

Concussion Guidelines Step 1: Systematic Review of Prevalent Indicators

Supplemental Content 6

Evidence Table. Included Studies For Key Questions 1, 2, and 3 – Medium Potential For Bias – N = 53

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
Anderson 2000 ¹ Hospital Pediatrics KQ 1	Exclusive Case Definition Documented evidence - Period of altered consciousness - GCS 13–15 - No mass lesion evidence on CT - No neurologic deficits	LOC		Not for LOC		Wechsler Verbal, Performance, and Full Scale IQ; Digit Span; Tapping Test; Story Recall; Spatial Learning; Rivermead BMT (mean scores and proportions with abnormal memory) Measured at a range of 0 – 30 days Uninjured controls PCE N = 96 Control N = 35 Recovery graphs show comparisons Significance NR for Wechsler NSD for Digit Span, Tapping Test, Story Recall, and Rivermead. Significance for Spatial Learning NR	ANOVA	Not Fixed
Bazarian 1999 ² Hospital Adults and Pediatrics KQ 1	Exclusive Case Definition All of: - LOC ≤ 10 min (or none) - GCS 15 - No skull fracture - No new focality to neurologic exam	LOC Amnesia		Yes. But, by definition if trauma controls had LOC or PTA, they would be in the TBI group.		NCSE, Trails A and B, Digit Span, Symbol Digit, Hopkins Verbal Learning A and B, and Symptom Checklist 90-R Measured in ED Orthopedic controls PCE N = 71 Control N = 59 PCE significantly worse on Trails A, Hopkins A, NCSE Total, NCSE Memory, Digits Forward Data for recovery graphs only for tests that were significant	Chi-square unpaired t-tests	Fixed
Broglio 2007 ³ Sports Adults KQ 1	Inclusive Case Definition AAN Grade 1: - Confusion - No LOC - Symptoms <	LOC 5/75 had LOC (6.7%)	Could not use symptoms (composite); 51/75 clinically sign. increase in duration or severity.	Self as own controls in pre-injury assessment	NeuroCom SOT 39/63 (61.9%) Clinically sign. impairment on at least 1 SOT variable Composite – 36.5% impaired	<u>3 Independent Samples – N = 75</u> a. Pencil and Paper Neuropsych Battery – n=23 b. HeadMinder – n=28 c. ImPACT – n=24 Measured at baseline and within 24 hours of PCE.	RCI Symptoms: 1SD below baseline for sum. Balance: 1SD below on any variable.	Fixed Baseline Day 1

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	15 m Grade 2: - No LOC - Symptoms > 15 m Grade 3: - LOC				Somatosensory ratio – 36.5% impaired Visual ratio – 31.7% impaired Vestibular ratio – 23.8% impaired	Self as own controls. <u>Proportion of sample with clinically sign. decrements</u> NeuroCom Composite: 36.5%, Somatosensory ratio: 36.5%, Visual ratio: 31.7%, Vestibular ratio: 23.8% Hopkins Verbal Learning Test (HVLT): 39.1% Trails A & B: 52.2% Symbol Digit: 52.2% Digit Span: 30.4% Controlled Oral Word Association Test (COWAT): 34.8% ImPACT Verbal: 41.7%, Visual: 20.8%, Motor: 20.8%, Reaction Time: 41.7% HeadMinder Simple Reaction Time: 71.4%, Complex Reaction Time: 71.4%, Processing Speed: 50%	Neuropsych: 1SD on 2 or more.	
Broglio 2007 ⁴ Sports Adults KQ 1	Inclusive Case Definition Simple: - No LOC <u>and</u> - Symptoms res. within 10 days Complex: - LOC > 1 minute <u>or</u> - Symptoms > 10 days			Self as own controls in pre-injury assessment		ImPACT Timepoints vary because all were assessed while symptomatic (mean 1.24 days; SD 0.70), and again when post-symptomatic (mean 8.14 days; SD 6.48). Self as own controls. N = 21 Simple concussion: No LOC <u>and</u> no symptoms within 10 days. Complex concussion: LOC > 1 min. <u>or</u> symptoms > 10 days. Total Sample: T1: 15/21 (71%) impaired on at least 1. 7 – Verbal, 8 – Visual, 5 – Motor, 9 – Reaction Time. T2: 8/21 (38%) impaired on at least 1 Simple Concussion: T2: 6/17 impaired Complex Concussion: T2: 2/4 impaired	RCI	Not Fixed Baseline Mean: 1.24 days (symptoms) 8.14 days (no symptoms)

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						At symptom resolution, 8/21 (38%) still had impairment on at least one cognitive measure, based on RCI. 6 – simple concussion 2 – complex concussion 1 – Verbal, 2 – Visual, 3 – Motor, 4 – Reaction Time		
Broglia 2009 ⁵ Sports Adults KQ 1 and 3	Inclusive Case Definition AAN Grade 1: - Confusion - No LOC - Symptoms < 15 min Grade 2: - No LOC - Symptoms > 15 min Grade 3: - LOC		Balance problems Dizziness Feeling mentally foggy Difficulty concentrating Difficulty remembering KQ3 Post Hoc significant correlation between: - balance and feeling foggy (r = 0.59, p < 0.00); concentration (r = 0.67, p < 0.00); memory (r = 0.58, p < 0.00). - dizziness and feeling foggy (r = 0.55, p < 0.00); concentration (r = 0.66, p < 0.00); memory (r = 0.55, p < 0.00)	Not for symptoms. Participants were own controls for Neurologic and Neurocognitive. Symptoms used in KQ3 analysis.	NeuroCom SOT Baseline and within 48 hours Self as own controls N = 26 RCI – 5/26 (19.2%) had clinically sign. decline in balance. 3 of the 5 reported balance symptoms. KQ3: Correlations between self-report of balance symptoms and objective measures of balance. Significant diff: - Balance symptom with SOT Composite (p < 0.00), Somatosensory (p = 0.03), Visual (p = 0.04) , and Vestibular (p < 0.00). - Dizziness symptom with SOT Composite (p < 0.00) and Vestibular (p = 0.01).	ImPACT Baseline and within 48 hours Self as own controls. N = 32 Cannot use for KQ1 because did not report which function. RCI – 22/32 (68.8%) had clinically significant declines in cognitive function. 14 of the 22 reported cognitive symptoms. KQ3: Correlations between self-report of cognitive symptoms and objective measures of cognition. Significant diff: - Foggy symptom and Reaction Time (p = 0.03). - Concentration symptom and Verbal Memory (p = 0.01). - Memory symptom and Verbal Memory (p < 0.001); Reaction Time (p = 0.03).	Spearman Correlations RCI	Not fixed, but within 48 hours of injury
Bryant 1999 ⁶ Hospital Adults KQ 1	Exclusive Case Definition PTA < 24 hours		Acute stress disorder symptoms PTSD symptoms – refer to publication Measured between 2 and 25 days post-	Yes, but by definition, if trauma controls had PTA, they would be in the mTBI group.			Chi-square; Bonferroni adj. alpha 0.003 for 0.05 rejection level	Not Fixed

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			<p>trauma. All patients were MVAs. Controls were MVAs without mTBI.</p> <p>PCE N = 79 Control N = 92</p> <p>Sign. > Fear, Helplessness, and Recurrent Memories for Controls on ASDI at 2-25 days.</p>					
<p>Cavanaugh 2005⁷</p> <p>Sports Adults</p> <p>KQ 1</p>	<p>Inclusive Case Definition Immediate but temporary:</p> <ul style="list-style-type: none"> - LOC, - Blurred vision, - Dizziness, - Amnesia, <u>or</u> - Memory impairment 				<p>NeuroCom SOT</p> <p>Measured at pre-trauma baseline and within 48 hours. Self as own controls. N = 27</p> <p>Measured 6 conditions each for: <u>ApEn AP</u> – Mean approximate entropy values for center of pressure anterior-posterior time series. <u>ApEn ML</u> – Mean approximate entropy values for center or pressure medial-lateral time series.</p> <p>Recovery graphs show comparisons. ANOVA showed a 3-way interaction, so further statistical analysis was not conducted</p> <p>Described magnitude of decline across days for each SOT condition</p>		ANOVA	Not fixed, but within 48 hours

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					For ApEn AP – CSD for Sensory Conditions 1 and 2. For ApEn ML – CSD for all conditions			
Collins 1999 ⁸ Sports Adults KQ 1 and 2	Inclusive Case Definition AAN Practice Parameters: Traumatically induced alteration in mental status with or without LOC	LOC 2/19 (10.5%) had LOC Symptoms recorded for entire sample pre-trauma, but post-trauma symptoms not compared to pre-trauma baseline.		Self as own controls in pre-injury assessment, but outcome data reported used comparison group of uninjured athletes.		Hopkins Verbal Learning Test (HVLTL), Trails A and B, Symbol Digit, Grooved Pegboard, and Controlled Oral Word Association Test (COWAT) Measured at pre-trauma baseline and 1, 3, 5, and 7 days. Self as own controls, but data reported for comparison group of uninjured athletes. PCE N = 16 (3 of 19 excluded) Control N = 10 Recovery graphs show comparisons. Standard scores created to convert neuropsych test scores to common metric. Group differences of ½ SD were considered moderate difference between groups. <u>Results:</u> 1 SD difference between groups at 24 hrs. for HVLTL Total (trials 1-3) and HVLTL Total Delay Score. ½ SD persisted until 5 days post-injury. <u>Group Differences (Previous Concussions)</u> <u>Mean pre-injury baseline scores grouped by previous concussion:</u> Trails B – significant diff. between ≥ 2 previous concussions and 0 previous concussions p = 0.02. Trails B – significant diff. between ≥ 2 previous concussions and 1 previous concussion p < 0.001. Symbol Digit – significant diff. between ≥ 2 previous concussions and 0 previous concussions p = 0.008. Symbol Digit – significant diff. between ≥ 2 previous concussions and 1 previous	RCI	Fixed

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						concussion $p < 0.001$. <u>Mean pre-injury baseline scores grouped by learning disability:</u> No significant diff.		
Collins 2006 ⁹ Sports Adolescents KQ 1	Inclusive Case Definition One or more of: - Observable alteration in mental status or consciousness - LOC, disorientation, Amnesia - Self-reported symptoms such as headache, photosensitivity, nausea/vomiting, or dizziness.	LOC Amnesia 10/74 (13.5%) had LOC 19/74 (25.7%) had Retrograde Amnesia 19/74 (25.7%) had PTA	21 item ImPACT Symptom Scale; measured pre- and post-trauma, but only composite reported	This was an intervention study (Revolution helmets vs standard helmets). Only used control group data		ImPACT Measured at pre-trauma baseline and between 0 and 11 days post Self as own controls N = 74 Post-trauma scores sign. worse than pre-trauma for all 4 domains Verbal $p < 0.001$, $d = 0.78$ Visual $p < 0.001$, $d = 0.92$ Reaction Time $p < 0.001$, $d = 0.79$ Processing Speed $p < 0.001$, $d = 0.54$	Paired t-tests	Fixed - Signs Not fixed - Neurocog
Comerford 2002 ¹⁰ Hospital Adults KQ 1	Exclusive Case Definition GCS 13 – 15	LOC		Yes. But, by definition if trauma controls had LOC, they would be in the mTBI group.		Rapid Screen of Concussion: Sentence Comprehension, No. Sentences Completed, Reaction Time to Complete Sentences, Immediate Memory, Learning Trial 1, Learning Trial 2 Measured in E.D. Orthopedic controls PCE N = 56 Control N = 85 PCEs significantly worse on all but Immediate Memory and Learning Trial 1	ANCOVA	Fixed
Cooper 2010 ¹¹ Military Hospital Adults KQ 1	Exclusive Case Definition - LOC < 30 min, - Amnesia < 24 hrs, - Alteration of mental state (dazed, disoriented,					RBANS: Immediate Memory, Visuospatial/Constructional, Language, Attention, and Delayed Memory Assessments occurred after patients were determined medically stable – mean 8.12 wks (SD 7.763) Military study	ANOVA	Not Fixed

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	confused), and - GCS \geq 13					Burn injury controls. PCE N = 50 Control N = 117 PCEs significantly worse on Visuospatial/Constructional, Attention, and Total Score		
Covassin 2007 ¹² Sports Adults KQ 1 and 2	Inclusive Case Definition AAN: - Altered mental state - With or without LOC	LOC Vomiting 3/79 had LOC (3.8%) Sign. > vomiting for males than females (F 1, 77 = 5.95; p = 0.017)	Sadness Sign. greater sadness for males than females (F 1, 77 = 13.05; p = 0.001) Did not report results for individual symptoms.	Self as own controls in pre-injury assessment		ImPACT Measured at 1-3 days; 7-10 days Self as own controls N = 79 Based on RCI: T1 – 58% had 1 or more declines in performance or increase in symptoms T2 – 30% had 1 or more declines (cannot use for KQ1 because composite) Based on univariate post-hoc analysis, concussed females performed sign. worse than concussed males on visual memory at 1-3 days. NSD on verbal, reaction time, or processing speed.	ANOVA RCI	Signs: Fixed Neurocog: Not Fixed 1-3 d 7-10 d
Covassin 2010 ¹³ Sports Adolescents KQ 1	Case Definition Not Specific Concussion in Sport Group definition: Complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces.		ImPACT symptoms reported as composite			ImPACT Measured at pre-trauma baseline and 2, 7, 14, 21, and 30 days post-injury. N = 72 Significantly slower reaction time \leq 14 days post-injury compared to baseline (p = 0.001); lower verbal memory scores at 7 days post-injury (p = 0.003); lower motor processing speed scores at 7 days post-injury (p = 0.000);	ANOVA and RCI to determine when the athlete had recovered	Fixed
De Monte 2006 ¹⁴ Hospital Adults and Pediatrics	Inclusive Case Definition GCS 13 – 15 Negative CT	PTA 42/90 PCEs (46.7%) had		Yes		Cannot use most of neurocognitive measures because they were adapted and not validated. Can only use Digit Symbol.	p value	Fixed

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KQ 1 and 3	scan <u>and</u> any of: - Loss of balance - Loss or altered consciousness - Amnesia - Disorientation - Confusion - Vomiting - Nausea - Blurred Vision - Headache	PTA 6/35 (17.1%) Orthopedic Controls had PTA				Measured in E.D. <u>Four groups:</u> mTBI/No PTA N = 48 mTBI/With PTA N = 42 Orthopedic N = 35 Uninjured N = 43 KQ3: NSD on Digit Symbol between mTBI/No PTA, Orthopedic, and Uninjured groups. Significant diff. on Digit Symbol between mTBI/No PTA and mTBI/With PTA ($t_{88} = 6.25, p < 0.001$)		
Dikmen 1986 ¹⁵ Hospital Adults and Pediatrics KQ 1	Inclusive Case Definition - GCS 13 – 15 - Coma < 1 hour <u>or if no coma</u> - PTA at least 1 hour - No evidence of cortical or brain stem contusion		Headache Fatigue Dizziness Blurred vision Noise sensitivity Light sensitivity Insomnia Difficulty concentrating Irritability Loss of temper easily Memory difficulties Anxiety Sign. greater Noise, Insomnia, Memory for PCEs	Yes		Finger Tapping, Speech Sounds Perception, Seashore Rhythm, Trails A and B, Wechsler Memory Scale, Selective Reminding Test, Category Test E.D. Sample Measured at 1 month Uninjured controls PCE N = 20 Control N = 19 Significantly worse for PCEs on Seashore, and Selective Reminding 4 hr. Delay	Wilcoxon and McNemar's	Not fixed Target 1 month, no variance reported
Dischinger 2009 ¹⁶ Hospital Adults KQ 1	Inclusive Case Definition GCS 13 – 15 At least of one: - LOC < 30 min - Amnesia - Altered mental state (confusion,		Headache Dizziness Blurred vision Fatigue Sensitivity to light Sensitivity to noise Concentration problems Memory problems	Self as own controls – self-report of prevalence of symptoms prior to injury that was provided post-injury (retrospectively)			Contingency tables, t-test, ANOVA, and correlations. However, performed on composite or to predict long-term PCS. Statistical	T1 Fixed: pre-injury T2 Not Fixed: range T3 Not fixed Targeted, no variance reported.

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	disorientation, feeling dazed) - Acceptable score on the Mini Mental State Examination (8/10)		Trouble thinking Anxiety Depression Irritability Measured at Pre-injury, 3-10 days, and 3 months Self as own controls N = 180, 164, and 110 at T1, 2, and 3 Recovery curves show comparisons in changes but significance NR.				analysis of proportions NR.	
Echemendia 2001 ¹⁷ Sports Adults KQ 1	Not defined					HVLT, Symbol Digit, Symbol Digit Memory, Digit Span, Penn State Cancellation Test, Trail Making Test, COWAT, Stroop, Vigil Continuous Performance Measure at pre-trauma, 2 hours, 48 hours, 1 week, and 1 month. 2-hour assessment only included Digit Span, HVLT, and Stroop. Uninjured matched athletic controls PCE N = 29 Control N = 20 At 2 hours, PCEs significantly worse on Digits Forward and 4 HVLT measures. At 48 hours, PCEs significantly worse on Digits Backwards, 3 HVLT measures, and Stroop Time. At 1 week, NSD on MANOVA. Recovery curves only for statistically significant results, so had to add separate graphs for each time point.	MANOVA – 2 hours, 48 hours, and 1 week ANOVAs – 1 week and 1 month	Fixed – 2 hours and 2 days Uncertain – 1 week. Target with no variance reported – 1 month.
Fay 1993 ¹⁸	Exclusive Case	LOC		Not for GCS		WISC-R, Category Test, Tactual Performance	Wilcoxon signed	Not Fixed

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Hospital Pediatrics KQ 1	Definition - GCS 13 – 15 - GCS 15 within 3 days - Documented LOC	GCS Authors report that 48 of 53 had an initial GCS of 15, and the remaining 5 achieved 15 within 3 days. They report that 50 had LOC < 10 min, and 3 LOC 10 min to 1 hr. So we don't know if the LOC < 10 min. includes no LOC.				Test, Progressive Figures and Color Form (younger) or Trails B (older), Sensory Perceptual Examination, Tapping, Grip Strength, CVLT-C Measured between 14-40 days Uninjured matched controls PCE N = 53 Control N = 53 NSD on 29 subtests. Only significant diff. was on 3 of 9 functional measures.	rank test	
Field 2003 ¹⁹ Sports Adults and Adolescents (Has Group Differences data, but was rated high PFB for those data, medium PFB for KQ1 data.) KQ 1	Inclusive Case Definition 1) Observable alteration in mental status or consciousness 2) Constellation of self-reported symptoms (eg, headache, fogginess, nausea/vomiting) <u>and/or</u> 3) LOC, disorientation, and/or amnesia	LOC		Not for LOC		HHLT for subgroups of [a] high school and [b] college athletes. BVMT-R for high school athletes only. Measured within 24 hours, and at 3, 5, and 7 days. High School PCE N = 19 High School Control N = 20 College PCE N = 35 College Control N = 18 <u>Results</u> 24 hours – High School PCE significantly worse on HHLT Total (p < 0.003), BVMT-R Total (p < 0.002), and BVMT-R Delayed (p < 0.002). College PCE significantly worse on HHLT Total (p < 0.002) and HHLT Delayed (p < 0.002). 3 days – High School PCE significantly worse	MANOVA and analysis of univariate main effects	Fixed for baseline, and 24 hours. After that, uncertain.

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						<p>on BVMT-R Total ($p < 0.002$) and Delayed ($p < 0.02$).</p> <p>5 days – High School PCE significantly worse on BVMT-R Total ($p < 0.008$).</p> <p>7 days – High School PCE significantly worse on HVL T Total ($p < 0.005$).</p>		
Gagnon 2004 ²⁰ Hospital Pediatrics KQ 1	Inclusive Case Definition ACRM At least one of: - LOC \leq 30 min - Amnesia - GCS 13 – 15	GCS 13, 14, 15 LOC PTA Nausea/vomiting	Headache Dizziness Visual problems Drowsiness Auditory problems	Not for signs and symptoms	<p>BOTMP Balance Subtest, P-CTSIB, and PST</p> <p>Measured during week 1, and at 4 and 12 weeks post-injury. Uninjured controls PCE N = 38 Control N = 38</p> <p>PCE significantly worse on BOTMP raw score at 1, 4, and 12 weeks. PCE sign. worse on 1 of 12 P-CTSIB measure (Tandem, Floor, Eyes Closed) NSD on PST</p>		ANOVA with Greenhouse-Geiser correction t-tests with Bonferroni adjustment	Not fixed
Gagnon 2004 ²¹ Hospital Pediatrics KQ 1	Inclusive Case Definition ACRM At least one of: - LOC \leq 30 min - Amnesia - GCS 13 – 15	GCS 13, 14, 15 LOC PTA Nausea/vomiting	Headache Dizziness Visual problems Drowsiness Auditory problems	Not for signs and symptoms	<p>BOTMP Response Speed Subtest</p> <p>Measured during week 1, and at 4 and 12 weeks post-injury. Uninjured controls PCE N = 38 Control N = 38</p> <p>NSD between groups across time points.</p>		ANOVA with Greenhouse-Geiser correction t-tests with Bonferroni adjustment	Not fixed
Gasparovic 2009 ²² Hospital Adults KQ 1	Exclusive Case Definition ACRM Guidelines - GCS 13 – 15 - Alteration in mental status			Yes		<p>Trails A and B, PASAT, Stroop, Digits Forward, CVLT, WAIS, Grooved Pegboard, Digit Symbol, WISC, COWAT, Beck Depression Inventory, State-Trait Anxiety Scale</p> <p>Measured between 4 and 19 days post-injury</p>	t-tests	Not fixed

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	(confusion, LOC ≤ 30 min, PTA ≤ 24 hours)					Uninjured controls PCE N = 9 Control N = 9 NSD on any test.		
Grubenhoff 2011 ²³ Hospital Pediatrics KQ 1 and KQ 3	Case definition not specified	LOC PTA GCS 13-14 Sub-divided PCE group into with or without Altered Mental State (AMS – presenting LOC, and/or PTA, and/or GCS 13-14).	Dizziness, Nausea, Photophobia, Fatigue, Phonophobia, Vision changes, Headache, Tinnitus, Not feeling “sharp,” Poor concentration, Poor balance, Irritable, Vomiting, Sadness Cases with AMS had significantly more symptoms than controls for all 15 symptoms. Significant associations between cases with AMS and dizziness, nausea, phonophobia, photophobia, vision changes, headache, and tinnitus.	Yes for signs, but by definition if a patient presented LOC, PTA, or GCS 13-14, they would be placed in the other injury control group. Yes for symptoms.			chi-square, logistic regression	Fixed
Hajek 2011 ²⁴ Hospital Pediatrics KQ 1	Exclusive Case Definition Observed LOC <u>or</u> GCS of 13 – 14 <u>or</u> at least two of: - PTA		Multiple symptoms – refer to publication Recovery curves show comparisons in changes but sign. NR.	Yes. But, by definition if controls had LOC or PTA, they would be in the mTBI group.			Significance tests only for rater agreement, or with composite scores.	Not fixed Targeted, no variance reported

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	<ul style="list-style-type: none"> - Neurological deficits - Vomiting - Nausea - Headache - Visual disturbances - Dizziness - Disorientation - Other mental status changes 		Analysis was about agreement between parent and child ratings.					
Hajek 2010 ²⁵ Hospital Pediatrics KQ 1	Exclusive Case Definition Observed LOC <u>or</u> GCS of 13 – 14 <u>or</u> at least two of: <ul style="list-style-type: none"> - PTA - Neurological deficits - Vomiting - Nausea - Headache - Visual disturbances - Dizziness - Disorientation - Other mental status changes 		Hyperarousal Re-experiencing Significant group x time interaction for Hyperarousal. NSD for Re-experiencing.	Yes. But, by definition if controls had LOC or PTA they would be in the mTBI group.			Repeated measures MANOVA	Not fixed Targeted, no variance reported
Heitger 2007 ²⁶ Hospital Pediatrics KQ 1	Inclusive Case Definition GCS 13 – 15		Multiple symptom checklists – refer to publication Recorded percent reporting “problem status” of 2 or higher For proportions, recovery curves show comparisons	Yes Non-hospital control group measured once and same measures used for 1 week and 3 month comparisons.			Non-parametric Wilcoxon for means NR for proportions	Not fixed, Targeted with variance reported

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			in changes but sign. NR. For means, sign. diff. at 1 week for all measures; at 3 months for headache, dizziness, noise sensitivity, fatigue, memory, concentration, thinking, and double vision.					
Hinton-Bayre 1999 ²⁷ Sports Adults KQ 1	Inclusive Case Definition Immediate and transient post-traumatic disturbance in neural function, such as an alteration in consciousness, disturbance of vision or equilibrium. However, players were included if symptoms were delayed or not reported immediately.	LOC 4/20 had LOC (20%)		Self as own controls in pre-injury assessment, as well as control group.		Speed of Comprehension (Silly Sentences), Digit Symbol, and Symbol Digit Measured at pre-season baseline, 1-3 days, and 1-2 weeks. Self as own controls and uninjured control group PCE N = 20 Control N = 13 Recovery curves show comparisons in changes. PCEs significantly worse than own baseline on all three measures at 1-3 days; NSD at 1-2 weeks Based on RCI: Across 3 tests, 16 of 20 concussed players were significantly impaired (3 on all 3 tests; 6 on 2 tests; 7 on 1 test). 3 of 13 controls were significantly impaired.	ANOVA RCI	Fixed – Signs Not fixed Neurocog
Iverson 2004 ²⁸ Sports Adults and Adolescents KQ 1 and 2	Inclusive Case Definition 1) Observable alteration in mental status or consciousness 2) Constellation of self-reported symptoms such	LOC Amnesia Disorientation Mental status change 2/38 (5.3%) had LOC 6/38 (15.8%)	Disorientation, and 5 or more min. of mental status change were on-the-field assessments and considered signs. 21 item ImPACT	Self as own controls in pre-injury assessment.		ImPACT Measured at pre-season baseline and 1-5 days Self as own controls N = 38 (19 previous concussions, 19 no previous concussions) Based on ANOVA: NSD for ImPACT Reaction Time or Processing	ANOVA	Fixed - signs Not fixed – Neuroc

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	<p>as:</p> <ul style="list-style-type: none"> - Headache - Fogginess - Nausea/ Vomiting - Dizziness <p><u>and/or</u> 3) LOC, Disorientation, <u>and/or</u> Amnesia</p>	<p>had Retrograde Amnesia 8/38 (21%) had PTA 17/38 (44.7%) had Disorientation 7/38 (18.4%) had ≥ 5 min. Mental Status Change</p> <p>Compared group with previous concussions to group without. LOC – 0/19 no previous; 2/19 previous. RTA – 3/19 no previous; 3/19 previous. PTA – 1/19 no previous; 7/19 previous. Disorientation 5/19 no previous; 12/19 previous. Mental Status – 1/19 no previous; 6/19 previous.</p>	<p>Symptom Scale; measured pre- and post-trauma, but only composite reported.</p>			<p>Speed for either effect of time or effect of group.</p> <p>Sign. diff. on Memory for effect of time and for effect of group (previous concussions performed worse).</p> <p><u>Group Differences</u> NSD on scores of Reaction Time and Processing Speed by number of previous concussion groups. Greater proportion of 3+ previous concussion group sustained major decline from baseline than 0 group (chi-squared [1, 38] = 6.3, p < 0.013). Odds of significant drop in memory function 7.7 times greater for 3+ group than 0 group (95% CI = 1.4-42.7).</p>		

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
Kashluba 2004 ²⁹ <u>and</u> Paniak 2002 ³⁰ (same patients in two studies at 1 and 3 month follow-up) Hospital Adults KQ 1	Inclusive Case Definition ACRM – any one of: - GCS 13 – 15 - Alteration in mental status (confusion, LOC ≤ 30 min, PTA ≤ 24 hours) - Focal neurologic deficits		Symptom checklist – refer to publication Paniak = 1 month follow-up Significant diff. on severity for all but 8/43 symptoms. Significantly higher incidence for PCE on 25/43 symptoms. Significantly higher incidence for controls on 2/43 symptoms. Kashluba = 3 month follow-up for same patients Significant difference on severity for 10/43 symptoms. Significantly higher incidence for 3/43 symptoms (balance, doing things slowly, fatigue). Abstracted all data from Paniak 2002 and Kashluba 2004 into Paniak 2002 records.	Yes			t-tests Bonferroni-adjusted (0.5/43) .00116 level (two-tailed)	Not fixed Targeted with variance reported
Kontos 2010 ³¹ Sports Adults and	Inclusive Case Definition Altered mental	LOC PTA		Self as own controls in pre-injury assessment.		ImPACT Measured at pre-trauma baseline, 2 days, and 7	ANOVA with Bonferroni correction	Fixed

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
Adolescents KQ 1 and 2	state (with or without LOC).	1/96 (1%) had LOC 2/96 (2%) had PTA				<p>days Self as own controls N = 96</p> <p>Based on ANOVA: Scores for Verbal [F(3, 93) = 11.19, p = 0.001], Visual [F(3, 93) = 5.59, p = 0.004], Motor [F(3, 93) = 4.87, p = 0.009], and Reaction Time [F(3, 93) = 4.42, p = 0.013] sign. worse at 2 days than baseline.</p> <p>Scores for Verbal, Visual, and Motor significantly better at 7 days than 2 days.</p> <p>NSD on Reaction Time between 2 days and 7 days.</p> <p>NSD on any tests between baseline and 7 days.</p> <p>Post-hoc: Caucasians significantly better than African Americans on motor processing at 7 days (practice effect in Caucasians).</p> <p>RCE for race differences only. Based on Reliable Change Estimates and odds ratios: At 7 days African Americans were 2.4 times more likely to have one clinically significant cognitive decline than Caucasians (chi-square = 4.29, p = .03).</p>	RCE and odds ratios for race Chi-squared	
Kwok 2008 ³² Adults KQ 1	Exclusive Case Definition - GCS 13 – 15 - LOC < 30 min or PTA < 24 hours - Abnormal CT within 24 hours					<p>Stroop, Digit Vigilance Test, Symbol Digit Modalities Test, CAVLT, Benton Visual Retention Test, Verbal Fluency Test</p> <p>Measured within 1 week, and at 1 and 3 months post-injury Uninjured controls PCE N = 31, 20 and 15 at 1 wk, 1 mo, and 3 mo Control N = 32, 19, and 19</p> <p>PCE significantly worse at 1 week on Digit</p>	ANOVA, t-tests Bonferroni correction to 0.006	Not fixed

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
						Vigilance, Symbol Digit, and Verbal Fluency-fruits and vegetables. PCE significantly worse at 1 month on Digit Vigilance, Symbol Digit, CAVLT-recognition, and Verbal Fluency-fruits and vegetables. PCE significantly worse at 3 months on Digit Vigilance, and CAVLT-recognition.		
Landre 2006 ³³ Hospital Adults KQ 1	Exclusive Case Definition ACRM Guidelines - Minimum score of 20 on the Mini-Mental Status Examination <u>and</u> at least one of: - GCS 13 – 15 - LOC ≤ 30 min - PTA < 24 hours - Alteration in mental state (dazed, disoriented, confused) - Focal neurological deficits	LOC		Yes. But, by definition if trauma controls had LOC, they would be in the mTBI group.		Trails A and B, GDS-V, GDS-D subtests, and the Wechsler MS-R Logical Memory subtests 1 (LM1) and 2 (LM2) Measured at an average of 4.5 days post-injury Trauma controls PCE N = 37 Control N = 39 PCEs significantly worse on GDS-V (t = -2.04, p = 0.046), and GDS-D (t = -2.32, p = 0.24); Trails A (t = -2.97, p = 0.004); Trails B (t = -2.35, p = 0.022); LM1 (t = -3.36, p = 0.001); LM2(t = -2.81, p < 0.006).	t tests	Not fixed
Lovell 2003 ³⁴ Sports Adolescents KQ 1 and 3	Inclusive Case Definition 1) Observable alteration in mental status/level of consciousness such as LOC, amnesia, disorientation, <u>and/or</u> 2) Self-reported symptoms	LOC Amnesia Disorientation 7/64 (10.9%) had LOC 13/64 (20.3%) had RTA 19/64 (29.7%) had PTA 28/64 (43.75%) had disorientation		Self as own controls in pre-injury assessment and control group.		ImPACT Memory Composite Measured at pre-trauma baseline, 36 hours, 4 days, 7 days Self as own controls and control group PCE N = 64 (57 for outcomes) Control N = 24 PCE divided into More Severe (n = 13) and Less Severe (n = 433) based on duration of amnesia or disorientation > or < 5 min. Based on ANOVA: Significantly diff. lower scores on memory	ANOVA t-tests	Fixed

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
	following collision such as fogginess, grogginess, headache, nausea/vomiting, dizziness, balance problems, and/or visual changes.	on the field				<p>composite at 36 hrs., 4 days, and 7 days compared to baseline [F(3, 189) = 1.26, p < 0.00001].</p> <p>Did not enter control group data into Heat Map. Only participants as own controls.</p> <p>KQ3: Based on ANOVA, More Severe significantly worse than Less Severe on Memory Composite [F(1, 54) = 5.5, p < 0.024].</p>		
Lovell 2004 ³⁵ Sports Adolescents KQ 1	Exclusive Case Definition Only Grade 1 concussions included			Self as own controls		<p>ImPACT Memory Composite, Reaction Time, and Processing Speed</p> <p>Measured within 72 hours, and between 5 – 10 days. Self as own controls. N = 43</p> <p>For Memory, significantly diff. across time points. For Reaction Time, NSD from baseline to T1. Sign. better at T2 than baseline and T1. For Processing Speed, NSD from baseline to T1. Sign. better at T2 than baseline and T1.</p>	ANOVA	Not fixed
Lovell 2007 ³⁶ Sports Adolescents KQ 1	Inclusive Case Definition 1. Diagnosed with concussion (defined as one or more of (a) observable change in mental status, (b) LOC or amnesia, (c) symptoms) <u>and</u> 2. Reported symptoms, <u>and/or</u> 3. Had cognitive dysfunction on IMPACT or	LOC Amnesia 6/28 (21.4%) had LOC 7/28 (25%) had RTA 16/28 (57.1%) had Anterograde Amnesia		Control group and self as own controls in pre-injury assessment, but only control group data in analysis (not PCE group pre-trauma data)		<p>ImPACT</p> <p>Measured at pre-trauma baseline, 7 days, and 35 days Self as own controls and control group, but pre-trauma baseline not in analysis. PCE N = 28 Control N = 13</p> <p>PCE sign. worse on Verbal, Visual, Motor, and Reaction Time composites at 7 days (p < 0.01); NSD at 5 weeks.</p>	NR (p values reported)	Fixed - Signs Not Fixed - Neurocog

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
	reported symptoms.							
Lundin 2006 ³⁷ Hospital Adults and Adolescents KQ 1	Inclusive Case Definition - LOC \leq 30 min and/or PTA \leq 24 hours - GCS 14 – 15		Headache Dizziness Nausea/vomiting Fatigue Taking longer to think Poor memory Poor concentration Double vision Blurred vision Sensitivity to light Sensitivity to noise Depressed Frustrated Restlessness Irritability Sleep disturbances Recovery curves show comparisons at 3 months but sign. NR.	Yes			Chi-square	Not fixed
Maddocks 1996 ³⁸ Sports Adults KQ 1	Not defined (Unclear if this is a subset of the data from Maddocks 1995)	LOC PTA		Self as own controls in pre-injury assessment, but data presented for control group of uninjured umpires.		Digit Symbol, PASAT, and Four Choice Reaction Time (Decision Time and Movement Time). Measured at baseline and 5 days post-injury. Self as own controls and control group of uninjured umpires. PCE N = 10 Control N not specified (assume 10) PCE significantly worse on Digit Symbol and Four Choice Reaction Time (Decision Time). NSD on PASAT or Four Choice Reaction Time (Movement Time).	ANCOVA	Not fixed
Maddocks 1995 ³⁹ Sports Adults	Inclusive Case Definition - LOC <u>or</u> altered consciousness	LOC 11/28 (39.3%) had LOC	Headache Dizziness Blurred vision Nausea	Yes			NR	Fixed

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
KQ 1	- Symptoms (eg, headache, dizziness, blurred vision)		Double vision Noise sensitivity Light sensitivity Symptoms measured at 2 hours post-injury Uninjured matched control athletes PCE N = 28 Control N = 28 Recovery graphs show comparisons at 2 hours but sign. NR.					
Maillard-Wermelinger 2009 ⁴⁰ Hospital Pediatrics KQ 1	Exclusive Case Definition 1) Observed LOC <u>or</u> 2) GCS 13 or 14 <u>or</u> 3) At least two symptoms (eg, PTA, neurological deficits, vomiting, nausea, headache, diplopia or dizziness)	LOC GCS		Yes. But, by definition if trauma controls had LOC or GCS < 15, they would be in the mTBI group.		CANTAB: Stockings of Cambridge and Spatial Working Memory Measured within 3 weeks post-injury, and at 3 months. Orthopedic Injury Controls PCE N = 186 Control N = 99 NSD on Stockings of Cambridge. OI group significantly worse on Spatial Working Memory.	MANCOVA	Not fixed
McAllister 1999 ⁴¹ Hospital Adults KQ 1	Inclusive Case Definition <u>Either</u> Alteration of level of consciousness (eg, dazed and confused and having amnesia for the event) <u>or</u>	LOC PTA		Not for LOC and PTA.		Trails A & B, COWAT, Wisconsin Card Sorting Test, Continuous Performance Test, Stroop, CVLT, Wechsler Memory Scale III Facial Memory, n-Back Measured between 6 and 35 days post-injury. Uninjured controls. PCE N = 12 Control N = 11	t-tests	Not Fixed

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
	LOC < 30 min, PTA < 24 hours, and GCS 13 – 15					PCEs significantly worse than controls on 2 Continuous Performance subtests – Simple Reaction Time and Reaction Time Distractibility.		
McClincy 2006 ⁴² Sports Adults and Adolescents KQ 1	Criteria not clearly specified. Concussions were <u>graded</u> according to AAN criteria, but authors do not state AAN criteria were used to ascertain cases.	LOC Amnesia 9/104 (8.7%) had LOC 23/104 (22.1%) had Anterograde Amnesia 19/104 (18.3%) had RTA 53/104 (51%) had Confusion	Confusion recorded as an on-field marker, considered a sign.	Self as own controls in pre-injury baseline.		ImPACT Verbal, Visual, Processing Speed, Reaction Time Measured Day 2, 1 week, and 2 weeks post-injury. Self as own controls N = 104 for 3 measures N = 76 for Visual score PCE significantly worse than own baseline for Verbal score at 2, 7, and 14 days; for Visual score at 2 and 7 days; for Processing Speed score at 2 days (sign. better than own baseline at 14 days); for Reaction Time score at 2 and 7 days.	MANOVA Post-hoc Bonferroni analysis	Not fixed
McCrea 2002 ⁴³ Sports Adults and Adolescents KQ 1 and 3	Inclusive Case Definition 1) AAN: Alteration in mental status With or without LOC 2) ACRM: Alteration in mental state LOC ≤ 30 min PTA ≤ 24 hours 3) Criteria contributing to diagnosis: Symptoms - Confusion - Headache - Dizziness - Memory problems	LOC PTA LOC and PTA data reported in McCrea 2003, for total sample.		Self as own controls in pre-injury baseline assessment.		This paper reports outcomes at baseline, time of injury, 15 minutes, 2 days, and 90 days. However, of 91 total, 45 had their own pre-trauma baseline, and 46 did not. But sample sizes for each time point are not broken out, so we can't compare the data reported because it combines data from participants with baseline and without baseline. Only Table 1 provides a comparison of the 45 who had pre-season baseline testing, and the only comparison is with the immediate post-trauma measure. SAC Measured immediately after PCE Self as own controls N = 45 Divided into severity levels based on no LOC/no PTA, PTA, and LOC (sample sizes unclear) Result: SAC Total Score (t =	Paired sample t-tests, Bonferroni corrections	Fixed for the data used in the analysis.

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
						-10.07, $p < 0.0001$), Orientation ($t = -2.91$, $p < 0.006$), Immediate Memory ($t = -5.76$, $P < 0.0001$), Concentration ($t = -5.67$, $p < 0.0001$), and Delayed Recall ($t = -6.44$, $p < 0.0001$) all significantly lower at immediate post-trauma than at pre-trauma baseline. KQ3: LOC group most severely impaired; no LOC/no PTA least severely impaired ($F[2, 88] = 53.08$, $p < 0.0001$).		
McCrea 2003 ⁴⁴ Sports Adults KQ 1	Inclusive Case Definition Alteration in mental state <u>and</u> one or more of (AAN): - Headache - Nausea - Vomiting - Dizziness or balance problems - Fatigue - Difficulty sleeping - Drowsiness - Light sensitivity - Noise sensitivity - Blurred vision - Memory difficulty - Difficulty concentrating	LOC Amnesia 6/94 (6.4%) had LOC 18/94 (19.1%) had PTA 7/94 (7.4%) had RTA		Self as own controls in pre-injury assessment, and uninjured control group athletes.		McCrea 2005 provided duplicate data. Used Baseline data from McCrea 2005 for recovery curves in this paper. HVLTL, Trails B, Symbol Digit, Stroop, and COWAT Measured at baseline, 2 days, 7 days, and 90 days Self as own controls and control group of uninjured athletes PCE N = 94 Control N = 56 Recovery curves show comparisons but significance NR. Visual inspection shows difference at 7 days for HVLTL Delayed Recall. From McCrea 2005, using SRB: 23% of PCE group impaired on 2 or more neurocog. measures at day 2 and 17% at day 7; compared to 8% and 9% at days 2 and 7 for controls; can't use data because does not specify which measures. Largest proportion of abnormal scores for PCE group on Delayed Recall and Recognition Memory of HVLTL, Trails B, Symbol Digit, and COWAT on days 2 and 7.	Multivariate Regression Models SRB Method	Fixed - Signs Not fixed – Neurocog, but 86% complete and statistical comparisons and imputations were used.
McCrea 2005 ⁴⁵	Inclusive Case	LOC		Self as own controls	BESS	Same data as McCrea 2003.	SRB	Fixed

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/ Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
Sports Adults KQ 1	Definition Alteration in mental state <u>and</u> one or more of (AAN): - Headache - Nausea - Vomiting - Dizziness or balance problems - Fatigue - Difficulty sleeping - Drowsiness - Light sensitivity - Noise sensitivity - Blurred vision - Memory difficulty - Difficulty concentrating	PTA Same data as McCrea 2003		in pre-injury assessment.	Measured at pre-trauma baseline, 10 minutes, 3 hours, and days 1, 2, 3, 5, and 7. Self as own controls and control group of uninjured athletes PCE N = 94 Control N = 56 Based on SRB: At 10 minutes, 36% PCE impaired, compared to 5% Controls. At day 2, 24% PCE impaired. At day 7, 9% PCE impaired.			
McIntire 2006 ⁴⁶ Sports-related and non-sports related injuries Adults KQ1	Exclusive Case Definition AAN Grade 1: - Confusion - No LOC - Sympt < 15 m Grade 2: - No LOC - Sympt > 15 m <u>Excluded LOC</u>			Not for signs and symptoms.		RSVP – validity uncertain Measured between 12 and 40 hrs post-injury. Uninjured controls PCE N = 17 Control N = 17 NSD	ANOVA	Not fixed
Meares 2011 ⁴⁷ Hospital Adults KQ1	Inclusive Case Definition WHO - GCS 13-15 > 30 min - Confusion/	GCS Levels PTA Duration	Headache Dizziness Irritability Memory Concentration Fatigue	Trauma Control Group		Cognitive measures taken but only used in regressions to predict Post-concussive syndrome.	Multi-level logistic regression	Not fixed Used T1 only (within 14 days post-injury)

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
	Disorientation - LOC - PTA and/or - other transient abnormalities		Noise Anxiety Depression Mood Swings Insomnia Malaise Measured average 4.9 days post-injury (with 14 days) PCE N = 62 Control N = 58 No significant difference between PCEs and Controls on any symptom except Controls reported significantly more Aggravation with Noise than PCEs.					
Mittenberg 1997 ⁴⁸ Hospital Pediatrics KQ 1	Inclusive Case Definition - GCS 13 – 15 - Normal CT - No evidence of skull fracture Decided to consider this inclusive, although children with abnormal CTs were excluded.		Multiple symptoms – refer to publication, Table 2. Measured 6 weeks post-injury. Orthopedic controls PCE N = 38 Control N = 47 PCEs significantly more self-report of headaches, remembering, light sensitivity, spinning head,	Yes			F statistic, precise analysis not specified	Not Fixed

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
			nervous or scared, and attention.					
Shores 2008 ⁴⁹ Hospital Adults KQ 1	Ambiguous definition: ACRM criteria, with revision by World Health Organization, except that patients with intracranial lesions were excluded.	GCS Revised Westmead PTA Scale (R-WPTAS) Measured within 24 hrs of injury Other injury controls PCE N = 79 Control N = 86 GCS 13, 14, 15 was 2%, 11%, and 87% for PCEs; 0%, 2%, and 98% for Controls. PCE sign. worse on R-WPTAS (p = 0.001; effect size (d) = 1.07		Yes Other injury controls PCEs had significantly more morphine and alcohol, and self-report of previous head injuries, than controls, but controlled for in the MANOVA.		ImPACT Verbal, Visual, Processing Speed, Reaction Time Measured within 24 hrs of injury Other injury controls PCE N = 79 Control N = 86 PCEs significantly worse on Verbal, Visual, Processing Speed, and Reaction Time	MANOVA	Fixed
Sim 2008 ⁵⁰ Sports Adolescents KQ 1	Inclusive Case Definition ACRM: Any alteration in mental status (such as confusion or disorientation) and may or may not involve LOC or amnesia.	LOC PTA 2/14 (14.3%) had LOC 4/14 (28.6%) had PTA		Self as own controls in pre-injury assessment		ANAM: Simple Reaction Time, Code Substitution, Continuous Performance Test, Math Processing, Spatial Processing, and Code Substitution Delayed Measured at pre-trauma baseline, 1-3 days, 4-7 days, and 8 – 11 days post Self as own controls N = 14 PCE performance at Time 1 significantly worse than baseline for Simple Reaction Time (t = 3.80, p = 0.002, d = 0.860), Code Substitution (t = 2.855, p = 0.014, d = 0.539), and Code	ANOVA	Fixed – Signs Not fixed - Neurocog

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
						Substitution Delayed (t = 2.875, p = 0.013, d = 0.543).		
Sosnoff 2007 ⁵¹ Sports Adults KQ 1	Not defined			Yes		CRI subtests of Response Time, Cued Response Time, Visual Recognition 1 and 2, Animal Decoding and Symbol Scanning Measured within 48 hours Uninjured controls PCE N = 22 Control N = 22 For mean response time, day x group interactions for Response Time, Cued Response Time, and Visual Recognition 2. PCEs significantly worse for Visual Recognition 1 and Symbol Scanning.	ANOVAs	Not fixed, but within 48 hrs
Van Kampen 2006 ⁵² Sports Adults and Adolescents KQ 1	Inclusive Case Definition Alteration in mental status With or without LOC <u>and/or</u> Symptoms (headache, dizziness, balance dysfunction, or nausea)	LOC Amnesia 15/122 (12.3%) had LOC 65/122 (53.3%) had RTA 2/122 (1.6%) had Anterograde Amnesia 22/122 (18%) had Confusion as an on-field marker	Because Confusion was identified as an “on-field marker”, it was categorized as a sign.	Self as own controls and control group of uninjured athletes Control group used for Signs and Symptoms Outcome data for self as own controls		ImPACT Measured at pre-trauma baseline and 2 days post. Self as own controls and control group of uninjured athletes PCE N = 122 Control N = 70 Recovery curves show comparisons but significance NR. Verbal, Visual, and Processing Speed subtests appear different. Based on RCI: 101/122 (83%) of PCE group had at least 1 ImPACT score that exceeded the RCI for that score, compared to 21/70 (30%) of comparison group. Data only reported for participants as their own controls. Average scores for individual composites in ImPACT indicate PCE post-trauma scores exceeded the RCI value when compared to pre-trauma scores on Verbal Memory, Reaction Time, and Symptoms.	RCI	Fixed – Signs Not Fixed – Neurocog, but within 48 hrs.

Reference Setting Key Questions	Inclusion Criteria	Signs Reported	Symptoms Reported	Comparison Group for Signs/Symptoms?	Neurologic Deficits Reported	Cognitive Deficits Reported	Significance Measure	Time-point
Warden 2001 ⁵³ Sports – West Point Adults KQ 1	Exclusive Case Definition - No LOC - Returned to full activity after 4 days			Self as own controls, but baseline symptoms were not measured.		ANAM sub-tests: Simple Reaction Time, Continuous Performance, Math Processing, Sternberg Procedure, Matching to Sample, and Code Substitution Delayed Memory Measured at baseline, and 1 and 4 days post-injury. Self as own controls N = 14 PCEs significantly worse on Simple Reaction Time than own baseline scores	t-tests with Bonferroni correction (0.009)	Fixed

AAN = American Academy of Neurology, ACRM = American Congress of Rehabilitation Medicine, ANAM = Automated Neuropsychological Assessment Metrics, ANCOVA = Analysis of Covariance, ANOVA = Analysis of Variance, ASDI = Acute Stress Disorder Structured Interview, BESS = Balance Error Scoring System, BMT = Behavioral Memory Test, BOTMP = Bruininks-Oseretsky Test of Motor Performance, BVMT-R = Brief Visuospatial Memory Test – Revised, CANTAB = Cambridge Neuropsychological Testing Automated Battery, CAVLT = Chinese Auditory Verbal Learning Test, CI = Confidence Interval, COWAT = Controlled Oral Word Association Test, CRI = Concussion Resolution Index, CSD = Clinically Significant Difference, CVLT = California Verbal Learning Test, CVLT-C = California Verbal Learning Test – Children, ED = Emergency Department, GCS = Glasgow Coma Scale, GDS-V = Gordon Diagnostic System’s Adult Vigilance, GDS-D = Gordon Diagnostic System’s Adult Distractibility, ImPACT = Immediate Post-Concussion Assessment and Cognitive Testing, LOC = Loss of Consciousness, MANCOVA = Multivariate Analysis of Covariance, MANOVA = Multivariate Analysis of Variance, MVA = Motor Vehicle Accident, NCSE = Neurobehavioral Cognitive Status Exam, NR = Not Reported, NSD = No Significant Difference(s), Trails A and B, PASAT = Paced Auditory Serial Addition Test, PCE = Potential Concussive Event, PCS = Post-Concussion Syndrome, P-CTSIB = Pediatric Clinical Test of Sensory Interaction for Balance, PST = Postural Stress Test, PTA = Post-Traumatic Amnesia, RCI = Reliable Change Index, RBANS = Repeatable Battery for the Assessment of Neuropsychological Status, RSVP = Rapid Serial Visual Presentation, RTA = Retrograde Amnesia, SAC = Standardized Assessment of Concussion, SD = Standard Deviation, SOT = Sensory Organization Test, SRB = Standard Regression-Based, WAIS = Wechsler Adult Intelligence Scale, WISC-R = Wechsler Intelligence Scale for Children – Revised

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