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Monthly Program Status Report – PROJECT

Reporting Period:	**March 2016**
Contracting Agency:	Food and Drug Administration (FDA)
FDA Project Manager:	Shaila Shaheed, Shaila.Shaheed@fda.hhs.gov, Thomas Permutt, thomas.permutt@fda.hhs.gov,
FDA Subject Matter Expert:	Thomas Permutt, thomas.permutt@fda.hhs.gov, 301-796-1271
FDA COTR:	Shaila Shaheed, Shaila.Shaheed@fda.hhs.gov,
Contract / Order:	HHSF223201310230C
Contractor PI:	Daniel Scharfstein, dscharf@jhu.edu, 410-955-2420
Project Team:	Aidan McDermott (Computer Programmer)
Description of Activity:	A recent FDA-sponsored National Research Council Report recommended that "examining sensitivity to the assumptions about the missing data mechanism should be a mandatory component of reporting." While the Report outlines a framework for conducting sensitivity analysis, there are two major problems with existing methods: (1) they have not been implemented in software packages and (2) they do not adequately address non-monotone missing data patterns (i.e., patients provide data irregularly). The objective of this project is to address these gaps by: 1) creating unified and coherent methods for global sensitivity analysis of clinical trials with monotone and non-monotone missing data, 2) developing free, open source and reproducible software in SAS and R to implement the methods, and 3) demonstrating the methods and software using real clinical trial data.

Project Health Check							
Health ▶	**Budget**	🟥	**Schedule**	🟨	**Resources**	🟩	**Deliverables**	
Notes ▶	Within Budget		On Schedule		Adequate		On Target	

Budget Tracking – (TOTAL CONTRACT CEILING)

POP	Ceiling Remaining	Cumulative Funding	Year Funding (Year 1)	Spent to Date	Year Funding Remaining	Month Invoice	Funding Covers
Base	$1,094,565	$1,094,565	$1,094,565	$962,894.82 ($164,747.12 committed)	$131,670.19	$758,357.07	Salary, fringe, other expenses, and indirect costs

Activity Summary and Highlights

We completed a revision of the main SAMON manuscript which was submitted to *Journal of Royal Statistical Society Series B*. (see attachment). We completed revision of death/missing data paper, which was re-submitted to *Biometrics* (see attachment). We completed a user-friendly version of SAMON manuscript which we plan to submit to *Clinical Trials* within the next two weeks (see attachment). We worked in Youtube video that explains how to use SAMON. We conducted a simulation study data to evaluate the performance of non-monotone missing data procedure.

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Key Accomplishments	
Current Reporting Period	*Planned for Next Period*
• Completed *JRSS-B* manuscript • Completed *Biometrics* manuscript. • Completed *Clinical Trials* manuscript. • Youtube video • Simulation study for non-monotone missing data procedure.	• Submit *Clinical Trials* manuscript • Non-monotone missing data software package. • Finish Youtube video

Issues and Risks					
Category	**Priority**	**Status**	**Opened**	**Issue**	**Description**
Contract (FDA)	1	Closed	9/30/13	Intellectual Property	Revision to contract regarding intellectual property language.
Dissemination (FDA)	2	Closed	2/15/14	Website	FDA Personnel cannot connect to www.missingdatamatters.org from their office computers.
Software (JHU)	1	Closed	3/15/14	Coverage of Confidence Intervals	Simulations indicate that standard procedures for constructing confidence intervals are not providing adequate coverage with typical sample sizes.
Computing (JHU)	1	Closed	4/21/14	Periods of slow performance of computing cluster	A new computing cluster was installed at Johns Hopkins. We are experiencing periods of slow performance on the cluster.
Personnel (JHU)	1	Closed	5/21/14	Re-Distribution of Effort	Starting April 1, Aidan McDermott has reduced his percent effort by 20%. Chenguang Wang joined the project starting July 15.
Invoicing (FDA)	1	Open	6/6/14	Payment of Invoices	Invoices have not been paid.
Computing (FDA)	1	Open	6/6/14	Software on FDA Cluster	Investigate the steps needed to run software on FDA cluster
Personnel (JHU)	1	Open	1/13/15	New Effort	Yi Lu joined the project to work on confidence intervals.

Other Activities

Attachments and References
JRSS-B Manuscript, *Biometrics* Manuscript, *Clinical Trials* Manuscript, Intermittent Missing Data Simulation Results

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Upcoming Short Courses/Webinars
- May 24 or May 26 (TBA): American Statistical Association Biopharmaceutical Section Webinar
- June 22 (8:30-5) Johns Hopkins University Summer Institute in Epidemiology and Biostatistics, Baltimore, MD
- July 26 (8:30-5) University of Washington Summer Institute in Statistics for Clinical Research, Seattle, WA
- October 26-28 BASS Conference, Rockville, MD

Status of Milestones
- 4: Create Non-Monotone Missing Data Product (due 9/15/16, on schedule)
  - 4.3: SAS implementation (due 6/30/16, on schedule)
  - 4.4: R Implementation (due 6/30/16, on schedule)
  - 4.5: Two Case Studies (due 6/30/16, on schedule)