San Antonio
Polytrauma Clinical Research
Long-term outcomes and treatments
Carlos Jaramillo MD, PhD
San Antonio Polytrauma Research

OBJECTIVES

• How we built the San Antonio Polytrauma Research Program
• Clinical questions
• Types of studies and team science approach
• New directives
• Lessons learned
Iraq and Afghanistan
“Polytrauma occurs when a person experiences injuries to multiple body parts and organ systems...”

- Traumatic Brain Injury (TBI)
- Amputation
- Burns
- Spinal Cord Injury
- Auditory and visual damage
- Post-traumatic stress disorder (PTSD)
- Other medical conditions...
Polytrauma Clinical Triad

TBI

Pain

PTSD

Lew et al. (2009)
Clinical definitions, classifications of TBI severity

<table>
<thead>
<tr>
<th>Severity</th>
<th>Glasgow Coma Scale Score</th>
<th>Duration of Loss of Consciousness</th>
<th>Duration of Posttraumatic Amnesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>13–15</td>
<td>&lt;30 minutes and/or</td>
<td>&lt;1 hour</td>
</tr>
<tr>
<td>Moderate</td>
<td>9–12</td>
<td>1–24 hours and/or</td>
<td>&lt;24 hours</td>
</tr>
<tr>
<td>Severe</td>
<td>8 or less</td>
<td>&gt;24 hours and/or</td>
<td>&gt;24 hours</td>
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</tbody>
</table>

TABLE 1. TBI Severity Rating Scale
DoD Numbers for Traumatic Brain Injury
Worldwide – Totals

2017

- Penetrating: 73
- Severe: 134
- Moderate: 2,559
- Mild: 15,042
- Not Classifiable: 33

Total - All Severities: 17,841

Source: Defense Medical Surveillance System (DMSS), Theater Medical Data Store (TMDS) provided by the Armed Forces Health Surveillance Center (AFHSB)

Prepared by the Defense and Veterans Brain Injury Center (DVBIC)

*Percentages do not add up to 100% due to rounding

2017, as of June 21, 2018
Concussion: Definition

1. any period of loss of consciousness;
2. any loss of memory for events immediately before or after the accident;
3. any alteration in mental state at the time of the accident (eg, feeling dazed, disoriented, or confused); and
4. focal neurological deficit(s) that may or may not be transient; but where the severity of the injury does not exceed the following:

- loss of consciousness of approximately 30 minutes or less;
- after 30 minutes, an initial Glasgow Coma Scale (GCS) of 13–15; and
- posttraumatic amnesia (PTA) not greater than 24 hours.

From American Congress of Rehabilitation Medicine (ACRM)
Mild Traumatic Brain Injury (TBI)

Concussion: Definition

This definition includes:
1. the head being struck,
2. the head striking an object
3. the brain undergoing an acceleration/deceleration movement (ie, whiplash) without direct external trauma to the head.
OEF/OIF/OND Veterans

Complex, multifaceted problems...

Require the integration of two or more scientific/clinical approaches for solution
VHA Polytrauma System of Care

- **Level 1: Polytrauma Rehabilitation Centers (5)**
  - Regional referral centers for acute, comprehensive rehabilitation
  - Lead clinical care, research, education, program development
  - Tampa, Minneapolis, Richmond, Palo Alto, San Antonio

- **Level 2: Polytrauma Network Sites (23)**
  - Veteran Integrated Service Network referral sites for post-acute rehabilitation

- **Level 3: Polytrauma Support Clinic Teams (86; 2-8 per VISN)**
  - Interdisciplinary team follow-up and management of stable TBI/Polytrauma symptoms at local VA facilities

- **Level 4: Polytrauma Points of Contact (41 VA medical centers)**
  - Care coordination and referral to appropriate services
VA Polytrauma Rehabilitation Centers

Richmond

Minneapolis

Palo Alto

Tampa

San Antonio
San Antonio PRC/STVHCS
San Antonio Polytrauma Center

2011: SA PRC opened

2012: Research Program - $0

Dr. Carlos Jaramillo, MD, PhD
- Physical Medicine and Rehabilitation (PM&R)
- Basic research, geriatric rehabilitation, aging/longevity research – focus on the effect of aging on TBI
- 60% research/40% clinical

Dr. Blessen Eapen, MD
- PM&R/TBI Board Certified
- 100% clinical
San Antonio Polytrauma Center

Year one: 2012-2013

Partnership: Dr. Mary Jo Pugh – outcomes and epidemiology

Multiple grant applications

• pilot studies
• CDA
• Health Services/epidemiology
• Long-term outcomes clinical research
• Consortium projects
• Clinical interventions
Polytrauma Research Objectives

1. Understand the population: injuries, diagnoses, conditions, symptoms
2. Understand the clinical trajectories of these patients and long-term outcomes from these injuries/conditions
3. Understand the relative benefits of current interventions, medications, and treatment guidelines
4. Develop new clinical approaches that provide the most benefit and least harm
Clinical Case

• 35 y/o male
• Multiple deployments – OEF/OIF
• Referred to Polytrauma Network Site clinic for evaluation of possible history of TBI
• Headache, LBP, poor concentration
Clinical Case

- 35 y/o male
- Multiple deployments – OEF/OIF
- Referred to Polytrauma Network Site clinic for evaluation of possible history of TBI
- HA, LBP, poor concentration
- **Served 10 years – combat engineer**
- **Not employed – considering school?**
- Headaches; +photosensitivity
- LBP; 5 years
- Cognition: conversations, written text, grocery lists, medical appointments, medications
Clinical Case

• Review of Systems
  Fatigue
  Dizziness
  Insomnia
  Nightmares
  Photosensitivity
  Tinnitus
  Decreased appetite +/- nausea
  Anxiety
  Irritability – with occ aggressive outbursts
  Neck pain
Clinical Case

TRAUMATIC BRAIN INJURY

Two combat related events with loss-of-consciousness of 1-5 minutes: one in 2010, and one in 2012. IEDs that resulted in casualties and the deaths of friends and colleagues.
Clinical Case

- VA and MTF - treatment guidelines for PTHA, PTSD, and pain. (9 CNS; 12 total)
- divalproex sodium and sumatriptan - headaches
- sertraline and buspirone – PTSD/anxiety
- quetiapine, zolpidem, and prazosin – sleep/nightmares
- gabapentin, cyclobenzaprine, and meloxicam - pain
- omeprazole - reflux
- sildenafil - erectile dysfunction.
Polytrauma Clinical Triad

TBI

Pain

PTSD

Lew et al. (2009)
Polytrauma Clinical Trials: Population

Prevalence of Chronic Pain, PTSD and TBI in a sample of 340 OEF/OIF veterans with polytrauma

Chronic Pain
N=277
81.5%

PTSD
N=232
68.2%

TBI
N=227
66.8%

12.6%
6.8%
5.3%

42.1%

10.3%
16.5%
2.9%

Other Health Comorbidities
Depression
Socioeconomic Factors
SUD

Mild TBI: Recovery Patterns

• The majority of patients with **sport-related** concussion recover within a 7- to 10-day period

• Approximately 10% of athletes have persistent signs and symptoms of concussion beyond 2 weeks.

• Cognitive dysfunctions typically resolve 3 months post-injury
mTBI: Post-concussive symptoms

Physical
- Headaches
- Neck pain
- Dizziness
- Photosensitivity
- Insomnia
- Fatigue

Cognitive
- Poor concentration
- Memory problem
- poor recall
- mental fatigue

Emotional
- Anxiety
- Depression
- Irritability
OEF/OIF/OND Veterans

Headaches

- Tinnitus
- Anxiety
- Depression

Insomnia

- Irritability

Dizziness/Vestibular

- Neck pain

Photosensitivity

- Fatigue
- Low back pain

Memory dysfunction
Epidemiology and Outcomes Research

• Dr. Mary Jo Pugh, PhD

Secondary data analysis, big data analytics, retrospective studies, latent class/cluster analysis, machine based learning

- Partnership on multiple grant submissions
- Co-authors
- Bridge and network building
- Mentoring
14 peer review since 2014


Polytrauma Clinical Research Program

Epidemiology + Clinical Research → Clinical Applications
Funded Projects 2013

- Chronic Effects of Neurotrauma Consortium Study Site: Longitudinal Study
- Consortium to Alleviate PTSD Study Site: PTHA RCT
- TRACC: Identifying and Validating Complex Comorbidity Clusters in OEF-OIF Veterans
Multi-center collaborative (VA, DoD, Private, Academic): links basic, translational, clinical neuroscience research.

David X. Cifu, MD: Principle Investigator and CENC Director, Virginia Commonwealth University, VA.

- Fill knowledge gaps – basic science of mild TBI
- Determine effects on late-life outcomes and neurodegeneration
- Identify individuals most susceptible to effects
- Identify the most effective treatment strategies

www.cenc.rti.org
Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat: Study 1

- 5- year longitudinal: observational cohort study
- Multi-site: Richmond VA, Tampa FL, Houston TX, San Antonio TX, Fort Belvoir VA, Portland OR
- Study Chair: William Walker, MD; Virginia Commonwealth University
- Characterize the late effects of mild TBI, assess the influence and interaction of potential risk factors for early dementia.
Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat: Study 1

- Late effects of mild TBI, risk factors for early dementia.
- 880 mild TBI; 220 no TBI
- Patient reported outcomes + cognitive/neurologic function
- Serum biomarkers: USUHS
- Neuroimaging

San Antonio: $1,326,194

[www.cenc.rti.org](http://www.cenc.rti.org)
2019 – 2024: LIMBIC
Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat: Study 1

• Late effects of mild TBI, risk factors for early dementia.
• 880 mild TBI; 220 no TBI
• Patient reported outcomes + cognitive/neurologic function
• Serum biomarkers: USUHS
• Neuroimaging
• Integration with other long-term studies

San Antonio: $1,326,194

www.cenc.rti.org
Epidemiology of mTBI: Aim 3
(Mary Jo Pugh, PhD)
The Nexus of Mild TBI and Trajectories of Persistent Comorbidity in Warfighters with Mild TBI

Data: 2002-2016
DoD Trauma Registry
DoD Diagnoses, Type of Care, Medications Prescribed
VA Diagnoses, Type of Care, Medications Prescribed
DoD, VA approve $45 million to fund the Consortium to Alleviate PTSD

Award to be managed by the UT Health Science Center San Antonio and the VA National Center for PTSD, leaders of the national PTSD research consortium

SAN ANTONIO (Aug. 12, 2013) — In an unprecedented show of support for our nation's wounded warriors, the U.S. Department of Defense and the U.S. Department of Veterans Affairs have agreed to provide approximately $45 million over five years for post-traumatic stress disorder (PTSD) research to advance PTSD diagnosis, prevention and treatment for service members and veterans. The University of Texas Health Science Center at San Antonio and the VA National Center for PTSD lead the consortium, announced over the weekend by the White House and DoD and VA officials.

The Consortium to Alleviate PTSD (CAP) will provide an array of cutting-edge clinical treatment trials and biological studies for active military and veterans with PTSD and related conditions, said CAP Consortium Director Alan L. Peterson, Ph.D., professor of psychiatry in the School of Medicine at the UT Health Science Center San Antonio. The consortium's initiatives will include efforts to learn more about the biology/physiology of PTSD development and treatment response to inform diagnosis, prediction of disease outcome, and new or improved treatment methods.
CAP: Randomized Clinical Trial of Cognitive-Behavioral Therapy for Posttraumatic Headache

Principal Investigator: Donald McGearry, PhD

Aim: Evaluate the effectiveness of a manualized behavioral health intervention for posttraumatic headache in Iraq and Afghanistan war veterans with co-occurring symptoms of posttraumatic stress.

More than 100,000 military service members and veterans

Alan Peterson, PhD – CAP overall PI
Don McGearry PhD – Study PI
Carlos Jaramillo MD, PhD – Site PI
Posttraumatic Headache: 5-year clinical trial

Consortium to Alleviate PTSD: Alan Peterson, PhD: Don McGeary PhD – Study PI
Carlos Jaramillo MD, PhD – Site PI

- 3 arm Randomized Control Trial: Cognitive behavioral therapy PTHA
- Outcomes including headache symptoms, PTSD, PCS
- Serum biomarkers
- 200 participants

- $3,074,337 five years
FORT-A

(Don McGeeary PhD; Carlos Jaramillo MD, PhD)

• Functional Orthopedic Rehabilitation Treatment—with mindfulness and Acceptance and Commitment therapy.
  • 5 year clinical trial-NIH NCAM
  • Establishing Efficacy of a Functional Restoration-Based CAM Pain Management Program in a Combat Injured Veterans Population
  • A randomized clinical trial of an interdisciplinary program with a strong CAM component (the FORT-A Program) to address chronic pain management and persistent opioid use in a sample of 130 OEF/OIF/OND Veterans with polymorbid chronic musculoskeletal pain
Polytrauma Clinical Trials: FORT A

- NCCIH: R01 AT008422-01
- **Project Title**: Establishing efficacy of a functional-restoration-based CAM pain management program

- $2,782,957 for five years
TBI Model Systems

Justin O’Rourke PhD – PI
Carlos Jaramillo MD, PhD – Medical Director

• Longitudinal Observational Study
  – Civilians and Veterans with TBI
  – Primarily Mild to Severe TBI
  – Parallel to Civilian TBIMS (16 centers)
TRACC: Identifying and Validating Complex Comorbidity Clusters in OEF-OIF Veterans

Mary Jo Pugh, PhD

- Big Data analytics
- Epidemiology
- LCA – clusters
- Predictive modeling
Polytrauma Clinical Trials

- DoD - CDMRP
- **Project Title:** Implementation of a Brief Cognitive Rehabilitation Intervention to Enhance Efficiency of Service Delivery for Service Members and Veterans with mTBI: Core-SCORE

$1,417,456 for three years
Current Funding

- Core-SCORE: $1,471,456
- IMAP – TBI Model Systems: $53,535 annually
- Pain Collaboratory – Chronic pain in Primary Care: $7,351,951 (6 years)
- CENC/LIMBIC - $1,326,194
- Epidemiology of Epilepsy - $1,198,195 (4 years)
- FORT A - $2,782,957 (5 years)
- PTHA - $3,074,337 (5 years with extension year)
Collaborators

- Dr. Blesson Eapen, MD
- Dr. Mary Jo Pugh, PhD

- CENC/LIMBIC
  Dr. David X. Cifu, MD
  Dr. William Walker, MD
  Dr. Lisa Wilde, PhD
  Dr. David Tate, PhD

- TBI Model Systems
  Dr. Risa Richardson, PhD
  Dr. Justin O’Rourke, PhD

- Consortium to Alleviate PTSD – STRONG STAR
  Dr. Don McGeary, PhD
  Dr. Cindy McGeary, PhD
  Dr. Alan Peterson, PhD

- Dr. Donald Royall, MD

Defense Veterans Brain Injury Center
- Dr. Doug Cooper, PhD
LESSONS LEARNED

- Grant submission!
- Team Science, collaborations, strategic partnership: Grant evaluation – strength of the team!
  - Formalized by grant funding and academic interests
  - Choosing collaborators and projects
- Growth management
  - Too fast? Too slow?
- Follow up studies
- Financial and human resources management
  - part-time employees
  - sharing employees with collaborators
  - long-term finance planning
  - employee turnover
  - incentive based pay
- Staying flexible and relevant