Norgan Radler, Charlene R. Continuous quality improvement at the clinical research site: implementing methods for coordinators in the Heart and Lung Transplant and Pulmonary department at Baylor Scott and White Research Institute
Master of Science (Clinical Research Management), April 2020

Introduction:

The following research project is a Quality Improvement (QI) study to assess resource utilization for six ongoing clinical trials and evaluate the impact of quality improvement methods on the completion of critical trial activities in the Heart and Lung Transplant and Pulmonary (HLTP) department at Baylor Scott and White Research Institute (BSWRI).

Methods:

The project design is a case series in which observations were made on research staff before and after an intervention, with no control group. Non-probability sampling with purposeful, maximum variation was used due to the study's qualitative research design. Metrics were collected regarding the completion of key trial activities of subject screening, subject enrollment, and data entry before and after intervention using a spreadsheet tool. Collected metrics were reviewed to identify areas for improvement and QI interventions were designed and implemented to reallocate resources as appropriate. The data was maintained in a run chart to monitor changes during the pre-intervention and post-intervention periods. Statistical analysis was performed on the data to evaluate the effect of the intervention.

***Results*:**

The Wilcoxon Signed-Rank test was used to statistically analyze differences in medians of activity metrics across all studies before and after intervention. All variables improved in the direction of the applied interventions except time screening subjects and data entered in the electronic data capture (EDC) system. Median differences were found statistically non-significant, except the combined variable of number of open queries and case report forms (CRF) not entered weekly which demonstrated a statistically significant decrease following intervention. Median time screening subjects demonstrated a non-significant decrease following intervention while median number of subjects screened showed a non-significant increase.

Median time enrolling subjects and median number of subjects enrolled increased post intervention, but statistical testing was not performed due to the small sample size below the minimum critical threshold required. Median time entering data in the EDC demonstrated a non-significant increase following intervention while median number of CRFs entered in the EDC showed a non-significant decrease.

Conclusion:

Implementation of the quality improvement process for clinical research staff provided a tool for our site to continuously assess and improve trial outcomes. Five of the seven variables receiving quality improvement interventions improved in the direction of the intervention, with one demonstrating a statistically significant difference. The small sample size used may have decreased the power of the study to detect statistical significance. Future studies should be completed to apply the quality improvement methodology used to a larger sample size. In conclusion, this study established 'proof of concept' for the completion of future, larger-scale quality improvement projects at our research site.

Continuous quality improvement at the clinical research site: Implementing methods for coordinators in the Heart and Lung Transplant and Pulmonary department at Baylor Scott and White Research Institute

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INTERNSHIP PRACTICUM REPORT

Presented to the Graduate Council of the
Graduate School of Biomedical Sciences
University of North Texas Health Science Center
at Fort Worth, Texas

In Partial Fulfillment of the Requirements
for the Degree of
MASTER OF SCIENCE IN CLINICAL RESEARCH MANAGEMENT

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Fort Worth, Texas
April 2020

ACKNOWLEDGEMENTS

I would like to express my sincere appreciation to my major professor, Dr. Stephen Mathew, for his constant guidance and mentorship during my academic journey at UNT Health Science Center. I would also like to thank my entire committee including Dr. Joost Felius, Dr. Pankaj Chaudhary, and Horacio Martinez for their dedicated support as I prepared and defended my internship practicum report. As site managers, Dr. Felius and Horacio went above and beyond to ensure abundant learning opportunities were available throughout my internship and facilitated an engaging, dynamic site experience. The statistical analysis presented in my project would not have been possible without the patient, expert guidance of biostatistician Johanna Van Zyl. I am grateful for the countless hours of training provided by Clinical Research Coordinator Christine Brooks, RN, and Research Enrollment Analyst II, Lesia Parker. The time invested by these wonderful ladies to further my professional knowledge will reap dividends in the future of clinical research.

Each member of the HLTP Department at BSWRI displayed a friendly, welcoming attitude, and never hesitated to lend their time to teach and train me. Notably, Clinical Research Coordinator II Amanda Doss facilitated my flawless onboarding process and continuously engaged me with new and unique learning experiences. Her positive, caring attitude helped me feel “part of the team” from day one and reflected BSWRI’s core values. I am also grateful to Dr. Parag Kale for the time he took out of his busy schedule to teach me about patient care in the field of cardiology. His kind, attentive bedside manner and dedication to advancing medicine through research are two principles I will practice throughout my career. I appreciate the many physicians and clinical staff within Baylor Scott and White Health who provided invaluable time and opportunities to further my knowledge of medicine and research.

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CHAPTER I

INTRODUCTION

The purpose of this practicum project was to evaluate whether there is improved effort and outcomes of key clinical research trial activities by administration of quality improvement methods. Trials were selected within the Heart, Lung, Transplant and Pulmonary (HLTP) research department at Baylor Scott and White Research Institute (BSWRI). The project was conducted with the assistance of Dr. Joost Felius, HLTP department manager, and Horacio Martinez, HLTP office manager.

This study is designed as an uncontrolled longitudinal case-series in which observations are made on BSWRI HLTP staff completion of key trial activities of subject screening, subject enrollment, and data entry before and after a quality improvement intervention. The study sought to identify areas of improvement within staff completion of key trial activities by analyzing activity metrics, in order to reallocate resources to reduce staff burden and improve operational efficiency through the quality improvement program. Applying a quality improvement approach to the challenge of limited time and personnel resources at clinical research sites may alleviate overburdening of Clinical Research Coordinators (CRC) and other staff and improve completion of critical trial activities.

CHAPTER II

BACKGROUND AND LITERATURE REVIEW

Clinical Research Coordinators at large, active sites are often assigned to oversee multiple trials and thus must improvise individualized methods to divide their finite resources amongst competing critical activities. Methods not aligned with site priorities may lead to inconsistent results such as over exceeding subject enrollment goals while data entry lags with multiple open queries. Sites can attain consistently high levels of performance among all CRC's when they incorporate a structured continuous quality improvement system that identifies and corrects performance gaps. Sites deficient in these processes can utilize a quality improvement project designed to answer their specific local, improvement question.

Clinical research sites that implement quality improvement methods may require staff effort tracking to record the time employees spend completing trial activities. When sites track staff workloads, they profit by developing an in-depth knowledge of trial activities, which enables them to construct budgets that sufficiently compensate their staff[1]. Staff effort tracking also helps sites to substantiate budget negotiations with sponsors by providing documentation of staff time spent in the completion of trial activities[1]. Lastly, staff workload tracking may assist sites to accurately determine the number of trials they can conduct, and to maintain a suitable number of employees to efficiently and effectively meet study goals without overburdening or under employing them[1].

Despite these overwhelming benefits, numerous challenges arise during the implementation of site-level staff effort tracking such as difficulty determining project goals and types of data to collect, struggling to dedicate staff time to consistently collect quality data, and trouble managing staff perception and participation[1]. Numerous healthcare organizations

including Indiana University Simon Cancer Center and Holden Comprehensive Cancer Center have overcome these challenges by conducting quality improvement projects that incorporate standardized effort-tracking approaches, datasets, and tools to guarantee consistent assessments, minimize staff time requirements, and enable easy data comparison and identification of operational inefficiencies[1]. The success of these projects can be observed through results such as an organization using collected data to justify hiring new employees and increase budgeting for key trial activities[1]. Sites that intend to implement staff effort tracking benefit from using a standards-based approach with clearly defined processes and tools[1].

Successful management is related to the effective use of performance measures as instruments to continuously compare performance and assess trends over time[2]. Benchmarking is an important component of the continuous improvement program that initially appeared in U.S. healthcare in 1990 through the requirements of the Joint Commission on Accreditation of Healthcare Organizations (JCAHO)[3]. Benchmarking had been pioneered by Xerox about 10 years previously as a means to decrease production costs in comparison to competitors in the same sector[3]. Though it originated from outside of healthcare, benchmarking is a tool that reaps dividends when applied within healthcare fields, including Clinical Research Management. As a process, benchmarking consists of measuring performance, making comparisons, and identifying areas requiring improvement[2]. It should be designed as a regulated process arranged around best practices that integrates feedback and measures factors critical to an organization's success[2]. Sites may identify opportunities for improvement by determining the difference between current and desired performance levels[2].

An important step of the quality improvement process lays within the selection of critical trial activities on which to observe and collect data. Two studies conducted by researchers at

Nottingham Clinical Trials Unit incorporated a systematic database search and Delphi survey to identify metrics commonly used to monitor site performance in multicenter trials[4]. The metrics they identified were finalized into three categories: recruitment and retention, data quality, and protocol compliance[5]. Monitoring performance metrics in these groups may improve trial performance by enabling sites to identify and respond to issues before trials are negatively affected[5]. The critical trial activities selected in our study generally fall within these groups, and thus should be beneficial to analyze.

In the peer-reviewed article "Using Metrics to Measure and Monitor Performance in Clinical Trials" published in the April 2014 edition of *Clinical Researcher*, Dr. Randy Krauss advises sites on strategies for selecting and monitoring appropriate metrics to improve clinical trials[6]. He advises the first step is to determine organizational goals to ensure selection of metrics which align with them[6]. Metrics should be clearly defined, accessible, verifiable, and adapted to reasonable goals[6]. Data from implemented metrics should be compared against the target to assess performance[6]. When analyzed against a benchmark or goal, metrics serve as indicators of process performance and may illuminate areas of concern for quality improvement[6]. Performance data from metrics may also inform future decision making and goal setting[6].

Another report advocated the use of a "balanced scorecard", or set of key performance indicators, to assess site processes intended to produce high quality data through clinical research trials[7]. This concept is not novel to the business sector, as it was first proposed in *Harvard Business Review* in 1992[8]. Incorporating this tool into clinical research enables a multi-faceted assessment of site performance that allows for the observation of both direct intended effects and unintended effects on non-targeted metrics[7]. Just as clinical research trials measure the safety and

efficacy of new drugs, clinical researchers should measure the efficacy of newly implemented processes in the workplace.

Dr. Kingsley defined key performance indicators as a select few critical metrics able to efficiently and accurately measure the performance of a process[7]. A key performance indicator (KPI) may be likened to a pulse or blood pressure reading which quickly assesses health, while an out of range reading initiates the investigation of other available measurements to find the cause[7]. A balanced scorecard is a set of multi-perspective KPIs that maximize organizational health when within range and allow for change to be affected when out of range[7]. A strength of the balanced scorecard lies in its capacity to illustrate improvements in one area that are at the expense of another area, which may happen when an organization redirects effort to improve one metric[7].

Dr. Kingsley provided a few words of caution in the selection of KPIs for the balanced scorecard[7]. He advocated that selected KPIs should be aligned with organizational goals to ensure time and effort spent is well-matched to potential benefit[7]. Sites should be aware of potential unintended effects of quality improvement efforts such as reducing efforts in non-targeted areas or the potential of fraud to meet selected goals[7]. Thus, it is important to select a balanced set of KPIs to maximize performance in all areas critical to organizational goals[7]. When conducting quality improvement projects, sites should also be conscious of the Hawthorne effect which is similar to the placebo effect in clinical research trials[7]. The Hawthorne effect can lead to apparent improvement of the targeted variable in the absence of a significant intervention simply due to the effect of observation[9].

Strategies for defining key performance indicators in clinical research sites were also discussed in another report where they noted that while sponsors and contract research

organizations have largely been successful at targeting metrics to optimize clinical trials, efforts by sites have been intermittent and lacking in a systematic methodology[10]. Sahai, 2016 proposed best practices and strategies for developing a metrics monitoring program at a clinical research site[10]. They argued that there is not a standard way of developing a KPI program or a universal list of KPIs applicable to all sites[10]. Instead, they advised the use of strategies and considerations for KPI program development that may be used and tailored by individual sites[10].

Strategies advocated by Sahai, 2016 include common themes already reviewed, such as identifying KPIs relevant to organizational goals and defining KPIs to ensure accurate metrics collection[10]. A significant strategy discussed is the timely implementation of findings from KPI monitoring[10]. Collection of metrics alone may not improve performance aside from the Hawthorne effect, but incorporating results into a continuous quality improvement process can maximize benefits[10]. Analysis of collected metrics must occur, and an appropriate plan for action developed[10].

In keeping with this same theme in her 2016 article in *Clinical Researcher*, Linda Sullivan, the president of the Metrics Champion Consortium (MCC) asked "are we simply using performance metrics to determine if we are doing things right and according to plan, or are we using them to improve the plan by doing the right things from the beginning?"[11] She argued that standardized KPIs may be applied across the clinical trials industry to benchmark and improve clinical trial operations[11]. Standardization enables organizations to measure the right things instead of focusing on metrics that may not improve performance[11]. To measure the right things, KPIs should be aligned with critical success factors which are those select key areas that ensure organizational performance[11].

MCC identified the following critical success factors with the input of stakeholders across the clinical trials industry[11]:

1. All studies have more than 85% of sites enrolling more than one subject
2. Develop a quality protocol in a timely manner
3. Use quality sites that deliver clean data in a timely manner while following GCP compliance regulations
4. Ensure that sites have drugs and other clinical supplies onsite when needed
5. Collect/Analyze safety and endpoint data required for submission
6. Monitor and respond to subject safety events in a compliant manner

With standardized critical success factors identified, sites can develop KPIs aligned with organizational roles and responsibilities[11]. When designing KPIs, a balance among time, quality, and cost metrics is important to enhance trial results and minimize rework[11].

SPECIFIC AIM

Clinical research sites managing multiple ongoing trials face a problem of overburdened coordinators and other staff due to limited resources such as time and personnel. Staff burden generally depends on the number of active studies, number of subjects per study, and number, duration, and difficulty of study visits, among other variables. Subject enrollment (e.g., "5 subjects enrolled towards a goal of 10" etc.) often receives central focus when measuring the intermediate performance of clinical studies, but all study activities require resources to achieve success. Critical factors that may limit trial success if allotted insufficient time or resources include identification and screening of potential study subjects, enrollment and informed consent, subject follow-up, data entry, and processing of adverse events. By analyzing

performance metrics for the key activities of subject screening, subject enrollment, and data entry by clinical research staff, the site may reallocate resources to improve resource utilization, staff burden, and operational efficiency.

Research Question:

Several studies were identified by BSWRI HLTP department to evaluate whether there is a difference in CRC performance of key trial activities by administration of quality improvement methods.

Null Hypothesis:

There is no difference in CRC performance of key trial activities by administration of selected quality improvement methods.

Alternate Hypothesis:

There is improved efficiency in CRC performance of key trial activities by administration of selected quality improvement methods.

***Aim 1*:**

Assess current resource utilization for and completion of the key activities of subject screening, subject enrollment, and data entry by clinical research staff at our site.

***Aim 2*:**

Implement reallocation of resources to improve resource utilization, staff burden, and operational efficiency of clinical research staff at our site.

***Aim 3*:**

After completion of the implementation period, reassess resource utilization for the key activities of subject screening, subject enrollment, and data entry by clinical research staff, and measure the change, if any, in completion of the activities.

***Aim 4*:**

Determine if collected trial activity metrics demonstrate statistically significant quality improvement upon study completion.

SIGNIFICANCE

Implementation of a quality improvement process for clinical research staff in the Heart and Lung Transplant and Pulmonary Research department will provide a tool for the research team to continuously assess and improve performance and influence future outcomes. The quality improvement methodology initiated in this project is the first of its kind for this site, and thus may provide 'proof of concept' to promote the completion of future, larger-scale quality improvement projects.

MATERIALS AND METHODS

Design and Sampling Technique:

An uncontrolled longitudinal study, or case series, was conducted in which observations were made on a series of clinical research staff before and after they receive a defined study intervention. A control group was not used. The study was divided into pre-intervention, intervention, and post-intervention periods. The pre-intervention and post-intervention periods consisted of equal, four-week long periods. Following the pre-intervention period, tailored quality improvement interventions were developed within a three-week period. The interventions were then implemented during an ensuing four-week intervention period. The non-probability technique of purposive sampling was used to analyze the issue from all angles by selecting a wide variation of data relating to clinical trial key activities.

We used a quality improvement process tailored from guidance issued by the Agency for Healthcare Research and Quality (AHRQ)[12] in this study. Run charts were maintained throughout the pre and post intervention periods to monitor the effectiveness of the intervention. The run chart is a visual tool that displays changes over time, and enables researchers to better assess whether changes are related to the intervention[12].

Clinical Trials Involved:

The following clinical research trials were selected for the quality improvement study:

1) Targeting Inflammation and Alloimmunity in Heart Transplant Recipients with Tocilizumab (ALL IN) is a Phase II randomized, prospective, multi-center placebo-controlled clinical drug trial in the United States. The study sample population is 200 primary heart transplant recipients, of which 15 will be enrolled at Baylor University Medical Center (BUMC) Dallas.

Subjects are randomized 1:1 into either an intervention group receiving study drug tocilizumab plus standard of care immunosuppression, or a control group receiving placebo plus standard of care immunosuppression. Screening, consent, and enrollment into the study takes place while the subject is on the UNOS waitlist, but randomization only occurs once the subject is transplanted. Randomized subjects will be followed for up to 24 months after transplant, with study visits occurring weekly for the first month, biweekly for the second month, monthly for months 3-6, bimonthly for months 8-12, and then yearly for a final visit at 24 months. Study activities performed or managed by the study coordinator include collection of research specimens, research labs, research procedures, study drug or placebo infusions, medical record reviews, and recording of clinical procedures.

2) Transplant of Redeemed Organs by Judicious Administration of New Direct-Acting Antivirals for Hepatitis-C Heart Recipients (TROJAN-C) is a Phase II prospective, multi-center open-label clinical trial. The study sample population is 20 subjects who receive Hepatitis C virus (HCV) Nucleic Acid Test (NAT) positive heart transplants and subsequent Epclusa® treatment, of which 12 will be enrolled at BUMC Dallas. The study aim is to determine the safety and efficacy of using HCV NAT positive donors for heart transplant in HCV NAT negative recipients who develop viremia post-transplant and are treated with Epclusa®. Consented subjects who receive a heart from a standard donor who appear HCV NAT negative will not be enrolled into the study. Study activities performed or managed by the study coordinator include collection of research specimens, study drug administration, research labs, medical record reviews, and recording of clinical procedures including immunological testing and labs.

3) Hemodynamic-GUIDEd Management of Heart Failure (GUIDE-HF) is a prospective, multi-center, clinical trial under an Investigational Device Exemption (IDE) to obtain pre-market approval (PMA) for an expanded indication for the CardioMEMS© heart failure system. The trial consists of a randomized, controlled arm that completed enrollment in December 2019, and a single arm with enrollment currently ongoing. The randomized arm study sample population is 1000 NYHA Class II, III, or IV heart failure (HF) subjects with either elevated NT-proBNP (or BNP) and/or a prior heart failure hospitalization (HFH). 34 subjects were enrolled for the randomized arm at BUMC Dallas. The single arm study sample population is 2600 NYHA Class III HF subjects with either elevated NT-proBNP (or BNP) and/or a prior HFH. In the single arm, study subjects receive the CardioMEMS© device and HF management guided by readings from the device. In the randomized arm, study subjects were randomized 1:1 into either a treatment group receiving the device and HF management guided by readings from the device, or a control group receiving the device and HF management based on standard of care not guided by readings from the device. The study duration following successful device implantation in both single and randomized arms is 12 months, with follow-up visits at 6 and 12 months. Study activities administered or managed by the study coordinator include device implantation, HF assessment, six-minute hallway walk (6MHW), collection of research labs, quality of life questionnaires, medical record reviews, subject contact calls at regularly scheduled intervals (randomized arm only) and recording of clinical procedures including labs and pulmonary artery catheterization.
4) REDUCE is a randomized controlled, prospective, double-blinded multi-center international clinical device trial to evaluate the Corvia Medical, Inc. IASD© System II to reduce elevated left atrial pressure in subjects with heart failure. The study sample population is 608 heart

failure subjects, 12 of which will be enrolled at BUMC Dallas. Subjects are randomized 1:1 into either a treatment arm receiving device implant, or a control group not receiving device implant. Subjects assigned to the control arm may cross-over to the treatment arm after the 24 month follow up visit. All subjects will be followed for five years post-implant, with follow-up visits occurring at 1, 3, 6, and 12 months, and then annually up to five years. Study activities administered or managed by the study coordinator include pre-randomization resting and supine bike exercise with right heart catheterization, device implantation, 6MHW, collection of research labs, quality of life questionnaires, electrocardiogram (ECG), issuance of device monitoring patches, and recording clinical procedures including labs, transthoracic echocardiogram (TTE), and physical exams.

5) The CHRONICLE study is a longitudinal, prospective multi-center observational study of the characteristics, treatment patterns, and health outcomes of individuals with severe asthma in the United States. Study activities will occur for a period of at least three years following consent and are composed of data collection from healthcare records review and web-based subject surveys collected at regular intervals. The study sample population is 1500 subjects in the US with a confirmed diagnosis of severe asthma.
6) BOSTON-2 is a Phase III randomized, prospective, multi-center, controlled, international clinical drug trial to demonstrate the effectiveness and safety of Liposomal Cyclosporine A inhalation solution in the treatment of Bronchiolitis Obliterans Syndrome in subjects post double lung transplant. The study sample population is 110 double lung transplant recipients diagnosed with Bronchiolitis Obliterans Syndromes, 5 of which will be enrolled at BUMC Dallas. Subjects are randomized 1:1 into either an intervention group receiving study drug Liposomal Cyclosporine A plus standard of care therapy, or a control group receiving

standard of care therapy only. Randomized subjects will complete a total of 11 visits during a 48-week treatment period, with visits scheduled every 4-8 weeks. Study activities administered or managed by the coordinator include collection of research labs, nebulized study drug administration, and administration of spirometry tests.

Data Collection Methodology:

Coordinators entered the following data into Smartsheets® on a weekly basis for each of their trials involved in this study:

1. Number of subjects screened
2. Hours spent screening subjects
3. Number of subjects enrolled
4. Hours spent enrolling subjects
5. Number of CRFs entered in EDC
6. Number of CRFs not entered in EDC
7. Number of open queries
8. Hours spent entering data in EDC

Collected data was processed as follows:

1. Transformed time spent completing screening, enrollment, and data entry to proportional data by determining the mean hours spent on each activity weekly for pre-intervention and post-intervention study periods.
2. Transformed outcomes of screening, enrollment, and data entry activities to proportional data by calculating mean subjects screened weekly, mean subjects enrolled weekly, and mean case report forms (CRF's) entered weekly for pre-intervention and post-intervention periods.

3. Transformed amount of data entry not completed and number of open queries to proportional data by calculating the mean of the sums of CRF's not entered and open queries weekly for pre-intervention and post-intervention study periods.

Quality Improvement Design and Implementation Process:

This study uses a quality improvement design modified from the benchmarking process introduced by Robert Camp at Xerox. First, activities critical to the success of clinical research trials were identified to target factors directly impacting trial outcomes for quality improvement. Experienced research site managers identified key trial activities as subject enrollment, subject screening, and data entry. Next, metrics were selected which could accurately define the effort and outcomes of enrollment, screening, and data entry activities. The metrics selected to define activity effort were hours spent screening subjects, hours spent enrolling subjects, and hours spent entering data in the EDC. The metrics selected to define activity outcomes were number of subjects screened, number of subjects enrolled, number of case report forms entered in the EDC, number of CRF's not entered in the EDC, and number of open queries.

A methodology for metric collection was then developed. Collection frequency, means and duration were planned to enable the construct of a dataset which could be analyzed to test the quality improvement hypothesis. Collection frequency and duration were determined within the constraints of a four-month study timeline due to the author's thesis deadline requirements. The platform for the metrics collection tool was carefully selected to maintain simplicity and thus encourage team acceptance and participation. A spreadsheet style metrics collection tool was built using Smartsheets® due to the platform's features of automated data requests and simple user interface.

Metrics were collected during a pre-intervention period to develop a baseline for key trial activity efforts and outcomes. Following the pre-intervention period, the metrics were reviewed by the study team to identify potential areas for quality improvement. Meetings were then conducted with the coordinators of each trial to discuss their metrics, collect input regarding challenges experienced, and learn about their past and current efforts or ideas to improve these areas. The area selected for quality improvement for each trial was finalized during the coordinator discussions. Following the discussions, the study team developed interventions tailored to each trial's area selected for quality improvement.

The quality improvement interventions were implemented over a five-week long period to ensure full effects could be measured during the ensuing post-intervention period. The study team worked closely during intervention implementation to maintain manager involvement within areas of change and continuously receive and incorporate coordinator feedback. Metrics were then re-collected during a four-week post-intervention period and analyzed to determine effect of the intervention.

Statistical Analysis Methodology:

In this study the dependent variables are defined as weekly number of subjects screened, hours spent screening, number of subjects enrolled, hours spent enrolling, missing data, open queries, and hours spent entering data. The dependent variables were measured across the pre-intervention period and post-intervention period. The independent variable is defined as the quality improvement intervention.

Run charts were maintained throughout the pre-intervention and post-intervention periods as a visual tool to monitor the effects of the intervention. Separate run charts were maintained

for each study, using weekly pre-processed metrics as data points. The run charts were analyzed for trends and changes in means over time to help determine whether the quality improvement intervention led to process improvement or degradation.

Inferential, non-parametric statistical analysis was performed on transformed data, with limitations clearly stated due to the non-generalizable nature of this study's design and sampling technique. It is appropriate to conduct non-parametric statistical tests for this study since our data violates normality assumptions due to sampling methods and size. Mean weekly time spent performing critical trial activities was compared before and after intervention using the Wilcoxon Signed-Rank test. Performance metrics for screening, enrollment, and data entry were also compared before and after intervention using the Wilcoxon Signed-Rank test. The Wilcoxon Signed-Rank test is appropriate to conduct since our study seeks to evaluate whether differences exist on a continuous dependent variable before and after intervention.

RESULTS

Median time screening subjects weekly across all studies decreased from 2.41 hours to 2.0 hours following intervention (Figure 1). This decrease was not found to be statistically significant. Studies receiving a QI intervention for screening included GUIDE, REDUCE, CHRONICLE, and BOSTON-2. These studies either showed either an increase or no change in median time screening subjects following intervention. GUIDE median time screening subjects weekly increased from 4.5 hours to 6 hours following intervention. REDUCE median time screening subjects increased from 1 hour to 2 hours following intervention. CHRONICLE median time screening subjects weekly remained constant at 3.5 hours post intervention. BOSTON-2 median time screening subjects remained constant at 1.5 hours post intervention.

Median time enrolling subjects weekly across all studies increased from 0.5 hours to 1.0 hours following intervention (Figure 2). Statistical testing was not performed due to sample size below Wilcoxon Signed Rank minimum critical value of n=5. Studies receiving a QI intervention for enrollment included GUIDE, REDUCE, and CHRONICLE. GUIDE median time enrolling subjects weekly increased from 0 hours to 2.5 hours following intervention. REDUCE median time enrolling subjects decreased from 1 hour to 0 hours following intervention. CHRONICLE median time enrolling subjects weekly decreased from 1 hour to 0 hours following intervention.

Median time entering data weekly across all studies increased from 2.63 hours to 3.0 hours following intervention (Figure 3). This increase was not found to be statistically significant. ALL-IN, GUIDE, and REDUCE received a QI intervention for data entry and all showed an increase in median time spent entering data post intervention. ALL-IN median time entering data weekly increased from 4 hours to 5 hours following intervention. GUIDE median

time entering data weekly increased from 2.5 hours to 6 hours post intervention. REDUCE median time entering data weekly increased from 3 hours to 4.5 hours post intervention.

Box Plots: Time Completing Trial Activities Across All Studies Pre and Post Intervention

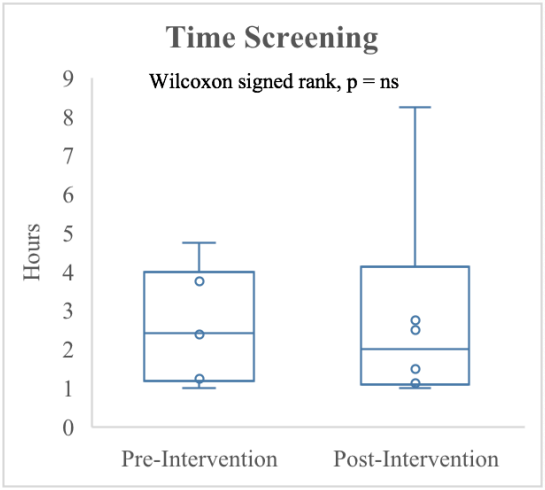

Figure 1. Median hours screening subjects pre and post quality improvement intervention, n = 6

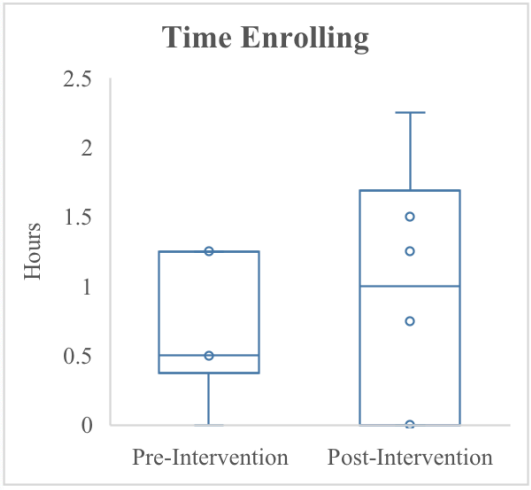

Figure 2. Median hours enrolling study subjects pre and post quality improvement intervention, n = 6

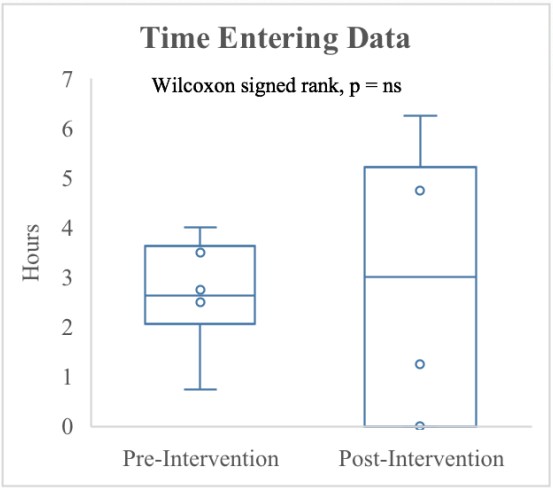

Figure 3. Median hours entering study data pre and post quality improvement intervention, n = 6

Median subjects screened weekly across all studies increased from 4 hours pre-intervention to 4.5 hours post-intervention (Figure 4). This increase was not found to be statistically significant. Studies receiving a QI intervention for screening included GUIDE, REDUCE, CHRONICLE, and BOSTON-2. GUIDE median subjects screened weekly decreased from 6 subjects to 5 subjects following intervention. REDUCE median subjects screened weekly remained constant at one subject before and after intervention. CHRONICLE median subjects screened weekly decreased from 32 subjects to 30 subjects following intervention. BOSTON-2 median subjects screened weekly increased from 3 subjects to 15 subjects following intervention.

Median subjects enrolled weekly across all studies increased from 0.25 subjects pre-intervention to 0.5 subjects post-intervention (Figure 5). Statistical testing was not performed due to sample size below Wilcoxon Signed Rank minimum critical value of n=5. Studies receiving a QI intervention for enrollment included GUIDE, REDUCE, and CHRONICLE. GUIDE median subjects enrolled weekly increased from 0 subjects to 1 subject following intervention. REDUCE median subjects enrolled weekly remained constant at 0 subjects before and after intervention. CHRONICLE median subjects enrolled weekly decreased from 0.5 subjects to 0 subjects following intervention.

Median data entered weekly across all studies decreased from 5.63 CRF's pre-intervention to 3.63 CRF's post-intervention (Figure 6). This decrease was not found to be statistically significant. Studies receiving a QI intervention for data entry included ALL-IN, GUIDE and REDUCE. ALL-IN median data entered weekly increased from 6 CRF's to 34 CRF's post intervention. GUIDE median data entered weekly decreased from 6.5 CRF's to 4.5 CRF's post intervention. REDUCE median data entered weekly increased from 0 CRF's to 3 CRF's following intervention.

Median open queries and data not entered weekly across all studies decreased from 28.75 CRF's and queries pre-intervention to 19.50 CRF's and queries post-intervention (Figure 7). This decrease was found to be statistically significant. Studies receiving a QI intervention for open queries and/or data entry included ALL-IN, GUIDE, REDUCE, and CHRONICLE. ALL-IN median open queries and data not entered weekly remained constant at 76 queries and CRF's before and after intervention. GUIDE median open queries and data not entered weekly decreased from 13.5 to 5.5 queries and CRF's following intervention. REDUCE median open queries and data not entered weekly decreased from 9 to 7 queries and CRF's following intervention. CHRONICLE median open queries and data not entered weekly increased slightly from 43.5 to 44.0 queries and CRF's following intervention.

Box Plots: Completion of Key Trial Activities Across All Studies Pre and Post Intervention

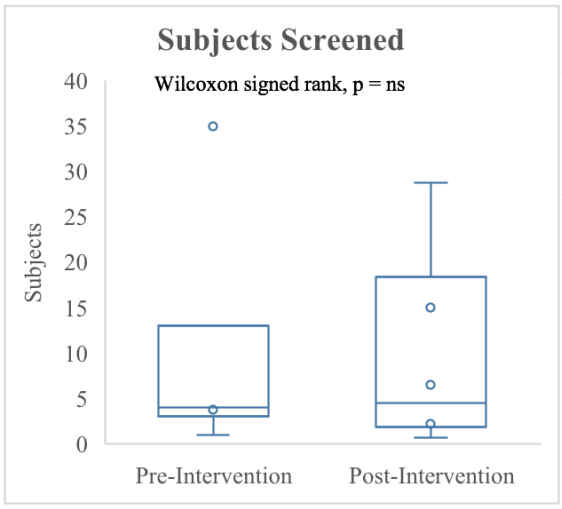

Figure 4. Median subjects screened pre and post quality improvement intervention, n = 6

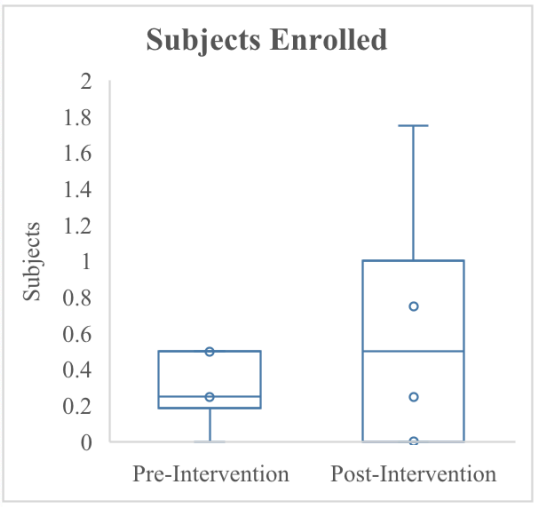

Figure 5. Median study subjects enrolled pre and post quality improvement intervention, n = 6

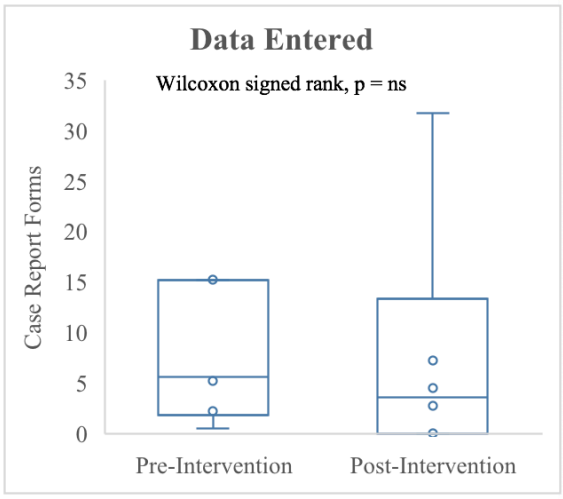

Figure 6. Median study data entered pre and post quality improvement intervention, n = 6

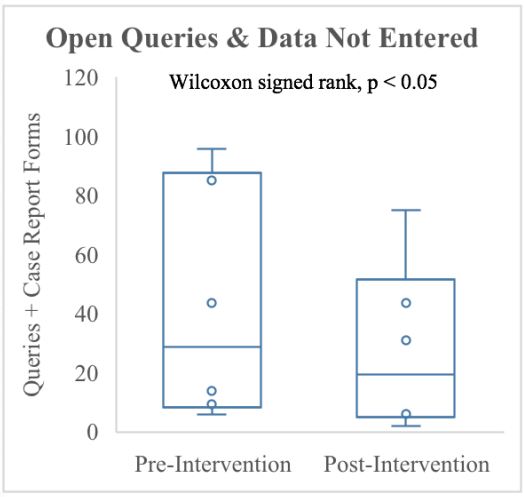

Figure 7. Median open queries and study data not entered pre and post improvement intervention, n = 6

Run Charts Pre vs Post Intervention:

The following run charts serve as a visual tool to help determine whether the quality improvement intervention led to process improvement or degradation in the targeted variables. Since at least ten data points are needed to statistically interpret the trends observed, we are unable to use the run chart to statistically determine whether observed changes are due to normal random variation or may be attributed to non-random change (i.e. effect of the intervention).

1. Screening

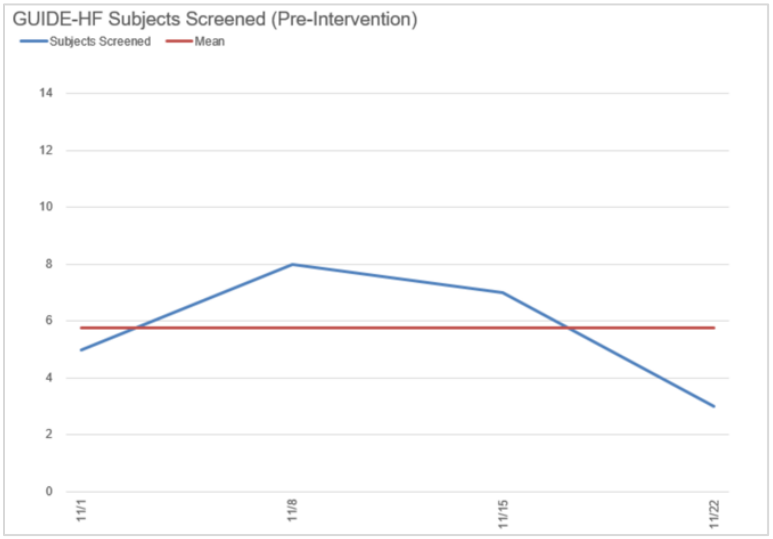

Figure 8. Run chart of GUIDE-HF subjects screened pre-intervention

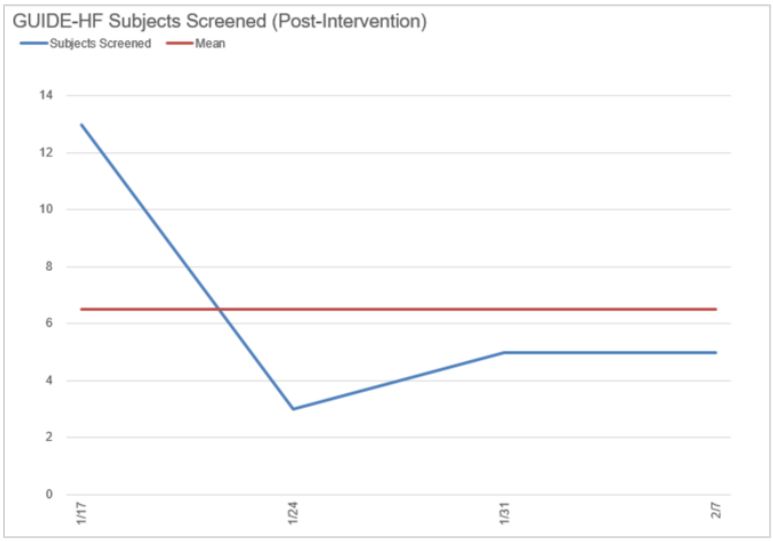

Figure 9. Run chart of GUIDE-HF subjects screened post-intervention

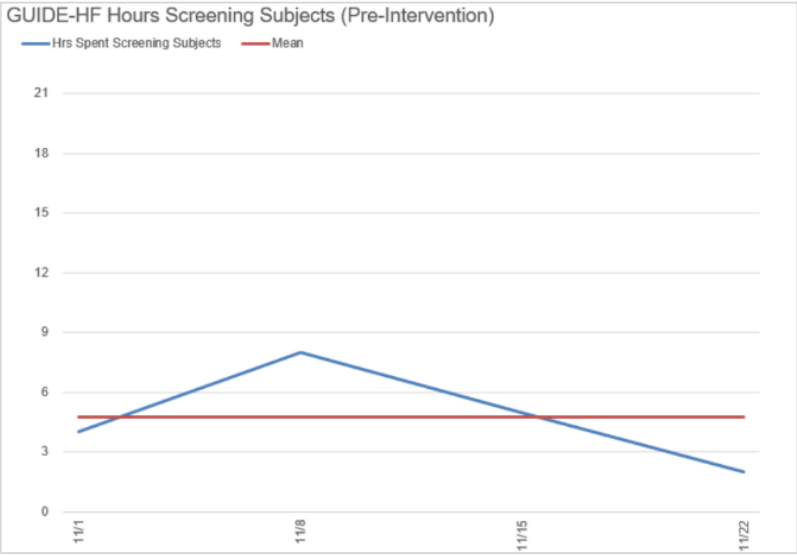

Figure 10. Run chart of hours screening GUIDE subjects pre-intervention

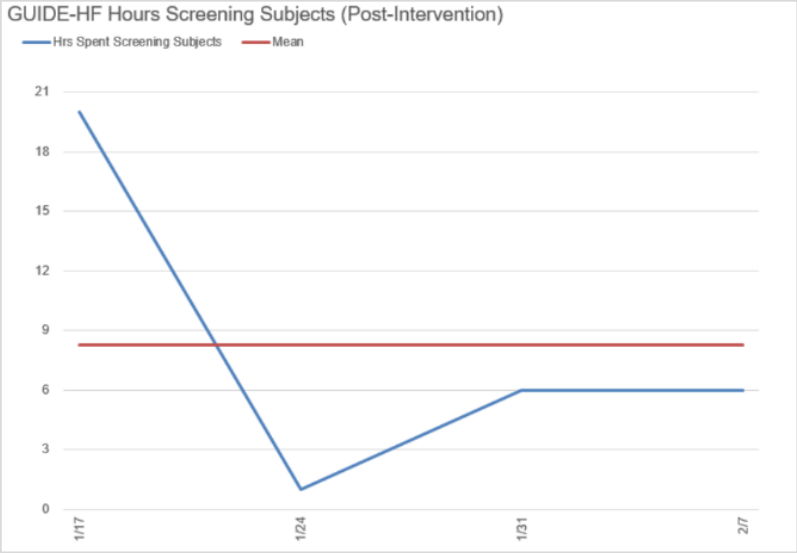

Figure 11. Run chart of hours screening GUIDE subjects post-intervention

GUIDE-HF received a quality improvement intervention for screening. Mean GUIDE-HF subjects screened weekly increased from 5.8 subjects pre-intervention (Figure 8) to 6.5 subjects post-intervention (Figure 9). Mean GUIDE-HF weekly time spent screening increased from 4.8 hours pre-intervention (Figure 10) to 8.3 hours post-intervention (Figure 11). The highest number of subjects screened and most time spent screening occurred in Week 1 of the post-intervention period and trended below the mean in ensuing weeks.

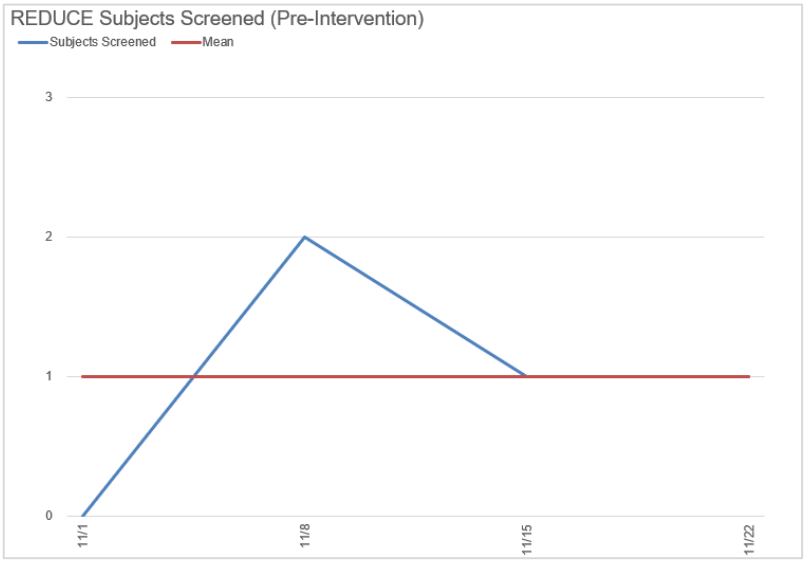

Figure 12. Run chart of REDUCE subjects screened pre-intervention

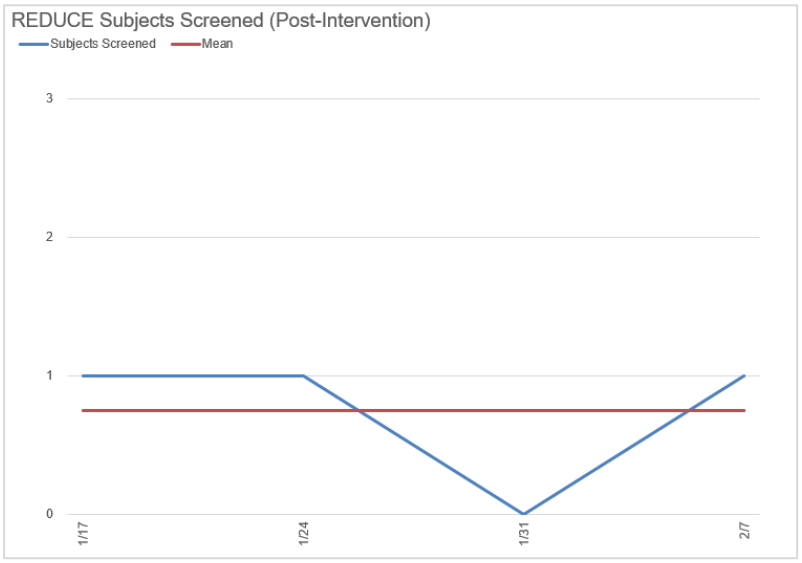

Figure 13. Run chart of REDUCE subjects screened post-intervention

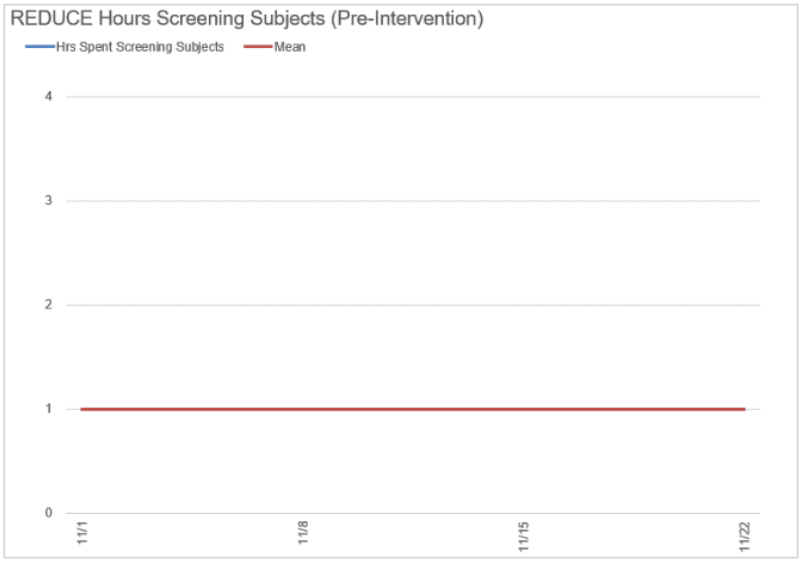

Figure 14. Run chart of hours screening REDUCE subjects pre-intervention

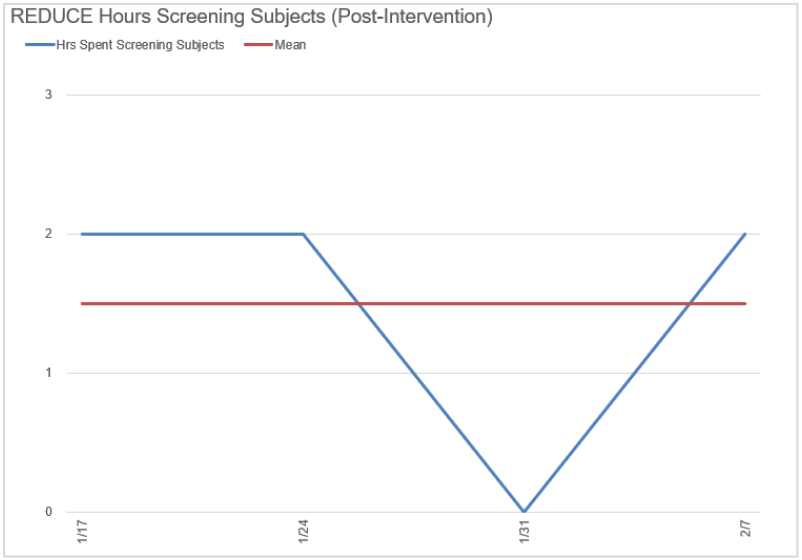

Figure 15. Run chart of hours screening REDUCE subjects post-intervention

REDUCE received a quality improvement intervention for screening. Mean REDUCE subjects screened weekly decreased from one subject pre-intervention (Figure 12) to 0.8 subjects post-intervention (Figure 13). Mean time screening subjects weekly increased from one hour pre-intervention (Figure 14) to 1.5 hours post-intervention (Figure 15).

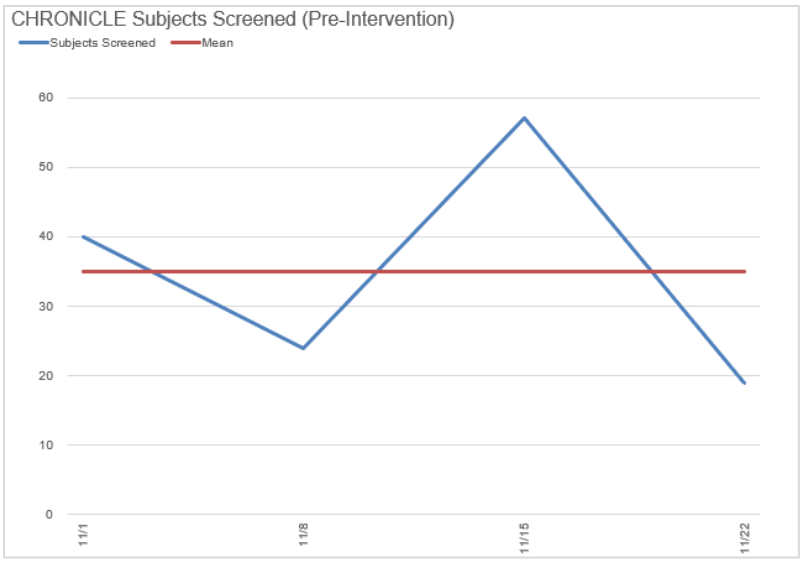

Figure 16. Run chart of CHRONICLE subjects screened pre-intervention

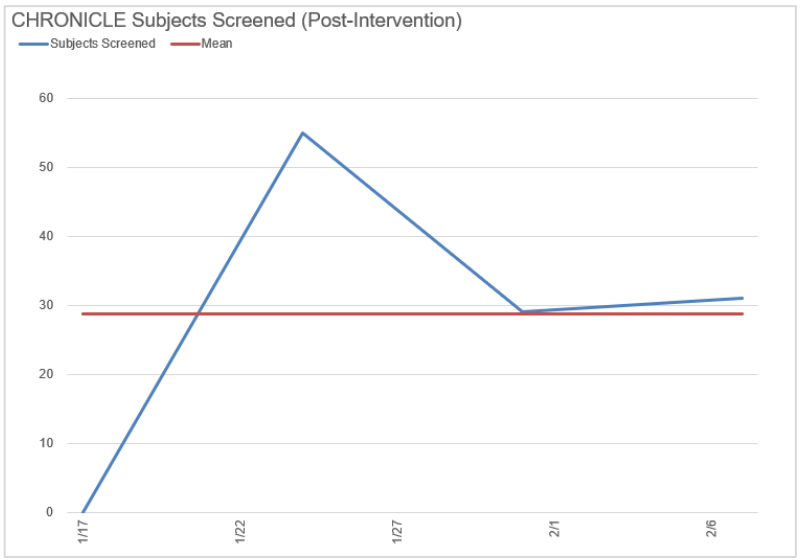

Figure 17. Run chart of CHRONICLE subjects screened post-intervention

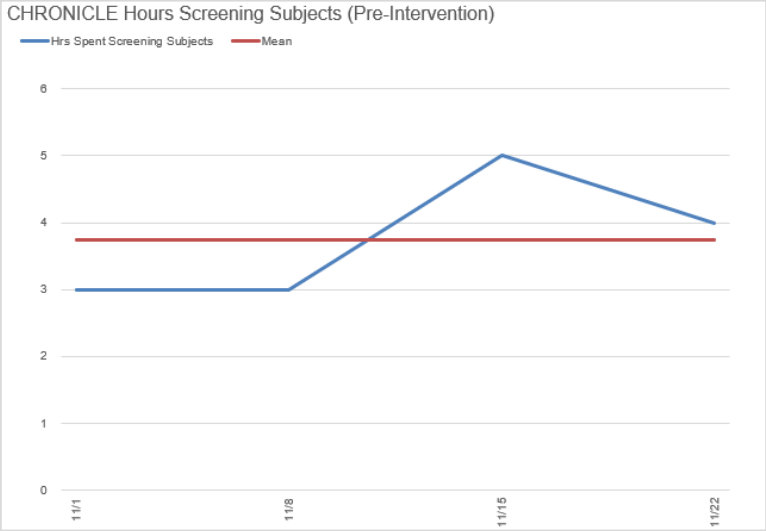

Figure 18. Run chart of hours spent screening subjects pre-intervention

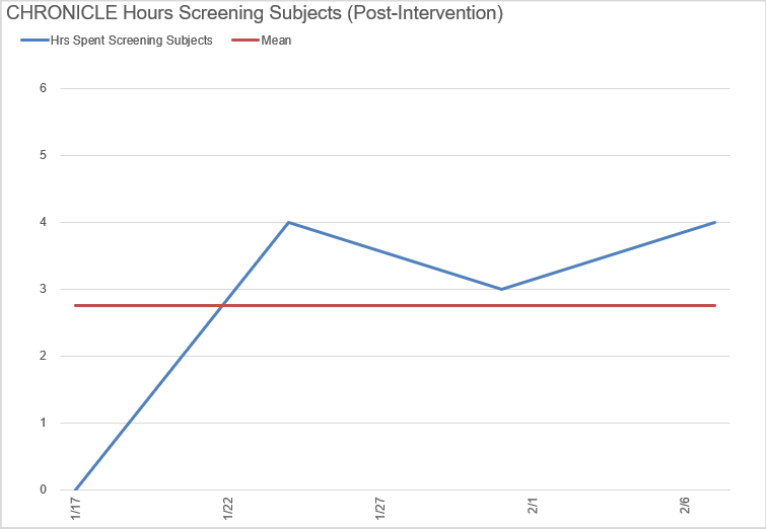

Figure 19. Run chart of hours spent screening subjects post-intervention

CHRONICLE received a QI intervention for screening. Mean subjects screened weekly decreased from 35 subjects (Figure 16) to 28.8 subjects (Figure 17), and mean time screening weekly decreased from 3.8 hours (Figure 18) to 2.8 hours post intervention (Figure 19). The lowest number of subjects screened and time screening occurred week one post intervention. The CRC planned to use pre-screened referrals from the clinic to improve screening efficiency per the planned intervention during this week. Clinic referrals were not received so the CRC returned to her high-volume screening process during the remaining period.

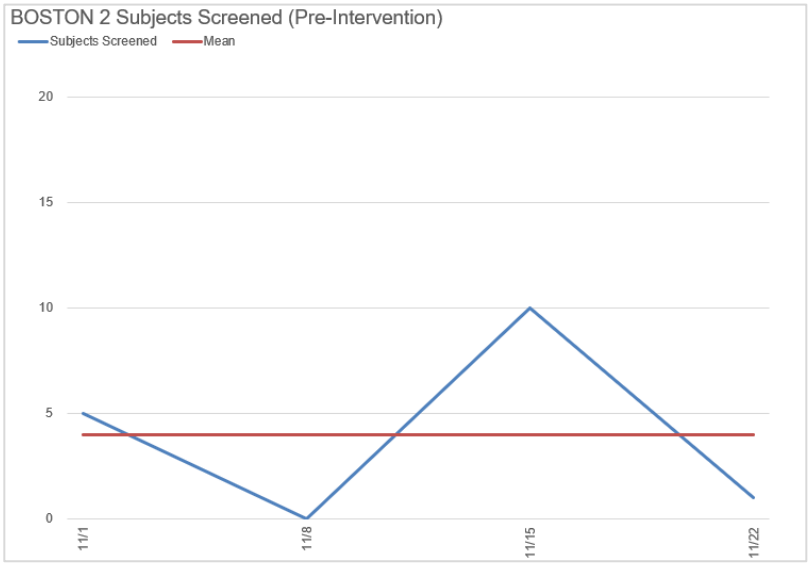

Figure 20. Run chart of BOSTON 2 subjects screened pre-intervention

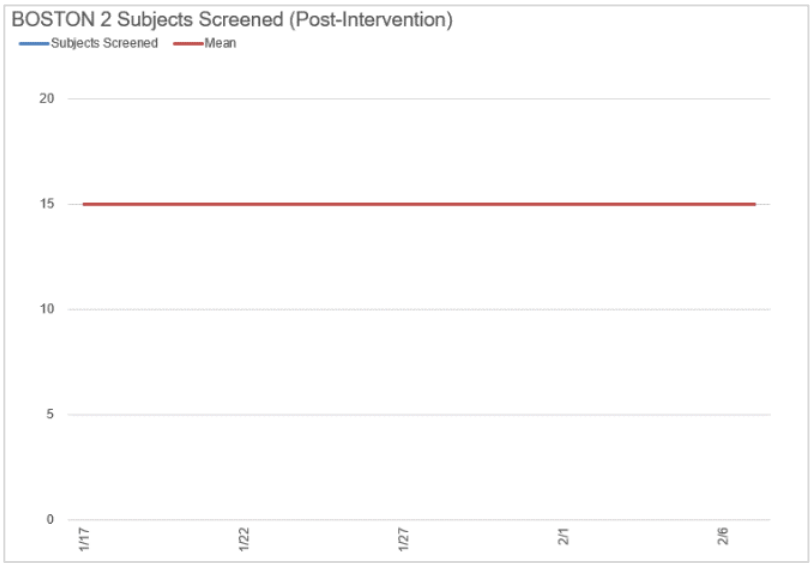

Figure 21. Run chart of BOSTON 2 subjects screened post-intervention

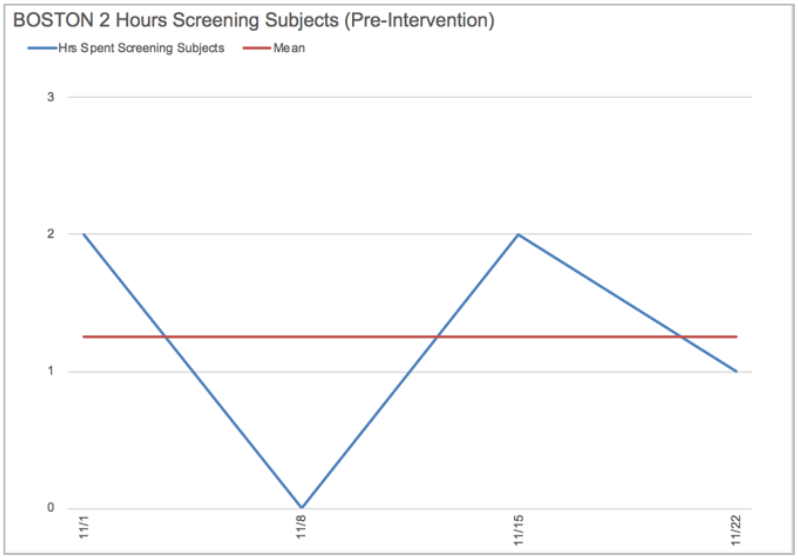

Figure 22. Run chart of hours screening BOSTON 2 subjects pre-intervention

Figure 23. Run chart of hours screening BOSTON 2 subjects post-intervention

BOSTON-2 received a quality improvement intervention for screening. Mean subjects screened weekly increased from 4.0 subjects (Figure 20) to 15 subjects post intervention (Figure 21). Mean time screening subjects weekly increased from 1.3 hours (Figure 22) to 1.5 hours post intervention (Figure 23). 15 subjects were screened each week post intervention due to the CRC meeting the intervention screening goal. Post-intervention screening time increased only slightly despite the larger number of subjects screened, reflecting an improved screening efficiency.

2. Enrollment

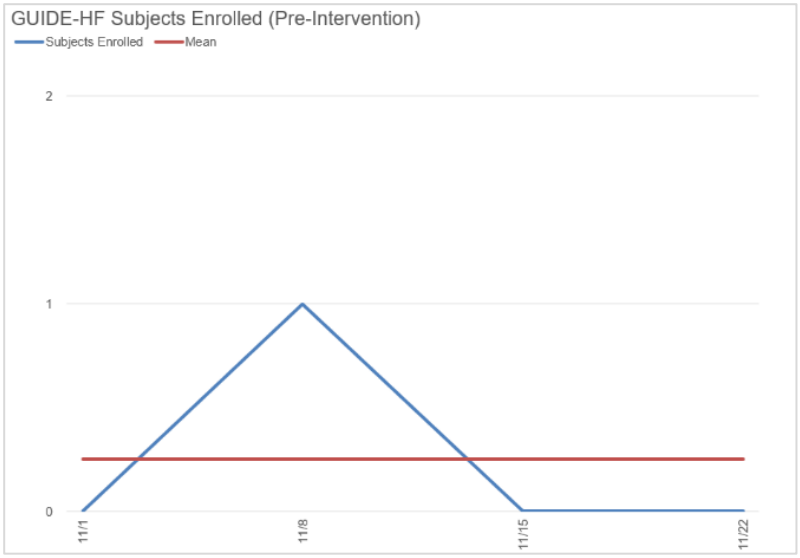

Figure 24. Run chart of GUIDE-HF subjects enrolled pre-intervention

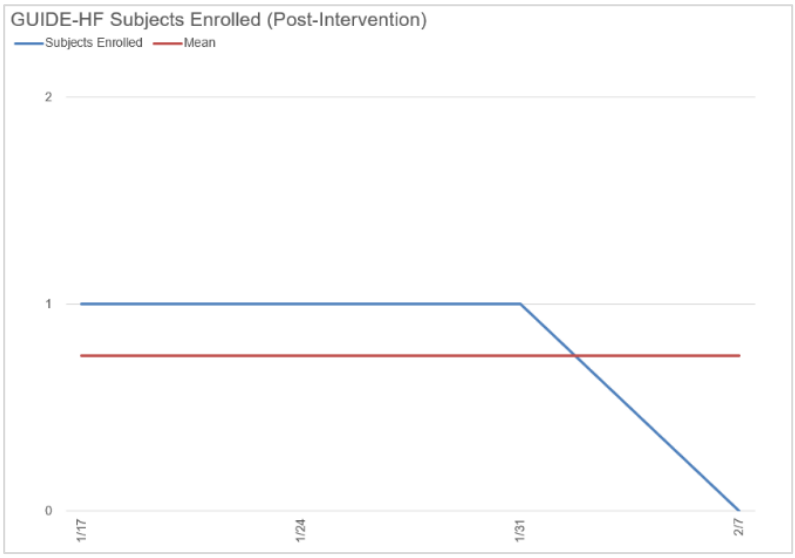

Figure 25. Run chart of GUIDE-HF subjects enrolled post-intervention

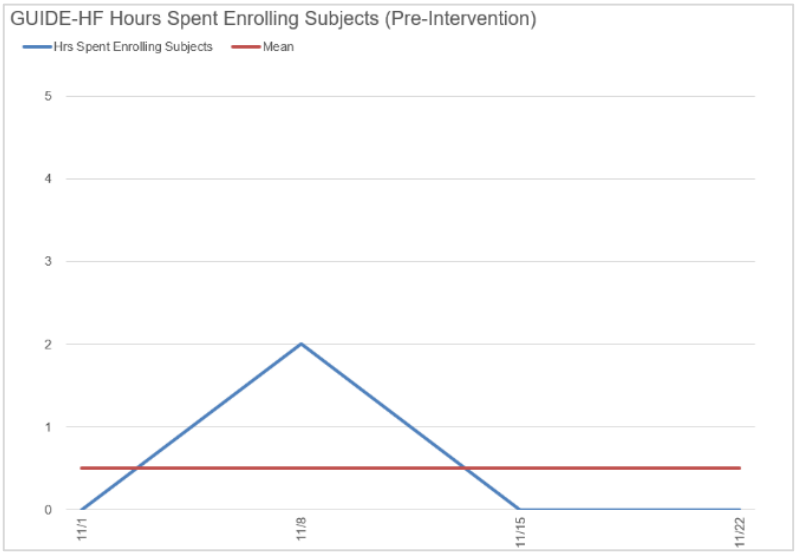

Figure 26. Run chart of hours enrolling GUIDE-HF subjects pre-intervention

Figure 27. Run chart of hours enrolling GUIDE-HF subjects post-intervention

GUIDE-HF received a quality improvement intervention for enrollment. Mean GUIDE-HF subjects enrolled weekly increased from 0.3 subjects (Figure 24) to 0.8 subjects (Figure 25) post intervention. Mean time enrolling subjects weekly increased from 0.5 hours (Figure 26) to 2.3 hours (Figure 27) post intervention. Three of four weeks pre-intervention resulted in zero subjects enrolled, while three of four weeks post-intervention accrued subject enrollment.

Figure 28. Run chart of REDUCE subjects enrolled pre-intervention

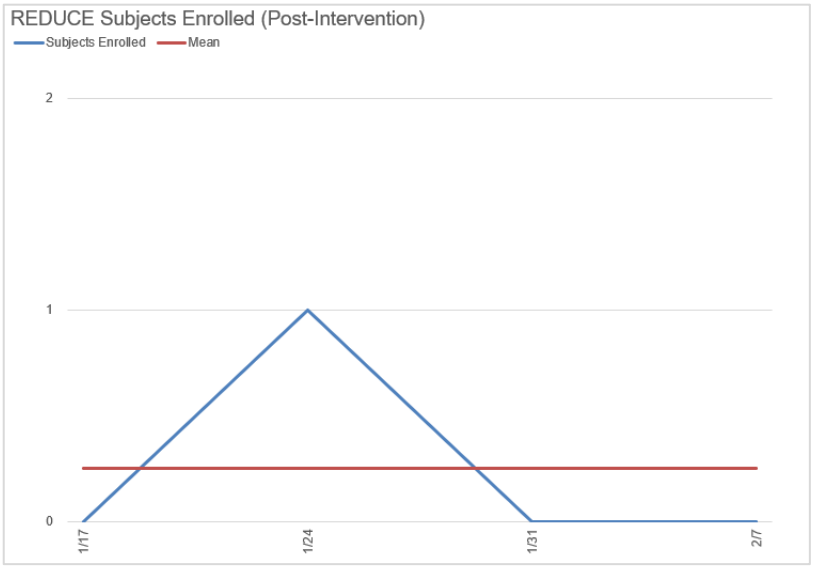

Figure 29. Run chart of REDUCE subjects enrolled post-intervention

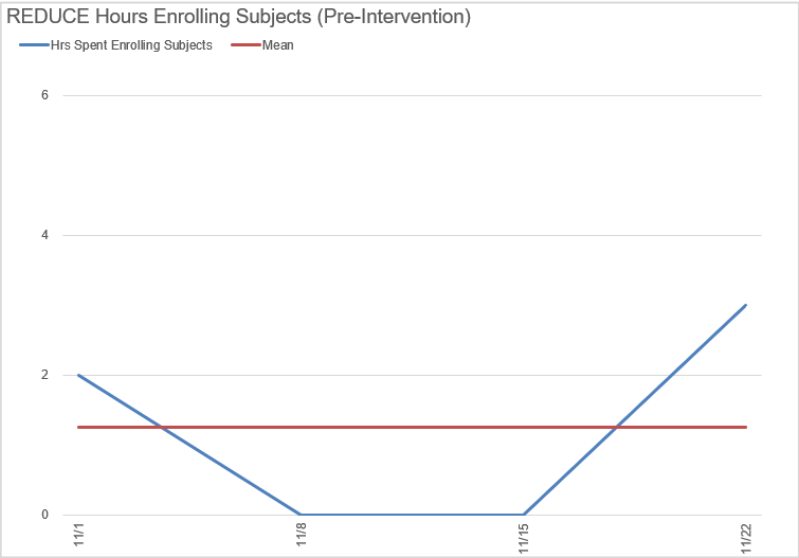

Figure 30. Run chart of hours enrolling REDUCE subjects pre-intervention

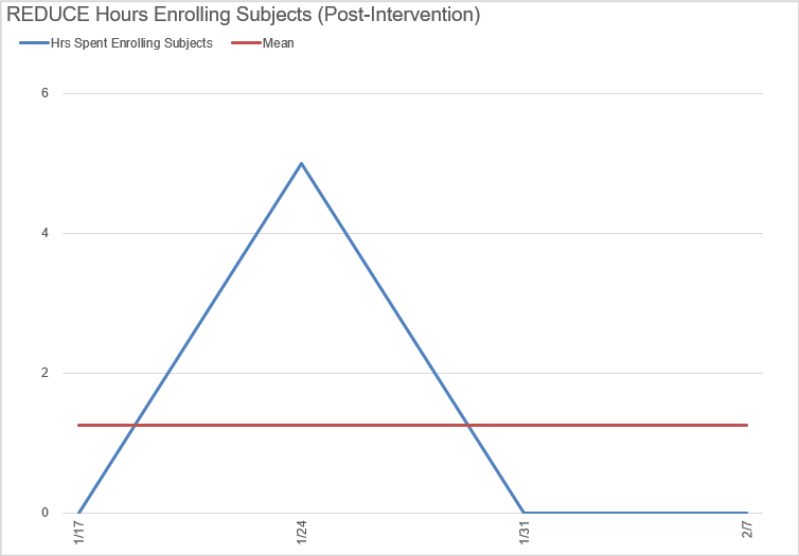

Figure 31. Run chart of hours enrolling REDUCE subjects post-intervention

REDUCE received a quality improvement intervention for enrollment. Run charts were maintained for number of subjects enrolled and time spent enrolling during pre and post-intervention periods. Mean REDUCE subjects enrolled weekly remained the same at 0.3 subjects pre (Figure 28) and post intervention (Figure 29). Mean time enrolling subjects weekly remained the same at 1.3 hours pre (Figure 30) and post intervention (Figure 31).

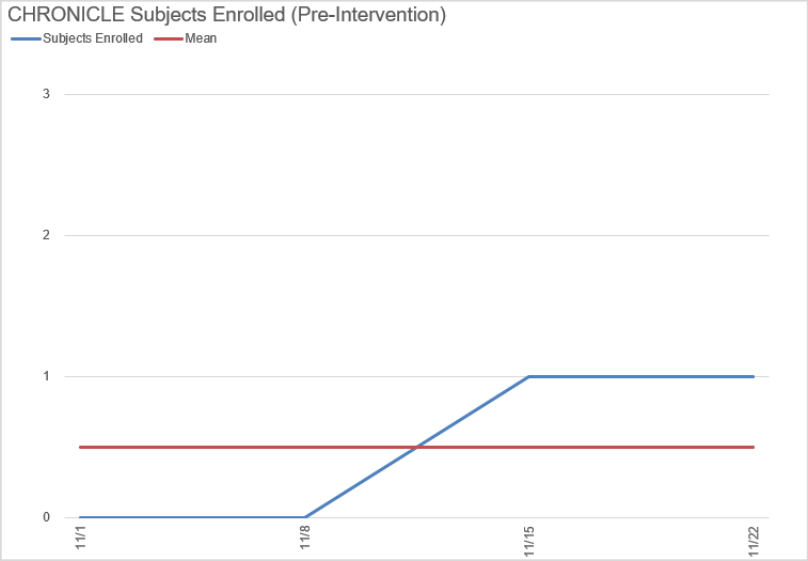

Figure 32. Run chart of CHRONICLE subjects enrolled pre-intervention

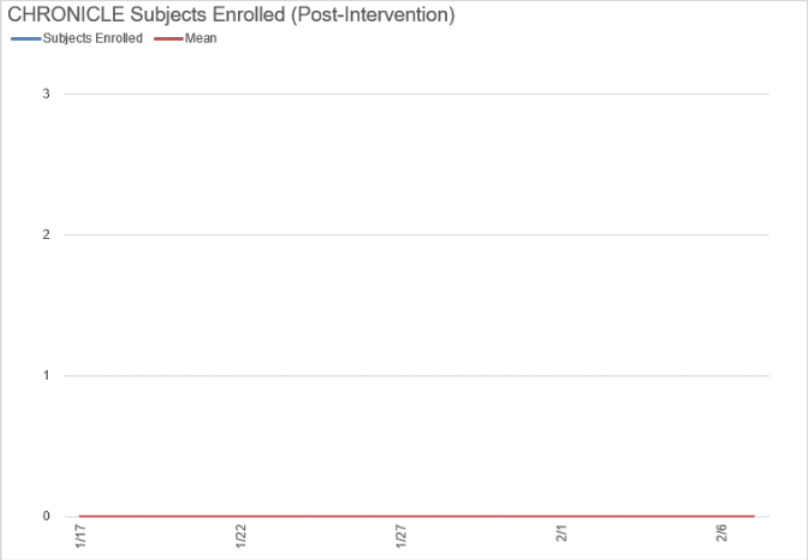

Figure 33. Run chart of CHRONICLE subjects enrolled post-intervention

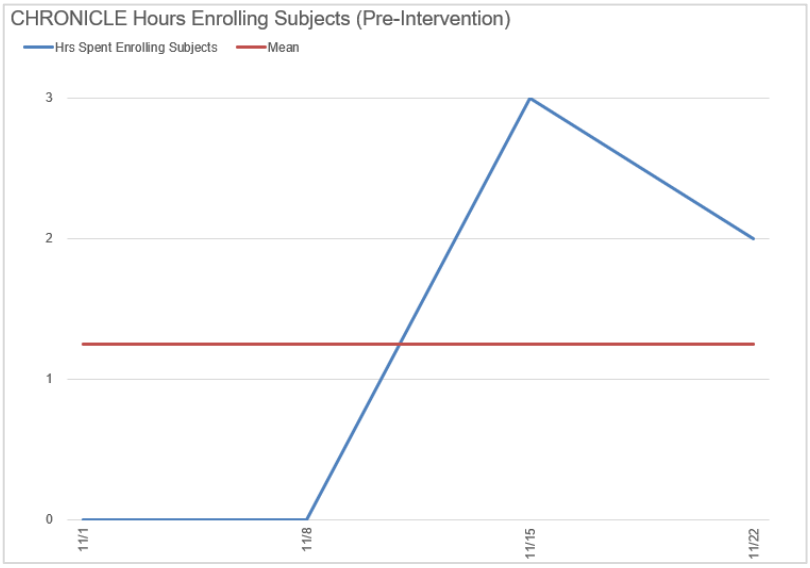

Figure 34. Run chart of hours enrolling CHRONICLE subjects pre-intervention

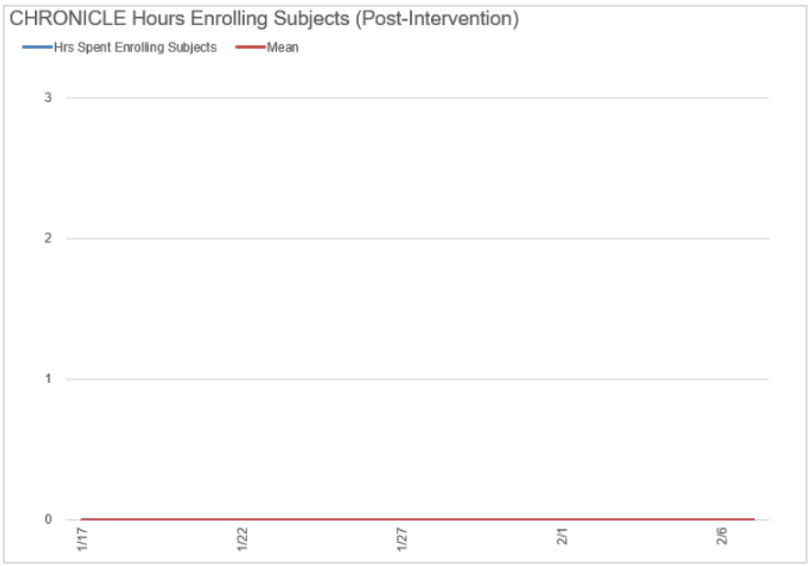

Figure 35. Run chart of hours enrolling CHRONICLE subjects post-intervention

CHRONICLE received a quality improvement intervention for enrollment. Run charts were maintained for subjects enrolled and time spent enrolling during pre and post-intervention periods. Mean CHRONICLE subjects enrolled weekly decreased from 0.5 subjects (Figure 32) to zero subjects following intervention (Figure 33). Mean time enrolling subjects weekly decreased from 1.3 hours (Figure 34) to zero hours following intervention (Figure 35).

3. Data Entry

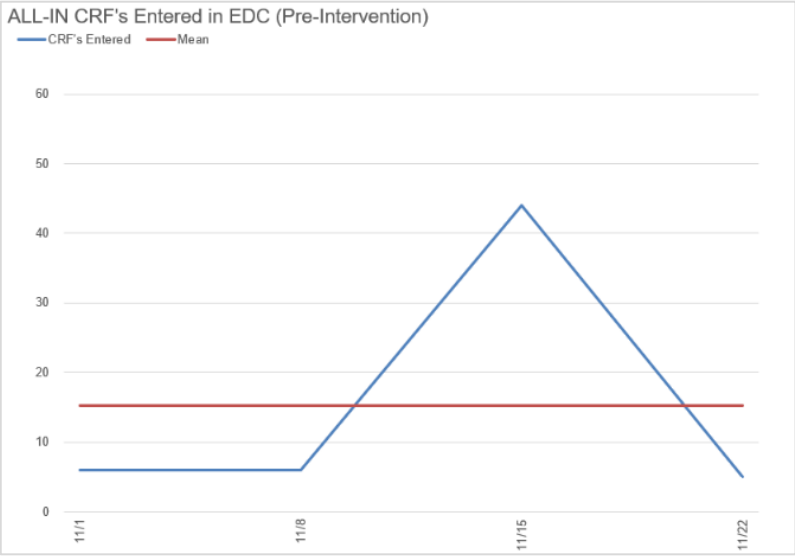

Figure 36. Run chart of ALL-IN CRFs entered in EDC pre-intervention

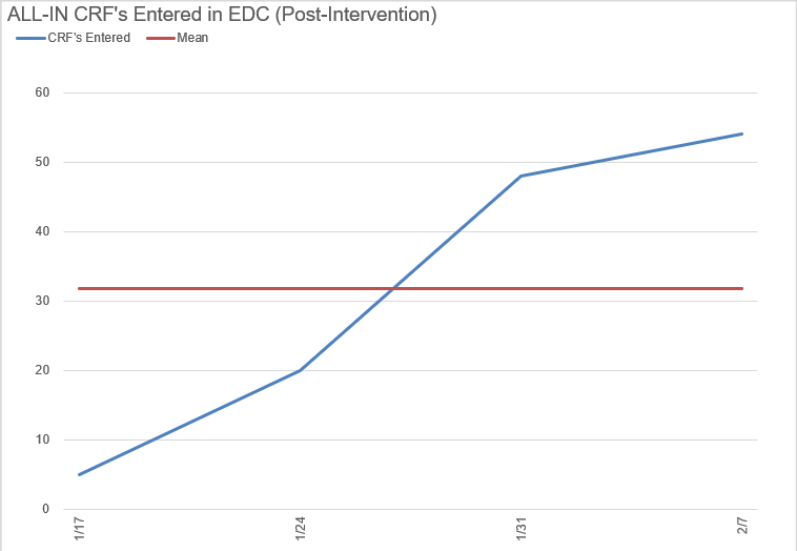

Figure 37. Run chart of ALL-IN CRFs entered in EDC post-intervention

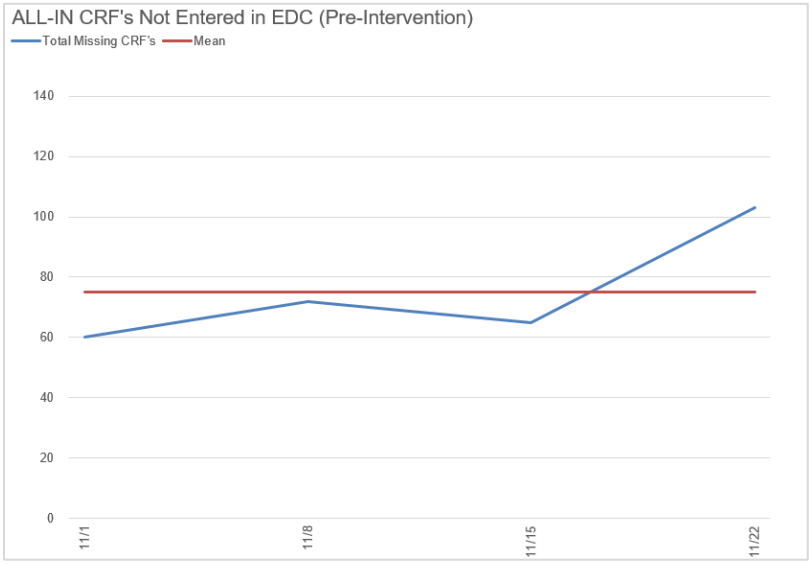

Figure 38. Run chart of ALL-IN CRFs not entered in EDC pre-intervention

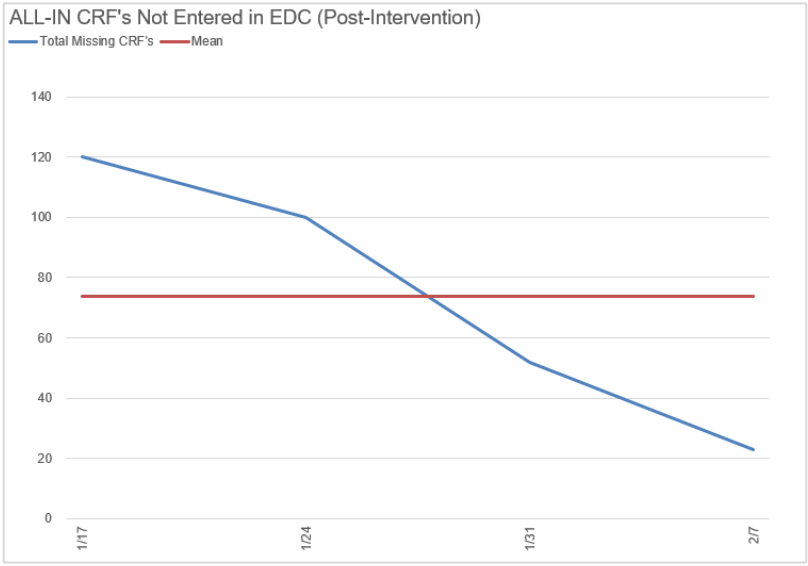

Figure 39. Run chart of ALL-IN CRFs not entered in EDC post-intervention

ALL-IN received a quality improvement intervention for data entry. Mean ALL-IN CRF's entered in the EDC weekly increased from 15.3 CRF's pre-intervention (Figure 36) to 31.8 CRF's post-intervention (Figure 37). Mean ALL-IN CRF's not entered in the EDC weekly decreased from 75 CRF's (Figure 38) to 73.8 CRF's following intervention (Figure 39).

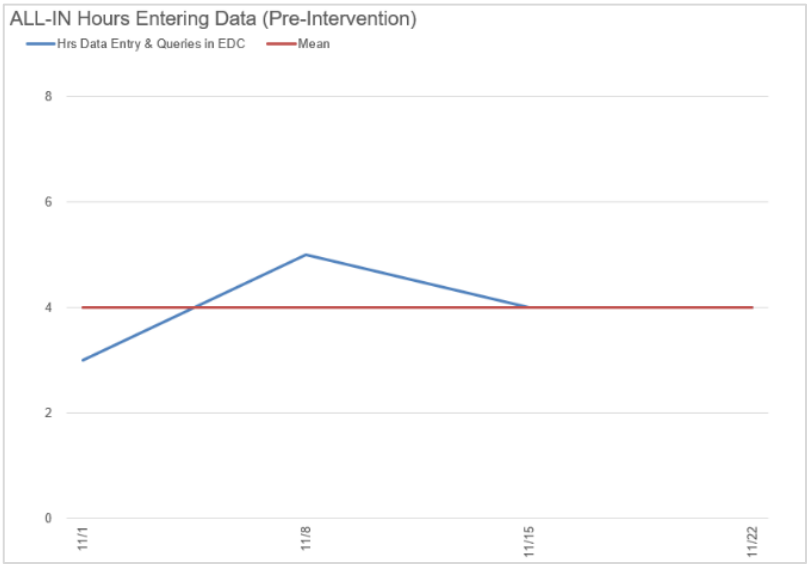

Figure 40. Run chart of hours entering ALL-IN data pre-intervention

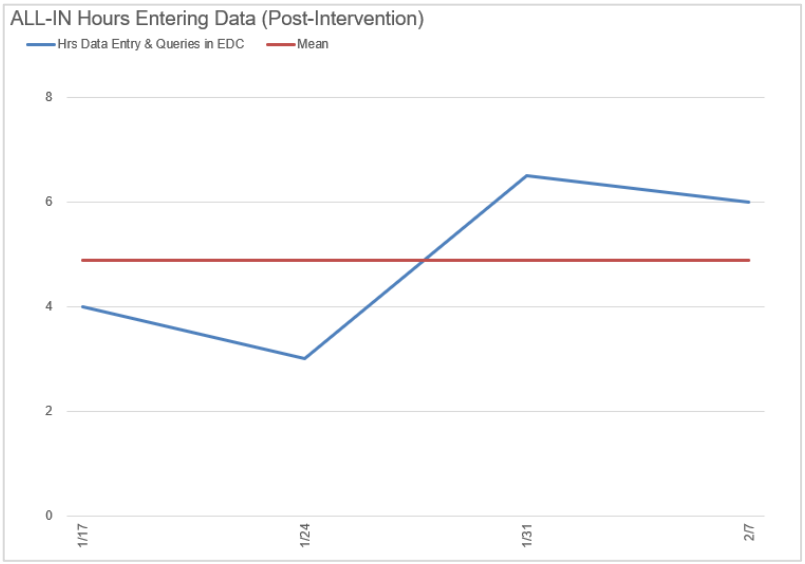

Figure 41. Run chart of hours entering ALL-IN data post-intervention

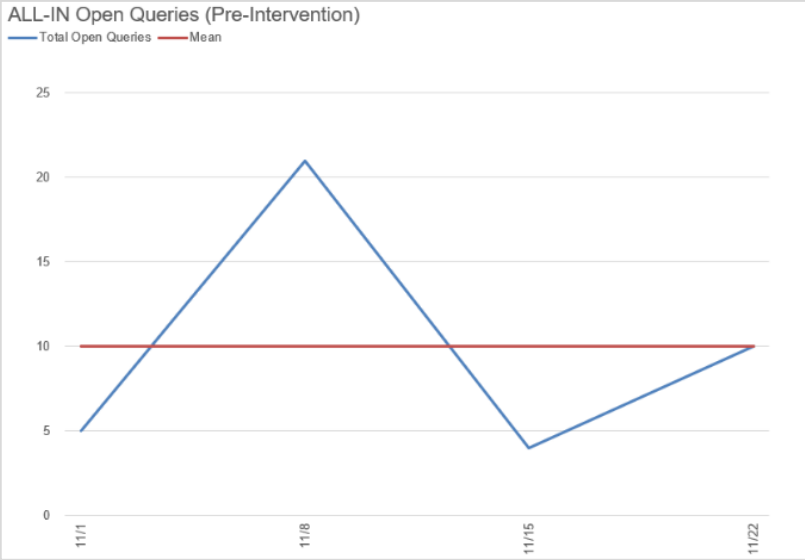

Figure 42. Run chart of ALL-IN open queries pre-intervention

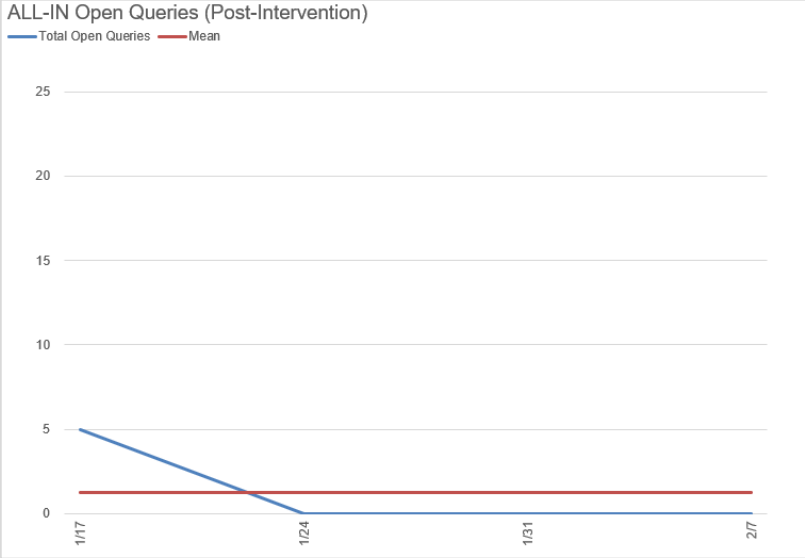

Figure 43. Run chart of ALL-IN open queries post-intervention

Mean weekly time entering CRF's for ALL-IN increased from 4.0 hours pre-intervention (Figure 40) to 4.9 hours post-intervention (Figure 41). Mean open queries weekly for ALL-IN decreased from 10 queries pre-intervention (Figure 42) to 1.3 queries post-intervention (Figure 43).

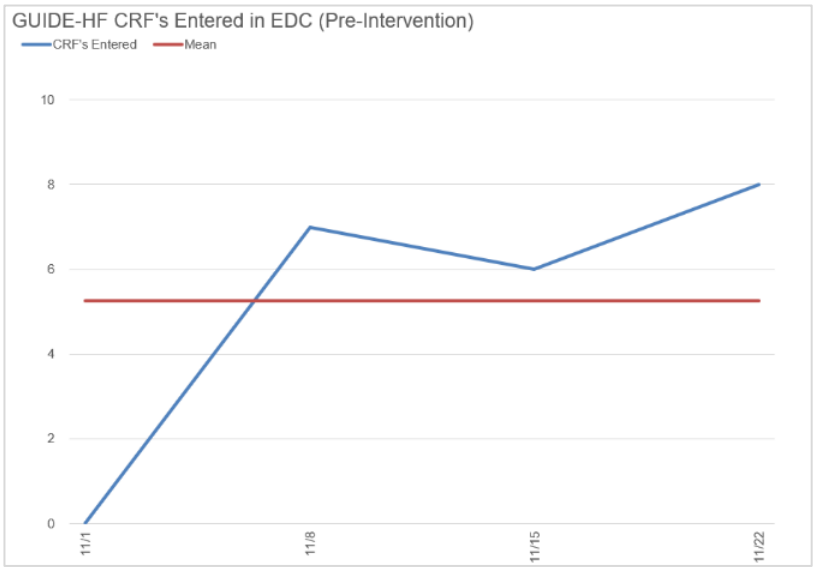

Figure 44. Run chart of GUIDE-HF CRFs entered in EDC pre-intervention

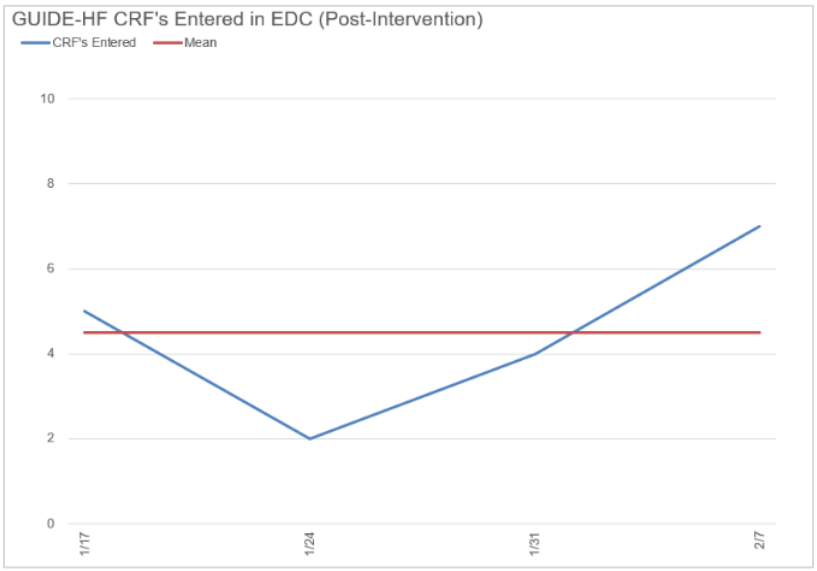

Figure 45. Run chart of GUIDE-HF CRFs entered in EDC post-intervention

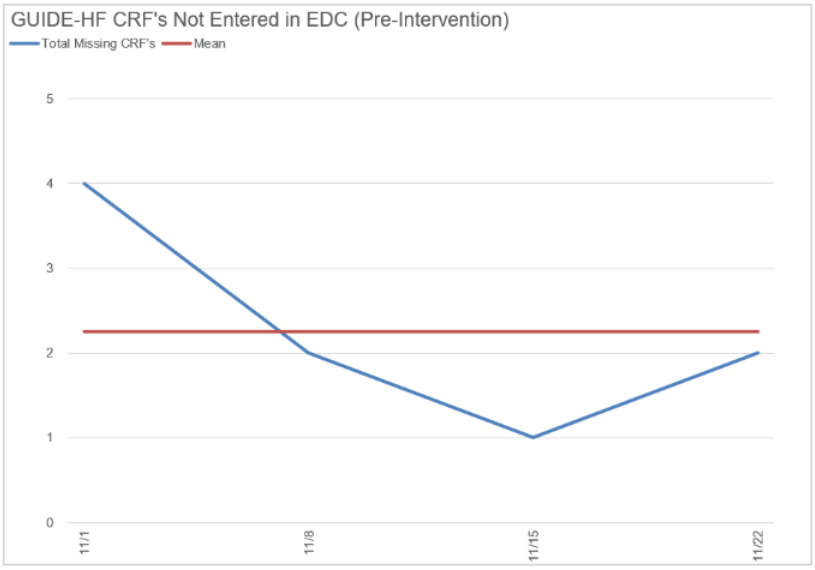

Figure 46. Run chart of GUIDE-HF CRFs not entered in EDC pre-intervention

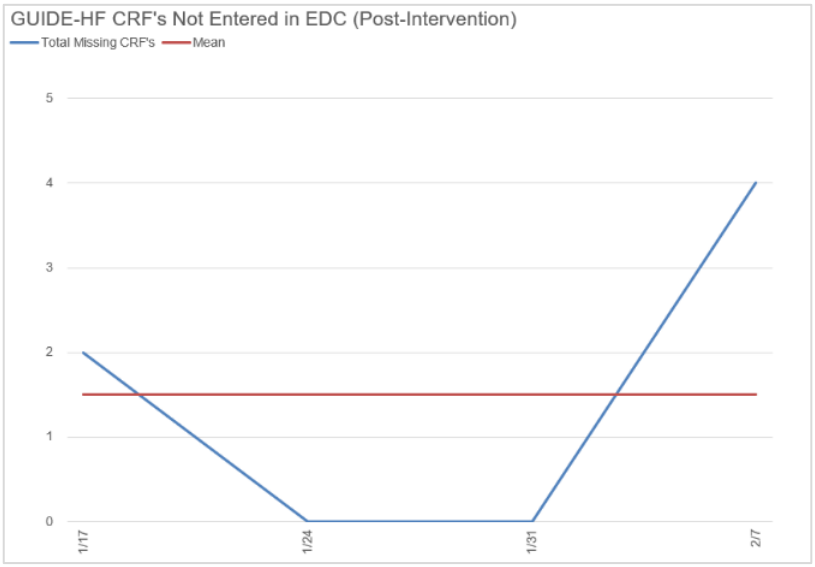

Figure 47. Run chart of GUIDE-HF CRFs not entered in EDC post-intervention

GUIDE-HF received a quality improvement intervention for data entry. Mean GUIDE-HF CRF's entered in the EDC weekly decreased from 5.3 CRF's pre-intervention (Figure 44) to 4.5 CRF's post-intervention (Figure 45). Mean CRF's not entered in the EDC weekly decreased from 2.3 CRF's pre-intervention (Figure 46) to 1.5 CRF's post-intervention (Figure 47).

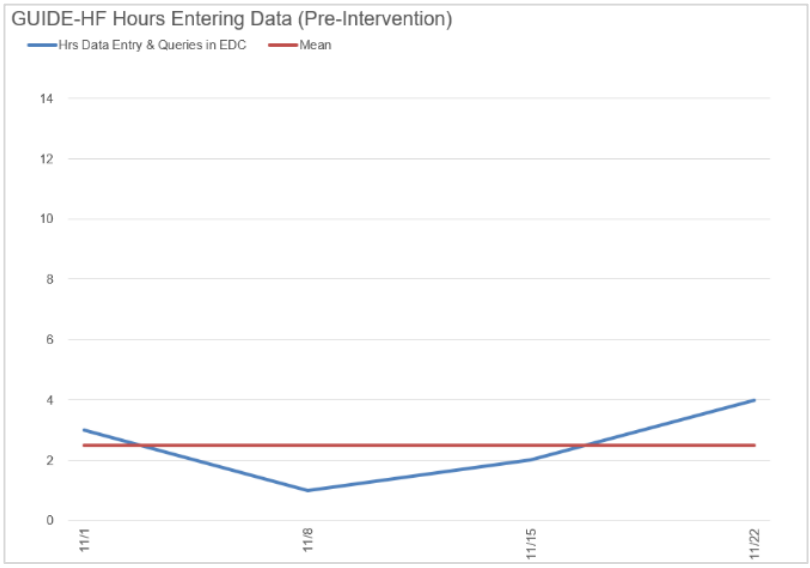

Figure 48. Run chart of hours entering GUIDE-HF data pre-intervention

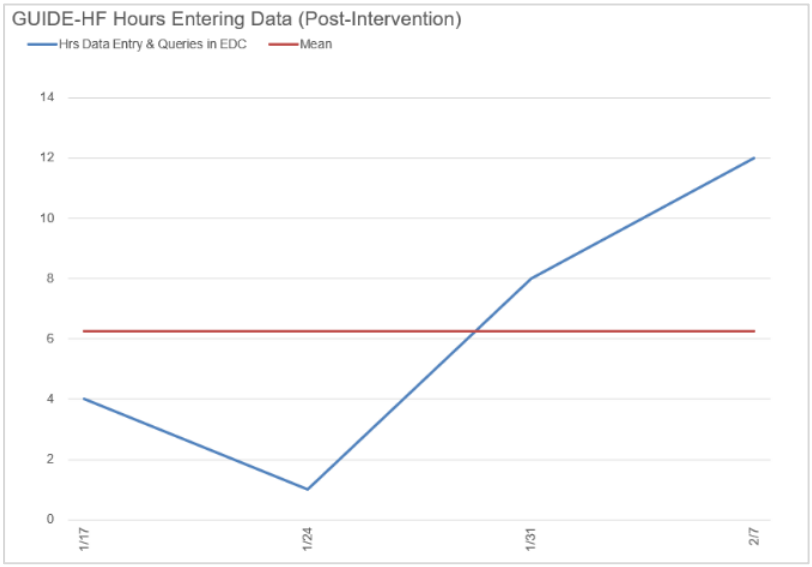

Figure 49. Run chart of hours entering GUIDE-HF data post-intervention

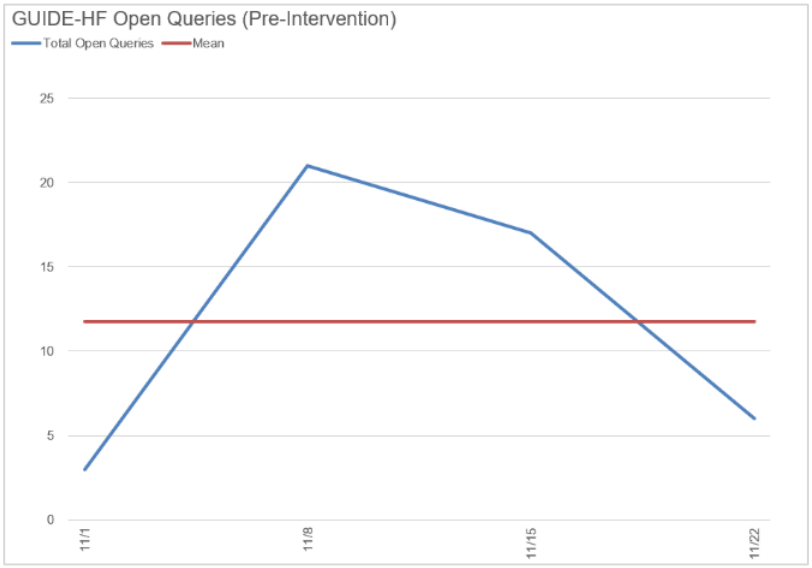

Figure 50. Run chart of open GUIDE-HF queries pre-intervention

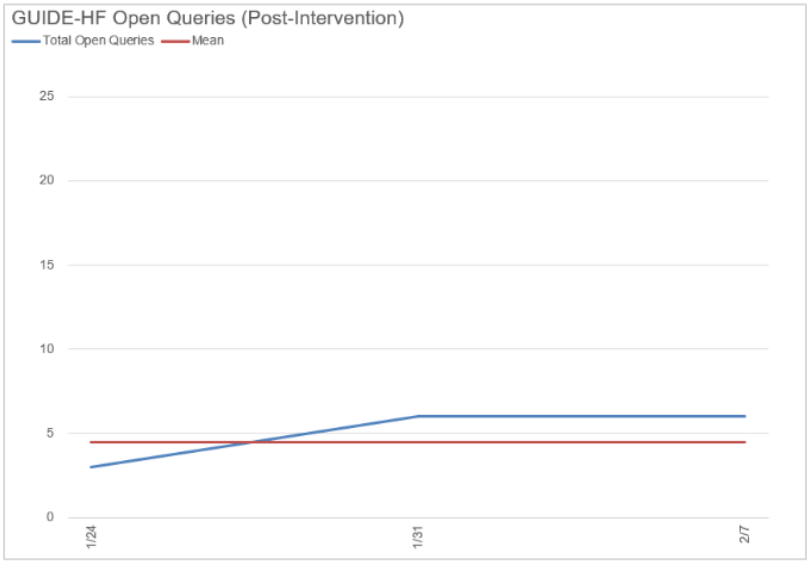

Figure 51. Run chart of open GUIDE-HF queries post-intervention

Mean time entering CRF's weekly for GUIDE-HF increased from 2.5 hours pre-intervention (Figure 48) to 6.3 hours post-intervention (Figure 49). Mean open queries weekly decreased from 11.8 queries pre-intervention (Figure 50) to 4.5 queries post-intervention (Figure 51).

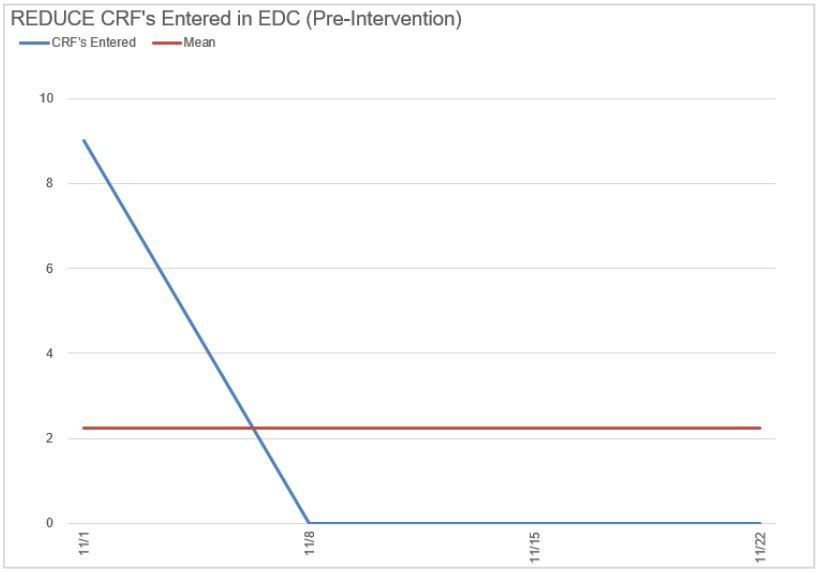

Figure 52. Run chart of REDUCE CRFs entered in EDC pre-intervention

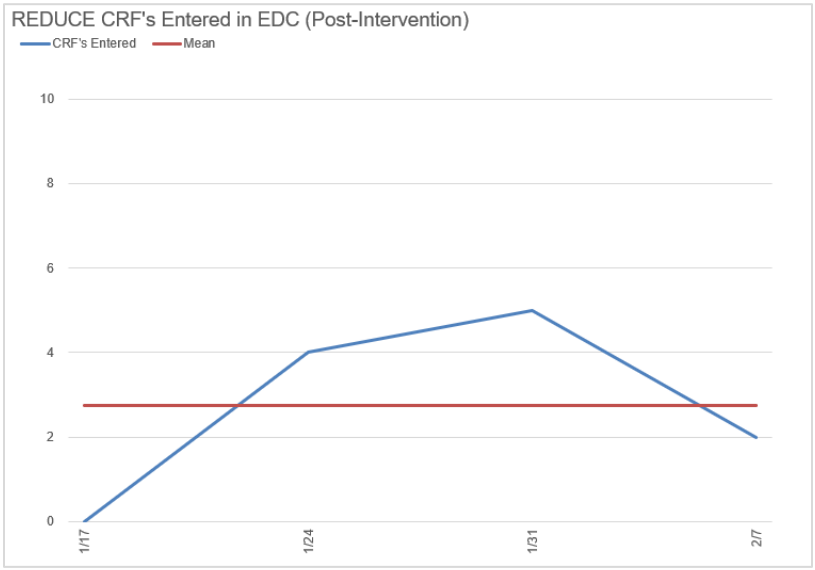

Figure 53. Run chart of REDUCE CRFs entered in EDC post-intervention

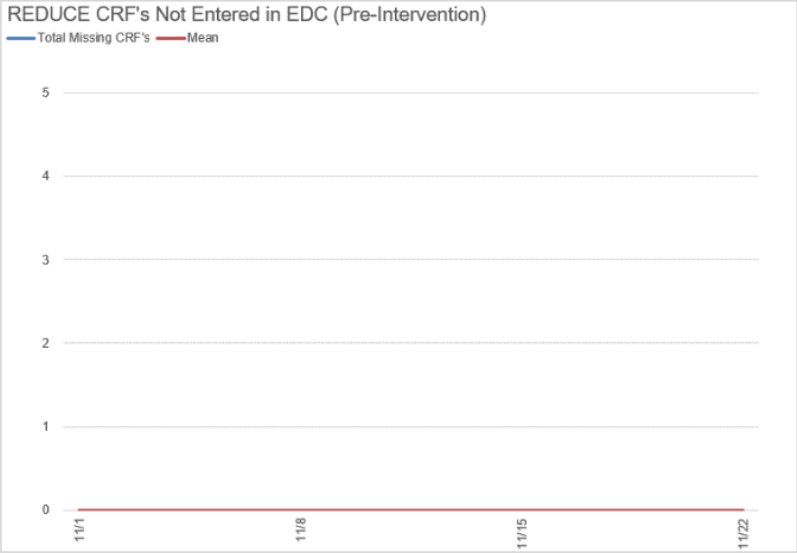

Figure 54. Run chart of REDUCE CRFs not entered in EDC pre-intervention

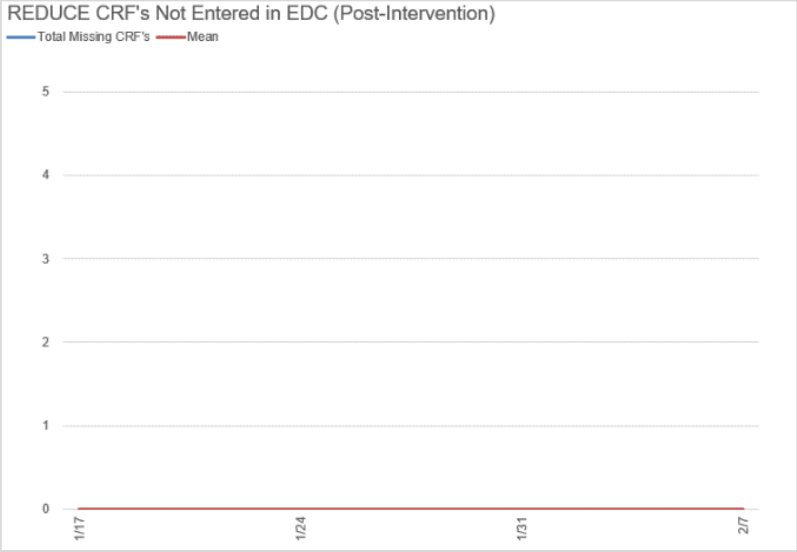

Figure 55. Run chart of REDUCE CRFs not entered in EDC post-intervention

REDUCE received a quality improvement intervention for data entry. Run charts were maintained for number of CRF's entered in the EDC and number of CRF's not entered in the EDC during pre and post-intervention periods. Mean REDUCE CRF's entered in the EDC weekly increased from 2.3 CRF's pre-intervention (Figure 52) to 2.8 CRF's post-intervention (Figure 53). Mean CRF's not entered in the EDC weekly remained constant at zero CRF's pre-intervention (Figure 54) and post-intervention (Figure 55).

Figure 56. Run chart of hours entering REDUCE data pre-intervention

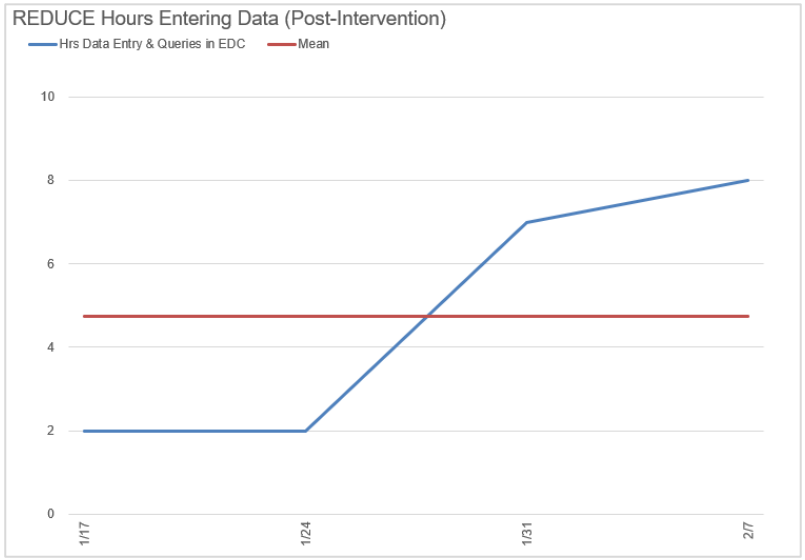

Figure 57. Run chart of hours entering REDUCE data post-intervention

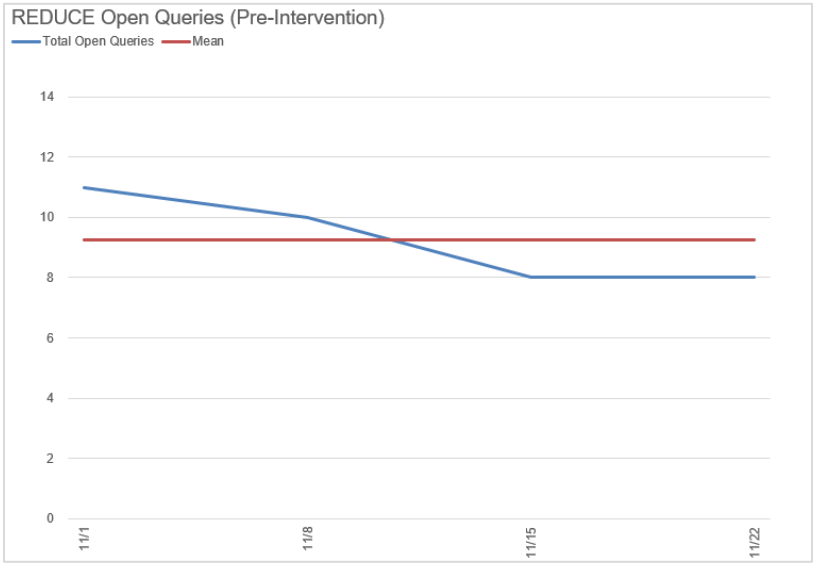

Figure 58. Run chart of open REDUCE queries pre-intervention

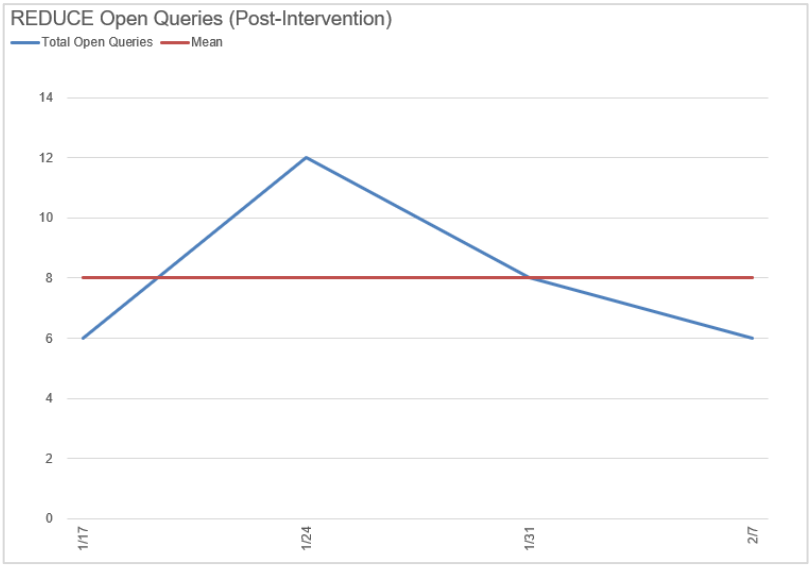

Figure 59. Run chart of open REDUCE queries post-intervention

REDUCE received a quality improvement intervention for data entry. Run charts were maintained for time spent entering CRF's, and number of open queries during pre and post-intervention periods. Mean time entering CRF's weekly increased from 2.8 hours (Figure 56) to 4.8 hours following intervention (Figure 57). Mean open queries weekly decreased from 9.3 queries (Figure 58) to 8.0 queries following intervention (Figure 59).

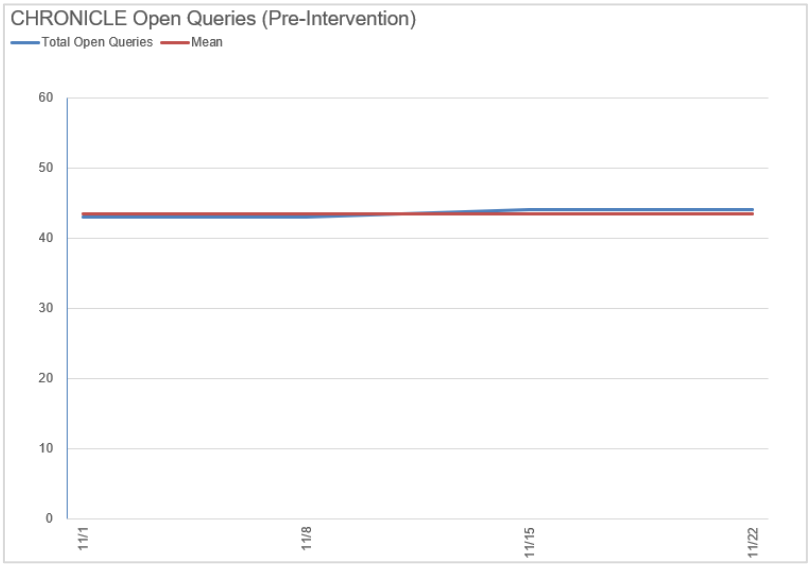

Figure 60. Run chart of open CHRONICLE queries pre-intervention

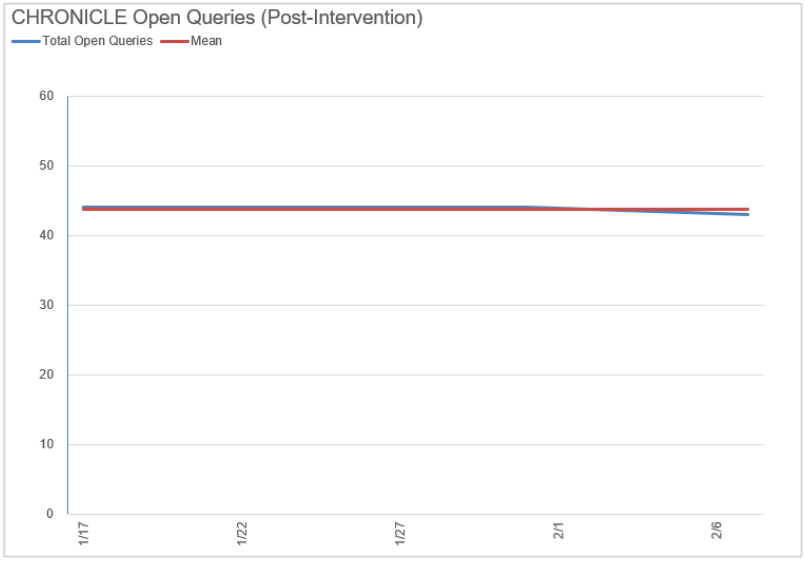

Figure 61. Run chart of open CHRONICLE queries post-intervention

CHRONICLE received a quality improvement intervention for open queries. Run charts were maintained for number of open queries during pre and post-intervention periods. Mean CHRONICLE open queries weekly increased from 43.5 queries pre-intervention (Figure 60) to 43.8 queries post-intervention (Figure 61).

Statistical Analysis of Interventions:

The Wilcoxon Signed-Rank test was used to statistically analyze differences in medians of key trial activity metrics before and after intervention. Statistical analysis was performed on metrics from the group of trials in our study regardless of differences in assigned interventions between trials. Trials were grouped in this manner to create a sufficient *n* value for statistical analysis. Time screening subjects and number of CRF's entered in the EDC demonstrated non-significant decreases in medians following intervention. The combined variable of number of open queries and CRF's not entered weekly demonstrated a statistically significant decrease in median following intervention. Time entering data in the EDC and number of subjects screened weekly demonstrated non-significant increases in medians following intervention. Statistical testing was not performed for number of subjects enrolled and time spent enrolling subjects due to sample sizes below the minimum critical value of n=5. In summary, five of the seven variables receiving quality improvement interventions improved in the direction of the intervention, with one demonstrating a statistically significant difference. The small sample size used may have decreased the power of the study to detect statistical significance.

DISCUSSION

Pre-intervention Processes vs. Selected Interventions:

The coordinator for ALL IN identified an area of improvement she encountered while completing key trial activities was entering complex immunological data. She implemented process improvement on her own initiative to improve data entry efficiency but experienced limitations from improving further due to time constraints. The coordinator directly spent 16 hours entering 61 CRF's into the EDC during the pre-intervention period. Of the six clinical trials involved in this study, ALL IN had both the highest number of CRF's and largest amount of time spent in data entry during the pre-intervention period. Due to the complexity of the study, it was common for 20-50 CRF's to be created each week leading to an accumulation of CRF's needing to be entered into the EDC.

Since the coordinator had self-improved her data-entry process flows, it was determined that the resource of time was needed to yield further improvement. Staff workloads and background in the data subject area were evaluated to select an additional team member to assist in data entry. Redirecting staff time in this manner maximized positive benefit to ALL IN while minimizing negative impact to other trials. Key and supplemental trial activities delegated to study members were assessed to determine if time spent completing each activity was advantageously matched to the complexity of the activity. It was determined that creation of study binders could be delegated to a Clinical Research Assistant in order to redirect coordinator time to the key activity of data entry.

Coordinator feedback was obtained, and metrics collected for TROJAN-C during the pre-intervention period to identify potential areas of improvement in the completion of key trial activities. No major unresolved challenges or resource-based limitations were identified, and key

activity workflows appeared to operate efficiently. Notably, of the six clinical trials involved in this study, TROJAN-C had the second highest number of CRF's and second largest amount of time spent in data entry during the pre-intervention period. TROJAN-C and ALL IN are managed by the same coordinator, requiring a significant time commitment for data entry. This is eased by delegation of data entry to more than one research staff on the study.

A quality improvement intervention was not selected for TROJAN-C due to the efficiency observed in trial processes and key activity completion. Since the coordinator for TROJAN-C also manages another trial receiving a quality improvement intervention of additional personnel for data entry, indirect benefits may be seen in TROJAN-C if the coordinator is able to reallocate time to it.

The coordinator for GUIDE-HF and REDUCE identified an area for improvement in her completion of key trial activities for both studies was allocating time across multiple competing responsibilities. She recognized that utilizing a scheduling approach to allocate time to complete key trial activities might improve the efficiency of her normal processes. Our study team observed that completion of key trial activities in the pre-intervention period already met departmental standards. Notably, GUIDE-HF maintained ranking within the top 10 enrolling sites nationwide throughout the duration of our quality improvement study. Additionally, both GUIDE-HF and REDUCE maintained a low number of open queries and CRF's not entered in the EDC. The study team sought to optimize productivity in already well-running processes by implementing the use of time blocking as a time management technique for both studies.

Coordinator feedback was obtained, and metrics collected for CHRONICLE during the pre-intervention period to identify potential areas of improvement in the completion of key trial activities. The coordinator for CHRONICLE faced the challenge of a high number of

queries remaining open despite following procedures to resolve them. The study team observed from CHRONICLE pre-intervention metrics that although there were many open queries, data entry was completed on time weekly resulting in zero missing data.

Another potential area of improvement identified was the process of screening subjects. The coordinator normally used the Principal Investigator's (PI) daily clinic schedule to review major inclusion/exclusion criteria for all visiting patients, resulting in a weekly screening rate of around 35 subjects. Though 15 hours were spent screening a total of 140 subjects during the pre-intervention period, only two subjects enrolled into the trial. Causative factors were identified to explain the discordance between screening effort and enrollment outcomes. The screening process used resulted in nearly half of the total screened subjects immediately found ineligible due to failure to meet major inclusion criteria. Eligible subjects first learned about the study from the coordinator when approached for consent, and usually declined enrollment due to lack of interest.

Our study team decided to implement quality improvement interventions within CHRONICLE's screening and enrollment processes, and data entry for open queries. The HLTP office research manager facilitated an inter-departmental effort to foster PI and clinic staff engagement with eligible subjects before the subject was approached for consent by the research team. The manager additionally coordinated a multi-site coordinator meeting to compare best enrollment and screening practices. Practices identified with proven efficiency and results included clinic staff using their knowledge of patient medical history and major inclusion/exclusion criteria to focus prescreening efforts on easily identifiable patient groups for optimized screening. Another successful practice was for clinic staff to discuss the study with eligible subjects and provide referrals to the coordinator. The direct involvement of clinic staff in

trial screening and enrollment processes improved screening efficiency and increased subject interest in trial participation. CHRONICLE's research team incorporated these identified best practices into their screening and enrollment efforts at our site by meeting with clinic staff to review trial inclusion/exclusion criteria and request subject referrals.

Coordinator feedback was obtained, and metrics collected for BOSTON-2 during the pre-intervention period to identify potential areas of improvement in the completion of key trial activities. The BOSTON-2 research team faced challenges identifying eligible subjects due to recently amended trial eligibility criteria that excluded more of the available patient population. Though the team screened four subjects weekly including prescreened referrals received from the clinic staff, zero subjects were enrolled during the pre-intervention period. Our study team decided to focus quality improvement efforts to increase the number of subjects screened in hopes of increasing enrollment. The HLTP office research manager established a weekly screening goal of 15 subjects for BOSTON-2.

Effect of Interventions:

Though the coordinator for ALL-IN directly spent 16 hours entering 61 CRF's into the EDC during the pre-intervention period, it was common for 20-50 CRF's to be created each week leading to an accumulation of outstanding CRF's. Improvement in data entry completion was limited by time constraints. Implementation of an intervention to redirect time to ALL-IN data entry improved median time entering data weekly from 4 hours to 5 hours and increased median CRF's entered weekly from 6 CRF's to 34 CRF's. The median number of open queries and CRF's not entered weekly remained constant at 76 queries and CRF's following intervention. This lack of improvement in the median likely resulted from our inability to fully

implement the intervention until beyond the middle of the post-intervention period. This is reinforced by observing the change in period totals vs medians for the variables in question. Following intervention, the total number of open queries decreased from 10 to zero and the total number of missing CRF's decreased from 103 to 23. Overall, despite the delayed implementation of the intervention, ALL-IN data entry completion improved following a target quality improvement intervention.

Since the coordinator for ALL-IN also manages TROJAN-C, our study team hypothesized that ALL-IN's intervention might indirectly benefit TROJAN-C if the coordinator was able to reallocate time to the trial. TROJAN-C did not receive a directed intervention due to already efficiently operating key activity workflows and productivity. Improvements were not observed within TROJAN-C key trial activity completion during the post-intervention period.

Implementation of time blocking as a time management technique for both GUIDE-HF and REDUCE trials enabled the coordinator to improve the efficiency of her normal processes by intentionally allocating time across multiple competing responsibilities in order to effectively complete data entry, screening, and enrollment activities. Variables that improved in the direction of the intervention for GUIDE-HF included median weekly time screening subjects, time enrolling subjects, time entering data, and number of open queries and data not entered. Variables that improved in the direction of the intervention for REDUCE included median weekly time screening subjects, time entering data, data entered, and number of open queries and data not entered. Post-intervention effects optimized productivity in already well-running processes for GUIDE-HF and REDUCE trials.

The coordinator for CHRONICLE faced the challenge of a high number of queries remaining open during the pre-intervention period despite following procedures to

resolve them. The coordinator continued efforts to close the open queries throughout our study, but no change resulted. Screening and enrollment processes used for CHRONICLE during the pre-intervention period resulted in large screening efforts with minimal enrollment outcomes. During the intervention period, CHRONICLE implemented best practices within screening and enrollment processes with the goal of improving efficiency and increasing subject interest in trial participation. Screening and enrollment metrics did not improve following intervention. This effect is likely due to an inability to fully implement the selected intervention within the four-week implementation period since it required changing inter-departmental processes.

The BOSTON-2 research team faced challenges identifying eligible subjects during the pre-intervention period despite screening four subjects weekly and receiving prescreened referrals from the clinic staff. The quality improvement intervention implemented increased the number of subjects screened weekly in hopes of increasing trial enrollment. BOSTON-2 median subjects screened weekly increased from 3 subjects to 15 subjects following intervention. Despite increased screening effort and a patient referral system already in place, the number of subjects enrolled remained at zero following intervention. The lack of effect following intervention is likely due to a limited study population not currently accessible to the research team.

Factors Affecting Study Results:

Our study team was unable to fully implement ALL-IN's quality improvement intervention until beyond the middle of the post-intervention period. This likely affected post-intervention results by limiting effect of change. This effect was most noticeable in the median

number of open queries and CRF's not entered weekly remaining constant following intervention.

The coordinator for CHRONICLE increased efforts to close resolved queries but no change was observed in the number of open queries. This lack of improvement following intervention likely results from sponsor-related factors beyond control of the coordinator. Since these contributing factors limit the effect of increased coordinator efforts, quality improvement efforts may be more effective if redistributed or retargeted. Additionally, CHRONICLE screening and enrollment metrics did not improve following intervention. This effect is likely due to an inability to fully implement and sustain the selected quality improvement intervention. Additional time is required beyond the four-week implementation period allocated for our study to effect sustained change within inter-departmental processes.

The BOSTON-2 research team successfully implemented a quality improvement intervention to increase the number of subjects screened weekly, but subject enrollment remained at zero. A major contributing factor to low enrollment identified by the coordinator during the pre-intervention period was recently amended trial eligibility criteria which excluded much of the previously available patient population. The lack of improved enrollment following intervention likely results from a limited study population not currently accessible to the research team. This contributing factor limits the effect of increased screening effort on enrollment.

Lessons Learned:

When assigning quality improvement interventions that reallocated staff time resources amongst studies, we first evaluated staff workloads and background in the subject area. Redirecting staff time in this manner maximized positive benefit to the trial receiving the

intervention while minimizing negative impact to other trials. We also learned that it is worthwhile to evaluate the efficiency of all studies together versus each study individually, to observe positive and negative effects of any resource reallocation involved in the quality improvement intervention.

The duration of periods within our study was short due to the research internship length, which affected our ability to fully implement each trial intervention. We learned that when constructing a quality improvement study design, it is important to maximize the length of the implementation period to optimize collection of data post-intervention that fully captures the effect of the intervention. Additionally, we noted that feasible study goals should be set in consideration of sample size limitations on statistical analysis. Our study goal for "proof of concept" was feasible considering our small sample size, but a future study goal to validate the quality improvement process and interventions should use a larger sample size for increased power to detect significant effects.

LIMITATIONS

A major limitation of this study is the non-generalizability of results to all trials and their coordinating staff due to the qualitative research design and non-random sampling technique. Qualitative research on performance measures may only be representative of the individual clinical research site and not applicable to other sites due to natural variation in site processes. Results from this study are just one part of a continuous quality improvement process that bears repeating several times with slight adjustments to interventions, to incorporate information learned from previous cycles[12]. Additionally, the non-random sampling technique used in this

study may create a sample that is not representative of a larger population, thus any statistical inferential analysis performed is non-generalizable.

Performance measures can be expected to have slight changes within sites due to natural process variations over time, but this makes it difficult to determine whether observed changes are naturally occurring or due to a study intervention. Statistical process control methods such as run charts were used to analyze variation over time and objectively determine whether the variation was naturally occurring or actually due to the study intervention[13]. Performance measures also vary between sites due to non-standardization of processes, so it is important for readers to understand that study results are not generalizable to sites outside of BSWRI HLTP department.

Another study limitation results from subjective collection techniques for data capturing CRC time spent in completion of key trial activities. The technique used in this study allows CRC's to record their own time spent in completion of the activities. The accuracy of this data thus depends on the CRC's ability to record unbiased data that reflects reality. The absence of an independent, objective means of collecting time allocation data ensues a limitation of possible respondent bias and inaccurate data. This limitation was mitigated by educating CRC's on the importance of accurate data collection to meet the study goal of optimizing employee workload and efficiency. CRC's were informed that it was not a study goal to measure employee performance.

Lastly, a negative perception of the study and/or intervention by CRC's as inconvenient or time-consuming may have restricted full implementation, resulting in skewed results. This limitation was mitigated by using a study design that did not greatly increase coordinator burden, and by receiving CRC feedback at multiple points throughout the study to monitor both their

burden and adherence to the intervention. Site managers were involved throughout the entire study process to ensure study feasibility and top down support.

CONCLUSION

The quality improvement methodology initiated in this project was the first of its kind for our department and provided our team with a tool to continuously assess and improve trial activity performance and outcomes. Five of the seven variables receiving quality improvement interventions had medians that improved in the direction of the intervention, with one demonstrating a statistically significant improvement. The lack of statistical significance for the improvement observed in the remaining four variables may be due to the effect of the small sample size we used decreasing the power of the study. It may be beneficial to validate our quality improvement methodology using a larger sample size in future projects. This study established 'proof of concept' for the completion of future, larger-scale quality improvement projects at our research site.

The quality improvement interventions that produced improvements in trial activities may be considered for standardization or further validation. These interventions include:

1) Evaluating staff workloads and backgrounds to redirect additional time for data entry to trials that typically generate or accumulate a large amount of complex data.
2) Evaluate key and supplemental trial activities delegated to trial members to determine if activities are advantageously assigned based on time, effort, and complexity. For example, delegating the creation of study binders to a research assistant may be beneficial if it allows the coordinator to spend more time entering complex data.

3) Implement the use of time management techniques for all research staff such as using personal Outlook calendars to block out time dedicated to completing key trial activities.
4) Set weekly screening goals for trials based off the trial screening effort (number of subjects screened) needed to generate one enrollment.
5) Evaluate efficiency of trial screening processes by determining screening effort (number of subjects screened) needed to generate one enrollment. Determine whether inefficiencies can be resolved by process improvement or are intrinsic to the trial due to unavailable study populations.
6) Managers should facilitate meetings between research staff on the same study at different sites to improve efficiency of trial activity process by incorporating proven best practices.
7) Managers should facilitate the development and continuation of an active process for clinic staff to send subject referrals to trial coordinators.
8) Managers should facilitate the development and continuation of an active process for the PI and clinic staff to inform eligible patients of research studies prior to the coordinator approaching the subject for consent.

FUTURE RESEARCH

Future research is important in the quality improvement process to continuously reassess methodology and effect of the intervention. A future study should be conducted to validate our methodology using a larger sample size to increase power to observe effect. Based on staff feedback, minimal effort was required to participate in this study, so it is feasible to include all trials in our department in future quality improvement studies. In this case, a longer intervention period should be used to ensure full implementation and effect of the intervention. It may be

beneficial to evaluate all trials managed by a coordinator to observe the effect of a trial intervention on the performance of other trials. It is unknown without this comparison whether quality improvement is a result of the intervention or is at the expense of the quality of other trials. Lastly, future research may be conducted to determine the effect of incorporating standardize quality improvement interventions within our department, such as setting weekly screening goals and using time management techniques.

CHAPTER III

INTERNSHIP EXPERIENCE

In addition to the proposed original study, I performed duties as an intern in the Heart and Lung Transplantation and Pulmonary clinical research department at BSWRI in support of the following trials:

1) Multi-Center Study of MagLev Technology in Subjects Undergoing MCS Therapy with HeartMate 3 (MOMENTUM 3)
2) Hemodynamic-GUIDEd Management of Heart Failure (GUIDE-HF)
3) REDUCE LAP-HF RANDOMIZED TRIAL II: A study to evaluate the Corvia Medical, Inc. IASD® System II to REDUCE Elevated Left Atrial Pressure in Subjects with Heart Failure (REDUCE)
4) Bioelectrical Impedance Spectroscopy in Heart Transplantation: Tracking Post-Transplant Changes in Body Composition and Correlation with Conventional Preoperative Risk Assessment Modalities (BIS)
5) Shear Wave Elastography of the Liver and Prediction of Morbidity and Mortality in Subjects Undergoing Advanced Heart Failure Therapy (Shearwave)

I was trained on Human Subjects Protection, Good Clinical Practice, Electronic Health Record systems, standard operating procedures, and study-specific activities. Study activities included electronic data entry, subject visit scheduling, and any additional administrative tasks assigned by the CRC or office manager. I had the opportunity to experience all aspects of clinical trial site activity in addition to shadowing physicians in their clinics.

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Appendix A: Journal Entries

Internship Daily Journal *August*

Week of 19-23 AUG:

19AUG

- Received department tour
- Obtained parking permit
- Obtained employee badge
- Completed Citi COI training (1 hr)
- Completed Citi GCP training (4 hrs)
- Scheduled mandatory trainings
- Completed initial set up of Cisco phone and desktop workstation

20AUG

- Attended department staff meeting (1 hr)
- Completed Encore merit system training with Rania (30 mins)
- Reviewed REDUCE study protocol (3 hours)
- Completed Office installation on desktop with IT support
- Reviewed and signed department protocols
- Updated staff binder with my CV and certifications

21AUG

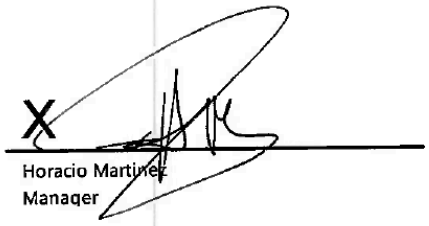
- Attended BSWRI mandatory Focused Orientation (5.5 hours)
- Completed review of BIS ICF and protocol

22AUG

- Reviewed EKG and Cardiac Monitoring skill sheets (1.5 hrs)
- Attended mandatory OR Training (1.5 hrs)
- Completed review of GUIDE ICF and half of GUIDE protocol (4 hrs)
- Completed Office Tools training with CRC Amanda Doss

23AUG

- Attended BIS trial one-month patient assessment with CRC Lesia Parker (4 hours)
- Completed review of Guide-HF protocol (2 hrs)
- Submitted OOO for 14 academic testing dates
- Reviewed EvaHeart protocol



Week of 26-30 AUG:

26AUG

- Scheduled internship practicum advisory committee meeting
- Scheduled mandatory GUIDE trial training with sponsor
- Reviewed internship practicum guidelines
- Planned internship practicum proposal (4 hours)
- Observed BIS ICF and baseline measurements with CRC Lesia (2 hours)

27AUG

- Attended Heart Research Team meeting where trials were discussed by PI's & CRC's (1 hr)
- Continued review of REDUCE ICF and Protocol
- Established location for advisory committee meeting
- Drafted template for internship practicum proposal

28AUG

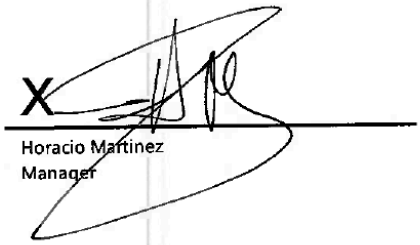
- Attended HLTP Patient Orientation (research presentation to patients) (1 hour)
- Continued working on research practicum proposal (4 hours)
- Received tour of hospital and lab orientation from CRC RN Shelby (1.5 hrs)
- Reviewed HM3 ICF and protocol (1 hour)

29AUG

- Discussed transplant/device selection process and meeting with Christine (1 hour)
- Reviewed GUIDE-HF protocol and ICF in prep for sponsor training on 30AUG (1 hour)
- Attended AHF lecture series "Sleep Apnea in Heart Failure" by Puneet Garcha, MD (1 hour)
- Conducted literature review for research proposal

30AUG

- Continued work on research proposal draft (2 hours)
- Continued literature review for research proposal (2 hours)
- Received Site Initiation Visit training from Sponsor (Abbott) for GUIDE trial (2 hours)



Horacio Martinez
Manager

Internship Daily Journal *September*

Week of 02-06 SEP:

02SEP

- Labor Day Holiday

03SEP

- Completed mandatory PeopleSoft training (3 hours)
- Reviewed sponsor-provided resources for GUIDE trial
- Reviewed REDUCE study ICF and Protocol

04SEP

- Completed GUIDE HF electronic data training with sponsor (Brooke from Abbott)
- Reviewed Reduce study patient binder and visit schedule with CRC Christine
- Completed thesis planning meeting with practicum mentor and research supervisor (Joost and Horacio)
- Continued work on practicum proposal draft

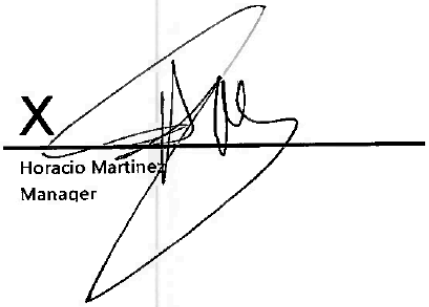
05SEP

- Completed review of REDUCE study EDC and patient binders with CRC Christine
- Reviewed shipping procedures for REDUCE study materials with CRC Christine
- Completed review of Momentum 3 ICF and Protocol
- Completed review of Shearwave ICF and Protocol
- Continued literature review for research proposal

06SEP

- Attended BSWRI General Orientation (4 hours)
- Completed CITI training GCP (FDA Focus) and HIPS (1.5 hours)
- Created proposal summary PowerPoint for committee meeting (1.5 hours)

- Attended LVAD removal and heart transplant (3:15pm-8:45pm)



Week of 09-13 SEP:

09SEP

- Held initial Advisory Committee Meeting (1 hour)
- Updated proposal with committee meeting notes
- Completed required BSWH Disclosure Statement
- Activated IRIS account
- Continued literature review for and background/timeline section of proposal

10SEP

- Attended departmental staff meeting
- Summarized three associated studies for proposal background section

11SEP

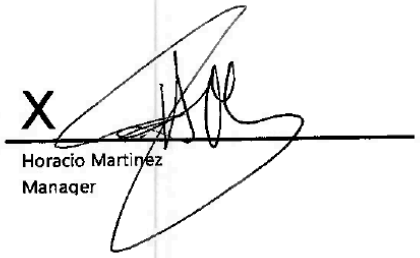
- Received training on Shearwave scheduling
- Conducted scheduling for Shearwave

12SEP

- Continued work on proposal draft

13SEP

- OOO for Military drill



Week of 16-20 SEP:

16SEP

- Continued work on proposal draft, emailed to major professor Dr. Mathew for review

17SEP

- Completed scheduling for Shearwave
- Completed scheduling for GUIDE-HF
- Attended NTX BSWRI staff meeting

18SEP

- Compiled list of GUIDE-HF patients screened "green" for potential enrollment
- Attended HLTP research meeting with Chief Dr. Hall where CRC's provided trial updates

19SEP

- Created patient daily asthma log for site study
- Continued work on proposal draft
- Attended surgical pod meeting with office manager and CRC's to review progress of studies, etc

20SEP

- Created practicum study summary for UNTHSC IRB submission, emailed to Dr. Mathews
- Incorporated Dr. Mathews proposal edits into draft

X

Horacio Martinez
Manager

Week of 23-27 SEP:

23SEP

- Emailed updated proposal draft to Dr. Mathews
- Reviewed practicum study timeline changes with Joost
- Emailed updated proposal draft and study summary documents to Dr. Mathews
- Created subject visit binder for BIS study

24SEP

- Attended Heart Research Committee Meeting
- Created subject visit binder for BIS study
- Attended sponsor EDC training (Merlin EDC for GUIDE-HF study)

25SEP

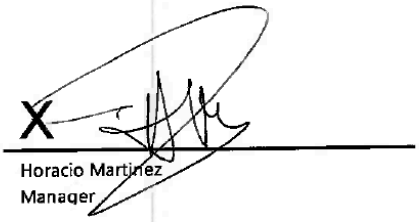
- Completed scheduling for Shearwave study
- Completed scheduling for BIS study
- Updated DOA log for Shearwave study

26SEP

- Attended AHF lecture. Topic: Durable Mechanical Circulatory Support (1 hr)
- Trained by CRC on entering data into EDC for GUIDE-HF study
- Entered data into EDC for GUIDE-HF study

27SEP

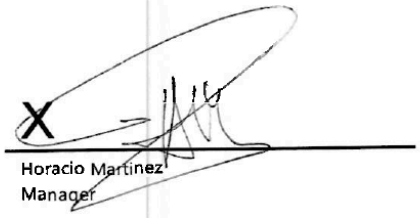
- OOO for academic testing at UNTHSC



Week of 30 SEP:

30SEP

- OOO for academic testing at UNTHSC



Internship Daily Journal *October*

Week of 01-04 OCT:

01OCT

- Shadowed cardiologist Dr. Kale in Advanced Heart Failure clinic (3 hours)
- Completed scheduling for Shearwave trial
- Completed scheduling for BIS trial

02OCT

- Observed CardioMEMS implant for GUIDE-HF trial in catheterization lab (4 hours)
- Created staff presentation for practicum study; Will present at staff meeting on 08OCT
- Created data collection tool for practicum study

03OCT

- Attended AHF lecture; Topic: Acute Heart Failure-Evaluation & Management

04OCT

- OOO for military drill

X

Horacio Martinez
Manager

Week of 07-11 OCT:

07OCT

- OOO for academic testing

08OCT

- Completed scheduling for Shearwave study
- Completed scheduling for BIS study
- Presented practicum study summary to HLTP staff at staff meeting
- Completed data entry for Shearwave study

09OCT

- Completed data entry for Shearwave study
- Attended meeting with Shearwave PI, CRC, supervisor
- Attended department research meeting with Chief cardiac physician, Dr. Hall

10OCT

- Created patient binder for Shearwave trial
- Scrubbed patient records for Shearwave trial
- Entered and updated patient data in REDCap EDC for Shearwave trial
- Updated master enrollment spreadsheet for Shearwave trial
- Attended AHF lecture "LVAD Management Approaches: More is Merrier vs. Less is More" by cardiologists Robert Gottlief, MD and Detlef Wencker, MD

11OCT

- Completed data entry for Shearwave study
- Continued scrubbing and updating Shearwave patient binders
- Conducted scheduling for Shearwave
- Trained on data entry for BIS study by manager Horacio
- Completed data entry for GUIDE-HF trial (phone calls entered)

X

Horacio Martinez
Manager

2

Week of 14-18 OCT:

14OCT

- Entered patient data for BIS study into REDCap EDC
- Scheduled patients for research assessments and procedures for BIS and Shearwave trials
- Met with site managers Horacio and Joost to discuss next step in practicum study

15OCT

- OOO for academic testing

16OCT

- Entered patient data for BIS study into REDCap EDC

17OCT

- Entered patient data for BIS study into REDCap EDC
- Attended Advanced Heart Failure lecture discussing LVAD speeds and their clinical impacts on heart failure patients
- Reviewed data collection points and tool for practicum study with manager Horacio
- Email practicum study participants reminder about pre-intervention data collection phase of practicum study starting 10/21

18OCT

- Entered patient data for BIS study into REDCap EDC
- Office half-day for Dallas fair

X

Horacio Martinez
Manager

Week of 21-25 OCT:

21OCT

- OOO for academic testing

22OCT

- Scheduled patients for research assessments and procedures for BIS and Shearwave trials
- Entered patient data for BIS study into REDCap EDC
- Entered patient data for GUIDE-HF trial into Abbott EDC
- Updated iRIS web-based research information system with patient enrollment data for Shearwave study

23OCT

- Entered patient data for BIS study into REDCap EDC
- Completed data entry for Shearwave study

24OCT

- Entered patient data for BIS study into REDCap EDC
- Completed data entry for Shearwave study
- Attended AHF Grand Rounds cardiology lecture

25OCT

- Shadowed cardiologist Dr. Kale on ICU rounds, observed TEE and cardioversion (3hr)
- Entered patient data for BIS study into REDCap EDC
- Created surgical device studies information binder for physician's clinic

X

Horacio Martinez
Manager

Week of 28-31 OCT:

28OCT

- Scheduled patients for research assessments and procedures for BIS and Shearwave trials
- Updated Shearwave patient binder
- Completed surgical device studies information binder for physician's clinic
- Entered patient data for BIS study into REDCap EDC

29OCT

- Entered patient data for BIS study into REDCap EDC
- Entered patient data for Shearwave study into EDC

30OCT

- Entered patient data for Shearwave study into EDC
- Reviewed data collection points and tool for practicum study with project manager Jillian Clark and manager Horacio
- Entered patient data for BIS study into REDCap EDC
- Attended research department update meeting with cardiologists

31OCT

- OOO for academic testing

X

Horacio Martinez
Manager

Internship Daily Journal *November*

Week of 01 NOV:

01NOV

- Reminded practicum study participants to submit metrics for week 2 pre-intervention period, and resolved their questions/concerns
- OOO for academic testing

X
Horacio Martinez
Manager

Week of 04-08 NOV:

04NOV

- Assisted CRC's with entering metrics for QI practicum study
- Verified accuracy of QI practicum study metrics entered for previous week, and created run charts and summary charts for metrics

05NOV

- Scheduled patients for research assessments and procedures for BIS and Shearwave trials
- Entered elastography scan results for Shearwave patients into EDC

06NOV

- Performed data entry for Shearwave study

- Performed data entry for BIS study

07NOV

- OOO for academic testing

08NOV

- Observed SAE reporting by CRC Amanda Doss for All-In trial
- Data entry BIS
- Finalized week 1 pre-intervention period metrics and run charts for practicum study and emailed them to managers Joost and Horacio
- Reminded practicum QI study participants to submit metrics for week 2 pre-intervention period, and resolved their questions/concerns

X

Horacio Martinez
Manager

Week of 11-15 NOV:

11NOV

- Performed data entry for Shearwave study
- Performed data entry for BIS study
- Shadowed CRC Amanda Doss during pt Tocilizumab infusion for All-In trial
- Learned about CCRC tasks (contract budget negotiations and approval process, and elements of a study budget) from research project manager/CRC Victoria Flores
- Reviewed Week 2 data for practicum study pre-intervention period, updated run charts and summary charts
- Scheduled patients for research assessments and procedures for BIS and Shearwave trials

12NOV

- Performed data entry for Shearwave study
- Performed data entry for BIS study
- Scheduled patients for research assessments and procedures for BIS and Shearwave trials

13NOV

- OOO for academic testing

14NOV

- Attended feasibility review of new study
- Performed data entry for BIS study
- Updated BIS patient binders
- Attended AHF lecture series "The Surgical Perspective of LVAD Therapy"
- Briefed staff about practicum project status during staff meeting

15NOV

- Reminded practicum QI study participants to submit metrics for week 3 pre-intervention period, and resolved their questions/concerns
- Performed data entry for BIS study

X

Horacio Martinez
Manager

Week of 18-22 NOV:

18NOV

- OOO for academic testing

19NOV

- Attended NTX staff meeting where basic clinical trial operations knowledge was reviewed
- Scheduled patients for research assessments and procedures for BIS and Shearwave trials
- Reviewed Week 3 data for practicum study pre-intervention period, updated run charts and summary charts
- Updated research committee lead Dr. Mathew on practicum study status

20NOV

- Uploaded raw patient data files from BIS study Imp Device. Exported data to individual excel files using study software and shared with research staff on study.
- Observed patient screening for All-In and Trojan-C studies
- Began learning R programming language for practicum study data analysis
- Created patient binder for REDUCE study
- Performed data entry for BIS study
- Attended department research meeting with staff and Chief cardiac physician, Dr. Hall
- Entered elastography scan results for Shearwave patient into EDC

21NOV

- Performed data entry for BIS study
- Attended AHF Grand Rounds cardiology lecture series
- Sent email update to manager Horacio on status of current assigned tasks/work

22NOV

- Reminded practicum QI study participants to submit metrics for week 4 pre-intervention period, and resolved their questions/concerns
- Performed data entry for BIS study
- Attended departmental lunch off campus

X

Horacio Martinez
Manager

Week of 25-29 NOV:

25NOV

- Shadowed cardiologist Dr. Kale on hospital rounds (2hr)
- Attended cardiology grand rounds lecture series about heart CT scans
- Attended Dr. Roberts' cardiopathology lecture during which he prosected hearts, heart valves, etc to interrogate disease etiology
- Reviewed Week 4 data for practicum study pre-intervention period, updated run charts and summary charts

26NOV

- OOO for academic testing

27NOV

- Reviewed practicum study pre-intervention phase metrics with Joost and Horacio
- Emailed summary of meeting for practicum study to Joost and Horacio
- Sent meeting schedule requests to CRC's of trials in my practicum study to discuss pre-intervention phase metrics
- Office early release for Thanksgiving holiday

28NOV

- Thanksgiving holiday

29NOV

- Received training from REA Hira for Guide-HF patient screening
- Screened four patients for Guide-HF trial

X

Horacio Martinez
Manager

Internship Daily Journal *December*

Week of 02-06 DEC:

02DEC

- OOO for academic testing

03DEC

- Conducted QI pre-intervention meetings with three coordinators and managers for practicum study (2 hrs)
- Summarized discussion points of QI practicum study meetings and sent to managers
- Updated internship journals
- Screened one patient for Guide-HF trial
- Created two patient binders for Reduce trial

04DEC

- OOO for academic testing

05DEC

- Reviewed study protocol in preparation for feasibility review
- Attended study feasibility review with site manager
- Observed Continuing Review by CRC Amanda Doss (3 hours)
- Attended AHF grand rounds, lecture "Heart Transplant Surgical Considerations"

06DEC

- OOO for military drill

X

Horacio Martinez
Manager

Week of 09-13 DEC:

09DEC

- OOO

10DEC

- OOO for academic testing

11DEC

- Attended HM3 PAS new study logistics meeting with manager Horacio and REA Lesia
- Screened one patient for GUIDE trial
- Observed Serious Adverse Event entry by CRC Christine Brooks
- Created report of patient status for enrollment and procedures for Shearwave study, emailed to PI Dr. Asrani
- Updated GUIDE patient binders with phone call visit CRF's

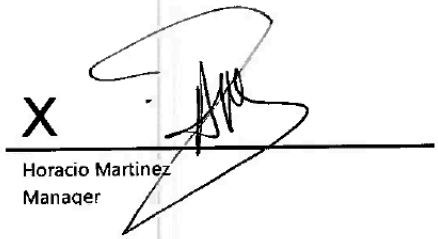
12DEC

- Trained on submission of IND Safety Reports in iRIS by REA Anne Elizabeth
- Attended AHF Grand Rounds lecture "Cardiac Amyloidosis: From Basics to Advances" by cardiologist Dr. Kale
- Drafted template of master spreadsheet for new HM3 PAS trial and emailed to REA Lesia and manager Horacio. Spreadsheet will be used to track consented patients and their study visits.
- Updated GUIDE-HF study tracker with dates of phone call visits and EDC entry for six subjects.
- Met with CRC of GUIDE-HF and REDUCE trials and managers Joost and Horacio to review metrics collected during pre-intervention phase, identify possible challenges in completion of key trial activities, and discuss possible QI intervention

13DEC

- Met with Dr. Asrani and manager Horacio to review Shearwave study subject visit completion. Discussed plan to schedule active subjects for remaining scans with Dr. Asrani.

- Reviewed active, in-window Shearwave subjects' upcoming clinic appointments in Epic and scheduled Shearwave scans with Dr. Asrani for three subjects.
- Resolved QI practicum study issues with CRC's (issue with spreadsheet tool and determining trial's local enrollment goal)
- Updated summary of CRC meetings for QI intervention to include meeting with CRC of Guide-HF and Reduce trials.
- Scheduled meeting with site managers Joost and Horacio to finalize practicum study QI interventions
- Prepared practicum study thesis manuscript template to include abstract, signature page, title page, acknowledgment page, and table of contents
- Entered subject study visit data into EDC for BIS study



Week of 16-20 DEC:

16DEC

- Entered CRF's for Six-Minute Walk test (6MWT), Body Composition, and height/weight (H/T) for 18 patients for BIS study, and updated study tracker

17DEC

- Attended Heart Research Committee Meeting with PI's and all research staff
- Attended iRIS training by Project Lead Aayla Jamil (1 hr)
- Designed QI intervention worksheets to use during meeting with Joost and Horacio
- Completed meeting with Joost and Horacio to finalize practicum study interventions (1 hr)
- Drafted emails containing proposed QI interventions to CRC's in my practicum study
- Made edits to HM3 PAS Master spreadsheet as requested by REA Lesia Parker

18DEC

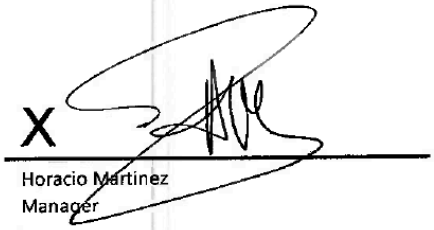
- Observed CRC Stephanie Carter consent subject for Intermacs. My goal is to get checked off to consent for registry/minimal risk studies by Research Educator Michelle Acker.
- Observed CRC/RN Christine Brooks enter Reduce study subject visits for screen-fail and implant into EDC
- Moved patient samples from a different office to our department's -80 freezer (2 hours)
- Coordinated scheduling of liver scan procedure for Shearwave study with PI
- Reviewed email drafts containing proposed QI interventions with manager Horacio and sent them to the CRC's in my practicum study
- Emailed requests to two CRC's in my study to update pre-intervention phase enrollment metrics to reflect patients consented not just randomized. This is due to lengthy enrollment visits that are not currently being captured in metrics.
- Updated Shearwave Master spreadsheet as instructed by manager Horacio

19DEC

- OOO

20DEC

- OOO



Week of 23-27 DEC:

23DEC

- Completed data entry for BIS study up to current date
- Printed off source documentation for height & weight measurements taken during office visits on or around BIS study visits
- Began reading ALL-IN protocol in order to be added to the study

24DEC

- Read 40 pages of ALL-IN protocol
- Printed off source documentation for height & weight measurements taken during office visits on or around BIS study visits
- Began self-review of HM3 PAS protocol training Webex recording

25DEC

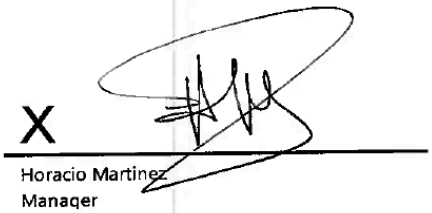
- Christmas holiday

26DEC

- OOO

27DEC

- Updated and printed off internship daily journal for manager signature
- Discussed next week's shadowing plan with surgical pod lead CRC/RN Christine Brooks
- Resent request for updated Guide / Reduce metrics to CRC. Updated numbers needed to ensure we are capturing work spent enrolling all subjects not just those randomized.
- Read remaining 35 pages of ALL-IN protocol
- Entered updated metrics for ALL-IN trial into practicum study metrics tracker
- Transferred practicum study Week 2 Intervention phase metrics from Smartsheets collection tool to metrics tracker
- Completed self-review of HM3 PAS protocol training Webex recording and documents
- Coordinated shadowing of study randomization visit on Monday 30DEC with pulmonary pod lead, REA Nick
- Coordinated attending IRB evaluation of PRESERVED-HF study on 02JAN



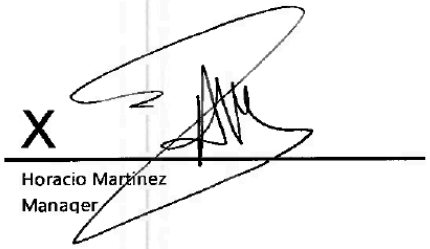
Week of 30-31 DEC:

30DEC

- Shadowed patient randomization visit for idiopathic pulmonary fibrosis study with REA Nick Maldonado including collection and prep of blood and urine samples (4 hours)
- Continued writing practicum report draft and updated study timeline
- Sent email to practicum committee to schedule date for defense/ seminar
- Discussed practicum seminar/ defense experience with CRC Eva Patel (UNTHSC alumni)

31DEC

- Shadowed CRC/RN Christine Brooks during new study start-up preparation including making visit binders, completing documents from sponsor, etc
- Office early release for holiday



Internship Daily Journal *January*

Week of 01-03 JAN:

01JAN

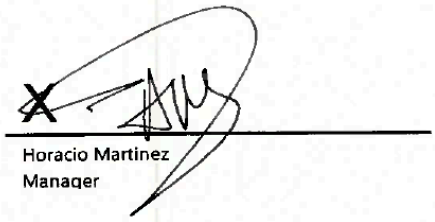
- New Year's Holiday

02JAN

- Attended NuPulse trial logistics meeting with CRC/RN Christine Brooks, REA Lesia Parker, and manager Horacio
- Attended IRB meeting where CR's and new studies were reviewed
- Reviewed upcoming appts for subjects enrolled in HM3 PAS and BIS trials in order to schedule them for research visits
- Updated HM3 PAS master spreadsheet with subject demographics, contact info, and status
- Updated subject statuses in EDC for BIS study

03JAN

- A.M. dentist appointment in Fort Worth
- Assisted in removing and packing office Christmas decorations
- Conducted literature review and generated introduction outline for practicum study report



Horacio Martinez
Manager

Week of 06-10 JAN:

06JAN

- Prepared December internship journal for manager signature
- Shadowed CRC Amanda Doss perform study drug pick-up at BUMC pharmacy
- Sent practicum study update email to CRC's involved in study, and followed-up with verbal discussions about intervention implementation
- Transposed previous weeks metrics from collection tool to practicum study metrics tracker
- Entered BIS study subject visit paper CRF's into EDC and filed them into subject binders

07JAN

- Performed pick-up of study drug at BUMC pharmacy and delivered to CRC/RN Michelle
- Attended surgical pod huddle with CRC Christine and REA's Lesia and Yasmeen to discuss status of ongoing clinical trials
- Corrected minor mistakes on CRF's for BIS study such as missing patient heart transplant numbers, printing off source for height and weight, etc
- Entered BIS study subject visit paper CRF's into EDC
- Scheduled patient study visits for BIS and HM3 PAS trials

08JAN

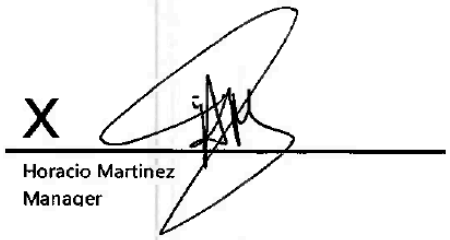
- Shadowed cardiologist Dr. Kale in Advanced Heart Failure clinic (3 hours)
- Entered BIS study subject visit paper CRF into EDC, printed off height and weight source from Epic, and filed the documents into the subject binder
- Attended department heart research meeting with Chief Cardiologist Dr. Hall
- Created condensed copy of HM3 PAS spreadsheet for REA Lesia

09JAN

- Attended AHF Grand Rounds lecture by chief cardiologist Dr. Hall
- Completed EDC training by CRC Amanda Doss for All-In study
- Completed sponsor training for All-In study
- Entered Guide-HF trial paper CRF's into EDC and filed them into subject binders

10JAN

- Reviewed previous students' CRM practicum reports from UNTHSC library site
- Reviewed and updated practicum study metrics tracker and run charts



Week of 13-17 JAN:

13JAN

- Escorted HELIOS monitor to BUMC pharmacy and observed monitoring activities
- Reviewed upcoming clinic appts for subjects enrolled in BIS trial to schedule them for research visits
- Sent email update about practicum study post-intervention period to CRC's involved
- Attended department staff meeting where study updates were provided

14JAN

- Shadowed RA Lesia to get BIS subject nutrition CRF's signed by nutritionist
- Transposed previous weeks metrics from collection tool to practicum study metrics tracker

15JAN

- Entered BIS study subject visit paper CRF's into EDC and filed them into subject binders
- Discussed CRC duties with RN Christine Brooks including subsite management and completion of documents for site initiation

16JAN

- Attended AHF grand rounds lecture by cardiologist Dr. Gottlieb
- Reviewed and updated practicum study run charts

- Submitted trouble ticket to maintenance service desk for office electrical issue

17JAN

- OOO for MCAT

Week of 20-24 JAN:

20JAN

- Shadowed CRC Shane Blankenship during subject visit for Galactic study
- Shadowed research assistant Russelia during lab sample preparation
- Transposed metrics from QI study data collection tool to metrics tracker
- Sent practicum study update to site managers Joost and Horacio

21JAN

- Scheduled patient study visits for BIS trial
- Scheduled room for thesis defense and seminar
- Completed mandatory DiSC assessment
- Attended leadership development training (2 hours)

22JAN

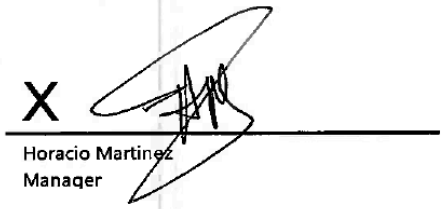
- Attended pulmonary transplant education session
- Assisted RN Shelby put together shelving units and organize staff storage room
- Attended heart research committee meeting

23JAN

- Attended Advanced Heart Failure Grand Rounds lecture about bariatrics in transplant
- Transposed metrics from QI study data collection tool to metrics tracker
- Entered BIS study subject visit paper CRF's into EDC and filed the documents into the subject binder, added new labeled tabs to binder
- Entered new BIS subjects into study in iRIS database
- Reviewed protocol for Intermacs study and completed documents to be added to the study

24JAN

- Completed review of protocol for Intermacs study
- Sent update to site managers regarding internship involvement and learning
- Continued working on literature review for practicum study
- Planned Intermacs study responsibilities with manager Horacio, and REA's Lesia and Hira
- Observed LVAD explant and heart transplant performed by surgeon Dr. Meyer (5 hours)



Week of 27-31 JAN:

27JAN

- Completed EDC site training for All-In trial
- Attended Dr. Robert's heart pathology demonstration (2 hours)
- Created SOP for Intermacs enrollment and consent process
- Reviewed Intermacs ICF
- Scheduled patient study visits for BIS trial
- Received email about possible Intermacs subject from clinic staff, checked binders and spreadsheets to determine if subject was consented. Since enrollment period is past, emailed manager Horacio with update.

28JAN

- Attended Heart Research Committee Meeting with PI's and all research staff
- Transposed metrics from QI study data collection tool to metrics tracker and created pre-intervention and post-intervention run charts.
- Scheduled ICF check-off with research nurse educator Michelle Acker
- Entered 10 CRF's for All-In study into EDC, printed source documents and filed in binders
- Filed BIS paper CRF's into subject binders

29JAN

- Shadowed cardiologist Dr. Kale during ICU rounds and research subject visit (3 hours)
- Tracked potential Intermacs subject in Epic. Notified CRA Lesia and REA Hira that subject would be discharged from ICU and could be approached for consent
- Printed QI study metrics tracker and run charts for meeting with Joost and Horacio
- Met with site managers Joost and Horacio to review metrics and status of interventions
- Entered 16 CRF's for All-In study into EDC, printed source documents and filed in binders
- Filed BIS paper CRF's into subject binders

30JAN

- Created detailed outline for practicum report
- Entered 8 CRF's for All-In study into EDC, printed source documents and filed in binders
- Attended AHF Grand Rounds lecture about new drug use for diabetes and heart failure
- Reviewed BSWRI Informed Consent training powerpoint in preparation for mock checkoff

31JAN

- Prepared for and completed ICF checkoff with research nurse educator Michelle Acker
- Trained by CRC Amanda to enter screen fail data into All-In EDC
- Shadowed two inpatient Intermacs subject consents and enrollment visits with REA Lesia
- Shadowed one BIS inpatient subject visit and two BIS inpatient consents with REA Lesia

X

Horacio Martinez
Manager

Internship Daily Journal *February*

Week of 03-07 FEB:

03FEB

- OOO for academic testing

04FEB

- OOO for academic testing

05FEB

- Created Intermacs activity log to track study activities including screening, consenting, etc
- Consented one Intermacs inpatient subject and completed enrollment visit
- Approached two inpatient subjects for Intermacs but was unable to consent due to ongoing procedures, etc
- Prepared ten sets of screening visit CRF's for Intermacs consents
- Coordinated with BSWRI staff member Brigid to complete necessary CITI training, and iRIS & study documents to be added to Intermacs study
- Obtained list of patients implanted with VAD's at BUMC from Analytics Developer II, Aayla; will use this list to find subjects needing to be approached for consent to Intermacs

06FEB

- Sent Shearwave study procedure status update to manager Joost
- Reviewed selection committee notes and determined Intermacs action items for VAD-approved subject, emailed to team
- Attended AHF lecture
- Attended research surgical pod finance/iRIS meeting
- Scheduled subjects for Intermacs visits
- Created Intermacs subject study visit spreadsheet

07FEB

- Entered 42 CRF's for All-in study
- Approached Intermacs subject for consent with REA Lesia Parker
- Reviewed and updated Intermacs training binders
- Created Reduce subject binder for CRC Yazmeen
- Filed Guide paper CRF's into subject binders

X

Horacio Martinez
Manager

Week of 10-14 FEB:

10FEB

- Entered 8 BIS CRF's into EDC and filed into subject binders
- Entered three new subjects into Intermacs EDC
- Attended departmental monthly staff meeting where new and current studies were reviewed
- Consented inpatient subject to Intermacs, completed enrollment visit, added subject to EDC

11FEB

- Entered demographics for two outstanding Intermacs consents in EDC, filed paper CRF's for five subjects in binders
- Scheduled F/U appts for Intermacs, confirmed appts with subjects
- Prepared ten sets of F/U visit CRF's for Intermacs appointments
- Created patient lists in Epic to streamline scheduling process
- Reviewed process for Intermacs data entry with REA Hira and manager Horacio
- Attended mandatory Epic Billing review Training WebEx for staff

12FEB

- OOO for medical appointment and procedure
- Began writing descriptions of clinical trials involved in QI study for thesis report

13FEB

- Completed writing descriptions of clinical trials involved in QI study for thesis report
- Began writing descriptions of coordinator pre-intervention and intervention study processes for thesis report, emailed completed sections to coordinators for review and input
- Transposed QI study metrics from collection tool to metrics tracker, emailed coordinators requesting missing week of metrics
- Updated run charts for QI study with all metrics received
- Scheduled Intermacs subject visits, confirmed visits with subjects

14FEB

- Completed Intermacs subject follow-up visit
- Scheduled inpatient Intermacs consent for Monday 02/17
- Rescheduled Intermacs subject visits due to subject missing visit
- Reviewed practicum study metrics for completion and accuracy, validated data with CRC's
- Worked on statistical analysis for research practicum study

X

Horacio Martinez
Manager

Week of 17-21 FEB:

17FEB

- Reviewed statistics methodology for practicum project with biostatistician Johanna
- Continued statistical analysis for research practicum study
- Scheduled Intermacs subjects for F/U visits and confirmed appts with subjects
- Consented inpatient subject to Intermacs, completed enrollment visit, added subject to EDC

18FEB

- OOO for academic testing

19FEB

- Completed Intermacs subject visit (questionnaires and neurocognitive exam)
- Waited for Intermacs subject, no show due to cancelled appointment
- Updated Dr. Mathews on practicum study thesis progress
- Filed 10 papers CRF's into subject binders for GUIDE study
- Updated department study board with number of new Intermacs subject consents
- Entered five paper CRF's into EDC for BIS and filed into subject binders
- Reviewed transplant selection committee notes for potential Intermacs consents. Reviewed medical records of two potential subjects, confirmed one already enrolled in Intermacs and the other will not be receiving VAD

20FEB

- Rescheduled practicum defense date and room
- Continued statistical analysis for research practicum study
- Waited for Intermacs subject to arrive to clinic visit, subject was no-show
- Attended cardiology grand rounds lecture

21FEB

- Continued statistical analysis for research practicum study
- Scheduled inpatient subject to be approached for Intermacs consent Monday, 24FEB

X

Horacio Martinez
Manager

Week of 24-28 FEB:

24FEB

- Consented inpatient subject to Intermacs, completed enrollment visit, added subject to EDC
- Submitted first draft of thesis to site managers Joost and Horacio
- Created master Intermacs subject spreadsheet

25FEB

- Continued working on thesis discussion section
- Updated master Intermacs subject spreadsheet with subject status and completed visits

26FEB

- Continued working on thesis discussion section
- Updated master Intermacs subject spreadsheet with subject status and completed visits

27FEB

- Entered 3 BIS CRF's into EDC and filed them into subject binders
- Discussed thesis edits with manager Joost
- Attended cardiology grand rounds lecture "Primary Allograft Failure" by Dr. Guerrero
- Approached potential Intermacs inpatient subject for consent twice
- Consented inpatient subject to Intermacs, completed enrollment visit, added subject to EDC
- Ran copies department Informed Consent Forms (ICF's) to Gabe for entry into Epic

28FEB

- Worked on thesis edits, continued working conclusion
- Scheduled Intermacs subjects for follow-up visits, called subjects to confirm

X

Horacio Martinez
Manager

Internship Daily Journal *March*

Week of 02-06 MAR:

02MAR

- Submitted maintenance request for office electrical issue
- Completed Intermacs subject follow-up visit (quality of life questionnaires & neurocog exam)
- Scheduled Intermacs subject follow-up and called subject to inform them
- Submitted first draft of practicum report to major professor

03MAR

- Entered 28 BIS CRF's in EDC, filed paper copies in subject binders
- Entered five new BIS subjects in iRIS including demographics
- Consented inpatient subject to Intermacs study
- Printed newly approved Intermacs ICF for subject packages and updated study department folder with electronic copy
- Filed IRB documents into Shearwave and Intermacs study binders

04MAR

- OOO for UNTHSC academic testing

05MAR

- Completed and printed February internship journal for manager signature
- Trained in Intermacs data entry by REA Hira (1.5 hours)
- Completed Intermacs subject follow-up visit
- Completed ""lessons learned", "conclusion", and "future research" for practicum first draft, emailed updated copy to site managers and major professor for review

06MAR

- Scheduled 44 Intermacs subject visits

- Completed concomitant medication training with CRC Amanda Doss for ALL-IN data entry
- Ran copies of department ICF's to Gabe for entry into Epic and ran department invoices to Debbie on different floor

X
Joost Felius
Manager

Week of 09-13 MAR:

09MAR

- Transposed data from GUIDE-HF spreadsheet copy to actual spreadsheet
- Waited for Intermacs subject post clinic appt for follow-up visit
- Entered 3 BIS CRF's in EDC, filed paper copies in subject binders
- Attended department staff meeting where biostatistics training was presented, and department updates were presented
- Updated iRIS subject status for 20 Intermacs subjects
- Sent our site flowcharts and spreadsheets for Intermacs to Plano CRC

10MAR

- Entered 8 Intermacs CRF's in EDC
- Worked on results section of research practicum report
- Completed Intermacs subject follow-up visit (questionnaires and neurocognitive exam)
- Filed 12 paper CRF's for GUIDE-HF into subject binders
- Created medications of interest and concomitant medications drug charts for ALL-IN to ease data entry process

11MAR

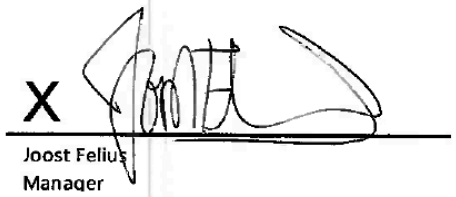
- Completed two inpatient subject follow-up visits for Intermacs
- Completed one outpatient subject follow-up visit for Intermacs
- Attended department research meeting with chief cardiologist Dr. Hall
- Began writing logs of concomitant meds and meds of interest for subject transplant visit for ALL-IN study

12MAR

- OOO for UNTHSC academic testing

13MAR

- Finished writing logs of concomitant meds and meds of interest for one ALL-IN subject, spot-checked by CRC Amanda
- Rescheduled one Intermacs subject follow-up visit
- Updated Intermacs visit window tracker with completed visits
- Entered two Intermacs CRF's into EDC
- Entered concomitant meds and meds of interest for one ALL-IN subject into EDC
- Ran copies of department ICF's to Gabe for entry into Epic and ran department invoices to Debbie on different floor



Week of 16-20 MAR:

16MAR

- Wrote concomitant meds log and meds of interest log for one ALL-IN subject
- Entered concomitant meds and meds of interest for one ALL-IN subject into EDC
- Canceled Intermacs follow-up visits due to COVID-19
- Met with manager Joost to discuss research practicum
- Scanned research internship daily logs to file
- OOO until further notice due to COVID-19 response by BSWRI