche Cobas 6000 chemistry analyzer at Visit 6 and Visit 7 (Roche Diagnostics, Indianapolis, IN) using a creatinase enzymatic method (Roche Diagnostics). In this enzymatic method creatinine is converted to creatine under the activity of creatininase. Creatine is then acted upon by creatinase to form sarcosine and urea. Sarcosine oxidase converts sarcosine to glycine and hydrogen peroxide, and the hydrogen peroxide reacts with a chromophore in the presence of peroxidase to produce a colored product that is measured at 546 nm (secondary wavelength = 700 nm). This is an endpoint reaction that agrees well with recognized HPLC methods, and has the advantage over Jaffe picric acid-based methods that are susceptible to interferences from non-creatinine chromogens. The laboratory inter-assay CV at Visit 5 was

4.3% at a concentration of 18.39 mg/dL and 1.5% at a concentration of 96.57 mg/dL. At Visit 6 and Visit 7 the laboratory inter-assay CVs were 4.5% at a mean concentration of 16.8 mg/L and 2.6% at a mean concentration of 88.1 mg/L.

2.2.11. Urine Albumin/creatinine Ratio - UMALCR (mg/g Cr) – Visits 5 through 7

The urine albumin/creatinine ratio was determined by dividing urinary albumin (mg/L) by creatinine (mg/dL) and multiplying by 0.01 to obtain mg of albumin/g of creatinine.

2.2.12. Vitamin B12 (pg/mL) – Visit 5

Vitamin B12 was measured in serum using a direct chemiluminescent competitive immunoassay method on the Roche Elecsys 2010 Analyzer (Roche Diagnostics, Indianapolis, IN). The sample is first incubated with the vitamin B12 pretreatment 1 and pretreatment 2 during which bound vitamin B12 is released. The pretreated sample is then incubated with the ruthenium labeled intrinsic factor and a vitamin B12-binding protein complex is formed, the amount of which is dependent upon the analyte concentration in the sample. After addition of streptavidin-coated microparticles and vitamin B12 labeled with biotin, the still-vacant sites of the ruthenium labeled intrinsic factor become occupied, with formation of a ruthenium labeled intrinsic factor-vitamin B12 biotin complex. The entire complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode. The laboratory CV is 7.39% at a concentration of 469 pg/mL and 8.32% at a concentration of 258 pg/mL.

2.2.13. Glucose (mg/dL) – Visits 5 through 7

Glucose was measured in serum by the Roche hexokinase method on a Roche Cobas 6000 chemistry analyzer (Roche Diagnostics, Indianapolis, IN). In this enzymatic method, glucose is converted to glucose-6-phosphate by hexokinase in the presence of ATP. Glucose-6-phosphate dehydrogenase then converts the G-6-P to gluconate-6-P in the presence of NADP. The

resulting increase in absorbance as NADP is reduced to NADPH is measured at 340 nm. The method is calibrated and checked quarterly against Standard Reference Material 965 from National Institute of Standards and Technology (NIST) traceable to the NIST definitive method for glucose by Isotope Dilution Mass Spectroscopy (IDMS). The laboratory inter-assay CVs are 1.3% at a mean concentration of 97.2 mg/dL and 1.8% at a mean concentration of 223.3 mg/dL.

2.2.14. Fructosamine (umol/L) – Visits 5 through 7

Fructosamine was measured in serum on the Roche Cobas 6000 Analyzer (Roche Diagnostics, Indianapolis, IN) using a colorimetric assay based on the ability of ketoamines to reduce nitrotetrazolium-blue (NBT) to formazan in an alkaline solution. The rate of formation of formazan is directly proportional to the concentration of fructosamine. Uricase serves to eliminate uric acid interference and detergent eliminates matrix effects. The rate of reaction is measured photometrically at 546 nm. The laboratory inter-assay CVs are 3.2% at a concentration of 220 umol/L and 2.0% at a concentration of 898 umol/L.

2.2.15. Glycated albumin (%) – Visits 5 through 7

Glycated albumin and total albumin were measured in serum by an enzymatic, endpoint reaction on the Roche Cobas 6000 chemistry analyzer (Roche Diagnostics, Indianapolis, IN). This is an open channel test using Asahi Kasei Pharma Corporation reagents (Tokyo, Japan). Two tests are performed on each specimen: glycated albumin and total albumin. These two values are reported along with the calculated glycated albumin percentage. Glycated albumin is measured in a multi-enzyme, stepwise reaction. First, ketoamine oxidase (KAOD) eliminates endogenous glycated amino acids. Then, an albumin-specific protease converts glycated albumin to glycated amino acids, and these react with the KAOD, producing hydrogen peroxide. In the presence of peroxidase, the hydrogen peroxide reacts with 4- aminoantipyrine to produce a visible chromogen whose intensity is directly proportional to the concentration of glycated albumin. The primary measuring wavelength is 546 nm and the secondary wavelength is 700 nm. It is a two-point, end-point reaction. Total albumin is determined by first treating the specimen with a solution to treat SH groups and convert reduced albumin to oxidized albumin. Bromcresol purple is added and a blue conjugate is formed. The intensity of the color is directly

proportional to the total albumin concentration. The primary measuring wavelength is 600 nm and the secondary wavelength is 660 nm. It is a two-point, end-point reaction. The calculation of glycated albumin percentage on the Cobas 6000 also incorporates a correction for methodologic deviation from the HPLC technique. The formula is:

[((GALB/AALB) / 1.14) * 100] + 2.9 = GALB %.

This formula is loaded into the Cobas 6000 and glycated albumin automatically calculated and reported in units of percent (%) when both tests are performed on a single specimen. The laboratory inter-assay CVs for the glycated albumin measurement are 4.4% at a mean concentration of 0.45 g/dL and 2.8% at a mean concentration of 1.64 g/dL. The laboratory inter-assay CVs for the albumin measurement are 3.0% at a mean concentration of 3.94 g/dL and 2.4% at a mean concentration of 4.45 g/dL.

2.2.16. 1,5-Anhydroglucitol (ug/mL) – Visits 5 through 7

1,5AG was measured in serum on the Roche Cobas 6000 chemistry analyzer (Roche Diagnostics, Indianapolis, IN) using GlycoMark reagent (GlycoMark Inc, New York, NY). First the sample is pretreated by glucokinase (GK) to convert glucose to glucose 6-phosphate in the presence of adenosine triphosphate (ATP), pyruvate kinase (PK) and phosphoenol pyruvate (PEP). The purpose of this reaction is to alter glucose so it can not react in the primary assay for 1,5-AG. Then pyranose oxidase oxidizes the second hydroxyl of 1,5-anhydroglucitol. The amount of hydrogen peroxide generated in this reaction is directly related to serum 1,5-AG concentrations and is detected by colorimetry using peroxidase. The laboratory inter-assay CVs are 0.9% at a concentration of 18.0 ug/mL and 9.7% at a concentration of 3.8 ug/mL.

2.2.17. Beta-2-Microglobulin (mg/L) – Visits 5 through 7

Beta-2-Microglobulin was determined immunoturbidimetrically in serum using the Roche Cobas 6000 chemistry analyzer (Roche Diagnostics, Indianapolis, IN). Latex-bound anti-*2-microglobulin antibodies react with antigen from the sample to form antigen/antibody complexes which are determined turbidimetrically after agglutination. The laboratory inter-assay CVs are 3.2% at a concentration of 1.63 mg/L and 4.3% at a concentration of 0.6 mg/L.

2.2.18. Magnesium (mg/dL) – Visits 6 and 7

Magnesium was measured in serum using a colorimetric method on the Roche Cobas 6000 chemistry analyzer (Roche Diagnostics, Indianapolis, IN). The method is based on the reaction of magnesium with xylidyl blue in alkaline solution containing EGTA to mask the calcium in the sample. In alkaline solution, magnesium forms a purple complex with xylidyl blue, diazonium salt. The magnesium concentration is measured photometrically via the decrease in the xylidyl blue absorbance. The laboratory inter-assay CVs are 3.5% at a concentration of 1.82 mg/dL and 1.9% at a concentration of 3.44 mg/dL.

*2.2.19. Potassium (*mmol/L*) – Visits 6 and 7*

Potassium was measured in serum by an indirect ion-selective electrode (ISE) method on the Roche Cobas 6000 chemistry analyzer (Roche Diagnostics, Indianapolis, IN). A 1:31 dilution of the sample is prepared by the analyzer and aspirated into the electrode chamber. An Ion-Selective Electrode (ISE) makes use of the unique properties of certain membrane materials to develop an electrical potential (electromotive force, EMF) for the measurements of ions in solution. The electrode has a selective membrane in contact with both the test solution and an internal filling solution. The internal filling solution contains the test ion at a fixed concentration. Due to the particular nature of the membrane, the test ions will closely associate with the membrane on each side. The membrane EMF is determined by the difference in concentration of the test ion in the test solution and the internal filling solution The laboratory inter-assay CVs are 1.3% at a mean concentration of 4.55 mmol/L and 2.0% at a mean concentration of 3.24 mmol/L.

2.2.20. Aspartate Aminotransferase (U/L) – Visits 5 through 7

Aspartate Aminotransferase (AST) was measured in serum using a kinetic rate reaction method on the Roche Cobas 6000 chemistry analyzer (Roche Diagnostics, Indianapolis, IN). AST activity is determined by a modification of the method recommended by the International Federation of Clinical Chemistry (IFCC). AST catalyzes the reaction of alpha-ketoglutarate with L-aspartate to form L-glutamate and oxaloacetate. Under the action of malate dehydrogenase (MDH), oxaloacetate converts to malate, and NADH is oxidized to NAD. The decrease in absorbance of

NADH, measured at 340 nm (secondary wavelength = 700 nm), is directly proportional to the serum activity of AST. The laboratory inter-assay CVs are 2.4% at a concentration of 21 U/L and 3.3% at a concentration of 141 U/L.

2.2.21. Alanine Aminotransferase (U/L) – Visits 5 through 7

Alanine Aminotransferase (ALT) was measured in serum using a kinetic rate reaction method on the Roche Cobas 6000 chemistry analyzer (Roche Diagnostics, Indianapolis, IN). ALT catalyzes the reaction of alpha-ketoglutarate with L-alanine to form L-glutamate and pyruvate. Under the action of LDH, pyruvate converts to lactate, and NADH is converted to NAD. The decrease in absorbance of NADH, measured at 340 nm (secondary wavelength is 700 nm), is directly proportional to the serum activity of ALT. The laboratory inter-assay CVs are 2.4% at a concentration of 21 U/L and 2.0% at a concentration of 133 U/L.

2.2.22. Gamma-Glutamyltransferase (U/L) – Visits 5 through 7

Gamma-Glutamyltransferase (GGT) was measured in serum by a kinetic rate reaction method on the Roche Cobas 6000 chemistry analyzer (Roche Diagnostics, Indianapolis, IN). In the presence of glycylglycine, L-gamma-glutamyl-3-carboxy-4-nitroanilide is converted by GGT to 5-amino-2-nitrobenzoate and L-gamma-glutamyl-glycylglycine. The rate of colored product formation is directly related to the amount of GGT in the specimen, and the rate of its appearance is measured at 415 nm (secondary wavelength 700 nm). The laboratory inter-assay CVs are 2.0% at a mean concentration of 25 U/L and 1.7% at a mean concentration of 174 U/L.

2.2.23. Hemoglobin (g/dL) – Visits 6 and 7

Hemoglobin was measured in EDTA whole blood that had been previously frozen for up to 9 weeks* using a Sysmex XS-1000i (Sysmex America, Inc., Lincolnshire, IL). The Sysmex XS-1000i is a quantitative automated hematology analyzer for *in vitro* diagnostic use for determining 21 hematological parameters. Hemoglobin is converted to SLS-hemoglobin and read photometrically. The laboratory inter-assay CVs are 0.8% at a mean concentration of 5.73 g/dL and 0.6% at a mean concentration of 16.95 g/dL. In a pilot study[1], hemoglobin was measured in previously frozen samples stored for 15 or 30 days as part of a complete blood count (CBC) and compared to measurements made in fresh blood samples. While the instrument provided

values for most CBC parameters, only the hemoglobin measurement was stable over time. Other CBC parameters were far less reliable when measured in these frozen samples.

*Time frozen for the whole blood vials ranged from 1 to 63 days (mean = 13.7 days; median = 13 days; standard deviation = 8.4 days). So, time frozen of "up to 9 weeks" is noted in the assay description, even though that does not reflect the majority of samples.

References

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2.3. Laboratory Analyte Measurements – Atherosclerosis Clinical Research Laboratory (ACRL) – Visits 5 through 7

2.3.1. Complete Blood Count – Visit 5

Instrument: ABX Horiba Diagnostics MICROS 60-CS

Test: Complete Blood Count

Method: A fully automated hematology analyzer is used for in-vitro diagnostics testing of whole blood specimens, platelet-rich plasma (PRP) samples, and whole blood component concentrates. The instrument implements both impedance technology and spectrophotometry to determine a Complete Blood Count (CBC) with 3-part differential. The 16 parameters are determined with a microsampling of only 10µL. The Micros 60 can analyze approximately 55 samples per hour.

2.3.2. Cholesterol – Visits 5 through 7

Instrument: Beckman Olympus AU400 Series

Test: Cholesterol (mg/dL)

Method: Enzymatic. Colorimetric. Cholesterol esters in serum are hydrolyzed by cholesterol esterase (CHE). The free cholesterol produced is oxidized by cholesterol oxidase (CHO) to cholest-4-en-3-one with the simultaneous production of hydrogen peroxide (H202), which oxidatively couples with 4-aminoantipyrine and phenol in the presence of peroxidase to yield a

chromophore. The red quinonimine dye formed can be measured spectrophotometrically at 540/600 nm as an increase in absorbance.

2.3.3. Triglycerides – Visits 5 through 7

Instrument: Beckman Olympus AU400 Series

Test: Triglycerides (mg/dL)

Method: Enzymatic. Color without GBw/SB. This Olympus Triglyceride procedure is based on a series of coupled enzymatic reactions. The triglycerides in the sample are hydrolyzed by a combination of microbial lipases to give glycerol and fatty acids. The glycerol is phosphorylated by adenosine triphosphate (ATP) in the presence of glycerol kinase (GK) to produce glycerol-3-phosphate. The glycerol-3-phosphate is oxidized by molecular oxygen in the presence of glycerol phosphate oxidase (GPO) to produce hydrogen peroxide (H2O2) and dihydroxyacetone phosphate. The formed H2O2 reacts with 4-aminophenazone and N, N-bis(4-sulfobutyl)-3,5-dimethylaniline, disodium salt (MADB) in the presence of peroxidase (POD) to produce a chromophore, which is read at 660/800 nm. The increase in absorbance at 660/800 nm is proportional to the triglyceride content of the sample.

2.3.4. High Density Lipoprotein Cholesterol – Visits 5 through 7

Instrument: Beckman Olympus AU400 Series

Test: High Density Lipoprotein (HDL-C) Cholesterol (mg/dL)

Method: Direct (Homogenous) HDL. The HDL Ultra Cholesterol assay is a homogenous method for directly measuring HDL-C concentrations in serum or plasma without the need for any off-time pretreatment or centrifugation steps. The assay is comprised of two distinct phases. In phase one, free cholesterol in non-HDL-lipoproteins is solubilized and consumed by cholesterol oxidase, peroxidase, and N, N-Bis (4-sulfobutyl)-m-toluidine disodium salt (DSBmT) to generate a colorless end product. In phase two, a unique detergent selectively solubilizes HDL-

lipoproteins. The HDL cholesterol is released for reaction with cholesterol esterase, cholesterol oxidase, and a chromogen system to yield a blue color complex, which can be measured bichromatically at 600/700nm. The resulting increase in absorbance is directly proportional to the HDL-C concentration in the sample.

2.3.5. Low Density Lipoprotein Cholesterol, Calculated – Visits 5 through 7

Instrument: Beckman Olympus AU400 Series

Test: Low Density Lipoprotein (LDL) Cholesterol, Calculated (mg/dL)

Method: Freidwald Formula. The Freidwald Formula is used to calculate the LDL cholesterol. The formula is: [LDL-chol] = [Total chol] - [HDL-chol] - ([TG]/5) the quotient ([TG]/5) is used as an estimate of very low-density lipoprotein (VLDL) cholesterol concentration. It assumes, first, that virtually all the plasma TG is carried on VLDL, and second, that the TG, cholesterol ratio of VLDL is constant at about 5:1.

2.3.6. Non-High-Density Lipoprotein Cholesterol, Calculated – Visits 5 through 7

Instrument: Beckman Olympus AU400 Series

Test: Non-High-Density Lipoprotein (non-HDL-C) Cholesterol, Calculated (mg/dL)

Method: Calculation. Non-HDL-C is calculated as total cholesterol minus HDL. The addition of non-HDL-C to the lipid panel reflects the recognition of this calculated value as a predictive factor in cardiovascular disease based on the National Cholesterol Education III studies. The reference ranges for non-HDL-C are based on National Cholesterol Education III guidelines: Desirable: < 130 mg/dL Borderline high: 139-159 mg/dL High: 160-189 mg/dL Very high: > or = 190 mg/dL

2.3.7. Glucose – Visit 5

Instrument: Beckman Olympus AU400 Series

Test: Glucose (mg/dL) (v5 only for ACRL)

Method: Enzymatic. In this Beckman Coulter procedure, glucose is phosphorylated by hexokinase (HK) in the presence of adenosine triphosphate (ATP) and magnesium ions to produce glucose-6-phosphate (G-6-P) and adenosine diphosphate (ADP). Glucose-6-phosphate dehydrogenase (G6P-DH) specifically oxidizes G-6-P to 6-phosphogluconate with the concurrent reduction of nicotinamide adenine dinucleotide (NAD+) to nicotinamide adenine dinucleotide, reduced (NADH). For the AU400 the change in absorbance at 340/380 nm is proportional to the amount of glucose present in the sample. For the AU480 the change in absorbance at 340/660 nm is proportional to the amount of glucose present in the sample.

2.3.8. High Sensitivity C-Reactive Protein – Visits 5 through 7

Instrument: Beckman Olympus AU400

Test: hs C-Reactive Protein (mg/L)

Method: C-reactive protein is measured by latex particle enhanced immunoturbidimetric assay. Latex particles coated with antibody specific to human CRP aggregate in the presence of CRP from the sample forming immune complexes. The immune complexes cause an increase in light scattering which is proportional to the concentration of CRP in the serum. The light scattering is measured by reading turbidity at 572 nm. The sample CRP concentration is determined versus dilutions of a CRP standard of known concentration. EDTA plasma was used.

2.3.9. Insulin – Visits 5 through 7

Instrument: Roche Cobas e411

Test: Insulin (µU/mL) (v5)

Conversion Factors:

µU/mL x 6.945 = pmol/L

pmol/L x 0.144 = µU/mL

Method: Immunoassay. Electrochemiluminescence (ECLIA) sandwich principle. A biotinylated monoclonal insulin-specific antibody and a monoclonal insulin-specific antibody labeled with a ruthenium complex form a sandwich complex. After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode.

2.3.10. Nterminal Pro-Brain Natriuretic Peptide – Visits 5 through 7

Instrument: Roche Cobas e411

Test: NT-proBNP (pg/mL)

Conversion Factors:

pmol/L x 8.457 = pg/mL

pg/mL x 0.118 = pmol/L

Method: Immunoassay. Electrochemiluminescence immunoassay (ECLIA) Sandwich principle. A biotinylated monoclonal NT-proBNP-specific antibody and a monoclonal NT-proBNP-specific antibody labeled with a ruthenium complex a form a sandwich complex. After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin. The microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell inducing a chemiluminescent emission which is measured by a photomultiplier. Results are

determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode.

2.3.11. High Sensitive Cardiac Troponin I – Visits 5 through 7

Instrument: Abbott ARCHITECT i2000SR

Test: hs Troponin I (ng/L)

Method: The ARCHITECT STAT High Sensitive Troponin-I assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of cardiac troponin I (cTnI) in human plasma and serum on the ARCHITECT i System with STAT protocol capability. EDTA plasma was used.

2.3.12. High Sensitive Cardiac Troponin T – Visits 5 through 7

Instrument: Roche Cobas e411

Test: hs Troponin T (pg/mL)

Method: Sandwich principle. Chemiluminescent. A biotinylated monoclonal anti-cardiac troponin T-specific antibody and a monoclonal anti-cardiac troponin T-specific antibody labeled with a ruthenium complex reaction to form a sandwich complex. After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin. Microparticles are magnetically captured onto the surface of the electrode. Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve (S-point calibration) provided via the reagent barcode.

2.3.13. Testosterone – Visits 5 through 7

Instrument: Abbott ARCHITECT i2000SR

Test: Testosterone (ng/dL)

Method: The ARCHITECT Testosterone assay is a Chemiluminescent microparticle Immunoassay (CMIA) for the quantitative determination of testosterone in human serum and plasma. EDTA plasma was used.

2.3.14. Sex Hormone Binding Globulin – Visits 5 through 7

Instrument: Abbott ARCHITECT i2000SR

Test: SHBG (nmol/L)

Method: The ARCHITECT Sex Hormone Binding Globulin (SHBG) assay is a Chemiluminescent microparticle Immunoassay (CMIA) for the quantitative determination of SHBG in human serum and plasma. EDTA plasma was used. It is a two-step immunoassay to determine the presence of SHBG using the chemiluminescent technology with flexible assay protocols referred to as Chemiflex.

2.3.15. Dehydroepiandrosterone Sulfate – Visits 5 through 7

Instrument: Abbott ARCHITECT i2000SR

Test: DHEA-S (µg/dL)

Method: The ARCHITECT Dehydroepiandrosterone Sulfate, S assay is a Chemiluminescent microparticle Immunoassay (CMIA) for the quantitative determination of DHEA-S in human serum and plasma. EDTA plasma was used.

2.3.16. Galectin-3 – Visits 5 through 7

Instrument: Abbott ARCHITECT i2000SR

Test: Galectin-3 (ng/mL)

Method: The ARCHITECT Galectin-3 assay is a Chemiluminescent microparticle Immunoassay (CMIA) for the quantitative determination of DHEA in human serum and plasma. EDTA plasma was used.

2.3.17. Growth Differentiation Factor-15 – Visits 6 and 7

Instrument: Roche Cobas e411

Test: Growth Differentiation Factor-15 (GDF-15) (pg/mL) (v6, & v7).

Method: Sandwich principle. Electrochemiluminescence Immunoassay (ECLIA). A quantitative determination of Growth Differentiation Factor-15 (GDF-15) currently limited by Federal (United States) law to investigational use.

2.4. Echo – Visits 5 and 7

Design and methods of echocardiography in ARIC Visit 5 have been previously described.[1] Briefly, measurements of participants attending Visit 5 and Visit 7 were obtained by certified study sonographers using uniform imaging equipment and image acquisition protocols. Studies were acquired digitally and sent to the Echocardiography Reading Center at the Brigham and Women's Hospital, where quantitative measures were performed by dedicated Reading Center analysts and independently over-read by staff echocardiographers with both readers blinded to clinical information.

Left ventricular (LV) volumes were calculated by the modified Simpson's method using the apical 4 and 2 chamber views. LV ejection fraction (LVEF) was derived from volumes in the standard manner. LV dimensions and wall thickness were measured from the parasternal long axis view according to the recommendations of the American Society of Echocardiography (ASE).[2] LV mass was calculated from LV linear dimensions and indexed to body surface area also as recommended by ASE guidelines. LV hypertrophy (LVH) was defined as LV mass indexed to body surface area (LV mass index, LVMi) >115 g/m^2 in men or >95 g/m^2 in women. Relative wall thickness (RWT) was calculated from LV end-diastolic dimension and posterior wall thickness. Left atrial (LA) volume was measured by the uniplane Simpson's method of discs using apical 4- and 2-chamber views at an end-systolic frame preceding mitral valve opening and was indexed to body surface area to derive LA volume index (LAVi). Early (E wave) and late (A wave) transmittal velocities were measured by pulsed wave Doppler, and the peak early diastolic lateral and septal mitral annular relaxation velocities (E') were assessed using tissue Doppler imaging, both from the apical 4-chamber view.[3] E/E' ratio, calculated as early transmittal velocity (E wave) divided by E'. Longitudinal strain was measured in the apical 4 and 2 chamber views using the TOMTEC software.

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2.5. Electrocardiograph (ECG) – Visit 5

Standard 10-second resting 12-lead electrocardiogram at rest was digitally acquired using a GE MAC 1200 electrocardiograph (GE, Milwaukee, WI) at 10 mm/mV calibration and a speed of 25 mm/s. ECG reading was performed centrally at the Epidemiological Cardiology Research Center (EPICARE), Wake Forest School of Medicine, Winston Salem, NC. All electrocardiograms were initially inspected visually for technical errors and inadequate quality before being automatically processed using GE 12-SL Marquette Version 2001 (GE, Milwaukee, WI). ECG abnormalities were classified and coded using the Minnesota ECG Classification.

2.6. Pulse Wave Velocity – Visits 5 through 7

Electrocardiogram, bilateral brachial and ankle blood pressures, and carotid and femoral arterial pulse waves were simultaneously measured with a vascular testing device (VP-1000plus, Omron Healthcare, Kyoto, Japan).[1] This machine was originally developed as a screening device for hypertension (via blood pressure), peripheral artery disease (via ankle brachial index), and arterial stiffness (via pulse wave velocity). This necessitated the use of four blood pressure cuffs on each limb. Carotid and femoral arterial pressure waveforms were stored for 30 sec by applanation tonometry sensors attached on the left common carotid artery (via a neck color) and left common femoral artery (via elastic tape around the waist). Bilateral brachial and post-tibial arterial pressure waveforms were stored for 10 sec by extremities cuffs connected to a plethysmographic sensor and an oscillometric pressure sensor wrapped on both arms and ankles.

Pulse wave velocity was calculated from the distance between two arterial recording sites divided by transit time. Transit time was determined from the time delay between the proximal and distal "foot" waveforms. The foot of the wave was identified as the commencement of the sharp systolic upstroke, which was automatically detected by a band-pass filter (5~30 Hz). Time delay between right brachial and tibial arteries (Tba), between carotid and femoral arteries (Tcf), and between femoral and tibial arteries (Tfa) were obtained. The path length from the carotid to the femoral artery (Dcf) was directly assessed in duplicate with a random zero length measurement over the surface of the body with a non-elastic tape measure.[2] The path lengths from the suprasternal notch to brachial artery (Dhb), from suprasternal notch to femoral artery (Dhf), and from femoral artery and ankle (Dfa) were calculated automatically by the machine using the following equations[3]:

Dhb = (0.220 x height {cm} - 2.07)

Dhf = (0.564 x height {cm} - 18.4)

Dfa = (0.249 x height {cm} + 30.7)

PWV were calculated by the following equations:

Carotid-femoral PWV = Dcf / Tcf

Brachial-ankle PWV = (Dhf + Dfa – Dhb) / Tba

The validity and reliability of the automatic device for measuring PWV have been established previously.[1,4]

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2.7. Coronary Artery Calcium (CAC) – Visit 7

During Visit 7, ARIC participants free of existing coronary heart disease (prior myocardial infarction or coronary revascularization) were invited to undergo a non-contrast cardiac-gated computed tomography (CT) scan to evaluate vascular and valvular calcification of the heart and thoracic aorta. After removal of upper body undergarments that might interfere with imaging, three electrodes were placed on the participant's chest and limbs. The participant was then placed on the scanner bed for the standard protocol of CAC (detailed specifications of CT scanners across the four sites are depicted in the table below).

The evaluation of calcification was based on both the Agatston score and the volume score.[1] Specifically, calcification was defined as lesions with attenuation >130 Hounsfield Units (HU) and area ≥1mm^2 in each slice level. Area of each calcified lesion was then multiplied by the density factor of calcified plaque depending on the highest HU in the area (130 to 199 HU = 1, 200 to 299 HU = 2, 300 to 399 HU =3, and ≥400 HU = 4) and scores for all lesions were summed across all slices.[1] The calcified volume score in cubic millimeters was based on isotropic interpolation using calcified voxel area and slice section thickness. Further details on volumetric reconstruction of calcified plaques and automated quantification have been previously documented.[2]

Table 2.7.1. CT Scan specifications for CAC evaluation at each ARIC site

Study Site	System	Tube Voltage	Tube Current	Gantry Speed	Exposure Time	ECG Trigger*	Slice Thickness	Reconstruction Field of View
Maryland	Siemens Somatom Sensation 64/Cardiac 64 (2009)	120 kVp	50 mA (63 mA)**	330 msec	220 msec	70 %	3.0 mm	32-35 cm
Minnesota	Siemens Somatom Sensation 64/Cardiac 64 (2008)	120 kVp	50 mA (63 mA)**	330 msec	220 msec	70 %	3.0 mm	32-35 cm
Mississippi	Siemens Somatom Definition Dual Source Cardiac 64 (2007)	120 kVp	50 mA (63 mA)**	330 msec	220 msec	70 %	3.0 mm	32-35 cm
North Carolina	GE 64-slice PET/CT Discovery MI scanner (2016)	120 kVp	320 mA (400 mA)**	350 msec	326 msec	75 %	2.5 mm	32-35 cm

***Percentage of R-R interval**

****For participants weighing more than 220 pounds**

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2.8. Ziopatch – Visits 6 and 7

Asymptomatic or subclinical atrial fibrillation (AF) was measured using the Zio® XT Patch — an innovative Food and Drug Administration (FDA)-cleared, leadless, noninvasive, water-resistant, ambulatory ECG monitoring adhesive patch that can record ECG data continuously for up to 2 weeks (iRhythm Technologies, Inc).[1-4] ECG monitoring beyond 24 hours increases the diagnostic yield of AF, by detecting subclinical AF that otherwise could not be detected.[5,6]

Diagnostic algorithm: Arrhythmia adjudication by iRhythm was performed and coded using a 2-step process. First, the ECG data were interrogated using an FDA-cleared, proprietary algorithm to identify potential arrhythmia episodes based on detection of the heart rate, irregularity, and morphology. Next, trained and certified cardiovascular technicians re-examined the detected arrhythmia episodes to confirm the diagnoses and classify the arrhythmia. A standard report was generated and uploaded to a secure website. The standard report included a cover page summarizing the main arrhythmia diagnoses and ECGs of the arrhythmias; the latter allowed verification of reported arrhythmias. Data on whether AF episodes were symptomatic or not, wear time, and analyzable time were obtained from the standard report.

iRhythm's original **AF detection algorithm** was a rule-based engine that looked at specific thresholds around measures of R-R irregularity, rate, and rate change to detect AF. The improved algorithm additionally incorporated a number of ECG features, such as current and previous R-R interval durations and both temporal and spectral P-wave characteristics. The Zio® XT Patch was designed to provide **optimal signal quality** by eliminating the wires and snap connections common to Holter/electrode connections, both of which are sources of artifact in recorded signals. Instead, the Zio® XT Patch design incorporated electrodes into the housing with permanent connections. The **current improved second-generation patch,** Zio® XT Patch, additionally incorporated flexible electrodes, a more compliant form factor, and other circuit improvements which yielded a median analyzable signal of 98% in all received devices

(iRhythm's Q4 2014 statistics). These statistics reflect any time the patch was not on the patient (Holter must be removed during showers, Zio need not), and significantly exceeded experience with Holter devices. Holters also have a form factor that reduces patient compliance, e.g., during sleep. The Zio® XT Patch platform records at a **sampling rate** of 200 Hz, a level that provides, per physician feedback, **excellent signal resolution**.[1,2] Further, a previous study has shown excellent agreement between simultaneous Zio and Holter for AF during the first 24 hours of recording; thereafter, the longer monitoring of the Zio was superior in identifying additional AF events.[3]

Quality control: Based on data from iRhythm—benchmarked against a publicly available cardiologist-annotated database from the Massachusetts Institute of Technology Beth Israel Hospital of 98 AF episodes—the sensitivity and positive predictive value for detecting AF are 100% and 85.0%, respectively. To avoid false positive findings, Dr. Elsayed Soliman and his team of physician ECG readers in the Epidemiological Cardiology Research Center (Wake Forest University) downloaded the standard report from the iRhythm website on a daily basis and verified the accuracy of reported AF.

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2.9. Spirometry – Visit 5

Spirometry was conducted in accordance with the American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines[1] using a dry rolling-seal Spirometer (Ohio SensorMed model 827, Ohio Medical Instruction Company, Cincinnati, Ohio). Each spirometer was attached to a computer running dedicated software that provided expiratory curves, calculated lung function parameters and determined the acceptability of the tests (Occupational Marketing, Inc., Houston, TX). The spirometry system has been independently tested and found to exceed ATS spirometry equipment recommendations.

All technicians were trained and certified in spirometry procedures. Technicians either participated in a central training, or, in cases of staff turn-over, were trained locally at their clinic location by a centrally-trained supervisor. All technicians were required to take an online course in spirometry and pass a written certification exam with a 70% or higher. A technician was allowed to retake the written exam one time if their initial score was lower than 70%.

Participants were asked to perform three to eight forced expiratory maneuvers in the seated position in an effort to meet the ATS acceptability and repeatability criteria. The highest value of FVC and FEV_1 from the acceptable maneuvers was used. All spirometry exams were reviewed by one investigator and each test was graded for quality. Only tests with FVC and FEV_1 grades of "C" or higher were used in our analysis. Predicted and lower limit of normal values were

obtained from the published reference equations derived from National Health and Nutrition Examination Survey (NHANES) III.[2]

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2.10. Diabetes – Visits 1 through 7

Diabetes was defined at Visits 1 through 7 using information on self-reported physician diagnosis (except at visit 5), current glucose-lowering medication use, and glucose levels. Participants were asked to bring current medication bottles to the visits and medications were recorded. The glucose-based definition of diabetes is defined as a fasting glucose ≥ 126 mg/dL, or a non-fasting glucose ≥ 200 mg/dL. Additionally, for Visits 2, 5, 6, and 7 elevated Hemoglobin A1c (HbA1c) can be incorporated into the definition of diabetes (HbA1c≥6.5%).

After Visit 4, new cases of diabetes can be identified using annual telephone calls. Annual follow-up (AFU) contacts are scheduled approximately every 12 months and are routinely completed by telephone. Beginning in 2012, the cohort was contacted semi-annually. The AFU data includes information on self-reported physician diagnosis of diabetes and current glucose-lowering medication use. In defining diabetes at Visit 5, self-reported physician diagnosis and current glucose-lowering medication use can be pulled from the AFU data, since self-reported physician diagnosis was not asked at the actual visit.

2.11. Microbiome

(*Content in development*)

2.12. Audiology – Visit 6

2.12.1. Pure-Tone Audiometry

Pure-tone audiometry is the gold-standard clinical measure of hearing and represents the peripheral encoding of sound. The audiometric procedures in ARIC were based, in-part, on the National Health and Nutrition Examination Survey (NHANES) audiometry protocol.[1] During on-site visits, pure-tone audiometry was measured in a single-walled sound isolation room (Whisper Room, Knoxville, TN) using insert earphones (Etymotic, Elk Grove, IL) on a calibrated audiometer (Interacoustics Equinox 2.0., Assens, Denmark). Audiometers underwent annual calibration and weekly biometric assessment using a bioacoustics simulator to ensure proper functioning. Trained and certified technicians performed otoscopy prior to assessment to ensure an unobstructed ear canal. Hearing thresholds were assessed in each ear separately at 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hertz (Hz) using best-practice manual Hughson-Westlake[2] presentation procedures. The threshold was defined as the lowest intensity or volume (decibel hearing level [dB HL]) at which a tone has been recognized by the participant at least 50 percent of the time following a minimum of three ascending (i.e., increasing) presentations at a level (i.e., 2 out of 3, 2 out of 4, 3 out of 5, etc). A repeat measure of 1000 Hz was included for internal reliability of the participant's responses. The two thresholds at 1000 Hz should be within 10 dB HL of one another to indicate consistent responses.

During in-home visits, pure-tone audiometry was assessed using a tablet-based (iPad, Apple, Cupertino, CA) Shoebox[3] portable audiometer (Ottowa, CA) and DD450 circumaural headphones (RadioEar, Eden Prairie, MN). The Shoebox portable audiometer is listed as a class II medical devices with the United States Food and Drug Administration and meets American National Standards Institute (ANSI) standards for a type 3 audiometer (ANSI/ASA S3.6-2018 and IEC 60645-1:2017). It has been shown to be reliable when compared with convention sound booth audiometers.[3] Ambient room noise was measured prior to and during testing to ensure compliance with ANSI standards for permissible ambient noise during audiometric testing. Shoebox devices underwent annual calibration and weekly biometric assessment using a bioacoustics simulator to ensure proper functioning and no deviation from calibration. Hearing

thresholds were assessed in each ear separately at 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hertz (Hz) using an automated algorithm that mimics best-practice threshold seeking methods and includes repeated measures to ensure internal reliability of the participant's responses. Compliance with ambient noise levels during testing is recorded on the data collection form. Thresholds that do not comply with ambient noise levels should be excluded from analysis. Please note, that if permissible noise levels in the home setting were too high, some frequency thresholds may be missing due to inability to assess without interference from background noise.

Pure-tone thresholds can be utilized in research using multiple methods. Please consult an ARIC researcher familiar with hearing loss for further information. A lower threshold represents "better" hearing. The most common method of measuring hearing loss is the pure-tone average (PTA) which represents the average of 500, 1000, 2000, and 4000 Hz in a given ear. These frequencies are considered the most important for speech-understanding. Most commonly, the better ear (i.e., lower score) is used. It can be used as a continuous measure or categorized using World Health Organization criteria (Normal ≤ 25 dB HL, Mild 25-40 dB HL, Moderate 41-60 db HL, Severe 61-80 dB HL, Profound ≥ 81 dB HL). Note that severe and profound categories are often collapsed into a "severe or greater".[4]

2.12.2. Speech-in-Noise (QuickSIN) Measurement

Speech-in-noise understanding is a higher-level hearing task that involves both auditory processes of encoding sound and cognitive processes of decoding the signal and separating the speech from noise. During on-site visits, speech-in-noise understanding was measured in a single-walled sound isolation room (Whisper Room, Knoxville, TN) using insert earphones (Etymotic, Elk Grove, IL) on a calibrated audiometer (Interacoustics Equinox 2.0., Assens, Denmark). Audiometers underwent weekly biometric assessment to ensure proper functioning and no deviation from calibration and annual calibration. Trained and certified technicians performed otoscopy prior to assessment to ensure an unobstructed ear canal.

The Quick Speech-in-Noise (QuickSIN)[5] test was used to assess speech-in-noise understanding. The QuickSIN presents sentences in the presence of multitalker babble background noise. Each

QuickSIN list consists of six sentences that are presented binaurally (i.e., simultaneously to both ears) at a fixed level of 70 dB HL while the background noise gradually increases in 5 dB HL increments with each sentence list until it is the same intensity level as the sentences (i.e., both the sentence and background noise are at 70 dB HL). Note that as background noise increases, the task becomes more difficult. Participants are asked to repeat back the sentences to the best of their ability. Each sentence is graded on a score of 0-5 based on the number of words correctly repeated by the participant. Participants were given a practice sentence list to familiarize them with the task and then completed 2 lists of 6 sentences each. The final score for each list is 0-30. Clinically, the QuickSIN is converted to a signal-to-noise ratio, which roughly represents the signal to noise level needed for the participant to understand speech in a noisy setting, by subtracting the total correct score from 25.5. Clinical cutoffs provided by the parent company are not standardized. In research, ARIC investigators recommend taking the average score of the 2 QuickSIN lists and using it on scale of 0-30 or a percent correct (0-100%) scale.

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2.13. Retinal – EyeDOC and Visit 5

2.13.1. Assessment of Retinal Vessel Diameters, Retinopathy, Focal Retinal Arteriolar Narrowing and Arterio-Venous (A/V) Nicking – Visit 5

Retinal vessel diameters were measured using a computer-assisted technique based on a standard protocol and formula.[1] For the assessment of retinal vessel diameters, retinal images of field 1 (centered at the optic nerve head) were used. Trained graders, masked to participant characteristics, measured the diameters of all arterioles and venules coursing through a specified area one-half to one disc diameter surrounding the optic disc using a computer software program shown in Figure 1a. On average, between 7 and 14 arterioles and an equal number of venules were measured per eye. Individual arteriolar and venular measurements were combined into summary indices that reflect the average retinal arteriolar and venular diameter of an eye based on the Parr-Hubbard-Knudtson formula.[2] Figure 1b shows an eye with narrow retinal arteriolar diameter and normal retinal venular diameter while Figure 1c depicts an eye with normal retinal arteriolar diameter and wide retinal venule diameter in a person with type 1 diabetes.

Figure 1a

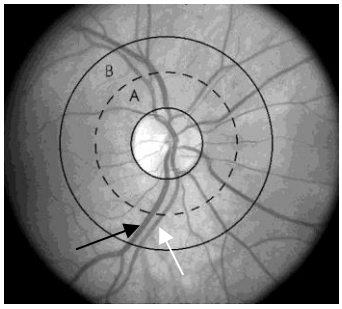


Figure 1b

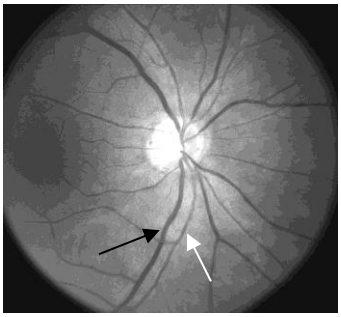
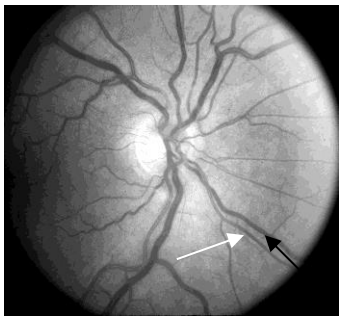


Figure 1c



1. Three scanned retinal images from eyes of persons with diabetes. a. grid over digitized image centered on right disc showing arterioles (white arrows) and venules (black arrows) coursing through a specified area one-half to one disc diameter (zone B) surrounding optic nerve head; b. right eye with narrow retinal arteriolar diameter and normal retinal venular diameter; c. right eye with normal retinal arteriolar diameters and wide retinal venular diameters.

Graders regularly participated in quality control exercises; the inter- and intra-grader variability was small (interclass and intraclass correlations > 0.90 for central retinal arteriole equivalent [CRAE] and central retinal venule equivalent [CRVE]). Measurements were done independently for each examination and each eye.

The grader assessed the absence, presence, and severity of retinopathy lesions by comparing them with standard images. The presence and severity of these lesions were then used to assign an overall disease severity for the eye, based on the ordinal ETDRS diabetic retinopathy severity scale. The following component lesions were used in assigning the severity level.

1. Retinal hemorrhages and microaneurysms (HMA)
2. Hard exudate (HE)
3. Venous loops (Loops)
4. Soft exudates or cottonwool spots (SE)
5. Intraretinal microvascular abnormalities (IRMA)
6. Venous beading (VB)

7. New vessels on the disc and elsewhere (NVD and NVE)
8. Fibrous proliferation on the disc and elsewhere (FPD and FPE)
9. Vitreous and/or preretinal hemorrhage (VH/PRH);

The presence of macular edema and clinically significant macular edema (ME and CSME) were also assessed. These lesions were graded using the Modified Airlie House protocol and definitions adapted for the ETDRS clinical trial.[3]

The presence of other retinal arteriolar characteristics, focal arteriolar narrowing, and arterio-venous (A/V) nicking, was evaluated. Focal narrowing was graded by comparing to a standard photograph from the Wisconsin Age-Related Maculopathy Grading protocol in which focal narrowing of small arterioles in the posterior pole (Field 2) involves a total length of 1/3 disc diameter.[4] Focal arteriolar narrowing was graded as absent, questionable, less than the standard, or greater than or equal to the standard for all arterioles more than 900 µm from the disc margin in two standard fields. When there were multiple but separate areas of focal arteriolar narrowing, the composite length of involvement was compared to the standard. For purposes of analyses, two categories were used—(1) absent or questionably present and (2) present. A/V nicking was graded for all arterio-venous crossings that were more than 900 µm from the disc margin in both fields. A/V nicking was graded as present if there was a decrease in the diameter of the venule on both sides of the arteriole that was crossing it.

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2.13.2. Retinal Pathology Review – EyeDOC

The assessment of retinal pathology was completed by ophthalmologists at the Wilmer Eye Institute. Optical coherence tomography (OCT) scans and retinal photographic images were reviewed to document pathology. For more prevalent eye conditions seen in this population, such as epiretinal membrane, the presence of pathology was indicated when the disease was considered clinically significant. All retinal photographic images were graded by an ophthalmologist. Images documenting retinal pathology were graded by a second ophthalmologist. The second ophthalmologist also re-graded a random sample of 10% of the retinal images with no pathology identified. The grading was based on two 45° retinal photographic images centered at the macular and the optic nerve head, respectively. Identification of retinal pathology was in accordance with the ARIC Retinal Grading Protocol[1] and the Early Treatment Diabetic Retinopathy Study Retinal Grading Protocol. [2] The grading for the OCT images is based on the system of International Nomoenclature for Optical Coherence Tomography Panel,[3] and The International Vitreomacular Traction Study Group Classification of Macular Hole.[4] The graders assessed the absence and presence of a series of retinal pathology lesions. *For detailed information please refer to the EyeDOC retinal pathology review (ERR) form QxQ instructions.*

Specific pathology lesions graded included the following:

- Active proliferative retinopathy
    - New vessels of the disc (NVD)
    - New vessels elsewhere (NVE)
    - Preretinal hemorrhages (PRH)
    - Vitreous hemorrhage (VH)
    - Tractional retinal detachment
    - Scatter / local photocoagulation treatment
- Preproliferaitve retinopathy

    - Venous beading
    - Significant intraretinal microvascular abnormalities (IRMA)
    - Significant hemorrhages and microaneurysms (HMA)
- Macular edema
    - Cystoid lesion or condition
    - Clinically significant macular edema (CSME)
    - Focal / grid photocoagulation treatment
- Age-related macular degeneration (AMD)
    - Clinically significant drusen / dry AMD
    - Choroidal neovascularization (CNV)
- Others
    - Hollenhorst plaque
    - Elevated nevus
    - Macular hole
    - Branch vein occlusion (BRVO) / central vein occlusion (CRVO)
    - Optic nerve pallor
    - Epiretinal membrane (ERM) with associated pathology
- Optic nerve cup-to-disc ratio
    - Optic nerve notching or rim thinning
    - Possible glaucoma
- Rhegmatogenous retinal detachment
- Papilledema

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2.14. Brain Magnetic Resonance Imaging (MRI) – Visits 5 through 11

Between 1993 and 1995, 1,949 participants without a contraindication from Forsyth County, NC and Jackson, MS completed two-dimensional (2D) MRI scans. These participants were invited to complete follow-up 2D MRI scans between 2004 and 2006. Both the baseline and follow-up scans were obtained utilizing 1.5 Tesla General Electric or Picker scanners. Axial 5-mm contiguous T1, T2, and proton density-weighted images were interpreted[1] using protocols based on the Cardiovascular Health Study.[2] Data from these 2D MRI scans are available for analysis. However, since 2D MRI scans are not directly comparable to the three-dimensional (3D) MRI scans obtained between Visits 5 and 11 these earlier scans have been excluded from longitudinal MRI and PET datasets.

At Visit 5 (2011-2013), participants without a contraindication from all sites were invited to complete 3D MRI scans if they were diagnosed with mild cognitive impairment (Section 2.18) or if they completed a prior 2D MRI scan. An age- and site-stratified random sample of cognitively normal individuals were also asked to complete a 3D MRI scan. Scans were performed on 3 Tesla Siemens scanners. The protocol included the following.

1. *Sagittal T1-Weighted Magnetization Prepared Rapid Acquisition Gradient-Echo (MPRAGE)* - Used for anatomic measures such as brain volume and thickness within regions of interest (ROI). Image pre-processing operations designed to correct intensity inhomogeneity and gradient non-linearity were applied to each set of MPRAGE images prior to image analysis.[3]
2. *Axial T2 Star* - Used for the assessment of microhemorrhages.
3. *Sagittal T2 Fluid-Attenuated Inversion Recovery (FLAIR)* - Used for the assessment of infarctions.

4. *Axial Diffusion Tensor Imaging (DTI)* - Used for ROI-wise diffusion measurements such as mean diffusivity (MD) and fractional anisotropy (FA).

5. *3D Pulsed Arterial Spin Labeling (PASL)* - Performed at sites with a PASL license. Used for assessing regional brain perfusion.

Abnormalities, such as infarcts and microhemorrhages, were identified by trained analysts and confirmed by a radiologist blinded to all clinical information. FLAIR images assessed white matter hyperintensities (WMH) in 2D using a semi-automated algorithm[4] and MPRAGE images assessed brain volume and thickness in 3D. The Freesurfer atlas[5,6] was used to quantify volume and thickness in each region of the brain. Volumetric measures were summed across regions into composite ROIs. Thickness measures were aggregated into composite ROIs utilizing weighted averages. ROI-wise MD and FA values were generated using a modified Johns Hopkins University "Eve" atlas[7] and the Mayo Clinic Adult Lifespan Template's Lobar atlas.[8]

Between Visits 6 and 7 (2016-2019), a subsample of participants completed a 3D MRI scan for one of several ancillary studies offered to members of the ARIC cohort. The same methodology employed at Visit 5 was utilized except that WMH was quantified using 3D technology.

From Visits 8 to 11 (2020-2024), willing participants without a contraindication completed a 3D MRI scan. The methodology employed was identical to Visits 6 and 7 except that the arterial spin labeling (ASL) sequence was eliminated at all sites except Jackson, MI and a T2 Space sequence was added. The protocol at Jackson, MI remained the same from Visits 6 to 11.

At each visit, scans were reviewed by a neuroradiologist at each site following local standard clinical care methods to screen for clinically significant abnormalities, such as hemorrhage and/or mass effect. In addition, the Mayo Aging and Dementia Imaging Research (ADIR) Lab reviewed all scans for medically significant abnormalities. All scans were evaluated by a trained image analyst for protocol compliance and scan quality. This quality control data was entered into data forms and transmitted to the coordinating center. Quality problems with any scan resulted in a request for a rescan.

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2.15. Vascular Magnetic Resonance Imaging (MRI) – Visits 5 through 7

The vascular MRI protocol was designed to estimate the prevalence of intracranial atherosclerotic disease (ICAD), determine whether it is associated with dementia or mild cognitive impairment, and characterize features of ICAD and estimate their associations with risk factors. The exam was carried out on 3T MRI Siemens scanners (Forsyth County: Skyra, 32 channel head coil; Jackson: Skyra, 20 channel head coil; Minneapolis: Trio, 12 channel head coil; and Washington County: Verio, 12 channel head coil). The MRI protocol consisted of a 3-dimensional time-of-flight MR angiogram through the Circle of Willis, centered to include the distal vertebral artery segments inferiorly and the middle cerebral artery branches superiorly (acquired resolution, 0.50 x 0.55 x 0.55 mm^3; 152 slices, 8.4cm SI coverage). This was followed by a 3-dimensional high-isotropic resolution black blood MRI (BBMRI) scan[1] oriented in a coronal plane and centered at the Circle of Willis (0.5 x 0.5 x 0.5 mm^3; 128 slices, 6.4 cm AP coverage). This vascular protocol was implemented at the end of the ARIC NCS brain MRI protocol.

MRI images were examined by trained analysts certified by successfully completing complex sample cases. Each analyst used picture archiving and communication system (PACS) software (Ultravisual; Emageon, Birmingham, AL) for the qualitative analysis of the MRA and BBMRI scans. Using the PACS software, the BBMRI and MRA images were co-registered and reconstructed in both short and long axes relative to the flow direction for each vascular territory. The number of plaques identified for each territory was recorded, with categorical stenosis recorded for the most stenotic plaque per territory.

Quantitative measurements of lumen size and stenosis from the MRA and wall/plaque size from the BBMRI were acquired using LAVA software (LAVA, Leiden University Medical Center, the Netherlands), which uses a deformable tubular model based on Non-Uniform Rational B-Splines (NURBS) surface modeling to contour each vessel segment. This technique provides

semi-automated contour detection of the arterial lumen and performs an iterative linear regression fit of the lumen area over the entire segment. Standard vessel segments were measured (e.g., proximal Circle-of-Willis branches such as M1 and basilar artery segments) over a fixed segment length, and the largest plaque identified for each vascular territory in the qualitative assessment was also measured.

Exam reliability was assessed by repeating 102 exams with evidence for plaque. Inter- and intra-observer variability was also assessed by repeat readings. A peer-review process was implemented twice per exam in which an observer re-evaluated each exam read by a different observer and disagreements were arbitrated by the Principal Investigator.

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2.16. Positron Emission Tomography (PET) – Visits 5 to 11

A subsample of participants from Forsyth County, NC, Jackson, MS, and Washington County, MD completed a florbetapir PET scan during Visit 5 (2011-2013) within one year of a 3D brain MRI scan (Section 2.14). Participants with dementia, renal dysfunction (creatinine .2 mg/dL), prolonged electrocardiogram corrected QT intervals (.450 ms), or who reported heavy alcohol use were excluded. The scanners utilized included the GE Discovery ST (Forsyth), GE Discovery 690 (Jackson), and Philips TruFlight (Washington). Weekly phantom scans were conducted to ensure quantitative accuracy and spatial uniformity.

PET images were spatially smoothed to arrive at a resolution of (***information not yet provided by PET reading center***). Preprocessed mean PET images were coregistered with structural MRI images and normalized to the MUlti-atlas region Segmentation utilizing Ensembles of registration algorithms and parameters (MUSE) space.[1] A total of 146 regions of interest (ROIs) were manually drawn. Standard uptake value ratio (SUVR) images relative to the cerebellum were calculated for each ROI.

From Visits 6 to 7 (2016-2019), a subsample of participants without a contraindication completed a MRI scan and PET scan for one of several ancillary studies offered to members of the ARIC cohort. From Visits 8 to 11 (2020-2024), willing participants without a contraindication completed a MRI scan (Section 2.14) and PET scan. Starting with Visit 9, PET scans were also conducted at Minneapolis, MN using a (***information not yet provided by PET reading center***).

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2.17. Neurocognitive Factor Scores – Visit 2 and Visits 4 to 9

Beginning in 1990, a series of neurocognitive tests were administered to the ARIC cohort. During Visit 2 (1990-1992) and Visit 4 (1996-1998) three neurocognitive tests were administered.

Delayed Word Recall (DWR) – A 10-word test of delayed episodic verbal memory[1] in which participants were presented with 10 common nouns that they were asked to use in a sentence. After a five-minute delay, participants were given 60 seconds to recall the words. The score ranges from 0 to 10 and represents the number of words correctly recalled.

Digit Symbol Substitution (DSS) – A test of executive functioning[2] in which participants were asked to translate numbers to symbols using a key. The score is a count of numbers correctly translated to symbols within 90-seconds. The score ranges from 0 to 93.

Word Fluency Test (WFT) – A measure of phonemic fluency[3] in which participants were given 60 seconds to state as many words as possible that begin with the letters F, A, or S. 60 seconds were given for each letter. The score ranges from 0 to 25 per letter and denotes the total number of acceptable words generated.

Between 2004 and 2006, five additional tests were added to the neurocognitive battery to provide a more thorough evaluation of a subsample of participants who took part in a brain MRI sub-study.

Incidental Learning (ILR) – A test for delayed recall[4] of elements from the DSS. Immediately following completion of the DSS, participants were asked to remember digit-symbol pairs. The score ranges from 0 to 9 and represents the number of symbol-pairs correctly recalled.

Animal Naming Score (ANS) – A test of semantic fluency[3] that involved naming as many animals as possible within 60 seconds. Names of extinct, imaginary, and magical animals were permitted. Credit was also given for breeds, different names for males, females, or infants of the same species (e.g. bull, cow, calf) as well as superordinate and subordinate titles (e.g. dog and terrier). The score is the total number of animals stated.

Logical Memory Test (LMT) – A test of recall[2] from two short stories read aloud to the participant. Initially, participants were asked to recall the details immediately following the reading of each story. Participants were then informed there will be additional questions about these stories at a subsequent point in time. After a delay of approximately 20 minutes, the participants were again asked to recall the details of each story. The score reflects the number of details correctly recalled with a maximum score of 25 per story.

Trail Making Test A (TMTA) – A test of processing speed[5] in which participants were presented with numbers ranging from 1 to 25. Each number was placed in a separate circle and distributed haphazardly across a page. Participants were asked to draw lines connecting the numbers sequentially. The score denotes the number of seconds the participant takes to complete the test. Participants who took longer than four minutes or who made more than 5 errors were given the maximum score of 240 seconds.

Trail Making Test B (TMTB) – A variation of the previous test[5] in which participants were presented with numbers ranging from 1 to 13 and letters ranging from A to L. Each of the numbers and letters was placed in a separate circle and distributed haphazardly across a page. Participants were asked to draw lines connecting the numbers and letters in a sequential, alternating fashion. The score represents the number of seconds required for

the participant to complete the test and is calculated using the same rules applied to the TMTA.

At Visit 5 (2011-2013) and in subsequent visits the neurocognitive battery was expanded to include the Digit Span Backwards and the Boston Naming Test.

Digit Span Backwards (DSB) – A test of attention[2] in which participants were read a string of numbers ranging from 2 to 7 digits. For each number string, the participant was asked to repeat the numbers backwards. Two trials were administered for each digit span length. The score ranges from 0 to 12 and catalogs the number of trials in which the participant correctly stated the reverse of the number string.

Boston Naming Test (BNT) – A 30-item test[6] that entailed naming common objects from a series of 30 line drawings. Participants were given 20 seconds to name the object in each drawing. The score ranges from 0 to 30 and indicates the number of objects correctly identified.

Due to the outbreak of COVID-19 during Visit 8 (2020), in-person neurocognitive testing was halted in March of 2020 after only 449 participants were assessed. Four months later, a modified six-test battery was administered over the phone. The modified neurocognitive battery included the DSB, the ANS, and a version of the WFT limited to the letters F and A. Three additional tests were incorporated into the battery for the first time.

Consortium to Establish a Registry for Alzheimer's Disease Word List (CERAD) – A 10-word test of immediate and delayed episodic verbal memory[7] comparable to the DWR. The test consisted of four trials. During the first three trials, participants were read ten common nouns and asked to repeat as many words as they could remember. The order in which the words were stated to the participant varied with each trial. The fourth trial was administered several minutes later. The score for each trial ranges from 0 to 10 and represents the number of words correctly remembered.

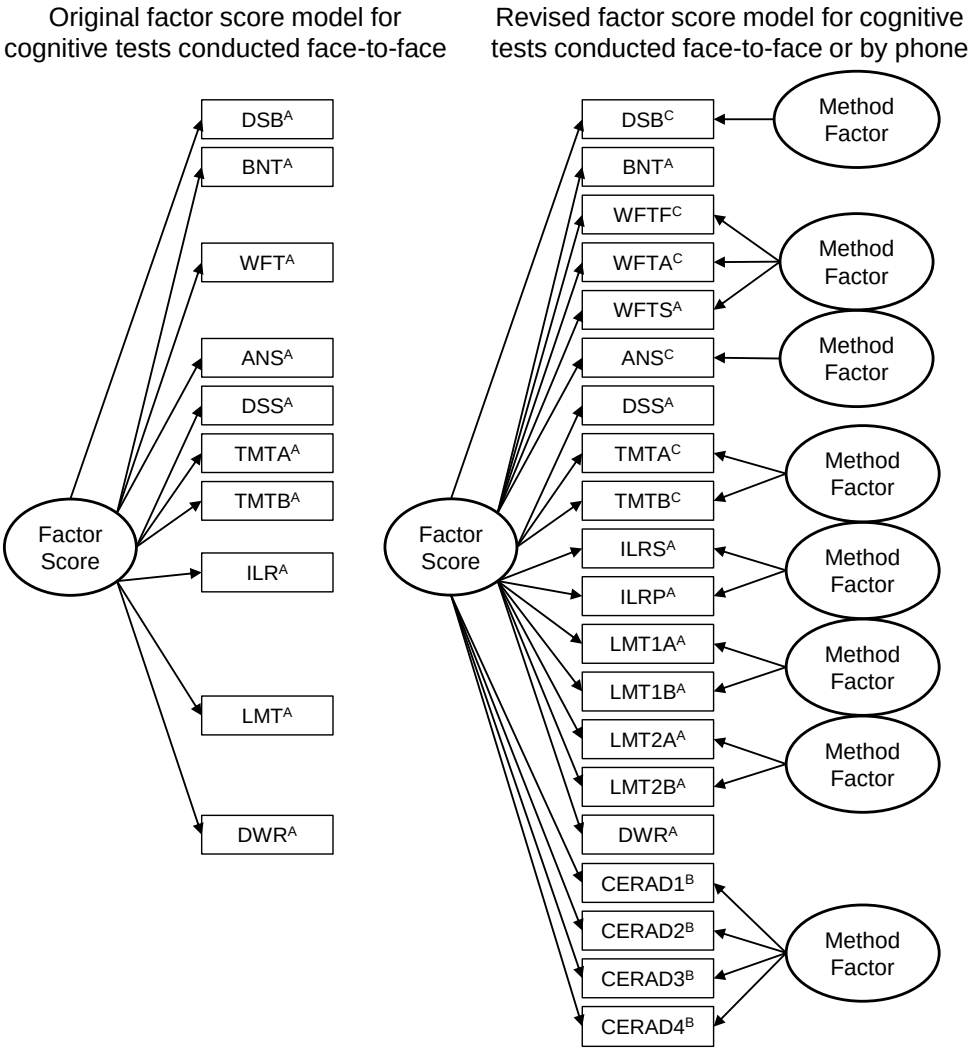
Oral Trail Making Test A (TMTA) – A variation of TMTA[5] in which participants were asked to recite the numbers 1 through 25 in sequence. The score denotes the number of seconds it

takes a participant to complete the test. Participants who took longer than four minutes or who made more than 5 errors were given the maximum score of 240 seconds.

Oral Trail Making Test B (TMTB) – A variation of the TMTB[5] in which participants were asked to verbally alternate between the numbers 1 through 13 and the letters A through L. The test is scored using the same rules applied to the oral TMTA.

To compare neurocognitive function across visits, Gross and colleagues[8] developed a model (Figure 2.17.1) for calculating factor scores ([V2_V#_CNFA] GLOBALFS1) for global cognition (Appendix A.1) as well as three previously identified cognitive domains[9-11] designated executive function, language, and memory ([V2_V#_CNFA] EXECFUNCFS1, LANGUAGEFS1, and MEMORYFS1). Each neurocognitive test administered in-person was discretized into ten or fewer categories.[12] When a participant did not possess the cognitive ability to complete a specific neurocognitive test, they were assigned a value that placed them in the category associated with the lowest test scores.

Figure 2.17.1. Confirmatory factor analysis models for global cognition



Abbreviations: ANS, Animal Naming Score; BNT, Boston Naming Test; CERAD1, Consortium to Establish a Registry for Alzheimer's Disease Word List (Immediate Recall Trial 1); CERAD2, Consortium to Establish a Registry for Alzheimer's Disease Word List (Immediate Recall Trial 2); CERAD3, Consortium to Establish a Registry for Alzheimer's Disease Word List (Immediate Recall Trial 3); CERAD4, Consortium to Establish a Registry for Alzheimer's Disease Word List (Delayed Recall); DSB, Digit Span Backwards; DSS, Digit Symbol Substitution; DWR, Delayed Word Recall; ILR, Incidental Learning (sum of ILRS and ILRP); ILRS, Incidental Learning (Symbols Recalled); ILRP, Incidental Learning (Digit-Symbol Pairs Recalled); LMT, Logical Memory Test (sum of LMT1A, LMT1B, LMT2A, and LMT2B; LMT1A, Logical Memory Test (Story A, Immediate Recall); LMT1B, Logical Memory Test (Story B, Immediate Recall); LMT2A, Logical Memory Test (Story A, Delayed Recall); LMT2B, Logical Memory Test (Story B, Delayed Recall); TMTA, Trail Making Test A; TMTB, Trail Making Test B; WFT, Word Fluency Test (sum of Letters A, F, and S); WFTA, Word Fluency Test (Letter A); WFTF, Word Fluency Test (Letter F); WFTS, Word Fluency Test (Letter S)
[A]Denotes test administered face-to-face. [B]Denotes test administered over the phone. [C]Denotes test administered face-to-face and over the phone. A method factor linked to a test marked [C] denotes a correlation between the two test modalities except for the Trail Making Tests which were found to have substantially different scores when administered face-to-face versus over the phone.

A confirmatory factor analysis (CFA) model with categorical indicators was performed to identify common covariation among the neurocognitive tests administered in-person. This analytic approach had the advantage of reducing measurement error and accommodating test

scores with non-normal distributions[13] by placing thresholds between categories along a normally distributed latent factor. The model also gave greater weight to neurocognitive tests that were highly correlated with other neurocognitive tests.

In 2020, a second model (Figure 2.17.1) was developed (Appendices A.2, A.3, B.1, and B.2.) that harmonized in-person and phone-based neurocognitive tests through co-calibration.[14-16] Co-calibration can be performed when one of two assumptions are met. The first assumption is that one or more tests are psychometrically equivalent regardless of modality. These tests are used as linking items to produce factor scores that are comparable even if the battery of tests varies over time. The second, alternative assumption is that the underlying construct of global cognition has not changed in a representative subsample of individuals who complete both in-person and phone-based tests. Test and modality specific measurement error is estimated in this subsample and the resulting measurement model is applied to the remaining sample.

Co-calibration was employed to compute four additional versions of global cognition based on either continuous ([V2_V#_CNFA] GLOBALFS2 and GLOBALFS3) or categorical ([V2_V#_CNFA] GLOBALFS4 and GLOBALFS5) indicators. Factor scores were generated from each type of indicator so that analysts can evaluate the implications of preventing data coarsening by using continuous indicators versus accommodating skewed distributions by using categorical indicators. Two versions of the factor score (GLOBALFS2 and GLOBALFS4) were based on models that assumed the ANS, DSB, and WFT were invariant to mode of administration.[17] Building on this assumption, the CERAD, OTMTA, and OTMTB were co-calibrated[14-16] to the global cognition factor score derived from in-person cognitive tests. The remaining versions (GLOBALFS3 and GLOBALFS5) utilized a subsample of participants (N=331) who completed in-person neurocognitive tests between January and March of 2020 and phone-based neurocognitive tests between July and December of 2020 to construct a model that assumed global cognition did not change in the relatively short timeframe. Two additional versions ([V2_V#_CNFA] GLOBALFS6 and GLOBALFS7, Appendices A.4 and B.3.) were computed from phone-based neurocognitive tests.

Table 2.17.1. Factor score versions

	Modality	Indicators	Co-Calibration Assumption
Version 1	In-Person Only	Categorical	-
Version 2	In-Person & Phone	Continuous	Invariant Tests
Version 3	In-Person & Phone	Continuous	Invariant Subsample Cognition
Version 4	In-Person & Phone	Categorical	Invariant Tests
Version 5	In-Person & Phone	Categorical	Invariant Subsample Cognition
Version 6	Phone Only	Continuous	-
Version 7	Phone Only	Categorical	-

To reduce measurement error, separate sub-scores from neurocognitive tests were incorporated into the models when possible. For example, separate sub-scores for the letters F, A, and S from the WFT were utilized instead of a sum score. A method factor (Figure 2.17.1) was specified to account for common variation among sub-scores. In the models with continuous indicators, test scores from the BNT, TMTA, and OTMTA that were below the 3rd percentile were winsorized. Based on a visual inspection of the distribution, scores from the BNT, TMTA, TMTB, OTMTA, and OTMTB were treated as left-censored while other cognitive tests were assumed to have a normal distribution.

The same methodology that produced seven versions of the global cognition factor score was employed to compute factor scores for the cognitive domains of language, executive function, and memory. However, Bland-Altman plots revealed systemic bias in the co-calibrated factor scores for executive function and memory. Consequently, these factor scores are not included in distributed datasets (V2_V#_CNFA).

The factor scores for each participant at each visit were generated using a measure harmonization and item banking approach.[18,19] This process involved estimating factor loadings, latent means, and thresholds for each neurocognitive test utilizing the data from Visit 5 for tests administered in-person or Visit 8 for tests only administered over the phone. The mean of the factor scores were set to 0 and the standard deviations were set to 1. Fixed parameter estimates were then integrated into separate models that estimated the factor mean and standard deviation at each visit. This ensured that changes over time represented changes in the underlying factor rather than changes in the scaling or meaning of the constructs. The assumption of longitudinal measurement invariance inherent to this approach was supported

by prior studies that utilized similar neurocognitive tests.[9,10] A final model with fixed parameters and data from all visits was used to compute factor scores for each participant at every visit in which one or more neurocognitive tests were completed. Factor scores computed from in-person and phone-based neurocognitive tests were standardized to Visit 5. Factor scores computed from only phone-based neurocognitive tests were standardized to Visit 8. The resulting factor scores represent the mean of the posterior probability distribution of cognitive function given observed performance on neurocognitive tests.[14]

Factor scores were estimated in Mplus.[20] Missingness was handled via a full-information maximum likelihood estimator with robust standard errors, which assumed that missingness within specific neurocognitive tests was missing at random conditional on the other neurocognitive tests in the model. This assumption was deemed reasonable since structural missingness in individual tests at earlier visits was based on study design and not on participants' cognitive ability.[8] A Markov chain Monte Carlo algorithm was used for numerical integration when necessary (Appendices A and B).

The correlation between factor scores across visits was fixed at 0. This ensured that the factor score for a given participant was determined solely by their performance on the neurocognitive tests administered at a specific visit and not by their performance at prior or subsequent visits. Global cognition factor scores were computed for Visit 2, Visits 4 through 9, the brain MRI sub-study, and the Aging and Cognitive Health Evaluation in Elders (ACHIEVE) randomized controlled trial. Factor scores for the domains of executive function, language, and memory were calculated for Visits 5 through 9 and the ACHIEVE RCT.

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2.18. Dementia or Mild Cognitive Impairment – Visits 5 through 9

For participants who attended Visit 5 or subsequent visits, a level 1 diagnosis (normal, mild cognitive impairment (MCI), or dementia) was determined based on an in-person cognitive evaluation consisting of a 10-test neurocognitive battery[1], the Mini-Mental State Exam (MMSE),

the Clinical Dementia Rating (CDR) scale, the Functional Activities Questionnaire (FAQ), and calculations of annualized cognitive decline. An algorithmic diagnosis based on this information was assigned, but algorithmic diagnoses were overruled by expert committee review when necessary. The algorithm developed was consistent with the formulation of dementia defined by the National Institute on Aging-Alzheimer's Association (NIA-AA) workgroups [2, 3] and Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5).[4]

Phone-based cognitive evaluations were initiated during Visit 8 (2020) and comprised a 6-test neurocognitive battery (Section 2.17), a shortened MMSE limited to the orientation subscale, the CDR, the FAQ, and calculations of annualized cognitive decline derived from co-calibrated factor scores (Section 2.17). An algorithmic diagnosis was assigned, but a lack of precision in the algorithm and conflicting classifications rendered by members of the review committee prompted a change from a level 1 diagnosis with three classifications (normal, MCI, and dementia) to the creation of a level 1 diagnosis with only two classifications (non-dementia or dementia) when only a phone-based cognitive evaluation was performed during a visit.

Level 1 incident dementia ascertained from an in-person cognitive evaluation was treated as an absorbing state. Level 1 incident dementia ascertained from a phone-based cognitive evaluation was also treated as an absorbing state unless a subsequent in-person evaluation rendered a diagnosis of MCI or normal. In that situation, the prior diagnosis from the phone-based evaluation was disregarded when defining level 1 incident dementia. If a participant had both an in-person evaluation and a phone-based evaluation during the same visit, then two diagnoses were generated. The first diagnosis was rendered using data from only the in-person evaluation and was defined as occurring on the date of the in-person assessment. The second diagnosis was rendered using data from the in-person and phone-based evaluations and was defined as occurring on the date of the later assessment.

The CDR, FAQ, education-adjusted score from the Telephone Interview for Cognitive Status (TICS), Six-Item Screener (SIS), and Eight-item Interview to Differentiate Aging and Dementia (AD8) were used to define level 2 incident dementia. Prior to 2015, only the CDR, FAQ, and education-adjusted TICS were used. Starting in June 2015, the SIS was assessed annually, and the AD8 was administrated to participants with hearing impairment or with impaired cognitive

function indicated by poor SIS scores. AD8 was also administered to a deceased participant's proxy even if no previous impairment was indicated. For participants who had neither an in-person evaluation nor available phone interview information, level 3 incident dementia was determined based solely on ICD9/10 codes (Table 2.18.1) from hospital discharge records or death certificates[5,6], each of which has been available since the start of cohort follow up.

Table 2.18.1. ICD9/10 codes for dementia diagnosis

Code Sources	Code [a]
ICD-9-CM	Starting with or equal to 290 (including: 290.0, 290.1x, 290.2x, 290.3, 290.4x, 290.8, 290.9); 294 (including: 294.0, 294.1x, 294.2x, 294.9); 331 (including: 331.0, 331.1x, 331.2, 331.7, 331.8x, 331.9; but excluding 331.83 – mild cognitive impairment)
ICD-10-CM	Starting with or equal to F01 (including: F01.5x); F02 (including: F02.8x); F03 (including: F03.9x); F04; F06.8; G30 (including: G30.1, G30.8, G30.9); G31 (including: G31.0x, G31.1, G31.8x, G31.9; but excluding G31.84 – mild cognitive impairment); G94 R41 (including: R41.8x, R41.9)

a. Code with a suffix "x" can have one subsequent digit from 0 to 9 in the place of "x" when applicable.

Level 1 represents the highest degree of confidence in a diagnosis but has the most missing data. Level 3 represents the lowest degree of confidence but has the least missing data because it is defined from all available sources of information (Table 2.18.2).

Table 2.18.2. Incident dementia versions

	Source
DEMDXL1CENS **COXDATE_DEMDXL1**	1. Reviewer diagnosis based on neuropsychological tests 2. Algorithmic diagnosis based on neuropsychological tests
DEMDXL2CENS **COXDATE_DEMDXL2**	1. Reviewer diagnosis based on neuropsychological tests 2. Algorithmic diagnosis based on neuropsychological tests 3. Results from Education-adjusted Telephone Interview for Cognitive Status 4. Results from Clinical Dementia Rating and Functional Activities Questionnaire 5. Results from Eight Item Dementia Screening Interview 6. Results from two Six Item Screeners 7. Results from one Six Item Screener if participant lost to follow-up or deceased
DEMDXL3CENS **COXDATE_DEMDXL3**	1. Reviewer diagnosis based on neuropsychological tests 2. Algorithmic diagnosis based on neuropsychological tests 3. Results from Education-adjusted Telephone Interview for Cognitive Status 4. Results from Clinical Dementia Rating and Functional Activities Questionnaire 5. Results from Eight Item Dementia Screening Interview 6. Results from two Six Item Screeners 7. Results from one Six Item Screener if participant lost to follow-up or deceased 8. Hospitalization discharge codes 9. Death certificate codes
DEMDXPHONECENS **COXDATE_DEMDXPHONE**	1. Results from Education-adjusted Telephone Interview for Cognitive Status 2. Results from Clinical Dementia Rating and Functional Activities Questionnaire 3. Results from Eight Item Dementia Screening Interview 4. Results from two Six Item Screeners 5. Results from one Six Item Screener if participant lost to follow-up or deceased
DEMDXSURVCENS **COXDATE_DEMDXSURV**	1. Hospitalization discharge codes 2. Death certificate codes

When multiple sources of information exist for a given participant, the order of priority utilized to diagnosis incident dementia is (1) reviewer diagnosis based on an in-person cognitive evaluation, (2) algorithmic diagnosis based on an in-person cognitive evaluation, (3) reviewer diagnosis based on a phone-based cognitive evaluation, (4) algorithmic diagnosis based on a phone-based cognitive evaluation, (5) education-adjusted TICS, (6) the CDR and FAQ from an informant interview, (7) AD8 result, (8) two SIS results, (9) one SIS result if the participant is lost to follow up or deceased, (10) hospitalization discharge codes, and (11) death certificate codes. Once dementia has been diagnosed, the order of priority for determining the date of incident dementia is (1) date of in-person or phone-based cognitive evaluation or date of hospitalization discharge record if the latter is earlier, (2) date of the earliest informant interview, education-adjusted TICS, AD8, or SIS that detected dementia, and (3) date of death. When examining time to incident dementia utilizing censored variables ([STATUS##] DEMDXL1CENS_##,

DEMDXL2CENS_##, DEMDXL3CENS_##, DEMDXPHONECENS_##, and DEMDXSURVCENS_##) 180 days is subtracted from the hospitalization discharge date or date of death if dementia was ascertained from a hospitalization record, death certificate, or informant interview that occurred after the date of death.

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(4) American Psychiatric Association. *Diagnostic and statistical manual of mental disorders (DSM-5®)*: American Psychiatric Pub; 2013.

(5) Alonso A, Mosley TH Jr, Gottesman RF, Catellier D, Sharrett AR, Coresh J. Risk of dementia hospitalisation associated with cardiovascular risk factors in midlife and older age: the Atherosclerosis Risk in Communities (ARIC) Study. *Journal of Neurology, Neurosurgery, and Psychiatry*. 2009;80(11):1194-1201.

(6) Schneider AL, Gottesman RF, Mosley T, Alonso A, Knopman DS, Coresh J, Sharrett AR, Selvin E. Cognition and incident dementia hospitalization: results from the Atherosclerosis Risk in Communities Study. *Neuroepidemiology*. 2013;40(2):117-124.

3. STATISTICAL ANALYSES

This section provides suggestions to analysts. These suggestions are designed to support the development of new ARIC manuscripts while also promoting methodological consistency with prior publications. The following subsections detail methodology used when examining specific outcomes.

3.1. Cognitive Decline Analyses

Two types of measures have been made available for examining cognitive decline. The first type consists of z-scores of the Delayed Word Recall (DWR), the Digit Symbol Substitution (DSS), and the Word Fluency Test (WFT). Each test was administered in-person starting at Visit 2 (1990-1992). The tests were standardized to Visit 2 by calculating the mean ($mean_{V2}$) and standard deviation (sd_{V2}) at Visit 2, subtracting $mean_{V2}$ from all values, and dividing all values by sd_{V2}. A 3-test combined z-score was calculated for participants with three non-missing scores by averaging the individual z-scores. The second type of measure is derived factor scores for global cognition and the domains of executive function, language, and memory (Section 2.17). Factor scores have been created at all visits in which at least one cognitive test was administered either in-person or over the phone.

In most situations, analysts modeling cognitive decline use the derived factor scores. The rationale behind this decision is twofold. The first issue that leads most analysts to choose the derived factor scores over the 3-test combined z-score is that factor scores give greater weight to neurocognitive tests that are highly correlated with other neurocognitive tests whereas z-scores assume that each neurocognitive test should be given equal weight. The second issue that analysts must consider is that factor scores integrate information from all available cognitive tests whereas the 3-test combined z-score is limited to in-person assessments in which the DWR, DSS, and WFT were all completed.

Different versions (Section 2.17) of the factor scores have been created for different analyses. In most situations, analysts are encouraged to use Version 5 of the factor score for

global cognition ([V2_V#_CNFA] GLOBALFS5) and Version 1 of the factor score for the domains of executive function, language, and memory ([V2_V#_CNFA] EXECFUNCFS1, LANGUAGEFS1, and MEMORYFS1). However, some analyses may require the use of a different version. Recommendations are depicted below (Table 3.1.1).

Table 3.1.1. Suggested use of factor scores

	Modality	Indicators	Co-Calibration Assumption	Recommended Use
Version 1	In-Person Only	Categorical	-	Original factor score developed by Gross and colleagues.[1] **Recommended for analyses of executive function, language, and memory.** May also be used when comparing estimates of global cognition to results from prior publications that only analyzed in-person assessments.
Version 2	In-Person & Phone	Continuous	Invariant Tests	May be used in sensitivity analyses that compare the recommended version to a version that mitigated data coarsening by using continuous indicators and was co-calibrated based on the assumption that the ANS, DSB, and WFT were invariant to mode of administration (Section 2.18).
Version 3	In-Person & Phone	Continuous	Invariant Subsample Cognition	May be used in sensitivity analyses that compare the recommended version to a version that mitigated data coarsening by using continuous indicators.
Version 4	In-Person & Phone	Categorical	Invariant Tests	May be used in sensitivity analyses that compare the recommended version to a version that was co-calibrated based on the assumption that the ANS, DSB, and WFT were invariant to mode of administration (Section 2.18).
Version 5	In-Person & Phone	Categorical	Invariant Subsample Cognition	**Recommended for analyses of global cognition.**
Version 6	Phone Only	Continuous	-	May be used in sensitivity analyses when only phone-based assessments are of interest to compare the recommended version to a version that mitigated data coarsening by using continuous indicators.
Version 7	Phone Only	Categorical	-	**Recommended for analyses in which only phone-based assessments are of interest.**

The choice of which measure of cognitive decline to utilize ultimately depends on the specifics of the analysis being performed. Analysts who are uncertain about which measure to use are

encouraged to select [V2_V#_CNFA] GLOBALFS5 from the most recent V2_V#_CNFA dataset. This includes analyses that do not extend to the latest visit in the most recent dataset. For example, if an analyst is conducting a cross-sectional investigation at Visit 6 then they should employ the Visit 6 values within the latest V2_V#_CNFA dataset rather than the V2_V**6**_CNFA dataset. Utilizing the latest V2_V#_CNFA dataset will ensure that values from the most current and accurate iteration of the factor score model are being analyzed.

3.1.1. Exploratory Analyses

Before assessing cognitive decline within the ARIC cohort, analysts typically remove participants who are not white or black and participants in Maryland or Minnesota who are not white due to the small number within each subgroup. A combined race-center variable can then be created comprised of five categories: (1) White, Forsyth County, North Carolina, (2) Black, Forsyth County, North Carolina, (3) White, Minneapolis, Minnesota, (4) White, Washington County, Maryland, and (5) Black, Jackson, Mississippi. Following this, most analysts exclude participants whose level of education is unknown and participants for whom the primary exposure is missing.

Analysts must also decide whether to include or exclude supplemental cognitive scores from ARIC ancillary studies. Longitudinal analyses that focus on the time between assessments, such as generalized estimating equations (GEEs) and mixed effects models, may benefit by the inclusion of extra observations. In contrast, statistical techniques that focus on the observations associated with a specific visit, such as a latent growth curve models, may find it preferable to remove supplemental cognitive scores.

After preparing the dataset, analysts should examine visit-specific univariate statistics and generate spaghetti plots of cognitive decline. These procedures should be replicated for each pertinent subpopulation and by the various levels of the exposure being examined, such as smokers and nonsmokers.

3.1.2. Longitudinal Models

To model the trajectory of cognitive decline in relation to an exposure, analysts are encouraged to use GEEs or mixed effects models with robust standard errors. GEEs generate parameter estimates with population-averaged interpretations. Mixed effects models provide both population-averaged and subject-specific interpretations when the outcome is continuous and normally distributed. Parameter estimates from mixed effect models with a discrete or non-normally distributed outcome typically have subject-specific interpretations.

GEE models that analyze cognitive decline may utilize an unstructured correlation matrix for the within-person observations and robust variance estimates. Depending on the nature of the analysis, an alternative correlation structure may be preferable. Please note that in most cases an independent correlation matrix is not encouraged for GEE models as this approach has been known to underestimate cognitive decline in the latter years of study.

Mixed effects models may include a random intercept and random slopes. An unstructured covariance matrix is frequently used for the random effects. If the model fails to converge or exhibits other problematic properties, it may be necessary to choose an alternative covariance matrix or remove random effects for the time splines described below.

In most cases, both GEE and mixed effects models will examine time on the study in years while adjusting for the age of each participant at the baseline assessment. For instance, an analyst might specify Visit 2 as the baseline assessment, calculate the time in years between Visit 2 and each subsequent visit, and calculate the mean-centered age at Visit 2. A common sequence of steps is depicted below.

1. Compute the mean-centered age at the baseline assessment (age) and create a quadratic term for mean-centered age (age^2).
2. Allow for non-linearity by adding a linear spline (Slope 1) with a knot at six years (Slope 2) and twenty-one years (Slope 3). Six years from Visit 2 is the approximate time of Visit 4 while twenty-one years is the approximate time of Visit 5. Additional knots may also be required if data from subsequent visits are included in the statistical model.

3. Include age and age^2 in the statistical model as well as the interactions between these covariates with Slope 1, Slope 2, etc.
4. If age^2 or the interactions from the previous step are not statistically significant, consider removing them from the model.

Additional examples for specific analyses are depicted below (Table 3.1.2).

Table 3.1.2. Suggested approach for longitudinal analyses

	Cognitive Decline Timeframe		
	Visit 2 to Visit 8	**Visit 2 to Visit 5**	**Visit 5 to Visit 8**
Outcome	Global cognition factor score (Version 5) or 3-test z-score		Global cognition factor score (Version 5) or language, memory, and executive function factor scores (Version 1)
Time term(s)	Time splines with knots at 6 and 21 years	Time splines with a knot at 6 years	Splines should be tested but are usually not needed
Mixed-effects model	A random intercept and a random slope(s) with an unstructured covariance matrix for the random effects		
GEE model	Unstructured correlation matrix for the within-person observations and robust variance estimates		
Covariates	Include covariates and their interaction with time and time splines		

An alternative approach that is occasionally proposed by analysts is to calculate cognitive decline by computing the difference between visits and dividing by the number of years between visits. Annualized cognitive decline is then used as the outcome in a linear regression model. Please note that this approach is ***not*** recommended because the differential follow-up durations will cause differential inflation in the variance of annualized cognitive decline, which is likely to result in increased standard errors as well as biased parameter estimates.

3.1.3. Addressing Informative Attrition

Within the ARIC cohort, cognitive decline is associated with attrition. Consequently, all longitudinal analyses should involve a careful consideration of how to address informative attrition. In ARIC, a common approach is to use multiple imputation by chained equations (MICE).[2-4] Analysts familiar with alternative approaches, such as pattern mixture models,[5-7]

selection models,[6,8] shared parameter models,[6,9] or inverse probability weighting[10-12] may employ these techniques as a sensitivity analysis or as the primary analysis.

Before imputing values utilizing MICE, the dataset should be restricted to the sample that will be analyzed. Key variables that are typically incorporated into the imputation model include the following.

1. The exposure. If multiple iterations of the exposure (e.g. standardized, dichotomized, quartiles, etc.) will be examined then analysts are encouraged to include the original version of the variable in the imputation model and then apply the necessary transformations post-imputation.
2. The primary outcome at both concurrent and prior assessments.
3. A bifurcated version of the Clinical Dementia Rating scale ([CDS]CDS7) completed during Visit 5 that can be derived using the following formulas.
    - CDSA = CDS7+1
    - CDSB = ((CDSA)>1)*(CDS7)
4. A winsorized version of the Mini-Mental State Exam ([DERIVE##]PRORATEDMMS##) in which all values less than 14 are set to a minimum value of 14.
5. The Six-Item Screener ([V2_V#_CNFA]SIS) obtained during annual follow-up assessments. To facilitate longitudinal analyses, the SIS closest to each neurocognitive assessment is provided in the dataset with neurocognitive factor scores and 3-test combined z-scores.
6. Variables indicating the level 3 dementia status of the participants during all visits in which neurocognitive assessment values are imputed. Visit-specific variables should be generated using the latest version of [STATUS##]DEMDXL3CENS_## and [STATUS##]COXDATE_DEMDXL3_## since updated dementia records are frequently obtained after the datasets from a visit have been finalized.
7. Time-invariant covariates measured at the baseline assessment such as sex ([DERIVE##]GENDER##), race-center ([DERIVE##]RACEGRP## and [DERIVE##]CENTER),

education ([DERIVE1#]ELEVEL02), mean-centered age ([DERIVE##]V#AGE##), and the presence of the apolipoprotein ε4 genotype ([APOE_NEW_P]APOEA_112) which is typically defined as dichotomous (0 alleles versus 1 or more alleles) but may alternatively be defined as trichotomous (0 alleles, 1 allele, or 2 alleles).

8. Time-varying covariates present in DERIVE## such as diabetes, hypertension, and cigarette use. Please note that continuous covariates are typically mean-centered.
9. A count of key medical events that occurred between cognitive assessments such as the number of hospitalizations, strokes, incidents associated with coronary heart disease, or instances in which the participant self-reported poor health. These events are documented in the surveillance and annual follow-up datasets.
10. A dichotomous indicator reflecting whether the participant reported key risk factors between cognitive assessments such as diabetes or hypertension. These factors are also documented in the surveillance and annual follow-up datasets.

Before performing the imputation, analysts must consider whether to include or remove deceased participants. Retaining only participants who were alive at all visits is likely to underestimate the rate of cognitive decline. Retaining participants who are deceased will produce inferences for an immortal cohort that does not exist but may provide relevant insights into etiology. A common compromise in ARIC is to impute pre-death cognitive scores by removing participants who died prior to the start of a visit. For instance, when imputing values for a neurocognitive measure that would have been obtained between 2016 and 2017 when Visit 6 was conducted, participants who died before 2016 are removed while participants who died after 2016 are retained.

When analyzing pre-death cognitive scores utilizing mixed effects models, which implicitly calculate cognitive decline beyond the date of death[13], the resulting parameter estimates can be interpreted as the annualized rate of cognitive decline had participants remained alive and continued to complete neurocognitive measures at subsequent visits. When analyzing pre-death cognitive scores using generalized estimating equations with an independent correlation matrix, cognitive decline beyond the date of death is not calculated[13] but the parameter

estimates may be unreasonably attenuated. Faced with these tradeoffs, most analysts opt to use mixed models and carefully describe the estimands generated. Ultimately, the decision will depend on the hypotheses proposed and the focus of the scientific investigation.

A related issue that analysts must contemplate is whether to include a dichotomous indicator that denotes if a participant is living or dead during each visit. In most situations, analysts are encouraged to generate imputed values based on concurrent and past variables, but not future variables, to preserve the causal sequence of time. One notable exception is death. If an analyst chooses to include this variable in their imputation model, then visit-specific variables should be generated using the latest version of [STATUS##]DATEOFDEATH as updated death records are frequently obtained after the datasets from a visit have been finalized.

Another critical consideration is how to determine the time at which each participant who is missing a neurocognitive measure would have been assessed. If the participant completed the SIS during the timeframe in which a visit was conducted (e.g. 2016 to 2017 for Visit 6), then the date of the SIS can be designated as the date of the neurocognitive assessment. If a participant was diagnosed with level 3 dementia during the visit, then the date of incident dementia can serve as the date of the neurocognitive assessment. If a participant died during the visit, then the date of the neurocognitive assessment is often calculated as occurring 180 days before the date of death but can be adapted based on the nature of the analysis. If none of the typical sources are available, then the median of all completed neurocognitive measures with a date can be specified as the date of assessment.

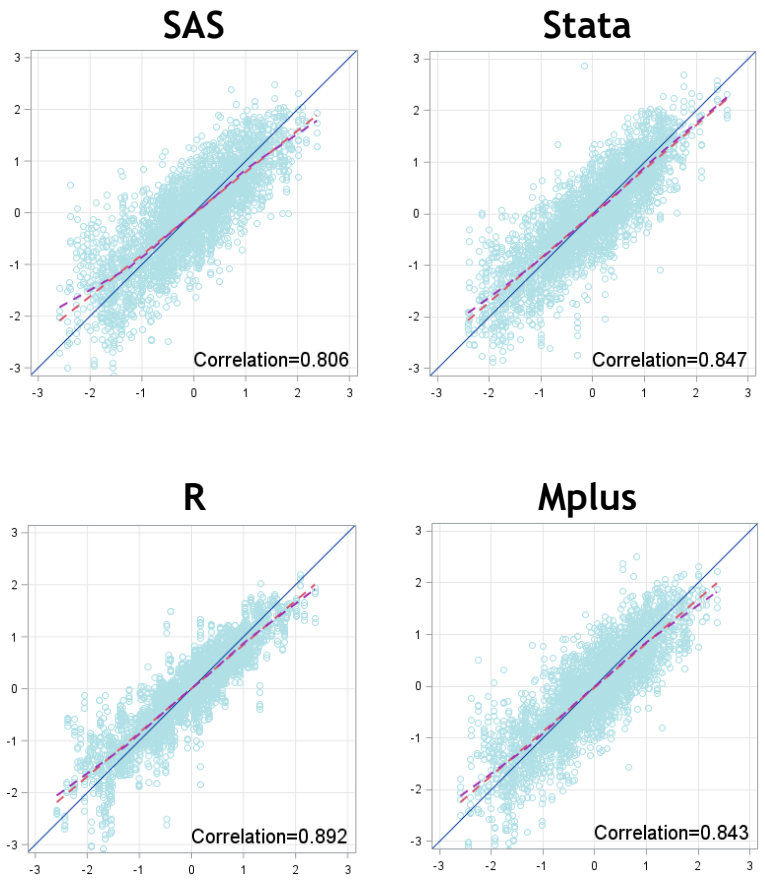
Once the timing of neurocognitive assessments has been resolved, analysts examining changes in global cognition and each of the cognitive domains should decide whether to employ one imputation model to generate missing values for all outcomes simultaneously or separate imputation models for each outcome. The benefit of using only one imputation model is that the correlation between global cognition and cognitive domains often results in more precise estimates of missing measures of cognitive function. The drawback is that differences in the associations between an exposure and the cognitive domains may be minimized. Given the efficiency of running one imputation model, many analysts choose the former. However, if

differences across domains is a critical aspect of the research question then separate models may be advantageous.

The next decision that analyst must make is whether to perform a single level or multilevel imputation.[14] Multilevel imputation models can be specified in programs like Mplus (Appendix C) and R. These models permit the analyst to decompose variables into both fixed and random effects with different correlation structures. In contrast, single level models can be easily performed in Stata (Appendix D), R (Appendix E), SAS (Appendix F), or Mplus and are therefore more commonly utilized. However, these models implicitly adopt an autoregressive correlation structure which can introduce bias in certain analyses, such as the examination of cognitive decline between Visits 2 and 7. Consequently, analysts may want to compare the results from both approaches if the initial parameter estimates are counterintuitive.

A comparison of programs conducted for ARIC (Figure 3.1.1) suggests that Stata and Mplus often produce superior results because these programs permit the use of link functions and distributions not permitted in SAS (e.g. the Poisson distribution) while preserving plausible variability that is suspiciously absent from imputations performed with the standard MICE package in R.

Figure 3.1.1. Correlation between observed and imputed values when the dataset and imputation model are the same but different analysis programs are utilized

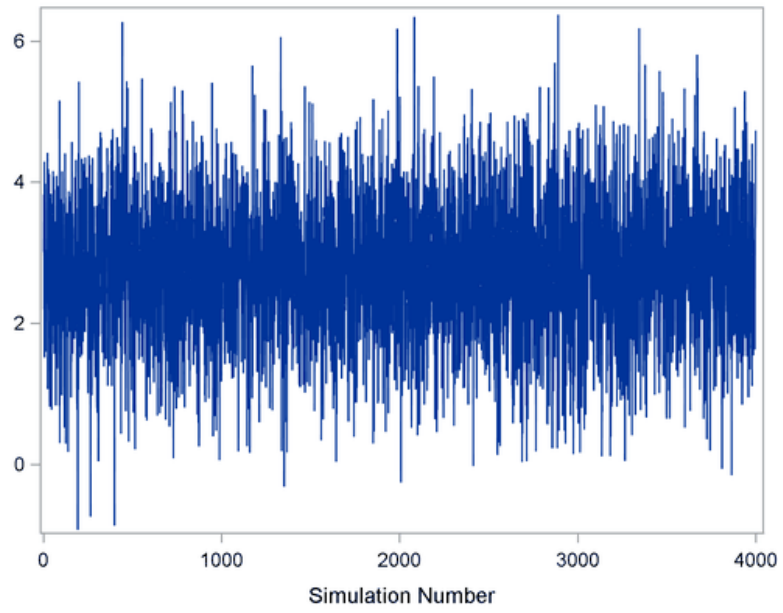


In ARIC, the most common approach is to generate 10 imputed datasets utilizing a single level imputation in Stata that includes variables denoting the time between the initial neurocognitive assessment and each follow-up neurocognitive assessment. An interaction between time and each neurocognitive assessment is incorporated into the imputation model. A series of imputations are then performed to ensure that concurrent and past variables, but not future variables, inform the values generated. The sequence below depicts an example for an analysis of longitudinal data from Visit 5 through Visit 7. Example Stata code is provided in Appendix G. Example Stata code for an analysis of longitudinal data from Visit 4 through Visit 6 is provided in Appendix H. Adaptable Stata code is provided in Appendix I.

1. Impute values at Visit 5 using all analytic and auxiliary variables obtained prior to January 1st, 2016 which marks the start of Visit 6. Retain the original and imputed values for both time-invariant and time-varying variables.
2. Impute values at Visit 6 using all analytic and auxiliary variables obtained prior to January 1st, 2018 which marks the start of Visit 7. This includes assessments from Visits 5 and 6. Incorporate an interaction between the neurocognitive assessment at Visit 5 and the time between Visits 5 and 6. Retain the original and imputed values for time-varying variables from Visit 6.
3. Impute values at Visit 7 using all analytic and auxiliary variables obtained prior to January 1st, 2020 which marks the start of Visit 8. This includes assessments from Visits 5 through 7. Incorporate interactions between (a) the neurocognitive assessment at Visit 5 and the time between Visits 5 and 7 and (b) the neurocognitive assessment at Visit 6 and the time between Visits 6 and 7. Retain the original and imputed values for time-varying variables from Visit 7.
4. Combine original and imputed values from the prior steps into a single dataset.

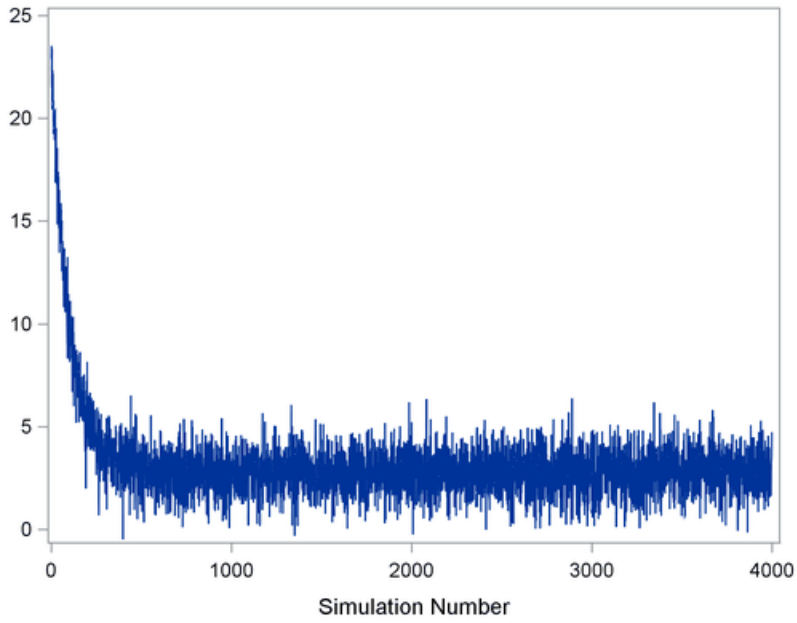
After each imputation, analysts should examine trace plots to evaluate convergence. An ideal trace plot is depicted below (Figure 3.1.2).

Figure 3.1.2. Ideal trace plot



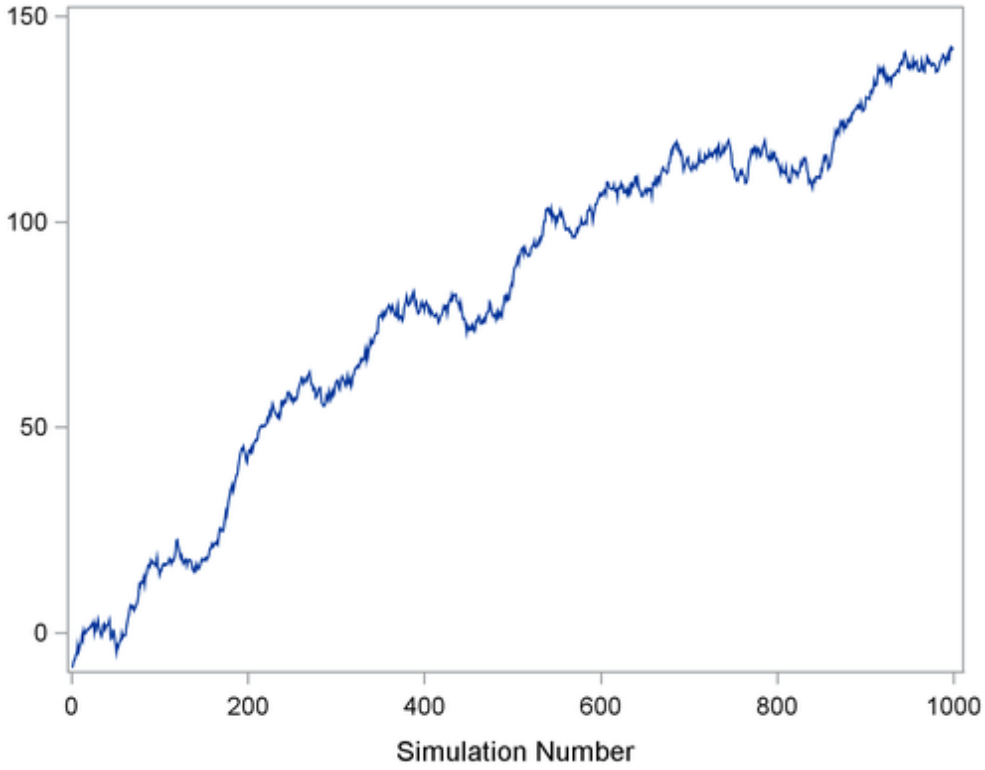
When analyzing data from the ARIC cohort, it is often the case that a trace plot starts at a remote initial value before reaching the target distribution (Figure 3.1.3). If this occurs, the analyst may need to increase the burn-in sample size to ensure samples are selected after the Markov chain reaches the target distribution. In ARIC, most analysts begin with a burn-in sample size of 50 and then adapt accordingly after examining the trace plots.

Figure 3.1.3. Trace plot indicating a sizable burn-in may be required



Trace plots that exhibit serious issues (Figure 3.1.4) may require a re-specification of the imputation model or potentially the use of an alternative approach such as inverse probability weighting (Section 3.2), pattern mixture modeling,[5-7] selection modeling,[6,8] or shared parameter modeling.[6,9]

Figure 3.1.4. Problematic trace plot



A recommended supplemental analysis to evaluate the imputation model is to randomly select 20% of the observed values from each neurocognitive assessment (Visit 5, Visit 6, Visit 7, etc.) and convert the value to missing. The imputation model can be utilized to generate five imputed values for each randomly selected observed value. A scatterplot with a standard and localized regression line will permit the analyst to compare the observed and imputed values (Figure 3.1.5). A Bland-Altman plot (Figure 3.1.6) may also be informative.

Figure 3.1.5. Scatterplot of observed and imputed values

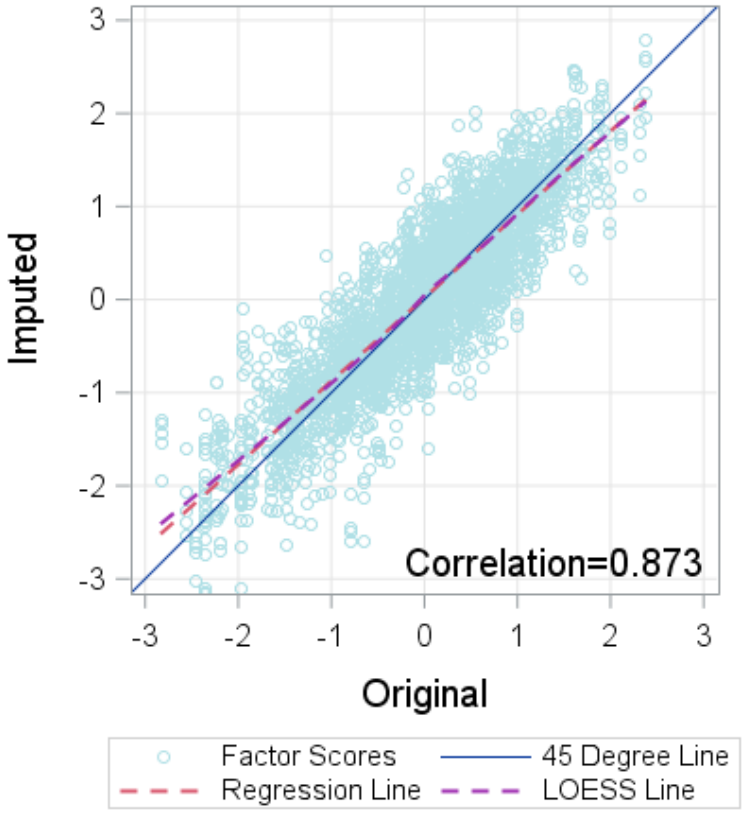
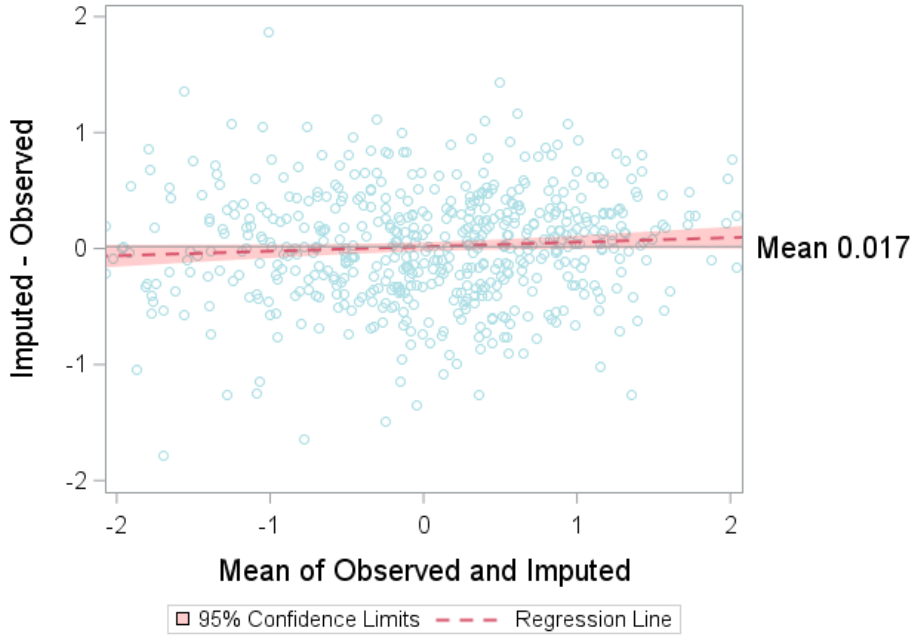


Figure 3.1.6. Bland-Altman plot of observed and imputed values



When the correlation between observed and imputed values is less than 0.40 it is often a sign that the imputation model is misspecified and needs to be refined. Even more important is the extent to which the regression lines digress from the 45-degree line in the scatterplot or deviate from 0 in the Bland-Altman plot. In an ideal scenario, the regression lines will be placed directly on top of or close to the 45-degree line in the scatterplot and will not dramatically differ from 0 in the Bland-Altman plot. If the deviation is sizable, analysts should attempt to improve the imputation model as well as describe the potential impact on the parameter estimates. For example, the minor deviation depicted in the above figures reveal that imputed values tend to be underestimated at the extremes of the distribution. Consequently, associations between an exposure and cognitive decline may be less precise and more attenuated than they would have been if the data were not missing.

To further assess the robustness of the imputation model, the same supplemental analysis can be repeated with a minor modification. Instead of randomly selecting 20% of the observed values, a logistic regression model can be fit to the data. The outcome will be whether a participant has a missing neurocognitive assessment and the predictors will be variables from the imputation model with little or no missing data. Utilizing this model, the probability of missingness at each assessment can be determined for each participant. Among the subsample of participants with an observed value at a specific assessment, the top quintile (i.e. 20%) with the highest probability of missingness can be converted to missing. Imputed values can then be generated and compared to the observed values. Please note that this test assumes the data is missing not at random (MNAR), which is a direct violation of a key assumption of multiple imputation which posits that the data is missing at random (MAR) conditional on the analytic and auxiliary variables in the imputation model. Nonetheless, the comparison is informative in that it depicts how effective the imputation model is even when a key assumption is violated. Additional techniques for examining imputed values are available and have been documented.[15] Future iterations of this manual will provide additional instruction for such approaches as posterior predictive checking.

In a few rare cases, such as when multilevel imputation models are utilized, the prior analyses will indicate that the initial imputation model is reasonable. In most situations though, analysts

will need to improve the model by incorporating interactions. Common interactions employed in ARIC imputation models include the following.

1. Cognition X Time
2. Cognition X Level 3 Dementia
3. Cognition X Mini-Mental State Exam
4. Education X Mini-Mental State Exam
5. Level 3 Dementia X Time
6. Level 3 Dementia X Age
7. Level 3 Dementia X Education
8. Level 3 Dementia X Race-Center
9. Level 3 Dementia X Clinical Dementia Rating
10. Level 3 Dementia X Mini-Mental State Exam
11. Level 3 Dementia X Six-Item Screener
12. Level 3 Dementia X Diabetes
13. Level 3 Dementia X Hypertension
14. Level 3 Dementia X Cigarette Use

Once a suitable imputation model has been developed, analysts should examine the means, frequencies, and distributions of observed and imputed variables. If imputed values defy plausibility (e.g. a negative score on the DWR), then it may be necessary to transform the data post-imputation through winsorization or a similar technique. It may also be necessary to revise the imputation model, such as by using predictive mean matching rather than regression for some continuous variables.

At this point, the imputed data can be analyzed and diagnostic measures evaluated. If the variance between datasets is substantially larger than the variance within each dataset, then the analyst may want to increase the number of imputed datasets. The same solution also

applies when the percentage of missing information is high or the relative efficiency is poor. Publicly available SAS macros and Stata commands[16] can also be used to analyze the imputed data and determine how many imputations are needed.

To ascertain the robustness of the results, analysts should perform a sensitivity analysis that compares parameter estimates and standard errors from the following models.

1. A model that includes only participants with complete data for each variable.
2. A model that uses only imputed values for covariates.
3. A model that includes imputed values for covariates as well as the exposure. Missing outcomes are not imputed in this model.
4. A model that includes imputed values for all variables in the analytic model.

Within the ARIC cohort, participants with lower cognitive scores are less likely to return for subsequent visits. As a result, the association between an exposure and cognitive decline is often greatest in the final model.

3.1.4. Utilizing Model Diagnostics

Regardless of the mechanism used to address informative attrition, analysts should employ diagnostics to assess the primary model(s). One common approach is to generate a scatter plot of the residuals across time. The scatterplot should include a locally weighted scatterplot smoothing (LOWESS) line. Plots should be created for (1) the entire population, (2) each racial subpopulation, (3) the various levels of the exposure being examined such as smokers and nonsmokers, and (4) the various levels of the exposure by racial subpopulation. Ideally, the LOWESS line will be horizontal at zero. If it is not, a model with additional time splines should be considered.

After assessing the LOWESS line across time, analysts are encouraged to evaluate the following:

1. The mean of model residuals overall, by visit, and by levels of key covariates such as gender and race.
2. A histogram or Q-Q plot of model residuals to assess the normality of errors.

3. Scatterplots of model residuals against predicted values from the model.
4. Scatterplots of continuous covariates across time if they have a statistically significant interaction with time.

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3.2. Dementia and Mild Cognitive Impairment Analyses

A summary of the different definitions of incident dementia is provided in Section 2.18. A detailed depiction of the definitions can be found in the STATUS## Derived Variable Dictionary available on the ARIC website.

3.2.1. Longitudinal Analysis of Incident Dementia

When examining incident dementia, analysts should use the censored level 3 dementia diagnosis as the event indicator ([STATUS##] DEMDXL3CENS_##) and the corresponding adjusted date as the event time ([STATUS##] COXDATE_DEMDXL3_##). Level 3 is recommended because it minimizes missing cases by relying on the best source of information available (Section 2.18). Level 1 dementia ([STATUS##] DEMDXL1CENS_## and COXDATE_DEMDXL1_##) can be utilized in sensitivity analyses that examine incident dementia when it is defined with the highest degree of confidence. However, analysts that use Level 1 dementia must keep in mind that the resulting parameter estimates are often biased due to informative attrition. Level 2 dementia ([STATUS##] DEMDXL2CENS_## and COXDATE_DEMDXL2_##) may be useful when comparing estimates from level 3 to a definition of incident dementia that excludes information from medical records and death certificates. Analysts who wish to compare parameter estimates from ARIC to other studies that only used medical records and death certificates to define dementia should select the surveillance only dementia diagnosis ([STATUS##] DEMDXSURVCENS_## and COXDATE_DEMDXSURV_##). Comparison to studies that only conducted phone-based assessments may be performed by using the phone only dementia diagnosis ([STATUS##] DEMDXPHONECENS_## and COXDATE_DEMDXPHONE_##).

Table 3.2.1. Suggested use of incident dementia variables

	Source	Recommended Use
DEMDXL1CENS **COXDATE_DEMDXL1**	1. Reviewer diagnosis based on neuropsychological tests 2. Algorithmic diagnosis based on neuropsychological tests	May be used in sensitivity analyses. Parameter estimates may be biased due to informative attrition.
DEMDXL2CENS **COXDATE_DEMDXL2**	1. Reviewer diagnosis based on neuropsychological tests 2. Algorithmic diagnosis based on neuropsychological tests 3. Results from Education-adjusted Telephone Interview for Cognitive Status 4. Results from Clinical Dementia Rating and Functional Activities Questionnaire 5. Results from Eight Item Dementia Screening Interview 6. Results from two Six Item Screeners 7. Results from one Six Item Screener if participant lost to follow-up or deceased	May be used in sensitivity analyses. Parameter estimates may be biased due to informative attrition.
DEMDXL3CENS **COXDATE_DEMDXL3**	1. Reviewer diagnosis based on neuropsychological tests 2. Algorithmic diagnosis based on neuropsychological tests 3. Results from Education-adjusted Telephone Interview for Cognitive Status 4. Results from Clinical Dementia Rating and Functional Activities Questionnaire 5. Results from Eight Item Dementia Screening Interview 6. Results from two Six Item Screeners 7. Results from one Six Item Screener if participant lost to follow-up or deceased 8. Hospitalization discharge codes 9. Death certificate codes	**Recommended for analyses of incident dementia.**
DEMDXPHONECENS **COXDATE_DEMDXPHONE**	1. Results from Education-adjusted Telephone Interview for Cognitive Status 2. Results from Clinical Dementia Rating and Functional Activities Questionnaire 3. Results from Eight Item Dementia Screening Interview 4. Results from two Six Item Screeners 5. Results from one Six Item Screener if participant lost to follow-up or deceased	Recommended for analyses in which dementia ascertained from only phone-based assessments are of interest.
DEMDXSURVCENS **COXDATE_DEMDXSURV**	1. Hospitalization discharge codes 2. Death certificate codes	Recommended for analyses in which dementia ascertained from only medical records and death certificates are of interest.

In time-to-event analysis, the baseline should be chosen according to specific needs. Dementia cases which occurred prior to the baseline specified for the analysis should be excluded. The suggested models for analyzing incident dementia are Cox proportional hazards models that employ Efron's approximation to handle ties and incidence rate models such as modified Poisson regression with robust error variance. Alternative models including accelerated failure time models or log-linear models with a Gamma distribution that assess time until incident dementia may also be utilized. Note that the dementia event time naturally occurs at an ARIC visit for dementia cases that were ascertained at the visit. Consequently, models handling interval censoring, such complementary log-log, should be considered as a sensitivity analysis to evaluate the robustness of the results.

When level 3 dementia is employed as the outcome, there is no need to correct for cohort attrition since the methods of ascertainment of cases who do not attend visits are thought to be nearly complete. However, analysts evaluating etiologic hypotheses[1] may wish to utilize inverse probability-of-censoring weights (IPCW)[2] to assess the onset of dementia while simultaneously treating [STATUS##]DATEOFDEATH as a competing risk.

3.2.2. Longitudinal Analysis of Mild Cognitive Impairment

Post-Visit 5 incident mild cognitive impairment (MCI) should be studied among cognitively normal participants at Visit 5. The cognitive status of Visit 5 attendees is defined by the variable [DERIVE5#]COGDIAG51 with the category "N" indicating cognitively normal. Cognitive status at subsequent visits is defined by the variable [DERIVE##]COGDIAG#1 with the category "M" indicating MCI.

MCI status was only assessed during in-person cognitive evaluations (Section 2.18), so the visit date can be used as an estimate of the event time for incident MCI in time-to-event analyses. However, considering that the event time is arbitrary and discretized according to visit time an interval censoring model, such as a complementary log-log model, is suggested for time-to-event analysis. Logistic regression can also be utilized when odds ratios are of interest.

If an analyst wishes to examine the onset of both MCI and dementia, either complementary log-log or logistic regression models can be employed. An ordinal logistic regression may be

appropriate if the proportional odds assumption is valid. Alternatively, a multinomial logistic model that treats MCI and dementia as two separate endpoints can be fit to the data. A four-category outcome of normal, MCI, dementia, or death may also be informative.

Attrition correction methods, such as inverse probability weighting (IPW), can be adopted to address the potential differential loss of MCI and dementia cases due to non-visit attendance. The practice of weighting observed data to account for missing data comes from weighting for non-response in sample surveys to correct for bias. To quote Rathouz and Preisser[3]:

> "…when non-responders differ from responders according to their distribution of measured characteristics, the responders' data is weighted so that analysis restricted to the complete data sample would resemble analysis of the combined data of responders and non-responders had it been observed. Use of weights assumes there exists knowledge of some variables, such as demographic characteristics, on the non-responders so that they can be placed in groups or bins with responders. The bin-specific inverse probability of being a responder is then calculated and used as the weight for observations in that bin. The same principle can be applied in a prospective study where the outcome Y at the end of the follow-up period is missing for some subjects. The general idea is to weight records inversely to their probability of being observed such that observed data with a low likelihood of being observed receive relatively high weight. Incorporating continuous as well as categorical baseline variables instead of bins, a logistic regression model can be used to estimate the probability of being observed at follow-up for each study participant. The resulting inverse probability is then the weight used in the complete-data analysis for the outcome."

When using IPW, analysts should omit any observed visit that occurs after the first missed visit. Depending on the nature of the research question, analysts may also wish to create pseudo-visits (e.g. Visit 4.1 = 1999-2005, Visit 4.2 = 2005-2010) to account for the large gap in time between Visit 4 and Visit 5. Once a monotone dataset has been generated, an IPW analysis can be implemented.[4-6] The suggested sequence of steps is:

1. Determine visit-specific probabilities of being observed conditional upon not dropping out at the previous visit.
2. Calculate the cumulative (unconditional) probabilities of not dropping out as a product of the conditional probabilities up to the visit.
3. Compute a visit-specific weight as the inverse of the cumulative probabilities up through the visit. The weight is 1 at the first visit since all subjects are present.
4. Apply the weights in a set of weighted estimating equations and solve them to estimate the regression parameters in the model for the marginal means.

The choice of estimating equations when using IPW is critical. IPW estimating equations with observation-specific weights are encouraged since this approach is more efficient than cluster-specific weights.[7] Analysts are encouraged to use an independence correlation matrix which provides parameter estimates that are less likely to underestimate incident MCI and dementia. Independence IPW estimating equations with observation-specific weights and conservative estimation of standard errors can be implemented in STATA or SAS. The SAS macro WGEE provides the option to generate bootstrapped estimates of standard errors.

IPW analyses can accommodate a wide range of variables in the model used to estimate the probability of a missing response. Key variables that should be included are:

1. The primary outcome at each visit.
2. The risk or protective factors of interest at each visit.
3. All covariates included in the analytic model from all visits.
4. Auxiliary covariates from primary and secondary datasets such as the annual follow-up.
5. Appropriate interaction terms between the variables listed above.

When developing the model analysts may use standard selection criteria, such as Akaike information criterion (AIC) and Bayesian information criterion (BIC), while keeping in mind that there is no penalty to pay in terms of efficiency loss by overfitting the missingness model.[8] Variables with extremely small or large coefficients should also be scrutinized since they may

result in extreme weights. An examination of the weights themselves can also be informative and may prompt the analyst to trim the weights using winsorization.

Another issue that deserves consideration is whether attrition is due to death or dropout. For IPW, analysts are encouraged to develop separate models for dropout and death. Note that this requires estimating the probability of dropout conditional on remaining alive and a determination of when someone should be classified as lost to follow-up versus deceased. This can be ascertained utilizing the latest version of [STATUS##]DATEOFDEATH. If a participant is known to be alive at the start of the next visit, they are classified as lost to follow-up. If a participant has a date of death before the start of the next visit, they are classified as deceased. At this point, the analyst should decide whether to apply weights for total attrition (death + dropout) or only for non-death dropout. This choice affects the interpretation of the findings. Findings weighted for non-death dropout hope to recover the association only in the case of perfect follow-up conditional upon being alive. Findings weighted for both death and dropout hope to recover the association where death is random or a competing event. While this is helpful for understanding etiology, the association corresponds to a hypothetical population that does not and cannot exist.

3.2.3. Time-Varying Covariates

When conducting time-to-event analyses, all available sources of data should be used to define time-varying covariates. Some covariates, such as systolic blood pressure, are obtained only during clinic-based assessments. Other covariates, such as diabetes and smoking status, are ascertained during clinic-based assessments and annual follow-up phone calls. Surveillance data may also provide pertinent information that can be used to define a time-varying covariate.

Continuous time models, such as the Cox proportional hazards model, can integrate time-varying covariates using a counting process method.[9] When a counting process is paired with an approach that requires specific intervals to be defined, such as IPW or IPCW, then the appropriate value for each interval should be included in the analytic dataset. When a value is missing from a specific interval, analysts are encouraged to utilize multiple imputation. When two or more values are present in the same interval, analysts may choose a method that is

suitable for the specific variable. For example, in some cases it may be appropriate to compute the mean of the two values while in other cases it may be preferable to choose the earliest or latest observation within the interval. These suggestions also apply to discrete time models, such as the complementary log-log model.

3.2.4. Cross-sectional Analysis of Dementia and MCI

For cross-sectional analysis of dementia and/or MCI, analysts should use the variable [DERIVE5#]COGDIAG5# for Visit 5 analyses, [DERIVE6#]COGDIAG6# for Visit 6 analyses, etc. A summary is provided in Table 3.2.1 below.

Table 3.2.2. Suggested approach for longitudinal analyses

	Outcome	
	Dementia	**MCI**
Permitted analytical timeframe	Incident events since visit 1; Better ascertainment after visit 5	Incident events after visit 5 only
Study population	Dementia free (cognitively normal or MCI) at the baseline	• Cognitively normal at baseline • Participants who completed in-person cognitive evaluations
Suggested modeling approach	• Time-to-event analysis: Cox model using Efron's method • Incidence rate: Poisson model with robust error variance	Time-to-event analysis: Complementary log-log model
Alternative modeling approach	Time-to-event analysis: Complementary log-log model	• Relative risk: Logistic model • Incidence rate: Poisson model
Methods to address cohort attrition	Not needed if using level 3 dementia	Needed. Recommend use of inverse probability of attrition weighting. However, not needed if the exposure is not related to attrition.
Methods to address competing risk of death [STATUS##]DATEOFDEATH	Recommend use of inverse probability-of-censoring weighting. However, this technique may not be warranted if the exposure is not related to death.	Recommend use of inverse probability-of-censoring weighting. However, this technique may not be warranted if the exposure is not related to death.
Variations on Outcomes	Based on the research question, analyst can study the following three potential conversion types: • Dementia free to dementia • Normal to dementia • MCI to dementia	• Analyst needs to decide whether to combine incident MCI and dementia together as the outcome.
	When studying the progression of cognitive impairment (i.e. normal to MCI and MCI to dementia), analysts can decide whether to separate out MCI cases who convert back to normal. For example, among participants who attended visit 5 and visit 6, about 55% of MCI cases at visit 5 converted back to normal at visit 6. This type of reverse conversion may be a result of measurement error.	

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3.3. Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) Analyses

Magnetic resonance imaging (MRI) and positron emission tomography (PET) were performed at ARIC Visit 5 (2011-13), Visits 6 and 7 (2016-19), and Visits 8 to 11 (2020-23). Beginning in 2020, all scans (Sections 2.14 and 2.16) were reanalyzed to produce harmonized measures designed for longitudinal analyses. Findings from readings by radiologists, such as infarcts and microhemorrhages, were not reanalyzed but derived variables have been created to reconcile inconsistent trends over time (Section 3.3.5).

The datasets distributed by the Coordinating Center (CC) facilitate region of interest (ROI) analyses. ROI analyses use probabilistic brain atlases to generate anatomical templates. Images from individual participants are mapped to the template and used to calculate region-specific measures of cortical thickness, white matter hyperintensities (WMH), standardized uptake value ratios (SUVRs) of florbetapir, etc.

An alternative analytic approach is to employ voxel-based morphometry (VBM).[1] VBM is a whole-brain measurement technique that tests for residual tissue concentration differences that remain after MRI scans are spatially normalized to a template, modulated, and smoothed. A statistical parametric mapping general linear model framework is used to estimate differences on a voxel-wise basis between groups, such as participants with and without cognitive impairment. VBM datasets have not been provided to the CC, but may be obtained by contacting the Mayo Aging and Dementia Imaging Research (ADIR) Lab.

3.3.1. Selection Bias

When performing ROI analyses of MRI and PET scans, analysts should initially generate descriptive statistics that characterize the differences between ARIC participants who completed a scan and those who did not. Since the size of the ARIC cohort decreased over time and the inclusion and exclusion criteria for MRI and PET scans varied at each visit (Sections 2.14 and 2.16), it is important to assess whether selection bias may impact the interpretation of results. If selection bias is present, this should be noted as a limitation or addressed analytically through the use of appropriate techniques such as probability weighting.

At Visit 5, weights (Section 2.1.2) designed to mitigate inaccurate inferences were calculated. The dataset V5_V11_MRI_DERV includes a weight (BASEWT1) that accounts for the MRI scan

selection criteria at Visit 5, a weight (REFADJ1) that adjusts for participant refusal, and the product of the two weights (SAMWT1). If the analytic sample is restricted to all participants who completed a MRI scan at Visit 5 and robust standard errors are specified in the model, then analysts may use SAMWT1 to obtain inferences that generalize to the ARIC cohort at Visit 5. The same methodology may be used to calculate weights that generate parameter estimates which correspond to the ARIC cohort at different points in time.

3.3.2. MRI: Brain Volume and Cortical Thickness

The dataset V5_V11_MRI_DERV has a two-level structure with visits (Visit) nested within participants. The Freesurfer atlas[2,3] was used to define measures of brain volume (*_vol*) in cubic millimeters for 60 regions of which 49 regions were subdivided into the left and right hemisphere. The same approach was utilized to define measures of cortical thickness[4] (*_thk*) in millimeters for 34 regions, each of which was subdivided into the left and right hemisphere. Since all field centers used Siemen scanners, analysts may use either measure without having to account for differences caused by a specific scanning technology.

In most cases, analysts are encouraged to examine both brain volume and cortical thickness. If forced to prioritize, cortical thickness may be reported as the primary outcome and brain volume as a sensitivity analysis.[4] The rationale for this approach is that correcting for head size, which is required when examining brain volume, may not adequately address the underlying confounding[5] and can produce inconsistent results based on the method of correction employed.[6-8]

Composite brain regions for both brain volume and cortical thickness have been derived by the Mayo ADIR Lab. Regions without measures of cortical thickness, such as the amygdala, are included in the brain volume definition but excluded from the cortical thickness definition.

Table 3.3.1. MRI composite brain regions of interest

Region	Brain Volume Definition	Cortical Thickness Definition
Deep Grey and White	Sum in the insula, thalamus proper, caudate, putamen, and pallidum regions	Not applicable
Ventricular	Sum in the left lateral, right lateral, 3rd, 4th, and 5th ventricle regions	Not applicable
Frontal Lobe	Sum in the caudal anterior cingulate, caudal middle frontal, lateral orbitofrontal, medial orbitofrontal, paracentral, pars opercularis, pars orbitalis, pars triangularis, precentral, rostral anterior cingulate, rostral middle frontal, superior frontal, and frontal pole regions	Surface area weighted average in the caudal anterior cingulate, caudal middle frontal, lateral orbitofrontal, medial orbitofrontal, paracentral, pars opercularis, pars orbitalis, pars triangularis, precentral, rostral anterior cingulate, rostral middle frontal, superior frontal, and frontal pole regions
Temporal Lobe	Sum in the bankssts, entorhinal, fusiform, inferior temporal, middle temporal, parahippocampal, superior temporal, temporal pole, transverse temporal, hippocampus, and amygdala regions	Surface area weighted average in the bankssts, entorhinal, fusiform, inferior temporal, middle temporal, parahippocampal, superior temporal, temporal pole, and transverse temporal regions
Occipital Lobe	Sum in the cuneus, lateral occipital, lingual, and pericalcarine regions	Surface area weighted average in the cuneus, lateral occipital, lingual, and pericalcarine regions
Parietal Lobe	Sum in the inferior parietal, isthmus cingulate, postcentral, posterior cingulate, precuneus, superior parietal, and supramarginal regions	Surface area weighted average in the inferior parietal, isthmus cingulate, postcentral, posterior cingulate, precuneus, superior parietal, and supramarginal regions
Temporal Lobe Meta-ROI	Sum in the entorhinal, fusiform, inferior temporal, middle temporal, hippocampus, and amygdala regions	Surface area weighted average in the entorhinal, fusiform, inferior temporal, and middle temporal regions
Temporal-Parietal Lobe Meta-ROI	Sum in the entorhinal, fusiform, inferior temporal, middle temporal, hippocampus, amygdala, and precuneus regions	Surface area weighted average in the entorhinal, fusiform, inferior temporal, middle temporal, and precuneus regions
Total	Estimated total intracranial volume	Mean cortical thickness across all regions in the brain

3.3.3. MRI: White Matter Hyperintensities

An algorithm[9] was used to compute WMH volume in the brain in cubic millimeters ([V5_V11_MRI_DERV] WMH_vol_2D or WMH_vol_3D) and the percentage of WMH in the brain ([V5_V11_MRI_DERV] WMH_vol_2D or WMH_vol_3D) relative to total intracranial volume. To facilitate comparisons between 2D scans at Visit 5 and 3D scans at subsequent visits (Section 2.14), a derived variable ([V5_V11_MRI_DERV] GLOBAL_ADJUSTED_ARIC5) has been provided. Region-specific analyses can be performed utilizing V5_V11_WMH, which has a three-level structure with brain regions (Region_No or Region_Name) nested within visits (Visit) nested within participants.

3.3.4. MRI: Mean Diffusivity and Fractional Anisotropy

The datasets V5_V11_DTI_JHU and V5_V11_DTI_MCALT_LOBAR have a three-level structure with brain regions (Region_No or Region_Name) nested within visits (Visit) nested within participants. Each dataset contains region-specific measures of mean diffusivity (MD) and fractional anisotropy (FA). MD is a scalar measure of how quickly water molecules diffuse (mm^2/s). FA measures the directional constraint of water diffusion and ranges from 0 to 1 (unitless). Higher mean diffusivity (MD) and lower fractional anisotropy (FA) usually indicate damaged or impaired microstructural integrity.[10]

The V5_V11_DTI_JHU dataset contains 110 brain regions defined using the John's Hopkins University (JHU) Diffusion Tensor Imaging (DTI) atlas. The mean and median of MD and FA is provided for each region. The V5_V11_DTI_MCALT_LOBAR dataset contains 16 regions defined utilizing the Mayo Clinic Adult Lifespan Template (MCALT) DTI atlas. The mean and median of MD for white matter and gray matter and the mean and median of FA for white matter have been calculated. Both datasets contain the number of voxels associated with each region so composite regions can be computed utilizing voxel-weighted averages.

When neighboring voxels are aggregated into a ROI, edge voxels that may be considered a part of multiple ROIs may cause partial volume contamination that can bias the mean of MD and FA. Consequently, analysts are encouraged to examine the median as the primary outcome and treat the mean as a sensitivity analysis.

3.3.5. MRI: Infarctions and Microhemorrhages

Infarctions and microhemorrhages were identified, counted, and measured by a trained imaging technician and confirmed by a radiologist blinded to all clinical information.[11-13] Each finding was categorized as possible or definite. The dataset V5_V11_MRI_FINDINGSREPORT documents these findings in a three-level structure with findings (uniqueid) nested within visits (Visit) nested within participants.

To simplify analyses, derived variables have been provided in V5_V11_MRI_DERV that quantify the number of large cortical infarctions (LARGECORTFREQ), small cortical infarctions (SMALLCORTFREQ), subcortical infarctions (SUBCORTFREQ), superficial siderosis (SUPERSIDFREQ), microhemorrhages (CMHFREQ), deep cerebral microhemorrhages

(DEEPCMHFREQ), lobar microhemorrhages (LOBARCMHFREQ), and infratentorial microhemorrhages (INFRATCMHFREQ) at each visit. Only findings classified as definite were counted.

Table 3.3.2. Definitions of infarctions and microhemorrhages

Type	Definition
Microhemorrhage	A discrete, roughly spherical hypointense region inside the brain with clear borders and a definite contrast between tissue and lesion. Identified via T2 Star sequence.
Lobar Microhemorrhages	A microhemorrhage found in the frontal, temporal, occipital, or parietal lobe.
Cerebral Microhemorrhages	A microhemorrhage found in the external capsule, internal capsule, corpus callosum, insula, thalamus proper, caudate, putamen, or pallidum regions.
Infratentorial Microhemorrhages	A microhemorrhage found in the pons, midbrain, medulla, cerebellum, or brainstem.
Superficial Siderosis	A curvilinear hypointense band located on the cortical surface or in the cortical sulci. Identified via T2 Star sequence.
Large Cortical Infarctions	A T2 hyperintense lesion (gliosis) that includes cortical gray matter, may include underlying white matter, and extends to the cortical edge. Identified via FLAIR sequence and may be confirmed by presence of a T1 hypointense cortical defect. Defined as greater than or equal to 10mm in greatest dimension (of gliosis) on an axial slice.
Small Cortical Infarctions	A T2 hyperintense lesion that includes cortical gray matter, may include underlying white matter, and extends to the cortical edge. Identified via FLAIR sequence and may be confirmed by presence of a T1 hypointense cortical defect. Defined as less than 10mm in maximum diameter (of gliosis) on an axial slice.
Subcortical Infarctions	A T2 hyperintense lesion with a dark center seen in the white matter, infratentorial, and central gray or capsular regions. Must be distinguished from perivascular spaces and ruled out as a cortical infarction. In most regions, the dark area (tissue loss areas) must be greater than or equal to 3mm in diameter as measured on the FLAIR or T1 based on whichever image shows the finding more clearly. The terms “subcortical” and “lacunar” infarction are often used interchangeably. A lacunar infarction is a more specific definition, i.e. a subcortical infarction that is 3 to 15 mm in diameter.

Two versions of each derived variable have been developed. The first version (FREQ1) does not reconcile within-participant differences over time. Consequently, it is possible for a participant to have more infarctions or microhemorrhages at Visit 5 then at subsequent visits. The second version (FREQ2) uses data from all available visits to ensure that there is a logical progression such that the number of infarctions or microhemorrhages increase but never decrease with time. For example, the first version (FREQ1) may indicate that a participant has 2 infarcts at Visit 5 and 1 infarct at Visit 6. In contrast, the second version would indicate that the same participant has 1 infarct at Visit 5 and 1 infarct at Visit 6. Analysts are encouraged to explore both versions when conducting longitudinal analyses, although the second version (FREQ2) is typically reported as the primary outcome while the first version (FREQ1) is treated as a sensitivity analysis.

3.3.6. MRI: Quality Control

The dataset V5_V11_MRI_IMAGEQC contains quality control information documented in a three-level structure with scanning series (SeriesDescription) nested within visits (Visit) nested within participants. Quality control assessments (SeriesQC) and assessments of protocol adherence (SeriesProtocol) are provided for some series. The V5_V11_MRI_DERV dataset also documents head motion (RMS_Displacement_mm) which can impact scan quality.

3.3.7. PET: Standardized Uptake Value Ratio

The dataset V5_V11_PET has a two-level structure with visits (Visit) nested within participants. All PET scans were co-registered with MRI scans (Section 2.16). Both scans were typically performed less than a year apart. The MUlti-atlas region Segmentation utilizing Ensembles of registration algorithms and parameters (MUSE) atlas[14] was used to document Standardized Uptake Value Ratios (_*suvr*) in 77 regions of which 69 regions were subdivided into the left and right hemisphere. Composite brain regions were derived by the Mallinckrodt Institute of Radiology at Washington University School of Medicine in St. Louis.

Table 3.3.3. PET composite brain regions of interest

(***Information not yet provided by PET reading center***)

3.3.8. Cross-sectional Analyses

Cross-sectional analyses may be performed using all scans from a single visit or a single scan per individual across visits. The latter approach provides a larger analytic sample but careful consideration must be given to how age differences may impact parameter estimates and whether the time between the exposure and the outcome introduces bias. Since scans of later visits used 3D technology, the use of 2D scans at Visit 5 (Section 2.14) may also limit the types of analyses that can be performed.

Measures of brain volume and cortical thickness (Section 3.3.2) have a normal distribution and can be analyzed utilizing linear regression models. When analyzing volumes, total intracranial volume ([V5_V11_MRI_DERV] EstimatedTotalIntraCranialVol) must be included as a covariate to adjust for differences caused by head size. When analyzing cortical thickness, this covariate

does not need to be integrated into the model.[15,16] In prior publications, ARIC investigators referred to composite regions linked to Alzheimer's disease as a 'Alzheimer disease signature region.' [17,18] This terminology is no longer considered accurate. Composite regions provided by the Mayo ADIR Lab should be referred to as 'temporal lobe meta-ROI' or 'temporal-parietal lobe meta-ROI' regions.

Measures of WMH (Section 3.3.3) have a strong right skewed distribution. As a result, WMH volume is typically log transformed prior to being analyzed as the outcome in a linear regression model. A natural log transformation is the most common choice but a log base 2 transformation is equally reasonable. A generalized linear model with a gamma distribution and a log link function is a viable alternative. Regardless of the model utilized, total intracranial must be included as a covariate to adjust for differences caused by head size.

Measures of MD and FA (Section 3.3.4) have a normal distribution with a modest right skew. Consequently, many analysts treat the distribution as normal and apply a linear regression model. An alternative approach is to fit a quantile regression model to the data. In most situations, analysts treat the median of MD and FA as the primary outcome and examine the mean of MD and FA in sensitivity analyses.

Counts of infarctions and microhemorrhages (Section 3.3.5) have a negative binomial distribution. Some analysts choose to dichotomize the outcome to indicate whether an infarction or microhemorrhage is absent or present. A logistic regression model is employed to generate odds ratios. Alternatively, a Poisson model with robust error variance can be used to calculate the relative risk. Other analysts prefer to leave counts in their original form and fit a negative binomial regression model to calculate rate ratios. A zero-hurdle or zero-inflated negative binomial regression model may also be adopted when a sizable number of the participants in the analytic sample do not have any infarctions or microhemorrhages. These models provide an odds ratio indicating the probability of not having any findings and a rate ratio for the subsample of participants with a finding (zero-hurdle) or the subsample of participants susceptible to having a finding (zero-inflated).

Measures of SUVR (Section 3.3.7) have a right skewed distribution and are typically dichotomized at the sample median before being analyzed with a logistic regression model.

Sensitivity analyses that dichotomize the outcome at previously reported thresholds of 1.2,[19] 1.1,[20] and 1.0[21] are encouraged to facilitate comparisons with prior studies. Dichotomizing the outcome at the 75th percentile is another common sensitivity analysis.[19] Fitting a quantile regression to a continuous measure of SUVR may also offer valuable insights.

Some analysts choose to fit a two-level mixed effects model that examines brain regions nested within participants. These models employ the same variable transformations and link functions described above. However, before fitting the mixed effects model outcomes from different regions of the brain are often placed on the same scale by standardizing or calculating a percentage. Alternative techniques, such as applying a scaled marginal model,[22] can also be adopted.

Table 3.3.4. Suggested approaches for cross-sectional analyses

Outcome	Distribution	Levels	Models
Brain Volume	Normal	One-level model or two-level mixed effects model	• Linear regression with total intracranial volume as a covariate
Cortical Thickness	Normal		• Linear regression
White Matter Hyperintensities	Strong Right Skew		• Linear regression after applying log transformation to outcome with total intracranial volume as a covariate • Generalized linear regression with a gamma distribution and a log link function with total intracranial volume as a covariate
Mean Diffusivity	Modest Right Skew		• Linear regression • Quantile regression to account for skew
Fractional Anisotropy	Modest Right Skew		• Linear regression • Quantile regression to account for skew
Infarctions and Microhemorrhages	Negative Binomial		• Logistic regression after dichotomizing outcome • Poisson regression with robust error variance after dichotomizing outcome • Negative binomial regression model assuming minimal number of excess zeroes • Zero-inflated negative binomial regression model when excess zeroes are present • Zero-hurdle negative binomial regression model when excess zeroes are present
Standardized Uptake Value Ratio	Right Skew		• Logistic regression after dichotomizing outcome • Poisson regression with robust error variance after dichotomizing outcome • Quantile regression to account for skew

3.3.9. Longitudinal Analyses

Like longitudinal analyses of cognitive decline and incident dementia, longitudinal analyses of MRI and PET scans need to account for bias caused by informative attrition. A common solution is to employ multiple imputation by chained equations (MICE) described in detail in Section 3.1.[23,24] Alternative approaches include the use of pattern mixture models,[25-27] selection

models,[28-30] shared parameter models,[27,28] or inverse probability weighting (Section 3.2). When appropriate, more than one method may be applied. For example, an analyst might use MICE to impute missing values for a longitudinal analysis restricted to all participants who completed a MRI scan at Visit 5 and use probability weighting (Section 3.3.1) in a model with robust standard errors to generate parameter estimates that correspond to the ARIC cohort at Visit 5. Before imputing values, the dataset should be restricted to the analytic sample. Key variables commonly incorporated into the imputation model include the following.

1. The exposure. If multiple iterations of the exposure (e.g. standardized, dichotomized, quartiles, etc.) will be examined then analysts are encouraged to include the original version of the variable in the imputation model and then apply the necessary transformations post-imputation.
2. The primary outcome at both concurrent and prior assessments.
3. Time-invariant covariates measured at the baseline assessment such as sex ([DERIVE##]GENDER##), race-center ([DERIVE##]RACEGRP## and [DERIVE##]CENTER), education ([DERIVE1#]ELEVEL02), mean-centered age ([DERIVE##]V#AGE##), and the presence of the apolipoprotein ε4 genotype ([APOE_NEW_P]APOEA_112) which is typically defined as dichotomous (0 alleles versus 1 or more alleles) but may alternatively be defined as trichotomous (0 alleles, 1 allele, or 2 alleles).
4. Time-varying covariates present in DERIVE## such as diabetes, hypertension, and cigarette use. Please note that continuous covariates are typically mean-centered.

Future versions of this manual will provide more detailed recommendations based on ongoing analyses.

Analysts utilizing MICE must also consider how specific choices made when constructing the imputation model may impact the interpretation of parameter estimates (Section 3.1). Pertinent decisions include the following.

1. Whether to include or remove deceased participants[31] and whether to include a dichotomous indicator that denotes if a participant is living or dead during each visit.

2. How to define when a participant with a missing assessment might have completed a MRI or PET scan. The definition may involve calculating the median time from baseline for all participants who completed a scan as well as calculating the date 180 days before the date of death for deceased participants.
3. Whether to impute all outcomes of interest in the same imputation model or in separate imputation models.
4. Whether imputed values that defy plausibility need to be winsorized, such as a negative value for brain volume.
5. Whether to employ single level or multilevel imputation.[32]
6. How to evaluate the performance of the imputation model[33] and determine whether it should be refined by integrating auxiliary variables or specifying interactions.
7. The number of imputed datasets to generate.[34]

After appropriate steps have been taken to address informative attrition, most analysts perform one of three types of longitudinal analyses. The first type is prospective and involves analyzing MRI or PET scans from two points in time. The same variable transformations, models, and link functions utilized when conducting cross-sectional analyses can be applied to prospective analyses. The value of the outcome at the baseline and the time between assessments are typically included as covariates, but this decision rests on the proposed hypotheses and envisioned causal pathways.[35] Some analysts also opt to compute a new outcome that reflects the change or rate of change between two time points. However, this approach is strongly discouraged as it can introduce error into causal analyses[34] and reduce power (Section 3.1.2). A better alternative is to perform the second type of longitudinal analysis which utilizes generalized estimation equations (GEEs) or mixed effects models. GEE and mixed effects models permit analysts to incorporate measures from multiple points in time and calculate the rate of change by specifying an interaction with time. GEEs with robust standard errors and an unstructured correlation matrix generate estimates of change with population-averaged interpretations. Mixed effects models with a random intercept, a random time slope, and an unstructured covariance matrix calculate estimates of change with subject-specific

interpretations. Details and modeling options, such as alternative specifications of the covariance matrices and random effects, are described in Section 3.1.2. The third type of analysis is three-level or cross-classified mixed effects models that examine brain regions nested within visits nested within participants. This analysis often requires the measure from each region to be placed on the same scale prior to model fitting (Section 3.3.8).

Table 3.3.5. Suggested approaches for longitudinal analyses

Outcome	Distribution	Levels	Models
Brain Volume	Normal	One-level prospective model, generalized estimating equation, two-level mixed effects model, two-level cross-classified mixed effects models, or three-level mixed effects model	• Linear regression with total intracranial volume as a covariate
Cortical Thickness	Normal		• Linear regression
White Matter Hyperintensities	Strong Right Skew		• Linear regression after applying log transformation to outcome with total intracranial volume as a covariate • Generalized linear regression with a gamma distribution and a log link function with total intracranial volume as a covariate
Mean Diffusivity	Modest Right Skew		• Linear regression • Quantile regression to account for skew
Fractional Anisotropy	Modest Right Skew		• Linear regression • Quantile regression to account for skew
Infarctions and Microhemorrhages	Negative Binomial		• Logistic regression after dichotomizing outcome • Poisson regression with robust error variance after dichotomizing outcome • Negative binomial regression model assuming minimal number of excess zeroes • Zero-inflated negative binomial regression model when excess zeroes are present • Zero-hurdle negative binomial regression model when excess zeroes are present
Standardized Uptake Value Ratio	Right Skew		• Logistic regression after dichotomizing outcome • Poisson regression with robust error variance after dichotomizing outcome • Quantile regression to account for skew

3.3.10. Utilizing Model Diagnostics

For both cross-sectional and longitudinal analyses, diagnostics should be employed to evaluate the primary model(s). Common visualizations include the following.

1. The mean of model residuals overall, by levels of the exposure, and by levels of key covariates such as gender and race. Examining residuals across time or visits is also pertinent when fitting longitudinal models.

2. A histogram or Q-Q plot of model residuals to assess the normality of errors.
3. Scatterplots of model residuals against predicted values from the model.
4. Scatterplots of continuous covariates across time if the covariates have a statistically significant interaction with time in a longitudinal model.

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Appendix A: Confirmatory Factor Analysis Models With Categorical Indicators

Prior to analysis in Mplus, neurocognitive tests were converted into the derived variables depicted below. The Trails Making Tests were also reversed so that the lowest possible score was 0 and the highest possible score was 240.

Variable	Label	Definition
DWRC	Delayed Word Recall Categorized	If DWR is 0 or 1 then DWRC is 0 Else if DWR is 2 then DWRC is 1 Else if DWR is 3 then DWRC is 2 Else if DWR is 4 then DWRC is 3 Else if DWR is 5 then DWRC is 4 Else if DWR is 6 then DWRC is 5 Else if DWR is 7 then DWRC is 6 Else if DWR is 8 then DWRC is 7 Else if DWR is 9 then DWRC is 8 Else if DWR is 10 then DWRC is 9
DSSC	Digit Symbol Substitution Categorized	If DSS is equal to or greater than 0 and less than 26 then DSSC is 0 Else if DSS is equal to or greater than 26 and less than 33 then DSSC is 1 Else if DSS is equal to or greater than 33 and less than 38 then DSSC is 2 Else if DSS is equal to or greater than 38 and less than 43 then DSSC is 3 Else if DSS is equal to or greater than 43 and less than 46 then DSSC is 4 Else if DSS is equal to or greater than 46 and less than 50 then DSSC is 5 Else if DSS is equal to or greater than 50 and less than 55 then DSSC is 6 Else if DSS is equal to or greater than 55 and less than 60 then DSSC is 7 Else if DSS is equal to or greater than 60 then DSSC is 8
WFTFC	Phonemic Fluency Categorized (F)	If WFTF is equal to or greater than 0 and less than 4 then WFTFC is 0 Else if WFTF is equal to or greater than 4 and less than 6 then WFTFC is 1 Else if WFTF is equal to or greater than 6 and less than 8 then WFTFC is 2 Else if WFTF is equal to or greater than 8 and less than 10 then WFTFC is 3 Else if WFTF is equal to or greater than 10 and less than 12 then WFTFC is 4 Else if WFTF is equal to or greater than 12 and less than 14 then WFTFC is 5 Else if WFTF is equal to or greater than 14 and less than 16 then WFTFC is 6 Else if WFTF is equal to or greater than 16 and less than 18 then WFTFC is 7 Else if WFTF is equal to or greater than 18 then WFTFC is 8
WFTAC	Phonemic Fluency Categorized (A)	If WFTA is equal to or greater than 0 and less than 4 then WFTAC is 0 Else if WFTA is equal to or greater than 4 and less than 6 then WFTAC is 1 Else if WFTA is equal to or greater than 6 and less than 8 then WFTAC is 2 Else if WFTA is equal to or greater than 8 and less than 10 then WFTAC is 3 Else if WFTA is equal to or greater than 10 and less than 12 then WFTAC is 4 Else if WFTA is equal to or greater than 12 and less than 14 then WFTAC is 5 Else if WFTA is equal to or greater than 14 and less than 16 then WFTAC is 6 Else if WFTA is equal to or greater than 16 and less than 18 then WFTAC is 7 Else if WFTA is equal to or greater than 18 then WFTAC is 8
WFTSC	Phonemic Fluency Categorized (S)	If WFTS is equal to or greater than 0 and less than 4 then WFTSC is 0 Else if WFTS is equal to or greater than 4 and less than 6 then WFTSC is 1 Else if WFTS is equal to or greater than 6 and less than 8 then WFTSC is 2 Else if WFTS is equal to or greater than 8 and less than 10 then WFTSC is 3 Else if WFTS is equal to or greater than 10 and less than 12 then WFTSC is 4

Variable	Label	Definition
		Else if WFTS is equal to or greater than 12 and less than 14 then WFTSC is 5 Else if WFTS is equal to or greater than 14 and less than 16 then WFTSC is 6 Else if WFTS is equal to or greater than 16 and less than 18 then WFTSC is 7 Else if WFTS is equal to or greater than 18 then WFTSC is 8
WFTTC	Phonemic Fluency Categorized (FAS)	If WFTT is equal to or greater than 0 and less than 19 then WFTTC is 0 Else if WFTT is equal to or greater than 19 and less than 24 then WFTTC is 1 Else if WFTT is equal to or greater than 24 and less than 28 then WFTTC is 2 Else if WFTT is equal to or greater than 28 and less than 32 then WFTTC is 3 Else if WFTT is equal to or greater than 32 and less than 35 then WFTTC is 4 Else if WFTT is equal to or greater than 35 and less than 39 then WFTTC is 5 Else if WFTT is equal to or greater than 39 and less than 43 then WFTTC is 6 Else if WFTT is equal to or greater than 43 and less than 49 then WFTTC is 7 Else if WFTT is equal to or greater than 49 then WFTTC is 8
ILRPC	Incidental Learning Categorized (Digit-Symbol Pairs Score)	ILRPC is equal to variable ILRP
ILRSC	Incidental Learning Categorized (Symbols Score)	ILRPC is equal to variable ILRS
ANSC	Semantic Fluency Categorized	If ANS is equal to or greater than 0 and less than 11 then ANSC is 0 Else if ANS is equal to or greater than 11 and less than 13 then ANSC is 1 Else if ANS is equal to or greater than 13 and less than 15 then ANSC is 2 Else if ANS is equal to or greater than 15 and less than 16 then ANSC is 3 Else if ANS is equal to or greater than 16 and less than 17 then ANSC is 4 Else if ANS is equal to or greater than 17 and less than 19 then ANSC is 5 Else if ANS is equal to or greater than 19 and less than 21 then ANSC is 6 Else if ANS is equal to or greater than 21 and less than 23 then ANSC is 7 Else if ANS is equal to or greater than 23 then ANSC is 8
LMTAC	Logical Memory Categorized (I Story A)	If LMTA is equal to or greater than 0 and less than 6 then LMTAC is 0 Else if LMTA is equal to or greater than 6 and less than 8 then LMTAC is 1 Else if LMTA is equal to or greater than 8 and less than 9 then LMTAC is 2 Else if LMTA is equal to or greater than 9 and less than 10 then LMTAC is 3 Else if LMTA is equal to or greater than 10 and less than 11 then LMTAC is 4 Else if LMTA is equal to or greater than 11 and less than 12 then LMTAC is 5 Else if LMTA is equal to or greater than 12 and less than 13 then LMTAC is 6 Else if LMTA is equal to or greater than 13 and less than 15 then LMTAC is 7 Else if LMTA is equal to or greater than 15 and less than 17 then LMTAC is 8 Else if LMTA is equal to or greater than 17 then LMTAC is 9
LMTBC	Logical Memory Categorized (I Story B)	If LMTB is equal to or greater than 0 and less than 6 then LMTBC is 0 Else if LMTB is equal to or greater than 6 and less than 8 then LMTBC is 1 Else if LMTB is equal to or greater than 8 and less than 9 then LMTBC is 2 Else if LMTB is equal to or greater than 9 and less than 10 then LMTBC is 3 Else if LMTB is equal to or greater than 10 and less than 11 then LMTBC is 4 Else if LMTB is equal to or greater than 11 and less than 12 then LMTBC is 5 Else if LMTB is equal to or greater than 12 and less than 13 then LMTBC is 6 Else if LMTB is equal to or greater than 13 and less than 15 then LMTBC is 7 Else if LMTB is equal to or greater than 15 and less than 17 then LMTBC is 8 Else if LMTB is equal to or greater than 17 then LMTBC is 9

Variable	Label	Definition
LMTCC	Logical Memory Categorized (II Story A)	If LMTC is equal to or greater than 0 and less than 3 then LMTCC is 0 Else if LMTC is equal to or greater than 3 and less than 5 then LMTCC is 1 Else if LMTC is equal to or greater than 5 and less than 7 then LMTCC is 2 Else if LMTC is equal to or greater than 7 and less than 8 then LMTCC is 3 Else if LMTC is equal to or greater than 8 and less than 9 then LMTCC is 4 Else if LMTC is equal to or greater than 9 and less than 10 then LMTCC is 5 Else if LMTC is equal to or greater than 10 and less than 11 then LMTCC is 6 Else if LMTC is equal to or greater than 11 and less than 13 then LMTCC is 7 Else if LMTC is equal to or greater than 13 and less than 15 then LMTCC is 8 Else if LMTC is equal to or greater than 15 then LMTCC is 9
LMTDC	Logical Memory Categorized (II Story B)	If LMTD is equal to or greater than 0 and less than 3 then LMTDC is 0 Else if LMTD is equal to or greater than 3 and less than 5 then LMTDC is 1 Else if LMTD is equal to or greater than 5 and less than 7 then LMTDC is 2 Else if LMTD is equal to or greater than 7 and less than 8 then LMTDC is 3 Else if LMTD is equal to or greater than 8 and less than 9 then LMTDC is 4 Else if LMTD is equal to or greater than 9 and less than 10 then LMTDC is 5 Else if LMTD is equal to or greater than 10 and less than 11 then LMTDC is 6 Else if LMTD is equal to or greater than 11 and less than 13 then LMTDC is 7 Else if LMTD is equal to or greater than 13 and less than 15 then LMTDC is 8 Else if LMTD is equal to or greater than 15 then LMTDC is 9
LMTTC	Logical Memory Categorized	If LMT is equal to or greater than 0 and less than 20 then LMTTC is 0 Else if LMT is equal to or greater than 20 and less than 26 then LMTTC is 1 Else if LMT is equal to or greater than 26 and less than 31 then LMTTC is 2 Else if LMT is equal to or greater than 31 and less than 36 then LMTTC is 3 Else if LMT is equal to or greater than 36 and less than 41 then LMTTC is 4 Else if LMT is equal to or greater than 41 and less than 45 then LMTTC is 5 Else if LMT is equal to or greater than 45 and less than 50 then LMTTC is 6 Else if LMT is equal to or greater than 50 and less than 57 then LMTTC is 7 Else if LMT is equal to or greater than 57 then LMTTC is 8
DSBC	Digit Span Backwards Categorized	If DSB is between 0 and 2 then DSBC is 0 Else if DSB is 3 then DSBC is 1 Else if DSB is 4 then DSBC is 2 Else if DSB is 5 then DSBC is 3 Else if DSB is 6 then DSBC is 4 Else if DSB is 7 then DSBC is 5 Else if DSB is 8 then DSBC is 6 Else if DSB is 9 then DSBC is 7 Else if DSB is between 10 and 12 then DSBC is 8
BNTC	Boston Naming Test Categorized	If BNT is equal to or greater than 0 and less than 16 then BNTC is 0 Else if BNT is equal to or greater than 16 and less than 22 then BNTC is 1 Else if BNT is equal to or greater than 22 and less than 24 then BNTC is 2 Else if BNT is equal to or greater than 24 and less than 26 then BNTC is 3 Else if BNT is equal to or greater than 26 and less than 27 then BNTC is 4 Else if BNT is equal to or greater than 27 and less than 28 then BNTC is 5 Else if BNT is equal to or greater than 28 and less than 29 then BNTC is 6 Else if BNT is equal to or greater than 29 and less than 30 then BNTC is 7 Else if BNT is equal to or greater than 30 then BNTC is 8
TMTAC	Trails Making Test A Reversed Categorized	If TMTA is equal to or greater than 0 and less than 160 then TMTAC is 0 Else if TMTA is equal to or greater than 160 and less than 180 then TMTAC is 1

Variable	Label	Definition
		Else if TMTA is equal to or greater than 180 and less than 189 then TMTAC is 2 Else if TMTA is equal to or greater than 189 and less than 196 then TMTAC is 3 Else if TMTA is equal to or greater than 196 and less than 201 then TMTAC is 4 Else if TMTA is equal to or greater than 201 and less than 205 then TMTAC is 5 Else if TMTA is equal to or greater than 205 and less than 209 then TMTAC is 6 Else if TMTA is equal to or greater than 209 and less than 214 then TMTAC is 7 Else if TMTA is equal to or greater than 214 then TMTAC is 8
TMTBC	Trails Making Test B Reversed Categorized	If TMTB is equal to or greater than 0 and less than 1 then TMTBC is 0 Else if TMTB is equal to or greater than 1 and less than 54 then TMTBC is 1 Else if TMTB is equal to or greater than 54 and less than 96 then TMTBC is 2 Else if TMTB is equal to or greater than 96 and less than 121 then TMTBC is 3 Else if TMTB is equal to or greater than 121 and less than 137 then TMTBC is 4 Else if TMTB is equal to or greater than 137 and less than 150 then TMTBC is 5 Else if TMTB is equal to or greater than 150 and less than 162 then TMTBC is 6 Else if TMTB is equal to or greater than 162 and less than 175 then TMTBC is 7 Else if TMTB is equal to or greater than 175 then TMTBC is 8
TCRDAC	CERAD Word List Categorized (Immediate Trial 1) - Phone	TCRDAC is equal to TCRDA If TCRDA is equal to 10 then TCRDA is 9
TCRDBC	CERAD Word List Categorized (Immediate Trial 2) - Phone	TCRDBC is equal to TCRDB If TCRDB is equal to 10 then TCRDB is 9
TCRDCC	CERAD Word List Categorized (Immediate Trial 3) - Phone	TCRDCC is equal to TCRDC If TCRDC is equal to 10 then TCRDC is 9
TCRDDC	CERAD Word List Categorized (Delayed) - Phone	TCRDDC is equal to TCRDD If TCRDD is equal to 10 then TCRDD is 9
TWFTFC	Phonemic Fluency Categorized (F) - Phone	If TWFTF is equal to or greater than 0 and less than 4 then TWFTFC is 0 If TWFTF is equal to or greater than 4 and less than 6 then TWFTFC is 1 If TWFTF is equal to or greater than 6 and less than 8 then TWFTFC is 2 If TWFTF is equal to or greater than 8 and less than 10 then TWFTFC is 3 If TWFTF is equal to or greater than 10 and less than 12 then TWFTFC is 4 If TWFTF is equal to or greater than 12 and less than 14 then TWFTFC is 5 If TWFTF is equal to or greater than 14 and less than 16 then TWFTFC is 6 If TWFTF is equal to or greater than 16 and less than 18 then TWFTFC is 7 If TWFTF is equal to or greater than 18 then TWFTFC is 8
TWFTAC	Phonemic Fluency Categorized (A) - Phone	If TWFTA is equal to or greater than 0 and less than 4 then TWFTAC is 0 If TWFTA is equal to or greater than 4 and less than 6 then TWFTAC is 1 If TWFTA is equal to or greater than 6 and less than 8 then TWFTAC is 2 If TWFTA is equal to or greater than 8 and less than 10 then TWFTAC is 3 If TWFTA is equal to or greater than 10 and less than 12 then TWFTAC is 4 If TWFTA is equal to or greater than 12 and less than 14 then TWFTAC is 5 If TWFTA is equal to or greater than 14 and less than 16 then TWFTAC is 6 If TWFTA is equal to or greater than 16 and less than 18 then TWFTAC is 7 If TWFTA is equal to or greater than 18 then TWFTAC is 8
TANSC	Semantic Fluency Categorized - Phone	If TANS is equal to or greater than 0 and less than 11 then TANSC is 0 If TANS is equal to or greater than 11 and less than 13 then TANSC is 1 If TANS is equal to or greater than 13 and less than 15 then TANSC is 2

Variable	Label	Definition
		If TANS is equal to or greater than 15 and less than 16 then TANSC is 3 If TANS is equal to or greater than 16 and less than 17 then TANSC is 4 If TANS is equal to or greater than 17 and less than 19 then TANSC is 5 If TANS is equal to or greater than 19 and less than 21 then TANSC is 6 If TANS is equal to or greater than 21 and less than 23 then TANSC is 7 If TANS is equal to or greater than 23 then TANSC is 8
TDSBC	Digit Span Backwards Categorized - Phone	If TDSB is between 0 and 2 then TDSBC is 0 Else if TDSB is 3 then TDSBC is 1 Else if TDSB is 4 then TDSBC is 2 Else if TDSB is 5 then TDSBC is 3 Else if TDSB is 6 then TDSBC is 4 Else if TDSB is 7 then TDSBC is 5 Else if TDSB is 8 then TDSBC is 6 Else if TDSB is 9 then TDSBC is 7 Else if TDSB is between 10 and 12 then TDSBC is 8

The derived variables were integrated into a confirmatory factor analysis model. Global cognition factor scores were produced using the following Mplus syntax. The number appended to the end of each derived variable indicates the corresponding ARIC visit. For example, DWRC2 is the categorized version of the DWR from Visit 2. When the letter M is appended, the derived variable is from the brain MRI sub-study.

A.1. In Person Assessments Only (Version 1)

```
DATA: FILE = FactorsMplus.dat;

VARIABLE:
NAMES = MPLUSID
DWRC2 DSSC2 WFTTC2
DWRCM ILRPCM DSSCM LMTTCM TMTACM TMTBCM
WFTTCM ANSCM ILRSCM
LMTACM LMTBCM LMTCCM LMTDCM WFTFCM
WFTACM WFTSCM
DWRC4 DSSC4 WFTTC4
DWRC5 WFTTC5 DSSC5 ILRPC5 ANSC5 DSBC5
BNTC5 LMTTC5 TMTAC5 TMTBC5 ILRSC5
LMTAC5 LMTBC5 LMTCC5 LMTDC5 WFTFC5 WFTAC5 WFTSC5
DWRC6 WFTTC6 DSSC6 ILRPC6 ANSC6 DSBC6
BNTC6 LMTTC6 TMTAC6 TMTBC6 ILRSC6
LMTAC6 LMTBC6 LMTCC6 LMTDC6 WFTFC6 WFTAC6 WFTSC6
DWRC7 WFTTC7 DSSC7 ILRPC7 ANSC7 DSBC7
BNTC7 LMTTC7 TMTAC7 TMTBC7 ILRSC7
LMTAC7 LMTBC7 LMTCC7 LMTDC7 WFTFC7 WFTAC7 WFTSC7
DWRC8 DSSC8 WFTTC8 WFTFC8 WFTAC8 WFTSC8
ILRPC8 ILRSC8 ANSC8
LMTC8 LMTAC8 LMTBC8 LMTCC8 LMTDC8 DSBC8 BNTC8
TMTAC8 TMTBC8
TCRDAC8 TCRDBC8 TCRDCC8 TCRDDC8
TWFTFC8 TWFTAC8 TANSC8 TDSBC8 TTMTAC8 TTMTBC8
DWRC9 DSSC9 WFTTC9 WFTFC9 WFTAC9 WFTSC9
ILRPC9 ILRSC9 ANSC9
LMTC9 LMTAC9 LMTBC9 LMTCC9 LMTDC9 DSBC9 BNTC9
TMTAC9 TMTBC9
TCRDAC9 TCRDBC9 TCRDCC9 TCRDDC9
TWFTFC9 TWFTAC9 TANSC9 TDSBC9 TTMTAC9 TTMTBC9;

USEVARIABLES =
DWRC2 DSSC2 WFTTC2
DWRCM ILRPCM DSSCM LMTTCM TMTACM
TMTBCM WFTTCM ANSCM
DWRC4 DSSC4 WFTTC4
DWRC5 WFTTC5 DSSC5 ILRPC5 ANSC5
DSBC5 BNTC5 LMTTC5 TMTAC5 TMTBC5
DWRC6 WFTTC6 DSSC6 ILRPC6 ANSC6
DSBC6 BNTC6 LMTTC6 TMTAC6 TMTBC6
DWRC7 WFTTC7 DSSC7 ILRPC7 ANSC7
DSBC7 BNTC7 LMTTC7 TMTAC7 TMTBC7
DWRC8 WFTTC8 DSSC8 ILRPC8 ANSC8
DSBC8 BNTC8 LMTTC8 TMTAC8 TMTBC8
DWRC9 WFTTC9 DSSC9 ILRPC9 ANSC9
DSBC9 BNTC9 LMTTC9 TMTAC9 TMTBC9;

MISSING = ALL (-9999);
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CATEGORICAL =
DWRC2 DSSC2 WFTTC2
DWRCM ILRPCM DSSCM LMTTCM TMTACM
TMTBCM WFTTCM ANSCM
DWRC4 DSSC4 WFTTC4
DWRC5 WFTTC5 DSSC5 ILRPC5 ANSC5
DSBC5 BNTC5 LMTTC5 TMTAC5 TMTBC5
DWRC6 WFTTC6 DSSC6 ILRPC6 ANSC6
DSBC6 BNTC6 LMTTC6 TMTAC6 TMTBC6
DWRC7 WFTTC7 DSSC7 ILRPC7 ANSC7
DSBC7 BNTC7 LMTTC7 TMTAC7 TMTBC7
DWRC8 WFTTC8 DSSC8 ILRPC8 ANSC8
DSBC8 BNTC8 LMTTC8 TMTAC8 TMTBC8
DWRC9 WFTTC9 DSSC9 ILRPC9 ANSC9
DSBC9 BNTC9 LMTTC9 TMTAC9 TMTBC9;

IDVARIABLE = MPLUSID;

ANALYSIS:
ESTIMATOR=MLR;
ALGORITHM=EM;
COVERAGE=.0001;
INTEGRATION=MONTECARLO;

MODEL:
GCV21 BY WFTTC2@1.497;
GCV21 BY DSSC2@2.779;
GCV21 BY DWRC2@1.139;
[GCV21@0.688];
GCV21@1.069;

GCV41 BY WFTTC4@1.497;
GCV41 BY DSSC4@2.779;
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[GCV41@0.631];
GCV41@0.964;

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GCVM1 BY ANSCM@1.667;
GCVM1 BY DSSCM@2.779;
GCVM1 BY TMTACM@2.337;
GCVM1 BY TMTBCM@3.310;
GCVM1 BY ILRPCM@1.375;
GCVM1 BY LMTTCM@1.414;
GCVM1 BY DWRCM@1.139;
[GCVM1@-0.120];
GCVM1@0.915;

GCV51 BY DSBC5@1.351;
GCV51 BY BNTC5@1.752;
GCV51 BY WFTTC5@1.497;
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GCV51 BY ANSC5@1.667;
GCV51 BY DSSC5@2.779;
GCV51 BY TMTAC5@2.337;
GCV51 BY TMTBC5@3.310;
GCV51 BY ILRPC5@1.375;
GCV51 BY LMTTC5@1.414;
GCV51 BY DWRC5@1.139;
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GCV51@1;

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GCV61 BY BNTC6@1.752;
GCV61 BY WFTTC6@1.497;
GCV61 BY ANSC6@1.667;
GCV61 BY DSSC6@2.779;
GCV61 BY TMTAC6@2.337;
GCV61 BY TMTBC6@3.310;
GCV61 BY ILRPC6@1.375;
GCV61 BY LMTTC6@1.414;
GCV61 BY DWRC6@1.139;
[GCV61@-0.103];
GCV61@0.920;

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GCV71 BY WFTTC7@1.497;
GCV71 BY ANSC7@1.667;
GCV71 BY DSSC7@2.779;
GCV71 BY TMTAC7@2.337;
GCV71 BY TMTBC7@3.310;
GCV71 BY ILRPC7@1.375;
GCV71 BY LMTTC7@1.414;
GCV71 BY DWRC7@1.139;
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GCV71@1.011;

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GCV81 BY BNTC8@1.752;
GCV81 BY WFTTC8@1.497;
GCV81 BY ANSC8@1.667;
GCV81 BY DSSC8@2.779;
GCV81 BY TMTAC8@2.337;
GCV81 BY TMTBC8@3.310;
GCV81 BY ILRPC8@1.375;
GCV81 BY LMTTC8@1.414;
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GCV81@0.765;

GCV91 BY DSBC9@1.351;
GCV91 BY BNTC9@1.752;
GCV91 BY WFTTC9@1.497;
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GCV91 BY TMTAC9@2.337;
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GCV91 BY ILRPC9@1.375;
GCV91 BY LMTTC9@1.414;
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[DSSC6$8@5.721];

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[TMTAC6$2@-2.053];
[TMTAC6$3@-1.1];
[TMTAC6$4@-0.143];
[TMTAC6$5@0.658];
[TMTAC6$6@1.424];
[TMTAC6$7@2.286];
[TMTAC6$8@3.68];

[TMTBC6$1@-2.588];
[TMTBC6$2@-1.856];
[TMTBC6$3@-0.775];
[TMTBC6$4@0.199];
[TMTBC6$5@1.141];
[TMTBC6$6@2.084];
[TMTBC6$7@3.123];
[TMTBC6$8@4.644];

[ILRPC6$1@-2.406];
[ILRPC6$2@-1.235];
[ILRPC6$3@-0.376];
[ILRPC6$4@0.41];
[ILRPC6$5@1.205];
[ILRPC6$6@2.06];
[ILRPC6$7@2.746];
[ILRPC6$8@3.709];
[ILRPC6$9@4.705];

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[LMTTC6$2@-1.626];
[LMTTC6$3@-0.899];
[LMTTC6$4@-0.225];
[LMTTC6$5@0.416];
[LMTTC6$6@0.949];
[LMTTC6$7@1.641];
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[DWRC6$3@-1.897];
[DWRC6$4@-0.906];
[DWRC6$5@0.238];
[DWRC6$6@1.416];
[DWRC6$7@2.712];
[DWRC6$8@4.336];
[DWRC6$9@6.299];

[DSBC7$1@-3.141];
[DSBC7$2@-2.173];
[DSBC7$3@-1.05];
[DSBC7$4@0.087];
[DSBC7$5@1.374];
[DSBC7$6@2.298];
[DSBC7$7@3.18];
[DSBC7$8@4.11];

[BNTC7$1@-3.25];
[BNTC7$2@-1.848];
[BNTC7$3@-1.185];
[BNTC7$4@-0.303];
[BNTC7$5@0.211];
[BNTC7$6@0.891];
[BNTC7$7@1.838];
[BNTC7$8@3.276];

[WFTTC7$1@-2.497];
[WFTTC7$2@-1.476];
[WFTTC7$3@-0.673];
[WFTTC7$4@0.007];
[WFTTC7$5@0.499];
[WFTTC7$6@1.162];
[WFTTC7$7@1.853];
[WFTTC7$8@2.901];

[ANSC7$1@-2.674];
[ANSC7$2@-1.606];
[ANSC7$3@-0.568];
[ANSC7$4@-0.07];
[ANSC7$5@0.44];
[ANSC7$6@1.323];
[ANSC7$7@2.158];
[ANSC7$8@2.997];

[DSSC7$1@-2.943];
[DSSC7$2@-1.135];
[DSSC7$3@0.106];
[DSSC7$4@1.417];
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[DSSC7$5@2.279];
[DSSC7$6@3.213];
[DSSC7$7@4.431];
[DSSC7$8@5.721];

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[TMTAC7$2@-2.053];
[TMTAC7$3@-1.1];
[TMTAC7$4@-0.143];
[TMTAC7$5@0.658];
[TMTAC7$6@1.424];
[TMTAC7$7@2.286];
[TMTAC7$8@3.68];

[TMTBC7$1@-2.588];
[TMTBC7$2@-1.856];
[TMTBC7$3@-0.775];
[TMTBC7$4@0.199];
[TMTBC7$5@1.141];
[TMTBC7$6@2.084];
[TMTBC7$7@3.123];
[TMTBC7$8@4.644];

[ILRPC7$1@-2.406];
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[ILRPC7$5@1.205];
[ILRPC7$6@2.06];
[ILRPC7$7@2.746];
[ILRPC7$8@3.709];
[ILRPC7$9@4.705];

[LMTTC7$1@-2.543];
[LMTTC7$2@-1.626];
[LMTTC7$3@-0.899];
[LMTTC7$4@-0.225];
[LMTTC7$5@0.416];
[LMTTC7$6@0.949];
[LMTTC7$7@1.641];
[LMTTC7$8@2.668];

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[DWRC7$2@-2.761];
[DWRC7$3@-1.897];
[DWRC7$4@-0.906];
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[DWRC7$9@6.299];
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[DSBC8$5@1.374];
[DSBC8$6@2.298];
[DSBC8$7@3.18];
[DSBC8$8@4.11];

[BNTC8$1@-3.25];
[BNTC8$2@-1.848];
[BNTC8$3@-1.185];
[BNTC8$4@-0.303];
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[BNTC8$6@0.891];
[BNTC8$7@1.838];
[BNTC8$8@3.276];

[WFTTC8$1@-2.497];
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[WFTTC8$5@0.499];
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[ANSC8$1@-2.674];
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[ANSC8$3@-0.568];
[ANSC8$4@-0.07];
[ANSC8$5@0.44];
[ANSC8$6@1.323];
[ANSC8$7@2.158];
[ANSC8$8@2.997];

[DSSC8$1@-2.943];
[DSSC8$2@-1.135];
[DSSC8$3@0.106];
[DSSC8$4@1.417];
[DSSC8$5@2.279];
[DSSC8$6@3.213];
[DSSC8$7@4.431];
[DSSC8$8@5.721];

[TMTAC8$1@-3.539];
[TMTAC8$2@-2.053];
[TMTAC8$3@-1.1];
[TMTAC8$4@-0.143];
[TMTAC8$5@0.658];
[TMTAC8$6@1.424];
[TMTAC8$7@2.286];
```

```
[TMTAC8$8@3.68];

[TMTBC8$1@-2.588];
[TMTBC8$2@-1.856];
[TMTBC8$3@-0.775];
[TMTBC8$4@0.199];
[TMTBC8$5@1.141];
[TMTBC8$6@2.084];
[TMTBC8$7@3.123];
[TMTBC8$8@4.644];

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[ILRPC8$3@-0.376];
[ILRPC8$4@0.41];
[ILRPC8$5@1.205];
[ILRPC8$6@2.06];
[ILRPC8$7@2.746];
[ILRPC8$8@3.709];
[ILRPC8$9@4.705];

[LMTTC8$1@-2.543];
[LMTTC8$2@-1.626];
[LMTTC8$3@-0.899];
[LMTTC8$4@-0.225];
[LMTTC8$5@0.416];
[LMTTC8$6@0.949];
[LMTTC8$7@1.641];
[LMTTC8$8@2.668];

[DWRC8$1@-3.313];
[DWRC8$2@-2.761];
[DWRC8$3@-1.897];
[DWRC8$4@-0.906];
[DWRC8$5@0.238];
[DWRC8$6@1.416];
[DWRC8$7@2.712];
[DWRC8$8@4.336];
[DWRC8$9@6.299];

[DSBC9$1@-3.141];
[DSBC9$2@-2.173];
[DSBC9$3@-1.05];
[DSBC9$4@0.087];
[DSBC9$5@1.374];
[DSBC9$6@2.298];
[DSBC9$7@3.18];
[DSBC9$8@4.11];

[BNTC9$1@-3.25];
[BNTC9$2@-1.848];
[BNTC9$3@-1.185];
```

```
[BNTC9$4@-0.303];
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[WFTTC9$1@-2.497];
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[WFTTC9$5@0.499];
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[ANSC9$1@-2.674];
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[ANSC9$5@0.44];
[ANSC9$6@1.323];
[ANSC9$7@2.158];
[ANSC9$8@2.997];

[DSSC9$1@-2.943];
[DSSC9$2@-1.135];
[DSSC9$3@0.106];
[DSSC9$4@1.417];
[DSSC9$5@2.279];
[DSSC9$6@3.213];
[DSSC9$7@4.431];
[DSSC9$8@5.721];

[TMTAC9$1@-3.539];
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[TMTAC9$6@1.424];
[TMTAC9$7@2.286];
[TMTAC9$8@3.68];

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[TMTBC9$2@-1.856];
[TMTBC9$3@-0.775];
[TMTBC9$4@0.199];
[TMTBC9$5@1.141];
[TMTBC9$6@2.084];
[TMTBC9$7@3.123];
[TMTBC9$8@4.644];

[ILRPC9$1@-2.406];
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[ILRPC9$8@3.709];
[ILRPC9$9@4.705];

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[LMTTC9$2@-1.626];
[LMTTC9$3@-0.899];
[LMTTC9$4@-0.225];
[LMTTC9$5@0.416];
[LMTTC9$6@0.949];
[LMTTC9$7@1.641];
[LMTTC9$8@2.668];

[DWRC9$1@-3.313];
[DWRC9$2@-2.761];
[DWRC9$3@-1.897];
[DWRC9$4@-0.906];
[DWRC9$5@0.238];
[DWRC9$6@1.416];
[DWRC9$7@2.712];
[DWRC9$8@4.336];
[DWRC9$9@6.299];

GCV21 WITH GCV41@0 GCVM1@0
GCV51@0 GCV61@0 GCV71@0 GCV81@0 GCV91@0;

GCV41 WITH GCVM1@0 GCV51@0
GCV61@0 GCV71@0 GCV81@0 GCV91@0;

GCVM1 WITH GCV51@0 GCV61@0
GCV71@0 GCV81@0 GCV91@0;

GCV51 WITH GCV61@0 GCV71@0 GCV81@0 GCV91@0;

GCV61 WITH GCV71@0 GCV81@0 GCV91@0;

GCV71 WITH GCV81@0 GCV91@0;

GCV81 WITH GCV91@0;

OUTPUT:
STDYX RESIDUAL TECH1;

SAVEDATA:
save=fscores;
file=GloCog1.dat;
```

A.2. In Person and Phone Assessments, Invariant Tests (Version 4)

```
DATA: FILE = FactorsMplus.dat;

VARIABLE:
NAMES = MPLUSID
DWRC2 DSSC2 WFTTC2
DWRCM ILRPCM DSSCM LMTTCM TMTACM TMTBCM
WFTTCM ANSCM ILRSCM
LMTACM LMTBCM LMTCCM LMTDCM WFTFCM
WFTACM WFTSCM
DWRC4 DSSC4 WFTTC4
DWRC5 WFTTC5 DSSC5 ILRPC5 ANSC5 DSBC5
BNTC5 LMTTC5 TMTAC5 TMTBC5 ILRSC5
LMTAC5 LMTBC5 LMTCC5 LMTDC5 WFTFC5 WFTAC5 WFTSC5
DWRC6 WFTTC6 DSSC6 ILRPC6 ANSC6 DSBC6
BNTC6 LMTTC6 TMTAC6 TMTBC6 ILRSC6
LMTAC6 LMTBC6 LMTCC6 LMTDC6 WFTFC6 WFTAC6 WFTSC6
DWRC7 WFTTC7 DSSC7 ILRPC7 ANSC7 DSBC7
BNTC7 LMTTC7 TMTAC7 TMTBC7 ILRSC7
LMTAC7 LMTBC7 LMTCC7 LMTDC7 WFTFC7 WFTAC7 WFTSC7
DWRC8 DSSC8 WFTTC8 WFTFC8 WFTAC8 WFTSC8
ILRPC8 ILRSC8 ANSC8
LMTC8 LMTAC8 LMTBC8 LMTCC8 LMTDC8 DSBC8 BNTC8
TMTAC8 TMTBC8
TCRDAC8 TCRDBC8 TCRDCC8 TCRDDC8
TWFTFC8 TWFTAC8 TANSC8 TDSBC8 TTMTAC8 TTMTBC8
DWRC9 DSSC9 WFTTC9 WFTFC9 WFTAC9 WFTSC9
ILRPC9 ILRSC9 ANSC9
LMTC9 LMTAC9 LMTBC9 LMTCC9 LMTDC9 DSBC9 BNTC9
TMTAC9 TMTBC9
TCRDAC9 TCRDBC9 TCRDCC9 TCRDDC9
TWFTFC9 TWFTAC9 TANSC9 TDSBC9 TTMTAC9 TTMTBC9;

USEVARIABLES =
DWRC2 DSSC2 WFTTC2
DWRCM ILRPCM DSSCM
TMTACM TMTBCM ANSCM
ILRSCM LMTACM LMTBCM LMTCCM LMTDCM
WFTFCM WFTACM WFTSCM
DWRC4 DSSC4 WFTTC4
DWRC5 DSSC5 ILRPC5 ANSC5
DSBC5 BNTC5 TMTAC5 TMTBC5
ILRSC5 LMTAC5 LMTBC5 LMTCC5 LMTDC5
WFTFC5 WFTAC5 WFTSC5
DWRC6 DSSC6 ILRPC6 ANSC6
DSBC6 BNTC6 TMTAC6 TMTBC6
ILRSC6 LMTAC6 LMTBC6 LMTCC6 LMTDC6
WFTFC6 WFTAC6 WFTSC6
DWRC7 DSSC7 ILRPC7 ANSC7
DSBC7 BNTC7 TMTAC7 TMTBC7
```

```
ILRSC7 LMTAC7 LMTBC7 LMTCC7 LMTDC7
WFTFC7 WFTAC7 WFTSC7
DWRC8 DSSC8 ILRPC8 ANSC8
DSBC8 BNTC8 TMTAC8 TMTBC8
ILRSC8 LMTAC8 LMTBC8 LMTCC8 LMTDC8
WFTFC8 WFTAC8 WFTSC8
TTMTAC8 TTMTBC8 TANSC8 TDSBC8 TWFTAC8 TWFTFC8
TCRDAC8 TCRDBC8 TCRDCC8 TCRDDC8
DWRC9 DSSC9 ILRPC9 ANSC9
DSBC9 BNTC9 TMTAC9 TMTBC9
ILRSC9 LMTAC9 LMTBC9 LMTCC9 LMTDC9
WFTFC9 WFTAC9 WFTSC9
TTMTAC9 TTMTBC9 TANSC9 TDSBC9 TWFTAC9 TWFTFC9;

MISSING = ALL (-9999);

CATEGORICAL =
DWRC2 DSSC2 WFTTC2
DWRCM ILRPCM DSSCM
TMTACM TMTBCM ANSCM
ILRSCM LMTACM LMTBCM LMTCCM LMTDCM
WFTFCM WFTACM WFTSCM
DWRC4 DSSC4 WFTTC4
DWRC5 DSSC5 ILRPC5 ANSC5
DSBC5 BNTC5 TMTAC5 TMTBC5
ILRSC5 LMTAC5 LMTBC5 LMTCC5 LMTDC5
WFTFC5 WFTAC5 WFTSC5
DWRC6 DSSC6 ILRPC6 ANSC6
DSBC6 BNTC6 TMTAC6 TMTBC6
ILRSC6 LMTAC6 LMTBC6 LMTCC6 LMTDC6
WFTFC6 WFTAC6 WFTSC6
DWRC7 DSSC7 ILRPC7 ANSC7
DSBC7 BNTC7 TMTAC7 TMTBC7
ILRSC7 LMTAC7 LMTBC7 LMTCC7 LMTDC7
WFTFC7 WFTAC7 WFTSC7
DWRC8 DSSC8 ILRPC8 ANSC8
DSBC8 BNTC8 TMTAC8 TMTBC8
ILRSC8 LMTAC8 LMTBC8 LMTCC8 LMTDC8
WFTFC8 WFTAC8 WFTSC8
TTMTAC8 TTMTBC8 TANSC8 TDSBC8 TWFTAC8 TWFTFC8
TCRDAC8 TCRDBC8 TCRDCC8 TCRDDC8
DWRC9 DSSC9 ILRPC9 ANSC9
DSBC9 BNTC9 TMTAC9 TMTBC9
ILRSC9 LMTAC9 LMTBC9 LMTCC9 LMTDC9
WFTFC9 WFTAC9 WFTSC9
TTMTAC9 TTMTBC9 TANSC9 TDSBC9 TWFTAC9 TWFTFC9;

IDVARIABLE = MPLUSID;

ANALYSIS:
ESTIMATOR=MLR;
ALGORITHM=EM;
```

```
COVERAGE=.0001;
INTEGRATION=MONTECARLO(10000);

MODEL:
GCV24 BY WFTTC2@1.525;
GCV24 BY DSSC2@2.491;
GCV24 BY DWRC2@1.248;
[GCV24@0.684];
GCV24@1.025;

GCV44 BY WFTTC4@1.525;
GCV44 BY DSSC4@2.491;
GCV44 BY DWRC4@1.248;
[GCV44@0.629];
GCV44@0.932;

GCVM4 BY WFTFCM@2.157;
GCVM4 BY WFTACM@2.266;
GCVM4 BY WFTSCM@2.379;
GCVM4 BY ANSCM@1.739;
GCVM4 BY DSSCM@2.491;
GCVM4 BY TMTACM@2.339;
GCVM4 BY TMTBCM@3.301;
GCVM4 BY ILRPCM@2.219;
GCVM4 BY ILRSCM@2.792;
GCVM4 BY LMTACM@3.166;
GCVM4 BY LMTBCM@2.995;
GCVM4 BY LMTCCM@3.169;
GCVM4 BY LMTDCM@3.511;
GCVM4 BY DWRCM@1.248;
[GCVM4@-0.121];
GCVM4@0.848;



GCV54 BY DSBC5@1.353;
GCV54 BY BNTC5@1.811;
GCV54 BY WFTFC5@2.157;
GCV54 BY WFTAC5@2.266;
GCV54 BY WFTSC5@2.379;
GCV54 BY ANSC5@1.739;
GCV54 BY DSSC5@2.491;
GCV54 BY TMTAC5@2.339;
GCV54 BY TMTBC5@3.301;
GCV54 BY ILRPC5@2.219;
GCV54 BY ILRSC5@2.792;
GCV54 BY LMTAC5@3.166;
GCV54 BY LMTBC5@2.995;
GCV54 BY LMTCC5@3.169;
GCV54 BY LMTDC5@3.511;
GCV54 BY DWRC5@1.248;
[GCV54@0];
```

```
GCV54@1;

GCV64 BY DSBC6@1.353;
GCV64 BY BNTC6@1.811;
GCV64 BY WFTFC6@2.157;
GCV64 BY WFTAC6@2.266;
GCV64 BY WFTSC6@2.379;
GCV64 BY ANSC6@1.739;
GCV64 BY DSSC6@2.491;
GCV64 BY TMTAC6@2.339;
GCV64 BY TMTBC6@3.301;
GCV64 BY ILRPC6@2.219;
GCV64 BY ILRSC6@2.792;
GCV64 BY LMTAC6@3.166;
GCV64 BY LMTBC6@2.995;
GCV64 BY LMTCC6@3.169;
GCV64 BY LMTDC6@3.511;
GCV64 BY DWRC6@1.248;
[GCV64@-0.088];
GCV64@0.960;

GCV74 BY DSBC7@1.353;
GCV74 BY BNTC7@1.811;
GCV74 BY WFTFC7@2.157;
GCV74 BY WFTAC7@2.266;
GCV74 BY WFTSC7@2.379;
GCV74 BY ANSC7@1.739;
GCV74 BY DSSC7@2.491;
GCV74 BY TMTAC7@2.339;
GCV74 BY TMTBC7@3.301;
GCV74 BY ILRPC7@2.219;
GCV74 BY ILRSC7@2.792;
GCV74 BY LMTAC7@3.166;
GCV74 BY LMTBC7@2.995;
GCV74 BY LMTCC7@3.169;
GCV74 BY LMTDC7@3.511;
GCV74 BY DWRC7@1.248;
[GCV74@-0.088];
GCV74@1.036;

GCV84 BY DSBC8@1.353;
GCV84 BY BNTC8@1.811;
GCV84 BY WFTFC8@2.157;
GCV84 BY WFTAC8@2.266;
GCV84 BY WFTSC8@2.379;
GCV84 BY ANSC8@1.739;
GCV84 BY DSSC8@2.491;
GCV84 BY TMTAC8@2.339;
GCV84 BY TMTBC8@3.301;
GCV84 BY ILRPC8@2.219;
GCV84 BY ILRSC8@2.792;
GCV84 BY LMTAC8@3.166;
```

```
GCV84 BY LMTBC8@2.995;
GCV84 BY LMTCC8@3.169;
GCV84 BY LMTDC8@3.511;
GCV84 BY DWRC8@1.248;
GCV84 BY TDSBC8@1.353;
GCV84 BY TWFTFC8@2.157;
GCV84 BY TWFTAC8@2.266;
GCV84 BY TANSC8@1.739;
GCV84 BY TTMTAC8@0.747;
GCV84 BY TTMTBC8@1.655;
GCV84 BY TCRDAC8@1.368;
GCV84 BY TCRDBC8@2.217;
GCV84 BY TCRDCC8@2.383;
GCV84 BY TCRDDC8@1.870;
[GCV84@-0.197];
GCV84@0.928;

GCV94 BY DSBC9@1.353;
GCV94 BY BNTC9@1.811;
GCV94 BY WFTFC9@2.157;
GCV94 BY WFTAC9@2.266;
GCV94 BY WFTSC9@2.379;
GCV94 BY ANSC9@1.739;
GCV94 BY DSSC9@2.491;
GCV94 BY TMTAC9@2.339;
GCV94 BY TMTBC9@3.301;
GCV94 BY ILRPC9@2.219;
GCV94 BY ILRSC9@2.792;
GCV94 BY LMTAC9@3.166;
GCV94 BY LMTBC9@2.995;
GCV94 BY LMTCC9@3.169;
GCV94 BY LMTDC9@3.511;
GCV94 BY DWRC9@1.248;
GCV94 BY TDSBC9@1.353;
GCV94 BY TWFTFC9@2.157;
GCV94 BY TWFTAC9@2.266;
GCV94 BY TANSC9@1.739;
GCV94 BY TTMTAC9@0.747;
GCV94 BY TTMTBC9@1.655;
[GCV94@-0.105];
GCV94@0.791;

[WFTTC2$1@-2.527];
[WFTTC2$2@-1.501];
[WFTTC2$3@-0.695];
[WFTTC2$4@-0.011];
[WFTTC2$5@0.484];
[WFTTC2$6@1.148];
[WFTTC2$7@1.840];
[WFTTC2$8@2.888];

[DSSC2$1@-2.743];
```

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VMMF2 BY TMTACM@1.036 TMTBCM@1.036;
VMMF3 BY ILRPCM@1.819 ILRSCM@1.819;
VMMF4 BY LMTACM@3.289 LMTCCM@3.289;
VMMF5 BY LMTBCM@3.584 LMTDCM@3.584;

V5MF1 BY WFTFC5@2.375 WFTAC5@2.090 WFTSC5@2.365;
V5MF2 BY TMTAC5@1.036 TMTBC5@1.036;
V5MF3 BY ILRPC5@1.819 ILRSC5@1.819;
V5MF4 BY LMTAC5@3.289 LMTCC5@3.289;
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V6MF2 BY TMTAC6@1.036 TMTBC6@1.036;
V6MF3 BY ILRPC6@1.819 ILRSC6@1.819;
V6MF4 BY LMTAC6@3.289 LMTCC6@3.289;
V6MF5 BY LMTBC6@3.584 LMTDC6@3.584;

V7MF1 BY WFTFC7@2.375 WFTAC7@2.090 WFTSC7@2.365;
V7MF2 BY TMTAC7@1.036 TMTBC7@1.036;
V7MF3 BY ILRPC7@1.819 ILRSC7@1.819;
V7MF4 BY LMTAC7@3.289 LMTCC7@3.289;
V7MF5 BY LMTBC7@3.584 LMTDC7@3.584;

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V8MF4 BY LMTAC8@3.289 LMTCC8@3.289;
V8MF5 BY LMTBC8@3.584 LMTDC8@3.584;
V8MF6 BY DSBC8@1.149 TDSBC8@1.149;
V8MF7 BY ANSC8@0.899 TANSC8@0.899;
V8MF8 BY TCRDAC8@1.647 TCRDBC8@2.544
TCRDCC8@2.607 TCRDDC8@2.310;

V9MF1 BY WFTFC9@2.241 WFTAC9@1.847 WFTSC9@2.135
TWFTFC9@2.160 TWFTAC9@2.039;
V9MF2 BY TMTAC9@1.036 TMTBC9@1.036;
V9MF3 BY ILRPC9@1.819 ILRSC9@1.819;
V9MF4 BY LMTAC9@3.289 LMTCC9@3.289;
V9MF5 BY LMTBC9@3.584 LMTDC9@3.584;
V9MF6 BY DSBC9@1.149 TDSBC9@1.149;
V9MF7 BY ANSC9@0.899 TANSC9@0.899;

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GCV24 WITH GCV44@0 GCVM4@0
GCV54@0 GCV64@0 GCV74@0 GCV84@0 GCV94@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
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V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV44 WITH GCVM4@0
GCV54@0 GCV64@0 GCV74@0 GCV84@0 GCV94@0
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V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
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GCVM4 WITH
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VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
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V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
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V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
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V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV64 WITH GCV74@0 GCV84@0 GCV94@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV74 WITH GCV84@0 GCV94@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV84 WITH GCV94@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV94 WITH
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
```

```
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF1 WITH VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF2 WITH VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF3 WITH VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF4 WITH VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF5 WITH
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF1 WITH V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF2 WITH V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF3 WITH V5MF4@0 V5MF5@0
```

```
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF4 WITH V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF5 WITH
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF1 WITH V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF2 WITH V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF3 WITH V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF4 WITH V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF5 WITH
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF1 WITH V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF2 WITH V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF3 WITH V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
```

```
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF4 WITH V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF5 WITH
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF1 WITH V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF2 WITH V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF3 WITH V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF4 WITH V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF5 WITH V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF6 WITH V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF7 WITH V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF8 WITH
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF1 WITH V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF2 WITH V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF3 WITH V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF4 WITH V9MF5@0 V9MF6@0 V9MF7@0;

V9MF5 WITH V9MF6@0 V9MF7@0;

V9MF6 WITH V9MF7@0;

OUTPUT:
STDYX RESIDUAL TECH1;

SAVEDATA:
save=fscores;
file=GloCog4.dat;
```

A.3. In Person and Phone Assessments, Invariant Cognition (Version 5)

```
DATA: FILE = FactorsMplus.dat;

VARIABLE:
NAMES = MPLUSID
DWRC2 DSSC2 WFTTC2
DWRCM ILRPCM DSSCM LMTTCM TMTACM TMTBCM
WFTTCM ANSCM ILRSCM
LMTACM LMTBCM LMTCCM LMTDCM WFTFCM
WFTACM WFTSCM
DWRC4 DSSC4 WFTTC4
DWRC5 WFTTC5 DSSC5 ILRPC5 ANSC5 DSBC5
BNTC5 LMTTC5 TMTAC5 TMTBC5 ILRSC5
LMTAC5 LMTBC5 LMTCC5 LMTDC5 WFTFC5 WFTAC5 WFTSC5
DWRC6 WFTTC6 DSSC6 ILRPC6 ANSC6 DSBC6
BNTC6 LMTTC6 TMTAC6 TMTBC6 ILRSC6
LMTAC6 LMTBC6 LMTCC6 LMTDC6 WFTFC6 WFTAC6 WFTSC6
DWRC7 WFTTC7 DSSC7 ILRPC7 ANSC7 DSBC7
BNTC7 LMTTC7 TMTAC7 TMTBC7 ILRSC7
LMTAC7 LMTBC7 LMTCC7 LMTDC7 WFTFC7 WFTAC7 WFTSC7
DWRC8 DSSC8 WFTTC8 WFTFC8 WFTAC8 WFTSC8
ILRPC8 ILRSC8 ANSC8
LMTC8 LMTAC8 LMTBC8 LMTCC8 LMTDC8 DSBC8 BNTC8
TMTAC8 TMTBC8
TCRDAC8 TCRDBC8 TCRDCC8 TCRDDC8
TWFTFC8 TWFTAC8 TANSC8 TDSBC8 TTMTAC8 TTMTBC8
DWRC9 DSSC9 WFTTC9 WFTFC9 WFTAC9 WFTSC9
ILRPC9 ILRSC9 ANSC9
LMTC9 LMTAC9 LMTBC9 LMTCC9 LMTDC9 DSBC9 BNTC9
TMTAC9 TMTBC9
TCRDAC9 TCRDBC9 TCRDCC9 TCRDDC9
TWFTFC9 TWFTAC9 TANSC9 TDSBC9 TTMTAC9 TTMTBC9;

USEVARIABLES =
DWRC2 DSSC2 WFTTC2
DWRCM ILRPCM DSSCM
TMTACM TMTBCM ANSCM
ILRSCM LMTACM LMTBCM LMTCCM LMTDCM
WFTFCM WFTACM WFTSCM
DWRC4 DSSC4 WFTTC4
DWRC5 DSSC5 ILRPC5 ANSC5
DSBC5 BNTC5 TMTAC5 TMTBC5
ILRSC5 LMTAC5 LMTBC5 LMTCC5 LMTDC5
WFTFC5 WFTAC5 WFTSC5
DWRC6 DSSC6 ILRPC6 ANSC6
DSBC6 BNTC6 TMTAC6 TMTBC6
ILRSC6 LMTAC6 LMTBC6 LMTCC6 LMTDC6
WFTFC6 WFTAC6 WFTSC6
DWRC7 DSSC7 ILRPC7 ANSC7
DSBC7 BNTC7 TMTAC7 TMTBC7
```

```
ILRSC7 LMTAC7 LMTBC7 LMTCC7 LMTDC7
WFTFC7 WFTAC7 WFTSC7
DWRC8 DSSC8 ILRPC8 ANSC8
DSBC8 BNTC8 TMTAC8 TMTBC8
ILRSC8 LMTAC8 LMTBC8 LMTCC8 LMTDC8
WFTFC8 WFTAC8 WFTSC8
TTMTAC8 TTMTBC8 TANSC8 TDSBC8 TWFTAC8 TWFTFC8
TCRDAC8 TCRDBC8 TCRDCC8 TCRDDC8
DWRC9 DSSC9 ILRPC9 ANSC9
DSBC9 BNTC9 TMTAC9 TMTBC9
ILRSC9 LMTAC9 LMTBC9 LMTCC9 LMTDC9
WFTFC9 WFTAC9 WFTSC9
TTMTAC9 TTMTBC9 TANSC9 TDSBC9 TWFTAC9 TWFTFC9;

MISSING = ALL (-9999);

CATEGORICAL =
DWRC2 DSSC2 WFTTC2
DWRCM ILRPCM DSSCM
TMTACM TMTBCM ANSCM
ILRSCM LMTACM LMTBCM LMTCCM LMTDCM
WFTFCM WFTACM WFTSCM
DWRC4 DSSC4 WFTTC4
DWRC5 DSSC5 ILRPC5 ANSC5
DSBC5 BNTC5 TMTAC5 TMTBC5
ILRSC5 LMTAC5 LMTBC5 LMTCC5 LMTDC5
WFTFC5 WFTAC5 WFTSC5
DWRC6 DSSC6 ILRPC6 ANSC6
DSBC6 BNTC6 TMTAC6 TMTBC6
ILRSC6 LMTAC6 LMTBC6 LMTCC6 LMTDC6
WFTFC6 WFTAC6 WFTSC6
DWRC7 DSSC7 ILRPC7 ANSC7
DSBC7 BNTC7 TMTAC7 TMTBC7
ILRSC7 LMTAC7 LMTBC7 LMTCC7 LMTDC7
WFTFC7 WFTAC7 WFTSC7
DWRC8 DSSC8 ILRPC8 ANSC8
DSBC8 BNTC8 TMTAC8 TMTBC8
ILRSC8 LMTAC8 LMTBC8 LMTCC8 LMTDC8
WFTFC8 WFTAC8 WFTSC8
TTMTAC8 TTMTBC8 TANSC8 TDSBC8 TWFTAC8 TWFTFC8
TCRDAC8 TCRDBC8 TCRDCC8 TCRDDC8
DWRC9 DSSC9 ILRPC9 ANSC9
DSBC9 BNTC9 TMTAC9 TMTBC9
ILRSC9 LMTAC9 LMTBC9 LMTCC9 LMTDC9
WFTFC9 WFTAC9 WFTSC9
TTMTAC9 TTMTBC9 TANSC9 TDSBC9 TWFTAC9 TWFTFC9;

IDVARIABLE = MPLUSID;

ANALYSIS:
ESTIMATOR=MLR;
ALGORITHM=EM;
```

```
COVERAGE=.0001;
INTEGRATION=MONTECARLO(10000);

MODEL:
GCV25 BY WFTTC2@1.525;
GCV25 BY DSSC2@2.491;
GCV25 BY DWRC2@1.248;
[GCV25@0.684];
GCV25@1.025;

GCV45 BY WFTTC4@1.525;
GCV45 BY DSSC4@2.491;
GCV45 BY DWRC4@1.248;
[GCV45@0.629];
GCV45@0.932;

GCVM5 BY WFTFCM@2.157;
GCVM5 BY WFTACM@2.266;
GCVM5 BY WFTSCM@2.379;
GCVM5 BY ANSCM@1.739;
GCVM5 BY DSSCM@2.491;
GCVM5 BY TMTACM@2.339;
GCVM5 BY TMTBCM@3.301;
GCVM5 BY ILRPCM@2.219;
GCVM5 BY ILRSCM@2.792;
GCVM5 BY LMTACM@3.166;
GCVM5 BY LMTBCM@2.995;
GCVM5 BY LMTCCM@3.169;
GCVM5 BY LMTDCM@3.511;
GCVM5 BY DWRCM@1.248;
[GCVM5@-0.121];
GCVM5@0.848;

GCV55 BY DSBC5@1.353;
GCV55 BY BNTC5@1.811;
GCV55 BY WFTFC5@2.157;
GCV55 BY WFTAC5@2.266;
GCV55 BY WFTSC5@2.379;
GCV55 BY ANSC5@1.739;
GCV55 BY DSSC5@2.491;
GCV55 BY TMTAC5@2.339;
GCV55 BY TMTBC5@3.301;
GCV55 BY ILRPC5@2.219;
GCV55 BY ILRSC5@2.792;
GCV55 BY LMTAC5@3.166;
GCV55 BY LMTBC5@2.995;
GCV55 BY LMTCC5@3.169;
GCV55 BY LMTDC5@3.511;
GCV55 BY DWRC5@1.248;
[GCV55@0];
GCV55@1;
```

```
GCV65 BY DSBC6@1.353;
GCV65 BY BNTC6@1.811;
GCV65 BY WFTFC6@2.157;
GCV65 BY WFTAC6@2.266;
GCV65 BY WFTSC6@2.379;
GCV65 BY ANSC6@1.739;
GCV65 BY DSSC6@2.491;
GCV65 BY TMTAC6@2.339;
GCV65 BY TMTBC6@3.301;
GCV65 BY ILRPC6@2.219;
GCV65 BY ILRSC6@2.792;
GCV65 BY LMTAC6@3.166;
GCV65 BY LMTBC6@2.995;
GCV65 BY LMTCC6@3.169;
GCV65 BY LMTDC6@3.511;
GCV65 BY DWRC6@1.248;
[GCV65@-0.088];
GCV65@0.960;

GCV75 BY DSBC7@1.353;
GCV75 BY BNTC7@1.811;
GCV75 BY WFTFC7@2.157;
GCV75 BY WFTAC7@2.266;
GCV75 BY WFTSC7@2.379;
GCV75 BY ANSC7@1.739;
GCV75 BY DSSC7@2.491;
GCV75 BY TMTAC7@2.339;
GCV75 BY TMTBC7@3.301;
GCV75 BY ILRPC7@2.219;
GCV75 BY ILRSC7@2.792;
GCV75 BY LMTAC7@3.166;
GCV75 BY LMTBC7@2.995;
GCV75 BY LMTCC7@3.169;
GCV75 BY LMTDC7@3.511;
GCV75 BY DWRC7@1.248;
[GCV75@-0.088];
GCV75@1.036;

GCV85 BY DSBC8@1.353;
GCV85 BY BNTC8@1.811;
GCV85 BY WFTFC8@2.157;
GCV85 BY WFTAC8@2.266;
GCV85 BY WFTSC8@2.379;
GCV85 BY ANSC8@1.739;
GCV85 BY DSSC8@2.491;
GCV85 BY TMTAC8@2.339;
GCV85 BY TMTBC8@3.301;
GCV85 BY ILRPC8@2.219;
GCV85 BY ILRSC8@2.792;
GCV85 BY LMTAC8@3.166;
GCV85 BY LMTBC8@2.995;
GCV85 BY LMTCC8@3.169;
```

```
GCV85 BY LMTDC8@3.511;
GCV85 BY DWRC8@1.248;
GCV85 BY TDSBC8@1.239;
GCV85 BY TWFTFC8@2.126;
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VMMF5 BY LMTBCM@3.584 LMTDCM@3.584;

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GCV45 WITH GCVM5@0
GCV55@0 GCV65@0 GCV75@0 GCV85@0 GCV95@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCVM5 WITH
GCV55@0 GCV65@0 GCV75@0 GCV85@0 GCV95@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV55 WITH GCV65@0 GCV75@0 GCV85@0 GCV95@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV65 WITH GCV75@0 GCV85@0 GCV95@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV75 WITH GCV85@0 GCV95@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV85 WITH GCV95@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV95 WITH
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
```

```
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF1 WITH VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF2 WITH VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF3 WITH VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF4 WITH VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF5 WITH
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF1 WITH V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF2 WITH V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;
```

```
V5MF3 WITH V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF4 WITH V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF5 WITH
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF1 WITH V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF2 WITH V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF3 WITH V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF4 WITH V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF5 WITH
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF1 WITH V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF2 WITH V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;
```

```
V7MF3 WITH V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF4 WITH V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF5 WITH
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF1 WITH V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF2 WITH V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF3 WITH V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF4 WITH V8MF5@0 V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF5 WITH V8MF6@0 V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF6 WITH V8MF7@0 V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF7 WITH V8MF8@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF8 WITH
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF1 WITH V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF2 WITH V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF3 WITH V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF4 WITH V9MF5@0 V9MF6@0 V9MF7@0;

V9MF5 WITH V9MF6@0 V9MF7@0;

V9MF6 WITH V9MF7@0;

OUTPUT:
STDYX RESIDUAL TECH1;

SAVEDATA:
```

```
save=fscores;
file=GloCog5.dat;
```

A.4. Phone Only (Version 7)

```
DATA: FILE = FactorsMplus.dat;

VARIABLE:
NAMES = MPLUSID
TCRDAS8 TCRDBS8 TCRDCS8 TCRDDS8
TWFTFS8 TWFTAS8 TANSS8
TDSBS8 TTMTAS8 TTMTBS8
TCRDAC8 TCRDBC8 TCRDCC8 TCRDDC8
TWFTFC8 TWFTAC8 TANSC8
TDSBC8 TTMTAC8 TTMTBC8
TCRDAS9 TCRDBS9 TCRDCS9 TCRDDS9
TWFTFS9 TWFTAS9 TANSS9
TDSBS9 TTMTAS9 TTMTBS9
TCRDAC9 TCRDBC9 TCRDCC9 TCRDDC9
TWFTFC9 TWFTAC9 TANSC9
TDSBC9 TTMTAC9 TTMTBC9;

USEVARIABLES =
TTMTAC8 TTMTBC8 TANSC8 TDSBC8 TWFTAC8 TWFTFC8
TCRDAC8 TCRDBC8 TCRDCC8 TCRDDC8
TTMTAC9 TTMTBC9 TANSC9 TDSBC9 TWFTAC9 TWFTFC9
TCRDAC9 TCRDBC9 TCRDCC9 TCRDDC9;

MISSING = ALL (-9999);

CATEGORICAL =
TTMTAC8 TTMTBC8 TANSC8 TDSBC8 TWFTAC8 TWFTFC8
TCRDAC8 TCRDBC8 TCRDCC8 TCRDDC8
TTMTAC9 TTMTBC9 TANSC9 TDSBC9 TWFTAC9 TWFTFC9
TCRDAC9 TCRDBC9 TCRDCC9 TCRDDC9;

IDVARIABLE = MPLUSID;

ANALYSIS:
ESTIMATOR=MLR;
ALGORITHM=EM;
COVERAGE=.0001;
INTEGRATION=MONTECARLO;

MODEL:
GCV87 BY TCRDAC8@1.335;
GCV87 BY TCRDBC8@2.157;
GCV87 BY TCRDCC8@2.318;
GCV87 BY TCRDDC8@1.807;
GCV87 BY TWFTFC8@2.053;
GCV87 BY TWFTAC8@2.360;
GCV87 BY TANSC8@1.443;
GCV87 BY TDSBC8@1.169;
GCV87 BY TTMTAC8@0.735;
```

```
GCV87 BY TTMTBC8@1.646;
[GCV87@0];
GCV87@1;

GCV97 BY TCRDAC9@1.335;
GCV97 BY TCRDBC9@2.157;
GCV97 BY TCRDCC9@2.318;
GCV97 BY TCRDDC9@1.807;
GCV97 BY TWFTFC9@2.053;
GCV97 BY TWFTAC9@2.360;
GCV97 BY TANSC9@1.443;
GCV97 BY TDSBC9@1.169;
GCV97 BY TTMTAC9@0.735;
GCV97 BY TTMTBC9@1.646;
[GCV97@0.070];
GCV97@1.000;

[TCRDAC8$1@-6.153];
[TCRDAC8$2@-4.654];
[TCRDAC8$3@-2.827];
[TCRDAC8$4@-1.162];
[TCRDAC8$5@0.459];
[TCRDAC8$6@1.894];
[TCRDAC8$7@3.311];
[TCRDAC8$8@4.408];
[TCRDAC8$9@5.616];

[TCRDBC8$1@-10.456];
[TCRDBC8$2@-8.641];
[TCRDBC8$3@-6.741];
[TCRDBC8$4@-4.739];
[TCRDBC8$5@-2.72];
[TCRDBC8$6@-0.62];
[TCRDBC8$7@1.441];
[TCRDBC8$8@3.396];
[TCRDBC8$9@5.406];

[TCRDCC8$1@-11.475];
[TCRDCC8$2@-10.202];
[TCRDCC8$3@-8.229];
[TCRDCC8$4@-6.249];
[TCRDCC8$5@-4.328];
[TCRDCC8$6@-2.378];
[TCRDCC8$7@-0.27];
[TCRDCC8$8@1.911];
[TCRDCC8$9@4.028];

[TCRDDC8$1@-5.797];
[TCRDDC8$2@-5.099];
[TCRDDC8$3@-4.055];
[TCRDDC8$4@-2.828];
[TCRDDC8$5@-1.323];
```

```
[TCRDDC8$6@0.009];
[TCRDDC8$7@1.455];
[TCRDDC8$8@2.895];
[TCRDDC8$9@4.446];

[TWFTFC8$1@-5.778];
[TWFTFC8$2@-3.959];
[TWFTFC8$3@-2.244];
[TWFTFC8$4@-0.53];
[TWFTFC8$5@0.928];
[TWFTFC8$6@2.317];
[TWFTFC8$7@3.605];
[TWFTFC8$8@4.932];

[TWFTAC8$1@-4.508];
[TWFTAC8$2@-2.452];
[TWFTAC8$3@-0.736];
[TWFTAC8$4@0.811];
[TWFTAC8$5@2.148];
[TWFTAC8$6@3.447];
[TWFTAC8$7@4.976];
[TWFTAC8$8@6.093];

[TANSC8$1@-1.75];
[TANSC8$2@-0.818];
[TANSC8$3@0.065];
[TANSC8$4@0.449];
[TANSC8$5@0.945];
[TANSC8$6@1.806];
[TANSC8$7@2.608];
[TANSC8$8@3.528];

[TDSBC8$1@-2.803];
[TDSBC8$2@-1.956];
[TDSBC8$3@-0.887];
[TDSBC8$4@0.106];
[TDSBC8$5@1.122];
[TDSBC8$6@1.854];
[TDSBC8$7@2.497];
[TDSBC8$8@2.955];

[TTMTAC8$1@-2.405];
[TTMTAC8$2@-1.423];
[TTMTAC8$3@-0.924];
[TTMTAC8$4@-0.39];
[TTMTAC8$5@0.293];
[TTMTAC8$6@1.07];
[TTMTAC8$7@2.112];

[TTMTBC8$1@-2.953];
[TTMTBC8$2@-1.807];
[TTMTBC8$3@-1.043];
```

```
[TTMTBC8$4@-0.395];
[TTMTBC8$5@0.167];
[TTMTBC8$6@0.747];
[TTMTBC8$7@1.339];
[TTMTBC8$8@2.168];
[TTMTBC8$9@3.187];

[TCRDAC9$1@-6.153];
[TCRDAC9$2@-4.654];
[TCRDAC9$3@-2.827];
[TCRDAC9$4@-1.162];
[TCRDAC9$5@0.459];
[TCRDAC9$6@1.894];
[TCRDAC9$7@3.311];
[TCRDAC9$8@4.408];
[TCRDAC9$9@5.616];

[TCRDBC9$1@-6.741];
[TCRDBC9$2@-4.739];
[TCRDBC9$3@-2.72];
[TCRDBC9$4@-0.62];
[TCRDBC9$5@1.441];
[TCRDBC9$6@3.396];
[TCRDBC9$7@5.406];

[TCRDCC9$1@-8.229];
[TCRDCC9$2@-6.249];
[TCRDCC9$3@-4.328];
[TCRDCC9$4@-2.378];
[TCRDCC9$5@-0.27];
[TCRDCC9$6@1.911];
[TCRDCC9$7@4.028];

[TCRDDC9$1@-5.797];
[TCRDDC9$2@-5.099];
[TCRDDC9$3@-4.055];
[TCRDDC9$4@-2.828];
[TCRDDC9$5@-1.323];
[TCRDDC9$6@0.009];
[TCRDDC9$7@1.455];
[TCRDDC9$8@2.895];
[TCRDDC9$9@4.446];

[TWFTFC9$1@-5.778];
[TWFTFC9$2@-3.959];
[TWFTFC9$3@-2.244];
[TWFTFC9$4@-0.53];
[TWFTFC9$5@0.928];
[TWFTFC9$6@2.317];
[TWFTFC9$7@3.605];
[TWFTFC9$8@4.932];
```

```
[TWFTAC9$1@-4.508];
[TWFTAC9$2@-2.452];
[TWFTAC9$3@-0.736];
[TWFTAC9$4@0.811];
[TWFTAC9$5@2.148];
[TWFTAC9$6@3.447];
[TWFTAC9$7@4.976];
[TWFTAC9$8@6.093];

[TANSC9$1@-1.75];
[TANSC9$2@-0.818];
[TANSC9$3@0.065];
[TANSC9$4@0.449];
[TANSC9$5@0.945];
[TANSC9$6@1.806];
[TANSC9$7@2.608];
[TANSC9$8@3.528];

[TDSBC9$1@-2.803];
[TDSBC9$2@-1.956];
[TDSBC9$3@-0.887];
[TDSBC9$4@0.106];
[TDSBC9$5@1.122];
[TDSBC9$6@1.854];
[TDSBC9$7@2.497];
[TDSBC9$8@2.955];

[TTMTAC9$1@-2.405];
[TTMTAC9$2@-1.423];
[TTMTAC9$3@-0.924];
[TTMTAC9$4@-0.39];
[TTMTAC9$5@0.293];
[TTMTAC9$6@1.07];
[TTMTAC9$7@2.112];

[TTMTBC9$1@-2.953];
[TTMTBC9$2@-1.807];
[TTMTBC9$3@-1.043];
[TTMTBC9$4@-0.395];
[TTMTBC9$5@0.167];
[TTMTBC9$6@0.747];
[TTMTBC9$7@1.339];
[TTMTBC9$8@2.168];
[TTMTBC9$9@3.187];

V8MF1 BY TCRDAC8@1.651 TCRDBC8@2.550
TCRDCC8@2.633 TCRDDC8@2.358;
V8MF2 BY TWFTFC8@1.977 TWFTAC8@1.977;

V9MF1 BY TCRDAC9@1.651 TCRDBC9@2.550
TCRDCC9@2.633 TCRDDC9@2.358;
V9MF2 BY TWFTFC9@1.977 TWFTAC9@1.977;
```

```
V8MF1@1 V8MF2@1
V9MF1@1 V9MF2@1;

GCV97 WITH GCV87@0 V8MF1@0 V8MF2@0 V9MF1@0 V9MF2@0;

GCV87 WITH V8MF1@0 V8MF2@0 V9MF1@0 V9MF2@0;

V8MF1 WITH V8MF2@0 V9MF1@0 V9MF2@0;

V8MF2 WITH V9MF1@0 V9MF2@0;

V9MF1 WITH V9MF2@0;

OUTPUT:
STDYX RESIDUAL TECH1;

SAVEDATA:
save=fscores;
file=GloCog7.dat;
```

Appendix B: Confirmatory Factor Analysis Models With Continuous Indicators

Prior to analysis in Mplus, neurocognitive tests were converted into the derived variables depicted below. The Trails Making Tests were also reversed so that the lowest possible score was 0 and the highest possible score was 240.

Variable	Label	Definition
DWRS	Delayed Word Recall Standardized - In Person	Calculate the mean and standard deviation from Visit 5 for the variable DWR. Subtract the calculated mean and divide by the calculated standard deviation.
DSSS	Digit Symbol Substitution Standardized - In Person	Calculate the mean and standard deviation from Visit 5 for the variable DSS. Subtract the calculated mean and divide by the calculated standard deviation.
WFTTS	Phonemic Fluency Standardized (FAS) - In Person	Calculate the mean and standard deviation from Visit 5 for the variable WFTT. Subtract the calculated mean and divide by the calculated standard deviation.
WFTFS	Phonemic Fluency Standardized (F) - In Person	Calculate the mean and standard deviation from Visit 5 for the variable WFTF. Subtract the calculated mean and divide by the calculated standard deviation.
WFTAS	Phonemic Fluency Standardized (A) - In Person	Calculate the mean and standard deviation from Visit 5 for the variable WFTA. Subtract the calculated mean and divide by the calculated standard deviation.
WFTSS	Phonemic Fluency Standardized (S) - In Person	Calculate the mean and standard deviation from Visit 5 for the variable WFTS. Subtract the calculated mean and divide by the calculated standard deviation.
ILRPS	Incidental Learning Standardized (Digit-Symbol Pairs Score) - In Person	Calculate the mean and standard deviation from Visit 5 for the variable ILRP. Subtract the calculated mean and divide by the calculated standard deviation.
ILRSS	Incidental Learning Standardized (Symbols Score) - In Person	Calculate the mean and standard deviation from Visit 5 for the variable ILRS. Subtract the calculated mean and divide by the calculated standard deviation.
ANSS	Semantic Fluency Standardized - In Person	Calculate the mean and standard deviation from Visit 5 for the variable ANS. Subtract the calculated mean and divide by the calculated standard deviation.
LMTS	Logical Memory Standardized - In Person	Calculate the mean and standard deviation from Visit 5 for the variable LMT. Subtract the calculated mean and divide by the calculated standard deviation.
LMTAS	Logical Memory Standardized (I Story A) - In Person	Calculate the mean and standard deviation from Visit 5 for the variable LMTA. Subtract the calculated mean and divide by the calculated standard deviation.
LMTBS	Logical Memory Standardized (I Story B) - In Person	Calculate the mean and standard deviation from Visit 5 for the variable LMTB. Subtract the calculated mean and divide by the calculated standard deviation.
LMTCS	Logical Memory Standardized (II Story A) - In Person	Calculate the mean and standard deviation from Visit 5 for the variable LMTC. Subtract the calculated mean and divide by the calculated standard deviation.
LMTDS	Logical Memory Standardized (II Story B) - In Person	Calculate the mean and standard deviation from Visit 5 for the variable LMTD. Subtract the calculated mean and divide by the calculated standard deviation.

Variable	Label	Definition
DSBS	Digit Span Backwards Standardized - In Person	Calculate the mean and standard deviation from Visit 5 for the variable DSB. Subtract the calculated mean and divide by the calculated standard deviation.
BNTS	Boston Naming Test Standardized - In Person	Calculate the mean and standard deviation from Visit 5 for the variable BNT. Subtract the calculated mean and divide by the calculated standard deviation. Winsorize the lower distribution at the 3rd percentile.
TMTAS	Trails Making Test A Reversed Standardized - In Person	Calculate the mean and standard deviation from Visit 5 for the variable TMTA. Subtract the calculated mean and divide by the calculated standard deviation. Winsorize the lower distribution at the 3rd percentile.
TMTBS	Trails Making Test B Reversed Standardized - In Person	Calculate the mean and standard deviation from Visit 5 for the variable TMTB. Subtract the calculated mean and divide by the calculated standard deviation.
TCRDAS	CERAD Word List Standardized (Immediate Trial 1) - Phone	Calculate the mean and standard deviation from Visit 8 for the variable TCRDA. Subtract the calculated mean and divide by the calculated standard deviation.
TCRDBS	CERAD Word List Standardized (Immediate Trial 2) - Phone	Calculate the mean and standard deviation from Visit 8 for the variable TCRDB. Subtract the calculated mean and divide by the calculated standard deviation.
TCRDCS	CERAD Word List Standardized (Immediate Trial 3) - Phone	Calculate the mean and standard deviation from Visit 8 for the variable TCRDC. Subtract the calculated mean and divide by the calculated standard deviation.
TCRDDS	CERAD Word List Standardized (Delayed) - Phone	Calculate the mean and standard deviation from Visit 8 for the variable TCRDD. Subtract the calculated mean and divide by the calculated standard deviation.
TWFTFS	Phonemic Fluency Standardized (F) - Phone	Calculate the mean and standard deviation from Visit 5 for the variable TWFTF. Subtract the calculated mean and divide by the calculated standard deviation.
TWFTAS	Phonemic Fluency Standardized (A) - Phone	Calculate the mean and standard deviation from Visit 5 for the variable TWFTA. Subtract the calculated mean and divide by the calculated standard deviation.
TANSS	Semantic Fluency Standardized - Phone	Calculate the mean and standard deviation from Visit 5 for the variable TANS. Subtract the calculated mean and divide by the calculated standard deviation.
TDSBS	Digit Span Backwards Standardized - Phone	Calculate the mean and standard deviation from Visit 5 for the variable TDSB. Subtract the calculated mean and divide by the calculated standard deviation.
TTMTAS	Trails Making Test A Reversed Standardized - Phone	Calculate the mean and standard deviation from Visit 8 for the variable TTMTA. Subtract the calculated mean and divide by the calculated standard deviation. Winsorize the lower distribution at the 3rd percentile.
TTMTBS	Trails Making Test B Reversed Standardized - Phone	Calculate the mean and standard deviation from Visit 8 for the variable TTMTB. Subtract the calculated mean and divide by the calculated standard deviation.

The derived variables were integrated into a confirmatory factor analysis model. Global cognition factor scores were produced using the following Mplus syntax. The number appended

to the end of each derived variable indicates the corresponding ARIC visit. For example, DWRS2 is the standardized version of the DWR from Visit 2. When the letter M is appended, the derived variable is from the brain MRI sub-study.

B.1. In Person and Phone Assessments, Invariant Tests (Version 2)

```
DATA: FILE = FactorsMplus.dat;

VARIABLE:
NAMES = MPLUSID
DWRS2 DSSS2 WFTTS2
DWRSM ILRPSM ILRSSM DSSSM
LMTSM LMTASM LMTBSM LMTCSM LMTDSM
TMTASM TMTBSM
WFTTSM WFTFSM WFTASM WFTSSM ANSSM
DWRS4 DSSS4 WFTTS4
DWRS5 DSSS5 WFTTS5 WFTFS5 WFTAS5 WFTSS5
ILRPS5 ILRSS5 ANSS5
LMTS5 LMTAS5 LMTBS5 LMTCS5 LMTDS5
DSBS5 BNTS5 TMTAS5 TMTBS5
DWRS6 DSSS6 WFTTS6 WFTFS6 WFTAS6 WFTSS6
ILRPS6 ILRSS6 ANSS6
LMTS6 LMTAS6 LMTBS6 LMTCS6 LMTDS6
DSBS6 BNTS6 TMTAS6 TMTBS6
DWRS7 DSSS7 WFTTS7 WFTFS7 WFTAS7 WFTSS7
ILRPS7 ILRSS7 ANSS7
LMTS7 LMTAS7 LMTBS7 LMTCS7 LMTDS7
DSBS7 BNTS7 TMTAS7 TMTBS7
DWRS8 DSSS8 WFTTS8 WFTFS8 WFTAS8 WFTSS8
ILRPS8 ILRSS8 ANSS8
LMTS8 LMTAS8 LMTBS8 LMTCS8 LMTDS8
DSBS8 BNTS8 TMTAS8 TMTBS8
TCRDAS8 TCRDBS8 TCRDCS8 TCRDDS8
TWFTFS8 TWFTAS8 TANSS8 TDSBS8 TTMTAS8 TTMTBS8
DWRS9 DSSS9 WFTTS9 WFTFS9 WFTAS9 WFTSS9
ILRPS9 ILRSS9 ANSS9
LMTS9 LMTAS9 LMTBS9 LMTCS9 LMTDS9
DSBS9 BNTS9 TMTAS9 TMTBS9
TCRDAS9 TCRDBS9 TCRDCS9 TCRDDS9
TWFTFS9 TWFTAS9 TANSS9 TDSBS9 TTMTAS9 TTMTBS9;

USEVARIABLES =
DWRS2 DSSS2 WFTTS2
DWRSM ILRPSM ILRSSM DSSSM
LMTASM LMTBSM LMTCSM LMTDSM
TMTASM TMTBSM WFTFSM WFTASM WFTSSM ANSSM
DWRS4 DSSS4 WFTTS4
DWRS5 DSSS5 WFTFS5 WFTAS5 WFTSS5
ILRPS5 ILRSS5 ANSS5 LMTAS5 LMTBS5 LMTCS5 LMTDS5
DSBS5 BNTS5 TMTAS5 TMTBS5
DWRS6 DSSS6 WFTFS6 WFTAS6 WFTSS6
ILRPS6 ILRSS6 ANSS6 LMTAS6 LMTBS6 LMTCS6 LMTDS6
DSBS6 BNTS6 TMTAS6 TMTBS6
DWRS7 DSSS7 WFTFS7 WFTAS7 WFTSS7
ILRPS7 ILRSS7 ANSS7 LMTAS7 LMTBS7 LMTCS7 LMTDS7
```

```
DSBS7 BNTS7 TMTAS7 TMTBS7
DWRS8 DSSS8 WFTFS8 WFTAS8 WFTSS8
ILRPS8 ILRSS8 ANSS8 LMTAS8 LMTBS8 LMTCS8 LMTDS8
DSBS8 BNTS8 TMTAS8 TMTBS8
TCRDAS8 TCRDBS8 TCRDCS8 TCRDDS8
TWFTFS8 TWFTAS8 TANSS8 TDSBS8 TTMTAS8 TTMTBS8
DWRS9 DSSS9 WFTFS9 WFTAS9 WFTSS9
ILRPS9 ILRSS9 ANSS9 LMTAS9 LMTBS9 LMTCS9 LMTDS9
DSBS9 BNTS9 TMTAS9 TMTBS9
TCRDAS9 TCRDBS9 TCRDCS9 TCRDDS9
TWFTFS9 TWFTAS9 TANSS9 TDSBS9 TTMTAS9 TTMTBS9;

CENSORED =
TMTASM (b) TMTBSM (b)
BNTS5 (b) TMTAS5 (b) TMTBS5 (b)
BNTS6 (b) TMTAS6 (b) TMTBS6 (b)
BNTS7 (b) TMTAS7 (b) TMTBS7 (b)
BNTS8 (b) TMTAS8 (b) TMTBS8 (b)
TTMTAS8 (b) TTMTBS8 (b)
BNTS9 (b) TMTAS9 (b) TMTBS9 (b)
TTMTAS9 (b) TTMTBS9 (b);

MISSING = ALL (-9999);

IDVARIABLE = MPLUSID;

ANALYSIS:
ESTIMATOR=MLR;
ALGORITHM=EM;
COVERAGE=.0001;
INTEGRATION=MONTECARLO(10000);

MODEL:
GCV22 BY WFTTS2@0.648;
GCV22 BY DSSS2@0.835;
GCV22 BY DWRS2@0.592;
[GCV22@0.661];
GCV22@0.990;
[DWRS2@0.010]; DWRS2@0.650;
[WFTTS2@0.001]; WFTTS2@0.581;
[DSSS2@-0.004]; DSSS2@0.325;

GCV42 BY WFTTS4@0.648;
GCV42 BY DSSS4@0.835;
GCV42 BY DWRS4@0.592;
[GCV42@0.596];
GCV42@0.901;
[DWRS4@0.010]; DWRS4@0.650;
[WFTTS4@0.001]; WFTTS4@0.581;
[DSSS4@-0.004]; DSSS4@0.325;

GCVM2 BY WFTFSM@0.567;
```

```
GCVM2 BY WFTASM@0.603;
GCVM2 BY WFTSSM@0.605;
GCVM2 BY ANSSM@0.688;
GCVM2 BY DSSSM@0.835;
GCVM2 BY TMTASM@0.602;
GCVM2 BY TMTBSM@1.247;
GCVM2 BY ILRPSM@0.600;
GCVM2 BY ILRSSM@0.763;
GCVM2 BY LMTASM@0.654;
GCVM2 BY LMTBSM@0.614;
GCVM2 BY LMTCSM@0.638;
GCVM2 BY LMTDSM@0.653;
GCVM2 BY DWRSM@0.592;
[GCVM2@-0.094];
GCVM2@0.873;
[WFTFSM@0.001]; WFTFSM@0.250;
[WFTASM@0.000]; WFTASM@0.274;
[WFTSSM@-0.001]; WFTSSM@0.227;
[ANSSM@0.012]; ANSSM@0.531;
[DSSSM@-0.004]; DSSSM@0.325;
[TMTASM@0.043]; TMTASM@0.094;
[TMTBSM@-0.253]; TMTBSM@0.401;
[ILRPSM@-0.007]; ILRPSM@0.424;
[ILRSSM@-0.009]; ILRSSM@0.204;
[LMTASM@-0.005]; LMTASM@0.122;
[LMTBSM@-0.005]; LMTBSM@0.147;
[LMTCSM@-0.016]; LMTCSM@0.157;
[LMTDSM@-0.017]; LMTDSM@0.113;
[DWRSM@0.010]; DWRSM@0.650;

GCV52 BY DSBS5@0.617;
GCV52 BY BNTS5@0.755;
GCV52 BY WFTFS5@0.567;
GCV52 BY WFTAS5@0.603;
GCV52 BY WFTSS5@0.605;
GCV52 BY ANSS5@0.688;
GCV52 BY DSSS5@0.835;
GCV52 BY TMTAS5@0.602;
GCV52 BY TMTBS5@1.247;
GCV52 BY ILRPS5@0.600;
GCV52 BY ILRSS5@0.763;
GCV52 BY LMTAS5@0.654;
GCV52 BY LMTBS5@0.614;
GCV52 BY LMTCS5@0.638;
GCV52 BY LMTDS5@0.653;
GCV52 BY DWRS5@0.592;
[GCV52@0];
GCV52@1;
[DSBS5@-0.008]; DSBS5@0.626;
[BNTS5@-0.002]; BNTS5@0.404;
[WFTFS5@0.001]; WFTFS5@0.250;
[WFTAS5@0.000]; WFTAS5@0.274;
```

```
[WFTSS5@-0.001]; WFTSS5@0.227;
[ANSS5@0.012]; ANSS5@0.531;
[DSSS5@-0.004]; DSSS5@0.325;
[TMTAS5@0.043]; TMTAS5@0.094;
[TMTBS5@-0.253]; TMTBS5@0.401;
[ILRPS5@-0.007]; ILRPS5@0.424;
[ILRSS5@-0.009]; ILRSS5@0.204;
[LMTAS5@-0.005]; LMTAS5@0.122;
[LMTBS5@-0.005]; LMTBS5@0.147;
[LMTCS5@-0.016]; LMTCS5@0.157;
[LMTDS5@-0.017]; LMTDS5@0.113;
[DWRS5@0.010]; DWRS5@0.650;

GCV62 BY DSBS6@0.617;
GCV62 BY BNTS6@0.755;
GCV62 BY WFTFS6@0.567;
GCV62 BY WFTAS6@0.603;
GCV62 BY WFTSS6@0.605;
GCV62 BY ANSS6@0.688;
GCV62 BY DSSS6@0.835;
GCV62 BY TMTAS6@0.602;
GCV62 BY TMTBS6@1.247;
GCV62 BY ILRPS6@0.600;
GCV62 BY ILRSS6@0.763;
GCV62 BY LMTAS6@0.654;
GCV62 BY LMTBS6@0.614;
GCV62 BY LMTCS6@0.638;
GCV62 BY LMTDS6@0.653;
GCV62 BY DWRS6@0.592;
[GCV62@-0.077];
GCV62@0.951;
[DSBS6@-0.008]; DSBS6@0.626;
[BNTS6@-0.002]; BNTS6@0.404;
[WFTFS6@0.001]; WFTFS6@0.250;
[WFTAS6@0.000]; WFTAS6@0.274;
[WFTSS6@-0.001]; WFTSS6@0.227;
[ANSS6@0.012]; ANSS6@0.531;
[DSSS6@-0.004]; DSSS6@0.325;
[TMTAS6@0.043]; TMTAS6@0.094;
[TMTBS6@-0.253]; TMTBS6@0.401;
[ILRPS6@-0.007]; ILRPS6@0.424;
[ILRSS6@-0.009]; ILRSS6@0.204;
[LMTAS6@-0.005]; LMTAS6@0.122;
[LMTBS6@-0.005]; LMTBS6@0.147;
[LMTCS6@-0.016]; LMTCS6@0.157;
[LMTDS6@-0.017]; LMTDS6@0.113;
[DWRS6@0.010]; DWRS6@0.650;

GCV72 BY DSBS7@0.617;
GCV72 BY BNTS7@0.755;
GCV72 BY WFTFS7@0.567;
GCV72 BY WFTAS7@0.603;
```

```
GCV72 BY WFTSS7@0.605;
GCV72 BY ANSS7@0.688;
GCV72 BY DSSS7@0.835;
GCV72 BY TMTAS7@0.602;
GCV72 BY TMTBS7@1.247;
GCV72 BY ILRPS7@0.600;
GCV72 BY ILRSS7@0.763;
GCV72 BY LMTAS7@0.654;
GCV72 BY LMTBS7@0.614;
GCV72 BY LMTCS7@0.638;
GCV72 BY LMTDS7@0.653;
GCV72 BY DWRS7@0.592;
[GCV72@-0.095];
GCV72@1.030;
[DSBS7@-0.008]; DSBS7@0.626;
[BNTS7@-0.002]; BNTS7@0.404;
[WFTFS7@0.001]; WFTFS7@0.250;
[WFTAS7@0.000]; WFTAS7@0.274;
[WFTSS7@-0.001]; WFTSS7@0.227;
[ANSS7@0.012]; ANSS7@0.531;
[DSSS7@-0.004]; DSSS7@0.325;
[TMTAS7@0.043]; TMTAS7@0.094;
[TMTBS7@-0.253]; TMTBS7@0.401;
[ILRPS7@-0.007]; ILRPS7@0.424;
[ILRSS7@-0.009]; ILRSS7@0.204;
[LMTAS7@-0.005]; LMTAS7@0.122;
[LMTBS7@-0.005]; LMTBS7@0.147;
[LMTCS7@-0.016]; LMTCS7@0.157;
[LMTDS7@-0.017]; LMTDS7@0.113;
[DWRS7@0.010]; DWRS7@0.650;

GCV82 BY DSBS8@0.617;
GCV82 BY BNTS8@0.755;
GCV82 BY WFTFS8@0.567;
GCV82 BY WFTAS8@0.603;
GCV82 BY WFTSS8@0.605;
GCV82 BY ANSS8@0.688;
GCV82 BY DSSS8@0.835;
GCV82 BY TMTAS8@0.602;
GCV82 BY TMTBS8@1.247;
GCV82 BY ILRPS8@0.600;
GCV82 BY ILRSS8@0.763;
GCV82 BY LMTAS8@0.654;
GCV82 BY LMTBS8@0.614;
GCV82 BY LMTCS8@0.638;
GCV82 BY LMTDS8@0.653;
GCV82 BY DWRS8@0.592;
GCV82 BY TDSBS8@0.617;
GCV82 BY TWFTFS8@0.567;
GCV82 BY TWFTAS8@0.603;
GCV82 BY TANSS8@0.688;
GCV82 BY TTMTAS8@0.257;
```

```
GCV82 BY TTMTBS8@0.712;
GCV82 BY TCRDAS8@0.528;
GCV82 BY TCRDBS8@0.619;
GCV82 BY TCRDCS8@0.640;
GCV82 BY TCRDDS8@0.595;
[GCV82@-0.151];
GCV82@0.930;
[DSBS8@-0.008]; DSBS8@0.626;
[BNTS8@-0.002]; BNTS8@0.404;
[WFTFS8@0.001]; WFTFS8@0.250;
[WFTAS8@0.000]; WFTAS8@0.274;
[WFTSS8@-0.001]; WFTSS8@0.227;
[ANSS8@0.012]; ANSS8@0.531;
[DSSS8@-0.004]; DSSS8@0.325;
[TMTAS8@0.043]; TMTAS8@0.094;
[TMTBS8@-0.253]; TMTBS8@0.401;
[ILRPS8@-0.007]; ILRPS8@0.424;
[ILRSS8@-0.009]; ILRSS8@0.204;
[LMTAS8@-0.005]; LMTAS8@0.122;
[LMTBS8@-0.005]; LMTBS8@0.147;
[LMTCS8@-0.016]; LMTCS8@0.157;
[LMTDS8@-0.017]; LMTDS8@0.113;
[DWRS8@0.010]; DWRS8@0.650;
[TDSBS8@-0.008]; TDSBS8@0.626;
[TWFTFS8@0.001]; TWFTFS8@0.250;
[TWFTAS8@0.000]; TWFTAS8@0.274;
[TANSS8@0.012]; TANSS8@0.531;
[TTMTAS8@0.089]; TTMTAS8@0.433;
[TTMTBS8@0.032]; TTMTBS8@0.744;
[TCRDAS8@0.076]; TCRDAS8@0.437;
[TCRDBS8@0.088]; TCRDBS8@0.243;
[TCRDCS8@0.088]; TCRDCS8@0.242;
[TCRDDS8@0.079]; TCRDDS8@0.296;

GCV92 BY DSBS9@0.617;
GCV92 BY BNTS9@0.755;
GCV92 BY WFTFS9@0.567;
GCV92 BY WFTAS9@0.603;
GCV92 BY WFTSS9@0.605;
GCV92 BY ANSS9@0.688;
GCV92 BY DSSS9@0.835;
GCV92 BY TMTAS9@0.602;
GCV92 BY TMTBS9@1.247;
GCV92 BY ILRPS9@0.600;
GCV92 BY ILRSS9@0.763;
GCV92 BY LMTAS9@0.654;
GCV92 BY LMTBS9@0.614;
GCV92 BY LMTCS9@0.638;
GCV92 BY LMTDS9@0.653;
GCV92 BY DWRS9@0.592;
GCV92 BY TDSBS9@0.617;
GCV92 BY TWFTFS9@0.567;
```

```
GCV92 BY TWFTAS9@0.603;
GCV92 BY TANSS9@0.688;
GCV92 BY TTMTAS9@0.257;
GCV92 BY TTMTBS9@0.712;
GCV92 BY TCRDAS9@0.528;
GCV92 BY TCRDBS9@0.619;
GCV92 BY TCRDCS9@0.640;
GCV92 BY TCRDDS9@0.595;
[GCV92@-0.046];
GCV92@0.787;
[DSBS9@-0.008]; DSBS9@0.626;
[BNTS9@-0.002]; BNTS9@0.404;
[WFTFS9@0.001]; WFTFS9@0.250;
[WFTAS9@0.000]; WFTAS9@0.274;
[WFTSS9@-0.001]; WFTSS9@0.227;
[ANSS9@0.012]; ANSS9@0.531;
[DSSS9@-0.004]; DSSS9@0.325;
[TMTAS9@0.043]; TMTAS9@0.094;
[TMTBS9@-0.253]; TMTBS9@0.401;
[ILRPS9@-0.007]; ILRPS9@0.424;
[ILRSS9@-0.009]; ILRSS9@0.204;
[LMTAS9@-0.005]; LMTAS9@0.122;
[LMTBS9@-0.005]; LMTBS9@0.147;
[LMTCS9@-0.016]; LMTCS9@0.157;
[LMTDS9@-0.017]; LMTDS9@0.113;
[DWRS9@0.010]; DWRS9@0.650;
[TDSBS9@-0.008]; TDSBS9@0.626;
[TWFTFS9@0.001]; TWFTFS9@0.250;
[TWFTAS9@0.000]; TWFTAS9@0.274;
[TANSS9@0.012]; TANSS9@0.531;
[TTMTAS9@0.089]; TTMTAS9@0.433;
[TTMTBS9@0.032]; TTMTBS9@0.744;
[TCRDAS9@0.076]; TCRDAS9@0.437;
[TCRDBS9@0.088]; TCRDBS9@0.243;
[TCRDCS9@0.088]; TCRDCS9@0.242;
[TCRDDS9@0.079]; TCRDDS9@0.296;

VMMF1 BY WFTFSM@0.654 WFTASM@0.606 WFTSSM@0.638;
VMMF2 BY TMTASM@0.378 TMTBSM@0.378;
VMMF3 BY ILRPSM@0.489 ILRSSM@0.489;
VMMF4 BY LMTASM@0.680 LMTCSM@0.680;
VMMF5 BY LMTBSM@0.698 LMTDSM@0.698;

V5MF1 BY WFTFS5@0.654 WFTAS5@0.606 WFTSS5@0.638;
V5MF2 BY TMTAS5@0.378 TMTBS5@0.378;
V5MF3 BY ILRPS5@0.489 ILRSS5@0.489;
V5MF4 BY LMTAS5@0.680 LMTCS5@0.680;
V5MF5 BY LMTBS5@0.698 LMTDS5@0.698;

V6MF1 BY WFTFS6@0.654 WFTAS6@0.606 WFTSS6@0.638;
V6MF2 BY TMTAS6@0.378 TMTBS6@0.378;
V6MF3 BY ILRPS6@0.489 ILRSS6@0.489;
```

```
V6MF4 BY LMTAS6@0.680 LMTCS6@0.680;
V6MF5 BY LMTBS6@0.698 LMTDS6@0.698;

V7MF1 BY WFTFS7@0.654 WFTAS7@0.606 WFTSS7@0.638;
V7MF2 BY TMTAS7@0.378 TMTBS7@0.378;
V7MF3 BY ILRPS7@0.489 ILRSS7@0.489;
V7MF4 BY LMTAS7@0.680 LMTCS7@0.680;
V7MF5 BY LMTBS7@0.698 LMTDS7@0.698;

V8MF1 BY WFTFS8@0.645 WFTAS8@0.539 WFTSS8@0.604
TWFTFS8@0.632 TWFTAS8@0.605;
V8MF2 BY TMTAS8@0.378 TMTBS8@0.378;
V8MF3 BY ILRPS8@0.489 ILRSS8@0.489;
V8MF4 BY LMTAS8@0.680 LMTCS8@0.680;
V8MF5 BY LMTBS8@0.698 LMTDS8@0.698;
V8MF6 BY ANSS8@0.320 TANSS8@0.320;
V8MF7 BY TCRDAS8@0.551 TCRDBS8@0.635 TCRDCS8@0.620 TCRDDS8@0.619;

V9MF1 BY WFTFS9@0.645 WFTAS9@0.539 WFTSS9@0.604
TWFTFS9@0.632 TWFTAS9@0.605;
V9MF2 BY TMTAS9@0.378 TMTBS9@0.378;
V9MF3 BY ILRPS9@0.489 ILRSS9@0.489;
V9MF4 BY LMTAS9@0.680 LMTCS9@0.680;
V9MF5 BY LMTBS9@0.698 LMTDS9@0.698;
V9MF6 BY ANSS9@0.320 TANSS9@0.320;
V9MF7 BY TCRDAS9@0.551 TCRDBS9@0.635 TCRDCS9@0.620 TCRDDS9@0.619;

VMMF1@1 VMMF2@1 VMMF3@1 VMMF4@1 VMMF5@1
V5MF1@1 V5MF2@1 V5MF3@1 V5MF4@1 V5MF5@1
V6MF1@1 V6MF2@1 V6MF3@1 V6MF4@1 V6MF5@1
V7MF1@1 V7MF2@1 V7MF3@1 V7MF4@1 V7MF5@1
V8MF1@1 V8MF2@1 V8MF3@1 V8MF4@1 V8MF5@1 V8MF6@1 V8MF7@1
V9MF1@1 V9MF2@1 V9MF3@1 V9MF4@1 V9MF5@1 V9MF6@1 V9MF7@1;

GCV22 WITH GCV42@0 GCVM2@0 GCV52@0 GCV62@0 GCV72@0 GCV82@0 GCV92@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV42 WITH GCVM2@0 GCV52@0 GCV62@0 GCV72@0 GCV82@0 GCV92@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCVM2 WITH GCV52@0 GCV62@0 GCV72@0 GCV82@0 GCV92@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
```

```
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV52 WITH GCV62@0 GCV72@0 GCV82@0 GCV92@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV62 WITH GCV72@0 GCV82@0 GCV92@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV72 WITH GCV82@0 GCV92@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV82 WITH GCV92@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV92 WITH
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF1 WITH VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;
```

```
VMMF2 WITH VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF3 WITH VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF4 WITH VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF5 WITH
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF1 WITH V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF2 WITH V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF3 WITH V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF4 WITH V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;
```

```
V5MF5 WITH
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF1 WITH V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF2 WITH V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF3 WITH V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF4 WITH V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF5 WITH
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF1 WITH V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF2 WITH V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF3 WITH V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF4 WITH V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF5 WITH
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;
```

```
V8MF1 WITH V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF2 WITH V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF3 WITH V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF4 WITH V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF5 WITH V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF6 WITH V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF7 WITH V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF1 WITH V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF2 WITH V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF3 WITH V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF4 WITH V9MF5@0 V9MF6@0 V9MF7@0;

V9MF5 WITH V9MF6@0 V9MF7@0;

V9MF6 WITH V9MF7@0;

OUTPUT:
STDYX RESIDUAL TECH1;

SAVEDATA:
save=fscores;
file=GloCog2.dat;
```

B.2. In Person and Phone Assessments, Invariant Cognition (Version 3)

```
DATA: FILE = FactorsMplus.dat;

VARIABLE:
NAMES = MPLUSID
DWRS2 DSSS2 WFTTS2
DWRSM ILRPSM ILRSSM DSSSM
LMTSM LMTASM LMTBSM LMTCSM LMTDSM
TMTASM TMTBSM
WFTTSM WFTFSM WFTASM WFTSSM ANSSM
DWRS4 DSSS4 WFTTS4
DWRS5 DSSS5 WFTTS5 WFTFS5 WFTAS5 WFTSS5
ILRPS5 ILRSS5 ANSS5
LMTS5 LMTAS5 LMTBS5 LMTCS5 LMTDS5
DSBS5 BNTS5 TMTAS5 TMTBS5
DWRS6 DSSS6 WFTTS6 WFTFS6 WFTAS6 WFTSS6
ILRPS6 ILRSS6 ANSS6
LMTS6 LMTAS6 LMTBS6 LMTCS6 LMTDS6
DSBS6 BNTS6 TMTAS6 TMTBS6
DWRS7 DSSS7 WFTTS7 WFTFS7 WFTAS7 WFTSS7
ILRPS7 ILRSS7 ANSS7
LMTS7 LMTAS7 LMTBS7 LMTCS7 LMTDS7
DSBS7 BNTS7 TMTAS7 TMTBS7
DWRS8 DSSS8 WFTTS8 WFTFS8 WFTAS8 WFTSS8
ILRPS8 ILRSS8 ANSS8
LMTS8 LMTAS8 LMTBS8 LMTCS8 LMTDS8
DSBS8 BNTS8 TMTAS8 TMTBS8
TCRDAS8 TCRDBS8 TCRDCS8 TCRDDS8
TWFTFS8 TWFTAS8 TANSS8 TDSBS8 TTMTAS8 TTMTBS8
DWRS9 DSSS9 WFTTS9 WFTFS9 WFTAS9 WFTSS9
ILRPS9 ILRSS9 ANSS9
LMTS9 LMTAS9 LMTBS9 LMTCS9 LMTDS9
DSBS9 BNTS9 TMTAS9 TMTBS9
TCRDAS9 TCRDBS9 TCRDCS9 TCRDDS9
TWFTFS9 TWFTAS9 TANSS9 TDSBS9 TTMTAS9 TTMTBS9;

USEVARIABLES =
DWRS2 DSSS2 WFTTS2
DWRSM ILRPSM ILRSSM DSSSM
LMTASM LMTBSM LMTCSM LMTDSM
TMTASM TMTBSM WFTFSM WFTASM WFTSSM ANSSM
DWRS4 DSSS4 WFTTS4
DWRS5 DSSS5 WFTFS5 WFTAS5 WFTSS5
ILRPS5 ILRSS5 ANSS5 LMTAS5 LMTBS5 LMTCS5 LMTDS5
DSBS5 BNTS5 TMTAS5 TMTBS5
DWRS6 DSSS6 WFTFS6 WFTAS6 WFTSS6
ILRPS6 ILRSS6 ANSS6 LMTAS6 LMTBS6 LMTCS6 LMTDS6
DSBS6 BNTS6 TMTAS6 TMTBS6
DWRS7 DSSS7 WFTFS7 WFTAS7 WFTSS7
ILRPS7 ILRSS7 ANSS7 LMTAS7 LMTBS7 LMTCS7 LMTDS7
```

```
DSBS7 BNTS7 TMTAS7 TMTBS7
DWRS8 DSSS8 WFTFS8 WFTAS8 WFTSS8
ILRPS8 ILRSS8 ANSS8 LMTAS8 LMTBS8 LMTCS8 LMTDS8
DSBS8 BNTS8 TMTAS8 TMTBS8
TCRDAS8 TCRDBS8 TCRDCS8 TCRDDS8
TWFTFS8 TWFTAS8 TANSS8 TDSBS8 TTMTAS8 TTMTBS8
DWRS9 DSSS9 WFTFS9 WFTAS9 WFTSS9
ILRPS9 ILRSS9 ANSS9 LMTAS9 LMTBS9 LMTCS9 LMTDS9
DSBS9 BNTS9 TMTAS9 TMTBS9
TCRDAS9 TCRDBS9 TCRDCS9 TCRDDS9
TWFTFS9 TWFTAS9 TANSS9 TDSBS9 TTMTAS9 TTMTBS9;

CENSORED =
TMTASM (b) TMTBSM (b)
BNTS5 (b) TMTAS5 (b) TMTBS5 (b)
BNTS6 (b) TMTAS6 (b) TMTBS6 (b)
BNTS7 (b) TMTAS7 (b) TMTBS7 (b)
BNTS8 (b) TMTAS8 (b) TMTBS8 (b)
TTMTAS8 (b) TTMTBS8 (b)
BNTS9 (b) TMTAS9 (b) TMTBS9 (b)
TTMTAS9 (b) TTMTBS9 (b);

MISSING = ALL (-9999);

IDVARIABLE = MPLUSID;

ANALYSIS:
ESTIMATOR=MLR;
ALGORITHM=EM;
COVERAGE=.0001;
INTEGRATION=MONTECARLO(10000);

MODEL:
GCV23 BY WFTTS2@0.648;
GCV23 BY DSSS2@0.835;
GCV23 BY DWRS2@0.592;
[GCV23@0.661];
GCV23@0.990;
[DWRS2@0.010]; DWRS2@0.650;
[WFTTS2@0.001]; WFTTS2@0.581;
[DSSS2@-0.004]; DSSS2@0.325;

GCV43 BY WFTTS4@0.648;
GCV43 BY DSSS4@0.835;
GCV43 BY DWRS4@0.592;
[GCV43@0.596];
GCV43@0.901;
[DWRS4@0.010]; DWRS4@0.650;
[WFTTS4@0.001]; WFTTS4@0.581;
[DSSS4@-0.004]; DSSS4@0.325;

GCVM3 BY WFTFSM@0.567;
```

```
GCVM3 BY WFTASM@0.603;
GCVM3 BY WFTSSM@0.605;
GCVM3 BY ANSSM@0.688;
GCVM3 BY DSSSM@0.835;
GCVM3 BY TMTASM@0.602;
GCVM3 BY TMTBSM@1.247;
GCVM3 BY ILRPSM@0.600;
GCVM3 BY ILRSSM@0.763;
GCVM3 BY LMTASM@0.654;
GCVM3 BY LMTBSM@0.614;
GCVM3 BY LMTCSM@0.638;
GCVM3 BY LMTDSM@0.653;
GCVM3 BY DWRSM@0.592;
[GCVM3@-0.094];
GCVM3@0.873;
[WFTFSM@0.001]; WFTFSM@0.250;
[WFTASM@0.000]; WFTASM@0.274;
[WFTSSM@-0.001]; WFTSSM@0.227;
[ANSSM@0.012]; ANSSM@0.531;
[DSSSM@-0.004]; DSSSM@0.325;
[TMTASM@0.043]; TMTASM@0.094;
[TMTBSM@-0.253]; TMTBSM@0.401;
[ILRPSM@-0.007]; ILRPSM@0.424;
[ILRSSM@-0.009]; ILRSSM@0.204;
[LMTASM@-0.005]; LMTASM@0.122;
[LMTBSM@-0.005]; LMTBSM@0.147;
[LMTCSM@-0.016]; LMTCSM@0.157;
[LMTDSM@-0.017]; LMTDSM@0.113;
[DWRSM@0.010]; DWRSM@0.650;

GCV53 BY DSBS5@0.617;
GCV53 BY BNTS5@0.755;
GCV53 BY WFTFS5@0.567;
GCV53 BY WFTAS5@0.603;
GCV53 BY WFTSS5@0.605;
GCV53 BY ANSS5@0.688;
GCV53 BY DSSS5@0.835;
GCV53 BY TMTAS5@0.602;
GCV53 BY TMTBS5@1.247;
GCV53 BY ILRPS5@0.600;
GCV53 BY ILRSS5@0.763;
GCV53 BY LMTAS5@0.654;
GCV53 BY LMTBS5@0.614;
GCV53 BY LMTCS5@0.638;
GCV53 BY LMTDS5@0.653;
GCV53 BY DWRS5@0.592;
[GCV53@0];
GCV53@1;
[DSBS5@-0.008]; DSBS5@0.626;
[BNTS5@-0.002]; BNTS5@0.404;
[WFTFS5@0.001]; WFTFS5@0.250;
[WFTAS5@0.000]; WFTAS5@0.274;
```

```
[WFTSS5@-0.001]; WFTSS5@0.227;
[ANSS5@0.012]; ANSS5@0.531;
[DSSS5@-0.004]; DSSS5@0.325;
[TMTAS5@0.043]; TMTAS5@0.094;
[TMTBS5@-0.253]; TMTBS5@0.401;
[ILRPS5@-0.007]; ILRPS5@0.424;
[ILRSS5@-0.009]; ILRSS5@0.204;
[LMTAS5@-0.005]; LMTAS5@0.122;
[LMTBS5@-0.005]; LMTBS5@0.147;
[LMTCS5@-0.016]; LMTCS5@0.157;
[LMTDS5@-0.017]; LMTDS5@0.113;
[DWRS5@0.010]; DWRS5@0.650;

GCV63 BY DSBS6@0.617;
GCV63 BY BNTS6@0.755;
GCV63 BY WFTFS6@0.567;
GCV63 BY WFTAS6@0.603;
GCV63 BY WFTSS6@0.605;
GCV63 BY ANSS6@0.688;
GCV63 BY DSSS6@0.835;
GCV63 BY TMTAS6@0.602;
GCV63 BY TMTBS6@1.247;
GCV63 BY ILRPS6@0.600;
GCV63 BY ILRSS6@0.763;
GCV63 BY LMTAS6@0.654;
GCV63 BY LMTBS6@0.614;
GCV63 BY LMTCS6@0.638;
GCV63 BY LMTDS6@0.653;
GCV63 BY DWRS6@0.592;
[GCV63@-0.077];
GCV63@0.951;
[DSBS6@-0.008]; DSBS6@0.626;
[BNTS6@-0.002]; BNTS6@0.404;
[WFTFS6@0.001]; WFTFS6@0.250;
[WFTAS6@0.000]; WFTAS6@0.274;
[WFTSS6@-0.001]; WFTSS6@0.227;
[ANSS6@0.012]; ANSS6@0.531;
[DSSS6@-0.004]; DSSS6@0.325;
[TMTAS6@0.043]; TMTAS6@0.094;
[TMTBS6@-0.253]; TMTBS6@0.401;
[ILRPS6@-0.007]; ILRPS6@0.424;
[ILRSS6@-0.009]; ILRSS6@0.204;
[LMTAS6@-0.005]; LMTAS6@0.122;
[LMTBS6@-0.005]; LMTBS6@0.147;
[LMTCS6@-0.016]; LMTCS6@0.157;
[LMTDS6@-0.017]; LMTDS6@0.113;
[DWRS6@0.010]; DWRS6@0.650;

GCV73 BY DSBS7@0.617;
GCV73 BY BNTS7@0.755;
GCV73 BY WFTFS7@0.567;
GCV73 BY WFTAS7@0.603;
```

```
GCV73 BY WFTSS7@0.605;
GCV73 BY ANSS7@0.688;
GCV73 BY DSSS7@0.835;
GCV73 BY TMTAS7@0.602;
GCV73 BY TMTBS7@1.247;
GCV73 BY ILRPS7@0.600;
GCV73 BY ILRSS7@0.763;
GCV73 BY LMTAS7@0.654;
GCV73 BY LMTBS7@0.614;
GCV73 BY LMTCS7@0.638;
GCV73 BY LMTDS7@0.653;
GCV73 BY DWRS7@0.592;
[GCV73@-0.095];
GCV73@1.030;
[DSBS7@-0.008]; DSBS7@0.626;
[BNTS7@-0.002]; BNTS7@0.404;
[WFTFS7@0.001]; WFTFS7@0.250;
[WFTAS7@0.000]; WFTAS7@0.274;
[WFTSS7@-0.001]; WFTSS7@0.227;
[ANSS7@0.012]; ANSS7@0.531;
[DSSS7@-0.004]; DSSS7@0.325;
[TMTAS7@0.043]; TMTAS7@0.094;
[TMTBS7@-0.253]; TMTBS7@0.401;
[ILRPS7@-0.007]; ILRPS7@0.424;
[ILRSS7@-0.009]; ILRSS7@0.204;
[LMTAS7@-0.005]; LMTAS7@0.122;
[LMTBS7@-0.005]; LMTBS7@0.147;
[LMTCS7@-0.016]; LMTCS7@0.157;
[LMTDS7@-0.017]; LMTDS7@0.113;
[DWRS7@0.010]; DWRS7@0.650;

GCV83 BY DSBS8@0.617;
GCV83 BY BNTS8@0.755;
GCV83 BY WFTFS8@0.567;
GCV83 BY WFTAS8@0.603;
GCV83 BY WFTSS8@0.605;
GCV83 BY ANSS8@0.688;
GCV83 BY DSSS8@0.835;
GCV83 BY TMTAS8@0.602;
GCV83 BY TMTBS8@1.247;
GCV83 BY ILRPS8@0.600;
GCV83 BY ILRSS8@0.763;
GCV83 BY LMTAS8@0.654;
GCV83 BY LMTBS8@0.614;
GCV83 BY LMTCS8@0.638;
GCV83 BY LMTDS8@0.653;
GCV83 BY DWRS8@0.592;
GCV83 BY TDSBS8@0.617;
GCV83 BY TWFTFS8@0.692;
GCV83 BY TWFTAS8@0.782;
GCV83 BY TANSS8@0.780;
GCV83 BY TTMTAS8@0.352;
```

```
GCV83 BY TTMTBS8@0.812;
GCV83 BY TCRDAS8@0.599;
GCV83 BY TCRDBS8@0.729;
GCV83 BY TCRDCS8@0.714;
GCV83 BY TCRDDS8@0.761;
[GCV83@-0.009];
GCV83@0.679;
[DSBS8@-0.008]; DSBS8@0.626;
[BNTS8@-0.002]; BNTS8@0.404;
[WFTFS8@0.001]; WFTFS8@0.250;
[WFTAS8@0.000]; WFTAS8@0.274;
[WFTSS8@-0.001]; WFTSS8@0.227;
[ANSS8@0.012]; ANSS8@0.531;
[DSSS8@-0.004]; DSSS8@0.325;
[TMTAS8@0.043]; TMTAS8@0.094;
[TMTBS8@-0.253]; TMTBS8@0.401;
[ILRPS8@-0.007]; ILRPS8@0.424;
[ILRSS8@-0.009]; ILRSS8@0.204;
[LMTAS8@-0.005]; LMTAS8@0.122;
[LMTBS8@-0.005]; LMTBS8@0.147;
[LMTCS8@-0.016]; LMTCS8@0.157;
[LMTDS8@-0.017]; LMTDS8@0.113;
[DWRS8@0.010]; DWRS8@0.650;
[TDSBS8@0.031]; TDSBS8@0.991;
[TWFTFS8@-0.002]; TWFTFS8@0.354;
[TWFTAS8@-0.018]; TWFTAS8@0.271;
[TANSS8@-0.121]; TANSS8@0.270;
[TTMTAS8@-0.089]; TTMTAS8@0.474;
[TTMTBS8@-0.130]; TTMTBS8@0.928;
[TCRDAS8@-0.116]; TCRDAS8@0.439;
[TCRDBS8@-0.109]; TCRDBS8@0.234;
[TCRDCS8@-0.160]; TCRDCS8@0.242;
[TCRDDS8@-0.109]; TCRDDS8@0.292;

GCV93 BY DSBS9@0.617;
GCV93 BY BNTS9@0.755;
GCV93 BY WFTFS9@0.567;
GCV93 BY WFTAS9@0.603;
GCV93 BY WFTSS9@0.605;
GCV93 BY ANSS9@0.688;
GCV93 BY DSSS9@0.835;
GCV93 BY TMTAS9@0.602;
GCV93 BY TMTBS9@1.247;
GCV93 BY ILRPS9@0.600;
GCV93 BY ILRSS9@0.763;
GCV93 BY LMTAS9@0.654;
GCV93 BY LMTBS9@0.614;
GCV93 BY LMTCS9@0.638;
GCV93 BY LMTDS9@0.653;
GCV93 BY DWRS9@0.592;
GCV93 BY TDSBS9@0.617;
GCV93 BY TWFTFS9@0.692;
```

```
GCV93 BY TWFTAS9@0.782;
GCV93 BY TANSS9@0.780;
GCV93 BY TTMTAS9@0.352;
GCV93 BY TTMTBS9@0.812;
GCV93 BY TCRDAS9@0.599;
GCV93 BY TCRDBS9@0.729;
GCV93 BY TCRDCS9@0.714;
GCV93 BY TCRDDS9@0.761;
[GCV93@-0.036];
GCV93@0.777;
[DSBS9@-0.008]; DSBS9@0.626;
[BNTS9@-0.002]; BNTS9@0.404;
[WFTFS9@0.001]; WFTFS9@0.250;
[WFTAS9@0.000]; WFTAS9@0.274;
[WFTSS9@-0.001]; WFTSS9@0.227;
[ANSS9@0.012]; ANSS9@0.531;
[DSSS9@-0.004]; DSSS9@0.325;
[TMTAS9@0.043]; TMTAS9@0.094;
[TMTBS9@-0.253]; TMTBS9@0.401;
[ILRPS9@-0.007]; ILRPS9@0.424;
[ILRSS9@-0.009]; ILRSS9@0.204;
[LMTAS9@-0.005]; LMTAS9@0.122;
[LMTBS9@-0.005]; LMTBS9@0.147;
[LMTCS9@-0.016]; LMTCS9@0.157;
[LMTDS9@-0.017]; LMTDS9@0.113;
[DWRS9@0.010]; DWRS9@0.650;
[TDSBS9@0.031]; TDSBS9@0.991;
[TWFTFS9@-0.002]; TWFTFS9@0.354;
[TWFTAS9@-0.018]; TWFTAS9@0.271;
[TANSS9@-0.121]; TANSS9@0.270;
[TTMTAS9@-0.089]; TTMTAS9@0.474;
[TTMTBS9@-0.130]; TTMTBS9@0.928;
[TCRDAS9@-0.116]; TCRDAS9@0.439;
[TCRDBS9@-0.109]; TCRDBS9@0.234;
[TCRDCS9@-0.160]; TCRDCS9@0.242;
[TCRDDS9@-0.109]; TCRDDS9@0.292;

VMMF1 BY WFTFSM@0.654 WFTASM@0.606 WFTSSM@0.638;
VMMF2 BY TMTASM@0.378 TMTBSM@0.378;
VMMF3 BY ILRPSM@0.489 ILRSSM@0.489;
VMMF4 BY LMTASM@0.680 LMTCSM@0.680;
VMMF5 BY LMTBSM@0.698 LMTDSM@0.698;

V5MF1 BY WFTFS5@0.654 WFTAS5@0.606 WFTSS5@0.638;
V5MF2 BY TMTAS5@0.378 TMTBS5@0.378;
V5MF3 BY ILRPS5@0.489 ILRSS5@0.489;
V5MF4 BY LMTAS5@0.680 LMTCS5@0.680;
V5MF5 BY LMTBS5@0.698 LMTDS5@0.698;

V6MF1 BY WFTFS6@0.654 WFTAS6@0.606 WFTSS6@0.638;
V6MF2 BY TMTAS6@0.378 TMTBS6@0.378;
V6MF3 BY ILRPS6@0.489 ILRSS6@0.489;
```

```
V6MF4 BY LMTAS6@0.680 LMTCS6@0.680;
V6MF5 BY LMTBS6@0.698 LMTDS6@0.698;

V7MF1 BY WFTFS7@0.654 WFTAS7@0.606 WFTSS7@0.638;
V7MF2 BY TMTAS7@0.378 TMTBS7@0.378;
V7MF3 BY ILRPS7@0.489 ILRSS7@0.489;
V7MF4 BY LMTAS7@0.680 LMTCS7@0.680;
V7MF5 BY LMTBS7@0.698 LMTDS7@0.698;

V8MF1 BY WFTFS8@0.621 WFTAS8@0.552 WFTSS8@0.584
TWFTFS8@0.564 TWFTAS8@0.639;
V8MF2 BY TMTAS8@0.378 TMTBS8@0.378;
V8MF3 BY ILRPS8@0.489 ILRSS8@0.489;
V8MF4 BY LMTAS8@0.680 LMTCS8@0.680;
V8MF5 BY LMTBS8@0.698 LMTDS8@0.698;
V8MF6 BY ANSS8@0.485 TANSS8@0.485;
V8MF7 BY TCRDAS8@0.552 TCRDBS8@0.649
TCRDCS8@0.649 TCRDDS8@0.604;

V9MF1 BY WFTFS9@0.621 WFTAS9@0.552 WFTSS9@0.584
TWFTFS9@0.564 TWFTAS9@0.639;
V9MF2 BY TMTAS9@0.378 TMTBS9@0.378;
V9MF3 BY ILRPS9@0.489 ILRSS9@0.489;
V9MF4 BY LMTAS9@0.680 LMTCS9@0.680;
V9MF5 BY LMTBS9@0.698 LMTDS9@0.698;
V9MF6 BY ANSS9@0.485 TANSS9@0.485;
V9MF7 BY TCRDAS9@0.552 TCRDBS9@0.649
TCRDCS9@0.649 TCRDDS9@0.604;

VMMF1@1 VMMF2@1 VMMF3@1 VMMF4@1 VMMF5@1
V5MF1@1 V5MF2@1 V5MF3@1 V5MF4@1 V5MF5@1
V6MF1@1 V6MF2@1 V6MF3@1 V6MF4@1 V6MF5@1
V7MF1@1 V7MF2@1 V7MF3@1 V7MF4@1 V7MF5@1
V8MF1@1 V8MF2@1 V8MF3@1 V8MF4@1 V8MF5@1 V8MF6@1 V8MF7@1
V9MF1@1 V9MF2@1 V9MF3@1 V9MF4@1 V9MF5@1 V9MF6@1 V9MF7@1;

GCV23 WITH GCV43@0 GCVM3@0 GCV53@0 GCV63@0 GCV73@0 GCV83@0 GCV93@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV43 WITH GCVM3@0 GCV53@0 GCV63@0 GCV73@0 GCV83@0 GCV93@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;
```

```
GCVM3 WITH GCV53@0 GCV63@0 GCV73@0 GCV83@0 GCV93@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV53 WITH GCV63@0 GCV73@0 GCV83@0 GCV93@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV63 WITH GCV73@0 GCV83@0 GCV93@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV73 WITH GCV83@0 GCV93@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV83 WITH GCV93@0
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

GCV93 WITH
VMMF1@0 VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF1 WITH VMMF2@0 VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
```

```
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF2 WITH VMMF3@0 VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF3 WITH VMMF4@0 VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF4 WITH VMMF5@0
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

VMMF5 WITH
V5MF1@0 V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF1 WITH V5MF2@0 V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF2 WITH V5MF3@0 V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF3 WITH V5MF4@0 V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF4 WITH V5MF5@0
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
```

```
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V5MF5 WITH
V6MF1@0 V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF1 WITH V6MF2@0 V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF2 WITH V6MF3@0 V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF3 WITH V6MF4@0 V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF4 WITH V6MF5@0
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V6MF5 WITH
V7MF1@0 V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF1 WITH V7MF2@0 V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF2 WITH V7MF3@0 V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF3 WITH V7MF4@0 V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF4 WITH V7MF5@0
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V7MF5 WITH
V8MF1@0 V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
```

```
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF1 WITH V8MF2@0 V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF2 WITH V8MF3@0 V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF3 WITH V8MF4@0 V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF4 WITH V8MF5@0 V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF5 WITH V8MF6@0 V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF6 WITH V8MF7@0
V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V8MF7 WITH V9MF1@0 V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF1 WITH V9MF2@0 V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF2 WITH V9MF3@0 V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF3 WITH V9MF4@0 V9MF5@0 V9MF6@0 V9MF7@0;

V9MF4 WITH V9MF5@0 V9MF6@0 V9MF7@0;

V9MF5 WITH V9MF6@0 V9MF7@0;

V9MF6 WITH V9MF7@0;

OUTPUT:
STDYX RESIDUAL TECH1;

SAVEDATA:
save=fscores;
file=GloCog3.dat;
```

B.3. Phone Only (Version 6)

```
DATA: FILE = FactorsMplus.dat;

VARIABLE:
NAMES = MPLUSID
TCRDAS8 TCRDBS8 TCRDCS8 TCRDDS8
TWFTFS8 TWFTAS8 TANSS8
TDSBS8 TTMTAS8 TTMTBS8
TCRDAC8 TCRDBC8 TCRDCC8 TCRDDC8
TWFTFC8 TWFTAC8 TANSC8
TDSBC8 TTMTAC8 TTMTBC8
TCRDAS9 TCRDBS9 TCRDCS9 TCRDDS9
TWFTFS9 TWFTAS9 TANSS9
TDSBS9 TTMTAS9 TTMTBS9
TCRDAC9 TCRDBC9 TCRDCC9 TCRDDC9
TWFTFC9 TWFTAC9 TANSC9
TDSBC9 TTMTAC9 TTMTBC9;

USEVARIABLES =
TCRDAS8 TCRDBS8 TCRDCS8 TCRDDS8
TWFTFS8 TWFTAS8 TANSS8 TDSBS8 TTMTAS8 TTMTBS8
TCRDAS9 TCRDBS9 TCRDCS9 TCRDDS9
TWFTFS9 TWFTAS9 TANSS9 TDSBS9 TTMTAS9 TTMTBS9;

CENSORED =
TTMTAS8 (b) TTMTBS8 (b)
TTMTAS9 (b) TTMTBS9 (b);

MISSING = ALL (-9999);

IDVARIABLE = MPLUSID;

ANALYSIS:
ESTIMATOR=MLR;
ALGORITHM=EM;
COVERAGE=.0001;
INTEGRATION=MONTECARLO;

MODEL:
GCV86 BY TCRDAS8@0.492;
GCV86 BY TCRDBS8@0.585;
GCV86 BY TCRDCS8@0.608;
GCV86 BY TCRDDS8@0.559;
GCV86 BY TWFTFS8@0.574;
GCV86 BY TWFTAS8@0.626;
GCV86 BY TANSS8@0.609;
GCV86 BY TDSBS8@0.623;
GCV86 BY TTMTAS8@0.259;
GCV86 BY TTMTBS8@0.704;
[GCV86@0];
```

```
GCV86@1;
[TCRDAS8@-0.007]; TCRDAS8@0.437;
[TCRDBS8@-0.010]; TCRDBS8@0.243;
[TCRDCS8@-0.012]; TCRDCS8@0.242;
[TCRDDS8@-0.014]; TCRDDS8@0.296;
[TWFTFS8@-0.122]; TWFTFS8@0.282;
[TWFTAS8@-0.124]; TWFTAS8@0.265;
[TANSS8@-0.263]; TANSS8@0.571;
[TDSBS8@0.057]; TDSBS8@1.016;
[TTMTAS8@0.049]; TTMTAS8@0.427;
[TTMTBS8@-0.078]; TTMTBS8@0.718;

GCV96 BY TCRDAS9@0.492;
GCV96 BY TCRDBS9@0.585;
GCV96 BY TCRDCS9@0.608;
GCV96 BY TCRDDS9@0.559;
GCV96 BY TWFTFS9@0.574;
GCV96 BY TWFTAS9@0.626;
GCV96 BY TANSS9@0.609;
GCV96 BY TDSBS9@0.623;
GCV96 BY TTMTAS9@0.259;
GCV96 BY TTMTBS9@0.704;
[GCV96@0.123];
GCV96@0.742;
[TCRDAS9@-0.007]; TCRDAS9@0.437;
[TCRDBS9@-0.010]; TCRDBS9@0.243;
[TCRDCS9@-0.012]; TCRDCS9@0.242;
[TCRDDS9@-0.014]; TCRDDS9@0.296;
[TWFTFS9@-0.122]; TWFTFS9@0.282;
[TWFTAS9@-0.124]; TWFTAS9@0.265;
[TANSS9@-0.263]; TANSS9@0.571;
[TDSBS9@0.057]; TDSBS9@1.016;
[TTMTAS9@0.049]; TTMTAS9@0.427;
[TTMTBS9@-0.078]; TTMTBS9@0.718;

V8MF1 BY TCRDAS8@0.567 TCRDBS8@0.647
TCRDCS8@0.630 TCRDDS8@0.633;
V8MF2 BY TWFTFS8@0.588 TWFTAS8@0.588;

V9MF1 BY TCRDAS9@0.567 TCRDBS9@0.647
TCRDCS9@0.630 TCRDDS9@0.633;
V9MF2 BY TWFTFS9@0.588 TWFTAS9@0.588;

V8MF1@1 V8MF2@1
V9MF1@1 V9MF2@1;

GCV96 WITH GCV86@0
V8MF1@0 V8MF2@0 V9MF1@0 V9MF2@0;

GCV86 WITH
V8MF1@0 V8MF2@0 V9MF1@0 V9MF2@0;
```

```
V8MF1 WITH V8MF2@0 V9MF1@0 V9MF2@0;

V8MF2 WITH V9MF1@0 V9MF2@0;

V9MF1 WITH V9MF2@0;

OUTPUT:
STDYX RESIDUAL TECH1;

SAVEDATA:
save=fscores;
file=GloCog6.dat;
```

Appendix C: A Brief Introduction to Multilevel Multiple Imputation in Mplus

C.1. Dataset Preparation

When performing multilevel multiple imputation in Mplus, begin by creating a *.dat* dataset with a long format (see https://www.statmodel.com/download/usersguide/Mplus%20user%20guide%20Ver_7_r6_web.pdf). Key points to remember when creating, importing, and defining the dataset in Mplus include the following.

- Variable names must be specified in Mplus rather than in a header row in the *.dat* dataset.
- Variable names cannot exceed eight characters
- Only numeric values are allowed. Character values are not permitted. This applies to all variables including the ARIC participant ID which should be converted to an MPLUSID.
- Variables that need to be retained in the imputed dataset, such as visit number, must be designated as auxiliary variables.
- Missing values are identified by using a unique numeric value such as -9999.
- When conducting a multilevel imputation in which there are multiple observations per participant, the ARIC participant ID should be designated as the clustering variable.
- Time-invariant variables should be listed after `BETWEEN`.
- Time-varying variables should be listed after `WITHIN`.
- Key variables that require a fixed and random effect, such as the global cognition factor score, should ***not*** be listed after `BETWEEN` or `WITHIN`.
- Categorical variables or variables with nonnormal distributions must be specified.

```
DATA: FILE = Long.dat;

VARIABLE:

NAMES =
APOE CIG DIAB HT GFS
FEMALE RC1 RC2 RC3 RC4 ED2 ED3 AGE
AFUHT AFUDIAB AFUPX
AFUHOSP AFUPH AFUCHD AFUSTRK
DEM DEATH TIME
MPLUSID VISIT;
```

```
USEVARIABLES =
APOE CIG DIAB HT GFS
FEMALE RC1 RC2 RC3 RC4 ED2 ED3 AGE
AFUHT AFUDIAB AFUPX
AFUHOSP AFUPH AFUCHD AFUSTRK
DEM DEATH TIME;

AUXILIARY = VISIT;

MISSING = ALL (-9999);

CLUSTER = MPLUSID;

BETWEEN = AGE FEMALE APOE
RC1 RC2 RC3 RC4 ED2 ED3;

WITHIN = CIG DIAB HT
AFUHT AFUDIAB AFUPX
AFUHOSP AFUPH AFUCHD AFUSTRK
DEM DEATH TIME;

CATEGORICAL =
APOE FEMALE RC1 RC2 RC3 RC4 ED2 ED3
CIG DIAB HT
AFUHT AFUDIAB AFUPX
DEM DEATH;
```

C.2. Imputation

A two-level, random model with a Bayesian estimator should be specified. Other features, such as the use of Gibbs sampling, are optional.

```
ANALYSIS:
ESTIMATOR = bayes;
TYPE = twolevel random;
BSEED = 4893;
ALGORITHM = GIBBS(RW);
BITERATIONS = 50000;
```

Time-invariant and time-varying variables must be listed under `%WITHIN%` or `%BETWEEN%` as appropriate. Variables with both random and fixed effects should be specified as depicted below for global cognition (`GFS`). Categorical variables must be denoted with the symbol `$1` or `(c)`. Other features are documented in the Mplus user manual (see https://www.statmodel.com/download/usersguide/Mplus%20user%20guide%20Ver_7_r6_web.pdf).

```
MODEL:
%WITHIN%
[CIG$1 DIAB$1 HT$1
AFUHOSP AFUPH AFUCHD AFUSTRK
AFUHT$1 AFUDIAB$1 AFUPX$1
DEM$1 DEATH$1 TIME];

S | GFS ON TIME;

GFS on CIG DIAB HT
AFUHT AFUDIAB AFUPX
AFUHOSP AFUPH AFUCHD AFUSTRK
DEM DEATH;

%BETWEEN%
[AGE FEMALE APOE$1
RC1$1 RC2$1 RC3$1 RC4$1
ED2$1 ED3$1];

GFS ON AGE FEMALE APOE
RC1 RC2 RC3 RC4 ED2 ED3;

S ON AGE FEMALE APOE
RC1 RC2 RC3 RC4 ED2 ED3;

GFS with S;

DATA IMPUTATION:
NDATASETS = 5;
THIN = 50;
IMPUTE =
GFS AGE FEMALE
APOE (c)
RC1 (c) RC2 (c) RC3 (c) RC4 (c)
ED2 (c) ED3 (c)
CIG (c) DIAB (c) HT (c)
TIME;

SAVE = Imputed*.dat;
```

The resulting imputed data can be analyzed in Mplus or another statistical program.

Appendix D: A Brief Introduction to Single Level Multiple Imputation in Stata

D.1. Dataset Preparation

To conduct a single level multiple imputation in Stata, begin by creating a wide dataset and indicating the structure of the resulting imputed datasets. For example, *Mlong* instructs Stata to stack the imputed datasets. Following this, specify which variables will be imputed (*mi register imputed*) and which variables will be used as covariates but do not require imputation (*mi register regular)*.

```
mi set mlong

mi register imputed ///
apoe cig5 diab5 ht5 gfs5

mi register regular ///
female rc1 rc2 rc3 rc4 ed2 ed3 age ///
afuhyper5 afudiab5 afuproxy5 ///
afuhosp5 afuph5 afuchd5 afustroke5 ///
demv5 deathv5

capture mi xtset, clear
```

D.2. Imputation

The code for performing multiple imputation by chained equations (MICE) in Stata is documented online (see https://www.stata.com/manuals13/mimiimputechained.pdf for details). For imputed variables, designate the imputation method based on the variable type (binary=logit, continuous=regress, etc.). Interactions between variables can be specified within the imputation model (*incl*).

mi impute chained ///

(logit) apoe diab5 ht5 ///
(ologit) cig5 ///
(regress, incl(demv5#ed2 demv5#ed3 ///
demv5#rc1 demv5#rc2 demv5#rc3 demv5#rc4 ///
*(demv5*c.age))) gfs5 ///*
= c.age c.afuhosp5 c.afuph5 c.afuchd5 c.afustroke5 ///
female rc1 rc2 rc3 rc4 ed2 ed3 afuhyper5 afudiab5 afuproxy5 ///
demv5 deathv5 ///
, add(20) burnin(50) rseed(040918) force dots augment ///

The resulting imputed data can be analyzed in Stata or another statistical program.

Appendix E: A Brief Introduction to Single Level Multiple Imputation in R

E.1. Software Packages

To perform a single level multiple imputation in R, download and install the following packages.

1. 'mi': https://cran.r-project.org/web/packages/mi/mi.pdf
2. 'mice': https://cran.r-project.org/web/packages/mice/mice.pdf
3. 'mitools': https://cran.r-project.org/web/packages/mitools/mitools.pdf

These packages are used to generate imputed data and process the resulting datasets.

E.2. Dataset Preparation

Read in a dataset and make sure all variables are formatted correctly. For example, it may be necessary to reformat categorical variables using as.factor:

```
V5a$female<-as.factor(V5a$female)
```

If either the analytic or imputation model has interactions, they can be included as just another variable (JAV).[1] Interactions between continuous variables can be computed directly.

```
V5b$gfs5_age<-V5b$gfs5*V5b$age
```

Interactions with categorical variables require additional code.

```
v5b$demv5_ed2<-(as.numeric(v5b$demv5)-1)*(as.numeric(v5b$ed2)-1)
v5b$demv5_age<-(as.numeric(v5b$demv5)-1)*v5b$age
```

E.3. Imputation

Before implementing MICE, examine the method matrices and structure using a zero-iteration imputation.

```
gcd2imp0<-mice(gcd2, maxit=0, seed=137)
summary(gcd2imp0)
```

This allows the analyst to see the default methods R uses. It also allows the analyst to extract the method and predictor matrices and then make changes or set model specifications.

Additional information about the types of imputation methods available in R are provided at https://www.rdocumentation.org/packages/mice/versions/3.11.0/topics/mice.

Prior analyses involving continuous variables suggest that linear regression with predicted values (code: norm.predict) performs better than the default predictive mean matching (code: pmm). The following code permits the analyst to changes these specifications.

1. Save the method matrix from the zero iteration imputation.

methgcd2<-gcd2imp0$method

2. Create a vector of the variable names.

gcd2_reg<-c('apoe', 'cig5', 'diab5', 'ht5,', 'gfs5')

3. Change the default method.

methgcd2[gcd2_reg]='norm.predict'

MICE can now be implemented using the selected dataset, updated method matrix, and desired imputation specifications (number of iterations, seed, burn-in number).

gcd2imp1<-mice(gcd2, maxit=5, method=methgcd2,
seed=137, print=TRUE, n.burn=50)

After generating imputed data, convert the dataset into a long format. The resulting dataset can be analyzed in R or another statistical program.

gcd2imp<-mice::complete(gcd2imp1, action='long', include=FALSE)

References

(1) White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Statistics in Medicine*. 2011;30(4):377-399.

Appendix F: A Brief Introduction to Single Level Multiple Imputation in SAS

F.1. Dataset Preparation

To generate imputed datasets in SAS, read in a dataset and make sure all variables are formatted correctly. If either the analytic or imputation model has interactions, they can be included as just another variable (JAV)[1] using the same approach employed for single level multiple imputation in R (Appendix E).

F.2. Imputation

The code for performing multiple imputation by chained equations (MICE) in SAS is documented online (see https://support.sas.com/en/documentation.html for details). For each variable, specify the imputation method based on the variable type (categorical=discrim, continuous=regression, etc.).

```
proc mi data=WIDE seed=876 nimpute=5 out=Imputed;
      class FEMALE APOE RC1 RC2 RC3 RC4 ED2 ED3
      CIG5 DIAB5 HT5 AFUHYPER5 AFUDIAB5 AFUPROXY5 DEMV5 DEATHV5;
      fcs nbiter=100
      discrim (FEMALE APOE RC1 RC2 RC3 RC4 ED2 ED3
      CIG5 DIAB5 HT5 AFUHYPER5 AFUDIAB5 AFUPROXY5 DEMV5 DEATHV5
      /classeffects=include)
      regression (GFS5 AGE AFUHOSP5 AFUPH5 AFUCHD5 AFUSTROKE5);
      var GFS5 AGE AFUHOSP5 AFUPH5 AFUCHD5 AFUSTROKE5
      FEMALE APOE RC1 RC2 RC3 RC4 ED2 ED3
      CIG5 DIAB5 HT5 AFUHYPER5 AFUDIAB5 AFUPROXY5 DEMV5 DEATHV5;
run;
```

The resulting imputed data can be analyzed in SAS or another statistical program.

References

(1) White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Statistics in Medicine*. 2011;30(4):377-399.

Appendix G: Example Global Factor Score Imputation in Stata from Visits 5 through 7

In the example below, the analyst created one imputation model for the global cognition factor score (gfs) and another imputation model for the cognitive domain factor scores (mem, lang, exfunc). Participants who died prior to the start of each visit were removed. Death was included as an auxiliary variable but only pre-death cognitive scores were imputed.

G.1. Imputation for Global Cognition at Visit 5

```
use "$pwv\pwv_v5.dta", clear

describe

mi set mlong

mi register imputed ///
pwvu5 pwvu6 pwvu7 ///
apoe cds1 ///
diab5 hyptmdcode5 map5 pulse5 cog5

mi register regular ///
 age age2 deathv5 demsurv5 ed2 ed3 female gfs5 ///
 afudiab5 afuhyper5 afuproxy5 afustroke5 ///
 vtime56 vtime57 ///
 tmmse5 rc1 rc2 rc3 rc4

capture mi xtset, clear

mi impute chained ///
 (ologit) apoe diab5 hyptmdcode5 cog5 ///
 (regress) cds1 ///
 (regress) map5 pulse5 ///
(regress, incl((c.vtime56*c.pwvu6) (c.vtime57*c.pwvu7))) pwvu5 pwvu6 pwvu7
///
 = c.age c.age2 c.gfs5 ///
 c.tmmse5 deathv5 demsurv5 ///
 afudiab5 afuhyper5 afuproxy5 ///
 ed2 ed3 female rc1 rc2 rc3 rc4 ///
 c.afustroke5 ///
 , add(25) burnin(50) rseed(040918) force dots augment ///

saveold "$pwv\V5STATAGFS", replace version(11)
```

G.2. Imputation for Global Cognition at Visit 6

```
use "$pwv\pwv_v6.dta", clear

describe

mi set mlong

mi register imputed ///
pwvu5 pwvu6 pwvu7 ///
gfs6 ///
apoe cds1 ///
diab5 diab6 ///
sisv6 ///
hyptmdcode5 hyptmdcode6 ///
map5 map6 pulse5 pulse6 cog5

mi register regular ///
 age age2 deathv6 demsurv5 demsurv6 ed2 ed3 female gfs5 ///
 afudiab5 afudiab6 ///
 afuhyper5 afuhyper6 ///
 afuproxy5 afuproxy6 ///
 afustroke5 afustroke6 ///
 tmmse5 tmmse6 ///
 vtime56 vtime57 ///
 rc1 rc2 rc3 rc4

capture mi xtset, clear

mi impute chained ///
 (ologit) apoe diab5 diab6 hyptmdcode5 hyptmdcode6 cog5 ///
 (regress) cds1 sisv6 ///
 (regress) map5 map6 pulse5 pulse6 ///
 (regress, incl(demsurv5#ed2 demsurv5#ed3 demsurv5#rc1 ///
demsurv5#rc2 demsurv5#rc3 demsurv5#rc4 demsurv6#ed2 demsurv6#ed3 ///
demsurv6#rc1 demsurv6#rc2 demsurv6#rc3 demsurv6#rc4 ///
(c.gfs6*c.vtime56) ///
(demsurv5*c.gfs5) (demsurv6*c.gfs6) ///
(demsurv6*c.vtime56) ///
(demsurv6*c.sisv6) ///
(c.tmmse5*c.gfs5) (ed2*c.tmmse5) (ed3*c.tmmse5) (demsurv5*c.tmmse5) ///
(c.tmmse6*c.gfs6) (ed2*c.tmmse6) (ed3*c.tmmse6) (demsurv6*c.tmmse6) ///
)) gfs6 ///
(regress, incl((c.vtime56*c.pwvu6) (c.vtime57*c.pwvu7))) pwvu5 pwvu6 pwvu7
///
 = c.age c.age2 c.gfs5 ///
 c.tmmse5 c.tmmse6 ///
 c.vtime56 ///
 deathv6 demsurv5 demsurv6 ///
 afudiab5 afudiab6 ///
 afuhyper5 afuhyper6 ///
 afuproxy5 afuproxy6 ///
 ed2 ed3 female rc1 rc2 rc3 rc4 ///
 c.afustroke5 c.afustroke6 ///
 , add(25) burnin(50) rseed(040918) force dots augment ///
```

```
saveold "$pwv\V6STATAGFS", replace version(11)
```

G.3. Imputation for Global Cognition at Visit 7

```
use "$pwv\pwv_v7.dta", clear

describe

mi set mlong

mi register imputed ///
pwvu5 pwvu6 pwvu7 ///
gfs6 gfs7 ///
apoe cds1 ///
diab5 diab6 diab7 ///
sisv6 sisv7 ///
hyptmdcode5 hyptmdcode6 hyptmdcode7 ///
map5 map6 map7 pulse5 pulse6 pulse7 cog5

mi register regular ///
 age age2 deathv7 demsurv5 demsurv6 demsurv7 ed2 ed3 female gfs5 ///
 afudiab5 afudiab6 afudiab7 ///
 afuhyper5 afuhyper6 afuhyper7 ///
 afuproxy5 afuproxy6 afuproxy7 ///
 afustroke5 afustroke6 afustroke7 ///
 tmmse5 tmmse6 tmmse7 ///
 vtime56 vtime57 ///
 rc1 rc2 rc3 rc4

capture mi xtset, clear


mi impute chained ///
 (ologit) apoe diab5 diab6 diab7 hyptmdcode5 hyptmdcode6 hyptmdcode7 cog5 ///
 (regress) cds1 sisv6 sisv7 ///
 (regress) map5 map6 map7 pulse5 pulse6 pulse7 ///
 (regress, incl(demsurv5#ed2 demsurv5#ed3 demsurv5#rc1 ///
demsurv5#rc2 demsurv5#rc3 demsurv5#rc4 demsurv6#ed2 demsurv6#ed3 ///
demsurv6#rc1 demsurv6#rc2 demsurv6#rc3 demsurv6#rc4 demsurv7#ed2 ///
demsurv7#ed3 demsurv7#rc1 demsurv7#rc2 demsurv7#rc3 demsurv7#rc4 ///
(c.gfs6*c.vtime56) (c.gfs7*c.vtime57) ///
(demsurv5*c.gfs5) (demsurv6*c.gfs6) (demsurv7*c.gfs7) ///
(demsurv6*c.vtime56) ///
(demsurv7*c.vtime57) ///
(demsurv6*c.sisv6) (demsurv7*c.sisv7) ///
(c.tmmse5*c.gfs5) (ed2*c.tmmse5) (ed3*c.tmmse5) (demsurv5*c.tmmse5) ///
(c.tmmse6*c.gfs6) (ed2*c.tmmse6) (ed3*c.tmmse6) (demsurv6*c.tmmse6) ///
(c.tmmse7*c.gfs7) (ed2*c.tmmse7) (ed3*c.tmmse7) (demsurv7*c.tmmse7) ///
)) gfs6 gfs7 ///
(regress, incl((c.vtime56*c.pwvu6) (c.vtime57*c.pwvu7))) pwvu5 pwvu6 pwvu7
///
 = c.age c.age2 c.gfs5 ///
 c.tmmse5 c.tmmse6 c.tmmse7 ///
 c.vtime56 c.vtime57 ///
 deathv7 demsurv5 demsurv6 demsurv7 ///
```

```
 afudiab5 afudiab6 afudiab7 ///
 afuhyper5 afuhyper6 afuhyper7 ///
 afuproxy5 afuproxy6 afuproxy7 ///
 ed2 ed3 female rc1 rc2 rc3 rc4 ///
 c.afustroke5 c.afustroke6 c.afustroke7 ///
 , add(25) burnin(50) rseed(040918) force dots augment ///

saveold "$pwv\V7STATAGFS", replace version(11)
```

G.4. Imputation for Cognitive Domains at Visit 5

```
use "$pwv\pwv_v5.dta", clear

describe

mi set mlong

mi register imputed ///
pwvu5 pwvu6 pwvu7 ///
exfunc5 lang5 mem5 ///
apoe cds1 ///
diab5 hyptmdcode5 map5 pulse5 cog5

mi register regular ///
 age age2 deathv5 demsurv5 ed2 ed3 female ///
 afudiab5 afuhyper5 afuproxy5 afustroke5 ///
 vtime56 vtime57 ///
 tmmse5 rc1 rc2 rc3 rc4

capture mi xtset, clear

mi impute chained ///
 (ologit) apoe diab5 hyptmdcode5 cog5 ///
 (regress) cds1 ///
 (regress) map5 pulse5 mem5 lang5 exfunc5 ///
(regress, incl((c.vtime56*c.pwvu6) (c.vtime57*c.pwvu7))) pwvu5 pwvu6 pwvu7
///
  = c.age c.age2 ///
 c.tmmse5 deathv5 demsurv5 ///
 afudiab5 afuhyper5 afuproxy5 ///
 ed2 ed3 female rc1 rc2 rc3 rc4 ///
 c.afustroke5 ///
 , add(25) burnin(50) rseed(040918) force dots augment ///

saveold "$pwv\V5STATADOM", replace version(11)
```

G.5. Imputation for Cognitive Domains at Visit 6

```
use "$pwv\pwv_v6.dta", clear

describe

mi set mlong
```

```
mi register imputed ///
pwvu5 pwvu6 pwvu7 ///
exfunc5 exfunc6 ///
lang5 lang6 ///
mem5 mem6 ///
apoe cds1 ///
diab5 diab6 ///
sisv6 ///
hyptmdcode5 hyptmdcode6 ///
map5 map6 pulse5 pulse6 cog5

mi register regular ///
 age age2 deathv6 demsurv5 demsurv6 ed2 ed3 female ///
 afudiab5 afudiab6 ///
 afuhyper5 afuhyper6 ///
 afuproxy5 afuproxy6 ///
 afustroke5 afustroke6 ///
 tmmse5 tmmse6 ///
 vtime56 vtime57 ///
 rc1 rc2 rc3 rc4



capture mi xtset, clear


mi impute chained ///
  (ologit) apoe diab5 diab6 hyptmdcode5 hyptmdcode6 cog5 ///
  (regress) cds1 sisv6 ///
  (regress) map5 map6 pulse5 pulse6 mem5 lang5 exfunc5 ///
  (regress, incl(demsurv5#ed2 demsurv5#ed3 demsurv5#rc1 ///
demsurv5#rc2 demsurv5#rc3 demsurv5#rc4 demsurv6#ed2 demsurv6#ed3 ///
demsurv6#rc1 demsurv6#rc2 demsurv6#rc3 demsurv6#rc4 ///
(c.mem5*c.vtime56) (demsurv5*c.mem5) (demsurv6*c.mem5)  ///
(c.tmmse5*c.mem5)   ///
(c.lang5*c.vtime56) (demsurv5*c.lang5) (demsurv6*c.lang5) ///
(c.tmmse5*c.lang5) ///
(c.exfunc5*c.vtime56) (demsurv5*c.exfunc5) (demsurv6*c.exfunc5) ///
(c.tmmse5*c.exfunc5) (demsurv6*c.vtime56) ///
(demsurv6*c.sisv6) ///
(demsurv5*c.tmmse5) (demsurv6*c.tmmse6) ///
)) mem6 lang6 exfunc6 ///
(regress, incl((c.vtime56*c.pwvu6) (c.vtime57*c.pwvu7))) pwvu5 pwvu6 pwvu7
///
 = c.age c.age2 ///
 c.tmmse5 c.tmmse6 ///
 c.vtime56 ///
 deathv6 demsurv5 demsurv6 ///
 afudiab5 afudiab6 ///
 afuhyper5 afuhyper6 ///
 afuproxy5 afuproxy6 ///
 ed2 ed3 female rc1 rc2 rc3 rc4 ///
 c.afustroke5 c.afustroke6 ///
 , add(25) burnin(50) rseed(040918) force dots augment ///

saveold "$pwv\V6STATADOM", replace version(11)
```

G.6. Imputation for Cognitive Domains at Visit 7

```
use "$pwv\pwv_v7.dta", clear


describe

mi set mlong

mi register imputed ///
pwvu5 pwvu6 pwvu7 ///
exfunc5 exfunc6 exfunc7 ///
lang5 lang6 lang7 ///
mem5 mem6 mem7 ///
apoe cds1 ///
diab5 diab6 diab7 ///
sisv6 sisv7 ///
hyptmdcode5 hyptmdcode6 hyptmdcode7 ///
map5 map6 map7 pulse5 pulse6 pulse7 cog5

mi register regular ///
 age age2 deathv7 demsurv5 demsurv6 demsurv7 ed2 ed3 female ///
 afudiab5 afudiab6 afudiab7 ///
 afuhyper5 afuhyper6 afuhyper7 ///
 afuproxy5 afuproxy6 afuproxy7 ///
 afustroke5 afustroke6 afustroke7 ///
 tmmse5 tmmse6 tmmse7 ///
 vtime56 vtime57 ///
 rc1 rc2 rc3 rc4



capture mi xtset, clear


mi impute chained ///
 (ologit) apoe diab5 diab6 diab7 hyptmdcode5 hyptmdcode6 hyptmdcode7 cog5 ///
 (regress) cds1 sisv6 sisv7 ///
 (regress) map5 map6 map7 pulse5 pulse6 pulse7 mem5 lang5 exfunc5 ///
 (regress, incl(demsurv5#ed2 demsurv5#ed3 demsurv5#rc1 ///
demsurv5#rc2 demsurv5#rc3 demsurv5#rc4 demsurv6#ed2 demsurv6#ed3 ///
demsurv6#rc1 demsurv6#rc2 demsurv6#rc3 demsurv6#rc4 ///
(c.mem5*c.vtime56) (demsurv5*c.mem5) (demsurv6*c.mem5)  ///
(c.tmmse5*c.mem5)   ///
(c.lang5*c.vtime56) (demsurv5*c.lang5) (demsurv6*c.lang5) ///
(c.tmmse5*c.lang5) ///
(c.exfunc5*c.vtime56) (demsurv5*c.exfunc5) (demsurv6*c.exfunc5) ///
(c.tmmse5*c.exfunc5) (demsurv6*c.vtime56) ///
(demsurv6*c.sisv6) ///
(demsurv5*c.tmmse5) (demsurv6*c.tmmse6) ///
)) mem6 lang6 exfunc6 ///
 (regress, incl(demsurv5#ed2 demsurv5#ed3 demsurv5#rc1 ///
demsurv5#rc2 demsurv5#rc3 demsurv5#rc4 demsurv6#ed2 demsurv6#ed3 ///
demsurv6#rc1 demsurv6#rc2 demsurv6#rc3 demsurv6#rc4 demsurv7#ed2 ///
demsurv7#ed3 demsurv7#rc1 demsurv7#rc2 demsurv7#rc3 demsurv7#rc4 ///
(c.mem5*c.vtime56) (c.mem5*c.vtime57) (demsurv7*c.mem6) ///
```

```
(c.tmmse5*c.mem5) (c.tmmse6*c.mem6) (c.tmmse7*c.mem6) ///
(c.lang5*c.vtime56) (c.lang5*c.vtime57) (demsurv7*c.lang6) ///
(c.tmmse5*c.lang5) (c.tmmse6*c.lang6) (c.tmmse7*c.lang6) ///
(c.exfunc5*c.vtime56) (c.exfunc5*c.vtime57) (demsurv7*c.exfunc6) ///
(c.tmmse5*c.exfunc5) (c.tmmse6*c.exfunc6) (c.tmmse7*c.exfunc6) ///
(demsurv6*c.vtime56) (demsurv7*c.vtime57) ///
(demsurv6*c.sisv6) (demsurv7*c.sisv7) ///
(demsurv5*c.tmmse5) (demsurv6*c.tmmse6) (demsurv7*c.tmmse7) ///
)) mem7 lang7 exfunc7 ///
(regress, incl((c.vtime56*c.pwvu6) (c.vtime57*c.pwvu7))) pwvu5 pwvu6 pwvu7
///
 = c.age c.age2 ///
 c.tmmse5 c.tmmse6 c.tmmse7 ///
 c.vtime56 c.vtime57 ///
 deathv7 demsurv5 demsurv6 demsurv7 ///
 afudiab5 afudiab6 afudiab7 ///
 afuhyper5 afuhyper6 afuhyper7 ///
 afuproxy5 afuproxy6 afuproxy7 ///
 ed2 ed3 female rc1 rc2 rc3 rc4 ///
 c.afustroke5 c.afustroke6 c.afustroke7 ///
 , add(25) burnin(50) rseed(040918) force dots augment ///

saveold "$pwv\V7STATADOM", replace version(11)
```

Appendix H: Example 3-Test Combined Z-Score Imputation in Stata from Visits 4 through 6

In this example, the analyst chose to impute individual z-scores for the Delayed Word Recall (z_dwrt), Digit Symbol Substitution (z_dsst), and Word Fluency Test (z_wft). Winsorization was performed post-imputation and a 3-test combined z-score was then computed. For this particular analysis, death was included as a variable and post-death cognitive scores were imputed.

```
mi set wide
mi misstable sum

***Variable to be recalculated after imputation***;
mi register passive ///
z_dwrt4 z_dwrt5 z_dwrt6 z_global5 z_global6

***Variables to be imputed***;
mi register imputed ///
 v4prvhtn v4drink123 v4bmi diabts42 v4smoke123 v4prvchd v4stroke income35 apoe /// V4fixed risk factors
 dwrt2 dsst2 wft2 /// V2 z-scores
 v5bmi diabts57 v5drink123 v5prvhtn v5smoke123 v5prvchd v5stroke /// V5 risk factors
 z_dsst4 memory4 z_wft4 /// V4 z-scores, complete but put here anyway
 z_dsst5 memory5 z_wft5 /// V5 z-scores
 z_dsst6 memory6 z_wft6 /// V6 z-scores
 surv_score mmse_truncated mmse_ind24 tic23 cdr_sp1 cdr_sp2 sis /// screening tool for dementia
 v5v6_poorhealth v5v6_hosp_total

 ***Complete variables***;
mi register regular ///
 v4age_c v4age_sq educ1 educ2 female rc_1 rc_2 rc_3 rc_4 /// age, sex, racecenter, education
 knwndeadbyvisit61 knwndeadbyvisit51 /// indicator of death
 copp cu zinc iron /// copper zinc, iron
 time_v45 time_v46 time_v56 time_ss_v6 /// time
 v5dementia v6dementia /// level-3 dementia indicator
 diet_score saturate_fat tcal /// covariates
 v4v5_proxy v4v5_poorhealth v4v5_hosp_total

***MICE***;
mi impute chained ///
(regress if !missing(imputedate51), omit (time_ss_v6 time_v46 time_v56 z_dsst6 memory6 z_wft6 sis
mmse_truncated )) v5bmi ///
```

```
(regress, omit (time_ss_v6 time_v46 time_v56 z_dsst5 memory5 z_wft5 z_dsst6 memory6 z_wft6 sis cdr_sp1
cdr_sp2 tic23 mmse_truncated i.mmse_ind24 v5bmi ///
 i.v5prvhtn i.diabts57 i.v5stroke i.v5prvchd i.v5drink123 i.v5smoke123 ///
 time_v45 v5v6_hosp_total i.v5v6_poorhealth)) ///
 wft2 dwrt2 dsst2 v4bmi z_dsst4 memory4 z_wft4 ///
(logit if !missing(imputedate51), ///
omit (time_ss_v6 time_v46 time_v56 z_dsst6 memory6 z_wft6 sis mmse_truncated )) ///
v5prvhtn diabts57 v5stroke v5prvchd ///
(logit, omit (time_ss_v6 time_v46 time_v56 z_dsst5 memory5 z_wft5 z_dsst6 memory6 z_wft6 ///
 sis cdr_sp1 cdr_sp2 tic23 mmse_truncated i.mmse_ind24 v5bmi i.v5prvhtn i.diabts57 i.v5stroke i.v5prvchd
i.v5drink123 i.v5smoke123 ///
 time_v45 v5v6_hosp_total i.v5v6_poorhealth )) ///
 v4prvhtn diabts42 v4stroke v4prvchd income35 apoe ///
(logit if !missing(imputedate51), ///
omit (time_ss_v6 time_v46 time_v56 z_dsst6 memory6 z_wft6 mmse_truncated sis v5v6_hosp_total))
v5v6_poorhealth ///
 (regress if !missing(imputedate51), ///
 omit(z_dsst6 memory6 z_wft6 time_ss_v6 time_v46 time_v56 mmse_truncated sis i.v5v6_poorhealth))
v5v6_hosp_total ///
(ologit, omit (time_ss_v6 time_v46 time_v56 z_dsst5 memory5 z_wft5 z_dsst6 memory6 z_wft6 sis cdr_sp1
cdr_sp2 tic23 mmse_truncated i.mmse_ind24 ///
 v5bmi i.v5prvhtn i.diabts57 i.v5stroke i.v5prvchd ///
 i.v5drink123 i.v5smoke123 time_v45 v5v6_hosp_total i.v5v6_poorhealth)) v4drink123 v4smoke123 ///
 (ologit if !missing(imputedate51), omit (time_ss_v6 time_v46 time_v56 z_dsst6 memory6 z_wft6 sis
mmse_truncated )) ///
 v5drink123 v5smoke123 ///
 (regress if !missing(imputedate51), ///
 omit(z_dsst6 memory6 z_wft6 time_ss_v6 time_v46 time_v56 sis mmse_truncated )) tic23 ///
 (regress if !missing(imputedate51), ///
 omit(z_dsst6 memory6 z_wft6 time_ss_v6 sis mmse_truncated time_v46 time_v56 cdr_sp2) ///
 incl(v5dementia (v5dementia#c.z_dsst4) (v5dementia#c.memory4) (v5dementia#c.z_wft4) (v5dementia*educ1)
(v5dementia*educ2) ///
 v5dementia#rc_1 v5dementia#rc_2 v5dementia#rc_3 v5dementia#rc_4 v5dementia#c.v4age_c)) cdr_sp1 ///
 (regress if !missing(imputedate51), ///
 omit(z_dsst6 memory6 z_wft6 time_ss_v6 sis mmse_truncated time_v46 time_v56 cdr_sp1) ///
 incl((v5dementia#c.z_dsst4) (v5dementia#c.memory4) (v5dementia#c.z_wft4) ///
 (v5dementia*educ1) (v5dementia*educ2) v5dementia#rc_1 v5dementia#rc_2 v5dementia#rc_3 v5dementia#rc_4
v5dementia#c.v4age_c)) cdr_sp2 ///
 (regress if !missing(imputedate51), ///
 omit(z_dsst6 memory6 z_wft6 sis mmse_truncated time_ss_v6 time_v56 time_v46) ///
```

```
 incl((v5dementia*educ1) (v5dementia*educ2) (v5dementia*z_dsst4) (v5dementia*memory4) (v5dementia*z_wft4)
(v5dementia*dsst2) (v5dementia*dwrt2) (v5dementia*wft2) ///
 (v5dementia*cdr_sp1) (v5dementia*cdr_sp2) (v5dementia*rc_1) (v5dementia*rc_2) (v5dementia*rc_3)
(v5dementia*rc_4) ///
 (v5dementia*diabts42) (v5dementia*v4prvhtn) (mmse_ind24*educ1) (mmse_ind24*educ2) )) z_dsst5 z_wft5
memory5 ///
 (logit if !missing(imputedate51), ///
 omit(z_dsst6 memory6 z_wft6 time_ss_v6 time_v46 time_v56 sis mmse_truncated )) mmse_ind24 ///
 (regress if !missing(imputedate61)) mmse_truncated ///
 (regress if !missing(imputedate61), ///
 incl((v6dementia*c.z_dsst5) (v6dementia*c.memory5) (v6dementia*c.z_wft5) ///
 v6dementia#educ1 v6dementia#educ2 v6dementia#rc_1 v6dementia#rc_2 v6dementia#rc_3 v6dementia#rc_4
v6dementia#c.v4age_c)) sis ///
 (regress if !missing(imputedate61), ///
 incl((c.mmse_truncated*c.z_dsst5) (c.mmse_truncated*c.memory5)(c.mmse_truncated*c.z_wft5)
(c.mmse_truncated*educ1) (c.mmse_truncated*educ2) ///
 (copp*c.sis) (cu*c.sis) (sis*z_dsst5) (sis*memory5) (sis*z_wft5) (v6dementia*c.z_dsst5)
(v6dementia*c.memory5) (v6dementia*c.z_wft5) ///
 (v6dementia*sis) (v6dementia*educ1) (v6dementia*educ2) (v6dementia*rc_1) (v6dementia*rc_2)
(v6dementia*rc_3) (v6dementia*rc_4) ///
 (v6dementia*diabts42) (v6dementia*v4prvhtn) (sis*c.time_v56) (sis*c.time_ss_v6))) z_dsst6 z_wft6 memory6
///
 = v4age_c v4age_sq educ1 educ2 female rc_1 rc_2 rc_3 rc_4 knwndeadbyvisit61 knwndeadbyvisit51 copp cu zinc
iron time_ss_v6 time_v45 time_v46 time_v56 v5dementia v6dementia diet_score v4v5_proxy v4v5_poorhealth
v4v5_hosp_total saturate_fat tcal, add(30) burnin(50) rseed(040918) report force dots augment savetrace
("F:\ARIC\Projects\traceplot.dta", replace)
 save "F:\ARIC\Projects\imputed_30 sets.dta", replace

use "F:\ARIC\Projects\imputed_30 sets.dta"

***Recalculate DWRT***;
mi passive: replace z_dwrt5 = memory5 if z_dwrt5==.
mi passive: replace z_dwrt6 = memory6 if z_dwrt6==.

***Winsorization of DWRT, since the range of the possible DWRT z-score should be between -2.98 and 2.13***;
mi passive: replace z_dwrt6 = -2.98 if z_dwrt6 < -2.98
mi passive: replace z_dwrt5 = -2.98 if z_dwrt5 < -2.98
mi passive: replace z_dwrt6 = 2.19 if z_dwrt6 > 2.19 & !missing(z_dwrt6)
mi passive: replace z_dwrt5 = 2.19 if z_dwrt5 > 2.19 & !missing(z_dwrt5)

***Calculate Global Z-Score***;
```

```
quietly sum z_global4
mi passive: replace z_global5 = ((z_dwrt5 + z_dsst5 + z_wft5)/2.3025864) if z_global5==.
quietly sum z_global4
mi passive: replace z_global6 = ((z_dwrt6 + z_dsst6 + z_wft6)/2.3025864) if z_global6==.
save "F:\ARIC\Projects\imputed_30_mice sets.dta", replace
```

Appendix I: Adaptable Stata Code for Multiple Imputation

Please note that this code can also be downloaded from https://github.com/Jennazhu/MI.

```
/*
cd ../..
*/

clear all
global atr "1-data/atrophy"



*** import  data
      use "$atr/dat_wide.dta", clear
      codebook id
      codebook id if !missing(atrophy)

  *rename time-invariant (baseline) vars to make cross-temporal MI spec easier to read
  rename (age  htn  smoke  drink  dm  apoe  educ)  ///
         (age1 htn1 smoke1 drink1 dm1 apoe1 educ1)
  rename (atrophy  male  siterace  wmh)  ///
         (atrophy1 male1 siterace1 wmh1)


*******************************************************************************
*Step 1:  Declare multiple-imputation data
  mi set wide


  *examine missingness patterns
  mi misstable summarize globz1 globz2 globz3 globz4 globz5 // summerize missingness of each variable
  mi misstable patterns  globz1 globz2 globz3 globz4 globz5, asis freq // summerize missingness of each
variable


*******************************************************************************
*Step 2: "Register" the missing variables
```

```
** Step 2.1: register imputed variables
** All baseline variables should be here (everyone is alive at baseline)
  global impvars ///
          globz1 globz2 globz3 globz4 globz5  ///
            age1 htn1 smoke1 drink1 dm1 apoe1 educ1 // v2globz

       * summarize impvars
     summ idnum $impvars
       * registeer
        mi register imputed  $impvars


** Step 2.2: register regular variables
      * Variables that do NOT contain missing data should be included after the
      * "mi register regular" statement
  global regvars ///
           atrophy1 male1 siterace_JB1 siterace_FB1 siterace_FW1  wmh1  ///
           alive1 alive2 alive3 alive4 alive5 ///
           dem1 dem2 dem3 dem4 dem5

      summ idnum $regvars
      mi register regular $regvars



*************************************************************************
*Step 3 : imputation

    * xtset for mi data
      capture mi xtset, clear

      *create inclusion variable statements for each visit (here 1 to 5)
  global incl0 // blank, nothing earlier to include than v1
      forvalues i = 1(1)5 {
    local j = `i'-1 // used in the global incl statements
    global incl`i'  (atrophy1*time`i') (atrophy1*male1) (atrophy1*htn1) (atrophy1*educ1) ///
                    (atrophy1*apoe1) (atrophy1*siterace_JB1)  (atrophy1*siterace_FB1)
(atrophy1*siterace_FW1) ///
                    (atrophy1*c.age1) (atrophy1*drink1) ///
```

```
                  (dem`i'*time`i') (alive`i'*time`i') ///
                  ${incl`j'}
  di
  di "Global macro var incl" `i' ": " "${incl`i'}"
    }

    *create omitted variable statements for each visit (here 1 to 4)
*omit anything from a future time
global omit5 // blank, nothing future to omit from last visit but needed for loop
forvalues i=5(-1)1 {
  local j = `i'-1 // used in the global omit name
  global omit`j' alive`i' time`i' dem`i'  globz`i' ${omit`i'}
  di
  di "Global macro var omit" `i' ": " "${omit`i'}"
}



* global seed for imputation
global mseed = 042020 // set MI random seed (change this every once in awhile)

*choose which types of death information to include:
*global keepdeathcat = 2 // don't use the visit if they died during
*global keepdeathcat = 1 // don't use the visit after death if they died in-between visits
global keepdeathcat = 0 // keep an observation in the dataset if they died in-between visits
    * start imputation
    mi impute chained ///
       (regress, omit( $omit1) ) age1   /// baseline normally distb covs ///
       (logit,   omit( $omit1) ) htn1  dm1  /// baseline binary covs
       (ologit,  omit( $omit1) ) apoe1 educ1 drink1 smoke1  /// baseline ordinal covs
       (regress if alivecat1 > $keepdeathcat , incl( $incl1 ) omit( $omit1) ) globz1 ///
       (regress if alivecat2 > $keepdeathcat , incl( $incl2 ) omit( $omit2) ) globz2 ///
       (regress if alivecat3 > $keepdeathcat , incl( $incl3 ) omit( $omit3) ) globz3 ///
       (regress if alivecat4 > $keepdeathcat , incl( $incl4 ) omit( $omit4) ) globz4 ///
       (regress if alivecat5 > $keepdeathcat , incl( $incl5 ) omit( $omit5) ) globz5 ///
            = atrophy1 male1 i.siterace1 wmh1 ///
     time1 time2 time3 time4 time5  ///
                 alive1 alive2 alive3 alive4 alive5 ///
              dem1 dem2 dem3 dem4 dem5 ///
           , add(30) burnin(50) rseed($mseed) report force dots augment
```

```
*check:
  forvalues i = 1(1)5 {
tab alivecat`i' if alivecat`i' > 0
  }

    save "$atr/impute/midat", replace


  ****************************
  ** change it into long format
  ****************************

  use "$atr/impute/midat", clear


  * reshape the data
  mi reshape long vdate time alive alivecat globz , i(idnum) j(visit)

  * xtset the data
  mi xtset idnum visit


  save "$atr/impute/midat_long", replace
```