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14. ABSTRACT

The Major Extremity Trauma and Rehabilitation Consortium (METRC) consists of a network of clinical centers and one data-coordinating center that work together with the DoD to conduct multi-center clinical research studies. The goal of the consortium is to produce the evidence needed to establish treatment guidelines for the optimal care of the wounded warrior and ultimately improve the clinical, functional and quality of life outcomes of both service members and civilians who sustain high energy trauma to the extremities. Funding for METRC has helped us to develop and sustain the data-coordinating center, establish the network of sites conducting METRC research studies, facilitate ongoing training for studies and support study specific research requirements.

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None listed.

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1. INTRODUCTION:

The Major Extremity Trauma and Rehabilitation Consortium (METRC) consists of a network of clinical centers and one data-coordinating center that work together with the military to conduct multi-center clinical research studies. The goal of the consortium is to produce the evidence needed to establish treatment guidelines for the optimal care of the wounded warrior and ultimately improve the clinical, functional and quality of life outcomes of both service members and civilians who sustain high energy trauma to the extremities. Funding for METRC has helped us develop and sustain the data-coordinating center, establish the network of sites for conducting METRC research studies, and conduct specific research studies in response to the gaps DoD has identified in orthopaedic trauma research. Initial funding for METRC was received through two cooperative agreements, referred to as METRC 1 and METRC 2. In 2016, METRC received a third consortium award- METRC 3- and was approved to conduct an additional 5 studies (this progress report focuses on METRC 3 activities):

- **PRECISE**: A Multi-Center, Prospective Observational Study to Evaluate the Use of Patient-Specific Precision Injury Signatures to Optimize Orthopaedic Interventions in Multiply Injured Patients.
- **EMS-BinD**: Early Mechanical Stabilization and Bleeding Disruption of the Pelvic Ring: A Multi-Center, Prospective Observational Study
- **Alter-G**: Early Advanced Weight Bearing for Peri-Articular Knee and Pilon Injuries: An RCT Using the Anit-Gravity Treadmill
- **CBPT**: Improving Recovery after Orthopaedic Trauma: Cognitive Behavioral Based Physical Therapy
- **LTE**: Long-Term Consequences of Major Extremity Trauma: A Pilot Study

2. KEYWORDS:

Clinical research consortium, extremity war injuries, trauma related outcomes, orthopaedic outcomes research

3. ACCOMPLISHMENTS:

o What were the major goals of the project?

Study 1: Measuring Patient Specific Injury and Progression of Immunologic Response to Optimize Orthopaedic Interventions in Multiply Injured Patients (PRECISE), PI: McKinley

Study 1 Specific Aims: (1) Measure patient-specific indices that quantify injury and immunologic response to injury; (2) Evaluate the impact of surgical magnitude on patient specific physiologic and immunologic biomarkers; (3) Using patient-specific indices that quantify injury and response to injury, develop surgical decision rules that optimize clinical outcomes. **Patient Population**: Multiply injured patients 18-55 years of age requiring full trauma activation in the ER with a qualifying axial or appendicular orthopaedic injury.

	Timeline	**Status**
Major Task 1: Study Initiation	Months	
Subtask 1: Finalize master protocol	8-16	Complete
Subtask 2: Develop case report forms (CRFs) for data capture, program and pilot test REDCap	17-19	Complete
Subtask 3: Obtain initial IRB approval at JHSPH and USAMRMC	19-23	Complete
Subtask 4: Distribute approved protocol and obtain IRB approval at all participating sites	22-24	Ongoing
Subtask 5: USAMRMC Human Research Protections Office review and approval of site-specific IRB-approved human use documents	24-28	Ongoing
Milestone Achieved: Local IRB approval at METRC sites and HRPO	28	Ongoing
Major Task 2: Training Research Staff		
Subtask 1: Develop and conduct training for Research Coordinators on procedures for enrolling patients within first 48 hours of admission, collecting and shipping blood samples, and data collection procedures	19-22	Ongoing
Subtask 2: Certify sites to begin screening and enrolling patients	24-28	Ongoing

Subtask 3: Conduct study initiation calls with each site	24-28	Ongoing
Milestone Achieved: Research Staff Trained	28	Ongoing
Major Task 3: Conduct Study		
Subtask 1: Clinical site Research Coordinators will screen and enroll 400 eligible study patients. Coordinators will enter data collected on paper case report forms into the REDCap database and serum samples will be shipped to the core lab.	24-41	Ongoing
Subtask 2: Generate and distribute monthly enrollment and follow-up reports; provide ongoing training and support to address problems with enrollment and follow-up as they are identified	30-47	Ongoing
Subtask 3: Generate and distribute data quality reports to monitor data completeness; check for errors and inconsistencies	24-47	Ongoing
Milestone Achieved: Patients enrolled	41	Ongoing
Milestone Achieved: All laboratory data analyzed	41	Ongoing
Major Task 4: Data Analysis and Report Writing		
Subtask 1: Develop final analysis files	40-48	Not Started
Subtask 2: Conduct analysis and write final reports and peer-reviewed publications	48-60	Not Started
Subtask 3: Disseminate results- publication in peer reviewed journals and presentation at professional and scientific meetings	48-60	Not Started
Milestone Achieved: Report findings from final analysis	60	Not Started

Study 2: Early Advanced Weight Bearing for Peri-articular Knee and Pilon Injuries: an RCT using the Anti-Gravity Treadmill (Alter-G), PI: Stinner

Study 2 Specific Aims: (1) To compare functional outcomes and return to usual major activities between patients randomized to receive the intervention versus standard of care; (2) to compare patterns of recovery in range of motion and strength between; and (3) to compare performance in 4 domains of physical function- speed, power, strength, and agility. **Patient Population**: Adults ages 18-55 with periarticular fractures about the knee or distal tibia (pilon) fractures treated with ORIF (plate) for whom there are no established contra-indications that would preclude randomization to early or delayed weight bearing.

	Timeline	**Status**
Major Task 1: Study Initiation	Months	
Subtask 1: Finalize master protocol	21	Complete
Subtask 2: Develop case report forms (CRFs) for data capture, program and pilot test REDCap	21-22	Complete
Subtask 3: Obtain initial IRB approval at JHSPH and USAMRMC	22-23	Complete
Subtask 4: Distribute approved protocol and obtain IRB approval at all participating sites	23-24	Ongoing
Subtask 5: USAMRMC Human Research Protections Office review and approval of site-specific IRB-approved human use documents	23-24	Ongoing
Milestone Achieved: Local IRB approval at METRC sites and HRPO	24	Ongoing
Major Task 2: Training Research Staff		
Subtask 1: Develop and conduct training for Research Coordinators on procedures for enrolling patients, data collection, and maintaining good follow-up	24	Complete
Subtask 2: Develop and conduct training for physical therapists on the standardized 10 week therapy protocol	24	Complete
Subtask 3: Certify sites to begin screening and enrolling patients	24	Complete
Subtask 4: Conduct study initiation calls with each site	24	Complete
Milestone Achieved: Research Staff Trained	24	Complete
Major Task 3: Conduct Study		
Subtask 1: Clinical site Research Coordinators will screen and enroll 200 eligible study patients. Coordinators will enter data collected on paper case report forms into the REDCap database.	24-48	Ongoing

Subtask 2: Generate and distribute monthly enrollment and follow-up reports; provide ongoing training and support to address problems with enrollment and follow-up as they are identified	24-48	Ongoing
Subtask 3: Generate and distribute data quality reports to monitor data completeness; check for errors and inconsistencies	24-60	Ongoing
Milestone Achieved: All patients enrolled	48	Ongoing
Milestone Achieved: All patients followed	60	Ongoing
Major Task 4: Data Analysis and Report Writing		
Subtask 1: Develop final analysis files, conduct analysis and write final reports and peer-reviewed publications	60	Not Started
Subtask 2: Disseminate results- publication in peer reviewed journals and presentation at professional and scientific meetings	60	Not Started
Milestone Achieved: Report findings from final analysis	60	Not Started

Study 3: Improving Pain and Function Following Orthopaedic Trauma: A Cognitive-Behavioral Based Physical Therapy Approach (CBPT), PI: Archer

Study 3 Specific Aims: (1) To determine the efficacy of the CBPT program for improving outcomes; (2) to determine whether changes in pain catastrophizing, fear of movement, and self-efficacy at 6 months are associated with improvement in outcomes; (3) to determine whether subgroups of service members and civilians are more likely to benefit from the CBPT Program. **Patient Population**: Adults ages 18-60 who are having surgical treatment for an orthopaedic injury to the lower-extremity and have psychosocial risk factors for poor outcomes.

	Timeline	**Status**
Major Task 1: Study Initiation	Months	
Subtask 1: Finalize master protocol	6-12	Complete
Subtask 2: Develop case report forms (CRFs) for data capture, program and pilot test REDCap	9-13	Complete
Subtask 3: Obtain initial IRB approval at JHSPH and USAMRMC	14-18	Complete
Subtask 4: Distribute approved protocol and obtain IRB approval at all participating sites	19-23	Complete
Subtask 5: USAMRMC Human Research Protections Office review and approval of site-specific IRB-approved human use documents	21-24	Complete
Milestone Achieved: Local IRB approval at METRC sites and HRPO	24	Complete
Major Task 2: Training Research Staff		
Subtask 1: Conduct training of the MTF therapist on administering the intervention to military patients (civilian therapists have already received training)**	-- **	*Not Applicable*
Subtask 2: Develop and conduct training for Research Coordinators on procedures for screening and enrolling patients; procedures for data collection and maintaining good follow-up	19-22	Complete
Subtask 3: Certify sites to begin screening and enrolling patients	21-24	Complete
Subtask 4: Conduct study initiation calls with each site	20-24	Complete
Milestone Achieved: Research Staff Trained	24	Complete
Major Task 3: Conduct Study		
Subtask 1: Clinical site Research Coordinators will screen and enroll 320 eligible study patients. Coordinators will enter data collected on paper case report forms into the REDCap database.	22-36	Complete
Subtask 2: Study therapist will administer treatment	23-40	Ongoing
Subtask 3: Generate and distribute monthly enrollment and follow-up reports; provide ongoing training and support to address problems with enrollment and follow-up as they are identified	22-48	Ongoing
Subtask 3: Generate and distribute data quality reports to monitor data completeness; check for errors and inconsistencies	22-48	Ongoing
Milestone Achieved: All patients enrolled	36	Complete

Milestone Achieved: All patients followed	48	Ongoing
Major Task 4: Data Analysis and Report Writing		
Subtask 1: Develop final analysis files, conduct analysis and write final reports and peer-reviewed publications	46-60	Not Started
Subtask 2: Disseminate results- publication in peer reviewed journals and presentation at professional and scientific meetings	46-60	Not Started
Milestone Achieved: Report findings from final analysis	60	Not Started

** This subtask was on hold due to the low numbers of military participants and ultimate determined to be not applicable to the study.

Study 4: Early Mechanical Stabilization and Bleeding in Disruption of the Pelvic Ring (EMS-BinD), PI: Gary

Study 4 Specific Aims: Among patients with Young-Burgess APC 2 and 3, LC-3, vertical shear, and combined mechanism (Tile B and C) injury patterns, (1) determine if longer time to application of CPC increases need for a defined set of interventions (resuscitation with blood products, number of ventilator days, the need for angioembolization and/or pre-peritoneal pelvic packing and/or REBOA) and mortality; (2) determine if application of CPC prior to definitive hospitalization results in decreased need for a defined set of interventions and mortality; and (3) set the stage for the design and implementation of future randomized clinical trials of the use of adjuvant resuscitation approaches to improve outcomes in this patient population. **Patient Population**: Adult patients with severe high-energy pelvic ring disruptions (OTA codes 61-B and 61-C) who arrive to a level 1 trauma center within 6 hours of injury.

	Timeline	**Status**
Major Task 1: Pilot study	Months	
Subtask 1: Develop pilot protocol	3-5	Complete
Subtask 2: Develop case report forms (CRFs) for data capture, program and pilot test REDCap	3-5	Complete
Subtask 3: Obtain initial IRB approval at JHSPH and USAMRMC	6-7	Complete
Subtask 4: Distribute approved protocol and obtain IRB approval at all participating sites	8-10	Complete
Subtask 5: Clinical site Research Coordinators review records for eligible study patients; abstract data	9-14	Complete
Subtask 6: Generate and distribute data quality reports to monitor data completeness; check for errors and inconsistencies	9-16	Complete
Subtask 7: Analyze pilot study data	16-23	Complete
Subtask 8: Generate manuscript based on pilot study data	24-30	Complete
Milestone Achieved: Preliminary retrospective pilot results inform prospective study design	20	Complete
Major Task 2: Study Initiation		
Subtask 1: Finalize master protocol	23-24	Complete
Subtask 2: Develop case report forms (CRFs) for data capture, program and pilot test REDCap	23-25	Complete
Subtask 3: Obtain initial IRB approval at JHSPH and USAMRMC	23-25	Complete
Subtask 4: Distribute approved protocol and obtain IRB approval at all participating sites	25-26	Ongoing
Subtask 5: USAMRMC Human Research Protections Office review and approval of site-specific IRB-approved human use documents	25-26	Ongoing
Milestone Achieved: Local IRB approval at METRC sites and HRPO	26	Ongoing
Major Task 3: Training Research Staff		
Subtask 1: Develop and conduct training for Research Coordinators on procedures for screening patients in the ED, collecting data from the EMS and ED flow sheets and, when applicable, obtaining autopsy data, best practices for contacting EMS providers to obtain missing data, and consenting patients or LARs.	27-28	Complete
Subtask 2: Certify sites to begin screening and enrolling patients	27-28	Ongoing
Subtask 3: Conduct study initiation calls with each site to ensure procedures are in place to allow access to EMS and autopsy data	27-28	Ongoing
Milestone Achieved: Research Staff Trained	28	Ongoing

Major Task 4: Conduct Study		
Subtask 1: Clinical site Research Coordinators will screen and enroll eligible study patients	27-52	Ongoing
Subtask 2: Generate and distribute monthly enrollment and follow-up reports; provide ongoing training and support to address problems with enrollment as they are identified	27-52	Ongoing
Subtask 3: Generate and distribute data quality reports to monitor data completeness; check for errors and inconsistencies	28-58	Ongoing
Subtask 4: Generate and submit request for SSDI data to evaluate 30-day mortality of enrolled patients	56	Ongoing
Milestone Achieved: All patients enrolled	52	Ongoing
Major Task 5: Feasibility Study		
Subtask 1: Develop data presentation profiles of cases to demonstrate variability in patterns of care	46-52	Not Started
Subtask 2: Convene protocol committee to provide ratings of equipoise and willingness to randomize selected cases to alternative treatments	52-54	Not Started
Milestone Achieved: Document acceptability and equipoise of surgeons regarding adjuvant resuscitation approaches	54	Not Started
Major Task 6: Data Analysis and Report Writing		
Subtask 1: Develop final analysis files	52-58	Not Started
Subtask 2: Conduct analysis and write final reports and peer-reviewed publications	54-60	Not Started
Subtask 3: Disseminate results- publication in peer reviewed journals and presentation at professional and scientific meetings	54-60	Not Started
Milestone Achieved: Report findings from final analysis	60	Not Started

Study 5: Follow-up of METRC Participants to Examine Secondary Health Effects and Long Term Costs (LTE), PI: MacKenzie

Study 5 Specific Aims: (1) To define the research questions of greatest importance and formulate hypotheses that will drive the study design of the main study; (2) to pilot procedures for locating and consenting METRC participants for a long-term (3-5 years post-injury) follow-up evaluation, identifying barriers for participation and appropriate use of alternative incentives; (3) to develop and pilot the evaluation procedures to include interviews, clinical exams, performance testing, medical record retrieval, and laboratory and radiographic assessments; and (4) to prepare for the successful implementation of the main study by establishing protocols and procedures, satisfying regulatory requirements, and submitting a competitive application for funding. **Patient Population**: Participants originally enrolled in the following METRC studies: FIXIT, OUTLET, TAOS, TCCS, BIOBURDEN, PAIN, PACS, OXYGEN, VANCO, PRIORITI-MTF, and OXYGEN

	Timeline	**Status**
Major Task 1: Study Initiation	Months	
Subtask 1: Finalize master protocol	25-27	Ongoing
Subtask 2: Develop case report forms (CRFs) for data capture, program and pilot test REDCap	25-27	Ongoing
Subtask 3: Obtain initial IRB approval at JHSPH and USAMRMC	27-29	Not Started
Subtask 4: Distribute approved protocol and obtain IRB approval at all participating sites	29-32	Not Started
Subtask 5: USAMRMC Human Research Protections Office review and approval of site-specific IRB-approved human use documents	30-33	Not Started
Milestone Achieved: Local IRB approval at METRC sites and HRPO	33	Not Started
Major Task 2: Training Research Staff		
Subtask 1: Develop and conduct training for Research Coordinators in developing contact files, tracing potential participants, and documenting all attempts at follow-up, as well as conducting interviews and scheduling follow-up visits	30-31	Not Started
Subtask 2: Certify sites to begin screening and enrolling patients	30-33	Not Started
Subtask 3: Conduct study initiation calls with each site to ensure procedures in place for	30-33	Not Started

contacting participants and completing in-person clinical examinations		
Milestone Achieved: Research Staff Trained	33	Not Started
Major Task 3: Conduct Study		
Subtask 1: Clinical site Research Coordinators will screen and re-consent 75 eligible study patients, including scheduling in person appointments	31-37	Not Started
Subtask 2: Generate and distribute monthly enrollment and follow-up reports; provide ongoing training and support to address problems with enrollment and follow-up as they are identified	31-37	Not Started
Subtask 3: Generate and distribute data quality reports to monitor data completeness; check for errors and inconsistencies	32-39	Not Started
Milestone Achieved: Patients complete all study related activities	39	Not Started
Major Task 4: Feasibility Study		
Subtask 1: Obtain feedback from research staff on procedures to track and bring participants back to clinic	31-37	Not Started
Milestone Achieved: Refined procedures for following patients and encouraging return for in-person clinic visit	37	Not Started
Major Task 4: Data Analysis and Report Writing		
Subtask 1: Develop final analysis files	39-41	Not Started
Subtask 2: Conduct analysis and write final reports and peer-reviewed publications	41-48	Not Started
Subtask 3: Prepare grant submission funding long term follow-up of full METRC cohort	41-48	Not Started
Milestone Achieved: Report findings from final analysis	48	Not Started
Milestone Achieved: Grant submission for full cohort study	48	Not Started

- **What was accomplished under these goals?**

Major Activities

COVID-19

METRC worked proactively at the beginning of the COVID-19 pandemic to ensure that the Coordinating Center would be able to transition to the remote setting immediately and without interruption to our operations. Prior to the Johns Hopkins University shutdown, and prior to the nation-wide shutdown, the MCC had already established a new platform for daily engagement and communication. Staff of the Coordinating Center had been asked to identify any computing or other resources that they would require in order to be productive while working from home; every team member confirmed that they were prepared to work entirely remotely.

The Executive Committee was engaged very early and approved the following actions per the timeline noted:

- March 12, 2020: Communication was sent to all METRC sites asking them to reschedule 'research-only' visits, to screen for COVID-19 symptoms before any clinic follow-ups, and to ensure that research staff had remote access to study files and electronic medical records systems. These requests were aligned with the national/CDC guidance at the time.

- March 17, 2020: METRC issued a consortium-wide pause on screening and enrollment. Screening and enrollment forms in REDCap databases were deactivated.

- Every few weeks following March 17th, the Executive Committee reevaluated the consortium-wide pause on research activity.

- May 5, 2020: The Executive Committee approved a 'Safe Re-Opening Plan', which was communicated to all sites, and which allowed sites to reopen specific studies in accordance with local policies and after MCC review and approval.

- The PIs of each study made the overarching decision as to whether their studies could feasibly and safely reopen. While all METRC 3 studies were reopened at the sites where local guidance permitted them to do so, other METRC studies remained paused due to the impossibility of conducting them safely (e.g., they required close physical contact between participants and research staff).

Despite the impact of the COVID-19 pandemic on METRC 3 study enrollment and follow-up, each of the five projects made significant strides towards successful completion. The details of each study's progress are described below.

While the METRC 3 studies were temporarily derailed, the METRC Coordinating Center continued to function at full operational capacity in the remote setting; it is still functioning in this way to this day. Moreover, during the period where the studies weren't enrolling, the MCC was able to aggressively shift its priorities and devote focused time and energy to building tools and establishing new processes which will serve the consortium for years to come. The most significant of these achievements was the development of a state-of-the-art, robust, fully automated data querying tool. With this resource in place we can generate, distribute, and address data queries on a near-constant prospective basis. This close-to-real time feedback loop between the MCC and the sites is critical to monitoring study progress and to reducing the length of time it has taken to clean and close out data and to lock the study databases once the final follow-ups are completed.

CBPT

The CBPT Study reached its target enrollment in February 2020. Follow-ups are ongoing and the study team continues to work closely with participating centers to ensure that these visits are as complete as possible. We expect to complete the final follow-up visit by April 2021.

In recognition of the need to clean and close out the data on a prospective basis, the CBPT study team continues to generate in-depth data quality and performance monitoring reports. These reports are distributed to sites and reviewed during bi-weekly phone calls.

One major amendment was approved during the project year. Due to the impact of COVID-19 on the ability to conduct in-person follow-up visits, the study team proposed and received approval to modify the primary study outcome to be patient reported outcomes (PROs) instead of PROs *and* physical assessments, the latter of which would have required in-person visits. The physical assessments remain an important part of the study outcomes; they are now considered secondary outcomes and will be reported upon in manuscripts arising from the study. With the gradual lifting of restrictions on in-person research, some sites have reinitiated in-person visits and are again obtaining both PROs and physical assessments.

AlterG

As of the end of the project year, 9 sites are actively screening and enrolling patients into the AlterG study. To date, there are a total of 38 participants enrolled. Of the 38, there are 18 patients in the control arm and 20 patients in the intervention arm. Four patients withdrew from the study after randomization, 5 patients completed the study and 29 patients are actively being followed. While enrollment has always been slow in this logistically challenging study, screening and enrollment were further impacted by the pause in research activities due to the METRC-mandate (March 17, 2020-May 4, 2020) and/or local/site-level mandate. After following each state and site regulation on re-opening clinical research studies, each site received approval to re-open the study.

There were three changes made to the protocol since the last annual report:

1. The protocol was updated to provide flexibility in the data collection process between surgery and the first study visit. Patient-reported outcomes at the baseline visit were removed and additional detail on the progression of the AlterG treadmill was provided
2. The protocol was updated to allow for remote study evaluations at the study sites affected by the COVID-19 pandemic. The remote study evaluations include consent, baseline instruction, and/or data collection, and follow-up visit data collection. If research staff are not available, surgeon investigators will be asked to complete screening, enrollment, and in-clinic visits.

3. In addition, the timeline of the non-weight bearing period for the patients randomized to the standard of care group has been adjusted to at least 8 weeks from 10-12 weeks, in line with current weight-bearing protocols. This was also addressing the concern that was raised by the DSMB.

We are providing real-time data quality checks on the main study outcome measures by utilizing the tools on REDCap. A physical therapist is reviewing the clinical assessment data periodically to address any data collection errors early on. All the study sites are receiving a weekly report on screening, enrollment, and follow-up activities. Additional data queries are being developed as of now.

EMS-BinD

Activity on EMS-BinD continued to increase over the past project year. Overall, 18 sites have initiated the process of obtaining regulatory approval and 14 of those are certified to screen and enroll participants. This represents an increase of 8 sites starting regulatory review and 10 sites certified over those reported last year. An additional 3 sites have indicated interest in participating in the study as well. During the previous reporting period, a study orientation presentation was held in November 2019 following the Annual Orthopaedic Trauma Association meeting to boost study site participation.

Of the 14 certified sites, 11 have screened and enrolled at least one participant while the remaining 3 are just beginning the screening process. There are 6 certified sites (including those that have yet to screen) that are still in a provisional status as they have yet to enroll 3 participants for a data review by the MCC. The provisional certification process has worked will over the past year and has provided another opportunity for detailed monitoring of data collection as well as process for maintaining site enthusiasm and resolving any problems as quickly as possible. To date, 756 patients have been screened and 88 enrolled (15% of target).

As anticipated, the unique data collection and data quality challenges associated with this study have led to lower screening and enrollment rates than are needed to successfully complete the study. In response, the study team and protocol committee recognized a need to amend the protocol as a way to improve screening and enrollment and to address some of the specific challenges identified by sites during the early part of the study. The protocol committee met in July 2020 and endorsed a set of changes to the protocol that has been submitted as an amendment (currently in review by JHSPH IRB) and to change the "per patient" invoicing process to better align payment with the revised study procedures. Study changes enacted include: 1) modifying the screening process so more complex data points are grouped together; 2) removing 2 exclusion criteria deemed unnecessary for this study; 3) expanding the allowable period for conducting the screening; 4) relaxing the precision required for the timestamp representing the placement of a pelvic binder from a to-the-minute response to a 15-minute window; 5) creating an adjudication process where all potentially eligible injuries are reviewed by a surgical panel to ensure only appropriate injury patterns are enrolled; and 6) allowing remote consent if necessary (change initiated in response to hospital operation changes related to COVID pandemic).

Lastly, during the previous year, the pilot study that preceded the current study was selected for a podium presentation by the study PI at the Extremity War Injuries conference in January 2020. Effort to develop a manuscript for submission related to the pilot study is ongoing.

During the upcoming quarter of the study period, we will roll out the approved amendment described above and continue to screen and enroll patients while closely monitoring for an uptick in these numbers. Additionally, the study team will be continuing to focus on data completeness and data quality through additional automated study reports and expanding the data query system for this project (which has already begun).

PRECISE

Eight of the ten centers participating in this study have completed all study certification activities and seven have enrolled study patients. Of the 2 remaining uncertified sites, one is pending certification and is expected to begin study implementation shortly while the other is still pending approval by their local IRB.

Between Oct 1st, 2019 and Sept 30, 2020, sites screened 1,189 patients and enrolled 79 participants, bringing total enrollment to 128 (roughly 30% of target). Of the 128 enrolled, 89 participants have completed follow-up and concluded their time on study. An amendment extending the window for obtaining consent was approved in December 2019.

Recruitment into the PRECISE study was significantly impacted for a brief period of time due METRC-mandated and/or local/site-mandated research closures. While 5 of the 8 certified sites have reopened the study to enrollment, the rate of enrollment remains lower than it was pre-COVID. The study team continues to work very closely with the sites that have reopened to identify and address the specific issues contributing to the slowed pace of enrollment.

In the meantime, other study activities are ongoing. Monthly enrollment, follow-up, and data quality reports are distributed regularly. Work on data quality assurance continues and we have begun piloting the study analysis to identify incomplete or potentially inaccurate data. We are pleased to report that the data quality for this study is excellent, based on all indicators, and we do not anticipate that there will be data cleaning related delays at the end of the study prior to completing the main analyses.

Long-Term Effects

The Long Term Effects study has spent the past project year focusing on preparations for patient enrollment and data collection during the upcoming year. The three working groups of the protocol committee each met at least once during the past year to fulfill their charges. The Patient Reported Outcomes group met in October 2019 and developed a list of constructs to consider for collection as part of this study. Suggestions for which instruments should be used for the data collection were also offered with a particular focus on using PROMIS measures where possible. The Clinical working group met in March 2020 and developed a list of constructs as well as a list of tests, procedures and measures that would be suited to these domains. The Logistics working group met three times over the past year (November 2019, August 2020 and September 2020). This group used the outputs of the other two working groups to gather additional information about the data collection methods and workflow as well as scheduling, costs, and operational concerns for the study overall. The suggested list of domains, collection instruments and tests has been winnowed into the final proposed list included in the draft protocol document. The draft protocol is to be reviewed and discussed by the full protocol committee during an upcoming meeting within the upcoming project quarter.

Based on the detailed discussions of the three working groups, the MCC proposed a revision to the scope of work at a meeting with the DOD Government Steering Committee (GSC) in May 2020. The change, which was approved, reduced the required number of participants to 75 (from 100) and the number of participating facilities to 4 from 8. The GSC agreed that the reduced scope of work could be achieved with no ill effects to the projected timeline nor to the utility of the study's findings since the successful completion of this pilot study remains the development and demonstration of appropriate procedures for executing a larger future study. This reduction allows for focused attention to be given in shepherding the four participating facilities (CMC, UMD, UWA, and WRD) through this work and facilitate the identification and correction of any problems encountered along the way. Given the task in getting each site fully ready to conduct this study, we would rather create the strongest and most ideal sites using a smaller group than to potentially encounter difficulties and create readiness challenges with a larger group. The four sites selected also reflect the larger set of METRC facilities and study participants quite well, with a variety of institutional characteristics still represented, including military and civilian centers, those affiliated with universities as well as without, and those drawing patients from both large and relatively small catchment areas.

Specific Objectives

Nothing to report.

Significant Results, Key Outcomes

Nothing to report.

Other Achievements

Updates Pertaining to METRC 3 Standing Committees

<u>Publications Committee</u>

The Publications Committee met periodically over the course of the past year and continued updating policies regarding multiple issues of importance. These policies are now posted to the METRC website, both within the METRC Policy & Procedure Manual and on the Publications page, making them easily accessible for all members of the Consortium.

The Committee reviewed and approved the abstracts that were submitted to the Orthopaedic Trauma Association call. Three of the abstracts pertained to main results from completed METRC studies. Each of these was accepted for podium presentation at the OTA Annual Meeting. The OTA Annual Meeting was held remotely this year due to COVID-19 concerns. From a scientific and dissemination perspective, the remote presentation really benefited METRC. The presentations were attended by a much larger audience than we're accustomed to seeing during the in-person meetings. In addition to the larger attendance, the question and answer format was particularly useful because attendees could enter their questions into the remote meeting platform where other attendees could see them and 'up vote' them if they had the same question. Ultimately, the presenters (the METRC study PIs) were able to address the 'room's' most widely held questions.

Science Committee

The Science Committee met periodically throughout the project year and continued to function as the 'gatekeepers' for appropriate requests for study-related data and/or papers. It also reviewed and approved a few grant proposals which were responsive to bridge funding due to COVID-19. Both the Science and Executive Committees agreed that the COVID-19 related proposals were critical to METRC's ongoing success and need to self-sustain its funding. Otherwise and by design, METRC did not submit proposals for new studies in response to the DoD PRORP, as it has done in every previous year with the facilitation of the Science Committee. The one-year pause on PRORP grant proposals was intended to allow the consortium to focus on publications and the ongoing studies.

Emerging Investigators Committee

The EI Committee had a light year. Beyond the ad hoc assistance provided to last year's awardees, the committee did not meet as it was decided not to fund a 3rd round of EI awards. The other major activity of the Emerging Investigators Committee is to plan and implement the Emerging Investigator Workshop. The workshop has taken place during the summertime in past years. This year, the EI Workshop was postponed in order to focus attention and efforts on COVID-19 related issues impacting the main METRC 3 studies. We hope to be able to offer the EI Workshop one more time in the next project year and we are hopeful that it will draw a larger group of participants given that it will take place in the remote setting.

Rehab Engagement Committee

The role of the Rehab Engagement Committee this project year has been, primarily, to act as an advisor to the rehab-focused study teams. The rehab studies have shown themselves to be logistically challenging under normal circumstances. With additional logistical pressure applied as a result of the pandemic, experts in rehab were essential in carefully evaluating whether METRC rehab studies could reopen safely and if they could be successful under additional constraints.

Data Standards Committee & Implementation & Quality Committee

The work of the Data Standards Committee (DSC) and the Implementation & Quality Committee (IQC) continued to move forward largely internally to the MCC during the year. These committees have continued to work together to address issues related to the committees' core missions, improve study development processes, and to move forward in addressing study data quality. During this past year, METRC has worked to launch several studies with additional studies expected to begin enrollment during the upcoming period. This formative work, combined with the data cleaning and analysis efforts of older METRC studies and prospective data cleaning of ongoing METRC studies, have provided a unique opportunity to highlight lessons learned and implement improvements to advance data quality in the upcoming period. The foundation of this work are the data dictionaries associated with all of our existing studies, which have been combined into an integrated collection of study questions, data domains and constructs and applicable study metadata. This resource continues to support the management of ongoing projects and the development of newer studies, ensuring consistency and improving efficiency in the time needed to launch a study.

Furthermore, the data dictionary work has supported a streamlined case report form (CRF) development process, embraced by the MCC and its Informatics Core. It also improves our data standardization efforts when reviewing the data requirements of a given study or as part of an "all hands" review of data collection materials prior to study initiation.

Finally, the work of the DSC and IQC is further supported by a growing and robust, state-of-the-art, automated data query system used to prospectively clean study data. The many ongoing analyses and data monitoring efforts associated with all METRC studies in turn yield additional items for consideration and review by the DSC.

The DSC and IQC expect to continue the specific activities noted above. Additionally, the DSC plans to conduct in depth reviews of several injury/fracture classification systems to develop guidance documents to help site personnel interpret questions correctly and ensure proper usage as part of studies. Finally, the committees will have an active role in developing a repository of standards for analysis, scoring of data collection instruments, and in the development of analytic data sets and related materials for release outside the MCC.

- **What opportunities for training and professional development has the project provided?**

Nothing to report.

- **How were the results disseminated to communities of interest?**

Nothing to report.

- **What do you plan to do during the next reporting period to accomplish the goals?**

We will continue to move the METRC 3 studies forward during the coming project year. The 3 enrolling studies will continue to enroll- PRECISE, EMS-BinD, and AlterG. The LTE protocol, with its new scope, will be submitted to the Johns Hopkins School of Medicine single IRB for approval. Once it is approved, it will be implemented very quickly at the 4 participating centers. The CBPT study will complete follow-up and analyses.

COVID-19 is sure to continue to impact the rate of study progress. We will remain nimble and focused on maximizing all possibilities and opportunities for forward motion and success while taking utmost care that the research teams and research participants at METRC sites are protected to the extent possible. It is impossible to know exactly how COVID will impact our studies in the next project year and each site's institutional response will matter a great deal. Although the overall situation remains unfortunate, we have established the processes and communication channels to address the challenges as they come.

4. **IMPACT:** *Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

   - **What was the impact on the development of the principal discipline(s) of the project?**

Nothing to report.

   - **What was the impact on other disciplines?**

Nothing to report.

   - **What was the impact on technology transfer?**

Nothing to report.

   - **What was the impact on society beyond science and technology?**

Nothing to report.

5. **CHANGES/PROBLEMS:** *The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants*

Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

- **Changes in approach and reasons for change**

Please see the study-specific notes in the 'Major Activities' section above for a detailed description of significant study amendments, changes in scope of work, and the impact of COVID-19. All significant changes were first proposed to the DoD and approved prior to implementation. We will continue to keep the DoD apprised of any changes in approach related to the ongoing COVID-19 pandemic.

- **Actual or anticipated problems or delays and actions or plans to resolve them**

We expect that we will not be able to complete all major tasks for each study by the end of the original project period. This is due to multiple significant factors, the two foremost being 1) that we started the METRC 3 studies later than planned while awaiting decisions from the Government Steering Committee, and 2) the impact of COVID-19 on study progress. We will submit a request for a No Cost Extension, asking for approval to continue working on MTERC 3 so that we can complete the studies during a 6th year.

- **Changes that had a significant impact on expenditures**

Nothing to report.

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

Nothing to report.

- **Significant changes in use or care of human subjects**

Nothing to report.

- **Significant changes in use or care of vertebrate animals.**

Nothing to report.

- **Significant changes in use of biohazards and/or select agents**

Nothing to report.

6. **PRODUCTS:** *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**

Nothing to report.

- **Website(s) or other Internet site(s)**

All METRC publications and presentations are posted on the METRC website: www.metrc.org.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

Nothing to report.

7. **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

   - **What individuals have worked on the project?**

See Appendix A – Personnel (Annual effort).

   - **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

     Effort support for Dr. Renan Castillo reduced from 34% for the period Oct 2018 – Sep 2019 to 20% for the period Oct 2019 – Sep 2020.

   - **What other organizations were involved as partners?**

See Appendix B.

8. **SPECIAL REPORTING REQUIREMENTS**

   - **COLLABORATIVE AWARDS:**

   - **QUAD CHARTS:**

9. **APPENDICES:**

Appendix A: Personnel (Yr4 - Annual)

METRC III

Personnel	Role	Calendar Months	
Ellen Mackenzie	Principal Investigator, Director	1.20	
Renan Castillo	Deputy Director	2.40	
Daniel Scharfstein	Lead Statistician	1.80	
Richard Thompson	Statistician	1.20	
Stephen Wegener	Co-Investigator	0.96	
Lisa Reider	Project Director	1.80	
Katherine Frey	Project Director	2.10	
Lauren Allen	Operations Director	7.20	
Suna Chung	Program Manager	3.85	*New Program Manager effective March 2020*
Andrea Deluca	Program Manager	0.55	*Role ended on the project effective March 2020, replaced by Suna Chung*
Linda Gai	Data Analyst	5.40	
Rachel Zamoiski	Data Analyst	9.35	*Effective November 2019*
Yanjie Huang	Data Analyst	7.20	
Kuladeep Sudini	Data Analyst	1.20	
Jack Dagg	Data Analyst	1.40	*New Analyst effective March 2020*
Vadim Zipunnikov	Statistician	0.24	
Susan Collins	Study Manager	9.00	
Tara Joseph	Study Manager	0.60	
Dana Alkhoury	Study Manager	7.80	
Craig Remenapp	Study Manager	9.00	
Andre Hackman	Statistician	0.96	
Anthony Carlini	Project/Technical Director	2.40	
Christina Owens	Research Assistant	9.00	
Rebecca Pickard	Editorial Assistant	4.80	*Effort support ended June 2020, no longer at METRC*
Manisha Kumar	Financial Manager	3.00	
Chris Witczak	Financial Analyst	9.00	
Cathy Epstein	Administrative Coordinator	9.60	
Elena Staguhn	Research Assistant	7.20	
Alina Grigorvitch	Programmer	1.40	*Role ended effective 01/15/2020*
Lucie Wiedefeld	Programmer	6.00	*Replaced Alina Grigorvich*
Elias Weston Farber	Research Assistant	2.10	
Trisha Chaffee	Research Assistant	4.20	
Aiden Mcdermot	Research Assistant	0.60	
Virgil DeMario	Research Assistant	0.60	*Started August 2020*
Danielle Drye	Research Assistant	0.60	

Table 1. METRC 3 Participating Sites: Approval Status and Enrollment

Code	Site Name	METRC 3 Studies			
		CBPT*	AlterG*	PRECISE	EMS-BinD
BAM	San Antonio Military Medical Center (SAMMC)	Actively Enrolling 15 screened 7 enrolled 3 randomized	Actively Screening 21 screened 0 enrolled 0 randomized Reopen Approval: 6/25/2020		Provisionally Certified 30 screened 2 enrolled Reopen Approval: 5/22/2020
BMC	Boston Medical Center				Pending Submission to DoD
CMC	Carolinas Medical Center	Actively Enrolling 708 screened 114 enrolled 56 randomized		Actively Enrolling 210 screened 15 enrolled Has not reopened enrollment	Actively Enrolling 80 screened 6 enrolled Reopen Approval: 5/8/2020
HCM	Hennepin Healthcare Research Institute		Actively Enrolling 5 screened 5 enrolled 5 randomized Reopen Approval: 6/17/2020	Pending Certification	Actively Enrolling 4 screened 3 enrolled Reopen Approval: 6/17/2020
HOU	UT Health: The University of Texas Health Science Center at Houston Medical School	Actively Enrolling 695 screened 181 enrolled 74 randomized	Actively Enrolling 98 screened 8 enrolled 6 randomized Reopen Approval: 5/19/2020	Actively Enrolling 63 screened 6 enrolled Reopen Approval: 5/28/2020	Actively Enrolling 274 screened 38 enrolled Reopen Approval: 5/8/2020
IFH	Inova Fairfax Hospital		Actively Enrolling 88 screened 15 enrolled 14 randomized Reopen Approval: 5/7/2020		Plans to participate
MTH	Methodist Hospital	Actively Enrolling 698 screened 106 enrolled 68 randomized		Actively Enrolling 361 screened 73 enrolled Reopen Approval: 5/18/2020	Actively Enrolling 74 screened 12 enrolled Reopen Approval: 5/12/2020
NSD	Naval Medical Center San Diego		Actively Enrolling 2 screened 1 enrolled 1 randomized Reopen Approval: 6/4/2020		
PIT	University of Pittsburgh			Actively Enrolling 2 screened 1 enrolled Reopen Approval: 7/6/2020	Submitted to IRB
RYD	University of Miami Ryder Trauma Center			Withdrew from Participating	Pending Submission to DoD
TGH	Tampa General Hospital	Actively Enrolling 292 screened 55 enrolled			

		35 randomized			
UKY	University of Kentucky		Actively Enrolling 9 screened 4 enrolled 4 randomized Reopen Approval: 7/9/2020	Actively Enrolling 3 screened 2 enrolled Has not reopened enrollment	
UMD	University of Maryland, R Adams Cowley Shock Trauma Center	Actively Enrolling 654 screened 106 enrolled 48 randomized		Actively Enrolling 255 screened 16 enrolled Reopen Approval: 9/14/2020	Actively Enrolling 75 screened 10 enrolled Reopen Approval: 5/11/2020
UVA	University of Virginia Medical Center		Actively Enrolling 26 screened 5 enrolled 5 randomized Reopen Approval: 5/14/2020		
UWA	University of Washington / Harborview Medical Center			Actively Enrolling 512 screened 15 enrolled Reopen Approval: 6/9/2020	Provisionally Certified 140 screened 1 enrolled Reopen Approval: 5/27/2020
VMC	Vanderbilt University Medical Center	Actively Enrolling 601 screened 64 enrolled 42 randomized		Provisionally Certified	Actively Enrolling 10 screened 5 enrolled Certified after Reopen Plan
WFU	Wake Forest University Baptist Medical Center				Actively Enrolling 51 screened 5 enrolled Reopen Approval: 6/5/2020
WRD	Walter Reed National Military Medical Center (WRNMMC)	Certified *No screening initiated*	Certified *No screening initiated* Reopen Approval: 6/25/2020		
MET	MetroHealth Medical Center				Actively Enrolling 17 screened 5 enrolled Reopen Approval: 5/8/2020
BJH	Washington University, Barnes-Jewish Hospital				Plans to Participate
ESK	Eskenazi Health				Provisionally Certified
HRV	Harvard Orthopaedic Trauma Service				Provisionally Certified 1 screened 1 enrolled
PSU	Penn State University M.S. Hershey Medical Center				Provisionally Certified

UMS	University of Mississippi Medical Center				Plans to Participate
UOK	University of Oklahoma/ OU Medical Center				Provisionally Certified
UAB	University of Alabama at Birmingham				Submitted to IRB
USF	University of California San Francisco		Actively Enrolling 15 screened 3 enrolled 3 randomized Reopen Approval: 6/18/2020		
NPM	Naval Medical Center Portsmouth		Pending IRB Submission		