The Trauma-Related Infections Research Area is part of the Infectious Disease Clinical Research Program based at the Uniformed Services University of the Health Sciences, Department of Preventive Medicine and Biostatistics. There are three primary research protocols: 1) Trauma Infectious Disease Outcomes Study (TIDOS); 2) Trauma-Associated Osteomyelitis; and 3) Invasive Fungal Wound Infection (IFI) Molecular Diagnostics.

TIDOS is the centerpiece protocol of the Trauma-Related Infections Research Area and involves investigators from a variety of disciplines, including infectious disease, trauma surgery, orthopedics, surgical pathology, epidemiology, statistics, microbiology, molecular biology, and immunology. Both TIDOS and Trauma-Associated Osteomyelitis are made possible through the cooperative research of investigators and personnel across multiple clinical sites, including the Uniformed Services University of the Health Sciences, Walter Reed National Military Medical Center, San Antonio Military Medical Center, Landstuhl Regional Medical Center, and the St. Louis Veterans Affairs Medical Center. In addition, TIDOS includes collaborations with the U.S. Army Institute of Surgical Research, Walter Reed Army Institute of Research, Naval Medical Research Center, and the United Kingdom Wound Infection Surveillance Programme. The IFI Molecular Diagnostics protocol also includes collaborations with the DoD Joint Pathology Center and the University of Texas Health Science Center at San Antonio.

TIDOS is supported by the U.S. Navy Bureau of Medicine and Surgery (BUMED) Wounded, Ill, and Injured Program (WII), the National Institute of Allergy and Infectious Diseases (NIAID), the DoD Global Emerging Infections Surveillance and Response System (GEIS), the Military Infectious Diseases Research Program (MIDRP) through the Defense Health Program, and U.S. Army Defense Medical Research and Development Program (DMRDP) funding. Trauma-Associated Osteomyelitis is supported by BUMED WII and NIAID. The IFI Molecular Diagnostics protocol is supported by DMRDP.
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Overview of the
Trauma Infectious Disease Outcomes Study

Advances in battlefield surgical practice and technology resulted in a higher rate of survival following deployment-related traumatic injuries during Operations Iraqi Freedom and Enduring Freedom. As a result, the number of complex polytrauma cases managed in military treatment facilities increased dramatically. Infection is a complication of battlefield injuries that can lead to significant morbidity and mortality. In addition, infections due to multidrug-resistant organisms are common in this population, necessitating broad-spectrum antibiotic coverage, which in turn, is likely contributing to their increasing prevalence. Furthermore, a large portion of the war wounded patients sustained blast-related trauma (often while dismounted), resulting in traumatic/surgical amputations, multiple surgeries, and prolonged courses of antibiotics for wound infections. Treatment of these infections is both clinically challenging and resource intensive. The burden and long-term impact of these infections is poorly understood and coupled by a lack of evidence-based practice guidelines for clinicians managing these infections.

The Departments of Defense (DoD) and Veterans Affairs Multicenter Cohort Study evaluating Infection-Associated Clinical Outcomes in Hospitalized Medical Evacuees following Traumatic Injury (TIDOS) was developed with the following objectives:

- Establish a cohort of DoD beneficiaries and active-duty personnel with trauma-related injuries to determine short- and long-term outcomes and potential risk factors associated with infections.
- Describe the infectious disease epidemiology of trauma-related injuries or other nosocomial infections in the cohort population.
- Establish a database and bacterial / fungal isolate repository to support future approved sub-studies focused on informing clinical management, disease prevention, or clinical trial design.
- Inform DoD efforts to develop real-time tools for combat-related health event/outcome analysis secondary to trauma-related infections during wartime.

The eligible study population included DoD beneficiaries and active-duty personnel receiving inpatient treatment at a participating tertiary care facility for a traumatic injury experienced during an overseas deployment. The observational cohort design targeted informed consent and enrollment prior to discharge or transfer during a subject’s initial hospitalization at a participating site in the United States (Walter Reed National Military Medical Center and San Antonio Military Medical Center). The longitudinal follow-up period for each subject was estimated at approximately five years. Trauma history, post-injury hospital management, potential risk factors associated with infections, and clinical outcomes were determined for the cohort study using various follow-up approaches (as appropriate): in-person and telephonic interviews, interaction with healthcare providers, medical record review, and query of electronic healthcare databases (such as the DoD Trauma Registry or the National Department of Veterans Affairs Healthcare Databases).
Letter from the Trauma-Related Infections Research Area Director

The Trauma-Related Infections Research Area has had another successful year marked by multiple accomplishments. In particular, following the closure of the Trauma Infectious Disease Outcomes Study (TIDOS) enrollment period in January 2015, our team undertook a massive effort to comprehensively review and finalize the 5-year TIDOS dataset, and analyses utilizing this dataset are already underway. We also continued to improve characterization of extremity wounds to refine in-depth analyses that will support practice guidance recommendations related to the prevention and management of infections. Furthermore, multiple analyses under the TIDOS Multidrug-Resistant and Virulent Organisms (MDR/VO) Initiative, a collaborative effort to maximize understanding of complex polytrauma (and polymicrobial) wounds, were completed and additional analyses are in development. These investigations include examining the interaction of wound bacteria (e.g., Enterococcus spp.), assessing clinical relevance of difficult-to-treat pathogens, and evaluating biofilm dispersal agents.

As part of the Invasive Fungal Wound Infection (IFI) Molecular Diagnostics study, the TIDOS registry of IFI patients was reviewed and updated. Data abstraction of medical records and operating room notes allowed for detailed examination of data on the level of the IFI wound. A retrospective study of archived tissue specimens is underway and anticipated to be completed in early 2017. Collaboration with the DoD Joint Pathology Center to perform a blinded review of archived specimens is also ongoing. These analyses will allow critical assessment of diagnostic techniques with eventual translation of validated methods for future clinical use within U.S. military hospitals.

There has also been a great deal of progress with the Trauma-Associated Case-Control Osteomyelitis Study. In particular, we have completed the case-control risk factor and case-case analyses related to open tibia and femur fractures. For the arm long bones, a case-control analysis and case series were completed. These studies have identified risk factors for the development of osteomyelitis with open fractures, as well as examining characteristics associated with osteomyelitis cases and recurrent episodes of the disease. Data abstraction through the VA is ongoing with completion planned in 2017, which will provide further follow-up assessment and allow an investigation of comorbidities and economic impact.

In 2017, TIDOS analyses will continue to focus on extremity wound infections, wound microbiology, and effectiveness research. New collaborations with USAISR Military Orthopaedic Trauma Registry are being discussed, which have the potential for more detailed analyses. Additional studies involving our updated IFI case registry are also in development.

Our aims and objectives remain high priorities for military medicine and continue to have significant clinical relevance during inter-war periods for the purpose of improved understanding and care of wounded personnel, and to enhance efforts with evidence-based approaches for the next conflict.

Lastly, I would like to congratulate Lt Col Heather Yun for receiving the American Society of Federal Health Professionals (AMSUS) Conference 2016 Military Medicine Article of the Year award for her TIDOS investigation on healthcare-associated pneumonia.

David R. Tribble, MD, DrPH
Science Director, IDCRP
Director, Trauma Infections Research Area
Scientific Strategic Plan for Trauma-Related Infections

The Infectious Disease Clinical Research Program has focused efforts on evaluation and development of new treatment strategies for combat-related trauma infectious complications. Infections in these complex wounds remain a major challenge, requiring well-designed clinical research in the areas of prevention and management. Treatment strategies have been complicated by the emergence of multidrug-resistant bacterial organisms and aggressive new threats, such as invasive molds. Furthermore, infections of the bone or on rehabilitative/restorative hardware may recur at a much later date.

Five research aims have been identified that, if accomplished, will advance Trauma-Related Infections in the desired direction, in line with IDCRP’s overall mission, vision and goals.

**Aim 1:** Describe the clinical characteristics, risk factors, and clinical outcomes among infections complicating deployment-related injuries, particularly associated with combat trauma

**Aim 2:** Evaluate short- and long-term health impacts (quality of life, healthcare utilization, and cost) of combat-related infections

**Aim 3:** Assess novel diagnostic modalities and biomarkers for traumatic wound-related infection

**Aim 4:** Evaluate existing and new therapies for treatment or prevention of trauma-related infections with focus on emerging and multidrug resistant organisms

**Aim 5:** Compare clinical outcomes and antibiotic exposure to specific microbiologic pathogenicity factors such as clonal patterns, resistance mechanisms, and/or additional genotypic/phenotypic characteristics in colonizing or infecting organisms isolated from trauma patients

Within each of the different trauma-related study protocols, a great deal of progress has been made to complete these research aims.

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<th>Protocol</th>
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<td>Femur analyses completion</td>
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Blast-Related Trauma and Wound Infections

Explosive blast results in grievous injuries with high morbidity and potential long-term infectious complications. Approximately 25% of blast trauma patients developed at least one infection during their initial hospitalization (Table) with a median of two infections per patient. Among blast trauma patients with infections, 69% were diagnosed with an extremity wound infection.

On 29 November through 2 December 2016, the DoD Blast Injury Research Program held their International State-of-the-Science (SOS) meeting entitled Minimizing the Impact of Wound Infections following Blast-Related Injuries. The overall goal of the meeting was to assess the current state-of-the-science on strategies to diagnose, prevent, and treat infections following combat-related blast injury. This was the first SOS Meeting on blast-related wound infections and included an Expert Panel comprised of both civilian and military clinicians. Dr. David Tribble, a member of the Expert Panel, presented information on blast wound infection rates and bacteriology from the TIDOS dataset.

Table: Frequent Infection Syndromes Among Blast Trauma Patients

<table>
<thead>
<tr>
<th>Infection Syndrome</th>
<th>Blast Trauma Patients (N=2962)</th>
<th>Median days to diagnosis post-injury (Interquartile Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Infection</td>
<td>24.7%</td>
<td>6 (3, 11)</td>
</tr>
<tr>
<td>SSTI</td>
<td>18.0%</td>
<td>8 (4, 16)</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>3.5%</td>
<td>16.5 (8, 26.5)</td>
</tr>
<tr>
<td>Bloodstream infections</td>
<td>6.7%</td>
<td>7 (4, 14)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2.4%</td>
<td>5 (3, 18)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>7.9%</td>
<td>5 (3, 8)</td>
</tr>
</tbody>
</table>

Blast-related findings from multiple TIDOS analyses on extremity wound infections, wound microbiology, and invasive fungal infections were also presented (Photos). Additional topics of presentations included the challenges related to treatment of blast wounds, DoD-sponsored research on wound infections, impact of colonization on host response and outcomes, industry considerations for anti-infective drug development, biofilms, genomics-based microbial detection, and antibiotic-resistant bacteria and treatment options.

During the meeting, attendees were split into working groups led by members of the Expert Panel to discuss key questions related to blast wound infection risk factors, candidate biomarkers for infection diagnosis and management, and infection prevention and treatment strategies. The primary themes of discussion were host and environmental factors, current treatment practices, microbiology, and data gaps. As current clinical practice guidelines focus on prevention and early wound care, it was noted that new guidelines on treatment of wound infections are needed. On the last day, the Expert Panel met in a closed session for further discussion of research priorities to improve the outcomes of patients with blast trauma.

Photos: Blast Injury SOS Meeting. Dr. David Tribble (left), Drs. Katrin Mende and Laveta Stewart (middle), and Dr. Anuradha Ganesan (right).
Extremity injuries among combat casualties are frequently complicated by infections, resulting in extended hospitalizations, significant morbidity, and mortality. During the past year, TIDOS investigators refined methodology for classifying polytraumatic extremity wounds related to the assessment of infectious outcomes. In brief, wounds were mapped to TIDOS anatomic extremity sites (i.e., upper arm, forearm, wrist, hand, thigh, knee, lower leg, ankle, and foot) using Abbreviated Injury Scale codes and injury descriptions. All wounds located at the same anatomic site and side were collapsed into one injury group and classified by the most severe wound at that site (Figure 1).

Amputation injury groups included amputations alone, amputations plus open fractures, amputations plus other open wounds, or amputations plus both open fractures and other wounds. Open fracture injury groups included fracture alone or a fracture with other open wounds. Other open wounds were defined as wounds without amputations or open fractures. Using these wound groups, combat-related extremity wound infections (CEWIs) during the first three years of TIDOS were analyzed.

Criteria for inclusion in the 3-year analysis was sustaining a combat-related open extremity injury between June 2009 and May 2012 and being admitted to Landstuhl Regional Medical Center within six days of injury. In addition, the analysis was restricted to patients who were transferred to participating hospitals in the United States.

A total of 1858 patients were admitted to U.S. hospitals with combat-related injuries, of which 1409 (76%) had at least one open extremity wound. Predominantly, patients were injured in Afghanistan (94%) and sustained severe or life-threatening injuries due to blast injuries (81%). Overall, 323 (23%) of patients had at least one infection.

A total of 5068 wounds (947 amputations, 1618 fractures, and 3043 other open wounds) were collapsed into 4342 open extremity wound groups, of which 11% had an infection. Patients with amputation wound groups had the highest proportion of infections (20%). In particular, 40% of patients with only amputations had an infection (Table). For the patients in the open fracture and other open injury wound groups, 5% and 1% developed infections.

Approximately 77% of patients with CEWIs during their initial hospitalization had organisms isolated from their infection wound sites with *Acinetobacter* spp., *Pseudomonas* spp., *Enterococcus* spp., and *Enterobacter* spp. being the most common. In addition, patients frequently had polymicrobial wound infections (64% of patients with positive cultures). Approximately 61% of the polymicrobial wounds recovered bacterial organisms alone, while 38% identified a combination of bacteria, mold, and/or yeast. Monomicrobial infections were largely the result of Gram-negative bacteria (57%).

![Figure 1: Wound location, injury group development and infection matching](image-url)
In a separate investigation, infectious outcomes were examined among 1043 combat casualties with open extremity fractures (2009 - 2014) with regards to use of different post-trauma antibiotic prophylactic regimens. The antibiotic regimens were defined as narrow if it followed DoD-directed guidance (i.e., any combination of IV cefazolin, clindamycin, amoxicillin-clavulanate with/without other antibiotics) and expanded Gram-negative coverage (EGN) if a fluoroquinolone and/or aminoglycoside was added to a narrow regimen. Approximately 56% and 44% of the patients received narrow and EGN coverage, respectively.

Understanding the complicated microbiology of CEWIs can lead to improvements in combat casualty care and infection control strategies. Analyses to evaluate the clinical outcomes of multidrug-resistant bacterial wound infections are underway. Data from the 3-year CEWI analyses were presented by Dr. Laveta Stewart at the 2016 Military Health System Research Symposium (MHSRS) and IDSA ID Week (Photo). A manuscript is in preparation.

In a separate investigation, infectious outcomes were examined among 1043 combat casualties with open extremity fractures (2009 - 2014) with regards to use of different post-trauma antibiotic prophylactic regimens. The antibiotic regimens were defined as narrow if it followed DoD-directed guidance (i.e., any combination of IV cefazolin, clindamycin, amoxicillin-clavulanate with/without other antibiotics) and expanded Gram-negative coverage (EGN) if a fluoroquinolone and/or aminoglycoside was added to a narrow regimen. Approximately 56% and 44% of the patients received narrow and EGN coverage, respectively.

Although a higher proportion of patients receiving EGN coverage sustained blast injuries (83% versus 74%), there was no significant difference in injury severity, length of hospitalization, or mortality between the groups. The proportion of patients with osteomyelitis was comparable between the antibiotic regimen groups (8% for both). Furthermore, there was also no significant difference related to the time from injury to diagnosis of osteomyelitis (Figure 2). In a Cox proportional hazard model, as well as a logistic regression model, use of a narrow prophylaxis regimen compared to EGN coverage was not a risk factor for osteomyelitis. Based on these data, use of EGN coverage with standard DoD-directed post-trauma antibiotic prophylaxis for open fractures does not convey an added benefit with regards to protecting against osteomyelitis. These data were presented by Col Bradley Lloyd at the 2016 IDSA ID Week (Photo) and a manuscript is in preparation.

<table>
<thead>
<tr>
<th></th>
<th>Any Amputation</th>
<th>Open fracture (no amputations)</th>
<th>Other open wounds (no amputations/fractures)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amputation</td>
<td>40%</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Open fracture</td>
<td>16%</td>
<td>8.5%</td>
<td>NA</td>
</tr>
<tr>
<td>Other open wound</td>
<td>4%</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Total</td>
<td>20%</td>
<td>5%</td>
<td>1%</td>
</tr>
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</table>

Total number of wound groups is 4342

Figure 2. Kaplan-Meier plot of time from injury to osteomyelitis diagnosis. Log-rank chi-square: 0.58; p=0.447

Table: Proportion of Injury Groups with ≥1 Infection

Photos: Dr. Laveta Stewart (left) and Col Bradley Lloyd (right) at 2016 IDSA ID Week
Invasive Fungal Wound Infections

Invasive fungal wound infections (IFIs) are well-recognized for having high morbidity and mortality. Early diagnosis and timely initiation of surgical/antifungal treatment is crucial to improve clinical outcomes. Over the past year, the TIDOS database has been systematically reviewed with regards to histopathological fungal evidence, mold growth from wound cultures, and antifungal chemotherapy. Following the comprehensive, large-scale effort, the TIDOS IFI Case Registry has been updated to include 95 IFI patients, of which 40 were classified as Proven (i.e., angioinvasion of viable tissue), 31 as Probable (i.e., fungal elements on histopathology without tissue invasion), and 24 as Possible (i.e., mold culture growth without histopathology).

Approximately 97% of the IFI patients were injured by a blast mechanism (~80% dismounted) with the majority sustaining critical or life-threatening injuries. In addition, 66% of patients required mechanical ventilation at both Landstuhl Regional Medical Center and the hospitals in the United States. A large-scale evaluation of the epidemiology of combat-related IFIs is underway.

Mold from the Mucorales order (e.g., Mucor, Saksenaea, and Apophysomyces spp.) and genus Aspergillus were the predominant molds identified from the IFI wound cultures. A smaller proportion also grew Fusarium spp. Nevertheless, mold etiology was unknown for a number of Proven and Probable cases, likely due to a lack of culture growth.

Clinical decision support tools related to IFIs have also been assessed through a collaborative effort between TIDOS investigators and the USU Surgical Critical Care Initiative (SC2i) team. Specifically, a web-based clinical decision tool (http://www.sc2i.org/tools/) was developed for use by clinicians in theater and after medical evacuation to Landstuhl Regional Medical Center to predict the likelihood of combat casualties developing an IFI (Figure). The tool is a Bayesian Belief Network built using trauma and clinical data from 227 combat casualties and validated using a separate dataset of 350 trauma patients. Use of this clinical tool may facilitate earlier diagnosis of patients with (or at risk for) IFIs, resulting in timely treatment and improved outcomes. A manuscript with details of the Bayesian models is in preparation.
With the high morbidity associated with osteomyelitis, examination of risk factors for developing the disease is considered high priority. Under the Trauma-Associated Osteomyelitis Study protocol, retrospective data from patients with open fractures of the tibia, femur, and long bones of the arm were examined in case-control analyses. In addition, a case-case analysis was conducted for the open fracture tibia and femur populations, while the arm long bones was assessed as a case series.

In the open tibia fracture case-case analysis, 130 patients with osteomyelitis were examined, of which there were 25 patients with either a definite or probable classification and 105 patients with a possible. The definite/probable and possible cases were not significantly different with regards to injury severity, injury mechanism, traumatic below knee amputations, initial infection symptoms (except for localized swelling), use of surgical hardware, and antibiotic management. There was also no significant difference related to timing of osteomyelitis diagnosis following injury, definitive orthopedic surgery, and radiographic union. These findings confirm that the possible classification is a valid diagnoses and should be treated definitively.

Among the 130 patients, 112 were followed for at least 30 days after resolution of the initial osteomyelitis to evaluate risk factors for osteomyelitis recurrence (i.e., new/recurrent infection at same site 30 days after initial infection was resolved). Approximately 28% of patients had an osteomyelitis recurrence. Characteristics between the patients with and without osteomyelitis recurrence were comparable, including classification of the initial osteomyelitis diagnosis (definite/probable and possible) (Figure). Bone loss and receipt of antibiotics for 22-56 days were significantly associated with osteomyelitis recurrence risk in a univariable analysis; however, no variables were retained in a multivariable analysis. Overall, risk factors associated with the development of initial osteomyelitis were not predictive of osteomyelitis recurrence.

The open femur (103 osteomyelitis cases and 64 controls) and arm long bones (64 osteomyelitis cases and 96 controls) fracture case-control studies have also been completed and significant risk factors include fracture severity, foreign body with hardware at bone site, use of antibiotic beads, muscle damage, and extensive degloving. Manuscripts with the results of the analyses are in preparation.

Under the bidirectional data use agreement with the St. Louis VA Health Care System, data abstraction was completed for over 360 patients, allowing for further assessment of follow-up data. Analyses of these data with regards to comorbidities and healthcare economics are forthcoming.

**Osteomyelitis Disease Classification**

- **Definite**: Bone culture and/or evidence of bone infection on direct examination
- **Probable**: Infection symptoms with either blood culture or radiographic evidence of infection
- **Possible**: Open fracture (or exposed bone) with contamination at time of injury, microorganism growth in deep wound tissue, and evidence of local/systemic inflammation

![Figure. Characteristics of Patients With and Without Osteomyelitis Recurrence](image)
Microbiological Analyses

Adding to the challenges related to treating complex extremity wound infections is that they are often polymicrobial and may involve multidrug-resistant organisms. As part of TIDOS, bacterial, yeast, and mold isolates collected from admission surveillance swabs and clinical work-ups (e.g., wound, blood, respiratory, and urine cultures) are retained in a microbiological repository. In an effort to comprehensively investigate the wound microbiome, TIDOS received funding from the Military Infectious Disease Research Program (MIDRP) to expand the scope of trauma-related infection microbiological studies on multidrug-resistant and virulent organisms (the MDR/VO Initiative), led by TIDOS investigator, Dr. Katrin Mende.

One objective of the MDR/VO Initiative is to assess interaction of wound bacteria, led by LTC Stuart Tyner and Rae Heitkamp. Enterococcus spp. are frequently isolated from polymicrobial wounds and have been shown to antagonize growth of other wound bacteria. Evaluation of 74 Enterococcus spp. isolates collected from polymicrobial extremity wounds (primarily from lower extremities) has been completed. Eight different species were identified with E. faecium and E. facecalis being predominant. Antimicrobial susceptibility testing of the isolates determined that while they were resistant to multiple antibiotics, vancomycin resistance was infrequent (Figure 1).

In general, patients with Enterococcus spp. isolated from wound cultures had significantly higher injury severity (80% with critical/life-threatening injuries versus 37%), sustained more traumatic amputations (81% versus 22%), and had a longer duration (>60 days) of initial inpatient trauma hospitalization (43% versus 9%).

Due to their association with persistent or recurrent extremity wound infections, evaluation of biofilm formation is another objective of the MDR/VO Initiative and is led by LTC Kevin Akers. In brief, formation of a biofilm allows pathogens to circumvent the host’s immune response and impede the effectiveness of antimicrobials. Clinical isolates (66 Acinetobacter baumannii and 74 Enterococcus spp.) collected from wounded military personnel were assessed for biofilm formation capacity with and without media supplementation of 10% human plasma (surrogate for the human wound environment). Biofilm formation and response to human plasma supplementation differed between the A. baumannii and Enterococcus spp. isolates. In particular, A. baumannii biofilm formation was significantly inhibited (83%) with human plasma supplementation, while Enterococcus spp. showed both an increase and decrease in biofilm formation.

Among Enterococcus spp. isolates, biofilm formation was low (16% with human plasma supplementation); however, assessment is ongoing. Moreover, clinical data will be examined to determine if biofilm formation is a wound infection risk factor, as well as to evaluate the impact of biofilms on clinical outcomes.

Findings from the Enterococcus spp. polymicrobial wound and biofilm analyses were presented at the 2016 Military Health System Research Symposium (MHSRS; Photos) by Ms. Heitkamp and Dr. Lee Mangum, respectively.
Laboratory testing of 226 *Stenotrophomonas maltophilia* isolates (a difficult-to-treat pathogen) collected from wounded personnel was recently completed by CPT Shane Patterson (ID Fellow) and Maj Dana Blyth (mentor). Approximately 66% of isolates were collected from wounds and 41% of patients had the organism isolated on serial cultures. Assessment of 50 patients with a *S. maltophilia* infection and critical injury severity (injury severity score >15) found that skin and soft-tissue infections (SSTIs) were predominant (59%) followed by pneumonia (12%). The overall infection incidence density was 1.3 per 100 person-days (95% CI: 1.1-16).

Overall, findings from the MDR/VO Initiative are providing a detailed picture of combat-related wound microbiology, leading to the potential development of novel infectious disease countermeasures. An update on the MDR/VO Initiative was presented by Dr. Mende at the 2016 MHSRS. Findings from the *S. maltophilia* analysis (Graduate Medical Education [GME] supported project) were presented by CPT Patterson at the 2016 IDSA ID Week (Photos).

Another GME supported analysis assessed characteristics related to MDR Gram-negative (GN) infections and was led by LCDR Wesley Campbell (MPH project) and Dr. David Tribble (mentor). A total of 913 patients (34% of 2699 trauma patients admitted to participating U.S. hospitals) developed an infection, of which 245 (27%) had MDRGN etiology (total of 543 infection events). Among the initial 286 MDRGN infections, SSTIs were prevalent (Figure 2). Patients with MDRGN infections frequently sustained blast injuries (84%) and traumatic amputations (58%) compared to patients without MDRGN infections (63% and 16%, respectively; p<0.001). In addition, 58% were colonized with a MDRGN prior to infection compared to 15% of patients without infections (p<0.001). When antibiotic usage was considered, there were significant differences in the distribution of prescribed antibiotics between the patients with and without MDRGN infections (p<0.001). Further research is underway to examine the association between antibiotic usage and MDRGN infection risk. Analysis findings were presented by LCDR Campbell at the 2016 IDSA ID Week (Photo). A manuscript has also been accepted for publication in *Surgical Infections*.

![Figure 2: Distribution of Initial MDRGN Infection Events (N=286)](image)
Joint Trauma System Combat Casualty Care Curriculum Conference [for CME credit]: Invasive Fungal Infection Update. 7 July 2016.

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Mangum LC, Garcia GR, Tribble D, Mende K, and Akers KS. Biofilm Formation Capacity among *Acinetobacter baumannii* and *Enterococcus* species isolates from Clinical Wound Infections of Injured U.S. Military Personnel. [Poster #1056]


Heitkamp R, Li P, Mende K, Tribble D, and Tyner S. *Enterococcus* spp. in Extremity Trauma Wounds [Poster #1018]

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Tribble DR. The U.S. Department of Defense Trauma Infectious Disease Outcomes Study (TIDOS).

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* Campbell WR, Li P, Whitman TJ, Blyth DM, Schnaubelt ER, Mende K, and Tribble DR. Characteristics and Predictive Factors for Multidrug-Resistant Gram-Negative Infections in Deployment-Related Trauma Patients. [Poster #375]

* Patterson SB, Mende K, Li P, Lu D, Murray CK, Tribble DR, and Blyth DM. *Stenotrophomonas maltophilia* Resistance in Military Trauma Patients. [Poster #326]

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* Stewart L. Assessment and Classification of Combat-Related Poly-Traumatic Extremity Wounds and Infectious Outcomes: Trauma Infectious Disease Outcomes Study 2009-2012.

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* Presentation/publication from analysis led by a resident, ID fellow, or post-doc
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Lloyd BA, Murray CK, Bradley W, Shaikh F, Aggarwal D, Carson ML, and Tribble DR. Variation in Post-Injury Antibiotic Prophylaxis Patterns over Five Years in a Combat Zone. Military Medicine. Accepted for publication.


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