



TBI-BH ECHO

Traumatic Brain Injury - Behavioral Health ECHO
UW Medicine | Psychiatry and Behavioral Sciences

Posttraumatic Headache Management

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Speaker disclosures

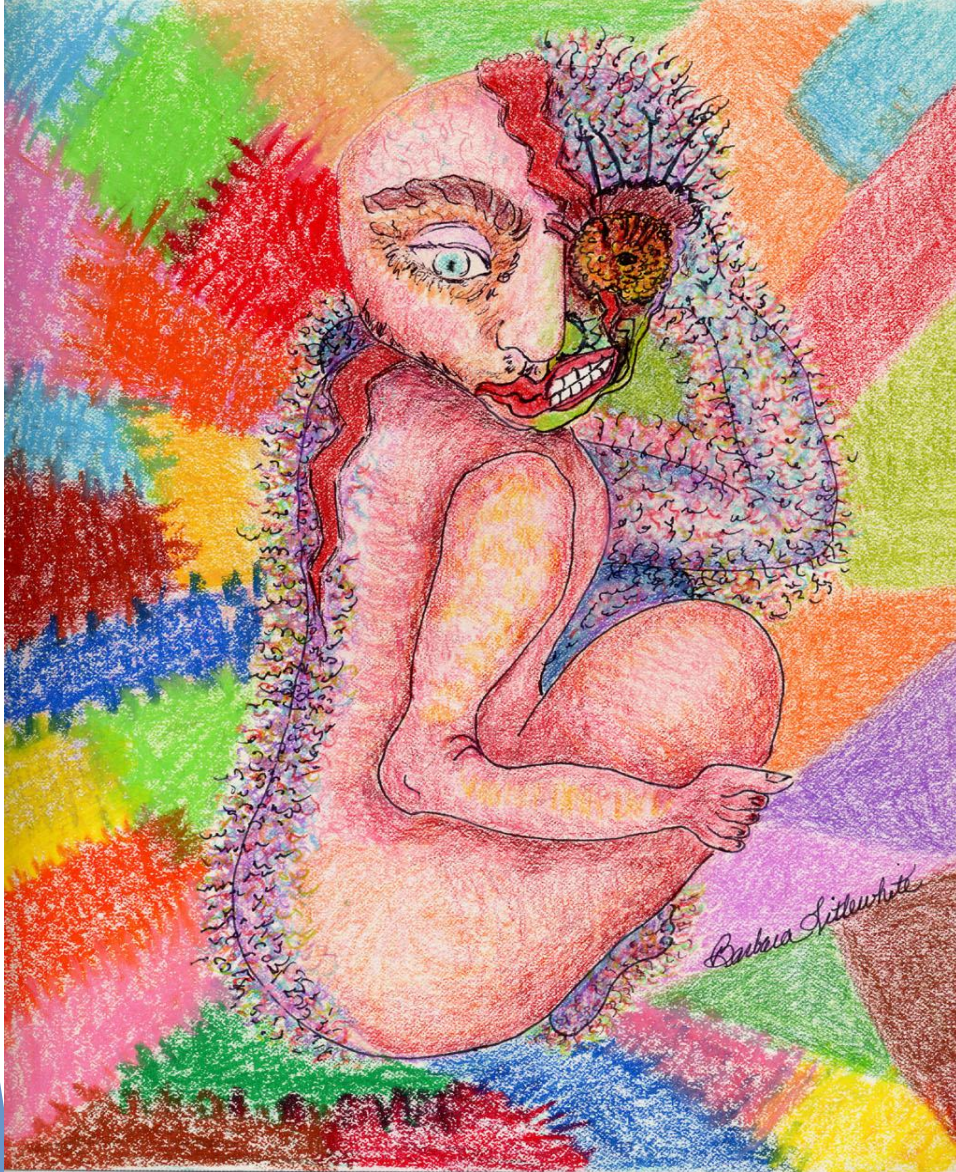
✓ No conflicts of interest

The following series planners have no conflicts of interest:

- ✓ Jennifer Erickson DO
- ✓ Jess Fann MD
- ✓ Cherry Junn MD
- ✓ Chuck Bombardier PhD
- ✓ Cara Towle MSN RN MA
- ✓ David Minor
- ✓ Amanda Kersey PhD
- ✓ Lauren Miles



Objectives



- ▶ Concept of primary vs secondary headache
- ▶ Analyze the ICHD-II criteria for PTH
- ▶ Epidemiology of PTH
- ▶ Creating a framework to understand an individual patient with PTH
- ▶ Taking a diagnostic approach to rational management of a patient with PTH including co-morbid conditions



A Sports-related Post-traumatic Headache

- ▶ A 13 year old right handed girl is referred to me 6 months after an injury for intractable headache.
- ▶ She was crouching ready to take shot during a soccer game when shouldered in the right temple by an opposing player.
- ▶ She was thrown to the ground, hitting the grass turf with the left side of her head. She saw stars. She does not remember a conversation with her coach immediately after the event.
- ▶ She rested on the sidelines with an ice-pack to treat a headache of immediate onset. Denied neck pain



Epidemiology of TBI

www.cdc.gov/traumaticbraininjury/statistics.html

- ▶ **Headache** is the most common physical symptom after TBI (Walker et al. 2005; Dikmen et al. 2010).
- ▶ **2.87 million** traumatic brain injuries (TBI) in 2014 (Centers for Disease Control and Prevention (2019). Surveillance Report of Traumatic Brain Injury-related Emergency Department Visits, Hospitalizations, and Deaths-US, 2014.).
 - ▶ Data do not include outpatient or office visits, military data or those not seeking care.
 - ▶ 75% of TBIs are mild TBI (mTBI).
 - ▶ Possibly up to **3.8 million** injuries per year among 44 million children and 170 million adults who play organized sports (likely underestimated for failure to recognize or minimize injury (Daneshvar et al. 2011).
- ▶ **Prevalence of PTH** in prospective cohort studies ranged from 30-60% at 1 month after injury and 26-65% 1 year after injury in civilian any intensity TBI (Dikmen et al. 2010, Faux & Sheedy 2005; Hoffman et al. 2011; Lieba-Samal 2011; Lucas et al. 2014; Stovner et al. 2009; Barlow et al. 2010; Eisenberg et al. 2013).
- ▶ **Higher symptom burden** in those with 2 or more concussions (Mannix et al. 2014).



Headache is part of the Post-Concussive Syndrome

- ▶ PTH usually does not exist in isolation
 - ▶ Somatic symptoms (dizziness, tinnitus, photophobia, phonophobia, fatigue, blurred vision)
- ▶ Cognitive symptoms
 - ▶ Impaired concentration, attention and memory
- ▶ Psychological symptoms
 - ▶ Depression, anxiety, apathy, insomnia, irritability
- ▶ These symptoms are often not recognized or volunteered



Headache Diagnosis in Perspective

▶ Primary Headache

- ▶ Headache has no known underlying treatable cause
- ▶ Clinical syndrome

▶ Secondary Headache

- ▶ Headache attributable to underlying definable condition
- ▶ No specific symptoms or definition of headache attributable to secondary headache pathology
- ▶ Treatment of underlying condition resolves headache



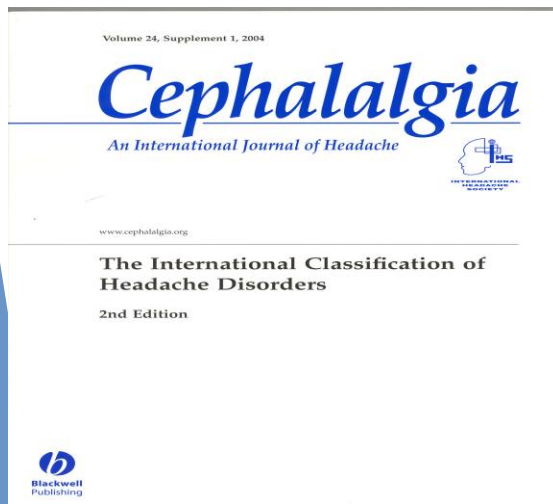
IHS Classification 2nd Edition - ICHD II

Primary HA

1. Migraine
2. Tension-type
3. Cluster and its relatives (TACs)
4. Other primary headaches (exertional, coital, hypnic, etc.)

Secondary HA

5. Posttraumatic
6. Vascular disease
7. Abnormal ICP, Neoplasm, etc
8. Substances
9. CNS infection
10. Metabolic
11. Cervicogenic, Eyes, Sinuses
12. Psychiatric HA
13. Neuralgias
14. Other



5. Headache attributed to trauma or injury to the head and/or neck

- ▶ **Acute vs. persistent** headache (less than vs. greater than 3 months)
 - ▶ Acute headache is reported to have developed within 7 days after injury, regaining consciousness or discontinuation of medication impairing ability to sense headache (delayed-onset headache in Appendix)
- ▶ **Moderate or severe vs. mild** traumatic injury to the head
- ▶ “There are no specific headache features known to distinguish the subtypes of 5. Most of these resemble tension-type headaches or migraine”.



The Post-Traumatic Headache

- ▶ PTH criteria define the severity, latency and duration of the headache
- ▶ No distinct presentation or unique signs for PTH
 - ▶ Location is anywhere
 - ▶ Characterization of pain is variable
 - ▶ Severity can vary widely
 - ▶ Disability may be greater relative to non PTH
 - ▶ Some retrospective studies report that when primary headache definitions are applied, most common phenotypes are migraine/probable migraine and tension type headaches though most primary headaches are represented



University of Washington Investigators:

- Kathy Bell MD
- Sureyya Dikmen PhD
- Jeanne Hoffman PhD (PI)
- Sylvia Lucas MD, PhD
- Nancy Temkin, PhD

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Natural History of Headache Following TBI

(studies funded by National Institute on Disability and Rehabilitation Research)

- ▶ **Moderate to Severe Cohort (TBI Model Systems)**
 - ▶ 7 Centers (UW, Mayo, Craig, Moss, Alabama, Texas, Virginia) participated
 - ▶ Objective: Describe headache in a prospective representative sample of individuals with moderate to severe TBI over 12 months.
- ▶ **Mild Cohort (field-initiated program)**
 - ▶ University of Washington
 - ▶ Objective: Describe headache in a prospective sample of individuals with mild TBI over 12 months



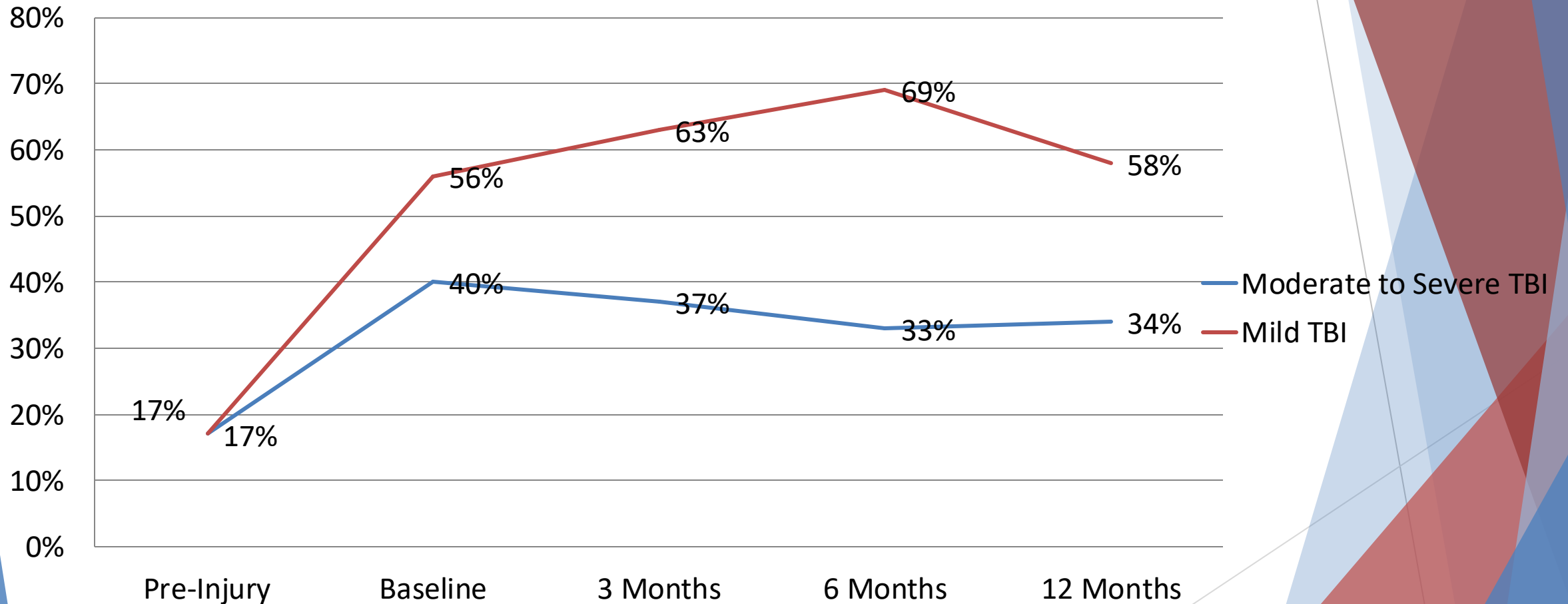
Methods

- ▶ **Baseline assessment:**
 - ▶ Mod/Severe in-person assessment prior to discharge from acute inpatient rehabilitation
 - ▶ Mild within 7 days of injury
- ▶ 3, 6, 12 month follow-up via telephone
- ▶ **Assessment of headache (NEW or WORSE)**
 - ▶ **Incidence and prevalence**
 - ▶ **Headache characteristics**
 - ▶ Pre-injury history of headache
 - ▶ Effectiveness of treatment from patient view



	Moderate to Severe TBI N=403	Mild TBI N=212
Age (years)	42.5	44.4
Male	72%	76%
Race (white)*	75%	75%
High School*	72%	83%
Cause of Injury*		
Vehicle	56%	58%
Assault	9%	5%
Sports	3%	3%
Fall	27%	24%
Hit by Object	2%	2%
Other	3%	8%

Prevalence of New or Worse Headache in the Year after TBI



(Hoffman et al. 2011; Lucas et al. 2014)



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Differentiating Primary Headache Types

Migraine/Probable Migraine	Tension-type
Moderate to severe	Mild to moderate
Throbbing, pulsatile	Vice-like, tight, squeezing
Activity worsens	No worsening with movement
Unilateral (60%)	Bilateral
Nausea/Vomiting	No nausea/vomiting
Photophobia & phonophobia	Photophobia OR phonophobia



Classification of New or Worse Headache

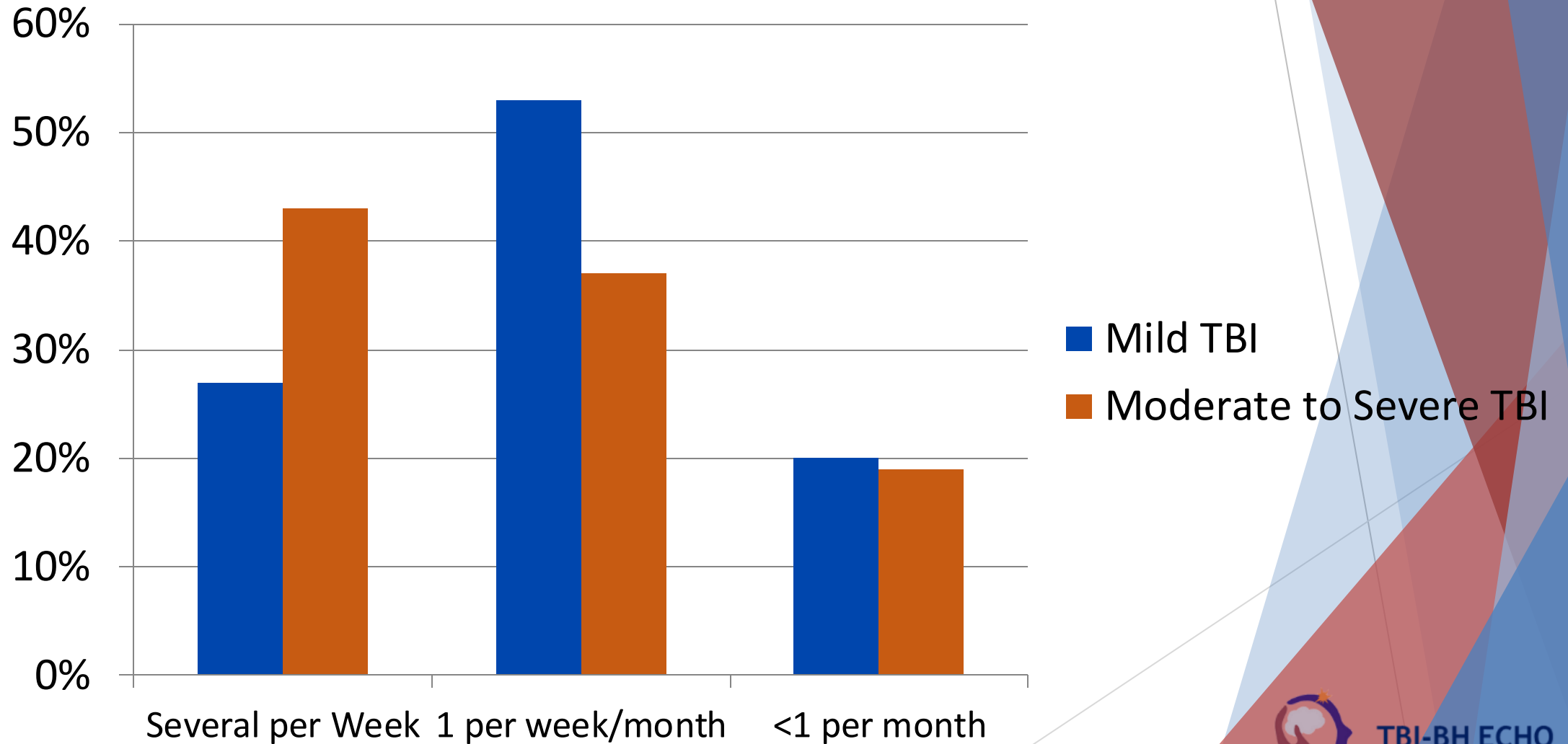
	Baseline		3 Months		6 Months		12 Months	
	Mod/Sev	Mild	Mod/Sev	Mild	Mod/Sev	Mild	Mod/Sev	Mild
Migraine/ Probable Migraine	54%	46%	63%	38%	67%	35%	61%	42%
Tension	7%	9%	13%	16%	14%	19%	14%	18%
Cervicogenic	10%	6%	5%	10%	2%	9%	5%	6%
Unclassifiable	29%	38%	20%	35%	17%	37%	20%	34%

(Lucas et al. 2012; Lucas et al. 2014)



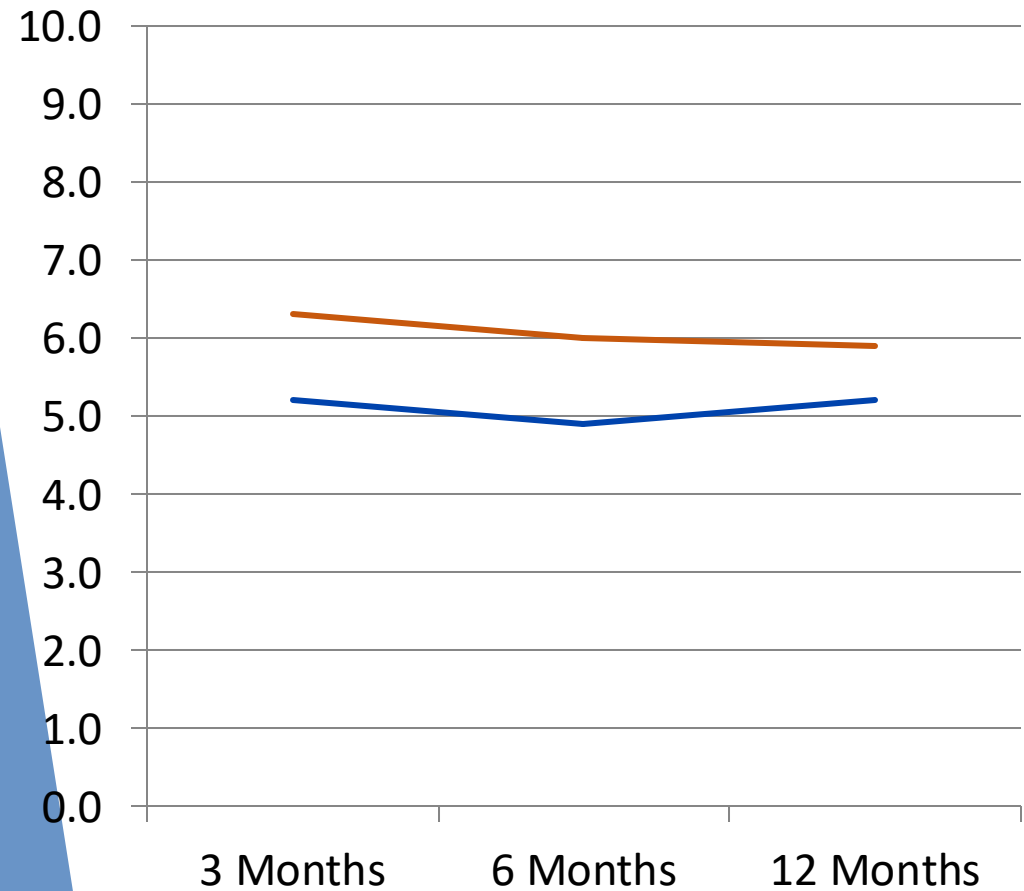
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Frequency of Headache at 1 Year



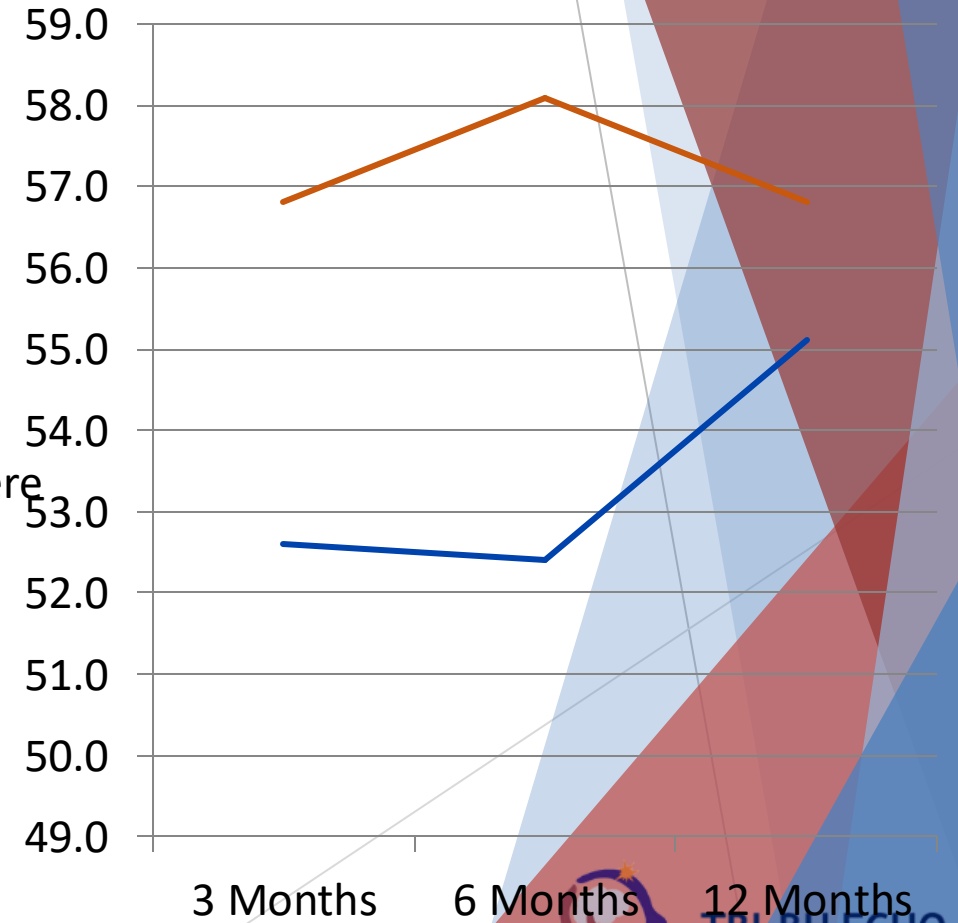
Impact of Headache

Pain Rating



— Mild TBI
— Moderate to Severe TBI

Headache Impact Test



Conclusions

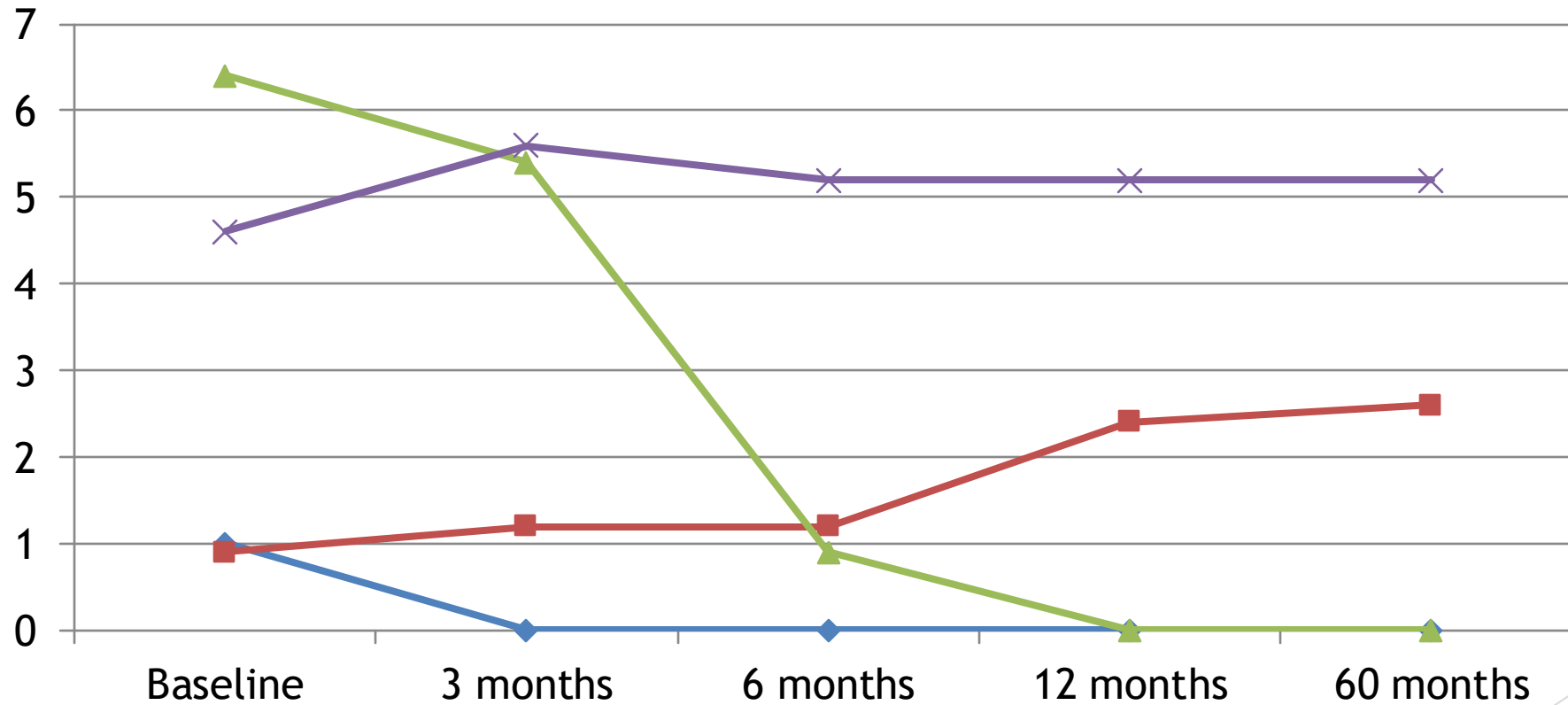
- ▶ Headaches are frequent after TBI with a higher prevalence after mild than moderate to severe TBI
 - ▶ However, headache appears to be more severe in those with moderate to severe TBI
- ▶ Majority meet ICHD classification as migraine and probable migraine
- ▶ Age appears to be a risk factor for the development of headache



Headache Pain

Best Model

Pain Rating



Group Percents: Minimal=25.4% Worsening=37.1% Improving=7.4% Chronic=30.1%



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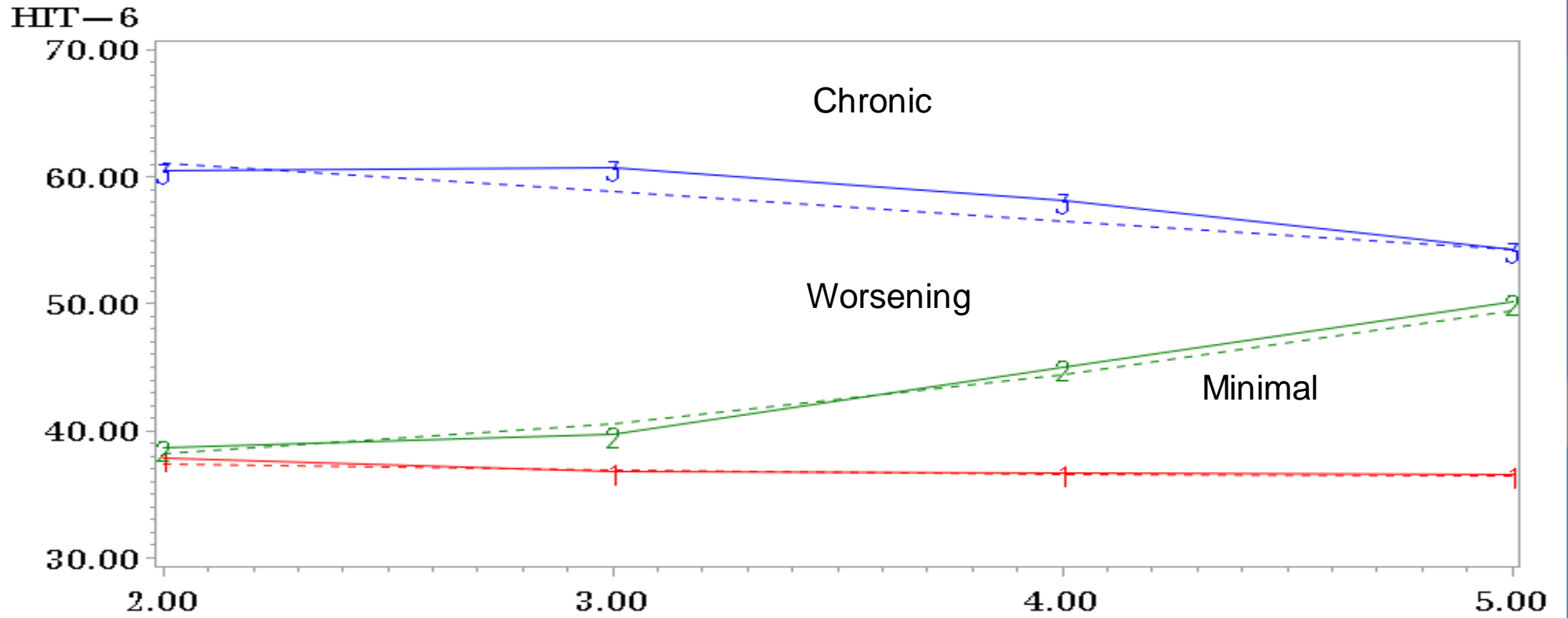
Pain and Headache Impact 5 years after Moderate to Severe TBI

- ▶ Discrete Mixture Modeling was used to estimate trajectory groups based on both pain rating (1-10) and impact score using HIT-6 (36-78)
 - ▶ HIT-6 scoring:
 - ▶ 49 or less=no impact
 - ▶ 50-55=some impact
 - ▶ 56-59=substantial impact
 - ▶ 60 or over=severe impact



Headache Impact

Best Model



Group Percents

48.4

27.3

24.3

Factors Related to Trajectory Membership

Chronic Pain

- ▶ Female
- ▶ Injured by violence
- ▶ Unemployed prior to injury
- ▶ History of headache or mental health problem

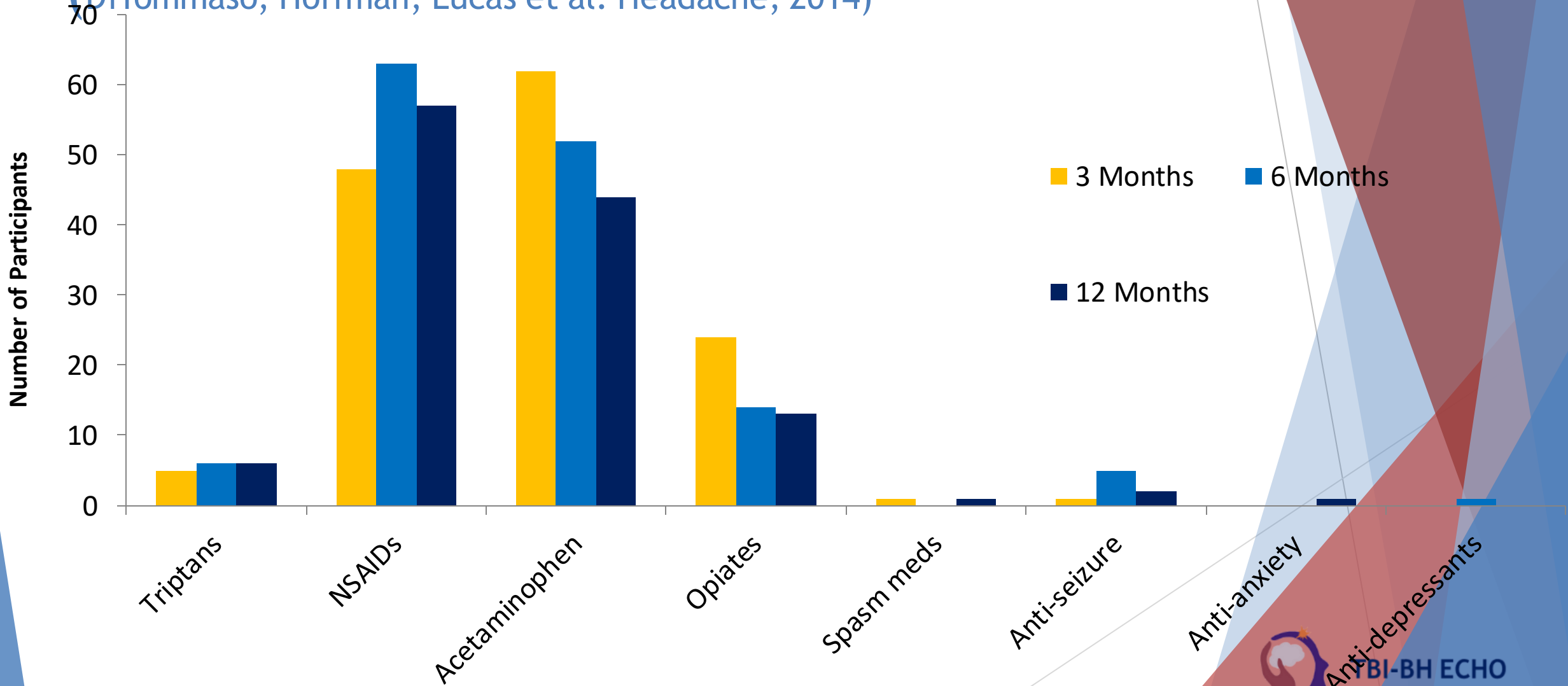
Chronic Impact

- ▶ Female
- ▶ Injured by violence
- ▶ Unemployed prior to injury
- ▶ History of headache



Self-Report of Treatment in those with mTBI

(DiTommaso, Hoffman, Lucas et al. Headache; 2014)



Subjects Reporting Headache, Depression, Both or Neither over One Year after mTBI

	Baseline N=212	Year 1 N=187
Headache only	112 (52%)	81 (43%)
Depression only	8 (4%)	4 (2%)
Headache and Depression	23 (11%)	46 (25%)
Neither	69 (33%)	56 (30%)
RR that subjects with headache will be depressed	1.64	5.43***
RR that subjects with depression will have headache	1.20	1.56***

*** p<0.001



Conclusions

- ▶ Rates of headache after mTBI were high at baseline (64%) and at 1 year (68%).
- ▶ Rates of depression after mTBI increased across 1 year from 15% at baseline to 27%.
- ▶ Headache with depression increased in comorbidity from baseline (11%) to 1 year (25%). However, few subjects had isolated depression without headache at baseline (4%) or 1 year (2%).
- ▶ At 1 year, subjects who had headache were 5.4 times more likely to be depressed than those without headache at 1 year. However, early after injury these two symptoms were unrelated with RR of 1.64.



A Sports-related Post-traumatic Headache

- ▶ A 13 year old right handed girl is referred to me 6 months after an injury
- ▶ She was crouching ready to take shot during a soccer game when shouldered in the right temple by an opposing player.
- ▶ She was thrown to the ground, hitting the grass turf with the left side of her head. She saw stars. She does not remember a conversation with her coach immediately after the event.
- ▶ She rested on the sidelines with an ice-pack to treat a headache of immediate onset. Denied neck pain



Next Day

- ▶ The following day she had trouble walking and a little imbalance and she was taken to a local ER
- ▶ Seen at Multicare Concussion Program
 - ▶ MRI brain normal
 - ▶ Braces artifact
 - ▶ Saw a chiropractor



The Headache

- ▶ Headache has been constant “24-7”, worse since school started with severity 5-6/10 to 10/10
- ▶ Cap-like over the vertex stopping at a band around her head
- ▶ Bilateral orbital pain
- ▶ Allodynia with severe pain-touch hurts if severe
- ▶ Squeezing and throbbing when severe
- ▶ Nausea and vomiting, photophobia and phonophobia
- ▶ Cant go to school, lays on the couch, watches TV, trouble getting to sleep



What Will Help Diagnosis and Treatment Options?

- ▶ No prior history of headache, though she recently started menarche.
- ▶ Family history of headache: paternal grandmother, father, and uncle have moderate to severe headaches
- ▶ Some recent weight loss and mother thinks she has mild depression



Diagnosis: Post-traumatic Headache

- ▶ Mild concussion
- ▶ Chronic lasting over 6 months increases in intensity with concentration but not watching TV
- ▶ Evaluate clinical features of headache:
 - ▶ Throbbing
 - ▶ Physical activity makes it worse
 - ▶ Moderate to severe
 - ▶ Nausea/occ vomiting, photo/phonophobia
- ▶ Decided to treat with drugs typically used for prevention of primary migraine headache



Medications

- ▶ Doxepin 10 mg at bedtime (sleep and pain blocker)
- ▶ Fluoxetine 10-20 mg (for chronicity of headache, mood, helps the TCA effect)
- ▶ Acute therapy: triptan
- ▶ Non-contact sports at school
- ▶ Gradual time increase at school 1 hour at first, building up, no television at home



Follow-up Visit 2/18/10

- ▶ No headache for a month
- ▶ Last headache Christmas break
- ▶ Stopped all drugs on her own at once and headache reoccurred
- ▶ Released by her sports doctor to play non-contact sports. I recommended restarting the preventives, then if no headache during the sports activity, taper off each slowly



Case

- ▶ 61 year old administrator with no prior h/o HA seen 4 months after injury
- ▶ She was running over wet marble tile handing a tool to her husband who is attempting to fix a water leak
- ▶ Slipped and fell backwards landing hard on her occiput. Possible very brief LOC; no PTA
- ▶ Immediate neck pain, back pain and nausea
- ▶ HA began 6 days later
- ▶ Diagnosis?



Case

- ▶ HA cap-like and occipital
- ▶ Daily, continuous 2-5/10 with 5/10 described as severe (10 is childbirth); 10 HA/month are migraine-type
- ▶ Sharp, stabbing “the worst hangover you could have”
- ▶ Severe photophobia, mild phonophobia
- ▶ Tried OTCs acetaminophen, naproxen, Excedrin, aspirin, ibuprofen with no relief. PCP gave her hydrocodone 5/325 mg up to 6/day, then changed to 10/325 mg up to 3/day with some relief; head CT normal
- ▶ Started on gabapentin 100 mg at bedtime for difficulty staying asleep, increased to 200 mg-groggy. Switched to amitriptyline 10 mg-not as good



Case

- ▶ The following month she was started on Botox
 - ▶ 155 units for three sets of injections
 - ▶ Before Botox daily HA; average pain 3/10
 - ▶ After Botox #1 2 HA-free days; average pain 2/10
 - ▶ After Botox #2 20 HA-free days; average pain 2/10
 - ▶ After Botox #3 19 HA-free days; average pain 2/10
- ▶ Improved MIDAS, HIT-6



TREAT THE PHENOTYPE

- ▶ Evaluate clinical features of PTH and treat as a primary headache disorder
 - ▶ Prior history of headache or family history of headache may make it more likely to respond to the treatment but this needs further study
- ▶ Severity of headache may determine need for non-specific vs specific migraine therapy
 - ▶ Frequency may determine need for preventive therapy
- ▶ Recognize co-morbid conditions
- ▶ Need to consider severity of TBI and cognitive impairment in the individual with PTH and choose therapy accordingly



Common Comorbidities

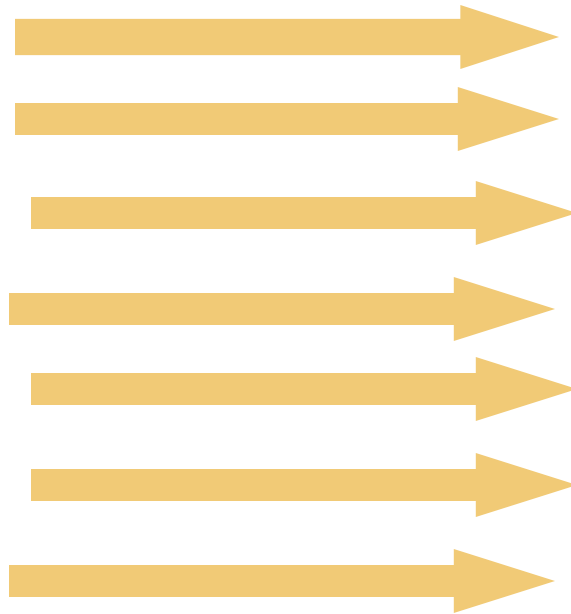
- ▶ Comorbid conditions often found in migraineurs include
 - ▶ Depression
 - ▶ Anxiety
 - ▶ Social phobias
 - ▶ Bipolar disorder
 - ▶ Irritable bowel syndrome
 - ▶ Sleep disorders



Migraine Comorbidity May Assist With Choice of Preventive Agent

Comorbidity

- ▶ Anxiety
- ▶ Frequent aura
- ▶ Depression
- ▶ Hypertension
- ▶ Insomnia
- ▶ Obesity
- ▶ Raynaud's



Agent

- ▶ beta-blockers
- ▶ verapamil, AEDs
- ▶ venlafaxine
- ▶ antihypertensives
- ▶ TCA, melatonin
- ▶ topiramate
- ▶ verapamil

AED=antiepileptic (anticonvulsant) drug; TCA=tricyclic antidepressant



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Lipton R, Silberstein S. *Clinician*. 2001;19:1-26.



Thank you



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Reference Slides



Goals of Acute Therapy

- ▶ The goal of treatment is to restore ability to function. Stratify care based on attack severity and disability and match efficacy of initial headache therapy to the treatment need.
- ▶ Treat a migraine attack as soon as possible after onset. If the headache reoccurs, re-treat.
- ▶ Minimize use of back-up and rescue medications by making sure the initial drug is effective.
- ▶ Optimize self care by patient education and an effective treatment plan with effective patient “tools” to avoid urgent care visits or lapse from physician care.
- ▶ Avoid or minimize side effects by choosing medication with good tolerability as initial therapy.



Acute Migraine Medications

- ▶ Nonspecific
 - ▶ Simple Analgesics
 - ▶ Combination analgesics
 - ▶ NSAIDS
 - ▶ Opioids
 - ▶ Corticosteroids
- ▶ Adjunctive therapies
 - ▶ Antiemetics/dopamine antagonists
- ▶ Specific
 - ▶ Ergotamine/Dihydroergotamine
 - ▶ Triptans
 - ▶ Gepants
 - ▶ Ditans



Ergots

- Known since the Middle Ages but orals have tolerability issues (nausea, vomiting, vasoconstriction)
- DHE (dihydroergotamine) synthesized 1945; dosed IV, IM, SQ, intranasal
- 5HT_{1B/1D/1F/1A/2A} as well as binding at cholinergic, dopaminergic, adrenergic receptors
- Long T_{1/2}; effective early or late in attacks
- 89% of patients treated with q8h IV DHE were pain free in 48 hours (refractory migraine; status migrainosus)
- AEs: nausea, vomiting, dizziness, site reactions, flushing, sweating
- Contraindicated in vascular disease and pregnancy



Triptans

- 5-hydroxytryptamine serotonin (5-HT)_{1b/d} agonists developed to cause vasoconstriction and block release of neuropeptides e.g. CGRP
- First line treatment for moderate to severe migraine
 - Generic and underprescribed
 - Long history of safety and efficacy
 - Pain free rates at 2 hrs 51% (3 mg SQ) vs 31% (placebo)
 - Seven available
 - Oral, ODT, nasal, subcutaneous, combination with NSAID
 - AEs: fatigue, dizziness, chest discomfort, paresthesias, flushing, heaviness sensation, sedation, nausea (mild, short-lived)
 - Treat early for best response
 - Recurrence in 30%
 - Contraindicated in vascular disease (and pregnancy in PI)



Gepants

- ▶ Calcitonin gene-related peptide (CGRP) antagonists (gepants)
 - ▶ CGRP levels correlated with migraine attacks
 - ▶ Ubrogepant, rimegepant
 - ▶ 2 hour pain freedom 22% (100 mg ubrogepant) vs 14% (placebo)
 - ▶ No vasoconstriction
 - ▶ AEs: nausea, somnolence, dry mouth

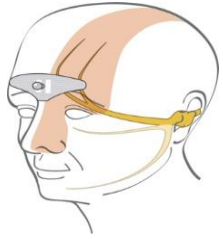


Ditans

- ▶ Selective 5-HT_{1F} agonists: Lasmiditan
- ▶ Not a vasoconstrictor
- ▶ AEs: dizziness, fatigue, paresthesia, sedation, driving impairment 90 min to 8 hours after dose
- ▶ Pain free at 2 hours 28-39% (50-200 mg) vs 15% placebo



NEUROMODULATION THERAPIES :



Supraorbital nerve stimulation - Cefaly device - acute migraine therapy



Transcranial magnetic stimulation
acute migraine therapy



Transcutaneous vagal nerve stimulation
acute cluster headache therapy



Sphenopalatine ganglion stimulation
acute (preventive?) cluster headache therapy



Occipital nerve stimulation
chronic headache



Preventive Therapies



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Guidelines for Initiating Preventive Medication in Post-Traumatic Headache

- ▶ Frequency of headache greater than 4-6 per month, disability more than 2-3 days per month or that significantly interferes with quality of life
- ▶ Use of acute medication more than 2-3 times per week on average or escalating use
- ▶ Acute medications contraindicated, not tolerated, or ineffective
- ▶ Use co-morbid conditions to select preventive therapy
- ▶ Difference between PTH and primary headaches may be the issues with cognitive changes following TBI
 - ▶ Compliance, memory, side effects of medication



Goals of Preventive Treatment

- ▶ Reduce attack frequency, severity, and duration
- ▶ Improve responsiveness to treatment of acute attacks
- ▶ Improve function and reduce disability
- ▶ Reduce use of acute medication and potential for rebound headache
- ▶ Prevent disease progression



Principles of Preventive Treatment

- ▶ Start with low dose and increase slowly
- ▶ Need adequate trial (1 to 2 months)
- ▶ Avoid drug overuse and interfering drugs
- ▶ Evaluate therapy
 - ▶ Use calendar
 - ▶ Taper (and stop?) if headaches well controlled
- ▶ Discuss family planning issues before initiating therapy



Classes of Treatments used for Preventive Migraine Treatment

- Antiepileptic
 - Divalproex sodium, topiramate, gabapentin
- Antidepressant
 - Amitriptyline (TCAs), venlafaxine, SNRIs
- Beta-blockers
 - Propranolol, timolol, metoprolol
- Other antihypertensive
 - Verapamil, lisinopril, candesartan
- Neurotoxins
 - onabotulinumtoxinA
- CGRP monoclonal antibodies
 - Erenumab, fremanezumab, galcanezumab, eptinezumab
- Herbal and nutritional supplements
 - Magnesium, riboflavin, feverfew, CoQ10, melatonin



Antibodies to CGRP or Its Receptor

	Eptinezumab	Erenumab	Fremanezumab	Galcanezumab
Target	Ligand	Receptor	Ligand	Ligand
Subclass	Humanized	Human	Humanized	Humanized
Dose	100-300 mg IV q 3 months	70 or 140 mg SQ monthly	225 mg SQ q month or 675 mg SQ q 3 months	240 mg SQ loading dose then 120 mg SQ monthly
Tmax	2-5 hours	5.5 days	5-7 days	7-13 days
Half-life	27 days	21-23 days	31 days	28 days



Occipital Nerve Block

- ▶ Occipital Neuralgia
- ▶ Cervicogenic Headache
- ▶ Migraine^{1,2}
- ▶ Cluster Headache³
- ▶ Hemicrania Continua⁴

1. Ashkenazi A, Young WB. Headache 2005;45:350-354

2. Cook BL, et al . Neurology (Abstract) 2006;66:A42

3. Ambrosini A et al . Pain 2005;118:92-96

4. Rozen T. Headache 2007;47:917-919



Behavioral Therapy

- ▶ Explanation
- ▶ Education
- ▶ Self control
- ▶ Relaxation
- ▶ Biofeedback
- ▶ Cognitive therapy
- ▶ Imagery
- ▶ Breathing

