METRC

Major Extremity Trauma Research Consortium
2015 Annual Report

Contents

METRC
Major Extremity Trauma Research Consortium

Dear Colleagues and Friends,

Limb injuries are much more common than most people realize. In trauma centers around the country two of every three patients are being treated for extremity injuries. More than half of all serious battlefield wounds in Iraq and Afghanistan are to the extremities—and these are the cases that end up causing the bulk of long-term disabilities among our veterans.

In the pages that follow you will meet both Service Members and civilians who have survived major limb trauma. You will get a glimpse of the challenges they and their loved ones face in the wake of these injuries, and you will get a sense for the daunting complexities involved in their care.

METRC is committed to finding the best way to address these complexities and, ultimately, to improve the clinical and quality-of-life outcomes for those who are injured. Currently, there is little in the way of rigorous evidence about which treatment decisions work best—in both the acute setting immediately after the injury and during the longer term transition to rehabilitation and reintegration back into everyday life.

Developing that evidence is what METRC is all about.

Our consortium was founded in 2009, with funding from the Department of Defense. The DOD recognized that the best way to address these gaps in our knowledge about which treatments work best is through a network of treatment centers and clinical experts, both military and civilian. Only such a network would have access to the shared expertise and patient populations needed to conduct studies of the scope and size needed to answer the most important questions. No single center, military or civilian, sees enough major limb trauma cases on its own to do that kind of work.

In military facilities, there is an additional challenge. The number of combat casualties is constantly in flux, depending on whether the nation is in a period with or without active military conflict. That makes a full partnership with the civilian sector essential to any effort to build a research enterprise capable of generating improvements in care and outcomes on a continuous basis. This partnership was designed from the outset to ensure that lessons learned in treating Service Members during periods of active combat are then translated to the civilian sector, where they can be further refined and improved in ways that will eventually benefit those injured on the battlefields in future conflicts.

Continued on page 3

Continued from page 1

A strong foundation for this work is now in place. We have established a robust infrastructure with access to the kinds of data-management expertise and project-management skills that are indispensable in large, multi-center trials. Working in partnership with expert clinicians in the military and civilian trauma communities, METRC has identified seven priority problem areas where gaps and uncertainties in our knowledge must be filled. Our consortium now numbers 26 core treatment facilities—four of them are military, while the other 22 are civilian trauma centers. Also important to the success of METRC are the contributions of more than 30 satellite centers from around the country.

Nearly 5,000 patients have been enrolled in 18 different studies. The coming year promises to be an exciting one, with results from the first of those projects starting to roll in and make an impact in the field.

That METRC has arrived at this point so quickly is a testament to the vision of the DOD, the capabilities of our clinical centers, and, perhaps most importantly, to the willingness of so many Service Members and civilian patients to volunteer their time and experience in order to make a difference for future patients. Their commitment to the research we are doing today will help ensure that people injured in the future will receive state-of-the-art care and live their lives to the fullest possible measure of their capabilities.

Sincerely,

Michael J. Bosse, MD
Chair of the Consortium

Ellen J. MacKenzie, PhD
Director of the Coordinating Center

“I’ve had this pain for more than one-third of my life now.”

Marine Gunnery Sgt. Mark Novello, far right in the background, participates along with veterans and active-duty service members, in physical therapy at Naval Medical Center San Diego’s gym.

A life changer?

IN THE YEARS AFTER a roadside bomb in Iraq tore up his right ankle, Mark Novello tried one kind of brace after another. But he found no relief from the chronic pain in his right ankle.

“Believe me, I tried everything,” says the 32-year-old Marine sergeant. “It felt like there was really nothing out there for us lower-leg extremity guys.”

The war in Iraq was still a relatively young affair when Novello got wounded in 2004. He wonders sometimes how much of the trouble he has endured is related to the fact that military doctors were still learning their way around the new types of injuries caused by IEDs.

“I try to explain sometimes why my situation is different,” Novello says. “Most people are used to injuries that come and go. I’ve had this pain for more than one-third of my life now.”

The shrapnel that surgeons removed from Novello’s leg measured one-and-a-half inches long and three quarters of an inch thick. Parts of his tibia were blown apart and gone forever. A key tendon was completely severed.

He spent six months in a full leg cast, then two months in cast that went up to his knee, and then two months after that in a boot. When he finally started therapy, he did so with the confidence and energy you’d expect in a marine.

“I’m 20 years old at that point, and I’m thinking that I’m young and strong and I’m like Superman, ready to tackle anything,” Novello says. “But it just never felt right.”

Today, Novello is finally feeling hopeful about his chances to find some relief from the pain. His wife was surfing Facebook one day when she saw a post about a METRC research project called PRIORITI-MTF.

The study is gauging the effectiveness of a new type of brace called the Intrepid Dynamic Exoskeletal Orthosis, or IDEO. When combined with a physical therapy program called Return to Run the IDEO is expected to improve function and reduce pain.

Three military treatment facilities host the study, including the San Diego Naval Medical Center near Camp Pendleton, where Novello is now stationed. METRC leaders are hopeful that if results from this trial are encouraging, it will be a step towards future studies involving civilian patients.

The IDEO brace is a three-part affair. There is a cuff at the knee, a strut running down the calf, and a plate under the foot. All three sections are custom fitted to each patient and designed to absorb the force of walking and running in ways that ease pressure on the ankle.

“It’s molded to my calf, to my shin, and to my knee,” Novello says. “I can’t even tell I’m wearing it, actually.”

Kevin Kuhn, an orthopaedic surgeon with the Navy, says that the specialized physical therapy regimen included in the study is critical. “The brace by itself does not necessarily improve performance,” he told the *San Diego Union Tribune* last year. “In previous studies, the return-to-duty rate was triple in the people who actually did the Return to Run program.”

For nearly a year now, Novello has been putting himself through a regimen that includes daily weight training and a three-mile run. He no longer feels the post-run pain that used to drive him straight to a couch.

Only time will tell if the brace will help Novello meet the physical fitness standards that the Marine Corps requires and hit his goal of a 20-year military career, but for the first time in years he finds himself able to go out on walks along the beach with his wife and take trips to a theme park with his stepchildren. Until recently he rarely felt up to taking his dog for a walk.

Plan of treatment was urgent debridement, provisional stabilization, and attempted salvage. Amputation was a possibility due to the large amount of soft tissue and bony destruction.

‘Should We Amputate?’

REMEMBERING THAT NIGHT, Erick Saunders marvels over all the dominos that had to fall into place for things to happen the way they did. He was headed out of town the next morning. The fuel coil on his father’s car conked out. He was one specialized tool short of what he needed to fix it. But a friend had the tool, so Erick asked if he could borrow it. The weather was gorgeous. Why not take the motorcycle?

And so the 26-year-old project manager with a manufacturing firm found himself on a two-lane back road near his home in Wellington, OH on the evening of Aug. 13, 2015. He remembers his attention wandering onto the list of things he wanted to get done before his trip. He didn’t see that the truck ahead had come at a dead stop until it was too late.

His first instinct was to veer into the other lane and loop around the truck. But he couldn’t see whether there was any oncoming traffic, so he played it safe, dropping his bike into a slide that then sent his body tumbling and bouncing its way into a roadside ditch.

“I was able to sit right up,” Saunders recalls. “My adrenalin was going, and I didn’t really feel the pain. But when I tried to stand up, that didn’t work out so well. I remember thinking, ‘Did I break my femur?’”

An onlooker dialed 911. A Life Flight helicopter from the trauma center at MetroHealth Medical Center in Cleveland arrived soon thereafter.

Doctors at MetroHealth told Saunders that the broken femur in his left leg was actually the lesser of his two biggest problems. They were worried that he might lose his right foot, where nearly every bone from the ankle on down was dislocated or fractured.

This decision point—should we amputate?—is the focal point of the OUTLET study, which has over 650 patients signed on at 35 trauma centers around the country. The project compares the physical functioning and quality of life outcomes for patients who undergo amputation after suffering severe foot and ankle trauma with those for patients whose foot is salvaged.

Saunders ended up having his foot salvaged. He endured nine surgeries in the month after his accident, with physicians moving step by step from stabilizing his situation to reconstruction and plastic surgery. The most painful operation, he says, involved taking muscle from his abdomen and putting it into his foot—the arteries and veins in that muscle tissue are now helping him maintain a healthy flow of blood.

Saunders describes the decision to participate in the OUTLET study as an easy one. He cites two motivations—first, a feeling of gratitude toward the surgeons who had worked so hard on his behalf, and second, a hope that his experience might be of some benefit to future patients.

“The weather was gorgeous. Why not take the motorcycle?”

◄ **Mr. Saunders presented with contaminated open type 3B fractures and dislocations of the midfoot. The dorsal skin and soft tissue of the foot were destroyed. The radiograph of the foot shows displaced fractures of the 2nd and 3rd mid metatarsals with dislocations of all 3 cuneiforms and all 5 tarsometatarsal joints.**

‘Should We Amputate?’

“If just one person is helped, that will make it worth it to me,” he says.

Heather Vallier, an orthopaedic trauma surgeon at MetroHealth, says that such thinking is typical of the study participants she works with. “When we ask about participating, a lot of patients approach it from this generous angle of ‘paying it forward,’” she explains. “They feel like this is an opportunity to take an awful event in their lives and give it a positive aspect.” She added that many also see their participation as a way to help the men and women who have been injured in service to the Country.

This decision point—should we amputate?—is the focal point of the OUTLET study, which now has over 650 patients signed on at 35 trauma centers around the country.

Saunders is happy with the steady progress he has been making up to this point. He received the all clear to start putting weight on the broken foot just before Thanksgiving 2015.

“That was such a great feeling,” he says. “Everyone in my family was so supportive during this, and being up and around a little bit with them at the holiday—it was like I was saying, ‘Look everybody, I’m going to be OK.’”

With Saunders now back on his old job at MTD Products, Vallier is counting him as “one of the lucky ones” among her patients. Many patients with severe extremity trauma are unable to return to their jobs, especially those with positions involving a lot of physical demands.

“The challenges that these patients face when it comes to simply getting out and making a living can be quite daunting,” says METRC co-chair Andrew N. Pollak. “The latest data I’ve seen show that half of them are never able to get back to work, in any capacity. Numbers like that really demonstrate the urgency of the work the Consortium is doing.”

The X-ray shows an open femoral shaft fracture (comminuted and markedly displaced with apex posterior angulation). He underwent debridement and stabilization of the femur with an intramedullary rod on the day of injury.

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 consists of a network of clinical centers and one data-coordinating center that work together to conduct multi-center clinical research studies that help define best practices for treating serious limb injuries.

The mission of METRC, simply put, is to improve outcomes and quality of life following major orthopaedic trauma. The urgency of this mission stems from an unfortunate fact that extremity trauma is involved in more than half of the serious injuries suffered on the battlefield. Caring for these wounded warriors is complex and costly. Many are burdened with injuries to multiple limbs. Some require amputation, a life-altering event that can affect function and everyday activities. And even those whose limbs are spared often require multiple surgeries and are at risk of short and long-term complications that make full recovery challenging. Extremity injuries account for two-thirds of the disability costs associated with serious combat casualties.

In everyday civilian life, extremity trauma is also common; fully two-thirds of patients admitted to U.S. trauma centers are treated for extremity injuries. Many of the challenges involved in treating injuries resulting from serious motor vehicle and motor cycle crashes, industrial accidents and assaults are similar to those faced in treating combat casualties. Both military and civilian centers are faced with critical decisions regarding the treatment of segmental bone defects, vascular injuries with ischemia, severe soft tissue injuries, and wounds with severe contamination. Challenges do not end with the acute phase of treatment; most patients require rehabilitation and post-acute services to optimize recovery and reintegration back into everyday life.

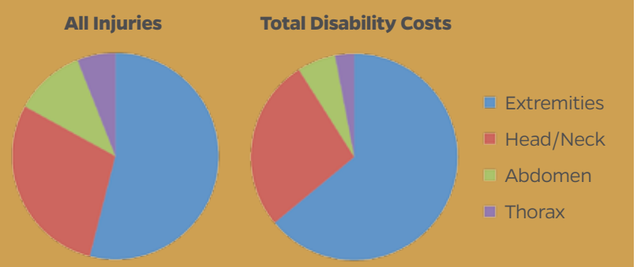
The evidence base to support best practices for the care of these injuries is lacking. METRC is committed to developing this evidence base. By combining the population of injured Service Members and combat expertise of military treatment facilities with the patients and clinical research expertise of civilian trauma centers we are able to conduct studies of sufficient size to address the gaps in our understanding of what works best and for whom. The military- civilian partnership embodied by METRC is particularly relevant now, given the de-escalation of combat activity. Continued investment in the METRC network will advance the care of injured service members that will be applicable in the event of future conflicts and contribute to the medical readiness of current forces by addressing ways to optimize recovery and return to duty following in-garrison musculoskeletal injuries.

Improving outcomes through collaborative research

The goal of METRC is to produce the evidence needed to establish treatment guidelines for 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 major orthopaedic trauma

Extremity Wounds in OIF/OEF Account for over 50% of all Wounds and 64% of Projected Disability Benefit Costs

(adapted from Masini et al, *J Orthop Trauma*, 23:261; 2009)



The work of METRC is guided by six overarching objectives. Our approach to the research we do emphasizes:

A Multi-Center Approach: Large, multi-center, prospective studies are needed to address knowledge gaps. Too many contributions to the orthopaedic literature end with the conclusion … "adequately powered studies are needed to definitively answer this question." No civilian trauma center or military treatment facility sees enough limb trauma patients by itself to conduct the kind of large scale clinical trials needed to address the questions of most concern to providers and patients. METRC now partners with over 50 clinical centers who are participating in one or more of the 18 on-going studies. Collectively, the METRC centers have already enrolled nearly 5,000 patients into these studies.

A Multi-Disciplinary Approach that Addresses Gaps in Research Across the Continuum of Care: To effectively address knowledge gaps across the continuum of care from point of injury through rehabilitation and re-integration, METRC engages multidisciplinary teams in the identification of study topics and in the design and execution of studies. These teams include experts in orthopaedic surgery, trauma surgery, physical medicine and rehabilitation, physical and occupational therapy, rehabilitation psychology, bioinformatics, as well as other specialty areas, such as emergency medical services, anesthesiology and regenerative medicine.

An important advantage of the Consortium is the ability to identify trauma patients during the very initial phases of treatment and follow them forward in time through their hospital care, rehabilitation, and reintegration back into everyday life with the goal of identifying opportunities for intervention along the complete continuum of care.

A Coordinated Approach to Ensure Quality Research: METRC is anchored by a Data Coordinating Center housed at one of the premier schools of public health in the Country. The Coordinating Center ensures that study protocols are appropriately designed and executed by providing essential expertise in protocol development; data management and analysis; regulatory oversight; and data quality control. It supports a web-based data entry system, develops and maintains case report forms, maintains data quality assurance procedures, and prepares performance and safety reports for interim monitoring by the METRC Data Safety Monitoring Board.

A Gaps-Driven Approach to Defining our Research Agenda: The Consortium is dynamic and responsive to evolving clinical challenges and the evaluation of promising new therapies of benefit to the wounded warrior and trauma patients more generally.

A close collaboration with our military colleagues helps maintain a focus on clinical questions of relevance to combat casualties. The METRC research agenda focuses on seven priority problem areas in limb trauma care. The identification of these areas was guided by the focus areas prioritized by the DoD's Peer Reviewed Orthopaedic Research Program and the Extremity War Injury Symposia work products. These priorities guide the work of the METRC Steering Committee, which approves study protocols and conducts essential oversight of research activities.

A Sustainable Approach: METRC works to mentor young surgeons and rehabilitation specialists in the design and conduct of clinical trials. The consortium is also building partnerships with basic scientists and engineers so that the field will have the capacity to facilitate the translation of new and emerging technologies into clinical practice. The infrastructure in place at the Coordinating Center and the Core centers enables us to compete successfully for grants to support studies that address priority areas for the Consortium. To date, METRC has been successful in obtaining over $18 million in funding from the DoD and the National Institutes of Health to conduct ten studies in addition to those funded by the core METRC grants.

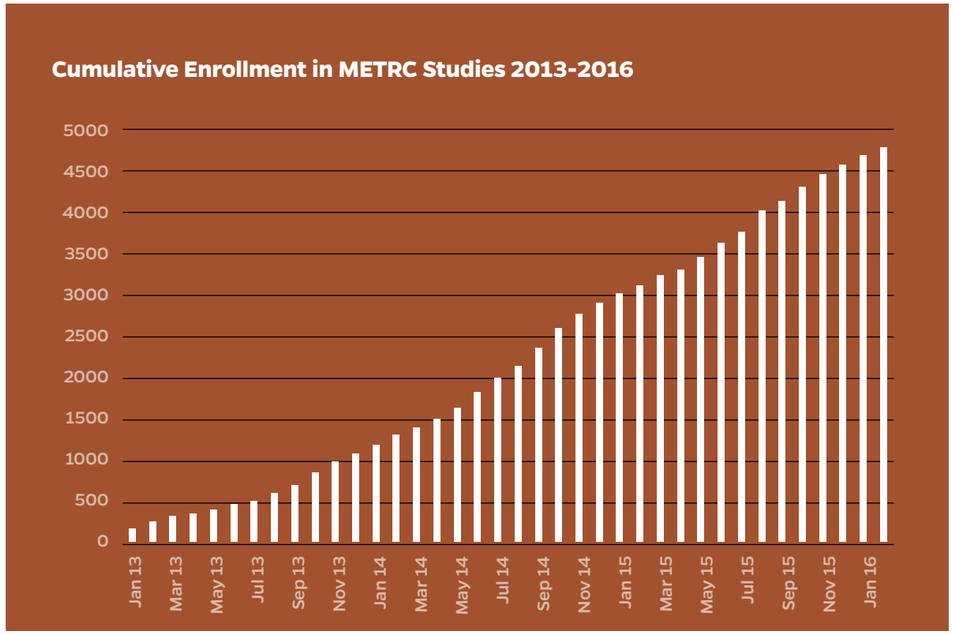
METRC Clinical Centers

The backbone of the Consortium consists of a dedicated group of core and satellite clinical centers located throughout the United States. They represent several regions of the country and are located in over 25 states.

The core centers include the 4 Military Treatment

The work of the METRC Consortium is guided by six overarching objectives.

1) Develop and maintain a research agenda in orthopaedic trauma and rehabilitation that directly responds to the needs of patients, clinicians, and key decision-makers in the military, VA and civilian health care systems;
2) Foster a multidisciplinary approach that brings together teams of investigators to include surgeons, emergency medicine providers, physiatrists, physical and occupational therapists, engineers, psychologists and health services researchers to address the most pressing issues identified by the agenda setting process;
3) Design and conduct multi-center research studies aimed at improving care and outcomes through the comparative evaluation of current and promising new treatments;
4) Partner with basic scientists, engineers, and clinicians to facilitate the evaluation and translation of new and emerging technologies into clinical practice;
5) Mentor the next generation of military and civilian orthopaedic trauma surgeons and rehabilitation specialists in the design and conduct of rigorous clinical research;
6) Contribute to the science of conducting clinical trials in a challenging patient population and treatment environment.



Facilities (MTFs) that receive the majority of combat casualties:

- San Antonio Military Medical Center and the Center for the Intrepid (CFI)
- Walter Reed National Military Medical Center and the Military Advanced Training Center (MATC)
- Naval Medical Center Portsmouth
- Naval Medical Center San Diego and the Comprehensive Combat and Complex Casualty Care (C-5) Program

Also core to the Consortium are 22 civilian trauma centers. These institutions treat a high volume of major trauma patients and have a robust research infrastructure to conduct multiple studies. Together with the MTFs, they provide the Consortium with a strong scientific and operational base from which to plan and conduct studies. They contribute patients to most, if not all, studies sponsored by the Consortium.

Together, the core centers treat over 15,000 serious fractures each year, of which 79% are to the lower extremity. Nearly one quarter (22%) of all fractures are open and of these, 49% are the most severe, Gustilo Type III fractures (33 % IIIA, 12% IIIB, 4% IIIC). An estimated 400 major amputations are performed annually across the core sites.

Total Number of Fractures Treated Annually at Core METRC Sites

All upper limb fractures	**3,291**
Traumatic amputations	29
Closed fractures	2,397
Open fractures	865
Gustilo Type I or II	565
Gustilo Type III	300
All lower limb fractures	**12,141**
Traumatic amputations	201
Closed fractures	9,352
Open fractures	2,588
Gustilo Type I or II	1,235
Gustilo Type III	1,353

While ongoing commitment of these core centers is critical to success, sample size targets are not achievable for large clinical studies without involvement of many other centers – our satellite centers - that choose to contribute to METRC on a more limited basis. These centers are important for the future of the Consortium and our commitment to conducting large, adequately powered studies to definitively address important research questions.

The investigators at both core and satellite centers represent a distinguished group of clinical investigators who are deeply committed to improving the lives of our wounded warriors and civilian trauma patients.

The Johns Hopkins Bloomberg School of Public Health

The Coordinating Center at the Johns Hopkins Bloomberg School of Public Health.

METRC is anchored by a Data Coordinating Center housed in the Johns Hopkins Bloomberg School of Public Health. Staff of the Coordinating Center provide a broad range of expertise in study design, biostatistical and economic analysis, data management, statistical programming, clinical trials management and grants management, all of which are critical to the ongoing success of the consortium.

The activities of the Coordinating Center are organized around five core functions:

- Protocol Development and Implementation
- Monitoring and Quality Assurance
- Computer Support and Informatics
- Data Management and Analysis
- Finance and Administration.

Teams are formed for each study and led by one of two Associate Directors for Trial Management. These teams tap into the expertise of each of the 5 cores as needed in varying phases of protocol development, study initiation, ongoing monitoring and reporting, data analysis and study closeout.

A set of 20 Policies and Standard Operating Procedures are maintained to ensure efficient and effective processes involved in the design, implementation, monitoring and analysis of all studies. The Coordinating Center also executes subcontracts and task order agreements with all centers and manages the distribution of payments to centers based on enrollment and follow-up reports generated from the METRC patient database.

METRC is committed to efficient and high quality research design, data collection, and analysis. What makes this possible is the coordination of activities

at the Coordinating Center which emphasize the following:

Standardized Approaches to Data Collection. 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. Primary functions of the system include: registration study participants, randomization, data entry (including images), and automatic alerts when serious adverse events occur or adjudication is required. 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.

Standard Data Collection across all METRC studies

- **Patient Demographics**
- **Socioeconomic Status**
- **Usual Major Activity**
- **Health Insurance**
- **Psychosocial Predictors of Outcome**
- **Smoking History**
- **Height and Weight**
- **Co-morbidities**
- **Pre-Injury Health Status**
- **General Injury Characteristics**
- **Mechanism and Type of Injury**
- **Functional Outcomes**

What and how we collect information relevant to each of our studies is guided by a Data Standards and Data Collection Policy. Core data elements are collected uniformly across most METRC studies allowing additional analyses to address cross-cutting questions of interest in the treatment of similar injuries.

In addition to these core data elements, standard procedures for collecting data common to many studies (e.g. infection, fracture healing, and functional performance) are applied. Since an analysis of cost-effectiveness is an objective for many METRC studies, procedures for collecting and analyzing billing data and assessing lost productivity costs have also been developed.

Data Quality Assurance and Data Quality Control. Critical to the success of any multi-center trial or study is a robust data quality assurance and data quality control plan. Quality assurance involves fostering productive, shared attitudes among collaborators as well as communicating expectations regarding institutional procedures clearly and in a timely fashion. Key elements of this quality assurance plan include training and certification of study personnel involved in data collection, and their re-training or re-certification as necessary over the course of the trial.

At the time that approved master study materials are distributed, the Coordinating Center conducts extensive training on study protocol and data collection procedures. Once each clinical site has received all required regulatory approvals, the Coordinating Center certifies the site on the basis of their having demonstrated thorough understanding of the study protocol and standard operating procedures. Prior to the initiation of patient recruitment, the Coordinating Center facilitates a one-on-one training call between the participating clinical site and the Principal Investigator.

The Coordinating Center's equally robust data quality control plan is based on an extensive set of surveillance and communication tools designed to actively monitor the performance of clinical sites relative to data collection. Data quality checks and data queries are generated and reported to sites on a monthly basis. Once enrollment and follow-up are underway at clinical sites, monitors from the Coordinating Center conduct site visits during which critical data elements, reported in the trial database, are verified against medical records. If data collection issues or patterns of discrepant data are detected, the Coordinating Center works closely with the site to follow the issues to resolution.

Applying State of the Art Statistical Methods. The Coordinating Center collaborates closely with a world renowned Department of Biostatistics at the Johns Hopkins Bloomberg School of Public Health to ensure that state of the art methods are used to enhance the design, analysis and interpretation of METRC studies. Some examples of methods we continue to refine include:

- Enrolling patients into a study where they are randomized to different surgical procedures can be challenging. For this reason, several METRC studies have been designed using a comprehensive cohort design, whereby patients are first offered enrollment into a randomized controlled trial (RCT) and those who refuse are then offered enrollment into an observational study. While these studies have been powered to detect effects using data only from the RCT, METRC biostatisticians have developed methods that make maximal use of all the data and will allow current and future studies with this type of design to require fewer patients enrolled into the RCT part of the study.
- METRC biostatisticians are developing methods for analyzing staged performance outcome assessments. In such assessments, patients are given a sequence of timed performance tests to determine their maximal functioning with patients only proceeding to the next test if their time on the previous test meets a specified performance threshold.
- METRC biostatisticians are developing statistical methods for analyzing complex time-series data. In one study, time series data on continuously collected tissue oxygenation and intramuscular pressure are being used to predict the risk of developing compartment syndrome. In several other studies, times series data collected from wearable step watch monitors are being used to understand the functional performance of competing treatments.

Research Priorities And Current Studies

Areas of Focus for METRC Research

- **Early Acute Management of the Orthopaedic Injury**
- **Prevention and Management of Acute and Chronic Musculoskeletal Infections**
- **Reconstructive Surgery and Non-Surgical Management to Improve Bone Healing**
- **Prediction, Prevention, and Amelioration of Secondary Conditions and Long-Term Physical Health Effects**
- **Management of Pain and Psychosocial Sequelae**
- **Rehabilitation Interventions to Improve Functional Outcomes and Quality of Life**
- **Optimization of Prosthetic and Orthotic Device Function, Durability, and Use**

METRC is aiming to fill the gaps in orthopaedic research to improve the care and outcomes of both Service Members and civilians who sustain major orthopaedic trauma. To that end we have developed a research agenda that focuses on critical topics along the entire continuum of care, from point of injury through rehabilitation and re-integration.

Gaps in research have been identified across seven broad problem areas.

These gaps were identified in partnership with military leaders at the Department of Defense and expert clinicians who are challenged in caring for both Service Members and civilians with serious limb injuries.

METRC is currently conducting 18 clinical research studies that address some of the challenges discussed below. We will continue to seek additional funding from public and private agencies to support the METRC research agenda.

Early Acute Management of the Orthopaedic Injury

The treatment decisions made soon after the injury are critical for survival and optimal recovery from the limb trauma. Several key questions must be addressed: What is the best way to manage severe bleeding, especially those from proximal (junctional) injuries and pelvic fractures? What is the best way to minimize dangers associated with the aggressive inflammatory response of the body to these injuries? Can we develop new biomarkers that help gauge the level of these responses in ways that improve clinical decision-making?

Compartment syndrome, a phenomenon in which internal tissue swelling stops the flow of blood to an injured extremity, can present life-threatening risks soon after injury. Currently, the only way to influence the progression of compartment syndrome is to perform a fasciotomy – an operation that completely opens the injured muscle region. Is there a screening test that can identify earlier and more accurately which cases need a fasciotomy? Just as important, is there a better technique to determine the patient who does not need the additional surgery and associated risks of a fasciotomy?

The PACS Study described on page 21 is an example of METRC's work in this priority area.

Prevention and Management of Acute and Chronic Musculoskeletal Infection

Infection following severe extremity trauma is a complication that can significantly impact the prospects for a patient's long-term recovery. Strategies to diagnose, prevent and treat infection are critical to the care of the wounded warrior and civilian trauma patient. Currently, METRC has four studies under way that are looking at ways to prevent infections and/or minimize their dangers.

The goals in these projects range from developing a better understanding the bacteria that are present on the patient's wounds at the time of tissue closure and the relationship of these bacteria to later infections … to evaluating new ways to prevent infection … and evaluating the effectiveness of different approaches to treating infections with antibiotics.

These studies include BIOBURDEN (description on page 20), OXYGEN (page 23), VANCO (page 24) and POvIV (page 23).

Reconstructive Surgery and Non-Surgical Management to Improve Bone Healing

Extremity and pelvic injuries often involve collateral damage to a patient's skin, muscle, arteries, nerves, and bones. This damage can be so extensive that reconstructive surgery is necessary, but questions abound when it comes to identifying best practices in this area.

What are the best ways to help patients recover from the loss of bone, muscles, nerves, and cartilage? Can we improve results here through a more detailed understanding of the way nerves and muscles facilitate and coordinate limb functioning? Are there novel clinical strategies that could prevent or delay the onset of major complications—in both the short and long-term?

METRC studies under way in this area include pTOG (description on page 20), FIXIT (description on page 20), OUTLET (page 21), and NERVE [page 25).

Prediction, Prevention, and Amelioration of Secondary Conditions and Long-Term Physical Health Effects

Patients often endure long-term limitations in joint motion and other physical functions in the wake of extremity injuries. They are also at elevated risk for trauma-related arthritis and long-term physical health problems such as obesity, cardiovascular disease, and osteoporosis.

Projects in this priority area will take a long view at the health and physical well-being of patients. Can we develop new strategies that keep patients clear of soft-tissue contracture and heterotopic bone formation, which are associated with decreased joint motion? Are there ways to prevent or delay the onset of arthritis? How big a problem is obesity and heart disease among these patients later in life? What strategies might bring those numbers down?

METRC studies under way in this area include PTOA (description on page 22) and METALS II (page 24).

Management of Pain and Psychosocial Sequelae

Pain control and addressing the psychosocial needs of patients following severe trauma are a crucial part of any treatment plan involving severe limb injuries. Research has shown that early problems with pain management are related not only to poor outcomes in physical functioning but also to psychological distress. Research has also shown that psychologic conditions, particularly post-traumatic stress disorder (PTSD) and depression, as well as lack of social support and poor coping skills can result in poor outcomes, even for those who do not suffer from clinical complications.

Can the early use of novel multi-modal pharmacology strategies in concert with supportive and behavioral therapy help control pain while minimizing the risks of opioid addiction and abuse? Can we better identify early on which patients are at risk for depression and post-traumatic stress? Which interventions are most effective for those patients in order to improve their ability to cope with these injuries?

METRC studies under way in this area are PAIN (description on page 22) and TCCS (page 22).

Rehabilitation Interventions to Improve Functional Outcomes and Quality of Life

The dose, timing, frequency, duration, and intensity of rehabilitation interventions are not currently based on evidence coming from well designed studies. For instance, despite significant clinical advances in the fixation of fractures, there is little data on the optimal time to start weight bearing to maximize the recovery of leg strength. Finding new ways to accelerate the recovery of leg strength will be important in getting service members back to full duty sooner; decreasing time to return to duty after surgery is critical to maintaining the fighting force.

Two related areas in need of research are psychology-enhanced physical therapy and regenerative rehabilitation. Strategies employing the former may be able to decrease the pain catastrophizing and fear of movement experienced by many patients. Innovations in the latter will become increasingly important as the use of regenerative medicine takes hold in the field. The new treatments that evolve will need to be paired with new rehab protocols in order to optimize the recovery process.

Concepts from the emerging field of individualized medicine will be important here as well. What are the best ways to tailor rehabilitation strategies to the specific condition and situation of a given patients, rather than relying on traditional practices developed according to an old one-size-fits-all model?

The REPAIR study (description on page 25) is an example of a METRC project in this area.

Optimization of Prosthetic and Orthotic Device Function, Durability, and Use

Advances in prosthetics and orthotics will continue to offer opportunities for improved function for both amputation and limb salvage patients. Osseous integration, a promising new strategy for prosthetic attachment to a residual limb, is expected to win FDA approval for use in the United States in the near future. Already used in Europe and Australia, osseous integration could have a significant positive impact on the future treatment of wounded warrior amputees, but well-designed prospective studies will be needed to understand all of the risks involved and to identify which patients are best suited to it.

Research on amputee care suffers from a recurring problem—the absence of a standardized and reliable measure for the proper fit and alignment of prosthetic devices. A current METRC research project is looking to fill that gap.

It is important to keep in mind, however, that severe extremity trauma is most commonly treated with limb reconstruction, not amputation. Often, this approach involves the acceptance of long-term limitations in joint motion and strength. Exciting new research is evaluating how the latest prosthetic technology can be adapted to enhance functioning for these patients as well.

METRC studies under way in this area are TAOS (description on page 21), ProFit, (page 21), and PRIORITI (page 24).

Spanning the Gaps: New and Refined Clinical and Functional Outcome Measures

A cross cutting theme to all the research METRC does is the development of new and refined measures of both clinical and functional outcome needed to advance the field of orthopaedic and rehabilitation research. While several measures now exist, few have been validated for major extremity trauma. In addition, many of the measures are not designed to adequately assess the ability to perform physically demanding activity as would be required for return to active duty or engagement in vigorous sports and recreational activities that contributes to the overall quality of life for many of the injured. Equally important is the application of these measures in real-time clinical practice so this information can be used to inform clinical decision making and modify treatment plans.

A METRC study that speaks directly to this cross-cutting theme is STREAM (description on page 23).

METRC Study Summaries

The **BIOBURDEN** Study aims to provide surgeons with more reliable and actionable information about the bacteria content, or "bioburden," of severe extremity wounds at the time a wound is closed or covered. Many surgeons have come to doubt the usefulness of traditional tissue culture reports, which are based on twenty-plus-year-old methodologies. This study will compare those reports with tissue-sample analyses based on new polymerase chain reaction (PCR) technologies. Researchers will also look for relationships between the pathogens present at wound coverage/closure and infections that arise later in 25 to 40 percent of cases. The usefulness of current antibiotic strategies will be evaluated as well.

- 39 trauma centers are participating in the study
- 705 patients have been enrolled (78% of eligible)
- We have reached our target sample size; enrollment is complete
- 69% of participants have completed the final 12 month follow-up
- Sponsor: DoD OETRP W8XWH-09-2-0108

The **FIXIT** Study aims to determine which of two surgical treatments is more effective for patients with severe (Gustilo Type IIIB and selected Type IIIA) open tibia shaft or metaphyseal fractures. One-half of the study's patients is randomized to receive internal fixation with intramedullary nails or plates. The other half is randomized to receive external ring fixators. Patients who refuse randomization are offered the opportunity to participate in a prospective cohort study. This study will compare 12 month rates of re-hospitalization for major limb complications between the two treatment groups. The study will also compare functional outcomes, patient satisfaction and one-year treatment costs between the groups.

- 31 trauma centers are participating in the study
- 203 patients have been enrolled in the RCT (48% of eligible); 154 patients have been enrolled in the observational study (36% of eligible)
- We have reached 90% of our target sample size
- 62% of participants have completed the final 12 month follow-up
- Sponsor: DoD OETRP W8XWH-09-2-0108

The **pTOG** Study looks at whether a manufactured bone-graft substitute (rhBMP-2) is as effective as traditional bone grafts taken from the patient's hip bone in the treatment of open tibia fractures with a large bone gap (circumferential bone defect of at least one centimeter comprising at least 50% of the circumference). Eligible patients requiring a bone graft are randomized to one of these two treatments. The study will compare the rates of bone healing, infection, physical function and one-year treatment costs between the two groups.

- 14 trauma centers are participating in the study
- 32 patients have been enrolled (62% of eligible)
- We have reached 64% of our target sample size
- 63% of participants have completed the final 12 month follow-up
- Sponsor: DoD OETRP W8XWH-09-2-0108

The **OUTLET** Study evaluates outcomes following treatment of severe foot and ankle injuries that involve major soft tissue damage and/or bone loss. The goal of this study is to identify the types of injuries that would have better outcomes had they been amputated instead of salvaged. This information will help clinicians and patients make better treatment decisions in the future. This study will assess self-reported function, physical performance and return to normal activities including work and active duty 18 months after injury.

- 35 trauma centers are participating in the study
- 664 patients have been enrolled (80% of eligible)
- We have reached our target sample size; enrollment is complete
- 39% of participants have completed the final 18 month follow-up
- Sponsor: DoD PRORP W81XWH-10-2-0090

The **TAOS** Study is a randomized trial comparing outcomes of patients that need a transtibial amputation. Patients are randomized to have an amputation using the standard posterior flap method, known as the Burgess procedure, or to have an amputation that involves a tibia-fibula bone bridge called the Ertl procedure. Patients who refuse randomization are offered the opportunity to participate in an observational study. This study will compare the number of revision surgeries and limb function 18 months following amputation. This study will also look at physical performance following amputation and overall treatment cost.

An ancillary study **(ProFit)** aims to validate and refine an objective assessment of prosthetic fit and alignment through the evaluation of photos, video and radiographs collected as part of the TAOS trial. There are currently no validated measures of fit and alignment of these prosthetic devices—factors known to impact the comfort, functioning, and overall outcomes of amputees.

- 26 trauma centers are participating in the study
- 59 patients have been enrolled in the RCT (43% of eligible); 43 patients have been enrolled in the observational study (31% of eligible)
- We have reached 35% of our target sample size
- 15% of participants have completed the final 18 month follow-up
- Sponsor: DoD PRORP W81XWH-10-2-0090 (TAOS); DoD PRORP W81XWH-14-1-0563 (ProFit)

The long term objective of the **PACS** Study is to develop a tool that will help clinicians make a timely and accurate diagnosis of acute compartment syndrome (ACS), a complication associated with some traumatic injuries in which severe internal tissue swelling can stop the blood flow to part of an injured extremity. Physicians do not currently have a reliable test to determine if ACS is present and whether to perform a fasciotomy (an invasive operation that completely opens the injured muscle region) to correct the condition. As a result, some patients end up undergoing operations they may not have been needed, and some patients end up with

long term problems because they did not get the needed operation. This study will specifically look at the usefulness of data available in the first 48-72 hours of injury in predicting the likelihood of ACS. These data include 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).

- 4 trauma centers are participating in the study
- 196 patients have been enrolled (33% of eligible)
- We have reached our target sample size; enrollment is complete
- 84% of participants have completed the final 6 month follow-up
- Sponsor: DoD PRORP W81XWH-10-2-0090

■ The **PAIN** Study examines whether additional pain medication administered during the period surrounding surgery for severe limb fractures can improve pain control and pain-related outcomes without increasing the adverse side effects associated with these medications. Patients with isolated fractures of the ankle, tibia, femur, or humerus are randomized into one of three groups and receive a placebo or one of two classes of analgesic therapy (nonsteroidal anti-inflammatory drugs or gabapentin) in addition to standard pain-management care. Researchers will be evaluating pain, complications, and the incremental cost effectiveness associated with each option.

■ A subset of patients in the Pain Study were enrolled into the **PTOA** study, which aims to lay the foundation for the next generation of prevention and treatment strategies for post-traumatic osteoarthritis (PTOA) and chronic pain. By following patients for up two years after they undergo fracture reduction surgery, researchers are looking to validate a potentially important new measure of fracture severity which correlates strongly with the development of PTOA.

- 22 trauma centers are participating in the study
- 226 patients have been enrolled (31% of eligible)
- We have reached 46% of our target sample size
- 9% of participants have completed the final 12 month follow-up
- Sponsor: DoD PRORP W81XWH-10-2-0090 (PAIN); NIH NIAMS R21AR061808 (PTOA)

■ The **TCCS** Study is looking at the effectiveness of a program called Trauma Collaborative Care (TCC) in helping patients with a severe extremity injury deal with their pain and other stressors that often follow trauma, such as PTSD and depression. The goal is to help these patients succeed at returning to pre-injury levels of activity. The intervention being evaluated is multi-modal. Patients are provided with access to a stand-alone program, the Trauma Survivors Network, which provides information and peer support; providers are given training to help their patients access services in the network; and dedicated "recovery coaches" work with patients to motivate their use of the network and to facilitate communication between them and their providers.

- 12 trauma centers are participating in the study
- 906 patients have been enrolled (61% of eligible)
- We have reached our target sample size; enrollment is complete
- 89% of participants have completed the final 12 month follow-up; follow up is complete
- Sponsor: DoD PRORP W81XWH-10-2-0090

■ The **STREAM** Study is looking at the potential of the Patient-Reported Outcomes Measurement Information System (PROMIS) in the orthopaedic trauma setting. The PROMIS tools use computer adaptive testing to provide concise measurement of respondent function. If the tools are validated in this population, clinicians will be able to use these brief, easily administered, standardized instruments to evaluate the status of patients at clinic visits and respond to problems that surface during recovery and rehabilitation.

- 47 trauma centers are participating in the study
- 556 patients have been enrolled (79% of eligible)
- We have reached 56% of our target sample size
- 28% of participants have completed the final 12 month follow-up
- Sponsor: NIH NIAMS R01AR064066

■ The **Oxygen** Study will evaluate whether receiving supplemental oxygen during the perioperative period before and after surgery can help patients avoid surgical-site infections after undergoing plate and screw fixation for high-energy calcaneus, pilon, or tibial plateau fractures. Researchers will also be comparing the types of bacteria present in patients who received the supplemental oxygen with those who did not in order to ensure this novel treatment does not exchange fewer infections for more serious ones. A final goal of this project is to validate a new method of predicting the risk of post-operative infections in this population.

- 19 trauma centers are participating in the study
- 477 patients have been enrolled (51% of eligible)
- We have reached 48% of our target sample size
- 41% of participants have completed the final 12 month follow-up
- Sponsor: DoD PRORP W81XWH-12-1-0588

■ The **POvIV** Study is comparing two ways of treating infections that can occur after a fracture fixation or fusion of a joint. Patients are randomized into two groups, one receiving standard regimens of intravenous antibiotics and the other receiving oral antibiotics that have the potential to be just as effective with fewer complications and lower costs. Patients who refuse randomization are offered the opportunity to participate in an observational study. Researchers will be evaluating the rate of surgical interventions, re-hospitalizations, and the incremental cost effectiveness associated with the two types of treatment in the year following the acute infection.

- 21 trauma centers are participating in the study
- 99 patients have been enrolled in the RCT (31% of eligible); 46 patients have been enrolled in the observational study (14% of eligible)
- We have reached 37% of our target sample size
- 37% of participants have completed the final 12 month follow-up
- Sponsor: DoD PRORP W81XWH-10-2-0133

■ The **VANCO** Study will evaluate the efficacy of the application of local vancomycin powder in the prevention of surgical site infections in patients who undergo plate and screw fixation for high-energy pilon and tibial plateau fractures. Researchers will look at whether and how local treatment affects the antibiotic sensitivities of the bacteria in patients who do develop infections. The researchers will also use the data to develop a more robust model for predicting infection risk in this population.

- 34 trauma centers are participating in the study
- 302 patients have been enrolled (65% of eligible)
- We have reached 30% of our target sample size
- 21% of participants have completed the final 6 month follow-up
- Sponsor: DoD PRORP W81XWH-10-2-0134

■ The **PRIORITI-MTF** Study is examining the benefits of an integrated orthotic and rehabilitation program that incorporates the Intrepid Dynamic Exoskeletal Orthosis (IDEO™) and the Return to Run (RTR) physical therapy program for service members and veterans who had a serious leg injury 2 or more years ago. The IDEO™ is custom-fit to each patient and incorporates a strut that acts as a spring and energy storing device, which is meant to help re-create power in the muscles of the lower leg and ankle. It is anticipated that use of the IDEO™ will improve function and reduce pain in the long run. Researchers will be evaluating the cost-effectiveness of IDEO™ as well as its scalability to military environments beyond its point of origin, the Center for the Intrepid at the San Antonio Military Medical Center.

- 3 military treatment facilities are participating in the study
- 91 patients have been enrolled (92% of eligible)
- We have reached our target sample size; enrollment is complete
- 2% of participants have completed the final 12 month follow-up
- Sponsor: DoD TATRC W81XWH-12-2-0032

■ The **METALS II** Study builds on the earlier METALS I study, which examined data on outcomes of Service Members who underwent either amputation or limb salvage after experiencing major limb trauma in Iraq and Afghanistan. METALS II will follow these same individuals 6-8 years out from their injury and bring new patients into the overall analysis. The aim is to use these longitudinal data to understand and compare the clinical, functional and mental health consequences of amputation and reconstruction in a military population. The study will also look at where patients accessed support services and whether they encountered obstacles that kept them obtaining the services they needed.

- 2 military treatment facilities are participating in the study
- The study protocol is under development
- Target sample size is 1,147 (429 cohort 1; 718 cohort 2); enrollment has not yet begun
- Sponsor: DoD PRORP W81XWH-15-2-0058

■ The **NERVE** Study aims to capture data on the treatment and outcomes of peripheral nerve injuries in the upper extremity. Little is known about the volume and impact of these injuries, and there are no evidence based guidelines to inform their treatment. This study will gather detailed information about different types of injuries, their treatment and outcomes following treatment across multiple trauma centers, which will be used to design future clinical trials comparing the efficacy of these treatment approaches.

- 15 trauma centers are participating in the study
- The study protocol is under regulatory review
- Target sample size is 450; enrollment has not yet begun
- Sponsor: DoD PRORP W81XWH-15-2-0074

■ The **REPAIR** Study is testing a physical therapy (PT) regimen that aims to help patients build muscle strength and endurance after suffering lower leg limb trauma. Many of these patients are unable to reach exercise intensity levels needed to achieve the gains they need and want to make, especially early on in their recoveries. The new PT strategy being studied here involves the use of a tourniquet to restrict arterial inflow and venous outflow to the limb while exercising. This has been shown in other settings to help patients build muscle and endurance even at low-intensity levels. Following treatment for a closed diaphyseal femur fracture, participants in the REPAIR study will be randomized to either a usual care PT program or to a PT program with blood flow restricted training. Muscle strength and muscle volume will be compared, as will functional outcomes.

- 8 trauma centers are participating in the study
- The study protocol is under regulatory review
- Target sample size is 250; enrollment has not yet begun
- Sponsor: DoD PRORP W81XWH-15-2-0067

After falling off a ladder, Officer O'Neill presented with a comminuted, open displaced fracture of his calcaneus with a large medial wound and exposed bone.

Controlling the pain

THE SECOND TIME he fell, Tim O'Neill wasn't so lucky. The 48-year-old police officer had emerged unscathed in the summer of 2012 after tumbling from a ladder at his home in Strongsville, OH, though he did put an elbow through the gutter on his way down.

"For the next two years I got to look at that bashed in piece of gutter every time I came up the driveway," he says with a laugh.

Fast forward to June 27, 2014. Looking to fix that gutter at last, O'Neill grabbed a rickety old aluminum ladder that, he admits ruefully, "I never, ever should have been using." This time, he landed at an awkward angle on his left foot. He knew immediately that he couldn't get up. He lay waiting until a passerby heard him call out.

The first hint that this second fall was a very serious affair came when an emergency room physician ordered him transferred to the regional Trauma Center. There, when physicians forcibly pushed his blown-out heel back into place, O'Neill felt pain like he'd never felt before.

He had an open fracture of the calcaneus, his heel bone, and he had destroyed the critical subtalar joint that connect his heel and his ankle. The first surgery was all about stabilizing his leg. The second one focused on reconstruction.

But the prognosis was still discouraging. He might never run again. He would have trouble walking on uneven surfaces. Arthritis would likely be a problem sooner rather than later.

O'Neill is not the sort of patient to sit back and accept such predictions. The surgeons who had operated on his back a few years before had advised him to transfer into a desk job at the Westlake Police Department or find a new line of work. Six months later, O'Neill was back out on patrol.

But this new prognosis proved a tougher nut to crack. A year into his rehab, he was still walking with a limp and feeling a lot of pain.

In the fall of 2015, O'Neill underwent a third surgery, a subtalar fusion. By forcing two bones to heal together in the heel at a point where they used to be connected by a joint, surgeons hoped to lessen O'Neill's pain, even if his mobility remained limited.

O'Neill is participating in the METRC-sponsored PAIN Study. In this study, researchers are comparing three different pain management strategies in the "perioperative" period just before and after an operation. Two of those strategies add a regimen of pain-relieving analgesics on top of standard pain management care. The four-year study of 500 patients is in process

He also liked METRC's core mission of helping wounded warriors.

◄ **Police Officer Timothy O'Neill is on restrictive duty and hoping to return to full time patrol duty.**

Controlling the pain

at 21 trauma centers around the country.

O'Neill says he had no qualms about signing up as a research subject. He had worked on a couple of research-related assignments during his college years and remembered how hard it was to recruit volunteers. He also liked what he heard about METRC's core mission of helping wounded warriors.

"There are a couple of guys I work out with who went through a lot overseas," O'Neill says. "I know there are guys out there working on their injures who have some emotional stuff to deal with on top of everything else. It's the kind of thing that makes me realize, 'What do I have to complain about?'"

The early results on that third surgery have been encouraging, O'Neill reports. He stayed off of his left leg for three full months, but he feels like he is on the road to a fuller measure of recovery at last. He is in the gym for one to two hours a day now, and footwork is an important part of his regimen during every workout.

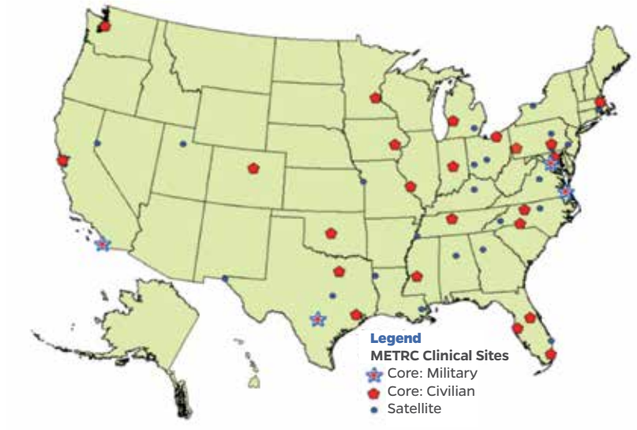
O'Neill remains hopeful that this recovery will end in a return to patrol duty on the job, but whether that works out in the end or not, he is confident the quality of his life over the long haul will be better than it would have been without that last surgery.

O'Neill has been participating in the METRC-sponsored PAIN Study which compares three pain management strategies in the periods just before and after an operation.

"Lifting weights is a good example," he says. "It's one of the things I enjoy doing most in life, and I can tell now that I'm going to be able to keep doing it for a long time to come. Before, I wasn't so sure."

Officer O'Neill was treated urgently with debridement and irrigation and temporary fixation with wires. This photograph depicts his wound 2 days later when he returned to the OR for definitive management of his fracture. The radiographs show intraoperative images obtained at that time.

METRC core sites



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Mark Richardson and Dr. Anna Miller, MD, at Wake Forest University Baptist Medical Center, one of METRC's Core Civilian Sites.

Looking Forward

THE COMING YEAR promises to be an exciting one for METRC as many of the studies will be presented to the medical community and begin to impact patient care. This will represent a new phase in the development of our consortium. As our work moves out of the study phase, it will reach the bedside, guiding clinical decisions and informing best practices.

We plan to continue to cultivate new research projects that tackle our priority problem areas and build on the evidence being gathered in current research. Under consideration are studies that would address several of our prioritized problem areas.

- Evaluate the use of patient-specific measures of magnitude of, and response to, injury in guiding surgical decisions in multiply injured patients (MIPs) with major skeletal trauma;
- Evaluate short-term outcomes of pelvic ring disruptions requiring advanced resuscitation. Of interest is the effectiveness (and timing) of circumferential pelvic compression and, in patients with hemorrhage, resuscitative endovascular balloon occlusion of the aorta (REBOA);
- Compare early versus delayed weight bearing for young adult patients with a closed ankle fracture without syndesmotic fixation;
- Compare outcomes and onset of post-traumatic osteoarthritis following screw retention vs. screw removal for treatment of ankle fractures with injury to the syndesmosis;
- Examine the effectiveness of advanced early weight bearing progression using the Alter-G anti-gravity treadmill compared to standard of care physical therapy following surgical treatment of a periarticular fracture about the knee or distal tibia (pilon);
- Test the efficacy of a phone-based cognitive-behavioral based physical therapy (CBPT) program for managing pain in service members and civilians at-risk for poor outcomes;
- Develop and validate a computer adaptive testing (CAT) based instrument to measure resiliency and reintegration for orthopaedic trauma;
- Pilot a home-based exercise physical therapy (PT) program in MTFs and civilian centers and determine which patients can rehabilitate independently without formal outpatient PT;
- Pilot the long-term follow-up of over 3,000 patients who were enrolled in METRC studies to estimate the prevalence of secondary physical health effects and determine factors related to the risk of developing a secondary health effect.

Summaries of ongoing studies are always available at www.METRC.org.

METRC provides the platform to ensure that military–civilian collaboration is maintained and strengthened. Securing the capability of such a research network is critical if we are to continue to advance the science that will make a difference in the lives of our wounded warriors and civilian trauma patients, some of whom you learned about in this report. We thank them and the nearly 5,000 other study participants who have already volunteered their time and experience so we can do better in the future.

We are particularly grateful to our wounded warriors for their service and commitment and their eagerness to improve the care of future combat casualties.

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