Michael Spriggs 16 December 2013

*F*olic *A*cid for *V*ascular *O*utcome *R*eduction *I*n *T*ransplantation
(FAVORIT)

A Randomized, Controlled Clinical Trial of the Effect of a High Dose Combination of Folic Acid, Vitamin B6 and Vitamin B12, on Arteriosclerotic Cardiovascular Disease Outcomes in Chronic, Stable Renal Transplant Recipients

FAVORIT is a multicenter, randomized, double-blind clinical trial to determine whether total homocysteine (tHcy)-lowering treatment with a standard multivitamin augmented by a high dose combination of folic acid, vitamin B12, and vitamin B6, versus treatment with an identical multivitamin containing no folic acid and Estimated Average Requirement (EAR) amounts of vitamin B6 and vitamin B12 reduces cardiovascular disease [CVD] outcomes among clinically stable renal transplant recipients (RTRs) with elevated tHcy levels. The FAVORIT data archive contains study data collected from screening, baseline, and follow-up for 4,110 randomized participants from 30 clinical sites. Data collection for the study began in August 2002 and follow-up ended June 2011. The Repository archive includes the study protocol and related descriptive documentation, data collection forms and study data, and a dataset integrity check.

The files in the archive are organized into the following directories:

1. Documentation
2. Forms
3. Data
4. Dataset Integrity Check

1. Documentation Directory

The FAVORIT Documentation Directory contains study and data documentation:

- The FAVORIT **Manual of Procedures,** FAVORIT MOP 130130.pdf, includes the official protocol and manual of procedures as of August 2009, 229 pgs.
- The FAVORIT **Protocol,** chap1 PROTOCOL 061129.pdf, dated November 2006, summarizes key elements of the FAVORIT study.
- A list of FAVORIT P**ublications** through December 2012 can be found in "All FAV Publication as of December 2012.pdf."
- A **Data Dictionary**, NIDDK Data Dictionary V2.pdf, version 6.0, dated October 18, 2013, provides an overview of the study design and methodology, describes the database structure, data and variable naming conventions, and study and analysis datasets. In addition, this useful document describes and defines primary and secondary study endpoints as well as laboratory methods and assays. Finally, contents and listing of the first 10 observations from each dataset, frequencies of categorical variables, means and other modal measures of continuous variables, and distributions of all study variables are provided. 611 pgs.

2. Forms Directory

The FAVORIT Forms Directory contains 48 files as follows:

- A total of 30 data collection forms, including 22 study data collection case report forms (CRFs, in pdf format) corresponding to data transferred to the Repository from the screening (n=4), baseline and follow-up visits (n=18). In addition, 8 outcomes forms document death, serious adverse events, as well as potential myocardial infarction, stroke, etc.

Some data forms include multiple versions. Each data set is a composite of all data items from all versions of the corresponding form. Consequently some data items may be missing from individual data records based on the version of the data form completed. Each form is named using a three-letter combination (e.g., REL for Randomization Eligibility Form) followed by a character string indicating the visit number and data set version.

- Question by question (Q x Q) specifications of 18 forms also are provided. These Q x Qs provide general and specific instructions for form completion.

A brief description of the study forms, their corresponding PDF and SAS file names, and Q x Q specifications is summarized in Table 1.

3. Data Directory

The FAVORIT data directory contains:

- 51 SAS datasets that correspond to: 27 CRFs including 5 screening datasets and 27 baseline/follow-up datasets and 8 outcome datasets (see Table 1) and 11 derived datasets (Table 2)

Table 1. Study data collection forms, corresponding SAS datasets and form names, and Q x Qs, FAVORIT files in NIDDK Repository

FORM	SAS DATA FILE NAME	FORM NAME (.pdf)	Q X Q
SCREENING			
Screening Creatinine	CREA_NIDDKV1	CRE	
Screening Creatinine Blind Matching Replicates	CREA_BRM_NIDDKV1		
Informed Consent Form	ICTA_NIDDKV1	ICT	ICT QxQ
Screening Phlebotomy Form:Collection	SPC_NIDDKV1	SPC	SPC QxQ
Screening Phlebotomy Form: Processing & Inventory	SPP_NIDDKV1	SPP	SPP QxQ
BASELINE AND FOLLOW-UP			
Creatinine, Glucose and Uric Acid	CRC_NIDDKV1	CRC	
Creatinine, Glucose and Uric Acid Blind Matching Replicates	CRC_BRM_NIDDKV1		
Participant Exit Form	EXTA_NIDDKV1	EXT	EXT QxQ
Follow-up Contact Form	FUP_NIDDKV1	FUP	FUP QxQ
Total Homocysteine	HCYA_NIDDKV1	HCY	
Total Homocysteine Blind Matching Replicates	HCYA_BRM_NIDDKV1		
Hospitalization Form	HOS_NIDDKV1	HOS	HOS QxQ
Informed Consent Modifications or Withdrawals	ICM_NIDDKV1	ICM	ICM QxQ
Informant Interview Form	INF_NIDDKV1	INF	INF QxQ
Low Density Lipoproteins	LDLA_NIDDKV1	LDL	
Low Density Lipoproteins Blind Matching Replicates	LDLA_BRM_NIDDKV1		
Lipids	LIP_NIDDKV1	LIP	
Lipids Blind Matching Replicates	LIP_BRM_NIDDKV1		
Medication Survey Form	MSR_NIDDKV1	MSR	MSR QxQ

Metabolic Panel Form	PCFA_NIDDKV1	PCF	
Metabolic Panel Form Blind Matching Replicates	PCFA_BRM_NIDDKV1		
Baseline/Follow-up Phlebotomy:Collection	PHC_NIDDKV1	PHC	PHC QxQ
Baseline/Follow-up Phlebotomy:Processing & Inventory	PHP_NIDDKV1	PHP	PHP QxQ
Pyridoxal Phosphate	PLPA_NIDDKV1	PLP	
Pyridoxal Phosphate Blind Matching Replicates	PLPA_BRM_NIDDKV1		
Randomization Eligibility Form	REL_NIDDKV1	REL	REL QxQ
Baseline Visit Form:Patient Characteristics	RPC_NIDDKV1	RPC	RPC QxQ
Urine Creatinine & Microalbumin	URNA_NIDDKV1	URN	
Urine Creatinine & Microalbumin Blind Matching Replicates	URNA_BRM_NIDDKV1		
Vitamin B12 and Folic Acid	VBFB_NIDDKV1	*VBF*	
Vitamin B12 and Folic Acid Blind Matching Replicates	VBFB_BRM_NIDDKV1		
Vitamin Distribution Log	VDL_NIDDKV1	VDL	VDL QxQ
OUTCOMES			
Death Adjudication Form	DAD_NIDDKV1	DAD	
Initiation of Dialysis Fax Notification	DIAA_NIDDKV1	DIA	DIA QxQ
Dialysis Post-Event Surveillance Form	DPEA_NIDDKV1	DPE	DPE QxQ
Death, Serious Adverse Event, or Elevated Amylase Fax Notification	DSAB_NIDDKV1	DSA	DSA QxQ
MI Adjudication Form	MAD_NIDDKV1	MAD	
Outcomes Documentation Form	OUTA_NIDDKV1	OUT	OUT QxQ
RSD Adjudication Form	RAD_NIDDKV1	RAD	
Stroke Adjudication Form	SAD_NIDDKV1	SAD	

Derived datasets are not associated with any particular CRF but contain variables merged across several forms and/or reflect recoded variable values created by the DCC. Some data were collected on different forms within a visit so a single variable spans multiple CRFs. **Eleven** derived datasets are provided. File names and a brief description of derived datasets are noted in Table 2. Corresponding sections of the NIDDK Data Dictionary for detailed discussions of the variables included in these datasets are indicated.

Table 2. FAVORIT Derived Datasets

FORM	SAS FILE NAME	DESCRIPTION	DATA DICT.*
Primary Outcome and All Cause Mortality	ADJPROCEP_ALL_NIDDKV2	First primary CVD outcome either adjudicated or procedural	5.5 p459
CVD Death	ADJ_DEATH_EP_NIDDKV1	Records CVD-related death	5.5 p468
MI	AJ_MI_EP_NIDDKV1	First myocardial infarction event	5.5 p473
Stroke	ADJ_STROKE_EP_NIDDKV1	First stroke event	5.5 p481
RSD	ADJ_RSD_EP_NIDDKV1	First resuscitated sudden death outcome	5.5 p486
Procedures	PROCEDURE_EP_NIDDKV1	First FAVORIT procedural outcome	5.5 p494
Treatment	TREAT_NIDDKV1	Treatment group assignment	5.5

Assignment			p499
Other Derived Datasets			
Screening	SCREEN_DERV_NIDDKV1	Various screening demographic and clinical data	5.1
Randomization	RAND_DERV_NIDDKV2	Derived variables on all randomized subjects, Baseline thru Visit 16	5.3
Adherence	ADHER_NIDDKV1	Vitamin adherence variables for each follow-up	5.2
ICD 9 Codes	DIAG_NIDDKV1	ICD 9 codes for all hospitalizations	5.4

*See NIDDK Data Dictionary V2.pdf provided in the Documentation directory. Page numbers for descriptions of outcome derived data are noted.

Linking subject data across datasets. Subjects are indentified in data records by the variable, BLINDID. Study visit number, VISIT, is coded as "00" for screening, "01" for baseline, and "02-16" for follow-up visits. FSEQNO, form sequence number, identifies multiple forms per visit (but is not applicable to screening or baseline visit forms). These three variables may be used to link subject data across all datasets.

4. Dataset Integrity Check Directory

The FAVORIT Dataset Integrity Check directory contains a report based on an examination of the data in the repository by statisticians and quality control specialists at the Repository. Datasets were checked for completeness, consistency, and usability. The published data from the manuscript in *Circulation* by Bostom et al (2011), Homocysteine-Lowering and Cardiovascular Disease Outcomes in Kidney Transplant Recipients : Primary Results From the Folic Acid for Vascular Outcome Reduction in Transplantation Trial were compared to values recalculated from the FAVORIT data in the NIDDK Repository.