

Monthly Program Status Report – PROJECT

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| Reporting Period: | June 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 | \$963,018.34 (\$81,198.98 committed) | \$131,546.66 | \$853,456.30 | Salary, fringe, other expenses, and indirect costs |

| Activity Summary and Highlights |
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| We completed two case studies and two simulation studies for non-monotone missing data methodology. We worked on completing the software package. Gave short course at Johns Hopkins. <i>Biometrics</i> paper on handling death and intermittent missing data was accepted and an associated software package, called <i>i dem</i> , was posted on CRAN. |

| Key Accomplishments | |
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| Current Reporting Period | Planned for Next Period |
| <ul style="list-style-type: none"> Gave short course at Johns Hopkins Completed two cases studies and two simulation studies for non-monotone missing data methods. Worked on non-monotone missing data software package. <i>Biometrics</i> paper on handling death and intermittent missing data accepted and associated software package, <i>idem</i>, posted on CRAN. | <ul style="list-style-type: none"> Short course at University of Washington Submit <i>Clinical Trials</i> manuscript Complete non-monotone missing data software package. |

| 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 | Closed | 6/6/14 | Payment of Invoices | Invoices have not been paid. |
| Computing (FDA) | 1 | Closed | 6/6/14 | Software on FDA Cluster | Investigate the steps needed to run software on FDA cluster |
| Personnel (JHU) | 1 | Closed | 1/13/15 | New Effort | Yi Lu joined the project to work on confidence intervals. |
| Software (JHU) | 1 | Open | 6/15/16 | Coverage of Confidence Intervals | Simulations indicate that standard procedures for constructing confidence intervals are not providing adequate coverage with typical sample sizes. |

| Other Activities |
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| Attachments and References |
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Upcoming Short Courses/Webinars

- July 26 (8:30-5) [University of Washington Summer Institute in Statistics for Clinical Research](#), Seattle, WA
- September 20 (12-3) ASA Webinar
- 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 (7/31/16)
 - 4.4: R Implementation (7/31/16)
 - 4.5: Two Case Studies (completed, need to write-up)