METRC

Major Extremity Trauma Research Consortium

2013 ANNUAL REPORT

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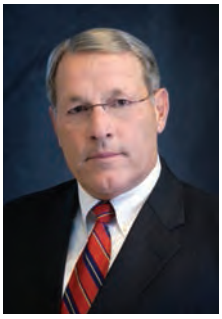
METRC
Major Extremity Trauma Research Consortium



Dear Colleagues and Friends,

We are beginning to see the potential of a large clinical research consortium. All 8 Core Studies funded under METRC 1 and METRC 2 are in the field and all of the METRC Core sites are enrolling patients. At the current enrollment rate, we should pass the 1000 patient mark by the end of 2013. We anticipate that an additional 5 main studies (which are supported by METRC but funded outside the Core funding mechanism) will be actively enrolling early 2014.

The Satellite centers remain a key to our long-term success. We continue to engage satellite centers - 12 are screening and enrolling patients and 20 are completing study certification requirements and should be active by the end of 2013. We are still accepting applications for new METRC centers (both Core and satellite).

Over the summer, METRC collaborated with investigators to prepare and submit 3 grants addressing areas of research important to the mission of the Consortium. Two of the proposals targeted different modalities of local antibiotic delivery to the traumatic wound. The third proposal was developed in collaboration with the BADER Consortium and is designed to validate new measures of prosthetic fit and alignment that could be used in large multi-center studies to provide a less subjective means to determine the impact of the prosthetic – tissue interface on the performance, function and outcomes of the amputee patient.

Critical to the conduct of clinical trials is a Quality Assurance and Performance Improvement (QA/PI) process that works to identify gaps in study enrollment and data completeness with the goal of targeting opportunities for enhancing overall site performance. METRC initiated a major QA/PI initiative this year to provide feedback to our centers related to their performance in comparison to other centers and internally defined benchmarks. We also recognized that site work demands varied and developed a program in concert with the Steering Committees to better align site activity with critical resources.

The present challenge for every site is the identification and capture of all eligible patients and the timely follow-up of all enrolled. Our congratulations go out to the six top enrolling sites as of September 1, 2013: Carolinas Medical Center, University of Maryland Shock Trauma Center, University of Texas at Houston, Vanderbilt University, University of Mississippi, and Wake Forest University.

Thanks to all of our investigators and research coordinators for their continued efforts and dedication to the goals of METRC. METRC provides the infrastructure and leadership necessary to tackle critical issues facing our trauma patients, soldiers and civilians alike, and demonstrates the capacity and talent of the Orthopaedic Trauma community for engaging in large clinical trials.

Sincerely,
Michael J. Bosse, MD
Ellen J. MacKenzie, PhD

About METRC

Advancing Limb Trauma Care through Research

The Major Extremity Trauma Research Consortium (METRC) was established in September of 2009 with funding from the Department of Defense (DoD). It is comprised of a network of clinical centers and one data coordinating center that work together with the DoD to conduct multi-center clinical research studies relevant to the treatment and outcomes of orthopaedic trauma sustained in the military.

Improving outcomes through collaborative research

The overall goal of the METRC 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.

The need for a Consortium dedicated to improving outcomes following major limb trauma is evident. Approximately 55% of all service members injured in OIF/OEF sustain significant extremity trauma. Many are burdened with injuries to multiple limbs. Complex wound management, infection, bone loss, articular surface loss, blast-related extremity heterotopic ossification, segmental nerve loss, complete muscle tendon unit loss and compartment syndrome have been identified as critical challenges in caring for our wounded warriors. These challenges are only compounded by the needs in the post-acute and rehabilitation phases of recovery. Rigorous clinical research is sorely needed to address these challenges. This research must rely on a multi-disciplinary approach that combines the clinical insights of the military and civilian orthopaedic surgeons and rehabilitation specialists, the research acumen of a world renowned clinical research center and the high volumes of patients with severe injuries that are treated at major Level I trauma centers and the military treatment facilities (MTFs). METRC is designed to meet these needs.

Anchored by a Data Coordinating Center at the Johns Hopkins Bloomberg School of Public Health and its Center for Injury Research and Policy, the Consortium includes 22 Core Level I civilian trauma centers and 4 Core MTFs – with the ability to expand patient recruitment to more than 30 additional satellite trauma centers. The Consortium works collaboratively with the DoD to:

1. *Continuously identify the most critical issues that challenge recovery from major orthopaedic trauma;*
2. *Develop and sustain a research infrastructure to support the conduct of multi-center research studies aimed at the rigorous evaluation of current standards of orthopaedic care;*
3. *Partner with basic scientists and engineers to facilitate the translation of new and emerging technologies into clinical practice;*
4. *Mentor young orthopaedic trauma surgeons and rehabilitation specialists in the design and conduct of clinical trials;*
5. *Contribute to the science of fracture and soft tissue repair;*
6. *Contribute to the science of conducting clinical trials in a challenging patient population and treatment environment.*

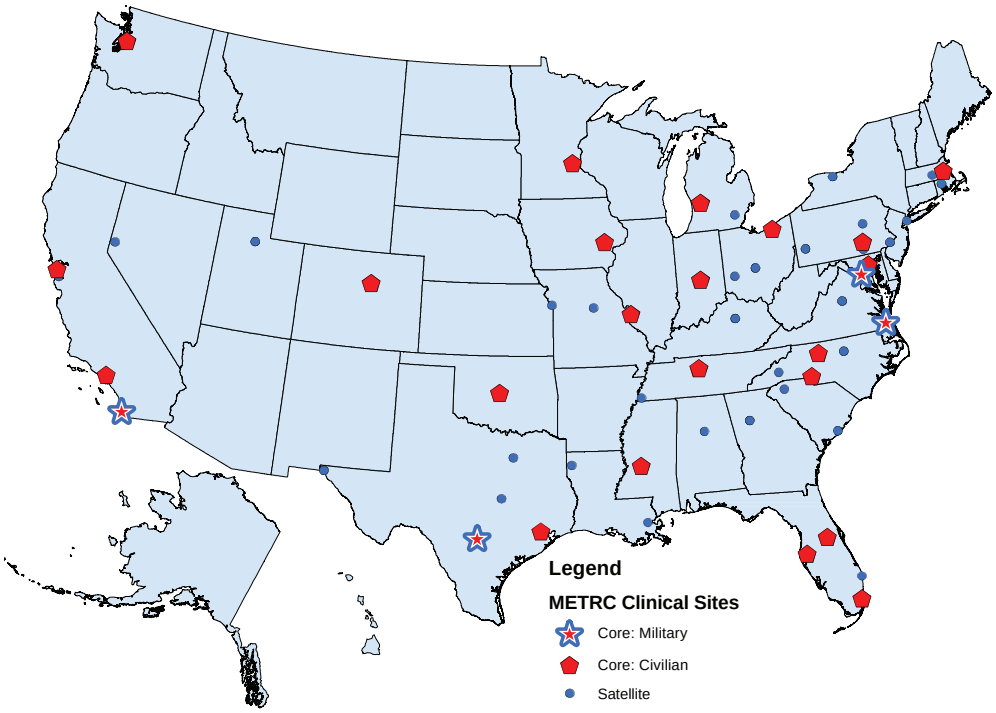
METRC is committed to conducting high quality clinical research that will make a difference in the lives of those who sustain major orthopaedic trauma. It does so by establishing a clinical research network that is dynamic and responsive to new clinical challenges or the emergence of new, promising novel therapies. The success of the Consortium depends on the identification of critical topics, the design of clinical trials that are sensitive to the realities of surgical patient research, rapid and high volume recruitment to those studies and excellent post-treatment follow-up. It also depends on the responsiveness of the network to specific centers and studies that are not meeting expectations and its ability to re-allocate resources and re-focus priorities accordingly.

Core funding for METRC is provided through the Orthopaedic Extremity Trauma Research Program (OETRP) (Award # W81XWH-09-2-0108) and a cooperative agreement with the DoD Peer Reviewed Orthopaedic Research Program (PRORP) of the Congressionally Directed Medical Research Program (CDMRP) (Award # W81XWH-10-2-0090).

The backbone of the Consortium consists of a dedicated group of Core and satellite clinical centers located throughout the United States (see Appendix A).

The Core Clinical Centers include 22 civilian trauma centers and the four military hospitals receiving the majority of major casualties, including Walter Reed National Military Medical Center (WRNMMC), San Antonio Military Medical Center (SAMMC), the Naval Medical Center in San Diego (NMCSD) and the Naval Medical Center in Portsmouth (NMCP). The civilian Core centers are large, level I trauma centers with leading orthopaedic trauma programs and established research infrastructures. The Core clinical centers are provided with resources to support METRC activities and participate in most trials sponsored by the Consortium. These centers were chosen on the basis of their volume of major extremity trauma cases, commitment to research, experience in participating in large multi-center studies, and academic qualifications.

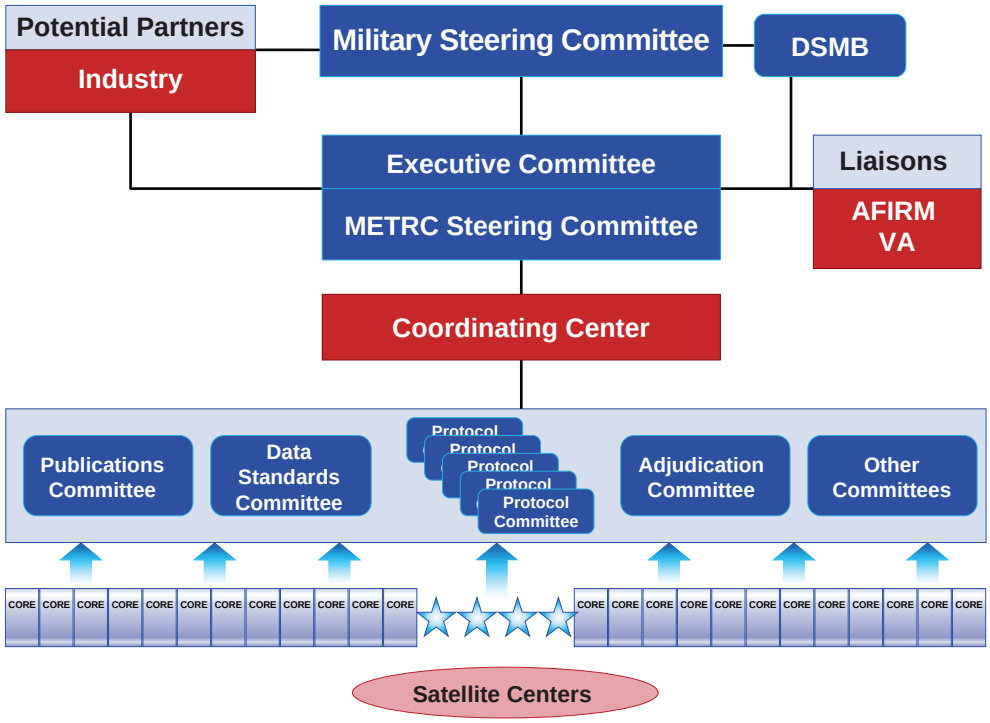
The Satellite Clinical Centers are civilian trauma centers with an established orthopaedic trauma program. They are invited to participate in individual METRC studies to ensure adequate numbers and appropriate mix of patients. Their participation is supported by a start-up payment as well as payments provided for each patient screened, enrolled and successfully followed.



The primary decision-making body of METRC is the Steering Committee, which is a representative body of the investigators and the U.S. Military. The Steering Committee provides ongoing oversight in planning and conducting each study sponsored by the Consortium and approves all study protocols. The Steering Committee meets monthly by WebEx-facilitated conference calls and in-person at least twice each year.

The Executive Committee serves as the agent of the Steering Committee in carrying out the day-to-day administrative responsibilities of the Consortium and Consortium-sponsored studies. The Consortium is supported by a network of Standing Committees, including: (1) Publications and Presentations; (2) Data Standards; (3) Clinical Outcomes Adjudication; and (4) Study-Specific Protocol Committees.

The Military Steering Committee was established by the DoD to (1) review progress of METRC; (2) provide advice and guidance on scientific and military relevance; (3) coordinate proposed projects with other military relevant orthopaedic trauma initiatives; (4) provide approval on all proposed Consortium studies prior to implementation; and (5) recommend areas of future study to the Consortium.



The Coordinating Center for METRC is located at the Johns Hopkins Bloomberg School of Public Health. The Coordinating Center works closely with the METRC Steering Committee to ensure that study protocols are appropriately designed, executed and analyzed. The Center is organized around three cores: (1) Protocol Development, Implementation and Monitoring; (2) Administration and Regulatory Affairs and (3) Informatics and Biostatistics. Resources of the Johns Hopkins Biostatistics Center are used to further support the data management and analysis activities of the Center. The Director, Deputy Director, Principal Biostatistician, and Principal Economist oversee the three Core activities of the Coordinating Center. A list of key personnel of the Coordinating Center is available in Appendix B.

JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

The METRC Data Safety Monitoring Board (DSMB):

A DSMB was established for METRC and acts in an advisory capacity to the DoD and the METRC Steering Committee to monitor patient safety and evaluate the efficacy of the interventions under study. Dr. Marc Swiontkowski of the University of Minnesota is Chair of the DSMB and serves as Medical Monitor. Other members of the board are listed here. The DSMB meets at least two times a year and more frequently as necessary.

METRC Data Safety Monitoring Board

Marc Swiontkowski, MD (CHAIR)
Department of Orthopaedics
University of Minnesota

Baruch Brody, PhD
Department of Philosophy
Rice University

Hans Kreder, MD, MPH
Department of Orthopaedics
Sunnybrook Health Sciences Centre

Stephen Walter, PhD
Department of Clinical Epidemiology & Biostatistics
McMaster University

Capt. Christopher Ayres USMC (Ret.)
OIF Combat Wounded
Hewlett-Packard Enterprise Services

Thomas Decoster, MD
Department of Orthopaedics
University of New Mexico Medical Center

Eli Powell, MD Col (Ret.)
Alaska Orthopaedic Surgery and Sports Medicine
Anchorage, AK

Ensuring Quality Research

METRC is committed to efficient and high quality research design and data collection. To this end, procedures have been put in place to document Consortium-wide and study-specific policies and procedures, facilitate communication across the Consortium, standardize approaches to data collection, and support rigorous continuous data quality assurance.

Policies and Standard Operating Procedures (SOPs):

The policies governing METRC were developed in 2010 and are re-visited on a regular basis and amended as appropriate. They include polices on:

- Governance
- Approval and Initiation of Studies
- Conflict of Interest and Commitment
- Publications and Presentations
- Data Standards and Data Collection

In an effort to standardize the processes and procedures utilized by the Consortium, we have developed several Standard Operating Procedures (SOPs) and compiled them into a Manual of Operations (MOP) for METRC. These SOPs are distributed to all participating centers and made available on the website. Amendments to these SOPs are made as necessary.

METRC has developed Standard Operating Procedures (SOPs)

1. **METRC Overview and Policies**
2. **METRC Communications**
3. **Data Safety and Monitoring Board**
4. **Study Initiation**
5. **IRB Submission and Study Documentation**
6. **Clinical Site Certification**
7. **Patient Screening**
8. **Reporting Requirements**
9. **METRC Data Management**
10. **Patient Payments**
11. **Patient Follow-up**
12. **Case Report Form Management**
13. **HIPAA Compliance**
14. **Medical Care Costs Data**
15. **Data Quality Assurance**
16. **Clinical Site Monitoring**
17. **Research Coordinator Advisory Committee**
18. **Data Sharing Policies for METRC**

Data Standards:

METRC has developed a Data Standards and Data Collection Policy that governs the development of case report forms (CRFs) and strategies for data collection. Core data elements are collected uniformly across all studies except in specific studies of limited scope. Collecting Core data across studies allows us to combine and analyze outcomes across studies, compare study populations, conduct METRC-wide secondary data analyses and serve as a starting point for CRF development for any given study. The twelve Core domains for data collection are summarized here.

In addition to developing the Core data elements to be collected across all studies, we have developed standard procedures for collecting data common to many studies. Standards have been developed for measuring infection, fracture healing and functional performance.

Standard Data Collection across all METRC studies

1. **Patient Demographics**
2. **Socioeconomic Status**
3. **Usual Major Activity**
4. **Health Insurance**
5. **Psychosocial Predictors of Outcome**
6. **Smoking History**
7. **Height and Weight**
8. **Co-morbidities**
9. **Pre-Injury Health Status**
10. **General Injury Characteristics**
11. **Mechanism and Type of Injury**
12. **Functional Outcomes**

REDCap
Research Electonic Data Capture

The centerpiece of the METRC data management infrastructure is the Research Electronic Data Capture (REDCap) system hosted at the Coordinating Center. REDCap is a state of the art, metadata driven application for distributed data collection and data management in clinical studies. The REDCap data management functionality allows for a secure, web-based data entry system that uses a web browser to access an internet-connected database server.

The system permits both the Coordinating Center and clinical sites to have access to data as soon as they are entered, allowing for near-real-time recruitment reports and increased data entry availability and convenience for the clinical sites. The primary functions of the data system include the following features: registration of all candidates for the trial; randomization to study arms; entry of all study data forms; inventory, management, and editing of study data; maintenance of full audit trails of all data entry and editing; and generation of real time performance reports. The REDCap data entry system also includes extensive data validation functionalities, including field level validation.

Continuous Quality Improvement:

Critical to the success of any multi-center trial is a robust data quality assurance and improvement plan. Quality assurance involves development and maintenance of proper attitudes among all investigators and research staff as well as the use of study designs that protect the results from bias. Beyond these strategies, assurances depend on procedures used for training, data collection and analysis. Paramount among these is the training and certification of study personnel involved in data collection, and the maintenance of those certifications throughout the trial. Additionally, data audits are performed to ensure collection of quality data. Monthly and Quarterly Reports are generated to monitor site performance and overall progress on each study:

- **Study and Site Specific Monthly Reports** summarize the numbers of patients screened and enrolled by month and track patient follow-up and data completeness by study ID. Sites are required to incomplete data within two weeks.
- **Study Specific Quarterly Reports** include updates on overall and site specific recruitment and enrollment and compare actual enrollment against projected enrollment. These reports are reviewed by the Study Protocol Committees and actions taken as necessary to improve the rate of enrollment and data quality.
- **DSMB Reports** are generated at least two times each year and more often as requested by the DSMB. These reports consist of both open and closed reports and are used as a basis for discussion at the DSMB meetings.

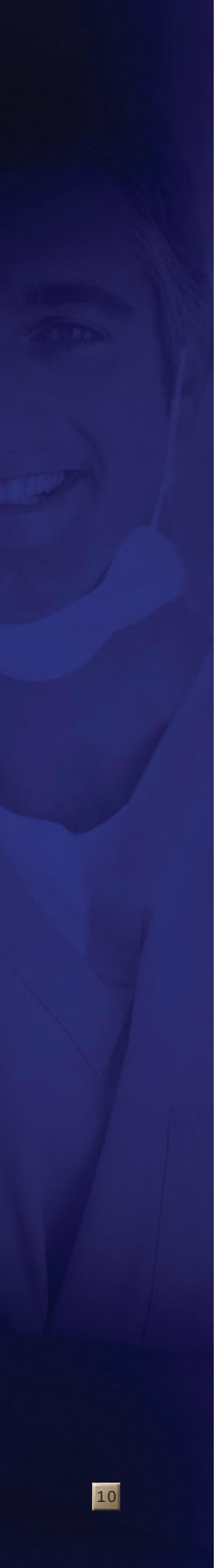
Also important ti assuring quality are formal on-site monitoring visits of METRC sites that are actively recruiting into one or more studies.

In 2013, the METRC Coordinating Center set to the task of developing site specific performance reports that could be used to improve the process of study implementation by defining areas of excellence, establishing benchmarks for success and looking critically at areas in need of improvement. These reports were also used to assist METRC leadership in making decisions regarding study involvement and alignment of resources with the level of site activity.

Site performance was evaluated in five domains that span the implementation life cycle of METRC studies, from initial regulatory review and approval through study follow-up and data quality assurance efforts. These domains constitute five pillars of excellence with one or more quality indicators used to define each pillar (*Figure C*). An indicator of volume which is based on number of participants enrolled and followed is also used in evaluating the overall contribution of each site.

Domain specific and overall performance scores are produced for each center and graphically displayed showing center performance compared to internally set benchmarks and to the average performance of all Core sites.

The work done by METRC clinical sites is vast and complex and such was the task of measuring their overall success. This critical activity described here was a preliminary approach for evaluating site performance. As a working group, we are looking forward to the evolution of this process over time, in concert with the shifting demands and priorities of the Consortium.



The METRC Registry

In 2010, a 'start-up' registry was established to assist the Consortium in determining the feasibility of future studies that could address critical research questions with adequate power. The registry is also used to monitor enrollment of current studies by estimating the expected number of patients to be screened for any one study and then comparing the expected numbers to the observed numbers screened. The registry was recently expanded to include information on nerve injuries.

All Core centers were asked to implement and maintain the registry for at least 365 consecutive days. The registry contains a limited set of data on patients between the ages of 18 and 84 who were admitted with fractures requiring surgery of the upper or lower extremity, pelvis or acetabulum, and foot (calcaneus, talus or crush injuries only). Excluded from the registry are hip fractures in patients 60 years or older and fractures to the wrist, hand, ankle, clavicle, patella, and the foot other than calcaneus/talus/crush.

All but two of the 26 Core civilian and military centers have implemented the registry and entered cases for 365 consecutive days. The table on the right provides annual estimates of the number of 'registry' fractures treated per site and across the 24 Core sites who contributed to the registry. Estimates are shown by upper and lower limb and by OTA code. The 24 sites together treat a total of 14,893 'registry' type fractures each year (including 226 traumatic amputations). Over three quarters (78%) of all fractures are to the lower extremity. Nearly one quarter (22%) of all fractures are open and of the open fractures, 49% are Gustilo type III (33 % IIIA, 13% IIIB and 3% IIIC).

An estimated 397 amputations (traumatic and surgical) are registered annually across the 24 Core sites (42 to the upper limbs and 355 to the lower limbs).

The registry data have added value to the Consortium and its ability to plan for future studies. Patients with type III tibia fractures are the subject of several potentially competing METRC projects–driving the need for the addition of new centers. Despite a high number of upper extremity, pelvic, and femur fracture patients, these injuries are currently the focus of few METRC studies. This information is being used to design future research.

Annual Number of Registry Fractures by Upper and Lower Limb and OTA Code

(based on data as of September 1, 2013)

	Annual Number of Registry Fractures	
	Average Per Site	**Total for 24 Sites**
All Upper Limb Fractures	**135**	**3245**
Traumatic Amputations	1	28
Closed Fractures	98	2361
Open Fractures	36	856
Gustilo Type I or II	23	557
Gustilo Type III	12	299
Humerus	**66**	**1572**
11 A,B,C (% open)	25	607 (6%)
12 A,B,C (% open)	21	493 (24%)
13 A,B,C (% open)	20	472 (38%)
Radius/Ulna	**69**	**1667**
21 A,B,C (% open)	30	723 (27%)
22 A,B,C (% open)	39	944 (35%)
All Lower Limb Fractures	**485**	**11648**
Traumatic Amputations	8	198
Closed Fractures	374	8964
Open Fractures	104	2486
Gustilo Type I or II	48	1157
Gustilo Type III	55	1329
Pelvis /Acetabulum	**85**	**2050**
61 A,B,C (% open)	42	1012 (6%)
62 A,B,C (% open)	43	1038 (2%)
Femur	**150**	**3578**
31 A,B,C (% open)	43	1021 (3%)
32 A,B,C (% open)	74	1777 (20%)
33 A,B,C (% open)	33	780 (31%)
Tibia	**200**	**4802**
41 A,B,C (% open)	66	1580 (12%)
42 A,B,C (% open)	79	1896 (49%)
43 A,B,C (% open)	55	1326 (32%)
Foot	**45**	**1087**
81 A,B,C (% open)	14	342 (26%)
82 A,B,C (% open)	28	677 (17%)
83 A,B,C (% open)	3	68 (56%)

Ongoing Research of the Consortium

Research Cores have been established to facilitate the development of research priorities and identification of studies (see box). These are the priorities used by the METRC and Military Steering Committee in selecting and approving specific studies to be conducted by the Consortium. Each decision is made after careful consideration of the importance and relevance of the research question, integrity of the proposed study design, feasibility, and availability of funding (either through the Core funds of the Consortium or through outside funding).

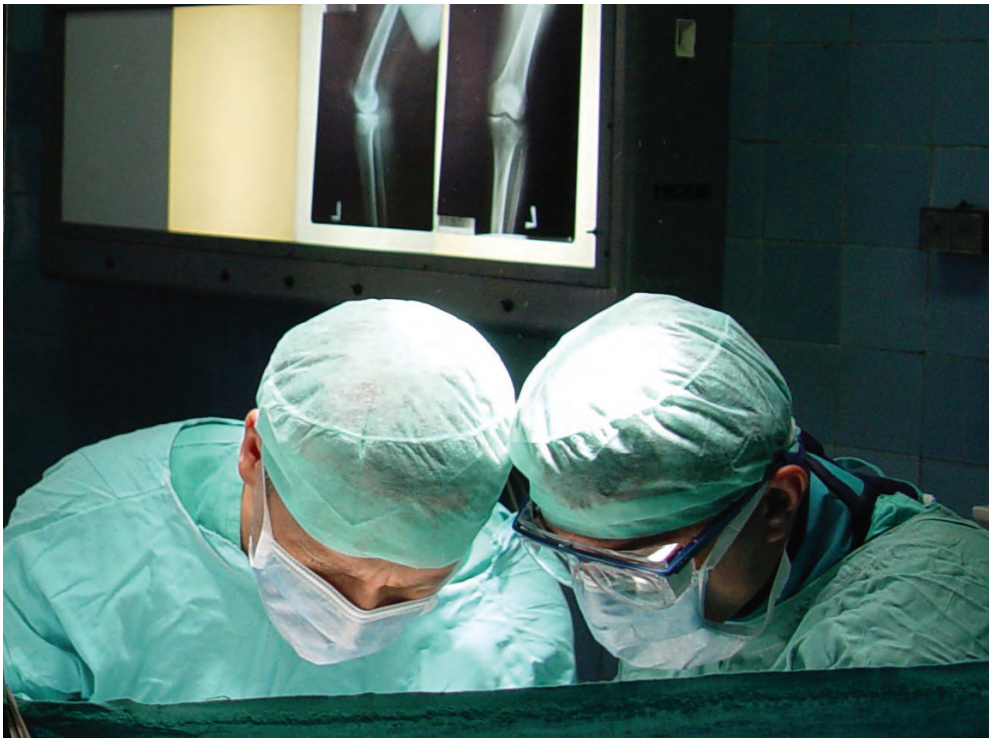
METRC encourages collaboration with industry in the evaluation of proprietary investigational agents under guidelines set forth by the Consortium. These guidelines, established to maintain the independence and scientific integrity of the Consortium, pertain to protocol development, data access, publication review and intellectual property. In particular, all industry sponsored studies must involve METRC investigators in protocol development and the final study protocol must be approved by the METRC Steering Committee. Collection and analysis of the data remain the responsibility of METRC and its Coordinating Center, independent of industry involvement.

Core Research Areas

- **Bone Defect Reconstruction and Fracture Healing**
- **Prevention and Treatment of Acute and Chronic Infections**
- **Diagnosis and Treatment of Compartment Syndrome**
- **Wound Care and Closure**
- **Prevention and Treatment of Post-Traumatic Osteoarthritis (PTOA)**
- **Limb Salvage and Amputation Outcomes**
- **Long-term and Rehabilitation Outcomes**

METRC is currently funded to conduct 14 studies that address six of the seven Core areas of research.

These studies are listed to the right, organized by the source of funding.



DoD OETRP
(core funding for METRC 1)

- **pTOG:** An RCT comparing rhBMP-2 vs. autograft for critical size tibial defects
- **FIXIT:** An RCT comparing ring external fixation vs. locked IM nail as the definitive stabilization of Grade IIIB tibia fractures
- **BIOBURDEN:** Assessment of severe extremity wound bioburden at the time of definitive wound closure or coverage: correlation with subsequent post-closure deep wound infection

DoD CDMRP
(core funding for METRC 2)

- **OUTLET:** Outcomes following severe distal tibia, ankle and/or foot trauma: comparison of limb salvage vs. transtibial amputation
- **PACS:** Predicting acute compartment syndrome using optimized clinical assessment, continuous pressure monitoring, and continuous tissue oximetry
- **PAIN:** An RCT comparing efficacy of standard pain management vs. standard care combined with use of perioperative pregabalin or ketorolac in the treatment of severe lower limb fractures
- **TAOS:** An RCT comparing transtibial amputation with and without a tibia-fibula synostosis
- **TCCS:** Using a collaborative care model to improve quality of life following extremity trauma

DoD PRORP Clinical Trial Awards

- **APS:** An RCT evaluating a novel therapy to reduce infection after operative treatment of fractures at high risk of infection *(primary award to University of Maryland)*
- **OXYGEN:** An RCT evaluating supplemental perioperative oxygen to reduce surgical site infection after high-energy fracture surgery *(primary award to University of Maryland)*
- **POvIV:** An RCT to assess oral vs. intravenous antibiotics for treatment of early post-op infection after plate fixation of extremity fractures *(primary award to Vanderbilt University)*

NIH National Institute of Arthritis, Musculoskeletal and Skin Disorders (NIAMS)

- **PTOA:** Multi-center investigation of the mechanical determinants of post-traumatic osteoarthritis *(primary award to University of Iowa)*
- **STREAM:** Reliability and Responsiveness of PROMIS tools in Orthopaedic Trauma Patients *(primary award to Johns Hopkins University)*

DoD USMRMC TATRC

- **PRIORITI-MTF:** Patient response to an integrated orthotic and rehabilitation initiative for lower extremity injuries in the military *(primary award to Johns Hopkins University)*

Each study currently funded by METRC is described in a one page brief that follows. For more information, visit the METRC **website www.metrc.org**

Assessment of Severe Extremity Wound Bioburden at the Time of Definitive Wound Closure or Coverage: Correlation with Subsequent Post-Closure Deep Wound Infection

The BIOBURDEN Study

Sponsored by: DoD OETRP
Award Number: W8XWH-09-20108 (METRC 1)
PI/Protocol Chair: Michael Bosse, MD

The primary objective of this study is to characterize the contemporary extremity wound "bioburden" at the time of definitive wound coverage/ closure of severe extremity military and civilian wounds. Routine tissue samples collected as part of standard care will be analyzed employing both standard tissue culture microbiology and modern polymerase chain reaction (PCR) technologies. The secondary objectives of the study are to determine 1) the correlation of the identified wound pathogens at the time of wound closure/ coverage with subsequent deep wound infections; 2) the correlation of the PCR results with those obtained from standard hospital microbiology; and 3) the efficacy, if any, of antibiotics used in the care of the wound.

There are 41 trauma centers participating in this study (33 are certified)

697 patients have been screened for eligibility and of these, 363 (52.1%) were eligible at time of consent.

289 (79.6% of eligible) were consented and enrolled into the study.

We have now reached 48.2% of our total enrollment

66 patients have completed the study

Study design: Multi-center, prospective cohort study.

Study duration: 3.5 years (2 year enrollment period, 1 year patient follow up and 6 month data analysis period). Participants are followed for one year after injury.

Sample size: 600.

Number of study sites: 40 core and satellite centers.

Principal Inclusion criteria: All open Type III tibia fractures (plateau, shaft and pilon) requiring a second procedure following fixation, or traumatic transtibial amputations requiring delayed primary closure, skin grafting and/ or flap coverage.

Protocol committee: M Bosse, MD, LCDR J Carney, MD, G Ehrlich, PhD, CDR J Forsberg, MD, T Miclau, MD, C Murray, MD, A Pollak, MD, G Russell, MD, R Seymour, PhD, CDR J Toledano, MD, J Wenke, PhD, D Wilson, BA, CCRP. From the Coordinating Center: R Castillo, PhD, E MacKenzie, PhD, G deLissovoy, PhD, D Scharfstein, ScD, A Carlini, MS, M Zadnik Newell, ScD, MEd, OTR/L.

A Prospective Randomized Trial to Assess Fixation Strategies for Severe Open Tibia Fractures: Modern Ring External Fixators vs. Internal Fixation

The FIXIT Study

Sponsored by: DoD OETRP
Award Number: W8XWH-09-20108 (METRC 1)
PI/Protocol Chair: Robert O'Toole, MD

There are 29 trauma centers participating in this study (28 are certified)

374 patients have been screened for eligibility and of these, 189 (50.5%) were eligible at time of consent.

93 (49.2% of eligible) were consented and enrolled in the RCT; 76 (40.2% of eligible) were consented and enrolled in the observational study.

We have now reached 29.8% of our total enrollment

41 patients have completed the study

The primary objective of this study is to compare outcomes for patients with severe open tibia shaft or metaphyseal fractures with or without a bone defect of any size randomized to treatment with a modern ring external fixator versus standard internal fixation techniques. Primary outcomes include rate of re-hospitalization for major limb complications, infection, fracture healing, limb function and pain. Secondary objectives are to: 1) determine the percentage of Gustilo IIIB open tibia shaft fractures that can be treated successfully (i.e. without amputation) without a soft tissue flap secondary to the use of ring external fixators; 2) compare the one year treatment costs associated with internal vs. external fixation; and 3) compare patient reported satisfaction with fixation method and overall treatment between the two groups.

Study design: Multi-center, prospective phase III randomized clinical trial. Patients who refuse randomization are eligible to enroll in a prospective cohort study.

Study duration: 60 months (6 month planning period, 36 month enrollment period, 12 month patient follow-up, and 6 month data and analysis and writing). Participants are followed for 12 months after injury.

Sample size: 312 in randomized study (156 per arm) and 312 in observational study.

Number of study sites: 24 Core sites, 5satellite sites.

Principal Inclusion criteria: All Gustilo Type IIIB and selected Gustilo Type IIIA diaphyseal or metaphyseal tibia fractures.

Protocol committee: R O'Toole, MD, M Bosse, MD, R Crichlow, MD, W Gordon MD, J Hsu, MD, C Jones, MD, JS Reid, MD, J Sontich, MD, E Carroll, MD, J Gary, MD, J Hutson, MD, A Jahangir, MD, S Quinnan, MD, D Sietsema, PhD, A Holmes, MS. From the Coordinating Center: E MacKenzie PhD, R Castillo PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, L Reider, MHS.

rhBMP-2 vs. Autograft for Critical Size Tibial Defects: A Multi-center, Randomized Trial

The pTOG Study

Sponsored by: DoD OETRP
Award Number: W8XWH-09-20108 (METRC 1)
Co-PIs/Protocol Co-Chairs: Lisa Cannada, MD and Paul Tornetta, III MD

There are 17 trauma centers participating in this study (11 are certified)

489 patients have been screened for eligibility and of these, 21 (4.3%) were eligible at time of consent.

13 (61.9% of eligible) were consented and enrolled into the study.

We have now reached 26% of our total enrollment

3 patients have completed the study

The primary objective of this study is to compare rate of fracture healing among patients that have a tibia shaft fracture with a critical size bone defect randomized to treatment with recombinant human bone morphogenetic protein (rhBMP-2/ACS) versus autogenous iliac crest bone graft (ICBG). rhBMP-2 is currently approved for use within the first 14 days in open tibia fractures treated with an intramedullary nail and is commercially available (Medtronic Sofamer Danek, Memphis TN). The FDA has granted an Investigational Device Exemption (IDE) for use of rhBMP-2 in this study. Secondary objectives are to 1) compare rates of infection and functional status between groups; and 2) compare one year medical cost for patients receiving a bone graft randomized to treatment with rhBMP-2 versus ICBG.

Study design: Multi-center, prospective phase III randomized clinical trial.

Study duration: 36 months (18 month enrollment period, 12 month patient follow-up, and 6 month data analysis period). Participants are followed for 12 months after bone graft treatment.

Sample size: 50 (25 per treatment group).

Number of study sites: 17 core sites.

Principal Inclusion criteria: Open diaphyseal tibia fractures with a circumferential bone defect of at least one centimeter in length compromising at least 50% of the circumference of the bone treated with an intramedullary nail.

Protocol Committee: L Cannada, MD, P Tornetta, III MD, M Bosse, MD, D Hak, MD, J Hsu, MD, C Jones, MD, S Morshed, MD, W Obremskey, MD, D Teague, MD, B Sangeorzan, MD, C Sagi, MD, H Vallier, MD, A Schmidt, MD, J Langford, MD, W Virkus, MD, G Zych, MD, J Marsh. From the Coordinating Center: E MacKenzie, PhD, R Castillo, PhD, G deLissovoy, PhD, D Scharfstein, ScD, A Carlini, MS, L Reider, MHS.

A Retrospective Study of the Treatment of Long Bone Defects

The Retro Defect Study

Sponsored by: DoD OETRP
Award Number: W8XWH-09-20108 (METRC 1)
PI/Protocol Chair: William Obremskey, MD

There are 20 trauma centers participating in this study (10 are certified)

60 records have been abstracted and entered into REDCap.

Data abstraction continues, with an expected completion date of November 1, 2013

The primary objective of this study is to characterize the methods of treatment currently being used to repair segmental defects > 1 cm with at least 50% cortical bone loss resulting from an open long bone fracture and to describe the outcomes and incidence of major complications associated with existing treatment methods. The secondary objective is to examine the relationships between treatment modality, union and re-hospitalization for a defined set of complications including amputation (at or proximal to the defect), infection (superficial or deep), flap failure, non-union, mal-union, loss of reduction, or hardware failure. This investigation will provide background data where there is otherwise a knowledge gap due to the relatively low numbers of patients treated with segmental long bone defects at individual institutions.

Study design: Retrospective, multi-center cohort design

Study duration: 1 year (3 month planning, 6 month accrual, 3 month analysis and writing). There is no follow up in this retrospective study.

Sample size: 1000 participants.

Number of study sites: 20 Core and satellite sites.

Principal Inclusion criteria: Long bone fractures (diaphyseal or metaphyseal fracture of either the tibia, femur or humerus) with a circumferential bone defect greater than one centimeter in length with at least 50% cortical loss treated with stable internal or external fixator.

Protocol Committee: W Obremskey, MD, M Bosse, MD, L Cannada, MD, C Jones, MD, D Stinner, MD, P Tornetta, MD. From the Coordinating Center: R Castillo, PhD, E MacKenzie, PhD, D Scharfstein ScD, A Carlini, MS, K Frey RN, MPH

Outcomes Following Severe Distal Tibia, Ankle and/or Foot Trauma: Comparison of Limb Salvage vs. Transtibial Amputation Protocol

The OUTLET Study

Sponsored by: DoD CDMRP PRORP
Award Number: W8XWH-10-2-0090 (METRC 2)
PI/Protocol Chair: Michael Bosse, MD

The primary objective of this study is to compare 18 month functional outcomes and health related quality of life (HRQoL) among patients undergoing salvage versus amputation following severe distal tibia, ankle and/or foot injuries with major soft tissue, bone and/or ankle articular surface loss. Secondary objectives are to 1) compare 18 month assessments of physical impairment using objective performance measures of agility, strength/power, speed and balance; and 2) compare levels of participation that will be evaluated by rate and time to return to major usual activity and participation in light, moderate or vigorous recreational or sports activities for patients treated with salvage versus amputation.

There are 31 trauma centers participating in this study (25 are certified)

369 patients have been screened for eligibility and of these, 212 (57.5%) were eligible at time of consent.

177 (83.5% of eligible) were consented and enrolled into the study.

We have now reached 40.1% of our total enrollment

No patients have completed the study

Study design: Multi-center, prospective longitudinal observational study.

Study duration: 51 months (30 month enrollment period, 18 month patient follow up and 3 month data analysis period). Participants are followed for 18 months after injury.

Sample size: 464

Number of study sites: 24 Core sites, 7 satellite sites.

Principal Inclusion criteria: Patients with either (1) Gustilo type III distal tibia and foot or ankle fractures with fracture pattern consistent with one of OTA codes: 43B1.3, 43B2-B3, 43C, 44B, 44C, 81B2-B3, 82B, and 82C; (2) open or closed industrial foot crush injuries; or (3) open or closed foot blast injuries.

Protocol committee: M Bosse, MD, L Cannada, MD, W Gordon MD, C Jones, MD, G Klute, PhD, T Miclau, MD, S Morshed, MD, W Racette CPO, B Sangeorzan, MD, R Seymour, PhD, B Steverson RN, MHA, CCRP, R Teasdall, MD, CDR, J Toledano, M.D, J Wenke, PhD, K Archer-Swygert, PhD, DPT. From the Coordinating Center: E MacKenzie PhD, R Castillo, PhD, G deLissovoy, PhD, D Scharfstein, ScD, A Carlini, MS, L Reider, MHS.

Comparison of Transtibial Amputation with and without a Tibia-Fibula Synostosis

The TAOS Study

Sponsored by: DoD CDMRP PRORP
Award Number: W8XWH-10-0090 (METRC 2)
Principal Investigator/Protocol Chair: Michael Bosse, MD

The primary objective of this study is to compare levels of impairment and functional outcomes for patients undergoing a transtibial amputation and randomized to receive an end-bearing tibia-fibula synostosis (Ertl procedure) versus a standard posterior flap procedure (Burgess procedure). Secondary objectives are to 1) compare the fit and the alignment of the prosthesis together with levels of comfort and satisfaction between treatment groups; and 2) compare rates of re-hospitalizations for complications, resource utilization, and overall treatment costs for patients undergoing a below the knee amputation who are randomized to receive an end-bearing tibia-fibula synostosis versus a standard posterior flap procedure.

There are 21 trauma centers participating in this study (6 are certified)

10 patients have been screened for eligibility and of these, 8 (80.0%) were eligible at time of consent.

5 (62.5% of eligible) were consented and enrolled into the study.

We have now reached 2% of our total enrollment

No patients have completed the study

Study design: Multi-center, prospective phase III randomized clinical trial.

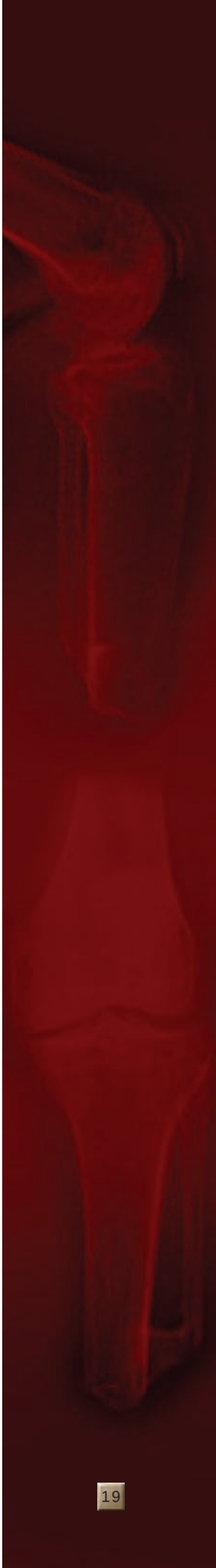
Study duration: 51 months (30 month enrollment period, 18 month patient follow up and 3 month data analysis period). Participants are followed for 18 months after injury.

Sample size: 250 (125 per arm).

Number of study sites: 19 Core sites, 2 satellite sites.

Principal Inclusion criteria: Transtibial amputation regardless of underlying injury.

Protocol committee: M Bosse, MD, L Cannada, MD, W Ertl, MD, W Gordon, MD, C Jones, MD, G Klute, PhD, T Miclau, MD, S Morshed, MD, W Racette CPO, B Sangeorzan, MD, R Seymour, PhD, B Steverson RN, MHA, CCRP, R Teasdall, MD, CDR, J Toledano, MD, J Wenke, PhD. From the Coordinating Center: E MacKenzie PhD, R Castillo, PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, L Reider, MHS.



Predicting Acute Compartment Syndrome using Optimized Clinical Assessment, Continuous Pressure Monitoring, and Continuous Tissue Oximetry

The PACS Study

Sponsored by: DoD CDMRP PRORP
Award Number: W8XWH-10-2-0090 (METRC 2)
PI/Protocol Chair: Andrew Schmidt, MD

The long-term objective of this research is to develop a tool that can aid clinicians in making a timely and accurate diagnosis of acute compartment syndrome (ACS) so that early fasciotomy can be done and unnecessary fasciotomy avoided. The immediate objective is to develop a model that accurately predicts the likelihood of ACS based on data available to the clinician within the first 48-72 hours of injury. Such data will include specific clinical findings, physiologic monitoring using muscle oxygenation measured with near-infrared spectroscopy (NIRS), continuous monitoring of intramuscular pressure (IMP) and perfusion pressure (PP), and serum markers of muscle injury (CPK levels).

There are 8 trauma centers participating in this study (8 are certified)

225 patients have been screened for eligibility and of these, 138 (61.3%) were eligible at time of consent.

41 (29.7% of eligible) were consented and enrolled into the study.

We have now reached 20.5% of our total enrollment

13 patients have completed the study

Study design: Multi-center, prospective cohort study.

Study duration: 32 months (6 month planning, 6 month accrual, 6 month final follow-up, 8 month analysis and writing). Participants are followed for six months after injury.

Sample size: 200.

Number of study sites: 8 core sites.

Principal Inclusion Criteria: Closed or open (Gustilo Type I, II or IIIA) tibial shaft or tibial plateau fractures, or severe soft tissue injuries or crush injuries to the lower leg resulting from a high-energy mechanism or gunshot wound.

Protocol committee: A Schmidt, MD, E Carroll, MD, M Bosse, MD, J Evans, MD, R Hayda, MD, R O'Toole, MD, G Russell, MD, R. Seymour, PhD. J.R. Westberg. From the Coordinating Center: E MacKenzie, PhD, R Castillo, PhD, D Scharfstein, ScD, A Carlini, MS, K Frey RN, MPH.

Improving Pain Management in High-energy OrthopaedicTrauma:

The PAIN Study

Sponsored by: DoD CDMRP PRORP
Award Number: W8XWH-10-2-0090 (METRC 2)
Co-PI/Protocol Co-Chairs: Renan C. Castillo, PhD and Srinivasa N. Raja, MD

The primary objective of this study is to test whether adjunctive analgesic therapy during the pre and peri-operative period, in addition to standard of care pain management, can improve overall pain control and pain related outcomes without increasing analgesic related side effects. Participants will be randomized into three groups: (Group 1) standard pain management plus oral placebo for up to two weeks and intravenous and oral placebo for up to 48 hours at each surgical procedure; (Group 2) standard pain management plus oral NSAIDS (meloxicam) for up to two weeks and intravenous ketorolac and oral placebo for up to 48 hours at each surgical procedure; or (Group 3) standard pain management plus oral pregabalin for up to two weeks and intravenous placebo and oral pregabalin for up to 48 hours at each surgical procedure. The secondary objective is to estimate the incremental cost effectiveness of each adjunctive therapy relative to standard of care analgesic therapy in the treatment of severe lower limb fractures.

There are 20 trauma centers participating in this study. Centers are in the process of submitting the JHBSPH and DoD approved master protocol to local IRBs and the DoD.

1 site is DoD approved.

4 sites are pending DoD approval

3 sites are pending local IRB approval

12 sites are pending local IRB submission

Study design: Three-arm, double blind, randomized, placebo controlled Phase III clinical trial.

Study duration: 4 years (12 month planning, 18 month accrual, 12 month final follow-up, 3 month analysis and writing). Patients are followed for 12 months following injury.

Sample size: 495 (165 per arm).

Number of study sites: 20 Core and satellite sites.

Principal Inclusion Criteria: Isolated, unilateral, Grade I &II open or closed pilon (distal tibial plafond) or calcaneus fractures requiring operative treatment with fixation.

Protocol Committee: S Raja, MD, D Anderson, PhD, K Archer, PhD, MAJ B Goff, DO, A Gottschalk, MD, PhD, D Hak, MD, T Higgins, MD, M Holden, C Jones, MD, L Marsh, MD, R O'Toole, MD, G Russell, MD, B Sangeorzan, MD, P Tornetta, MD, H Vallier, MD, S Wegener, PhD. From the Coordinating Center: PhD, E MacKenzie PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, K Frey RN, MPH.

Multi-center Investigation of the Mechanical Determinants of Post-Traumatic Osteoarthritis

The PTOA Study

Sponsored by: National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
Award Number: 1R21AR061808-01
Co-PI/Protocol Co-Chairs: Lawrence Marsh, MD and Donald D Anderson, PhD

The primary objective of this study is to measure the incidence of PTOA and chronic pain for up to 24 months following fracture reduction surgery and quantify the extent to which fracture severity and post-reduction contact stress are related to the development of PTOA. Colleagues at University of Iowa have developed techniques to measure the fracture severity which correlate strongly with PTOA development. In this multi-center feasibility study, mechanical metrics of acute injury severity and contact stress challenge will be further validated and extended to a large and geographically diverse group of patients with tibial pilon fractures treated using a range of current techniques. Making these techniques widely available for clinical research will help lay the foundation for the development of the next generation of treatment strategies for the prevention of PTOA.

This study is being conducted in conjunction with the PAIN trial.

There are 20 trauma centers participating in this study. Centers are in the process of submitting the JHBSPH and DoD approved master protocol to local IRBs and the DoD.

1 site is DoD approved.

4 sites are pending DoD approval

3 sites are pending local IRB approval

12 sites are pending local IRB submission

Study design: Multi-center, prospective cohort study.

Study duration: 45 months (9 month planning, 18 month accrual, 18 month final follow-up, 6 month analysis and writing). Participants are followed for up to two years from the time of injury.

Sample size: 150.

Number of study sites: 20 Core and satellite sites.

Principal Inclusion criteria: Isolated pilon (distal tibial platform) fractures requiring operative treatment with fixation at the discretion of the treating surgeon.

Protocol committee: S Raja, MD, D Anderson, PhD, K Archer, PhD, MAJ B Goff, DO, A Gottschalk, MD, PhD, D Hak, MD, T Higgins, MD, M Holden, C Jones, MD, L Marsh, MD, R O'Toole, MD, G Russell, MD, B Sangeorzan, MD, P Tornetta, MD, H Vallier, MD, S Wegener, PhD. From the Coordinating Center: R Castillo PhD, E MacKenzie PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, K Frey RN, MPH.

Improving Activity and Quality of Life Following Lower Extremity Trauma: The Trauma Collaborative Care Study

The TCCS Study

Sponsored by: DoD CDMRP PRORP
Award Number: W8XWH-10-2-0090 (METRC 2)
Co-PI/Protocol Co-Chairs: Stephen Wegener, PhD and Ellen MacKenzie, PhD

There are 12 trauma centers participating in this study (10 are certified)

149 patients have been screened for eligibility and of these, 64 (43.0%) were eligible at time of consent.

42 (65.6% of eligible) were consented and enrolled into the study.

We have now reached 4.7% of our total enrollment

No patients have completed the study

The primary objective of this study is to develop and evaluate the effectiveness of Trauma Collaborative Care (TCC) in improving a composite outcome comprised of patient reported assessment of function, depression and post-traumatic stress. The TCC intervention has three multi-modal components: 1) the Trauma Survivors Network (TSN) – an integrated approach to provide efficient access to information, peer support, and self-management training; 2) training of providers to promote patient use of TSN Program services and; 3) the use of a 'Recovery Coach' to motivate use of services and promote communication between providers and patients. The secondary objectives are to 1) evaluate differences in pain, health related quality of life, and return to usual major activity; and 2) compare use of services in the year following injury between the two groups.

Study design: Multi-center cluster design.

Study duration: 4 years (18 month planning, 12 months developing TCCI, 12 month accrual, 12 month final follow-up, 6 month analysis and writing). Participants are followed for one year from the time of injury.

Sample size: 900 (450 per arm).

Number of study sites: 11 Core site and 1 satellite site.

Principal Inclusion Criteria: Patients treated surgically for one or more orthopaedic injuries of AIS 3 or greater with initial admission to the trauma service of the participating hospital and a length of stay >=5 days or >= 3 days with planned readmission for additional procedures

Protocol Committee: S Wegener, PhD, M Bosse, MD, A Bradford, PhD, R Hymes, MD, C Jones, MD, D Sietsema, PhD, RN, H Vallier, MD. From the Coordinating Center: E MacKenzie, PhD, R Castillo, PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, K Frey RN, MPH.

Streamlining Trauma Research Evaluation with Advanced Measurement

STREAM Study

Sponsored by: NIH National Institute of Arthritis, Musculoskeletal and Skin Disorders (NIAMS)
Award Number: 1R01AR064066-01
PI/Protocol Chair: Renan Castillo, PhD

The Stream study protocol is pending approval from the JHBSPH IRB.

Target date for enrollment is November, 2013.

The primary objective of this study is to examine the measurement properties of existing PROMIS (patient reported outcomes measurement information system) computer adaptive tests (CATs) and item banks in patients with orthopaedic trauma. The secondary objectives are to examine the responsiveness of existing PROMIS domains in patients with orthopaedic trauma, and to evaluate the participant burden associated with the administration of these instruments. As part of the NIH Roadmap initiative, PROMIS has developed tools, including item banks, short forms and CATs that can help standardize measurement for many health-related quality of life domains. These tools are being tested in large general population samples across the lifespan. The STREAM study will assess the performance and research utility of these new tools in an orthopaedic trauma patient population for future comparative effectiveness research projects.

Study design: Multi-center, prospective longitudinal observational study

Study duration: 3 years (6 month planning, 12 month accrual, 12 month final follow-up, 6 month analysis and writing). Patients are followed for up to 12 months from the time of injury.

Sample size: 1000 participants

Number of study sites: All METRC sites participating in FIXIT, PAIN, OUTLET, or TAOS

Principal Inclusion Criteria: Patients currently enrolled in the METRC FIXIT, OUTLET and TAOS studies.

Protocol Committee: R O'Toole, MD, M Bosse, MD, S Wegener, PhD, S Morshed, MD, J Agel, MA, M Weaver, MD, T Higgins, MD, R Hayda, MD, K Chan, PhD, A Wu, PhD. From the Coordinating Center: R Castillo, PhD, E MacKenzie, PhD, D Scharfstein ScD, A Carlini, MS, L Reider, MS, K Frey RN, MPH

Supplemental Perioperative Oxygen to Reduce Surgical Site Infection After High-energy Fracture Surgery

The Oxygen Study

Sponsored by: DoD CDMRP PRORP
Award Number: W8XWH-09-20108
PI/Protocol Chair: Robert V. O'Toole, MD

The primary objective of this study is to assess the efficacy of supplemental perioperative oxygen in the prevention of surgical site infections. The secondary objectives are to 1) compare species and antibacterial sensitivities of the bacteria in the patients who develop surgical site infections in study patients treated with supplemental oxygen compared to those who were not treated with supplemental oxygen; 2) validate the previously developed risk prediction model for the development of surgical site infections after fracture surgery; and 3) measure and compare resource utilization and cost associated with surgical site infection in study patients treated with supplemental oxygen compared to those who were not treated with supplemental oxygen.

The Master Protocol has been approved by the JHBSPH IRB and is awaiting approval by the DoD.

Core and satellite centers are in the process of submitting the protocol to their local IRB and DoD for approval.

Study design: Phase III randomized controlled clinical trial.

Study duration: 3 years (6 month start up, 18 months of recruitment, 6 months follow up, 6 months analysis and writing). Participants are followed for one year after injury.

Sample size: 1000 (500 per arm).

Number of study sites: 27 core and satellite centers.

Principal Inclusion criteria: High-energy tibial plateau, pilon and calcaneous fractures treated operatively with pate and screw fixation.

Protocol committee: R O'Toole, MD, MSME, G Altman, MD, C Arndt, RN, M Bosse, MD, A Dagal, MD, JC D'Alleyrand, MD, T Dipasquale, DO, J Gary, MD, A Holmes, MS, M Joshi, MD, M Karunakar, MD, C Murray, MD, N Rao, MD, M Sen, MD, A Schmidt, MD, R Sikorski, MD, P Watkins, RN, M Weaver. MD. From the Coordinating Center: R Castillo, PhD, E MacKenzie, PhD, D Scharfstein, ScD, A Carlini, MS, M Zadnik Newell, ScD, MEd, OTR/L.

A Prospective Randomized Trial to Assess PO versus IV Antibiotics for the Treatment of Early Post-op Wound Infection after Plate Fixation of Extremity Fractures

The POvIV Study

Sponsored by: DoD CDMRP PRORP
Award Number: W81XWH-10-2-0133
PI/Protocol Chair: William T. Obremskey, MD, MPH

The primary objective of this study is to investigate the efficacy of oral (per os, (PO)) antibiotic therapy versus intravenous (IV) antibiotics in the treatment of acute infection after fixation of fractures or fusion of joints. The secondary objective is to build and validate a risk prediction model for failure of treatment of early post-op wound infections after fixation of fractures.

There are currently 5 trauma centers participating in this study. The study was rolled out to the rest of 35 sites in mid-September of 2013.

95 patients have been screened for eligibility and of these, 11 (11.5%) were eligible at time of consent.

4 (36% of eligible) were consented and enrolled into the study.

We have now reached 1.5% of our total enrollment

No patients have completed the study

Patients with post-operative infections routinely receive up to six weeks of intravenous antibiotic therapy following surgical debridement, despite growing evidence that oral antibiotic therapy is equally effective, with a reduced risk of complications and lower medical costs. The equivalence of oral versus intravenous therapy to treat wound infection after plate fixation of extremity fractures has not been definitively established in a randomized clinical trial.

Study design: Phase III randomized controlled clinical trial.

Study duration: 4 years (6 month planning, 24 month accrual, 12 month follow-up, 6 month analysis and writing). Participants are followed for 12 months following diagnosis of infection.

Sample size: 264 (132 per arm).

Number of study sites: 35 Core and satellite sites.

Principal Inclusion criteria: Patients with fractures (defined as femurs, tibias, and fibulas of the legs, and the humeri, radii, and ulnas of the arms) treated with a plate or IMN, or patients undergoing fusion of subtalar, ankle, knee, wrist or elbow that develop a post op wound infection.

Protocol committee: W Obremskey, MD, MPH, J Anglen, MD, K Archer, PhD, DPT, M Bosse, MD, M Fleming, MD, M Holden, CDR J Keeling, MD, T Miclau, MD, S Morshed, MD, MPH, LTC C Murray, MD, A Schmidt, MD, T Talbot, MD, MPH, P Tornetta, III, MD, H Vallier, MD. From the Coordinating Center: R Castillo PhD, E MacKenzie PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, M Zadnik Newell, ScD, MEd, OTR/L.

Novel Therapy to Reduce Infection after Operative Treatment of Fractures at High Risk of Infection: A Multi-center Randomized Controlled Trial

The APS Study

Sponsored by: DoD CDMRP PRORP
Award Number: W81XWH-10-2-0134
PI/Protocol Chair: Robert O'Toole, MD

The APS study has had delays associated with obtaining FDA approval. To overcome this issue, the protocol committee has proposed changes in the study design, pending approval by the DoD.

The primary objective of this study is to investigate whether the use of an Antibacterial Plate Sleeve (APS) reduces the rate of deep surgical site infections (SSIs) after operative treatment of high energy fractures. The treatment of high-energy military fractures continues to result in poor outcomes and be associated with high rates of infection. Local antibiotic delivery systems associated with fracture hardware have the potential to reduce complications by lowering infection rates in these patients. Although there is strong theoretical and animal study data as well as some promising preliminary clinical data regarding the use of local antibiotics to reduce infection, it is not yet clear that Antibacterial Plate Sleeves will perform better than treatment without Antibacterial Plate Sleeves in a rigorous head-to-head clinical trial The results of this trial have potential to reduce surgical site infection in both the military and civilian patients, and improve patient outcomes from these potentially devastating injuries.

Study design: Phase III randomized controlled multi-center trial.

Study duration: 44 years (12 months planning and regulatory approval, 18 month accrual, 12 month final follow-up, 6 month analysis and writing). Participants are followed for 12 months following injury.

Sample size: 800 (400 per arm).

Number of study sites: 25-35 core and satellite sites.

Principal Inclusion criteria: Tibial plateau and pilon fractures initially treated in a staged fashion and then treated definitively with plate and screw fixation more than 5 days later after swelling has resolved; and calcaneus fractures initially treated in a splint or with limited percutaneous fixation or both, and then definitively more than 5 days later with plate and screw fixation after swelling has resolved.

Protocol committee: R O'Toole, MD, D Chan, MD, M Graves, MD, D J Hak, MD, MBA, J Hsu, MD, M Joshi, MD, J Langford, MD, H Mir, MD, N Rao, MD, Z Roberts, MD, D Sietsema, PhD, RN, D Tsukayama, MD, D Wilson, BA, CCRP. From the Coordinating Center: R Castillo PhD, E MacKenzie PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, M Zadnik Newell, ScD, MEd, OTR/L.

Patient Response to an Integrated Orthotic and Rehabilitation Initiative for Traumatic Injuries

The PRIORITI-MTF Study

Sponsored by: DoD TATRC and CRMRP
Award Number: W81XWH-12-2-0032
Co-PI/Protocol Chair: Joseph Hsu, MD and Ellen MacKenzie, PhD

The Master Protocol has been approved by the JHBSPH IRB and is awaiting approval by the DoD.

The primary objective of this study is to examine the benefits (and cost-benefits) of an integrated orthotic and rehabilitation program that incorporates the Intrepid Dynamic Exoskeletal Orthosis (IDEO) and the Return to Run (RTR) physical therapy regimen, but designed for scalability in the broader military environment (i.e. beyond San Antonio Military Medical Center where the program was developed). The secondary objectives of the study are to 1) document patterns of device use, use of ambulatory aids, shoe wear and patient reported satisfaction associated with the Intrepid Dynamic Exoskeletal Orthosis (IDEO); and 2) to assess the economic impact of the PRIORITI program by (i) measuring one-year costs associated with participation in PRIORITI and compare these costs to those projected under standard of care; and (ii) estimating lifetime cost-effectiveness of the PRIORITI program relative to standard of care.

Study design: Multi-center before-after program evaluation where participants serve as their own controls.

Study duration: 3 years (6 month planning and training, 10 month accrual, 12 month final follow-up, 8 month analysis and writing).

Sample size: 85 Participants.

Number of study sites: 3 Military Treatment Facilities.

Principal Inclusion criteria: Patients who are currently two or more years out from a traumatic unilateral lower extremity injury at or below the knee at or below the knee, who are able to bear weight and who have chronic muscle weakness and/or limited range of motion at the ankle that translates into functional deficits that interfere with daily activities and overall quality of life.

Protocol committee: J Hsu, MD, M Bosse, MD, CDR D Dromsky, MD, J Ferguson CPO, LTC DA Gajewski MD, W Gordon, MD, R Hooper PT, PhD, J Owens MPT, LTC BK Potter MD, COL (Ret.) C Scoville PT, Capt J Town NC. From the Coordinating Center: E MacKenzie PhD, M Bosse MD, R Castillo PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, M Zadnik Newell ScD, MEd, OTR/L.

Funding Sources

The activities of METRC are currently funded exclusively by federal grants. Core funding for METRC is provided through the Orthopaedic Extremity Trauma Research Program (OETRP) (Award # W81XWH-09-2-0108) (METRC 1) and a cooperative agreement with the DoD Peer Reviewed Orthopaedic Research Program (PRORP) of the Congressionally Directed Medical Research Program (CDMRP) (Award # W81XWH-10-2-0090) (METRC 2). These awards provide funding for specific studies and support the infrastructure of the Consortium. Four of our METRC Investigators have successfully obtained individual grants that use the METRC consortium as a foundation for the research. These individuals are the prime recipients of the awards (three from DoD CDMRP, two from NIH NIAMS and one from the DoD Clinical Telemedicine & Advanced Technology Research Center and the Clinical and Rehabilitative Medicine Research Program) but they subcontract with the Coordinating Center to help with the design, implementation, and analysis of the studies. These subcontracts also provide funding to support the participation of METRC Centers in the study. A summary of these awards (total amounts) is provided on the following page.

Overview of Budget
METRC Coordinating Center

	METRC 1	METRC 2	UMd PRORP #1	UMd PRORP #2	Vanderbilt University PRORP	University of Iowa NIH R21	Johns Hopkins TATRC	Johns Hopkins NIH R01
Personnel - MCC	3,135,912	5,834,433	537,224	208,550	332,973	46,341	274,864	469,574
Non Personnel Costs	674,127	1,874,374	53,466	55,144	30,431	2,748	103,679	145,280
Equipment and Major Supplies		1,540,220			76,770			23,896
Core Civilian Centers								
Direct Costs	6,855,638	10,040,449						
Indirect Costs to Centers	2,975,824	4,737,484						
Patient Enrollment Costs	1,755,000	3,296,000	1,200,000*	1,112,000*	600,000*	75,000*	27,000*	250,000
Core MTF Centers								
Direct Costs	2,243,281	1,659,333					1,511,096	
Indirect Costs to Centers	446,413	330,207					316,424	
Satellite Center Enrollment								
Patient Enrollment Costs	735,000	687,500						
Total Direct Costs	18,821,195	30,000,000	1,790,690	1,383,694	1,040,174	124,089	2,233,063	888,750
IDC on the Direct Costs (IDC to JHU)	2,678,425	8,657,995	117,731	233,883	225,736	87,165	438,904	551,025
Total Award	21,499,620	38,657,995	1,923,353	1,956,114	2,306,775	223,360	2,500,000	1,439,775

**These amounts may be used to support patient enrollment in either cores, military training facilities or satellite centers*

Looking Forward

This has been a productive year for METRC. All 8 Core studies funded under METRC 1 and METRC 2 are in the field and we anticipate that an additional 5 studies supported by METRC but funded outside the Core will be actively enrolling in early 2014.

In the coming year we will continue to focus on study enrollment and continuous quality improvement activities. In addition, we will begin the development of analysis files for several studies that have accrued greater than 25% of their projected sample size.

Practice Surveys relevant to study questions under investigation are being distributed to all METRC investigators and their partners. The primary goal of these Practice Surveys is to document variation in knowledge, beliefs, and practices among orthopaedic trauma surgeons in the United States. A secondary goal is to prospectively assess the impact of METRC research projects on clinical practice.

We continue to cultivate new research ideas that address the priorities of the DoD and the Consortium. Currently under discussion are studies to:

- ✔ Investigate the effect of local adjuvant antibiotics on wound infection rates in the surgical treatment of high-energy thoracolumbar spine fractures and dislocations) (PI: J Patt, MD, MPH);
- ✔ Evaluate the safety and efficacy of an antibiotic-loaded chitosan sponge delivery system used adjunctively for the prevention of infections in open fractures and severe extremity wounds (PI: J Hsu, MD);
- ✔ Validate new measures of prosthetic fit and alignment that can be used in large multi-center studies to provide a less subjective means to determine the impact of the prosthetic – tissue interface on the performance, function and outcomes of the amputee patient (PI: S Morhsed, MD)

Please continue to check our website www.metrc.org to monitor the progress of our activities.

Appendix A

Participating Centers

MILITARY TREATMENT FACILITIES

San Antonio Military Medical Center, BAM
Principal Investigator: MAJ Daniel Stinner, MD

Walter Reed National Military Medical Center, WRD
Principal Investigator: LTC Wade T. Gordon, MD

Naval Medical Center Portsmouth, NPM
Principal Investigator: LCDR Christopher Smith, MD

Naval Medical Center San Diego, NSD
Principal Investigator: CDR James E. Toledano, MD, MC, USN

CORE CIVILIAN SITES

Boston Medical Center, BMC
Principal Investigator: Paul Tornetta, III, MD

Carolinas Medical Center, CMC
Principal Investigator & Chair of the METRC Consortium: Michael J. Bosse, MD

Denver Health and Hospital Authority, DHA
Principal Investigator: David J. Hak, MD, MBA

Florida Orthopaedic Institute / Tampa General & St. Joseph's Hospitals, FOI
Principal Investigator: Roy W. Sanders, MD

Hennepin County Medical Center / Regions Hospital, MIN
Principal Investigators: Andrew H. Schmidt, MD & Paul Lafferty, MD

LAC + USC Medical Center, LAC
Principal Investigator: Jackson Lee, MD

MetroHealth Medical Center, MET
Principal Investigator: Heather A. Vallier, MD

Orlando Regional Medical Center, ORL
Principal Investigator: Joshua R. Langford, MD

Methodist Hospital, MTH
Principal Investigator: Todd McKinley, MD

Orthopaedic Associates of Michigan / Spectrum Health, SPC
Principal Investigator: Clifford B. Jones, MD

Penn State University M.S. Hershey Medical Center, PSU
Principal Investigator: J. Spence Reid, MD

St. Louis University Hospital, STL
Principal Investigator: Lisa K. Cannada, MD

University of California at San Francisco, USF
Principal Investigator: Theodore Miclau, III, MD

University of Iowa Hospitals & Clinics, UIA
Principal Investigator: J. Lawrence Marsh, MD

University of Maryland R Adams Cowley Shock Trauma Center, UMD
Principal Investigator & Co-Chair of the METRC Consortium: Andrew N. Pollak, MD

University of Miami Ryder Trauma Center, RYD
Principal Investigator: Gregory A. Zych, DO

University of Mississippi Medical Center, UMS
Principal Investigator: George Russell, MD

University of Oklahoma Medical Center, UOK
Principal Investigator: David Teague, MD

University of Washington / Harborview Medical Center, UWA
Principal Investigator: Jens Chapman, MD

UT Health: The University of Texas Health Science Center at Houston, HOU
Principal Investigator: Joshua Gary, MD

Vanderbilt University Medical Center, VMC
Principal Investigator: William T. Obremskey, MD, MPH

Wake Forest University Baptist Medical Center, WFU
Principal Investigator: Eben Carroll, MD

SATELLITE CENTERS

Allegheny General Hospital, AGY
Principal Investigator: Gregory Altman, MD

Barnes-Jewish Hospital at Washington University, BJH
Principal Investigator: William M. Ricci, MD

Duke University Hospital, DUK
Principal Investigator: Robert D. Zura, MD

Emory University, EMU
Principal Investigator: William M. Reisman, MD

Geisinger Health System, GMC
Principal Investigator: Michael Suk, MD, JD, MPH, FACS

Grant Medical Center, GRT
Principal Investigator: Benjamin Taylor, MD

Harvard Orthopaedic Trauma Service, HRV
Principal Investigator: Michael Weaver, MD

Inova Fairfax Hospital, IFH
Principal Investigator: Robert A. Hymes, MD

Louisiana State University Health Sciences Center, SHV
Principal Investigator: Massimo Morandi MD, FACS

Louisiana State University, LSU
Principal Investigator: Peter C. Krause, MD

Medical University of South Carolina, MSC
Principal Investigator: Langdon A. Hartsock, MD

Mission Hospital, ASH
Principal Investigator: Harold M. Frisch, MD

Ohio State University Medical Center, OSU
Principal Investigator: Laura Phieffer, MD

Regional Medical Center at Memphis, CAM
Principal Investigator: John Weinlein, MD

Reno Orthopaedic Clinic, RNO
Principal Investigator: Peter L. Althausen, MD, MBA

Rhode Island Hospital, Brown University, RIH
Principal Investigator: Roman A. Hayda, MD

Scott and White Memorial Center, SWM
Principal Investigator: Michael Brennan, MD

Stanford University Medical Center, STN
Principal Investigator: Julius A. Bishop MD

St. Mary's Medical Center, STM
Principal Investigator: Robert Borrego, MD, PA

St Vincent Indianapolis Hospital, STV
Principal Investigator; Renn Crichlow, MD

Temple University Hospital, TMP
Principal Investigator: Saqib Rehman, MD

Texas Tech University Health Sciences Center, ELP
Principal Investigator: Amr A. Abdelgawad, MD

University of Alabama at Birmingham, UAB
Principal Investigator: Jason Lowe, MD

University of Kansas Medical Center, UKS
Principal Investigator: Terence McIff, MD

University of Kentucky, UKY
Principal Investigator: Brandon T. Bruce, MD

University of Pennsylvania, PEN
Principal Investigator: Samir Mehta, MD

University of Pittsburgh, PIT
Principal Investigator: Andrew R. Evans, MD

University of Rochester, ROC
Principal Investigator: John T. Gorczyca, MD

University of Texas Health Science Center, San Antonio, SAN
Principal Investigator: Animesh Agarwal, MD

University of Texas Southwestern Medical Center, UTX
Principal Investigator: Adam J. Starr, MD

University of Utah, UUT
Principal Investigator: Thomas F. Higgins, MD

University of Virginia Medical Center, UVA
Principal Investigator: David B. Weiss, MD

Wright State University, WSU
Principal Investigator: Richard Laughlin, MD

York Hospital / WellSpan Health, YRK
Principal Investigator: Thomas DiPasquale, DO, FACOS, FAOAO

Appendix B

Staff of the Coordinating Center

Ellen J. MacKenzie, PhD, Director

Renan C. Castillo, PhD, Deputy Director

Daniel O. Scharfstein, ScD, Principal Biostatistician

Gregory deLissovoy, PhD, MPH, Principal Economist

Junya Zhu, PhD, Investigator

CORE: Informatics and Biostatistics

Anthony R. Carlini, MS, Director

Andre Hackman, MS, Senior Programmer

Grace Ha, PhD, Senior Research Assistant

Jason Luly, MS, Biostatistician

Greg Mettee, BS, Research Assistant

Steve Samudrala, MS, Programmer Analyst

CORE: Protocol Development, Implementation & Monitoring

Lisa Reider, MHS, Director

Katherine Frey, RN, MPH, MS, Associate Director

Mary Zadnik Newell, ScD, MEd, OTR/L, Associate Director

Lauren Allen, MA, Study Manager

Susan Collins, MSc, Study Manager

Tara Taylor, MPH, Study Manager

CORE: Administration and Regulatory Affairs

Rachel Holthaus, MS, CIP, Director

Avanti Aparentado, BS, Financial Officer

Cathy Epstein, Administrative Assistant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Major Extremity Trauma Research Consortium