



Mild Traumatic Brain Injury In U.S. Troops Returning from Iraq and Afghanistan:

Public Health Considerations

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Mild Traumatic Brain Injury (mTBI) Definition

- Blow or jolt to the head that causes physiological disruption of brain function:
 - Brief loss of consciousness (<30 min)
 - Transient alteration in consciousness
 - Post-traumatic amnesia of <24 hours
- “Mild TBI” is synonymous with “concussion”.
- Distinct from moderate / severe TBI
- Acute symptoms may be followed by persistent post-concussion symptoms / syndrome (PCS)
 - e.g. headaches, sleep disturbance, fatigue, irritability, dizziness, concentration problems, cognitive problems, balance problems, ringing in ears, blurred vision, reduced ability to tolerate stress / alcohol / emotions



The mTBI Express Train

- CDC Report to Congress on mild TBI (2003)
- Incidence reported to be 20% among troops deployed to Iraq/Afghanistan; often “blast” related
 - As many as half continue to report symptoms post-deployment
- Labeled “signature injury” of this war
- Subject of various Commissions/Boards
 - AFEB memo to DoD Health Affairs, Aug '06
 - Independent Review Group (West, Marsh), April '07
 - DoD Mental Health Task Force Report, June '07
 - President’s Commission (Dole, Shalala), July '07
 - Army TBI Task Force Report, May 2007 (released Jan '08)
- \$900M FY07 Congressional appropriation
- Key recommendations: population-wide screening post-deployment and neurocognitive assessments



What DoD Has Done So Far

- Established common DoD-VA definition of TBI (Dec '06; Oct '07)
- Published in theater CPG (MACE) (Dec '06)
- Published clinical guidance for garrison settings (Oct '07)
- Initiated population-wide screening/assessments for mTBI as part of PDHA/PDHRA (phased in)
- Mandated baseline neurocognitive assessment testing for deploying population using NCAT (ANAM) (Jan '08)
- TBI specialty clinics (various forms)
- Education efforts



Assumptions That Are Driving DoD Policies

- Mild TBI is on same continuum as moderate / severe TBI.
- Mild TBI caused by blast may have unique health effects.
- Case definitions for mTBI and PCS are sufficiently valid.
- Symptoms usually resolve in 1-3 months, but persistent post-concussive symptoms are not uncommon (~15%).
- Mild TBI “overlaps” with and may be confused with PTSD.
- A careful clinical history (perhaps with the help of cognitive testing) can distinguish symptoms due to mild TBI.
- The “silent” epidemic; requires “high index of suspicion”.
- It doesn’t matter what label we use, since “mild TBI” means the same thing as “concussion”.
- Screening for mTBI is imperative for appropriate care.
- There is specific treatment available for mild TBI.



mTBI is Not on Same Continuum as Mod / Severe TBI

	Mild TBI (concussion)	Mod/Severe TBI
Focal neurological signs	Generally None / Transient	Yes
Natural History / Recovery	Full recovery is expected; No consensus on post-concussive symptoms / syndrome	Directly related to injury severity and functional neuroanatomy
Case definitions and specificity of physical, behavioral, cognitive symptoms / sequelae	Very poor, low validity (e.g. low kappa b/w ICD-10 & DSM-4; high baseline rates and with other injuries)	High
CT / MRI	Usually negative / equivocal	Diagnostic
Neurocognitive testing	Inconclusive; evidence for clinical utility lacking	Diagnostic
Neuronal cell damage	Twisting / Stretching	Shearing / Death
Predictors of Persistent Symptoms / Disability	Debated: neurological vs. psychological	Based directly on injury characteristics
Epi. evidence of causation	Inconsistent	Consistent

Adapted from McCrea, Oxford Univ Press, 2008 and Iverson. In: Brain Injury Medicine 2008



mTBI: What the Evidence Indicates

- Blast physics and casualty data suggest that primary blast overpressure injuries are very rare.
- Neither mTBI or PCS case definitions have been validated using clinical interviews and adequate control groups.¹⁻³
- Incidence of mTBI during deployment is unknown:
 - Only 5% of OIF/OEF Soldiers report injury with LOC, usually very brief (<3 min).
 - It is impossible to know how many of the other Soldiers with “altered mental status” actually had physiological disruption of brain function.
- Acute concussion symptoms usually resolve within a few hours to a few days, not 1-3 months^{1,4}
- A re-analysis of the classic studies indicate that persistent PCS occur in about 3-5% of concussion cases, not 15+%.¹

1. McCrea M. Oxford Univ Press 2008 (chapters 15-17); 2. Schwab, et. al. J Head Trauma Rehab 2007, 3. Meares, et. al. J Neurol Neurosurg Psych 2008; 4. Iverson 2007



mTBI/PTSD “Overlap”: The Evidence

- Concussion (mTBI), by definition, does not “overlap” with PTSD, because it is the injury event itself.
- However concussion in combat is strongly associated with subsequent PTSD, likely because of the high threat context.¹
- PTSD, in turn, is strongly associated with somatoform and post-concussive symptoms due to neuroendocrine, autonomic nervous system, and immune system dysregulation; as well as altered perception of symptoms.²
- Post-concussive symptoms overlap with hundreds of medical conditions, and all historical post-war syndromes.
- Two studies have found that PTSD explains the majority of symptoms categorized as “post-concussive” in Soldiers who have had concussions during Iraq deployment.^{1,3}

1. Hoge, et. al. NEJM 2008; CDC 2003; 2. Boscarino JA, Ann NY Acad Sci 2004; 3. Schneiderman, et. al. Am J Epi 2008



PCS and NC Testing: What The Evidence Indicates

- A careful clinical history is not sufficient to attribute persistent symptoms to mTBI (especially months after injury).¹⁻⁴
 - ICD-10 and DSM-4 definitions correlate poorly.
 - High baseline rates of symptoms in normal populations
 - Several studies have shown that the PCS symptoms occur just as frequently after non-head traumas as after mTBI.
- The available data indicate that neurocognitive assessment testing in concussion lacks reliability, validity, and clinical utility.⁵⁻⁸

1. McCrea M. Oxford Univ Press 2008; 2. Meares, et. al. J Neurol Neurosurg Psych 2008; 3. Iverson. In: Brain Inj Med 2007; 4. Carroll LJ, et. al. (WHO Task Force) J Rehabil Med 2004; 5. Vasterling, ISTSS 2007; 6. Randolph, McCrea. J Athletic Training 2005 7. Blieberg, et. al. Neurosurg 2004; 8. Cernick, et. al. Arch Clin Neuropsychol 2007



New DoD mTBI Post-Deployment Screening Revised PDHA/ PDHRA

9

a. During this deployment, did you experience any of the following events? *(Mark all that apply)*

- | | Yes | No |
|--|-----------------------|-----------------------|
| (1) Blast or explosion (IED, RPG, land mine, grenade, etc.) | <input type="radio"/> | <input type="radio"/> |
| (2) Vehicular accident/crash (any vehicle, including aircraft) | <input type="radio"/> | <input type="radio"/> |
| (3) Fragment wound or bullet wound above your shoulders | <input type="radio"/> | <input type="radio"/> |
| (4) Fall | <input type="radio"/> | <input type="radio"/> |
| (5) Other event (for example, a sports injury to your head). Describe: | <input type="radio"/> | <input type="radio"/> |

b. Did any of the following happen to you, or were you told happened to you, IMMEDIATELY after any of the event(s) you just noted in question 9.a.? *(Mark all that apply)*

- | | Yes | No |
|---|-----------------------|-----------------------|
| (1) Lost consciousness or got "knocked out" | <input type="radio"/> | <input type="radio"/> |
| (2) Felt dazed, confused, or "saw stars" | <input type="radio"/> | <input type="radio"/> |
| (3) Didn't remember the event | <input type="radio"/> | <input type="radio"/> |
| (4) Had a concussion | <input type="radio"/> | <input type="radio"/> |
| (5) Had a head injury | <input type="radio"/> | <input type="radio"/> |

c. Did any of the following problems begin or get worse after the event(s) you noted in question 9.a.? *(Mark all that apply)*

- | | Yes | No |
|-----------------------------------|-----------------------|-----------------------|
| (1) Memory problems or lapses | <input type="radio"/> | <input type="radio"/> |
| (2) Balance problems or dizziness | <input type="radio"/> | <input type="radio"/> |
| (3) Ringing in the ears | <input type="radio"/> | <input type="radio"/> |
| (4) Sensitivity to bright light | <input type="radio"/> | <input type="radio"/> |
| (5) Irritability | <input type="radio"/> | <input type="radio"/> |
| (6) Headaches | <input type="radio"/> | <input type="radio"/> |
| (7) Sleep problems | <input type="radio"/> | <input type="radio"/> |

d. In the past week, have you had any of the symptoms you indicated in 9.c.? *(Mark all that apply)*

- | | Yes | No |
|-----------------------------------|-----------------------|-----------------------|
| (1) Memory problems or lapses | <input type="radio"/> | <input type="radio"/> |
| (2) Balance problems or dizziness | <input type="radio"/> | <input type="radio"/> |
| (3) Ringing in the ears | <input type="radio"/> | <input type="radio"/> |
| (4) Sensitivity to bright light | <input type="radio"/> | <input type="radio"/> |
| (5) Irritability | <input type="radio"/> | <input type="radio"/> |
| (6) Headaches | <input type="radio"/> | <input type="radio"/> |
| (7) Sleep problems | <input type="radio"/> | <input type="radio"/> |

Problems with this include the lack of validation and: a. "experience" of a blast is not the same thing as an injury, blow or jolt to the head. b. "IMMEDIATELY after" is confusing. "Felt dazed, confused, or saw stars" may not correlate with physiological disruption of brain function, and had low specificity in NEJM study. c. and d. are not independent from the injury questions.



Foundations of Population Screening

Understand Risk Factors:

What do we know about the risk factors for developing persistent post-concussive symptoms after concussion?



Risk Factors for Persistent PCSs

- 4 principal risk factors have been associated with persistent post-concussive symptoms:
 - **Repeated concussive events (e.g. recovery mean 14 days vs. <1-7 days in NCAA Concussion Study)**
 - Guskiewicz K, et. al., JAMA 2003;
 - **Depression, anxiety, PTSD**
 - Bryant RA, Harvey AG. J Nerv and Mental Disorder 1999;
 - **Presence of medical disability and legal processes**
 - Carroll LJ, et. al. (WHO Task Force). J Rehabil Med 2004
 - **Expectations and beliefs that patients have about the seriousness of their condition**
 - Carroll LJ, et. al. (WHO Task Force). J Rehabil Med 2004
 - Ferguson RJ. Neuropsychology 1999
 - Whittaker R. J Neurol. Neurosurg. Psychiatry 2007



Foundations for Population Screening

Effective interventions:

What evidence-based treatments are available for mTBI identified through post-deployment screening assessments?



Evidence-Based mTBI Treatment

- None, ...except cognitive education to normalize symptoms and provide the expectation of rapid recovery.¹⁻⁴

1. Peloso PM, et. al. (WHO Task Force); J Rehab Med 2004;
2. Borg J, et. al. (WHO Task Force); J Rehab Med 2004;
3. Mittenberg W, et. al. Arch Clin Neuropsych 1996;
4. Ponsford J, et. al. J Neurol Neurosurg Psych 2002

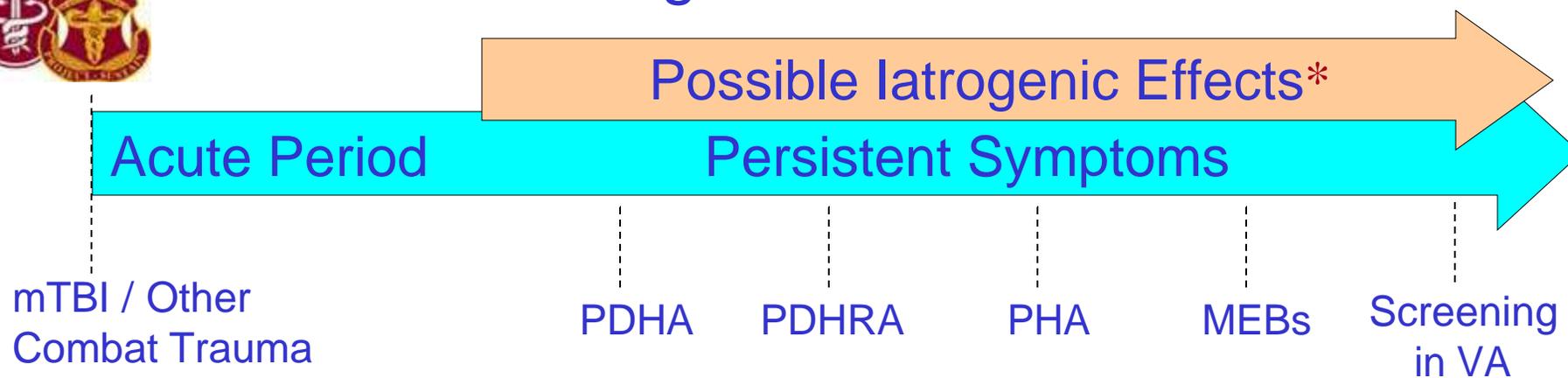


Necessary Criteria for Population-Level Screening Have Not Been Met

- Rona, et. al. JAMA 2005

- Important health problem
- Screening test should be simple, precise, and validated.
- High-quality research evidence demonstrates the effectiveness of screening in reducing morbidity.
- Adequate staffing and facilities are critical.
- Potential benefits from the screening program outweigh risks.

Screening: First Do No Harm



- ***Iatrogenic pathways:** labeling, inconclusive cognitive or neuroimaging studies, unproven interventions, medication side effects, failure to provide effective treatment for real problems, use of rehabilitation services designed for mod/severe TBI, poor risk communication, disability seeking, cost.

- **Expectation as etiology.** The belief that one is sick is well known to amplify symptoms (e.g. mTBI, hypertension, whiplash, chronic fatigue, irritable bowel, chest pain, herpes zoster, lactose intolerance). Perceptions are reinforced by the number of tests performed that legitimizes symptoms as “medical”.

- References: 1) Iverson, In: Brain Injury Medicine, Demos, 2007; 2) Wood, Brain Injury 2004; 3) Barksy AJ, Ann Int Med 1999



NEJM Study (Jan 31, 2008)

- Cross-sectional survey of 2525 Soldiers from 2 BCTs studied 3-4 months post-deployment
- Measures: Combat experiences, injuries, concussion history (using DVBIC questions); validated clinical scales for PTSD, depression, somatic/physical symptoms
- Soldiers with other injuries served as control group for all comparisons
- Clinical scales were independent from injury and combat experience measures
- Analyses controlled for demographics, combat intensity, injury mechanism, and multiple blast exposures.
- 60% availability, 98% participation rate



Mild TBI Prevalence (NEJM 2008)

Injury Type*	(N=2525)
Soldiers with mTBI**	
Loss of Consciousness	124 (4.9%)
Altered Mental Status ("dazed, confused, or seeing stars")	260 (10.3%)
Soldiers with Other Injuries	435 (17.2%)

* Blast was the most common mechanism for mTBI (75%), whereas falls were the most common mechanism of other injuries.

** LOC usually lasted <3 minutes. Of the 260 with altered MS, 253 reported being "dazed, confused, or seeing stars."



Mild TBI and Mental / Physical Health

- Soldiers who reported mTBI, particularly with loss of consciousness (LOC), were much more likely to have PTSD and physical health problems post-deployment than Soldiers with other injuries.

Health Measures Past-Month	mTBI with LOC (n=124) (%)	mTBI with Altered MS (n=260)(%)	Other Injuries (n=435)(%)	No Injury (n=1706) (%)
Mental Disorders				
PTSD	43.9*	27.3*	16.2	9.1
Major Depression	22.9*	8.4	6.6	3.3
Physical Health				
Poor General Health	12.6*	6.6	6.9	2.3
Sick-call \geq 2	42.5*	32.8	28.9	19.7
Missed work \geq 2 days	23.3*	15.6	14.6	7.3
High Physical Symptoms (Score \geq 15)	24.8*	16.1	11.3	5.1



However, That Was Not the Whole Story

- High physical symptoms (PHQ-15 score * 15) occurred almost exclusively among Soldiers with PTSD.
- Similar relationship observed for all outcomes, including PCSs.

Injury Type	Overall % with High PHQ-15	Stratified Analysis	
		<u>PTSD</u> % High PHQ-15	<u>No PTSD</u> % High PHQ-15*
LOC	24.8	50.9	4.5
Altered MS	16.1	41.8	7.0
Other Injury	11.3	42.0	5.3
Statistics	P<.001	NS	NS

N for all injuries = 801; N for PTSD = 189

N's for LOC = 123;54;69; Altered MS = 260;71;189; Other Injury = 433;79;363



Health Symptoms Stratified by PTSD

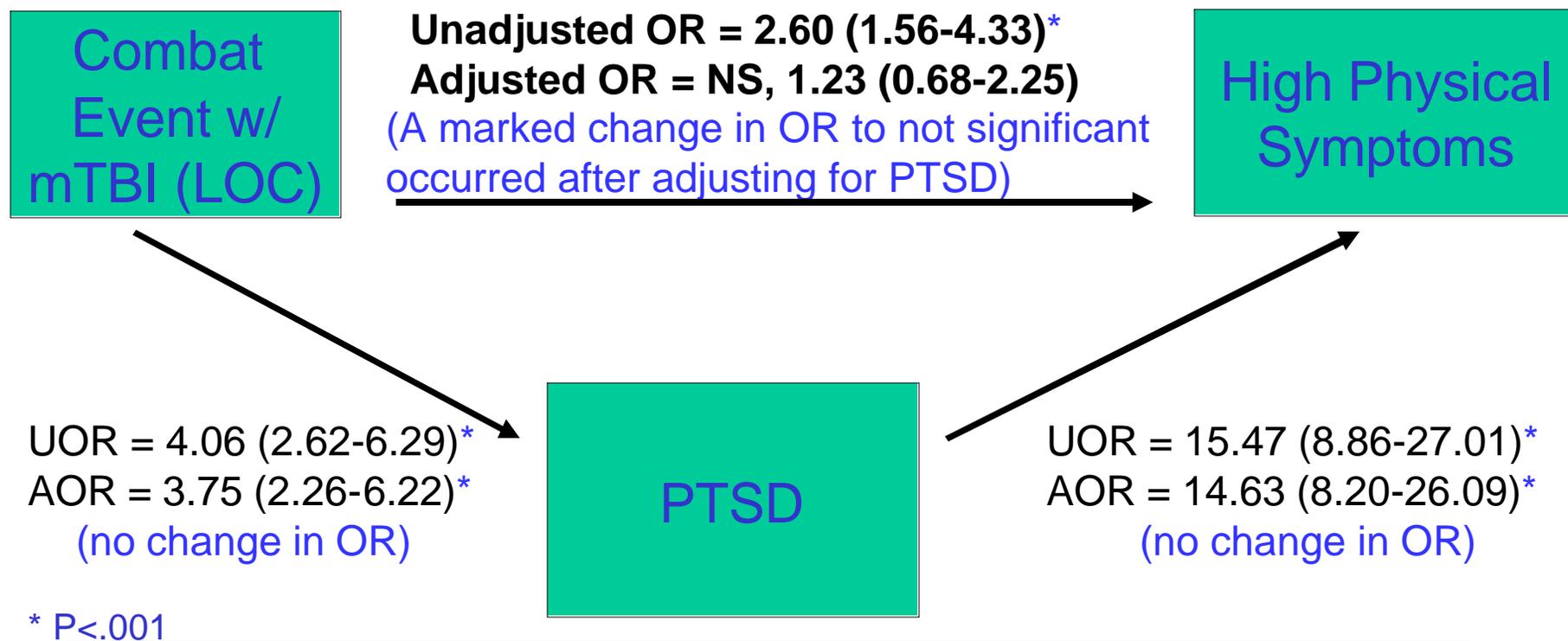
(analysis does not control for depression or other variables)

Health Symptoms	LOC	Altered MS	Oth Injury			
	(n=124)	(n=260)	(n=435)			
High PHQ-15 (15)	24.8*	16.1	11.3			
Headaches	32.2*	17.7*	12.1			
Sleep disturbance	53.8*	44.9*	37.2			
Concentration prob	31.4*	26.0*	18.1			
Irritability	56.8*	47.6*	36.8			
Memory Problems	24.6*	16.2	13.7			
Health Symptoms	PTSD			No PTSD		
	LOC (n=54)	Altered MS (n=71)	Oth Injury (n=70)	LOC (n=69)	Altered MS (n=189)	Oth Injury (n=363)
High PHQ-15 (15)	50.9	41.8	42.0	4.5	7.0	5.3
Headaches	49.1*	31.3	29.9	19.4*	12.8	8.8
Sleep disturbance	80.4	75.0	73.5	33.3	34.4	30.2
Concentration prob	58.8	61.5	54.4	10.4	13.5	11.1
Irritability	80.4	86.2	82.4	38.8	33.9	27.9
Memory problems	42.3	37.9	35.8	10.8	8.6	9.6



PTSD as Mediator

- A combat event associated with LOC reflects intense traumatic event with high threat to loss of life (near miss on one's life). This leads to PTSD.
- PTSD in turn leads host of health symptoms by well known mechanisms involving neuroendocrine, autonomic NS, and immune system dysregulation.





Clinical Implications

- Screening for mTBI months after injury will result in large numbers of service members being unnecessarily referred for evaluation and treatment of non-specific symptoms attributed to “brain injuries”.
 - “Brain injury” label likely to amplify symptoms.¹⁻⁸
 - Unintended iatrogenic consequences will occur.⁵⁻⁸

1. McCrea M. Oxford Univ Press 2008; 2. Peloso PM, et. al. (WHO Task Force); J Rehab Med 2004; 2. Borg J, et. al. (WHO TF; J Rehab Med 2004; 3. Mittenberg W, et. al. Arch Clin Neuropsych 1996; 4. Ponsford J, et. al. J Neurol Neurosurg Psych 2002; 5. Iverson, In: Brain Injury Medicine, Demos, 2007; 6. Wood, Brain Injury 2004; 7. Barksy AJ, Ann Int Med 1999



For example, DoD guidance for treating mTBI in non-deployed environment (Oct '07) includes recommendations that are not FDA approved.

- For sleep disturbance related to mTBI:
 - 14 day trial of trazodone / ambien
 - **If comorbid nightmares or other PTSD symptoms, give trial of quetiapine (seroquel)** (an atypical antipsychotic with metabolic side effects such as weight gain and hyperglycemia)
- For irritability related to mTBI:
 - **Six week trial of SSRI or SNRI (e.g. sertraline, venlafaxine)** (SSRIs commonly cause sexual side effects. Venlafaxine has significant risk of hypertension.)



There Are Some Simple Answers to This Problem: Recommendations

- Modify post-deployment screening assessments immediately (e.g. PDHA, PDHRA, PHA) to minimize risks.
- Build the structure of care for mild TBI on evidence-based step-care and collaborative care approaches centered in primary care, not TBI specialty clinics (or de-facto TBI clinics).
- Disseminate effective risk communication.



Modify Post-Deployment Screening for mTBI

- **Focus on point of injury evaluation. Modify post-deployment assessments to minimize risks:**
 - Screen for all injuries at the PDHA time point only.
 - Do not rescreen for mTBI at PDHRA or subsequently.
 - Screen for depression and PTSD.
 - Increase specificity of mTBI questions:
 - Focus on LOC. Remove or change non-specific “dazed or confused” question.
 - De-couple symptom questions from injury questions.



Treat Symptoms in Primary Care

- **Build foundation of mTBI care on evidence-based models centered in primary care:**
 - Step-care approaches in primary care have been proven to be effective in treating physical symptoms, while minimizing unnecessary and costly diagnostic evaluations, procedures, and referrals¹⁻³ (e.g. DoD-VA Post-Deployment Health CPG)
 - Collaborative care models in primary care, have been proven to be effective in reducing the medical morbidity associated with co-morbid mental disorders (depression, PTSD)^{4,5}
 - Educate providers about mTBI.

1. Kroenke K. Int J Methods in Psych Res 2003;
2. Engel CC, Katon WJ, Nat Acad Press 1999;
3. DoD-VA Post-deployment CPG
4. Gilbody, et. al. Arch Int Med 2006;
5. Katon, et. al. J Trauma Stress 2006



Disseminate Effective Risk Communication

- **Always convey reassurance and promote the expectation for rapid and full recovery:**
 - Utilize proven cognitive behavioral techniques¹⁻⁴
 - Throw out “mild TBI” label. Use “concussion” instead.
 - Lower stigma
 - Better understood term; more reassuring
 - Less likely to be confused with moderate / severe TBI
 - Reserve “brain injury” label for moderate and severe TBI
 - Draw on sports concussion analogies
 - Minimize speculation about possible blast effects. Instead talk about brain plasticity.
 - There is no evidence that being knocked unconscious for 30 seconds from a blast is any different clinically than being knocked unconscious for 30 sec. by another mechanism.

1. Peloso PM, et. al. (WHO Task Force); J Rehab Med 2004;
2. Borg J, et. al. (WHO TF; J Rehab Med 2004;
3. Mittenberg W, et. al. Arch Clin Neuropsych 1996;
4. Ponsford J, et. al. J Neurol Neurosurg Psych 2002



Thank You!

The views are those of the author(s) only and do not reflect the official position of the Army or DoD.

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Backups



ANAM Recommendations (Based on Literature Review)

- Discontinue routine or population-wide use of ANAM until there are clear guidelines for how test data should be utilized clinically.
- Continue to make ANAM available to neuropsychologists who want to use it, as part of their “tool kit”, but establish systematic program evaluation of clinical utility.
- Establish policy that ANAM test data should be interpreted only by neuropsychologists.
- Ensure that research portfolio includes an adequate number of NC studies that evaluate clinical utility.
- Insure scientific review of all guidelines and policies by independent experts (e.g. Defense Health Board).



Additional Recommendations to Primary Care Clinicians

- Post-concussion symptoms are like other unexplained symptom-based conditions.
- Develop a plan in collaboration with patient to evaluate and treat each symptom in step-wise manner.
- Acknowledge health concerns, but avoid attribution errors & potential iatrogenic harm:
 - The belief that one is sick amplifies symptoms
 - Belief is reinforced by number of medical tests / referrals
 - May lead to failure to provide effective treatment for the real problems
- Trust your clinical judgment.
- Screen for mental health problems, but don't label symptoms as "mental".