Economics of Traumatic Brain Injury (TBI) Biomarkers

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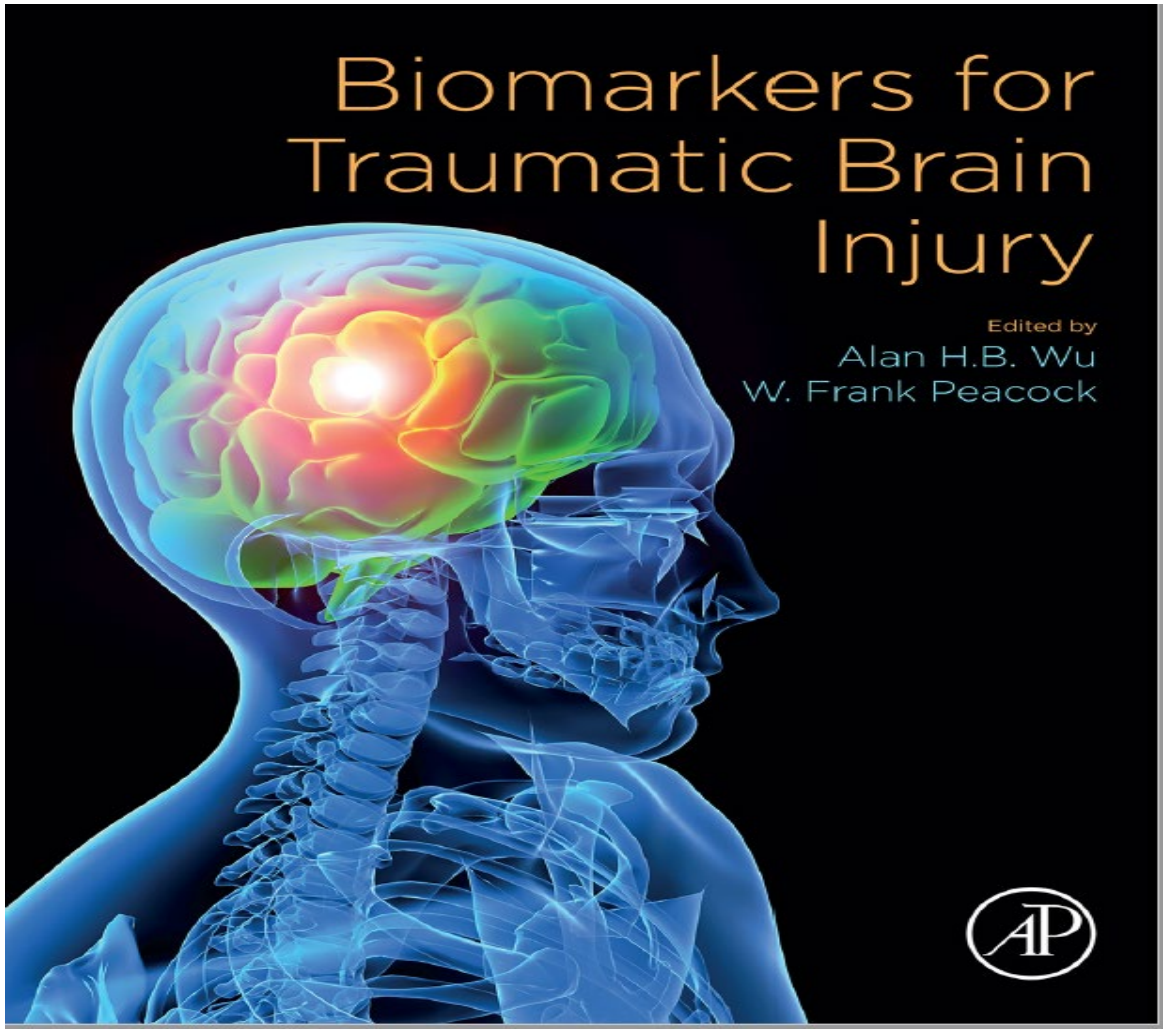

Outline

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Background

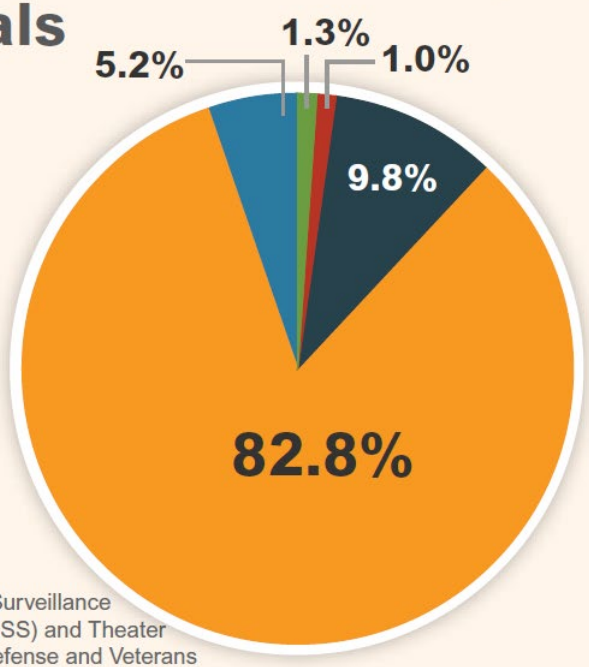
- Traumatic Brain Injury (TBI) is the leading cause of death and disability globally among all trauma-related injuries.[1]
- The global incidence of all-cause all-severity TBI has been estimated to be 939 per 100,000 population, resulting in an estimated 69 million individuals exposed to TBI each year.[2]
- Mild TBI affects about 740 per 100,000 individuals, approximately 55.9 million each year worldwide.[2]
- Severe TBI has been estimated to affect about 73 per 100,000, approximately 5.48 million individuals each year worldwide.[2]
- Between 2000-2019, there were 413,858 military TBIs worldwide, with 82.8% classified as mild.[3]

Military TBI

DoD Numbers for Traumatic Brain Injury
Worldwide — Totals

2000-2019 Q3

Penetrating	5,279
Severe	4,110
Moderate	40,378
Mild	342,747
Not Classifiable	21,344
Total - All Severities	**413,858**



Source: 2000 to 2018 Q1 data provided by the Armed Forces Health Surveillance Branch (AFHSB) using the Defense Medical Surveillance System (DMSS) and Theater Medical Data Store (TMDS); data starting 2018 Q2 provided by the Defense and Veterans Brain Injury Center (DVBIC) using the MHS Data Repository (MDR).

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

2000-2019 Q3, as of November 08, 2019

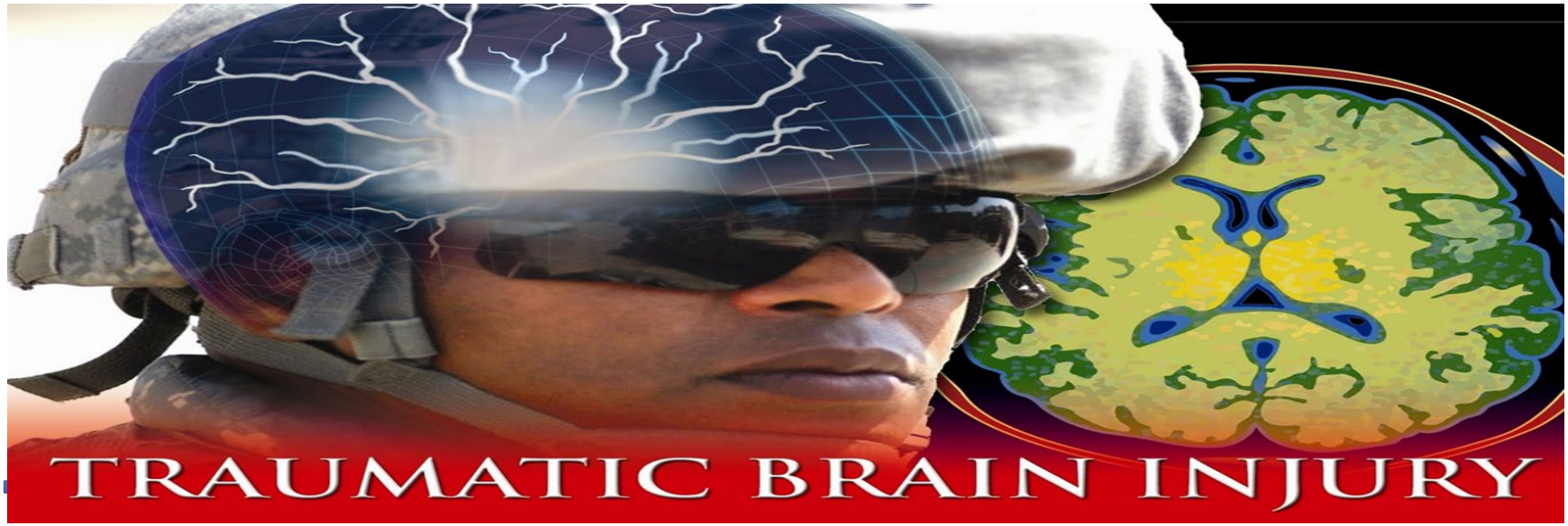
*Percentage may not add to 100% due to rounding.

Background
Blood Biomarker, CT and MRI

- As of this writing, there is one U.S. FDA approved TBI blood biomarker (Banyan Brain Trauma Indicator) and one internationally approved TBI blood biomarker in Sweden. Banyan predicted intracranial lesions with 97.5% accuracy and absence of intracranial lesions with 99.6% accuracy in individuals with head trauma [4,5]
- Pricing for the FDA approved biomarker has not been established in the United States and the Swedish Biomarker costs approximately 21 Euros ($24.34).[4,5]
- U.S. standard of care for Emergency Department TBI diagnosis and management is CT and Glasgow Coma Scale (GCS).[6]
- However, CT is not a very sensitive diagnostic tool as only 5% of patients suspected of having a mild TB will have abnormal findings on CT.[4]
- The FDA states that the availability of a blood test for mild TBI will providers to determine the necessity of CT in individuals suspected of mild TBI and reducing radiation exposure and health care costs.[4]
- Standard MRI is considered to be superior to CT 48 to 72 hours post injury, detecting white matter abnormalities, neuronal damage and brain stem injuries.[7]

Objective

- In absence of US biomarker pricing, we examined the per unit cost of CT and MRI in military Veterans diagnosed with TBI, along with associated inpatient, outpatient, pharmacy and total Veterans Health Administration (VHA) costs over a 14-year period, with costs adjusted for inflation to December, 2018.
- The results provide a benchmark for current standard of care, by which future TBI Blood Biomarker pricing can be compared for cost-effectiveness studies.



Poll Question

Are you aware that a TBI Blood Biomarker has been developed?

Yes

No

Methods

- 79,276 veterans were identified with a TBI diagnosis from VA Informatics and Computing Infrastructure (VINCI) inpatient and outpatient patient treatment file (PTF) databases between January 1, 2000, and December 31, 2010, with information on utilization and cost by VA clinic stop codes.
- Diagnosis and TBI severity were determined by International Classification of Diseases, Ninth Revision (ICD-9) codes for TBI, post-concussive syndrome, and TBI-related late effects, according to the Military Health System and Defense Health Agency Traumatic Brain Injury (TBI) DoD Standard Surveillance Case Definition for TBI Adapted for AFHSB Use.[8]
- Utilization and cost of CT and MRI were determined based on the VA clinic stop codes 150 and 151.[9]
- Health Economics Resource Center (HERC) files were linked to PTF files using a scrambled social security number to identify VHA annual costs per veteran from FY2000-2014.[10]
- Co-morbidities were obtained by applying the Elixhauser Enhanced algorithm to the PTFs.[11]

Methods

- CT and MRI utilization was identified using the VA clinic stop codes and counting the number of occurrences of those codes per veteran. CT and MRI costs were estimated using the HERC outpatient cost files whereby CT and MRI costs were identified based on their associated clinic stop codes.
- Annual per veteran total, inpatient, outpatient and pharmaceutical costs were obtained from HERC files for FY2000-2014.
- HERC inpatient costs consist of acute hospital care, inpatient non-acute care and long-term care, based on Medicare Diagnosis Related Groups (DRGs), Relative Value Units (RVUs) and Resource Utilization Groups (RUGs).[12]
- Outpatient Visit Costs are estimated using the relative values of all Current Procedures and Terminology (CPT) codes assigned to the visit. HERC uses the relative values from the Medicare Resource-Based Relative Value System (RBRVS), which is used to reimburse providers for services provided to Medicare patients.[12]
- Outpatient Pharmacy costs are estimated by HERC from the Managerial Cost Accounting (MCA) national extracts from VA facilities which include estimates of all prescriptions dispensed to an individual on a given day.[12]

Methods

- 31 Elixhauser comorbidities included 4 mental health comorbidities.[11]
- First, we examined the unadjusted % of veterans using CT and MRI by TBI severity status.
- Second and Third, we examined the unadjusted mean, median and interquartile range of cost per unit and utilization of CT and MRI by TBI severity status.
- Fourth, we examined the unadjusted mean, median and interquartile range of the annual per veteran cost of CT and MRI by TBI severity status.
- Our first models were a logit of the likelihood a veteran received a CT/MRI.
- Our second models were GLM (Poisson) models of annual CT and MRI utilization
- Our third models were GLM (Gaussian) models of annual CT and MRI cost per veteran.

Methods

- Our fourth models were total annual VHA annual cost per veteran by any CT/MRI use.
- Our fifth models were the marginal impact of any CT or MRI use on annual inpatient, outpatient and pharmacy VHA costs per veteran using seemingly unrelated regression (SURE), allowing for correlation between categories.
- All models were adjusted for Elixhauser comorbidities as well as TBI severity.
- All costs were converted to December 2018 using US Department of Labor Consumer Price Index Calculator.
- All analyses were performed inside VINCI using STATA 15.0.
- Statistical significance was determined at $P<0.05$

Unadjusted utilization and costs

TABLE 7.1 Unadjusted per unit and per veteran utilization and costs of CT and MRI 2000—14 in 2018 value by TBI severity level.

	CT			MRI		
Variables	All severity	Mild TBI (n = 21,283)	Higher severity TBI (*n* = 58,443)	All severity	Mild TBI (*n* = 21,283)	Higher severity TBI (*n* = 58,443)
Any use of imaging	67,588 (84.78%)	16,097 (75.63%)	51,491 (88.10%)	48,868 (61.29%)	14,959 (70.29%)	33,909 (58.02%)
Cost per unit						
Mean	$468	$460	$470	$732	$692	$750
Median	$422	$410	$425	$639	$595	$655
25 Percentile	$315	$309	$319	$532	$530	$534
75 Percentile	$554	$551	$556	$833	$795	$843
Annual utilization per veteran						
Mean	0.84	0.43	0.99	0.39	0.35	0.40
Median	0.5	0.25	0.64	0.21	0.20	0.21
25 Percentile	0.2	0.06	0.30	0	0	0
75 Percentile	1.125	0.53	1.33	0.54	0.46	0.60
Annual cost per veteran						
Mean	$409	$205	$484	$288	$240	$305
Median	$221	$100	$289	$136	$131	$138
25 Percentile	$77	$20	$113	$0	$0	$0
75 Percentile	$516	$244	$615	$393	$315	$425

CT, Computed tomography; *MRI*, magnetic resonance imaging; *TBI*, Traumatic brain injury.

Co-morbidity adjusted odds of any CT or MRI

TABLE 7.2 Odds ratios from logit models of any CT and MRI relative to no CT or MRI use per veteran.

	CT		MRI	
Variables	Odds ratio	95% CI	Odds ratio	95% CI
Severity				
Mild (reference)				
Higher severity	1.43*	1.37:1.49	0.68*	0.66:0.71

Co-morbidity adjusted utilization and costs

TABLE 7.3 Severity and comorbidity-adjusted annual CT and MRI utilization and costs per veteran 2000–2014 in 2018 values.

	CT		MRI	
Variables	Number (95% CI)	Cost (95% CI)	Number (95% CI)	Cost (95% CI)
Severity				
Mild (reference)				
Higher severity	0.42* (0.410:0.437)	$171* (164:177)	0.09* (0.083:0.102)	$78* (72:84)

Co-morbidity and severity adjusted cost impact of CT and MRI

TABLE 7.4 Severity and comorbidity-adjusted marginal effect of any CT and MRI use on total VHA cost per veteran 2000–2014 in 2018 values.

Variables	Total cost (95% CI)	Inpatient cost (95% CI)	Outpatient cost (95% CI)	Pharmacy cost (95% CI)
Any CT	$1775* (1514:2035)	−$245 (−551:61)	$1646* (1529:1763)	$373* (315:431)
Any MRI	$851* (582:1120)	−$1522* (−1742: −1302)	$1983* (1899:2067)	$389* (348:431)
Severity				
Mild (reference)				
Higher severity	$19 (−185:223)	$393* (160:626)	−$390* (−479:301)	$16 (−27:60)

Co-morbidity and severity adjusted predicted mean annual costs per veteran by CT/MRI use

TABLE 7.5 Severity and comorbidity-adjusted predicted mean annual CT, MRI, and total VHA cost per veteran 2000—2014 in 2018 values.

Variables	CT cost	MRI cost	Total cost	Inpatient cost	Outpatient cost	Pharmacy cost
Severity						
Mild	$284* (279:289)	$230* (225:235)				
Higher severity	$455* (451:459)	$309* (305:313)				
Any CT use						
No			$13,237* (12,981:13,494)	$6686* (6408:6963)	$5259* (5153:5365)	$1292* (1240:1344)
Yes			$15,012* (14,895:15,129)	$6441* (6331:6550)	$6906* (6864:6947)	$1665* (1645:1686)
Any MRI use						
No			$14,220* (14,003:14,438)	**$7411* (7244:7578)**	$5439* (5375:5503)	$1370* (1338:1401)
Yes			$15,072* (14,934:15,210)	**$5889* (5758:6019)**	$7423* (7373:7473)	$1759* (1735:1784)

CT, Computed tomography; *MRI*, magnetic resonance imaging; *VHA*, Veterans Health Administration.

Findings

- The comorbidity adjusted cost of CT was $284 in mild TBI and $455 in in higher severity TBI, which was higher than MRI at $230 in mild TBI and $309 in higher severity TBI.
- The mean 2018 value per unit cost of MRI has been shown to be approximately $732, with a range of $692 for mild TBI severity to $750 for higher TBI severity, in the same cohort.
- Interestingly, the unadjusted frequency of any CT use is higher among veterans with higher TBI severity, but the unadjusted frequency of any MRI use is higher among veterans with lower TBI severity. It is possible that this is due to providers, when facing an absence of findings on CT, but symptoms which could be associated with TBI, choose to perform MRI exams.
- This result is reinforced in the comorbidity-adjusted logit models, which showed that higher TBI severity is associated with a much lower likelihood of any MRI use.

Findings

- Finally, the exciting result that any MRI use was associated with a significant marginal reduction in annual inpatient cost of $1,522 per veteran suggests that MRI use is being used in TBI diagnosis and management to reduce inpatient hospital care and cost.
- This is consistent with the literature stating that CT is better for detecting anatomical pathology and early bleeds, while MRI's ability to detect hematomas improves over time.
- Also, MRI is superior to CT in detecting axonal injury, indirect neuronal damage, and small areas of contusion. In fact, some studies have shown that CT has missed about 10% to 20% of abnormalities detected by MRI.
- In addition, MRI is generally more sensitive than CT for detecting neuronal damage, with individuals whose brains show widespread MRI abnormalities or brain stem injuries, regularly failing to achieve significant neurological recovery, even in the presence of normal CT scans.
- Finally, for prognosis and rehabilitation guidance, MRI has been used to detect white matter abnormalities and provide better information.

Poll Question

Which technology is significantly associated with reduced inpatient cost among veterans diagnosed with TBI in severity and co-morbidity adjusted models?

- CT
- MRI
- Both
- Neither

Limitations

- Diagnoses via VHA administrative data ICD codes - not verified with structured clinical interviews.
- Reason for each CT and MRI was not ascertained. However, comorbidities were adjusted for in the models.
- Inpatient, Outpatient and Pharmacy costs may not be directly associated with TBI exposure: study did not subset the healthcare utilization data to only occur after a participant's initial mTBI exposure.
- Non-VHA care not included
- Our study has a higher percentage of higher severity veterans relative to that reported by DVBIC.
- However, only about a third of the veterans in our cohort were OEF/OIF/OND.

More recent study

- A more recent study published after this study went to press, "Cost-Effectiveness of Biomarker Screening for Traumatic Brain Injury, Journal of Neurtrauma 36:2083-2091 (July 2019) by Su et al, analyzed a cost-effectiveness model to determine the price at which Banyan Biomarker becomes cost-effective relative to CT.[13]
- This study used the literature to obtain estimates of the probability of intracranial lesions and the cost of CT scans as well as quality adjusted life-years (QALYs) and life-expectancy for their model.
- They estimated the cost of the biomarker screen is cost-effective up to $308.96 for mild TBI and $73.41 for moderate TBI.
- Their study was based on literature estimates and not actual data, but did include QALYS and estimated survival.
- This compares with our findings of the comorbidity adjusted cost of CT was $284 in mild TBI and $455 in in higher severity TBI, which was higher than MRI at $230 in mild TBI and $309 in higher severity TBI.

Future Directions

- The ideal would have been to be able to compare pricing and cost impact of the new blood biomarker.
- The S100B biomarker has a per unit cost of $21 in Sweden.
- However, the marginal impact of S100B biomarker on long-term inpatient, outpatient and pharmacy costs are not yet known.
- When the pricing has become available, and the technology has begun to spread through the VA system, a study comparing similar per unit, per Veteran and the marginal impact on total, inpatient, outpatient and pharmacy VA cost will be illuminating.
- This study has served to provide important benchmark information by which new TBI biomarkers could be compared in the future.
- The results are especially relevant, given the finding that though having a higher per unit cost than CT, any MRI use has been shown to reduce inpatient costs in veterans by approximately double the MRI's per unit cost in veterans diagnosed with TBI.

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