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Visual Deficits and Dysfunctions Associated with Traumatic Brain Injury: A Systematic Review and Meta-analysis

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SIGNIFICANCE: This study reports prevalence data combined independently for accommodative dysfunction, convergence insufficiency, visual field loss, and visual acuity loss in patients with traumatic brain injury in the absence of eye injury.

OBJECTIVE: The objective of this study was to conduct a systematic review and meta-analysis to determine the prevalence rates of accommodative dysfunction, convergence insufficiency, visual field loss, and visual acuity loss in TBI patients without concomitant eye injury.

DATA SOURCES: The data sources used in this study were PubMed, EMBASE, EBSCO, and Cochrane Library.

STUDY APPRAISAL AND SYNTHESIS METHODS: Publications reporting the prevalence of diagnosed accommodative dysfunction, convergence insufficiency, visual field loss, or visual acuity loss to the level of legal blindness in TBI patients of any age were included. Univariate metaregression analyses and subgroup analyses were performed to account for statistical heterogeneity.

RESULTS: Twenty-two eligible publications were identified across the four visual conditions. Random-effects models yielded combined prevalence estimates: accommodative dysfunction (42.8; 95% confidence interval [CI], 31.3 to 54.7), convergence insufficiency (36.3%; 95% CI, 28.2 to 44.9%), visual field loss (18.2%; 95% CI, 10.6 to 27.1%), and visual acuity loss (0.0%; 95% CI, 0.0 to 1.1%). Metaregression and subgroup analyses revealed that visual field loss was significantly more prevalent in moderate to severe (39.8%; 95% CI, 29.8 to 50.3%) compared with mild TBI (6.6%; 95% CI, 0 to 19.5%).

CONCLUSIONS AND IMPLICATIONS OF KEY FINDINGS: This study demonstrates that accommodative dysfunction, convergence insufficiency, and visual field loss are common sequelae of TBI. Prospective longitudinal research with rigorous and uniform methodology is needed to better understand short- and long-term effects of TBI on the vision system.

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Traumatic brain injury is defined as an alteration in brain function or other evidence of brain pathology caused by an external force.¹ In 2013 alone, an estimated 2.8 million people in the United States sustained a traumatic brain injury, most commonly from falls, being struck by or against an object, and motor vehicle accidents.² In the military, more than 375,000 cases of traumatic brain injury were reported in service members since 2000,³ many of them as a result of powerful explosive blast events. Retrospective studies show that 65 to 79% of traumatic brain injury patients report subjective visual complaints^{4–9}; however, prevalence of the underlying visual dysfunctions attributed to self-reported symptoms varies substantially between these studies for reasons including inconsistent diagnostic and reporting methods, varying sample population demographics, and the many possible mechanisms of injury. Given the limitations of available retrospective data and the dearth of studies that prospectively recruit unbiased patient samples, this study was undertaken to obtain more accurate prevalence estimates. Thus, the purpose of this study is to use available published scientific data to estimate the prevalence of four visual outcomes often considered to be associated with traumatic brain injury: accommodative dysfunction, convergence insufficiency, visual field loss, and visual acuity loss.^{10–16} Furthermore, univariate

metaregression and subgroup analyses were performed to better account for the observed heterogeneity.

METHODS

Systematic Literature Search

Four databases (PubMed, EMBASE, EBSCO, and Cochrane Library) were queried for relevant literature published before August 2, 2017. Although settings and interfaces varied between these databases, an identical search strategy was adapted for each database. The complete search strategy can be found in the Appendix (available at <http://links.lww.com/OPX/A408>). Briefly, search terms were organized into four concepts: (1) prevalence, (2) head injury, (3) vision, and (4) deficit/dysfunction. Terms within each category were separated by the Boolean operator “OR,” and each category was parenthesized and separated by the operator “AND.” When possible, Medical Subject Heading terms or the “explode” qualifier was used to expand the search language. All citations were imported and managed using EndNote X7.7.1 (Clarivate Analytics, Philadelphia, PA). Two authors of the current study (DWB, KM) worked independently to screen title and abstracts for relevant

articles; arbitration of disagreements was performed by an independent third author (RKM). Two authors (DWB, RKM) then worked independently to review full-text articles of all articles marked relevant to confirm eligibility; arbitration of disagreements was performed by two authors of the current study (FMB, NM). Recent systematic reviews on the topic were scanned for appropriate literature^{10,14,17}; bibliographies of all included articles were scanned for relevant references.

Inclusion and Exclusion Criteria

The criteria for literature inclusion were as follows: (1) traumatic brain injury or comparable head injury was diagnosed by a trained medical professional; (2) screening and/or diagnostic testing for accommodative dysfunction (insufficiency or infacility), convergence insufficiency, visual field loss, or visual acuity loss (visual acuity equal to 20/200 or worse) was performed by an eye care provider; and (3) the article was published in English in a peer-reviewed journal, and full text was available. There were no restrictions for period or patient age, with the exception that accommodation was only measured in nonpresbyopic traumatic brain injury populations 40 years or younger.

Studies were excluded based on the following criteria: (1) single-case report design was used; (2) the sample population was artificially selected for one of the visual outcomes (i.e., patients were recruited because of visual symptoms likely secondary to the visual outcome); (3) the sample population was previously diagnosed as having a chronic (or other) eye condition (e.g., glaucoma and diabetic retinopathy); (4) brain injury was acquired in a manner unrelated to trauma (e.g., stroke and infection); and (5) either traumatic brain injury or visual outcomes were self-reported or otherwise not clinically diagnosed. Efforts were made to remove the impact of ocular/orbital injury on visual diagnoses: patients/publications were excluded if there was evidence of eye injury (e.g., intraocular hemorrhage and open globe injury) that could explain visual symptoms. Applicable data were restricted to traumatic brain injury patients diagnosed as having one or more of these four visual outcomes. These data did not include baseline prevalence comparisons, calculation of risk statistics, or assessment of the effectiveness of interventions for these outcomes. Review articles rarely reported original data and were therefore excluded from statistical analysis; however, reviews were used as resources to find relevant literature.

Study Selection

Reported data regarding the prevalence of accommodative dysfunction, convergence insufficiency, visual field loss, and visual acuity loss were gathered by conducting the systematic literature search described previously. All reported accommodative dysfunction data reflect accommodative measures relative to age-related thresholds. Visual field loss was defined as any type of diagnosed visual field defect consistent with post-chiasmal injury such as hemianopia, quadrantanopia, or scotoma; visual field defects attributed to pre-chiasmal optic nerve or retinal damage were excluded. Visual acuity loss was defined as a Snellen visual acuity estimate or comparable measure at the level of “legal blindness” (20/200 or worse).¹⁸

Duplicate articles were removed, and the remaining publications were screened by title and abstract for possible inclusion. A thorough full-text review of all remaining articles was subsequently completed. Additional articles were added to the initial list after review of bibliographies contained in the included articles. All steps were performed independently by two reviewers (DWB, KM); arbitration of disagreements was performed by an independent third reviewer (RKM).

To the extent possible, an individual patient was represented only once for each visual outcome calculation. When necessary, study authors were contacted to determine the existence or degree of patient overlap between their publications. In instances of cohort overlap between two or more studies, the larger or more recent publication was chosen for inclusion¹⁴; some notable studies were excluded as a result of this process.^{5,6,19–21}

Data Extraction

Prevalence statistics of the four visual outcomes were extracted directly from tables or the reported text. Initial data extraction was performed by two authors who worked together (DWB, RKM); arbitration of disagreements was performed through discussion with two additional authors (FMB, NM). A second review of data extraction was performed by one author (RKM) with any issues resolved through discussion with two additional authors (FMB, NM). Confidence intervals were estimated according to the Clopper-Pearson method²² at the 95% level. When available, additional contextual data extracted from each study included the following: geographic location (by country), age of participants, participant sex ratio, target population (i.e., defining characteristics of the recruited population), causes of traumatic brain injury (i.e., mechanism of injury), time elapsed from the traumatic brain injury until the eye examination/screening, severity of traumatic brain injury, study design, and visual deficit/dysfunction testing criteria.

Statistical Analysis

All statistical analyses were conducted using R statistical software (3.4.2)²³ and its “meta” and “metafor” package.²⁴ Prevalence rates were calculated by dividing the number of individuals with traumatic brain injury diagnosed with the visual outcome by the total number of individuals diagnosed as having traumatic brain injury. These rates were transformed via Freeman-Tukey’s²⁵ double-arcsine method, as it best accounts for extreme values (near 0 or 1) and is appropriate for meta-analyses of prevalence.²⁶ Studies were weighted per their effect size using the reciprocal of variance (i.e., inverse variance) of the transformed proportions. A continuity correction of 0.5 was applied to all prevalence estimates of zero.²⁷ Forest plots of each visual outcome were presented as back-transformed data (i.e., raw prevalence) using the “metaprop” and “forest” commands. Variances were combined using the DerSimonian-Laird²⁸ random-effects model. Between-study variance (τ^2) was estimated using the restricted maximal likelihood method,²⁹ as it best accommodates meta-regression analyses, and heterogeneity was assessed using Cochran Q test and Higgins I^2 (I^2 values <40, 30 to 60, 50 to 90, and $\geq 75\%$ were deemed low, moderate, substantial, and considerable heterogeneity, respectively).³⁰ Cochran Q has demonstrated low power under certain circumstances and was therefore deemed statistically significant at P values less than .10.³¹ An iterative influence analysis using the leave-one-out method was performed for each outcome to determine whether any single study was disproportionately influential in any of the respective combined prevalence estimates.^{32,33} Subgroup analysis was performed for four moderators: (1) study design (prospective vs. retrospective), (2) traumatic brain injury severity, (3) diagnostic criteria, and (4) risk of bias to compare the prevalence rates among different levels of moderators by considering the meta-analysis result from each group separately. Methodological risk of bias of each study was appraised via criteria validated by Hoy et al.³⁴ Upon assessment of methodological risk of bias,³⁴ studies ranged from 0 to 6 (Table 1). The overall risk-of-bias score for each study was

TABLE 1. Risk-of-bias tool matrix

Study	Was the study's population a close representation of the national population in relation to your relevant variable?	Was the sampling frame a true or close representation of the target population?	Was some form of random selection used to select the sample?	Was the likelihood of nonresponse bias minimal?	Were data collected directly from the subjects?	Was an acceptable case definition used in the study?	Was the study instrument that measured the parameter of interest shown to have reliability and validity (if necessary)?	Was the same mode of data collection used for all subjects?	Was the length of the shortest prevalence period for the parameter of interest appropriate?	Were the numerator(s) and denominator(s) for the parameter of interest appropriate?
Alvarez et al. ³⁵	No (1)	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Brahm et al. ⁴	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	No (1)	Yes (0)	Yes (0)
Bulson et al. ³⁶	No (1)	No (1)	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	No (1)	Yes (0)	Yes (0)
Capó-Aponte et al. ⁷	No (1)	Yes (0)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Capó-Aponte et al. ³⁷	No (1)	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Ciuffreda et al. ³⁸	No (1)	Yes (0)	Yes (0)	No (1)	Yes (0)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Cohen et al. ³⁹	Yes (0)	No (1)	No (1)	No (1)	Yes (0)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Goodrich et al. ⁹	No (1)	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Hellerstein et al. ⁴⁰	No (1)	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Jackowski et al. ⁴¹	No (1)	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Lemke et al. ⁴²	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Magone et al. ⁴³	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Master et al. ⁴⁴	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Padula et al. ⁴⁵	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Poggi et al. ⁴⁶	No (1)	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Sabates et al. ⁴⁷	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Schrupp et al. ⁴⁸	No (1)	No (1)	No (1)	Yes (0)	Yes (0)	No (1)	No (1)	No (1)	Yes (0)	Yes (0)
Shokunbi and Agbeja ⁴⁹	No (1)	No (1)	No (1)	Yes (0)	Yes (0)	No (1)	No (1)	No (1)	Yes (0)	Yes (0)
Stelmack et al. ⁸	No (1)	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0) for AD, CI No (1) for VFL	Yes (0) for AD, CI No (1) for VFL	Yes (0) for AD, CI, VAL No (1) for VFL	Yes (0)	Yes (0)
Storey et al. ⁵⁰	No (1)	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Suchoff et al. ⁵¹	No (1)	No (1)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)
Van Stavern et al. ⁵²	Yes (0)	Yes (0)	Yes (0)	Yes (0)	Yes (0)	No (1) for CI Yes (0) for VFL	No (1) for CI Yes (0) for VFL	No (1) for CI Yes (0) for VFL	Yes (0)	Yes (0)

Yes (0) represents low risk of bias; No (1), high risk of bias. Subcategories: low risk, 0 to 3 score for risk of bias; moderate risk, 4 to 6 score for risk of bias; high risk, 7 to 9 score for risk of bias. AD = accommodative dysfunction; CI = convergence insufficiency; VAL = visual acuity loss; VFL = visual field loss.

grouped into low risk of bias (score of 0 to 3), medium risk of bias (score of 4 to 6), and high risk of bias (score 7 to 9); a higher score indicates greater risk of bias.³⁴ All of the studies in this article ranged from low to medium risk of bias.

Univariate metaregression analyses of prevalence by several moderators were conducted to investigate the sources of heterogeneity in each of the four visual outcomes. The moderators were considered as categorical variables with mostly binary outcomes. The risk-of-bias moderator was a binary outcome with low and moderate categories of risk of bias, and severity of traumatic brain injury was a binary outcome with mild (Glasgow Coma Scale score 13 to 15) and moderate-to-severe (Glasgow Coma Scale score 3 to 12) categories.

When Glasgow Coma Scale, or comparable metric, was not reported, explicit attribution of mild or moderate/severe traumatic brain injury in the publication text was considered; for this analysis, sports concussions were not considered mild traumatic brain injury. Study authors were contacted when traumatic brain injury severity distinctions were unclear. Many individual publications reported visual outcome prevalence statistics stratified by traumatic brain injury severity, which provided an opportunity to use subpopulations from a single article in more than one category.^{4,35,42} Statistics reported for metaregression analyses were the test statistic for

the omnibus test of coefficients (i.e., the test for the effect of a moderator; Cochran Q), percentage of heterogeneity accounted for R^2 , and Higgins I^2 for individual subgroups.

Bonferroni correction for multiple comparisons was applied to metaregression analyses such that Cochran Q was deemed statistically significant at less than 0.025.

RESULTS

Search Results

Database searches yielded 2104 unique publications. Of these, 2082 publications were excluded primarily because of a sample population comprising non-traumatic brain injury patients, lack of measurements for pertinent visual outcomes or being preselected for visual symptoms consistent with the visual outcome, not examined by an eye care provider, missing data, or being a foreign-language article. After title and abstract screening and full-text review, 22 publications met the criteria for inclusion.^{4,7–9,35–51} The selection process summarized in Fig. 1 is in accordance with standardized Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines.⁵⁴ On several occasions, data on more than one visual outcome were extracted from the same

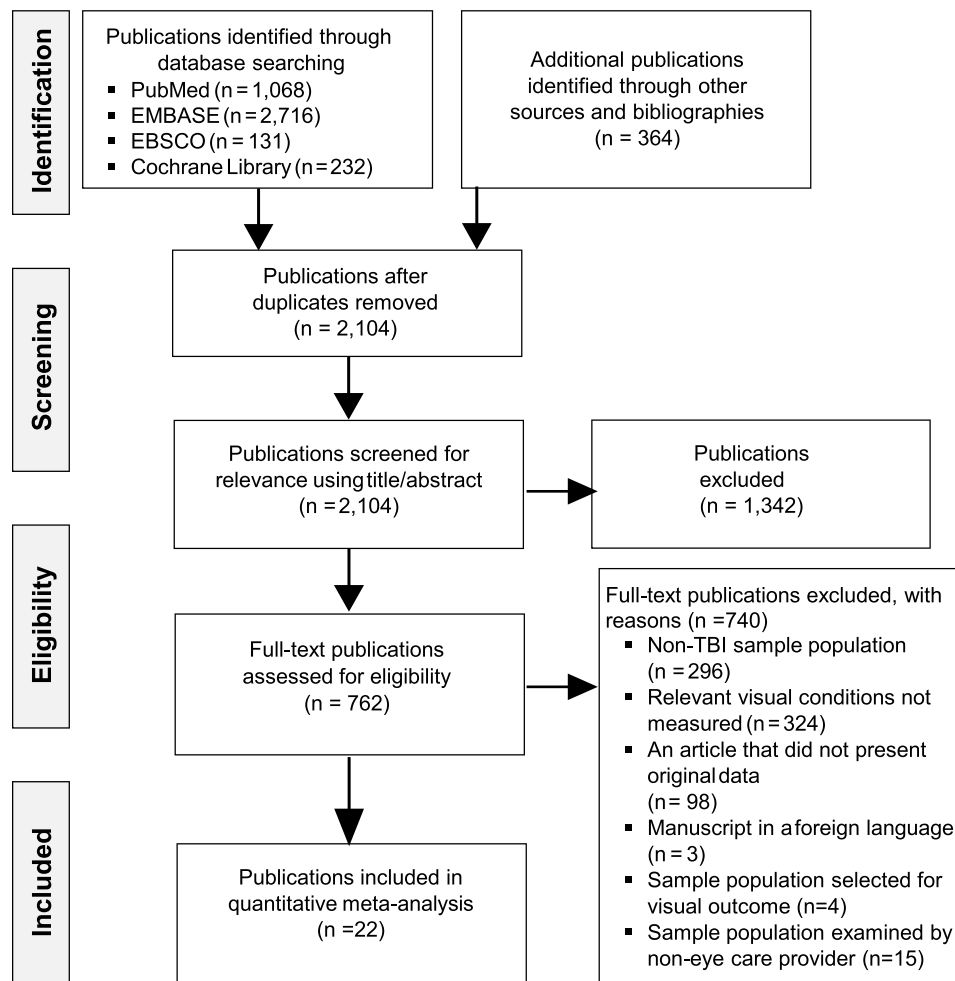


FIGURE 1. Flow diagram of the systematic literature search process according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses.⁵³

publication. Taking these into account, 11 publications reported accommodative dysfunction data,^{4,7-9,35-38,43-45} 14 reported convergence insufficiency data,^{4,7-9,35,37-41,43,44,50,52} 14 reported visual field loss data,^{4,7-9,35-37,42,46-49,51,52} and 6 reported visual acuity loss data.^{4,7,8,35,41,43}

Study Characteristics

Characteristics of the included studies can be found in Table 2. The studies were predominantly conducted in the United States (86.3%), but patients from Africa, Asia, and Europe were also represented. Patients ranged in age from 7 months to 91 years and were generally recruited from one of three subpopulations: (1) military service members and/or veterans, (2) athletes, or (3) the catchment area surrounding local hospitals; female patients were underrepresented, particularly among military groups. The most commonly reported mechanisms of traumatic brain injury were motor vehicle accidents, blast-related injuries, sports-related injuries, and falls.

Accommodative Dysfunction

The combined sample represents 1271 traumatic brain injury patients who were screened for accommodative dysfunction. The methods of assessing accommodation varied among the studies (Table 2); tests for accommodative insufficiency, infacility, or both were most common. Prevalence of accommodative dysfunction ranged from 13 to 80.0% across the included studies with a combined prevalence of 42.8% (95% confidence interval, 31.3 to 54.7%; Fig. 2). This estimate was considerably heterogeneous ($Q[10] = 115.64$; $P < .0001$; $I^2 = 91.35\%$), although no single study was disproportionately influential. None of the four metaregression analyses (study design, traumatic brain injury severity, diagnostic criteria, and risk of bias) accounted for a significant portion of heterogeneity. The combined prevalence estimate of studies explicitly reporting on mild traumatic brain injury patients, the most common form of traumatic brain injury, was 43.2% (95% confidence interval, 29.2 to 57.7%).

Convergence Insufficiency

Across all studies, 2140 traumatic brain injury patients were screened for convergence insufficiency. Other convergence dysfunctions were sought, but only one study evaluated for convergence excess,⁷ and none evaluated for convergence infacility. Testing methods for convergence involved the current state of the commonly used clinical criteria accepted by the field; hence, either the singular use of near point of convergence or any combination of near point of convergence, fusional vergence, and eye alignment testing was used (Table 2); diagnostic cutoffs for the near point of convergence test varied from 6 to 12.7 cm (5 inches). The estimated prevalence in each study ranged from 14.7 to 71.4%. The combined prevalence was 36.3% (95% confidence interval, 28.2 to 44.9%; Fig. 3); these data were considerably heterogeneous ($Q[13] = 129.20$; $P < .0001$; $I^2 = 89.94\%$), but influence analysis did not specify any single study as disproportionately influential. None of the four metaregression analyses (study design, traumatic brain injury severity, diagnostic criteria, and risk of bias) accounted for a statistically significant portion of the reported heterogeneity ($R^2 < 0.21$; $P > .03$). The combined prevalence estimate of the studies explicitly reporting on mild traumatic brain injury patients, the most common form, was 37.2% (95% confidence interval, 24.3 to 51.1%).

Visual Field Loss

In the combined sample, 2106 patients underwent visual field testing. The specific types of visual field loss experienced by these patients, when reported, included homonymous or nonhomonymous hemianop(s)ia,^{4,35,42,47,49,51} quadrantanop(s)ia,^{4,35,42,47} visual field constriction/tunnel vision,^{4,47,51} and central or paracentral scotoma.^{4,47,51} Two publications in the included literature presented diagnoses of cortical blindness resulting from damage to the occipital region of the brain causing visual acuity and visual field loss.^{47,49} The authors did not comment on the extent of visual impairment (i.e., partial or complete) or the visual acuity estimate associated with cortical blindness; therefore, cortical blindness was treated as a post-chiasmal visual field defect rather than a loss of visual acuity. Visual fields were most often assessed via confrontation and/or a handheld perimeter; however, Goldmann and automated perimetry were also used. Individual publications presented prevalence estimates between 0.0 and 50.5%. The combined prevalence estimate was 18.2% (95% confidence interval, 10.6 to 27.1%; Fig. 4); statistical heterogeneity was considerable ($Q[13] = 177.22$; $P < .0001$; $I^2 = 92.67\%$), but influence analysis did not reveal any single study as disproportionately driving the combined estimate. Metaregression analyses revealed that traumatic brain injury severity accounted for a significant portion of the observed heterogeneity. Patients with mild traumatic brain injury demonstrated visual field loss at a rate of 6.6% (95% confidence interval, 0 to 19.5%), whereas patients with moderate to severe traumatic brain injury had visual field loss at 39.8% (95% confidence interval, 29.8 to 50.3%; $R^2 = 64.80$; $P = .0006$). Risk of bias, study design, and diagnostic criteria were not statistically significant moderators ($R^2 = 0.22$; $P > .06$).

Visual Acuity Loss

Visual acuity was measured in 1333 traumatic brain injury patients. All studies used a Snellen chart/card or comparable metric to assess visual acuity (Table 2); therefore, an analysis comparing diagnostic testing criteria was not performed. Prevalence of visual acuity loss at increasingly worse levels was reported, but inconsistent reporting methods across the studies made combined prevalence estimates untenable. However, data regarding the prevalence of visual acuity worse than or equal to 20/200 (i.e., legal blindness)¹⁸ were available and ranged from 0.0 to 3.4%. This degree of visual acuity loss is rare; the combined prevalence estimate was 0.0% (95% confidence interval, 0.0 to 1.1%; Fig. 5); this estimate exhibited lower heterogeneity ($Q[5] = 13.21$; $P < .02$; $I^2 = 62.2\%$) compared with previous cases, and no single study was disproportionately influential. The current study was unable to confirm a single case of visual acuity loss in mild traumatic brain injury patients (0.0%; 95% confidence interval, 0.0 to 0.0%), whereas moderate-to-severe traumatic brain injury patients experienced this deficit at a rate of 3.2% (95% confidence interval, 0.3 to 9.3%). The result needs to be interpreted with caution because only one study with moderate-to-severe data was available for the analysis.

DISCUSSION

Accommodative dysfunction and convergence insufficiency are the most prevalent of the four visual outcomes examined in this study, occurring in 42.8 and 36.3% of traumatic brain injury patients, respectively. The accommodation and convergence

TABLE 2. Characteristics of included studies

Study	Geographic location	Age (y), mean age \pm SD (range)	Proportion, female (%)	Target population	Causes of TBI	Time since TBI	Severity	Study design	Risk of bias (0–10)	Visual deficit/dysfunction testing criteria
Alvarez et al. ³⁵	USA	40.3 \pm 17.4 (5–89)	39	General population	MVA, fall, strike or blow to the head from or against an object, sport	N/R	N/R	Retrospective	Low	AD: NPA, NRA, PRA, AC/A ratio, cover test, Maddox rod test; CI: NPC (no amount specified), fusional vergence, cover test; VFL: confrontation, Humphrey visual field, OKN nystagmus drum; VAL: Snellen chart, retinoscopy
Brahm et al. ⁴	USA	Inpatient: 28.6 Outpatient: 30.5	4	Military	Blast, MVA, gunshot, or fall	N/R	Moderate to severe; mild	Retrospective	Low	AD: pull-away method, cover test; CI: NPC (7 cm), cover test; VFL: confrontation, Goldmann; VAL: Feinbloom chart, Teller Acuity Cards, OKN drum, retinoscopy/refraction
Bulson et al. ³⁶	USA	29.9 (21–55)	1	Military	Blast, MVA, fall	N/R	N/R	Retrospective	Moderate	AD: visual acuity, cover test, further binocular testing performed at discretion of provider (including PRA/NRA, FCC, accommodative facility/amplitude, phorias, and ranges); VFL: confrontation
Capó-Aponte et al. ⁷	USA*	29.33 \pm 8.14	9	Military	Blast, fall, MVA rollover, blunt force	42 \pm 343 d	Mild	Retrospective	Low	AD: PRA, NRA; CI: NPC (no amount specified), fusional vergence, cover test, worth-4-dot, fixation disparity; VFL: confrontation; VAL: Snellen chart, Snellen card, refractive error
Capó-Aponte et al. ³⁷	USA	31.2 \pm 7.36	10	Military	Blast	15–45 d	Mild	Prospective	Low	AD: AC/A ratio, minus lens, facility tests with lens flippers; CI: NPC (no amount specified), fusional vergence, cover test, worth-4-dot, fixation disparity; VFL: confrontation; VAL: Snellen chart, refraction
Ciuffreda et al. ³⁸	USA	44.9 \pm 15.8 (8–91)	N/R	General population	N/R	4.5 y (0.1–43)	N/R	Retrospective	Low	AD: refraction, visual acuity, “binocular and oculomotor evaluation,” accommodation, version, vergence, facility testing; CI: accommodation, version, vergence, binocular and oculomotor evaluation
Cohen et al. ³⁹	Israel	Inpatient: 30 \pm 18.1 Outpatient: 29 \pm 9.9	N/R	General population	N/R	Inpatient: 3 y Outpatient: 3 mo	Severe	Prospective	Moderate	CI: NPC (RAF near-point rule; no amount specified)

Continued

TABLE 2. Continued

Study	Geographic location	Age (y), mean age \pm SD (range)	Proportion, female (%)	Target population	Causes of TBI	Time since TBI	Severity	Study design	Risk of bias (0–10)	Visual deficit/dysfunction testing criteria
Goodrich et al. ⁹	USA	Nonblast: 24 (19–63) Blast: 26 (19–55)	5	Military	Blast, MVA, fall, assault	Nonblast: 0.32 ± 0.52 y (0.02–3.13) Blast: 1.01 ± 1.18 y (0.03–4.79)	Moderate to severe; mild	Retrospective	Low	AD: pull-away method, monocular accommodative amplitude; CI: NPC (8 cm), cover test, Hirschberg test; VFL: confrontation, tangent screen, arc, Goldmann
Hellerstein et al. ⁴⁰	USA	38.88	N/R	General population	N/R	N/R	Mild	Prospective	Low	CI: fusional vergence, refraction, cover, test, stereopsis, NPC, relative accommodation, PRA, NRA (if able to be performed)
Jackowski et al. ⁴¹	USA	37.29 ± 4.3 (29–42)	57	General population	N/R	0.4–10.5 y	N/R	Prospective	Low	CI: NPC (12.7 cm); VAL: refraction
Lemke et al. ⁴²	USA	Median, 25 (19–45)	5	Military	Blast	Median, 2 mo (2 wk–6 y)	Mild; moderate; severe; penetrating	Prospective	Low	VFL: automated perimetry
Magone et al. ⁴³	USA	30.5 ± 8.3	6	Military	Blast	50.5 ± 19.8 mo (16–91)	Mild	Retrospective	Low	AD: amplitude of accommodation; CI: NPC (8 cm), fusional vergence, cover test; VAL: Snellen chart
Master et al. ⁴⁴	USA	14.5 (13.5–14.8)	58	Pediatric	Sports, fall	<1 mo; 1–3 mo; >3 mo	N/R	Prospective cross-sectional study	Low	AD: visual acuity, amplitude (push-up), accommodative facility; CI: NPC (6 cm), fusional vergence, eye alignment testing (modified Thorington test), vergence facility
Padula et al. ⁴⁵	USA	24 (22–46)	30	General population	MVA, fall	N/R	N/R	Prospective	Low	AD: bell and book retinoscopy, visual acuity (with Feinbloom and Lighthouse), NPC, cover test, refraction
Poggi et al. ⁴⁶	Italy	Median, 6.8 (0.5–12.1)	34	Pediatric	MVA, fall	Median, 3.2 mo (0.4–107.6)	Moderate to severe	Prospective	Low	VFL: Goldmann, ring perimeter, Crothers test
Sabates et al. ⁴⁷	USA	31 (5–74)	30.9	General population	MVA, direct trauma to the skull, fall, bicycle accident, mountain climbing, blast	8.5 mo (3 wk–3 y)	N/R	Retrospective	Low	VFL: Goldmann, tangent screen
Schrupp et al. ⁴⁸	USA	42 ± 12 (18–59)	71.4	General population	MVA, fall, blow to the head, and unknown	6.2 y (11 mo–22 y)	Mild	Prospective	Moderate	VFL: N/R
Shokunbi and Agbeja ⁴⁹	Nigeria	84.5 ± 57.3 mo (7 mo–16 y)	36	Pediatric	MVA, fall, miscellaneous	N/R	N/R	Retrospective	Moderate	VFL: N/R
Stelmack et al. ⁸	USA	31	8	Military	Military (OEF/OIF)	<30 d	N/R	Retrospective	Low (AD, CI, and VAL), moderate (VFL)	AD: accommodative facility, refraction; CI: fusional vergence, eye alignment test, vergence facility, refraction; VFL: N/R; VAL: refraction
Storey et al. ⁵⁰	USA	5–18 y	N/R	Pediatric	Sport, fall, recreation	N/R	N/R	Retrospective	Low	CI: NPC (6 cm)
Suchoff et al. ⁵¹	USA	44.9 ± 15.8 (8–91)	N/R	General population	N/R	4.5 y (0.1–42)	N/R	Retrospective	Low	VFL: confrontation, static or kinetic perimetry

Continued

TABLE 2. Continued

Study	Geographic location	Age (y), mean age \pm SD (range)	Proportion, female (%)	Target population	Causes of TBI	Time since TBI	Severity	Study design	Risk of bias (0–10)	Visual deficit/dysfunction testing criteria
Van Stavern et al. ⁵²	USA	30 (2–86)	37	General population	MVA, fall, bicycle accidents, projectile, pedestrian accident, and others	73.5 \pm 291.8 d (3 d–12 y)	N/R	Retrospective	Low	CI: N/R; VFL: Goldmann, Humphrey visual field

Risk of bias is based on 10 criteria formulated and validated by Hoy et al.,³⁴ where a higher score indicates greater bias; two scores are presented in some cases because of insufficient reporting of diagnostic criteria for some but not all visual outcomes. Information presented in the “visual deficit/dysfunction testing criteria” column is discretized by the visual condition. *Evaluation was done by an American at Landstuhl Regional Medical Center, Germany. AC/A = accommodative convergence per unit of accommodation; AD = accommodative dysfunction; CI = convergence insufficiency; MVA = motor vehicle accident; NPA = near point of accommodation; NPC = near point of convergence; N/R = not reported; NRA = negative relative accommodation; OEF = Operation Enduring Freedom; OIF = Operation Iraqi Freedom; PRA = positive relative accommodation; TBI = traumatic brain injury; UK = United Kingdom; USA = United States; VAL = visual acuity loss; VFL = visual field loss.

pathways rely on a decentralized and extensive neural architecture involving mesencephalic brainstem nuclei, premotor and motor cortex, cerebellum, and oculomotor, abducens, and trochlear nerves. Focal damage to a critical component of this system, diffuse or shearing forces along the visual pathway, or intracranial edema, hematoma, or hemorrhage therefore can commonly lead to deficient ability of the eyes to accommodate and/or converge,⁵⁵ which is usually independent of any decrement in visual acuity. The variety of damaging events that can lead to accommodative dysfunction and/or convergence insufficiency provides plausible reasoning for the high prevalence rates reported in this study.

Visual field loss occurs in approximately 18.2% of traumatic brain injury patients according to this study. The assessment of visual field loss in a traumatic brain injury patient is complicated by the varied nature of head injuries and the probability of an associated ocular injury. Individuals can demonstrate visual field loss by sustaining a direct ocular injury and/or an injury to the intracranial visual pathways resulting in damage to segments of the visual pathway ranging from the retina to the occipital cortex.^{56,57} To ensure that the results of the current study were based solely on the impact of a brain injury and not ocular injury, only visual field loss secondary to post-chiasmal injury was considered. Such defects are often perceived bilaterally by the patient (e.g., hemianopia and quadrantanopia)⁵⁷ and are considered to occur secondary to an injury to the intracranial portion of the visual pathway. The current study indicates that visual acuity loss at the level of legal blindness is rarely associated with only traumatic brain injury. A probable explanation is that visual sequelae resulting from ocular, retinal, or optic nerve damage were excluded from this analysis. In most cases, traumatic visual acuity loss is related to pre-chiasmal damage and occurs in the setting of severe head trauma associated with loss of consciousness.⁵⁸ The relatively low prevalence of visual acuity loss due to neurologic consequences of traumatic brain injury suggests that the test for visual acuity, which is the most commonly performed measure of the visual system, is an insufficient stand-alone surrogate for overall visual health. In fact, most traumatic brain injury patients in the current study had little if any loss of acuity; three studies reported that all patients with mild forms of traumatic brain injury had better than or equal to 20/25 vision.^{7,37,43} Therefore, patients with a history of head injury should be evaluated by an eye care provider (i.e., optometrist or ophthalmologist) who can render a comprehensive eye examination

to look for these subtle changes in visual function, including direct injuries to the eye, which were not included in this study but are known to be commonly associated with head injuries and traumatic brain injury.⁵⁹ Such a comprehensive examination would include the following: medical history, visual acuity, measurement of refractive error, external examination, pupillary testing, distance and near cover testing, visual field testing, extraocular muscle movement assessment including version and vergence functions, accommodative assessment, tonometry, slit-lamp biomicroscopy, binocular indirect ophthalmoscopy, and gonioscopy. The current study did not use comparative baseline rates of the studied visual outcomes in otherwise healthy individuals that would allow for risk metrics to be calculated. Although baseline rates or control groups were infrequently reported in the literature collected here, prevalence statistics for visual outcomes in populations with no history of head injury have been reported previously. Rates of accommodative dysfunction in otherwise healthy individuals were reported to be between 5.8 and 32.4%,^{37,60–64} which is lower than 42.8% reported in the current study. Convergence insufficiency was previously reported in 4.2 to 31.4% of otherwise healthy populations^{11,37,61,63–67} compared with 36.3% reported in traumatic brain injury patients here. Baseline visual field loss data are rare and generally measured in older adults; however, Capó-Aponte et al.³⁷ reported 0% visual field loss in otherwise healthy military personnel aged 20 to 43 years, and Ramrattan et al.⁶⁸ reported a prevalence of 3% in civilians aged 55 to 64 years. These estimates are notably lower than 18.2% in the current study. Lastly, baseline rates of visual acuity loss to the level of legal blindness were reported at less than 1%,^{60,69,70} which is comparable with the approximately 0% reported in traumatic brain injury patients here.

Prevalence Stratified by Traumatic Brain Injury Severity

The prevalence estimates harvested from each study included in the current analysis varied substantially. It was hypothesized that this heterogeneity could be partially explained by the severity of traumatic brain injury. To address this question, the prevalence of the four studied visual outcomes was stratified into either mild traumatic brain injury or moderate-to-severe traumatic brain injury categories, and metaregression analyses and subgroup analyses

Prevalence of Accommodative Dysfunction

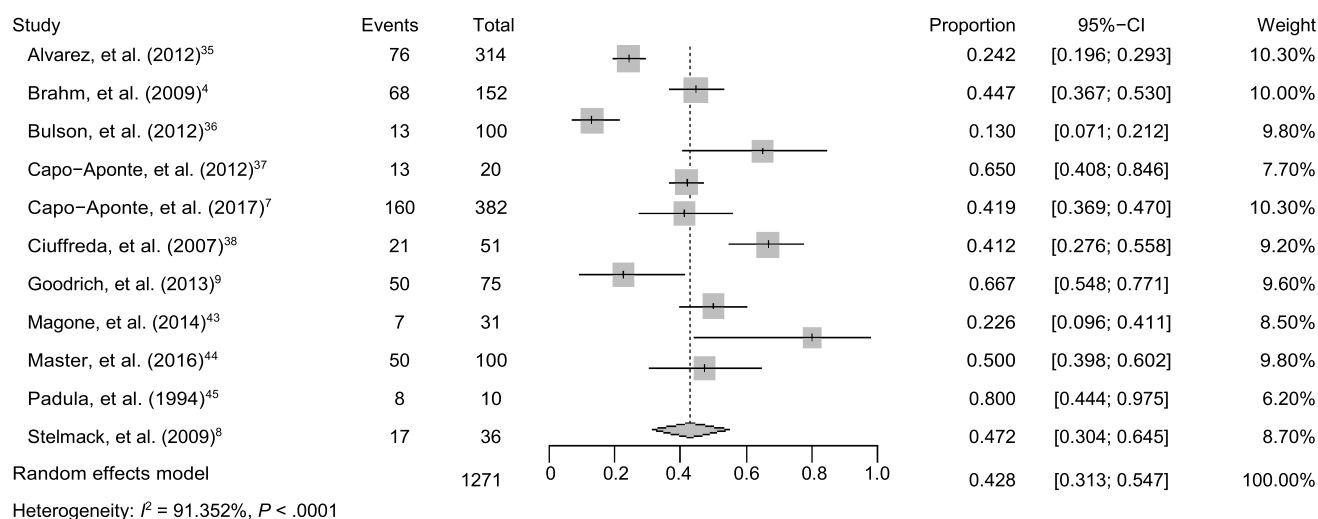


FIGURE 2. Forest plot of accommodative dysfunction prevalence in traumatic brain injury patients. Each data (square) and error band (horizontal line) represent mean prevalence and 95% confidence interval (CI), respectively. “Events” refer to the number of patients with a positive diagnosis of accommodative dysfunction; “total” is the sample size of each study. Weights and combined prevalence are calculated using the DerSimonian-Laird random-effects model. Sizes of the gray boxes are in proportion to the reported weights. Mean prevalence is presented as a broken vertical line. Asterisk indicates statistically significant heterogeneity ($P < .10$).

were performed (Fig. 6). The prevalence of accommodative dysfunction and convergence insufficiency did not differ in patients with mild versus moderate to severe traumatic brain injury according to the current analysis. However, the data for accommodative dysfunction need to be interpreted with caution because only one study with moderate-to-severe traumatic brain injury data was

available for the analysis. This study comparison combined data across studies frequently using different diagnostic approaches (Table 2) and often did not stratify prevalence by the types of accommodative issues (e.g., accommodative insufficiency and infacility). However, the study findings comport with Brahm et al.⁴ and Alvarez et al.,³⁵ who did report these traumatic brain injury

Prevalence of Convergence Insufficiency

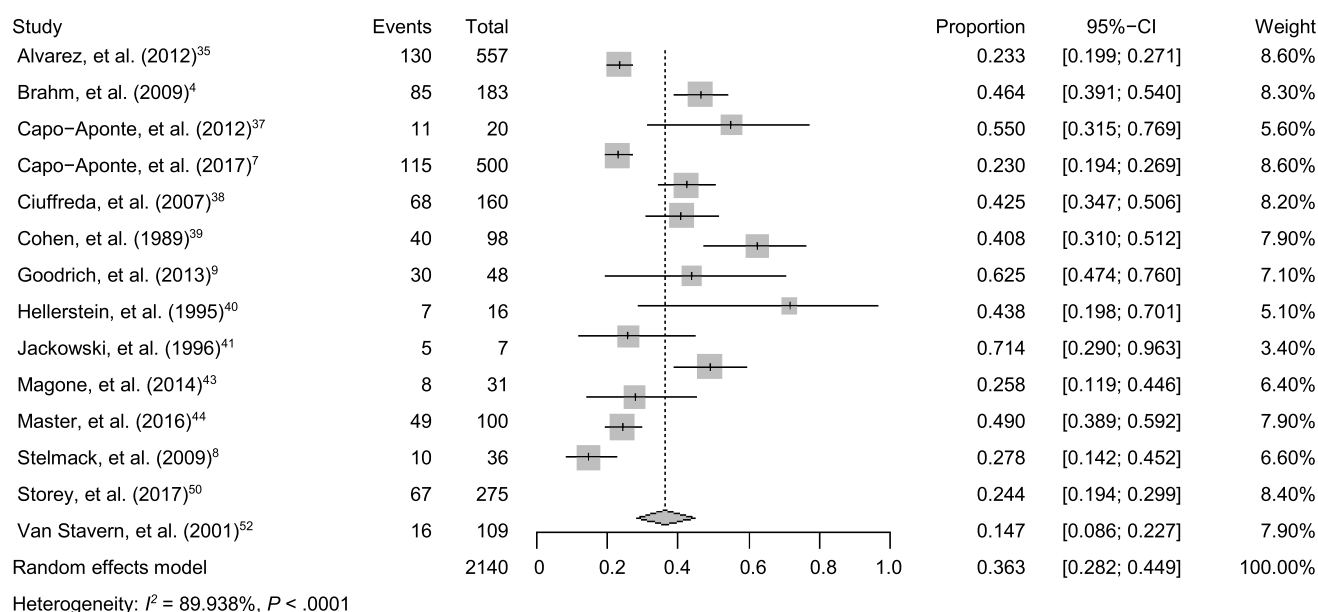


FIGURE 3. Forest plot of convergence insufficiency prevalence in traumatic brain injury patients. All conventions as in Fig. 2.

Prevalence of Visual Field Loss

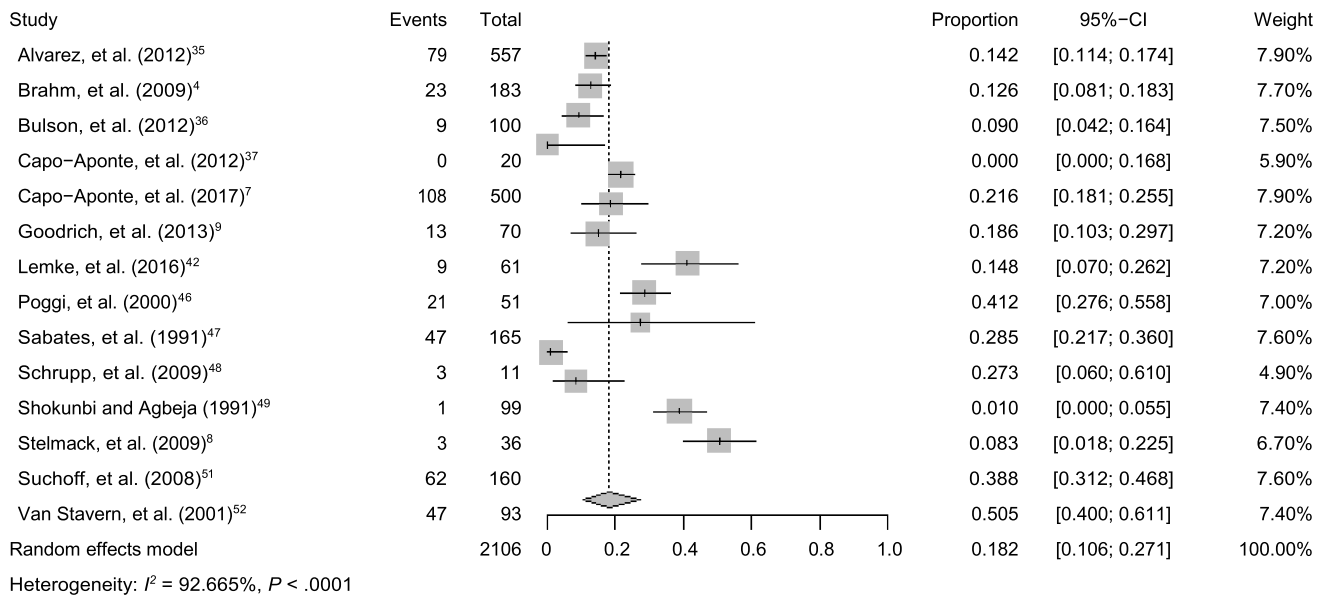


FIGURE 4. Forest plot of visual field loss prevalence in traumatic brain injury patients. All conventions as in Fig. 2. The x axis is truncated for clarity.

severity comparisons using their respective, internally consistent, diagnostic methodologies and found no differences in visual dysfunctions between traumatic brain injury severity levels. It should also be noted that the specific neurological abnormalities responsible for accommodative and convergence issues are rarely investigated in individual cases. More detailed research is likely to shed greater light on this issue.

In contrast, post-chiasmal visual field loss demonstrated significance for higher prevalence associated with moderate to severe traumatic brain injury (39.8%) compared with mild traumatic brain injury (6.6). This observation is consistent with previous research showing that more severe forms of traumatic brain injury, particularly with distributed cerebral pathology involving the occipital lobe, optic radiations, or optic tract, lead to higher rates of post-chiasmal visual field loss.^{57,71}

When the prevalence of visual acuity loss (legal blindness equal to or worse than 20/200) was stratified by the severity of traumatic brain injury, no cases were reported in mild traumatic brain injury

patients compared with 3.2% in moderate to severe traumatic brain injury, but these data need to be interpreted with caution because only one reference with moderate to severe traumatic brain injury was found. Although disparate visual acuity categorization presented in the existing literature precluded a comparison of visual acuity at less severe levels in the current study, one study did report infrequent moderate visual acuity loss (worse than 20/100) in Polytrauma Network Site outpatients (1.6%) compared with Polytrauma Rehabilitation Center inpatients (12.7%).⁴

Other Moderating Variables and Their Relationship with Visual Outcome Prevalence

In addition to traumatic brain injury severity, the studies were evaluated on the association of the prevalence rates with risk of bias, diagnostic criteria, and study design (prospective vs. retrospective). Methodological risk of bias was used not only to assess the literature at large but also to determine if biased studies impacted reported

Prevalence of Visual Acuity Loss

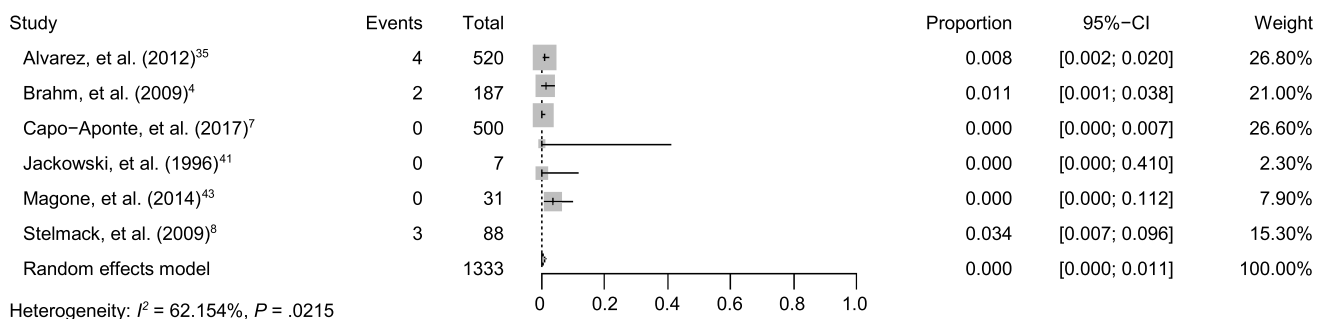


FIGURE 5. Forest plot of visual acuity loss (at the level of legal blindness) prevalence in traumatic brain injury patients. The x axis is truncated for clarity. All other conventions as in Fig. 2.

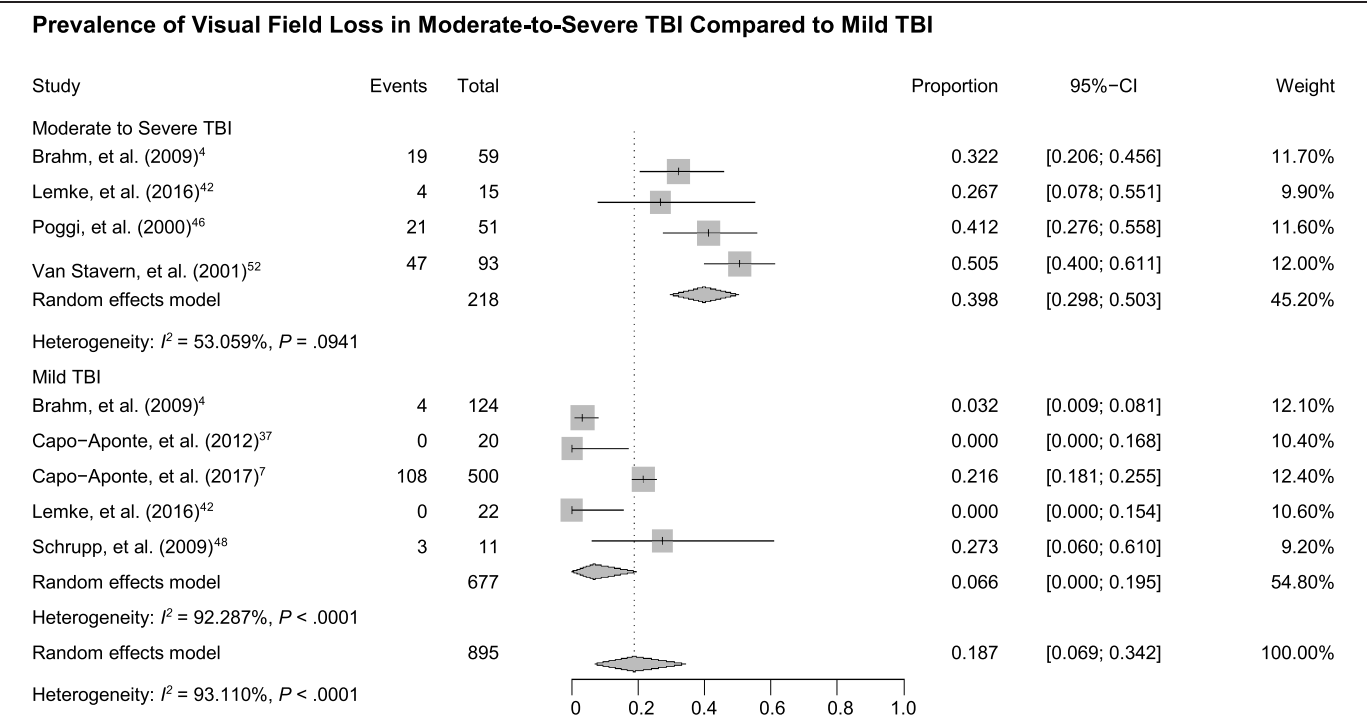


FIGURE 6. Forest plot of visual field loss prevalence in moderate-to-severe TBI compared with mild TBI. All other conventions as in Fig. 2. TBI = traumatic brain injury.

prevalence rates in a meaningful way. Criteria validated by Hoy et al.³⁴ were used to appraise the studies on the recruited sample population, the types of recruitment used, study instruments and measurement validation, and statistical approach. The general population was represented at higher rates (63%) than service members and/or veterans (37%), which decreased the bias of recruited samples. The studies used for the analysis had either low or medium risk of bias, with overall risk of bias in the low category (mean, 3.18/10). Most studies used validated screening/diagnostic criteria for both traumatic brain injury and visual outcome assessment (although some were not transparent about the tools used), and all used appropriate statistical procedures. The screening/diagnostic criteria for the visual dysfunctions varied significantly between different studies. Despite this variability, we did not observe an association between the screening/diagnostic methodology and the prevalence rates for all four visual outcomes. No association was observed between the type of study (prospective vs. retrospective) and the prevalence rates.

Traumatic Brain Injury Resulting from Blast versus Nonblast Events

Prevalence rates for the four studied visual outcomes may depend on the mechanism by which the brain injury was acquired. Of particular interest is whether head injuries resulting from an explosive blast event (i.e., due to the blast overpressure wave and/or head injury secondary to events of the blast) were related to differential visual dysfunction rates when compared with head injuries resulting from nonblast events (e.g., sports-related trauma, falls, and motor vehicle accidents). Several of the included publications provided descriptions of the type(s) of injuring event that resulted in traumatic brain injury (Table 2). Although the data for these parameters are very limited, our study did not show that the prevalence

for the four visual outcomes is different in blast versus nonblast traumatic brain injury events. Trauma secondary to direct, blunt, or penetrating injury to the brain, as well as damage resulting from brain displacement (e.g., coup-contrecoup injury), can occur both in explosive blast or nonblast scenarios. Animal studies, computational analyses, and human brain pathology research have been used to examine whether the physical impact of the blast overpressure wave, the only component unique to blast, produces specific brain injuries separate from other traumatic brain injury mechanisms of injury.^{53,72–77} In recent work, Tagge et al.⁷³ compared the effects of the blast overpressure wave with direct head impacts using computational simulation. This research showed that direct impact generated high-pressure force loading onto a focused contact area, whereas blast wave impact caused distributed, lower-magnitude force loading. Direct impact produced sevenfold greater peak shear stress to the brain as compared with the blast wave. Therefore, any effects due purely to blast overpressure on the visual system are likely to be subtle and may be obscured by the more powerful effects of direct impact during the same blast event. Indeed, Capó-Aponte et al.⁷⁸ studied the isolated effects of blast overpressure in Marine Corps “breachers” who encounter repetitive subconcussive blast exposure as part of their training. Although the results were suggestive of detrimental effects of the low-level repetitive blast on corneal endothelial cell count, near vertical phoria, and visual field sensitivity, all test results in the experimental group were within or only slightly lower than normative value ranges. No differences were found in convergence, accommodation, or visual acuity measures. Nevertheless, it should be acknowledged that, although the current study and others did not detect a difference between blast and nonblast events in visual symptoms measures, recent publications suggest that blast events may evoke specific cellular and molecular

effects in brain tissue. Shively et al.⁷² described a distinct pattern of interface astroglial scarring in tissues adjacent to cerebrospinal fluid at junctions between gray and white matter and around blood vessels in brain specimens from military service members who experienced blast exposure. Comparable glial deposition patterns were not observed in brain specimens from individuals with a history of impact (i.e., nonblast) and traumatic brain injury or control cases with no history of traumatic brain injury. Future research is needed to establish whether these neuropathological findings are associated with specific short- and/or long-term clinical manifestations.

It should also be noted that little is known about the visual complications that arise from the other possible mechanisms of traumatic brain injury (e.g., falls and assaults), as stratification by the mechanism of injury in the literature is rare (however, see Alvarez et al.,³⁵ who did stratify visual outcomes by specific etiology including motor vehicle accidents, falls, and sports injuries).

Persistence of Visual Dysfunctions Secondary to Traumatic Brain Injury

There is also conjecture in the field of vision science regarding the persistence of visual dysfunctions after an individual sustains a traumatic brain injury. Studies assessing a traumatic brain injury patient's visual status at numerous time points during recovery are infrequent and use subjective visual symptom data rather than administering comprehensive eye examinations.^{79,80} Despite the lack of optimal evidence, a small number of publications, which are included in the analyses previously, address the extent to which visual outcomes are diagnosed in the long-term (i.e., chronic) phase. Capó-Aponte et al.⁷ compared three cohorts whose constituents received diagnostic eye examinations at different periods (i.e., ≤ 45 days, between 46 and 365 days, or >365 days) after their traumatic brain injury. Although the small number of studies did not allow for the generalization of the conclusion, this study found no difference in the prevalence of accommodative dysfunction, convergence insufficiency, and visual field loss between the three groups. In addition, Kowal⁸¹ documented the prevalence of accommodative dysfunction (16%) and convergence insufficiency (14%) in 161 patients shortly after head injury. Most patients with accommodation and convergence issues were followed up for more than 1 year, and at least 58 and 35% of these patients, respectively, experienced persisting symptoms. Despite the paucity of evidence explicitly addressing the prevalence of visual outcomes in the chronic versus acute phase of traumatic brain injury recovery, it is evident that traumatic visual dysfunctions can and do persist in a substantial proportion of traumatic brain injury patients past 1 year after the injuring event.

Limitations

The nature of meta-analyses requires the combination of data collected from various locations, sources, and authors. There are, therefore, inherent limitations that should be acknowledged. A primary limitation of the current study is the extent of statistical heterogeneity in the data for accommodative dysfunction, convergence insufficiency, and visual field loss. Each of these combined prevalence estimates (Figs. 2 to 5) was associated with a significantly high I^2 statistic (each $>90\%$). To further account for some of the reported heterogeneity, univariate metaregression analyses were performed.

Limitations were apparent in the traumatic brain injury severity analysis; it was common that either publications did not report the severity of traumatic brain injury, or the patient sample was populated with individuals who sustained varying degrees of traumatic brain injury. The traumatic brain injury severity analysis was further complicated by the diagnosis of “concussion” in several publications,^{44,50} which lacks the same accepted severity distinctions used in traumatic brain injury and is often but not always^{82,83} deemed synonymous with mild traumatic brain injury. For these reasons, many publications were excluded from metaregression analyses, which reduced the power and generalizability of subsequent conclusions. Similar challenges restricted the utility of the screening/diagnostic testing criteria moderator.

Categorization of disparate approaches into logical categories was exceedingly difficult; for example, testing criteria in a distinct category necessarily overlapped with those of neighboring categories. This problem is magnified by some studies not providing sufficient methodological detail for their testing criteria. Additional attempts were made to account for differences between studies based on age of participants, sex ratio, target population, geographic location, and year of study, but these factors largely failed to explain variability among visual outcome prevalence estimates (data not shown). The metaregression analyses suggest that no single factor was responsible for the observed statistical heterogeneity.

Recommendations

Traumatic brain injury is a time-related process involving injury, short-term change, and longer-term recovery, which can persist chronically, all processes that are not well understood. A carefully constructed prospective trial with a large sample and consistent evaluation techniques would have a tremendous impact on the field and would address the various limitations outlined previously. An ideal trial would recruit unbiased samples of consecutive patients from hospitals, emergency departments, military treatment facilities, and/or Veterans Affairs; record demographic characteristics (e.g., age, sex, and occupation) and injury specifics (e.g., etiology, severity, comorbid conditions such as eye injuries, and imaging results); would require complete examinations from eye care providers within a restricted time after injury and additional follow-up, regardless of overt visual symptoms; would mandate application of consistent diagnostic testing criteria for each visual outcome; and would maintain detailed records of dosage, use, and compliance information for prescribed drugs, devices, or interventions. Furthermore, to better understand chronicity, recovery, and management outcomes, this study should be extended to incorporate a natural history design over a longitudinal timeline.

The current study clearly shows that traumatic brain injury damages the visual system in many ways and that, because visual acuity is often unaffected, these visual outcomes are frequently undetected. Therefore, all service members, veterans, and/or civilians who have experienced a traumatic brain injury should seek (or be referred to) an eye care provider for a comprehensive eye examination as specified by the Veterans Health Administration Notice 2017-35⁸⁴ and the Vision Center of Excellence Clinical Recommendations for the Eye Care Provider. Further detail regarding the detection and management of traumatic brain injury-associated visual dysfunctions is available in the Department of Defense- and Veterans Affairs-approved Vision Center of Excellence clinical recommendations.^{85–87}

ARTICLE INFORMATION

Supplemental Digital Content: The Appendix, available at <http://links.lww.com/OPX/A408>, demonstrates the search strategy used for searching the databases PubMed, EMBASE, EBSCO, and Cochrane Library to identify candidate literature articles for this meta-analysis.

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